EP001 / #1405

Topic: *AS01 Surgery - IPSO - if accepted, the abstract will be presented in the surgical programme*

SAFETY AND TOLERABILITY OF ANESTHETIC MANAGEMENT OF SUPERSELECTIVE OPHTALMIC ARTERIAL CHEMOTHERAPY FOR RETINOBLASTOMA IN CHILDREN

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Background and Aims: Superselective intraarterial chemotherapy (SIAC) significantly reduced number of enucleations in children with retinoblastoma. Life-threatening complication of SIAC, hemodynamic instability and bronchospasm (trigemino-pulmonary, trigemino-cardiac reflex), significantly limit the wider implementation of this technique. We aimed to describe our experience of SIAC, to report the serious adverse cardio-respiratory reactions we have observed.
Methods: Study includes patients (n = 383) underwent SIAC (n = 618) under general anesthesia in 2013–2021.
Results: Hemodynamic parameters in patients who underwent SIAC procedure for the first time (n = 246) were analyzed: in 88% cases smooth anesthesia was observed, the deviations of blood pressure and heart rate did not exceed 20% of the baseline values. In 12% cases, patients who underwent the first SIAC procedure developed bronchospasm of 5-12 seconds after catheterization of a. ophthalmica with microcatheter. Hemodynamic parameters analysis in patients who underwent repeated SIAC procedures (2nd, 3rd, etc.) (n = 137), in 58% cases, a clinical picture of the trigemino-pulmonary reflex of varying severity manifested: of a weak degree - 72%, of a moderate degree - 15%, of a severe degree - 13%.
Conclusions: Adverse cardio-respiratory reactions are commonly observed in SIAC for retinoblastoma. The adverse clinical signs represent an autonomic reflex response and all patients should be considered at-risk. Anesthesiologists must be vigilant for adverse reactions and deal with them quickly and effectively. However, further investigations are needed to improve the understanding and management of the described oculo-pulmonary reflex.

EP002 / #1490

Topic: *AS01 Surgery - IPSO - if accepted, the abstract will be presented in the surgical programme*

PARAMENINGEAL RHABDOMYOSARCOMA: A RETROSPECTIVE STUDY OF 22 CASES

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Background and Aims: Parameningeal location in rhabdomyosarcoma (RMS) is correlated with a poor prognosis. it represents 16% of all rhabdomyosarcomas. We aimed by this study to review parameningeal RMS treated at the pediatric oncology department of Salah Azaiez institute and to identify possible prognostic factors.
Methods: A monocentric retrospective study was conducted over a period of 25 years between 1994 and 2019 at the pediatric oncology department of Salah Azaïz Institute. Our study involved patients with parameningeal RMS. All data regarding patients were obtained from the medical record.
Results: Twenty-two patients were included. The mean age at diagnosis was 7 years old (range: 2-9 years) with a male predominance. The most frequent initial symptom was cranial nerve palsy (n=6). In 77% of cases (n=17), the location was the nasopharynx. Histological examination showed embryonal RMS in 91% of patients. Median tumor size was 72 mm. Eight patients had metastatic disease at diagnosis. Surgery was performed in 31% of cases (n=7) with negative margins in 50%. Five patients had lymph node involvement was observed in 23% of patients. Seven patients had radiotherapy. Twenty patients received chemotherapy. Intent for chemotherapy was neoadjuvant in 54%, adjuvant in 18% and palliative in 18% of patients. Overall survival (OS) was 75% at one year and 36% at three years. The prognostic factors influencing OS were age (5-10 years old) (p=0.008) and lymph node involvement (p<0.001). Relapse free survival (RFS) was 52% at one year and 31% at three years for patients with localized disease. The prognostic factor influencing RFS was lymph node involvement (p=0.002).
Conclusions: Parameningeal rhabdomyosarcoma is a particular neoplasm with a poor prognosis. Age (5-10 years old) and lymph node involvement were shown to significantly influence survival.

EP003 / #1602

Topic: *AS01 Surgery - IPSO - if accepted, the abstract will be presented in the surgical programme*

LONG TERM OTOTOXIC EFFECTS OF CISPLATIN IN SURVIVORS OF PEDIATRIC SOLID TUMORS

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Background and Aims: Cisplatin is an integral component of chemotherapeutic regimes of childhood tumors, but their use may impart a significant hearing deficit in long-term survivors. We aim to evaluate the long-term auditory effects of Cisplatin in survivors of pediatric solid tumors
Methods: The study included a cohort of survivors of Hepatoblastoma(HB) and Malignant Germ Cell tumors(MGCT) registered at pediatric surgical-oncology clinic from 1994 to 2016. The ototoxic effects of Cisplatin were evaluated in the patients by means of a pure-tone audiometry(PTA) done during follow up.
Results: A total 129 patients were deemed as survivors, with a mean duration of follow-up in HB and MGCT of 8.47(SD 4.27) years and 7.84(SD 4.25) years. Of the 117 survivors receiving Cisplatin, one patient had hearing difficulty at follow up. PTA was performed in 83 survivors, of which an audiogram was available for 51 survivors for evaluation, 28 (54.9%) of which were reported normal. Hearing loss was detected in 39(76.4%) out of 51 survivors by the SIOP grading system. Severe hearing loss was detected in 32(62.7%) survivors (grade 3,4). Hearing loss was detected in 26(51%) survivors according to the Brock's Grading system. Severe hearing loss was detected in 6 (11.7%) survivors. The survivors of MGCT had a significantly higher (92.3%) chance at developing hearing loss compared to 60% of HB survivors (p=0.012). A dose of Cisplatin of >/=420mg/m2 was found to be associated with hearing loss, with a sensitivity of 75% and specificity of 66.67%. The mean age at diagnosis was significantly higher in children with hearing loss(48.50,SD 47.54months) as compare to children without hearing loss(24.5,SD 32.12months) (p=0.01928). Age at audiometry did not correlate with hearing loss.
Conclusions: The SIOP grading system, being more sensitive, must be uniformly used to screen for hearing loss. Older age at diagnosis, higher dose and MGCT survivors need close monitoring.

EP004 / #1666

Topic: *AS01 Surgery - IPSO - if accepted, the abstract will be presented in the surgical programme*

ANTHROPOMETRIC OUTCOMES IN SURVIVORS OF PEDIATRIC SOLID TUMORS

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Background and Aims: The importance of nutritional status in childhood cancer patients cannot be overemphasized, not only due to its potential impact on the disease and survival, but also for its impact on their survivorship. We sought to evaluate the long-term arthropometric outcomes in pediatric solid tumor survivors
Methods: The study included a cohort of pediatric solid tumor survivors registered at pediatric surgical-oncology clinic from 1994 to 2016. Anthropometry was noted at the time of presentation, after completion of chemotherapy, and at last follow-up. The z-scores for weight-for-age and height-for-age were calculated using WHO growth charts for age <5 years and Indian Academy of Pediatrics growth charts for age >/= 5 years
Results: Of the survivors, 317 survivors, comprising of 48, 81 and 188 survivors of HB, MGCT and WT respectively, were included in the analysis. The median age at diagnosis was 24.5 (IQR 59-13.2) months, with range of 5-19.54years of follow-up. On evaluating the z-scores of the collective cohort of survivors at three time points, we found that the z-scores for height for age, weight for age and BMI showed an improving trend in nutrition. The difference in the prevalence of malnutrition and severe malnutrition was found to be statistically significant when any two time points were compared during follow-up. A similar trend was seen in the individual cohorts of HB, MGCT and WT, which showed 10% and 7.5%, 10.9% and 9%, 15.7% and 11.4% to be stunted and wasted at last follow-up. We found no significant effect of age at diagnosis on the anthropometric measures at last follow-up. On evaluating BMI in 28 adult survivors, we found 43% to be in the underweight category.
Conclusions: Anthrometric measures improve during follow-up, however, up-to 15% children persist being malnourished which is close to the national averages. Thus, the effect of therapy improves over time.

EP005 / #1157

Topic: *AS01 Surgery - IPSO - if accepted, the abstract will be presented in the surgical programme*

HEALTHCARE UTILIZATION OF EXTRACORPOREAL MEMBRANE OXYGENATION IN CHILDREN WITH CANCER: A NATIONAL EXPERIENCE

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Background and Aims: Extracorporeal Membrane Oxygenation (ECMO) is a resource-intensive, lifesaving form of resuscitation which is infrequently used in pediatric oncology patients. However, with the use of ECMO increasing overall in the pediatric population, the experience with ECMO in oncology patients should be updated. We sought to describe healthcare utilization and outcomes in pediatric oncology patients requiring ECMO cannulation.
Methods: We used the Kids Inpatient Database (2019) to identify a cohort of patients admitted with primary diagnosis of malignancy who subsequently underwent ECMO cannulation. This dataset contains a national representative sample of pediatric hospitalizations in the United States. We reported descriptive demographics, and baseline disease information. We then quantified length of stay, total hospitalization charges, and charges per day.
Results: We identified 31 patients with a primary oncology diagnosis who underwent ECMO cannulation. The most common malignancies included acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), and Non-Hodgkins Lymphoma. Children with solid tumors represented 22.5% of children cannulated (7/31). In hospital mortality was 51.6% (N=16), consistent with overall ECMO outcomes. Of these, 33% were discharged home, an additional 33% were discharged home with home healthcare. The median age was 7 (IQR 3-16), with 41.9% female patients, and 55.2% white patients. Patients were most commonly covered by private insurance (48%) and received care at an urban academic medical center (100%); 35.5% were transferred to these centers. Patients underwent a median of 13 procedures (IQR 11-20). Median hospital charges were $1,302,684 ($705,556-$2,167,772). Median charges per day were $26,887 ($19517-$57066).
Conclusions: ECMO is a lifesaving but resource intensive method of resuscitation. Although ECMO has been infrequently used in pediatric oncology patients, the survival of these patients is consistent with overall outcomes of non-oncology patients. Further studies, including international collaborations, are needed to further investigate indications and outcomes of ECMO cannulation in these patients.

EP006 / #216

Topic: *AS01 Surgery - IPSO - if accepted, the abstract will be presented in the surgical programme*

REVIEW OF NEONATAL HEPATIC TUMORS REQUIRING HEPATIC RESECTION IN THE EARLY POSTNATAL PERIOD

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Background and Aims: Neonatal liver tumors may require early postnatal hepatic resection owing to tumor rupture, respiratory failure, and circulatory failure. In this study, we reviewed such cases in our hospital.
Methods: This study included patients diagnosed with liver tumor and treated with liver resection in the early postnatal period at our hospital between 1980 and 2021. We retrospectively reviewed medical and surgical records with respect to data on gestational age and birth weight, clinical course, surgery, and complications.
Results: Seven patients were included in this study. The time of diagnosis was prenatal in four patients and postnatal in three patients, and the mode of delivery was vaginal in four patients and cesarean in three patients. The median gestational age was 38 (37–40) weeks, and the median birth weight was 3152 (2564–3898) g. The median tumor size was 10 (2.5–11.5) cm. The final diagnosis was hepatoblastoma in three patients, hemangioma in two, hamartoma in one, and focal nodular hyperplasia in one. The diagnosis was not confirmed preoperatively in six patients. The median age at surgery was 6 (0–62) days. Six of seven patients had a critical condition, including two with circulatory failure owing to tumor rupture, one owing to intratumoral hemorrhage, one owing to abdominal compartment syndrome, and two owing to respiratory failure. Five patients underwent complete hepatic resection without complications; however, one patient required intraoperative resuscitation owing to hyperkalemia from the tumor that resulted in cardiac arrest, and another patient required silo construction, Rex shunt, and hepatic ductal jejunal anastomosis.
Conclusions: Neonatal liver tumors can lead to serious systemic conditions and may require high-risk early postnatal hepatectomy. However, they can be managed by quick decision-making and troubleshooting.

EP007 / #856

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

MINIMAL RESIDUAL DISEASE IN ACUTE LYMPHOBLASTIC LEUKEMIA AND ITS RELATIONSHIP WITH OTHER PROGNOSTIC FACTORS – A SINGLE CENTER EXPERIENCE FROM INDIA

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Background and Aims: In low- and middle-income countries, Minimal Residual Disease (MRD) based therapy-intensification of acute lymphoblastic leukemia (ALL) isn't always possible since the test is expensive, time consuming and requires technical expertise. The purpose of this study is to assess the correlation of MRD with other prognostic factors at diagnosis.
Methods: In this retrospective study, patients <40 years of age with ALL who had immunophenotyping, cytogenetic studies, and CSF analysis done at diagnosis, completed BFM-based induction chemotherapy and underwent bone marrow analysis at the end of induction were included. Patients were classified as B or T cell ALL; NCI standard (SR) or high risk (HR); favorable risk [t(12:21), hyperdiploidy (FR)], poor risk [Hypodiploidy, t(9:22), MLL translocation, t(1:19), iAMP21, IKZF1 deletion (PR)] or intermediate risk (neither FR nor PR) cytogenetic]; CNS positive or negative; good (GPR) or poor prednisone response (PPR); and MRD (<0.01% or >0.01%) at the end of induction.
Results: Between 2015 and 2021, 60 patients met the inclusion criteria. Median age was 11.5 years; 40 (66.6%) were <18 and 20 (33.3%) were >18 years old. Male: Female ratio was 1.86. Forty-one (68.3%) had B-ALL and nineteen (31.6%) T-ALL. Forty-four patients (73.3%) met the NCI HR criteria. PR, IR, and GR cytogenetics were seen in 12 (20%), 30 (50%) and 18 (30%) patients respectively. Forty-four patients (73.3%) had GPR. Seventeen (28.3%) were MRD positive at the end of induction. Patients with B-ALL (24%), NCI-SR (6%), GR cytogenetics (22%) and GPR (22.7%) had a lower incidence of positive MRD; NCI risk status had the highest statistical significance [OR 0.12, 95% CI 0.01-0.97].
Conclusions: Efforts should be made to have standardized MRD testing routinely available in LMICs. Larger studies may be able to suggest other clinical predictors of positive MRD.

EP008 / #917

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

CYTOGENETIC AND MOLECULAR CHARACTERIZATION OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA WITH A CONSENSUS-DERIVED DIAGNOSTIC PANEL. EXPERIENCE FROM A COLLABORATIVE NETWORK IN MEXICO

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Background and Aims: The “Bridge Project”, a Mexico in Alliance with St. Jude (MAS) initiative, seeks to grant access to specialized diagnostic tests to identify cytogenetic and molecular alterations in childhood acute lymphoblastic leukemia (ALL) patients. From May 2019 to March 2022, newly diagnosed patients with ALL from six hospitals in Mexico have been benefited. We aim to describe results of molecular characterization for ALL patients in participating MAS centers.
Methods: A consensus-derived diagnostic panel including cytomorphology, immunophenotype, DNA index, karyotype (with analysis of 20 metaphases), fluorescence in situ hybridization (FISH) (including KMT2A, ETV6/RUNX1, BCR/ABL, E2A/PBX1 and iAMP21 for B-lineage ALL and KMT2A, BCR/ABL, E2A/PBX1, TLX1, TLX3, CDKN2A and TRA/D) for T-lineage ALL, and flow cytometry Minimal Residual Disease (MRD) was used. Samples were centrally analyzed at Hospital Infantil Teleton de Oncologia Molecular Genetics Laboratory.
Results: We included 276 children and a total of 1,369 samples were analyzed. A diagnosis of ALL was established in 229 (82.9%) cases, of which 213 (93%) were B-lineage and 16 (7%) were T-lineage. Studies performed on ALL cases were as follows: Cytomorphology 270 (98.5%), immunophenotype 276 (100%), DNA index 274 (99.2%), karyotype 266 (96.3%), FISH 259 (93.8%). MRD was determined for all confirmed ALL cases at previously established timepoints. Significant findings include abnormal karyotype in 113 (49.3%), hyperdiploidy in 53 (23.1%), complex karyotype in 15 (6.5%) cases. Recurrent structural alterations found were t(12;21) in 40 (17.4%), t(1;19) in 14 (6.1%), t(9;22) in 6 (2.6%), gene break MLL/t (4;11) in 9(3.9%), iAMP21 in 25 (10.9%) of B-lineage cases, and del(9)(p21) in 5 (2.1%), TRA/D (14)(q11.2) rearrangement in 3 (1.3%) of T-lineage cases.
Conclusions: Access to cytogenetic and molecular characterization for chilhood ALL and systematic follow-up evaluation with flow cytometry MRD have been possible with the "Bridge Project". This is resulting in better stratification and treatment allocation for patients.

EP009 / #552

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

CLINICOPATHOLOGICAL FEATURES AND PROGNOSTIC VALUE OF P16 (CDKN2) GENE DELETION AMONG PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS

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Background and Aims: The p16 is a tumor-suppressor protein encoded by a CDKN2 gene located in 9p21, which deletion has been found in various types of tumors. The aim of this study is to investigate the clinicopathological features and prognostic value of p16 gene deletion in pediatric Acute lymphoblastic leukemia (ALL).
Methods: The Hematology Center of Armenia is the only medical institution in Armenia performing diagnostics and treatment of pediatric ALL patients. A retrospective analysis of 81 pediatric patients, diagnosed with ALL between January 2019 and December 2021, was performed. Data were analyzed with the IMB SPSS version 23 statistical software. We carried out descriptive statistical analysis and presented all the continuous variables by means, medians, and standard deviations (SD). The overall survival rate was estimated using the Kaplan-Meier method.
Results: We analyzed 81 patients, 14 (17.2%) of which had p16 deletion. The annual incidence ranges from 7% to 27%. 92.9% of cases were B-cell and 7.1% were T-cell precursor ALL. No significant association was detected with age, sex, performance status (hepatosplenomegaly, lymphadenopathy, mediastinal mass, CNS involvement), laboratory indications (hyperleukocytosis, neutropenia, HGB, thrombocytopenia, LDG, peripheral and bone marrow blast cells), immunophenotypic features and other cytogenetic abnormalities (TEL/AML1, BCR/ABL, MLL, IGH, and C-MYC rearrangement, P53 deletion). All patients were treated according to the ALLIC-BFM-2009 protocol. Two patients (11.8%) abandoned treatment during the induction regimen. The distribution between standard, intermediate and high-risk groups was equable (28.6%). One patient had disease progression after the induction therapy. The 2-year overall survival (OS) was 92%.
Conclusions: No significant correlation between the p16 gene deletion and clinicopathological feathers, as well as the prognostic impact, was detected. The 2-year OS of the p16 deletion positive ALL is compatible with the 2-year OS of all pediatric ALL cases. However, due to the limited number of recruited patients and the short period of follow-up further investigation is needed.

EP010 / #343

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

MALNUTRITION AND FEBRILE NEUTROPENIA IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA AT MUHIMBILI NATIONAL HOSPITAL

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Background and Aims: Febrile neutropenia (FN) is common in Acute Lymphoblastic Leukemia (ALL). Malnutrition predisposes children with ALL to FN by alterations of body metabolism which aggravates low body immunity. The aim of this study was to determine the prevalence of malnutrition in ALL children with FN and to compare it with ALL children without FN
Methods: A retrospective cross sectional study involved data from the files of children aged 0 to 10 years diagnosed with ALL admitted at Muhimbili National Hospital from January 2019 to December 2020. Data included Age, Sex, ALL type, body weight on admission, history of fever with body temperature ≥ 38°C at any point from diagnosis to the end of remission induction treatment, and absolute neutrophil count <1/mm^3 during fever presentation. Weight for Age was interpreted using WHO Z scores. Malnutrition was defined as Mild to moderate underweight (>-3 to -1SD) and Severe underweight (≤-3 SD). FN was defined as body temperature of ≥ 38°C with Absolute neutrophil count <1/mm^3. Frequency percentages, Pearson Chi square test and Fischer exact test were used in data analysis
Results: A total of 59 children, 28(47.5%) males and 31(52.5%) females were included in the study. Mean age was 5.2 ± 2.0 years. Children with FN were 45(76.3%) and those without FN were 14(23.7%). FN mostly affected age group 1 to 5 years (p value 0.004). The prevalence of Malnutrition in children with FN was 28.9% where severe underweight was 11.2% and mild to moderate underweight was 17.7%. Prevalence of Malnutrition in children without FN was 28.6% (mild to moderate underweight), none had severe underweight (0%)
Conclusions: Severe malnutrition predisposes ALL children to FN. Early nutritional intervention is important in children with ALL to reduce the incidence of FN.

EP011 / #1620

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

LONG NON-CODING RNAS CONTRIBUTING FOR CRLF2 OVEREXPRESSION IN ACUTE LYMPHOBLASTIC LEUKAEMIA

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Background and Aims: CRLF2 overexpression (CRLF2-high) has been associated with unfavourable prognosis in B-cell acute lymphoblastic leukaemia (B-ALL) cases. The presence of CRLF2 rearrangements (CRLF2-r) and CRLF2 F232C mutations can explain only half of the cases with this gene overexpression. Long non-coding RNAs (lncRNAs) play a role in the development and progression of leukaemia and can interfere in the transcriptional regulation of protein-coding genes. In this scenario, we hypothesise that the dysregulation of lncRNAs might be a potential mechanism underlying CRLF2-high in B-ALL patients.
Methods: We included 126 diagnostic B-ALL cases from the TARGET cohort and delineated their molecular profile based on WGS and RNA-seq data. Differentially expressed (DE) lncRNAs in CRLF2-high patients were identified using DESeq2 v.1.28.1. Lncpath package was used to obtain functional pathways influenced by the DE lncRNAs. The DE lncRNA-targets experimentally validated were obtained from the LncRNA2Target v3.0 database, and the interactions were tested by correlation analysis using RNA-seq TARGET data. All analyses were conducted using the GRCh37-hg19 genome as reference.
Results: A total of 293 up- and 70 down-regulated DE lncRNAs were identified in CRLF2-high patients. KEGG analysis demonstrated that these DE lncRNAs were mainly involved in ribosome and leukocyte transendothelial migration pathways. Among them, we identified five potential interactions lncRNA-target positively correlated including RPL34-AS1-MIR3663, LINC00161-MIR21, LINC00161-MIR590, PWRN1-MIR21 and PART1-MIR149. Interestingly, RPL34-AS1 and MIR21 were also closely correlated with CRLF2, showing a high expression in CRLF2-high patients (p=0.036 and p=0.004, respectively). Considering the functional role of these lncRNAs in cell proliferation, invasion, migration and apoptosis, we will validate these potential interactions using B-ALL cell lines as models.
Conclusions: Our findings indicate a potential mechanistic role for these lncRNAs interactions on leukemogenesis which could unravel novel biomarkers, and clarify how the expression of CRLF2 is regulated.

EP012 / #293

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

SAFETY AND EFFICACY OF ALENDRONATE TO TREAT OSTEOPENIA IN CHILDREN DURING THERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: Low bone mineral density (osteopenia) is encountered commonly in children with acute lymphoblastic leukemia (ALL) before, during and after therapy. Prior experience with alendronate, a third generation bisphosphonate administered orally, demonstrated high tolerability and evident clinical efficacy. Moreover, some bisphosphonates have exhibited apparent anti-cancer activity. However, concerns have been expressed about the long term safety and utility of such agents in children, including the occurrence of hematological abnormalities. These concerns were addressed in this retrospective cohort study of sequential outcomes.
Methods: Of 217 children with ALL, 63% with standard risk disease, treated between 2000 and 2015 on Dana Farber Cancer Institute protocols, 69 received alendronate for a mean of 87 weeks after dual energy X ray absorptiometry (DXA). DXA was repeated after completion of alendronate and again, in a subgroup of 32 children, 5-9 years later. Lumbar spine areal bone mineral density (LSaBMD) Z scores were obtained and values corrected for height, age and weight (HAW) were calculated for subjects 3-18 years of age.
Results: Almost 80% (172/217) of the children remain in continuous complete remission at a mean of 14.5 years from diagnosis. Of those who received alendronate, which was almost uniformly well tolerated, 7/69 (10.3%) relapsed compared to 19/89 (21.3%) who did not receive the drug ($p=0.06$). The mean unmodified LSaBMD Z score rose from -1.78 to -0.47. This gain was statistically significant for both unmodified ($p<0.0001$) and HAW corrected Z scores (-1.32 to -0.42, $p<0.0001$). There was a modest, statistically insignificant median reduction (0.045) of LSaBMD Z score ($p=0.09$) subsequently in the subgroup (N=32) on long term follow-up.
Conclusions: Alendronate is well tolerated and appears to be moderately and sustainably effective in osteopenic children with ALL. Whether it offers protection against relapse of leukemia needs further study.

EP013 / #382

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

AMPK EPIGENETICALLY REPROGRAMS GENE EXPRESSION AND PROMOTES ADAPTATION/SURVIVAL IN RESPONSE TO ENERGY/METABOLIC STRESS THROUGH BINDING TO A CHROMATIN-ASSOCIATED TRANSCRIPTION COMPLEX IN ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: Survival rates for relapsed/refractory acute lymphoblastic leukemia (ALL), the most common cancer in children and adolescents, remain poor. We and others have reported that ALL cells are vulnerable to energy/ER-stress conditions mediated by AMPK activation. We hypothesized that in ALL cells undergoing energy/metabolic stress, activation of AMPK epigenetically modifies the transcriptome to promote a compensatory survival/adaptation response.
Methods: To identify genome-wide genes regulated by direct association of AMPK to chromatin in response to energy/metabolic stress, we constructed T-ALL (CCRF-CEM/CN2) stable cell line expressing HA-AMPKα2 and performed ChIP-seq assays using HA and Rpb1 antibodies in CN2 cells grown in RPMI ± glucose for 24h. To correlate the level of AMPKα2 recruitment with the level of gene mRNA expression, we used RNA-seq. Interactions between AMPK and chromatin-associated proteins were identified using co-immunoprecipitation (Co-IP) and kinase assays.
Results: ChIP-seq identified 612 gene loci exhibiting recruitment of HA-AMPKα2. Among them, 431 were unique to untreated control whereas 171 were unique to no-glucose conditions. RNA-seq indicated that of 3497 genes altered by AMPK activation, two-thirds were downregulated. Among these, we uncovered a cluster of histone genes exhibiting both decreased recruitment of HA-AMPKα2 to chromatin and mRNA downregulation. Further ChIP-qPCR using AMPKα2 antibody confirmed these data in KASUMI-2 (Bp-ALL). Co-IP uncovered that AMPKα2 interacted with putative members of an AMPK/chromatin-associated transcription factor complex including the TATA-Box Binding Protein Associated Factor (TAF), integrator (INT), and RNA polymerase II. More importantly, we uncovered for the first time that TAF1 is phosphorylated by the AMPKα2β1γ1 heterotrimer.
Conclusions: Our data show that in response to energy/metabolic stress, AMPKα2 binds directly to a chromatin-associated transcription complex to epigenetically reprogram gene expression promoting cellular adaptation/survival. Further elucidation of AMPK's interactions with members of this putative AMPK/chromatin-associated transcription complex may lead to unique opportunities for epigenetic-based therapeutic interventions or combination strategies in relapse/refractory ALL.

EP014 / #1682

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

DEVELOPMENT OF A GENE EXPRESSION AND SPLICING BASED CLASSIFICATION METHOD FOR PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA USING RNA PANEL SEQUENCING

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Background and Aims: Acute lymphoblastic leukemia (ALL) is the most common malignancy of childhood. Whole transcriptome-based sequencing studies revealed distinct, gene expression-based ALL subgroups. These subgroups may provide prognostic or predictive information and therefore improve clinical outcome. In this study, we aimed to determine ALL subgroups using an RNA-based sequencing panel, that investigates 1385 clinically and diagnostically relevant genes. As alternative splicing events are relatively poorly investigated in pediatric ALL, we started developing an alternative splicing based subgroup classification, complementing gene expression- based information.
Methods: Diagnostic bone marrow samples from 191 children with B-, and T-cell precursor ALL were sequenced using the Illumina TruSight RNA Pancancer kit on the Illumina MiSeq platform. Gene-expression levels were determined using kallisto, and alternative splicing events were analyzed by SUPPA2. Normalization of RNA-seq data was followed by principal component analysis, hierarchical clustering of genes or samples and differential expression or differential splicing analysis between known subgroups.
Results: Hierarchical clustering of samples and genes at the gene expression level revealed 10 patient subgroups, that is comparable with literature information. Clustering of alternative splicing events detected 9 groups that showed a different sample composition compared to gene expression- based groups. Gene expression-based sample groups showed a 65% mean overlap with existing WHO-subgroups, while only 31% overlap was found in alternative splicing-based groups. One sample group was separated by gene expression as well as alternative splicing and was dominated by T-ALL samples.
Conclusions: Our results show that categorization of ALL patient-subgroups based on gene expression may be feasible using not only whole transcriptome sequencing, but also panel sequencing technologies. This could improve molecular diagnostics of pediatric ALL, while lowering costs. Additionally, results indicate that splicing analysis is feasible with panel sequencing technologies and may broaden the spectrum of clinical diagnostics in pediatric ALL.

EP015 / #926

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

TIME TO DIAGNOSIS OF HEMATOLOGICAL MALIGNANCIES IN CHILDREN IN AN ONCOLOGY UNIT OF A COUNTRY WITH LIMITED RESOURCES

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Background and Aims: The prognosis of hematological malignancies in pediatrics remains poor in developing countries. One of the main causes is the delay in diagnosis. Studies assessing the factors associated with the time-to-diagnosis of hematological malignancies are rare in Africa. The objective of our study is to identify diagnostic delays in hematological malignancies in children and analyze the risk factors for diagnostic latency.
Methods: We performed a study of 112 cases of children with hematological malignancies referred to the Pediatric Hematology and Oncology Unit of University Hospital Hassan II of Fez between January 2017 and January 2020. We recorded patients' data through parents' interview and review of the medical records. We studied the time intervals between onset and final diagnosis and start of treatment, and investigated associated factors with shorter intervals.
Results: The median latency to diagnosis in our study is 66.14 days. The median physician interval is higher than the median patient interval (37 vs. 28 days). Acute leukemia and the transfer to our unit after the first consultation are associated with a shorter delay of the physician interval (23.3 days, P=0.003, and 14.2 days, P=0.00 successively). Isolated lymphadenopathy as a revealing sign is associated with a prolonged delay of the patient's interval (40.9 days, P=0.017). The gender, the age, the family size, the distance from the hospital, the parents' employment and level of education, and the type of health insurance have no significant association with the diagnostic latency.
Conclusions: The index of suspicion for hematological malignancy in children remains low in our country. Our findings shows that acute leukemia and the fast transfer to a specialized unite of cancer are factors of shorter diagnosis delay. Thus, the increase in practitioner and public awareness, and the establishment of a well-identified circuit of the patient would reduce diagnostic delays.

EP016 / #410

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

COMPARISON OF PEDIATRIC ALL LYMPHOBLAST'S PROTEIN EXPRESSION PROFILES ACCORDING TO TREATMENT RESPONSE MEASURED BY MINIMAL RESIDUAL DISEASE.

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Background and Aims: In Mexico, cancer represents the leading cause of death by disease. Almost half of the cases are due to acute Lymphoblastic leukemia (ALL). Once chemotherapy treatment is started 98% of patients will achieve remission. Despite the use of clinical, biochemical, immunological, and genetic variables, risk stratification is not yet precise enough to predict which patients will relapse once remission is achieved, although it is recognized that treatment response is the best predictor of the outcome. This study aims to describe the lymphoblast's protein expression profile from pediatric patients diagnosed with B-ALL according to their response to remission induction treatment.
Methods: Bone marrow samples from pediatric patients with suspected ALL were obtained before the start of treatment. Mononuclear cells were isolated with Ficoll-Hypaque, then, proteins were isolated for further identification by shotgun proteomic analysis using a mass spectrometer coupled to liquid chromatography and applying computational tools for identification and analysis. Patients were grouped according to MRD levels (good response: <0.01, slow response: 0.01-0.99) at the end of induction treatment.
Results: Four samples were analyzed, two patients had a good response and two had a slow response. Identification of a large number of proteins (886-1724) per patient was achieved, from which 631 were identified in all patients. A principal component analysis revealed that the expression profile of patients is more similar between patients who have the same type of response to treatment when measured by MRD. In addition, differentially expressed proteins in poor responders describe a cell cycle activation through MYC, YAP1, and SRF.
Conclusions: This methodology is useful to identify proteins that have clinical use as diagnostic biomarkers, that are used to determine the efficacy of treatment, or as therapeutic targets. Finally, mass spectrometry proteomics is useful for identifying therapeutic targets in precision medicine strategies.

EP017 / #411

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

FEASIBILITY OF A STANDARDIZED NEXT-GENERATION SEQUENCING PANEL FOR PRECISION MEDICINE IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: Conventionally, improvements in survival of pediatric patients with Acute Lymphoblastic Leukemia (ALL) have been based on the optimization of chemotherapy schemes and a risk-oriented intensity assignment strategy. Recent evidence shows that precision medicine, which looks for interpersonal tumor differences at the molecular level in order to provide tailoring of medical treatment to the individual characteristics of patients. The aim of this study was to evaluate the utility of a standardized next-generation sequencing (NGS) panel to find targets for directed therapies in pediatric patients with ALL.
Methods: Bone marrow samples from seven pediatric patients diagnosed with ALL were preserved in paraffin and analyzed by NGS (FoundationOne Heme); the targets included 406 genes and 31 selected introns involved in DNA rearrangements, and RNA of 265 genes known to participate in oncogenesis or to be modified by target therapy.
Results: BET domain inhibitors were predicted to have biological effects in two patients with rearrangements of IGH. MEK inhibitors could be used in one patient who had an alteration of NRAS. One patient had an alteration of JAK2 predicted to be sensitive to ruxolitinib. An alteration in PIK3CA was found in one patient, suggesting the benefits of using mTOR inhibitors. A patient had an alteration in FLT3, indicating a possible biologic effect by using kinase inhibitors, multikinase inhibitors, tyrosine kinase inhibitors, or MEK inhibitors. Two patients showed no positive results.
Conclusions: The presence of molecular targets with known drug-triggered biological effects was found in five of seven patients, indicating that this standardized NGS-sequencing panel could be useful for precision medicine in pediatric ALL. It is expected that improvements in patient survival could be reached by using targeted drugs in addition to standard schemes.
Acknowledgments: We deeply thank Roche who kindly provided the tests for this work.

EP018 / #1462

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

PRELIMINARY ANALYSIS OF RISK FACTORS FOR SEVERE MUCOSITIS IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: High-dose methotrexate (HD-MTX) is a critical component of acute lymphoblastic leukemia (ALL) treatment. Racial/ethnic disparities in MTX toxicities have been reported, including a disparate risk of MTX neurotoxicity and delayed clearance. Patient-related risk factors for severe MTX-associated mucositis are unknown. Refinement of these risk factors may help predict patients at greatest risk, which may help reduce morbidity and mortality by offering opportunities for early intervention. We evaluated the incidence of MTX-associated mucositis following doses of HD-MTX in an ethnically diverse population of patients with ALL.
Methods: We retrospectively reviewed patients diagnosed with ALL and treated with HD-MTX (5 g/m2) at Texas Children's Cancer Center (2010-2017). Clinical, treatment, and sociodemographic factors were systematically collected from the electronic medical record. Mucositis was graded according to a modified CTCAE scale. Mixed effects multivariable logistic regression was used to estimate the odds ratios (OR) and corresponding 95% confidence intervals (CI) for the association between clinical factors and mucositis.
Results: We identified 316 patients who received a total of 1,110 doses. The majority of patients were male (58%) and self-reported Hispanic ethnicity (53%). One-third (n=108, 34%) of patients experienced at least one episode of Grade 3 or 4 mucositis. Patients who did not clear MTX by hour 24 had a significantly higher odds of Grade 3 or 4 mucositis (OR 2.16, p=0.05), though this was not significant in an adjusted model of risk. In our preliminary analysis, the risk of severe mucositis was not associated with sex, race, ethnicity, or obesity.
Conclusions: The ability to predict which patients are at greatest risk of mucositis remains a challenge. We continue to evaluate potential risk factors, including age, leucovorin dosing, use of oral glutamine, malnutrition, area deprivation indices, oral/dental health, pharmacogenomics, and the microbiome. Furthermore, we continue to improve the precision and accuracy of risk prediction models for severe mucositis.

EP019 / #1508

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

IMPROVING SURVIVAL BY DECREASING INDUCTION MORTALITY AND ENHANCING SUPPORTIVE CARE: A SUSTAINABLE STEPWISE APPROACH IN PEDIATRIC PATIENTS WITH ALL IN WESTERN KENYA

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Background and Aims: Since 2010, we have treated children with acute lymphoblastic leukemia (ALL) on resource-adapted protocols at Moi Teaching and Referral Hospital (MTRH) in Western Kenya. Working with twining partners from Princess Máxima Center for Pediatric Oncology in the Netherlands and Indiana University in the United States, we recently published outcomes of children diagnosed with ALL from 2010-2016. We showed increased mortality during induction phase and high rates of treatment abandonment. Initially, our induction phase comprised of vincristine, doxorubicin, and prednisone with eventual addition of L-asparaginase. Based on these results, we focused on strategies to mitigate both causes of poor outcome. This included active enrollment of families into health insurance, structured parental education, and use of flow cytometry to improve diagnostic accuracy. Doxorubicin was dropped from our induction regimen as the supply of Vincristine, Prednisone, and L-asparaginase was improved.
Methods: Children diagnosed with ALL from 2017- 2020 were identified from our registry. A retrospective review was done of the outcomes of 161 children receiving modified treatment with improved social or financial support for diagnostic testing, insurance coverage, and transportation.
Results: Mortality in induction (6 weeks) decreased from the historical rate of 26% to 13%. Abandonment of treatment was reduced from 26% to 8%. Overall survival at three years improved from 20% to over 50%. Each of these comparisons achieved statistical significance ($p<0.003$ or better).
Conclusions: Sustainable improvement in the care of children with ALL in low- and middle-income countries happens as many small steps, that add up to significant advances in outcomes. Our studies highlight the importance of collaboration, need for proper documentation of data, and continuous quality improvement strategies adapted to available resources. Future strategies will include improved recognition and diagnosis of ALL, proper risk stratification, risk-adapted protocols for management of central nervous system disease, improved supportive care, and further reduction of treatment abandonment.

EP020 / #1266

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

PHAGOCYTE-RELATED S100 PROTEINS AND CYTOKINES IN ACUTE LYMPHOBLASTIC LEUKEMIA AT DIAGNOSIS AND FOLLOW-UP MAY IMPROVE PREDICTION OF MINIMAL RESIDUAL DISEASE.

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Background and Aims: Few studies investigated S100 proteins and single cytokines in ALL at diagnosis and found low levels of S100A9, S100A12, and IL-18 compared to both juvenile idiopathic arthritis and other autoinflammatory diseases but higher levels than in healthy controls. The aim of this study was to evaluate whether biomarkers of inflammation like phagocyte-related S100 proteins and a panel of cytokines at diagnosis could predict the outcome of ALL expressed as minimal residual disease (MRD), relapse, and death. Further we evaluated the level of the biomarkers at diagnosis and during antileukemic therapy and their correlation with basic laboratory values.
Methods: In this retrospective cohort study, we evaluated the serum levels of biomarkers of inflammation like phagocyte-related S100 proteins and a panel of cytokinesin 150 ALL patients diagnosed at Aalborg and Aarhus University Hospitals from January 2001 to December 2018. Serum concentrations of the proteins were determined by multiplexed bead array assay on a MAGPIX instrument using Luminex software. We performed internal validation using repeated ’10- fold cross- validation’ computing the area under the curve (AUC) as well as positive and negative predictive values in order to evaluate the predictive performance.
Results: The levels of S100A9, S100A12, IL-1beta, IL-12p70, IL-13, IL-17, IL-18, and MPO serum levels increased significantly as chemotherapy was initiated. The difference was most pronounced for S100A9 and S100A12, which had strong positive correlations with the neutrophils counts. In contrast, TNF-alpha, IL-6, IL-10, CCL-2, MMP-3, and CD25 serum levels decreased after chemotherapy. In a multivariate predictive models with MRD as the outcome, AUC increased from 75% (95% CI 66-81%) when using initial risk group stratification alone to 83% (95% CI 73-91%) including the biomarkers TNF-alpha, S100A12, and CCL-2.
Conclusions: A multivariate predictive model including CCL-2, TNF-alpha, and S100A12 could improve the ability to predict MRD compared to conventional risk-group stratification alone.

EP021 / #1713

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

OUTCOME OF INFANTILE ACUTE LYMPHOBLASTIC LEUKEMIA TREATED AT KING HUSSEIN CANCER CENTER

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Background and Aims: Infantile Acute lymphoblastic leukemia (ALL) is rare; despite excellent cure rates in most children with ALL; infants continue to have poor outcomes with overall survival of 30-40%. Historically, relapse and therapy related mortality have been the major leading cause of treatment failure.
Methods: Retrospective chart review for all infants (age less than one year) treated at King Hussein Cancer Center per modified total XV protocol.
Results: Between Feb2005 and Jan2022 a total of 23 patients (13 males) were treated and followed for a median of 71 months (range, 2-205). Median age at diagnosis was 6.7 months (range, 2.5-11.5). Median WBC at diagnosis was 99k/µl (rang, 0.7-570). CNS status at diagnosis were: CNS1 (N=18), CNS2 (N=3) and CNS3 (N=2). Immunophenotypes were consistent with B-ALL (CD10 negative, n=15; CD10 positive, n=7) and, T-ALL (n=1). MLL gene rearrangement was positive in 15 patients (65%). Five patients had positive MRD >=0.01% at the end of induction. The estimated 5-year-EFS and OS were 62% and 69%, respectively. No prognostic factors were identified using univariate and multivariate analysis. Mortalities were due to disease relapse/progression (N=4) or infection (N=2).
Conclusions: The outcome of infants with ALL at our institution is in line with published literature. This highlights the importance of upfront intensive therapy and optimal supportive care: Pre-emptive admissions during intensive blocks, prophylactic anti-fungals, nutritional support and immunoglobulin replacement.

EP022 / #1578

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

CAR T-CELL PEDIATRIC PATIENTS ADMITTED TO A PEDIATRIC INTENSIVE CARE UNIT (PICU): SUPPORTIVE TREATMENT AND OUTCOMES

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Background and Aims: Chimeric antigen receptor (CAR) T-cell CD 19 therapy is an effective treatment for relapsed or refractory B-cell acute lymphoblastic leukemia (ALL). It can be associated to life-threatening toxicities, being cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) frequent adverse effect. PICU admission is often required. Our main purpose is to describe clinical characteristics, treatment and outcomes of patients admitted to PICU.
Methods: Prospective observational cohort study conducted in a tertiary pediatric hospital from 2016-2021. Children who received CAR-T therapy admitted to PICU were included. Epidemiological, clinical characteristics, ICANS and CRS scales (ASTCT scale), supportive treatment, length of stay (LOS) and mortality variables were collected.
Results: CAR-T cells (41BB construct, 18 Tisa-cel/CTL019, 5 ARI-0001 cells) were infused in 59 patients. Twenty-three patients (38.9%) required PICU admission, LOS was 4 days (IQR 2-7) and hospital LOS 24 days (IQR 16-38). Median age was 8 years (IQR 6-11). Patients admitted to PICU presented higher tumoral burden before infusion: 23%(IQR 5-72) vs. 0(0-4), $p<0.001$. Main reasons for admissions were CRS (n=19, 82.6%) and neurotoxicity (n=3, 13%). Fourteen patients (60.9%) required inotropic support, 13 (56%) received respiratory support, 5 of them mechanical ventilation. Regarding specific CAR-T toxicities, 15 patients (65.2%) received tocilizumab, 4(17.4%) anakinra, 4(17.4%) siltuximab and 10 (43.5%) steroids. Fourteen patients (60.9%) had neurological involvement, one of them was severe (ICANS 4). Patients who required inotropic drugs had higher procalcitonin and ferritin levels ($p<0.05$). Two patients died during PICU stay (8.7%), both because of refractory CRS-macrophage activation syndrome. There were no differences in relapse rate after CAR-T ($p=0.396$).
Conclusions: PICU admission after CAR-T therapy is frequent, mainly due to CRS. Supportive treatment allowed effective management of toxicities and high survival. Our data confirm that high tumoral burden is a risk factor for severe CRS and ICANS and thus PICU

EP023 / #845

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS FROM A TERTIARY CENTER IN TURKEY

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Background and Aims: Acute lymphoblastic leukemia (ALL) is the most common type of cancer in children accounting for approximately 25% of all pediatric cancers and 5-year survival is approximately 85% in developed countries. We reviewed our ALL patients in order to evaluate their outcome and survival.
Methods: A total of 41 (16 female, 25 male) patients with ALL diagnosed between 2011 to 2022 were included in the study. All patients were stratified and treated according to COG Protocols.
Results: The mean age of the patients were 6 (2-16) years. There were 32 (78%) standard risk patients. Thirty-four (82%) B-ALL and 7 T-ALL patients with a mean duration of follow-up 107 months were treated. Central nervous system involvement was present in 3 patients. Minimal residual disease at 28. day was negative in 36 (87%) patients. The 10-year overall survival was 85.2%. The only cause of death in our study was due to infections (14.6% [6/41 patients]). Only one patient, with t(9;22) BCR-ABL translocation, relapsed after seven years and attained remission with allogeneic stem cell transplantation.
Conclusions: Our success rate is promising but the infectious complications are still the most common cause of death in developing countries (etc. Turkey) during treatment of children with ALL.

EP024 / #977

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

THERAPEUTIC MECHANISMS OF CD9 NEUTRALIZING ANTIBODIES IN PEDIATRIC B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: Despite advances in CD19- and CD22-based immunotherapies for children with relapsed/refractory B-cell precursor acute lymphoblastic leukemia (BCP-ALL), a substantial proportion of cases subsequently relapse with antigen loss, underscoring the need to develop salvage therapies. We recently demonstrated that neutralizing antibodies against CD9 endowed potent single-agent activities in patient-derived xenografts of refractory BCP-ALL and enhanced chemosensitivity. This study was designed to further characterize their underlying mechanisms.
Methods: Standard parameters of assessing cell death, including phosphatidylserine externalization, mitochondrial potential dissipation, cytochrome c release and caspase activation, were characterized by flow cytometry in BCP-ALL cell lines following exposure to anti-CD9. Proteins shaping different modes of cell death was investigated by Western blotting and compared with vincristine, coupled with genome-wide expression microarray, qPCR and functional validation to dictate the downstream pathways.
Results: Anti-CD9 significantly increased Annexin V^+ cells comparing with IgG control. Loss of mitochondrial potential and release of cytochrome c were also witnessed following antibody exposure. Surprisingly, anti-CD9 did not mediate changes in proteins related to apoptosis (caspase-3/7/8/9, PARP, Bax/Bim/Bad/Bcl-2/Bcl-xL/Mcl-1), necroptosis (RIP/MLKL), autophagy (LC3/Beclin-1/Atg-5/Atg-7) or mitophagy (DRP-1), whereas vincristine induced classical apoptosis reversible by a pan-caspase inhibitor. Anti-CD9 differentially regulated 192 genes enriched with E2F transcription targets and G2M cell cycle checkpoint. Up-regulation of DRAM1, IKZF2 and RANBP3L, and down-regulation of ARRDC3 were validated in 10 BCP-ALL cell lines and 17 patient samples. Low expression of IKZF2 was associated with poor outcomes in a pediatric BCP-ALL cohort, and that overexpression of IKZF2 significantly suppressed leukemia proliferation, phenocopying the beneficial effects of anti-CD9.
Conclusions: Anti-CD9 exhibits its leukemia suppressive activities via induction of a previously unrecognized form of cell death possibly involving reactivation of the tumor suppressor IKZF2. This study collectively provides the first mechanistic description of anti-CD9 in BCP-ALL and a promising therapeutic target worth to be considered in future clinical trials.

EP025 / #415

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

TREATMENT OUTCOME OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA ACCORDING TO RISK-GROUP STRATIFICATION: 20-YEAR PERIOD EXPERIENCE IN A SINGLE INSTITUTION

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Background and Aims: Acute lymphoblastic leukemia (ALL) is the most common malignant disease in children and adolescents. In this study, the treatment outcomes and prognostic factors of ALL patients were investigated during a 20-year period in a single institution.
Methods: This study analyzed patients aged <19 years old who were diagnosed with ALL at Ajou University Hospital from January 2001 to December 2019. Patients were classified and treated under the low-risk (LR), standard-risk (SR), high-risk (HR), and very HR (VHR) groups.
Results: Among 112 patients, there were 7 patients (6.3%) in LR, 37 (33.3%) in SR, 52 (46.4%) in HR, and 16 (14.3%) in VHR groups. Relapse occurred in 22 patients, with 15 occurring during ALL treatment and 7 occurring within a median 18 months following the end of chemotherapy (range, 2–53 months). The 10-year relapse-free survival (RFS) and overall survival (OS) were 76.6 ± 4.5% and 83.3 ± 4.8%, respectively. The RFS and OS according to risk groups were as follows: LR: 68.6% ± 18.6%, 80.0 ± 17.9%; SR: 83.5% ± 6.8%, 100%; HR: 76.1% ± 7.3%, 81.1 ± 5.8%; and VHR: 63.0% ± 13.3%, 63.3 ± 16.6%. On multivariate analysis, white blood cell count >200,000/mm^3 at diagnosis (relative risk: 5.120, 95% confidential interval [CI] 1.454–18.028, P = 0.011) and BCR/ABL mutation (relative risk: 3.863, 95% CI 10.98–13.591, P = 0.035) were associated with a lower RFS. On subgroup analysis, the LR group had a lower OS than the SR group (80.0 ± 17.9% vs 100%, P = 0.025).
Conclusions: Our study indicated that patients with hyperleukocytosis at diagnosis and BCR/ABL mutation exhibited a lower RFS. The OS of the LR group was lower than that of the SR group. Therefore, the treatment for these patients should be modifed to improve the treatment outcomes.

EP026 / #113

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

EFFECTIVENESS OF A METHOTREXATE-FREE CHEMOTHERAPY REGIMEN IN LOW-RISK ACUTE LYMPHOBLASTIC LEUKEMIA FOR UNINSURED HISPANIC CHILDREN.

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Background and Aims: The high rates of toxicity and mortality related to the treatment of patients with acute lymphoblastic leukemia (ALL) in low- and middle-income countries (LMIC) have generated the need to adapt treatment protocols according to the capacity of support therapy to less intensive regimens, especially in low-risk (LR) patients. The primary objective of our study was to determine the 3-year overall survival (OS) and event-free survival (EFS) in LR ALL protocol.
Methods: One hundred and seven children were diagnosed with ALL from 2017 to 2019 in University hospital “José Eleuterio González”. LR was defined as ≤6 years, with ≤20,000 leukocytes, without extramedullary infiltration, good response to steroids, and minimal residual disease (MRD) ≤0.01% after the induction phase. The chemotherapy regimen on an outpatient basis includes 4 doses of anthracycline, 15 doses of L-asparaginase, high-doses of methotrexate were not included.
Results: Twenty-seven patients (34%) met LR criteria. The median follow-up was 41 (17-58) months. Of 22 evaluated patients (81%), the karyotype was normal in 13 (59%), 5 (9%) had hyperdiploidy, and 4 were not analyzable quality. There were no induction deaths. Nine patients (33%) received their chemotherapy scheme completely as outpatients. Thirteen patients (48%) never had treatment interruption for more than 7 days. The 3-year OS was 96.3%, and EFS was 82.4%. One patient presented a bone marrow late relapse, and other presented an isolated early relapse to the CNS. Currently both alive and in a second remission. One patient died during maintenance, in remission, due to viral pneumonia.
Conclusions: The treatment of low-risk Hispanic ALL patients with our adapted regimen showed promising results with good 3-year OS and EFS. Also, it was possible to counteract the lack of hospital beds and poor support therapy in our environment due to low toxicity and no induction mortality.

EP027 / #397

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

LOW TOXICITY BORTEZOMIB-BASED OUTPATIENT REGIMEN IN RELAPSED/REFRACTORY ACUTE LYMPHOBLASTIC LEUKEMIA IN THE TARGETED THERAPY ERA.

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Background and Aims: There are multiple treatment strategies in patients with refractory or relapsed (R/R) acute lymphoblastic leukemia (ALL). Currently, the use of agents targeting surface receptors such as CD19, CD20, and CD22, including bispecific T cell engagers, monoclonal antibodies, and chimeric antigen receptor (CAR) T cells, have shown promising results; however, their costs make their use unaffordable in low or middle-income countries. Therefore, alternative chemotherapy combinations and repurposed agents should continue to be explored. We aimed to describe our experience with a bortezomib (BZ) based regimen in children, adolescents, and young adults diagnosed with R/R ALL.
Methods: We performed a retrospective analysis between 2014-2020 of patients who received our bortezomib-based regimen. The reinduction protocol consisted of BZ 1.3 mg/m^2/day on days 1, 4, 8, and 11; dexamethasone 10 mg/m^2/day for 21 days, vincristine 1.5 mg/m^2/day on days 1, 8, 15, and 22; doxorubicin 50 mg/m^2/day or mitoxantrone on day 1 IV; L-asparaginase 6000 U/m^2 (nine doses). Treatment response was assessed on day 30.
Results: We included 35 patients; the median age was 12 years (3-33). A complete response (CR) was achieved by 23 patients (65%); 13 patients achieved CR with MRD negativity (CRxMRD). 17.1% achieved partial response after 1 cycle. No treatment-related mortality occurred, 21 patients (60%) were not hospitalized, and 24 (68%) did not require blood component transfusions, 23 patients (65%) did not have significant treatment-related adverse events. Indications for hospitalization were neutropenic fever (n=9), one event of mild pancreatitis, and one event of superficial venous thrombosis of the upper limb. One patient presented severe neurological toxicity with seizures. Eighteen patients (52.9%) underwent hematopoietic stem cell transplantation consolidation, The 5-year OS and RFS were 41% and 37.2% in the whole group.
Conclusions: The addition of BZ to a simple protocol of chemotherapy is effective, safe, economically, and logistically feasible in the low resources setting.

EP028 / #1227

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

PHARMACOKINETICS AND IMMUNOGENCICITY OF THE FIRST DOSES OF PEG-ASPARAGINASE

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Background and Aims: PEG-asparaginase is an indispensable part of the multiagent treatment of acute lymphoblastic leukemia (ALL). However, PEG-asparaginase treatment comes with substantial toxicity leading to discontinuation of therapy, which threatens survival. The most common toxicity is hypersensitivity, defined as either clinical allergy or silent inactivation both associated with increased clearance and inactivation of PEG-asparaginase. Pharmacokinetic (PK) analyses are essential in detecting inactivation of PEG-asparaginase. Therefore, we aimed to investigate the possibility to identify PK parameters to predict hypersensitivity before the allergic reaction occurred.
Methods: Patients with ALL aged 1-45 years treated according to the ALLTogether Pilot Protocol from December 2018 to December 2021 in the Nordic and Baltic countries were eligible. A total of 2,228 samples from 256 patients were analyzed real-time for asparaginase enzyme activity (AEA) levels. A transit compartment model to characterize the PK of PEG-asparaginase was developed, representing increased clearance over time. AEA was represented by the sum of all compartments.
Results: Inactivation of PEG-asparaginase was identified in 44 of 256 patients (17.2%); 9 patients with silent inactivation (20.5%), 12 patients with mild allergy (27.3%) and 23 patients with severe allergy (52.3%). Hypersensitivity mainly occurred after 4th or 5th dose (n=22 (50%) and n=6 (13.6%), respectively). A 10-compartmental transit model that allowed an exponential increase in clearance over time described the AEA-time profile best. The model divided patients into stable or exponentially increasing clearance over time. All patients with inactivation of PEG-asparaginase demonstrated an increased clearance over time. Patients with clinical symptoms demonstrated the most prominent increase.
Conclusions: PK analysis of AEA enables early identification of changing clearance, which opens new possibilities to predict inactivation of PEG-asparaginase contributing to improvement of treatment.

EP029 / #446

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

AN IMPLEMENTATION APPROACH TO CHARACTERIZE SUCCESSFUL FACTORS OF INTERNATIONAL COLLABORATION IN A DRUG-DONATION PROGRAM AND FACILITATION EFFORT

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Background and Aims: International partnerships and supply chain innovation have been identified as promising solutions to bridge the pediatric cancer survival gap. Collaborator engagement leverages complementary expertise to improve system level integration of evidence-based interventions. Despite recent emphasis on the critical nature of engagement, there has been little formal reporting of partnership composition. As part of a larger effort to evaluate the implementation of blinatumomab in low- and middle-income countries, this study examined the experiences of collaborators in a blinatumomab drug-donation program after two years of program involvement.
Methods: We hypothesized that the collaborative approach established at program initiation would result in improved collaborator satisfaction. An electronic survey comprised of 47 questions was developed. This included 40 close-ended questions from the Wilder Collaboration Factors Inventory 2nd ed., a tool identifying 20 factors that influence collaboration success. Responses were scored on a 5-point Likert-type scale.
Results: The survey was administered to 16 collaborators (14/16, 87.5% response rate), with diverse, multidisciplinary composition; nurse practitioner (n=1), pharmacists (n=2), physicians (n=6) (United States [3], India [3], and Pakistan [1]), industry (n=4), and non-governmental organization (n=1). Females comprised 43% of respondents. Average scores >4 represented partnership strengths. Twelve out of twenty collaborative factors received scores >4.5. Factor ratings for "mutual respect and trust," "shared stake in process and outcome", and "shared vision" scored highest (>4.9) indicating strengths in the partnership with an overall program satisfaction of 9.28 on a 10-point scale. Ratings for factors related to process and structure were identified as opportunities for improvement.
Conclusions: As a result of this survey, additional structure will be established to improve transparency of processes. As new partners join the project and their dynamics evolve, we will reevaluate collaborator responses overtime. Integration of this tool provides an opportunity to identify areas for improvement and guide decisions to foster long-term, sustainable engagement amongst international collaborations.

EP030 / #1206

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

HIGH DOSE METHOTREXATE USE IN CHILDREN WITH HIGH RISK ALL IN A LMIC- A 10-YEAR EXPERIENCE

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Background and Aims: High dose methotrexate has proven to be very effective in treatment of high-risk Precursor B Acute Lymphoblastic Leukemia in children. Cytotoxic concentrations in lymphoblasts can cause severe adverse effects such as neutropenia, mucositis, renal and hepatic injury. Treatment related toxicity warrants precautions such as hyperhydration, monitoring levels, leucovorin rescue and urine alkalinization. This study aims to provide tolerance of HDMTX in LMIC setting.
Methods: Records of patients with high risk ALL between 2010-2019 were reviewed retrospectively , data recorded in Resonance study manager. All patients were treated with a uniform treatment regimen based on the BFM protocol. Interim maintenance included HDMTX 5gm/m2 biweekly for 4 doses. TALL patients were shifted to Capizzi MTX. Study variables included sex, age, disease type, blood counts, methotrexate levels, creatinine levels and liver function tests.
Results: 372 doses of high dose methotrexate were administered to 105 HR ALL patients, 72 (68.5%) males, median age of 9.5 years. Most patients had B ALL(n=98, 93.3%), while 7(6.7%) had T-ALL. The median methotrexate level at 24 hours was 7.14 (IQR 2.34-12), at 48 hours was 1.41 (IQR 0.98-4.56) & at 72 hours was 0.29 (IQR 0.02-4.2) umol/L. The mean hospital stay for administration of each dose of HD MTX was 4.8 days. The most common side effects were vomiting and diarrhea (n=20, 5.4%) followed by leukopenia (n=19, 5.1%), dermatological reactions (n=18, 4.8%) and increased creatinine levels(n=15, 4.03%).Thrombocytopenia was reported in (n=7, 1.88%) and mucositis(n=4, 1.07%). Median follow up time of the study group was 19.5 months (IQR 7.5-35 months) with an overall survival of 70% (95% CI).
Conclusions: High dose MTX was well tolerated in our study population from LMIC with acceptable side effects needing aggressive support, adequate hydration and leucovorin rescue based on MTX level monitoring. This encourages other centers in using HDMTX as standard of treatment for HR BALL.

EP031 / #1579

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

PEGASPARGASE LEVELS IN INFANTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP TRIAL AALL15P1

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Background and Aims: Asparaginase is an essential component of therapy for acute lymphoblastic leukemia (ALL). Very limited data on pharmacokinetics and therapeutic drug monitoring using serum asparaginase activity (SAA) levels exist in infants. We aimed to describe SAA levels in infants with ALL and correlate with age/dose or treatment cycle.
Methods: AALL15P1 enrolled infants with ALL between 2017-2020, treating with pegaspargase dosed at indicated units/m^2 as follows: Induction: <7days 1250; 7days-6months 1750; 6-12months 2000; Post-induction: <6months 1650; 6-12months 1875; >/=12months 2500. An optional study obtained SAA levels, recommended on day 7 following administration.
Results: 78 patients enrolled on AALL15P1, and 34 patients submitted 60 SAA levels. Levels were measured during Induction (n=30), Interim Maintenance (n=17) and Delayed Intensification (n=13). Age at the time of pegaspargase administration varied from 1-17 months. There were no significant demographic differences between patients with at least one level and those without. All SAA levels were >/=0.1 IU/mL and the majority (n=55, 92%) were >/=0.4 IU/mL. Mean levels increased with prescribed dose (and thus age), with mean levels of 0.57 IU/mL for <6 months (n=10), 0.82 IU/mL for 6-11 months (n=31), and 1.31 IU/mL for >/=12 months (n=19) ($p<0.001$). This trend persisted when sub-analyzed by treatment cycle and age. There were no pegaspargase hypersensitivity reactions reported.
Conclusions: This represents the largest cohort of infant ALL patients with SAA levels reported. All reported levels were >/=0.1 IU/mL (proposed minimum therapeutic level) and the majority were >/=0.4 IU/mL (proposed optimal therapeutic level), suggesting that, despite a reduced BSA-based pegaspargase dose compared to older children, infants achieve adequate asparagine depletion. No SAA levels were indicative of silent inactivation and there were no patients with hypersensitivity, highlighting that the asparaginase immune response relationship may differ in infants. Ongoing analysis will assess for correlation of SAA levels with patient demographics and incidence of pegaspargase-associated toxicities.

EP032 / #287

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

DOES DIETARY ASPARAGINE AFFECT PEGASPARGASE THERAPY AND THE GUT MICROBIOME? A PILOT STUDY IN MICE.

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Background and Aims: Pegaspargase (PEG) is key to the treatment of pediatric Acute Lymphoblastic Leukemia. PEG depletes blood asparagine (Asn), killing leukemic but not healthy cells. Guidelines on optimum dosing of PEG are unclear. Asn is made by healthy cells and diffuses from the gut. We sought to determine if dietary Asn can impact PEG-mediated Asn depletion and its association with gut bacteria.
Methods: Pre-diet blood and stool samples from 10 mice were collected. The mice were then divided into 2 cages and given an Asn rich or depleted diet. Blood and stool were sampled after 72 days (post-diet). The mice were then injected with 200 IU/kg PEG. Four days post-PEG stool and 5-day post-PEG blood samples were collected. Stool 16S ribosomal DNA was sequenced. Blood Asn was measured using mass spectrometry.
Results: Blood Asn levels were similar between post-diet samples. Asn was depleted in all post-PEG samples. Analysing bacteria within a diet, the depleted diet had 36 species change in abundance between baseline and post-diet, and the rich diet had 17. Of the 17, 8 changed in the same direction for both diets. The depleted diet had 15 species change abundance from post-diet to post-PEG, the rich diet had 1. Comparing diets, 29 species were different between groups at baseline, 11 post-diet, and 26 post-PEG. Three changed post-diet but were similar at baseline, and 19 changed post-PEG that were similar post-diet.
Conclusions: Blood Asn was depleted in mice with PEG regardless of dietary Asn. Thus, modifying dietary Asn before PEG is unlikely to be impactful. Despite differences at baseline, we observed bacterial changes based on diet and PEG injection, which require further investigation. The impact of dietary Asn on PEG efficacy over a longer period should be explored, to determine whether Asn depletion can be sustained and if changes in gut bacteria have any impact.

EP033 / #1460

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

DEVELOPMENT OF RAPID MOLECULAR TESTING TO DIAGNOSE PEDIATRIC CANCERS IN SUB-SAHARAN AFRICA

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Background and Aims: Risk stratification and molecular targeting have been key to increasing cure rates for pediatric cancers in high-income countries. Precise diagnosis and successful treatment in low-resourced settings is hindered by insufficient pathology infrastructure. The Global HOPE program aims to improve outcomes for pediatric cancer in Sub-Saharan Africa (SSA). The goal of this study was to develop rapid molecular assays to improve pediatric cancer diagnoses in low-resourced settings.
Methods: The NanoString nCounter platform was chosen due to minimal technical expertise required, ability to test sub-optimal RNA, and turn-around-time (2-3 days). To address the high frequency of gene fusions in pediatric cancers, custom panels were designed to detect 439 specific breakpoints of fusions associated with hematologic malignancies and 436 fusions for solid tumors. The NanoString Cancer Copy Number Variation (CNV) assay was tested to determine the effectiveness of detecting aneuploidy and gene amplification, also common in pediatric cancers.
Results: Validation of the custom gene fusion panels was performed using >140 samples with known fusion status. The results had a 99% accuracy after follow-up sequencing of any potential false negative/positive results. Testing the CNV assay confirmed that amplification and CNV in a diploid background are easily detectable in pediatric cancer samples. In the presence of high chromosome number, an alternative analysis algorithm is required to reset the background ploidy, similar to microarray analysis of aneuploid cancer samples.
Conclusions: Validation studies of the NanoString assays confirmed them as highly accurate, tolerant of variable nucleic acid quality, and requiring small sample amounts. Global HOPE is currently implementing the platform in SSA, starting with the custom gene fusion panels. Testing will allow children in SSA to be treated according to the specific molecular characteristics of their cancers to maximize their chances of a cure, the same approach now considered standard-of-care in the US.

EP034 / #790

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

EARLY RESULTS AND COST-ANALYSIS OF MAS-ALL-18 TREATMENT GUIDELINE FOR ACUTE LYMPHOBLASTIC LEUKEMIA IN MEXICO

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Background and Aims: Acute Lymphoblastic Leukemia (ALL) was treated until June 2019 in Mexico mainly using TOTAL-XV based protocols, with an early treatment-related mortality/abandonment rate (TRMR) of 12% during induction and 25% in the first year of treatment. Since July 2019, a treatment guideline based on strategic deintensification of therapy in carefully selected patients, based on genetic profiling and minimal residual disease, has been used in 4 centers within the Mexico in Alliance with St. Jude (MAS) collaborative network.
Methods: We compared our preliminary results with the MAS-ALL-18 treatment guideline with results from ALL patients treated at MAS-affiliated centers prior to July 2019, focusing on early TRMR at end of induction and during the first year of therapy. We also calculated approximate chemotherapy expenditure per patient for TOTAL-XV standard and high-risk, and MAS-ALL-18 favorable, intermediate and high-risk, and estimated cost per 100 patients considering risk-group assignment distribution documented for both cohorts.
Results: Our cohort prior to July 2019 included 578 patients, of which 18.7% were treated as standard and 81.3 as high-risk. We previously reported early results from a MAS-ALL-18 cohort, among which 49.5% of patients were classified as favorable, 20.8% as intermediate and 29.7 as high-risk. Early TRMR for 138 MAS-ALL-18 patients who have completed 1 year of treatment was 7.4% during induction, and 15.4% during the first year of treatment. Chemotherapy expenditure per patient was estimated at 10,353.51USD for standard and 15,510.78USD for high-risk TOTAL-XV and 8,008.00USD for favorable, 13,041.25USD for intermediate and 14,774.38USD for high-risk MAS-ALL18 patients. Chemotherapy expenditure per 100 patients, considering risk-group assignment distribution documented for both cohorts, was estimated at 1,454,637.05 for TOTAL-XV and 1,106,441.80 for MAS-ALL-18.
Conclusions: MAS-ALL-18 has proven to have lower early TRMR at end-of-induction (7.4 Vs 12%) and after one year of therapy (15.4 Vs 25%), whilst permitting an estimated 24% cost reduction in chemotherapy expenditure.

EP035 / #1003

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

RB TRANSCRIPTIONAL COREPRESSOR 1 (RB1) GENE DELETIONS ADVERSELY AFFECT THE OUTCOME IN PEDIATRIC B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: There is a need for newer biomarkers to improve the risk-stratification of B-ALL. The aim of the study was to estimate the prevalence and effect of RB transcriptional corepressor1(RB1) deletion in childhood B-ALL, when present alone or along with IKAROS family zinc finger1 (IKZF1) deletion.
Methods: The pediatric B-ALL cases were analyzed for RB1 and IKZF1 deletions using multiplex ligation-dependent probe amplification(MLPA).
Results: There were 357 pediatric B-ALL patients with a median age of 7 years(1-18). This included 320 BCR-ABL1 negative and 37 BCR-ABL1 positive patients. Overall, 33/357(9.2%) patients had RB1 deletions (RB1del); 30/320(9.4%) BCR-ABL1 negative and 3/37(8.1%) BCR-ABL1 positive. The IKZF1 deletions (IKZF1del) were present in 70(19.6%) patients. The concomitant RB1 and IKZF1 deletions (RB1del/IKZF1del) were present in 11(3.1%) cases. RB1 deletions alone in absence of IKZF1 deletions (RB1del/IKZF1wt) were seen in 22 cases. Their comparison was done with 59 cases with IKZF1 deletions alone with no RB1 deletion (RB1wt/IKZF1del) and cases without any RB1 or IKZF deletions (RB1wt/IKZF1wt). The post-induction remission rate (55.6%;p=0.052) was worst in the group with both RB1 and IKZF1 deletion (RB1del/IKZF1del) compared with 81.8% in RB1del/IKZF1wt, 78.7% in RB1wt/IKZF1del & 86.6% in RB1wt/IKZF1wt. The median EFS (8.9 months;p=0.0001) and median OS (11.5 months;p=0.007) were least in the RB1del/IKZF1del group compared to RB1del/IKZF1wt (28.5, 41.2 months), RB1wt/IKZF1del (22.6, 30.3 months) and RB1wt/IKZF1wt (48.8 months, median OS not reached) respectively.
Conclusions: RB1 deletions were seen in 9.2% with similar distribution in BCR-ABL1 negative and positive B-ALL subgroups. The concomitant RB1/IKZF1 deletions were seen in 3.1% of B-ALL patients. The patients with concomitant RB1/IKZF1 deletions had much poorer outcomes than cases without any of these deletions or having RB1 deletions or IKZF1 deletions alone. Thus, the presence of RB1 deletions and IKZF1 deletions, particularly if present together, can be used as a predictive marker for poor outcome in B-ALL.

EP036 / #1220

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

ANALYSIS OF PHARMACOGENETIC INDICATORS OF METHOTREXATE HEPATOTOXICITY DURING TREATMENT ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN

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Background and Aims: Acute lymphoblastic leukemia (ALL) in children is a potentially curable disease, but patients still suffer adverse drug reactions that sometimes require dose reduction or discontinuation of cytostatics and contribute to a decrease in overall therapy effectiveness. One of the main drug used in ALL therapy protocols is methotrexate, which treatment is complicated by the development of hepatotoxicity (HT). HT can be caused by various genetic polymorphisms as seen with ABCB1 and SLCO1B1. In this study, we examined the relationship of single nucleotide polymorphisms (SNPs) of the SLCO1B1 (T521C rs4149056) and ABCB1 (rs4148738 C>T, rs2032582, rs1128503, C3435T rs1045642) genes with the development of clinically relevant HT in children treated with high-dosed (>1g/m2) methotrexate. Aim. To evaluate the association of pharmacogenetics (PG) indexes with HT of methotrexate during ALL therapy.
Methods: 67 children with ALL who received methotrexate therapy with ALL IC-BFM 2009 protocol were enrolled the study. To assess the side effects, the patients were evaluated using laboratory methods and NCI toxicity scales (CTCAE v5.0 2018). We used a real-time PCR method to study gene's SNP. The material was a peripheral blood. Material was sampled once, irrespective of the duration of methotrexate therapy.
Results: Mean age of the patients was 7.56±4.8. The HT stage 1-2st. was in 44.8%, 3-4st. - 55.2%. Toxicity was assessed in the postcytostatic period, the relationship with polymorphisms of these genes was assessed using contingency tables, as follows: Pearson's χ^2 for ABCB1C 3435T rs1045642 and GT was 6.7, p-value 0.347, for ABCB1 rs2032582 – 9.206, p-value: 0.162, for ABCB1 rs1128503 – 6.692, p-value 0.669, ABCB1 rs4148738 – 7.582, p-value 0.577, for SLCO1B1 T521C rs4149056 – 5.919, p-value 0.432. Thus, the compared signs were statistically unsignificant.
Conclusions: Determination of polymorphisms of genes providing cytostatic transport and metabolism, PGx aspects of toxicity, is a promising and dynamically developing area of clinical oncology.

EP037 / #996

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

PATTERNS AND OUTCOMES OF ACUTE CENTRAL NERVOUS SYSTEM COMPLICATIONS DURING TREATMENT OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA, NATIONAL CANCER INSTITUTE-CAIRO UNIVERSITY EXPERIENCE

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Background and Aims: Central nervous system (CNS) complications are heterogeneous, varying from very mild and transient symptoms to extremely severe and debilitating or even lethal syndromes.The study aimed to assess the incidence, risk factors, patterns, and outcomes of different CNS complications during treatment of pediatric acute lymphoblastic leukemia (ALL)
Methods: A retrospective study included 390 patients with ALL, treated according to St. Jude total XV protocol at National Cancer Institute, Cairo University between January 2012 to December 2017. Clinical and radiological findings of all patients, were reviewed and analyzed.
Results: among the whole study cohort, there were 39(10%)patients diagnosed with different types of CNS complications.Cerebrovascular Events were the most frequent, diagnosed in 19 (4.9%) patients, 12(3.1%)patients diagnosed with posterior reversible encephalopathy syndrome (PRES), and 6 (1.5%) patients diagnosed with leukoencephalopathy, Both CNS infections and leukemic infiltrates were diagnosed in one patient each. The incidence of CNS complications was significantly higher in patients older than 10 years old(P value 0.04), those with initial high-risk disease, and in patients who were classified as CNS III status Most of patients (79.5%) with CNS achieved complete recovery, while 6(15.4%) patients died, and 2(5.1%) patients developed residual neurological deficits. Regarding the onset of CNS complications, there were 15 (38.4%) patients who had complications during the induction of remission phase of treatment, 12 (30.8%) patients had complications during the early maintenance phase of treatment, 9 (23.1%) patients had complications during the late maintenance phase of treatment, and 3 (7.7%) patients had complications during the consolidation phase of treatment
Conclusions: Patients with older age at presentation,high-risk disease,and initial CNS III status were at higher risk of developing acute CNS complications during treatment of childhood ALL. Despite of high recovery rate in patients with CNS complications, still 15% of them died that warranted prompt intervention.

EP038 / #1703

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

CLINICAL AND MANAGEMENT OF PATIENTS WITH CAR-T THERAPY IN A TERTIARY PEDIATRIC HOSPITAL

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Background and Aims: Chimeric antigen receptor (CAR) T-cell therapy is a novel treatment for children with relapsed or refractory acute lymphoblastic B leukemia. Although complete remission rates are high, it involves serious health risks. The most frequent complications are cytokine release syndrome (CRS) and neurotoxicity. Almost 30-50% of pediatric patients require intensive treatment and close monitoring in pediatric intensive care units (PICU). The aim of this study is to describe CAR-T patients' clinical characteristics and follow up in a Tertiary Pediatric Hospital.
Methods: Retrospective study including CAR-T infusions between January 2020 and March 2022. Epidemiological and clinical data were collected.
Results: Ten patients received CART therapy. The median age was 8.8 years (1.25-20.8). There were nine cases of bone marrow relapse and one combined relapse. Two primary refractory leukemias, four refractory relapses and four second leukemia relapses. 100% of second relapses were after hematopoietic stem cell transplantation (HSCT). The median time to relapse after HSCT was 13 months (12-17) and the median minimal residual disease prior to infusion was 23.6% (0.46-76.7%). Seven patients developed CRS, 57% grade 3 or more. Three patients developed neurotoxicity, 66% grade 3 or more. Seven cases (70%) required PICU admission, two of them only for monitoring. Hemofiltration was necessary in three cases. Five cases required corticoisteroids, six Tocilizumab, four Siltuximab and two Anakinra. Four patients relapsed after infusion (100% CD19-) and two lost B-cell aplasia during the next months. 100% suffered from hypogammaglobulinemia. One patient died by fulminant CRS and three due to progression. Nine patients achieved complete remission (CR). At the moment six patients are alive with CR. The median of follow up is 10 months (7-20).
Conclusions: In patients with relapse or refractory ALL, CAR-T cell therapy has achieved lasting remission. These patients often need PICU admission and monoclonal antibody treatment due to its side effects and complications.

EP039 / #610

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

TREATMENT OUTCOME IN PEDIATRIC ACUTE LEUKEMIA WITH HYPERLEUKOCYTOSIS AT HOSPITAL INFANTIL DE MÉXICO FEDERICO GÓMEZ.

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Background and Aims: Hyperleukocytosis caused by acute leukemia (AL) is associated with early morbidity and mortality due to hyperviscosity arising from the excessive number of leukocytes. This study was designed to assess the incidence of hyperleukocytosis, survival outcomes, and adverse features among pediatric AL patients with hyperleukocytosis.
Methods: Between January 2018 and December 2020, 52 children with previously untreated AL and hyperleukocytosis were enrolled at the Hospital Infantil de México Federico Gòmez The medical charts of these patients were retrospectively reviewed.
Results: Of the 52 children with AL 35 had initial leukocyte counts of >100×10(9)/L, and 9 patients had a leukocyte count of >250×10(9)/L. and 8 with leukocite count of > 400 x 10(9)/L. Eighty-eight had acute lymphoblastic leukemia and twelve acute myeloid leukemia. Thirty-one were females (59.6%) . Three had SNC3 status at diagnosis , 9 were unclassified. Common early complications during induction therapy included tumor lysis syndrome (63.5%) renal dysfunction (28.8%) , respiratory distress (28.8%) and central nervous system hemorrhage (5.8%). Infectious were presents in 36.5% of the cases. All patients were treated with hyperhidration, urinary alcalinization , blood transfusions , antibiotics if they required. Eighteen(34.6%) were treated with leukapheresis and 11 required hemodyalisis. Twelve patient died , 6 in the group of leukapheresis. The reduction of leukocite counts were observed in 15 patient, in three there was no reduction. In the group on acute lymphoblastic leukemia 37 were responders to prednisone. The complete remission (CR) rate for the pediatric AL patients with hyperleukocytosis was 86% . The estimated 3-year overall survival of AL children with hyperleukocytosis was 64.3% However in the group of patients with leukapheresis the overall survival was 49.6%. and 69% in patients without leukapheresis.
Conclusions: The optimal management hyperleukocytosis is still uncertain, and there are no randomized studies demonstrating one is superior to each other.

EP040 / #562

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

TREATMENT OUTCOME FOR ESCALATING INTRAVENOUS METHOTREXATE IN CHILDREN WITH STANDARD-RISK ACUTE LYMPHOBLASTIC LEUKEMIA: A SINGLE-CENTER ANALYSIS

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Background and Aims: Recently, survival rate have significantly improved for children with ALL, with 5-year survival rates over 90%, especially in standard risk (SR) group. This report analyzed the outcome of children treated on escalating IV methotrexate (MTX) without leucovorin rescue during the 2 cycle of interim maintenance (IM) phases, compared with existing standard IM regimen.
Methods: From January 2010 to December 2020, patients diagnosed and treated for SR ALL at Pusan National University Children's Hospital were included. Patients diagnosed before September 2015 were treated with standard IM regimen and defined as group 1, and all subsequent diagnosed patients were treated with escalating IV MTX and defined as group 2. The results was analyzed in these two groups.
Results: Total 100 standard-risk ALL patients were diagnosed. Among 100 patients, 42 patients were included in group 1, and the remaining 52 were included in group 2. At the time of initial diagnosis, none of the patients had CNS involvement, and there was only one patient in group 2 who relapsed with CNS. One patient died in each of the two groups, and the cause of death was septic shock during neutropenic state. The 5-year event-free survival (EFS) was 88.1±5.0% and 91.9±4.6% (p=0.336) in group 1 and group 2, respectively. The 5-year overall survival (OS) was 95.2±3.3% and 95.7±4.3% (p=0.593) in group 1 and group 2, and there were no statistically significant. Comparing the toxicity, the rate of hospitalization due to delayed chemotherapy or neutropenic fever was higher in group 1, but it wasn't statistically significant. Although the rate of hepatotoxicity was high in the 2 group, it didn't require hospitalization, and other toxicities were favorable, resulting in a relatively low hospitalization rate.
Conclusions: In our study, escalating IV MTX without leucovorin rescue during the IM phases didn't improved EFS compared with standard IM regimen with oral MTX.

EP041 / #679

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

INDUCTION FAILURE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN JAPAN: CCLSG/KYCCSG/JACLS/TCCSG JOINT STUDY.

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Background and Aims: Reports from the Western countries showed subjects who failed to achieve complete remission after induction chemotherapy ('induction failure' [IF]) survived poorly even in the modern era. The characteristics and prognosis of subjects who experienced IF have not been poorly understood in Japan.
Methods: The clinical data of patients, who were enrolled in CCLSG ALL2000, CCLSG ALL2004, KYCCSG ALL96, KYCCSG ALL02, JACLS ALL 97, JACLS ALL-02, TCCSG L99-15, or TCCSG L04-16 (during the period from 1996 to 2009) and failed to achieve remission after one course of induction therapy, were retrospectively collected and analyzed.
Results: Eighty-nine patients with IF (1.8%) were identified among 4,956 participants. The 5-year overall survival (5y-OS) was 43.0% +/- 5.5% (95%CI: 32.0%-53.4%). No difference was found in the survival rates between patients with B-ALL and T-ALL. In the B-ALL cohort (n=64), 5y-OS was significantly higher in NCI-SR Patients than NCI-HR patients (p=0.031). In the T-ALL cohort (n=25), 5y-OS was significantly lower in patients with CNS-3 than those without (p=0.017). Due to limited data availability, we were unable to analyze the effect of re-induction chemotherapy on survival. We found no survival benefit in the use of allogeneic SCT.
Conclusions: The IF rate in the current study seems comparable to that observed in the Ponte di Legno international collaborative study (2.4% among 44,017 patients; NEJM 2012). The 5y-OS in the current study was also comparable to that reported by the Ponte di Legno group study (5y-OS 32% +/- 1%).

EP042 / #1134

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

WEIGHT VARIABILITY IN A PEDIATRIC POPULATION DURING TREATMENT OF ACUTE LYMPHOBLASTIC LEUKEMIA WITH A GRADUATED INTENSITY PROTOCOL FOR LOW-INCOME COUNTRIES

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Background and Aims: Obesity is a well-documented problem associated with childhood acute lymphoblastic leukemia (ALL) with increasing body mass index often observed during therapy, and it can diminish the quality of life of survivors. Our objective was to describe the weight variability during treatment of ALL patients, and to identify which subgroups were affected by overweight and obesity at the end of therapy.
Methods: Records of pediatric patients between the ages of 2 and 15 years with ALL between 2011 and 2015 at the Hospital Universitario in Monterrey, Mexico were reviewed. We evaluated weight, and height at each treatment phase, and from the beginning of follow-up until the last visit to the clinic. Patients were classified in four groups using BMI z-score adjusted by age and sex using WHO tables.
Results: Of the remaining 80 patients, median age was 5 (2-15) years, of which 45(56%) were male, and 35(44%) were female. At diagnosis 45(56%) had high-risk disease, and 36(44%) where low risk. Median follow up in months was 74.5 (1-121). BMI z-score increased from induction to consolidation (mean= 0.34 ± 0.1, $p< 0.001$), from consolidation to intermediate maintenance (mean= 0.32 ± 0.07, $p<0.0001$), and from intensification to the first year after diagnosis (mean=0.23 ± 0.1, $p=0.03$). BMI increased from diagnosis to follow-up (mean=0.81± 0.19, $p<0.0001$) In a subgroup of 52 (65%) survivor patients, we analyzed the BMI Z-score changes over the course of treatment for the main risk factors related with obesity (sex, age, and ALL risk at diagnosis), in which no significant differences were found. However, a positive correlation was found between the first and last Z-score means. ($r= 0.567$, $p<0.0001$).
Conclusions: Ideally ALL survivors should be healthy children by the end of treatment, it is important that we focus in the prevention of overweight and obesity of these patients from the diagnosis of disease.

EP043 / #349

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

ASSESSMENT OF DISSEMINATED INTRAVASCULAR COAGULATION IN CHILDREN DURING WITH ACUTE LYMPHOBLASTIC LEUKAEMIA DURING INDUCTION CHEMOTHERAPY IN A TERTIARY CARE HOSPITAL IN BANGLADESH

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Background and Aims: The overall cure rate for childhood acute lymphoblastic leukemia has improved from virtually zero to the current event-free survival rate (EFS) of more than 90%. Disseminated intravascular coagulation is the commonest hemostatic abnormality in patients with acute lymphoblastic leukemia. It might cause serious hemorrhagic complications and warrants proper medical attention in due time. Aim of the study was to detect the frequency, identify the risk factors and outcome of disseminated intravascular coagulation in children with acute lymphoblastic leukemia during induction chemotherapy.
Methods: This prospective observational study was carried out in 55 diagnosed cases of ALL children in the department of pediatric hematology and oncology, Bangabandhu Sheikh Mujib Medical University, Bangladesh from November 2020 to October 2021. Patients were kept on follow-up with risk-directed UKALL 2003 regimen.DIC was detected by using the International Society of Thrombosis and Haemostasis scoring system by using Prothrombin time, Platelet count, S. fibrinogen, and D-dimer at baseline, on day 7, 14, and 21. Statistical analysis was obtained by using SPSS-version 22.
Results: Out of 55 patients, DIC was encountered in 12 (21.8%) patients. At diagnosis, DIC was found in 8 patients (14.54%), on day 7, DIC was found in 4 patients (8%).A total of 8(14.54%) patients have developed DIC at diagnosis, among them 4(50%) had persisted DIC after starting chemotherapy and 4 patients resolved. But, 4 patients (8.5%) newly developed DIC during hospitalization (p=0.001) on day 7. The use of Daunorubicin had 6.252 times significantly increased risk to developed DIC. Patients with DIC had more bleeding 10(83.3%) than the non-DIC group 20(46.6%). The mortality rate was higher,3(25.0%) in the DIC group and 6(14.0%) in the non-DIC group.
Conclusions: The frequency of DIC was 21.8% during the induction period, use of daunorubicin was identified as the risk factor for the development of DIC. Mortality was higher in patients with DIC.

EP044 / #1163

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

OUTCOMES OF CHILDREN WITH RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA- EXPERIENCE FROM INDIA

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Background and Aims: Paediatric Acute Lymphoblastic Leukemia(ALL) is highly curable with the current treatment, but about 15%patients relapse after an initial response. The published 5year OS ranges between 36- 50% after first relapse. These figures are further affected in developing countries where treatment cost, infections and abandonment are major hindrances to successful outcomes. Data from developing world is meagre. We aim to discuss the outcomes of children with relapsed-ALL.
Methods: Medical records of children diagnosed as first relapse of ALL between October2016 and December2021 were retrospectively analysed for outcomes. Patients were risk-stratified and initiated on treatment as per BFM-REZ-2002. Treatment was modified based on patients' condition and response to therapy. Targeted therapy aided remission achievement in 7patients. Category S3, S4 and MRD>0.1% by Flowcytometry post F1+F2 were considered indications for HSCT.
Results: We managed 23patients of first relapse of ALL, with median age 9years(range:3-16years)(Males-18, Females-5). ALL Phenotype: precursor-B-cell-19/23, T-cell-4/23. Original disease treatment comprised of BFM-95protocol-15patients, ICICLE-3patients, others-5patients. Median time to relapse-20months from initial diagnosis(range:8-57months). Relapse site: Isolated bone-marrow-13patients, isolated extra-medullary-4, combined-6patients. Extramedullary sites:CNS -7, testis-2, one each in bone and mediastinal-mass. Patient risk-stratification upon relapse:S1group-2patients, S2group-9, S3group-4 and S4group-8patients. Sixteen patients were considered for HSCT. Four of twenty-three didn't achieve CR2. Nineteen patients achieved CR2, of which 12underwent HSCT(4-Matched-sibling, 8-Haploidentical) and 7were managed with only chemotherapy-radiotherapy. Of these, 7/19 relapsed after CR2. Follow-up ranged from 12-1992days. On last follow-up, the OS and EFS of the cohort is 47% and 39% respectively. Mortality: refractory disease -6patients and treatment related mortality-6patients(sepsis-5, arrythmia-1). Analyzing the outcomes of sub-groups, the OS and EFS: S1group-100% and 50%, S2group-66% and 55%, S3group-50% and 50%, S4group-12.5% and 12.5%. Amongst those who underwent HSCT in CR2 the OS and EFS was 41.6% each.
Conclusions: Treatment of relapsed-ALL is possible and should be pursued. HSCT is a good treatment option for high-risk patients.

EP045 / #636

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

LOST TO FOLLOW-UP DURING TREATMENT OF ALL IN LMIC SINGLE CENTER EXPERIENCE IN YOGYAKARTA, INDONESIA

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Background and Aims: Lost to follow up (LOFU), defined as no contacts after cessation of maintenance treatment is one of the obstacles to evaluate the effectiveness of ALL - protocols. In the low- and middle-income countries (LMIC), there is still inequality to access health facilities or communication services. We would like to describe the feasible way to contact the LOFU patients.
Methods: Data were obtained from 362 patients diagnosed with ALL from February 2013 until November 2018 who were treated for 2 years using ALL-Protocols 2013 and 2016 in Sardjito General Hospital, Yogyakarta, Indonesia, a LMIC. All LOFU patients who had not visited the clinic for more than 6 months between January - June 2021 were contacted by short message, mobile phone call, or letters to the parents or to the local Health Centers if no response was obtained.
Results: A total of 182 patients were off therapy. The median time from diagnosis was 4 years. There were 111/182 (61%) LOFU patients. Among them, 93/111 (83.8%) were successfully contacted, 68/111 (61.3%) by short message and mobile phone call, 25/111 (22.5%) via letter, and no response was obtained from 18/111 (16.2%) patients. Of the 93 patients, 85 (91.4%) were alive and 8 (8.6%) died. Two patients had sequelae after chemotherapy and two patients experienced relapse.
Conclusions: To contact LOFU patients by phone and formal letters was in our situation effective for more than four-fifths of patients. Therefore, simple and cheap methods can be effective to decrease the number of patients lost to follow-up. Long term follow-up is essential to analyze the results of ALL treatments. A LMIC should have special consideration for long term follow-up.

EP046 / #1739

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

PH(+) ALL. EXPERIENCE OF 20 YEARS IN ONE GREEK PEDIATRIC ONCOLOGY DEPARTMENT.

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Background and Aims: Acute lymphoblastic leukemia(ALL) is the most common malignancy in children. There are some subtypes of leukemia associated with specific chromosomal translocations. The identification of these rearrangements is of great prognostic value, and can play a major role in the selection of appropriate anti-leukemic therapy. Ph(+)ALL t(9;22)(q34;q11), was associated with poor prognosis until we included TKIs in therapy.
Methods: All Ph(+)ALL treated in our department from 01.01.2002-31.12.2021 were analyzed. Characteristics, response to therapy and final outcome were studied.
Results: From 01.01.2002-31.12.2021 445 children were treated with ALL.Seven of them(1,57%)were found to be Ph(+).Additional cytogenetic abnormalities were detected in 5/7.Female were 3/7(42,8%).The median age was 5,75 years(3,4 -13,3).Six patients were diagnosed with common B-ALL and 1 with biphenotypic T-ALL+B-ALL.All children were treated with backbone BFM-HR protocols(BFM 95,ALLIC 2009) and TKIs from Day15.Two patients underwent BMT in CR1.At diagnosis median value(MV) of WBC was 17400/ml(3700 to 334200),MV of Hb 10,4gr/dl(5,3 to 12,0)and MV of Plt was 153000/ml(16000 to 225000).All seven on Day8 were PDN good responders.On Day15 BM was M1 to 6/7 and M3 to 1/7.FC-MRD on Day15 was negative in 3/7,<10 in 3/7 and >10 to 1/7.On Day33 5/7 patients had FC-MRD negative whereas 2 boys had MRD 0,01 and 0,4.Six patients on Day33 had quantitative BCR-ABL/ABL negative whereas 1 patient had BCR-ABL/ABL 3,31.Five of them are in CR1 for 0,58y(still under therapy),10,25y,14,08y,16,25y and 18,33y and 2/7 relapsed in 15 and 50 months from diagnosis.One of the relapsed patients underwent BMT and is in CR2 for 7,9y.The second one underwent BMT in CR2 but relapsed 8 months after BMT and died with progression of his disease.
Conclusions: EFS of our patients with Ph(+) ALL is 71,5% and OS is 85,7%.The use of TKIs improved the EFS and the OS in children with Ph(+)ALL and our results are comparable to the ones of the national literature.

EP047 / #417

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

RISK FACTORS FOR THROMBOSIS IN CHILDREN RECEIVING ASPARAGINASE-BASED CHEMOTHERAPY FOR ACUTE LYMPHOBASTIC LEUKEMIA

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Background and Aims: Thrombosis is a known complication of acute lymphoblastic leukemia (ALL) therapy, but there are few strategies for identifying at-risk patients; thus, prophylactic anticoagulation is rarely utilized. The purpose of this study was to identify risk factors for thrombosis during treatment for ALL to identify patients who may benefit most from prophylactic anticoagulation.
Methods: We conducted a retrospective cohort study of all children with newly diagnosed ALL treated at Texas Children's Hospital for the time period 2012-2020. The primary outcome was incident deep venous thrombosis, dural sinus thrombosis, or pulmonary embolism during therapy, identified through electronic query of the medical record followed by manual review of radiology reports. We used multivariable logistic regression to determine odds of thrombosis given demographic, clinical and/or laboratory variables.
Results: We identified 630 patients: 550 (87.3%) with B-ALL, and 80 (12.7%) with T-ALL. Twenty-eight (5.1%) patients with B-ALL and 12 (15.0%) with T-ALL developed thrombosis, most often occurring during Induction (63%) or Consolidation (20%) cycles. In unadjusted analyses, increasing year of life (OR, 1.16; 95%CI, 1.09-1.24), T phenotype (OR, 3.29; 95%CI, 1.55-6.64), d-dimer >20 µg/ml at diagnosis (OR, 6.7; 95%CI, 1.4-25.9), and being overweight at diagnosis (OR, 2.5; 95%CI, 1.3-4.9) were associated with increased odds of thrombosis. The strongest association with thrombosis was observed with peripherally inserted central catheters (PICC) (OR, 6.0; 95%CI, 3.0-12.4). On adjusted analysis, T phenotype (OR, 3.9; 95%CI, 1.2-12.1), use of PICC lines (OR, 4.1; 95%CI, 1.4-13.8), being overweight (OR, 3.3; 95%CI, 1.1-10.8), and diagnostic d-dimer ≥20 µg/ml (OR, 8.9; 95%CI, 1.4-46.8) were independently associated with thrombosis risk.
Conclusions: Thrombosis during ALL therapy occurs most often early in therapy among patients with easily identifiable risk factors. These findings merit validation, and they identify a population in whom intervention with prophylactic anticoagulation may be most beneficial.

EP048 / #1431

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

SYNERGY OF VENETOCLAX AND DUAL MTOR/PI3K INHIBITION IN BCP-ALL

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Background and Aims: Deregulation of cell death is a hallmark of many cancers contributing to leukemogenesis and treatment failure in B-cell precursor acute lymphoblastic leukemia (BCP-ALL). We previously showed that deficient apoptosis signaling is an indicator for poor outcome in ALL. Cell death induction is counter-regulated by anti-apoptotic molecules like BCL-2 and MCL-1 and selective inhibition of BCL-2 by venetoclax showed clinical activity in CLL and promising results in preclinical and first clinical studies in ALL. Previously, we identified that hyperactivation of the mammalian target of rapamycin (mTOR) signaling pathway in ALL cells is associated with inferior relapse-free survival. Here, we evaluated anti-leukemia activities of BCL-2 (venetoclax) and mTOR/PI3K pathway (NVP-BEZ-235) inhibition in BCP-ALL and analyzed the interplay of both inhibitors.
Methods: Half maximal effective concentrations (EC_{50}) were assessed in BCP-ALL cell lines (N=8) and patient-derived xenograft (PDX) samples (N=10). Protein expression was assessed by immunoblotting. Synergies were analyzed in dose-response matrices (Bliss synergy model).
Results: We analyzed sensitivities of BCL-2 inhibition in BCP-ALL samples. Interestingly, we identified high expression of anti-apoptotic MCL-1 in venetoclax insensitive ALL cell line and PDX samples pointing to MCL-1 as a mediator of venetoclax insensitivity. Exposure of ALL cells to NVP-BEZ235 resulted in decreased phosphorylation of the downstream targets S6 and 4E-BP1, reduced cellular proliferation and downregulated MCL-1 protein expression. 4E-BP1 has been described as translational regulator of MCL-1 and mTOR inhibition associated MCL-1 downregulation might prime venetoclax insensitive ALL to cell death induction by BCL-2 inhibition. Interestingly, co-treatment with venetoclax and NVP-BEZ-235 synergistically reduced cellular proliferation and induced cell death (max. Bliss scores >40) in cell line and PDX-ALL samples including apoptosis deficient, venetoclax-insensitive, poor outcome ALL.
Conclusions: Taken together, we show anti-leukemia activity of simultaneous PI3K/mTOR and BCL-2 inhibition priming apoptosis deficient, venetoclax insensitive BCP-ALL samples to synergistic cell death induction along with downregulation of anti-apoptotic MCL-1.

EP049 / #1644

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

SYNERGISTIC AND ON-TARGET ACTIVITY OF DUAL BCL-2/BCL-XL INHIBITION TOGETHER WITH INHIBITION OF MCL-1

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Background and Aims: Targeting the intrinsic apoptosis pathway has become a promising treatment approach in acute lymphoblastic leukemia (ALL). Selective BCL-2 inhibition (venetoclax) has shown heterogeneous activity in ALL and other apoptosis regulators like MCL-1 and BCL-XL promote insensitivity. However, targeting BCL-XL resulted in thrombocytopenia. The dual BCL-2/BCL-XL inhibitor AZD4320 and its drug conjugate AZD0466 demonstrated anti-tumor activity in hematological cancers, but only transient thrombocytopenia. Here, anti-leukemia activities of combined BCL-2/BCL-XL and MCL-1 inhibition (AZD5991) were analyzed and compared to other BH3-mimetics investigating on-target activities and combination effects.
Methods: Half maximal effective concentrations (EC_{50}) were assessed in seven B-cell precursor ALL cell lines and 19 patient-derived xenograft (PDX) samples. Protein expression and complexes were assessed by immunoprecipitation and immunoblotting. BH3-profiling was performed to determine dependencies on BCL-2 family proteins. Combination effects were analyzed by dose-response matrix analyses.
Results: First, we determined activities of dual BCL-2/BCL-XL (AZD4320), BCL-2 (venetoclax), BCL-XL (A-1331852) and MCL-1 (AZD5991, S63845) inhibition. Sensitivity to dual BCL-2/BCL-XL inhibition correlated significantly with BCL-2 (N=19; r_s=0.63; p=0.004) but not BCL-XL inhibition, and sensitivities to both MCL-1 inhibitors also correlated (N=19; r_s=0.66; p=0.002). Interestingly, highest sensitivities (lowest EC_{50} values) were found for dual BCL-2/BCL-XL inhibition (p<0.001). Mechanistically, analysis of protein complexes showed disrupted binding of the apoptosis executor BIM to BCL-2 and BCL-XL upon BCL-2/BCL-XL inhibitor exposure, while BIM-binding to MCL-1 was reduced upon MCL-1 inhibition, demonstrating on-target activity of both drugs. Functionally (BH3-profiling), BCL-2/BCL-XL inhibition induced increased MCL-1-dependence, while inhibition of MCL-1 resulted in a shift towards dependence on BCL-2 and BCL-XL, indicating mutual binding/dependence and potential effectivity of concomitant inhibition. Importantly, combining BCL-2/BCL-XL and MCL-1 inhibitors resulted in synergistic activity (mean Bliss synergy score of +8.77; N=5).
Conclusions: In summary, we identified sensitivity, on-target and synergistic activity of the dual BCL-2/BCL-XL inhibitor AZD4320 together with inhibition of MCL-1.

EP050 / #1012

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

THE TETRASPANIN CD9 SHAPES GLUCOCORTICOID SENSITIVITY IN PEDIATRIC B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: Resistance to glucocorticoids (GCs) confronts therapeutic success in B-cell precursor acute lymphoblastic leukemia (BCP-ALL). Identification of predictive biomarkers and mechanisms underlying GC resistance is of scientific/clinical importance. This study aims to demonstrate the association between CD9 and GC susceptibility and uncover its mechanisms driving resistance.
Methods: BCP-ALL cell lines (n=6) and primary lymphoblasts (n=18) with differential CD9 expression were profiled for their sensitivity to prednisolone (Pred) and dexamethasone (Dex). Association of CD9 with patient responses to Pred prophase was investigated in a pediatric BCP-ALL cohort (n=182). Functional impact of CD9 on GC susceptibility was determined by gain- and loss-of-function experiments in BCP-ALL cells, coupled with mechanistic dissection of pathways downstream of GC receptor NR3C1 through genomics, transcriptomics and proteomics.
Results: CD9- and CD9+ cell lines had distinct drug sensitivity profiles, with the former showing resistance to GCs but not other chemotherapeutics. CD9- samples exhibited resistance to Pred (IC50s: 8,185 vs. 268 nM) and Dex (IC50s: 2,761 vs. 31 nM) comparing with CD9+ samples. More poor Pred responders were identified in CD9- than CD9+ patients (19.4% vs. 6.2%, P=0.018). CD9 overexpression in CD9- cells (SEM, KOPN-8) significantly enhanced sensitivity to GCs by 2.8-17.7-fold, whereas CD9 knockout in CD9+ cells (697) decreased GC sensitivity. The expression and cytoplasm-to-nucleus translocation of GC receptor was similar in CD9- and CD9+ cells but CD9 was physically interacted with NR3C1. Upon GC stimulation, the presence of CD9 facilitated DNA binding of NR3C1 and increased the number and magnitude of GC-responsive genes (TSC22D3, ZBTB16). CD9- cells showed constitutive activation of MAPK pathway and were preferentially susceptible to reversal of GC resistance by the MEK1/2 inhibitor trametinib.
Conclusions: CD9 confers GC susceptibility through modulation of GC signaling in childhood BCP-ALL. Patients with CD9- phenotype might be more prone to trametinib therapy for counteracting GC resistance.

EP051 / #1411

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

HEALTH OUTCOMES IN ADULT SURVIVORS OF CHILDHOOD ALL AND THEIR SIBLINGS – A NATIONAL LONG TERM FOLLOW UP

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Background and Aims: The treatment of acute lymphoblastic leukaemia (ALL) has improved and resulted in increased survival and reduction in late effects. However, health outcomes of survivors can be affected later in life. An increased understanding of health outcomes is therefore important to be able to provide promotional and supportive resources. The aim of this study is to investigate health outcomes in adult survivors of childhood ALL (ASCALL) and their siblings.
Methods: A national cross-sectional study including ASCALL, diagnosed between 1985 and 2007, registered in the Swedish Childhood Cancer Registry. 440 (51%) out of 860 ASCALL and 135 siblings responded to a questionnaire. T-test and chi square test were used to compare groups regarding HRQL (SF-36) health related factors including sleep quality/quantity, stress, anxiety and depression (DASS 21), several dimensions of fatigue (MFI 20), prevalence of chronic pain, diabetes, cardiovascular disease, headache/migraine, rheumatism, and workability (WAI).
Results: The mean age of the ASCALL and their siblings was 30.9y (19y -49y) and 32.5y (18y-54y) respectively. 49% of ASCALL and 62% of the siblings were female. Time since diagnose was 24.1 y (13y-36y). ASCALL had significantly lower sleep quality (22% poor sleepers vs 10% p=0.01), quantity (p=0.049), and mean workability (8.17 vs 8.66, p=0.032), higher scorings on fatigue (physical fatigue (12.09 vs 9.41, p=<0.001), reduced motivation (12.07 vs 8.21, p<0.001), and reduced activity (12.85 vs 9.90, p=<0.001)) than the siblings. No significant differences between the groups on BMI, chronic pain, depression, anxiety,stress, prevalence of diabetes, cardiovascular disease, or rheumatism. The ASCALL scored significantly worse on the general health domain (SF-36) (64.9 vs 72.3, p=0.002).
Conclusions: Adult survivors of childhood ALL report more fatigue, more sleeping problems, poorer general health and poorer workability compared to a group of siblings. The differences indicate that adult ALL survivors may be more vulnerable to poor health later in life.

EP052 / #1081

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

OUTCOME OF IMMUNOTHERAPY WITH BLINATUMOMAB AND DONOR LYMPHOCYTE INFUSIONS IN PEDIATRIC R/R B-ALL AFTER ALLO-HSCT

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Background and Aims: Patients with relapsed/refractory (R/R) acute B - lymphoblastic leukemia (B-ALL) following allogeneic hematopoietic stem cell transplantation (allo-HSCT) have a poor prognosis. Blinatumomab is effective salvage option for R/R patients after allo-HSCT, however relapses still occur in most patients. We suppose, that adding infusions of donor lymphocyte (DLI) to blinatumomab may improve immunoadoptive pressure on leukemic cells. We evaluated overall survival (OS), incidence of responses and graft-versus-host-disease (GVHD) in R/R B-ALL children, who were treated with combination immunotherapy blinatumomab and DLI after allo-HSCT.
Methods: The data of 15 children with the median age 10 (0-18) years, who underwent immunotherapy with blinatumomab and DLI after allo-HSCT, were analyzed. Allo-HSCT was performed in complete remission (CR) in 5 (33%), MRD+ in 2 (13%)., relapse – in 8 (53%) pts. Haploidentical donor was in 11 (73%) pts. Myeloablative conditioning was used in 9 (60 %) pts. All pts received cyclophosphomyde on day +3, +4. Indication for therapy was MRD+ in 6 (40%), relapse - in 9 (60%) pts. Blinatumomab was administrated after prior chemotherapy in 5 (33%) relapsed pts. The first dose of DLI (median $=1*10^6$ CD3+/kg) was administrated during the first course blinatumomab in 12 (80%) pts. Six pts (40%) received 2-3 courses of therapy.
Results: At the median follow up 10 months OS is 73%. CR was achieved in 12 (80%) children, the median duration of remission was 7 months (1-52, months). Bone marrow relapse occurred in 5/12 (40%). Grade III acute GVHD was reported in 2 pts, classic chronic GVHD – in 2 (mild and severe), moderate overlape syndrome – in 1 child. All cases of death were associated with relapses of leukemia.
Conclusions: Combination of blinatumomab and DLI may induce durable remission in patients with R/R B-ALL. This immunotherapy is safe even in children after haplo-HSCT. Further experiences are necessary for finally outcomes.

EP053 / #1176

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

VITAMIN D LEVELS AND METABOLIC SYNDROME AT DIAGNOSIS IN CHILDHOOD LYMPHOBLASTIC LEUKEMIA

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Background and Aims: Vitamin D is associated with alterations in bone metabolism, immunity, and metabolic syndrome (MS). It has been described those children with acute lymphoblastic leukemia (ALL) and low vitamin D values at diagnosis are associated with lower survival. The study aimed to determine the prevalence of low levels of Vitamin D and risk factors associated with MS in ALL.
Methods: Descriptive and prospective study including patients was conducted between 2017- 2022. Patients were evaluated from November 2017 to March 2022. Vitamin D levels, waist circumference, arterial pressure (AP), triglycerides, HDL-cholesterol, and glucose levels were recorded at study entry. Vitamin D deficiency was defined as a serum < 20 ng/mL, insufficiency was 20–30 ng/mL, and sufficiency >30 ng/mL. Cook's criteria for < 10 years old and 10 or more years old International Diabetes Federation's criteria were used to diagnose MS. This study was Approval by Ethical Committee. The chi-square test was used to analyze the relationship between the variables.
Results: Fifty-eight patients were enrolled, and 11 of them were excluded. Finally, 47 were studied. The median age at the time of diagnosis was 7,58 years, and the median time of follow-up post-diagnosis was 22 months. Twenty-seven patients were males. Vitamin D levels were deficient at 55%, insufficient at 28%, and sufficient at 17% of patients. Twenty-six percent had MS at diagnosis. There were no differences in the incidence of metabolic syndrome between patients with sufficient vitamin D levels and those with deficient or insufficient levels. All relapsed patients (N=7) and one patient died from COVID infection in remission. All patients have low levels of vitamin D (insufficient =1 and deficient=7).
Conclusions: It is essential to study vitamin D at the time of diagnosis, supplement with vitamin D throughout treatment and periodically assess vitamin D levels.

EP054 / #860

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

COVID-19 MRNA VACCINATION APPEARS SAFE IN PEDIATRIC PATIENTS WITH A HYPERSENSITIVITY REACTION TO PEGYLATED ESCHERICHIA COLI L-ASPARAGINASE

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Background and Aims: L-Asparaginase is an established component of acute leukemia therapy. PEG-Asparaginase (PEGAsp), Escherichia coli L-asparaginase linked to polyethylene glycol (PEG) is the common first-line formulation, however, hypersensitivity reactions to PEGAsp occur in 10-15% of patients, with PEG component suggested as the antigenic culprit. As current mRNA COVID-19 vaccines contain PEG, albeit of different molecular weight, the safety of administration of these vaccines to leukemia patients with prior PEGAsp hypersensitivity has been questioned. The purpose of this case series is to describe a single institution’s experience administering the COVID-19 vaccination to patients with PEGAsp allergy.
Methods: We performed a retrospective chart review of pediatric patients with PEGAsp hypersensitivity who received COVID-19 mRNA vaccination at the Children’s Hospital of Philadelphia (CHOP). Chart abstraction was performed to determine the occurrence and grading of hypersensitivity reactions to PEGAsp and adverse events associated with COVID-19 mRNA vaccination.
Results: Forty patients with PEGAsp allergy (grade 2: n=12; grade 3: n=9; grade 4: n=4) received COVID-19 vaccination at a median of 54.4 months (range 2-154 months) after documented hypersensitivity. Of those, 33 (82.5%) had been challenged with an alternative form of Asparaginase and 30/33 (91%) had not experienced hypersensitivity with an alternative formulation, suggesting PEG as the hypersensitivity trigger for the majority. All patients received both doses of the vaccine, and no patients experienced any allergic or anaphylactic symptoms from the vaccination.
Conclusions: Based on our institutional experience, COVID-19 mRNA vaccination appears to be safe in patients with PEGAsp allergy despite the presence of PEG in the vaccine. The specific molecular weight of PEG may play a critical role in triggering a reaction. As efforts are underway to vaccinate all eligible patients to COVID-19 for individual protection and herd immunity, these data suggest that patients with PEGAsp allergy should be included.

EP055 / #1126

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

PREDICTORS OF PRE-MAINTENANCE DELAYS DURING THERAPY AND ASSOCIATIONS WITH OUTCOME AMONG CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA: A POPULATION-BASED STUDY.

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Background and Aims: Therapy delays occur in children with acute lymphoblastic leukemia (ALL), causing stress among caregivers. Limited data exists on whether prolonged delays lead to inferior outcomes.
Methods: Children <18 years at diagnosis of ALL were identified at pediatric centers in Ontario, Canada between 2002-2012, treated according to Children's Oncology Group protocols for standard- or high-risk ALL. Abstractors obtained demographic, disease, treatment, and outcome-related data, including dates of therapy phases. Phase-specific delays were calculated by comparing actual duration to that expected by protocol. Pre-Maintenance phase-specific delays were summed to obtain "total delay" at the time of Maintenance. Predictors of prolonged delay (>/=75th percentile) were determined through logistic regression. The association between prolonged delay and event-free and overall survival (EFS, OS from start of Maintenance) was adjusted for demographic and disease factors.
Results: Among 489 patients, the longest delays were associated with Intensified Consolidation [median 14 days, interquartile range (IQR) 7-23] and Intensified Delayed Intensification (14 days, IQR 8-21). Among 477 (97.5%) children reaching Maintenance therapy, median total delay was 29 days (IQR 13-50), higher among those receiving high-risk therapy (49, IQR 34-61) vs. standard-risk therapy (16, IQR 8-29). In multivariable analysis, predictors of prolonged delay (>50 days) included high-risk ALL and positive end Induction minimal residual disease. Prolonged delay was not associated with inferior EFS [hazard ratio (HR) 1.4, 95th confidence interval (95CI) 0.7-2.7; p = 0.40] but was with inferior OS (HR 4.8, 95CI 1.3-17.1; p = 0.01). When adjusted for other disease-related variables, the magnitude of association with OS remained similar though statistical significance was lost (HR 4.1, 95th CI 0.9-17.5; p = 0.07).
Conclusions: These results can inform counselling of caregivers of children with ALL on phase specific delays. Prolonged delays may be associated with increased risk of poor outcomes, though validation in larger cohorts is required.

EP056 / #1963

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

HAPLOIDENTICAL HEMATOPOYESIS STEM CELL TRANSPLANTATION FOR RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN TREATED IN URUGUAY

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Background and Aims: The prognosis of relapsed Acute Lymphoblastic Leukemia (ALL) remains por due to resistance to chemotherapy agents. This study evaluate the efficacy and feasibilty of Haploidentical Hematopoietic Cell Transplantation (Haplo HSCT) for pediatric relapsed ALL.
Methods: 40 patients with relapsed ALL, 14 underwent Haplo HSCT between 2010 and 2021 at the Hospital Pereira Rossell (Montevideo-Uruguay. All patients were transplanted in Complete Remission (CR) following different protocols, only 3 had positive MRD(0.1%,0.6%,1.9%). Conditioning regimens employed were TBI based in 11 patients. Graft versus host disease (GVHD) prophylaxis was administered with cyclosporine and methotrexate.
Results: 8 patients received peripheral blood and 6 received bone marrow as the stem cell source. Among 14 patients who achieved engraftment, acute GVHD ocurred in 8 patients. (GI6, GII4,GIII1,GIV 1, skin was the most comon organ involve) and chronic GVHD was observed in 6(GI 2, GII 2, GIII 2,GIV 2 Skin was involve in the mayority of cases and severe cases was because of the Lung). The 5 year overall survival (OS) between al LAL relapsed patients was 32.5% +_7.4% and in patients who underwent and haplo was 33.3% +- 12% , leukemia free survival rates were 16% and 20% respectively.
Conclusions: Haploidentical transplantation is a feasible solution for relapsed leukemia patient in Uruguay with promesing results.

EP057 / #773

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

OUTCOMES OF MSK-NY-II THERAPY IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH PRECURSOR B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: Despite improving cure rates in children with Acute lymphoblastic leukemia (ALL), high risk (HR) ALL poses unique challenges. Intensified therapy has been the standard for augmenting increased early remission and improving long term survival. Treatment with the New York II protocol (MSK-NY-II) intensified chemotherapy regimen was developed to improve efficacy and reduce toxicity. We report here our center's experience treating pediatric and young adult patients with precursor B-cell (pre-B) ALL with MSK-NY-II at Memorial Sloan Kettering Cancer Center (MSKCC).
Methods: We retrospectively analyzed all pediatric and young adult patients from 2000-2016, <30 years of age, with de novo pre-B ALL treated at MSKCC with the MSK-NY-II protocol.
Results: We identified a total of 124 patients. Median starting age was 6.8 years [0.1-29.6] with median initial bone marrow blasts of 61% [1-99]. CNS3 involvement was seen in 3.2% (4/124) of patients and no testicular involvement identified. There were 94.1% (96/102) of evaluable patients who achieved a complete remission (CR) of <5% bone marrow blasts by D29 of Induction. There were 21 patients (16.9%) who received an allogeneic hematopoietic stem cell transplant in CR1. Median time to relapse was 736 days [113-1208] with 15 total relapses (13.1%); 9 medullary, 4 extramedullary, and 2 combined relapses. Overall survival (OS) at 5-years was 88.7%. MSK-NY-II cumulative doxorubicin dose was 300mg/m2. Cardiac dysfunction with abnormal shortening fraction was observed in 1 patient. There were 2 infectious deaths during MSK-NY-II therapy, 1 during Induction and 1 with PJP pneumonia during Maintenance. There was a low total number of inpatient days, median 26.5 days [range 0-157].
Conclusions: The intensive MSK-NY-II protocol for pre-B ALL was tolerated well and outcomes in this large single institution cohort are similar to that of contemporary regimens for pre-B ALL. MSK-NY-II warrants consideration in patients with HR pre-B ALL.

EP058 / #1663

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

LOW FREQUENCY OF T(12;21) B-CELL ACUTE LYMPHOBLASTIC IN COLOMBIA: A REPORT FROM VIGICANCER WORKING GROUP

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Background and Aims: Children with acute lymphoblastic leukemia (ALL) and t(12;21) (ETV6-RUNX fusion) have excellent overall survival. Prevalence in children is approximately 20-25%, however reports suggest prevalence has geographical and ethnic variability. We assessed the prevalence of t(12;21) in children with ALL from Colombia.
Methods: We conducted a cross-sectional study to estimate the prevalence of the t(12;21) in patients with newly diagnosed B-cell ALL (<15 years of age) included in 27 pediatric oncology units (POU) in 10 Colombian cities reporting to VIGICANCER (Childhood Cancer Surveillance System). In Colombia, detection of t(12;21) is performed by fluorescence in situ hybridization (FISH) at several commercial laboratories; however, no centralized validation is carried out.
Results: From January 2019 to December 2021, VIGICANCER included 965 children with ALL (871 B-cell, 80 T-cell; 14 mixed/unclassified). In the B-cell ALL cohort, the median age was 5.5 years (IQR: 3, 10), 52% were male, 9% were afro-descendants and/or native Colombians, and 50% had public insurance. FISH for t(12;21) was performed in 67% of patients and for t(9;22) in 83%. Frequencies for t(12;21) and t(9;22) were 11% (95%CI: 8, 13) and 5% (95%CI:3, 7), respectively. We found an 8% prevalence of t(12;21) in patients with public health insurance vs. 14% in semi-private (P=0.02). There was high heterogeneity in detection among the different POUs, and in two, the prevalence was 20-28%
Conclusions: Prevalence of t(12;21) in B-cell childhood ALL in a sizeable sample of patients in Colombia was lower than reported in other regions. Two POUs achieved the expected prevalence reported in high-income countries. There were differences by insurance, suggesting that the low prevalence in our sample could be related to the quality of FISH methodology used in Colombia. Our findings impact the survival of Colombian children and present an opportunity to improve ALL diagnosis, classification, and treatment in resource-constrained settings by developing targeted strategies.

EP059 / #1998

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

IMPACT OF NUTRITIONAL STATUS ON SURVIVAL AND UNSCHEDULED DAYS OF HOSPITALIZATION FOR INFECTIOUS PROCESSES IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: In children with acute lymphoblastic leukemia (ALL), the most important cause of hospitalization is infections. The objective of this study was to describe the nutritional status and unscheduled hospitalized days due to infectious processes on the survival of children with acute lymphoblastic leukemia.
Methods: A retrospective cohort study was designed to describe the survival of a convenience sample of patients according to their nutritional status and the number of unscheduled days of hospitalization in a referral center in the state of Jalisco, Mexico.
Results: 203 patients were included. The male-female ratio was 1.5. Ninety-six children (47.2%) had an optimal nutritional status at diagnosis, whereas this was not optimal in 107 patients (52.8%). 34 patients (16.7%) presented global malnutrition. According to the body mass index, 10% of the patients were overweight and 12% were obese. The average number of days of unscheduled hospitalization for children without optimal nutritional status was higher in the remission induction and consolidation treatment stage (8.3 and 2.3 days, respectively) related to children with optimal nutritional status (8.2 and 1.2 days respectively). In the statistical analysis, a significant association between survival and nutritional status was not found
Conclusions: In this cohort, although nutritional status was not associated with lower survival in children with ALL, we found that most children do not have an optimal nutritional status at diagnosis, therefore they are more susceptible to complications secondary to chemotherapy toxicity.

EP060 / #2002

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

RISK FACTORS FOR TREATMENT ABANDONMENT FOR CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA. A STUDY FROM A TERTIARY CARE HOSPITAL IN MEXICO

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Background and Aims: In low and middle-income countries, one of the main causes of treatment failure is treatment abandonment. This study shows the characteristics of children with acute lymphoblastic leukemia and its associated risk factors for abandonment in the first 90 days of treatment.
Methods: A retrospective cohort study was designed that included patients younger than 18 years of age diagnosed in an oncology unit in a middle-income country.
Results: 643 children were included; the average age of the patients was 7.1 years. Family nucleus status was recorded in 616 patients, of which, 93 cases (15%) had a single-parent family. Regarding the place of residence (n=638) 335 children (52%) lived outside the urban area of the city. As for parents, incomplete primary education was the most frequent level of education; mothers and fathers 40% and 33% respectively. Forty-one patients (6.4%) abandoned treatment. The economic household-income monthly average was $6039 MXN. With the logistic regression model, a significant association was found with single-parent family (p=0.000), father's age <30 years (p=0.000), positive minimal residual disease after induction treatment (p=0.001) and residence outside the city (p=0.02)
Conclusions: The socioeconomic factors associated with treatment abandonment were related to the family burden that cannot be covered by families who have to travel longer distances from care centers, in some cases in single-parent families, and according to the father's age, being the families with parents under 30 years of age are at higher risk. In this study, children who did not achieve remission after induction treatment had a higher risk of treatment abandonment.

EP061 / #2007

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

A MIXED-METHOD APPROACH TO THE ANALYSIS OF TRENDS IN SURVIVAL RATE OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA. EXPERIENCE OF SINGLE INSTITUTION IN A MIDDLE-INCOME COUNTRY

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Background and Aims: In low-and middle-income countries, the survival of children with acute lymphoblastic leukemia (ALL) decreases dramatically in the initial treatment phase. The objective of this study was to analyze the survival trend of pediatric patients with ALL in the first 90 days of treatment.
Methods: A sequential mixed-method approach was used. Interventions that decreased early events were found using the qualitative model. The trend of the annual percentage change (APC) of the survival rate was analyzed with the Jump Model and Comparability Ratio and time periods that presented changes with statistical significance ($p < 0.05$) were identified
Results: 12 semi-structured interviews were applied using seven categories that described the main interventions implemented to improve the survival rate. 643 children were included from 2007 until April 2021. After one year of implementing the Total XV Therapy (2012), a change in the trend of the event-free survival rate (EFS) was identified (APC=+2.08) and was statistically significant. The EFS trend rates increased in 2009 once there was an adjustment in the treating personnel and chemotherapy dose intensity protocol improvement (APC=+7.85) although it was not statistically significant. There was a point in 2014 when the overall survival rate (OS) trend (APC=+1.8) had a significant increase. This was one year after the leukemia clinic staff increased and a pediatric infectious disease specialist was included on the team
Conclusions: In this cohort of patients, changes in the survival rate were significantly associated with the implementation of the Total XV Therapy and adjustment in the treating personnel

EP062 / #354

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

CHILDHOOD LATE BONE MARROW RELAPSES IN B CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA IN SPAIN. ANALYSIS OF TREATMENT OUTCOMES.

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Background and Aims: Acute lymphoblastic leukemia (ALL) is the most common cancer in childhood, with relapse occurring in 10-15% of cases. In Spain, the current therapeutic recommendation (LAL/SEHOP-PETHEMA 2015) for relapse is based on the IntReALL SR and HR protocols and recommend allogeneic stem cell transplantation (HSCT) to patients with B-cell precursor (BCP) late bone marrow relapse and inadequate response (minimal residual disease ≥ 0.1%) after induction. Here we describe our overall results and analyse the impact of this stratification.
Methods: Data from pediatric patients with late bone marrow relapse of BCP ALL recorded within the SEHOP/PETHEMA 2015 registry from January 2015 to April 2021 were reviewed. Overall survival (OS), event-free survival (EFS), cumulative incidence of relapse (CIR) and treatment-related mortality (TRM) were calculated both in the whole cohort and stratified by response to induction (MRD < 0.1% vs MRD ≥ 0.1%). The Kaplan-Meier method, Log Rank test and Gray's methods were used to estimate and compare OS, EFS, CIR and TRM with the help of R statistical software.
Results: A total of 42 patients were included. Median follow-up was of 33 months (range 7-47). The 3-year OS, EFS, CIR and TRM were of 81.1%, 60.7%, 33.4% and 11.2%, respectively in the entire cohort. We found no statistically significant differences in OS (87.3% vs 71.4%; p = 0.3), EFS (72.7% vs 42.9%; p = 0.052), CIR (27.9% vs 39.3%; p = 0.43) and TRM (4.5% vs 21.4%; p = 0.16) among good responders versus poor responders.
Conclusions: Overall results are comparable to those previously reported with the ALL-REZ 2002 BFM study. The application of HSCT was able to rescue a proportion of patients with poor response to inducction after relapse which is translated into non-significant differences in survival results.

EP063 / #1339

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

ANALYSIS OF THE OUTCOME OF PRE-B STANDARD RISK RELAPSES REGISTERED IN THE SEHOP-PETHEMA 2015 GUIDELINES

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Background and Aims: The classification fo early combined relapses of pre-B phenotype in the standard risk group is controversial. In fact, the Children Oncology Group classifies these patients in the high-risk group and the Nordic Society of Paediatric Haematology and Oncology found an overall survival of only 38%, which are intermediate results between the rest of the standard-risk and the high risk relapses. We analyse our own results in a Spanish cohort of patients undergoing treatment with an IntReALL-based approach.
Methods: Data from all patients registered in the Spanish registry "SEHOP-PETHEMA 2015" between January 2015 and April 2021 with a diagnosis of standard-risk first relapse were reviewed. Overall survival (OS), event-free survival (EFS), cumulative incidence of relapse (CIR) and treatment-related mortality (TRM) of pre-B early combined relapses were calculated and compared with the rest of standard-risk pre-B first relapses. The Kaplan-Meier method was used for the estimation of the survival functions and the Log-Rank test was use for comparisons. Gray's method was used for the analysis of CIR and TRM. All these calculations were performed with R.
Results: There were 71 cases of first relapse of standard-risk pre-B phenotype, of wich 7 were early combined relapses. EFS was significantly lower in the early combined relapse group compared with the other standard-risk relapses (33.3% vs 76.2%; p=0.04). Furthermore, this was consequence of an increased CIR (50% vs 10.1%; p=0.048), with no difference in TRM (16.7% vs 12.1%; p=0.074). OS was also lower, although this difference did not reach statistical significance (41.7% vs 82.3%; p=0.08).
Conclusions: In early combined relapses of pre-B phenotype, we found inferior results than in other standard-risk pre-B relapses due to a higher incidence of second relapses. This should lead us to consider treatment intensification in this group, using new therapies or throug the inclusion of these patients in the high-risk group.

EP064 / #270

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

MEDICATION INDUCED DIABETES DURING INDUCTION THERAPY IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: IMPACT OF RISK GROUPING

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Background and Aims: Medication induced diabetes (MID) is common during induction therapy for pediatric acute lymphoblastic leukemia (ALL) and has potentially significant negative consequences. Reported risk factors for MID are variable with limited data comparing patients treated with standard-risk (SR) vs high-risk (HR) regimens. This study aims to evaluate the incidence and risk factors for MID during induction in patients with ALL from the Maritimes over a 20-year period, assess the complication rates of MID, and compare the risk of MID in SR versus HR regimens.
Methods: We performed a retrospective single-center study of 262 patients (142 males, 120 females) diagnosed with ALL at the IWK Health Centre from 2000 to 2019. Demographic and treatment data was extracted from the Pediatric Oncology Research Database and EMRs.
Results: Twenty-two patients developed MID (8.4%). Patients with MID were significantly older (10.3 vs 6.2 years, $p < 0.001$), had higher BMI z-scores (1.2 vs 0.3, $p=0.003$), and had higher rates of Trisomy 21 (9.5% vs 1.3%, $p=0.012$). Patients with MID had significantly higher rates of CNS disease (36.4% vs 14.2%, $p=0.007$) but did not have increased rates of infection, relapsed disease, or death. HR patients (n=122) had significantly more complications than SR patients (n=140) including MID (13.1% vs 4.3%, $p=0.01$), CNS disease (23.8% vs 9.3%, $p=0.001$), infection (68.3% vs 45.7%, $p<0.001$), relapsed disease (10.7% vs 4.3%, $p=0.047$), and death (11.5% vs 1.4%,<0.001). HR patients treated with 28-days of prednisone developed significantly more MID than those treated with 14-28 days of dexamethasone (21.5% vs 3.5%, $p=0.003$) and were significantly older (12.7 vs 4.2 years, $p<0.001$).
Conclusions: Older age, higher BMI, CNS disease, Trisomy 21, and steroid type were risk factors associated with MID in our cohort. HR patients developed significantly more complications including MID. Screening for MID should be routine during ALL induction therapy, particularly for those with HR disease.

EP065 / #818

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

TREATING RELAPSED B-ALL IN IN CHILDREN WITH A SETTING-ADAPTED MITOXANTRONE BASED INTENSIVE CHEMOTHERAPY PROTOCOL (TMH RALL PROTOCOL)-EXPERIENCE FROM TATA MEMORIAL HOSPITAL MUMBAI

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Background and Aims: The outlook of relapsed ALL in LMICs is particularly dismal due high treatment related toxicity, inadequate resources and unavailability of targeted therapy. We report our experience of using a locally adapted mitoxantrone based protocol for non-high risk (HR) relapses.
Methods: Eighty-two children with non-HR B-cell ALL relapses were treated on TMH rALL-18 protocol between November 2018-January 2021. The protocol (adapted from COG/UKALL-R3/Int-Re-ALL), comprising of 7 blocks of multi-agent chemotherapy (including mitoxantrone in induction) followed by local radiation and maintenance, underwent serial modifications based on our experience with initial patients. Major modifications included reducing number of dexamethasone pulses during induction, dose-reduction and spacing apart of high-dose cytarabine during Block-3. Unlike in the original protocols, we introduced blood count cut-offs for various post-induction time-points.
Results: Thirty/82 and 52/82 patients were early and late relapses respectively. Though induction chemotherapy was outpatient based, 65/82 patients needed hospitalization for supportive care of which 22 (26.8%) had blood-stream infection, 20(24.4%) required ICU care and 12(14.6%) died. Forty-five of 60 assessable patients (75%) cleared MRD post-induction. Post-induction toxic deaths were seen in 7 patients (5 in Block 3, 1 during
maintenance and 1 post-transplant). Multidrug resistant organism (MDRO) sepsis was seen in 8/19 toxic deaths. No further block 3 deaths were encountered post modification of cytarabine dose and interval. Till last analyzed 175 grade 3/grade 4 toxicity events were seen in induction and 182 further episodes during the rest of the phases taken together. The EFS and OS of the cohort were 53.9±7.5% and 68.4±8% respectively at median follow-up of 10 (2-39) months.
Conclusions: Toxic events including MDRO infections remain a major hurdle in the LMICs. Toxicity can be mitigated by local adaptation of protocols that strike a fine balance between efficacy and tolerability. Until the time, targeted therapies are freely accessible, treatment with setting-adapted chemotherapy protocols can produce acceptable outcomes at least in the non-HR relapses.

EP066 / #1127

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

THE CHOICE OF CONVENTIONAL CHEMOTHERAPY OR IMMUNOTHERAPY AS BRIDGING THERAPY DOES NOT APPEAR TO IMPACT CLINICAL RESPONSE TO CD19 DIRECTED CAR-T THERAPY IN PEDIATRIC B-ALL

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Background and Aims: Bridging therapy (BT) is indicated for most children with B-ALL during the period while awaiting manufacture of tisagenlecleucel (tisa-cel), a CD19 directed CAR-T therapy. Both conventional chemotherapy agents and immunotherapies have been used. We aim to investigate outcomes after tisa-cel therapy for patients treated with conventional or immunotherapy-based BT
Methods: Patients treated with tisa-cel at our institution with bone marrow disease (with or without extramedullary disease) were included. Patients with isolated extramedullary disease were excluded as systemic BT was infrequently administered.
Results: 33 patients received systemic BT. 24 received conventional chemotherapy and 9 received immunotherapy. There was no consensus conventional chemotherapy regimen; methotrexate containing regimens were most common (n=12). 8/9 patients receiving immunotherapy received inotuzumab and 1/9 received blinatumomab. One patient in each group died of infectious toxicity before infusion. Failure to achieve MRD negative or molecular remission at day 28 after infusion occurred in 5/23 (21.7%) conventional and 2/8 (25%) of immunotherapy recipients. Amongst responders, 6/18 (33%) conventional BT patients and 3/6 (50%) immunotherapy BT patients relapsed. 1 relapse was CD19-, occurring in a patient who received inotuzumab. There was one second malignancy in a patient with Li-Fraumeni. At last follow up (median 493 days [range 76-2548 days]), 15/23 (65.2%) conventional BT patients and 5/8 (62.5%) were alive. B-cell aplasia was maintained for at least 6 months in 8/23 (34.7) conventional BT patients and 2/8 (25%) immunotherapy BT patients although 2 additional patients in the immunotherapy group went to planned HSCT prior to 6 months.
Conclusions: No obvious differences were seen in initial response, relapse, or survival between patients treated with conventional and immunotherapy BT. As low disease burden at time of infusion is a positive prognostic factor, it is reasonable to bridge with whatever regimen is felt to be most likely to give the lowest disease burden with tolerable toxicity.

EP067 / #1857

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

RELIABILITY OF PERIPHERAL BLOOD MINIMAL RESIDUAL DISEASE ON DAY 8 OF INDUCTION FOR RISK STRATIFICATION OF PEDIATRIC PRECURSOR B ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: During the early phases of treatment for childhood (ALL), MRD is a statistically significant predictor of prognosis . For outcome prediction and therapy stratification in pediatrics with ALL, flow-cytometric monitoring of MRD in the bone marrow (BM) during induction therapy is commonly used. Although using peripheral blood (PB) instead of BM has been adopted by several leukemia groups , data on its effectiveness is limited
Methods: This is a prospective study on a cohort of 64 children with B- ALL, who were treated at the King Hussein Cancer Center (KHCC)(ALL 1102 protocol). Patients underwent PB MRD assessment on day 8 of induction , followed by BM MRD evaluation on day 15 And at end of induction
Results: 69 patients were included (median age, 4.98 years; range, 1.5 to 18.2). Median WBC was 34.43k/ul . Risk stratification was : HR (N=23), SR (26), LR(n=18) and VLR (n=1). Cytogenetics were favorable in 16 (24%), neutral in 39 (58%) and unfavorable in 12(18%). On day 8, 41 had negative MRD and on day 15, 40 were negative.Day 35 showed negative MRD in 46 (72%). Day 8 and day 15 BM showed significant correlation ($R=0.64$, $p<0.001$). When correlated with EOI MRD, day 15 showed significant correlation ($R=0.54$, $p<0.01$), while day 8 did not ($R=0.23$, $P=0.82$). Studied for prediction of EOI, the AUC for day 8 (AUC=0.65) was significantly less than day 15(AUC=0.85) ($p=0.033$). Using an MRD level of 0.1 % for days 8 and 15, 53 samples were concordant while 7 were not.
Conclusions: Results of our study showed that although the day 8 and day 15 MRD levels were significantly correlated. However, the day 15 marrow MRD measurement was the one significantly correlating with the EOI MRD. This study is still ongoing and recruiting patients. More data will be available for analysis that may strengthen our results.

EP068 / #1196

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

LONG-TERM TREATMENT RESULTS OF PEDIATRIC AND YOUNG ADULT ACUTE LYMPHOBLASTIC LEUKEMIA WITH ALL IC-BFM 2002 PROTOCOL

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Background and Aims: Acute lymphoblastic leukaemia (ALL) is the most common childhood cancer. The great progress in treatment has been made with BFM (Berlin-Frankfurt-Munster) protocols. Overall survival rate in pediatric patients with ALL is over 90%. We present the results of Pediatric ALL Russian group with ALL IC-BFM 2002 protocol. Evaluated long-term overall survival (OS), event-free survival (EFS) and disease- free survival (DFS) for ALL with ALL IC-BFM 2002 protocol.
Methods: From 2003 to 2021, 451 patients with primary ALL were enrolled in ALL IC-BFM 2002 protocol. Median age was 7.2 year (range 0-21). T-ALL was diagnosed in 150 (33,3% of patients), B-ALL 301 (66,7%). At diagnosis and after induction therapy, the patients were stratified into three groups: standard (SR), intermediate (IR), and high-risk (HR) groups.
Results: On 8 days of steroid therapy, 8.4% of patients were prednisone poor responders. Bone marrow response on day 15 was M1 (<5% blasts) in 80.9% patients, M2 (5 ≥ to <25% blasts) in 14.4%, and M3 (≥25% blasts) in 4.7% patients. On day 33 bone marrow response M1 was in 88.9%, M2 - in 9.1%, and M3 - in 2.0% of patients. According to risk stratification, 77,6% of the patient were qualified for SR, 17,7% - IR, and 4,7% as HR. Complete remission was achieved in 98,4% of patients. 10y OS for all patients was 91±1,6%. The OS for the SR was 91,2±1,9%, 93,3±3,1% for IR, and 73,1±10,6% for HR, p<0,05. 10y EFS for SR, IR and HR was 86±2%, 83,3±5,1%, and 67,7±11,5%, respectively. p<0,05. 10y DFS for SR group was 86±2%, for IR - 83,3±5,1%, and 67,7±11,5% - for HR, p<0,05.
Conclusions: ALL IC-BFM 2002 is highly effective protocol for treatment of children with ALL in Russian pediatric oncology centers. This program, based on inexpensive and reproducible stratification criteria, has been successfully carried out in both large and small centers.

EP069 / #873

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

IKZF1 PLUS PROFILE AND OUTCOME ANALYSIS IN A COHORT OF PEDIATRIC B-CELL ACUTE LYMPHOBLASTIC LEUKAEMIA

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Background and Aims: IKZF1 deletion occurs in 15% of paediatric B-cell ALL (B-ALL) and has been shown to be associated with an increased risk of relapse and poor outcome. Recently described IKZF1^{Plus} profile shows association with worse minimal residual disease (MRD), poor prednisolone response (PPR) and high cumulative incidence of relapse. The current study aimed to evaluate the frequency and prognostic impact of IKZF1 and IKZF1^{Plus} deletion in a cohort of pediatric B-ALL.
Methods: A total of 178 pediatric B-ALL cases were analysed for IKZF1 deletion and IKZF1^{Plus} profile using MLPA based probes (P-335 and P-202). IKZF1^{Plus} profile was defined by presence of IKZF1 deletion with an additional deletion of CDKN2A/2B, PAX5 or PAR1 region, in the absence of ERG deletion.
Results: The mean age of cohort was 5.3 years and mean TLC at presentation was 82000/ul. Forty eight patients (N=175, 27%) had a positive MRD and eleven (N=176, 6.2%) had remission failure post induction. Sixty three (N=118, 54%) patients were positive for recurrent translocations and/or hyperdiploidy. As per final risk categorisation, 78/178(44%) were high risk, 58(33%) intermediate and 41(23%) were of standard risk. Forty (N=178, 22%) cases had an IKZF1 deletion, out of which 27 (67%) had an IKZF1^{Plus} profile. Relapse free survival (RFS) and event free survival (EFS) at 4 years for IKZF1 deletion group was statistically poor as compared to non-IKZF1 deletion group (58% vs. 78%, p=0.046; 38% vs. 60%, p=0.0103); however no difference for overall survival (OS) was noted. RFS and EFS at 4 years was even worse for IKZF1^{Plus} group as compared to non- IKZF1^{Plus} group (50% vs. 70%, p=0.026; 36% vs. 58%, p=0.0103).
Conclusions: IKZF1 deletions is associated with unfavorable clinical outcome in pediatric B-ALL cohort. Our data highlights the importance of routine incorporation of testing for IKZF1 deletion and plus profile for better risk stratification in treatment trials.

EP070 / #1348

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

BACTERIAL ISOLATES AMONG INFANTS WITH LEUKEMIA

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Background and Aims: Infantile leukemia has worse outcomes when compared to other childhood leukemias. Understanding patterns of bacterial infections and spectrum of antibimicrobial resistance may help in managing these patients.
Methods: Patients with infantile leukemia diagnosed from January2006 and January2021 were identified. We linked there records to our microbiology records. We selected only first-isolates to remove duplicates and repeated positive cultures caused by the same pathogen. Antimicrobial resistance were used to label samples as Negative, Multidrug-resistant (MDR),and extensively drug-resistant (XDR) according to the Clinical Laboratory Standards Institute (CLSI) guidelines.
Results: We identifed 32 patients (ALL, 18; AML, 14; 48% females). The median age was 0.58 year (range, 0.14-1). There were 102 isolates, with blood (N=86, 84%) being the most common site. The median number of isoltes per patient were 2(range,1-8) and the median time of infection after diagnosis was 3.8months(range, 0.1-32). There were 71 gram-positive(GPB) and 31 gram-negative(GNB) bacteria. GNB represented 40% of peripheral blood cultures, but only 15% of central catheter cultures. The most common pathogens were coagulase-negative staphylococcus species(CONS, N=44, 43%), followed by Viridans Group Streptococcus(VGS, N=11, 11%), E. Coli(N=8, 7.8%), Klebsiella pneumoniae(N=8, 7.8%), Pseudomonas aeruginosa(N=5, 4.9%) and Streptococcus pneumoniae(N=4, 3.9%). Sixteen isolates were labeled as MDR(16%): E coli(N=7), Klebsiella pneumoniae(N=5), Staphylococcus aureus(N=2), Enterococcus faecium(N=1) and Serratia odorifera(N=1). Only one respiratory sample grew an XDR Acinetobacter calcoaceticus. These resistant isolates(N=17) were identified in 11 patient (median=1 isolate per patient). Estimated 4-week survival after an infection was 94%+/-2.3% and was not different according to site of isolate, antimicrobial resistance or gramstain. Also, there was no difference in survival after having multiple isolates.
Conclusions: Bacterial isolates among infants with leukemia are predominantly gram-positive. Survival of our patients following these infections was acceptable and reflects adequate supportive care. One third of our infants were infected with MDR/XDR bacteria and these were predominantly GNB.

EP071 / #633

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

RISK AND BENEFIT OF LESS INTENSIVE TREATMENT FOR STANDARD RISK GROUP OF CHILDHOOD ALL, AN EXPERIENCE IN LMIC

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Background and Aims: It is challenging to develop less toxic chemotherapy regimen in LMIC with limited resources. ALL2013 showed too many toxic deaths and abandonments. Our study provides an experience of two protocols, Indonesian ALL2013 SR and a lower intensity protocol, ALL2016 SR. The major changes in ALL2016 were omitting the anthracycline in induction, shortening the pulses of two weeks dexamethasone in maintenance into one week, and rescheduling L-asparaginase from three to two times a week.
Methods: SR group was defined as age 1-10 years, leucocyte count less than $50x10^9$/L, no CNS involvement, no mediastinal mass, no T-cell phenotype, and good prednisone response. The 4-year-pOS and pEFS were analyzed using Kaplan Meier method.
Results: ALL2013 SR included 106 patients and ALL2016 91 patients. ALL2016 showed a non-significant advantage for SR patients (4-year-pEFS 56.0% vs 47.2%; P=0.220 and 4-year-pOS 70.3% vs 61.3%; P=0.166) due to less toxic deaths (7% vs 20%; P=0.011) and less abandonment (5% vs 11%; P=0.142). The cumulative incidence of relapses in ALL2016 was 40% and in ALL2013 34% (P=0.432). Relapses frequently occurred between weeks 80-120.
Conclusions: Overall, the outcome improved. The less intensive treatment succeeded to reduce toxic deaths and abandonments, although at the cost of more relapses.

EP072 / #124

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

ASPARAGINASE-SPECIFIC ANTIBODY MEASUREMENT IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) UNDER NATIVE E. COLI ASPARAGINASE-BASED AND ITS POTENTIAL FACTORS ASSOCIATION.

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Background and Aims: Asparaginase is one of the chemotherapy backbones for pediatric acute lymphoblastic leukemia (ALL) treatment. But its foreign protein origin can produce the antibody which causes an allergic reaction together with lowering activity made drug ineffectiveness.
Methods: The primary objective is to prove the association of asparaginase-specific antibodies with post-48-hours activity. The secondary objective is to study the potential factors influencing the antibody concentration. A single-center cross-sectional study conducted from September 2020 through June 2021 at King Chulalongkorn Memorial Hospital, Thailand. 51 eligible patients (25 males and 26 female) age between 1-15 years old were enrolled. Native E. coli asparaginase was administrated intramuscularly. Whole blood was drawn for measuring post-48-hours activity from the last dose (21 cases), and asparaginase-specific antibody at any time (51 cases) which later processed with the coupled enzymatic reaction.
Results: The empirical optimal cut-off of antibodies was newly calculated which shows a ratio of 2.2 times above healthy volunteers. The mean activity is 1.94 and 2.42 ng/ml for an antibody positive and negative group respectively. The asparaginase antibody was proved non-linear, independently invert correlation with activity by multivariate mix-model analysis (p-value: 0.031 (95%CI: -1.51 to -0.07). The asparaginase allergic reaction and asparaginase accumulation dose were proved not associated but some inflammatory event as proved-invasive fungus infection shows significant positive trend considering as confounding factor (p-value <0.001, 95%CI: 5.06 to 10.90).
Conclusions: Due to weak invert and non-linear antibody-activity relationship and no standard cut-off positivity criterion, our opinion still affirms to discourage employing the asparaginase-specific antibody measurement for justification of the treatment change. Furthermore, this trial raises the concern of cross-reaction of antibodies with some inflammatory/infection event.

EP073 / #743

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

EXPRESSED AND DIFFERENTIALLY METHYLATED GENES ASSOCIATED WITH INDUCTION TREATMENT RESPONSE IN PEDIATRIC PATIENTS WITH B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: Colombian survival rate for pediatric acute lymphoblastic leukemia (ALL) is less than 60%, which could be related to genetic and epigenetic alterations specific to our population. Some genetic alterations are used to classify patients into a risk group, but a genetic profile capable of sensitively predicting response to chemotherapy induction, improving risk classification, and predicting survival is greatly needed. Our objective was to identify genes associated with the response to induction chemotherapy in pediatric patients with B-cell ALL.
Methods: RNA sequencing and genome-wide DNA methylation assay were done in blasts from 27 patients newly diagnosed with B-cell ALL. Statistics analyses were done using DEseq2 and Partek Flow software. We selected genes that were differentially expressed (DEGs), differentially methylated, and had a correlation between both. Response to induction treatment was assessed by minimal residual disease (MRD) detected by flow cytometry and analyzes were performed between patients who did or did not respond to induction treatment at two-time points (15 and 33 days) and complete response (patients who did or did not respond on time points). Selected genes were verified with RT-PCR in a different cohort of patients.
Results: We identified 50 DEGs in common for all comparisons. Differential methylation analysis showed that 4 of them had differentially methylated CpGs and had a correlation between expression and methylation levels. Six more interesting genes that met the previous criteria and were present only in the complete response were also further validated by RT-PCR. Genes DAPK1, BOC, ITGA6, MIR4435-2HG, and NDPC1 have been confirmed to be overexpressed in non-responder patients.
Conclusions: We identified 5 genes present in patients with poor response to induction chemotherapy and could be used as predictive biomarkers of response to chemotherapy in Colombian pediatric patients with B-cell ALL.

EP074 / #257

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

MINIMAL RESIDUAL DISEASE COMPARISON BETWEEN IG/TCR PCR VERSUS NGS ASSAYS IN CHILDREN WITH PHILADELPHIA CHROMOSOME-POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA: A REPORT FROM THE COG AALL1631 STUDY

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Background and Aims: Minimal residual disease (MRD) assessment by immunoglobulin/T-cell receptor (Ig/TCR) polymerase chain reaction (PCR) is currently being used in the international pediatric Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph^+ALL) trial EsPhALL2017/COG AALL1631 for risk stratification. MRD concordance has previously been demonstrated between Ig/TCR PCR and flow cytometry. We sought to assess concordance of MRD assessment between conventional Ig/TCR PCR and next-generation sequencing (NGS) assays.
Methods: MRD was assessed in all patients on AALL1631 by Ig/TCR PCR at end-induction IB; those with MRD $<5x10^{-4}$ were classified as standard-risk (SR), whereas patients with MRD $>=5x10^{-4}$ were considered high-risk (HR) and assigned to hematopoietic stem cell transplant (HSCT). Residual diagnostic and end-induction IB samples from consenting patients were assessed for NGS MRD and subsequently compared to Ig/TCR MRD to determine concordance as related to MRD-based HSCT recommendations. MRD values were calculated using the kappa statistic for agreement above chance.
Results: Sixty-seven patients had matched samples available for MRD assessment at end-induction 1B by both Ig/TCR PCR and NGS. NGS MRD was evaluable for all 67 patients and stratified as 62 SR and 5 HR. In contrast, Ig/TCR PCR results were inevaluable for 3 patients (unsatisfactory sample quality) and indeterminate (positive, but not quantifiable) in 4 patients. Of the remaining 60 patients, 55 met SR and 5 HR criteria using Ig/TCR PCR. There was only 1 discordant case between the two methods for MRD-based HSCT recommendation among these 60 patients with a kappa statistic for agreement above chance of 0.88.
Conclusions: NGS and Ig/TCR PCR assays were highly concordant in MRD assessment for risk stratification in pediatric Ph^+ALL patients enrolled on AALL1631. The NGS assay yielded MRD results amenable for risk stratification in 100% patients compared to 89.6% for the Ig/TCR PCR methodology. These data support the use of NGS MRD testing for risk stratification in pediatric Ph^+ALL.

EP075 / #991

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

SINGLE NUCLEOTIDE POLYMORPHISMS IN THIOPURINE ASSOCIATED MYELOSUPPRESSION IN MAINTENANCE THERAPY IN ACUTE LYMPHOBLASTIC LEUKEMIA: THE MYSTERY REMAINS.

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Background and Aims: Mercaptopurine (6-MP), the mainstay of maintenance therapy (MT) in acute lymphoblastic leukemia (ALL), is associated with hematological and hepatic toxicities with germline genetic variations being determinants of interpatient variability in susceptibility, drug response, and toxicity. NUDT15 & TPMT are the main SNP's implicated, incidence varying with ethnicity. This prospective study aimed at evaluating the prevalence of SNP's in children who tolerated lower doses of 6-MP.
Methods: One hundred and ninety children with ALL (age: 5.29±2.9 years) were evaluated for the NUDT15 (c.415C>T) & TPMT *2 (c.238 G>C), *3A (c.460 G>A and c.719 A>G),*3B (c.460 G>A) and *3C (c.719 A>G) SNP prior to start of MT. Data with regards to 6-MP dosing and toxicities over 6 months of MT was noted.
Results: NUDT15 and TPMT SNP's were demonstrated in 12% and 4.5% patients respectively (all heterozygous, one patient testing positive for both). The dose of 6-MP in patients with the NUDT15 SNP was lower (49±8.1mg/m2/day vs. 54±6mg/m2/day (p=.002). Ten patients with NUDT15 SNP received ≥50/mg/m2/day but had higher dose interruptions [4 weeks (IQR: 2-8] as compared to those without SNP [2weeks (IQR1-4)] (p=.06). Only 2/7 children with TPMT SNP required dose reduction. Fifty seven of 190 children on MT (30%) received ≤50mg/m2/day of 6-MP (mean 45.46±5.9mg/m2/day), with 13/57 receiving ≤40mg/m2/day (36.3±4.8 mg/m2/day). Fifteen children (26%) who received lower doses had a demonstrable SNP (13: NUDT15 and 2 TPMT). Five patients (38%) who received ≤40mg/m2/day demonstrated a SNP (NUDT15 in all).
Conclusions: Only 26% cases of ALL on MT tolerating lower doses demonstrated a known SNP. A lower dose in 42/57 children could not be attributed to the known SNP's. Whole exome sequencing (WES) or large scale GWAS (Genome wide association studies) studies are required to identify novel candidate SNPs that are likely to be associated with 6mercaptopurine myelotoxicity in south east Asian population

EP076 / #8

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

PHARMACOGENOMICS OF VINCRISTINE-INDUCED PERIPHERAL NEUROPATHY IN CHILDREN WITH CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims: Vincristine-induced peripheral neuropathy (VIPN) is a debilitating side-effect of vincristine in children with cancer. It remains a challenge to predict which patients will suffer from VIPN. Pharmacogenomics may explain an individuals' susceptibility to side-effects. In this systematic review and meta-analysis, we describe the influence of pharmacogenomic parameters on the development of VIPN in children with cancer.
Methods: PubMed, Embase and Web of Science were searched up to 30-09-2021. In total, 1597 records were identified and 21 studies were included. A random-effects meta-analysis including nine studies was performed for the influence of cytochrome P450 (CYP) 3A5 expression on the development of VIPN.
Results: Single-nucleotide polymorphisms (SNPs) in four transporter-associated genes (e.g. ATP binding cassette subfamily C member 2 (ABCC2)), three metabolism-associated genes (e.g. vitamin D receptor (VDR)), six cytoskeleton-associated genes (e.g. centrosomal protein 72 (CEP72)), one hereditary neuropathy-associated gene (solute carrier family 5 member 7 (SLC5A7)), and ten genes previously unrelated to vincristine or neuropathy (e.g. Ewing's tumor-associated antigen 1 (ETAA1)) were associated with VIPN. CYP3A5 expression status was not significantly associated with VIPN (pooled odds ratio 0.69, 95% confidence interval 0.38-1.26, I^2 = 50%, τ^2 = 0.33). The comparison and interpretation of the results of the included studies was limited due to heterogeneity in the study population, treatment protocol and assessment methods and definitions of VIPN.
Conclusions: Pharmacogenomic parameters have a significant influence on VIPN in children with cancer and show potential for clinical relevance. However, CYP3A5 expression status was not a significant risk factor. Independent replication is essential to validate the clinical significance of the reported associations. Future research should aim for prospective VIPN assessment in a discovery and replication cohort. Ultimately, the goal would be to stratify patients based on the presence of SNPs and provide a tailored dosage that limits the risk of VIPN while maintaining the highest therapeutic efficacy.

EP077 / #340

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

PHYSICAL FITNESS THROUGHOUT CHEMOTHERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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Background and Aims: Due to improving survival rates of patients with childhood acute lymphoblastic leukaemia (ALL), there is an increasing focus on long-term effects of treatment. ALL and its treatment cause a range of physiological changes, interfering with normal physical functioning. So far, it remains unclear how physical fitness (PF) (including muscle strength, functional mobility and endurance) evolves throughout treatment for ALL.
Methods: Sixty-two patients treated for ALL according to the EORTC 58081 protocol underwent physical testing at nine timepoints throughout their 2-year-treatment (last measurement at 6 months post-treatment). Four tests were conducted. Quadriceps and tibialis anterior muscle strength were assessed using a hand-held dynamometer. Standing broad jump test (SBJ) and six-minute walk test (6MWT) were assessed for functional mobility and endurance, respectively. Z-scores were calculated based on gender- and aged-matched test-specific normative values, which were predicted based on time of assessment, ALL risk group and age at diagnosis, using linear mixed models. We added an interaction factor to test whether evolution over time is subject to age.
Results: The strongest decreases in Z-scores are observed after induction therapy in quadriceps strength (Z=-1.36 to Z=-2.62), SBJ (Z=-1.15 to Z=-2.22) and 6MWT scores (Z=-2.20 to Z=-3.57). Age at diagnosis is a significant predictor for tibialis anterior strength ($p=0.025$), SBJ ($p<0.001$) and 6MWT ($p<0.001$) performance. Adolescents (>13 years) tend to have lower results on all performed tests from diagnosis onwards. Muscle strength seems to recover 6 months after treatment (Z=-0.8 for quadriceps strength, Z=0.5 for tibialis anterior strength). However, 6MWT and SBJ scores remained below expected levels, especially for adolescents (Z=-1.63 and Z=-2.58 respectively).
Conclusions: We conclude that future interventions might need to target early decline in PF after induction phase, the low functional mobility and endurance post-treatment, specifically in the adolescent subgroup. These observations can be used to better tailor individualized physiotherapy throughout treatment.

EP078 / #1044

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

EVALUATION OF SKIN TOXICITY PROFILE OF HIGH DOSE METHOTREXATE THERAPY IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: High dose Methotrexate(HDMTX) has a variety of cutaneous side effects. In this study we assessed the skin toxicity profile of HDMTX in acute lymphoblastic leukemia(ALL) in a Low-Middle Income countries(LMIC) setting with detailed monitoring of clinical and lab parameters along with limited serum MTX estimation.
Methods: This is a prospective observational study done from 1st January 2019 to 31st December 2019. Children with age<14 years diagnosed with High Risk ALL who received a total of 4 HDMTX courses were included. Administration of HDMTX was done by trained nursing staff at a dose of 5gram/metre^2 in an inpatient setting with strict hydration and alkalinization with urine pH monitoring. Data regarding skin and toxicity profile, leucovorin rescue and serum MTX levels starting at 54-hour from start of HDMTX until subsequent normalization (<0.2micromole/liter) were analyzed.
Results: During the study period, 488 HDMTX infusions were administered. Skin toxicity was noted in 13.1%(n-64) of infusions. Most common manifestation was focal and diffuse hyperpigmentation(n-25). Others included itchy papular rash(n-14), bullous lesions(n-11), skin peeling(n-6), perioral, perianal and eyelid excoriation(n-4), itchy crusty rash (n-3) and generalized desquamation(n-1). Mean day of onset was 6.4(SD 2.01) days from start of HDMTX. Majority were managed with supportive care. One infusion required intravenous methyl prednisolone and extra doses of folinic acid. Mean duration for symptom resolution was 5.4(SD 1.82) days. Among all the 4 HDMTX infusions, the incidence of skin toxicity progressively decreased with highest in 1st cycle(26.2%) and lowest in 4th cycle(4.1%)(p-0.001). There was no relation between delayed MTX clearance with skin toxicity. Among other toxicities, skin toxicity had significant association with thrombocytopenia and infection(P-0.017 and 0.001 respectively).
Conclusions: Skin toxicity can be observed in limited number of infusions (<15%) when HDMTX is given at 5 gram/meter^2 with highest incidence being in the 1st cycle. Nearly all skin manifestations are transient and can be managed with supportive care.

EP079 / #249

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

NOVEL ADAPTION TO THE PEDIATRIC SARC-F SCORE TO CLASSIFY PEDIATRIC HEMATO-ONCOLOGY PATIENTS WITH FUNCTIONAL SARCOPENIA

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Background and Aims: The SARC-F questionnaire is recommended as a screening tool for sarcopenia in elderly, and consists of five self-reported questions addressing strength, walking, rising, stairclimbing and falling. The aim of this study was to investigate the accuracy of the pediatric SARC-F (PED-SARC-F), for identifying sarcopenia in pediatric hemato-oncology patients, including determination of a cut-off for clinical use.
Methods: Patients 3-20 years, under active treatment or within 12 months after treatment cessation at the hemato-oncology department of the Princess Máxima Center for Pediatric Oncology, were eligible. Patients had a physiotherapy assessment including PED-SARC-F, as part of standard of care. The physiotherapy assessment consisted of muscle strength measures (handheld dynamometry), physical performance (various tests) and muscle mass (bio-impedance analyses). Structural sarcopenia was defined as low muscle mass in combination with low muscle strength and/or low physical performance. Functional sarcopenia indicated low muscle strength combined with low physical performance.
Multiple logistic regression models were estimated to study the associations between PED-SARC-F, and the endpoints: structural and functional sarcopenia. To evaluate which PED-SARC-F cut-off point (0-10) provides the most accurate classification of functional sarcopenia, the area under the receiver operating characteristic curve (AUCs), sensitivity and specificity per point were calculated.

Results: In total, 215 assessments were included, 62% were performed in boys and median age was 12.9 years (IQR: 8.5-15.8).
The PED-SARC-F had an AUC of 0.90 (95%CI = 0.84-0.95) for functional sarcopenia and 0.69 (95%CI = 0.57-0.80) for structural sarcopenia.
A cut-off point of ≥5 had the highest specificity of 96% and sensitivity of 74% for functional sarcopenia.

Conclusions: We adapted the SARC-F to a pediatric version and confirmed its excellent accuracy for identifying functional sarcopenia and defined a clinically useful cut-off in a pediatric hemato-oncology setting. This easy self-report score can identify children that may need physiotherapy interventions during and shortly after treatment.

EP080 / #713

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

POINT-OF-CARE MUSCULOSKELETAL ULTRASOUND CORRELATES WITH BODY COMPOSITION, MUSCLE STRENGTH AND PHYSICAL PERFORMANCE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: Non-invasive and reliable tools to measure muscle mass and muscle quality in children with acute lymphoblastic leukemia (ALL) are limited.
The aim of the study was to explore the association of muscle ultrasound outcomes with standard-of-care assessments of body composition, muscle strength and physical performance in children with ALL.
Methods: In this cross-sectional study we included Dutch ALL patients, aged 3-18 years during maintenance therapy.
Bilateral ultrasound measurements of the rectus femoris (RF) muscles were captured using a portable linear array transducer connected to a tablet. Artificial intelligence image analysis was used to estimate RF muscle thickness, cross-sectional area, intramuscular adipose tissue (IMAT) and raw pixel intensity (RPI), as a proxy for glycogen.
Assessments of body composition (bio-impedance analysis and thigh circumference), muscle strength (hand-held dynamometry) and physical performance (timed up and go test [TUG] and time to rise from floor test [TRF]) were performed during the same visit.
Spearman's rank correlation analyses (rho) were calculated to study correlations between ultrasound outcomes and measures of body composition, muscle strength and physical performance.
Results: Muscle ultrasound was performed in 60 patients, 37/60 boys (61.7%), median age 6.1 years (range: 3–18.8 years).
RF thickness and cross-sectional area correlated moderately with muscle mass (rho=0.58, rho=0.6), handgrip strength (rho=0.6, rho=0.65), knee extension strength (rho=0.65, rho=0.68), and highly with thigh circumference (rho=0.76, rho=0.78). IMAT correlated moderately with TUG (rho=0.52) and TRF (rho=0.53), i.e. increased fat infiltration correlated with slower performance. RPI correlated moderately with handgrip strength (rs=-0.48), knee extension strength (rho=0.51), and TUG (rho=0.5), lower glycogen correlated with lower strength and slower performance. All p-values were <0.001.
Conclusions: Muscle ultrasound may be useful for measuring muscle mass and muscle quality in children with ALL, allowing rapid and non-invasive assessments. Further validation using golden standard assessments in children is needed to determine the accurateness in pediatric populations.

EP081 / #643

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

COMPARATIVE ASSESSMENT OF DIFFERENT BIOINFORMATIC PIPELINES FOR GENE FUSION DETECTION FROM RNA-SEQ DATA IN ACUTE PEDIATRIC LEUKEMIA

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Background and Aims: Background: RNA sequencing (RNA-seq) is a well-established tool for detecting gene fusions in acute leukemia. Multiple bioinformatics pipelines have been developed to analyze RNA-seq data in leukemia, but an agreed gold standard has not been established. Aim: To compare and define an integrative bioinformatics pipeline to detect gene fusions in acute pediatric leukemia.
Methods: Applicability assessment of five fusion calling pipelines (Arriba, deFuse, CICERO, FusionCatcher, and STAR-Fusion) individually, and development of a set of scripts that standardize and combine fusion results of all of them to detect leukemia driver fusion genes in data from cell lines and pediatric patients.
Results: We analyzed RNA-seq data from 18 cell lines and 15 previously characterized pediatric patients with leukemia. Each algorithm individually called most of the fusions with similar sensitivity and precision. However, not all rearrangements were called, so choosing a single pipeline might cause the missing of important fusions. To solve this, we integrated the results of the five algorithms in just one pipeline. We compared the output from the agreement of 5/5, 4/5, and 3/5 algorithms. The maximum sensitivity was achieved with the agreement of 3/5 algorithms, with a sensitivity of 79% in cell lines and a sensitivity of 100% in patient data. The obtained precision for the agreement of 3/5 algorithms was 10.2% and 23% for cell lines and patients, respectively, due to the high rate of false-positive variants. We applied different manual filters to discard false-positive rearrangements improving the precision to 36.7% (cell lines) and 84% (patients).
Conclusions: Conclusion: The five fusion caller pipelines worked well individually but missed some fusions. The best strategy to achieve a high sensitivity is to combine results from all five callers and keep those fusions called by 3/5 pipelines. Moreover, manual filtering would improve precision.

EP082 / #828

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

IMMUNOPHENOTYPIC AND CHROMOSOMAL CHARACTERIZATION OF KMT2A GERMLINE ACUTE LYMPHOBLASTIC LEUKEMIA IN INFANTS

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Background and Aims: KMT2A germline (KMT2A-g) acute lymphoblastic leukemia (ALL) configure approximately 20% of ALL in infants, and show distinct clinical and genetic features (e.g., NUTM1 rearrangement), and better prognosis compared with KMT2A gene-rearranged (KMT2A-r) ALL. However, its pathophysiology remains obscure due to the rarity of the disease. We aimed to investigate immunophenotypic and chromosomal characteristics in infants with KMT2A-g ALL.
Methods: Patients registered to the Japanese Pediatric Leukemia/Lymphoma Study Group MLL-10 trial (Tomizawa D. Blood 2020) were analyzed.
Results: Fifteen infants with KMT2A-g ALL were identified. Median age at diagnosis was 307 days, and three patients were <180 days old. Skewing towards male sex was observed (67%). Median white blood cell counts at diagnosis were 43.7 x10^9/L. No patients showed CNS involvement. Unsupervised clustering analysis of leukemic cell immunophenotype grouped many of the KMT2A-g ALL patients, which differentiated from the KMT2A-r ALL patients. Dominant cell surface antigens expressed in KMT2A-g ALL were CD10, CD20, CD24, cytoplasmic CD22, and cytoplasmic Igμ, whereas expression of CD34, NG2, CD15, and CD65 were low. Karyotype of KMT2A-g ALL showed chromosomal translocation, deletion, or addition of chromosome 15 in 7 cases among the 13 cases analyzed. One case showed t(1;19)(q23;p13.3) and TCF3-PBX1. Minimal residual disease at the end of induction was negative in all patients analyzed either by flow cytometry and Ig/TCR PCR. Three cases showed poor response to initial prednisolone therapy; one patient developed secondary acute myeloid leukemia with KM2TA-MLLT3, but was successfully treated with hematopoietic cell transplantation. The 3-year and 5-year EFS and OS rates of all infants with KMT2A-g ALL were 93.3% and 100%, respectively.
Conclusions: KMT2A-g ALL showed distinct immunophenotypic and karyotypic profiles compared to KMT2A-r ALL. While aberration of chromosome 15 suggests involvement of NUTM1 gene rearrangements, further analysis will be needed to elucidate mechanisms of this rare disease.

EP083 / #1358

Topic: *AS05.a Acute Lymphoblastic Leukaemia*

THE TOPOISOMERASE-I INHIBITOR GIMATECAN POTENTLY SUPPRESSES B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA WITHOUT CONCURRENT CARDIOTOXICITY

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Background and Aims: Topoisomerase-II inhibitors such as daunorubicin are the standard chemotherapeutic agents for treatment of acute leukemia. However, their well-recognized myelosuppressive and cardiotoxic natures could mediate severe complications and unwanted late effects. This study aims to evaluate the efficacy, toxicity and mechanism of a topoisomerase-I inhibitor, gimatecan, in a preclinical setting of childhood leukemia.
Methods: Activities of gimatecan were screened in vitro on BCP-ALL and AML cell lines, and on CD34+ hematopoietic stem/progenitor cells (HSPCs). Efficacy in vivo was assessed in cell line- and patient-derived xenografts of leukemia. Hematologic toxicity was evaluated on an animal model of stem cell transplantation. Cardiotoxicity was measured on human iPSC-derived cardiomyocytes. Mechanisms of action were dissected by RNA-seq and validated by Western blot.
Results: Gimatecan had a markedly higher potency against leukemia cell lines (median IC50: 1.2 nM) than standard chemotherapeutics (median IC50s:182-361 nM), with profound selectivity on BCP-ALL over AML (3.6-fold) and HSPCs (75-fold). Oral administration of single-agent gimatecan resulted in complete disease remission in xenografts of BCP-ALL cell lines bearing favorable (ETV6-RUNX1), intermediate (TCF3-PBX1), adverse (KMT2A-AFF1) and fatal (TCF3-HLF) cytogenetics, and was equally effective in patient-derived xenografts of refractory childhood BCP-ALL failing salvage chemotherapy or upfront immunotherapies. Gimatecan exhibited a moderate suppression of normal hematopoiesis, and did not mediate prominent damages on cardiomyocytes as opposed to daunorubicin. Exposure of BCP-ALL cells to gimatecan triggered dose- and time-dependent cell death, G2/M cell cycle arrest, caspase/PARP/Bax cleavage, suggestive of extrinsic apoptosis. Transcriptome profiling of gimatecan-treated cells revealed up-regulation of the p53 tumor suppressive and down-regulation of the MYC oncogenic pathways. Effectors downstream of p53 such as Chk1 and Chk2 were activated by gimatecan, indicating DNA damage.
Conclusions: Gimatecan is an exceptionally potent agent against childhood BCP-ALL. Its tolerable toxicity profile favors further development for resistant leukemia and should be prioritized for clinical trials.

EP084 / #181

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

CHILDHOOD ACUTE PROMYELOCYTIC LEUKEMIA IN IRAQ: A 16-YEAR EXPERIENCE IN A PEDIATRIC CANCER REFERRAL CENTRE IN BAGHDAD

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Background and Aims: Despite advances in the treatment of children with acute promyelocytic leukemia (APL), survival rates in low-income countries remain poor. In September 2003, within a collaborative program between Children-Welfare-Teaching-Hospital in Baghdad and Hematology, “Sapienza”, University of Rome, a specific all-trans retinoic (ATRA)-based protocol was designed for the management of Iraqi children with APL and adapted to local difficulties.
Methods: Children (age<17 years) with a morphological diagnosis of APL entered the study. Treatment consisted of ATRA (25mg/m^2/dayx30days) induction, associated with an anthracycline for high-risk (HR; baseline WBC>10x10^9/L) patients and for those with an increasing WBC during ATRA therapy; three anthracyline-based consolidation courses and 2 years standard maintenance with ATRA (14days/3months). From June 2010, ATRA was introduced in each consolidation course. Intrathecal prophylaxis was given to HR patients. Arsenic trioxide was not available.
Results: From September 2003 to August 2019, 118 APL children (M/F 64/54; hypergranular 81; variant 37; HR 68) were diagnosed in Baghdad (first cohort 54; second cohort 64). Six (3 HR) died before starting therapy (hemorrhages) and 4 refused treatment for parents’ decision. Ninety-four/108 (87%) evaluable children achieved a complete remission (CR); 12 (11%) died during induction (HR 9), due to hemorrhages in 8, differentiation-syndrome in 3, infection in 1; 2 abandoned therapy. Thirty-one (33%) relapsed in the bone marrow (first-period 20/31); 2 are alive in second CR. The 5-year overall survival and event-free survival rates are 61.8% and 64.1% for the entire patients’ series; 51.7% and 43.5% for first cohort and 68.4% and 55.5%, for second. Baseline WBC was a risk factor for induction mortality (HR 75%, low-risk 25%; p=0.011).
Conclusions: Induction therapy with ATRA and anthracycline confirmed its efficacy with a virtual absence of resistant disease. Early death, mainly due to hemorrhage, remains a major cause of failure. ATRA extended consolidation improved the overall results.

EP085 / #838

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

PEDIATRIC ACUTE MYELOID LEUKEMIA WITH T(8;21)- IS IT REALLY FAVOURABLE ?

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Background and Aims: t(8;21) is a common recurrent cytogenetic abnormality in pediatric Acute Myeloid Leukemia(AML) and is considered to have favourable prognosis. However, recent reports suggest heterogeneity in survival outcomes in this subgroup. We report clinical features and outcome of our cohort of childhood t(8;21)positive AML.
Methods: Data of 13consecutive t(8;21)positive AML treated between January2014- December2021 was retrospectively analysed with primary aim to analyse OS and EFS. Sub-analysis was done to decipher the difference in outcome amongst subgroups based on age, gender, initial TLC, presence of additional cytogenetic abnormality, MRD positivity at end of 2ndinduction, myeloid sarcoma, aberrant CD19 and maintenance chemotherapy.
Results: Demographics: male-9, female-4; mean age-10.3years (Range:3-15years). At diagnosis, myeloid sarcoma-3patients, CNS involvement-1patient. AML1-ETO fusion transcript was detected by PCR in all patients. Combination of t(8;21) with loss of sex chromosome was the most common cytogenetic abnormality(n=6), 3patients had aberrant CD19 expression on flowcytometry. One patient abandoned treatment after 1stinduction chemotherapy and was excluded from analysis. Twelve patients received 2cycles of 3+7(Daunorubicin 45mg/m^{2}x3days, Cytarabine200mg/m^{2}x7days) followed by 4cycles high-dose Cytarabine(12gm/m2), 1patient received MRC AMLXII protocol. All patients achieved morphological remission post 2induction cycles, whereas negative MRD (<0.1% by flowcytometry) and molecular remission seen in 6/8 and 8/10 patients respectively. Six patients relapsed with mean interval of 8.8months after diagnosis and received Hematopoietic stem cell transplant(HSCT) in CR2. Of the transplanted patients, 2died due to treatment-related complications and 3 had 2ndrelapse (2-died,1-lost to follow-up). Median follow up duration-22months (Range:4-120months) with EFS and OS of 50% and 63% respectively. Of the features analysed, only high initial TLC(>50000/uL) showed association with poor outcome($p<0.05$).
Conclusions: Our data suggests that outcome of t(8;21)positive pediatric AML is inferior than what was traditionally believed. Further research into role of other co-existing molecular markers may help in identifying this ‘not-so-favourable’ subgroup where treatment may be intensified to achieve long-term cure.

EP086 / #1646

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

REAL WORLD OUTCOME OF CHILDREN WITH ACUTE MYELOID LEUKEMIA PRESENTING TO A TERTIARY CARE CENTER IN INDIA

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Background and Aims: Treatment of pediatric AML remains a challenge in the LMICs as well as HICs. We report real-world data of pediatric AML treated in a tertiary-care center in India.
Methods: We analysed outcomes of AML patients <15 year of age who received atleast 1 week of treatment at our center. Initial workup included cytogenetics, flowcytometry and molecular studies. Patients at high risk of infections received oral metronomic chemotherapy(OMCT) prior to 3+7 induction followed by 3 cycles of high-dose cytarabine +/- cladribine and 1 year of oral maintenance therapy. Bone-marrow responses were assessed by morphology and 10-color flowcytometry at the end of each chemotherapy cycle until negative. A positive BM-MRD was defined as ≥0.01% by flowcytometry.
Results: Two-hundred-fourteen children <15 years of age were analysed. Ninety-eight received OMCT while 116 received 3+7 induction upfront. Total 194 received Induction I of which 152 proceeded to consolidation. Total 130 patients completed prescribed intensive chemotherapy. Median age was 8 years(0.1 – 16.0), Male:Female ratio was 2.05:1, median baseline count of 25.02(0.02 – 418)x10^3/µL and median follow up was 26 months (95% CI: 23.96-28.04). Two year EFS and OS were 39.5 ± 3.6 % and 42.6 ± 3.6 % respectively. After excluding 4 patients who had M3 marrow at the end of induction, 55/149 (36.91%) patients were MRD positive. MRD positive patients had a significantly poor 2 year EFS of 31.1 ± 7.5 % vs 66.2±5.4% (p=0.00035) who were MRD neg. Those who cleared MRD at the end of consolidation still had an EFS of 43.5%+11.9% as compared to 17.5± .6% for those who continued to be MRD positive (p = 0.005).
Conclusions: Treatment of AML remains a challenge. MRD at the end of induction I was a significant predictor of outcome in pediatric AML treated with 3+7 induction. Newer therapies are needed to improve outcomes without increasing infection related mortality.

EP087 / #772

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

MESOTHELIN TARGETING CHIMERIC ANTIGEN RECEPTOR THERAPY FOR PEDIATRIC ACUTE MYELOID LEUKEMIA

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Background and Aims: Despite advances in targeted therapies, one in four children with AML will relapse. There remains an urgent unmet need for improved therapies. About 25% of pediatric AML patients aberrantly express mesothelin (MSLN). We aimed to assess the efficacy of a second generation MSLN targeting chimeric antigen receptor (CAR) T cell with a 28-zeta costimulatory domain (M28z) against pediatric AML. We hypothesized that M28z CAR T cells have antitumor efficacy against MSLN+ AML.
Methods: AML human cell line, Kasumi-1, was retrovirally transduced to stably express MSLN and GFP-firefly-luciferase fusion protein. In vitro efficacy at varying effector to target (E:T) ratios was evaluated using luciferase assays. $3x10^6$ MSLN+ tumor cells were injected systemically via tail vein into NSG mice to produce clinically relevant mouse models with high disease burden. $5x10^5$ M28z CAR T cells (E:T 0.2:1) were injected systemically at day 7. Overall Survival was analyzed via Kaplan-Meier estimate and compared between groups using a log-rank test. Secondary outcomes included tumor burden as measured noninvasively with bioluminescent imaging (BLI) and flow cytometry of bone marrow/spleen.
Results: In vitro assays demonstrated >50% MSLN+ tumor cell lysis with E:T as low as 1:1, without toxicity against MSLN- controls. M28z treated mice (E:T 0.2:1) demonstrated significantly prolonged survival (median 62 days, $p < 0.0007$). Control mice were euthanized at median 38 days for progressive disease, as measured by BLI and flow cytometry after necropsy. Disease burden was eradicated by 7 days after treatment in the M28z group. By 62 days, the M28z mice did not show signs of acute cytokine release (no weight loss, reduced activity, or malaise).
Conclusions: M28z CAR T cells specifically target MSLN+ cells in vitro and significantly prolong survival in vivo at low E:T ratios wiithout off-target effects. Second generation MSLN Targeting CAR T cells could be an alternative therapy for MSLN+ pediatric AML patients.

EP088 / #1834

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

IMMUNOPHENOTYPIC PROFILE OF PAEDIATRIC ACUTE PROMYELOCYTIC LEUKEMIA

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Background and Aims: Acute promyelocytic leukemia (APL) has distinct morphologic, biologic, and clinical features. Diagnosis is predominantly based on morphology which is characterized by presence of abnormal promyelocytes with bilobed nuclei and frequent Auer rods and a cytogenetic/molecular hallmark of t(15;17)(q22;q21) PML-RARA. APL patients account for 2-20% of pediatric AML. Aim of the study is to discuss immunophenotic profile of pediatric APL.
Methods: Children of age <18 years with APL diagnosed in the department of Laboratory Oncology were retrospectively analyzed. The diagnosis was made based on morphological, phenotypical, cytogenetic and molecular features.
Results: Out of total 302 paediatric AML patients, 30 (9.9%) were diagnosed as APL (median age-8.5 years, range 1 year -18years, M:F-2.3:1). Common presenting symptoms were fever (83.3%) and bleeding (73.3%). Median Hemoglobin was 68 g/L(range:3.9- 10.3g/L), TLC was 11. 82x10⁹/L (range:0.9-256.41x10⁹/L), platelets were 27x10⁹/L (range:6-182x10⁹/L) with peripheral blood and bone marrow promyelocyte percentage 76% (0-98%) and 90% (70-98%), respectively. Around 90% had classical hypergranular and 10% had hypogranular morphology. As per Sanz risk stratification, 14.3% had low, 25% intermediate and 60.7% high risk disease. On immunophenotyping, 24(80%) were CD34-HLADR-, 5(16.7%) were CD34+HLADR- and 1(3.3%) was CD34+HLADR+. All patients were positive for cMPO, CD13, CD33 and CD9. Other IPT marker as CD38, CD64, CD117, CD123, CD25, CD4, CD2, CD56, CD15, CD18,CD11b, CD19 and CD7 were positive in 96.6%, 89.7%, 83.4%, 55.2%, 50%, 31%, 25.9%, 20.7%, 16.7%, 10.3%, 10.3%, 10% and 6.7%, respectively.
Conclusions: APL constitute 9.9% of total paediatric AML in our cohort. All the cases were positive for cMPO, CD13, CD33 and CD9. A combination of cMPO, CD34, HLADR, CD117, CD33, CD15, CD11b/CD11c, CD9, CD18 with CD45 can diagnose APL with high specificity and sensitivity by excluding other hypergranular AML and also in cases with CD34 and HLA-DR negative cases of AML that can pose a diagnostic dilemma on morphology or on flow-cytometry.

EP089 / #1480

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

ANALYSIS OF BOSUTINIB FOR CHRONIC MYELOID LEUKEMIA IN THE MULTICENTER, PROSPECTIVE OBSERVATIONAL STUDY OF PEDIATRIC CHRONIC MYELOID LEUKEMIA (JPLSG CML-08)

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Background and Aims: Bosutinib is a second-generation tyrosine kinase inhibitor (TKI) indicated for treatment of chronic myeloid leukemia (CML) in adult patients. The safety and efficacy of bosutinib in pediatric patients have not yet been evaluated, except for only one pediatric patient reported. In this study, we report cases of chronic phase (CP) CML treated with bosutinib as a sub-analysis of the Japan Pediatric Leukemia/Lymphoma Study Group (JPLSG) CML-08 study.
Methods: The JPLSG CML-08 study enrolled 78 patients with CP CML under 18 years of age diagnosed between October 2009 and September 2014. Among them, 9 patients were treated with bosutinib.
Results: The median age at diagnosis was 11.1 (4.0-17.0) years. Males and females were 7 and 2, respectively. the 1st-line TKIs were imatinib (n=8) and dasatinib (n=1). The median age at start of bosutinib was 15.1 (7.7-21.5) years. The patients were treated with bosutinib as the 3rd-line (n=6), the 4th-line (n=2), and the 5th-line (n=1). The reasons of changing the TKI were resistance (n=6) and intolerance (n=3). The median starter dose was 79 (50-410) mg/m^2 and the median maximum dose was 320 (250-400) mg/m^2. The median duration of bosutinib administration was 27 (5-40) months, with 5 patients continuing bosutinib and 4 switching to other TKIs (3 resistant, 1 intolerant). BCR-ABL1 mutation analysis was performed in 6 patients before bosutinib administration, and 35bp insertion could be observed in exon 8/9 of 3 patients. Grade 3 toxicities, such as hypertension, elevated liver enzyme, creatine kinase and phosphorus levels, as well as grade 1/2 toxicities, such as diarrhea, rash, musculoskeletal pain, abdominal pain, headache, fever, elevated bilirubin, and hematotoxicity (anemia and neutropenia), were reported.
Conclusions: Adverse event profile was similar to the adult one. Bosutinib demonstrated manageable toxicity in the treatment of CP CML patients.

EP090 / #666

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

CLINICAL PROFILE, CYTO-MOLECULAR ANALYSIS AND OUTCOME OF PEDIATRIC ACUTE MYELOID LEUKEMIA: A REPORT FROM TERTIARY CARE HOSPITAL IN RESOURCE-CONSTRAINED SETTING

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Background and Aims: Despite the advancements in diagnostic techniques and discovery of newer chemotherapeutic agents, the outcome of acute myeloid leukemia (AML) remains dismal. The objectives of this study were to investigate clinical profile, cyto-molecular analysis, and survival outcome of pediatric AML.
Methods: This prospective study was carried out from October 2018 to December 2020 in a tertiary care hospital. Karyotype and cytogenetics analysis was done to identify chromosomal aberrations and PCR, RT-PCR, and fragment analysis were utilized for targeted molecular panel.
Results: A total of 70 patients of AML aged ≤18 years were enrolled in this study. The median age in this cohort was 6 years (IQR; 3,6 years), and males were predominant. About one-fifth of patients had malnutrition. The median duration of symptoms before presentation to the hospital was 25 days (IQR; 10,45 days). Fever was the commonest symptom, followed by bleeding, pallor, proptosis, and fatigue. The cytogenetic analysis revealed abnormal karyotype/cytogenetics (AKC) in 45 (64.3%) patients and normal karyotype/cytogenetics (NKC) in 25 (35.7%). The common chromosomal abnormalities were t(8;21) translocation (31.42%), monosomy/deletion 7 (7%), complex karyotype (4%) and monosomal karyotype (2%). AML-ETO fusion (37%) and CBFB-MYC11 gene fusion (2%) were detected by RT-PCR and FLT3-TKD (1.5%) by PCR. Fragment analysis revealed NPM1(7%) mutation and FLT-ITD (8%). The remission was achieved in 90.5% of enrolled patients post-induction-1. The median follow-up period of our patients was 221 days (IQR 28;415 days). The median event-free survival (EFS) in all patients was 11 months (95% CI, 5-12.5). The three-year overall survival probability (pOS) was 57% in all patients.
Conclusions: The delayed seeking to a health care facility and malnutrition are still prevalent in developing countries yet the overall survival has increased considerably. The majority of patients had AKC. The paucity of survival data in pediatric AML from developing countries lays out the importance of the conducted study.

EP091 / #1548

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

CHRONIC MYELOID LEUKEMIA IN LMICS- CHANGING PARADIGM OF CARE-LOOKING BEYOND TYROSINE KINASE INHIBITORS

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Background and Aims: There has been a paradigm shift in the management of chronic myeloid leukemia (CML) after the introduction of tyrosine kinase inhibitors (TKIs). In LMICs, it remains a less focused area. This study was aimed to investigate the clinical presentation, evolution in the management with the availability of generic forms of second-generation TKIs, and reasons for poor compliance.
Methods: A retrospective study was performed, and all the patients with CML from January 2015 through January 2022 were reviewed.
Results: Twenty-seven patients diagnosed with CML were included in the study. The mean age was 8.8 years (range 2.5-14 years). The most common symptoms were abdominal distension (100%), pallor (100%), and fever (89%). All the patients were positive for BCR-ABL1 (p210) fusion transcript, detected by RT-PCR. The most common presentation was CML-chronic chase (CP) 22 (81%), and 5 (19%) de novo blast crisis (BC) [de novo lymphoid BC (n=3), extramedullary lymphoid BC (n=1), and myeloid BC (n=1)]. There was progression in two patients with CML-CP, one to each lymphoid and myeloid BC. Imatinib was the 1st line in all cases earlier and recently shifted to 2nd generation TKI as 1st line for BC. Two patients with the suboptimal response received 2nd generation TKIs. The treatment for all the patients with BC included chemotherapy and TKI. The transplant could be performed on only one patient with progression. Five patients with BC and one with CP expired. Non-compliance to follow-up as well as to medication was a major issue. The reasons for non-compliance include unawareness, distance, social issues, drug availability, and financial constraints. This issue has been tried to be resolved by teleconsultation recently.
Conclusions: Compliance with follow-up and drugs is an important issue in LMICs. Repeated counseling, increasing awareness among the medical community and the patients, and telemedicine remain the mainstay of improving follow-up and compliance.

EP092 / #672

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

MOLECULAR EVALUATION OF GENE MUTATION PROFILE AND COPY NUMBER VARIATIONS IN PEDIATRIC ACUTE MYELOID LEUKEMIA

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Background and Aims: Cytogenetically normal acute myeloid leukemia (AML) is currently categorized as intermediate-risk, yet this group is quite heterogeneous. The objectives of this study were to investigate the mutation profile of targeted genes and copy number variations (CNVs) in normal karyotype and normal cytogenetics (NKC) AML and correlate it with treatment response.
Methods: This prospective study was conducted from October 2018 to December 2020. The next-generation sequencing (NGS) (30 gene panel) and chromosomal microarray analysis (CMA) using Affymetrix Cytoscan 750 K GeneChip were performed in NKC-AML.
Results: A total of 94 patients aged ≤18 years were screened. After excluding 24 patients, 70 patients with AML underwent conventional karyotyping/cytogenetic analysis. Forty-five (64.3%) had abnormal karyotype/cytogenetics (AKC) and 25 (35.7%) had NKC. Twenty-three out of 25 NKC-AML were further processed for gene mutation profile and CNVs using NGS and CMA, respectively. Twenty-two out of 23 (95.7%) patients were detected to have mutations in various genes. The common mutations were: NRAS (5), NPM1 (4), CEBPA (4), KRAS (3), KIT (3), RUNX1 (2), NOTCH1 (2), WT1 (2), GATA1 (2), FLT3 (2), GATA2 (2), KMT2D (2), FLT3-TKD (2), PHF6 (2). Copy number variations (CNVs) were detected in nine patients (39%), and the 4 (17%) had increased total homozygosity. A long contiguous stretch of homozygosity was detected on ch 9, ch11, and ch19. The gains were observed on ch 8, 9, 14, 19, 21, and 22, and the losses were seen on ch 7 and 10. The gains were more common than losses (8 vs 2). Monosomy was observed in three patients. Post-induction-1, 86% patients achieved remission.
Conclusions: NKC-AML patients have genetic abnormalities that can be detected by more advanced techniques like NGS and CMA. These genetic abnormalities play a role in risk stratification that may remain hidden in otherwise NKC-AML and eventually confer a poor prognosis.

EP093 / #968

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

EFFICACY OF POST-TRANSPLANT PROPHYLACTIC THERAPY IN CHILDREN WITH HR AML DEPENDING ON MRD STATUS BEFORE ALLO-HSCT

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Background and Aims: Relapse of AML remains one of the main causes of mortality after allo-HSCT. The role of prophylactic therapy after allo-HSCT has not been determined, especially with dependence on MRD(±) status before allo-HSCT in children with AML. One of the options for relapse prophylaxis in this case is usage of DLI±hypomethylating agents. The aim: studying the effect of anti-leukemia prophylaxis on overall and relapse-free survival (OS and RFS) of children with AML, depending on the MRD(±) status before allo-HSCT.
Methods: The retrospective analysis included 57 patients (pts.), age 0.5-18 years, who were in MRD(+) or MRD(-) AML remission at the time of allo-HSCT. Patients with primary graft failure, relapse within 2 months after alloHSCT, GVHD 2-4 grade who didn't allow performing prophylaxis of disease recurrence were excluded from analysis. Post-transplant prophylaxis of AML received 16 pts.: 1. 5-azacytidine 20-70 mg/m^2 from 3 to 5 courses in 7 (44%) pts, 2. DLI in 6 (37%) pts (total CD3+/kg dose was 1,5x10^6- 2x10^8), 3. DLI + hypomethylating agents in 3 (19%) pts. Patient's characteristics, including remission status, intensity of conditioning regimen, donor type, stem cell source, GVHD prophylaxis in groups with/without post-transplant AML prophylaxis were comparable.
Results: Median follow up is 68 months. Post-transplant prophylaxis of relapse in pts with MRD(+)status before allo-HSCT increased RFS - 100% vs 36.4% without post-transplant disease prophylaxis (p = 0.008), but did not affect on OS - 87.5% vs 92%, respectively (p = 0.268). In high risk AML pts with MRD(-) post-transplant prophylaxis of relapse had no effect on OS - 88.7% vs 100% (p = 0.083) and RFS - 87.5% vs 92 % (p = 0.671), respectively.
Conclusions: Post-transplant prophylaxis of relapse is advisable in children with AML with MRD(+) before allo-HSCT.

EP094 / #1528

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

RESULTS OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION WITH REDUCED-INTENSITY CONDITIONING REGIMEN IN PEDIATRIC CHRONIC MYELOID LEUKEMIA PATIENTS FAILING FIRST- AND SECOND-GENERATION TYROSINE KINASE INHIBITORS THERAPY

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Background and Aims: While tyrosine kinase inhibitors (TKIs) are first-line therapy in children with chronic myeloid leukemia (pCML), allogeneic hemopoietic stem cell transplantation (allo-HSCT) remains the only curative option in spite of associated toxicity/mortality. This study evaluates efficacy and toxicity of allo-HSCT with reduced-intensity conditioning (RIC) in patients with pCML.
Methods: Among 50 pediatric patients with a median age of 12(1-18) years 15(30 %) did not respond to first- and second-generation TKIs and were included into allo-HSCT cohort. At the moment of allo-HSCT patients achieved complete hematologic (CHR; 13/15, 86%) and cytogenetic response (CCyR; 7/15, 46%). None of the patients had complete molecular response (CMR), 2 were non-responders. In 4 cases BCR-ABL kinase domain mutations were found; T315I mutation in 3 cases, M244V and M351 mutations in 1 patient with lymphoid blast crisis. In 1 case DDX41 mutation was found. Most (14) patients received RIC prior to grafting with bone marrow (n=7) or peripheral blood stem cells (n=8) from matched related (n=4), matched (n=7) or mismatched unrelated (n=3), and haploidentical (n=1) donor. Calcineurin inhibitors-based GVHD prophylaxis in 6 and post-transplant cyclophosphamide-based one in 9 patients.
Results: Thirteen (86%) patients engrafted on a median of D+19(D+11-D+23). In 2 cases a second allo-HSCT was performed after primary graft failure, then in 1 a third one due to second graft failure (SGF). On D +100, 13 pts (86 %) achieved a CHR and CCyR, with 9 (60 %) patients also reaching CMR. Four patients received donor lymphocyte infusions due to molecular relapse (n=3) or SGF(n=1). With a median follow-up of 90 months the overall survival was 80%. Three patients died due to acute (n=1) or chronic (n=1) graft-versus-host disease, infection (n=1).
Conclusions: Allo-HSCT with RIC is an effective and relatively safe therapeutic modality in patients with pCML failing to achieve response to first- and second-generation TKIs.

EP095 / #1533

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

NEW ANTIGENS FOR A CAR-T THERAPY IN JUVENILE MYELOMONOCITIC LEUKEMIA

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Background and Aims: Juvenile myelomonocytic leukemia (JMML) is a rare leukemia with high morbidity and mortality, whose only curative option at present is hematopoietic stem cell transplantation. CAR-T Therapy against CD19 antigen has obtained impressive results in patients with acute lymphoblastic leukemia. Given that CAR-T therapy has significantly lower development costs and time than other conventional therapies, translational research with this advance therapy in rare diseases such as JMML presents a great opportunity. In this work we identified potential cell surface antigens differentially associated with tumors in JMML, good candidates for a CAR-T therapy.
Methods: Using Gene Expression Omnibus database we selected 2 published RNAseq data from hematopoietic stem cells in a cohort of 11 JMML patients and 9 controls (GSE111895 and GSE183252 series). Next, we performed a differential expression analysis with edgeR using an FDR (False Discovery Rate) < 0.05 as a threshold. Different bioinformatic tools, such as The in silico Human Surfaceome and The Human Protein Atlas, were used to select those cell surface proteins that are not highly expressed in healthy tissues.
Results: We identified around 1,000 differentially expressed genes in HSC from patients and controls. Of these, 700 overexpressed proteins on the cell surface were identified. In order to identify specific antigens, we analyzed the expression of the 30 best candidates in healthy tissues using in silico tools, selected the genes with low or undetected mean expression in 44 healthy human tissues, and identified the best ones for a potential CAR-T therapy in JMML, such as VNN1, GPR174 or MILR1.
Conclusions: The proteins identified in this study are potential candidates for a CAR T therapy in JMML. This therapy would be of great benefit for patients with this type of severe leukemia, with limited treatment options and very poor outcome.

EP096 / #2006

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

PEDIATRIC ACUTE MYELOID LEUKEMIA – OUTCOME FROM A GOVERNMENT FACILITY IN NORTH INDIA

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Background and Aims: Childhood AML is a heterogeneous disease with survival of >70 % in developed countries. In developing countries, it varies from 25-55%. We evaluated the profile and outcome of childhood AML at our centre.
Methods: Prospectively collected data from April-2017 to March-2022 is reported. Children aged 0–18 years diagnosed with AML & MPAL were included. Children presenting at relapse were included. Treatment consisted of 2 cycles of cytarabine with anthracycline followed by high dose cytarabine based intensification. APML was managed as per PETHEMA 2005 protocol. Relapsed AML was managed with 2 cycles of FLAG followed by bone marrow transplantation. Venetoclax-Azacytidine was used in those either refractory to FLAG or not fit.
Results: 47 patients with AML (AML: 36, APML: 8, MPAL: 3) were included. 3 children with relapsed AML were referred here for further treatment. Median age of 8.5 years (0.4-18 years), M:F 1.6:1. Of 44 denovo cases, 9 children had high-risk, 18 had intermediate and rest had favourable -isk genetic profile. FLT3-ITD was noted in 8. 1 had RAM phenotype. All achieved morphological remission at end of induction. 4 children died during induction and 3 died during intensification following sepsis. 2 children of other causes (GATA2 def, cardiac arrhythmias). 7 children discontinued treatment and 7 relapsed. Out of 3 relapsed patients, 2 continued to be refractory post relapse chemotherapy and one child with APML in CR3 with no sibling donor underwent autologous BMT 2 years ago and remains in CR. 26 children are alive and in complete remission (follow up 1 month-7 years post completion of treatment) 55% EFS was noted in the entire cohort. In APML, 7 are in CR; 1 LTFU. Response to Ven-Aza (n=3) was disappointing in relapsed settings.
Conclusions: The survival data of AML is sparse from LMIC. With standard protocols, more than 50% AML children survive the disease.

EP097 / #827

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

PATTERNS AND PREVALENCE OF INFECTION AND RELATED MORTALITY IN PEDIATRIC ACUTE MYELOID LEUKEMIA – A SINGLE CENTER EXPERIENCE FROM INDIA

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Background and Aims: Infection-related deaths remain a major cause of concern in the management of paediatric acute myeloid leukemia (AML). In India, unlike in the west, multi-drug resistant gram-negative organisms (MDRO) contribute significantly to treatment-related morbidity and mortality. Hereby, we report the patterns of infections and related mortality among paediatric AML patients receiving intensive chemotherapy at a tertiary care center in India.
Methods: Data collected from Electronic Medical Records of de-novo paediatric AML patients younger than 15 years who have received intensive chemotherapy from January 2014 to December 2019 were retrospectively analyzed. All patients received standard 3+7(Daunorubicin+Cytarabine) induction followed by 3-4 cycles of cytarabine-based consolidation chemotherapy. Azole-based anti-fungal prophylaxis was administered to all patients.
Results: A total of 277 patients were treated with 997 intensive chemotherapy cycles. Febrile neutropenia was observed during 65% of these cycles. Focus of infection included, gastrointestinal (n=121, 18.6%), skin and soft tissue (n=103, 15.8%), lung (n=95, 14.6%), paranasal sinuses (n=14, 2.1%) and none (n=272, 42%). Culture positive sepsis was seen in 140 (21.5%) patients, including gram-negative bacilli (n=108, 77%), gram-positive cocci (n=30, 21.4%) and fungi (n=2, 1.4%). An MDRO was in 44% of culture-positive sepsis, which was most commonly Klebsiella pneumoniae (56%). The incidence of proven/probable fungal infections was 7.5%. Overall, the incidence of sepsis-related mortality was 12.6% with the majority occurring during induction (7.2%). MDRO sepsis contributed to 75% of all sepsis-related deaths in induction.
Conclusions: Gram-negative sepsis, in particular, MDRO accounted for the majority of toxic deaths among paediatric AML at our centre. Hospital antibiotic stewardship programs along with the incorporation of novel treatment strategies including antibiotic cycling and granulocyte transfusions will help in curtailing MDRO sepsis.

EP098 / #1519

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

PROGNOSTIC SIGNIFICANCE OF METHYLATION PROFILE AND RNA EXPRESSION LEVEL OF WILMS TUMOR 1 GENE IN PRIMARY CASES OF ACUTE MYELOID LEUKEMIA

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Background and Aims: Acute myeloid leukemia (AML) is a genetically heterogeneous neoplastic disorder characterized by clonal expansion of myeloid precursor cells. Wilms tumor-1 (WT1) gene encodes a zinc-finger transcription factor involved in controlling cellular growth, differentiation, and proliferation of AML. There has been conflicting reports about association of WT1 gene expression with prognosis of AML. However epigenetic impact of WT1 is largely unknown.
Methods: This study aimed to investigate the RNA expression levels of the WT1 gene in BM and PB samples obtained from 69 AML patients (69 at diagnosis, 51 in hematological remission (day-28), and 9 relapse) using quantitative real-time PCR. The methylation status of the WT1 promoter was also analyzed using methylation-specific polymerase chain reaction (MSP) in all 69 cases at all time points. Finally, we correlated the methylation profile and gene expression level of WT1 gene to study the course of disease
Results: WT1 gene expression at the time of diagnosis, and relapse group were significantly higher when compared with the value at the time of remission or healthy control samples ($p = <0.001$). Moreover, higher levels of WT1 mRNA expression were found to be inversely correlated with normal hematopoiesis and positively associated with age, high marrow blast counts, M4 subtype, cytogenetic unfavorable risk groups, resistance to therapy, an inferior outcome, and a greater incidence of disease relapse compared to patients with low WT-1 mRNA expression. Robust hypermethylation of WT1 promoter was observed in 72% of cases of AML. Patients having hypermethylated profile of WT-1 gene had inferior relapse-free survival compared to normal WT1 patients. Significant positive correlations ($p<0.001$) between the WT1 expression and methylation levels with bone marrow blast counts at both initial diagnosis and after induction therapy was observed.
Conclusions: Together, these findings support that WT1 gene overexpression–hypermethylation signature is a distinctive feature that positively associates with the leukemic burden in AML.

EP099 / #1667

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

EXCELLENT REMISSION RATES AND SIGNIFICANT LESS TOXICITY WITH CHEMOTHERAPY-FREE APPROACH FOR ACUTE PROMYELOCYTIC LEUKEMIA (APL).

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Background and Aims: Acute Promyelocytic Leukemia (APL) in children is rare (5-7% of AML). Standard of care is a combination of chemotherapy with All-Trans Retinoic Acid (ATRA). There are limited data regarding chemotherapy-free approach using ATRA and Arsenic Trioxide (ATO) in children. This retrospective study shows our experience with chemotherapy-free approach in children with APL.
Methods: The study included children with APL treated at our department from 2012 until 2021. Efficacy was estimated by remission rates, while toxicity by hospitalization days and use of blood products.
Results: Ten patients were included, treated according to AML-BFM protocols. Mean age at diagnosis was 12.9 (range: 9-15) years and mean time of follow-up 3.5 (range: 0.5-9.5) years. Diagnosis was confirmed by cytogenetics and molecularly. Seven patients were stratified as standard and three as high risk. Hemorrhagic diathesis was present at diagnosis in all patients (mean platelet count: 36,670/μL, mean prothrombin time (PT) of 16.63 sec). Patients treated with ATO/ATRA attained PT normalization within two weeks (range: 5-14 days), significantly sooner compared to patients with chemo/ATRA (range: 25-40 days). All patients developed fever at least once during induction. None developed differentiation syndrome. Severe headaches and nausea, indicating pseudotumor cerebri, occurred in all patients treated with ATRA/ATO at induction and in one patient throughout treatment requiring prolonged and repetitive hospitalizations. All other patients continued treatment in outpatient basis. Initial hospitalization period for patients treated with chemo/ATRA was 40 days. Comparing transfusion requirements, total PLT and PRBC transfusions were statistically significant less in ATRA/ATO group ($p=0.016$ and $p=0.009$, respectively). On day 28, all patients achieved molecular remission and remain in remission up to last observation time point.
Conclusions: Our experience concurs with reported studies mainly in adults, showing high efficacy rates and acceptable toxicity profiles with ATRA/ATO treatment for pediatric patients with APL.

EP100 / #1230

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

EFFECT OF ANTIBIOTIC PROPHYLAXIS ON VIRIDANS GROUP STREPTOCOCCI BLOODSTREAM INFECTIONS IN DUTCH PEDIATRIC PATIENTS WITH ACUTE MYELOID LEUKEMIA: A TWO-CENTER RETROSPECTIVE STUDY

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Background and Aims: Viridans group streptococci (VGS) remain a prevalent cause of bloodstream infections (BSIs) during pediatric acute myeloid leukemia (AML) treatment. The associated high morbidity and mortality highlights the need to identify interventions to decrease VGS infections. We evaluated the effect of different prophylactic antibiotic regimens on the occurrence of (VGS) BSIs.
Methods: Medical records of 83 children (0-18 years) diagnosed with de novo AML at the Amsterdam UMC, location VUmc (n=42; January 1998-June 2018) and Princess Máxima Center (n=41; June 2018-March 2021) were studied. Within the study period, four consecutive treatment protocols were used. Pneumocystis jiroveci pneumonia prophylaxis included co-trimoxazole. Gram-negative prophylaxis with fluoroquinolones was introduced in 2006. Gram-positive prophylaxis comprised either no prophylaxis, penicillin, teicoplanin, or macrolides. BSI was defined as fever with a positive blood culture. Pearson's χ^2 test was used to test differences in proportions. Two-sided p-values ≤0.05 were considered statistically significant.
Results: Included patients underwent 323 chemotherapy courses, of which 21 (6.5%) were excluded because antibiotics were given therapeutically during the whole aplastic period (n=19), death during the chemotherapy course (n=1), or a treatment-related protocol violation (n=1). Of the 302 evaluable chemotherapy courses, 94 (31.1%) were given without prophylaxis, 137 (45.4%) with penicillin, 48 (15.9%) with teicoplanin, 10 (3.3%) with macrolides, and 13 (4.3%) with two different regimens, which were added to the above. The corresponding occurrence of BSIs and VGS BSIs, respectively, with these four prophylactic regimens were 68/102 (66.7%) and 25/102 (24.5%), 51/149 (34.2%) and 21/128 (14.1%), 3/51 (5.9%) and 0/51 (0%), and 7/13 (53.8%) and 2/10 (20%) ($p<0.0001$ and $p=0.001$).
Conclusions: The administration of teicoplanin antibiotic prophylaxis was significantly associated with a decrease in (VGS-associated) BSIs and seems a suitable and effective intervention in pediatric AML. A randomized trial in the NOPHO-DB-SHIP consortium is ongoing to address this important issue, including possible disadvantages of teicoplanin prophylaxis.

EP101 / #1525

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

INTRODUCING DIAGNOSTIC TESTING FOR CHRONIC MYELOID LEUKEMIA IN A PUBLIC HOSPITAL SETTING IN WESTERN KENYA

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Background and Aims: Chronic myeloid leukemia (CML) is a myeloproliferative disorder characterized by proliferation of the granulocytic cell line. The incidence of CML in Africa is estimated at 2,000 cases per year with children 0-19 years representing approximately 10% of the total cases. The disorder is associated with a poor prognosis without treatment. Tyrosine kinase inhibitors are approved for treatment in adults and children with confirmed disease. Diagnostic testing for CML in the public setting in Kenya is limited and not covered by the National Health Insurance Foundation (NHIF). We report the establishment of diagnostic testing for CML in the AMPATH Reference Laboratory (ARL) and Moi University Teaching and Referral Hospital (MRTH) in Eldoret, Kenya.
Methods: CML is characterized by the t(9;22)(q34;q11.2) resulting in a reciprocal exchange of ABL1 and BCR creating a chimeric fusion gene and protein with accelerated tyrosine kinase activity. Fluorescence in situ hybridization (FISH) methodology with the BCR/ABL1 probe set was applied to both peripheral blood and bone marrow smears. Patients with an elevated white count and clonal granulocytic proliferation were identified. Two slides of each specimen type were split for concordance studies between the ARL and the Indiana University School of Medicine FISH laboratory. Both laboratories followed the same protocol utilizing probes from the same vendor.
Results: Fifteen of 16 samples (94%) including both suspected cases and controls were concordant with WBC, hematological review and FISH results. There was one discordant peripheral blood specimen that was negative at ARL and positive in the Indianapolis FISH lab. Additional samples are under review at both laboratories.
Conclusions: Concordance studies reported here support the feasibility of diagnostic testing for CML in Western Kenya. Validated diagnostic testing is the first step to a rapid confirmation of CML and NHIF support for testing and tyrosine kinase inhibitor therapeutic coverage.

EP102 / #597

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

TREATMENT OF BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM IN PEDIATRIC PATIENTS WITH TAGRAXOFUSP, A CD123-TARGETED THERAPY

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Background and Aims: Blastic plasmacytoid dendritic cell neoplasm (BPDCN), a rare and aggressive hematologic malignancy, derives from plasmacytoid dendritic cells that overexpress CD123. Pediatric cases of BPDCN are uncommon, limiting available robust safety and efficacy data. A first-in-class, CD123-directed therapy, tagraxofusp (TAG, SL-401) is the only treatment approved by the FDA for patients aged ≥2 years with newly diagnosed (1L) and relapsed or refractory (R/R) BPDCN. TAG is also approved by the EMA for 1L treatment of adult patients with BPDCN. Herein we present safety and efficacy data of TAG therapy in pediatric patients with BPDCN.
Methods: Pediatric case reports of BPDCN were collected across the US and Europe. Data were summarized descriptively; analyses included tumor response, survival, and safety.
Results: Eight pediatric patients with BPDCN were treated with TAG. Median age was 15.5 years (range 2–21 years). All patients received 12 mcg/kg TAG throughout all treatment cycles [1–4 cycles], including a 2-year-old patient who also received 7 mcg/kg at second relapse. Five of eight patients experienced adverse events (AE): two had decreased albumin, two had increased transaminases, and one experienced capillary leak syndrome. All AEs were manageable and resolved. Three 1L patients achieved a complete response, one 1L patient showed partial response and one R/R patient had a minor response. One 1L and 1 R/R patient (each) had stable disease and one R/R patient had disease progression. Five patients were bridged to stem cell transplant following TAG treatment.
Conclusions: Here we expand the knowledge base of BPDCN treatment in pediatric patients. TAG treatment was tolerated in all patients, showing a manageable safety profile and promising efficacy that bridged 63% of our cohort to stem cell transplant.

EP103 / #899

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

PHARMACOGENETICS OF ABCB1, CDA, DCK, GSTT1 AND GSTM1 AND OUTCOMES IN A COHORT OF PEDIATRIC ACUTE MYELOID LEUKEMIA PATIENTS FROM COLOMBIA

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Background and Aims: Different studies have shown that ABCB1, CDA, DCK, GSTT1 and GSTM1 gene variants are related to drug toxicity in acute myeloid leukemia (AML) patients. Our aim was to identify the association between single nucleotide variants (SNV) in ABCB1, CDA and DCK and the presence or absence of GSTT1 and GSTM1 genes with clinical outcomes and toxicity in pediatric patients with de novo acute myeloid leukemia.
Methods: Fifty-one pediatric patients with confirmed de novo acute myeloid leukemia were included. We used a SNaPshot assay to evaluate ABCB1, CDA and DCK variants. GSTT1 and GSTM1 deletions were analyzed by conventional PCR. Clinical outcomes and toxicity associations were evaluated using odds ratios and Chi-square analysis.
Results: ABCB1 (1236G>A,rs1128503) GG genotype had a 6.8 OR (p 0.044) for cardiotoxicity. ABCB1 (3435G>A,rs1045642) genotype GG had a 4.51 OR (p 0.032) for transaminitis, genotype AA was a protective factor against relapse 0.69 OR (p 0.025). CDA (-451G>A,rs532545) and (79A>C,rs2072671) genotypes CC/AA were associated with increased risk for mucositis and liver toxicity 4.84 OR (p 0.016), while genotypes CT/CA were a protective factor against these adverse reactions 0.27 OR (p 0.026). For ABCB1 (1236G>A,rs1128503/2677C>A/T,rs2032582/3435G>A,rs1045642) combined genotypes AA/AA/AA, a strong association was found with death after HSCT 13.73 OR (p 0.009); combined genotypes and CDA (79A>C,rs2072671) or (-451G>A,rs532545) genotypes GG/CC/GG and CA/CT were associated with MRD >0.1. We did not find any association between GSTT1 and GSTM1 null alleles with clinical or toxicity outcomes in this cohort.
Conclusions: This is the first study of AML pharmacogenetics in Colombia, a country with a highly admix population. Our results highlight the importance of genetic analysis in pharmacogenetic response and suggest that pharmacogenetic profiles could be incorporated in the initial risk evaluation of Colombian pediatric patients with AML.

EP104 / #1016

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

GENOMIC ALTERATIONS AND OUTCOMES IN A PEDIATRIC ACUTE MYELOID LEUKEMIA COHORT FROM COLOMBIA

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Background and Aims: Few studies identifying genomic aspects in pediatric acute myeloid leukemia patients have been reported in Latin American countries. The aim of this study was to identify genomic alterations, clinical characteristics and outcomes in a cohort of pediatric patients with AML.
Methods: Patients with confirmed de novo acute myeloid leukemia until 18 years of age were included. Cytogenetics and conventional FISH analysis for t(8,21), Inv16, and KMT2A rearrangements, along with genomic analysis for 30 genes panel and 119 fusions by next generation sequencing and rapid testing for FLT3, NPM1 and CEBPA genes were performed. Genomic data was correlated with treatment response and outcomes.
Results: Fifty-one patients were analyzed, 67.4% had a cytogenetic abnormality. Genetic variants were identified in 74.5% of patients. FLT3 variants (ITD or TKD D835) were found in 14/51 patients (27.4%), followed by NRAS (21.6%), KRAS (13.7%) and WT1 and KIT (11.8%). Patients were stratified as high risk (66.6%) after the end of induction. During treatment, 96% of patients had at least one toxicity event. Twenty-two out of 33 (66%) patients who received HSCT had a related toxicity event. FLT3-ITD was associated with relapse and measurable residual disease >10 at day 21 11.25 OR (CI 1.89-66.72, p 0.006, and 10 OR (CI 1.61-62, p 0.018), respectively. NRAS was associated with death during induction 16.71 OR (CI 1.51-184.59, p 0.022).
Conclusions: To date, this is the first study in Colombian pediatric AML patients with a complete characterization from a clinical and genomic standpoint. Our study highlights the importance of a rapid and systematic incorporation of genetic analysis in pediatric AML in Colombia, as it directly affects treatment decisions and outcomes. The incorporation of targeted therapies with conventional chemotherapy is an increasingly urgent need in pediatric patients.

EP105 / #1843

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

A BRIEF OVERVIEW TO PEDIATRIC GRAY ZONE LYMPHOMAS

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Background and Aims: Gray zone lymphoma(GZL) is a rare B-cell lymphoma in childhood and adolescence, representing features between diffuse large B-cell lymphoma(DLBCL) and classical Hodgkin lymphoma. Due to its rarity, standard treatment options are lacking.
Methods: Herein, we describe three patients with GZL.
Results: Case-1: A 16-year-old female presented with cervical and supraclavicular LN swelling. The supraclavicular LN biopsy revealed a GZL(LBCL+cHL) with mediastinal, cervical, supraclavicular, axillary, and lung involvement (stageIII). The patient received chemotherapy according to the B-NHL BFM 2012. At the end of the therapy, PET-CT demonstrated a new axillary LN, which was shown to be a GZL(LBCL+HL). The patient received second-line treatment with 3×R-ICE followed by HD-BEAM with ASCT.She received brentuximab vedotin (BV) maintenance after ASCT. The patient has been in CR for 18 months. Case-2: A 14-year old female was admitted with cough and swelling of cervical LN. Initial diagnosis revealed classic HL, stage IIA. The patient received chemotherapy and radiotherapy according to the GPOH-HD 95. After eight months, she presented with axillary LN, and relapse was shown to be a GZL(LBCL+cHL).The patient received treatment with 3×B-IGEV followed by HD-BEAM with ASCT.She received BV maintenance after ASCT.The patient has been in CR for 18 months. Case-3: A 16-year-old male presented with cervical LN,and biopsy revealed a GZL(LBCL+cHL) with mediastinal, cervical, supraclavicular, and abdominal LN involvement(stageIII). The patient received chemotherapy according to the B-NHL BFM 2012. PET-CT demonstrated a complete remission at the end of the therapy, and he received involved-field irradiation.After two months, he relapsed with mediastinal, abdominal, and lung involvement. The LN biopsy was shown to be HL.The patient received 3×B-IGEV followed by HD-BEAM with ASCT. He received BV maintenance after ASCT.
Conclusions: GZL remains a therapeutic challenge.Most of the time, it has inferior outcomes compared to LBCL and HL and a tendency to relapse. Prospective studies evaluating effective treatment approaches are highly needed.

EP106 / #1425

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

AN EFFECTIVE COMBINATION THERAPY FOR THE TREATMENT OF PEDIATRIC PLASMA CELL MYELOMA TYPE POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER

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Background and Aims: Post-transplant lymphoproliferative disorder (PTLD) is a serious complication of immunosuppressive therapy following solid organ or hematopoietic cell transplantation. Here we report the first use of the CD38 monoclonal antibody daratumumab for the treatment of plasma cell myeloma (PCM) type PTLD in a pediatric patient. While the standard initial approach for PTLD is the reduction of immunosuppressive therapy with or without the addition of rituximab, the optimal therapy for PCM-PTLD is less clear.
Methods: We present the cases of three pediatric patients with PTLD including various degrees of plasma cell involvement and review their clinical and pathologic characteristics, therapeutic interventions, and outcomes. All data were acquired through review of the electronic medical record.
Results: Three pediatric patients were treated for plasma cell predominant PTLD at our institution between 2010-2020. The first (a 12-year-old female, status post heart transplant) and second (a 15-year-old female, status post heart transplant) received a standard rituximab-based approach and unfortunately relapsed, requiring additional chemotherapy. The third patient was a 9-year-old male, status post kidney transplant, who was diagnosed with PCM-PTLD (CD20 negative, CD38 positive) and treated with bortezomib, dexamethasone, and daratumumab. Despite the paucity of data governing the use of daratumumab in pediatric patients, our pediatric-adapted daratumumab administration approach allowed for safe administration of 4 cycles. This combined treatment regimen, including the anti-CD38 monoclonal antibody daratumumab, was safe, well-tolerated, and resulted in a sustained remission for 2 years.
Conclusions: In the third case for a pediatric patient, the combination therapy of bortezomib, dexamethasone, and daratumumab was well-tolerated and produced remission from PCM-PTLD. This treatment regimen is encouraging and supports further evaluation in larger studies, as well as further discussion of daratumumab maintenance therapy for the sustained remission of PCM-PTLD.

EP107 / #1770

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

INFRADIAPHRAGMATIC HODGKIN'S LYMPHOMA IN PEDIATRIC CANCER PATIENTS

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Background and Aims: Infradaiphragmatic Hodgkin's lymphoma (HL) is a rare disease occurring in <5% of pediatric patients. The prognostic impact of an infradiaphragmatic localization of this lymphoma is controversial.we aimed to evaluate the baseline clinicopathologic features, prognostic factors and outcome of pediatric patients with infradiaphragmatic HL diagnosed and treated at children cancer hospital 57357
Methods: Between 2007 and 2020, All patients with histologically confirmed clinical stage I/II infradiaphragmatic HL retrospectively were evaluated including clinical presentation, initial laboratories & radiological findings, response to initial treatment & their outcome in comparison with supradiaphragmatic stage I/II
Results: Among 999 Hodgkin's lymphoma staged I/II, there were 35 infradiaphragmatic HL patients with male to female ratio 2.5 :1, the mean age was 10 years, 28.6%(10/35) of cases were histologically NLPHL while 37.1% (13/35) were histologically Mixed Sclerosis CHL, 37%.1(13/35) of patients presented with B-symptoms, In 54.3%(19/35) of cases ESR was less 30, 62.9% of patients (22/35) did not receive Radiotherapy, 14.3% (5/35) of patients relapsed, Overall Survival was 87.7% while Event Free survival was 81.3% at 60 months, OS of the patient with negative interim PET/CT was 100% versus 50% in patients with inadequate response at 60 months with significant P-value:0.04.OS according to diaphragmatic site was highly statistically significant P-value: 0.009 (87.7% vs 98.3%) infradiaphragmatic HL versus supradiaphragmatic,Correlation of EFS according to diaphragmatic site was not statistically significant P-value:0.075 however infradiaphragmatic HL EFS was 81.39% which is still lower than supradiaphragmatic stage I/II 91.5% at 60 months.
Conclusions: in spite of infradiaphragmatic HL cases does not carry high risk features still this category of the patients has lower OS & EFS in comparison to patients who had supradiaphragmatic initial presentation which mandate further studies.

EP108 / #1499

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

IMMUNE CHECKPOINT INHIBITORS IN PEDIATRIC NON-HODGKIN LYMPHOMAS

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Background and Aims: The prognosis in pediatric relapsed or refractory (R-R) NHL is unfavorable; no matter what form of modern treatment is adopted. New treatment approaches need to be introduced.
Methods: We used CPIs in 11 children with R-R NHL. The median age was 12 (2–17) years. The distribution of the patients by diagnosis was as follows: PMBCL (n = 4), PTCL (n = 4), DLBCL (n = 1), LBL (n = 2). The median number of prior lines of therapy was 3 (2–5). Refractory NHL was observed in 7 cases, and 4 patients had had multiple relapses (≥ 3). Nivolumab was administered at a dose of either 1 mg/kg (n = 4) or 3 mg/kg (n = 3) every 2 weeks, Pembrolizumab - at a dose of 2 mg/kg every 3 weeks (n = 4). The median number of CPI doses received by the patients was 3 (1–12). In 7 patients, CPIs were administered as monotherapy, in 4 – in combination with cytostatic agents. Once remission was achieved, we used hematopoietic stem cell transplantation for consolidation.
Results: Response to the CPI therapy was observed in 4 out of 11 patients (complete response – in 2 patients); stabilization - 1 patient. Only patients with PMBCL (n=3) and PTCL (n=1) responded to the treatment. Two responders were PDL1-postive. At the median follow-up of 257 (13–1668) days, 6 patients were alive, with 4 of them remaining in durable remission.
Conclusions: This paper is one of the first reports on the successful use of CPIs in children with R-R NHL. PMBCL and PTCL turned out to be responsive to the treatment. This therapy can be used to achieve remission or possibly even cure in children whose only option would be palliative care if they were treated with standard approaches.

EP109 / #241

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

PROGNOSTIC SIGNIFICANCE OF PD1, PD-L1 EXPRESSION AND METABOLIC ACTIVITY ON 18F-FDG PET/CT IN REFRACTORY/RELAPSING PEDIATRIC HODGKIN LYMPHOMA

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Background and Aims: Hodgkin Lymphoma (HL) is a unique disease entity both in its pathology and the young patient population that it primarily affects. Several meta-analyses have demonstrated that high PD-L1 expression levels are correlated with adverse clinical and pathologic features. This study aims to evaluate the correlation between the expression of PD-L1 and clinicopathological features, as well as the prognostic significance of PD-L1 expression with regard to interim PET response in relapsing / refractory pediatric HL
Methods: We measured the expression of PD-1/PD-L1 in the baseline diagnostic samples of children with relapsing/ refractory classical HL. The results were correlated with the pathological subtypes as well as the clinical outcome in relation to PET response.
Results: Of the 88 included patients, 77% had advanced-stage HL. PD-1 expression was detected in 50% of cases, whereas PD-L1 (membranous) was expressed by tumor cells in 60% of the cases, and strongly expressed in 16% of cases. Notably, PD-L1 (cytoplasmic) was detected in 55% of the cases. There was a significant difference in the expression levels of PDL-1 between the different pathological subtypes ($p = 0.006$). OS of patients with PD-L1expression (Cytoplasmic) was 83% vs 91% in patients with absent expression ($P=0.001$). There was no prognostic significance of PD-L1 expression with regard to PET response ($p=0.31$).
Conclusions: Although PD-L1 expressions did not show statistical significance with well-established prognostic factors, our preliminary data indicate that pathological subtypes and cytoplasmic expression of PD-L1 may have a prognostic implication on survival in pediatric HL.

EP110 / #1006

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

HODGKIN LYMPHOMA. TEN YEARS EXPERIENCE FROM THE HELLENIC WORKING GROUP

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Background and Aims: Pediatric Hodgkin Lymphoma (HL) is the third most common childhood malignancy. Nowadays, it is a highly curable disease and this success is mainly related to the treatment risk-adaptive strategies applied. Aim:the retrospective study of the clinical-epidemiological data and survival-rate of pediatric HL during the last 10 years in Greece and the evaluation of possible late-occurring adverse events in this cohort.
Methods: We retrospectively reviewed data from the medical records of children diagnosed, treated, and followed up in all the Pediatric Oncology Departments in Greece, during the period 2010-2020. Demographic, clinical, radiological, laboratory data, treatment protocol and follow-up data were evaluated. All patients were followed-up until the end of 2021. Distributions of Overall Survival (OS) and Disease-Free Survival (DFS) were assessed with Kaplan–Meier curves.
Results: Data were collected from 183 patients. Median age was 12.93 years (range: 3.62-20.45 years). The cohort study included 105 males and 78 females. The most common subtype was nodular sclerosis in 132/183 (72.1%). Three patients (1,63%) had Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL). Seventy-six patients (41.8%) were diagnosed with early-stage disease, while 106 (58.2%) with advanced stage. B symptoms were present in 39/183 (21.3%). Since 2013, all patients in Greece were treated according to the EURONET-PHL protocol, 134 (82.2%) patients with EURONET-PHL-C1 and 29 with EURONET-PHL-C2. A total of 179/183 patients are alive. Relapse occurred in 14/183. Second malignancies are reported in 4 patients, 2 solid tumors (thyroid gland and breast) and 2 hematological malignancies (acute myelogenous leukemia). Endocrine abnormalities (abnormal thyroid function and gonadal dysfunction) were reported in 17.7% of the patients with available data. Overall survival for the whole cohort was 97.8% and DFS was 90.7%.
Conclusions: Excellent survival outcome has been achieved, in this cooperative Greek study. Longer follow-up will give valuable insight in the long-term outcome and late toxicity in order to optimize first-line and relapse treatment.

EP111 / #908

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

ANAPLASTIC LARGE CELL LYMPHOMA, EXPERIENCE IN 28 YEARS OF A PEDIATRIC CENTER IN ARGENTINA

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Background and Aims: Anaplastic large cell lymphoma (ALCL) represents 10 to 15% of pediatric Non-Hodgkin lymphomas (NHL). Different clinical, pathological and molecular characteristics are still being evaluated as prognostic factors. To analyse clinical and biological characteristics and therapeutic response of pediatric patients diagnosed with ALCL.
Methods: retrospective review analysis of clinical records of patients with ALCL from January 1994 to January 2022. Diagnosis confirmed according to WHO criteria. Clinical, histopathological and treatment data were collected. Therapeutic schemes based on BFM90 and ALCL99 protocols. Statistical analysis: SPSS 20.0 Software.
Results: One hundred forty patients with NHL were admitted, 18 patients (12.8%) with ALCL. Fifteen patients were evaluable, median age 7.9 years old (r3-15.3), 53% male. Median follow-up: 4.1 years (IQR0.3-9.2). Eleven patients (73%) presented B symptoms. Nodal commitment (100%). Most affected areas were: cervical, mediastinal and abdominal. Twelve patients (80%) presented extranodal involvement. Twelve patients presented advanced stage (III/IV) according to St.Jude staging system. Four patients presented Karnofsky Score (KPS) <50, this being a factor associated with lower OS compared to those with KPS ≥50 (OS 25% vs 90%, p0.013). Eight patients had LDH >500 IU/L. ALK determination in 11 patients: ten positive and one negative. Twelve patients (80%) achieved full remission. One patient (6.6%) relapsed 4 years after diagnosis, undergoing second line treatment and autologous hematopoietic stem cell transplantation Four patients (26.6%) died within first months of treatment: 2 due to infectious complications; one due to disease progression refractory to treatment; and another due to respiratory failure during prephase. The 5-year OS for this group was 73% and the EFS was 64%.
Conclusions: the incidence and OS of ALCL was similar to that reported. Deaths were observed in the first months of treatment. KPS<50 at admission was associated with poorer survival. Early clinical suspicion, timely diagnosis and adequate clinical support determined the evolution in this population.

EP112 / #1052

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

MICROBIOLOGICAL PROFILE OF BLOOD STREAM INFECTIONS IN PEDIATRIC CANCER PATIENTS AT KAMUZU CENTRAL HOSPITAL, IN LILONGWE, MALAWI

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Background and Aims: Febrile neutropenia is a serious treatment-related complication. There is scant literature on the microbiological profile of bloodstream infections (BSIs) in pediatric cancer across Sub-Saharan Africa (SSA).
Methods: A cross-sectional study from January 1, 2019, to December 31, 2021, of pediatric cancer patients aged <16 who had a peripheral blood culture performed. Routine bacteria identification and antibiotic susceptibility testing of bacterial isolates were performed. Patient file or database reviews were conducted on all patients with BSIs to determine clinical outcomes.
Results: Microbiologically confirmed BSIs were observed in 30(15%) of the 196 peripheral blood cultures performed. The mean age was 7 years (SD ±3.6) and 18(62%) were male. Patient files were reviewed in 24/30(80%) and the remaining 6/30(20%) clinical files were missing, so data was obtained from a database. Nineteen of 30(67%) BSIs were identified in patients with leukemia or lymphoma. Thirteen of 24(54%) patients had received >48 hours of antibiotics before blood culture collection. Thirty-seven bacterial isolates were identified, including 5 patients with multiple isolates. Gram-negative organisms were identified in 28(75%) of 37 isolates [9(32%) Klebsiella spp., 4(14%) Escherichia coli, 3(11%) Pseudomonas; and 12(43%) other]. Majority of gram-negative isolates were resistant to ceftriaxone (15/28,53%), but sensitive to piperacillin-tazobactam (3/3,100%) and meropenem (24/28,86%); and 8 multi-drug resistant (MDR) isolates sensitive to meropenem only. Gram-positive organisms were identified in 9(24%) of 37 isolates [7/9(78%) staphylococcal spp.; all resistant to penicillin]. Sixteen (53.3%) of 30 patients with a BSI died within 2 weeks of the culture.
Conclusions: BSI are common among pediatric cancer patients in Lilongwe, Malawi, with increased MDR bacterial isolates and high mortality. This study is limited by pre-treated cultures and incomplete data. Future prospective studies comprehensively looking at BSI among febrile neutropenic patients are urgently needed to improve clinical care and outcomes.

EP113 / #1162

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

OEPA/COPDAC THERAPEUTIC REGIME IN CHILDREN WITH ADVANCED-STAGE HODGKIN LYMPHOMA AND OMISSION OF RADIOTHERAPY IN ADEQUATELY RESPONDING PATIENTS: EXPERIENCE FROM A TERTIARY CARE CENTER IN MÉXICO.

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Background and Aims: Although the majority of children and adolescents diagnosed with advanced-stage Hodgkin lymphoma will achieve remission and cure, it has been associated with significant long-term side effects. The objective of this study is to describe the results of the use of the OEPA/COPDAC therapeutic regimen in patients with high-risk Hodgkin's lymphoma. In addition to investigating whether radiotherapy can be safely omitted in patients with an adequate response.
Methods: A retrospective study of patients younger than 18 years with high-risk Hodgkin's lymphoma, was done from January 2017 to February 2022 in a tertiary care center in Mexico
Patients received 2 cycles of OE*PA (vincristine, etoposide, prednisone, and doxorubicin) and 4 cycles of consolidation therapy with COPDAC (cyclophosphamide, vincristine, prednisone, and dacarbazine). Radiation therapy was omitted in patients with complete remission to induction chemotherapy.
Results: Twenty-one patients were included. The mean age at the presentation was 11.6 years, male predominance (61.9%), B symptoms were present in 61%, bulky disease in 71.4%, and CHIPS score of 3 in 33%. Histopathology was reported: mixed cellularity 57.2%, nodular sclerosis 38.1%, and rich in lymphocytes 4.7%.
After therapy with 2 cycles of OE*PA, 81% had complete remission, so radiotherapy was omitted and consolidation therapy was continued. Only 19% had partial remission, so involved-field radiotherapy was started at a dose of 25 Gy.
With a median follow-up of 36 months, we had 0% abandonment of therapy, 0% relapses and progressive disease, and no deaths. Overall survival and event-free survival were 100%. NCI-CTC grade 2 and 3 hematologic toxicities were observed in 9.5% and 38% respectively. NCI-CTC grade 1 sensory neurotoxicity was 42.8%.
Conclusions: The OEPA/COPDAC regimen is well tolerated with acceptable toxicity; radiotherapy could be omitted in patients with an adequate response to intensified induction, avoiding late repercussions; however longer follow-up is needed.

EP114 / #1670

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

EVOLVING CLINICAL EPIDEMIOLOGY OF PEDIATRIC BURKITT/MATURE B CELL LYMPHOMA IN SUB-SAHARA AFRICA (SSA) AND INTENSIFICATION OF CHEMOTHERAPY TO IMPROVE OUTCOMES

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Background and Aims: Mature B Cell Lymphoma (MBCL) is the commonest lymphoma in children, with survival in SSA lower than in high-income countries. This study aimed to demonstrate the evolution of clinical phenotypes and the feasibility and benefit of chemotherapy intensity escalation for MBCL to improve children's survival in the SSA setting.
Methods: From March 2019 to December 2021, children under 18 years with MBCL were diagnosed using standard WHO criteria and risk-stratified by BFM criteria. The treatment strategy was to escalate chemotherapy intensity methodically and serially from traditional low-dose regimens used in SSA to higher intensity BFM-based regimens. Children were followed prospectively for clinical outcomes. We evaluated the distribution of clinical phenotypes and compared response, treatment-related mortality (TRM), and survival by chemotherapy protocol using Kaplan-Meier survival analysis.
Results: Fifty-six children were included in the analysis, with a median age at diagnosis of 8 years, and 64% were male. Fifty-two (92.9%) had Burkitt lymphoma, while 7.1% had Diffuse Large B Cell lymphoma. The abdomen was the commonest disease site at 71.4%, while jaw masses accounted for 17.9%. The distribution of risk strata (based on Murphy Stage and LDH) was 83%, 15%, and 2% for high, intermediate, and low risk, respectively. The initial 13 patients (23.2%) received the 1g/m^2 methotrexate regimen with 30.8%(4) remissions, 0.08%(1) TRM, and 38.5% and 23% 1-year overall and relapse-free survival, respectively. We then escalated therapy for the subsequent 31 children to include doxorubicin (50mg/m^2), with 48.4%(15) remissions, 0.1%(3) TRM, and 74% and 70% 1-year overall and relapse-free survival, respectively.
Conclusions: MBCL in SSA is predominantly high-risk abdominal Burkitt lymphoma warranting higher intensity chemotherapy. Escalation of BFM-based chemotherapy was safe and resulted in improved outcomes in our experience. Future goals are to continue this diagnostic, risk stratification, and chemotherapy escalation strategy and disseminate it to other centers in SSA.

EP115 / #760

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

APPLICATION OF WEIBULL AFT PARAMETRIC REGRESSION MODEL ANALYSIS FOR PATIENTS WITH AGGRESSIVE LYMPHOMA IN AMPATH KENYA

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Background and Aims: Most models used in survival analysis assume a distribution-free model meaning no assumption has to be made about the survival times distribution. Approximating the survival distribution that includes log-normal, log-logistic, exponential, and Weibull distributions, we can employ parametric failure time analysis in parametric survival models. We aim to examine the use of the Weibull model in the parametric-failure analysis of children with NHL-B in a case of western Kenya.
Methods: A retrospective review of records that collected data that included clinical data, diagnostic procedures as well as treatment outcomes. Multivariate regression analysis was performed and the possible prognostic factors were put in the Weibull model and the Cox proportional hazard model. The Akaike Information Criterion (AIC) was used to find the best-fitted model.
Results: The prognostic factors included in the Weibull model gave more accurate estimates than the estimates from the Cox model. The AIC showed that the data fit the Weibull model better than the Cox model (218 and 230 respectively). Comparing the parametric and the Weibull regression models, the Weibull model fitted well with the non-parametric model. The hazard rates for age (1.088;95% CI, 0.9942-1.1343 and 1.082;95% CI, 0.9973 1.1430) and sex (1.889; 95% CI, 0.3873 1.6500 and 1.870;95% CI 0.4373 1.8681) are more than 1 both in the multivariate Weibull and Multivariate Cox models respectively implying that there is an increased risk of mortality from BL as age increases same as the sex.
Conclusions: The Cox model assumes a proportional hazard model and is distribution-free implying that if the assumption doesn't hold, then the model is likely to lead to unreliable conclusions. Thus, in cases where the distribution of population survival data is likely to be identified, a parametric approach to the accelerated failure time analysis is more powerful compared to the semi-parametric and non-parametric methods.

EP116 / #762

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

A TIME SERIES ARIMA MODEL APPROACH TO FORECASTING THE PREVALENCE OF BURKITT'S LYMPHOMA IN AMPATH KENYA

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Background and Aims: A time-series study determines the probable model and predicts its values in the future to facilitate statistical analysis of the variables based on time. Prevalence and incidence of cancers are getting increased with aging and population growth; thus, this study aims to predict the prevalence rate per 100 population of aggressive lymphoma in children in a case study of western Kenya using time series models.
Methods: Retrospective review of NHL-B cases from May 2018 to August 2020. The time variable was each month of the study years and using the number of daily registered cancers in each month, the time series of the monthly period prevalence rate per 100 population was designed. ARIMA methods were used to design a probable prediction model based on the autocorrelation model (ACF) and partial autocorrelation model (PACF). The goodness of fit of the final model was assessed using Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and Box Ljung.
Results: The model parameters namely, the p and q parameters were estimated as 0 and 1 respectively and the best ARIMA model was considered as ARIMA (p=0, d=1, q=1) that only had 1 moving average component and a difference of 1. This model had the least AIC (114.59) and BIC (117.73). The number of NHL-B cancer cases in May 2018 was 3 with a prevalence rate of 4.615. This study showed that the rate in February 2025 will be increased to 355 (95% CI, 276.35518 - 434.9839) based on forecasting with the ARIMA model.
Conclusions: The increasing trend of NHL-B will be continued which is considered based on the ARIMA method result. These results suggest that analyzing a time series ARIMA model helps to prognosticate the prevalence of NHL-B and improve the forecast precision.

EP117 / #509

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

EFFECTS OF TUMOR LOCALIZATION ON THE SURVIVAL FOR NHL-B

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Background and Aims: In sub-Saharan Africa, Burkitt lymphoma; an aggressive cancer of B lymphocytes with high mortality in low-income countries is a disease of children. We aim to evaluate the relevance of primary tumor location as a prognostic factor in the survival of patients with BL.
Methods: Retrospective review of histological cases diagnosed and confirmed BL in infants from 2018 to 2021 (n=65). Patients were categorized by primary tumor site into abdomen (80%, n = 52), jaw (18.46%, n = 12), and jaw and abdomen (1.54%, n = 1) groups. Subgroup analysis was used for comparative analysis of Event-free survival (EFS) and overall survival (OS) rates.
Results: Fifty-two patients (80%),12 patients (18.46%), and 1patient (1.54%) presented with abdominal, jaw, jaw-abdomen tumors respectively. Twenty-two patients (42.31%) with abdominal tumors had CR compared to 23 patients (44.23%) and 7 patients (13.46%) with PD and PR respectively. Six patients (50%) with jaw tumors had PD while 5 patients (41.67%) and 1 male (8.33%) had a CR and PR respectively. Thirty-four patients (65.38%) with abdominal tumors were alive, 16(30.77%) were deceased, and 2(3.85%) were LTFU. Six patients (50%) with jaw tumors were alive, 6 (50%) were deceased. Median EFS was 324 days (95% CI, 294-532) and median OS was 310 days (95% CI, 294-437). Median EFS for abdominal tumors was 320 days (95% CI, 294-539), jaw tumors were 324 days (95% CI, 229-502). Median OS for abdominal tumors was 310 days (95% CI, 294-497), jaw tumors were 324 days (95% CI, 294-502) and jaw-abdomen was 299 days
Conclusions: Tumor localization to the jaw is associated with an improved survival rate both from EFS and OS. Those localized to the abdomen had a worse survival rate compared with jaw tumors which may be due to biological differences between tumor sites.

EP118 / #645

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

PREVALENCE AND CHARACTERIZATION OF PEDIATRIC EBV-NEGATIVE POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER: SINGLE CENTER STUDY

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Background and Aims: Post-transplant lymphoproliferative disorder (PTLD) is the most common malignancy in pediatric post-solid organ transplant (SOT) patients. While the association of Epstein-Barr Virus (EBV) with the development of PTLD is well recognized, little is known about EBV-negative pediatric PTLD. Therefore, we aimed to characterize differences between pediatric EBV-positive and EBV-negative PTLD to better understand the pathogenesis of EBV-negative PTLD.
Methods: We retrospectively reviewed clinical data from SOT patients diagnosed with PTLD in a single pediatric center from 2005 to 2021. Data included demographics, SOT type, time from SOT transplant to PTLD diagnosis, PTLD site, histopathological morphology by WHO criteria, and tumor markers, including EBV. Cases were compared by tumor EBV expression using χ^2, Mann-Whitney, and Fisher's Exact tests.
Results: We identified 60 patients meeting the inclusion criteria. Of those, 25% (n=15) had EBV-negative PTLD while 75% (n=45) had EBV-positive PTLD. The distribution of sex and race/ethnicity did not differ by tumor EBV status. EBV-negative PTLD was more likely to occur in heart transplant patients (73.3% v. 42.2%, $p < 0.04$). The median interval (months) between SOT and PTLD diagnosis was longer in EBV-negative PTLD (105) than EBV-positive PTLD (28.5) ($p<0.02$). EBV-negative PTLD seemed more frequent in the gastrointestinal tract (42.9%) than EBV-positive PTLD (24.4%) ($p = 0.18$), while other sites were similarly distributed between the two groups. The distribution of morphologic subtypes did not differ overall between EBV positive and negative PTLD, but those with plasmacytic/plasmablastic features were more likely to be EBV-negative PTLD (33.3% v. 9.3%, $p<0.04$). Expression of CD30, CD20, or CD138 by immunohistochemistry did not differ by tumor EBV status.
Conclusions: Our single institution report suggests that EBV-negative PTLD exhibits distinct characteristics that differ from EBV-positive PTLD, especially in time from SOT to development of PTLD. Cooperative group research can help guide treatment for EBV-negative PTLD, particularly in those with plasmacytic/plasmablastic features.

EP119 / #780

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

REFRACTORY OR RELAPSED HODGKIN'S LYMPHOMA IN CHILDREN AND YOUNG ADULTS

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Background and Aims: Hodgkin's lymphoma (HL) is a pathology that can be cured in the first line in the majority of cases in children and young adults. The therapeutic failure rate found in the literature is 10% in the favorable group and 15 to 20% in the advanced stages. In our context, the salvage of refractory Hodgkin's lymphoma by chemotherapy followed by autologous hematopoietic stem cell transplantation sometimes remains difficult given the lack of resources that can delay treatment. The objective of our work is to draw up the clinical, therapeutic and evolutionary profile of patients refractory to the first line of treatment for Hodgkin's lymphoma.
Methods: This is a monocentric retrospective study, conducted over 7 years and 5 months (January 2011-May 2019) at the Casablanca hematology center. All patients aged under 21 with the diagnosis of Hodgkin's lymphoma were included.
Results: 19 patients were collected, 13 of whom were refractory to first-line treatment and 6 cases of relapse after a first complete remission, representing an overall rate of 12.7% and 6% respectively. In the table below, we summarize the characteristics of patients with primary failure. Relapsed patients had a median age of 12.5 years [10-18] and the median time to relapse was 24 months [15-69]. The latter were in the EORTC unfavorable prognosis group. In the first line, 5 patients had received the OEPPA/COPDAC protocol and one patient ABVD. As a catch-up protocol, 4 patients had received the ICE protocol and 2 the DHAP protocol. Five patients had undergone HSC autograft and at the final status 3 patients were put in maintained complete remission.
Conclusions: Catching up with refractory or relapsed Hodgkin's lymphoma leads to an increase in toxicity in this vulnerable population, which limits our therapeutic choices.

EP120 / #1722

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

CLINICAL FEATURES AND OUTCOMES OF ADOLESCENTS AND YOUNG ADULTS WITH B-CELL NON-HODGKIN LYMPHOMA MANAGED IN AN UNDERPRIVILEGED SETTING: A MULTICENTER COHORT STUDY

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Background and Aims: There is a paucity of real-world data on outcomes in adolescents and young adults (AYAs). We aimed to describe the clinical characteristics and survival outcomes of AYA treated in a resource-constricted setting.
Methods: We performed a multicenter retrospective cohort study on patients aged 15-39 years with a diagnosis of diffuse large B-cell lymphoma (DLBCL) or Burkitt lymphoma (BL) from 2008 to 2018. The Kaplan-Meier method and long-rank test were used to evaluate overall survival (OS) and progression-free survival (PFS).
Results: We identified a total of 95 patients, 90 (95%) with DLBCL and 5 (5%) with BL. The median age of all patients was 33 years (range, 15-39). Of all patients, 54% had a good performance status[BsVv1] , and 62% presented with early-stage cancer at diagnosis. RCHOP-like (88%) was the most frequent frontline regimen[BsVv2] , only 2% received a pediatric regimen. The overall response rate was 89%[BsVv3] (23% partial response and 66% complete response), the recurrence/progression was observed in 31% of patients. Second-line chemotherapy was given to 28% and 5% had a stem cell transplant. With a median follow-up of 49 months (95% CI 29-60), the 5-year OS and PFS were 78% and 67%, respectively.
Conclusions: This study report that AYAs with B-cell NHL mostly present with early-stage cancer at cancer diagnosis and had high treatment response rates. Despite the limitations to providing cancer care in Peru, we observed similar survival outcomes to those reported in high-income countries. Efforts should be made to increase the availability of novel cancer-directed therapy and ensure treatment compliance in AYAs to further improve the survival outcomes in resource-limited populations.

EP121 / #758

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

GEMCITABINE AND VINORELBINE (GV) VERSUS IFOSFAMIDE, CARBOPLATIN, ETOPOSIDE (ICE) REGIMEN IN TREATING PEDIATRIC PATIENTS WITH RECURRENT OR PROGRESSIVE HODGKIN'S LYMPHOMA

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Background and Aims: Pediatric Hodgkin lymphoma (HL) is a curable disease; however, at relapse or progression (R/P) the optimal salvage regimen is unclear. This study aimed to compare the response rate (RR), toxicities, and outcome of GV with ICE regimen after first-line ABVD (Doxorubicin-Bleomycin-Vinblastine-Dacarbazine) in patients with R/P HL.
Methods: This retrospective study included 132 pediatric patients with R/P HL (median age 13.9 years) treated from July-2012 to December-2020 with GV (n=50) or ICE (n=82). Patients were evaluated for RR to second-line, toxicities, factors predicting response at R/P, overall survival (OS), and event free survival (EFS).
Results: The RR was 54.3% to ICE and 28.6% to GV (P=0.004). Factors predicting poor RR were a higher stage, progressive disease (PD) during first-line or early relapse, female sex, age ≥13 years, B-symptoms, ESR >50 mm/h, WBC ≥13.5x10^9/L, hemoglobin <10.5 gm/dL. On multivariate analysis, only PD during first-line or early relapse (P=0.002), and B-symptoms (P=0.002) were independent factors to poor RR. Treatment-related mortalities were 2.4% for ICE and 2% for GV (P=0.86). Of the 380 ICE and 235 GV cycles given, grade-3/4 neutropenia, grade-3/4 thrombocytopenia, and grade-3 anemia were seen more frequent in ICE (98.9%, 83.9%, and 71% respectively) than GV regimen (18.7%, 4.6%, and 8% respectively) (P<0.00001). Fever neutropenia necessitating hospital admission occurred in 55.5% of ICE cycles compared with 2.1% of GV (P<0.00001) and clinically documented infections in 17.9% vs 2.1%, respectively (P<0.00001). Grade-3 hypokalemia, hypomagnesemia, hemorrhagic cystitis, blood-stream infection, and septic shock were reported in 29.5%, 26.8%, 8.1%, 5%, and 5.8% of ICE cycles, but none in GV. The 3-year OS was 69.3±10.6% for ICE and 74±12.9% for GV (P=0.3); while the 3-year EFS was 39.3±11.4% and 24.9± 12.5%; respectively (P=0.001).
Conclusions: ICE regimen had a better RR and EFS, but a higher toxicity profile than GV. However, toxic mortality was similar for both regimens.

EP122 / #966

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

REDUCING THE BURDEN OF ONCOLOGY CHEMORADIOTHERAPY AND RADIATION EXPOSURE FROM DIAGNOSTIC IMAGING BY UTILIZING TARGETED IMMUNOTHERAPY IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS WITH HODGKIN LYMPHOMA.

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Background and Aims: Significant chronic health conditions continues to increase over time among pediatric, adolescent, and young adult (CAYA) classical Hodgkin lymphoma (cHL) survivors. Targeting the tumor microenvironment (TME) and tumor-specific antigens is emerging as effective and safe treatments for cHL patients. Recently, we completed a phase 2 trial evaluating the use of antibody-drug conjugate targeting CD30 (brentuximab vedotin, Bv) and regulatory B-cells (rituximab, RTX) to risk-adapted chemotherapy in newly diagnosed cHL CAYA patients. The combination was safe and resulted in significant reduction to toxic chemotherapy and radiation therapy (RT), while keeping superior outcomes (5-year OS/EFS 100%; Hochberg/Cairo, JITC 2022). Adding the checkpoint inhibitor nivolumab to chemoimmunotherapy with RTX + Bv may allow further anthracycline dose reduction and RT in intermediate-/high-risk cHL in CAYA.
Methods: This is a multicenter study for patients with intermediate- and high-risk cHL. Intermediate-risk cHL patients receive 2 cycles of Bv, doxorubicin, vinblastine, dacarbazine, and RTX (Bv-AVD-R). Rapid early responders (RER) or slow early responders (SER) by FDG-PET scan receive 2 or 4 cycles of Bv, vinblastine, dacarbazine, nivolumab, and RTX (Bv-NVD-R), respectively. High-risk cHL patients receive 2 cycles of Bv-AVD-R. RERs by FDG-PET scan receive 4 cycles of Bv-NVD-R; SERs receive 2 cycles of Bv, nivolumab, doxorubicin, vinblastine, dacarbazine and RTX (Bv-NAVD-R), followed by 4 cycles of Bv-NVD-R. RT will be given to SER patients not achieving CR. Patients age ≥ 3 and ≤ 39 years will be enrolled with a primary objective to assess safety/feasibility of adding nivolumab to chemoimmunotherapy with RTX + Bv in intermediate-/high-risk cHL.
Results: Two patients have been enrolled to date and have had no DLT. Accrual is ongoing. Additional results will be presented at the meeting
Conclusions: Targeting the TME (regulatory B-cells) and PD1/PD-L1 axis is a promising approach in CAYA with cHL. (NCT05253495).

EP123 / #1412

Topic: *AS05 SIOP Scientific programme / AS05.c Lymphomas*

EVALUATION OF BONE MARROW INVOLVEMENT IN PAEDIATRIC NON-HODGKIN LYMPHOMA: 18F-FDG PET/CT VERSUS BONE MARROW BIOPSY

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Background and Aims: Non-Hodgkin lymphoma (NHL), fourth most common malignancy in chilren is characterized by high propensity to bonemarrow involvement (BMI). Accurate evaluation of BMI is essential for staging and affects management, treatment and prognosis. Its an indicator of infusion-related reaction with rituximab. Bone marrow biopsy (BMB) explores limited bonemarrow; potentially missing focal involvement and is invasive. Aims: 1) Evaluate the diagnostic accuracy of ^{18}F-FDG PET/CT in detecting BMI compared to BMB in newly diagnosed paediatric NHL. 2) Evaluate prognostic value of BMI detected by PET/CT
Methods: 55 consecutive, newly diagnosed treatmentnaive NHL patients (68% boys) who underwent baseline PET/CT and BMB recruited. FDG uptake evaluated qualitatively on fivepoint scale (0-4) scores 3/4 were taken positive for BMI. Results compared by two blinded NMphysicians. Groups: True positive: 1) Focal uptake matches site of positive BMB 2) No obvious CTchanges indicating alternative underlying pathology 3) Followup scan demonstrates disappearance of lesion post treatment. False positive: Positive scan not under above 3 criteria. True negative: Negative scan matches negative BMB. False negative: Negative scan mismatched with positiveBMB. Prognostic value of BMI demonstrated on PET/CT evaluated by OS/ 3-year PFS.
Results: Sensitivity and specificity of PET/CT in detecting BMI were 95%, and 100% respectively. BMB had similar specificity however the sensitivity was 24%. PET/CT demonstrated higher accuracy of 99% versus 81% of BMB. The negative predictive value of PET/CT scan was higher (98%) than BMB. BMI showed a strong correlation with PFS of 86% vs 97%; and OS of 83% vs 100% (p value<0.05) demonstrated in PET/CT positive and negative cases.
Conclusions: ^{18}F-FDG PET-CT demonstrated higher diagnostic accuracy than BMB. BMB maybe avoided in aggressive NHL, wherein PET/CT scan has high sensitivity and specificity. In indolent NHL, however BMB has a higher diagnostic value. We suggest that PET/CT be used as complementary tool to BMB for BMI evaluation.

EP124 / #625

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

OPTIMIZING CYCLOSPORINE (CSA) DOSE POST ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRIC CANCER PATIENTS.

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Background and Aims: Cyclosporine A (CSA) dosing has been complicated by considerable intra-patient and inter-patient variability in pharmacokinetics, which is affected by different factors such as patient age, and concurrent drug therapy. This study assessed various factors that might affect CSA dose and subsequent trough plasma level.
Methods: A retrospective study included pediatric cancer patients who underwent Allogeneic Hematopoietic Stem Cell Transplant at the Children's Cancer Hospital Egypt 57357 from October 2012 to August 2016 from matched related donors(MRD) with CSA as part of their GVHD prophylaxis regimen. CSA initial dose was 1.5mg/kg every 12 hours and then titrated according to the level and drug toxicity. The desired level was between 200 to 250 ng/ml.
Results: A total of 119 patients were included during the study period, with a median age of 9.9 years. Fluconazole as a prophylactic antifungal was used in 54.6% of the patients while voriconazole in 43% of them. Female patients and those who are older than 9 years old or received concomitant voriconazole had reached the target CSA level earlier with low initial doses. Also, those who received voriconazole had delayed CSA clearance and required lower CSA doses compared to other antifungal agents. A higher probability (above 90%) to reach the desired plasma level with doses ≤1.5mg/kg BID for those who are >9 years old and on voriconazole. Younger patients ≤9 years and on non-voriconazole antifungal required a CSA dose of more than 1.5 mg/kg BID with a probability to reach the desired plasma level of around 80%. CSA toxicity was reported in 21% of the patients.
Conclusions: Initial CSA dose individualization should consider patient age and concomitant antifungal used. Patients who are > 9 years old or receive concomitant voriconazole require initial lower doses of CSA.

EP125 / #50

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

NUTRITION SUPPORT PRACTICES AND OPINIONS TOWARD GASTROSTOMY USE IN PEDIATRIC BONE MARROW TRANSPLANT CENTERS: A NATIONAL SURVEY

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Background and Aims: Previous surveys have shown deviations in nutritional practices from international guidelines during bone marrow transplant (BMT). Guidelines recommend enteral nutrition first-line and nasogastric tubes are the mainstay for its provision. Gastrostomies provide an alternative, yet their use is less common. This survey aimed to investigate nutrition support practices in United Kingdom pediatric allogeneic BMT centers and compare clinicians' opinions on gastrostomy use.
Methods: An online survey was administered to all 12 centers. One response was requested from the lead BMT dietician, clinical nurse specialist and consultant in each center. Questions concerning gastrostomies were answered by all clinicians. In addition, the dietician answered questions regarding nutritional practices.
Results: A 100% response rate was achieved from 12 centers (36/36 clinicians). Nutritional counselling was provided in 92% of centers before and routinely throughout admission, 83% screened on and regularly throughout admission, 83% assessed nutritional status before transplant and 92% used enteral nutrition first-line. Enteral and parenteral nutrition were initiated under similar criteria. Forty-two percent of centers used gastrostomies in children with poor nutritional status prior to admission or likely to refuse a nasogastric tube. In those not using them, 76% of clinicians felt some children should be offered a gastrostomy. Clinicians perceived less displacements (78%) and cosmetic appearance (69%) as the most common advantages of gastrostomies over nasogastric tubes. Risk of surgery (92%) and tube/stoma complications (58%) were the most common perceived gastrostomy problems.
Conclusions: Centers employ proactive and similar approaches to nutritional counselling, screening, assessment and interventions. Gastrostomy use divided practice and opinion with differences in use and perceived advantages, but agreement on potential complications. Despite their risks clinicians wanted to utilize gastrostomies more in clinical practice. Placement requires careful consideration of the risks, benefits and family preferences. Future research needs to investigate complications, outcomes and family experiences of gastrostomy feeding in these children.

EP126 / #707

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

EXPERIENCE OF PEDIATRIC HAPLOIDENTICAL STEM CELL TRANSPLANTATION- REAL- WORLD DATA FROM A TERTIARY CARE CENTRE.

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Background and Aims: With the success of post-transplant cyclophosphamide based platform and improved clinical care, the number of haploidentical stem cell transplants (HaploSCT) have surged over the last decade. However, data from low-middle income countries (LMIC) is scarce. We aimed to evaluate the outcome of haploSCT in children and adolescent population (<18 years) at our centre.
Methods: We conducted a retrospective analysis of the haploSCT performed between January 2015 and February 2022. The graft versus host disease (GVHD) prophylaxis was post-transplant Cyclophosphamide (PTCy) with Mycophenolate-mofetil and Cyclosporine/tacrolimus. All patients were transfused peripheral blood stem cells from donors. Supportive care was given as per unit protocol. Post-transplant, patients continued regular follow up. Overall survival (OS) was calculated using the Kaplan–Meier method.
Results: Twenty-five patients underwent haploSCT. Median age was 11 Years (range 3-18 years). Benign hematological disorders included aplastic anemia (n=3), Inherited bone marrow failure syndromes (n=4), and primary immunodeficiency in one case. Malignant disorders included relapsed acute lymphoblastic leukemia (n= 9), relapsed acute myeloid leukemia (n=6), myelodysplastic syndrome (n=1) and hodgkin disease (n=1). Sibling donors were used in 10 patients, and parents in 15. Most common conditioning regimen used was Fludarabine + Busulphan based (n=19, 76%). Engraftment rates were 80% (n=20) with acute graft versus host disease in 24% (n= 6) and cytomegalovirus (CMV) reactivation in 60% (n=15) patients. Hemorrhagic cystitis was seen in 64% (n=16). Non-relapse mortality was 36% (n=9). Relapse related mortality was 24%. The median follow-up was 12 months and OS was 40%. Nine out of 25 patients are alive and on regular follow-up.
Conclusions: HaploSCT with a PTCy platform is a cost-effective, promising modality of treatment in children and adolescents who don't have matched sibling or matched unrelated donors. However, long-term outcomes in LMICs remain poor. CMV reactivation, hemorrhagic cystitis and multi-drug resistant bacterial infections remain a challenge.

EP127 / #876

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

FUNCTIONAL STATUS AND OUTCOMES IN PEDIATRIC AND YOUNG ADULT PATIENTS UNDERGOING HEMATOPOIETIC CELL TRANSPLANT

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Background and Aims: Pediatric and young adult patients undergoing hematopoietic cell transplantation (HCT) often experience decreased functional mobility and deconditioning. The benefits of functional status on outcomes in patients undergoing HCT is established in the literature. Physical therapy intervention can directly address the physical sequelae effects of HCT that include functional mobility, functional strength and endurance. Transplant Energize Me Patient Outcome (TEMPO©) is a multidisciplinary therapy standard of care that aims to optimize patient outcomes in these areas. In TEMPO©, the novel Functional Mobility Score (FMS©) is an objective outcome measure completed by physical therapists. The Karnofsky Performance Status Scale and Lansky Play Performance Scale (K/L) are gold standards for this population and are subjective in measure. We hypothesize that a patient's functional status, measured by FMS© and K/L, at admission and discharge will have an inverse relationship on outcomes such as length of stay (LOS) and time to engraftment.
Methods: A retrospective chart review included patients with data on functional status at HCT admission and discharge as well as information on outcomes. Data were summarized descriptively. Spearman correlation coefficients were used to estimate the correlation between FMS© and K/L performance scores and outcomes.
Results: A total of 37 patients were included in this study. Patients were 57% male and had median age at HCT of 12 years. There was a mild negative correlation between FMS© at discharge and length of stay (r_s=-0.40, p=0.0156).
Conclusions: The number of patients in this small study presents a limitation. This exploratory study identifies that these metrics alone are not robust enough to evaluate functional status and the multifactorial relationship of function to LOS and time to engraftment. Future studies will explore the effect of cardiorespiratory fitness and the level of activity during HCT admission and effect on patients'outcomes.

EP128 / #315

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION WITH ANTITHYMOCYTE GLOBULIN AND LOW DOSE POST-TRANSPLANT CYCLOPHOSPHAMIDE; A SINGLE-CENTER RETROSPECTIVE STUDY

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Background and Aims: Hematopoietic stem cell transplantation from a haploidentical donor (haplo-HCT) are increasingly used in patients lacking a matched donor, but the optimal strategy needs to be defined. This study aims to review the outcome of haplo-HCT with antithymocyte globulin with low dose post-transplant cyclophosphamide (ATG/LD-PTCy) in a single center for pediatric patients.
Methods: A retrospective analysis was done on patients who underwent haplo-HCT with ATG/LD-PTCy at Samsung Medical Center between 2019 and 2021. ATG was administered 2 mg/kg/day for 2 days (d-7, d-6) and cyclophosphamide 14.5 mg/kg/day was given for 2 days (d-3, d-2). As for PTCy, cyclophosphamide 25 mg/kg/day was administered at d3 and d4, and tacrolimus with mycophenolate mofetil was given from d5 for graft-versus-host disease (GVHD) prophylaxis.
Results: Total of fourteen patients (7 male) underwent haplo-HCT with ATG/LD-PTCy. The most common diagnosis was acute myeloid leukemia (AML; n=4), followed by acute lymphoblastic leukemia (ALL; n=3). Neutrophil and platelet engraftment was achieved at a median of 16 and 37 days in 13 patients. One patient with engraftment failure underwent 2nd haplo-HCT, but ALL relapsed at 3 months despite successful engraftment. Two patients with AML relapsed within 4 months. In patients with successful engraftment, the natural killer cells recovered most early, followed by B cell recovery. The overall and relapse-free survival rates were 83.3% and 74.1% at 6 months, and 71.4% and 74.1% at 12 months, respectively, with a median follow-up of 8.7 months. Acute GVHD occurred in 11 patients, of which 10 were grade I or II.
Conclusions: Haplo-HCT with ATG/LD-PTCy could achieve engraftment in a high proportion of patients, and disease-free status was maintained except for early relapse cases. Based on these findings, ATG/LD-PTCy might be a feasible option for patients undergoing haplo-HCT.

EP129 / #434

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

IS MIXED T-CELL CHIMERISM PREDICTIVE OF RELAPSE IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA AFTER ALLOGENEIC STEM CELL TRANSPLANTATION?

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Background and Aims: Chimerism studies post hematopoietic stem cell transplant (HSCT) are dynamic. The aim of this study was to review our data on presence of recipient cells in post-HSCT pediatric patients with acute lymphoblastic leukemia (ALL) to study its significance as a predictor of relapse of their primary disease.
Methods: Forty-six transplant naïve pediatric patients with ALL who underwent allogeneic HSCT from 2012-2017 at our institution were analyzed. Thirty-seven lived beyond Day+120 and are evaluated herein. Mixed T-cell Chimerism (MC) was defined as >1.0% of recipient's DNA spiking any time during post-HSCT follow-up beyond Day+30.
Results: Median age at transplant was 8.8 years (range, 0.5-14.0), 19(51.4%) were boys. Two(6.1%) had BCR/ABL and 3(9.1%) had MLL gene re-arrangement out of the 33 patients followed till Day+720. Bone marrow (BM) was the stem cell source in 28(75.7%), peripheral blood in 1(2.7%) and cord blood for 8(21.6%) patients. All patients received myeloablative conditioning regimen with cyclosporine and methotrexate as graft versus host disease (GVHD) prophylaxis. Post-HSCT relapse rate of primary disease was 51.4% (n=19) with a median time to relapse of 6.7 months from transplant. Relapse sites were blood in 13 (68.4%), CNS in 5 (26.3%) and bone marrow in 1 (5.3%). Post HSCT overall rate of MC till Day+720 was 51.4% (19 of 37). MC till Day+100 was seen in 45.9% (17 of 37) and beyond Day+100 in 12.9% (4 of 31 evaluable) patients. MC during D+100, D+100 to Day+720 or throughout till Day+720 was not significantly associated with relapse of primary disease (relapse rate: 11, 57.9%, 9, 52.9% and 3, 75%; P=0.517, 1.00 and 0.284 respectively).
Conclusions: Chimerism analysis is an essential tool for post-HSCT follow-up of engraftment. MC was not observed to be a significant predictor of post-HSCT relapse of primary disease in our patient cohort.

EP130 / #1248

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

MIXED T-CELL LYMPHOCYTE CHIMERISM IN PEDIATRIC ACUTE MYELOID LEUKEMIA AFTER ALLOGENEIC HEMATOPOIETIC TRANSPLANT

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Background and Aims: It is importance to identify the origin of the newly developing hematopoietic system in patients undergoing transplant for malignancies. We reviewed our data on mixed t-cell chimerism (MC) in pediatric patients with acute myeloid leukemia (AML) post hematopoietic stem cell transplant (HSCT) to investigate its significance as a predictor of relapse of primary disease and overall survival.
Methods: Forty-one pediatric patients with AML underwent allogeneic HSCT from 2012-2017 at our institution. Twenty-eight fared beyond Day+120 and are the focus of this report. Mixed T-cell lymphocyte Chimerism (MC) was defined as >1.0% of recipient's DNA spiking any time during post-HSCT follow-up at or beyond Day+30.
Results: Median age at transplant was 6.9 years (range, 0.1-13.9), 14(50.0%) were boys. For 20 (71.4%) bone marrow (BM) was the source of stem cells, 1 (3.6%) peripheral blood and for 7 (25.0%) cord blood. All patients received a myeloablative conditioning regimen with GvHD prophylaxis. Donor was a full matched relative in 16 (57.1%) and Haploidentical in 5 (17.9%) while unrelated in the remaining 7 (25%) recipients transplanted with CB. Rate of post-HSCT relapse of primary disease or progression was 7.1% (n=2) with a median time to relapse of 6.7 months from transplant. Rate of MC post-HSCT from Day+30 till Day+100 was 57.1% (n=16), Day+100 to Day+1825 40.0% (n=10 of 25 evaluable) and day+30 through Day+1825 was 64.3% (n=18 of 28). With a median follow-up of 58.4 months (95% CI: 48.2-68.5) and mortality rate of 21.4% (n=6 of 28), cumulative probability of overall survival of our cohort at 5 year was 77.5%±8.1%. MC during D+100, D+100 to Day+1825 or throughout till Day+1825 was not significantly associated with relapse of primary disease, mortality or overall survival.
Conclusions: MC was not found to be a significantly associated with post-HSCT relapse of primary, mortality rate or overall survival in pediatric AML patients.

EP131 / #1179

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

OUTCOME OF INFANT YOUNGER THAN 1 YEAR WITH ACUTE LYMPHOBLASTIC OR MYELOID LEUKEMIA FOLLOWING INTENSIVE CHEMOTHERAPY AND HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background and Aims: Infant leukemia is rare aggressive disease and has poor prognosis. And, neurocognitive dysfunction is an important long-term problem after transplantation of children. We reported the characteristics and outcomes including neurocognitive problem of infant acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) with intensive chemotherapy and hematopoietic stem cell transplantation (HSCT).
Methods: We present the results of 20 patients underwent allogeneic HSCT with infant ALL and AML at Seoul National University Children's Hospital from 1995 to 2020. All patients used busulfan-based myeloablative contioning regimen. Patients who visited a psychiatric outpatient clinic after transplantation were considered patients with predisposition of neurocognitive problems.
Results: In all 20 patients, the median age at diagnosis and HSCT was 7.2 months (range, 2.8-11.1 months) and 14.5 months (range, 7.5-22.4 months). The patients included 16 ALL (80%) and 4 AML (20%). Eight patients received HSCT from unrelated peripheral blood stem cell (PBSC), 7 from unrelated cord blood, 2 from haploidentical PBSC, and others from related bone marrow, unrelated bone marrow, and related PBSC. There was no engraftment failure. The cumulative incidence of acute graft-versus-host disease (GVHD) with grade II-IV was 31% and those with grade III-IV was 15.6%. Chronic GVHD appeared in only one case with moderate severity. The 5-year overall survival (OS) and event-free survival rates (EFS) and treatment-related mortality (TRM) were 84.4%, 83.3%, and 17.1%, respectively. Patients who visited a psychiatric outpatient clinic after transplantation were 37.3% (median 2.7 years after transplantation, range 2.0-9.1 years).
Conclusions: This study showed favorable outcomes of infant ALL and AML after intensive chemotherapy and HSCT during long period. And it is considered necessary to follow-up the neurocognitive function in patients who underwent intensive chemotherapy and HSCT at an early age. However, the number of patients was not large enough, further studies are needed for these high-risk patients.

EP132 / #561

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

A CROSS SECTIONAL SURVEY TO REVIEW FOOD SAFETY PRACTICES WITHIN PAEDIATRIC ONCOLOGY AND STEM CELL TRANSPLANT CENTRES IN THE UNITED KINGDOM

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Background and Aims: Neutropenia is a common complication of chemotherapy, which poses a high risk of infection and mortality. Neutropenic diet has historically been recommended for those undergoing high dose chemotherapy (HDC) for malignancy or stem cell transplants (SCTs). The rationale behind the diet is to reduce risk of foodborne infection by avoiding foods considered to be high microbial risk. However, evidence for this diet is limited and there is lack of national consensus guidelines. Aim: To establish what food safety guidance is being implemented across centres in the United Kingdom (UK) providing paediatric SCTs or HDC.
Methods: Twenty two principal treatment centres (PTCs) and centres providing SCTs registered with the British Society of Blood and Marrow Transplantation and Cellular Therapy or the Children's Cancer and Leukemia Group were identified. Specialist dietitians employed by these centres were contacted to complete an online questionnaire regarding food safety guidance implemented at their centres for paediatric patients undergoing HDC or SCT. Questions related to restricted foods, specific guidelines implemented, ward food provision and timings of food provision.
Results: Responses received from 16/22 centres (73%). Many aspects of the neutropenic diet were consistent across centres, including avoidance of unpasteurised dairy products (94%, P=0.50), raw or undercooked meat (94%, P=0.34), unpasteurised patê (88%, P=0.39), raw shellfish (94%, P=0.45), probiotics (75%, P=0.42). A lack of consistency in advice around the water source used on wards, vacuum packed meats and fish and unpeeled fruits and vegetables was apparent. There was great variation between which guidelines were being referenced at each centre, with trust own guidance being the most common (31%).
Conclusions: Food safety guidance for neutropenic patients differs greatly across UK centres, with some practices seeming outdated and non-evidence based. A national review of food safety guidance needs to be considered to provide a standardised approach for this population.

EP133 / #1664

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR CHILDREN IN JORDAN 2003-2021: ACTIVITY AND TRENDS

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Background and Aims: The first comprehensive pediatric HSCT program in Amman-Jordan was established in 2003 at King Hussein Cancer Center (KHCC).We describe activities and trends by Pediatric HSCT Program at KHCC.
Methods: Retrospective data review was conducted between 2003 to October 2021.
Results: Between January, 2003 and October 2021, 1051 HSCTs were performed with a median age of 8 years (0.13-31), of which 58% were males and 72 % were Jordanians (n=758). Median follow-up was 2.9 years (0.087-12.5). Allografts accounted for 77% of HSCTs (n=811); whereas, autografts accounted for 23 %(n=240). Allogeneic HSCTs included full-matched family/related donors in 79%(n=641), haploidentical in 16%(n=132) and unrelated donors in 5%(n=38). Stem cell sources included PBSCs in 75%(n=788), BM 21%(n=221) and CBUs 4% (n=38) of the HSCTs. Myeloablative and reduced intensity conditioning were employed in 71 % and 27% of HSCTs, respectively; and no conditioning in 2%. Malignant conditions were the main indications for HSCTs (56%;n=591), whereas, non-malignant accounted for 44%(n=460). The most common indication for allogeneic HSCTs were leukemia (37%;n=297), followed by hemogloinopathies (26%;n=212), bone marrow failures in 17%(n=137) and immune deficiencies in 11%(n=88); while solid tumors (69%;n=165), followed by lymphomas (41%;n=99) were the main indications for autologous HSCTs. The 5-year OS and EFS for all HSCTs were 81% ±2.3 and 75%±3.4, respectively; and for allogeneic 84%±3.1 and 77%±2.2. Cumulative incidence of TRM at 1 year for allogeneic HSCTs was 1.9%, compared to 5% in previous era (before 2010),p=0.004). Whereas, for autologous HSCT was 0.54%. Disease progression/ relapse of underlying condition was the main cause of mortality (76%).
Conclusions: Implementing contemporary practices, expertise of the treating teams and robust supportive care practices contributed to significant improvement in HSCTs outcomes at KHCC.A constant increment in HSCTs numbers performed at KHCC is evident. In particular, haploidentical HSCTs are increasingly employed as a readily available alternative donor option.

EP134 / #409

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

INTERFERON-GAMMA-PRIMED MESENCHYMAL STEM CELLS ENHANCE THE ENGRAFTMENT OF HUMAN CORD BLOOD HEMATOPOIETIC STEM CELLS IN NSG MICE

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Background and Aims: Hematopoietic stem cell transplantation (HSCT) is a curative option for a variety of hematologic diseases. Umbilical cord blood-derived HSCs (CB-HSCs) transplantation has shown relatively poor engraftment compared with other sources due to the limited cell numbers in a CB unit. Studies have demonstrated that co-transplantation of mesenchymal stem cells (MSCs) with HSCs enhances the engraftment of HSCs. We aimed to investigate if interferon-gamma (IFN-γ)-primed MSCs could further promote the engraftment of human CB-HSCs than naïve MSCs.
Methods: MSCs derived from Wharton jelly with or without IFN-γ-priming were analyzed by single cell RNA-sequencing. Then, we transplanted 1 x 10^4 CB-$CD34^+$ cells (Group A), $CD34^+$ cells plus naïve MSCs (Group B), and $CD34^+$ cells plus IFN-γ-primed MSCs (Group C) in busulfan-conditioned NSG mice. At 6 weeks post-transplant, engraftment rates were compared among groups by measuring the percentage of human $CD45^+$ cells in bone marrow by flow cytometry.
Results: Single cell RNA-sequencing revealed that 729 genes were up-regulated and 477 genes were down-regulated in IFN-γ- primed-MSCs. Gene Ontology analysis showed that most of those changes are related to external stimuli, defense responses and protein bindings. The median percentage of human $CD45^+$ cells in bone marrow of Groups A to C was not statistically different (3.54%, 3.61%, and 4.49%, respectively; P=NS). The highest engraftment rate achieved in each group was 7.58% (Group A), 13.20% (Group B), and 20.80% (Group C), respectively.
Conclusions: This study demonstrated that gene expression patterns of MSCs change upon IFN-γ-priming. With a limited number of $CD34^+$ cells, co-transplantation of IFN-γ-primed MSCs tended to promote engraftment better than naïve MSCs. Additional studies are needed to verify the engraftment promoting effect of IFN-γ-primed MSCs by limiting $CD34^+$ cell dose and optimizing conditioning for engraftment. Our findings suggest co-transplantation of IFN-γ-primed MSCs with CB could be a novel and promising approach to overcome poor graft performance following CB transplantation.

EP135 / #1259

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

PRETRANSPLANT MYELOID AND IMMUNE SUPPRESSION (PMIS) FOR HIGH-RISK THALASSEMIA PATIENTS RECEIVING MATCHED RELATED DONOR ALLOGRAFT

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Background and Aims: Patients with high risk thalassemia have a higher incidence of transplant related complications and graft failure.The introduction of PMIS, mainly for alternative donor transplants, is reported to be feasible and associated with good outcomes. We are reporting our results applying PMIC in MRD transplants for high risk thalassemia patients.
Methods: This is a retrospective chart review of patients who received PMIS for high risk thalassemia patients(age more than 14years or class 3 thalassemia)receiving matched related donor allografts, according to our new guidelines which were in effect since Oct2020. Accordingly, these patients received fludarabine 200 mg/m2 intravenously (iv) over 5 days in combination with dexamethasone 25 mg/m2/day iv over 5 days, given as two cycles 3 weeks apart in association with hydroxyurea, followed by fludarabine and busulfan based reduced toxicity conditioning (RTC).
Results: Seven patients received PMIS since Oct2020.None of these patients required admission after these infusions.Median age at transplant was 16.5 (range, 4-26.5 years), median ferritin 1020(440-7300 ng/ml); median liver span15.9 (9.6-17cm);median absolute lymphocyte count prior to transplant 500(range,200-1200).None of the patients had significant liver fibrosis as confirmed by pretransplant biopsy. The median time of neutrophil and platelets engraftment was on days 13(range, 13-20) and 18(range, 15-22), respectively. After a median follow up of 192 days (range, 101-499), five patients have full donor chimerism (above 95% donor cells), and 2 have stable mixed chimerism. There were no signs of acute or chronic graft vs host disease detected in any of our patients. Five patients developed molecular CMV reactivation but with no clinical manifestations. One patient developed BK cystitis that was treated conservatively.
Conclusions: Applying PMIS for high-risk thalassemia patients receiving MRD allografts was not associated with significant toxicity.This approach may improve the results for this group of patients and we will continue using PMIS for our high-risk transplants.Viral reactivation needs close monitoring.

EP136 / #385

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

IMMUNE RECONSTITUTION AFTER HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN WITH LEUKEMIA: A BRAZILIAN INSTITUTION EXPERIENCE

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Background and Aims: Allogeneic hematopoietic stem cell transplantation (HSCT) is an established treatment for children with high risk and relapsed leukemias, certain lymphomas, and various non-malignant diseases. Despite intensive efforts to control T cell and natural killer (NK) cell engraftment and recovery, the accomplishment of optimal balance between acute graft-versus-host disease (aGVHD), chronic graft-versus-host disease, viral infections and graft-versus leukemia/tumor effect remains a challenge. Increasing evidence suggests that early and rapid lymphocyte recovery following (HSCT) is associated with better survival.
Methods: A retrospective analysis of patients diagnosed with acute leukemia who underwent HCT between August 2018 and June 2021, in the BMT Unit of Erastinho's Hospital. We studied the dynamic analysis of immune recovery with regard to potential factors affecting its speed, including age, type of HCT, diagnosis, graft-versus-host disease (GvHD), and cytomegalovirus (CMV) infection reactivation. Absolute counts of different lymphocyte subsets and immunoglobulin serum levels were determined in peripheral blood of patients.
Results: 20 patients were included, 5F/15M, age 1-19 years old (M-10). They all underwent a myeloablative regimen; haploidentical donor (70%), male (60%), and a peripheral blood cell source (70%). Viral infections occurred in 90% mainly of cytomegalovirus (55%). Acute-GVHD occurred in 55% and chronic GVHD in 70%.
Conclusions: Distinct kinetics of recovery were observed in each subpopulation. NK cells are the first to recover, followed by memory T cells, meaning they could derive from the graft, while the number of B cells and auxiliary T cells (CD4+) increases only six months after the transplant. The factors analyzed interfere in the thymic production of T lymphocytes and the recovery of CD4+ lymphocytes. The results emphasize the importance of quantifying lymphocytes subpopulations in the peripheral blood as a way to improve monitoring in patients with acute leukemia who underwent a bone marrow transplant, in order to evaluate the best moment to revaccinate these individuals.

EP137 / #676

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

CHARACTERIZATION OF TENEURIN-4 AND ITS ROLE IN NEUROBLASTOMA TUMORIGENESIS

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Background and Aims: Neuroblastoma is the most common extracranial solid tumor in children, and the high-risk disease remains a therapeutic challenge. Neuroblastoma originates from neural crest cells and impairs neuronal differentiation during early embryonal development. Teneurins (TENM1-4) are cell adhesion molecules that are highly expressed during embryonal development and function in differentiation. We and others have identified somatic mutations and structural aberrations of TENM genes in tumors, including neuroblastoma. This study aims to identify the importance of TENM4 in neuroblastoma growth, tumorigenicity, and differentiation.
Methods: siRNA-mediated knock-down and RNA sequencing of TENM1-4 were performed in neuroblastoma cells to analyze the molecular effects of TENM1-4. CRISPR-Cas9-mediated knockouts of TENM4 ($TENM4^{-/-}$) in SK-N-BE(2) cells were evaluated for detailed molecular changes, proliferation, differentiation, and tumorigenicity.
Results: siRNA-mediated knockdown of TENM4 significantly decreased proliferation in all investigated neuroblastoma cell lines. Furthermore, knockdown of TENM4 led to upregulation of genes associated with neuronal differentiation and downregulation of genes related to cancer-associated pathways. Two $TENM4^{-/-}$ clones from the CRISPR-Cas9 gene-edited SK-N-BE(2) were uncovered; both clones induced a neuronal differentiation-like morphology with impaired clonogenic capacity compared to wildtype cells. Both knockout clones displayed decreased MYCN expression in comparison to wild-type cells. Importantly, $TENM4^{-/-}$ cells did not lead to tumor formation when grafted into nude mice as opposed to wild-type SK-N-BE(2) cells that formed tumors. We further examined primary neuroblastomas and detected a significantly higher protein and mRNA expression of TENM4 in high-risk vs. non-high-risk and MYCN-amplified vs. non-MYCN amplified tumors.
Conclusions: Our data suggest that TENM4 is expressed in a subpopulation of neuroblastomas with MYCN-amplification, and plays an important role in neuroblastoma growth and differentiation. TENM4 may be a potential therapeutic target in neuroblastoma.

EP138 / #1135

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

SINGLE CELL ANALYSIS OF HUMAN BONE METASTATIC NEUROBLASTOMA UNRAVELS EMERGING IMMUNE CELL POPULATIONS IN THE BONE MARROW

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Background and Aims: Introduction:
Neuroblastoma (NB) is a pediatric solid tumor with frequent metastasis. Patients with metastasis account for 50% of all NB cases at diagnosis, where 70% have bone marrow involvement. To better understand the cancer progression and metastatic processes, revealing unique relationships between tumor cells and cell populations in the bone marrow microenvironment is essential for future therapeutic strategies.
Methods:
Bone marrow aspirates were taken from eleven clinically diagnosed neuroblastoma patients. Five patients had clinically confirmed “tumor infiltration” in their bone marrow, two of which had confirmed bone metastasis. Six patients had “no tumor infiltration”, of which we sequenced the matched primary tumor from two of the patients. Bone tumors were dissociated into single cells. Both tumor and bone marrow samples underwent red blood cell removal, FACS sorting ($CD235^{neg}$) and proceeded for single-cell RNA sequencing (scRNA-seq) using the 10X Genomics platform (Chromium 3’ v2 kit, 10x Genomics). Bone marrow aspirates were enriched for: 1) mesenchymal cells ($PDGFRa^{pos}$), adrenergic tumor cells ($CD24^{pos}$), Schwann cell precursor (SCP)-like cells ($ERBB3^{pos}$) together with $CD235^{neg}$ cells, 2) solely sorting $CD235ab^{neg}$. These were combined prior to scRNA-seq.
Results:
scRNA-seq revealed eleven major cell populations including immune, tumor and erythroid cells. Tumor cells infiltrating the bone marrow in the metastatic patients showed an adrenergic phenotype (PHOX2B, TH, MYCN, DBH). We identified a significant increase in total cell fraction of immature B cells, NK $CD56^{bright}$ cell populations, as well as a distinct macrophage population in the metastatic patients compared to the non-metastatic neuroblastoma patients.
Conclusions: Conclusion:
Our discoveries provide novel biological insight for the bone and bone marrow metastatic field of neuroblastoma. Further evaluation might potentially bring novel and important insights to neuroblastoma research, and most importantly, a better understanding on how to target advanced and heterogenous disease at earlier stages prior to metastatic spread.

EP139 / #657

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

SAFETY AND PHARMACOKINETICS OF ALECTINIB FOR JAPANESE PEDIATRIC PATIENTS WITH RELAPSED/REFRACTORY MALIGNANT SOLID TUMORS OR MALIGNANT LYMPHOMA (NCCH1708): A SINGLE-CENTER PHASE I TRIAL

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Background and Aims: This study aimed to determine the safety, pharmacokinetics, and recommended phase-2 dose (RP2D) of alectinib, a highly selective ALK (anaplastic lymphoma kinase) inhibitor, for Japanese pediatric patients with relapsed/refractory malignant solid tumors or malignant lymphoma.
Methods: We conducted a single-center, phase 1 trial for patients aged 3–18 years who were refractory or intolerant to standard treatment. Patients confirmed to have an ALK overexpression by immunohistochemistry or ALK alteration by fluorescence in situ hybridization, or next generation gene sequencing were eligible. The primary endpoint was the incidence of dose-limiting toxicity.
Results: Nine patients with a median age of 7 years (range 4–15 years) were enrolled between May 2018 and January 2020, among whom eight had neuroblastoma and one had rhabdomyosarcoma. No dose-limiting toxicity was observed, and the level 2 dose of this study was determined as the RP2D. Grade ≥3 adverse effects were only observed in 4 patients (44.4%), with lymphopenia (22.2%), anemia (22.2%), neutropenia (11.1%), and fever (11.1%) being the most common grade ≥3 adverse events associated with alectinib. Japanese children had similar pharmacokinetic data as Japanese adults. Although all patients were confirmed to be positive by immunohistochemistry, ALK alteration could not be confirmed via NGS in seven patients NGS were performed, and no objective responses were observed in the patients enrolled.
Conclusions: Alectinib was safe and well-tolerated in Japanese children with malignant solid tumors. The RP2D determined in this trial was 150, 300, 450, and 600 mg/day for patients <15, ≥15 and <25, ≥25 and <35, and ≥35 kg, respectively. After this trial, enrollment of pediatric patients began in an ongoing phase 2 study with alectinib for patients with solid tumors with ALK alteration identified via next generation gene sequencing. Funding: Japan Agency for Medical Research and Development and Chugai Pharmaceuical Co.Ltd. Clinical Trial Information: JMA-IIA00354

EP140 / #1461

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

DISPENSING ORAL TEMOZOLOMIDE IN CHILDREN: PRECISION AND STABILITY OF A NOVEL READY-TO-USE LIQUID FORMULATION IN COMPARISON WITH CAPSULE DERIVED MIXTURES

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Background and Aims: Parents and caregivers often overcome the lack of commercially available pediatric formulations by mixing adult dosage forms with food. This study aimed at assessing the risks associated with handling of temozolomide (TMZ) capsules in comparison with a ready-to-use oral suspension specifically formulated for children (Ped-TMZ).
Methods: TMZ capsules were opened and their content (equivalent to 90 mg) mixed with food vehicles. Similar dose was sampled from Ped-TMZ. TMZ and its degradation product, amino-imidazole-carboxamide (AIC), were assayed using UV-HPLC at 0, 30 and 60 min. Statistical analysis was performed to evaluate TMZ recovery, AIC amount and impact of operator on accuracy. Acceptance criteria were pre-defined for TMZ (95.0-105.0%) and AIC (<1%) content.
Results: Mean TMZ recovery was 96.6±1.2% for Ped-TMZ and 91.0±1.5% and 91.6±1.4% for the capsule-derived preparations with apple juice and applesauce, respectively. The recovery of TMZ in Ped-TMZ was systematically and significantly higher than that observed after handling of TMZ capsules ($p<0.0001$) and within specifications. The recovery of TMZ from capsules in food never met acceptance criteria. In addition, the 4 tested food vehicles (applesauce, cream, milk, purée) had a significant effect on TMZ stability ($p=0.0042$) and AIC significantly increased with time in 3 of the 4 vehicles ($p<0.0001$). Only 1/72 preparations from capsules in food met the acceptance criteria, whereas Ped-TMZ showed no TMZ loss and AIC remained within specifications.
Conclusions: This study demonstrated a significant impact of handling TMZ capsules on dosing accuracy with a mean deliverable dose decreased by 9%, and possibly even greater in routine practice as complete food intake by the child is unlikely. Rapid degradation of TMZ was evidenced in certain food vehicles. When combined with the known effect of food on TMZ absorption, mixing capsule content with food may significantly reduce TMZ exposure, highlighting the need of age-appropriate TMZ formulations.

EP141 / #1089

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

PHENOTYPE SHIFT IN TUMOUR PATHOLOGY WITH GANGLIONEUROMA AND GANGLIONEUROMA INTERMIXED BETWEEN INITIAL LESION BIOPSY AND SURGICAL RESECTION - A UK CCLG NATIONWIDE STUDY.

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Background and Aims: Ganglioneuroma (GN) and ganglioneuroblastoma intermixed (GNBi) are neuroblastic tumours with typically a benign clinical course. To accurately discriminate between GN/GNBi and the more aggressive nodular ganglioneuroblastoma (GNBn) phenotype surgical resection is required however rate(s) of discrepancy between initial lesion biopsy and resection pathology are unknown. This study therefore analyses discrepancy rate(s) between histology diagnosis with initial biopsy and in the resected surgical specimen as part of a wider review in management of GN/GNBi.
Methods: Patients 0-24 yrs diagnosed with localized GN or GNBi between 1990-2020 and who underwent initial biopsy followed by surgical resection of the tumour were eligible.
Results: 112 of 242 patients with GN/GNBi were registered from 11 UK CCLG centres during the study period. Thirty-seven patients (33%) had a new tumour phenotype documented in their final pathology. In 25 (22%) index cases diagnosis changed from GN to GNBi. In 12 (11%) patients the changes were significant leading to a modification in oncological management (in 3 from GN to GNBn; in 6 from GNBi to GNBn; in 2 from GNBi to differentiating NB and in a single patient from GNBi to poorly differentiated neuroblastoma). Raised urinary VMA, HVA and MIBG avidity were found to be independent predictors of more aggressive pathology ($p=<0.05$, Fisher's exact test). One GNBn patient died from acute surgical complications and another index case with poorly differentiated neuroblastoma is still receiving ongoing active treatment 15 years after diagnosis. Five patients have ongoing symptoms.
Conclusions: In this study 33% of patients had a shift in their final tumour pathology with 11% cases being significant. Raised urinary VMA, HVA or MIBG avidity should raise clinical suspicion of a more aggressive pathology. Individualised management is crucial to offset poor outcomes.

EP142 / #769

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

COMBINATORIAL THERAPY OF IL-21 SECRETION ONCOLYTIC VIRUS AND ANTI-ROR1 CAR NK CELLS AGAINST NEUROBLASTOMA: SIGNIFICANT EFFECT IN-VITRO AND IN-VIVO

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Background and Aims: Novel therapies are desperately needed for children with recurrent and/or metastatic neuroblastoma (NB) (Chu/Cairo, JITC, 2021). ROR1 is highly expressed by most NB. Our group has successfully expanded peripheral blood NK cells (exPBNKs) with feeder cells and electroporated CAR mRNA to exPBNKs (Chu/Cairo, Cancer Immunol Res, 2015). Oncolytic herpes simplex viruses (oHSVs) have been safely used in clinical trials for a wide range of cancers (Cassady, et al, JITC, 2021). We sought to determine the anti-tumor efficacy of the therapy combination of oHSV engineered to express human IL21 with anti-ROR1 CAR engineered exPBNK cells (CAR exPBNKs) against ROR1^{+} NB.
Methods: ExPBNKs were expanded and electroporated with anti-ROR1-CAR mRNA (Chu/Cairo, JITC, 2021). oHSV C134 was modified to express hIL-21 gene (C021). The supernatants containing C134 and C021 were generated as previously described (Cassady, et al, JITC, 2021). In-vitro cytotoxicity of CAR exPBNKs against NB cell lines were examined by ELISA assays of IFN-g, granzyme and perforin levels. In-vivo hIL21 secretion and anti-tumor effect of the C021 with CAR exPBNKs was examined utilizing human NB xenografted NSG mice.
Results: C021 at MOI 0.025 or CAR exPBNKs significantly inhibited NB growth compared to controls. The combination of C021 and CAR exPBNKs significantly enhanced the killing of NB ($p<0.05$) with significantly enhanced secretion of IFN-g ($p<0.05$), granzyme B ($p<0.05$) and perforin ($p<0.05$) and significantly enhanced expression of NK activating marker CD25 ($p<0.05$) compared to controls. Our in-vivo animal study showed that NB infected with C021 secreted hIL21 and the combination of C021 and CAR exPBNKs reduced tumor burden in human NB xenografted NSG mice compared to the untreated group ($p<0.05$) and the CAR exPBNKs-treated group ($P=0.056$).
Conclusions: Our data demonstrate the significant anti-tumor efficacy of combining C021 with anti-ROR1 CAR exPBNKs to therapeutically target NB in-vitro and in-vivo. (Funded by U54 CA232561).

EP143 / #861

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

RECRUITMENT BARRIERS OF PATIENTS WITH NEUROBLASTOMA IN EARLY PHASE TRIALS: ANALYSIS OF THE EUROPEAN PRECISION MEDICINE TRIAL MAPPYACTS COHORT

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Background and Aims: Neuroblastoma is the most common extra-cranial solid tumor in children. In case of relapse/refractory high-risk disease, long-term survival is poor. The European prospective precision medicine trial MAPPYACTS defined molecular profiles of relapse/refractory pediatric malignancies to suggest the most adapted targeted treatment (Berlanga et al, Cancer Discovery 2022). The aim of this study was to analyze the outcome of the neuroblastoma cohort and identify recruitment barriers of these patients.
Methods: We analyzed clinical data, clinical molecular tumor board (CMTB) reports and follow-up of patients with neuroblastoma included in MAPPYACTS (NCT02613962).
Results: 104 of 787 included patients (13%) had neuroblastoma. Data of the first 46 patients included in 3 French centers are presented here. For them, 49 biopsy or surgery procedures were performed, 33 had successful sequencing analysis and 26 at least one potential actionable alteration. Patients had 1 to 6 (median, 2) prior treatment lines and received 0 to 5 (median, 1) treatments after the CMTB recommendation. Among the 26 patients with actionable alterations, 6 (23%) received a matched treatment, 3 (12%) within an early phase trial. 23 patients were not included in a clinical trial according to their molecular alteration because: patient in remission after prior treatment (6, 23%), death within 90 days after CMTB (4, 15%), another non-targeted therapy as per physician's choice (6, 23%), no trial open and received matched treatment off-label (3, 12%), parent's refusal to experimental therapy (2, 8%), biomarker trial not open (1, 4%), 1 patient without data. Data including all patients will be presented at the meeting.
Conclusions: Our results demonstrate that although most patients with neuroblastoma have potentially actionable alterations, there are limited adapted relevant clinical trials. It further highlights the importance of performing molecular profiling early to maximize the chance of patients to benefit from this approach.

EP144 / #1634

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

PRECISION MEDICINE IN CHILDHOOD CANCER – A REPRESENTATIVE CASE OF NBL

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Background and Aims: Over 80% of paediatric cancer patients will become long-term survivors, however two-thirds of all childhood cancer survivors will suffer from late effects after their treatment, which might have significant impact on their quality of life. Thus, there is a great need for new therapy approaches more precisely tailored for each individual paediatric patient. Through translational research, combining molecular diagnostics with preclinical cancer models, we aim to predict better treatment options for patients in order to improve their outcomes.
Methods: are included in Results.
Results: A paediatric patient presented with high-risk neuroblastoma (NBL), with primary tumour in the left adrenal gland and multiple skeletal metastases and bone marrow involvement. Through NGS, MYCN amplification in combination with 11q deletion were identified in the primary tumour, although these genetic alterations usually are mutually exclusive. There were no ALK aberration, ATRX or TERT rearrangements. The patient received treatment according to the European SIOPEN HR-NBL1 high-risk NBL treatment protocol with some modifications and is now in ongoing complete remission. Performing droplet digital PCR on blood samples, we were able to monitor the tumour burden, which in concordance with more invasive imaging and bone marrow sampling indicated complete response during treatment and follow-up . Both primary cell cultures and mural patient derived xenograft (PDX) models were established from this NBL and diverse treatments were tested with the aim to identify drug candidates for individualized therapy in case of refractory or relapsed disease. The primary cells showed resistance to most of the drugs tested, including Temozolomide, Cyclophosphamide and Etoposide. A combination of Venetoclax and Idasanutlin was found to have great synergistic impact on proliferation of the primary cells. In vivo PDX drug experiments are on-going.
Conclusions: We postulate that a combination therapy of Venetoclax and Idasanutlin may be an effective treatment option for patients with NBL presenting similar genetic profile.

EP145 / #339

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

SINGLE-CELL TRANSCRIPTOMICS REVEAL TUMOR CELL DIVERSITY IN NEUROBLASTOMA TRANSGENIC MOUSE AND ORGANOID MODELS

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Background and Aims: Neuroblastoma (NB) is the most common extracranial solid tumor of childhood. MYCN amplification is a frequent genetic abnormality, representing a critical stratifying prognostic marker. Given that MYCN plays a key role in NB tumorigenesis and aggressiveness, TH-MYCN transgenic mouse model is widely used in NB research, which is characterized by the overexpression of MYCN under the TH promoter. This overexpression gives rise to tumors exclusively in the sympathoadrenal system, reflecting NB features. We aimed to explore the transcriptional landscape of TH-MYCN tumors by single-cell RNA sequencing (scRNA-seq) and utilize the bioinformatically predicted essential interactions to establish NB organoid models (tumoroids).
Methods: Tumors from four homozygous and four hemizygous TH-MYCN mice were dissociated into single cells, enriched for viable non-erythroid cells, profiled by scRNA-seq (10x Chromium), sequenced on the NextSeq platform (Illumina), and analyzed using pagoda2 and seurat. Immunofluorescence was used to validate the bioinformatically predicted cell types. Harnessing scRNA-seq and spatial data, culture conditions for TH-MYCN tumoroids were optimized. Tumoroids were established and expanded for immunofluorescence whole-mount staining.
Results: scRNA-seq of TH-MYCN tumors revealed 16 major cell populations, spanning stromal, immune, and tumor compartments. MYCN+ tumor cells predominantly resembled sympathoblasts (Isl1, Stmn1, Nefl), while chromaffin cells (Th, Dbh, Chga) were rare. Immunofluorescence staining confirmed that tumors predominantly consisted of proliferating sympathoblasts. Tumor cell nests were surrounded by supportive stromal and immune cells. The adrenergic tumor cell composition in TH-MYCN tumors was highly reminiscent of human NB. Interestingly, we discovered transitioning immature adrenergic tumor cells (Sox11, Ptprs, Atrx). Furthermore, ex vivo tumoroid cultures were robust and highly proliferative. Whole-mount staining of tumoroids revealed adrenergic Phox2b+ expression, neurite outgrowth, proliferative inner core, and apoptotic outer edge of the tumoroids.
Conclusions: This comprehensive atlas of TH-MYCN tumors provides a resource for unmasking novel therapeutic targets. Tumoroid-based drug screening offers a tool for tailoring precision medicine.

EP146 / #228

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

USP44 DRIVES DISEASE AGGRESSION AND IS A POTENTIAL THERAPEUTIC TARGET IN NEUROBLASTOMA

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Background and Aims: Neuroblastoma is the most common solid tumor outside of the CNS that contributes disproportionately to cancer deaths in the young. Recent data, and the relative lack of recurrent nucleotide mutations in this disease, suggests that epigenetic and post-translational events play an important role in the pathogenesis of this disease. De-ubiquitinating enzymes (DUBs) are a class of highly drugable targets that regulate myriad cellular events including histone ubiquitination. We therefore sought to identify de-ubiquitinating enzymes that contribute to the development, progression, or therapeutic responses in neuroblastoma.
Methods: We performed a computational screen of 95 de-ubiquitinating enzymes followed by validation using three independent neuroblastoma datasets. We used model systems including neuroblastoma cell lines, genetically modified mouse cells, and a transgenic zebrafish system to study the role of USP44 in neuroblastoma.
Results: Through a computational screen, increased expression of USP44 - an enzyme that targets ubiquitinated histone H2B - had the greatest impact on neuroblastoma survival compared with 94 other enzymes. The impact on survival was confirmed in three independent datasets where USP44 was correlated with measures of disease aggression. We observed a direct relationship between USP44 and proliferation, migration, and invasion in three independent cell lines. Depletion of the histone H2B ubiquitin ligase RNF20 produced similar results. Enforced expression of USP44 impaired neurite outgrowth in cells cultured with retinoic acid. Transgenic expression of USP44 accelerated the development of MYCN-driven neuroblastoma in a zebrafish model.
Conclusions: Our data lead us to conclude that USP44 has oncogenic activity in neuroblastoma likely through removing ubiquitin from histone H2B. As this epigenetic mark affects global gene expression and has been tied with differentiation, we hypothesize that USP44 contributes to the differentiation block in these tumors. The ability of USP44 silencing to inhibit cell proliferation and metastatic behavior suggests that it may be an attractive therapeutic target in high-risk neuroblastoma.

EP147 / #1642

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

MOLECULAR MECHANISMS OF CHEMORESISTANCE IN NEUROBLASTOMA PATIENTS

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Background and Aims: The emergence of drug-resistance is the major cause of cancer treatment failure. Patients with high-risk neuroblastoma tumors (HR-NB) are treated with intensive multimodal therapy, however, approximately 60% suffer disease relapse. Achieving cure after relapse is challenging due to tumor heterogeneity and the development of resistance. We have investigated the molecular mechanisms of therapy-induced resistance in HR-NB, to identify cellular pathways promoting survival as potential therapeutic targets.
Methods: Drug-resistant NB cell models were generated using cytotoxics included in current chemotherapy protocols for HR-NB patients. Drug-resistant cells were characterized using gene expression and DNA methylation profiling, ChIP-seq assays and NGS sequencing. Functional in-vitro and in-vivo assays were performed. Paired diagnosis-relapse tumor samples were used for validation. High-throughput screening (HTS) was performed to test cytotoxicity of 2,400 FDA approved compounds (concentration range 1-0.1 µM) in both drug-resistant and native NB cells.
Results: Drug-resistant cells showed changes of expression levels of genes involved in cell differentiation, migration and DNA damage repair processes. A significant portion of these genes have been reported previously in NB associated with mesenchymal state and drug-resistance. Functionally, drug-resistant cells showed defects on cell proliferation, cell cycle and colony-forming capability whereas enhanced invasion and in-vivo tumor growth capacities. DNA methylation profiling identified extensive hypermethylation across the genome of drug-resistant cells, whereas hypomethylation affected super-enhancers previously described in NB mesenchymal phenotype. HTS identified cytotoxicity to compound treatment in drug-resistant cells, with 50 compounds inducing cell death (more than 80%) at low concentration (1µM). Compounds with high-activity target molecules associated with apoptosis/cell cycle/DNA damage (60%), infection (37%), metabolism (15%) and protein tyrosine kinase (9%) pathways.
Conclusions: We have identified a set of differentially expressed genes and signalling pathways potentially underlying acquired resistance in our NB model. HTS identified active compounds against our drug-resistant NB cells, providing insight into potential vulnerabilities of interest for therapeutic opportunities.

EP148 / #1261

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

CHARACTERIZATION OF HIGH RISK NEUROBLASTOMA. POTENTIAL BIOMARKERS FOR STRATIFICATION OF HIGH RISK NEUROBLASTOMA.

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Background and Aims: In the clinical practice, patients with high-risk neuroblastoma are treated uniformly without further stratification. However, high-risk neuroblastoma embodies a heterogeneous group of tumors, whereby patients can display response to treatment and long-term outcome or develop early progressive disease with poor outcome. We investigated high-risk neuroblastoma to identify epigenetic and molecular alterations underlying the divergent clinical evolution and treatment response of these tumors, and to identify biomarkers for their stratification into distinct subgroups.
Methods: We analyzed DNA methylation microarray and gene expression data from more than 500 high-risk neuroblastoma samples obtained at diagnosis. Snap-frozen and formalin-fixed paraffin-embedded samples were used for pyrosequencing, phospho-kinase array, immunoblotting and immunohistochemical analyses. Patients with disseminated neuroblastoma diagnosed after 18 months of age, or with MYCN amplified tumors were classified as high-risk. Cox-regression models and machine-learning analysis were used for survival analyses. Survival curves were estimated by Kaplan-Meier method and compared by log-rank test. Pathway analysis was performed using R package KEGGREST, ConsensusPathDB-MaxPlanck and R package topGO.
Results: We identified distinct DNA methylation profiles within high-risk neuroblastoma. Cox-regression models and machine-learning analysis, identified differentially methylated CpG sites that defined two subgroups of patients with substantially different overall survival (5-year OS: 91.48% versus 8.11%). Moreover, we identified methylation markers that could distinguish these clinically relevant subgroups of tumors. Integrative analysis of DNA methylation and matching gene expression data, identified differential expression of genes involved in cellular metabolism, purine biosynthesis and AKT/mTOR cell signaling. Protein expression analysis identified high levels of proteins involved in IMP metabolism and increased activation of AKT/mTOR pathways in highly aggressive neuroblastoma.
Conclusions: We have identified (epi)genetic changes underlying the heterogenous behavior of aggressive neuroblastoma, and revealed altered pathways of interest for potential therapeutic options. We identified a set of markers that enabled stratification of high-risk neuroblastoma into clinically relevant subgroups.

EP149 / #1025

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

MODULATION OF REDOX HOMEOSTASIS BY INHIBITION OF MTHFD1 IN MYCN AMPLIFIED NEUROBLASTOMA: MECHANISMS AND THERAPEUTIC IMPLICATIONS

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Background and Aims: Neuroblastoma (NB) is the most common solid tumor in childhood. MYCN amplification is tightly associated with poor prognosis of pediatric NB. Methylenetetrahydrofolate dehydrogenase, cyclohydrolase and formyltetrahydrofolate synthetase 1 (MTHFD1) is a key enzyme in the folate cycle. However, the underlying mechanisms of MTHFD1 in MYCN amplified neuroblastoma is still unknown.
Methods: We investigated MTHFD1 expression, clinical relevance, redox modification, and molecular mechanisms using the NB cells and tissues (n=63). The antitumor synergistic effects of Methotrexate (MTX) and JQ1 on NB tumorigenesis were evaluated in vitro and in vivo. Data analysis used Kaplan-Meier, Pearson's correlation, and two-sided Student's t-test.
Results: Here, we report that NB patients with high expression of MTHFD1 have a shorter progression-free survival (P=0.002) and the expression levels of MTHFD1 and MYCN are positively correlated (R=0.82). Suppression of MTHFD1 disturbs NADPH redox homeostasis, accelerates cell death, and suppresses growth (P<0.05 for all). Also, inhibition of MTHFD1 suppresses NB cell growth in cell-based xenografts (n=6 mice per group). We determined that MTHFD1 is transcriptionally activated by MYCN. The elevation of oxidative stress through MTHFD1 knockdown or the use of methotrexate, an antifolate drug, sensitizes cancer cells to JQ1, targeted therapy for NB.
Conclusions: Our study identifies that MTHFD1 confers redox homeostasis and promotes growth and suppressed apoptosis in NB cells, providing new targets and strategies for the treatment of neuroblastoma. The synergistic antitumor effects of MTX and JQ1 have important clinical significance.

EP150 / #792

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

MICRO-RNA IN NEUROBLASTOMA- NOVEL DIAGNOSTIC AND PROGNOSTIC MARKERS

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Background and Aims: The microRNAs(miRNA) are short-length RNA fragments which number approximately 2000 in mammals. These are approximately 22 nucleotide long and have a role in RNA silencing and post-transcriptional regulation of gene expression. Differential expression of miRNA has been found in various tumors. The detection of the miRNA in the neuroblastoma(NB) patients has potential of use as a diagnostic and prognostic modality.
Methods: This was prospective study including 8 cases of NB . During biopsy from cases with suspected NB, one extra tissue-core was collected in RNA- later and stored at -80°C. Three cores were sent in neutral buffer formalin for histopathological examination. After confirmation of diagnosis of NB, the total RNA was extracted. Next generation sequencing(miRNA seq) was done in S5(Ion-torrent) using 540-chip. Small RNA-seq pipeline of ion- reporter was used for data analysis and quantification. Three cases of Wilms tumor(WT) were used as control.
Results: A total of 8 patients of NB with median age of 13.5m(4-72m) months were included. The size of the NB core biopsy ranged from 1-1.5cms. Six were poorly differentiated NB while 2 were of differentiating type. Five patients had metastatic tumor and in one of these the n-myc gene was amplified. Seven patients got chemotherapy. Four patients are alive(one post autologous-HSCT), 2 patients are on palliation and 2 patients have died. On global miRNA expression profile of the NB patients miRNA 451a, 19b-3p, 106b-5p and 21-5p were consistently high .The data was normalised by logarithmic transformation.The Principal component analysis showed two distinct clusters of NB and WT tumor miRNA expression profile,indicating the miRNA expression is homogenous and unique for each.
Conclusions: miRNA451a,19b-3p,106b-5p and 21-5p can serve as potential diagnostic and prognostic biomarkers for NB and can be utilised as liquid-biopsy markers. The miRNA expression profile of NB can serve to differentiate from WT which has similar clinico-radiological presentations.

EP151 / #1650

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

PLASMA CELL-FREE DNA ANALYSIS UNCOVERED TUMOR HETEROGENEITY AND CLONAL EVOLUTION DURING TREATMENT FOR RELAPSED NEUROBLASTOMA

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Background and Aims: Treatment for relapsed neuroblastoma remains a challenge. Plasma cell-free DNA (cfDNA) can detect tumor mutations non-invasively and inform neuroblastoma therapy.
Methods: Plasma samples were collected from patients with high-risk neuroblastoma (HR-NB) at disease progression after informed consent. CfDNA analysis was done by targeted next-generation sequencing (NGS) using the CLIA-approved Foundation One Liquid (324 genes) assay or the MSK-IMPACT (322-468 genes) platform.
Results: 57/86 (66%) patients harbored at least 1 pathogenic genomic alteration in their cfDNA (mean=2, range 0-21): 43/64 (67%) by Foundation One Liquid and 14/22 (64%) by MSK-IMPACT. Recurring alterations for the entire cohort included MYCN amplification (n=8 patients), ALK point mutations (n=14); mutations and/or promotor alterations in genes involved in chromatin remodeling (ATRX n=6 ARID1A, n= 3, ARID1B n=2, TERT n=3 and ATM n= 3), and mutations in RAS-MAPK pathway (KRAS n=3, NRAS n=6, BRAF n=5, PTPN11 n=7, NF1 n=11). Other mutations included those in FGFR1 (n=5), MET (n=2) and IGF1R (n=1). NGS data on the primary tumor prior to relapse was available in 57 patients. In 23 (40%) patients, new genomic alterations appeared in their cfDNA not detected in the pre-relapse tumor. Therapy based on cfDNA analysis was instituted in 16/57 patients (28%) (using inhibitors of ALK, MET and BRAF in 14, 1 and 1 patients, respectively). After treatment, 12 patients had follow up cfDNA samples; new mutations were detected as disease progressed, enriched for the RAS-MAPK (n=6) and ALK (G1202R, n=1) pathways among others.
Conclusions: CfDNA analysis detected genomic aberrations in patients with HR-NB at relapse. Such analysis permits a relatively noninvasive profiling of tumor heterogeneity and clonal evolution, with the potential to guide therapy. When soft tissue is unavailable or if disease is limited to skeletal sites, cfDNA is a viable alternative for studying mutations. cfDNA monitoring should be more widely adopted in therapeutic trials for HR-NB.

EP152 / #128

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

INCREASED CD11B+-CD49B+NATURAL KILLER (NK) CELL TUMOR INFILTRATION AFTER CO-ADMINISTRATION OF ANTI-PD-1/PD-L1 ANTIBODIES IN A MURINE NEUROBLASTOMA MODEL

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Background and Aims: The infiltration of immune cells into the tumor microenvironment plays an important role in the anti-tumor immune response. Immune checkpoint inhibition has been shown to suppress tumors in a mouse neuroblastoma model but does not inhibit tumor growth. Here, we investigated in vivo anti-tumor effect of simultaneous administration of anti PD-1/PD-L1 antibodies and further analyzed the relationship between tumor growth inhibition and infiltration of immune regulatory cells infiltration.
Methods: Mouse neuroblastoma cells (Neuro-2a) were subcutaneously inoculated into A/J mice, and anti-PD-1/ PD-L1 monoclonal antibodies (mAbs; 200 μg/mouse) were intraperitoneally administered five times (on day 7,8,9,12 and 14 after the tumor cell inoculation). Tumor weight was assessed, and $CD4^+CD25^+$Fox $P3^+$ cell and $CD3^-CD49b^+$ cells were detected by flow cytometry, regulatory T cell and natural killer (NK) cell in the spleen and tumors of tumor-burden mice were measured.
Results: Simultaneous administration of anti-PD-1/PD-L1 mAbs significantly and moderately inhibited tumor growth in 80% of the mice, whereas no tumor suppression was not observed in the remaining 20% of the mice. The ratio of $CD4^+CD25^+FoxP3^+$ cells in the spleen was not significantly different among the treatment group: significant, moderate tumor suppression and isotype control. In addition, $CD4^+CD25^+$ tumor infiltrating lymphocytes were observed from all groups, but FoxP3 expression in these cells were not observed. Compared to isotype-treated or moderator tumor-suppressed mice, a significant increase in tumor infiltrating $CD3^-CD11b^+CD49b^+$ NK cells were observed in mice with significantly suppressed tumors. Ratio of NK cell infiltration and tumor weight were negatively correlated in the mAbs co-administered group.
Conclusions: $CD4^+CD25^+FoxP3^+$ regulatory T cells did not contribute the extent of tumor suppressive by co-administration of anti-PD-1/PD-L1 antibodies. The promotion of $CD11b^+$ $CD49b^+$ NK cell infiltration into the tumor microenvironment may play an important role in the anti-tumor immune response induced by immune checkpoint inhibition in neuroblastoma.

EP153 / #729

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

STRUCTURAL DISRUPTION OF BAF CHROMATIN REMODELLER IMPAIRS NEUROBLASTOMA METASTASIS BY REVERTING AN INVASIVENESS EPIGENOMIC PROGRAM

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Background and Aims: Epigenetic programming during development is essential for the determination of cell lineages, and its alteration contributes to the initiation of embryonal tumors. In neuroblastoma, neural crest progenitors block their natural differentiation course into sympathoadrenergic cells, leading to an aggressive and metastatic pediatric cancer. The study of the epigenetic regulators responsible for oncogenic epigenomic networks is crucial to develop new epigenetic-based therapies against these tumors. mSWI/SNF ATP-dependent chromatin remodeling complexes act genome-wide translating epigenetic signals into opened chromatin states. Our aim is to understand the role of mSWI/SNF complexes in the control of the oncogenic epigenomes of neuroblastoma in order to unveil new targets and to develop new epigenetic-based therapeutic strategies for this pediatric cancer.
Methods: Functional characterization of mSWI/SNF complexes in neuroblastoma cells was performed by proteomic, transcriptomic and chromatin accessibility analyses, and the effects of its inhibition on oncogenic features were assessed with in vitro functional assays and neuroblastoma metastasis mouse models.
Results: Neuroblastoma cells contain the three main mSWI/SNF subtypes, but only BAF complex disruption through silencing of its key structural subunits ARID1A and ARID1B impairs proliferation by promoting cell cycle blockade. Genome-wide chromatin remodeling analysis coupled with whole transcriptome data revealed that BAF disruption results in the epigenetic repression of an extensive invasiveness-related expression program, involving integrins, cadherins and key mesenchymal regulators, thereby reducing extracellular matrix adhesion and invasion in vitro, together with a drastic inhibition of neuroblastoma metastasis initiation and growth in vivo.
Conclusions: We define a novel ATPase-independent role for BAF complex in the maintenance of an epigenomic program that allows neuroblastoma invasiveness and metastasis, urging the need for new BAF pharmacological structural disruptors for its therapeutic exploitation in metastatic neuroblastoma.

EP154 / #1396

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

PROGNOSTIC VARIABLES AND OUTCOME OF HIGH RISK NEUROBLASTOMA TREATED IN A TERTIARY CANCER CENTRE IN INDIA

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Background and Aims: Outcomes of High-risk neuroblastoma (HR-NBL) in Lower-Middle Income Countries (LMICs) are adversely affected by toxicities, non-availability of(or delay in) Autologous-stem cell transplant(Auto-SCT) and immunotherapy. Herein, we study the clinical profile and outcomes of HR-NBL treated with intensive protocol without immunotherapy.
Methods: Treatment-naive children with biopsy-proven HR-NBL from July 2018 to December 2020 were retrospectively analysed. INRG stratification was used based on MIBG scan, FDG-PETCT scan, bone marrow studies, N-Myc/SCA reports. Rapid COJEC induction and surgery of primary after achieving metastatic Complete Response/Very Good Partial Response(mCR/VGPR) was followed by Auto-SCT and radiotherapy(RT). If end-induction bone marrow was involved, 2 cycles of TVD(topotecan,vincristine,doxorubicin) were administered. Oral maintenance consisting cis-retinoic acid, cyclophosphamide, etoposide and celecoxib was administered post RT. Survival was analysed by log rank test and prognostic factors by cox proportional-Hazard model using SPSS(Version-26).
Results: Among 64 eligible patients, median age was 39months(16-128months) with suprarenal primary in majority[42(65.6%)]. Molecular data was available for 43 of whom 17(39.5%) had N-Myc amplification. All but one were metastatic at presentation with bone-marrow, bone, lymph-nodes, lung metastases seen in 47(73%), 26(46%), 3(4.6%), 2(3.1%), respectively. At the end of Rapid COJEC induction, mCR/mVGPR was achieved in 39(60.9%). There were 6(9.4%) toxic-deaths, 5(7.8%) progression, 1(1.5%) palliation due to poor general condition. Half(7/14) of those who received TVD attained mCR. Out of 42 who underwent surgery, 31 achieved gross total resection. Thirty-eight(59.4%) underwent Auto-SCT(toxic-death post Auto-SCT-1). At a median follow-up of 29months (95%CI:9.0-20.99), 3year EFS/OS of the entire cohort was 24±7.2% and 25.2±5.8%, and of those who completed the multi-modality treatment was 32.7±11.1% and 36.6±8.7% respectively. On multivariate analysis, PET response (in mCR/mVGPR) [HR:2.9(1.01-8.53,p=0.04)] and gross total surgical resection[HR:3.1(1.03-9.88,p=0.49)] were prognostic.
Conclusions: Outcomes of HR-NBL even with a strategy including Auto-SCT is suboptimal in LMICs. Persistent bone marrow disease and inadequate metastatic response had a poor outcome in spite of intensive therapy.

EP155 / #169

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

CONGENITAL NEUROBLASTOMA: PRENATAL DIAGNOSIS AND CLINICAL COURSE

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Background and Aims: Neuroblastoma (NB) is the most common neonatal malignant solid tumor and amounts to 26% of all prenatally diagnosed neoplasms (Isaacs, 2002). The aim was to analyze NB cases detected in utero and to characterize the disease course and therapy outcomes.
Methods: 29 patients with a diagnosis of NB first suspected during the antenatal ultrasound examination for the period 01.2012-07.2021 (115 months) were included in the analysis. The diagnosis was made according to the international criteria. Staging was according to INSS, therapy was carried out per the modified German NB2004 protocol. Database was locked on 01.07.2021.
Results: The male:female ratio was 0.8:1. The median gestational age at the time of the first pathological changes detection (n=25) was 36 weeks (range 28-40). Adrenal/retroperitoneal masses were detected in 20/29 (69%), abdominal masses – 7/29 (24%), other topography – 2/29 (7%). Median age of NB diagnosis was 1.9 months (range 0.4-12.7). Most cases were detected before 3 months of age (21/29, 72.4%). In 10 patients (34.5%) of this group, the diagnosis was verified in the first month of life. Primary tumor topography included adrenal gland (26/29, 89.7%, among them 8 cases had bilateral involvement), retroperitoneal space (1/29, 3.4%), posterior mediastinum (2/29, 6.9%). MYCN was nonamplified in all detected cases (26/26). Stage distribution: stage 1 - 17/29 (58.6%), there was one case of stages 2, 3 and 4, stage 4S - 9/29 (31.0%). Patients were stratified to low (28/29, 96.6%), and intermediate (1/29, 3.4%) risk groups. 6 patients in the low-risk group with stage 4S were treated with chemotherapy. Relapse/progression was detected in 3/29 (6.9%) cases. The median follow-up period was 46.9 months (range 3.5-99.6). All patients were alive.
Conclusions: The long-term prognosis of prenatally diagnosed NB was excellent. Multidisciplinary discussion since detection of fetal masses and institutional collaboration are important for organization of timely postnatal NB management.

EP156 / #360

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

OCULAR ABNORMALITIES IN PATIENTS TREATED WITH AN ANTI-GD2 MONOCLONAL ANTIBODY DINUTUXIMAB BETA

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Background and Aims: The aim was to analyze the incidence and the type of ocular abnormalities (OA) in high-risk (HR) neuroblastoma (NB) patients treated with dinutuximab beta (DTB).
Methods: The medical records of 21 patients who received immunotherapy for HR NB were retrospectively analyzed. 16 (76.2%) patients received DTB in front-line settings, 5 (23.8%) at relapse/progression. All patients underwent a comprehensive ophthalmologic examination prior to each course of therapy. At the start of DNB, 7 patients had OA, where 2/7 wore bifocal reading glasses. Survival analysis was performed using the Kaplan-Meier method with appearance OA as an event.
Results: Median age at diagnosis of NB was 54 months (range 25–119). Male:female ratio – 0.75:1. OA observed in 13/21 (61.9%) cases. 3/13 (23%) patients were prescribed bifocals reading glasses for the first time. Following abnormalities were noted: impaired accommodation (n=9), mydriasis (n=3), impaired photoreaction (n=3), anisocoria (n=2), cycloplegia (n=1), no photoreaction (n=1). Patients might have several ocular abnormalities at the same time. Age (58 months (interquartile range (IQR) 43–84) with versus 51 months (IQR 37–58) without OA, p=0.336) and sex (8/12 (66.7%) females versus 5/9 (55.6%) males, p=0.673) were not associated with the incidence of OA. Patients who had ocular pathology prior to therapy with DTB were 4 times less likely to develop ophthalmologic toxicity (0/4 (0.0%) versus 13/17 (76.5%), p = 0.012, odds ratio – 0.24 (0.10–0.55). Based on Kaplan-Meier method OA developed in 50% of cases after 36.0 days from the start of DTB treatment. OA were detected between 2-40 days of therapy. OA developed in 50% of cases after receiving a total dose of 128 mg. In our study, no dose-related effect was found between DTB and OA.
Conclusions: Ocular abnormalities are a common complication of DTB. Careful monitoring of patients by an ophthalmologist is recommended.

EP157 / #388

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

'ULTRA-HIGH-RISK' NEUROBLASTOMA SUBGROUP: A TOOL TO PREDICT SURVIVAL IN CHILDREN WITH NEWLY DIAGNOSED HIGH-RISK NEUROBLASTOMA

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Background and Aims: The International Neuroblastoma Risk Group Staging System (INRGSS) and the NB-2004 protocol are important tools for risk assessment in patients with neuroblastoma (NB). In recent years, many research groups have attempted to define a subgroup of 'ultra-high risk' patients in order to apply alternative therapeutic approaches to such patients, but research results are still insufficient. The aim of this study was to develop widely available tool for use at the time of diagnosis to identify a subgroup of 'ultra-high risk' patients with NB at risk for very poor outcome.
Methods: This retrospective single-centre study included 107 high-risk patients (56 boys, median age 28.4 months, range 1-169 months) with newly diagnosed NB. Cox regression analysis was used to build a predictive model. Based on the results of the ROC analysis, the quality of the model was assessed in a three-stage cross-validation with the calculation of the sensitivity/specificity ratio.
Results: Three-year event-free survival was 39.9±5.1%, three-year overall survival - 64.7±5.0%. In multivariable regression analysis, ferritin levels ≥210 μg/L (risk ratio (RR): 1.78, score 10 if true), the presence of a 1p deletion (RR: 2.08, score: 6), and bone marrow metastasis (RR: 2.70, score: 5.5) were significant predictors of an unfavorable outcome. The patient is classified in a 'ultra-high risk' subgroup if the total score (sum of scores for each predictor) is ≥7. The developed tool was characterized by an acceptable prognostic quality (AUC = 0.768, sensitivity - 68.3%, specificity - 70.2%). The predictive value of the model was stable during validation ($p<0.05$ at each stage of validation).
Conclusions: The developed tool for identifying an additional subgroup of 'ultra-high risk' patients with neuroblastoma can be used by oncologists in clinical practice.

EP158 / #1401

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

IMMUNOTHERAPY AFTER AUTOLOGOUS OR ALLOGENEIC HEMOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH HIGH-RISK NEUROBLASTOMA, A SINGLE CENTER EXPERIENCE

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Background and Aims: The long-term results in patients with high-risk neuroblastoma (HR NB) are still unsatisfactory, especially if primary resistant or relapse (rrNB) develop. While there is a strong body of evidence supporting the use of anti-GD2 antibodies in patients with primary HR NB, it is less commonly used in rrNB cases. Although immunotherapy is not yet incorporated into local standard, it was used within pilot clinical trials recruiting autologous (auto-HSCT) and haploidentical hemopoietic stem cell transplantation (haplo-HSCT) recipients.
Methods: A total of 23 patients with a median age of of 3 (1-15) years at diagnosis with HR NB (n=19) or rrNB (n=4) treated in RM Gorbacheva Research Institute were included. All primary patients were initially treated according to national guidelines (modified GPOH NB2004 protocol) reaching complete (CR; n=16) or very good partial response (VGPR; n=3). Among 4 patients with rrNB 2 were in CR or VGPR, while other 2 achieved stable disease (SD) prior to haplo-HSCT. Immunotherapy consisted of 5 dinutuximab beta cycles (100 mg/m2 each) via prolonged 10-day infusion. One patient with SD it also received anti-PD1 antibodies (nivolumab).
Results: With a median follow-up of 20 months the 2-year EFS in auto-HSCT recipients was 78%, which is much better compared to similar cohort of 96 patients treated in 2008-2019 (p=0.02). Both patients with rrNB achieving response prior to haplo-HSCT are alive and disease-free 18 and 28 months post-transplant. One patient with SD died due to disease progression, another relapsed after a long-term (55 months) response to combined immunotherapy. Immunotherapy was well tolerated in all but 2 cases, in which it was ceased prematurely due to neurotoxicity development (both patients still retain the response).
Conclusions: Immunotherapy provides reproducible results in auto-HSCT recipients. It may also be a feasible post-consolidation strategy in NB patients with rr NB, although larger cohort studies are needed.

EP159 / #912

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

LATE COGNITIVE AND ADAPTIVE OUTCOMES OF PATIENTS WITH NEUROBLASTOMA-ASSOCIATED OPSOCLONUS-MYOCLONUS-ATAXIA-SYNDROME: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP (COG)

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Background and Aims: Opsoclonus-myoclonus-ataxia syndrome (OMAS) is a rare autoimmune disorder of the nervous system that presents with abnormal eye and limb movements, altered gait, and increased irritability. Between 2-4% of children diagnosed with neuroblastoma have neuroblastoma-associated OMAS (NA-OMAS). Children with NA-OMAS typically present with low-risk disease that is cured with surgery alone or surgery and less intensive chemotherapy. Despite excellent overall survival, however, patients with NA-OMAS can have persistent significant neurological deficits. COG protocol ANBL00P3, a randomized prospective therapeutic clinical trial for patients with NA-OMAS, demonstrated that the addition of intravenous immunoglobulin (IVIG) to prednisone and risk-adapted chemotherapy significantly improved the one year post-diagnosis response rate. Herein we report the evaluation of long-term neurocognitive and adaptive functioning.
Methods: Of 53 children enrolled on ANBL00P3, 29 submitted evaluable neurocognitive data at diagnosis and additional scheduled time points and were included in the analyses. Adaptive development was assessed via the Vineland Adaptive Behavior Scale, and validated, age-appropriate tools including the BSID, WPPSI-R, WISC-III were used to assess neurocognitive function.
Results: Eighteen patients were treated with chemotherapy and IVIG (IVIG+). The remaining eleven received chemotherapy only. Descriptive spaghetti plots suggest that treated patients, regardless of group, demonstrated relatively stable cognitive functioning and stable to improved adaptive development over time. Descriptively, the IVIG+ group demonstrated greater improvements in adaptive development compared to the chemotherapy-only group.
Conclusions: Study participants appear to demonstrate stable cognitive functioning and stable to improved adaptive functioning over time. The addition of IVIG to a chemotherapy-only regimen may offer some additional benefit by further improving long term adaptive outcomes. While statistical significance is limited by small sample size, findings suggest that aggressively treating NA-OMAS may be associated with improved long-term cognitive and adaptive functioning as compared to historical cohorts.

EP160 / #660

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

CELL-FREE MRNA FROM PLASMA IS ENRICHED IN EXTRACELLULAR VESICLES IN PATIENTS WITH NEUROBLASTOMA

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Background and Aims: Liquid biopsies have been studied as diagnostic modalities in patients with neuroblastoma, focusing mostly on detection of circulating tumor cells and cell-free DNA (cfDNA) from plasma. However, these approaches have their specific limitations. Plasma contains more particles that represent potential biomarkers, including cell-free RNA (cfRNA) and extracellular vesicles (EVs), which are shed by every cell in the body. We investigated the potential of cfRNA detection from plasma of patients with neuroblastoma, and whether these targets are associated to EVs.
Methods: We isolated cfRNA from 200ul of plasma from 20 healthy controls and from 40 patients with neuroblastoma (10 with localized and 30 with metastatic disease). We performed droplet digital PCR (ddPCR) for neuroblastoma-specific genes (PHOX2B, TH, CHRNA3), genes involved in cell cycle regulation (E2F1, CDC6, ATAD2, DHFR, H2AFZ, MCM2) and potential cfRNA reference genes (GUSB, B2M and HPA1a/b) using 4 multiplex assays. cfDNA was also analyzed by ddPCR for methylated RASSF1A and ACTIN beta. EVs were isolated by size exclusion chromatography (SEC).
Results: Thirteen out of 30 samples from patients with metastatic disease were positive for at least one neuroblastoma-specific gene in cfRNA, all patients with localized disease were negative. The cell cycle genes were expressed in both healthy controls as well as in patients, and were not significantly overexpressed, except for DHFR which was higher in metastatic disease. Analysis of EVs showed presence of the neuroblastoma-specific genes and the cell cycle genes in the EV-enriched SEC fractions in patients' plasma. Interestingly, cfDNA was mostly concentrated in the non-EV SEC fractions.
Conclusions: We explore the possibilities of different cfRNA markers from plasma as novel biomarkers in neuroblastoma and we demonstrate that these mRNA markers are mostly concentrated in EV-enriched SEC fractions. This study forms a starting point for further investigations into mRNA from plasma as biomarker.

EP161 / #1776

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

MAINTENANCE WITH NAXITAMAB COMBINED WITH GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR AND INTRATHECAL TOPOTECAN FOR METASTATIC RETINOBLASTOMA

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Background and Aims: Metastatic retinoblastoma (RB) requires intensive chemotherapy due to its poor prognosis, which may lead to severe complications and/or second neoplasms in patients with germline RB1 mutation, highlighting the need of safer and more effective therapies. Disialoianglioside GD2 is highly expressed in most RB, consequently, anti-GD2 monoclonal antibodies, responsible for increasing survival for high-risk neuroblastoma, may be a therapeutic option.
Methods: Report of two cases with metastatic RB who received five cycles of subcutaneous (SC) GM-CSF for 5 days at 250 µg/m2 /day (days -4 to 0) and 500 µg/m2/day (days 1-5), and naxitamab infused over 30 minutes at 3 mg/kg/day, days 1, 3, and 5, outpatient. Intrathecal topotecan was administered at 0.4 mg/dose for 6 cycles.
Results: Two patients (“A” and “B”) referred to our center at the age of 18 months and 5 years respectively with bilateral retinoblastoma. A systemic metastatic relapse was detected 6 years after diagnosis consisting of bone marrow and liver metastasis (“A”) and bone marrow and minimally disseminated disease in the CNS (qPCR positive for CRX on CSF) (“B”). Previous treatment included local (intravitreal melphalan, tandem intra-arterial topotecan-melphalan, thermotherapy) and systemic cytostatic therapy (>10 cycles), enucleation of one (“A”)/both eyes (“B”) and, in “A”, intrathecal topotecan due to CNS involvement. Both patients received COG-0321-based chemotherapy but in patient “A”, a severe hypersensitivity to Cisplatin occurred and, in “B”, ototoxicity, limiting the use of platinum derivatives. After achieving complete remission, patients underwent consolidation with high-dose chemotherapy with autologous stem cell rescue followed by maintenance with naxitamab and GM-CSF plus intrathecal topotecan in “B”. No major toxicities were reported. Both patients continue without evidence of disease 20 and 26 months after extraocular relapse.
Conclusions: Naxitamab and GM-CSF maintenance +/- Intrathecal topotecan were safe and well tolerated and may become potential therapeutic tools for high-risk retinoblastoma.

EP162 / #278

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

CATECHOLAMINE-NEGATIVE NEUROBLASTOMA PATIENTS: THE ROLE OF NORADRENERGIC-TO-MESENCHYMAL TRANSITION?

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Background and Aims: Urinary catecholamine metabolites play a role as diagnostic and prognostic biomarker in neuroblastoma. Two neuroblastoma-specific cell states are defined, namely noradrenergic (NOR) and mesenchymal (MES), with possible different catecholamine excretion profiles. In this study we investigated the biology of catecholamine excretion in vivo and in vitro.
Methods: Catecholamine metabolites were measured in 73 high-risk patients and in culture medium of 26 neuroblastoma cell lines. The presence of catecholamine enzymes in neuroblastoma cell lines and primary tumors was examined with qRT-PCR, western blot and immunohistochemistry (IHC). Additionally, catecholamine excretion was compared in 3 matched NOR- and MES neuroblastoma cell lines and tested after overexpressing TFAP2B and PRRX1.
Results: 71 out of 73 patients had at least one elevated metabolite at diagnosis (sensitivity 97%). In 18 out of 30 patients with relapse urinary data was collected, of whom 5 patients where catecholamine negative (28%). Catecholamine metabolite levels were detected in the medium of 8/26 of the tested cell lines, which was related to the presence of the enzyme tyrosine hydroxylase (TH). TH protein was present in all the excreting and absent in all the non-excreting cell lines. IHC staining for TH in primary tumors showed an identical pattern with all catecholamine positive patients being TH positive (n = 70), whereas all catecholamine negative patients were TH negative (n = 3). Finally, catecholamine excretion was observed in all NOR cell lines (3/3), but absent in all MES cell lines (0/3). Overexpression of PRRX1 induced mesenchymal transition and stopped catecholamine excretion. TFAP2B overexpression restored catecholamine excretion in NOR non-excreting cell line, but not in a MES cell line.
Conclusions: Catecholamine negative phenotype is due to downregulation of TH, which might be dictated to the fine balance between NOR- and MES cell types.

EP163 / #1679

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

IRINOTECAN AND TEMOZOLOMIDE ACTIVITY FOR RELAPSED/PROGRESSIVE NEUROBLASTOMA DURING NAXITAMAB IMMUNOTHERAPY

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Background and Aims: Anti-GD2 monoclonal antibodies are effective in preventing relapse in patients with high-risk neuroblastoma (HR-NB) in complete remission and show objective responses (OR) in relapsed/refractory HR-NB patients alone or combined (chemo-immunotherapy) with Irinotecan and Temozolamide (I/T). We hypothesized that relapsed/progressive neuroblastoma under naxitamab treatment may respond better to rescue I/T (chemo-immunotherapy effect) than historical cohorts from the pre-immunotherapy era.
Methods: This is a single-institution retrospective review of all patients with relapse or progressive HR-NB during treatment with naxitamab treated between June 2017 and January 2022 and rescued with 2 cycles of irinotecan (50 mg/m2/day x5) and temozolomide (150 mg/m2/day x5). Disease response was assessed by revised INRC criteria using 123I-MIBG SPECT/CT and four bone marrow aspirates.
Results: From June 2017 to January 2022, 165 patients received naxitamab based immunotherapy and forty-three relapsed or progressed during treatment. Nineteen received I/T as recue, 12 because of relapse (nine first relapse; two second relapse; and one fourth relapse) and seven with refractory disease and progression. Median age at the time of relapse or progression was 5.9 years (range: 3-15.8). Median number of naxitamab cycles received before I/T was four (range: 2-7). Four patients had MYCN amplified tumors. Relapse or progression was isolated to bone in sixteen patients; bone and soft tissue in three including one with bone marrow involvement. Ten patients had ≥ 3 lesions. Five (26.3%) patients presented OR (4 complete and 1 partial response) after two I/T cycles. Thirteen patients had stable disease and one progressive disease.
Conclusions: The OR rate with I/T in our series compares favorably to studies where I/T is used without immunotherapy suggesting anti-GD2 mAb as a mechanism of potentiating chemotherapy even when administered sequentially.

EP164 / #1760

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

EVALUATING CADO FOR PALLIATION IN A LOW-INCOME SETTING AMONG UGANDAN CHILDREN DIAGNOSED WITH NEUROBLASTOMA

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Background and Aims: In low-income settings, therapies are often not available during high-risk (HR) neuroblastoma (NB) management and treatment is with non-curative intent. Globally the CADO treatment protocol (oral cyclophosphamide 50 mg/m^2, IV doxorubicin 35 mg/m^2, IV vincristine 1.5 mg/m^2) has been used for palliative purposes in HR-NB. Our study aimed to determine the value of maintenance CADO after induction with OPEC/OJEC on outcomes in Uganda.
Methods: A multicentre, retrospective chart review of children younger than 16 years diagnosed with HR-NB between January 2010 to November 2020, and treated with either OPEC/OJEC induction chemotherapy alone or with maintenance CADO in addition to the induction, was conducted. Clinical characteristics at diagnosis and cytopaenias, numbers of blood product transfusions and infections during CADO, to evaluate treatment toxicity, were documented. Kaplan-Meier survival curves were used to determine the median survival time and two-year overall survival (OS) rates.
Results: Forty-five patients were included, 32 (71.1%) had received “induction only” and 13 (28.9%) “induction plus maintenance CADO”. The median age at diagnosis for the “induction only” and “CADO maintenance” group were 49.5 and 52 months respectively (p=0.9). Both groups compared similarly on sex, primary tumour site, LDH, ferritin, stage and MYCN. The total number of cycles administered in the “CADO maintenance” group was 99 cycles (range 1-11, median of 11). During the CADO cycles, only one neutropenic fever, one non-neutropenic fever and one platelet transfusion were documented. The median survival times for the “CADO maintenance” group and the “induction only” group were 38.5 and 12.6 months (p=0.5) respectively while the 2-year OS rates were 46.2% and 34.3% respectively (p=0.5). The five-year OS for both groups was <5.0%.
Conclusions: In settings where HR-NB therapies are limited, maintenance CADO appears to offer increased survival benefits with minimal toxicity during palliation. Studies of larger cohorts to evaluate CADO during HR-NB are recommended.

EP165 / #749

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

CLINICOPATHOLOGICAL IMPLICATIONS OF GANGLIONEUROBLASTOMA INTERMIXED

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Background and Aims: International Neuroblastoma Risk Group (INRG) consensus pretreatment classification schema stratifies patients into low, intermediate, and high-risk using the patient age, clinical stage, histology, 11q aberrations and amplification of MYCN gene. We studied patients with the primary pathologic diagnosis of Ganglioneuroblastoma Intermixed (GNBI) - regarded as a tumor with “favorable” histology by International Neuroblastoma Pathology Classification (INPC) system - to evaluate the correlation of this diagnosis with the clinicopathological features.
Methods: Retrospective search of the archives of the pathology department of our institution between 1995 and 2021 revealed 15827 specimens from 2805 patients. The term “Ganglioneuroblatoma Intermixed” was found in 237 cases. Of the 237 cases, 57 had initial diagnosis of GNBI. The clinical and follow up data (median 3.3 years, range 0.2-13.7), and MYCN amplification status were available for all patients; targeted exome sequencing data was available in 23 patients. Clinical stage was determined using clinical/radiological (including MIBG scanning) data and pathological confirmation.
Results: 25% (14/57) of patients with primary GNBI had metastatic disease at presentation (INRG stage M). 50% (7/14) of patients with metastatic GNBI relapsed, as opposed to 5% (2/43) in locoregional disease. MYCN gene amplification was only detected in metastatic group (n=2); one of these relapsed. Primary tumors of the abdomen were more likely to relapse than those of thorax (8 vs. 1 case). Somatic alterations were detected in 8 patients (represented in both the groups).
Conclusions: Localized GNBI at diagnosis has excellent long-term clinical outcome. However, a proportion of cases with this pathologic diagnosis have metastases at the time of initial diagnosis. Therefore, rendering “favorable” histology in the pathology reports of primary GNBI in the absence of concurrent clinical and radiologic data may not reflect the true nature of disease. Very few patients with the initial diagnosis of GNBI show MYCN amplification.

EP166 / #1655

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

INTEGRATIVE ANALYSIS OF FEN1 EXPRESSION AND PROGNOSTIC IMPACT IN NEUROBLASTOMA

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Background and Aims: Neuroblastoma-NB is the most common childhood solid tumor. Despite advances in diagnoses and treatments, the prognosis of NB still remains poor. FEN1-Flap endonuclease-1, involves in DNA replication, long-patch excision repair, and telomere maintenance. FEN1 overexpression has been reported to be associated with the different types of cancers and chemotherapy resistance. It might be a predictive biomarker and therapeutic target in multiple cancers. However, the role of FEN1 in NB has not been thoroughly investigated now.
Methods: NB mRNA expression data was downloaded from UCSC XENA. Survival analysis of FEN1 expression were performed using Kaplan Meier. In addition, FEN1 expression data were also extracted from Pediatric Neuroblastoma (TARGET, 2018) database. Survival analysis was performed using cBioPortal. Through STRING tool to determine FEN1 binding proteins and based on interacted proteins, Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis was performed.
Results: 85 NB samples were selected from GDC TARGET-NBL dataset. Most of NB patients belonged to high risk group, INSS stage 4 and 4s with unfavorable histology. Kaplan Meier analysis showed higher FEN1 expression was correlated with poor survival outcomes ($p<0.05$). FEN1 expression exhibited significant positive association with CDCA5 expression($r=0.9$). Its overexpression was also related with poor survival outcomes($p<0.05$) in NB. KEGG analysis suggested FEN1 mainly participated in the cell cycle, DNA replication and homologous recombination function. In addition, FEN1 mRNA expression data from 139 TARGET NB patients were also analyzed using cBioPortal, which confirmed FEN1 higher expression was also related with poor survival in NB($p<0.05$).
Conclusions: Our study detected that the expression level of FEN1 was elevated in NB. Higher FEN1 expression was found to be correlated with poor overall survival. FEN1 may be an independent prognostic factor for NB. Further studies are required to explore the relative mechanisms in NB and the relationship between FEN1 and CDCA5.

EP167 / #1786

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

DINUTUXIMAB BETA-BASED CHEMO-IMMUNOTHERAPY FOR RELAPSED/REFRACTORY HIGH-RISK NEUROBLASTOMA: PRELIMINARY RESULTS

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Background and Aims: Relapsed or refractory (R/R) high-risk (HR) neuroblastoma (NB) has a dismal prognosis. Anti-GD2-mediated chemo-immunotherapy has a considerable anti-tumor activity in patients with R/R HR-NB. In the present study, we purposed to investigate the impacts and adverse effects of the combination of immunotherapy with dinutuximab beta (DB) and chemotherapy in patients with R/R HR-NB.
Methods: Patients of over 12 months with documentation of a HR-NB diagnosis were eligible at relapse or designation of refractory disease status. Inclusion criteria were as follows: relapsed or refractory, measurable by contrast-enhanced magnetic resonance imaging (MRI) and/or computed tomography (CT) or metaiodobenzylguanidine (MIBG)/ fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT evaluable disease and/or demonstrated by bone marrow aspiration and biopsy. Chemotherapy scheme was irinotecan (IV, 50 mg/m² per dose, on Days 0-4) and temozolomide (PO, 100 mg/m² per dose, on days 0-4). Dinutuximab beta was administered intravenously for 10 days through continuous infusion with 10 mg/m2 per day (on Days 1-10). The patients received 2 to 12 successive cycles with duration of 28 days each. Disease assessment was performed after cycles 2, 4, and 6 and every 2 to 3 cycles thereafter.
Results: Between January 2020 and January 2022, nineteen (n=19) patients received a total of 116 cycles of DB+CT. Objective (complete or partial) responses were achieved in 12/19 (63%) patients, including complete remission (CR) in 6/19 and partial response (PR) in 6/19. Stable disease was observed in two patients. The remaining five patients developed bone/bone marrow and soft tissue progression after 2-4 cycles of treatment. The most common side effect was fever, which was more common in the first cycles of treatment. Grade ≥3 toxicities were leukopenia (62%), thrombocytopenia (27%), hypertransaminasemia (25%), fever (14%), and rash/itching (11%), respectively.
Conclusions: DB-based chemo-immunotherapy is suitable leading to an encouraging response rate in patients with R/R HR-NB

EP168 / #1257

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

THE OPTIMAL USE AND EFFECTIVENESS OF 131I-META IODOBENZYLGUANIDINE (131I-MIBG) MOLECULAR RADIOTHERAPY FOR HIGH-RISK AND RELAPSED/REFRACTORY NEUROBLASTOMA

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Background and Aims: ^{131}I-mIBG therapy, originally used for refractory/relapsed neuroblastoma or for palliative bone pain, is being incorporated into induction and consolidation treatments.
Methods: Retrospective review of patients with high-risk/relapsed/refractory neuroblastoma ^{123}I-mIBG-avid scanning treated with ^{131}I-mIBG at our institution over the last 14 years.
Results: Twelve patients received 21 ^{131}I-mIBG cycles. There were 10 boys. Median age was 5.3 years (1.83-22.58). All had metastatic disease. Three patients had MYCN amplification. In 7 cases ^{131}I-mIBG was used as induction therapy prior surgery [median time 10.5 days before surgery (8-154)] and in another 2 cases, as consolidation prior stem cell transplantation (21 and 23 days before). In patients undergoing transplantation after surgery, median time between ^{131}I-mIBG and transplantation was 76 days (27-154). In 12 cases ^{131}I-mIBG was administered for relapsed/refractory disease, two of them as pain-controlling palliative treatment. Three patients received chemotherapy concomitantly. Four patients received ^{131}I-mIBG treatment twice, one patient three cycles and another patient four. The administered activity of ^{131}I-mIBG median dose was 200 mCi (3.7 GBq). Five patients are dead of progressive disease. Four patients are in complete remission with a median follow-up time of 8.46 years (5.67-11.42), one of them despite harboring MYCN amplification. Tolerance was excellent: one grade 2 hypertension, one grade 2 vomiting and one infusion reaction. Median admission time was 3 days (3-5). Two cases developed grade 4 pancytopenia, with prolonged thrombocytopenia. Eight/nine patients developed chronic hypothyroidism requiring replacement therapy.
Conclusions: ^{131}I-mIBG therapy is feasible as induction therapy, consolidation and relapsed/refractory neuroblastoma, especially in chemo-resistant neuroblastomas. Ideally, blood stem cells should be collected before ^{131}I-mIBG treatment. When used pre-operatively, it seems to facilitate surgery. The most important side effect is thrombocytopenia, especially when the bone marrow is affected. Surgery should be performed early after the ^{131}I-mIBG treatment, before the thrombocytopenia is established. Stem cell rescue ameliorates the thrombocytopenia.

EP169 / #832

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

SCHWANN CELL PRECURSORS IS THE CELL-OF-ORIGIN IN HUMAN NEUROBLASTOMA

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Background and Aims: Malignant mechanisms of neuroblastoma are shaped by its developmental origin from the neural crest. Recent insights into the fetal development of the adrenal gland extended our knowledge of cellular identities in neuroblastoma. However, its cell-of-origin is still unknown. Schwann cell precursors (SCPs) are migrating neural crest-derived multipotent stem cells recently described to contribute to adrenal development in humans. Compared to other migrating neural crest cells, SCPs exist for a longer period of time and serve as a stem cell reservoir for various cell types. Thereby, SCPs constitute a central progenitor cell within a complex system of cellular transitions. We seek to understand how this embryonic plasticity translates to the origin of neuroblastoma, therapeutic resistance or relapse.
Methods: We sequenced seventeen human neuroblastoma samples by single-cell RNA-sequencing and profiled more than 72,000 cells identifying main cell types including immune, mesenchymal and neural crest-derived adrenergic cells. Interestingly, we identified SCP-like cells connecting the adrenergic and mesenchymal compartments by cellular transitions. To study the SCP-like cells in greater detail, we applied a new multi-omics sequencing method (DNTR-Seq) that allowed us to jointly analyze the whole genome and transcriptome from single cells sorted for specific markers.
Results: We revealed a complex clonal structure of neuroblastoma showing an unexpected heterogeneity not only of adrenergic cells but also of malignant SCP-like cells. Importantly, all malignant cells identified shared one genetic aberration, a gain of Chr17, that we identified as the first malignant hit initially present only in SCP-like cells. These pre-malignant SCP-like cells distinguish from stromal SCPs by the overexpression of potential druggable genes such as NGFR or KPNB1.
Conclusions: We identified an unexpected heterogeneity and plasticity in human neuroblastoma relevant for therapeutic resistance and relapse. Our data suggest that the newly identified malignant SCP-like cells is the cell-of-origin in neuroblastoma and possibly act as a cancer stem cell.

EP170 / #18

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

EFFECT OF KIGELIA AFRICANA FRUIT EXTRACT ON STAGE 4 NEUROBLASTOMA

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Background and Aims: Neuroblastoma (NB), an embryonal tumor deriving from the neural crest, is one of the most common solid pediatric tumors. Especially high-risk NBs, e.g. with MYCN amplification, still account for about 12-15% of cancer related deaths in children. Kigelia africana (KA), is a plant used in traditional African medicine which has already shown its anti-cancer potential in several studies. The aim of this study is to evaluate the effect of KA fruit extract on stage 4 high-risk NB cells on terms of cell survival and immunomodulation.
Methods: NB cells with and without MYCN amplification and non-neoplastic cell lines were treated with KA fruit extract at different concentrations. The effect of KA on cell viability and apoptosis rate were assessed by bioluminescence-/fluorescence-based assays. Expression levels of EGFR (epidermal growth factor receptor) and the NFkB (nuclear-factor kB) subunit p65 were analysed via Western blot and microscopy. Secretion of pro- and anti-inflammatory cytokines was determined by ELISA.
Results: At low doses and contrary to non-neoplastic cells, KA-treated NB cell lines show a significant reduced viability and induced cell death, especially in MYCN non-amplified tumor cells. Interestingly, incubation of tumor- and non-tumor cells with KA leads to a regulation of NF-kB p65 phosphorylation and EGFR expression. Furthermore, KA shows no effect on the cytokines expressed by NB but on several of those expressed by non-tumoral cells.
Conclusions: Our results demonstrate a cytotoxic effect of KA fruit extract on NB, especially in MYCN non-amplified tumor cell lines, but not on non-neoplastic cells. We propose a KA-mediated regulation of cell survival and apoptosis in tumor cells by modulating expression and activation of EGFR and NF-kB, respectively. Furthermore, immunomodulation by NB appears not to be directed by tumor cytokine production and thus, further research on NB immune-key rolers must be assessed.

EP171 / #722

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

COMBINATIONAL TREATMENT WITH ROCK INHIBITOR RKI-1447 AND BET INHIBITORS SYNERGISTICALLY IMPAIRS NEUROBLASTOMA GROWTH

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Background and Aims: Neuroblastoma originates from cells within the neural crest and is most commonly diagnosed in children under the age of two. In every fourth neuroblastoma patient, whole genome and whole exome sequencing previously revealed at least one somatic mutation or structural aberration in genes regulating the Rho/Rac signaling pathway; a pathway implicated in neural crest differentiation and migration. These mutations push active Rho, which increases downstream Rho-associated kinase (ROCK) activation. Formerly, ROCK was identified as a promising drug target in neuroblastoma and other cancer diagnoses.
Methods: The pan-ROCK inhibitor RKI-1447 was studied in viability assay, clonogenic assay and a neuroblastoma transgenic mouse model, TH-MYCN. Drug combination screening of RKI-1447 with FIMM oncology drug library yielded synergistic partners that were validated by drug matrices using WST-1. Further testing of synergistic concentrations was performed using clonogenic assays, western blots, immunohistochemistry and a 3D multicellular tumor spheroid (MCTS) model, composed of fibroblasts and neuroblastoma cells.
Results: Our studies demonstrate that ROCK inhibition by RKI-1447 suppressed neuroblastoma growth both in vitro in neuroblastoma cell lines and in vivo in TH-MYCN mice. Additionally, RKI-1447 impaired the clonogenic capacity of neuroblastoma cells. Combinational drug screening revealed synergistic effects between RKI-1447 and inhibitors of bromodomain and extraterminal (BET) proteins. Combining BET inhibitor ABBV075/mivebresib with RKI-1447 we evaluated the potential of these combinations and observed synergistic effects in monolayer cell viability assays and MCTS. Immunohistochemistry staining on MCTS indicated increased cell death, measured by cleaved caspase 3, impaired cell viability and decreased tumor growth, in comparison to single drug treatment. Moreover, western blot analysis of combined RKI-1447 and ABBV075 treatment in neuroblastoma cells displayed decreased MYCN protein expression.
Conclusions: BET inhibitors have previously demonstrated potential for the treatment of neuroblastoma. We show that combination treatments of BET inhibitors with the pan-ROCK inhibitor RKI-1447 may offer a promising therapeutic approach.

EP172 / #1891

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

FRACTURE PREVALENCE IN CHILDREN WITH HIGH-RISK NEUROBLASTOMA

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Background and Aims: Children with high-risk neuroblastoma (HR-NBL) undergo intensive multi-modal therapy that increase their risk of acute and long-term toxicities. The aims of this study were to determine fracture prevalence and associated clinical characteristics in children with HR-NBL from time of HR-NBL diagnosis.
Methods: We conducted a retrospective cohort study of patients aged 0-30 years with HR-NBL at our tertiary-care institution and within the Pediatric Health Information System (PHIS) database from 2010-2021.
Results: We discovered a fracture prevalence of 6.7% (n=6) in 89 HR-NBL patients at our institution. Four patients had a fracture within 6 weeks of therapy completion, one during consolidation, and one 3 years off therapy. Mean age at diagnosis was 4.9 years and 4 patients were female. Lower extremities accounted for 5/6 fractures (2 femurs, 1 tibia, one metatarsal, one calcaneus) and one fracture in the radius. Three patients historically had iodine123-meta-iodobenzylguanidine (MIBG)-avid disease in the fractured bone (femurs and tibia) and 3 patients had no history of MIBG avidity in the fractured bone. Only one patient had MIBG avidity (due to disease recurrence) in the fractured femur about 2 months prior to time of fracture. Two out of 3 patients with vitamin D measurements had insufficiency (serum 25-hydroxy vitamin D 19 and 21 ng/dL). Four patients had a mean lumbar bone mineral density Z-score of -0.275 (obtained shortly after fractures). In review of the PHIS database, we discovered a 3.35% fracture prevalence (with a 95% confidence interval: 2.97-3.75%).
Conclusions: Higher prevalence of fractures was observed in our cohort of children with HR-NBL during and shortly after treatment compared to general pediatric population. Metastatic bone disease commonly present at time of diagnosis in addition to high-dose chemotherapy are likely major risk factors. Further studies are needed to determine the optimal time for evaluation and intervention to prevent bone health complications in HR-NBL.

EP173 / #1788

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

INCIDENCE OF ADRENAL INSUFFICIENCY IN CHILDREN WITH HIGH-RISK NEUROBLASTOMA

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Background and Aims: Patients with high-risk neuroblastoma (HRNBL) are at increased risk of toxicities due to aggressive, multi-modal therapy. The incidence of adrenal insufficiency (AI) has not been reported. Our primary aim was to determine the incidence of AI among patients with HRNBL at our institution and nationally.
Methods: A retrospective cohort study was performed at our institution including patients with HRNBL from 1998 to 2021. Demographic and clinical characteristics were evaluated in association with AI incidence. Summary statistics were computed and bivariate analyses were conducted using Pearson chi-squared tests, Fisher's exact tests, and Wilcoxon tests. Cox hazard regression models were used to examine the effects of gender and age at neuroblastoma diagnosis on time to AI diagnosis. A review of the Pediatric Health Information Systems (PHIS) database from 2010 to 2021 was performed to estimate the national incidence of AI in HRNBL.
Results: Among the institutional cohort of 93 HRNBL patients, 13 developed AI (14%). The adrenal gland was the primary tumor site in 61.3%. Two patients developed AI within 6 months and the latest case was detected at 218 months from time of HRNBL diagnosis. Though not statistically significant, survival curves demonstrate that females had a higher probability of developing AI compared to males (22.2% vs 6.25%; log-rank Chi-square = 1.9310, P = 0.16). When adjusting for gender, each year increase in age at HRNBL diagnosis suggests a 96% decreased risk of developing AI (P = 0.67). From the PHIS database an AI incidence of 5.2% was identified (95% confidence interval for this prevalence: 4.75-5.70%).
Conclusions: We report a 5-14% incidence of AI in children with HRNBL. Larger multi-institutional studies are needed to validate these findings and determine which patients are at particular risk of developing AI during or after treatment.

EP174 / #1842

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

FAVORABLE OUTCOME OF NEUROBLASTOMA PATIENTS WITH MUTATIONS INVOLVING NEUROBLASTOMA BREAKPOINT FAMILY OF GENES

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Background and Aims: Neuroblastoma Breakpoint Family (NBPF) genes are altered in patients with neuroblastoma and other malignancies. We used the TARGET-Neuroblastoma dataset to study alterations in these genes and their relation to risk stratification and outcome of patients with neuroblastoma.
Methods: Clinical data, mutational data, expression tables, and processed copy number variation per gene were obtained. Comparisons of categorical and numeric data were conducted using the chi-square test and Student's t test. Kaplan–Meier curves, log-rank tests, and Cox proportional hazards regression tests were used to analyze survival data. Log-transformed gene expression values of high and low/intermediate risk tumors were compared. For all tests, p-value ≤0.05 were considered statistically significant.
Results: Among 1076 patients with mutational data, 24 patients (2.2%) had 30 mutations involving NBPF genes; half (N=15) of these mutations were missense nonsynonymous. Patients with NBPF mutations were less likely to have metastatic disease (p=0.02) or high-risk disease (p=0.004) and had significantly better 5-year OS (92+/-5.6 vs. 63+/-1.5, p=0.015). When combined with risk stratification in multivariable Cox proportional hazard models, lacking NBPF mutations was associated with a hazard ratio for death of 4.01 (1.00-16.09, p=0.050). Combining results of RNA-seq and microarray gene expression data, high-risk tumors had significantly lower levels of NBPF1, NBPF8, NBPF15, and NBPF24 and higher levels of NBPF4, NBPF6 and NBPF22p.
Conclusions: Having mutations in NBPF is an independent prognostic factor predicting favorable outcome, particularly in patients with high-risk neuroblastoma. Differential gene expression shows that different NBPF genes have different expression patterns in low/intermediate- and high-risk tumors.

EP175 / #277

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

HARNESSING CRISPR/CAS9 MUTAGENESIS SCREENING FOR RATIONAL DESIGN OF NEXT-GENERATION CAR-NKT THERAPY AGAINST NEUROBLASTOM

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Background and Aims: Natural killer T cells (NKTs) possess innate antitumor properties that provide advantages over conventional T cells for use in cancer immunotherapy. We found that NKTs expressing a chimeric antigen receptor (CAR) specific for neuroblastoma antigen GD2 showed better tumor infiltration and ability to modify the tumor microenvironment than GD2-CAR T cells. Genes that regulate NKT cell persistence, functional fitness, and central memory differentiation remain largely unknown. To address this gap, we have developed a CRISPR/Cas9 screening system to identify genes that regulate the persistence and antitumor activity of NKTs and GD2-CAR NKTs for therapeutic targeting.
Methods: We have developed the first CRISPR/Cas9 screening system for use in human NKTs and GD2-CAR NKTs to identify genes that regulate survival and proliferation of these cells during in vitro serial tumor challenge. As part of this system, we generated a library of guide (g)RNAs (five per gene) specific for a panel of 1,117 immune-related and 48 non-targeting gRNA controls. We have developed methods for graded lentiviral transduction of NKTs/CAR-NKTs followed by multiplexed functional testing and next generation sequencing of gRNA-transduced cells. We also established a system to validate candidate genes that includes in vitro and in vivo functional assays.
Results: Our first screening round in human NKTs yielded nine candidate genes of interest, which we are currently validating in a series of functional experiments. We are also performing a CRISPR/Cas9 library screen in GD2-CAR NKTs challenged with GD2+ neuroblastoma cells in a serial tumor challenge assay.
Conclusions: A CRISPR/Cas9-based screening system is feasible for use in human NKTs/CAR-NKTs to identify novel genes that regulate persistence and antitumor activity of NKTs in an unbiased manner. Results obtained from this study will ultimately help to enhance the antitumor efficacy of NKT cell-based immunotherapy against neuroblastoma

EP176 / #507

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

SYNERGISTIC EFFECT OF WIP1 INHIBITOR SL-176 AND H3K27 DEMETHYLASE INHIBITOR GSK-J4 ON NEUROBLASTOMA CELLS AND SPHEROIDS

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Background and Aims: The phosphatase WIP1, an oncoprotein encoded by PPM1D on chromosome 17q, impedes DNA damage response and is overexpressed in neuroblastoma, correlating to clinical prognosis. The WIP1 inhibitor SL-176 has proven anti-neuroblastoma effect. In a drug combination screening, the most promising candidate for combination with SL-176 was GSK-J4, an inhibitor of histone H3K27 demethylases previously implicated in neuroblastoma and other malignancies.
Methods: Potential synergy was assessed in a range of neuroblastoma cell lines using viability assays and dose-response matrices analyzed with the SynergyFinder tool. For immunoblot, qPCR and RNAseq, IMR-32, SK-N-BE(2) and SK-N-AS cells were exposed to vehicle, SL-176, GSK-J4, or the combination. Protein or RNA was extracted after 1-144 or 6-72 hours, respectively. We also treated neuroblastoma multi-cellular tumor spheroids, observing size and viability and subsequently collecting them for immunohistochemistry.
Results: Viability assays in five neuroblastoma cell lines confirmed the synergistic effect of combining SL-176 with GSK-J4. Tumor spheroids treated with the drug combination showed smaller size and decreased viability after six days. Immunoblot experiments demonstrated a marked effect on WIP1 downstream targets and apoptosis markers for cells treated with the combination, compared to vehicle or single drug treatment which differed little from each other. qPCR confirmed a clear synergism of SL-176 and GSK-J4 with upregulation of p53 downstream targets PUMA and p21, where expression in combination- vs. single drug-treated cells differed by one order of magnitude. In reference to vehicle, RNAseq data showed 2580 differentially expressed genes in the combination-treated SK-N-BE(2) cells compared to 48 and 140 for cells treated with only SL-176 or only GSK-J4, respectively. For IMR-32 cells, these numbers were 645, 30 and 30.
Conclusions: Combining the WIP1 inhibitor SL-176 and the epigenetic modifier GSK-J4 induces synergistic cytotoxicity in neuroblastoma cells. The vast numbers of differentially expressed genes suggest a pervasive effect of this drug combination on transcription.

EP177 / #1136

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

INVESTIGATING THE INTERACTIONS OF DISTINCT TUMOR SUBPOPULATIONS IN HUMAN NEUROBLASTOMA USING SINGLE-CELL RNASEQ AND NOVEL SPATIAL MULTI-OMICS

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Background and Aims: Neuroblastoma (NB) is the most common and deadly infant malignancy, accounting for approximately 15% of pediatric cancer-related deaths. Survival in the high-risk group is still less than 50% which creates the need to identify the subpopulation of tumor cells displaying therapy resistance.
Methods: In our study, we used single-cell RNA sequencing to profile 17 NB samples from 15 patients and generated a database of ~70,000 single cells. This was followed by spatial multi-omics using a combined multiplex single-molecule DNA and RNA-FISH approach on NB patient biopsies.
Results: Unbiased single-cell clustering revealed thirteen cell types spanning tumor, immune and stromal cells. Among the tumor population, we found two clusters expressing known mesenchymal (PRRX1, LEPR) and adrenergic (TH, DBH) genes, indicative of mesenchymal and adrenergic tumor origin, respectively. These two putative tumor populations were connected by a “bridge” population that expressed key neural crest and Schwann lineage markers (SOX10, S100B) and was annotated as Schwann Cell Precursor–like (SCPs). Transcriptional profiling of the three distinct tumor populations revealed a continuous transition to both the MES and ADR lineages via the SCP-like population which harbored malignant aberrations. To further define the three tumor cell states and investigate a possible transition from malignant SCPs to malignant MES and/or ADR cells, we are in the process of implementing a single-molecule DNA and RNA-FISH approach. This method allows us to simultaneously, detect and validate abnormal DNA allelic expression and study RNA signatures through which we distinguish tumor subpopulations from normal stroma cells.
Conclusions: We conclude that there are three subpopulations of malignant NB tumor cells, and are in the process of investigating possible links between them. Increasing our understanding of the interactions between SCPs and their downstream tumor subpopulations may provide novel information aiding in the strategy for therapeutic targeting of resistance tumor cell types in high-risk NB.

EP178 / #953

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

NOVEL DRUG COMBINATIONS FOR NEUROBLASTOMA THERAPY – EXPLORING THE FULL POTENTIAL OF THE ROCK2-SPECIFIC INHIBITOR KD025

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Background and Aims: Neuroblastoma (NB) is an aggressive cancer of early childhood and a clinical challenge as the prognosis for high-risk patients remains poor. Novel drug combinations are needed to support existing therapies, improve survival, and reduce late effects. Our research group has previously demonstrated that the Rho/ROCK signaling pathway is a promising therapeutic target in NB. This study aims to explore novel drug combinations with focus on the ROCK2-specific inhibitor KD025 (Belumosudil, Rezurock™).
Methods: Drug combination screening was performed using KD025 together with a cancer drug library containing 528 drugs. Cell viability, clonogenicity, and protein expression/ phosphorylation were evaluated in NB cell lines treated with single drugs or drug combinations. Furthermore, IncuCyte® Live Cell analysis was used to monitor NB tumor spheroid growth and assess cell death. The in vivo efficacy of KD025 was evaluated in 9464D allografts and the transgenic TH-MYCN mouse model.
Results: Our work demonstrates that KD025 impaired cell viability and clonogenicity of NB cell lines, decreased N-Myc levels, and increased phosphorylation of p38 and Akt. Moreover, KD025 promoted the release of the danger-associated molecular pattern HMGB1 from SK-N-BE(2) cells. In addition, we observed that KD025 impaired tumor growth in 9464D allografts and in homozygous TH-MYCN mice but did not completely suppress tumor growth. An extensive combinational drug screening revealed several synergistic combination partners for KD025 including the DRD2 antagonist TIC10/ ONC201 and the p97 inhibitor NMS-873. Synergistic effects of these drug combinations were confirmed in NB cell lines grown in monolayer and tumor spheroids. Immunohistochemistry on tumor spheroids demonstrated that combinations of KD025 and TIC10 or NMS-873 reduced the number of Ki67-positive cells and increased the number of cleaved Caspase-3 positive cells in comparison to single drug treatment.
Conclusions: In conclusion, combination treatments using the ROCK2-specific inhibitor KD025 together with NMS-873 or TIC10 may be promising therapeutic approaches for NB.

EP179 / #703

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

BARRIERS AND FACILITATORS IN THE TRANSLATION OF NEUROBLASTOMA RESEARCH: A PILOT STUDY

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Background and Aims: The translation of preclinical findings to clinical applications is a time-consuming process that often spans years. In neuroblastoma, where overall survival is still only 61%, there is a striking discrepancy between the size and activity of the preclinical research field and the number of resulting new clinical applications. In this pilot study, we identified key barriers and facilitators that play a role in the progress of a preclinical discovery towards clinical implementation in neuroblastoma care.
Methods: Researchers and clinicians in the field of neuroblastoma were asked to provide their views on the process of translation, and key accelerating and/or delaying factors, using surveys (n=21) and semi-structured interviews (n=12). Questions were based on existing theoretical frameworks and formulated to allow new themes to emerge.
Results: Participants identified 6 important barriers and 3 important facilitators in the translational process. Perceived barriers were practical difficulties to integrate research and clinical data, the current academic reward system and career disincentives, low incidence of patients, regulations and legislation, high research costs and lack of funding, and a lack of adequate models for translational research. Perceived facilitators were a high level of multidisciplinary collaboration, international collaborations, and a high level of patient willingness to participate in research.
Conclusions: There is an urgent need to continue to improve and accelerate the process of translating neuroblastoma research into clinical practice. The barriers and facilitators identified in this study provide a guide for further research and highlight the areas that need to be prioritized to accelerate the translational process for pediatric oncology patients, specifically those with neuroblastoma.

EP180 / #1676

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

PATTERN OF RELAPSE IN HIGH-RISK NEUROBLASTOMA (HR-NB) PATIENTS CONSOLIDATED WITH NAXITAMAB

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Background and Aims: Consolidation with anti-GD2 immunotherapy has proved to be effective in reducing the risk of relapse in high-risk neuroblastoma (HR-NB). We here aim to describe the pattern of first relapse in patients diagnosed with HR-NB who received Naxitamab as consolidation.
Methods: Single institution, retrospective analysis of HR-NB patients who received Naxitamab consolidation in first CR between June 2017 and December 2021 and subsequently relapsed. Consolidation consisted of 5 cycles of subcutaneous GM-CSF and i.v Naxitamab. Disease was assessed by the modified International Neuroblastoma Response Criteria using 123I-MIBG SPECT/TC and bone marrow (BM) aspirates.
Results: Seventy-six HR-NB patients in first CR were consolidated with Naxitamab and twenty-four (31.57%) relapsed. Fourteen (58,3%) of the 24 relapsed during immunotherapy and 10 (41.6%) off therapy. Among the 14 that relapsed during treatment, one relapsed after cycle 1, six after cycle 2, two after cycle 4, and five after cycle 5. Eight of the 24 relapsed patients were lost to follow-up. The relapse pattern was confirmed for 16 patients. Mean age at diagnosis was 2.9 years (1.7–7), and four were MYCN amplified. Twelve (75%) of the 16 patients relapsed in one compartment: 5 (31.2%) with isolated bone limited to 1-3 foci; 3 (18.75%) with >3 bone lesions; 3 (18.75%) with isolated soft tissue; and 1 (6.25%) with BM only disease. Relapse in more than one compartment occurred in 4 patients (25%): soft tissue and bone in 2 (12.5%); bone and BM in 1 (6.25%); and 1 in all three compartments (6.25%). No CNS relapses occurred. Eight (50%) of the 16 relapsed patients achieved second CR.
Conclusions: Relapse after first CR consolidated with Naxitamab occurs mostly limited to one compartment, being the bone the most common site. BM relapse is rare after Naxitamab consolidation. Second CR is highly achievable and may be related to the reduced burden of disease.

EP181 / #1727

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

HIGH RATE OF SERIOUS ADVERSE EVENTS IN HEAVIER PATIENTS RECEIVING NAXITAMAB DOSES >150 MG.

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Background and Aims: Naxitamab is an anti-GD2 monoclonal antibody (mAb) that has proved effective against GD2 expressing tumors like high-risk neuroblastoma (HR-NB), retinoblastoma, and osteosarcoma (OS). Clinical trials of naxitamab have reported 60% of patients experiencing grade 3-4 pain or hypotension. Pharmacokinetics of anti-GD2 mAbs have shown drug clearance is based on weight and age. For naxitamab, AUC was shown to correlate with patient body weight.
Methods: Single institution, retrospective analysis of >50 kg patients who received naxitamab doses >150 mg from June 2017 to February 2022. Grade 3 or 4 serious adverse events (SAEs) were evaluated according to the CTCAE v5. Naxitamab therapy consisted of 2.4-3 mg/kg/dose on days 1, 3 and 5 along with subcutaneous GM-CSF for 10 days.
Results: Nine patients received naxitamab doses >150 mg (1 female; 8 males), 7 for HR-NB and two in second CR for relapsed metastatic OS. Mean age is 17.5 years (11-23). All had grade 1-2 pain, hypotension, or allergy. Six (66.6%) of the 9 patients developed G3-4 AEs for a total of 10 events. Four (44.4%) patients required hospitalization. G3-4 events include two orthostatic hypotension (22.2%) requiring treatment with alpha pressors; two myocarditis (22.2%) receiving corticosteroids; one PRES (11.1%); two (22.2%) G3 hypotension during infusion; two (22.2%) G3 hypertension post-infusion; and one with G3 vomiting with secondary dehydration. All SAEs occurred during 1st naxitamab cycle. All SAES resolved. Patients with G4 toxicities (orthostatic hypotension and PRES) were taken off therapy.
Conclusions: First exposure to naxitamab in heavier patients receiving doses >150 mg is associated with a higher incidence of G3-4 SAEs. All SAEs were reversible with proper management.

EP182 / #835

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

DINUTUXIMAB BETA TREATMENT IN CHILDREN WITH ADRENAL GLANDS INSUFFICIENCY

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Background and Aims: Employment of dinutuximab beta (DB) in patients with high-risk neuroblastoma (NBL) improved survival and combination of DB with chemotherapy is promising treatment option. Symptoms of adrenal gland (AG) insufficiency and treatment with hydrocortisone (HC) may influence toxicities and results of therapy.
Methods: From May, 2017 till January, 2022, 73 patients with NBL were treated with DB, including 45 in monotherapy, 27 DB in combination with chemotherapy and 1 DB with Nivolumab. The occurrence of AG insufficiency and its influence on toxicities was evaluated. Of 73 patients, in 6 (8%) AG insufficiency was diagnosed before start of DB. Two children received DB as first line and 4 for relapsed/refractory disease; all were heavily pretreated.
Results: Of 6 children with AG insufficiency, in 3 no severe adverse events were observed during DB therapy. In two other patients exacerbation of AG insufficiency was observed during fever, diarrhea or vomiting. One patient had severe exacerbation from the 2nd day of DB infusion without any additional reasons. All symptomatic patients required increase of HC dose with good effect. In consecutive cycles, dose of HC was increased from beginning of the cycle with good effect, and additional doses were added if needed. Two children after DB therapy had disease relapse, the other 4 remain in CR.
Conclusions: The DB therapy is feasible in children with AG insufficiency. Patients must be observed very carefully and HC dose must be increased if symptoms occur. Increase of HC dose should be considered for next cycles. Symptoms of AE insufficiency may be similar to DB toxicities, so it should not be missed before therapy. Although HC may influence response to DB, its immunosuppressive effect is low and considering poor outcome in HR NBL, these patients should not be excluded from therapy. Influence of HC on treatment results needs further investigations.

EP183 / #2020

Topic: *AS05 SIOP Scientific programme / AS05.e Neuroblastoma*

NEUROBLASTOMA RESTAGING AND RESPONSE TO THERAPY EVALUATION: FUTURE OF 68GA DOTANOC PET/CT

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Background and Aims: Iodine 123 MIBG is the conventional mode of investigating neuroblastoma. In certain cases evaluation with FDG PET/CT might also be required. Newer PET agents offer a higher sensitivity and accuracy and have been demonstrated to be superior to MIBG SPECT/CT imaging. ^{68}Gallium DOTATATE is FDA approved radiotracer with significanty high sensitivity and specificity in the evaluation of neuroblastoma patients although data is limited.
Methods: Since Iodine 123 MIBG shipping became problamtic with the stoppe international flights amid the COVID pandemic, we evaluated neuroblastoma patients for follow-up studies with ^{68}Gallium DOTATATE as it was produced loco regionally at our centre.
Results: We imaged 10 follow-up neuroblastoma patients with Dotanoc PET/CT. Median age was 42 months (6 females and 4 males). 5 of these patients also had a baseline Dotanoc PET/CT. 8 scans had positive findings on follow-up imaging. 5 patients were in the high-risk group. No special preparation was required for the Dotanoc scans ias comapred to the MIBG scans. Radiation dosimetry is also more favorable.
Conclusions: ^{68}Gallium Dotanoc PET/CT imaging in neuroblastoma restaging and response to therapy evaluation is feasible and offers several advantages including high spatial resolution, high sensitivity and specificity. Advantages also include that it requires no special preparation and a relatively favorable dosimetry profile compared to traditional I131 MIBG scans.

EP184 / #984

Topic: *AS05.f Renal Tumours*

CLINICO-PATHOLOGICAL FEATURES AND THERAPY OUTCOME IN CHILDHOOD WILMS TUMOR: THIRTEEN YEARS EXPERIENCE OF TERTIARY CARE CENTER IN SAUDI ARABIA

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Background and Aims: Wilms Tumor (WT) is second most common abdominal tumor in children. It is usually presented as asymptomatic abdominal mass in otherwise healthy child. It needs multidisciplinary approach (chemotherapy, surgery and radiotherapy). Our aim is to assess our management and outcome of WT over a period of 13 years and comparing it with local, regional and international studies.
Methods: We reviewed 37 pediatric patients diagnosed with WT presented to Prince Sultan Military Medical City (PSMMC) a tertiary care hospital in Riyadh, Saudi Arabia, from January-2004 till December-2016.
Results: Median age at diagnosis 29 (range 4-99) months. Male 15/37(40.5%), female 22/37(59.5%). Most common presentation was abdominal mass (80%). Associated symptoms: hypertension (46%), hematuria (16%), anemia (51%) and hereditary predisposition syndromes (8%). Right and left sided tumor were equally distributed 15(40.5%) patients each, while bilateral involvement 7(19%) patients. Lung was the commonest metastatic site 8/37(21.6%). Stage I, II, III and IV were 10/37(27%), 10/37(27%), 9/37(24.4%) and 8/37(21.6%); respectively. Favorable histology (FH) and unfavorable histology (UH) were 34/37(91.9%) and 3/37(8.1%); respectively. Twenty-two (59.5%) patients received pre-operative chemotherapy, thirteen (35.1%) received post-operative chemotherapy and two (5.4%) had surgery alone. Fifteen(40.5%) patients received radiotherapy after surgery and chemotherapy, twenty(54.1%) received chemotherapy without radiotherapy, two(5.4%) had surgery alone. After median follow up period 60 (range 4-84) months, 33/37(89.2%) patients got complete remission while 4/37(10.8%) patients had persistent/refractory disease. Four patients relapsed after median follow up period 34 (range 18-46) months, two of them had FH as stage III and IV, the other two patients were stage IV with UH (diffuse/focal anaplasia). Four patients died, two were refractory (FH stage IV) and two were relapsed (UH stage IV). Five-years overall-survival 89.2% and event-free-survival 78.4%.
Conclusions: Our study demonstrated excellent survival rate for WT comparable with local and regional outcomes. Diffuse anaplasia and advanced stage have strong relationship with relapse and mortality.

EP185 / #1203

Topic: *AS05.f Renal Tumours*

SUBSEQUENT MALIGNANT NEOPLASMS OF THE KIDNEY AFTER TREATMENT OF PRIMARY MALIGNANCY DURING CHILDHOOD: ANALYSIS OF SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS DATA FROM 1975 TO 2016

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Background and Aims: Malignant renal neoplasms are rare before age 45. Age, gender, and genetic risk factors can influence the risk of these neoplasms. However, the risk in survivors of childhood cancer is not well established. This study aims to report the incidence of renal subsequent malignant neoplasms (SMNs) after treatment of a childhood primary malignancy.
Methods: Using the Surveillance, Epidemiology, and End Results (SEER) registry, we identified survivors of childhood cancer who developed a renal SMN. Survivors were under 20 years old at the time of primary cancer diagnosis and diagnosed between 1975-2016. We excluded survivors with a primary renal cell carcinoma or adenocarcinoma, and the SMN had to occur at least 13 months after the primary cancer diagnosis. The clinical characteristics of the survivors with SMNs of the kidney (including renal pelvis) were evaluated and standardized incidence ratios (SIRs[observed/expected]) were calculated. Kaplan-Meier estimates were performed to assess survival after renal SMN.
Results: Of 1,477 survivors of childhood cancer with SMNs, 53 developed a renal SMN (54 total cases). Of the 54 cases, 47 were a second cancer (43 carcinomas, 3 Wilms, and 1 Ewing sarcoma), 6 carcinomas were a third cancer and 1 carcinoma was a fourth cancer. Among these, there were 29 female (54.7%), 47 white (88.7%) and 7 Hispanic (13.2%) survivors. The most common primary cancers were Hodgkins lymphoma (n=9) and neuroblastoma (n=7). The mean ages of primary malignancy and renal SMN occurrence were 10.1 years and 31.1 years, respectively. The SIR of developing any renal SMN was 4.52 ($p<0.05$; 95%CI 3.39-5.89). The 5-year overall survival after a renal SMN was 71% (95%CI: 55%-82%).
Conclusions: Renal SMNs are rare but occur ~4.5 times more frequently in survivors of childhood cancer compared to the general population. This increased risk should be considered when providing long-term care for survivors of childhood cancer.

EP186 / #927

Topic: *AS05.f Renal Tumours*

EPIDEMIOLOGIC AND CLINICAL OUTCOMES OF PEDIATRIC RENAL TUMORS IN KOREA: A RETROSPECTIVE ANALYSIS OF THE KOREAN PEDIATRIC HEMATOLOGY AND ONCOLOGY GROUP (KPHOG) DATA

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Background and Aims: Renal tumors account for approximately 7% of all childhood cancers, including Wilms tumor (WT), clear cell sarcoma of the kidney (CCSK), malignant rhabdoid tumor (MRTK), renal cell carcinoma (RCC), congenital mesoblastic nephroma (CMN) and other rare tumors. We investigated the epidemiology of pediatric renal tumors in Korea.
Methods: From January 2001 to December 2015, data of pediatric patients (0–18 years of age) newly-diagnosed with renal tumors at 26 hospitals were retrospectively analyzed.
Results: Among 439 patients (male 240), the most common tumor was WT, at 77.9% (n=342), followed by RCC, CCSK, MRTK, CMN, and others at 8.2% (n=36), 5.5% (n=24), 3.6% (n=16), 2.7% (n=12), and 2.1% (n=9), respectively. Median age at diagnosis was 27.1 months (range 0-225.5) and median follow-up duration 88.5 months (range 0-211.6). Overall, 32 patients died, of whom 17, 11, 1, and 3 died of relapse, progressive disease, second malignant neoplasm, and treatment-related mortality. Five-year

overall survival and event free survival were 97.2% and 84.8% in WT, 90.6% and 82.1% in RCC, 81.1% and 63.6% in CCSK, 60.3% and 56.2% in MRTK, and 100% and 91.7% in CMN, respectively ($P < 0.001$).
Conclusions: The pediatric renal tumor types in Korea are similar to those of previous reports in other countries. WT accounted for a large proportion and survival was excellent. Non-Wilms renal tumor included a variety of tumors and showed inferior outcome especially in MRTK. Further efforts are necessary to optimize the treatment and to analyze the genetic characteristics of pediatric renal tumors in Korea.

EP187 / #952

Topic: *AS05.f Renal Tumours*

EPIDEMIOLOGICAL AND PATHOLOGICAL ASPECTS OF NEPHROBLASTOMA IN CRDCE TWO FIRST YEAR OF ACTIVITY.

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Background and Aims: Nephroblastoma is the one of most frequent tumor in children and the aim is to obtain an optimal and diligent diagnosis in the pathology pole of the CRDCE.
Methods: This is a retrospective study of pediatric renal tumors. The pieces of nephrectomies were received fresh. The macroscopy and histolpathologic techniques were carried out immediately. We used the SIOP classification for grade and stage.
Results: Over a period of the years 2020 and 2021, sixty (60) renal tumors were diagnosed, in the CRDCE, with 46 nephroblastomas, followed by rhabdoid tumors (5 cases), clear cell sarcomas (2 cases), and neuroblastoma (2 cases). Within the 46 cases of nephroblastoma, the gender ratio was around 1 with a slight male predominance, the age was between 15 years and 7 months with an average of 4 years and 3 months at the time of diagnosis. Upon receipt of the 46 specimens, the macroscopic examination showed a weight ranging from 100g to 3200g with an average of 570g. The histological examination confirmed the diagnosis and the classification of the cases according to histological subtypes, the mixed subtype: 14 cases, the regressive subtype: 13 cases, the stromal subtype: 8 cases, the blastematous subtype : 6 cases, the epithelial subtype: 3 cases, finally a necrotic case and a cystic case. 63% of nephroblastomas were classified as stage 2 (intermediate risk) according to the SIOP classification of 2001, stage 3 and stage 1 were respectively at 19.5% and 17.5%.
Conclusions: According to the findings of our study, nephroblastoma remains the most common histological type of pediatric renal tumors. With a predominance of histological subtypes low and intermediate risk.

EP188 / #1986

Topic: *AS05.f Renal Tumours*

ADVANCED STAGE OF NEPHROBLASTOMA : EXPERIENCE OF SINGLE CHILDHOOD CANCER UNIT IN KINSHASA - DRCONGO

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Background and Aims: Nephroblastoma is the most common malignant renal tumor in children and accounts for approximately 90% of kidney cancers. Management of patients diagnosed at advanced stage (stage III and IV) is challenging, especially in the context of sub-Saharan Africa. We present the experience of the paediatric oncology unit of Kinshasa, DRC.
Methods: This is a retrospective descriptive study, from January 2010 to December 2020 conducted at the paediatric oncology unit of Kinshasa university hospital.
Results: A total of 96 children was diagnosed with nephroblastoma during the period of study. Advanced stage (Stage III and IV) was found in 26 children (30%). Most of them were living in Kinshasa city (81%) with their ages between 2-5 years old (58%).The majority of parents completed at least primary school Abdominal mass was the main symptom at presentation (96.2%), with fever (56.8), abdominal pain (30.8%) and haematuria (23.2%). Abdominal ultrasound was done for all and chest X-ray for 92%. There was a predominance of stage IV (57.7%). Surgery has been done to only 50% of the children and children received preoperative and postoperative chemotherapy. No child received radiation therapy. In this study, 53.8% of the children had abandoned the treatment and 38.4% died. Only 2 patients (7.6%) are in remission
Conclusions: Mortality rate and abandonment of treatment are very high and need to be addressed. Improving access to medical care and providing radiation therapy services may help to increase the cure rate, but early diagnosis should be on top of priorities.

EP189 / #816

Topic: *AS05.f Renal Tumours*

AGE AS A PROGNOSTIC VARIABLE IN CHILDREN AND ADOLESCENTS WITH FAVOURABLE HISTOLOGY (FH) WILMS TUMOUR (WT)

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Background and Aims: There is limited and inconsistent data regarding the independent impact of age on outcomes of WT; age < 2 years is generally considered favorable. We report the presentation and outcomes with regards to age at presentation.
Methods: All patients with FH WT treated at our centre from January 2013 - December 2020 were analysed. While resectable tumours were operated upfront, unresectable tumours received preoperative chemotherapy (Vincristine-Dactinomycin (VA) x4 weeks in non-metastatic and VA+Doxorubicin x 6 weeks in metastatic tumors) followed by delayed nephrectomy. Local radiation and local treatment of metastatic sites were also done. Presentation and outcomes (Event free survival (EFS) and overall survival (OS))- were analysed by age.
Results: Of 257 patients treated during this period, 235(91.4%) had favourable histology, with median age at presentation of 23 months (range-3-372 months) and 145(61.7%) were males. Most children were aged 0-2 years(n=67),2-4 (n=83) and 4-10 years(n=68) ; only 17 patients were older than 10 years. The incidence of stage 3 and 4 disease in 0-2 years, 2-4 years,4-10 years and >10 years was 43.2%,62.6%,72% and 64.7% respectively; bilateral WT was 11.9%,2.4%, 4.1% and 5.8%.The proportion of patients with inoperable disease at presentation was 50.7%, 62.6%,63.2% and 41% respectively. The incidence of toxic deaths was higher in children <2 years at 57.1% compared to 28.5% in >2years, with 13.3 % grade ¾ haematological toxicities and 71% veno-occlusive disease(n=5). At a median follow-up period of 36 months, EFS and OS were 69.5% and 87.8% respectively; 3-year EFS and OS in 0-2 years,2-4 years,4-10 and >10 years were 67.6%,73.1%,71.9% and 64.2% and 84%,88%,91% and 88.2% respectively.
Conclusions: Age < 2 years and >10 years had poorer outcome in FH WT. Higher incidence of inoperable disease at presentation and increased toxicities including death might explain the unexpectedly low outcome in <2 years.

EP190 / #1442

Topic: *AS05.f Renal Tumours*

ACCURACY OF CT IN DIFFERENTIATING WILMS FROM NON-WILMS RENAL TUMOURS IN PEDIATRIC PATIENTS

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Background and Aims: Introduction: Pediatric renal tumors are histologically diverse, 85% being Wilms tumor (WT) and remaining being heterogeneous group of non-Wilms tumors (NWT). Lack of specific radiological criteria and tumour markers leads to misdiagnosis. Imaging needs to identify cases in which radiological uncertainty warrants preoperative histology. Aim : 1) To assess the utility of baseline CECT in differentiating WT from NWT. 2) To correlate the imaging findings with histopathological report (HPR). 3) To evaluate inter-observer variation between two dedicated pediatric oncoradiologists.
Methods: Type of study: Institutional Ethics Committee approved retrospective study done in Tata memorial Hospital Study population Comprise of sample size of 81 patients, with baseline WT and NWT in a ratio of 2 : 1 ie 54 Wilms tumors and 27 non-Wilms tumors. Methodology CT scans were assessed independently by two pediatric oncoradiologists blinded to the histpathology and overall impression was recorded as WT, non-WT, or indeterminate. The variations in the opinion of the two observers was also noted. Diagnostic accuracy of CT for predicting WT vs non-WT histology was assessed and κ-Coefficient value was calculated for the degree of agreement between the two observers.
Results: The average age presenatation of WT and NWT was statistically significant (p =.001). There was moderate agreement between CT diagnosis and HPR of observer 1 (k value of 0.61) and mild agreement in observer 2 (k value of 0.32). There was poor interobserver agreement in categorizing WT, NWT and indeterminate with K value of 0.196. The variors imaging characteristic assessed like tumoral calcification and fat, renal sinus, pelvicalyceal system, ureter and vascular involvement , metastasis, adenopathy and subcapsular fluid in Wilms and non-Wilms tumour were stastically not significant.
Conclusions: There are no specific CT features to differentiate WT and NWTs with statistical significance. The overall accuracy of CT to differentiate WT from NWT has high sensitivity but low specificity.

EP191 / #318

Topic: *AS05.f Renal Tumours*

FAMILIAL WILMS TUMOR ASSOCIATED WITH GERMLINE REST MUTATIONS

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Background and Aims: Wilms tumor (WT) is one of the most common childhood renal cancer. Although WT is primarily a non-familial condition, about 5% of cases have one or more relatives with a history of Wilms tumor. Most of the time, inherited WT cases harbour WT1 mutations. Besides that, germline inactivating mutations in REST, CTR9, TRIM28 have recently been considered as WT predisposition genes. This report presents WT cases with detected germline mutations in REST. This gene is also associated with the gingival fibromatosis. Aims: presentation of clinical cases with WT associated with germline pathogenic variants in REST in children from two unrelated families.
Methods: Patient 1 (a female, 4 y.o. with bilateral WT) is a proband from in vitro fertilization (IVF) triplets, with sister and brother without WT. Patient 2 (a male, 5 y.o. with unilateral WT) is a proband, who has 2 healthy siblings. We analyzed probands` DNA extracted from peripheral blood leucocytes with custom-targeted NGS-198 genes-panel. The detected variants were checked in family members by Sanger sequencing.
Results: Patient 1 had a pathogenic germline mutation in REST c.2668_2671del, p.(E891Pfs*6), as well as her sister. The mutation was probably inherited from their deceased father, as he had gingival fibromatosis. Patient 2 had a pathogenic germline variant in REST c.1035_1036insTA, p.(E346*), as well as his mother and both brothers. There were two other WT cases in this family (proband`s maternal uncles). Family members with REST mutations from both families had gingival fibromatosis.
Conclusions: We have demonstrated familial clinical cases of a rare WT form, associated with germline pathogenic variants in REST.

EP192 / #386

Topic: *AS05.f Renal Tumours*

CHEMOTHERAPY RELATED FEVER IN PATIENTS TREATED FOR WILMS TUMOUR

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Background and Aims: Fever is frequent in children with oncological diseases and can be associated to many infectious causes. Many drugs can also cause fever, as cytarabine, carboplatin or methotrexate. Fever induced by vincristine (VCR) is frequently observed during clinical practice, but no reliable data about its characteristics are available.
Methods: We conducted a retrospective study in patients < 18 years treated for Wilms tumour at the Division of Pediatric Haematology-Oncology, Padua, between 2010 and 2021. We divided febrile episodes in 5 categories: chemotherapy (CT) related fever, infective fever, febrile neutropenia, neoplastic fever and “other”. We compared infective/neutropenic episodes with the ones related to CT. We recorded data about characteristics of fever and chemotherapy, blood exams, radiological investigations, antibiotic therapy, hospitalization and delay of treatment in following cycles. Exact Fisher tests were used to compare proportions. Kruskal-Wallis test or ANOVA on ranks were used to compare continuous distributions. Statistical significance was settled for any p-value <0.05.
Results: We recorded 97 febrile episodes in 36 patients: 28 correlated to chemotherapy, and 69 identified as infective fever in patients with or without neutropenia. CT related fever occurred most frequently in the first weeks of treatment (median 4 weeks) compared to patients with infective fever (median 8 weeks, p<0.0001). The duration of fever resulted statistically significant, with a shorter resolution of the episodes in the group of CT related fever (median: 72 hours, p=0.0052). All episodes of CT related fever occurred after the administration of Vincristine, in combination or not with other drugs, and the majority of them happened within the first 24 hours of treatment (75%). Half of the patients with CT related fever received antibiotic therapy. Data about infectious markers were limited and no statistical differences were noted.
Conclusions: Rapid recognition of CT related fever is important in order to avoid extra testing, unnecessary antibiotic therapy and hospitalization.

EP193 / #482

Topic: *AS05.f Renal Tumours*

MRI-CHARACTERISTICS OF PEDIATRIC- AND YOUNG-ADOLESCENT RENAL CELL CARCINOMA: A SINGLE-CENTER RETROSPECTIVE STUDY AND LITERATURE REVIEW

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Background and Aims: Pediatric renal cell carcinoma (RCC) is a rare renal malignancy. Translocation-type RCC (MiT-RCC) is the most frequent subtype in children, in contrast to clear-cell RCC (ccRCC) in adults. MRI is the preferred imaging modality for assessment of pediatric renal tumors and plays a potential role in their non-invasive discrimination. Previous literature has suggested imaging findings differ between RCC-subtypes, however, studies focusing on MRI-characteristics are limited. Therefore, this study aims to identify MRI-characteristics of RCC, focused on its presentation in children and young adolescents, through a single-center case-series and literature review.
Methods: The identified diagnostic MRI-scans including diffusion-weighted imaging (DWI) were retrospectively assessed by two observers. An extensive literature review was conducted in Pubmed, Embase and Cochrane, focusing on MRI-characteristics of RCC-subtypes often seen in children and young adults.
Results: Six pediatric patients with a median age of 12 years (range 63-193 months) were included. Two/six patients had MiT-RCC, and 2/6 ccRCC. Median tumor volume was 393 cm^3 (range 29-2191 cm^3). Five tumors had a hypo-intense appearance on T2-weighted imaging, whereas 4/6 were iso-intense on T1-weighted imaging. Four/6 tumors showed well-defined margins, whereas other tumor characteristics were often inconsistent among patients. The median apparent diffusion coefficient (ADC)-values on DWI ranged from 0.70-1.20*10^{-3} mm^2/s. Thirteen articles (46 cases) focusing on MRI-characteristics of MiT-RCC could be identified. A majority of the patients showed T2-weighed hypo-intensity, similar to our MiT-RCC cases. T1-weighted hyper-intensity, an irregular growth pattern and limited diffusion restriction were often described for MiT-RCC.
Conclusions: The discrimination of RCC-subtypes and differentiation from other pediatric renal tumor types based on MRI remains difficult. Nevertheless, T2-weighted hypo-intensity of the tumor seems a potential distinctive characteristic in our case-series as well as in previous literature. This study stresses the importance of gaining specific knowledge of MRI in pediatric- and young adolescent RCC and focusing on innovative techniques.

EP194 / #725

Topic: *AS05.f Renal Tumours*

HOW TO IMPROVE INITIAL DIAGNOSTIC ACCURACY OF KIDNEY TUMOURS IN CHILDHOOD WITHOUT HISTOLOGY?

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Background and Aims: Treatment of nephroblastoma starts with preoperative chemotherapy in SIOP trials without proven histology. To test for a higher accuracy in the initial imaging diagnosis additional clinical and tumour-related parameters were analysed.
Methods: We conducted a retrospective analysis of a total of 3307 patients with histologically proven paediatric renal tumours enrolled in the consecutive SIOP-GPOH trials between 1989 and 2017. Our focus included Wilms tumour (WT), congenital mesoblastic nephroma (CMN), clear cell sarcoma (CCSK), malignant rhabdoid tumour of the kidney (MRTK) and renal cell carcinoma (RCC). The different entities were compared in view of metastasis, bilaterality, tumour volume (TV) and age at diagnosis. Statistical analysis was enhanced by ROC curves and Pearson correlations.
Results: Bilateral tumours occur exclusively in WT (253 patients, 8.6% of WT), with the exception of one patient with CCSK. In patients aged <3 years with localized disease, CMN (N= 96/1009 (9.5%)) and CCSK (N=57/1009 (5.6%)) occur in addition to WT (N=834/1009 (82.7%)). In TV<100 ml, CMN is present in 54 of 213 (25.4%) patients. MRTK is common in the <3 years age group with metastatic disease (N=12/59 (20.3%) in TV<500 ml). In the age group of 3-7 years, Non-WT is very rare, regardless of metastatic status or TV. In the age group >7 years, RCC occurs more frequently, especially when TV<150ml. Tumours >1000ml are observed only in WT and CCSK. None of the CMN patients have metastases at diagnosis. For the different entities ROC curves are shown.
Conclusions: The frequency profiles established for each paediatric renal tumour allow for a more specific initial diagnosis and can help radiologists differentiate WT from RCC, CMN, and MRTK. Differentiating WT from CCSK remains a challenge. Novel approaches like liquid biopsies may help to further increase diagnostic accuracy in the near future.

EP195 / #1330

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

IDENTIFICATION OF POTENTIALLY PATHOGENIC VARIANTS IN CANCER PREDISPOSITION GENES IN PEDIATRIC SARCOMAS BY NEXT GENERATION SEQUENCING

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Background and Aims: Although sarcomas can occur in the setting of a cancer predisposition syndrome, this association is often missed. The aim of this study was to identify pathogenic germline variants in pediatric patients with sarcomas, through the analysis of cancer susceptibility genes included in somatic panels, using next-generation sequencing (NGS).
Methods: Forty-three pediatric and young adult patients with different sarcoma subtypes were included in the analysis. Tumor profiling was performed using the Oncomine™ Childhood Cancer Research Assay (Thermo Fisher). Sequencing results were reviewed for potential germline alterations in genes associated with cancer predisposition syndromes (CPS). Jongmans´ criteria were considered for patient selection.
Results: 43 patients were included: 18 were diagnosed with osteosarcoma (41.9%), 12 Ewing's sarcoma (27.9%), 4 rhabdomyosarcoma (9.3%) and 9 other sarcoma (20.9%). Gender: 27 males/16 females. Mean age: 12 years (range 0.6-30.8). Eleven patients were metastatic at diagnosis (25.6%). Primary sites included lower extremities (53.5%), upper extremities (23.3%) and trunk (14%). We identified four patients with a family history of cancer, one of which had congenital anomalies and excessive toxicity to treatment. Three patients suffered from excessive toxicity to therapy, one of them had congenital anomalies and other presented two malignant tumors. Sixteen patients were selected with potentially germline pathogenic variants in the following genes: CDKN2A, NF1, NF2, RB1, SMARCA4, SMARCB1 and TP53. Variants were subsequently analyzed in DNA from peripheral blood. Three patients were excluded due to sample unavailability. The variants in NF1 and CDKN2A in two patients diagnosed with malignant peripheral nerve sheath tumor and osteosarcoma, respectively, were detected in the germline, confirming the diagnosis of a CPS.
Conclusions: The analysis and filtering of somatic mutations in pediatric tumors according to clinical and molecular criteria, could help to identify pathogenic germline variants in sarcoma. Identifying CPS is important for the management and genetic counselling of these patients and their families.

EP196 / #1321

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

TREATMENT RESULTS OF PEDIATRIC OSTEOSARCOMA: COMPARISON OF CISPLATIN/DOXORUBICIN AND EURAMOS REGIMENS IN TWO TIME PERIODS

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Background and Aims: To evaluate the treatment results of two regimens for the treatment of osteosarcoma in our center: cisplatin/doxorubicin (AP) and EURAMOS regimens.
Methods: A file search of 90 patients with newly diagnosed osteosarcoma performed and demographic features, surgical procedures, response to treatment and outcome of patients retrospectively analyzed. 59 patients treated with AP regimen from January 2000 to October 2015 and 31 patients treated with EURAMOS regimen from October 2015 to December 2020 were included into the study.
Results: The median age of the patients was 12.9 years (6.5-17.9) and M/F ratio was 1.5/1. Primary tumor sites were femur in 51%, tibia in 23% and humerus in 11% of the patients; 29% of the patients had metastatic disease, mostly in lungs (19%) and bone (12%). There were 59 patients treated with AP regimen and 31 received EURAMOS regimen. Limb-sparing surgery and amputation were performed for 79% and 11% of patients. Local tumor resection could be performed in 7 patients. Histological response to treatment was good in 32% and poor in 69% of the patients, and negative margins could be obtained in 94%. No statistical difference for tumor necrosis was found between two regimens. The 5-y EFS and OS rates for all patients were 32.9% and 59.6%, respectively. The 5-y EFS and OS rates were 39.9% and 65.3% for patients with non-metastatic disease whereas same rates were 16.9% and 45.7% for metastatic disease (p=0.01, p=0.009). For patients with non-metastatic osteosarcoma 5-y OS rates were 63.6% and 76.2% with AP and EURAMOS regimens, and 5-y EFS rates were 43.1% and 26.5%, respectively.
Conclusions: Although AP regimen provided considerably high survival rates in our group of patients, outcome with EURAMOS regimen increased 5-y OS rate to 76.2% in non-metastatic osteosarcoma. The outcome of our patients is comparable with EURAMOS results.

EP197 / #1242

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

THE DETERMINANTS OF TIME TO DIAGNOSIS AND ITS IMPACT ON CLINICAL OUTCOMES IN BONE SARCOMAS: A RETROSPECTIVE OBSERVATIONAL STUDY OF 1329 PATIENTS

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Background and Aims: Delayed disease presentation is common among cancer patients in developing countries. This study aims to identify the determinants of time to diagnosis and explore its impact on survival outcomes in bone sarcomas.
Methods: This is a retrospective single-centre observational study performed in India on subjects with bone sarcomas. We extracted clinico-demographic details, symptom duration before presentation, and treatment outcomes from hospital records of patients registered between 2003 and 2018. We performed stepwise univariable and multivariable logistic regression to identify the determinants of time to diagnosis. Cox regression analysis was used to identify the impact of time to diagnosis on overall survival.
Results: A total of 1329 subjects were analysed including 472 patients (35.5%) with osteosarcoma and 857 patients (64.5%) with primitive neuroectodermal tumour (PNET). The median age was 16 years (range: 0.1-71 years) with 92% of patients below 30 years and male:female ratio of 2.3. Median time to diagnosis was 4 months (IQR: 3-7 months). On univariable logistic regression, age above 16 years, absence of fever, lower total leukocyte count (<11000/mm^3), rural residence and distance from treating centre over 197 km were associated with longer time to diagnosis (more than 4 months). Among these, older age (HR 2.53, p-value <0.01) and rural residence (HR 0.75, p-value=0.04) remained significant on multivariable analysis. There was no difference in diagnosis interval based on disease type (osteosarcoma versus PNET), stage (localised versus metastatic) or gender. There was no significant association between time to diagnosis and outcomes in the whole cohort or in subsets based on disease type or disease stage.
Conclusions: Among patients with bone sarcomas, older age and rural residence are associated with delayed time to diagnosis. However, diagnostic delay does not impact disease survival, suggesting the dominant role of tumour biology in determining treatment outcomes, even in resource-challenged situations.

EP198 / #1794

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

PELVIC EWING SARCOMA: A SINGLE CENTER EXPERIENCE

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Background and Aims: The pelvis is considered one of the most common sites of ES and has a worse prognosis than ES located in the extremity.We aimed to examine patients with pelvic ES treated with multidisciplinary treatment methods in our center.
Methods: The clinical features and prognosis of 14 pelvic ES cases diagnosed between 2010-2021 were evaluated retrospectively.
Results: M/F ratio was 0.75. Median age was 14,75 years(2,25years-17,5years). Pain and swelling were the most common complaints. At diagnosis, lung involvement was present in eight patients, bone marrow in one patient, lymph nodes in two patients, and multi-bone involvement in five patients; four patients were non-metastatic. Treatment of all patients was started with neoadjuvant chemotherapy. Surgery could not be performed in seven patients due to extensive disease or morbid surgery; five patients underwent surgery and the rate of necrosis was above 95% in two patients and below in three patients. Eleven patients received radiotherapy to the primary site and/or metastasis areas simultaneously with chemotherapy. In the follow-up, two patients developed relapse after treatment discontinuation, and seven patients had progressive/refractory disease. Four patients died due to progressive disease, one patient died during neoadjuvant chemotherapy due to typhitis, three patients were out of follow-up as diseased, four patients are sick and their treatment continues. Two surviving patients have been followed up without any problem for 6 and 3 years, respectively, since the treatment cut. Overall survival rate was 21% in 3 year; 5 years was 7%.
Conclusions: Many studies have investigated the effects of multiple factors on survival in patients with pelvic ES, including tumor size, presence of metastases at diagnosis, and treatment modalities. Presence of metastasis at the time of diagnosis was found to be the most important prognostic factor, and 71% of our cases were metastatic at the time of diagnosis, and our 5-year overall survival rate was 7%.

EP199 / #118

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

A RETROSPECTIVE REVIEW TO MONITOR THE IMPACT OF EARLY NASOGASTRIC TUBE FEEDING IN THE ACUTE MYELOID LEUKAEMIA COHORT

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Background and Aims: Background/Aims: Children diagnosed with acute myeloid leukaemia (AML) undergo intensive chemotherapy, which adversely affects nutritional status; side effects include anorexia, vomiting, mucositis. Proactive nasogastric tube (NG) placement can facilitate adequate enteral nutrition provision early in treatment, offsetting associated malnutrition risk. Aim: to evidence benefit of early enteral nutrition on nutrition outcomes.
Methods: Retrospective data collected from electronic records. Patients with AML having completed first two chemotherapy cycles between June 2019-June 2021 without any extended intensive care stays (>7days) included. Outcomes assessed: weight, z-score, number of days on parenteral nutrition (PN), length of hospital stay.
Results: Twenty-one patients met inclusion criteria; 52% male. Ages: 2months-11years (mean = 2years). NG feeds started within 5 days in 56% during cycle 1: 88% during cycle 2. Comparing patients who received NG feeds <5days (early NG feeders) and >5 days (late NG feeders) of starting chemotherapy, no difference in number of patients started on PN, or number of PN days. Weight loss in both early & late NG feeders in cycle 1 (-0.5Z and -0.36Z respectively). Cycle 2; observed weight gain in early NG feeders(+0.29Z), late NG feeders experienced weight loss (-0.07Z). Irrespective of timing of NG tube insertion, paired t-test showed significant weight loss in cycle 1 (z-score -.49; $p<0.000$); by cycle 2, weight loss was ameliorated with observed weight gain overall (z-score +0.07, $p= 0.316$). In both cycles, length of hospital stay was longer in late NG feeders (cycle 1: +1day; cycle 2: +6days).
Conclusions: Conclusion: Sample was too small to note any significance of early versus late NG placement on nutritional status. However, findings re-enforce importance of early nutrition support with proactive dietetic contact and nasogastric feeding in preventing ongoing significant weight loss and potential to reduce hospital length of stay. Future research should include assessing barriers to initiation of early enteral nutrition.

EP200 / #573

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

DELAYED PRIMARY CONTROL IN PATIENTS WITH LOCALIZED EXTREMITY OSTEOSARCOMA IS ASSOCIATED WITH WORSE OUTCOME

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Background and Aims: Timing of local control is not well studied in osteosarcoma. We assessed the impact of delay of local control on survival outcome of patients with osteosarcoma.
Methods: We conducted a retrospective analysis of children (<18 years) with primary non-metastatic osteosarcoma of the extremities who presented to King Hussein Cancer Center (KHCC) from Jan2005 until Mar2020. Patients were treated according to EURAMOS-1 protocol. Patients' demographics, disease characteristics and outcomes were collected. Events were defined as death, progression or relapse. Cox proportional hazards regression was used for univariate and multivariate comparison of different covariates. Data collection and analysis were done in December 2021.
Results: Eighty-seven patients were included in this analysis, 45 (51.7%) were females; median age at diagnosis was 12.5 years (range, 5.9-18). Eighty-three patients (95%) underwent local control by surgery (Limb salvage surgery in 65 (75% of total), amputation in 18 (20%)), four patients (5%) refused amputation; one of them had radiotherapy as local control. After a median follow up of 50.7 months (range, 5.5-189.9) the 5-year event free survival (EFS) and overall survival (OS) were 53%+/-5.7% and 64%+/-6% respectively. On univariate analysis local control before 20 weeks, and good histologic response (≥90% necrosis) were associated with better EFS rates (p value 0.005 and 0.001 respectively) and OS (p, 0.049 and 0.002, respectively). On multivariate analysis, both were associated with better EFS (p, 0.03 and 0.006); however, only good histologic response was associated with better OS (p, 0.003).
Conclusions: Our findings suggest that delay in local control beyond 20 weeks after diagnosis predict lower EFS in patients with localized, extremity-primary osteosarcoma. Timely local control planning by a multidisciplinary team needs to be ensured.

EP201 / #659

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

NUTRITIONAL PROFILE AND OUTCOME OF PEDIATRIC PATIENTS WITH MALIGNANT BONE TUMOURS– EXPERIENCE FROM A TERTIARY CANCER CARE CENTRE FROM NORTH EAST INDIA

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Background and Aims: Pediatric patients with osteosarcoma and Ewing's sarcoma are at an increased risk for developing malnutrition. Early recognition and intervention are required to prevent morbidity and mortality. This study aims to describe the nutritional profile and outcome of these patients with special emphasis on nutritional intervention.
Methods: In this retrospective study ,104 pediatric patients attending Dr. Bhubaneswar Borooah Cancer Institute between October 2019 to February 2022 diagnosed with either osteosarcoma or Ewing's sarcoma were analysed. Informations were collected from pediatric oncology database. Nutritional status was assessed using WHO Z scores and Frisanco chart for MUAC in children above 5 years of age. The data was analysed using SPSS V21 software.
Results: Total 104 cases were studied, of which Ewing's sarcoma 58(55.8%) and osteosarcoma 46(44.2%). The mean age at diagnosis was 13.9+/- 4.13 years. The male: female ratio was 1.2:1. At presentation 22(21.2%) were well nourished and 82(78.8%) were malnourished. Amongst the female children,72% and males,78.8% were malnourished. High,low and moderate calorie interventions were given to 82(78.8%), 20(19.2%) and 2(1.9%) patients respectively. Out of 104 patients,39(37.5%) have completed treatment, 35(33.7%) did not complete treatment, 20(19.2%) are continuing treatment at present, 10(9.6%) did not take any treatment. Outcome assessment shows 56(53.8%) are alive, 34(32.7%) expired and 14(13.5%) lost to follow up. Significant association was found between baseline nutritional status and good outcome (p=0.03) and baseline nutritional status and completion of treatment (p=0.028). Significant association was seen between pre intervention and post intervention nutritional status in osteosarcoma(p=0.005). No significant association was observed between gender and nutritional status/completion of treatment/outcome.
Conclusions: In developing countries, malnutrition is a major comorbidity among children. Nutritional status plays an important role in cancer treatment compliance and outcome. Therefore, nutritional interventions should be planned at individual level and population level as well by authority to improve survival and enhance compliance.

EP202 / #1384

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

VALUE OF RADIOTHERAPY DOSE ON THE OUTCOME IN EWING SARCOMA

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Background and Aims: Radiotherapy (RT) is an integral part of Ewing Sarcoma (EWS) therapy. The Ewing 2008 protocol recommended radiotherapy doses in a range of 45 to 54 Gy but some patients (pts) received other doses of RT. We analyzed the value of different radiotherapy doses on event-free survival (EFS) in EWS patients.
Methods: The Ewing 2008 database consists of 534 radiotherapy-admitted patients with non-metastatic EWS. Recommended treatment consisted of multimodal chemotherapy and local treatment consisting of surgery and (S&RT group)/or radiotherapy (RT group). EFS was analyzed with univariable and multivariable Cox regression models including known prognostic factors age, sex, tumor volume, surgical margins and histological response.
Results: S and RT was performed in 336 patients (70.4%), and 145 patients (29.6%) received definite RT. In the S&RT group radiotherapy dose was (a) </=53Gy in 193 (57.4%), (b) 54-58Gy in 118 (35.1%) and (c) >/= 59Gy in 25 (7.4%) pts. In the RT group radiotherapy dose was (a) in 17 (11.7%), (b) in 64 (44.1%) and (c) in 64 (44.1%) pts. 3y-EFS of the S&RT group was .76 (SE=.03) for (a), .76 (SE=.04) for (b), and .69 (SE=.10) for (c) (P=.57), and in the RT group .58 (SE=.13), .69 (SE=.06), and .73 (SE=.06) (P=.63), respectively. Multivariable Cox regression revealed age >/= 15years (HR=2.3 95%CI 1.2-4.4), non-radical margins (HR=2.6 95%CI 1.4-5.0) for the S&RT group (Sex P=.81, Histological response P=.20, Tumor volume P=.13, Dose P=.35), and large tumor volume (HR 2.2 (95%CI 1.2-4.0) for the RT group as independent factors (Dose P=.15, Age P=.08, Sex P=.40).
Conclusions: We found no impact of RT dose on survival outcomes in our cohort, whether patients were

treated with combined local therapy modality or definitive radiotherapy. The upcoming iEuroEwing trial will assess the value of different radiotherapy dose in a randomized manner to control for potential selection bias.

EP203 / #1534

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

HIGH-DOSE CHEMOTHERAPY FOLLOWED BY AUTOLOGOUS STEM CELL TRANSPLANTATION IN PEDIATRIC PATIENTS WITH RELAPSED OSTEOSARCOMA

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Background and Aims: Patients with relapsed osteosarcoma have poor treatment outcomes. High-dose chemotherapy with autologous stem cell transplantation (HDCT/ASCT) has been used in several high-risk malignant solid tumors; however, few studies have evaluated their role in the treatment of osteosarcoma. We evaluated the effectiveness of HDCT/ASCT in relapsed pediatric osteosarcoma cases.
Methods: We retrospectively reviewed the medical records of 40 patients diagnosed with and treated for relapsed osteosarcoma at Asan Medical Center and Samsung Medical Center from January 1996 to July 2019.
Results: The median age of this cohort was 13.4 years (range, 6.1–18.2). The cohort's 5-year overall survival (OS) was 51.0±0.1% during a median follow-up period of 67.5 months. Twenty-five patients (62.5%) achieved complete remission (CR) with salvage treatment, and the 5-year OS was 82.4±0.1%, whereas none of the remaining 15 patients who did not achieve CR ($P<0.0001$) survived. Of the 25 CR cases, 15 underwent subsequent HDCT/ASCT. However, there were no significant differences in the 5-year OS outcomes between patients who did and did not receive HDCT/ASCT (83.9±0.1%, 13/15 vs. 80.0±0.1%, 8/10, respectively; $P=0.923$).
Conclusions: Our results indicate that HDCT/ASCT does not significantly improve survival outcomes in relapsed osteosarcoma. Achievement of CR remains the most crucial factor for good survival outcomes.

EP204 / #1193

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

DISIALOGANGLIOSIDE GD2 – PATTERN IN PEDIATRIC SOLID TUMOR

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Background and Aims: Immunotherapy using GD2-targeting antibodies has become a component of up-front treatment for high-risk neuroblastoma. GD2 has been found at varying levels of expression on a number of other tumor types including Ewing's sarcoma (ES), osteogenic sarcoma (OS), soft tissue sarcoma (STS). To date, there has been limited research on GD2 expression in listed tumors. The aim of the study is to investigate the frequency of GD2 expression in pediatric solid tumor.
Methods: Patients were eligible for inclusion if they satisfied the following criteria: if they were less than 18 years of age and had received a diagnosis of refractory solid tumors (5 OS, 4 ES and 4 STS). Flow cytometry was performed to investigate possible membranous expression of GD2. The percentage of GD2-positive tumor cells was assessed as a continuous parameter (0–100%).
Results: GD2 was found to be expressed in 10 of the 13 (76.9%) tumor samples. Among the tumor's subtypes, GD2 expression was observed predominantly in OS (ranged from 0% to 91.6%, mean 38.3 ± 21.2%) and STS (ranged from 4.3% to 84.2%, mean 42.5 ± 21.2%). The results of GD2 expression in ES ranged from no detectable surface expression to diffuse and/or intense staining in some tumors (GD2 expression levels ranged from 0.5 to 94.2% from diagnostic biopsy samples of ES, mean 25.1 ± 23.1%).
Conclusions: The present study revealed the presence of GD2 expression in a high proportion of pediatric solid tumors samples, with a significantly higher proportion of GD2-positive tumors in osteogenic sarcoma and soft tissue sarcoma versus Ewing's sarcoma. GD2 in childhood solid tumor might be a suitable tumor-associated antigen that could be targeted on the cell surface in patients with a poor prognosis.

EP205 / #191

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

SECONDARY OSTEOSARCOMA: A VERY CHALLENGING CHALLENGE

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Background and Aims: The risk of survivors developing a secondary bone sarcoma after receiving treatments for paediatric cancers is well established. The aim of this study was to assess secondary osteosarcoma (SOS) patients' clinical characteristics and clinical outcomes.
Methods: The study concerns survivors with a history of primary neoplasms (PN) during childhood and adolescence treated with chemotherapy +/- radiotherapy+/- surgery and subsequently diagnosed with SOS.
Results: We identified 26 survivors (13 Females, 13 Males) who developed SOS at a median of 7.3 years from diagnosis of the PN, of which 5/7 tested had a Li-Fraumeni syndrome. They were a median 8.6 and 15.1 years of age when their PN and SOS were diagnosed, respectively. Twenty four out of 26 underwent radiotherapy and 19 were treated with chemotherapy including doxorubicin, for the PN. A consistent number of SOS was located in unfavourable sites (8 hip bone, 6 skull) and all but one received chemotherapy with tailored schedule and omission of doxorubicin in 20 cases and 18 out of 26 underwent surgery: Fifteen patients died of SOS The 5- and 10-year event free survival, overall survival probabilities (95% confidence interval) were 73.1% (57.9-92.3%) / 30.8% (17.3-54.8%) and 92.3% (82.6-100%) / 69.2% (53.6-89.5%), respectively.
Conclusions: Judging from our experience, survival probabilities after SOS are lower than observed in patients with primary osteosarcoma but not negligible. It is therefore mandatory to discuss the best choice of treatment for such patients in terms of their chances of cure and quality of life in a referral center.Judging from our experience, survival probabilities after SOS are lower than observed in patients with primary osteosarcoma but not negligible. It is therefore mandatory to discuss the best choice of treatment for such patients in terms of their chances of cure and quality of life in a referral center.

EP206 / #1078

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

GERMLINE VARIANTS IN PEDIATRIC PATIENTS WITH OSTEOSARCOMA REVEALED BY MULTIGENE PANEL TESTING

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Background and Aims: Osteosarcoma (OS) is the most common bone tumor in children and young adults with a peak of incidence in the second decade of life. Most cases are sporadic but the risk of OS is substantially increased by germline variants in cancer-associated genes. The use of next-generation sequencing (NGS) to reveal the genetic predisposition to OS expands our knowledge of the molecular basis of the disease and is important for patient's management.
Methods: A total of 38 patients with OS were enrolled in the study. There were 18 girls and 20 boys aged 3-17 years (mean age 11,3 years). The NGS of genomic DNA was performed on the Illumina platform using a multigene panel of 882 cancer-associated genes. Libraries were prepared via enrichment by hybridization with KAPA HyperChoice probes (Roche).
Results: Pathogenic and likely pathogenic mutations predisposed to cancer development were revealed in heterozygous state in 9 patients (23%). Six patients had OS and at least one secondary tumor: nephroblastoma (n=2), soft tissue sarcoma (n=3), retinoblastoma (n=1). Most often the mutations occurred in the TP53 gene (n=4). In two cases, the patients with TP53 mutation had additional tumor: nephroblastoma or embryonic rhabdomyosarcoma. One patient with retinoblastoma at age 2 and OS at age 15 carried a novel mutation in RB1 gene (c.214_224del), leading to premature stop codon. Other potentially affected genes were the BRCA1 (2080delA), SMARCAL1 (c.2542G>T), RAD51 (splice site mutation:c.905-2_905-1del) and ATM (c.8565T>G) genes. The pathogenic stop-gained variant in the SMARCAL1 gene was previously described in patients with immuno-osseous dysplasia.
Conclusions: Germline mutations in cancer associated genes were revealed in 23% of our patients. Significant proportion (10%) of osteosarcomas were a part of Li-Fraumeni syndrome caused by alterations in the TP53 gene. Also, mutations in other genes (RB1, BRCA1, RAD51, ATM) associated with hereditary cancer syndromes were found.

EP207 / #972

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

COMMON PRACTICE OF THE OSTEOSARCOMA MANAGEMENT IN PEDIATRIC ONCOLOGY CENTERS. A NATIONWIDE REPORT

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Background and Aims: The survival of high-grade osteosarcoma, the most common primary bone tumor in children, in the last 40 years has reached a plateau. As a pan-European effort has recently been initiated to further improve survival, we surveyed the common practice of the 7 pediatric oncology centers in Greece, to create standardized national recommendations.
Methods: We conducted a survey about the common practice of all oncological centers in Greece regarding biopsy, use of p-glycoprotein, PET experience, chemotherapy, muramyl tripeptide, metastasectomy, palliative techniques.
Results: The 2/7 centers usually perform core needle biopsy, 3/7 open, 2/7 both. None measures p-glycoprotein or modify treatment with p-glycoprotein. The 3/7 perform PET as a routine when diagnosed, 2/7 before surgery, 2/7 at the end of treatment. All departments, use EURAMOS protocol. The 3/7 in the past evaluated the response to neoadjuvant treatment, with thallium scintigraphy. The 3/7 have given muramyl tripeptide in 4 patients. The 6/7 choose amputation surgeries when there is infiltration of blood vessels and nerves (4/7), disease progression (2/7), local recurrence (3/7), as palliative (1/7). Rotationplasty surgeries were used in 3/7 centers for 4 patients. All centers perform prosthetic and expanding surgeries in Greece, while 5/7 sent patients in European centers in the past. Metastasectomy is performed after the end of neoadjuvant (1/7), after the end of adjuvant (2/7), after surgery but before the end of adjuvant (4/7). Metastasectomy operations are performed with open surgery (5/7), or minimally invasive technique when possible (2/7). In cases of pulmonary recurrence 5/7 administer recurrent chemotherapy except metastasectomy, 2/7 omit chemotherapy individually. None used samarium, or any isotope to relieve symptoms. The most common chemotherapy for relapse was ifosfamide-etoposide. New treatments are used individually.
Conclusions: The common practice in Greece, co-insides with the usual practice in Europe. Patients need to be treated in new clinical trials to improve survival.

EP208 / #1000

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

INCIDENCE AND TIME TRENDS OF OSTEOSARCOMA. COMPARISON DATA OF SEER, USA WITH THE GREEK REGISTRY NARECHEM-ST

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Background and Aims: Despite success stories in prevention, screening, and treatment, cancer remains the second leading cause of childhood (0-14 years) death with increasing incidence trends for several disease types. Preliminary data on the descriptive epidemiology of childhood osteosarcoma are reported in Greece and compared to those of the SEER, USA.
Methods: From 839 osteosarcoma cases recorded in SEER collaborating registries (1975–2017), data on 204 cases (2010-2017) were extracted for the comparative analyses. Nationwide registry for childhood hematological malignancies and solid tumors (NARECHEM-ST) data comprise 55 incident cases reported during 2010-2020 in 6 pediatric Hematology-Oncology Centers and alternative data sources, apart from the island of Crete accounting for 5% of the total pediatric cancer burden. Preliminary analyses were performed for the comparison of the percentage of cases across the two registries and the distribution of cases by age and sex.
Results: The annual percentages of cases in both registries did not show any significant differences overall for the overlapping years (goodness-of-fit-p=0.95), whereas differences were noted with regards to sex and age distribution among the NARECHEM-ST registry which comprised mainly Caucasian populations. Most NARECHEM-ST cases (82%) were diagnosed after the 10th year of life, without significant reduction of the annual percentage of cases for smaller ages (p=0.469); median age at diagnosis was higher in NARECHEM-ST compared to SEER (12, 11respectively). A larger male preponderance was estimated in NARECHEM-ST compared to SEER in all age groups (male: female=1.12 vs 1.04) and in cases 10-14 years (1.25 vs 1.14). The overall NARECHEM-ST AIR was 2.8 without a significant change in the linear trend (p=0.93).
Conclusions: Variations in the descriptive epidemiology between the two examined registries with accessible final primary data as well as with published data derived from other European countries may imply variable risk factors shaping the respective geographical and temporal patterns and need to be further explored.

EP209 / #1018

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

SURVIVAL OF OSTEOSARCOMA IN GREECE: PRELIMINARY DATA FROM THE NATIONWIDE REGISTRY FOR CHILDHOOD HEMATOLOGICAL MALIGNANCIES AND SOLID TUMORS (NARECHEM-ST; 2010-2020)

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Background and Aims: Osteosarcoma is the most common primary bone sarcoma. We aimed to assess the 5-year overall survival (OS) and explore prognostic variables among incident cases with high-grade osteosarcoma aged 0-14 years reported in the NARECHEM-ST Registry.
Methods: Preliminary data of the 55 incident pediatric patients (0-14 years) with confirmed by biopsy high-grade osteosarcoma, diagnosed between 2010 and 2020 and followed-up to 31-12-2021 in six Pediatric Hematology- Oncology Departments were reviewed. One patient was lost to follow up. Descriptives for age, sex, primary site, stage, treatment and survival outcomes were examined; Kaplan-Meier curves were constructed, and 5-year overall survival (OS) and local and distant relapse-free survival (RFS) were estimated.
Results: The median age at diagnosis was 12 years (4–14 years) and the male-to-female ratio was 1.12. The most common sites at diagnosis were the extremities (47/55, 85%), skull (3/55, 5%) and trunk (5/55, 9%), whereas 8 patients had primary metastatic disease (15% stage III). Surgical resection of the primary tumor was performed in 53 patients. Most of the patients received EURAMOS based protocol. Good response to chemotherapy (necrosis >90%) was recorded in almost 40% cases. Ten patients had a local relapse (70% died), while 20 had a relapse on other sites (75% died). At the last follow up (median 4 years, range: 0.4-11.8 years) 34 patients were alive. The 5-year OS exceeded 63% (95% CI: 48%-75%). The 5-year OS was poorer (41%, p=0.3) in patients with metastatic or relapsed disease. The 5-year local and distant RFS were 81% (95% CI: 67%-59%) and 62% (95% CI: 47%-73%) respectively.
Conclusions: OS and RFS of patients with osteosarcoma in Greece is comparable to that reported by major collaborative trials. As expected, survival is influenced by the presence of metastases, and relapsed disease. Ongoing clinical cancer registration could facilitate comparison of outcomes between different study groups and modify treatment.

EP210 / #681

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

SINGLE-CELL TRANSCRIPTOME ANALYSIS OF TUMOR AND STROMAL COMPARTMENTS OF OSTEOSARCOMA PRIMARY TUMORS AND METASTATIC LESIONS

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Background and Aims: Osteosarcoma is a malignant bone tumor that most commonly affects children, adolescents, and young adults. The current standard of care involves surgical resection of the primary tumor and multi-agent chemotherapy which can result in 5-year survival rates up to 70% for patients with localized disease. However, approximately 20% of patients have clinical detectable metastases at diagnosis. In addition, tumors will relapse and generate metastasis in a third of patients with localized disease at the time of diagnosis. In patients with metastasis, more than 85% of the metastases occur in the lungs and tend to be resistant to chemotherapy. Importantly, the survival of patients with metastatic osteosarcoma has remained virtually unchanged over the past 30 years, with an overall 5-year survival rate of less than 20%.
Methods: In this study, we employed a single-cell RNA-sequencing technology to profile the transcriptomes of individual cells from dissociated primary or metastatic tumors of K7M2 osteosarcoma model. Additionally, Spatial RNA-sequencing was performed to determine localization and potential interactions of cells in TME.
Results: Our single-cell RNA-sequencing analysis revealed distinct cell types in primary and metastatic osteosarcoma tissues including tumor, endothelial, immune cells, and fibroblasts. We found an impaired immune response with a defective antigen presentation, immunoregulatory DCs, pro-tumoral macrophages and increased number of T-regulatory cells. Furthermore, spatial RNA-sequencing analysis, in combination with single cell data, shows a complex network of interactions between tumor cells and the rest of TME cell populations, especially immune cells.
Conclusions: Our work identifies an impaired immune response against tumoral cells and a complex network of interactions in TME. These findings provide valuable insights on how tumoral cells can interact with other cells in TME. The pathways through which tumor induces immunoregulatory phenotype of DCs or pro-tumoral macrophages can be a potential therapeutic target that we need to explore.

EP211 / #1609

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

PEDIATRIC BONE AND SOFT TISSUE SARCOMAS: CLINICAL PROFILE, MANAGEMENT AND OUTCOME; EXPERIENCE FROM A TERTIARY CARE CENTER IN INDIA

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Background and Aims: BACKGROUND AND AIM Sarcomas are a heterogeneous group of rare tumors that arise predominantly from the embryonic mesoderm. The aim of this study was to analyze the clinical features and outcome of pediatric sarcomas.
Methods: This was a retrospective study conducted at Mazumdar Shaw Medical Center at Bangalore, India. Data of all pediatric patients with bone and soft tissue sarcomas were analyzed from January 2015 to February 2022.
Results: A total of 68 cases were analyzed; 45 were bone sarcomas (62% osteosarcoma and 38% Ewing's sarcoma) and 23 were soft tissue sarcomas (91% rhabdomyosarcomas). The male female ratio was 1.1:1. The mean age of presentation of bone tumor was 13 years and soft tissue sarcoma was 7 years. Most common site being distal femur 59%(n=26) in bone tumors and orbit 38% (n=8) in rhabdomyosarcoma.12 patients presented with metastatic disease (5 cases of osteosarcoma ,3 cases of Ewing's sarcomas and 4 cases of Rhabdomyosarcomas) with lung being the most common site of metastasis. Among 21 cases of rhabdomyosarcoma;52% presented as high risk ,38% with intermediate risk and 9.5% presented with recurrent disease. All cases of Rhabdomyosarcomas and Ewing's sarcomas were treated with COG protocol based on risk stratification, and Osteosarcomas were treated with Methotrexate based regimen. Good histopathologic response (necrosis ≥90%) was achieved in 59% nonmetastatic and 56% metastatic patients .6 cases relapsed (4 children with rhabdomyosarcoma ,2 with osteosarcoma and 1 with Ewing's sarcoma). At a median follow-up of 48 months, the overall survival and disease-free survival of Osteosarcoma was 82% and 75%, Ewing's sarcoma was 88% and 82% and soft tissue sarcomas was 82% and 65% respectively.
Conclusions: The formation of disease management groups/clinics focused on sarcomas has resulted in better understanding and management of these uncommon tumors hence resulted in better outcome in terms of overall survival.

EP212 / #1453

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

FACTORS INFLUENCING OUTCOME OF PATIENTS WITH PRIMARY EWING SARCOMA OF THE SACRUM

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Background and Aims: Ewing Sarcoma (EWS) is a rare and highly malignant bone tumor. It represents the second most common bone tumor in children and adolescents following osteosarcomas. The sacrum as primary is very rare. Due to the anatomical location, local treatment is challenging especially regarding surgery.
Methods: To analyze prognostic factors we retrospectively analyzed databases of EURO-E.W.I.N.G. 99 and EWING 2008. Both clinical trials included 124 patients (pts) with localized (n=70) or metastasized (n=53) sacral EWS. All pts received systemic treatment according to the protocols. For local control 64.3% received definitive radiotherapy (followed by combined modality treatment (25.2%)) and surgery alone (4.3%). Some pts had no local treatment (6.1%) mainly due to early relapse. The study endpoint was event free survival (EFS). Factors probably associated with survival e.g., age, sex, tumor volume, local treatment modality and applied study protocol were included in the univariate and multivariable analyses.
Results: Age under 18 years was associated with better outcome (3y-EFS: .45 vs .12; P=.03) in patients with metastases at diagnosis. In general, metastases at diagnosis (3y-EFS: .33 vs .68; P<.001; HR=3.4, 95% CI 1.7 to 6.6), large tumor volume (3y-EFS: .36 vs .69; P=.002; HR=2.1, 95% CI 1.1 to 4.0) or age ≥ 18 years (3y-EFS: .41 vs .60; P=.10; HR=2.6, 95% CI 1.3 to 5.2) were associated with dismal outcome. Interaction was seen in patients with definitive radiotherapy compared to other patients by a higher EFS in localized disease in contrast to a lower EFS in metastatic patients (P<.001).
Conclusions: Young age is associated with a better outcome and interaction was observed between

definitive radiotherapy and metastases at diagnosis. Regarding local therapy modality, the anatomical location is decisive and the majority of pts received definitive radiotherapy.

EP213 / #1918

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

ANALYZING METHOTREXATE LEVELS: A LITERATURE REVIEW

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Background and Aims: Methotrexate is an antineoplastic anti-metabolite commonly used at high doses in pediatric oncology for the treatment of certain malignancies such as osteosarcoma, CNS malignancies and lymphomas. Toxicity from methotrexate is widespread involving multiple systems notably including the gastrointestinal, hematologic, renal, mucocutaneous and neural systems. Glucarpidase reduces the methotrexate concentration by cleaving it into non-toxic metabolites, 4-deoxy-4-amino-N10-methylpteroic acid (DAMPA) and glutamate which are eliminated by the liver. High performance liquid chromatography is the gold standard for evaluating methotrexate levels as DAMPA cross-reacts with immunoassay measurements.
Methods: A review of existing literature limited between the years 2000 and 2022 was conducted utilizing the PubMed database using the search terms “methotrexate” linked with the Boolean operator AND to the terms “high performance liquid chromatography (HPLC)” and “immunoassay”. Results were then analyzed for trends between HPLC and immunoassay measurements which recurred consistently throughout the literature.
Results: The initial search resulted in 26 articles. The prominent trends from these articles were discordance between the commonly used methotrexate immunoassays which overestimated the overall methotrexate concentrations compared to HPLC. Notably, these studies demonstrated a more pronounced overestimation for methotrexate concentrations below 0.2 micromoles.
Conclusions: In our pediatric patients the methotrexate threshold for discharge is set to reduce the risk of toxicity. However from literature HPLC is superior to the more commonly used immunoassay methods which may grossly overestimate methotrexate levels especially at lower concentrations. This is of critical importance as in our pediatric population we run the risk of unnecessarily prolonging hospital admissions thus further disrupting quality of life and so must be accurately balanced with the risk of toxicity to our patients.

EP214 / #31

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

CLINICAL OUTCOME OF PATIENTS WITH OSTEOSARCOMA EXPERIENCING RELAPSE OR PROGRESSION: A SINGLE-INSTITUTE EXPERIENCE

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Background and Aims: Patients with osteosarcoma who experience relapse or progression (R/P) have a poor prognosis. In the current study, we retrospectively analyzed the clinical outcomes of patients with osteosarcoma who recently experienced R/P and received novel salvage chemotherapy and/or molecular target therapy.
Methods: Between 2000 and 2019, 59 patients younger than 40 years old were diagnosed with high-grade osteosarcoma, among which 30 patients experienced R/P. Clinical data of those patients were retrospectively analyzed to identify prognostic and therapeutic factors influencing their outcomes.
Results: Twenty-two patients (73.3%) underwent curative local surgery for primary lesion and metastases, one of whom also received local radiotherapy, after first R/P. The 5-year progression-free survival (PFS) rate of the entire cohort was 51.9%. The 5-year overall survival (OS) rates after the last R/P of patients experiencing first (n = 30), second (n = 14), and third (n = 9) R/P were 50.3%, 51.3%, and 46.7%, respectively. Multivariate analysis did not identify any independent risk factors affecting OS. The 5-year PFS rate of the 30 patients after first R/P was 22.4%, and multivariate analysis identified histological subtype and curative local surgery as independent risk factors influencing PFS. The median relapse-free intervals between the first and second R/P and the second and third R/P were 1.06 and 1.14 years, respectively. Long (> 6 months) partial response was observed in three patients treated using temozolomide+etoposide, irinotecan+carboplatin, or regorafenib.
Conclusions: OS rate in the patients with osteosarcoma experiencing R/P included in this study was markedly higher than that reported previously, mainly due to the surgical total removal of tumors, even after subsequent R/P. The recent establishment of salvage chemotherapy or molecular targeted therapy may also increase survival rates in a subgroup of patients.

EP215 / #547

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

CLINICAL OUTCOMES OF LOCALIZED AND METASTATIC OSTEOSARCOMA PATIENTS TREATED BY TWO CONSECUTIVE PROTOCOLS (2006 -2021). RESULTS OF THE CHILEAN PEDIATRIC CANCER PROGRAM PINDA.

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Background and Aims: The aim of this study was to analyze clinical outcomes of children with osteosarcoma treated by 2 consecutive protocols.
Methods: Patients with high-grade osteosarcoma aged ≤15 years were treated with pre and post-operatively chemotherapy. Protocol A, June 2006-December 2015 : Carboplatin, Ifosfamide, Doxorubicin and Methotrexate for localized patients; Cisplatin, Doxorubicin, Ifosfamide, Etoposide and Methotrexate for metastatic ones Protocol B, January 2016 to March 2021: Cisplatin, Doxorubicin, Methotrexate for all patients with metronomic chemotherapy with oral cyclophosphamide and methotrexate in metastatic patients. All patients underwent surgery of the primary tumor.
Results: Protocol A, 131 patients, median follow-up 97 months. Fifty % were male, median age 12 years; 38 % presented with lung metastases, 62% bilateral. One patient with multicentric disease, 4 patients had second cancer. Seventy-eight % underwent conservative surgery; necrosis 90% in 53%. Overall survival (OS) 64%, localized 75% and metastatic 46%. Event-free survival (EFS) 60%, localized: 69%, metastatic: 46%. Twenty-two patients (27%) localized patients relapsed: bone 27%, lung 50%, combined 23%. Forty-seven patients died (36%). Protocol B, 64 patients median follow-up 33 months. Fifty-five % were male, median age 12 years.; 56% presented with lung metastases, 89% bilateral. Three patients with multicentric disease, 2 patients had second cancer Sixty-seven % underwent conservative surgery; necrosis 90% in 42%. OS: 72%; localized 90% and metastatic 58%. EFS 53%; localized: 71%, metastatic: 39%. Seven (25%) localized patients relapsed: 43% local, 57%, lung. Eighteen patients died (28%).
Conclusions: Our national data demonstrates similar survival rates as reported by larger series and reaffirms known prognostic factors.This highlights the importance of centers concentrating expertise and resources. Of note, the high proportion of metastasic patients. Acknowledgements to Data Manager Mariela Fuenzalida

EP216 / #197

Topic: *AS05 SIOP Scientific programme / AS05.g Bone Tumours*

PROGNOSTIC VALUE OF DETECTION OF CD99+, CD45− CELLS IN PERIPHERAL BLOOD BY FLOW CYTOMETRY IN CHILDREN WITH EWING SARCOMA

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Background and Aims: Early detection of metastasis and recurrence of Ewing sarcoma (ES) is important for early management. This work aimed to detect $CD99^+$, $CD45^-$ cells in peripheral blood by flow cytometry (FC) before and during chemotherapy and evaluate their prognostic significance.
Methods: This prospective cohort study was carried out on 60 children newly diagnosed with ES at Children Cancer Hospital-Egypt 57357 and 40 healthy children control group. Detection of $CD99^+$, $CD45^-$ cells in peripheral blood was accomplished by FC at baseline before treatment and after five cycles of chemotherapy. Samples were classified as positive if they had more than the upper limit of cells observed in the control cases. Correlation between FC results and relapse and overall survival (OS) after one year was performed.
Results: Median percentage of $CD99^+$, $CD45^-$ cells was significantly increased in patients compared with controls (0.002% vs 0%, respectively, $P < 0.001$). Post-cycle 5 $CD99^+$, $CD45^-$ cells were increased in 12 patients, of them 11 patients' disease had either relapsed or progressed. Post-cycle 5 $CD99^+$; $CD45^-$ cells had a 73.3% sensitivity and 97.8% specificity for predicting relapse or progression, whereas baseline only had 6.7% sensitivity and 77.8% specificity. The hazard ratio for mortality in the post-cycle 5 positive group was 18.4 [95% confidence interval (1.86 to 181.46)] times that of the negative group. One year OS was 91.67%.
Conclusions: Post-cycle 5 $CD99^+$, $CD45^-$ cells in peripheral blood by FC is a strong predictor for relapse, progression, and mortality whereas baseline is a poor predictor in newly diagnosed patients with ES

EP217 / #159

Topic: *AS05.h Soft Tissue Sarcomas*

RHABDOMYOSARCOMA WITH UNKNOWN PRIMARY TUMOR SITE. A REPORT FROM EUROPEAN PEDIATRIC SOFT TISSUE SARCOMA STUDY GROUP (EPSSG)

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Background and Aims: Rhabdomyosarcoma (RMS) is an aggressive malignancy, and 20% of children present with metastases at diagnosis. Patients presenting with disseminated disease very occasionally have no clear evidence of a primary tumor mass. Since these patients have rarely been investigated, we report on a series of patients with RMS and unknown primary tumor site registered in the MTS 2008 protocol (October 2008 - December 2016) coordinated by the European pediatric Soft tissue sarcoma Study Group.
Methods: Patients were administered 9 cycles of induction chemotherapy, and 48 weeks of maintenance chemotherapy. Surgery and/or radiotherapy was planned after the first assessment of tumor response, and implemented after six cycles of chemotherapy. If feasible, radiotherapy to all sites of metastasis was recommended.
Results: We identified 10 patients with RMS and unknown primary site, most of them adolescents (median age 15.8 years, range 4.6-20.4). Nine had fusion-positive alveolar RMS. Multiple organ involvement was identified in 7 patients, 2 only had bone marrow disease, and 1 only had leptomeningeal dissemination. All patients were given chemotherapy, 4 were irradiated, and none had surgery. Three patients underwent allogeneic bone marrow transplantation. At the time of this analysis, only 2 patients are alive in complete remission: 1 had received radiotherapy; and 1 had a bone marrow transplant.
Conclusions: RMS with unknown primary tumor occurs mainly in adolescents and is typically fusion-positive alveolar. Radiotherapy may be important, but survival is poor and patients should be offered enrollment in investigational trials.

EP218 / #1364

Topic: *AS05.h Soft Tissue Sarcomas*

NUTRITIONAL STATUS AND INTERVENTIONS OF CHILDREN WITH BONE AND SOFT TISSUE SARCOMAS

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Background and Aims: Malnutrition is an important condition common in pediatric oncology and causes many adverse events, including mortality. This study aims to determine the nutritional status, daily food consumption, and nutritional treatments in hospitalized children with solid tumors.
Methods: Patients with bone and soft tissue sarcomas admitted to the Ege University Hospital Pediatric Oncology Department between January 2018-December 2021 (59 patients; F/M: 26/33; mean age:10.3 years (0,5-18 years)) were followed. The nutritional status of the patients was evaluated with the StrongKids (SK) screening tool within 24 hours of hospitalization, and nutritional therapy was started for the patients who needed it. Anthropometric measurements (height, weight, upper-middle arm circumference (MUAC)), and daily food consumption were taken in 3 different times.
Results: Malnutrition was observed in 22% (n =13), moderate risk 78.0%(n=46) according to StrongKids. According to weight for age 32.2%(n=19) of patients were <25%, 33.9% (n=20) of the children had <25% MUAC. Children can get mean 47.9% (5-115%) of their daily energy requirements and 43% (0.5-120) of their protein requirements with oral foods. 33,9% (n=20) of the children were fed with ONS, 13,6% (n=8) fed by EN, and 1,7% (n=1) fed by TPN. Of the 40 patients, all 3 measurements were completed, 45,8% (n=27) gained weight. The patients weight for age <25% at the 1st, 2nd and 3rd follow-ups, respectively were 37.5% (n=15), 45% (n=18), 42.5% (n=17) (p=0.13). Those with SK>4 were respectively 27.5% (n=11), 47.5% (n=19), 27.5% (n=11) (p=0.029), those with MUAC<25 were found to be 37.5% (n=15), 45% (n=18), 35% (n=14) (p=0.22).
Conclusions: Malnutrition in pediatric cancers is an important issue that should not be ignored. It can occur at any time during the follow-up. Multidisciplinary teams regarding malnutrition should monitor pediatric cancer patients, and nutritional interventions should be performed without delay when necessary.

EP219 / #1021

Topic: *AS05.h Soft Tissue Sarcomas*

PAZOPANIB MAINTENANCE THERAPY FOR EWING SARCOMA IN PEDIATRIC PATIENTS

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Background and Aims: The prognosis of Ewing sarcoma is still not promising due to remarkable relapse rates. Thus, there is an need for novel therapies. Pazopanib is a multi-target tyrosine kinase inhibitor and there have been no reports on the long-term efficacy of it in pediatric patients with Ewing sarcoma.
Methods: We report 7 pediatric patients with Ewing sarcoma, received pazopanib in addition to cytotoxic chemotherapy
Results: The median age was 12 (8-15 years). 4 patients had metastatic disease and 3 patients were in the poor-risk group according to Euro Ewing 2012 Protocol. 6 patients underwent surgery and there was no viable tumour in the pathological examination. One patient could not be operated due to high morbidity. All patients received radiotherapy. 3 patients underwent high-dose chemotherapy and autologous stem cell transplantation. We started pazopanib to 6 patients as maintenance after the end of the treatment at a dosage of 200-400mg/day, which was eventually increased to 400-800mg/day. The inoperable patient had intracranial relapse at the 6th month of pazopanib. Other 5 patients are disease-free with a 7 months median follow-up time from the starting of pazopanib (3-13 months). One of the 7 patients had disseminated disease and he received VIT (vincristine- irinotecan- temozolamide) with pazopanib. He has also been followed-up with pazopanib as monotherapy for 10 months and he is disease-free. In all cases, whitening of hair was observed. Two patients had mild hepatotoxicity. One of these patients tolerated the dose reduction well and is now monitored. The other patient had to be discontinued at the 8th month of treatment. Median follow-up time from the diagnose is 18 months (15-27 months).
Conclusions: Pazopanib maintenance may be a therapeutic option as a continuation treatment for poor-risk Ewing sarcoma and also may be useful for disseminated disease. More studies are needed to demonstrate its efficacy and safety in pediatric patients.

EP220 / #1392

Topic: *AS05.h Soft Tissue Sarcomas*

IMPACT AND THERAPEUTIC EXPLOITATION OF HYPOXIA IN RHABDOMYOSARCOMAS

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Background and Aims: Rhabdomyosarcomas (RMS) are rare aggressive childhood cancers with poor prognosis at relapse. Hypoxia in cancer is associated with resistance to radio- and chemotherapy and is a negative prognostic factor. Data for the extent and effects of hypoxia in RMS are limited. Moreover, no hypoxia-targeted treatment strategy has entered clinical practice, due to a lack of biomarker-led clinical trials. The project aims to assess the effect of hypoxia in RMS on patient outcomes, develop a novel, more effective therapeutic strategy based on the hypoxia present in RMS.
Methods: Bioinformatic analysis was performed on RMS patient gene-expression profiling datasets. Protein and RNA levels of hypoxia markers and sensitivity to backbone drugs were compared in hypoxia and normoxia in vitro and three-dimensional models were generated to model hypoxia.
Results: High levels of hypoxia significantly correlated with worse overall survival (OS) in fusion negative (FN)-RMS (p=0.0436). A consistent upregulation of hypoxia inducible factor (HIF) downstream-targets glucose transporter-1 and carbonic anhydrase-IX, as well as reduced sensitivity to irinotecan in hypoxia, was demonstrated in cell line models. Hypoxia in 3D tumour spheroid cultures of RMS cell lines was alleviated by atovaquone, a repurposed antimalarial. Preliminary data suggests that atovaquone sensitises RMS spheroids to irinotecan.
Conclusions: Tumour hypoxia negatively impacts outcome in patients with FN-RMS and evidence suggests this contributes to resistance to current treatment options. Atovaquone provides a novel hypoxia-targeted strategy to improve oxygenation in tumours and increase sensitivity to current treatment options.

EP221 / #132

Topic: *AS05.h Soft Tissue Sarcomas*

PATIENTS WITH EMBRYONAL RHABDOMYOSARCOMA COMPLETELY RESECTED AT DIAGNOSIS: AN INTERNATIONAL ANALYSIS

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Background and Aims: The survival of patients with localized embryonal rhabdomyosarcoma (RMS) completely resected at diagnosis is above 90%. Most of them have paratesticular, uterus, or vaginal RMS, limiting specific analyses on RMS localized in other anatomic regions. We conducted this international study to define the outcome for completely resected embryonal RMS at sites other than paratesticular/uterine/vaginal primary sites,
Methods: We identified 113 patients, aged 0-18 years, enrolled from 1/1995 to 12/2016 in Children's Oncology Group (COG) (64 patients) and European protocols (49). Genito-urinary non-bladder/prostate RMS were excluded. The recommended chemotherapy was VA (vincristine, actinomycin-D) for 24 weeks or IVA (ifosfamide plus VA) in the European protocols and VA for 48 weeks or VAC (VA plus cyclophosphamide) in the COG protocols.
Results: The most common primary sites were non-parameningeal head and neck (40.7%), other (23.9%) and extremities (20.4%). In the COG studies, 42% of patients received VA and 58% VAC. In Europe 53% received VA and 47% IVA. With a median follow-up of 97.5 months the 5-year progression free and overall survival was 80.0% (71.2-86.4) and 92.5% (85.6-96.2), respectively, without significant differences between chemotherapy regimens. Tumor size (< or > 5 cm) significantly influenced overall survival: 96.2% (88.6-98.8) vs. 80.6% (59.5-91.4), respectively (p 0.01).
Conclusions: Survival of patients with non alveolar RMS completely resected at diagnosis is good among tumors arising from non-paratesticular/uterine/vaginal sites, and patients may be treated successfully with low intensity chemotherapy. To reduce the burden of treatment VA for 24 weeks may be considered in children with tumors <5 cm.

EP222 / #946

Topic: *AS05.h Soft Tissue Sarcomas*

PROGNOSTIC VALUE OF PATIENT-DERIVED XENOGRAFT ENGRAFTMENT IN PEDIATRIC SARCOMAS

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Background and Aims: The goals of this work were to identify factors favoring patient-derived xenograft (PDX) engraftment and study the association between PDX engraftment and prognosis in pediatric patients with Ewing sarcoma, osteosarcoma and rhabdomyosarcoma.
Methods: We used immunodeficient mice to establish PDX from patients at hospital Sant Joan de Deu, Barcelona, Spain. We addressed whether PDX tumors retained the main histologic, genomic and functional properties of patient tumors during successive passages in mice. Sample characterization included histopathology markers, chromosomal profiles (copy number alteration; CNA) and preclinical treatment assays (efficacy of irinotecan). We studied the association of the parameter “successful PDX engraftment” with the event free survival and overall survival of the patients from which the PDX were established.
Results: We established 30 subcutaneous PDX from patient tumor biopsies, with a successful engraftment rate of 44%. Age greater than 12 years and relapsed disease were patient factors associated with higher engraftment rate. PDX retained histology markers and most chromosomal aberrations of patient samples during successive passages in mice. Treatment with irinotecan resulted in significant activity in 20 of the PDX and replicated the response of rhabdomyosarcoma patients. Successive generations of PDX responded similarly to irinotecan, demonstrating functional stability of these models. Out of 68 tumor samples from 51 patients with a median follow up of 21.2 months, PDX engraftment from newly diagnosed patients was a prognostic factor significantly associated with poor outcome ($P = 0.040$). This association was not significant for relapsed patients. In the subgroup of patients with newly diagnosed Ewing sarcoma classified as standard risk, we found higher risk of relapse or refractory disease associated to those samples that produced stable PDX models ($P = 0.0357$).
Conclusions: Our study shows that PDX engraftment predicts worse outcome in newly diagnosed pediatric sarcoma patients

EP223 / #353

Topic: *AS05.h Soft Tissue Sarcomas*

RISK FACTORS IN PEDIATRIC MALIGNANT PERIPHERAL NERVE SHEATH TUMORS (MPNST): RESULTS FROM THE FRENCH PEDIATRIC ONCOLOGY SOCIETY (SFCE) COHORT

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Background and Aims: MPNST are very rare and aggressive tumors, which affect children, adolescents, and young adults. These tumors appear frequently in the context of type 1 neurofibromatosis (NF1). This study aims to determine risk factors in unselected pediatric MPNST in order to define an adapted therapeutic strategy.
Methods: Multicentric national retrospective study of all pediatric patients (0-18 yo) treated for MPNST, confirmed by a systematic pathology review, in France, from 1995 to 2017 and included in the SIOP MMT-95, EpSSG NRSTS-05 protocols and the French National Pediatric Tumor Registry (RNCE).
Results: Overall, 66 patients (median age 13.0 yo [range, 0.1-18.0]) developed a MPNST located in the limbs (36%), trunk (27%), head and neck (21%) and para-vertebral area (15%). Among them, 48% of patients had NF1, 44% had grade I-II FNCLCC grade tumors while 50% had grade III (not gradable, 4 cases). A majority of patients had localized (94%) and N0 (96%) tumors. The therapies consisted of surgery (94%), chemotherapy (neoadjuvant (36%) and/or adjuvant (27%)) and radiotherapy (52%). After a median follow-up of 3.8 y [range, 0.0-18.7], 5-year overall (OS) and event-free survivals (EFS) were respectively 46.7% [95%CI, 35.8-60.8] and 40.8% [95%CI, 30.3-54.9]. In multivariate analysis, unfavorable risk factors for overall survival were: presence of metastases (OR 6.4 [1.8; 22.0], p=0.001), FNCLCC grade 3 (OR 4.77 [1.4; 15.8], p=0.01), large tumor size (≥10 cm; OR 2.3 [1.1; 4.8], p=0.02) and NF1 status (OR 2.2 [1.1; 4.4], p=0.02).
Conclusions: MPNST had overall poor outcome especially in NF1 patients and in high grade, large and metastatic tumors. These risk factors should be considered to develop a more adapted risk stratification and develop new strategies to improve the survival of the patients. Regular monitoring for early MPNST detection in patients with NF1 also needs to be developed.

EP224 / #283

Topic: *AS05.h Soft Tissue Sarcomas*

METASTATIC RHABDOMYOSARCOMA: EVIDENCE OF THE IMPACT OF RADIOTHERAPY ON SURVIVALS, A RETROSPECTIVE SINGLE-CENTER EXPERIENCE

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Background and Aims: The prognosis of patients with metastatic rhabdomyosarcoma (RMS) remains largely unsatisfactory despite the adoption of intensive multimodal therapy. To evaluate the role of the different treatments adopted over the years, we retrospectively analysed a cohort of patients <21 years with metastatic RMS, treated from 1990 to 2020 at a referral center for pediatric sarcomas.
Methods: Patients were treated using a multimodal approach, which included surgery, radiotherapy and chemotherapy (with high-dose and maintenance chemotherapy in some cases). Patients' outcome was examined with univariable and multivariable analysis based on clinical features and treatment. Concerning radiotherapy, we categorized patients as: radical = radiotherapy to all disease sites; partial = radiotherapy to ≥ 1 site of disease, but not all; or none.
Results: The series included 80 patients. Event-free survival (EFS) and overall survival (OS) at 5 years were 17.3% and 21.3%, respectively. Survivals were significantly associated to radiotherapy, either on primary tumor and metastatic sites. In particular, EFS and OS were 70.6% and 76.0%, respectively, for patients who had radical irradiation. Lung irradiation was associated to superior survivals in patients with lung metastases only (5-year OS 77.8% versus 23.1%). EFS correlated also with maintenance chemotherapy, with also OS tending to be better for patients receiving it. At the Cox's multivariable analysis, OS correlated significantly with radiotherapy category.
Conclusions: While confirming the overall poor outcome of metastatic RMS patients, this study identified radiotherapy – on both primary tumor and metastatic sites – as the main variable influencing survival. As further finding, our study suggested a potential role of maintenance chemotherapy in improving survivals.

EP225 / #423

Topic: *AS05.h Soft Tissue Sarcomas*

PEDIATRIC ADULT-TYPE NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMAS: SALVAGE RATES AND PROGNOSTIC FACTORS AFTER RELAPSE

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Background and Aims: Though the prognosis for patients with pediatric non-rhabdomyosarcoma soft tissue sarcomas (NRSTS) is generally good, the chances of being cured after relapse are limited. This report describes a series of relapsing NRSTS patients treated at a referral center for pediatric sarcoma, investigating the pattern of relapse, salvage rates, and factors correlating with final outcome.
Methods: The analysis concerned 103 patients <21 years old with relapsing adult-type NRSTS treated from 1985 to 2020. For risk-adapted stratification purposes, patient outcome was examined using univariable and multivariable analyses based on patients' clinical features at first diagnosis, first-line treatments, clinical findings at first relapse, and second-line treatments.
Results: The first relapse occurred within 2-102 months (median 14 months) after patients' first diagnosis, and was local in 47%, metastatic in 34%, and both in 19%. Treatment at relapse included chemotherapy in 72 patients, radiotherapy in 38, and surgery in 55. The median overall survival (OS) was 20 months. Post-relapse OS was 56.1%, 25.8% and 19.1% at 1, 5 and 10 years, respectively. Cox's multivariable regression analysis showed that OS was significantly better for patients with local and late relapses (occurring more than 12 months after their first diagnosis), and for those achieving secondary remission.
Conclusions: The outcome of patients with recurrent NRSTS is poor. The abovementioned variables (type and time of relapse, and achievement of secondary remission) were combined in a risk-adapted model to develop a tool for estimating the chance of salvage, and deciding the best second-line treatment approach.

EP226 / #1043

Topic: *AS05.h Soft Tissue Sarcomas*

THE PROGNOSTIC ROLE OF THE C-REACTIVE PROTEIN AND SERUM LACTATE DEHYDROGENASE IN A SERIES OF PEDIATRIC PATIENTS AFFECTED BY EWING SARCOMA

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Background and Aims: Ewing sarcoma (ES) is a rare and aggressive pediatric cancer with different biological behaviours. The predictive value of serum lactate dehydrogenase (LDH) and C-reactive protein (CRP) has not been clearly assessed. The objective of our retrospective study was to investigate the prognostic value of LDH and CRP levels in a series of ES pediatric patients.
Methods: Between 2004 and 2019, 89 patients with ES were included. LDH and CRP were measured at diagnosis before treatment initiation for all patients. Multivariable Cox models for overall survival (OS) adjusting on commonly reported prognostic factors of Ewing sarcomas were used. For biomarkers, a classification and regression tree (CART) model was used to find a cut-off associated with survival. Kaplan-Meier estimates by biomarkers levels were derived for OS and progression-free survival (PFS) and compared with log-rank tests. All comparison tests were two-sided and considered significant at the 5% level.
Results: In univariable analyses, LDH and CRP high levels were associated with worst prognosis. In multivariable analyses, only higher LDH value remained associated with a lower OS. For LDH, the optimal cut-off to discriminate survival was 333 UI/L according to the CART model. The high LDH level group experienced all the 21 deaths registered in our population (24%) and about 90% of disease progressions. The 5-year OS was 66.4% in the high LDH level group while no death was observed in the low LDH level group. The 5-year PFS was 57.9% in the high LDH level group versus 80.4% in the low LDH level group.
Conclusions: Our study demonstrates that LDH levels at diagnosis strongly correlates to prognosis. Its feasibility with a very low cost and its reproducibility in almost all centers, make it suitable as a potential prognostic biomarker in clinical oncological practice.

EP227 / #692

Topic: *AS05.h Soft Tissue Sarcomas*

HEARING LOSS IN SURVIVORS OF HEAD AND NECK RHABDOMYOSARCOMA

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Background and Aims: Hearing loss (HL) can be a serious and permanent adverse effect of childhood cancer treatment and may be provoked by systemic, but also local therapies such as head and neck radiotherapy (RT) and surgery. The primary aim of this study was to assess the frequency and pattern of HL in survivors of head and neck rhabdomyosarcoma (HNRMS). The secondary aim was to explore the dose-effect relationship between dose to the cochlea and HL.
Methods: Between 1993 and 2017 Dutch patients treated for HNRMS were evaluated for HL with pure tone audiometry at least two years after end of treatment. HL was graded according to the Muenster, International Society for Paediatric Oncology (SIOP) and Common Terminology Criteria for Adverse Events (CTCAE) v4.03 classification. Deleterious HL was defined as Muenster ≥2b, SIOP ≥2 and CTCAE ≥2. A dose-effect relation was explored for cochlear irradiation dose and HL using logistic regression.
Results: Forty-two HNRMS survivors underwent audiological evaluation. According to Muenster, SIOP and CTCAE classification, 19.0% (n=8), 14.2% (n=6) and 11.9% (n=5) suffered from deleterious HL, respectively. Four survivors had low frequencies HL with normal hearing or milder hearing loss in the higher frequencies. Maximum cochlear radiation dose (D0.1cc) correlated best with HL as opposed to mean or minimum dose. The dose probability curve shows a trend that HL (≥Muenster 2b) occurs in 50% of the ears when receiving a maximum dose of 19.0 GyEQD2 (p=0.075).
Conclusions: HL occurred in up to 19% of survivors of HNRMS depending on ototoxicity grading scale. Four survivors revealed an atypical, but recurrent low frequency HL audiometric signature. More research is needed on the relevance of this specific HL pattern and on the development of radiotherapy-specific HL classification systems. RT dose-effect relation showed a trend but more research is needed. Long-term audiological follow-up is recommended for survivors of HNRMS.

EP228 / #720

Topic: *AS05.h Soft Tissue Sarcomas*

MALIGNANT AND BORDERLINE VASCULAR TUMORS IN CHILDHOOD: A REPORT OF FORTY CASES FROM SINGLE CENTER

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Background and Aims: Malignant and intermediate grade vascular tumors (MIVT) are a rare subtype of soft tissue sarcomas and consist of histologically and clinically heterogeneous group of neoplasm. The objective of this study was to report our institutional experience with VTM over a 45-year period.
Methods: From 1975 to 2021, 336 children with non- rhabdomyosarcoma soft tissue sarcoma (nRMS-STS) were admitted to the Pediatric Oncology Department of Hacettepe University. Of these, 40 children with MIVT were evaluated retrospectively. Patients' age and gender, the tumor's subtypes and location, treatment and survival rates were recorded.
Results: There were 17 males, 23 females with a mean age of 33.5±54.8 (0–192) months. Mean duration of symptoms from onset to diagnosis was 5.3±10.5 (0-56) months. The most common presentation symptoms were mass (42.5%) and skin rash (17.5%). The tumor arises from soft tissue in 45% of cases, skin in 25% of cases. Liver, lymph nodes bone, lung and heart were the other localization. Histopathologically 25 were intermediate tumor including 9 kaposi sarcoma (9 post-transplant, 4 classical, one endemic), 8 hemangioendothelioma, 4 hemangiopericytoma and 4 kaposiform hemangioendothelioma, while 15 were malignant including 12 angiosarcoma and 3 epitheloid hemangioendothelioma. Twenty patients underwent surgery, 4 of them received chemotherapy and 5 received both chemotherapy and radiotherapy. In addition, 8 patients received chemotherapy alone or with steroid and/or interferon and four received both chemotherapy and radiotherapy. One patient with intermediate group died of non-tumor cause. Five-year overall and event free survival in intermediate and were 100% and 27.5% in intermediate group, 43.3% and 26.8% in malignant group.
Conclusions: MIVT was rarely seen in childhood. It constitutes 11.9% of nRMS-STS in our clinics. Intermediate and malignant group constituted 62.5% and %37.5, respectively. Prognosis of malignant VT quite bad. Although no patient died in intermediate VT recurrence rate was high.

EP229 / #166

Topic: *AS05.h Soft Tissue Sarcomas*

OUTCOMES OF CHILDREN TREATED WITH PREOPERATIVE RADIOTHERAPY FOR LOCAL CONTROL IN PEDIATRIC EWING SARCOMA AND RHABDOMYOSARCOMA

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Background and Aims: The optimal local management of pediatric Ewing Sarcoma (ES) and rhabdomyosarcoma (RMS) requires careful multidisciplinary consideration, particularly when the tumour is large or located in a difficult area to address surgically. When radiotherapy (RT) is used in conjunction with surgery, the optimal timing of RT continues to be debated. Preoperative RT may reduce radiation dose and normal tissue exposure but is a less common approach. The study objective was to describe treatment outcomes and complications of children with ES or RMS treated with preoperative RT.
Methods: This was a retrospective chart review of children aged 0-19 years presenting to BC Children's Hospital in Vancouver, Canada with a new diagnosis of ES or RMS from 1998- 2020. Descriptive statistics and Kaplan-Meier method were used.
Results: Of the 169 eligible children, 79 (46.7%) were diagnosed with ES and 90 (53.3%) were diagnosed with RMS. Median follow-up duration was 5.86 years [range, 1.60-13.5]. Median age was 11.0 years [range, 5-15] and 95 (56.2%) were male. The cohort's 5-year overall survival (OS) and progression free survival (PFS) were 65.7% and 60.7%, respectively. Only thirteen children received preoperative RT, all of whom all had ES, and primary tumor locations included pelvis (6), thorax (3), lower extremity (2), and abdomen (2). The 5-year OS and PFS for patients with ES who received preoperative RT compared to postoperative RT (n=14) were 82.5% vs. 85.8% (P=0.898) and 48.9% vs. 78.7% (P=0.143), respectively. Children treated with preoperative RT had a higher rate of surgical complications compared to children treated with postoperative RT (30.7% vs 21.4%, P=0.674).
Conclusions: Preoperative RT did not impact survival outcomes in our institutional cohort of children with ES. There are potential advantages of reducing exposure of normal tissue to high doses of RT, and thus this approach could be considered in the treatment of children with ES.

EP230 / #1515

Topic: *AS05.h Soft Tissue Sarcomas*

NEXT GENERATION SEQUENCING ANALYSIS OF PEDIATRIC SOFT TISSUE SARCOMA REVEALS CLINICAL BENEFIT: MULTICENTER DATA FROM CHINA

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Background and Aims: To uncover the genomic characteristics and study the clinical value of Next Generation Sequencing (NGS) in pediatric soft tissue sarcoma (pSTS), we first report the genomic profiles in Chinese pSTS.
Methods: Tumor tissue, as well as peripheral blood from 210 psts patients, were collected in 11 centers in China. Samples were sequenced in a CLIA/CAP-accredited laboratory with a targeted NGS panel (Onco PanScan™ plus; GenetronHealth.inc) consisting of all exons of 831 cancer-related genes and mRNA of 395 genes. Bioinformatics analysis was conducted using a build-in computational pipeline.
Results: A total of 210 samples consisted of 28 histology types mainly including rhabdomyosarcoma (RMS) (n = 66), Ewing's sarcoma (n = 25), INI1-deficient sarcoma (n = 22), sarcoma with BCOR genetic alterations (n = 15), undifferentiated sarcoma (n = 13), synovial sarcoma (n = 8), and other mesenchymal tumors (n = 74). All patients were with progressed, relapsed, refractory disease, or the diagnosis was difficult, of which 81.0% samples were from initial diagnoses. Genomic analysis revealed frequent alterations in TP53 (11%), EWSR1-FLI1 (10%), BCOR (8%), NTRK fusion (10%), PAX3 fusion (6%), FLI1-EWSR1 (5%), MDM2 (5%), CTNNB1 (4%), NF1 (4%), MYCN (4%) and PIK3CA (4%). BCOR-internal tandem duplication (BCOR-ITD) was detected in 5 patients. In total, we identified 20 germline mutations, with a median tumor mutational burden of 0.47 (0-6.57) /Mb. The proportion of confirmed diagnosis was 56.2%. NGS contributed to a change of diagnosis in 30 patients (14.3%). Druggable alterations were detected in 56.7% of patients. Twenty-three patients received the treatment recommended by genetic testing, four of them with NTRK fusion were recruited in a matched clinical trial that could be evaluated and showed partial remission upon Larotrectinib.
Conclusions: NGS profiling revealed the molecular basis of pediatric soft tissue sarcoma in Chinese population, leading to be useful for diagnosis and clinical management for some patients.

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Topic: *AS05.h Soft Tissue Sarcomas*

COMBINING ONCOLYTIC VIROTHERAPY AND SMALL MOLECULE INHIBITORS: A NEW THERAPEUTIC STRATEGY FOR SOFT TISSUE SARCOMAS

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Background and Aims: The success of standard therapy for high-risk patients is low and new therapeutic concepts are lacking. Oncolytic viruses present new promising strategies, but the monotherapy rarely has the potency to induce complete remission. It was shown before that the addition of Cyclin-Dependent Kinases (CDK) 4/6 inhibitors can increase viral particle formation and cytotoxicity of the virus, while Bromodomain and Extra-Terminal motif (BET) inhibitors promote viral gene expression and production of infectious particles. Therefore, we assess respective combination therapies to boost the efficacy of the YB-1-based oncolytic adenovirus XVir-N-31.
Methods: Here, we study in vitro oncolysis, viral replication, infectious particle formation and antitumor immune responses of XVir-N-31 in combination with inhibitors of CDK 4/6 and BET proteins in clinically achievable concentrations.
Results: We observe high YB-1 expression in all cell lines which can be infected and lysed by the virus. Combination therapy greatly enhances cytotoxicity and the interaction of the components is highly synergistic according to the Chou-Talalay-Test. We show that the combination therapy leads to increased viral replication 24h and 48h after viral infection. In addition, the combination therapy significantly augments infectious particle formation 48h and 72h after viral infection. Our results also suggest an ameliorated antitumor immune response after the combination therapy due to MHC class I upregulation, induction of apoptosis and immunogenic cell death.
Conclusions: Combination therapies of XVir-N-31 and inhibitors of CDK 4/6 and BET proteins are new promising therapeutic approaches for pediatric soft tissue sarcoma in vitro, warranting further evaluation in vivo (phase I clinical trial combining Oncolytic Virotherapy with CDK 4/6 inhibitors in planning).

EP232 / #1600

Topic: *AS05.h Soft Tissue Sarcomas*

SYSTEMATIC REVIEW OF EARLY PHASE TRIALS FOR CHILDREN AND YOUNG PEOPLE WITH RELAPSED AND REFRACTORY RHABDOMYOSARCOMA: THE REFORMS-SR PROJECT

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Background and Aims: Around one-third of children and young people treated for rhabdomyosarcoma (RMS) experience relapsed and/or refractory (R+R) disease. Second line treatment with curative intent may be available but for around 80% this is not successful. Early phase trials explore new and innovative approaches, but are rarely reviewed or synthesised systematically. We systematically reviewed responses in early phase trials of paediatric R+R RMS to inform future research and provide accurate information to families and clinicians making treatment choices in this challenging situation.
Methods: Seven databases and six trial registries were searched in June 2021. All records were screened in duplicate. Eligible studies explored interventions aimed at disease control (curative or palliative) in patients under 18 years old with R+R RMS. Measured outcomes included survival, disease response and adverse events. Studies were limited to those performed after 2000. No language or geographical restrictions were applied. Quality assessment used the Downs and Black checklist. Given the considerable heterogeneity, synthesis was narrative. REFoRMS clinical and parent advisory groups were actively involved in the review. (PROSPERO: CRD42021266254)
Results: 16,965 records were identified. 197 trial registry records of 174 unique studies, and 115 full texts of completed studies (including over 1,100 R+R RMS patients) were included. Study quality was limited by poor and inconsistent reporting. 49 registered trials are currently ongoing, 16 were withdrawn/suspended, and 11 completed but have not reported data. Included studies mostly focus on systemic chemotherapy or targeted therapies with minimal data on local control approaches. Overall response rates across included studies were low. Adverse events vary dependent on intervention.
Conclusions: Improving reporting quality and consistency would facilitate synthesis of early phase studies in R+R RMS. The REFoRMS-SR will be converted into the first living systematic review in children's cancer, providing an up-to-date resource on early phase studies for researchers, clinicians and families.

EP233 / #717

Topic: *AS05.h Soft Tissue Sarcomas*

A SYSTEMATIC REVIEW AND META-ANALYSIS OF THE SIGNS AND SYMPTOMS OF CHILDHOOD SOFT TISSUE SARCOMAS

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Background and Aims: Time to diagnosis (TTD) of childhood soft tissue sarcomas (STS) has a significant independent association with survival. A greater understanding of clinical presentation is crucial to informing interventions to effectively reduce TTD. This study aims to provide an overview of the signs and symptoms observed in patients with childhood STS.
Methods: Studies detailing the signs and symptoms in >10 patients aged <18 years at diagnosis, published between 2010 and 2021, were searched for, without language restrictions. The pooled proportions of 43 signs and symptoms were analysed and ranked by frequency according to age and tumour location.
Results: Among 2,462 patients, the most common signs and symptoms were lump/swelling (38%), pain (6%), cutaneous changes (4%), localised eye swelling (3%), constitutional symptoms (2%), abnormal full blood count (2%), and cranial nerve deficits (2%). The signs and symptoms differed according to location. For head and neck tumours, these were localised eye swelling (20%), lump/swelling (16%), cranial nerve deficits (14%), and/or impaired visual function (6%). For abdomen and pelvic tumours, these were urinary symptoms (24%), abdominal distension/discomfort (22%), genital swelling (16%), pain (11%), constitutional symptoms (9%), vaginal bleeding (7%), change in bowel habit (6%), and/or obstructive jaundice (2%). The most frequent signs and symptoms differed according to age, reflecting an age-related distribution of STS. In patients <5 years, these were lump/swelling (44%), genital swelling (4%), reduced mobility (3%) and/or vaginal bleeding (2%), while consumptive coagulopathy (16%), cutaneous changes (5%), and bleeding/bruising/petechiae (2%) were strongly associated with diagnosis <1 year. Among patients >11 years, the most frequent were lump/swelling (57%), constitutional symptoms (52.4%), pain (28.6%) and/or headaches (19%).
Conclusions: The signs and symptoms of childhood STS differ according to tumour location and by age. Recognition of these age-specific clinical features, alongside a greater insight into their chronological development, is instrumental in developing effective interventions to successfully reduce TTD.

EP234 / #233

Topic: *AS05.h Soft Tissue Sarcomas*

VERY RARE SOFT TISSUE SARCOMAS WITH BCOR, CIC AND YWHAE REARRANGEMENTS IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS: AN EUROPEAN EXPERIENCE.

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Background and Aims: A subset of rare undifferentiated small round cell sarcomas harbor new identified specific molecular abnormalities: CIC-DUX4/other partner, BCOR-CCNB3/other partner, YWHAE fusions or BCOR-ITD (internal tandem duplication). “CIC rearranged” (CIC fused) and “BCOR rearranged” (BCOR fused/ITD/YWHAE) sarcomas are not well described in youths. Treatment and outcome data of pediatric patients with these new rare sarcomas are missing.
Methods: Multi-institutional retrospective analyze of young patients (0-21 years) treated for a “CIC” or “BCOR rearranged” soft tissue sarcoma (STS). Patients’ data from large European centers of Italy, France and the STS registry SoTiSaR were analyzed.
Results: Overall, 45 patients (25 males) had CIC-fused (n=27), BCOR-CCNB3 (n=8), BCOR-ITD (n=7), and YWHAE (n=3) STS. Main primaries were limbs (n=15) and abdomino-pelvic (n=15). Median ages were 14.3 years (ranges: 2.8-20.0) and 8.6 (0.1-19.1) respectively for “CIC” (27 cases) and “BCOR-rearranged” STS (18 cases; p=0.03). IRS stages were I (n=2), II (n=3), III (n=25) and IV (n=15). Overall, 35 patients had large tumors (≥ 5 cm) and 4 nodal involvement. Patients received chemotherapy (n=45), local surgery (n=34) and/or radiotherapy (n=28), with additional high-dose chemotherapy (n=3) or maintenance (n=4). After a median follow-up of 41.9 months (IC95%, 28.1-66.0), 23 patients had a tumor event, 17 patients died. Tumor events occurred after a median delay of 6.5 months (range, 0.5-114), mainly metastatic ± loco-regional (61%). Three year-event free survival (EFS) were 43.5% (95%IC, 27.4-69.2) and 42.6% (95%IC, 22.6-80.1) respectively for CIC and BCOR-STS (P=0.88). 3Y-overall survival were respectively 45.2% (95%IC, 28.0-73.0) and 73.4% (95%IC, 54.1-99.7; P= 0.28). Age, tumor size, and IRS stage do not impact survival (P>0.05), but outcome was superior in patients receiving anthracyclines (P=0.033).
Conclusions: Pediatric patients with these rare entities often present with large tumors and metastatic disease. Overall prognosis is unfavorable, even for small and localized tumors. Anthracyclines-based regimen is important but new treatment options are necessary.

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Topic: *AS05.h Soft Tissue Sarcomas*

EPITHELIOID HEMANGIOENDOTHELIOMA IN CHILDREN: THE EUROPEAN PEDIATRIC SOFT TISSUE SARCOMA STUDY GROUP (EPSSG) EXPERIENCE

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Background and Aims: Epithelioid hemangioendothelioma (EHE) frequently has an indolent presentation despite potential diffuse tumor spread. To better characterize EHE, the European pediatric Soft tissue sarcoma Study Group (EpSSG) analyzed all young patients prospectively registered in treatment protocols.
Methods: Patients with localized EHE were included in the NRSTS-05 study (EUDRACT 2005-001139-31) while metastatic tumors were registered in the academic MTS-2008 study (NCT00379457).
Results: Overall, 13 patients with localized and one with metastatic disease were included which represents 1% of all non-rhabdomyosarcoma cases registered. Sex ratio was 1, and median age 14 years (range, 0.1-19). Primary site was limbs (eight cases), trunk (five cases) and multifocal metastatic (one case). Tumors were smaller than 5 cm in 71% of cases. No patient had regional nodal involvement. IRS groups were group-I seven cases, II two cases, III four cases and IV one case. Local therapy was, initial primary surgery (10 cases) followed by an immediate primary re-resection (five cases). In addition, two patients had delayed surgery (R0, R2). No radiotherapy was delivered. Systemic therapy for localized tumors consisted of interferon (2 cases), vincristine with steroids (1), Temsirolimus (1) and paclitaxel (2 cases). Median follow-up for alive patients was 37 months (range, 6-176). One patient had metastatic relapse and died. The patient with stage IV disease developed tumor progression and received regorafenib, doxorubicine and interferon, and then died for cardiac failure. At the end of follow-up, 12 patients remain alive off therapy (11 in complete remission and one with stable residual 5 years after). Five-year progression free and overall survivals are respectively 82.1% (95%CI: 44.4 – 95.3) and 78.6% (95%CI: 36.1 – 94.4).
Conclusions: EHE is a very rare sarcoma in pediatrics and mainly occurs in adolescents. For localized disease, outcome is favorable. The role of systemic therapy for initially unresectable tumors needs to be further explored.

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Topic: *AS05.h Soft Tissue Sarcomas*

OUTCOMES OF PATIENTS TREATED FOR RHABDOMYOSARCOMA AT BUTARO CANCER CENTER OF EXCELLENCE, RWANDA: 2013-2019.

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Background and Aims: Rhabdomyosarcoma (RMS) is the most common childhood soft tissue sarcoma. Few studies have assessed its treatment outcomes in rural low resource settings. We aimed to describe the characteristics and outcomes of patients with RMS presenting at a rural cancer center in Rwanda.
Methods: A retrospective chart review was performed on all patients with RMS presenting at Butaro Cancer of Excellence (BCCOE) between January 2013 and December 2019. Patients were treated using a pediatric protocol adapted from Intergroup Rhabdomyosarcoma Study (IRS I-V) Group. Patient characteristics and outcomes were reported using descriptive statistics. Event-free survival (EFS) was estimated using the Kaplan-Meier where we considered death, disease progression, loss to follow-up and palliation events.
Results: Thirty-four patients were included in this study. The median age at presentation was 8.9 years (IQR: 3.1-14.8) and 19 patients (55.9%) were female. The head and neck region was the most common primary site of disease: 10 (29.4%) in the orbit. On pre-surgical staging, 22 (64.7%) were categorized as high risk. The most common histologic subtype was embryonal (n=22, 64.7%). Two-thirds of patients underwent surgery (n=23, 67.6%), 8 (34.8%) had uninvolved margins and 10 (43.5%) received radiation. At the end of study period, of those who received planned treatment (n=18), 10 (55.5%) died, 6 (33.3%) were alive. Of the 16 who did not get all planned treatment, 9 (56.3%) died (8 prior to surgery), 1 (6%) was alive. With a median follow-up time of 11.2 months, the one-year EFS was estimated to be 52.1% (95% CI: 34.1-67.3%) while two-year EFS was 21.5% (95%CI: 9.5-36.6).
Conclusions: The study demonstrated success in treating RMS in rural low resource setting with adaptation of the IRSG pediatric protocol although, the EFS is lower compared to reports from elsewhere. Efforts should focus on accessing early care, effective surgery and comprehensive social support.

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Topic: *AS05.h Soft Tissue Sarcomas*

NEUROFIBROMATOSIS TYPE 2: WHAT DO WE DO AND WHAT CAN WE DO?

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Background and Aims: Neurofibromatosis type 2 (NF2) is an AD disorder, occurring in 1/25,000-40,000 live births, relate to multiple sensory and motor disabilities throughout their lives, alongside with development of different types of tumors, seriously affecting their quality of life. To describe NF2 patient's situation, who underwent follow-up during childhood or adolescence in a neuro-oncology service.
Methods: Retrospective analysis of patients under 21 years of age with NF2 treated in the neuro-oncology service of a hospital in Buenos Aires, Argentina in the last 7 years.
Results: Twelve patients with NF2, M:F ratio 3:1. Average age 18 years, median age at the first consultation 18.5 years (8-21), one of the patients had not been previously diagnosed. Eleven patients developed more than 3 different types of tumors: multiple schwannomas including acoustic neuromas (91.6%), peripheral schwannomas (91.6%), meningiomas (66%), medullary ependymomas (58%) and neurofibromas (50%). Seven patients required 3 or more surgical interventions, due to neurosurgical treatments or infectious complications, among others. 55 total admissions. All patients had hearing loss and visual impairments, together with hemiparesis (25%), chronic pain (25%), epilepsy (17%). Half of the patients received more than 5 daily medications (30% indicated by psychiatry). Use of bevacizumab in 25% of patients show a good clinical and audiometric response. Three of 10 evaluable patients presented ECOG score > 2 and Lansky < 50. Follow-up loss: 3 patients, 3 died (20%) and 1 is currently in ICU due to an acute SARS-COV19 infection. It is noteworthy that the older the patients were, the more complication the added.
Conclusions: Multidisciplinary approach is mandatory with initial palliative care management, given the torpid evolution of the disease and its unfailing progression towards progressive disability. We believe that therapeutic accompaniment, psychological and spiritual approach of the patients and their families should be a priority, just as surgical approaches and imaging controls are today.

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Topic: *AS05.h Soft Tissue Sarcomas*

TARGETING THE CELLULAR DEVELOPMENTAL STATE WITH IPATASERTIB AS A NOVEL THERAPEUTIC OPPORTUNITY FOR AGGRESSIVE RHABDOMYOSARCOMA.

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Background and Aims: Pediatric Rhabdomyosarcoma (RMS) is a developmental tumor that affects individuals from birth to young adulthood. Patients with metastatic RMS at diagnosis or with relapse present a dismal prognosis. Previous inconclusive attempts aimed at blocking the AKT/mTOR pathway relied upon the sustained activation of the receptor tyrosine kinase (RTKs) signaling in RMS cells. The most transversal attribute across RMS tumors is the expression of myogenic lineage genes both in fusion-negative (FN) and fusion-positive (FP, PAX3/7-FOXO1 translocations) RMS subtypes. Here, we postulate that therapeutic vulnerabilities in RMS might depend on lineage dictates. The aim of this study is to describe the transcriptional myogenic signature of those RMSs sensitive to the pan-AKT inhibitor Ipatasertib.
Methods: The antitumoral activity of Ipatasertib was evaluated in vivo in patient-derived xenograft (PDX) established at HSJD, including FP-RMS and FN-RMS. NOD/SCID mice subcutaneously implanted received 100mg/kg or 25mg/kg Ipatasertib PO QD for four weeks. Blood and tumor samples were collected after a single dose for pharmacokinetic (PK) analysis. Transcriptomics was accomplished in RMS-PDX, primary cells, and their corresponding RMS patients' biopsies.
Results: Ipatasertib induced more than 50% of tumor volume reduction in 4 out of 8 PDXs evaluated after 10 doses of 100mg/kg. At 25mg/kg dose, Ipatasertib slowed tumor growth in a dose-dependent manner and the PK analysis exhibited an intratumoral Cmax over 11µM in one FN and one FP RMS-PDX. Such concentrations significantly inhibited phospho-S6 and induced PARP cleavage. Functional transcriptomic analysis revealed an enrichment in proliferative pathways mediated by E2F and MYC targets (ES=0.70 and 0.58) paralleled with a depletion in the expression of myogenesis-related genes (ES= -0.32) in most Ipatasertib-sensitive RMS tumors.
Conclusions: Clinically feasible doses demonstrated effectiveness in blocking the growth of PDX-RMS. RMS tumors and RMS-PDXs more sensitive to Ipatasertib displayed transcriptional profiles associated with proliferation and poor myogenic differentiation.

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Topic: *AS05.h Soft Tissue Sarcomas*

THE ONCOGENIC ROLE OF HEDGEHOG PATHWAY CO-RECEPTORS IN RHABDOMYOSARCOMA: EXPANDING KNOWLEDGE TO DISCOVER NEW THERAPEUTIC TARGETS

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Background and Aims: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children. The mortality rate for RMS still remains between 35-40%. A persistent activation of the Hedgehog (Hh) signaling pathway is well established and associated with worse prognosis and less muscle differentiation. Our group has been the first in publishing the important role of Hh Ligands in RMS, proposing an autocrine Hh activation model. The standard pathway activation entails ligand binding to Patched receptor, which allows the activation of Smoothened and the subsequent activation of Gli proteins, the main effectors of the pathway. However, there are other co-receptors (Gas1, CDO and BOC) that are also able to bind with ligands and even seem to be necessary for complete Hh activation.
Methods: Since the role of these co-receptors in RMS has not yet been characterized, we propose their study with the aim of finding new molecular targets and opening up new therapeutic possibilities. First of all, a consistent expression of these co-receptors in RMS tumors was verified, as a previous step to attribute them an oncogenic role. Moreover, we genetically downregulated BOC and CDO expression and studied the underlying molecular and functional consequences of their absence or pharmacollogic inhibition. An animal model is also provided to test the effects of the depletion of CDO.
Results: The results obtained permitted us to rule out an essential oncogenic role of BOC. Conversely, CDO genetic or pharmacologic inhibition caused strong anti-oncogenic effects in vitro as decreased cell proliferation, arrested cell cycle and, finally, cell differentiation and apoptosis induction. A rmarkable on tumor growth was also observed.
Conclusions: In conclusion, we propose the inhibition of CDO as a novel and potent therapeutic target against RMS.

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Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

IMPROVING KNOWLEDGE OF PRIMARY EYECARE WORKERS ON EARLY WARNING SIGNS AND SYMPTOMS OF RETINOBLASTOMA IN NORTHERN GHANA

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Background and Aims: Background Approximately 8000 new cases of retinoblastoma are diagnosed annually around the world with most of them in LMICs. In Ghana, about 65 – 70 children are affected annually based on reports from general ophthalmologists from peripheral eye centres in the country. This paper presents on a strategy for early detection of retinoblastoma in a LMIC with funding from Alliance Mondiale le Contre Cancer (AMCC) through World Child Cancer (WCC). Objectives Build capacity of Primary Eyecare Workers (PEWs) on early warning signs and symptoms of retinoblastoma Assess the knowledge of PEWs on early warning signs and symptoms of retinoblastoma
Methods: Northern, Northeast and Savannah Regions of Ghana were selected, and a simple random method used to select health facilities for the training. PEWs in these facilities were then selected. A structured question was used to assess PEWs before training on Early Warning Signs and Symptom (EWSS) of Retinoblastoma and same tool used post-training to assess knowledge gain. One Trainer of Trainers session was carried out for 10 trainers who later conducted 9 training sessions across the 3 regions for 200 PEWs.
Results: In the downstream training, average minimum score between pre and post-test improved by 17% whilst average maximum score between pre and post-test improved by 7.8% at the end of the training sessions. Results in the pretest showed an average minimum knowledge of 65.4% and this improved to 76.9% average knowledge on retinoblastoma EWSS at the end of the training. Average minimum score during post-test was 76.9% whilst average maximum score post-test was 82.9%.
Conclusions: The downstream training of PEWs has been effective. Similar models will be used for the training of PEWs in other regions in Ghana to improve on early detection, timely and appropriate referral of childhood eye conditions, especially retinoblastoma, for timely and prompt management.

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Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

SUSCEPTIBLE AND PROTECTIVE KILLER CELL IMMUNOGLOBULIN-LIKE RECEPTOR (KIR) POLYMORPHISM IN UNILATERAL, NON-FAMILIAL RETINOBLASTOMA

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Background and Aims: KIR regulates natural killer (NK) cell activity to detect and eliminate tumor cells via interaction with class-I HLA ligands. Both KIR and class-I HLA molecules exhibit extensive polymorphism. Inheritance of certain KIR and HLA combinations is associated with selected malignancies. RB1 inactivation triggers the initiation of retinoblastoma; however additional alterations are required for tumor development. The aim was to explore the protective and susceptible role of KIR/HLA polymorphism in the pathogenesis of retinoblastoma.
Methods: Patients with unilateral, non-familial retinoblastoma were enrolled as cases. Healthy individuals matched for ethnicity were enrolled as controls. KIR genotyping was performed by sequence-specific primer assay. The investigated KIR genes included: inhibitory (2DL1, 2DL2, 2DL3, 2DL4, 2DL5A, 2DL5B), activating (2DS1, 2DS2, 2DS3, 2DS4*FUL, 2DS4*DEL, 2DS5, 3DL1, 3DL2, 3DL3, 3DS1) and pseudogenes (2DP1, 3DP1*FUL, 3DP1*DEL). Both haplotypic and genotypic variations of KIR polymorphism were analyzed. In addition, HLA ligands were investigated by sequence-specific oligonucleotide assay for HLA-A, B, and C locus.
Results: KIR genotyping was performed in 48 cases and 107 controls. The mean age of cases was 2.9±2.2 years (range: 0.25-10). Among the 19 KIR genes, the frequency of KIR2DS4*FUL (p=0.0019) and 2DS5 (p=0.0095) was increased among cases. The distribution of AA and Bx genotypes was similar among cases and controls. The frequency of tel-A/B haplotype was decreased (p=0.0006), and tel-B/B increased in cases (p=0.021). HLA ligands were investigated in 25 cases and 50 controls. The frequency of HLA ligands (C1/C2, Bw4, A3/A11) was similar among cases and controls. However, the KIR/HLA combination frequency for KIR3DS1/HLA-Bw4 was decreased in cases (p=0.006).
Conclusions: It is the first study to report the association of killer cell immunoglobulin-like receptors in retinoblastoma. KIR2DS4*FUL and KIR2DS5 had a susceptible, and KIR3DS1/HLA-BW4 had a protective role in retinoblastoma. The results will aid in exploring the therapeutic potential of NK cell-based therapy for retinoblastoma.

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Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

DECIPHERING THE IMMUNOGENETIC PROFILE OF RETINOBLASTOMA

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Background and Aims: Human leukocyte antigen (HLA) genes, also known as major histocompatibility complex, are highly polymorphic. HLA class 1 genes are present on most human cells and are involved in antigen presentation to the cytotoxic T lymphocyte. The genetic variation of the HLA genes could lead to a heterogeneous immune response which may determine disease susceptibility. There is scarce literature on HLA polymorphism in retinoblastoma. The aim was to explore the potential role of HLA polymorphism as a risk factor for retinoblastoma.
Methods: The study was case-control and performed in a single center to analyze the frequency of HLA class I genes in retinoblastoma. Children on treatment or previously treated for unilateral, non-familial retinoblastoma were enrolled as cases. Healthy children matched for ethnicity were included as controls. The genomic DNA was extracted from blood samples of cases and controls and subjected to HLA class 1 genotyping. HLA typing was performed at intermediate resolution using LAB Type® sequence-specific oligonucleotide Class I kits for HLA A and B locus. HLA typing was carried out using a LUMINEX LABscan 3D instrument. The interpretation was performed using HLA Fusion™ software.
Results: Thirty-six cases and 86 controls were enrolled. The mean age of the cases and controls was 3.3±2.3 years (range: 0.58-10) and 6.9±3.7 years (range: 0.25-12), respectively. The tumor was intraocular in 27 (75%) and extraocular in 9 (25%). The frequency of the HLA-A*24:02 allele was reduced (95% CI 0.13-0.82, OR: 0.33, p-value: 0.0159) in cases as compared to controls. However, on applying Bonferroni correction, the frequency was not significant (corrected p-value: 0.38).
Conclusions: None of the HLA class 1 genes were associated with susceptibility to retinoblastoma. The study of the HLA polymorphism could aid in exploring HLA-dependent therapies, which are mainly cytotoxic T cell-based and include tumor-infiltrating lymphocytes and T cell receptor-engineered T cells.

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Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

RB1 GENE MUTATIONS IN TURKISH PATIENTS WITH RETINOBLASTOMA

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Background and Aims: Retinoblastoma (RB) is the most common intraocular malignancy in children, caused by mutations in the tumor suppressor RB1 gene. The aim of this study is to assess the frequency/type of RB1 gene mutations in a large cohort of Turkish RB cases.
Methods: RB1 gene mutation screening was performed in peripheral blood samples of 219 individuals (122 children with RB/14 family members with RB/83 healthy family members of 47 probands with RB1 mutations) followed in the Istanbul University, Oncology Institute. All 27 exons and close intronic regions of the RB1 gene were sequenced for small deletions and insertions using the Sanger sequencing (2013-2018) or Next Generation Sequencing (2019-2021); large deletions and duplications were investigated both by Multiplex Ligation Probe Amplification (MLPA) and copy number variation (CNV). Correlation with demographic and clinical data were evaluated.
Results: After RB1 mutation screening, mutations were detected in 57/136(41.9%) patients, in 23/84(27.4%)with unilateral, in 30/47(63.8%) bilateral RB, in 3/3 trilateral RB, and1/2 unilateral retinoma. Of these mutations, 45(78.9%) were small genetic rearrangements, 12(21.1%) large genetic rearrangements. Frameshift mutations were found in 11, nonsense in 18, splice error in 11, and missense mutation in 1, synonymous substitution in 2, upstream substitution in 2 patients. Ten novel mutations were found. Three of 83 healthy family members had germline RB1 mutation. The disease was hereditary in 13(22.8%); and de novo(77.2 %) in 44 of the 57 patients with mutations. Infants (p:0.021); bilateral/trilateral RB (p:0.0001); those with light(green-blue) iris color vs dark color (71.4% vs 36.5%. p:0.003) had higher frequency of RB1 gene mutation.
Conclusions: RB1 gene mutation was found in 41.9% of Turkish children with RB, 63.8% of bilateral, 27.4% of unilateral RB. 10 novel mutations of the RB1 gene were found according to the Leiden Open Variation Database and the Human Gene Mutation Database.

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Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

AN IMMUNOHISTOCHEMISTRY PANEL IS A USEFUL TOOL FOR IDENTIFYING RETINOBLASTOMA MOLECULAR SUBTYPES.

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Background and Aims: Two molecular subtypes of retinoblastoma were described by multi-omic analysis and subtype 2 has a higher propensity for metastasis. Since multi-omic analysis is not widely available, we propose an immunohistochemistry panel as a tool to identify both subtypes.
Methods: Two hundred fifty-five consecutive cases from Argentina and Barcelona were evaluated and an enhanced cohort of cases with extraocular relapse was enriched with patients from the remaining centers (n=21). Immunohistochemistry included ARR3, CRX, Ki67 and TFF1 antibodies. TFF1 was selected because its high expression in subtype 2 in transcriptomic analysis and lack of expression in subtype 1. The quick score (QS) value was calculated and subtype 2 was defined when the QS for TFF1 was>45. Validation of the immunohistochemistry panel was performed against multi-omic analysis in 39 cases.
Results: In 94.8% the immunohistochemistry characterization matched the results obtained by multi-omic analysis. Overall, of 276 cases evaluated, 103 (37.3%) were subtype 1, 160 (58%) subtype 2 and 13 (4.7%) were not evaluable because of tumor necrosis. Compared to subtype 1, children with subtype 2 tumors were older at diagnosis (median age 29 vs 14 months; p=0.0003), had more commonly unilateral disease (80.2% vs 68.93%; p=0.006) and presented more frequently high-risk pathology factors (HRPF) (76.25% vs 54.4%; p<0.0001), specifically massive choroid (p=0.0013) and retrolaminar optic nerve invasion (p=0.0354). Enucleated eyes of patients that experienced extraocular relapse (n=32) had a significantly higher TFF1 QS (median=210, range 60 to 300) than those with no extraocular relapse (n=208) (median=67.5, range 0 to 300) (p<0.0001). All metastatic sites studied (n=13) were positive for TFF1
Conclusions: This immunohistochemistry panel is an accessible tool for identifying retinoblastoma molecular subtypes with possible application when access to multi-omics diagnosis is not available. Subtype 2 is associated with HRPFand a higher risk for extraocular relapse.

EP245 / #1910

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

RETINOBLASTOMA (RB) IN SUB-SAHARAN AFRICA: A SINGLE TUMOR PROGRAM TO SUPPORT RB MULTIDISCIPLINARY TEAMS AND IMPROVE CURE RATE IN LINE WITH 2030 WHO OBJECTIVES

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Background and Aims: RB is a rare tumor with a potential high (close to 100%) cure rate when a recognized key role of the ophthalmologist is effective. In collaboration with the RB multidisciplinary team, ophthalmologists are strongly involved in the diagnosis, treatment (enucleation and local ophthalmological conservative procedures) and follow up. We present a RB program implemented since June 2019 with strong involvement of ophthalmologists. This program draws on the experience gained since 2011 with GFAOP and the Bamako team, and published in 2018.
Methods: The objective of this 10 year RB program is to improve cure rate from average of < 20 % to > 70% of expected cases of RB in each country by directly supporting the RB teams, thanks to a Swiss Foundation and Curie Institute. Five main areas are supported through this program: training, equipment (for enucleation and eye salvage), early diagnosis campaigns, improvement of data collection and discussions on challenging cases.
Results: Up to date (3rd year of implementation), a network of 31 RB teams from 22 countries is established with 11 early diagnosis multiyear plan underway. Equipment for eye salvage has been provided in 16 countries and ophtalmologists have been trained in Curie institute or in Bamako. An expert tumor board online meeting is held in regular basis or in demand.
Conclusions: This program represent a unique opportunity to learn about a single childhood cancer intervention in sub-Saharan Africa. Bringing ophthalmologists as key actors seem to be essential.

EP246 / #480

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

HUMAN PAPILLOMAVIRUS IN CERVICAL SMEAR OF MOTHERS OF CHILDREN WITH NON-FAMILIAL, UNILATERAL RETINOBLASTOMA: A CASE-CONTROL STUDY

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Background and Aims: The association between HPV and retinoblastoma is inconsistently reported from 0 to 69%. Interaction between RB1 tumor suppressor and oncoproteins of DNA viruses is described. Inactivation of retinoblastoma protein by HPV 16 and 18, suggests a possible role. We hypothesized maternal HPV to be an etiological factor for retinoblastoma. If so, the frequency of HPV in the cervical smear in mothers of children with retinoblastoma would be higher.
Methods: The case-control, single-center study was conducted during 2016-2020. Patients on treatment or previously treated for unilateral retinoblastoma, born by vaginal delivery, and lacking a family history of retinoblastoma were identified. The mothers of these patients/survivors were enrolled as cases. In addition, mothers whose children did not have retinoblastoma were enrolled as controls. A cervical smear was obtained with a cytobrush from the enrolled mothers and run for polymerase chain reaction for HPV. HPV Genoarray kit was utilized for genotyping and detection of high-risk (16,18,31,33,35,39,45,51,52,53,56,58,59,66,68) and low-risk [6,11,42,43,44,CP8304(81)] HPV subtypes.
Results: During the study period of 56 months, 42 patients/survivors with non-familial, unilateral retinoblastoma, born by vaginal delivery were identified. The mothers of the 42 patients/survivors were enrolled as cases. The controls included 57 women. The cases and controls did not differ in age at marriage (p=0.670), age at conception (p=0.170), or rural/urban locality (p=0.744). However, the cases had a higher socio-economic scale (modified-Kuppuswamy scale: I+II+III: 23.8% vs. 19.2%; p=0.021) and were older (27.4±3.0 vs. 26.1±3.1 years; p=0.047) than controls. High-risk HPV (predominantly 16 and 18) were detected in 9 (21.4%) cases and 14 (24.6%) controls (p=0.72).
Conclusions: The frequency of high-risk HPV in the cervical smears of mothers of children with non-familial retinoblastoma was not different from the mothers whose children lacked retinoblastoma. The hypothesis of maternal transmission of HPV during vaginal delivery to the baby as an etiology for non-familial retinoblastoma was not supported.

EP247 / #2016

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

A GLOBAL ONLINE RETINOBLASTOMA ACADEMY

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Background and Aims: Through a Global Retinoblastoma Need's Assessment, we identified a need for further education that focused on multidisciplinary management. The goal of the Online Retinoblastoma Academy was to provide an educational resource for multidisciplinary teams that focused on effective treatment and management of retinoblastoma while examining the impact of resource limitations.
Methods: The course had eight (8) modules to complete over 10-weeks. Resources were compiled to meet each learning objective. A mixture of video lectures, journal articles, readings, and case examples were used. Knowledge checks and discussion forums in each module ensured learning objectives were being met and provided an opportunity for collaboration. Teams completed project proposals at the end of the course to implement in their own centers.
Results: A total of 285 participants enrolled in the first 10-week course. 122 participants fully completed the course (43%). 38 centers registered which represented 22 different countries and all WHO global regions were represented. There were a wide range of specialties represented including 72 pediatric hematology/oncologists, 56 ophthalmologists, 31 pediatric ophthalmologists, and 25 pathologists. A total of 15 team project proposals were presented.
Conclusions: The academy was useful in creating a collaborative, global space for multidisciplinary teams to expand their knowledge of the treatment and management of children with retinoblastoma. The discussions during the academy initiated the development of the Global Retinoblastoma Advisory Group and the projects that should be addressed.

EP248 / #2019

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

EXTENDING THE REACH: THE IMPACT OF ORBIS CYBERSIGHT OVER ON GLOBAL RETINOBLASTOMA OVER TWO DECADES

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Background and Aims: Orbis is a non-profit organization devoted to blindness prevention and treatment in developing countries. Cybersight, which is an online training and mentorship service for healthcare professionals, provides online training and consultations. Cybersight works to increase capacity of healthcare professionals involved in eye health and health systems by providing live webinars, online courses, and consultations. The goal of Cybersight is to facilitate mentorship and training between healthcare professionals in developing countries by connecting individuals to specialists in developed countries and providing online resources. The telemedicine platform can be used to improve vision and survival outcomes, specifically in children with retinoblastoma.
Methods: Each case on Cybersight is assigned a mentee and a mentor that will work together through telemedicine consultations. The first retinoblastoma case in Cybersight occurred in July 2003. There are 10 mentors who specialize in retinoblastoma that help consult on cases.
Results: There have been 978 retinoblastoma cases via Cybersight since 2003. This averages to 4.4 retinoblastoma cases per month from 2003 to present. The consultations vary in length based on case. Consults have occurred with individuals from 31 countries. 35.7% of cases are from Guatemala and 32.1% of cases are from Jordan.
Conclusions: Cybersight provides a unique platform that allows for global communication and education. This resource is seen to produce impactful training opportunities through consultations, specifically in Guatemala, Jordan, and other developing countries.

EP249 / #2025

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

FORMATION OF A GLOBAL RETINOBLASTOMA ADVISORY GROUP

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Background and Aims: Participants in the Global Retinoblastoma Academy recognized similar challenges to caring for children with retinoblastoma across regions and sought further opportunities to connect and learn from one another while developing shared strategies for addressing gaps in care. The Global Retinoblastoma Advisory Group was organized to partner in the development, support, and implementation of strategic regional initiatives for improving the survival and vision outcomes of children with retinoblastoma.
Methods: Applications for membership were sent via email to academy participants (22 countries) and network members and were posted in the Retinoblastoma Global online community. The basic group structure was determined, with each organization allowed two full members and unlimited alternate members. The group nominated and elected a separate standing committee and global community co-chair, set term limits and proposed meeting schedule and initial project priorities.
Results: The Global Retinoblastoma Advisory Group has 77 members and 13 alternate members, including representation from pediatric oncology, ocular oncology, nursing and research, with plans to expand to include parent/patient representation and other social support members. The standing committee, representing all seven World Health Organization regions, has 15 members and will begin meeting in January 2022 to develop working groups for prioritized projects. The top areas of concern include early detection/education for diagnosis, abandonment of care, and acquisition of resources for ophthalmologic interventions.
Conclusions: Engagement of global stakeholders in developing and implementing initiatives to improve outcomes for children with retinoblastoma is essential.

EP250 / #1980

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

MULTIMODALITY TREATMENT INCLUDING INTRA-ARTERIAL CHEMOTHERAPY FOR DISSEMINATED RETINOBLASTOMA

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Background and Aims: Extraocular retinoblastoma remains difficult to cure with current treatments as high dose chemotherapy and radiotherapy leading to long-term sequelae. CNS involvement can't be cured with conventional treatment. Hence, innovative strategies aiming to increase survival rates with lower sequelae are needed.
Methods: Retrospective report from 3 institutions using a similar pilot approach for treating patients with overt orbital retinoblastoma with (stage IVb) and without CNS involvement (stage III).For stage III patients, the aim was avoiding orbital radiotherapy with intensive neoadjuvant chemotherapy and limited surgery followed by 3 cycles of intra-arterial chemotherapy(IAC) with topotecan-melphalan as local consolidation. For stage IV patients, intensive chemotherapy was used alternating with intra-arterial chemotherapy with high dose carboplatin,melphalan and topotecan and also added intrathecal chemotherapy with topotecan.
Results: From 2016 to 2021, 8 patients were treated (4 stage III; 4 stage IVb) (6 unilateral,2 bilateral).All 4 stage III patients received systemic chemotherapy and a median of 3 cycles of IAC and achieved complete remission for a median of 34 months (range 15 to 56) without orbital radiotherapy. Stage IVb patients (n=4), 3/4 patients had chiasmatic involvement and suprasellar lesions and 2/4 with leptomeningeal dissemination. Two of 3 patients with chiasmatic involvement achieved complete remission and one of them is disease-free for 25 months. One case abandoned therapy in complete remission and was lost to follow-up. The 2 leptomeningeal dissemination patients showed progressive disease and died within 2/3 months. Genomic profiling of 3 patients of stage IV showed MYCN gains/amplifications and BCOR mutations in 1.
Conclusions: In this small pilot study,a multimodal approach introducing intra-arterial chemotherapy at higher doses, in association with high dose chemotherapy seems promising for stage III retinoblastoma avoiding radiotherapy. Three cases with stage IVb and chiasmatic disease, which is not curable with conventional therapy, achieved complete remission but patients with leptomeningeal dissemination may need a different approach

EP251 / #416

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

TOPOTECAN IN REFRACTORY/RECURRENT INTRAOCULAR RETINOBLASTOMA: OUTCOME AND RESPONSE PREDICTIVE FACTORS

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Background and Aims: Topotecan showed efficacy in retinoblastoma, we report our experience with systemic topotecan in pediatric patients with refractory/recurrent retinoblastoma, and we looked for predictive factors for response.
Methods: This is a retrospective review for patients with refractory/recurrent retinoblastoma treated at King Hussein Cancer Center between Jun2007 and Jul2019 using topotecan. Topotecan was given as a second line chemotherapy for refractory/recurrent disease. Patients and disease characteristics, response to therapy, eye salvage and survival were depicted.
Results: Twenty-six patients, 37 eyes with refractory/recurrent retinoblastoma were reviewed, all received topotecan as second line chemotherapy (3 cycles in 31 eyes, and 4-6 cycles in 6). The median age at diagnosis was 6 months (range, 1-17). Seventeen (38%) were males and 22 (85%) had bilateral disease. Nineteen eyes (51%) were IIRC group D, 12 (32%) group C, and six were group B. Twenty-two eye (59%) had seeds (sub-retinal in 13 and vitreous in 9). Toptecan was given for residual active disease in 20 eyes (54%) and recurrent in 17 (46%). Nineteen eyes (51%) showed excellent response, five (14%) had partial-response, and 13 (35%) showed progression or no response. Twenty-three eyes (62%) were salvaged (no radiation or enucleation), 10 (27%) underwent enucleation, and five eyes received radiation. On multivariate analysis advance IIRC group, presence of seeds and vitreous seeds subtype were predictive factors for poor response to topotecan (p values were 0.038, 0.035, 0.024 respectively). At last follow up 2 patients died of metastatic disease and there was no active disease in 24.
Conclusions: Our findings suggest that topotecan is active as second line chemotherapy in refractory/recurrent retinoblastoma. Advance stage, presence of seeds in general and vitreous seeds in specific are predictors of poor response to topotecan.

EP252 / #602

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

THE ASSOCIATION BETWEEN MATERNAL NUTRIENT INTAKE DURING PREGNANCY AND THE RISK OF SPORADIC UNILATERAL RETINOBLASTOMA

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Background and Aims: Previous studies have associated maternal diet with the risk of retinoblastoma (RB) in offspring. However, most studies have examined the role of food groups rather than nutrients or supplements. The aim of the current study is to investigate the association between maternal nutrient intake during pregnancy and the risk of sporadic unilateral retinoblastoma in offspring.
Methods: A food frequency questionnaire which was modified for use in a phone interview was completed from 187 sporadic unilateral RB cases 155 controls. Supplement use during pregnancy was also asked. We performed logistic regression to estimate the odds ratios (ORs) and the 95% confidence intervals (CIs).
Results: In the unadjusted model, retinol activity equivalents (RAE) and vitamin D had significant inverse associations with the risk of sporadic unilateral RB (OR: 0.76, 95% CI: 0.62—0.94, p-value: 0.01; OR: 0.82, 95% CI: 0.70—0.96, p-value: 0.01). When adjusted for child's birth year, maternal race, maternal education, and total calorie intake, RAE and vitamin D significantly reduced the risk of sporadic unilateral RB (OR: 0.67, 95% CI: 0.51—0.88, p-value: 0.004; OR: 0.78, 95% CI: 0.65—0.94, p-value: 0.009). In the fully adjusted model, RAE and vitamin D continued to show an inverse association with the risk of sporadic unilateral RB (OR: 0.68, 95% CI: 0.51—0.91, p-value: 0.01; OR: 0.76, 95% CI: 0.61—0.93, p-value: 0.008).
Conclusions: Our study replicated the previous findings that vitamins A and D may reduce the risk of cancer development. However, the mechanisms that maternal nutrient intake influences the risk of sporadic unilateral RB in offspring still need to be investigated. Further study is warranted to enhance the understandings of the role of maternal nutrient intake in the etiology of sporadic unilateral RB.

EP253 / #168

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

RETINOBLASTOMA IN TURKEY: CLINICAL PRESENTATION AND OUTCOME 1983-2017

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Background and Aims: Retinoblastoma is the most common primary intraocular malignancy of childhood with different survival rates across the world. The aim of this study is to evaluate the clinical characteristics, treatment approach and outcome (patient survival, eye survival) in retinoblastoma cases treated in the Istanbul University, Istanbul Medical Faculty, Department of Ophtalmology and Oncology Institute, Division of Pediatric Oncology, Turkey between 1983 and 2017.
Methods: The medical records of 297 patients diagnosed with retinoblastoma between 1983-2017 were evaluated retrospectively. Information on gender, laterality, age at diagnosis, presenting signs, spread of tumor, treatment modality, survival rate, and family history were evaluated.
Results: Of 297 patients (403 eyes), 191 (64.3%) had unilateral and 106 (35.7%) had bilateral involvement. The mean age at diagnosis was 21.29 ±18,68 (1-216) months for all patients, 25.15 ±18.7 (1-216) for unilateral and 14.39 ±16.5 (1-180) months for bilateral cases. The most common presenting symptoms were leukocoria (54.2%) and strabismus (36.3%). Family history of retinoblastoma was present in 25 (8.4%) patients. Most of the eyes were ICRB group E (40.9%), and D (20.3%). Systemic chemotherapy, local ophtalmic treatment, intraarterial chemotherapy, radiotherapy, enucleation was used according to patient's clinical findings and treatment era. Enucleation was done primarily in 58.1% of unilateral, 21.6% of bilateral cases. The frequency of enucleation decreased from 64.9% to 32.5% after 2011. The 5-year eye protection rate was 100% in Group A, 88.4% in Group B, 66.7% in Group C, 55.4% in Group D and 4.5% in group E. The 5-year overall survival of all patients was 97.2 %.
Conclusions: The implementation of up-to-date treatments and multidisciplinary team approach has resulted in high survival and high eye salvage rates in our cohort. The intraocular advanced stage at presentation is still high which emphasizes the importance of public and healthcare staff education. The enucleation rate has significantly decreased over the years.

EP254 / #1737

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

EVALUATION AND ADAPTATION OF THE FACE-Q | CRANIOFACIAL PATIENT-REPORTED OUTCOME MEASURE FOR RETINOBLASTOMA

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Background and Aims: FACE-Q is a patient-reported outcome measure (PROM) that evaluates appearance-based and associated psychosocial outcomes of craniofacial surgery. This study aimed to assess the content validity of FACE-Q among retinoblastoma (RB) survivors and parents/guardians.
Methods: This was a cross-sectional qualitative study. Eligible participants included RB survivors ≥8 years old and parents/guardians of survivors <8 years old. Seven participants per type were recruited, as suggested by COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) guidelines. In cognitive debriefing interviews, participants reviewed FACE-Q sections measuring eye-related, appearance-based, and psychosocial outcomes, and provided feedback on their relevance, comprehensiveness, and comprehensibility relative to the RB experience. Interviews were transcribed, coded, and analyzed via constant comparative analysis to confirm or disprove the above factors, and identify new concepts and suggestions for modifications. The number of participants offering each specific feedback or suggestion was tallied; a minimum of three instances was required to modify the FACE-Q. Applicable FACE-Q questions were adapted and subsequently re-evaluated by survivors and parents/guardians for corroboration purposes.
Results: Participants deemed all FACE-Q sections reviewed as relevant to the RB experience. To improve the relevance and comprehensiveness of the measure, participants suggested additional concepts, including those related to prosthetic eyes and visual impairment. While survivors suggested adding the concept of interpersonal relationships, parents indicated that survivors <8 years old are not yet self-conscious or concerned about their appearance. To improve comprehensibility, a common consensus among participants was that certain terms, and existing response options and instructions should be altered to enhance clarity and appropriateness in relation to RB, visual impairment, laterality, and enucleation.
Conclusions: The study results suggest key modifications to FACE-Q to make it comprehensible, comprehensive, and relevant to RB survivors. In future, the adapted FACE-Q will undergo field testing for assessment of validity and reliability.

EP255 / #1225

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

ADJUVANT CHEMOTHERAPY FOR CHILDREN WITH ADVERSE HISTOLOGY POST-ENUCLEATION FOR RETINOBLASTOMA – A SINGLE CENTRE EXPERIENCE OVER 20 YEARS

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Background and Aims: Up to 25% of children with retinoblastoma undergoing primary enucleation have evidence of adverse histopathological features indicating the need for adjuvant chemotherapy. We aimed to review the experience at a single large national referral centre over a 20-year period to correlate pathological features with clinical outcome.
Methods: Patients diagnosed with retinoblastoma undergoing primary enucleation were identified from the Retinoblastoma Registry at a single institution which covers the UK and Ireland (population 46 million) and receives 60% of national referrals. Data were reviewed to identify which adverse histopathological feature required adjuvant chemotherapy. This was correlated with patient outcome.
Results: Between 1/1/2002 and 31/12/2021, 83 patients had adverse histological features of whom 62 (75%) were treated with 4 cycles of vincristine, etoposide and carboplatin (VEC). The patients excluded from 4 cycles of VEC included those with very high-risk disease (tumour at the cut-end of the optic nerve, scleral involvement) or those treated on an individualised regimen at the physician's discretion. The event free and overall survival for the group receiving 4 cycles of VEC was 98.4% at a medium time of 13 years from end of treatment. The indication for adjuvant chemotherapy was massive choroidal invasion in 22 (35.5%), post-laminar optic nerve involvement in 15 (24.2%), multiple adverse factors in 15 (24.2%), anterior chamber involvement in 6 (9.7%) and unknown in 4 (6.4%). The only patient who relapsed and died had massive choroidal invasion with tumour found in the peripapillary space which has been reported to increase the risk of central nervous system relapse.
Conclusions: Our data indicate that 4 cycles of adjuvant VEC are safe and effective for patients with adverse histopathological features following primary enucleation for retinoblastoma. Intensification of treatment may be warranted in patients with peripapillary involvement. Some patients may have treatment safely de-escalated further.

EP256 / #601

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

A SINGLE-BLINDED, RANDOMIZED CONTROLLED TRIAL OF STANDARD VERSUS HIGHER-DOSE CARBOPLATIN-BASED INTRAVENOUS CHEMOTHERAPY FOR GROUP D AND E RETINOBLASTOMA

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Background and Aims: There is limited access to intra-arterial chemotherapy for retinoblastoma in low- and middle-income countries. The aim was to compare the efficacy of standard versus higher-dose carboplatin-based intravenous chemotherapy in patients with Group D and E retinoblastoma.
Methods: The single-center, single-blinded, randomized study was conducted during 2019-2021. Patients with newly diagnosed Group D or E retinoblastoma were randomised to receive vincristine, etoposide, and higher-dose carboplatin (<36 months: 28 mg/kg; ≥36 months: 840 mg/m2) or standard-dose carboplatin (<36 months: 18.6 mg/kg; ≥36 months: 560 mg/m2) chemotherapy. The eyes were evaluated by examination under anesthesia and ultrasonography at diagnosis and following 3-cycles of chemotherapy. Group E eyes with poor likelihood of globe and vision salvage were excluded.
Results: Thirty-two eyes of 29 patients were enrolled: 17 Group D and 15 Group E eyes. Baseline demographic and tumor characteristics were similar in the two arms. Among the group D eyes (higher-dose: 6; standard-dose: 11), the response of the tumor to chemotherapy pertaining to regression pattern (p=1.00), reduction in tumor-size (diameter: p=0.78; height: p=1.00), subretinal fluid (p=1.00), subretinal seeds (p=0.69) and vitreous seeds (p=0.69) was comparable between the two arms. The globe-salvage (higher-dose: 100% vs. standard-dose: 81.8%; p=0.52) and salvage of meaningful vision (higher-dose: 60% vs. standard-dose: 81.8%; p=0.24) were comparable as well. Among the group E eyes (higher-dose: 7; standard-dose: 8), the response of tumor pertaining to regression pattern (p=1.00), reduction in tumor-size (diameter: p=0.48; height: p=0.89), subretinal fluid (p=0.64), subretinal seeds (p=1.00) and vitreous seeds (p=1.00) was comparable between the two arms. The globe-salvage (higher-dose: 57.1% vs. standard-dose: 12.5%; p=0.12) and salvage of meaningful vision (higher-dose: 42.9% vs. standard-dose: 12.5%; p=0.28) were non-significantly higher in the higher-dose arm. No excess treatment-related toxicity was observed in the higher-dose arm.
Conclusions: Higher-dose carboplatin-based intravenous chemotherapy did not improve globe or vision salvage in group D or E retinoblastoma.

EP257 / #1404

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

«INVISIBLE» RETINOBLASTOMA: SMALL PRIMARY TUMORS AND CONTINUED TUMOR GROWTH AFTER TREATMENT REVEALED BY OPTICAL COHERENCE TOMOGRAPHY

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Background and Aims: Background. Retinoblastoma is a malignant tumor in children whose diagnostic algorithm includes morphometric research. OCT allows to reveal visible tumors, but its informative in diagnosis of «invisible» retinoblastoma requires further study. Aim. To reveal diagnostic symptoms of «invisible» small primary retinoblastoma and continued tumor growth after treatment by OCT.
Methods: . The analysis of changes of the retina, revealed by OCT at 61 children with retinoblastoma at different stage of treatment with research of 108 tumors (primary small retinoblastoma - 24, new «invisible» focus after chemotherapy-5, residual tumour after local treatment by methods of brachytherapy and transpupillary thermotherapy – 34, chorioretinal scar - 36, «invisible» continued tumor growth - 9) was carried out.
Results: . OCT-symptoms of 24 primary retinoblastoma: homogeneous tumor in inner retinal layers, hyperreflectivity of tumour tissue with (18) or without (9) «shadow» effect, equal choroidal profile. There were no symptoms by Ret Cam and echography, but new «invisible» small retinoblastoma tumors after chemotherapy were carried out by OCT (5). The chorioretinal scar after treatment (36) - flat bright highreflective stripe replacing all retinal layers. Residual tumours (36) - elevation, homogeneity of structure and thickening of tomographical scan, hyperreflectivity of tumor tissue with «shadow» effect, equal choroidal profile; on periphery - bright flat highreflective retina were diagnosed. There were no symptoms by Ret Cam and echography, but flat hyperreflective tumor tissue between inner and external retinal layers were revealed by OCT (9).
Conclusions: Conclusion. The OCT allows to reveal changes in a retina and to diagnose «invisible» small primary retinoblastoma and continued tumor growth after treatment that is necessary for definition of further tactics of treatment.

EP258 / #1738

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

RETINOBLASTOMA RESEARCH IN AFRICA: A SCOPING REVIEW

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Background and Aims: Achieving equity in retinoblastoma care represents a global challenge. In Africa, where anticipated and reported mortality and morbidity of retinoblastoma is higher than in the rest of the world, the generation of quality local evidence is crucial to inform clinical retinoblastoma guidelines. This scoping review aims to identify the breadth and depth of retinoblastoma research conducted in Africa.
Methods: A systematic search of Embase, Medline, Scopus, Web of Science, and African Journals OnLine (AJOL) databases was conducted to identify peer-reviewed English-language publications published between 1/January/2003 and 28/March/2022. Medical subject headings ‘retinoblastoma’, ‘Africa’, and individual African country names were used as search terms. Articles were included if they were original research articles on retinoblastoma and conducted in any African country. Articles were excluded if retinoblastoma or Africa was not the primary study focus or location, respectively. Data collected included journal and citation information, authors affiliations and study type/site/summary.
Results: The search yielded 1,094 citations. After deduplication and initial title and abstract screening, 119 full-text articles were assessed for eligibility, and 59 were included in the review. The countries represented included Egypt, Kenya, Nigeria, South Africa, Uganda, Tanzania, Ethiopia, Morocco, Zimbabwe, Democratic Republic of the Congo, Ghana, Mali, Sudan, Tunisia, Côte d'Ivoire, Republic of the Congo, Senegal, and Zambia. Thirty-nine percent involved authors from outside Africa. All articles identified solely through AJOL had entirely African authorship. All studies were primary research studies (81% observational, 19% experimental). Experimental studies represented clinical (55%), applied basic (36%), and implementation (9%) research, and more often involved investigators from outside Africa (55%) than did observational studies (35%).
Conclusions: The results indicate a need for more support of African-led experimental research to build the local evidence for retinoblastoma management. AJOL revealed African-led studies not included in Western databases, suggesting a publication bias preventing dissemination of African science.

EP259 / #1119

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

THE ROLE OF INSURANCE AND THE MEDICAL CARE SYSTEM IN DIAGNOSTIC DELAY IN RETINOBLASTOMA

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Background and Aims: Diagnostic delay is considered to worsen clinical outcomes in retinoblastoma, though contributors to delay are multifactorial and poorly understood. Our work in a public hospital in Mexico showed delay impacts severity and survival in bilateral (but not unilateral) disease. Other studies suggest healthcare access may impact disease presentation but this has not been directly examined. We examined whether diagnostic delay differed between children diagnosed in two adjacent children's hospitals in Mexico City: one public (HIM) and one in the employer based social security system (IMSS).
Methods: Within the EpiRbMx study, consenting parents of 445 Mexican children with retinoblastoma were interviewed at diagnosis about initial symptoms and household demographic characteristics. Diagnostic delay or lagtime was defined as the time (months) between parents noting symptoms and diagnosis. Treatment hospital, sociodemographic, and clinical factors were examined as predictors for lagtime in multivariable linear regression.
Results: Clinical presentation, including disease laterality, age at diagnosis, and presenting symptoms did not differ by hospital, however mean lag time for HIM children(N=347) was 6.5 (range 0.0 to 66) months, compared with 4.6 (0.0–24) months for IMSS children (N=96), p=0.006 . Lag time was associated with strabismus (p=.009) but not other clinical presentations. Predictors of diagnostic delay differed between the two healthcare systems: paved streets and commuting time predicted a nearly 2 fold increase in lagtime at the IMSS but were not strong predictors of lagtime in the HIM. Importantly the two hospitals serve different populations as HIM and IMSS cases differed by socioeconomic factors and living conditions during pregnancy, including household income, maternal education and presence of home toilet (p<008, all).
Conclusions: Our results show healthcare systems impact diagnostic delay. Additionally, sociodemographic predictors of lag time also differ by healthcare system, suggesting that strategies to decrease delays in diagnosis need to be tailored to care settings.

EP260 / #810

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

MATHEMATICAL MODEL FOR MULTISTABILITY DETECTION IN RETINOBLASTOMA CONSIDERING GENETIC AND EPIGENETIC LANDSCAPE

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Background and Aims: Retinoblastoma is a childhood cancer of the retina which has a striking specificity. Alterations on the molecular circuitry for RB1 gene develop tumors in the eye in patients before the age of five. Tumorigenesis is the result of a complex interaction of intrinsic and extrinsic processes of cells which promote genomic instability, resistance to apoptosis, reprogramming and reorganization. Likewise, the levels of gene expression, loss of function of suppressor genes, microRNAs and non-coding RNAs in the cellular microenvironment as external factors are decisive to quantify the form in which a tumor grows and spreads.
Methods: The number of pathways on which these alterations occur are crucial to understand the origin and prognosis of the tumorigenesis. Thus, we propose a mathematical model for genetic and epigenetic landscape, in which the pathways between RB1 and E2F genes play a crucial role in the tumorigenesis. The model considers different interactions among the genes RB1, E2F, CDK2, P53, AKT and SYK, microRNAs miR-373 and miR-34, and non-coding RNAs miR17~92 and let-7 family, that regulate the cell cycle and the progression of RB.
Results: Our model provides a quantitative analysis for the negative feedback regulation RB1/E2F and demonstrates that the system presents a bistability for some range of feedback strengths, relate with the interactions.
Conclusions: In conclusion, the model provides a way for controlling the signaling pathways and the evolution of Retinoblastoma using the bistability of the system, that can be using as alternative strategies for cancer therapy.

EP261 / #1874

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

OPHTHALMIC ARTERY CHEMOSURGERY IMPROVES TOPOTECAN ORBITAL EXPOSURE COMPARED TO SYSTEMIC INFUSION IN PIGS

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Background and Aims: Orbital extension in retinoblastoma is frequent in developing countries and is a major cause of death. Despite multimodal therapy with high-dose chemotherapy, enucleation, and radiotherapy has improved life salvage, treatment is still associated with high toxicity and mortality. An alternative treatment strategy to improve clinical response would be to enhance chemotherapy delivery to the orbit and minimize systemic exposure. We aimed to study and compare the orbital exposure of chemotherapy after ophthalmic artery chemosurgery (OAC) and intravenous (i.v) infusion in an animal model.
Methods: Three landrace pigs received topotecan (4mg) 30-minutes OAC and samples were serially obtained from a peripheral artery and from a microdialysis probe inserted into the lateral rectus of the infused eye as a surrogate of the orbital vascular irrigation. The animal was recovered and after a wash-out period, the animals received an i.v infusion of 4mg of topotecan; plasma and samples from the non-treated lateral rectus muscle were obtained and all were quantified by HPLC.
Results: Median muscle exposure calculated as the area under the concentration versus time profile for total topotecan attained after OAC was significantly higher than after i.v infusion (139906 ng*h/ml (range: 116202-332938) and 758 ng*h/ml (range: 523-2616), respectively, $p<0.05$). The median (range) muscle-to-plasma exposure ratio was 37 (22-49) and 0.13 (0.11-0.51) after OAC and i.v, respectively. The median (range) ratio between topotecan exposure attained after OAC to i.v in the muscle was 222.3 (69.6-439.4) but systemic exposure remained comparable with a median (range) ratio for drug exposure in plasma of 1.05 (0.95-1.20).
Conclusions: OAC resulted in significantly higher topotecan exposure in the lateral rectus muscle of the pig compared to that attained after i.v while similar systemic exposure was attained after both routes of drug delivery. Patients with orbital retinoblastoma may benefit from OAC.

EP262 / #1265

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

CAN BONE MARROW EXAMINATION BE SKIPPED IN CHILDREN WITH LOW STAGE RETINOBLASTOMA?

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Background and Aims: To see the prevalence of bone marrow metastases in children with retinoblastoma presenting to our hospital and if bone marrow examinations be skipped in those with intra-ocular, low group disease.
Methods: Retrospective review of 164 patients with retinoblastoma registered at Shaukat Khanum Memorial Cancer Hospital from January, 2017 to December, 2018. Data fields included demographics, initial presenting symptoms, duration of symptoms, laterality, local group as per EUA, MRI findings, overall stage, metastatic sites, treatment modalities used, disease and patient status at 1 and 2 years follow up. Quantitative variables were analyzed using descriptive statistics.
Results: A total of 164 patient charts were reviewed. Eight patients could not complete their workup, so were excluded. Of 156 patients, male to female ratio was 1. Median age at presentation was 24 months. Family history of retinoblastoma was found in 16% patients. Major initial symptom was leucoria in 70% patients followed by squint in 11%. Median duration of symptoms was 3 months (range 1 week – 4 years). Bilateral disease was found in 30% (46) children. Majority patients presented with advanced disease. There were 42% (66) patients with group D eyes, 30% (46) with group E eyes and 10% (16) with localized extraocular spread at presentation. Distant metastases were seen in 9% (14) patients. Globe was salvaged in 33% (52) patients only while 66% (104) patients underwent enucleation at some point during their treatment. Of 156 patients reviewed, bone marrow involvement by retinoblastoma was seen in 3.8% (n=6). All these patients had either group E eyes or local extraocular spread.
Conclusions: If findings of MRI and EUA are combined for retinoblastoma patients, children with group D eyes can be spared of performing routine bone marrow examination;saving money, time and avoiding morbidity.

EP263 / #867

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

HYDROGEL IMPLANTS FOR TRANS-SCLERAL DELIVERY OF TOPOTECAN INTO EYE BULB – PROOF OF CONCEPT ON ANIMAL MODEL

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Background and Aims: Retinoblastoma (Rb) treatment with intra-arterial and intra-vitreal application of topotecan and melphalan is widely used for therapy of Rb. The aim of our study was to develop a relatively non-invasive system that delivers a cytotoxic drug by diffusion according to concentration gradient to a vitreous of an eye bulb.
Methods: Lens-shaped bilayered hydrogel implants loaded with topotecan (TPT) were developed for trans-scleral diffusion of TPT into an eye bulb. The implants were tested on a rabbit animal model.
Results: The implant is composed of inner poly(2-hydroxyethyl methacrylate) (pHEMA) layer – thickness 1.25±0.02mm - loaded with TPT and outer poly(2-ethoxyethyl methacrylate) (pEOEMA) layer -thickness 0.78±0.1mm - that TPT does not absorb and is impermeable for TPT; pEOEMA is a shield for surrounding tissues. pHEMA and pEOEMA without TPT are non-toxic for tissues confirmed in-vitro on cell lines and by chorioallantoic membrane assay. TPT-loaded pHEMA in-vitro is cytotoxic against Y79 Rb cell line (100% cytotoxicity until 6th round of repeated fresh cell culture). In-vitro release of TPT from pHEMA has two-phases (50% of TPT is released in first 24hours, subsequent in 13 days). In an animal rabbit in-vivo experiments, the lens-shaped TPT-pHEMA/pEOEMA implants were successfully implanted to the posterior segment of the eye bulb with minimal macroscopic and microscopic toxicity. To increase trans-scleral diffusion of TPT, transconjunctival cryotherapy was used. Median vitreous total TPT exposures (AUC) were 455.6 ng.h/ml, median plasma AUC were 50.3 ng.h/mL, plasma exposure accounts 11-12% of vitreous exposure.
Conclusions: The pilot study confirms the ability of the bilayered hydrogel implant to deliver TPT into the eye-bulb in an adequate concentration and minimal toxicity. Supported by MH CZ – RVO, UH Motol 00064203, GA UK 907019, AV21 Strategy (Czech Academy of Sciences)

EP264 / #503

Topic: *AS05 SIOP Scientific programme / AS05.i Retinoblastoma*

GERMLINE ALTERATIONS IN HEREDITARY RETINOBLASTOMA SURVIVORS WITH SUBSEQUENT MALIGNANT NEOPLASMS

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Background and Aims: Subsequent malignancies (SMNs) in hereditary retinoblastoma (RB) survivors have been broadly documented in the literature. However, it is unclear if germline genetic alterations, other than mutations in RB1, play a role in the development of SNMs in this population
Methods: Whole exome sequencing (WES) was performed on DNA extracted from peripheral blood from 5 RB survivors who developed SMNs, using SureSelect Clinical ResearchExome v2 followed by next generation sequencing. Variant calling and interpretation was done using open-source tools (GATK Haplotype Caller, CPSR) and manual curation. Genetic profile was correlated with clinicopathological characteristics, type of SMNs and treatment exposure.
Results: We analyzed five hereditary RB survivors with history of a SMN (renal cell carcinoma, sebaceous cell carcinoma, osteosarcoma, alveolar rhabdomyosarcoma and leiomyosarcoma). All subsequent neoplasms occurred in the irradiated field except for the renal cell carcinoma. Aside from pathogenic variants in RB1 in all patients, we did not identify any other recurrent pathogenic germline gene variants. After an exhaustive search that included genes associated with DNA repair and cancer predisposition genes, we identified 10 shared variants of unknown significance and one likely pathogenic variant in the gene ASAH2. None of them were apparently associated with the SMN's phenotype. In addition, a heterozygous nonsense variant in the XPC gene was detected in one patient that developed a sebaceous cell carcinoma.
Conclusions: We speculate that the loss of one functional allele of XPC in one patient could have affected the repair of the DNA damaged by radiotherapy exposure and might have played a role in the development of a SMN. Other than that, there is no sufficient evidence from this cohort to associate additional germline mutations to the development of SMNs. The exposure to carcinogenic treatments such as radiotherapy in a RB1-mutated genetic background may be the main responsible for the development of SMNs.

EP265 / #422

Topic: *AS05.j Liver Tumours*

COMPARATIVE MOLECULAR STUDY BETWEEN PEDIATRIC HEPATOCELLULAR CARCINOMA AND HEPATOBLASTOMA

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Background and Aims: The main pediatric liver tumors are hepatoblastoma (HB) and pediatric hepatocellular carcinoma (HCC). Whilst HB appears at early ages, HCC is mainly diagnosed in adolescents and it is usually associated to underlying metabolic diseases. HCN-NOS (Hepatocellular malignant neoplasm) is a recent entity with histopathological features of HB and HCC. Due to the rarity of the disease (<1 case/million children), the biology of HCC and their similarity with HB has been poorly explored. To characterize pediatric HCC at the genomic, transcriptomic and epigenomic level and to perform a comparative study with HB and HCN-NOS.
Methods: We performed a genomic (SNP-array), epigenomic (EPIC/850k) and transcriptomic (HTA2.0array) studies on 8 HCC and compared them with already published omics data of 31 HB, 2 HCN-NOS and 19 non-tumor liver (NT) samples (Carrillo-Reixach et al, JHepatol, 2020). The results obtained were validated in an independent series of 21 HCC, 56 HB, 7 HCN-NOS and 8 NTs using QUAlu and Nanostring techniques for assessing DNA methylation and gene expression.
Results: We identified CTNNB1 gene mutations in 73%, 50% and 36% of HB, HCN-NOS and HCC, respectively. Promoter-TERT mutations were found in HCN-NOS (22%) and HCC (8%) but not in HB. All except one of the FL-HCC cases with frozen samples had DNAJB1:PRKACA fusion-transcript; the only case without this fusion, had a deletion in the exon2 in PRKCA. The genome of HCC had higher number of chromosomal losses than HB ($p < 0.0001$). HCC was characterized by a CpG-island hypermethylation. Two different imprinting regions at 14q32 (DLK1/DIO3) and 15q11.2 (SNORD115/116) were upregulated in HB and HCC. Finally, we identified SPINK1 gene (Serine-peptidase-inhibitor, kazal-type-1) as overexpressed gene in HCC that was strongly associated with prognosis of patients with liver cancer in training (Log-Rank=0.008) and validation sets (Log-rank=0.012).
Conclusions: We identified molecular differences between pediatric HCC and HB and a common prognostic factor.

EP266 / #1754

Topic: *AS05.j Liver Tumours*

DELAYED PRESENTATION, ADVANCED AND METASTATIC DISEASE ARE ASSOCIATED WITH POOR OUTCOMES IN PRIMARY PEDIATRIC LIVER TUMOR-HEPATOBLASTOMA- STUDY FROM TERTIARY CARE HOSPITAL IN PAKISTAN

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Background and Aims: Primary hepatic tumors are rare entity; Hepatoblastoma is the most common childhood liver tumor. Over the years the overall survival of hepatoblastoma has increased from 35% to 90%.Risk stratified treatment protocols have been proposed over the years with the intention of reduced therapy for lower risk patients compared to intensified treatment for higher risk patients. In our study we aim to determine the risk factors in children diagnosed with hepatoblastoma and its effects on outcomes.
Methods: A retrospective study from June 2007 till January 2021 was carried out at Shaukat Khanum Memorial Cancer Hospital and Research Centre-Pakistan.
Results: Total 56 patients diagnosed with hepatoblastoma presented with mean age of 26.2 months (SD ± 21.1 months). Out of them 42 (75%) were males whereas 14 (25%) were females. The common presenting feature was abdominal distension present in 23 patients (41.1%). High risk disease was most seen in our cohort, present in 28 patients (50%) followed by standard risk disease present in 15 patients (26.8%). Surgical resection was offered to only 53.8% patients whereas in 32.1% disease was unresectable. At the end of treatment, complete remission was seen among 17 patients (30.4%), disease progression in 11 patients (19.6%). Death as first event was seen in 16 patients (28.6%). Patients with advanced disease had poor prognosis (p value 0.002). Significant number of patients (17.9%) with high risk and very-high risk disease abandoned the therapy. The 4-year overall survival seen was 48.5% whereas event free survival was 30%.
Conclusions: Advanced disease is commonly seen in low-middle income countries due to delayed presentation resulting in poor outcomes, although free treatment is offered there is still high number of abandonment seen among our patients. Nationwide campaign is needed to increase awareness regarding early detection of hepatoblastoma.

EP267 / #351

Topic: *AS05.j Liver Tumours*

STANDARD-RISK HEPATOBLASTOMA: RESULTS OF CISPLATIN MONOTHERAPY IN THE EXTENDED GROUP OF RUSSIAN PATIENTS

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Background and Aims: Risk-adapted therapy is the standard of care for hepatoblastoma (HB). The aim of this study was to analyses the efficacy of cisplatin monotherapy in a large population of Russian patients with standard-risk HB.
Methods: For the period 02.2012 - 12.2019 (95 months) 60 patients with standard-risk HB were treated within the framework of the cooperation of two large volume centers. The SIOPEL criteria were used for stratification into risk groups. Throughout the study period, standard-risk patients received therapy according to the SIOPEL-3 SR protocol, including cisplatin monotherapy (Perilongo G, 2009). Survival was assessed by the Kaplan-Meier method. For the purposes of this study, overall survival (OS), event-free survival (EFS), where any change in chemotherapy regimen towards its escalation were considered as an additional event, and progression-free survival (PFS) were calculated. The survival analysis was carried out on 15.01.2021.
Results: 54/60 (90%) patients were treated with cisplatin monotherapy and included in the final analysis. Median age at diagnosis was 11.3 months (range 0.0-87.7). Male:female ratio - 0.86:1. Distribution by PRETEXT stages: I - 14 (25.9%), II - 30 (55.6%), III - 10 (18.5%) patients. The median alpha-fetoprotein level at the time of diagnosis was 162979 ng/ml (range 129 - 2000000). Modification of therapy was required in 3/54 patients. Median follow-up was 47.1 months (range 2–99). Among 54 patients 52 (96.3%) are alive, 2 (3.7%) patients died (1/2 - complications of surgical treatment). Relapses/progressions were noted in 4/54 (7.4%) patients, one of whom died due to disease progression. 3-year OS was 98.1% (95% CI 94.6-100), EFS - 85.1% (95% CI 75.5-94.6), PFS - 90.5% (95% CI 82.5-98.4).
Conclusions: Our data are consistent with the original studies of the SIOPEL group and convincingly confirm the effectiveness of cisplatin monotherapy in patients with HB of the standard risk group in the Russian Federation.

EP268 / #580

Topic: *AS05.j Liver Tumours*

HEPATOBLASTOMA: SERVICES AVAILABLE ACROSS PEDIATRIC ONCOLOGY EAST & MEDITERRANEAN (POEM GROUP) COUNTRIES

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Background and Aims: Access to complete care in oncology is essential for good outcomes. This analysis evaluated the challenges in management of hepatoblastoma in the POEM group countries.
Methods: A Microsoft survey was sent three times to 96 centers in 25 countries, and responses were analyzed.
Results: Twenty-nine respondents from 27 institutions across 15 countries participated. Fourteen centers (48%) diagnosed ≤ 3 hepatoblastoma cases /year, while 7 centers (24%) diagnosed 15-30 patients /year. Alfa-fetoprotein testing was available at all centers, turnaround time being ≤3 days in 22 (76%). Imaging modalities (CT and/or MRI) were available in all, and 28/29 centers employed the PRETEXT staging. Fourteen centers (48%) performed a diagnostic biopsy in >90% of cases, while 10 (34%) reported a biopsy in ≤50%. Thirteen centers (45%) estimated ≤25 % cases and 5 (18%) reported 50-75% present with metastatic disease. Twenty-one centers had in-house surgery, 9 reported availabilities in the same city, and 1 in multiple locations. Surgery was performed by pediatric surgeons in 18 centers, onco-surgeons in 9, and general surgeons in 4. Four centers (14%) had access to liver transplant. Only 35% reported >90% of surgeries occurring on time, with lack of theatre or need for transplant being the main reasons for delay. Ten centers (34%) reported that >90% of surgeries resulted in complete excision with negative margins, whereas 11/29 (38%) reported ≤75% of surgeries resulting in negative margins. One fifth of centers reported requiring a second opinion for histopathology. Neoadjuvant chemotherapy was used by all. One third of respondents reported a delay in therapy in >90% patients, due to cytopenia or lack of beds.
Conclusions: This analysis provides an overview of the limitations in multidisciplinary treatment of hepatoblastoma in the POEM countries. Results will be used to enhance network collaborations to improve care, and to identify barriers for surgical availability and timeliness of care.

EP269 / #301

Topic: *AS05 SIOP Scientific programme / AS05.k Germ Cell Tumours*

GUIDELINE-CONGRUENT CARE IS ASSOCIATED WITH INCREASED SURVIVAL AMONG ADOLECENTS AND YOUNG ADULTS WITH PRIMARY MEDIASTINAL GERM CELL TUMORS: A POPULATION-BASE STUDY

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Background and Aims: Most prognostic factors and outcomes for primary mediastinal germ cell tumors (PMGCT) in adolescents and young adults (AYAs, 15–39 years) are obtained from single institutions or clinical trials with limited sample size. We aimed to assess, at the population-level, the impact of the delivery of guideline-congruent care (GCC), treating physician specialty, and location of care on survival among AYAs with PMGCT.
Methods: We used data from the California Cancer Registry (CCR) to ascertain all AYAs diagnosed with a PMGCT from 2004 to 2018, and to identify detailed treatment information from the CCR text-fields. GCC, defined based on the National Comprehensive Cancer Network and Children Oncology Group (COG) guidelines, includes chemotherapy alone (BEP: bleomycin, etoposide and cisplatin) or chemotherapy plus surgery. Multivariable Cox proportional regression was used to examine the associations between all-cause survival and GCC, location of care (COG/NCI-Designated Cancer Center versus other centers) and treating physician specialty, adjusting for sociodemographic and clinical factors. Results are presented as hazard ratios (HR) and corresponding 95% confidence intervals (CI).
Results: Of 300 patients, 56% were of Hispanic race/ethnicity, 42% had late-stage disease (III/IV), 55% were treated by adult Hematologists/Oncologists, 27% received all their care at COG/NCI-designated cancer centers, and 50% received GCC. The most common histology type was seminoma (40%). At five years after diagnosis, 189 (63%) patients were alive. AYAs with non-seminomas and late-stage disease were about 3-times more likely to die than those with seminoma tumors or earlier (I/II) stage disease (HR=3.14, CI 1.88–5.24 and HR= 2.60, CI 1.72–3.93, respectively). GCC (versus non-GCC) was associated with improved survival (HR=0.66, CI 0.44–0.99). We found no differences in survival by treating physician specialty, location of care or sociodemographic factors.
Conclusions: GCC was independently associated with improved survival, underscoring the importance of following clinical practice guidelines when caring for the high-risk population of AYAs with PMGCT.

EP270 / #1731

Topic: *AS05 SIOP Scientific programme / AS05.k Germ Cell Tumours*

GERM CELL TUMORS: INTRACRANIAL GONADAL, AND EXTRACRANIAL-EXTRAGONADAL

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Background and Aims: To present the long-term experience and outcome of patients with Germ cell tumors(GCTs) of a single Pediatric Hematology-Oncology center.
Methods: We analyzed 83 patients with GCTs(34/83 boys) with median age 8.2 years(range, 6 days-16 years) diagnosed and treated in our Department from 1977 to 2020.
Results: GCT were gonadal in 58/83, intracranial 7/83, extracranial-extragonadal 16/83 and 2/83 unspecified.Of 58 gonadal cases, 57/58 were GCTs and 1/58 gonadoblastoma, 24 mature teratomas, 17 immature teratomas, 7 yolk sac tumors, 4 dysgerminomas, 2 embryonal carcinomas and 3 mixed GCT tumors.One patient developed testicular embryonal carcinoma as a second malignancy after Burkitt lymphoma. 56/58 patients underwent total surgical excision and 16/58 received platinum-etoposide based chemotherapy.Disease-free and overall survival were 88% and 100% in patients with primary testicular disease and 90% and 94% respectively, in patients with ovarian cancer.Two patients with metastatic ovarian tumor histology died due to disease progression. Seven patients presented with intracranial GCT;3 immature teratomas(1 with yolk sac component), 4 germinomas. Three patients underwent complete surgical excision and four biopsy only.All patients underwent platinum-based chemotherapy, 1/7 received 2 autologous transplantations for teratoma, 4/7 additional radiotherapy. Two patients relapsed, and one died. Sixteen patients presented with extracranial-extragonadal GCT localized in:abdomen N=5, mediastinum N=3, sacrococcygeal region N=6, heart N=1, vagina N=1.Histologically:8 mature teratoma, 1 immature teratoma, 6 patients had yolk sac tumor, and 1 yolk sac/immature teratoma. Three patinets were metastatic(lungs/liver/vagina). Fourteen patients underwent complete surgical excision, and three biopsy only. Six patients received platinum-etoposide based chemotherapy. One patient died due to disease, and one patient developed a second malignancy.
Conclusions: GCTs present in children with heterogeneous histology and localization. Metastatic character is associated with increased disease mortality and is more common in patients with extragonadal-extracranial localization. Beyond surgery, allocation of watchful waiting and chemoradiation as well as chemo intensification in selected patients is determinant for outcomes.

EP271 / #294

Topic: *AS05 SIOP Scientific programme / AS05.k Germ Cell Tumours*

RETROSPECTIVE STUDY ON STAGE IV EXTRACRANIAL GERM CELL TUMORS IN JAPAN: A REPORT FROM THE GERM CELL TUMOR COMMITTEE IN JAPAN CHILDREN'S CANCER STUDY GROUP

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Background and Aims: While stage IV germ cell tumors have shown particularly poor prognosis, little consolidated information has been available given its rarity. Therefore, the Germ Cell Tumor Committee of the Japan Children's Cancer Study Group (JCCG) planned a retrospective survey to understand the actual situation in Japan.
Methods: A retrospective survey from January 1, 2000 to December 31, 2019 among patients under 20 years of age upon diagnosis was planned to ascertain the actual status of stage IV germ cell tumors based on the classification of the Children Oncology Group staging in Japan.
Results: Data were obtained from 50 cases across 31 institutes, among whom 30 and 20 were males and females, respectively. The median age at diagnosis was 4.0 years (0.6–18.8), with 19 cases at the age of ≥11 years and 31 cases at the age of <11 years. As for surgical treatment, 36 patients underwent only biopsy upon initial diagnosis, eight patients underwent aggressive resection, and six patients did not undergo surgery, including biopsy, and received chemotherapy based on tumor markers alone. The most common pathological diagnosis was yolk sac tumor with 32 cases. All patients received chemotherapy, and 40 underwent second-look surgery, including five of the six patients who did not undergo biopsy prior to chemotherapy. The 5-year overall survival was 64.3% (48.8%–76.2%), whereas the 5-year event-free survival was 63.4% (47.2%–75.8%). Patients younger and older than 11 years had a 5-year overall survival of 77.6% (56.4%–89.4%) and 42.1% (20.4%–62.5%), respectively, with only the age of ≥11 years being an independent prognostic factor ($p = 0.003$).
Conclusions: In pediatric patients with extracranial germ cell tumors, the age of ≥11 years was an independent poor prognostic factor. Age should be considered separately to select the optimal treatment.

EP272 / #1549

Topic: *AS05 SIOP Scientific programme / AS05.k Germ Cell Tumours*

EPIDEMIOLOGY & OUTCOMES OF PEDIATRIC EXTRACRANIAL GERM CELL TUMOR FROM A TERTIARY CARE HOSPITAL IN NORTH INDIA

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Background and Aims: Germ cell tumors(GCT) constitute only 3.5% of childhood malignancies but have excellent outcomes with surgery and chemotherapy as mainstay of treatment. We share our experience with pediatric extracranial GCT in a Lower-Middle Income Country(LMIC).
Methods: Electronic medical record of children upto 15 years of age registered in our unit from June 1st2018 through October 31st2021 and diagnosed with extracranial GCT was reviewed. Data pertaining to clinical characteristics, tumor markers, imaging, management and follow-up was retrieved. Cases were risk stratified as per COG criteria into low risk(LR), intermediate risk(IR) and high risk(HR) groups.
Results: Fifty-seven patients with extracranial GCT were registered during the study period of which 46 patients with de novo GCT were analysed (11 operated patients outside with presenting with recurrence were excluded) with median age 5.5 years(Range-0.5-15 years) and male:female ratio 0.64:1. Two-third cases were gonadal GCTs (63.04%; 21-Ovarian, 8-Testicular) while 36.95% were extragonadal (8-sacrococcygeal, 3-gastric, 2-mediastinal, 2-retroperitoneal, 1-parotid and 1-gluteal). Thirty-five(76.08%) patients had malignant GCT(MGCT) with 24 yolk sac tumors, 9 mixed GCT, 1 dysgerminoma and 1 choriocarcinoma, while 11(23.91%) had mature/immature teratoma. With a median follow-up of 15 months, the 1-year event free survival(EFS) and overall survival(OS) for MGCT was 76.4% and 89% respectively. Ten events seen in our cohort included 4 relapses, 4 treatment refusal/abandonment(TRA) and 2 deaths. For LR, IR and HR groups, the 1-year EFS was 100%, 83.7% and 62.5%(p=0.28) with 1-year OS being 100%, 93.7% and 80.2%(p=0.24) respectively. On univariate and multivariate analysis, age, baseline AFP, risk group, chemotherapy backbone (PEb vs JEb) and degree of resection did not significantly impact survival of MGCTs.
Conclusions: Our data shows satisfactory outcomes in pediatric GCT in LMIC setting with standard therapy, though longer follow-up is needed to determine final survival and late-effects of treatment. Measures to curb high TRA rate of 8.6% can further improve outcomes.

EP273 / #1756

Topic: *AS05 SIOP Scientific programme / AS05.k Germ Cell Tumours*

ANALYSIS OF SURVIVAL AND LATE EFFECTS OF PATIENTS TREATED FOR CHILDHOOD VAGINAL MALIGNANT GERM CELL TUMOR

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Background and Aims: Vaginal malignant germ cell tumors (GCT) are rare GCTs occuring in children <2years-old. The question of local treatment is crucial to control disease but can lead to late effects.
Methods: We included children treated for vaginal GCT in French TGM95 and TGM2013 studies or referred to Gustave Roussy in first-line during the inter-study period. Patients were classified as standard-risk (SR: localized disease and AFP<10000ng/ml) or high-risk (HiR: metastatic and/or AFP>10000ng/ml) and were treated with 3-5 VBP (vinblastine-bleomycine-cisplatin) or 4-6 VIP (etoposide-ifosfamide-cisplatin) courses, respectively. Conservative surgery (partial vaginectomy) and/or brachytherapy were used for local treatment in cases of post-chemotherapy residue.
Results: Fourteen patients were included (median age =12 months, range=6-20). Six of them (43%) were classified as HiR (AFP>10000ng/ml: n=4; lung metastases: n=2). After first-line chemotherapy, one patient (SR-group) did not achieve AFP normalization, leading to secondary VIP, whereas both metastatic patients had lung metastases cleared by chemotherapy. A vaginal post-chemotherapy residue (median size=8mm, range=1-24) was observed in 13/14 patients (8SR/5HiR), treated by complete resection in 9/13 (6SR/3HiR) with viable malignant cells in 3/9 (2SR/1HiR), incomplete microscopic resection with viable malignant cells completed by brachytherapy in 2/13 (2SR), and by brachytherapy only in 2/13 (2HiR, including 1 with residual viable cells on post-chemotherapy biopsy). Among the 5 patients with viable disease (4SR/1HiR), 4 patients (3SR/1HiR) received 2 adjuvant chemotherapy courses (VIP or Bleomycin-Carboplatin-Doxorubicin). One patient relapsed (SR) just after surgery (no residual cells) and was treated with 4 VIP and brachytherapy. At last news (median follow-up=4.6years, range=0.5-16), all patients remained in complete remission. Regarding long-term toxicity, 5 patients had vaginal sequelae with synechiae and/or stenosis (including 4 after brachytherapy).
Conclusions: Childhood vaginal GCTs carry very favorable prognosis with risk-adapted chemotherapy and local treatment, to remove post-chemotherapy residue, preferably with conservative surgery to minimize local late effects. Adjuvant chemotherapy remains to evaluate.

EP274 / #788

Topic: *AS05 SIOP Scientific programme / AS05.k Germ Cell Tumours*

PRESENCE OF SOMATIC MUTATIONS WITHIN MTOR, KIT, ATM, KRAS AND PIK3CA IN PEDIATRIC PATIENTS WITH GERM CELL TUMORS

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Background and Aims: Background and aims Germ cell tumors (GCTs) are a rare group of neoplasms that affect about 3.5% of pediatric patients. GCTs are benign or malignant neoplasms occurring in gonadal and extragonadal sites. Unlike to many other cancers, GCTs have a relatively low mutational burden including embryonic epigenetic state, copy number alterations (CNAs), and single nucleotide variant (SNV) or somatic insertion/deletion. Moreover, there is a lack of information about molecular alterations in pediatric GCTs. Therefore, the aim of this study was to perform a genomic profile by whole-exome sequencing (WES) of pediatric GCTs.
Methods: We performed the WES using Illumina paired-end sequencing strategy of 16 cases and respective matched normal, including ten ovarian, five testicular, and one mediastinal. Data analysis was performed as follows: Mutect, Pindel, and Mutsig for SNVs/Indels; HMMcopy, Nexus Copy Number and Gistic for CNAs; and Signal (Cosmic v3) for mutational signatures.
Results: The analyses of Single Base Substitution Signatures showed SBS39 and SBS22 in 68.75% and 12.5% of samples, respectively. Among the common genes involved in GCTs pathogenesis, we found CNAs on chromosomes 4, 7, 8, 10, 12, 21, 22, with gain of KRAS, CCND2, CDKN1B, ETV6, KDM5A, RAD52, RECQL, PIK3C2G, CRKL genes, and loss of KIT and PTEN genes. Somatic mutations of NYAP2 and RHBDF2 genes were identified in 25% of patients, in addition to MTOR (19%), KIT (12%), ATM (12%), KRAS (6%) and PIK3CA (6%) genes. Two patients presented concomitant MTOR and KIT missense mutations, both with ovarian tumor, which one was dysgerminoma and the other one mixed GCTs, comprising 60% choriocarcinoma and 40% dysgerminoma.
Conclusions: MTOR, KIT, ATM, KRAS, PIK3CA alterations are consistently described, suggesting that these are the main driver genes of pediatric GCTs. Further cohort studies are needed to elucidate these findings and to improve clinical management, leading to better therapeutic alternatives.

EP275 / #1954

Topic: *AS05 SIOP Scientific programme / AS05.k Germ Cell Tumours*

THE IMPACT OF PEI (CISPLATININ, ETOPOSIDE AND IFOSFAMIDE) USED FOR CHILDHOOD HR (HIGH RISK STAGE IV) GERM CELL TUMOR. THE BRAZILIAN STUDY GROUP EXPERIENCE.

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Background and Aims: The Brazilian Group started January 2009 the 2nd protocol and January 2008 the 3rd; both have used PEI for HR group. Good Rosponders received 4 PEI (99 protocol) and 5 PEI (2008 protocol) (same total dose for etoposide and ifosfamide and platinum changed from 420 mg/m^2 to 600 mg/m^2).The poor responders have received 2 complementary cycle of PEI (GCT-99) or new agents 3 PEI + 3 TIP (GCT-2008).
Methods: From 163 S IV eligible pts, 98 were treated with GCT-99 and 65 with GCT-2008. Testicular 69, Ovary 42, Sacrococcygeal 27, Mediastinal 11, retroperitoneum 8 and others 6; from 99 prot 60 pts received 4 cycles PEI, 38/6 cy PEI, from 2008 prot 50/5 cy PEI and 15/3PEI+3TIP, 64 YST, 5 IT, 7 Germinomas, 20 other malignant, 67 mixed tumors. Metastasis were 21 liver alone, 53 lung alone, 8 lymph node, 81 combination(including bone, brain).According to Age 70 <11 years, 34 (11-14 y) and 59 >15 y. Relapsed 32 pts (11 liver/and/or lung, 11 primary site, 4 lymp node, 6 others). BMT were performed for 20 pts (6 refractory/or in progression, 12 after relapsed and 2 as consolidation 1st remission).
Results: 10 yearsOS for the 163 pts was 72.0%; age 0-11 ys the 10y OS-75.1, 11-14y, 73.4% and >15y 67.4% (ns). Testicular 10y OS 73.4%, ovary 78.4, sacroc 77.6% and others 52.8 % (ns); prot 99-4 PEI 10yOS was 69.7%, 6 PEI 75.7%, Prot 2008 5 PEI 77.5% and 3 PEI+3TIP 59.3% (ns); metastasis at diag 10y OS for lung alone 75.4%, liver alone 71.4%, lymp node 75.0% and combination 70.0 (ns). For the patients who received BMT the 5 and 10y OS was 50.0%.
Conclusions: HR group patients do well but this is applicable in the context of further refinements in risk approaches to therapy. Challenges remain in our approaches to high risk disease

EP276 / #236

Topic: *AS05 SIOP Scientific programme / AS05.k Germ Cell Tumours*

SECOND MALIGNANCIES IN CHILDREN, ADOLESCENTS, AND YOUNG ADULTS WITH EXTRACRANIAL GERM CELL TUMORS: A REPORT FROM THE MALIGNANT GERM CELL TUMOR INTERNATIONAL CONSORTIUM

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Background and Aims: While men with testicular cancer have a two-fold increase in second malignant neoplasms (SMNs), the risk of SMNs in children and adolescents with extracranial malignant germ cell tumors (GCTs) is not fully quantified. The Malignant Germ Cell Tumor International Consortium (MaGIC) dataset includes 1,798 patients from 14 clinical trials from 5 countries. SMNs were identified using the MaGIC dataset.
Methods: We analyzed the cumulative incidence of SMNs in children with GCT within the MaGIC dataset. Patients managed with chemotherapy within trials which reported the date and diagnosis of SMN, were analyzed.
Results: A total of 917 patients from seven GCT clinical trials were included (INT-0097 [n=300], INT-0106 [n=121], P9749 [n=26], AGCT01P1 [n=19], AGCT0132 [n=211], TGM95 [n=179], GCIII [n=61]). Six hundred and three patients were female (65.8%). Primary tumor site included ovary (38.4%), testes (21.2%), sacrum/coccyx (21.0%), mediastinum (8.5%), retroperitoneum (5.8%), and other (5.1%). Metastases at diagnosis were noted in 231 patients (25.2%). The median follow-up was 66 months. SMNs were identified in 11 patients with a median time to SMN of 17 months (range 3–94 months). SMNs included acute myeloid leukemia/myelodysplastic syndrome (MDS) in 6 patients; solid tumors in 6 patients. At least 3 of the SMNs likely represent malignant transformations of teratoma. One patient had 2 SMNs (MDS and squamous cell carcinoma). The 5-year cumulative incidence of SMNs was calculated according to cooperative group (Children’s Oncology Group (1.1%), France (0.6%), United Kingdom (0%); p-value=0.61), patient sex (female (0.7%), male (1.3%); p-value=0.51), tumor site (ovary (0.9%), testes (1.0%), other (0.8%); p-value=0.90), and metastases at diagnosis (no (0.8%), yes (1.3%); p-value=0.49).
Conclusions: The risk for SMNs is not significantly elevated in this cohort, however long-term follow up of children with GCTs is warranted. Differentiating between treatment-related secondary malignancy, second malignancy, and somatic malignant transformation of the original GCT, a unique aspect of GCT, remains critical.

EP277 / #1150

Topic: *AS05 SIOP Scientific programme / AS05.k Germ Cell Tumours*

EVALUATION OF TUMOR GROWTH OF GERM CELL TUMORS IN XENOGRAFT MODEL

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Background and Aims: Background and aims: Despite the success with cisplatin treatment in germ cell tumors (GCTs), a small but significant number of patients will relapse. Several studies have been carried out to overcome cisplatin resistance with the use of other chemotherapeutic agents, in order to have a significant impact on the survival of these patients. An intensively used in vivo model for chemotherapy tests are the xenograft models, which can be generated through the tumor cell lines. Therefore, the development of in vivo models in GCTs is extremely important. In this study we have established the xenograft model derived from GCTs cell lines.
Methods: For this propose, $1x10^6$ of NTERA-2 and JEG-3 were diluted in HBSS and matrigel (1/1). They were injected subcutaneously into the right flank of athymic male mouse (Mus musculus), and the animals were observed and weighed weekly. Tumor volume was calculated using the following formula: $d \times D^2 \times 0.5$. Tumors were removed and stained with hematoxylin and eosin (H&E) and analyzed by pathology department.
Results: NTERA-2 tumors started to grow on the 22nd day after inoculation. The time from the beginning of growth to tumor excision ranged from 23 to 40 days. The volume of tumors ranged from 1,871 to 2,476 mm^3. JEG-3 tumors started to grow between the 11th and 20th day after inoculation. With the exception of one animal, whose growth was extremely rapid, the time from the beginning of growth to tumor excision ranged from 5 to 9 days. In animals, the tumors had a purplish color and a hemorrhagic appearance. The volume of removed tumors ranged from 990 to 4,694 mm^3.
Conclusions: NTERA-2 and JEG-3 cell lines were able to form tumors in mice model, which could be useful not only in basic research but also in the clinical setting.

EP278 / #1557

Topic: *AS05 SIOP Scientific programme / AS05.k Germ Cell Tumours*

PEDIATRIC TERATOMAS: A REVIEW OF THE BRAZILIAN COHORT

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Background and Aims: Teratomas are the most common histological subtype of germ cell tumors (GCT) of childhood, classified as mature or immature, may arise in the gonads or extragonadals. Mature teratomas (MT) are benign cystic solid tumors and contain well-differentiated tissues representative of all three germ cell layers. Immature teratomas (IT) contain neuroectodermal or blastematous tissue, classified by a system introduced by Norris, modified by Gonzales ± Crussi. Brazilian patients with extracranial GCTs began to be included in a single database in 1991 and to date there are 4 therapy protocols. Children with mature teratoma are treated only with surgical resection, however, children with immature teratoma with hematogenous metastasis receive postoperative chemotherapy.
Methods: This study describes the pediatric population with mature teratomas and Brazilian pediatric clinical trials (CT99 and GCT2008). Analyzes for patients aged 0 to 21 years with a diagnosis of teratoma were included. GCTs mixed with associated teratoma were excluded from the analysis.
Results: 414 patients were included among all teratomas, 76% were female. Seventy percent were TM (290), with 49.3% ovarian, 11% testicular, 20% sacrococcygeal and 36.7% other locations. All of them were considered localized disease and 96% were treated with total surgical resection, no patient received chemotherapy and 99% are alive and disease-free. Only 3 patients had recurrence at the primary site. Among the 124 ITs, 41.9% ovarian, 11.3% testicular, 27% sacrococcygeal and 25% from other locations (63.6% from the head and neck). Eighty percent received surgery alone as treatment, while 13.7% patients (stage IV) received postoperative chemotherapy. Twelve patients had recurrence and 87.1% are alive and disease-free.
Conclusions: This analysis shows an overview of the presentation of teratomas in children and adolescents in the Brazilian cohort, with the challenge of disseminating knowledge of the behavior of these tumors, as well as their treatment.

EP279 / #1340

Topic: *AS05 SIOP Scientific programme / AS05.k Germ Cell Tumours*

TREATMENT OUTCOMES OF ADOLESCENTS WITH EXTRA-CRANIAL GERM CELL TUMOR RECEIVING CISPLATIN VS CARBOPLATIN BASED CHEMOTHERAPY-A RETROSPECTIVE REVIEW

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Background and Aims: To compare outcomes using cisplatin or carboplatin-based chemotherapy in adolescent extracranial germ cell tumor (GCT)
Methods: A retrospective analysis of 75 patients with GCT aged 11 years to 17 years 364 days, recruited at Shaukat Khanum Memorial cancer Hospital, from January 2008 to December 2016. Data fields included site, histopathology, stage, risk groups, baseline AFP, β-HCG levels, metastatic sites and chemotherapy regimen give n. Data analysis involved quantitative analysis, mean and median calculations, event free survival (EFS) and overall survival (OS) calculations using Kaplan Meier curves.
Results: Sevent-five adolescent patients were recruited. Male: female ratio was 1:2. Alpha fetoprotein was raised in 56% (42) patients but level above 10,000 was seen in 21%(n=16) patients. Beta HCG was raised in 21% (n=16). Eighty-one percent had gonadal primaries (n=61; 46 ovarian, 15 testicular). Advanced stage was seen in 80% while 55% had high risk disease. Seminomatous GCTs were found in 1/3rd patients. Sixty-five patients received chemotherapy (JEB: 44%, BEP: 49%, JEV: 3%, VeIP:3.1%). 5-year EFS and OS of whole cohort were 62% and 75% respectively. 5-year EFS and OS of those receiving carboplatin vs cisplatin were 80% vs 53% (p= 0.01) and 86% vs 67% (p= 0.16) respectively. 5-year EFS and OS of ovarian, testicular and extragonadal GCTs were 73% vs 53% vs 36% (p: 0.01) and 82% vs 78% vs 63% (p= 0.17) respectively. Among ovarian GCTs, 55% received carboplatin while in testicular and extragonadal GCTs, 65% received cisplatin-based chemotherapy. There was no difference in EFS of seminomatous and non-seminomatous GCTs (p value=0.2) but OS was better in seminomatous tumors (p value=0.03).
Conclusions: Adolescent with testicular and extragonadal primaries have poorer outcomes than ovarian GCTs. Carboplatin-based chemotherapy showed better OS and EFS among adolescents in this study. Further studies are needed to identify poor responders in this group who might benefit from intensifying therapy

EP280 / #640

Topic: *AS05.I Rare Tumours and Histiocytosis*

SPECTRUM OF LIVER DISEASES IN CHILDREN WITH LANGERHANS CELL HISTIOCYTOSIS

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Background and Aims: Hepatic Langerhans cell histiocytosis (LCH) is characterized by proliferation and accumulation of Langerhans cells in the liver, causing liver dysfunction or mass lesion. The diagnosis of hepatic LCH is based on the following: (1) hepatomegaly, defined as a liver edge greater than 3 cm below the costal margin at the mid clavicular line (2) liver dysfunction defined as bilirubin > 3 times, transaminases > 3 times of normal, protein < 55 g/L, albumin < 3 g/dL, or by clinical entities including an intrahepatic nodular mass or ascites or edema, not as a result of other causes (3) histopathological findings of active disease. We carried out this retrospective review of cases to study the spectrum of liver diseases seen in our patients with LCH.
Methods: Medical records of children diagnosed to have LCH from 2001 to 2020 were reviewed after obtaining IRB approval. Those children who had features of liver involvement were included for further analysis.
Results: 64/304 children with LCH had hepatic involvement. 45 boys and 19 girls with a median age of 28.9 months at diagnosis. 61 had hepatomegaly, 14 had jaundice and 4 had ascites. Abnormal LFT was noted in 38 children; these included hypoalbuminemia (33) transaminitis (27) hyperbilirubinemia (24). 55/64 children had either /or ultrasound /CT scans done and the findings were as follows: hepatomegaly (44), coarse echotexture (17) hypoechoic nodules (9), portal hypoechogenecity (5) sclerosing cholangitis (5). 10 children had liver biopsy; 6, 1 and 3 had early, late or mixed stages of disease. 15/64 children developed chronic liver disease.
Conclusions: The incidence of hepatic LCH in our cohort was 21%. 60% of them had biochemical evidence of liver dysfunction. Up to 17% had features other than isolated hepatomegaly on imaging. 23% of those who had hepatic LCH progressed to chronic liver disease.

EP281 / #2000

Topic: *AS05.I Rare Tumours and Histiocytosis*

HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS AT A PEDIATRIC SPECIALTY HOSPITAL. OUTCOMES AND DIAGNOSTIC PATHWAY PROPOSAL FROM 2018 TO 2021.

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Background and Aims: BACKGROUND AND AIMS: Hemophagocytic lymphohistiocytosis (HLH) is an acute and rapidly progressive systemic inflammatory disorder characterized by cytopenias, hypercytokinemia, and hyperferritinemia. Common clinical manifestations of HLH are acute fever, lymphadenopathy, hepatosplenomegaly and multiorgan failure that requires prompt recognition of the symptoms and early treatment. The main objectives are to describe clinical and demographic characteristics of the patients who meet the criteria of HLH and develop a diagnostic algorithm.
Methods: METHODS: Patients diagnosed with HLH, between January 2018 and December 2021 in a pediatric hospital, were included in this study who met 4/8 criteria from HLH-2004 along with hyponatremia, hepatitis, neurological features and elevated LDH mainly in the emergency room. We performed bone marrow aspirate and based on the clinical characteristics and laboratory findings, we developed a diagnostic algorithm for its recognition and treatment substained in the literature with a simple pathway where we detected patients with suspicious of HLH and according to the first evaluation, we continue diagnostic work-up until treatment
Results: RESULTS: We analyzed clinical and laboratory findings from 23 pediatric patients, affecting mainly females (56%), fever was the most frequent clinical sign and hyperferritinemia the most prevalent laboratory abnormality. The mortality rate was 39%, with a mean time to diagnosis of 16 days, most of the patients present secondary HLH with infection demonstrated. Prevalence between 2018 and 2021 was 0.123%, however in 2018 the prevalence was 0.018% and increased to 0.377% in 2021 using diagnostic work-up based on literature and resources to perform a quick diagnosis.
Conclusions: CONCLUSION: HLH is a rare entity but with a high mortality rate which makes early recognition crucial for appropriate management. Using our diagnostic algorithm, we were able to recognize and treat prompty patients protocolizing initial pathway to decrease mortality index.

EP282 / #1504

Topic: *AS05.I Rare Tumours and Histiocytosis*

USE OF MAPK PATHWAY INHIBITORS IN PEDIATRIC HISTIOCYTOSIS IN SPAIN

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Background and Aims: The MAPK pathway is one of the most commonly altered pathways among childhood neoplasia. BRAF V600E mutations are common in histiocytosis, mainly in Langerhans Cell Histiocytosis (LCH). AIM: Review of the off-label use of BRAF inhibitors in pediatric patients diagnosed with histiocytosis in Spain.
Methods: Analysis of 127 patients included in LCH-IV international study from Spain and 12 cases treated with inhibitors. Review of the results of a survey about BRAF-MEK inhibitors use sent to the Spanish Society of Pediatric Hematology and Oncology members.
Results: Since LCH-IV study open in Spain in 2017 until 1/April/2022, 127 patients were enrolled, mainly in stratum I (21 multisystemic and 43 polyostotic/CNS risk bone lesions) and VI (54 Natural history) but also 4 in relapses and 3 in CNS tumors or Neurodegenerative-LCH (ND-LCH) stratum. Among LCH studies, inhibitors were use in 6 patients, due to ND-LCH in 3 cases, refractory high-risk in 2 and high-risk relapse in 1. After the survey, data from 8 Spanish hospitals were collected about six patients. The main causes for inhibitors use were: Langerhans cell histiocytosis in 11 and Erdheim-Chester Disease (ECD) in one patient. BRAF inhibitors were used in 12 (6-vemurafenib, 6-dabrafenib) and MEK in 2 patients (trametinib). Up-front inhibitors use was reported only in ECD. Oral tolerance was good, without severe adverse effects. Therapy duration ranged from five years to six month and most patients are still on-therapy.
Conclusions: The chemotherapy was used in 50% of LCH-IV cases and curative in most patients. BRAF inhibitors in refractory MS-LCH showed rapid tumor regression, but relapse after stopping therapy appeared in most cases. The efficacy in LCH-ND is still controversial. New international trials that incorporate inhibitors are needed, so that we learn rather than the off-label use. Targeted therapies are not enough, but might contribute to reduce burden by chemotherapy in LCH patients.

EP283 / #258

Topic: *AS05.I Rare Tumours and Histiocytosis*

SELF-RESOLVING CONGENITAL LANGERHAN CELL HISTIOCYTOSIS (LCH) WITH A NOVEL KLC1::RAF1 FUSION

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Background and Aims: We report the case of an infant with congenital Langerhans cell histiocytosis (LCH). She presented at birth with 'blueberry muffin syndrome', a descriptive term for the presence of multiple blue/purple nodules in the skin. Congenital LCH is rare, and the clinical course can vary from self-resolution to progression to multi-system LCH, and it carries the risk of re-activation. There is little available molecular data on these cases, particularly linking the relationship between genotype and phenotype in congenital LCH.
Methods: Microbiological, haematological, and biochemical testing was undertaken. A skin biopsy was performed for histological and molecular testing as standard-of-care. No tissue was used for experimental purposes.
Results: Screening for congenital infections was negative. Histology from the skin biopsy was consistent with LCH, and immunostains confirmed the diagnosis. A targeted next-generation sequencing panel did not identify V600E, or any other exon 15 BRAF mutations. Whole genome sequencing of paired tumour and germline DNA identified a somatic KLC1::RAF1 fusion, and no germline mutations. The expression of the KLC1::RAF fusion was validated through RNA sequencing. Staging investigations for LCH, including skeletal survey, bone marrow aspirate and ultrasound of liver and spleen revealed no other sites of disease. Blood tests both at diagnosis and follow-up were normal, apart from a transiently elevated alanine transaminase level. The infant is now 5 months old, remains well and is developing normally with no evidence of bone marrow, skin, or risk-organ involvement of LCH. She will continue to be monitored for re-activation.
Conclusions: We report a case of self-resolving congenital LCH, consistent with the Hashimoto-Pritzker variant. Importantly, we describe a novel fusion in LCH, KLC1::RAF1. We hypothesise that this fusion drives the constitutive activation of ERK characteristic of LCH. In the event of re-activation, this RAF fusion may be targeted through MEK inhibition.

EP284 / #1238

Topic: *AS05.I Rare Tumours and Histiocytosis*

TREATING ADRENOCORTICAL CARCINOMA WITHOUT MITOTANE LEVEL MONITORING: CHALLENGES AND OUTCOMES FROM A LMIC.

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Background and Aims: Treatment of adrenocortical carcinoma (ACC) depends on surgical resection of primary tumor and systemic therapy using chemotherapy and mitotane. While associated with significant short and long term toxicity, mitotane levels are not readily available in many centers, particularly in LMIC.
Methods: This is a retrospective chart review of children (<18years) diagnosed with ACC at KHCC between Jan2000 and Dec2021. Demographics, clinical features at diagnosis, outcome and toxicities were captured from written notes. All patients were labeled as steroid deficient and were given stress dose of hydrocortisone upon presentation to ER for any febrile illness after starting mitotane.
Results: Thirteen patients were included (6 males and 7 females) with a median age of 3-years (range, 1-16.5). At presentation, 85% had virilization, 54% had hypertension and 31% had cushingoid features. All patients underwent tumor resection. The median tumor weight of 116-grams (range 25 – 745mg). Postoperative stages were 1(N=5 , 38%), 2(N= 3, 23%), 3(N= 2,15%) and 4(N=3, 23%). Eight patients received mitotane with a median peak dose of 3.5gram/m2/day (range 1-4gram/m2/day). This dose was achieved by slow increments from a starting dose of 1g/m2/day and were maintained for a median of 8 months (range, 6-18). Toxicity was mainly hematologic and related to the use of chemotherapy. None of our patients were admitted to the intensive care unit. Only 2 patients required modifications of mitotane during therapy due to suspected toxicity. Also, 2 patients needed long-term steroid replacement. By the time of last follow 2 patients with stage 4 had died while the rest are still alive with no evidence of disease.
Conclusions: The outcome and toxicity of our patients are in line with published literature. The lack of mitotane level monitoring did not seem to impact our patients' outcome.

EP285 / #170

Topic: *AS05.I Rare Tumours and Histiocytosis*

ROSAI DORFMAN DISEASE – EXPERIENCES IN THE GERMAN RARE HISTIOCYTOSES REGISTRY AND CONSULTATION CASES

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Background and Aims: Rare or Non-Langerhans cell histiocytoses (non-LCH) include very different diseases. In pediatrics, besides juvenile xanthogranulomatosis, Rosai-Dorfman disease (RDD), is most frequent.
Methods: In 2012, the German registry/consultation service for non-LCH - part of International IRHDR - was initiated, including 97 patients so far.
Results: 20 RDD patients were reported, all but one survivors (3 months to 5 years follow-up); 9/10 female/male; 0 were infants, 2 1y old, 5 2-4 y old, 12 5-18 y old, 1 >18y. 7 had cervical lymph node involvement only (all <5 y); 4 had CNS involvement only (all 5-8y), 9 had special or multiple organ involvement (most bone, but also kidneys, skin, glands, and other organs, age from 1 to >18y). In two, a mixed/overlap histiocytosis was found (RDD/Erdheim-Chester disease, RDD/LCH), one patient had H-syndrome (germline), one patient first had systemic RDD, then Acute Lymphoblastic Leukemia, and died from it. Genetic analysis was performed in 6; showing 1 ALK, 1 KRAS, and 1 MAP2K1 mutation, and the H syndrome in 1 case, two were negative. 7 patients who had cervical lymph node disease only, received resection followed by observation in 5 cases, and steroids in 2. 4 patients having CNS involvement were treated by observation after resection in 1, steroids in 2, and targeted therapy in 1 case. The systemic cases received steroids in 2 cases, polychemotherapy in 3 cases, and targeted therapy in 1; the others combined therapies or unknown.
Conclusions: RDD is a heterogeneous disease. In localized lymph node cases, typically at age 1-5, observation or steroids are appropriate. CNS disease is typical for children in school age. Besides, individual courses like systemic or with mixed/overlap histology or malignant transformation, may require individual therapies. Molecular analyses are crucial to enable targeted therapies. Appropriate consultation depends on international registration, which should be propagated.

EP286 / #1313

Topic: *AS05.I Rare Tumours and Histiocytosis*

CAN EBV TITER BE USED AS A TUMOR MARKER IN EBV RELATED CHILDHOOD MALIGNANCY?

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Background and Aims: Ebstein-Barr virüs (EBV), a member of the herpes virus family, causes infectious mononucleosis. It is known that EBV may play a role in the etiology of patients with B-cell lymphomas, Hodgkin lymphoma and nasopharyngeal carcinomas in the childhood group.In this study, can serum EBV PCR titer increases in pediatric cases with EBV-associated cancer be a stimulating factor for the disease? search for an answer to the question.
Methods: File data of cases diagnosed with EBV-associated cancer in our center between 2011-2021 were retrospectively reviewed.
Results: 156 cases diagnosed as Non-Hodgkin Lymphoma (NHL), Hodgkin Lymphoma (HL) and Nasopharyngeal Carcinoma (NPC) in our center between 2011-2021, which are known to be associated with EBV, were retrospectively analyzed. These cases consisted of 31(19.8%) HL, 10 (6.4%) NPC, 115 (73.7%) NHL cases. EBV PCR positivity was present at the time of diagnosis in 15 (9.6%) cases out of 156 cases. Of the positive cases, 3 were HL, 7 were NPC, and 5 were NHL. Immunodeficiency was also detected in one HL and 2 NHL cases. One NPC case was excluded from the study because its detailed data were not available. Considering the follow-ups, relapse or progressive disease was detected in 6 cases, and it was observed that the EBV PCR titers, which had become negative, increased again at the time of relapse/progression in all of these cases. Of these cases, 3 were NPC, 2 were HL, and the other case was diagnosed as relapsed/refractory NHL with the diagnosis of immunodeficiency. No re-positive EBV PCR titers were detected in other cases followed up in remission.
Conclusions: We think that EBV PCR follow-ups should be done regularly in cases diagnosed with EBV-related tumors, especially nasopharyngeal cancer, since an increase in EBV titer may be a precursor of the disease.

EP287 / #1875

Topic: *AS05.I Rare Tumours and Histiocytosis*

NASOPHARYNGEAL CARCINOMA IN CHILDHOOD: ANALYSIS OF A SERIES OF 50 PATIENTS TREATED WITH COMBINED CHEMOTHERAPY AND RADIOTHERAPY

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Background and Aims: Nasopharyngeal carcinoma is a cancer arising from the nasopharynx epithelium. Within the boundaries of the nasopharynx, the tumour epicentre is frequently seen at the fossa of Rosenmüller, from where the tumour invades adjacent anatomical spaces or organs. The aim of our study is to investigate the epidemiological, clinical, radiological, therapeutic particularities of the nasopharyngeal carcinoma (NPC) in children, and to determine prognostic factors correlated with outcome and features of a series of 50 cases collected in the Pediatric Hematology Oncology Center, in Rabat (Morocco).
Methods: A total of 50 patients with NPC were treated in the Center of Pediatric Hematology and Oncology in Rabat, from January 2010 to December 2019. They were retrospectively analyzed. Overall survival (OS) and disease-free survival (DFS) were calculated.
Results: Most patients were males (73%). Median age was 13 years. The main presenting symptoms were neck mass (81%), tinnitus/hearing loss (53%), bloody nasal discharge (23%), headache (56%) and nasal obstruction (20%). Stage I, II, III, IVA, IVB and IVC patients accounted for 0%, 7.7%, 62%, 13.7%, 7.8% and 7.8%, respectively. All patients were treated by neoadjuvant chemotherapy. The complete response rate to chemotherapy was 68%. All patients were treated by radiotherapy: 60 to 70 Gy to primary tumors, 50 to 65 Gy to cervical lymph nodes. Locoregional relapses were observed in 4 patients, metastatic relapses in 4 cases. The 2 and 5- year overall survival (OS) rates were 91,7% and 84,3% respectively. Disease-free survival (DFS) was 72%. The main long-term complications of therapy were trismus (40%), hearing loss (25%), xerostomia (50%), hypothyroidism (8%), growth disorders (10%) and neck fibrosis (30%).
Conclusions: The majority of patients were diagnosed at advanced stages. Children and adolescents with NPC had excellent survival except metastatic disease. The TNM stage was the most relevant prognostic factor.

EP288 / #671

Topic: *AS05.I Rare Tumours and Histiocytosis*

NUT CARCINOMA IN CHILDREN: THE EXPERT EUROPEAN EXPERIENCE

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Background and Aims: NUT-carcinoma is a rare, probably underdiagnosed and highly aggressive tumor defined by the presence of a somatic NUTM1 rearrangement. The tumor occurs mainly in adolescents and young adults. We analyzed the clinical, radiologic, and biological features of pediatric patients (≤18 years) with NUT-carcinoma.
Methods: This retrospective multicenter international study was based on review of medical records of 24 children with NUT-carcinoma from 5 countries with specific rearrangement or positive anti-NUT nuclear staining.
Results: Twenty-four patients with a median age of 14.6 years (range: 3.9–18 years) were analyzed. Thoracic/mediastinal tumors were the primary in 14 patients, and head and neck in 7 cases. One patient had multifocal tumor with unknown primary, another a vocal cord and the last one a pancreas primary. Sixteen patients (67%) presented with regional lymph node involvement and 17 patients (71%) with distant metastases, in most cases lung (38%), distant lymph nodes (38%) and bone marrow (30%). Approximately half of patients were initially misdiagnosed and diagnosis was corrected after NUT immunochemistry or NUT fusion sequencing. Chemotherapy was administered in all patients; nine patients underwent major surgery and 19 radiotherapy. Median overall survival was 0.75 years (range 0.2-11 years) median event free survival 0.4 years (range 0.1-11 years), one patient is currently treated for a subsequent relapse (1.9 years after diagnosis). Three long-term survivors (11, 9.1 and 6.6 years after diagnosis) were identified, these cases were associated with non-metastatic cervical disease and non-metastatic disease with BRD3-NUT-fusion.
Conclusions: As in adults, NUT-carcinoma in pediatric patients is poorly sensitive to conventional therapy in most cases. In a minority of patients long-term survival is possible with multimodal treatment. Early diagnosis of undifferentiated or poorly differentiated carcinomas to identify the specific rearrangement of NUT-gene is necessary to initiate the optimal diagnostic and therapeutic strategy.

EP289 / #341

Topic: *AS05.I Rare Tumours and Histiocytosis*

BCOR-CCNB3-FUSION POSITIVE SARCOMA. THE IMPORTANCE OF TWINNING PROJECTS TO ADDRESS THE DIAGNOSTIC LIMITATIONS OF RARE TUMORS IN DEVELOPING COUNTRIES.

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Background and Aims: BCOR-CCNB3-fusion positive sarcoma is a recently defined rare subtype of undifferentiated round cell sarcomas. Like other molecular genetic tumor subtypes, it is a challenging diagnosis for developing countries.
Methods: Here we report a case of a 15-years-old boy diagnosed with BCOR-CCNB3-fusion positive sarcoma.
Results: A fifteen-years-old male was admitted to the hospital with complaint of a painful mass in the left leg. CT revealed pathological mass in the thickness of the left extensor digitorium longus muscle (5.3x4.9x17.6cm in size) and signs of active hemorrhage. The pathological mass was completely resected and histologically hematoma was diagnosed. Six months later, the patient returned with the same complaints. MRI revealed multichambered pathological mass in the anterior and lateral compartment of the left leg (4.0x2.8x15.6cm in size). The patient underwent second surgery, and the lesion was completely removed. According to the histological and immunohistochemical examinations low-grade fibromyxoid sarcoma was diagnosed. Postsurgical CT showed no signs of residual disease and distant metastases. After the patient was admitted to our clinic, review of paraffin-embedded tissue blocks of first surgery performed and diagnosis of low-grade fibromyxoid sarcoma was confirmed. After Musculoskeletal Multidisciplinary Working Group discussion via telemedicine, decision was made to review the paraffin-embedded tissue blocks and conduct molecular genetic testing in Germany, since there were discrepancies between histological reports and suspicion of recurrent disease. The final diagnosis was BCOR-CCNB3-fusion positive undifferentiated sarcoma, which was evaluated as a recurrent. The lack of molecular genetic testing in Armenia led to a delay in diagnosis by 3 months.
Conclusions: Diagnosis of rare pediatric tumors is challenging in developing countries like Armenia. The lack of molecular genetic testing not rarely leads to misdiagnosis. Twinning projects between clinics of developing and developed countries remain extremely important for the diagnosis of rare tumors and can reduce disparities in cancer treatment in developing countries.

EP290 / #1513

Topic: *AS05.I Rare Tumours and Histiocytosis*

EXPERIENCES WITH TREOSULFAN-BASED CONDITIONING FOR HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

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Background and Aims: Hemophagocytic lymphohistiocytosis (HLH) challenges hematopoietic stem cell transplantation (HSCT) due to the high graft failure rate, relapse, and simultaneous toxicity. This report evaluated the outcome of treosulfan-based conditioning in HLH patients.
Methods: Between January 2016 and April 2022, 21 patients with HLH received HCT with a treosulfan-based conditioning regimen using matched sibling (MSD, 1), unrelated (URD, 13), and haploidentical family donor (HFD, 7). Nine had familial HLH (3 PRF1 and 6 UNC13D), 6 had other genetic defects (4 XIAP, 1 XLP1, and 1 Griscelli syndrome), and 6 had secondary HLH. The conditioning regimen consisted of treosulfan, fludarabine, thiotepa, and rabbit ATG. The cyclosporine and mycophenolate mofetil were used for GVHD prophylaxis in MSD or URD. For the haploidentical HCT, an ex vivo αβ T cell-depleted graft was used without pharmacologic prophylaxis.
Results: All patients achieved engraftment at a median of 10 days without late graft failure. One patient developed VOD, which was successfully treated with defibrotide. Ten (48%) and 6 (29%) patients developed grade 2 and 3-4 acute GVHD, respectively. One patient developed moderate chronic GVHD, and 3 developed severe chronic GVHD. Nineteen survived with complete donor chimerism, and 2 died due to pneumonia and asphyxia, respectively. At a median follow-up of 28 months, the overall survival (OS) and disease-free survival (DFS) were 92.3% and 91.7% at 2 years, respectively. The 2-year probability of moderate-to-severe chronic GVHD-free and disease-free survival (CDFS) was 67.9%.
Conclusions: Our findings indicated that HCT using treosulfan/fludarabine/thiotepa/r-ATG shows a favorable outcome with excellent donor chimerism in pediatric patients with HLH. Furthermore, haploidentical HCT from an αβ T cell-depleted graft could be a possible alternative in patients who lack a matched related or unrelated donor. Our study's high incidence of acute GVHD requires further modification of the conditioning regimen or GVHD prophylaxis.

EP291 / #1859

Topic: *AS05.I Rare Tumours and Histiocytosis*

25 YEARS OF LANGERHANS CELL HISTIOCYTOSIS EXPERIENCE OF A SINGLE CENTER

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Background and Aims: Evaluation of patients diagnosed with Langerhans cell histiocytosis (LCH) and treated in our center.
Methods: The medical records of patients with LCH were rewieved. The clinical characteristics, treatment details and responses were analyzed retrospectively.
Results: There were 60 patients with LCH between 1987-2022. The median age of diagnosis was 55 months (2.5mos –18yrs), M/F=1.3. Single system involved LCH (SSIG-LCH) (68%, n:41); involvement sites were bone (88%), skin (7%), lymph node (2.5%), lung (2.5%). Nine patients had vertebral involvement. Surgery was performed in 66%, chemotherapy consisted vinblastin, prednisolone+methotrexate, mercaptopurine was given in 63%. Radiotherapy (RT) was given in 12% of cases (3 of them vertebral LCH). Relapse occured in 5 cases. The median follow-up time was 6.5yrs (1month -18yrs), 15-years OS rate was 100% and 5-year and 15-years EFS rates were 84%. Multisystem involved LCH (MSIG-LCH) (32%, n:19); involvement sites were bone (95%), skin (53%), lung (42%), pituitary gland (21%), Liver (16%), Gastrointestinal system (16%), spleen (5%). Eight of them had risky organ (RO) involvement, 4 of 8 patients had lung involvement as RO. Surgery was performed in 58% of cases, chemotherapy consisted vinblastin, prednisolone+methotrexate, mercaptopurine was given in all 19, and RT was given in two patients. Refractory disease (n:2) and relapse (n:6) occured in 8 patients. The median follow-up time was 5years (5months-17yrs), the 2-and 15- years OS rates were 88% and EFS rates were 39%. One infant had skin+pulmonary LCH (risky organ), and died with refractory LCH despite anticancer treatment at 21months. Other infant died from meningococcemia. Remission achieved with vemurafenib in two cases.
Conclusions: In MSI-LCH group age tends to be younger than SSI-LCH, these patients particularly had RO involvement. Although lung involvement is not considered as risky organ, pulmonary LCH can be fatal especially in the infancy. In relapsed/ refractory cases, remission can be achieved by anti-BRAF drugs.

EP292 / #851

Topic: *AS05.I Rare Tumours and Histiocytosis*

CARDIAC EVALUATION BEFORE AND AFTER ORAL PROPRANOLOL TREATMENT IN INFANTILE HEMANGIOMAS

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Background and Aims: Infantile hemangiomas (IHs) are the most common vascular tumor developing in children, and oral propranolol, a non-selective beta-adrenergic antagonist, is known as first-line treatment. This study prospectively assessed cardiac status initially and regularly to establish guidelines for monitoring cardiac function and toxicity in IHs treated with propranolol for ≥6 months.
Methods: 64 patients diagnosed with IHs and treated with oral propranolol before 2 years of age at the Department of Pediatrics, Kangbuk Samsung Hospital (Seoul, Korea) with cardiac evaluations between 2017 and 2021, were included. Cardiac evaluations including ECG, 24 hour Holter monitoring and echocardiography were performed initially and at 6 to 12 months after treatment with oral propranolol.
Results: 64 patients (21 male, 43 female) with IHs successfully underwent cardiac evaluations. The mean percentage of size decrease after 1 year of oral propranolol treatment was 71.8%. Pre-treatment echocardiography diagnosed congenital heart disease (CHD) in 25 of 64 patients (39.0%), including PDA (3); ASD (6); PFO (6). LV systolic function before and after treatment revealed no statistically significant differences in ejection fraction, fractional shortening, mitral annular plane systolic excursion, or global longitudinal strain. However, early (E) and late (A) diastolic mitral inflow velocities, and E/A ratio, together with early diastolic mitral annular velocity e′ (E/e′ ratio) measurements demonstrated a significant increase after treatment. Among the RV function measurements, peak systolic tissue velocity (S') and tricuspid annular plane systolic excursion (TAPSE) were significantly improved after treatment ($P < 0.05$). None of the 64 patients experienced adverse events such as arrhythmias, and no significant changes in heart rate, PR interval, and QTc, except for QRS duration on ECG during propranolol treatment.
Conclusions: Oral propranolol treatment ≥6 months was effective and safe without significant cardiac toxicity in IHs. Initial echocardiography is necessary to diagnose CHD. This study suggest the cardiac evaluation guidelines for IHs treated with oral propranolol.

EP293 / #904

Topic: *AS05.I Rare Tumours and Histiocytosis*

LONGTERM SURVIVORS WITH RHABDOID TUMORS ARE RARE: A NATIONAL REPORT FROM GREECE

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Background and Aims: Rhabdoid-tumors(RT) are rare, highly-aggressive neoplasms arising from renal (MRT), extrarenal soft-tissue(EERT) or central-nervous-system(ATRT). They usually present in infants or young children and have dismal prognosis. Almost 10% of pts present with synchronous tumors. If germline-mutations in SMARCB1 or SMARCA4-genes are found, diagnosis of Rhabdoid-Tumor-Predisposition-Syndrome 1 or 2 (RTPS1/RTPS2) is established, respectively. Data from national registries, on this entity are lacking.

Methods: All, 7 pediatric hematology-oncology centers in Greece participated in this retrospective study that covered the period between 1/2012-12/2021. Demographics, tumor characteristics and outcome were analyzed.

Results: Twenty-two pts with RT (11females), with a median age of 10m (range:1d-7.5y) were diagnosed in Greece during the study-period. Diagnosis included ATRT (14pts), EERT (8pts) and MRT(2pts). Two pts had synchronous and 1 metachronous tumors. The most common ATRT-location was posterior-fossa. Upon diagnosis, metastatic lesions were found in 57.1%. RTPS1 was diagnosed in 3 out of the 14pts evaluated. All pts underwent surgery (biopsy:6, partial resection:3, subtotal/total resection:13). Total/subtotal resection was achieved in 9/14 ATRT and in 3/8 extracranial-RT(ERT). Sixteen pts were treated according to the EuRHAB-Registry investigational-treatment protocol. Two patients did not receive therapy. Radiotherapy as per protocol was given in 8/22pts (6ATRT, 2ERT). High-dose chemotherapy was administered to 3 children. No treatment-related death occurred. The median follow-up was 9m(range:1m-8.77y). Overall survival was 50.0% (95%CI15.2-77.4%), 37.5% (95%CI8.7-67.4) and 12.5% (95%CI11.7-42.2) at 1y, 3y and 5y respectively. Median time of 1st relapse was 5.4m. Relapse/progression were local, metastatic or combined in 3, 3 and 12 cases respectively. Only 2pts are long-term survivors in 1st remission (1ATRT-SHH-subtype for 8.75y and 1MRT 5.25y post-diagnosis respectively).

Conclusions: Due to the rarity and extremely dismal prognosis of these tumors, further investigational efforts within an international framework, like in our study, are needed.

EP294 / #1029

Topic: *AS05.I Rare Tumours and Histiocytosis*

THE ROLE OF GENETIC TESTING IN DIFFERENTIAL DIAGNOSIS OF HAMARTOMATOUS POLYPOSIS SYNDROMES: SINGLE CENTER EXPERIENCE

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Background and Aims: Hamartomatous polyposis syndromes (HPS) are a heterogeneous group of rare hereditary diseases including juvenile polyposis syndrome, Peutz-Jeghers syndrome, and PTEN hamartoma tumor syndrome (Cowden syndrome). These conditions are characterized by similar clinical manifestations and a high risk of malignancy, but require different follow-up tactics since each syndrome carries different organ-specific risks of neoplasia. HPS should also be differentiated from other forms of hereditary polyposis (familial adenomatous polyposis and MUTYH-associated polyposis). Molecular genetic testing in such patients plays a leading role in the differential diagnosis at the early stages of the disease.
Methods: Retrospective review of hospital records from January 2011 to December 2021, molecular genetic testing.
Results: The study included 20 patients, 13 boys and 7 girls, from 5 to 22 years old. The clinical diagnosis of hamartomatous polyposis was based on diagnostic criteria (Beggs et al., 2010; Jass J. et al., 1988). The main symptoms included: abdominal pain in 17 cases (85%), vomiting in 11 cases (55%), mucosal pigmentation in 9 cases (45%), gastrointestinal bleeding in 4 cases (20%), and weight loss in 1 case (5%). The results of genetic testing were, as follows: 9 patients (45%) had a mutation in the STK11 gene (Peutz-Jeghers syndrome); 6 patients (30%) carried a mutation in the PTEN gene (Cowden syndrome); 5 patients (25%) had mutations in the genes SMAD4 or BMPR1A (juvenile polyposis). Family history was known for 14 patients. In 10 families (70%), no other cases of tumor diseases were observed. In three families, the first-line relatives were found to carry mutations in cancer-associated genes.
Conclusions: Molecular genetic testing is indicated in all patients with suspected HPS to determine the optimal follow-up strategy. Genetic testing is also important for the next of kin of such patients to identify asymptomatic carriers of pathogenic mutations and to assess the risk of developing malignancy throughout life.

EP295 / #858

Topic: *AS05.I Rare Tumours and Histiocytosis*

INTRAOCULAR MEDULLOEPITHELIOMA : CLINICO-PATHOLOGICAL FEATURES OF A RARE ENTITY.

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Background and Aims: Intraocular medulloepithelioma, though rare, forms the second most ocular tumour after retinoblastoma. It arises from the non-pigmented ciliary epithelium and typically manifests in the first decade of life. We present a case series of five intraocular medulloepithelioma in the paediatric population.
Methods: The cases were retrieved over a period of 10 years from the electronic medical records at Tata Memorial Hospital, Mumbai. The clinical and imaging findings, treatment records, histological features and follow-up data was noted.
Results: A total of 5 paediatric patients with intraocular medulloepithelioma were included in this series. The age range was from 2 to 15 years. We also found 2 adult cases diagnosed with intraocular medulloepithelioma; both the patients were of age 26 years. The presenting complaints were loss of vision (most common), followed by redness of eye and proptosis. Imaging findings demonstrated an anterior chamber mass originating from the ciliary body. The teenage patient had been diagnosed at the age of 3 years, but the family refused treatment and the patient presented at a later stage. Interestingly, this patient had limited ocular disease which was treated with enucleation followed by radiation therapy. The histology was a non-teratoid medulloepithelioma. The patient had an uneventful follow-up. All the other 4 patients showed evidence of extraocular extension, with two patients developing metastasis to intraparotid lymph node. The patients were treated with enucleation followed by radiation therapy. One patient showed recurrence of the disease after completion of treatment, with involvement of cervical lymph nodes and vertebral metastases, and is currently on palliative treatment. The other 3 patients are disease free on follow-up. Histology in all cases showed primitive neuropeithelial cells, rosette formation and teratoid component in one case.
Conclusions: Intraocular medulloepithelioma is a rare entity, with prognosis depending on stage of the tumour. Extraocular extension and metastatic disease confer a worse prognosis.

EP296 / #1187

Topic: *AS05.I Rare Tumours and Histiocytosis*

COMPARISON OF MODIFIED WEISS AND WIENEKE SCORING SYSTEM FOR PAEDIATRIC ADRENOCORTICAL TUMOURS

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Background and Aims: Wieneke scoring system is recommended by recent WHO classification of adrenocortical tumours (ACTs). We attempted to study and compare modified Weiss (MW) and Wieneke criteria with respect to their clinical behavior.
Methods: We studied 23 patients with ACTs in our institute from 2011 to 2021. Clinical details and follow up were derived from Electronic medical records. Histopathology was reviewed by applying both Wieneke and MW criteria.
Results: Age range was from 11 months to 11 years with median of 4 years. 13% patients were diagnosed with adrenocortical adenoma (ACA) by MW criteria while 87% as adrenocortical carcinoma (ACC). The range of Weiss score was from 4 to 8. On follow up, (n=12), 66% patients experienced disease relapse while 33% were alive without disease. Patients with relapse had a MW score of 5 and above. 3 of 2 patients with no relapse had a MW score of 7. By Wieneke system, a score of 2 and less was applied to 3 (15%), score 3 to 7 (35%) and score 4 and above to 50% of patients with ACC. One of the patients with Wieneke score 2 had relapse, 3 patients with score 3 had relapse whereas 2 patients with score 6 were alive without disease.
Conclusions: Diagnosis of adrenocortical carcinoma was offered to 86% patients by modified Weiss's criteria. We attempted to apply Wieneke criteria retrospectively in order to compare the two scoring systems. Disease relapse was correlated with MW score above 5; although 2 patients with score 7 had no disease progression. By Wieneke criteria, patients in benign and uncertain malignant potential category experienced relapse while 2 patients in malignant category were well. Our findings are more in endorsement of modified Weiss scoring system. However, we plan to undertake a prospective application of Wieneke system and review our results with adequate follow up.

EP297 / #1177

Topic: *AS05.I Rare Tumours and Histiocytosis*

CEREBROVASCULAR ACCIDENTS IN PATIENTS WITH CRANIOPHARYNGIOMA.

CEREBROVASCULAR ACCIDENTS IN PATIENTS WITH CRANIOPHARYNGIOMA.

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Background and Aims: Craniopharyngioma (CP) is a rare brain tumor, mainstay treatments include surgery and radiation, but have side effects relating to the damage of anatomical structures in the vicinity of the tumor. CPs often arise in close proximity to the Circle of Willis. Patients are at risk for cerebrovascular accidents (CVA). In this study we aim to describe the incidence and temporal relationship of CVA in CP with surgery and/or radiation.
Methods: Data was extracted From IRB approved database of craniopharyngioma patients seen at Children's Healthcare of Atlanta from 2000 to 2021 as a part of retrospective analysis. CVA was diagnosed if the patient had symptoms and/or radiologic imaging consistent with stroke. Medical course of the disease in relation to timeline of various treatment modalities was noted.
Results: Of 85 screened patients, 12 patients were found to have CVA. Median age at time of stroke was 10.7 years (range 2.4-21.2). One of 12 patients had intratumoral hemorrhage, all remaining had ischemic stroke. Majority of the CVAs (10/11 patients) occurred 24-48 hours following surgery involving tumor resection. Neither ommaya nor VP shunt placement were temporally related to CVA. Two patient events were not temporal related to surgery. Six of 12 patients received radiation therapy prior to CVA. One patient had stenosis of Circle of Willis and had CVA after 3 courses of radiation (1,2 and 8 years before CVA). Vascular stenosis in major vessels was noted in 5of 12 patients.
Conclusions: Risk of CVA in CP was about 14%, mostly ischemic, occurred mostly intraoperatively or immediately postoperatively within 24-48 hours of surgery involving tumor resection.

EP298 / #959

Topic: *AS05.I Rare Tumours and Histiocytosis*

CLINICAL SPECTRUM AND TREATMENT OUTCOME OF CHILDREN WITH LANGERHANS CELL HISTIOCYTOSIS-A SINGLE INSTITUTIONAL EXPERIENCE FROM INDIA

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Background and Aims: Langerhans cell histiocytosis (LCH) has heterogeneous clinical manifestations and unpredictable clinical course and outcome.We retrospectively analyze children with LCH over 12 year period.
Methods: Children aged ≤ 14 years pathologically diagnosed as LCH and treated at our institute between 1st January 2004 to 31stDecember 2015 were included for retrospective analysis. The extent of disease,treatment protocol and response assessment was done as per LCH III trial and three year event free survival (EFS) and overall survival (OS) was calculated.
Results: A total of 64 children were recruited.The median age of the cohort was 2 years (range: 2 months- 13 years).Male to female ratio was 2.2:1. Multisystem LCH (MSLCH) was seen in 32 (50%) patients in which 22 children had risk organ involvement. Single system (SS) LCH single site and multifocal (MF) involvement was present in 23 (35%) and 9 (15%) children respectively. The most common clinical manifestation was swelling (n=52) followed by skin rash (n=21) with bone (n=42) being the most common system involved.Nine patients (14%) had progressive disease among which two patients lost to follow up and seven patients died.Eight patients had reactivation. Three year EFS and OS for the cohort was 68.8% and 92.5% respectively. Three year OS for SSLCH Single Site /MF , MSLCH without risk organ involvement was 100% while it was only 75% in MSLCH with risk organ involvement. Three year EFS for SSLCH Single site ,SSLCHMF and MSLCH without risk organ involvement was 95.7% , 62.5% and 63.6% respectively and was 45.3% in risk organ involvement. Long term complication like diabetes insipidus, neuropsychiatric problem and dental abnormality was present in eleven (17%), two, five (7.8%) children respectively.
Conclusions: Multi system LCH with risk organ involvement was associated with inferior outcome.Progressive disease on chemotherapy was related with high mortality which needs to be addressed especially in resource limited countries

EP299 / #1898

Topic: *AS05.I Rare Tumours and Histiocytosis*

REFRACTORY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH) TRIGGERED BY CORONAVIRUS DISEASE (COVID-19) AND EPSTEIN BARR VIRUS (EBV) INFECTION IN A TEENAGER WITH AN UNDIAGNOSED PRIMARY IMMUNODEFICIENCY (PID)

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Background and Aims: Primary (familial HLH) results from an inherited immune disorder and secondary from a critical illness (autoimmunity, malignancies or infection) that induces an uncontrollable excessive immune response resulting in multiorgan failure. EBV can trigger HLH and recently COVID-19 has been reported in few adults. We present a HLH case triggered by COVID-19 and EBV in a teenager with undiagnosed PID.
Methods: Case report
Results: A 14-year-old female had PMH: colitis, perianal abscesses, meningitis, mild varicella post-vaccine, short stature and depression. Immunological work-up was not conclusive for any specific PID: immunodeficiency panel, NOBI, RTE, Th17, protein vaccine response and Immunoglobulins normal. Appropriate memory to naive CD4/CD8. Low memory B and T reg cells. Genetic Testing Panel PID and whole exome sequencing - no causative mutation. FH: recurrent infections and autoimmune disorders in immediate family. She presented early in the pandemic with five days: fever, rash, gastrointestinal symptoms, headaches, hypotension, respiratory distress and lethargy (no focal neurological deficit), hepatosplenomegaly and hyperferritinemia (20332 ug/L). Treatment included fluid resuscitation, inotropes, high flow oxygen, antibiotics, IVIG and methylprednisone boluses for presumed septic shock. She improved for 72 hours followed by deterioration with worsening hyperferritenemia. Further work-up showed 8/8 HLH-2004 diagnosis criteria, pleocytosis, SARS-CoV-2 IgG antibodies and EBV viral load (251766 IU/ml). Treatment included HLH 2004 induction and Rituximab. HLH improved and EBV viral load became negative. On week 6, she had HLH reactivation (increasing ferritin, soluble CD-25 and CD-163), treatment resulted in dexamethasone, weekly etoposide, ruxolutinib and ultimately emapalumab prior to hematopoietic stem cell transplant (conditioning Alemtuzumab, Treosulfan and Fludarabine), cyclosporine and mycophenolate for GVHD prophylaxis. Post transplant she has remained well with ongoing T cell mixed donor chimerims and no evidence of HLH or recurrent infection.
Conclusions: COVID-19 could trigger HLH in children with PID, further collaborative studies are required to further confirm this finding.

EP300 / #512

Topic: *AS05.I Rare Tumours and Histiocytosis*

PRKAB2 EMERGES AS A POTENTIAL PROGNOSTIC BIOMARKER IN PEDIATRIC ADRENOCORTICAL TUMOR

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Background and Aims: Paediatric adrenocortical tumour (ACT) is a rare neoplasm with high heterogeneity. Different from adult ACT, anatomopathological parameters are considered inaccurate in predicting patient's prognosis, which reflects difficulties in determining the progression of the disease, treatment strategies and tumour biology. AMP-activated protein kinases (AMPK), which have the PRKAB2 gene as a producer of one of the subunits of its complex, exert crucial activities for the maintenance of embryonic development, and are strongly associated with the main hallmarks of cancer. Thus, this study aimed to evaluate the clinical value of the expression of PRKAB2 in children with ACT.
Methods: Gene expression was determined by Real-time PCR (RT-qPCR), RNA-sequencing (RNA-seq), and in silico evaluation of two public datasets of paediatric cases of ACT. CEMITool package was used to identify co-expression gene modules and hub genes using data of our sequenced samples. Association analysis between PRKAB2 and clinical features were carried out using Mann-Whitney and log-rank tests.
Results: Co-expression analysis of the RNA-seq data of 14 paediatric tumour samples from our cohort identified the PRKAB2 as a hub gene in ACT. In addition, validation analysis of a higher number of samples of our cohort of Brazilian patients (n=56) and data expression of the public datasets GSE76019 (n=34) and GSE76021 (n=29) revealed the association between lower levels of PRKAB2 with the ACT unfavourable events recurrence and/or death (p=0.009, p=0.011 and p=0.048, respectively). Furthermore, the underexpression of PRKAB2 was significantly associated with lower 5-year event-free (0.002) and overall (p=0.003) survival in our cohort (n=56).
Conclusions: Collectively, our results suggest that PRKAB2 gene may be an important player in ACT biology and a promising predictive marker of prognosis for paediatric patients with ACT. (Grants FAPESP: 2021/10702-9 and 2014/20341-0)

EP301 / #1933

Topic: *AS05.I Rare Tumours and Histiocytosis*

TGF-BETA PATHWAY ACTIVATION COMBINED WITH WNT/BETA-CATENIN INHIBITION AS A POTENTIAL THERAPEUTIC STRATEGY FOR PEDIATRIC ADRENOCORTICAL TUMORS

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Background and Aims: Pediatric adrenocortical tumors (ACT) are rare and aggressive tumors with generally poor prognosis in advanced stages and limited treatment options. In this context, the aim of our study was to search for new potential therapeutic targets or approaches to improve treatment effectiveness by using an in-house RNA sequencing of ACT samples.
Methods: Total RNA of ACT tissues from 14 Brazilian patients were sequenced in order to search for differentially expressed genes (DEGs) between ACT cases that presented (n=5) or not (n=9) recurrence and/or death. Gene expression was validated in additional 56 ACT samples by RT-qPCR. In vitro, cell viability and colony formation of NCI-H295R were evaluated after stimulation with TGF-beta recombinants alone or in combination with the inhibitor of Wnt/Beta-catenin (PNU-74654). DESeq2 package, Mann-Whitney test, Kaplan-Meier curves and $p<0.05$ were used for analysis.
Results: Among the DEGs, we identified the TGFBR2 as one of the top 50 downregulated gene in the cases of ACT with unfavorable outcomes. Further validation in a larger cohort (n=56) revealed the association between TGFBR2 underexpression with worse 5-years event-free (56% versus 97%) and overall survival (69% versus 97%) ($P<0.01$). In vitro, stimulation of NCI-H295R cells with TGF-beta ligands (10ng/ml) decreased cell viability ($P=0.03$) and colony formation ($P<0.02$), which were accompanied by an increase in MYC expression, a Wnt target-gene. Then, we evaluated whether the combination of TGF-beta activation and Wnt inhibition would enhance this effect, since the inhibition of Wnt/beta-catenin is shown to reduce NCI–H295 proliferation. Although either TGFbeta ligands and PNU-74654 (50uM) were effective independently, the combination therapy had a higher impact in cell viability ($P=0.03$).
Conclusions: Collectively, our results suggest that TGF-beta signaling might have a role in pediatric act progression and in activating the Wnt/beta-catenin pathway, which could be useful as a potential combinatorial therapeutic strategy (FAPESP: 2014/203410 - 2018/044770).

EP302 / #947

Topic: *AS05.I Rare Tumours and Histiocytosis*

OUTCOMES OF CHILDREN WITH EXTRACRANIAL MALIGNANT RHABDOID TUMORS TREATED AT A TERTIARY CARE CENTRE IN INDIA

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Background and Aims: Extracranial malignant rhabdoid tumours(MRT) are rare childhood cancers with a poor outcome. We report our experience in children with extracranial MRT treated at a tertiary hospital in India.
Methods: Retrospective analysis of children (<15 years) with pathologically confirmed extracranial MRT, treated between January 2011 to December 2020 were performed. Staging was by ^{18}FDG-PET/CT. Initial chemotherapy regimen was adapted from the hospital Ewing sarcoma protocol (Vincristine, Ifosfamide/Cyclophosphamide,Etoposide, Doxorubicin) and from 2017 onwards, 8 cycles of chemotherapy (alternating cycles of Vincristine, Doxorubicin, Cyclophosphamide/Ifosfamide,Carboplatin,Etoposide) were administered.Local treatment at 10-12 weeks included surgery and/or radiotherapy. Survival analysis was performed by Kaplan-Meier Analysis, analysis of prognostic factors by cox proportional-Hazard model(IBM SPSS^{TM}v 24.0).
Results: A total of 78 children were diagnosed to have extracranial MRT during the study period. Of these, 25/78 were treated with a curative intent and 53 children were palliated in view of disseminated disease. Median age was 25 months(16-34months) and M:F was 1:1.5. Six patients (24%) had renal MRT and nineteen patients(76%) had extrarenal MRT. Five of 25 patients had metastatic disease(20%) at presentation. Local treatment was surgery in 5(20%), radiotherapy in 8(32%) and surgery plus radiotherapy in 9(36%). At a median follow-up of 14 months(6-21months), 3year EFS/OS was 20.753±5.3%(95%CI:10.28-31.22)/26.7± 6.75%(95%CI:13.4-39.9). Among all variables analysed for prognosis in non metastatic tumors, use of adjuvant radiotherapy alone had prognostic impact on EFS (p=0.035).
Conclusions: Extracranial MRT is a highly aggressive tumour in young children, with very poor outcomes. Radiotherapy as part of local treatment showed some benefit in survival. Further understanding of the biology of this disease and newer therapeutics are necessary to improve the survival of children with extracranial MRT.

EP303 / #1647

Topic: *AS05.I Rare Tumours and Histiocytosis*

MULTIDISCIPLINARY TUMOR BOARD FOR THE LATINAMERICAN PEDIATRIC ONCOLOGY GROUP (GALOP) RARE TUMOR INITIATIVE.

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Background and Aims: GALOP´s Rare Tumor Initiative was launched in 2011 to improve management and outcomes of children and adolescents with infrequent tumors in latinamerica. To address lack of standardized therapeutic guidelines, a virtual tumor board was established for multidisciplinary discussion of these patients. Our aim is to describe the activity of this tumor board.
Methods: Retrospective analysis of the Rare Tumor group monthly meetings, held through the web platform of Cure4Kids, from September 2013 to March 2022. Cases were presented virtually, including clinical history, complementary studies, and questions for discussion. Literature review was performed, and international experts were invited where possible.
Results: The Cure4Kids´s Rare Tumor Group has 151 registered participants from 18 countries, mostly from Latinamerica and Caribbean. Ninety-two cases of de-identified patients from 11 countries, were discussed in 74 meetings, by a median of 10 participants per session. Fifty-three cases corresponded to rare tumors, 14 rare sarcomas, 8 cases of tumors with unusual presentation and 17 cases for diagnosis. Six administrative meetings were held for discussion of the initiative, regional networks and data capture.
Conclusions: This report shows the feasibility of implementing an international tumor board for low-middle-income countries, focused on complex cancers where available expertise is limited. Further evaluation of how this translates into final patient management is warranted.

EP304 / #809

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

THE OUTCOME OF TANDEM HIGH-DOSE CHEMOTHERAPY FOR PATIENTS WITH MEDULLOBLASTOMA IN INFANT AND YOUNG CHILDREN: A SINGLE-CENTER STUDY

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Background and Aims: Medulloblastoma is the most common malignant brain tumor of childhood, accounting for 25% to 35% of all intracranial tumors. Multimodality therapy including surgery, radiotherapy, and chemotherapy has been treated for patients with medulloblastoma, the survival is affected by age, metastatic stage at diagnosis, and resection status after surgery. Young children under 3 years old are considered to avoid radiotherapy due to neurodevelopmental problems. Alternative therapeutic options are needed to overcome that.
Methods: From April 2005 through June 2021, we registered patients who were below years old and diagnosed with medulloblastoma and treated with Korean Society Pediatric Neurooncology (KSPNO) Protocol at Yonsei Cancer Center. Six cycles of chemotherapy and tandem high-dose chemotherapy(HDCT) with autologous stem cell transplantation(ASCT) were administered. Outcomes and complications of them were analyzed retrospectively.
Results: 12 patients were enrolled, and histologic subgroup was confirmed in 10 patients (4 classic, 2 desmoplastic/nodular, 4 medulloblastoma with extensive nodularity), and molecular subgroup of sonic hedgehog was confirmed in 9 patients. All patients underwent induction chemotherapy after tumor resection, and 1 HDCT, and only 9 patients underwent 2 HDCT. 2 patients experienced a relapse of leptomeningeal seeding before the second HDCT, one of them died due to the progression of the disease. One patient died from treatment-related mortality during the first HDCT. Median days to neutrophil engraftment are 13.5(IQR 11.7-15.7) and 12(IQR 11-13) days, median days of fever after ASCT are 5.5(IQR 5.0-7.5) and 4(IQR 2-6), in first and second HDCT, respectively. Median follow-up days are 3.67 (IQR 2.32-6.87) years and 9 patients (75%) are under complete remission.
Conclusions: Tandem HDCT following chemotherapy to avoid radiotherapy under 3 years old showed promising results in relapse rate. But modifications to reduce the risk of HDCT should be considered.

EP305 / #348

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

HIGHLIGHTING THE USE OF METHYLATION PROFILING IN MOLECULAR SUBGROUP OF MEDULLOBLASTOMA PATIENTS IN A DIFFERENT CLINICAL OUTCOME AND SURVIVAL

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Background and Aims: Medulloblastoma (MB) is aggressive embryonal tumor representing the most frequent primary malignant brain cancer in children . It classify to four subgroup: wingless (WNT), sonic hedgehog (SHH), group 3, and group 4. Gene expression array, next-generation sequencing, and methylation profiling revealed that medulloblastomas harbor a paucity of mutations ,.Afew data from Saudi Arabia (SA) and Arab world studing the molecular subgroup and its clinical implications thus we conduct this study to illuminate our population gentic background and implication in clinical outcome and surivival.
Methods: In this study, we analyzed 23 samples of MB treated in a single institute through genome-wide DNA methylation and targeted next generation sequencing .
Results: we conduct an analysis of MB-DNA methylation patterns in cohort using archival biopsy material (n = 41). Of the 23 materials available for methylation assessments, 13 could be classified into the major DNA methylation subgroups . We preformed methylation profiling for our medulloblastoma patients from our archival FFPE biopsy of post treated patients in our institute. Our assessments revealed high survival rates observed for WNT tumors with exclusively 100% survival and more commonly in female. Strikingly more than half of our population is either group 3 or group 4 . group 3 showed the most aggressive outcome with all cases died due to relapse. Also we found that group 4 showing high metastatic and relapse rate with nearly 75% relapse rate complicated by death.
Conclusions: In conclusion, we demonstrate that DNA methylation profiling empower the sub-classification of four disease sub-groups in archival FFPE biopsy material from MB patients. Moreover, we conclude that the incorporation of DNA methylation biomarkers can significantly improve the accuracy of current disease-risk stratification These findings have important implications for future clinical disease management in MB cases across the Saudi Arabia and Arab world.

EP306 / #1331

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

MALNUTRITION RISK AND INTERVENTIONS FOR CHILDREN WITH CENTRAL NERVOUS SYSTEM TUMORS

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Background and Aims: Nutrition screening and intervention time are vital during childhood cancer treatment.Though some central nervous system (CNS) tumors present a greater nutritional risk than others. This study aimed to determine the nutritional status, daily food consumption amounts, and nutritional treatments applied in hospitalized patients with CNS tumors.
Methods: CNS cancer patients admitted to the Ege University Hospital pediatric oncology clinic between January 2018 and December 2021 (62 patients; n=29, 46.8% F, n=33, 53.2% M; median age:8.0 (1-17 years) were followed in this study. The nutritional status was evaluated within 24 hours of hospitalization, and nutritional therapy was started for the patients who needed it. Height, weight, upper-middle arm circumference (MUAC)), daily food consumption were taken.
Results: Malnutrition was observed in 46,8% (n =29), moderate risk 53.2%(n=33) according to StrongKids. Height for age was <25% in 33.9% (n=21) of the children, 25-75% in 35.5% (n=22) and >75% in 30.7% (n=19). Weight for age ranged from <25% for 22.6% (n= 27), 25-75% for 22.6% (n=14), and >75% for 34% (n=21). BMI according to age of 43.5% (n= 27) <25%, 37.1% (n=23) ranged from 25-75%, 19.4% (n=17) >75% is in the range. According to MUAC measurements, 45.2% (n=28) of the children were <25%, 35.5% (n=22) 25-85%, and 19.3% (n=12) >85%. Children can get mean 39.1% (min:0,max:115) of their daily energy requirements and 38.4% (mean:0, max:157) of their protein requirements with oral foods. Of the children (n=55) 67.2% (n=37) received <50% of their daily energy requirement and 77.3% of them <50% of their protein requirement by orally. 29% (n=18) of the children were fed with ONS, 32.3% (n=20) fed by EN, and 3.2% (n=2) fed by TPN.
Conclusions: The frequency of malnutrition is common in children with CNS tumors. Multidisciplinary teams regarding nutrition should monitor pediatric cancer patients, and nutritional intervention should be performed without delay when necessary.

EP307 / #1648

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

IMPROVEMENT IN SURVIVAL BUT STILL LOW AND SLIGHT INCREASE IN THE INCIDENCE TREND RATE OF PEDIATRIC BRAIN TUMORS IN ARGENTINA: ARGENTINE PEDIATRIC ONCOLOGY REGISTRY-INC(ROHA)2000-19

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Background and Aims: Objective: To present the incidence and survival trends of the pediatric brain tumor (BT) population in Argentina between 2000-19.
Methods: ROHA is a population-based hospital registry that has been active since 2000 and is part of the National Pediatric Program at the Ministry of Health's National Institute of Cancer. ROHA's network data comes from different sources; most are reported by pediatric oncology units from all regions in the country. Estimated coverage is 92%. Age-standardized incidence rate (ASR) trends were calculated using Joinpoint regression analysis, which was used to assess trends of age-standardized incidence rates over time, and to estimate their annual percentage of change (APC) with 95% of confidence intervals. OS was calculated using the Kaplan-Meier method and was reported at 5 years (between 2005-14), and 3 years (between 2000-04; 2005-09; 2010-12).
Results: 27,016 new cases of cancer were recorded between 2000-19 with ASR 131.6 (95% CI [124.5-138.6]); 19.7% (5,320) were BT with ASR 24.9 (95% CI [21.8-27.9]). Between 2000 and 2019, ASR in BT increased slightly (APC: 0.7%; 95% CI [0.2; 1.2]; p=0.01). OS at 5 years for BT was 56.4% (54.4-58.3) between 2005-2014 (n:2453). OS at 3 years was 50.5% (47.8-53.0) between 2000-05 (n:1421) compared with 58.9% (56.4-61.4) between 2006-11 (n:1515) and 63.8% (61.2-66.3) between 2012-16 (n:1413).
Conclusions: Discussion and Conclusion: The incidence of BT in Argentina is similar to other countries in Latin America; however, it remains lower than in North American and European countries. The increase in the BT trend could be related to a better registry of these cases. Although survival outcome improvement was observed, it is still lower than in most developed countries.

EP308 / #117

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

TREATMENT-INDUCED PULMONARY TOXICITY IN PATIENTS WITH MEDULLOBLASTOMA: A RETROSPECTIVE ANALYSIS ON 2 ITALIAN INSTITUTIONS' COHORTS.

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Background and Aims: Incidence of iatrogenic pulmonary toxicity is around 20%. Apart from bleomycin fibrosis, the role of lomustine, HD-thiotepa, autologous stem-cells transplantation(APBSCT) and their synergy with craniospinal irradiation(CSI) are unclear. To elucidate their role in lung-function impairment, we retrospectively evaluated 39 medulloblastoma patients treated at INT-Milan and OPBG-Rome.
Methods: 39 patients (17 females, median RT age 8 years) treated for localized(29) or metastatic(10) medulloblastoma in 2000-2020 and with spirometric assessment, were considered. Treatment included: SIOP-like-PNET IV(19), high-risk protocol(19), infant protocol without RT(1). CSI doses were: 23.4Gy(20), 31.2Gy(8), 36Gy(6) and 39Gy(4); 4 received protons and 34 photons(9 VMAT, 25 3D), 11 hyperfractionated-accelerated-RT; 33 had 6 median CCNU cycles; 6 APBSCT.
Results: Median follow-up: 98 months. All patients performed at least one spirometry at median 5 years after RT. Eight (20.6%) had mildly pathological spirometries, 8 Forced Vital Capacity (FVC%)<90%. RT age was not associated with FVC%/ PEF% (p=0.319 and 0.405). A lower Peak Expiratory Flow(PEF%) was marginally associated to APBSCT group (p=0.062) with FVC%(≤90% vs >90%) similar but less significant(p=0.163). Median FVC%/PEF% were higher in the CCNU-group without reaching significance (p=0.436 and 0.062): this was a standard-risk group not receiving APBSCT nor higher RT doses. Even though the lung volume encompassed by 5-10 Gy isodoses was greater in VMATvs3D RT(p<0.001 and p=0.015), there were no significant differences in ventilatory parameters. FVC%/PEF% were negatively associated to CSI dose. Since no relevant lung volume is involved in high doses, a multifactorial etiology could be speculated.
Conclusions: Preliminary data show no significant FVC%/PEF% reduction. Small sample size and differences in spirometry techniques impose larger cohorts accrual to elucidate potential treatment-induced pulmonary impairment in the pediatric population thus validating the use of spirometry during treatment/follow-up.

EP309 / #1926

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

DIFFERENCES IN LONG-TERM NEUROPSYCHOLOGICAL PROFILE IN PEDIATRIC SURVIVORS OF POSTERIOR FOSSA TUMOR (TFP) TREATED WITH PROTON RADIOTHERAPY (PRT) COMPARED TO PHOTON RADIOTHERAPY (XRT).

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Background and Aims: Ependymoma (EP) is a malignant glial tumor of the Central Nervous System (CNS). Represents 10% of all Posterior Fossa Tumors (PFT) in children. The standard treatment for children with histology of EP, both supratentorial and infratentorial, consists of maximal resection Surgery (CIR), followed by treatment with Radiotherapy (RT) and complementary forms with Chemotherapy (CT). Neuropsychological deficits are common and have a multifactorial origin.
Methods: The aim was to analyze whether new treatment protocols used with Proton Radiotherapy (PRT) minimize the vulnerability of long-term cognitive dysfunctions on cognitive functions, compared to the traditional treatment of Photon Radiotherapy (XRT), which is already known to be toxic on neurocognitive domains.
Results: A sample of pediatric patients followed by the Neurology Service of the Sant Joan de Déu Hospital, between 2002 and 2021, with a history of EP that differed in the modality of treatment with radiotherapy (XRT vs PRT) was included. Cognitive test scores for intelligence, memory, visuoconstructive functions and Executive Functions (EF) were obtained. The analyses compared the neuropsychological assessments of each subject greater than or equal to 3 years after treatment with RT between the treatment modality groups and ages of onset of TFP. The cognitive functions of 23 subjects (6 XRT, 7 PRT and 10 CIR) were analyzed. The PRT group obtained superior results in relation to the Intelligence Quotient (IQ) compared to the XRT group. The age of onset of less than 3 years turned out to be a determining factor on EF, regardless of the RT treatment received.
Conclusions: Our findings presuppose the protective factor of PRT in relation to XRT in cognitive functions, but at the same time, highlight the impact of brain damage at an early age of less than or equal to 3 years on long-term neuropsychological sequelae.

EP310 / #1951

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

PEDIATRIC CRANIOPHARYNGIOMA: DESCRIPTION OF THE LONG-TERM NEUROPSYCHOLOGICAL AND BEHAVIORAL PROFILE.

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Background and Aims: Craniopharyngioma is a type of benign brain tumor that affects the central nervous system (CNS). It has an intrasellar and / or suprasellar location, around the midline. It represents between 3 and 5% of childhood brain tumors. Treatment usually includes neurosurgery and radiation therapy (RT). Hypothalamic involvement of the tumor and secondary injuries to treatment lead to a high rate of hypothalamic obesity and neuropsychological deficits. Such long-term cognitive deficits will significantly affect academic performance and quality of life. T The main objective is to evaluate and determine a neuropsychological profile and the long-term academic development of children with craniopharyngioma compared to a healthy control group. In turn, the aim is to study the relationship between medical variables and cognitive deficits.
Methods: Between 2013 and 2020, a total of 16 subjects were assessed. 8 subjects (6 boys and 2 girls) were included. The inclusion criteria were: age between 6 and 18 years , and have a complete neuropsychological assessment of 1-2 years after the end of active medical treatment. The healthy control groupof the was matched by age and gender with the craniopharyngioma grup.
Results: Show statistically significant differences beetwen two groups in quotient intellectual (p-value = .010), focused attention (p-value = .005), working memory (p-value = .021), speed processing (p-value =. 010) and, emotional control (p-value = .006). Only age (onset less than 8 years) showed a high correlation with QI, language and attention focused. Variables such as the number of surgery and / or RT treatment were not related to neuropsychological variables.
Conclusions: Executive dysfunction and emotional dysregulation, as well as attention deficit it appears to be the neuropsychologycal profile. It is important to establish early rehabilitation programs.

EP311 / #1598

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

METASTASIC MEDULLOBLASTOMA: RADIOLOGICAL FEATURES AND ITS CORRELATION WITH MOLECULAR SUBGROUPS AND DISSEMINATION PATTERN

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Background and Aims: Medulloblastoma (MB) is the most frequent malignant childhood brain tumor. At least, four molecular subgroups have been described (WNT, SHH, group3, group4), which are associated with different biology, prognosis, specific MRI characteristics and patterns of metastatic dissemination. We aimed to determine the imaging features of metastatic MB, its molecular classification and their outcomes.
Methods: Retrospective institutional analytic-observational study conducted from January 2004-January 2022 in a tertiary-care center. Pediatric patients with metastatic medulloblastoma at disease onset were included. We collected epidemiological and clinical characteristics, treatment received, and outcomes. The molecular subgroup was determined by its methylation profile.
Results: In the study period, from sixty-three identified patients, 17 (26.9%) were metastatic. The median age at diagnosis was 5.1 years (range 2.1-17.5 years), and 58.8% were male. According to histopathologic classification, fifteen patients (93.8%) were classic,1 (6.3%) desmoplastic. Molecular subgroup analysis showed 2 WNT (12.5%), 1 SHH (6.3%), 3 (18.8%) group 3 (G3) and 5 (31.2%) group 4 (G4). Four patients (25%) were classified as G3/G4 and 1 (6.3%) as mixed. Five patients (29.4%) were M2 and 12 patients (70.6%) were M3 according to Chang staging system. Localization in the cerebellar hemispheres was only observed in the SHH patient. G3 tumors characteristically presented homogeneous contrast enhancement. All WNT, G3 and G4 were located in IV ventricle. We found no association between molecular subgroup and metastatic site (intracranial vs spinal, Fisher test, p=0.45). All patients with a metastatic lesion in the third ventricular infundibular recess were G4. Four patients died, all of them were either G3 or G3/G4.
Conclusions: Our results support what has been previously reported. Molecular subgrouping can be suggested based upon certain radiologic characteristics. In our cohort, the presence of a metastasis in the infundibular recess suggests group 4 MB. However, the dissemination pattern not was associated with any particular subgroup.

EP312 / #239

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

OUTCOME OF CHILDREN AND ADOLESCENTS WITH INTRACRANIAL GERMINOMA TREATED WITH CHEMOTHERAPY AND REDUCED DOSE IRRADIATION: A BRAZILIAN CONSORTIUM.

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Background and Aims: Primary central nervous system (CNS) germ cell tumors (GCT) are rare malignancies, classified according to their histological components and tumor markers (TM) as either germinomas or non- germinomatous germ cell tumors (NGGCT). The aim of the present study is to evaluate the outcome of germinoma patients treated with a Brazilian CNSGCT consortium protocol.
Methods: Since 2013, 57 patients with histology and/or TM consistent with CNSGCT were diagnosed, 43 cases of germinoma with/without HCGß levels ≤ 200mIU/ml, five between 100-200mIU/ml. The treatment plan consists of four cycles of carboplatin/ etoposide followed by 18Gy ventricular field irradiation and primary site(s) boost up to 30Gy, and 24Gy craniospinal irradiation for disseminated disease.
Results: Mean age 13.2 years (4.7-25.5y), 29 males. Diagnosis was made by TM (n=6), biopsy (n=25) and both (n=10). Two bifocal cases, with negative TM were treated as germinoma. Primary tumor location was pineal (n=18), suprasellar (n=14), bifocal (n=10) and basal ganglia/ thalamus (n=1). Fourteen demonstrated ventricular/ spinal spread. Second-look surgery occurred in two patients (residual/ teratoma). Thirty-six patients have achieved complete responses (CR) after chemotherapy, seven showed residual teratoma/ scar. Radiotherapy was performed as described, except in one case. Toxicity was mostly grade 3/4 neutropenia/ thrombocytopenia during chemotherapy. At a median follow-up of 40 months, event-free and overall survival is 100%.
Conclusions: This treatment is tolerable and VFI dose reduction to 18Gy preserves efficacy with excellent outcome, even in patients with HCGß levels between 100-200mIU/ml.

EP313 / #1586

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

SURVIVAL OUTCOMES OF CHILDREN AND ADOLESCENTS WITH BITHALAMIC GLIOMAS: MULTICENTRIC EXPERIENCE AND POOLED DATA ANALYSIS.

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Background and Aims: Bithalamic gliomas (BG) are rare brain tumours with distinct molecular alterations. Prognosis is dismal. We analysed patients with BG from two neurosurgical centres in London and two tertiary Paediatric Neuro-Oncology Units in UK and Spain.
Methods: Patients aged ≤18 years with clinico-radiological diagnosis of BG between 2000-2021 were eligible. Those with unilateral involvement at presentation were excluded. Clinical, radiological, histological, molecular, and survival data were collected. Pooled data analysis of reported cases with individualised data was performed.
Results: Sixteen patients were included. Median age 6.3 years (range, 4.1-17.9). Male:female ratio 1.3:1. Thirteen (81%) had histology at diagnosis: 7 (54%) low grade gliomas -LGG-, 6 (46%) high grade gliomas -HGG-. Seven (54%) had molecular profiling: H3K27-altered (n=4), H3 wild-type (n=3). Among H3K27-altered cases: EGFR and TP53 mutations (n=1); EGFR mutation (n=1); BRAF V600E, PIK3CA and TERT mutations (n=1); no oncogenic drivers found (n=1). Among H3-Wt cases: EGFR and TP53 mutations (n=1); PIK3CA and PTPN11 mutations (n=1); no oncogenic drivers found (n=1). Fourteen (88%) underwent radiotherapy, of which 11 (79%) received concomitant Temozolomide. One child had only chemotherapy (vincristine/carboplatin/etoposide) and another had no treatment (parental decision). Two patients received targeted drugs post-radiotherapy: sirolimus (limited tissue for molecular profiling, but mTOR activation on immunohistochemistry) and afatinib (EGFR mutation), respectively. Median overall survival (OS): 12.5 months (range: 3.7-188); three long-term survivors: 4.5 years (no biopsy), 11 years (HGG) and 15 years (LGG), respectively. No significant differences between the survival of patients with LGG or HGG. In the pooled data analysis (34 independent cases) median OS was 12.6 months (range: 12.4-160).
Conclusions: Survival of patients with BG is very poor regardless of the underlying histology, although anecdotal long-term survivors are described. EGFR and mTOR pathway alterations are relatively frequent. Access to targeted therapies upfront should be prioritised in clinical trials for individuals with BG.

EP314 / #1637

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

A COMPUTATIONAL FRAMEWORK FOR THE ANALYSIS OF CHILDHOOD CANCER GENOME DATA. APPLICATIONS TO MEDULLOBLASTOMA

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Background and Aims: The H2020 project 'individualizedPaediatricCure' (iPC, GA 826121) combines knowledge-based and machine learning approaches for paediatric oncology aiming to generate computational models to produce personalised diagnostics and therapies recommendations within a cloud-based platform. Here we introduce a computational framework that we have developed in the context of the iPC project for the analysis of childhood cancer genome data. The framework consists of two main components: (1) a model for the generation of synthetic data and (2) a graph-based model for functional analysis. Both models have been applied to the study of medulloblastoma.
Methods: The synthetic data generation model, namely an explainable variational autoencoder, can be used to augment and interpolate available omic data with synthetic instances, which are automatically annotated with confidence scores to assess their reliability. The graph-based model, namely a multilayer network, consists of multiple layers of bio-entities connected through relational associations, which capture the complexity of omic information despite the small sample size.
Results: We used the synthetic data generation model to study the gene expression characteristics of the four medulloblastoma subgroups (WNT, SHH, G3, G4) and, in particular, those underlying the unexplored relationship between G3 and G4 subgroups. Furthermore, thanks to the multilayer network model, we identified the minimal number of genes, outlined by proteogenomic data, that define molecular subgroups of medulloblastoma. This work is published in iScience (Núñez-Carpintero et al. 2021, doi: 10.1016/j.isci.2021.102365).
Conclusions: Both synthetic data generation and multilayer networks are emerging as dominant solutions for precision medicine as they enable addressing critical challenges for paediatric oncology such as privacy-preservation, small data modelling, and explainability and interpretation of computational analysis of genome data.

EP315 / #545

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

EPENDYMOMA IN CHILDREN: EXPERIENCE OF A SINGLE-CENTER IN ARGENTINA

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Background and Aims: Ependymomas are the third most common pediatric CNS tumors (6-10%). Standard of care is gross total resection +/-radiotherapy, with 5 years overall survival rate of 60-80%. New 2021 Who classification identified 10 types of tumors based on localization, histological features.and molecular characteristics. The aims are to report experience of an Argentinian single center in diagnosis, treatment and outcome of patients with ependymoma; and to describe reviewed molecular findings.
Methods: Retrospectively review of records and tumor samples of patients treated at Hospital de Niños Ricardo Gutierrez, between January 2013 and December 2020. Inmunohistochemistry and molecular techniques were done to detect RELA, N- Myc, H3K27me3 status
Results: From 233 patients with CNS tumors in this period, 33(14%) were ependymomas. 28 evaluable. Male/female ratio 1.25:1. Median age 60 months (r:8-204m). Localized disease: 26 (93%). All 28 patients undrwent surgery, achieving gross total resection in 62.9% of the cases. 64% received radiotherapy. Posterior fossa in 13p (46%). Ten were reclassified as PF-A due to H3K27me3 mutation. Six alive in CR (median follow up: 72 months), 2 alive with disease, 2 dead due to disease progression Three p were reclassified as PF-B and are alive in CR . Supratentorial 10p(36%). Five RELA positive: 4 p dead due to disease progression, 1 p alive with disease. Five p RELA negative: 3 dead due to disease progression, 2 alive (28 qnd 48 months off treatment) Spinal cord in 5p(18%). One with N- myc amplification. All alive without RDT.
Conclusions: Poor results in patients with supratentorial tumors could be due to lack of radiotherapy. Standard treatment at that time was limited to surgery alone when CR could be achieved. Patients with PF ependymomas had similar results to reported in the literature probably related to frontline radioteraphy for its treatment. This highlights importance of molecular biology to be able to adapt treatments.

EP316 / #1143

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

MEDULLOBLASTOMA IN CHILDREN LESS THAN FIVE YEARS OLD: A REVIEW OF 20 CASES FROM BRAZIL

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Background and Aims: Medulloblastoma (MB) is the most common malignant brain tumor in children less than three-five years. Histological variants consist of classic, MB with extensive nodularity (MBEN), desmoplastic/nodular (MBDN), large-cell/anaplastic and are staged based on extent of resection, dissemination and more recently, molecular stratification. The report aim is to present the outcomes of infant MB treated in a middle-income-country between 2016-2019.
Methods: In a retrospective analysis, 20 patients were treated according to a modified Head Start backbone protocol followed by myeloablative chemotherapy with autologous stem cell rescue (ASCR). Radiogenomics/ Immunohistochemical correlation was used to stratify into molecular subgroups: MB with wingless (WNT) activation, sonic hedgehog (SHH) activation and non-WNT/non-SHH MB.
Results: Mean age 2.6 years (1.5-4.8y), 12 males. Mean time to initial symptoms to diagnosis was 3.9 months (0.2-12months). Sixteen had complete resection, thirteen no metastasis. Fourteen were classified as MB-SHH, four with P53 protein >50% and six as non-WNT/non-SHH. Progression-free survival (PFS) and overall survival (OS) across the entire cohort was 46.2% and 72% at a median follow-up of 27.5 months. According to histology, PFS and OS for MBDN was 68.6% and 90%, for classic-MB 35% and 67.5%, respectively. Two MBDN patients relapsed, both with M+ disease and radiogenomics/immunohistochemical correlation with SHH-activation and possible Tp53 mutation (p53>50%); One patient died without disease due to Coronavirus + and meningitis four months after ASCR. Among relapsed classic-MB, one had M+ disease and SHH characteristics and the other three were classified as non-WNT/non-SHH: two also had M+, one with MYCC+ on histology. Both MBDN and two/four relapsed classic-MB are alive after salvage therapy with craniospinal irradiation.
Conclusions: We report the outcome of children less than five years with medulloblastoma treated in a middle-income-country, showing a very acceptable outcome despite difficulties in referral and in performing properly the molecular evaluation on a routine basis.

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Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

RISK FACTORS OF MEDULLOBLASTOMA: A 10 YEARS' EXPERIENCE OF A SINGLE CENTER

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Background and Aims: Medulloblastoma (MB) is the most common embryonal central nervous system (CNS) tumor in children. The aim of this study was to assess the molecular and clinical profiles of patients with MB diagnosed in our center, identifying the risk factors for treatment failure.
Methods: A 10years (2012-2021) retrospective analysis of the clinical and molecular profile of patients with MB was performed, taking into account histopathological assessment, molecular data (DKFZ/Heidelberg), extent of resection and response to treatment.
Results: Among 37 patients (22 males) with mean age 5.7years (9months-16years), surgical resection was performed in 34 (Gross Total:19, Partial:15), and only biopsy in 3 patients. Based on CSF cytology, brain/spinal MRIs the patients were characterized as M0 (20/37 patients), M2 (2/37), or M3 (15/37), according to the Chang staging system. Histologically, 30 patients were diagnosed with classic MB, 3 with desmoplastic MB, 3 with large cell/anaplastic (LCA) MB and 1 patient with an embryonal tumor, non-otherwise specified, in whom the diagnosis of MB was suggested by DNA methylation analysis. Molecularly, 18 out of 37 patients have been classified into WNT-activated Medulloblastoma (3patients), SHH-activated with TP53-wildtype (1 infant patient) or TP53-mutant (2patients: 1somatic / 1germline), Group 3 (4patients) and Group 4 (8patients). Germline alterations predisposing to medulloblastoma (NBN, APC, TP53) were detected in 3 patients. During the follow-up period (mean: 58months, range: 8.5-111months), 6 patients succumbed to their disease. Specifically, 2 patients with classic MB (1 classified as Group4) relapsed and succumbed to their disease 4 and 6 years after initial diagnosis, 2 patients with metastatic LCA-MB (1 classified as Group3) and 2 patients with metastatic classic MB-SHH-TP53mutant progressed rapidly under their initial treatment.
Conclusions: Our experience concurs with worldwide published series and shows that the initially disseminated form, anaplastic type, and specific molecular groups (Group3 and SHH-TP53mut) are the most important risk factors for medulloblastoma treatment failure.

EP318 / #675

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

A SINGLE CYTOSINE METHYL PCR-GENOTYPING BASED DECISION SUPPORT SYSTEM FOR RAPID CLASSIFICATION OF MEDULLOBLASTOMA

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Background and Aims: Classification of medulloblastoma (MB) into clinically relevant molecular subgroups (WNT, SHH and non-WNT/non-SHH) is critical for patient prognostication and treatment. Genome-wide DNA methylation profiling enables precise MB classification, however the implementation of this diagnostic approach in daily clinical practice is challenging for many centres worldwide. We have applied a novel approach for MB classification based on single cytosine-methyl PCR-genotyping analysis of a reduced set of subgroup-specific differentially methylated cytosines, and developed a decision support system for automated subgroup assignment.
Methods: We analysed DNA methylation microarray data of 4,741 samples (3,094 MB and 1,647 non-MB tumors), qPCR data of tumor samples (50 MBs and 10 non-MB tumors) and blood samples (6 healthy individuals). Synthetic double-stranded DNA was used for primer testing and qPCR control references. The multistep decision support system (DNA methylation status predictor and subgroup classification) was developed using binary-based classification algorithms.
Results: We designed, tested and validated allele-specific qPCR genotyping primers capable of discriminating between single base-pair changes representing differential methylation states. When tested with tumor DNA, primers showed specific hybridization enabling detection of the methylation state of 93% analysed cytosines, and manual classification of 84% of MB samples (100% concordance). By using binary discrimination algorithms, we developed a DNA methylation predictor that enabled automated analysis of qPCR data, and increased methylation status prediction capacity (AUC 0.978, accuracy 93.9% (95%CI [89.9-96.6%]; k=0.88)). A hard-decision decoding classifier was then developed and validated using multi-institutional DNA methylation microarray data (n=3,044). MB subgroups were assigned with an accuracy >90%. When tested with tumor DNA qPCR-data, the decision support system assigned samples to a MB subgroup with >95% accuracy (95%CI [82.25%-99.36%]; k=0.87).
Conclusions: We have developed a multistep decision support system that allows for simple, accurate and cost effective classification of MB tumors into clinically relevant subgroups using a qPCR, a widespread molecular technique.

EP319 / #564

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

CLINICO-EPIDEMIOLOGICAL PATTERN AND TREATMENT OUTCOME OF PAEDIATRIC MEDULLOBLASTOMA: A SINGLE INSTITUTIONAL EXPERIENCE IN NORTH EAST INDIA

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Background and Aims: Medulloblastoma is one of the most common malignant brain tumours of childhood with aggressive clinical behaviour. There is limited published data of paediatric medulloblastoma from developing countries like India. The aim of the study is to evaluate the clinico-epidemiological pattern and treatment outcome in paediatric medulloblastoma in a cancer care centre of North-East India.
Methods: In this retrospective study, we analyzed the medical records of 52 children diagnosed with medulloblastoma at Dr. B. Borooah Cancer Institute, Guwahati, Assam from 2015 to 2019.
Results: The median age of diagnosis was 8±3.5 years (range 1-15 years) with male: female ratio of 2.25:1. Headache (73%), vomiting (69.2%), unsteadiness (46.1%) and cranial nerve palsy (11.5%) were the common presenting features. Staging showed that 39 (75%) patients presented with localised disease, 5 (9.6%) patients with malignant cells in CSF, 6 (11.5%) with spinal involvement and 2(3.8%) with distant metastasis. Majority of the patients (59.6%) had high risk disease. Ventriculo-peritoneal shunt was needed for 37(71.1%) patients. Thirty (57.6%) patients underwent total/near total excision and 19(36.5%) had subtotal excision. Four (7.6%) patients below 3 years of age received chemotherapy only. Thirty eight (73.07%) patients received craniospinal radiation upto 36 Gy followed by posterior fossa boost upto 54 Gy with concurrent vincristine. Adjuvant chemotherapy was received by 18 (34.6%) patients. Majority (48.7%) patients showed partial response and only 3(5.7%) achieved complete response. Among these 52 children, 9 (17.3%) refused treatment. Progression free survival at 2 year, 3 year and 4 year were 42.3%, 28.8% and 19.2% respectively. Overall survival at 2 year, 3 year and 4 year were 48.07%, 34.6% and 21.1% respectively. Most common treatment related toxicity was febrile neutropenia (23%).
Conclusions: The epidemiological patterns are quite similar to the worldwide data. The survival rates are low as compared to other studies because of poor follow up data.

EP320 / #1102

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

A NATIONAL PEDIATRIC NEURO-ONCOLOGY TUMOR BOARD INITIATIVE IN SPAIN: RESULTS OF A WEB-BASED SURVEY TO EVALUATE PARTICIPANT EXPERIENCE UTILIZING THIS RESOURCE

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Background and Aims: The Spanish Brain Tumor Group of the Spanish Pediatric Hematology-Oncology Society (SEHOP) launched in January 2020 an initiative to allow Pediatric Oncologists to weekly present their cases to the group. Between January 2020 and February 2022, 56 cases were reviewed. This survey explored the participants' experience utilizing this resource.
Methods: A cross-sectional electronic questionnaire was distributed to 35 participants in 24 institutions through email.
Results: Twenty-six respondents (74%) from all the participating institutions completed the survey. All participants (100%) found this a great initiative. Seventy-six percent found the contact form easy, and 73.1% the format convenient. Only 1 person had internet connectivity problems. Thirty-one percent reported frequent-attendance (75-100% meetings), 50% reported mid-attendance (50%), and 19% low-attendance (<25%). The most frequently reported attendance-barriers were the subspecialist's workload (44%), the timing of the teleconference (44%). More than 70% of attendees found the frequency and duration of the teleconference were sufficient. Cases were presented at diagnosis (42%), at first relapse (23,1%), or >/= second relapse (31%). In >90% the decisions suggested were very helpful, appropriate and reinforce the decisions of the presenter. In 77% of the cases, some complementary study was performed outside the consulting center, mainly methylation studies. The recommendations were followed in almost all cases, were transmitted to the rest of the multidisciplinary team and were generally well received, being considered an improvement in the quality of care. In all cases the decision was transmitted to the families and 92% of those surveyed reflect it in the patient's medical history. All the participants recommend professionals to share their cases and would do so again themselves.
Conclusions: The Spanish Pediatric Tumor Board initiative provided a valuable tool for the management of pediatric brain tumors in Spain as it provided a feasible and easy to access continued medical education opportunity for the participants.

EP321 / #620

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

REMISSION OF HYPOTHALAMIC OBESITY IN PEDIATRIC-ONSET CRANIOPHARYNIOMA DURING INTERFERON-BASED TUMOR TREATMENT

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Background and Aims: Craniopharyngioma is a rare tumor arising from the craniopharyngeal duct. Proposed treatments include surgical resection, local irradiation, intracystic and/or systemic interferon-alpha. Although long-term survival rates are high and metastatic potential is low, local recurrences and damage to adjacent structures from the tumor, surgery and/or radiation often result in endocrine and metabolic complications. Hypothalamic obesity (HO) is reported in 65-80% of craniopharyngioma patients after aggressive surgical resection. HO significantly impairs health-related quality of life, remains difficult to treat, and may reduce survival. We aim to describe the association between systemic interferon therapies and the trajectory of BMI in pediatric patients with craniopharyngioma-associated HO.
Methods: Subjects entered into an IRB-approved database at a single institution between 2000-2021 with the aim of determining progression free survival included children with craniopharyngioma treated with systemic interferon (Peginterferon alfa-2b, Interferon alfa-2b, or Peginterferon alfa-2a). We analyzed BMI trends before, during and after interferon therapy. Obesity was defined as BMI >/=95%tile.
Results: Twenty-three children (12F/11M) were diagnosed with craniopharyngioma at a median age 6 years. At diagnosis, 3 subjects (13%) were obese. At initiation of interferon, 8 subjects (35%) (4F/4M) were obese with median BMI 26.6 kg/m2, median standardized BMI (SDS) 2.47. Among these 8 obese subjects, 7 had reduction in BMI during interferon therapy (median duration 9 months) and one increased in BMI. Median BMI after interferon was 23.1 kg/m2, BMI SDS 2.0). The BMI reduction in obese children during interferon was followed by rapid rise in BMI in all who stopped interferon, except for one.
Conclusions: Systemic interferon-based therapy for craniopharyngioma may be considered an option for tumor control and may have specific off-target benefits in patients who present with co-morbid HO. Additional research is needed to understand the impact of interferon associated weight loss on body composition, weight-related co-morbidities, and quality of life.

EP322 / #1110

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

HIGH-GRADE AND DIFFUSE INTRINSIC PONTINE GLIOMAS IN GREEK PEDIATRIC PATIENTS: FIRST NATIONAL REPORT

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Background and Aims: The main characteristics of pediatric high-grade-gliomas (HGG) worldwide are aggressive clinical and biological behavior, high morbidity and mortality. Data from national registries, on this entity are lacking
Methods: All 7, pediatric hematology-oncology centers in Greece participated in this retrospective study that covered the period between 1/2012-12/2021. Demographics, tumor characteristics and outcome were analyzed.
Results: During the study period, 65 patients(36 females), median age: 8.48y(range:3 days-16.9y) were enrolled. The most common tumor-location were brainstem(41/65patients) and parietal lobe(12/65patients). DIPG based on imaging studies only was diagnosed in 29patients (9/29underwent biopsy). Surgical intervention was performed 46patients(VP-shunt insertion:9, biopsy:24, partial resection:12, total/subtotal resection:6). Histological diagnosis was feasible in 42patients(16 brainstem-tumors). Astrocytoma gradeIV was diagnosed in 78.6%(33/42) and gradeIII in 21.4%(9/42). Of notice, 3 patients with initial histological findings of low-grade (2gradeII and 1gradeI), were upgraded to gradeIV following molecular and DNA-methylation analyses. Out of the 16 biopsied midline-tumors, 9 had a positive H3K27M-immunohistochemistry (diffuse-midline-glioma, DMG), Furthermore, 6/20 patients had H3F3A-mutation, 4/20 EGFR-overexpression and 3/20 PTEN-loss. Six patients were elected by their caregivers to receive treatment in other countries. Patients>3years of age (52/59) were treated upfront mainly according to HIT-HGG2013 Protocol with radiotherapy-temozolomide (46/52patients). In 6DIPG-patients, following progression, re-irradiation resulted in temporary symptomatic improvement. In 4 of them, nivolumab was also administered. The most common regimen for HGG-patients upon progression was bevacizumab with irinotecan or CCNU. In 7 patients, targeted therapy was administered after end of RT, based on molecular results (3patients mTOR-inhibitor, 2patients Tyrosine-kinase-receptor inhibitor, 1MEK-inhibitor and 1 MET-inhibitor). Overall survival was 58.8%(95%CI32.5-77.8), 41.2%(95%CI18.5-62.6) and 2.3%(95%CI4.3-38.3) at 1, 2 and 3 years respectively. Median overall survival time was 1.29 years.
Conclusions: Our national experience concurs with worldwide published series and shows that pediatric HGG and DIPG, despite aggressive treatment continue to have a grave outcome, urgently needing other type of approaches. Re-irradiation may offer short survival prolongation.

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Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

COMPLEX TREATMENT EFFECTIVENESS IN PATIENTS WITH RELAPSED MEDULLOBLASTOMA, RM GORBACHEVA RESEARCH INSTITUTE EXPERIENCE

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Background and Aims: Medulloblastoma (MB) is the most common central nervous system malignancy in pediatric population. Despite majority of patients with MB achieving remission the prognosis in relapsed cases is still dismal. Complex intensive therapy including high-dose chemotherapy (HDCT) with autologous hemopoietic stem cell transplantation (auto-HSCT) could improve treatment results.
Methods: A total of 60 patients with relapsed MB received auto-HSCT in 2008-2021. The median age at relapse was 11.5 (5.0-37.0) years. Histological subtypes were classic (n=43), desmoplastic (n=12) and anaplastic (n=5). Molecular subgroups were assessed in 23 patients: WNT (n=2), SHH (n=7), Gr.III (n=2), Gr.IV (n=12). MYC and MYC-N amplification was found in 2/19 cases investigated. All patients received polychemotherapy prior to auto-HSCT achieving complete (CR, n=21), partial response (PR, n=32) or stable disease (SD, n=7). In most (n=57) cases Carbo-Eto-Thio HDCT regimen was used. Subsequently, 34 patients received craniospinal irradiation (CSI, n=23) or local radiation therapy (RT, n=11).
Results: Engraftment at a median of 13 (8-37) days past transplant was registered in 53/60 cases. With a median follow-up of 30 (0.1-164) months from auto-HSCT the 3-year overall survival (OS) is 56.8% (95%CI 42.9%-68.5%), event-free survival (EFS) is 29.8% (95%CI 18.8%-41.6%). All but 2 patients with pre-transplant SD died due to disease progression, one still has CR. The better OS and EFS were observed in RT recipients (68.7% and 36.9% vs. 40.0% and 16.7%, accordingly; p=0.005) and patients with classic MB (87.2% and 41.5% vs. 22.2% and 8.3%, accordingly; p=0.002). Grade 4 (CTCAE V 5.0) complications developed in 19.4% cases. Cumulative transplant-related mortality was 11.7% (95%CI 1.1%-35.9%).
Conclusions: Despite relatively high toxicity the complex therapy regimen allows achieving response in significant number of patients with relapsed MB. HDCT with auto-HSCT is effective in patients with CR and PR. RT improved HDCT results in assessed cohort.

EP324 / #541

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

OPTIC PATHWAY GLIOMAS IN CHILDREN: DEMOGRAPHIC, CLINICAL CHARACTERISTICS AND RESULTS OF AN ADAPTED PROTOCOL

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Background and Aims: Optic pathway gliomas (OPG) constitute 1-5% of childhood brain tumors. The aim of this study is to evaluate patients with optic pathway gliomas diagnosed/treated/ followed in a single center.
Methods: The medical files of 95 patients with OPG diagnosed/treated between 1990-2021 in the Istanbul University, Oncology Institute were retrospectively assessed for demographic, clinical characteristics, treatment and outcome.
Results: The median age of 95 patients (48 male, 47 female) was 54 (1-216) months, 58 (61.1%) had NF-1. Seven had diencephalic syndrome (7.4%). Twenty-seven(28.4%) had Dodge 1, 30(31.6%) Dodge 2 and 38(40%) Dodge 3 disease. Median follow up was 10.5 years (1-31 years). Nineteen (20%) patients had stable disease and were followed without treatment, 24 patients underwent surgery, 6 patients recieved radiotherapy (RT). 65 patients received chemotherapy (CT) due to symptomatic/progressive disease. Chemotherapy consisted of (adapted SIOP-LGG regimen) vincristine (VCR) 1.5 mg/m²/dose and carboplatinum 550 mg/m²/dose every 21 days for three courses with weekly VCR, followed by VCR and carboplatinum every 28 days for a total of 12 cycles (3 cycles induction, 9 cycles consolidation). Ocular findings in 86 patients were, vision was stable in 67(77.9%), improved in 18(20.9%), detoriated in 1(1.2%). Radiology (MRI) revealed stable disease/regression of tumor in 79 patients, and complete regression of spinal metastasis in 1 patient. Endocrinologic follow-up was done. Ten year overall survival(S) in all patients, in patients with NF1 and without NF1 were 96%, 98% and 92%, respectively; 10 year event free survival (EFS) in all patients, in patients with NF1 and without NF1 were 83%, 87.6% and 77.5% respectively.
Conclusions: In children with , symptomatic/progressive OPG, chemotherapy with an adapted regimen consisting of vincristine and carboplatinum for a total of twelve courses seems to be effective and provides a relatively good quality of life. Radiotherapy should be avoided especially in patients with NF-1.

EP325 / #1767

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

GERMLINE PTCH1 AND SUFU MUTATIONS IN PATIENTS WITH INFANT SHH MEDULLOBLASTOMA.

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Background and Aims: Germline mutations in PTCH1 and SUFU are the main causes of basal cell nevus syndrome (BCNS, Gorlin syndrome, GS) detected in 2% patients with medulloblastoma (MB), exclusively in SHH MB subgroup. The aim of the study was to investigate the incidence of Gorlin's syndrome and clinical outcome in the SHH MB cohort.
Methods: We analyzed a cohort of 19 patients (pts) with infant SHH MB (age < 3y/o) diagnosed between 2016 and 2020.
Results: The diagnosis of GS was genetically confirmed by NGS in 5 patients, among them 2 had PTCH1 and 3 had SUFU germline mutations. As to SUFU mutations, c.895C>T, p.(R299X) (rs1590066162) was found in 2 pts and c.708_711del, p.(D237Cfs*29) was not previously described. PTCH1 variants (c.290dupA, p.(N96Kfs*43) (rs1554708751); c.1160G>A, p.(W387*)) were previously described in pts with Gorlin syndrome. In two cases de novo status of mutations was confirmed (1 PTCH1, 1 SUFU), three others were family cases. Among these 5 pts with GS, the median age of MB manifestation was 18 months. Macrocephaly was presented in 4 pts and in 3 pts had high birth weight. Development delay was documented in 2 out of 5 pts. Histologically there were 4 MBEN and 1 DNMB. All pts received chemotherapy according to the HIT SKK protocol (3 SKK cycles followed by 2 modified SKK cycles). Intraventricular methotrexate was administrated in all cases. All patients are in complete remissions after the end of treatment with a median follow up for 3.1 years.
Conclusions: The incidence of Gorlin syndrome in our group of infant SHH is 26%, which is comparable to Waszak et al. data. HIT-SKK regimen with intraventricular methotrexate is an effective treatment option for these patients.

EP326 / #1362

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

PROFILE OF PAEDIATRIC OPTIC GLIOMAS - EXPERIENCE FROM A TERTIARY CARE CENTRE IN SOUTH INDIA.

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Background and Aims: Optic Pathway Gliomas(OPG) account for 3–5% of paediatric brain tumours. Profile and outcome data of these tumours from developing countries is limited. AIM- To study the clinical spectrum, imaging, treatment regimens and outcome in patients with OPG at our tertiary care paediatric oncology centre and our collaborating ophthalmology centre.
Methods: A retrospective descriptive study of paediatric patients diagnosed with OPG from 2018 to 2022. Clinical characteristics, radiological, treatment details, ocular assessment and overall outcome were analysed.
Results: Twenty patients were diagnosed with OPG during the study period. Seventy five percent were male. Mean age at diagnosis was 7.55 years. Neurofibromatosis-1 was present only in 15%. Visual disturbances, proptosis were the major symptoms in 80% and 70% respectively. Mean duration of symptoms was 7 months. Bilateral eye involvement was noted in 10%. Visual acuity was diminished in 95% of patients at diagnosis. Relative-Afferent-Pupillary-Defect was seen in 10 patients. Visual-Evoked-Potential (VEP) was done in 11 patients and 90% had delayed latency. Thirteen patients had isolated optic nerve, three had isolated chiasmal and four had involvement of both structures. Four patients were under observation (low risk features) with periodic evaluation, 3 were lost to follow up at diagnosis, 8 patients received only chemotherapy (Vincristine-carboplatin), 2 had undergone debulking surgery and 3 patients received radiation (54 Gy) in view of inadequate response to chemotherapy. At last follow-up, 12 patients underwent visual-assessment of which 75% had persistent abnormal fundus and 30% had delayed latency in VEP. Six patients were stable, 3 had progression of disease and 3 patients improved radiologically. No death was reported.
Conclusions: Patients with OPG usually present with nonspecific visual symptoms. Early diagnosis and multi disciplinary management can help stabilize the disease, prevent progression and improve outcome in these patients. However, targeted therapy for this rare paediatric tumour needs to be explored by clinical trials.

EP327 / #1911

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

BRAIN TUMOURS AT MBINGO BAPTIST HOSPITAL IN CAMEROON: IMPROVED DIAGNOSIS WITH MORE IMAGING CAPACITY

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Background and Aims: Introduction Reliable diagnostic capacity is required for effective childhood cancer management and epidemiology. In 2017, computed tomography (CT) was acquired at Mbingo Baptist Hosptial (MBH) with a qualified radiologist. Earlier analysis of existing hospital-based paediatric oncology registry reported a rarity of brain tumours. Our aim was to investigate the epidemiology and outcome of paediatric brain tumours at MBH.
Methods: Method This was a retrospective study by review of records of children below 15 years with brain tumours from September 2017 to December 2021. A case review form was used to abstract data on demographics, clinical presentation, management and outcome. Only descriptive analysis were reported.
Results: About 1700 CT scans have been performed at MBH in the study period of which 20 were children below 15 years with brain tumours; 9 males and 11 females. The diagnoses were medulloblastoma (n=4); ependymoma (n=4); brain stem glioma (n=3); and metastatic neuroblastoma (n=1) ,eight other children did not have diagnosis . The commonest presenting symptoms were headache (5, 25%), hemiplegia (3, 15%), vomiting (3, 15%), impaired vision (5, 25%) and status epilepticus (1, 5%). Eight had a ventriculo-peritoneal shunt, three were referred to another specialized hospital, two referred abroad, two patients had surgery and chemoradiation, one patient had only surgery, two placed on palliative care only, and two refused treatment. After a median follow up of twelve months, ten (50%) are alive, five (25%) dead and five (25%) lost to follow up.
Conclusions: Conclusion The availability of CT and the services of a radiologist at Mbingo Baptist Hospital has enabled the diagnosis of brain tumours. Pursuant to this study, there are ongoing efforts to implement and establish a network of referral for effective specialist management of brain tumours.

EP328 / #291

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

METASTATIC DIA/DIG: MOLECULAR CHARACTERIZATION AND TREATMENT RESPONSE

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Background and Aims: Desmoplastic infantile astrocytoma (DIA) and desmoplastic infantile ganglioglioma (DIG) are glioneuronal tumors of early childhood. Surgical resection is usually sufficient to cure these benign tumors. The presence of metastatic seeding is rare and has been reported as an adverse prognostic factor. We present 2 cases of children with recurrent metastatic DIA/DIG to describe their therapeutic management and outcome and to highlight the importance of molecular characterization of these rare tumors to guide adjuvant therapy.
Methods: Description of 2 cases including clinical presentation and response evaluation by MRI.Tumor burden was evaluated by calculating the sum of the maximum bi-perpendicular dimensions of the 3 most dominant lesions on MRI.
Results: The first patient developed metastatic recurrence after initial gross total resection (GTR) of localized DIG. Relapse was treated with monthly carboplatin and vincristine (CB/VCR). Complete response (CR) was achieved after 15 cycles and the patient has remained in CR for 5 years. Post-hoc molecular analysis of the tumor revealed a BRAF-RDX fusion. The second patient presented with a disseminated intraventricular relapse following an incomplete resection of a DIA associated with SPECC1L-NTRK2 fusion. Patient received 2 cycles of CB/VCR with minimal response and was then switched to Larotrectinib. The patient demonstrated positive treatment response with 67% and 77% decrease in tumor burden on follow-up MRI at 3 months and 6 months, respectively .The patients has remained on treatment since then with significant clinical improvement.
Conclusions: In our 2 cases, metastatic recurrence was responsive to adjuvant therapy leading to CR with conventional chemotherapy in one and to VGPR with NTRK inhibitor for the second patient. Early molecular characterization of these benign tumors is critical in case of incomplete resection or metastatic seeding to widen therapeutic options and maximize chance of cure. Response with NTRK inhibitor appears rapid and significant but the total duration of treatment remains unknown.

EP329 / #1049

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

INTRATUMORAL HEMORRHAGE IN PEDIATRIC LOW-GRADE-GLIOMAS: AN INTERNATIONAL CASE SERIES.

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Background and Aims: Pediatric low-grade gliomas (PLGG) are grade I and II WHO tumors. Intratumoral hemorrhage is a common complication (up to 8-20%), not well reported in the literature. It can happen at diagnosis, treatment, or follow-up. We have collected an International cohort of PLGG which developed an intratumoral hemorrhage.
Methods: International, multicentric, observational, descriptive and retrospective analysis of 28 patients with a PLGG who suffered an intratumoral hemorrhage. We gathered data on demographic characteristics, histology, molecular findings, treatment received, and information related to the hemorrhagic event.
Results: Twenty-eight patients were enrolled onto the study. Median age at tumor diagnosis was 10.1 years (range, 0.4 to 17.5 years). Three patients (10.7%) had a cancer predisposition syndrome (2 Neurofibromatosis type 1 and 1 Noonan syndrome). Most frequent histological subtypes: pilocytic astrocytoma (67.8%), pleomorphic xantoastrocytoma (10.7%) and pilomyxoid astrocytoma (7%). The most common locations: hypothalamic-chiasmatic (32.1%) and posterior fossa (25%). BRAF status was available in 16 patients (4 had a KIAA1549BRAF fusion and 2 a BRAFV600E mutation). NGS was performed in 10 patients, four of them had an FGFR alteration. Regarding therapy, all patients had initial surgery, with 42.8% needing further surgeries. Seventeen patients (60.7%) received at least one chemotherapy regimen, and six patients (21.4%) received radiotherapy. Twenty-four patients (85.7%) had a spontaneous intratumoral hemorrhage; other etiologies were post-traumatic (10.7%) and post-surgical (3.6%). In thirteen patients (46.4%), the hemorrhages occurred at the time of diagnosis. The main treatment strategies were surgery and observation (39.2% each group). Two patients (7.1%) died because of the bleeding event. To date, 75% of the patients are alive, although 4 of them (14.2%) had a recurrence of their hemorrhage.
Conclusions: Pediatric low grade gliomas are at risk of intratumoral hemorrhage, which occurs usually at diagnosis and spontaneously. Despite being a life-threatening situation, mortality and recurrence rates are low in these patients.

EP330 / #1050

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

PROGNOSTIC SIGNIFICANCE OF TUMOR METHYLTRANSFERASE ACTIVITY IN CHILDREN WITH DE NOVO METASTATIC MEDULLOBLASTOMA: RESULTS OF INTERCENTER PILOT STUDY

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Background and Aims: The aim of this study was to estimate event-free survival (EFS) according to the activity of tumor methyltransferases.
Methods: From 2017 till 2018 nineteen patients were included in trial. Children underwent adjuvant therapy: ArmB (n=11) - vincristine/cyclophosphamide/cisplatin/etoposide (OPEC)-based induction, CSI 36Gy + local RT to the tumor bed up to 54Gy with 5-azacytidine, 1 cycle OPEC and 2 cycles thiophosphamide/carboplatin with auto stem cell transplantation (auto-SCT); ArmC (n=8) - cyclophosphamide/cisplatin-based induction, CSI 23.4 Gy followed by 2 cycles 5-azacytidine/thiophosphamide/carboplatin with auto-SCT, local RT with 5-azacytidine. All patients was older 3 years, male/female ratio 11/8. R1 status was revealed in 10 patients, M1, M2, M3 status – in 1, 6 and 12 out of 19. Classic histological variant was identified in 16 tumor samples, large cell/anaplastic – in 3, MYC gene amplification in 1, MYC-N gene amplification in 3 (2 of them with TP53 mutation), Iso17q in 6. Molecular groups were determined in 12 samples (SHH – 2, Group3 – 3, Group4 – 7). MGMT and DNMT1,3a,3b proteins expression was assessed by immunohistochemical method in 19 samples (Score 0-3 – no/weak, Score 4-12 – moderate/strong).
Results: 3-year EFS was 54.5% in armB, 50.0% and in armC, median follow-up 29.8 ± 5.8 and 37.7 ± 9.1 months (p=0.915). Moderate/strong MGMT and DNMT1,3a,3b proteins expression was revealed in 8, 12, 10, 8 out of 19 tumor samples. All tumor samples with MYC/MYC-N gene amplifications were characterized by moderate/strong level of DNMT1 protein expression. There was not determined any prognostic significance of these proteins expression according to age group (3-7 years and older), gender, M+ variants, molecular group (SHH/Group3/Group4).
Conclusions: There are not enough patients in both arms to understand the predictive value of the activity of tumor methyltransferases. It is necessary to continue the study of these markers, especially in group with MYC/MYC-N gene amplification.

EP331 / #1501

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

PROGNOSTIC SIGNIFICANCE OF REDUCED-DOSE AND REDUCED-VOLUME RADIOTHERAPY IN CHILDREN WITH DE NOVO MEDULLOBLASTOMA: RESULTS OF INTERCENTER PILOT STUDY (LIKE-SJMB03)

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Background and Aims: The aim of this study was to estimate event-free survival (EFS) depending on the R/M group and therapeutic approaches.
Methods: From 2008 till 2016 forty eight patients were included in trial. Children underwent adjuvant therapy: for R0M0 – CSI 23.4Gy, for R1M0 and R0/1M+ – CSI 36.0Gy (instead of 39.6Gy and additional irradiation to the metastatic sites up to 50.4–55.8Gy for M2/M3) + local RT to the tumor bed up to 54Gy (instead of 55.8Gy and primary site up to 59.4Gy for R1) followed by 4 cycles vincristine/cyclophosphamide/cisplatin with auto stem cell transplantation. R0M0: n=25, 3–7 years of age/older – 13/12, vermis and 4-th ventricle/cerebellar hemisphere (primary site) – 21/4; tumor samples – classic/LCA/desmoplastic histology in 22/2/1, MYC-N amplification in 1, Iso17q in 2, WNT/SHH/Group3/Group4/no data in 3/1/3/8 and 10. R1M0: n=8, 3–7 years of age/older – 5/3, vermis and 4-th ventricle/cerebellar hemisphere – 8/0; tumor samples – classic/LCA histology in 7/1, Iso17q in 2, WNT/SHH/Group3/Group4/no data in 1/0/1/2 and 4. R0/1M+: n=15, 3–7 years of age/older - 10/5, vermis and 4-th ventricle/cerebellar hemisphere – 12/3; M1/M2/M3 – 4/2/9; tumor samples – classic/LCA/desmoplastic histology in 13/1/1, MYC amplification in 1, MYC-N amplification in 2, Iso17q in 4, WNT/SHH/Group3/Group4/no data in 1/2/3/6 and 3.
Results: 5-year EFS was 82.0% in R0M0 group (6 relapses – 1 WNT, 1 SHH, 3 Group4, 1 secondary osteosarcoma in Group3, 2 events after 5 years), 3–7 years of age/older 88.9% and 58.3% (p=0.044); 62.5% in R1M0 group (progression – 1 Group3, relapse – 1 Group 4, 1 case with fatal septic complication); 33.3% in R0/1M+ group (8 relapses – of them 1 SHH, 1 Group3, 3 Group4; progression – 1 Group3, 1 case with fatal septic complication).
Conclusions: Reduced-dose and reduced-volume radiotherapy led to a significant decrease in the EFS rate in children with R1M0 and R0/1M+ status.

EP332 / #1335

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

NATIONAL EXPERIENCE AND USEFULNESS OF CENTRALIZED PATHOLOGICAL AND MOLECULAR REVIEW IN PEDIATRIC MEDULLOBLASTOMA.

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Background and Aims: The implementation of molecular information is critical in the classification of pediatric medulloblastoma (MB). It´s mandatory not only for the inclusion of cases in clinical trials, but also for the initial diagnosis/management. This information should be reviewed and complemented when it's no available in some centers. We reviewed the implementation of molecular subgrouping-classification at national level, since it was included in the centralized pathological review.
Methods: Multi-center centralized prospective and retrospective study of frozen and FFPE tumor samples at diagnosis of pediatric MB patients from national hospitals, from February 2021 to March 2022. Local pathology, centralized histology review, immunohistochemical (IHC) subgrouping, and a molecular subgrouping based on the Minimal Methylation Classifier (MIMIC) from Schwalbe et al., 2017 were performed.
Results: Forty-eight cases were analyzed, 33 were prospective, and 45 in frozen tissue. Locally, 45.8% did not have any subgrouping classification information. The centralized review subclassified all cases using IHC. MIMIC classified in the non-WNT/non-SHH, 5 tumors (10.4%) in Group 3 and 29 (60.4%) in Group 4. WNT-activated were 3 cases (6,3%) and SHH-activated 7 (14.6%). 4 cases (8.3%) were unclassified (2 FFPE and 2 WNT, classified by IHC, monosomy 6 and CTNNB1 mutational status) Comparing with local diagnosis, the centralized review showed changes in initial histology in 9 cases (18.7%), and subgrouping classification remained the same in 6 cases (12.5%). In 4 cases (8.3%) the diagnosis changed, and in 38 cases (79.2%) the molecular subgrouping classification was added. .
Conclusions: The centralized pathological and molecular review in pediatric MB has allowed us to have a complete and homogeneous information in the initial classification of these tumors. Not all centers have this information available at diagnosis, and a centralized review at a national level allowed confirmation of the pathology and added this information in a significant number of cases.

EP333 / #1096

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

NEUROCOGNITIVE FUNCTIONS IN CHILDREN SURGICALLY TREATED FOR BRAIN TUMORS: A PRELIMINARY REPORT.

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Background and Aims: As survival outcomes in children with brain tumors have been improving over time, cognitive sequelae of treatment are becoming of interest. However, the role of histology and surgery in the development of these cognitive deficits remains unclear. This study aimed to evaluate cognitive functioning in children with brain tumors before and after surgery.
Methods: All children with a new diagnosis of primary brain tumor were prospectively assessed. Neurocognitive evaluations were performed at diagnosis (T0) and within 14 days after surgery (T1). Intelligence quotient, language, learning and memory, attention, executive functions, visuo-constructional and sensorimotor skills were explored.
Results: Twenty patients (12 males, mean age 10.6±3.2 years) were enrolled between January 2019 and December 2021. Tumor localization was mainly supratentorial (11/20, 55%). The histological type was low-grade in 9/20 (45%) patients and high in 11/20 (55%). All children underwent surgery, with gross total resection in 15/21 (71%) cases. At baseline, patients showed significant major deficits in sentence repetition ($p=0.002$), phonemic fluency ($p=0.03$), direct span ($p=0.006$) and copy design tasks ($p<0.001$) in comparison to normal values. Intrapatient evaluations did not change between T0 and T1. Children with low-grade lesions did not differ from those with high-grade disease for baseline and clinical characteristics. At T0, the high-grade group showed lower scores than the low-grade in the Rey-Osterrieth Complex Figure B test (5.6 ±4.4 vs 12.2±0.9; $p=0.01$) evaluating visuospatial memory. No significant difference emerged for T1 evaluations.
Conclusions: Children with brain tumors may present several neurocognitive deficits in memory and visuospatial capabilities, particularly those with high-grade diseases. Surgery, even when radical, didn't impact cognitive functions in our population, independently of grading. Prospective protocols with baseline and periodic neurocognitive evaluations should be encouraged to early detect functional difficulties and develop a tailored treatment approach for the patient.

EP334 / #971

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

PHYSICAL, PSYCHOLOGICAL AND QUALITY OF LIFE EFFECTS OF HORSE-ASSISTED REHABILITATION IN CHILDREN AND ADOLESCENTS AFTER ONCOLOGIC TREATMENT: RANDOMIZED OPEN LABEL CLINICAL TRIAL

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Background and Aims: Scientific evidence in Horse Assisted Rehabilitation shows advantages in physical and psychological variables in children and adults, whether healthy or with pathologies. Cancer therapy may cause some health implications forlong cancer survivors cancer. AIMS: Analyze if Horse Assisted Rehabilitation applied on padiatric cancer survivors, is safe, well tolerated and could improve symptoms derived from cancer or its treatments.
Methods: Randomized Open-label Clinical Trial including children (4-18y) who have completed a treatment for a Brain Tumor. Intervention Group (IG): 24 weekly sessions (45 minutes each) of Horse Assisted Rehabilitation; Control Group (CG) followed their normal interventions. Institutional Review Boards: CEEAH-UAB and Vall d'Hebron Hospita. CTG ID: NCT04070131.
Results: 17 children (9 girls, 8 boys; mean age: 9.4 y) randomized into two comparable groups were included. Horse Assisted Rehabilitation were safe and well tolerated by all IG participants, showing no discomfort or undesirable effects. Parents of IG participants reported improvements in children's mood, quality of life (QOL), and participation in activities. Motor coordination DCDQ07 test (Fine Motor subscale) showed a significant improvement in the IG (+2.662) compared to the CG (0.816, p=0.037). About QOL tests, in both groups there were significant improvements, more significant in the IG in the PEDSQL-C test, Health and Physical Activities subscales (CG: +1.40, GI: -3.36, p=0.028), Emotional State (CG:+3.00, IG:-0.54, p=0.043) and total score (CG:+15.00, IG:-0.91, p=0.032). There were no significant differences between groups in other physical (Ped.and Sitting Scale, Heart Rate Variability), psychological (Children's Depression Inventory, State-Trait Anxiety for Children) or quality of life variables.
Conclusions: Horse Assisted Rehabilitation is safe and well tolerated at every age and physical condition and could improve some physical and QOL parameters in children after cancer treatment. Despite the pandemia, who make difficult greater recruitment, It miight be a tool to be used to improve QOL of this particularly fragile population

EP335 / #1467

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

CNS PRIMARY MELANOCYTIC TUMORS IN CHILDREN

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Background and Aims: Primary melanocytic tumors of the CNS arise from leptomeningeal melanocytes, derived from the neural crest during embryonic life. They can occur as diffuse or solitary, benign or malignant tumors. Very rare in children, they include the diffuse leptomeningeal melanosis, meningeal melanoma, melanocytic meningioma and primary melanocytoma of the CNS, following the World Health Organization sub-classification. Our aim is to report two rare cases of primary melanocytic tumors of the CNS ocurring in two children, with particular emphasis in the peculiar imaging features of these unusual tumors in the pediatric age.
Methods: We report two rare cases of primary melanocytic tumors of the CNS: a primary melanocytic tumor of the occipital area in a 14-year-old boy (case 1), and a diffuse leptomeningeal melanomatosis in another 14-year-old boy (case 2). In contrast to melanocytoma, the diffuse leptomeningeal melanosis widely infiltrated the leptomeninges, and demonstrated features of malignancy. Main neuroimaging manifestations will be highlighted, emphasizing the diagnostic challenges and correlating the imaging features with the pathological results.
Results: By neuroimaging, the main characteristic on MRI is the hyperintense signal on T1-weighted images, due to the paramagnetic properties of melanin, with hypointense signal on T2-weighted images, and with enhancement after gadolinium administration. Pathologically, the main clue is that these tumors are black or brown depending on their melanin content. In contrast to melanocytoma, the diffuse leptomeningeal melanosis widely infiltrated the leptomeninges, and demonstrated features of malignancy. A review of the current literature for main clinical, radiological, surgical, and histological findings of these lesions will be also pesented.
Conclusions: Primary melanocytic tumors of the CNS are very rare in the pediatric age. Based on two recent cases seen in our tertiary centre, the main neuroimaging manifestations of these tumors will be highlighted, emphasizing the diagnostic challenges and correlating the imaging features with the pathological results.

EP336 / #57

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

CLINICAL AND PATHOLOGICAL CHARACTERIZATION OF DISSEMINATED PILOCYTIC ASTROCYTOMAS: A RETROSPECTIVE ANALYSIS FROM AN ONCOLOGICAL CENTER

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Background and Aims: BACKGROUND: Among pediatric CNS tumors, pilocytic astrocytoma (AP) is the most frequent tumor, presenting non-malignant features, like slow growth and non-infiltrative traits. Rearrangements in the BRAF gene are the main molecular alteration. Up to 10% may show dissemination. In such cases, radiation therapy, chemotherapy and targeted therapies can be used. AIM: To describe clinical and pathological aspects of patients with disseminated pilocytic astrocytoma at the Barretos Cancer Hospital from January 2000 to December 2019.
Methods: MATERIALS AND METHODS: Longitudinal cohort study, with retrospective data collection and analysis of clinical and molecular data from pediatric patients diagnosed with disseminated pilocytic astrocytoma from 2000 to 2019.
Results: RESULTS: From 93 patients diagnosed with AP during this time, 10 (10,7%) had disseminated disease at diagnosis or follow-up. Half (5/10, 50,0%) were in the hypothalamus/optical pathway region. Treatment modalities varied according to age and clinical conditions. BRAF V600E mutation was detected in 3 tumors from 8 analyzed (3/8, 37,5%) and one had KIAA1549:BRAF fusion (1/5, 20,0%). At this moment, 60% of patients are alive and the overall 3-year survival was 65%.
Conclusions: CONCLUSION: This study provided clinical and epidemiological data of patients with disseminated AP from a specialized group in pediatric neuro-oncology. Findings are similar to those described in the literature regarding the analyses described (clinical, radiological, morphological, molecular, therapeutic and survival).

EP337 / #878

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

PLATFORM OF EXPERIMENTAL MODELS FOR PEDIATRIC BRAIN TUMOR

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Background and Aims: Pediatric central nervous system (CNS) tumors are the leading cause of childhood cancer-related death. Then, more appropriated therapies are lacking, leading to develop pre-clinical models that are more predictable. In this sense, patient-derived xenografts models (PDX) have emerged as an important platform to search for a new treatment and to identify new biomarkers in oncology. These models try to mimic the cellular and histopathologic structure, tumor heterogeneity and are being used for preclinical drug evaluation and personalized medicine strategies. Then, the aim of this study was to established a panel of pre-clinical pediatric brain tumor (PDX and primary cell line) from Brazilian patient.
Methods: A total of 23 cancer specimens from patients were obtained from July 2021 to March 2022. The surgical specimens were transplanted to immunodeficient mice NSG or NUDE (Nu/J), or used to established primary cell culture. Solid tumor samples were cut into 2 mm^3 and implanted subcutaneously. The tumor was designated as generation F0, and the tumor was passaged to mice for further generations (F1, F2…). Pathological tissues (PDX and patient) were subjected to hematoxylin-eosin staining and immunohistochemistry. The protocol was approved by institutional Ethics Committee and all patients gave written informed consent. Animal experiments were performed in compliance with the guidelines of the Institutional Animal Care and Use Committees (IACUC).
Results: PDX model (6) and a panel of primary cell lines (16) were established of several tumor types (Low- or high-grade glioma, ependymoma, medulloblastoma, meningiomas). The histopathological analysis indicated that heterogeneity was recapitulated and the structures of the PDX tumors were retained when compared with the original patient tumors.
Conclusions: We established a pre-clinical panel of primary cell lines and PDX of pediatric brain tumor. We expect that these models allow for understanding tumor biology, identify new biomarkers and to investigate new therapies integrated into personalized medicine strategies.

EP338 / #1148

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

APPLICABILITY OF A NOMOGRAM INCLUDING CLINICAL AND MOLECULAR VARIABLES TO STRATIFY RISK GROUPS IN PEDIATRIC MEDULLOBASTOMAS.

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Background and Aims: Medulloblastoma is the most frequent and lethal malignant kind of pediatric brain tumors.A complex disease which comprises, at least, four different molecular subtypes (WNT, SHH, Group 3 and Group 4). These subgroups present with specific characteristics, distinct clinical presentations and different outcomes.Recently, a nomogram that assesses not only molecular subtype but also clinical variables and it can predict more accurately the survival of the patients in developed countries. AIM: Analyze the applicability of a prognostic nomogram for pediatric medullobastomas treated at Barretos Cancer Hospital.
Methods: 85 pediatric patients, between 0 to 18 years, with medulloblastomas treated between January 2000 and December 2017 was assessed. Clinical pathologic variables were considered and stored at RedCap. The molecular subgroups were performed using the NanoString platform.Variables such as age, type of tumor resection, molecular subgroups, presence, or not, of metastasis, and dose the craniospinal radiotherapy were assessed.
Results: 85 patients with descriptive analysis of the sample, the molecular classification could be performed on 62 of them due to the lack of biologic material. The distribution of molecular subgroups was SHH - 35.5%, WNT- 19.4%, Group 3 – 16.1%, Group 4 – 29.0%.It could be observed that the presence of metastasis ($p=0.03$),received chemotherapy or not ($p<0.0001$), and the dose of craniospinal radiotherapy ($p<0.0001$) were associated with worse outcomes. The combined analyses of clinic pathologic variables, and molecular subgroup, the nomogram was designed to predict, with a high level of accuracy, 1-year overall survival (AUC=60.9), 3-years overall survival (AUC=77.3) and 5-years overall survival (AUC=80). A calculator was designed to predict, in a fast and efficient way, survival in 1, 3 and 5 years.
Conclusions: This study showed the applicability of the nomogram for a Brazilian pediatric medulloblastoma and the utility of a calculator developed from the nomogram as an easy-to-use tool for the clinic routine.

EP339 / #1643

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

ESTABLISHMENT OF A NEW EPENDYMOMA PRIMARY CELL LINE AND PDX MODEL

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Background and Aims: Intracranial Ependymoma is a type of tumor that accounts 1.6% of all central nervous system (CNS) tumors and can affect adult and child. Cell lines and animal models are rare and therefore search for new treatments are limited. Thus, the aim of this work was to establish a primary cell line and a PDX (Patient Derived Xenograft) model using tissue from a patient diagnosed with ependymoma grade 3 according to WHO.
Methods: Patient tissue was collected and taken to our animal house facility. Excess vessels and necrotic tissue were removed and then tissue was divided into 4 pieces for: biobank, pathology, cell culture and PDX. For primary culture, tissue was prepared using accutase protocol, incubated 3 times at 37ºC for 5 min, cells were neutralized using complete media and centrifuged for 5min to remove enzyme excess. Pellet was resuspended in media and plated into T25 flasks. Cells were monitored and splitted after 80% of confluence. For the PDX model, tissue was mixed with matrigel (1:1) and injected subcutaneously into the flanks of NSG mouse (P0 – passage 0). Tumor grow was monitored using a caliper and once the tumor reached 1.5mm^3, animal was harvest and tumor was reimplanted into P1 mouse and successively until P3.
Results: In this study we were able to determine an ependymoma cell line, that was frozen and thaw, remaining stable in culture. Therefore, we established the cell line and injected into NSG mouse reaching P3. Regarding PDX model, using tissue directly from the patient, we were able to achieve P3, and tumors from patient and mouse slide were analyzed by our pathologist and were compatible, hence retaining the tumor primary characteristics.
Conclusions: We expect that this work will provide a useful and powerful tool to investigate new therapies using our primary cell line and PDX model.

EP340 / #1814

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

ANALYSIS OF THE GLOBAL SURVIVAL OF A REFERENCE CENTER IN PEDIATRIC NEURO ONCOLOGY DURING 10 YEARS

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Background and Aims: BACKGROUND: Central nervous system (CNS) tumors are the most common malignant neoplasm in children, being the main cause of morbidity and mortality in the pediatric population. At the Barretos Cancer Hospital, we observed a rise in the number of patients diagnosed with central nervous system tumors, which are the main malignant neoplasms among solid tumors. With the low overall survival rate of 20% in the country, there is a need for a multidisciplinary pediatric neuro-oncology group dedicated to better diagnosis and treatment with improved survival and patient care . AIM: Analyze the overall survival in two periods of patients diagnosed with brain tumor in the pediatric age group (under 18 years old).
Methods: METHODS: Retrospective and cross-sectional study, analysis of 445 pediatric patients aged from 0 to 18 years old with a diagnosis of CNS tumor, divided into two periods: January/2000 to June/2013 and August/2013 to July/2019. We evaluated gender, age group, histology, topography, type of treatment (surgery, chemotherapy and/or radiotherapy) and follow-up.
Results: RESULTS: Of the 445 patients with CNS neoplasia, 198 (44.49%) were diagnosed from January/2000 to June/2013 with OS at 2 years of 59.6%, 5 years of 51.5% and 10 years 43.2%. In the second 6-year period, 247 (55.5%) were diagnosed with a 2-year survival of 72.7% and a 5-year survival of 67% with statistical significance ($p < 0.0001$).
Conclusions: CONCLUSION: This study showed the importance of the team specialized in pediatric neurooncology, bringing significant data to the literature of a developing country.

EP341 / #208

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

EARLY RESULTS OF RANDOMIZED STUDY OF RADIOTHERAPY(RT), CONCOMITANT NIMOTUZUMAB/VINORELBINE VERSUS MULTIPLE ELECTIVE RADIOTHERAPY COURSES WITH CONCOMITANT VINORELBINE/NIMOTUZUMAB FOR NEWLY DIAGNOSED DIFFUSE INTRINSIC PONTINE GLIOMA (DIPG)

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Background and Aims: The purposes of this trial were to evaluate the feasibility, response, PFS/OS of a randomized study comparing two different RT schedules for DIPG while administering the same systemic treatment.
Methods: Patients: 2-21 years-old with a not-pretreated radiologically verified DIPG (MRI blindly reviewed at diagnosis and every 12 weeks thereafter) and symptoms duration below 6 months. Biopsy was required if suggested by atypical imaging. Vinorelbine 20 mg/m2+nimotuzumab 150 mg/m2 were administered weekly for 12 weeks; thereafter every other week until tumor progression or for up to 2 years. Standard(ST) arm included focal RT at total dose of 54Gy (1.8Gy/day); for local progression re-irradiation was proposed at 19.8Gy, in case of dissemination craniospinal irradiation(CSI) at 36Gy was adopted. Experimental(SP) arm included three elective courses of RT at defined timepoints at 36Gy, 19.8Gy and 19.8Gy with possible reirradiation for relapse at 9 Gy. Incidences of local(L) and distant(D) progression were assessed in a competing risk setting.
Results: Aggregated preliminary results are given for 4 Italian centers. 54 pts were screened and 51 included, 27 in ST, 28 males, median age 7 years (range 3-17). Median time of observation was 17.9 months. Twelve patients needed a shunt, 10 during treatment; 20 were biopsied, in 18 cases according local protocols. 19/20 tumors had H3.3 K27 mutation. 41 relapsed, 28 locally, 13 with a component of dissemination. 36 died, one for tracheotomy bleeding. SP irradiation was feasible and never produced significant radionecrosis. Median EFS/OS were 7.3/12.9 months, respectively; EFS/OS at 1 year were 19.0%/57.3%, not differing between patients with local vs. disseminated relapses. Patients submitted to biopsies had more dissemination (P=0.04) and less local progression (P=0.077).
Conclusions: Treatment was feasible and OS confirmed previous results obtained in a single center. Randomization results will be later reported.

EP342 / #48

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

INCIDENCE OF HEARING IMPAIRMENT IN CHILDHOOD MEDULLOBLASTOMA SURVIVORS TREATED AT KING FAHAD MEDICAL CITY KFMC SAUDI ARABIA.

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Background and Aims: Medulloblastoma MB is the most common childhood CNS tumor treated with combined therapy surgery with radiation and cisplatin chemotherapy causing significant hearing impairment (HI) with impact on child's quality of life.
Methods: Retrospective review for a total of 78 patients with confirmed MB diagnosis treated at KFMC between 2010 and 2020 (HI) was graded using the National Cancer Institute (NCI) Grades (1-4). All patients received 6 weeks of risk adapted CSI radiotherapy concurrent with daily oral Etoposide. Patients were treated with 2 different maintenance chemotherapy Group 1=30 patients (38.5%) treated with German HIT-MED MB protocol 8 Maintenance cycles. (Cisplatin /lomustine/VCR) Cumulative dose of Cisplatin 560 mg/m2 Group 2= 48 patients (61.5%) treated with MB Saudi Arabian Pediatric Hematology Oncology Society (SAPHOS) protocol 6 Maintenance cycle alternating A&B. cycle A: Cisplatin 90 mg/m² x 1d & 3 weeks of daily oral Etoposide. cycle B: Cyclophosphamide x 2 d & Vincristine Cumulative dose of Cisplatin 270 mg/m2
Results: A total of 78 patients completed the follow up duration up to 99 months. The median age was 82 months with 66.7% male and 33.3% female. Median time of onset of hearing decline was 7 months after start of radiation therapy Significant (HI) (NCI grade 3/4) in 26.9% of patients, and 23.1% required hearing aid use Using life table analysis: mean time to develop HI was significantly shorter 10.1 months and 16.0 months in group 1, vs 43.6 months and 61.1month in group 2
Conclusions: Our study showed that incidence of hearing impairment was not affected by high radiation dose however Higher Cisplatin cumulative dose in German HIT-MED protocol was associated with higher incidence and shorter time to develop HI than MB SAPHOS protocol Our study will form base line for future studies to modify therapy related Toxicity and improve outcome of childhood MB in Saudi Arabia

EP343 / #49

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

MANAGEMENT OF CNS TUMOR WITH BCOR INTERNAL TANDEM DUPLICATION WITH MULTIMODALITIES THERAPY: SURGERY, INTENSIVE CHEMOTHERAPY, AND RADIATION.

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Background and Aims: The 2021WHO CNS tumor classification includes CNS tumors with internal tandem duplications in the BCL6 corepressor (BCOR) gene as a new entity of CNS embryonal tumors labelled high-grade neuroepithelial tumors with BCOR alterations (HGNET-BCOR) are characterized by genetic aberrations in the BCOR gene located at Xp11.4, leading to increased expression of BCOR mRNA and distinct DNA methylation profiles. currently no agreement on the optimal strategy to manage these rare tumors, which mostly occur in young children These tumors are usually treated as high grade glioma HGG with upfront radiation therapy with poor outcome
Methods: We report 2.5 years old boy presenting with headache and vomiting. MRI showed a well-defined left cerebellar mass, hyperintense in T2 and hypointense in T1, with restricted diffusion and no spinal CSF seeding metastases. He underwent gross surgical resection of the tumor initial pathological diagnosis was epithelioid high grade malignant neoplasm. Brain tumor methylation classifier analysis of resected tumor tissue confirmed a CNS tumor with BCOR internal tandem duplication (WHO grade 4).
Results: The patient was treated per COG ACNS0334 (3 induction cycles of vincristine, cyclophosphamide, cisplatin, etoposide, HDMTX, followed by consolidation with 3 cycles of carboplatin and thiotepa with autologous hematopoietic stem cell rescue). MRI brain before the start of chemotherapy showed a small recurrent mass within the surgical cavity. post-induction MRI detected stable-sized residual lesion in the surgical cavity; however, post-consolidation MRI showed complete resolution of the residual mass. The patient subsequently received craniospinal irradiation (36 Gy [CSI]) with a boost to the tumor bed up to 54 GY. By the time of writing this report our patient is still in complete remission.
Conclusions: Our case showed that this aggressive brain tumor may respond well to intensive multimodalities therapy Further case studies and international prospective trials are needed to optimize the clinical management of these rare tumors

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Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

FUSION DETECTION OF PEDIATRIC HIGH-GRADE GLIOMA USING NANOSTRING

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Background and Aims: Gliomas are a heterogeneous group of brain tumors which represents an important cause of cancer related death in children and young adults. The identification of gene fusions involving tyrosine kinases (TK) receptors in glioma cases have been considered of major importance because tumors harboring these rare genetic events, may be targetable by specific drugs (TK inhibitors) which showed promising antineoplastic effects. Unfortunately, the most frequently technologies used for TK gene fusions detection needs high quality material and are expensive. In the present study, we aimed to identify TK gene fusions (ALK, ROS1, RET, NTRK1, NTRK2 and NTRK3) using an RNA based technology (nCounterâ) from formalin-fixed, paraffin-embedded (FFPE) glioma samples.
Methods: The RNA was extracted (RNeasy Mini Kitâ, Qiagen) from 16 gliomas samples from infant, pediatric and young adults (0.9 to 21 years) treated at Barretos Cancer Hospital, Brazil. Two different nCounterâ panels (Elements Tagset) were used for TK gene fusions detection. The findings were confirmed in nine cases using a commercial Next Generation Sequencing (NGS) panel (Archer FusionPlex Solid Tumorâ).
Results: We found one case with NTRK1 fusion based on the imbalance of NTRK1 3' and 5' probes (Ratio: 7.15). The presence of NTRK1 fusion was confirmed by NGS, which identified the TPR-NTRK1 fusion in tumor RNA.
Conclusions: nCounterâ showed to be a potential technology for the identification of a TK fusions using low amount of RNA from a FFPE sample and could be applied in clinical routine of health centers in the future for the detection of targetable gene fusions.

EP345 / #848

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

PROFILING PAEDIATRIC BRAIN TUMOUR AND MANAGEMENT IN A RESOURCE-LIMITED SETTING: A SINGLE CENTRE EXPERIENCE IN UGANDA

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Background and Aims: The outcome and survival of children with brain tumours in low-income countries are low. Besides, the epidemiological and treatment data for paediatric brain tumours are grossly lacking in these settings owing to a lack of resources and population-based cancer registries. We assessed the clinical profile, treatment and outcome of children with brain tumours in Uganda.
Methods: We retrospectively reviewed records of children with brain tumours at the Uganda Cancer Institute between 2017 and 2021. Patient and tumour characteristics, treatment and outcomes were sourced. In addition, we also surveyed the members of the multidisciplinary team (MDT).
Results: Thirty-five paediatric brain tumour cases were identified, with a median age of 8.0 years (IQR 4.0-11.0). Over one-half (57.1%) were male, and the median duration of symptoms was six months (IQR 3.0-8.5). The majority (62.9%) of the tumours were supratentorial. Craniopharyngioma was the most common brain tumour diagnosis (25.7%), followed by astrocytoma (14.3%), medulloblastoma (11.4%), and ependymoma (8.6%) and pineoblastoma (8.6%). Surgical resections were in 9(28.6%) of the cases, of which 6(17.1%) were gross total resections, and 4(11.4%) were subtotal resections. Ten (28.6%) of the children received chemotherapy, while 6(17.1%) and 5(14.3%) respectively were treated with radiotherapy and palliation. There was an increasing trend in the multidisciplinary management of cases over time. Only 17(48.6%) of the children with brain tumours were alive and active in care, 13(37.1%) lost to follow up/abandoned treatment, and 3(8.6%) died. The barriers to neuro-oncological care were lack of neurosurgical resources (46.7%), imaging (46.6%), diversity of MDT (26.7%), access to radiotherapy (20.0%) and pathology (20.0%).
Conclusions: Lack of neurosurgical resources, imaging, radiotherapy and histopathology, among others, continue to hamper the outcome of children with brain tumours in resource-limited settings - compounded by high rates of treatment abandonment and loss to follow-up.

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Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

PEDIATRIC BRAIN TUMORS: CLINICAL PROFILE, MANAGEMENT STRATEGIES AND OUTCOME EXPERIENCE FROM A TERTIARY CARE CENTER, INDIA

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Background and Aims: Pediatric brain tumors are the most common solid tumors and leading cause of mortality and morbidity in children worldwide. With multimodality treatment overall survival (OS) is around 70% in developed countries. We aim to describe the patterns of brain tumors in children, to evaluate affect of pretreatment factors and the treatment itself on the outcome.
Methods: A retrospective detailed analysis was performed on series of Pediatric Primary Brain Tumors who were referred for chemotherapy in our department from January 2014 to December 2021 based on presentation, histology, disease extent, treatment and response.
Results: Of 68 cases, 66% were males, age ranging between 4 months to 16 years. Medulloblastoma was the most common tumor (34 %) followed by Optic nerve glioma (12%), Pilocytic Astrocytoma, Ependymoma and Atypical rhabdoid tumor(6% each).Presentation with features of raised intracranial pressure was most frequent (68%) followed by Ataxia (37%) and focal neurological deficit (20%). All of 68 patients received chemotherapy, of which 31% received High dose chemotherapy (HDCx) followed by Tandem Autologous Hematopoietic Cell transplants (AuHCT). Surgery was initial modality of treatment in 87%. Radiotherapy was given to 63%. By univariate analysis factors predicting poor outcome were WHO grading and Extent of disease, while the factors predicting better outcome were type of resection and HDCx and AuHCT. In the present study group OS and Event free survival (EFS) at 1yr after diagnosis were 85 % and 82 % respectively .And the subgroup who underwent HDCx and AuHCT, the 2 yr OS and EFS after diagnosis were 86 % and 81 % respectively. There was no Transplant related mortality.
Conclusions: Multimodality management including surgery, chemotherapy and radiation therapy remains the cornerstone for management of Pediatric Brain Tumors. HDCx followed by AuHCT can deliver optimal outcome in developing countries in the sub group of High risk Pediatric Brain Tumors.

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Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

ACUTE TOXICITY OF CHEMOTHERAPY IN INTRACRANIAL GERM CELL TUMOURS ACCORDING TO AGE

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Background and Aims: Central nervous system germ cell tumours (GCT) usually develop in children, adolescents or young adults. The SIOP CNS GCT II European trial includes four courses of pre-irradiation chemotherapy. Whether chemotherapy-related acute toxicity (CRAT) depends on age remains debated.
Methods: CRAT was analysed in this trial according to three age groups: children (aged ≤11 years), adolescents (aged 12-17 years) and adults (aged ≥18 years) and to type of chemotherapy: carboPEI (alternating etoposide-carboplatin and etoposide-ifosfamide) for non-metastatic germinoma; PEI (cisplatin, etoposide and ifosfamide) for standard-risk non-germinomatous GCT (NGGCT); PEI and hyperPEI (higher dose of ifosfamide and etoposide) for high-risk or poorly responsive NGGCTs.
Results: Among 296 patients assessable for CRAT, 105 were children, 121 were adolescents and 70 were adults (age max 41 years).Tumour types (and thus chemotherapy) varied across age-groups: adults received mostly carboPEI (79% versus 62% of children and 62% of adolescents). Median chemotherapy cumulative doses/m² were similar among the three groups. Delay in chemotherapy ≥7 days (mostly for prolonged marrow aplasia) was noted in 27%, 38% and 19% of children, adolescents, and adults, respectively. Grade ≥3 haematological and non-haematological CRAT was observed in 94%/31%, 97%/36% and 77%/21% of children, adolescents, and adults, respectively. Grade ≥3 haematological and non-haematological CRAT was observed in 90%/21%, 92%/42% and 100%/79% of patients treated with CarboPEI, PEI, and PEI/hyperPEI, respectively. No toxic death was reported. In multivariate analysis, grade ≥3 overall (haematological and non-haematological) CRAT adjusted to treatment type was significantly higher in adolescents treated with CarboPEI when compared with adults: odds ratio: 0.1 [0.02-0.4] but not with children: odds ratio: 0.9 [0.1-6.3].
Conclusions: Chemotherapy is safe in all age-groups, but nevertheless with higher haematological and non-haematological toxicity in adolescents when compared with adults.

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Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

MOLECULAR FINDINGS IN A SERIES OF CHILDHOOD PLEOMORPHIC XANTHOASTROCYTOMAS WITH HISTOPATHOLOGICAL CONFIRMATION

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Background and Aims: Pleomorphic xanthoastrocytoma (PXA) is a circumscribed glioma arising more common in the cerebral hemispheres of children and young adults. Recent molecular studies demonstrate an activating mitogen-activated protein (MAP) kinase mutation (most frequently BRAF p.V600E hotspot mutation) with cooccurring deletion of CDKN2A/B encoding the p16 cell cycle regulator protein in most PXA.
Methods: Clinical data and tissue samples of a total of 30 primary cases that were diagnosed as PXA (grade 2 and 3) between 2013 and 2021 in Rogachev institute were provided for this study.
Results: Of the 30 cases, 9 (30%) were anaplastic PXA (A-PXA). Median follow up time is 4.0 years. The vast majority of tumors occurred in a supratentorial location (n=28), most frequently the frontal lobe (n=11), with rare posterior fossa (n=1) and spinal cord (n=1) tumors. The most frequent alterations were CDKN2A/B deletion (n=19; 68%; 95% CI 49 - 82) and BRAF p.V600E (n=17; 57%; 95% CI 39 - 73). Co-occurring two of this alterations was in 12 pts (43%; 95% CI 27 - 61). Gross total resection (GTR) was achieved for 11 (37%) pts. GTR was the main favorable prognostic factor, 3-year PFS is 91% (95% CI 75 – 100) compared to 17% (95% CI 5 – 57) for the rest. Neither CDKN2A/B deletion nor BRAF p.V600E was significantly associated with PFS after adjustment for GTR using Cox proportional hazards model (hazard ratios 1.1 (95% CI 0.4 – 3.7) and 0.6 (95% CI 0.2 – 1.8) respectively). PXA have higher PFS relative to A-PXA though it wasn't significant (HR 0.5 (95% CI 0.2 – 1.4) after adjustment for GTR).
Conclusions: our results confirm that the vast majority of PXA harbor either CDKN2A/B deletion or BRAFV600E mutation. In histologically defined PXA, tumor WHO grade and GTR remains a strong predictor of patient survival.

EP349 / #502

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

CLINICAL FACTORS, MANAGEMENT AND OUTCOMES OF PATIENTS UNDER 18 YEARS OLD WITH BRAIN TUMORS: SINGLE CENTER EXPERIENCE IN PERU

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Background and Aims: There are few published reports on clinical factors, treatment, and survival in children and adolescents with brain tumors in low- and middle-income countries in the region of the Americas. This study aims to retrospectively analyze demographic and clinical factors related to treatment and survival in children and adolescents diagnosed with brain tumors in a tertiary care center in Peru.
Methods: All cases of patients under 18 years of age with brain tumors diagnosed in a single-center during 11 years (2007 to 2017) were retrospectively reviewed. Clinical and demographic variables were analyzed to assess their association with OS and EFS. Variables including age, gender, tumor histology, extent of surgery, origin and time to diagnosis were available for analysis using the Kaplan-Meier method and the Cox hazards ratio regression.
Results: Seventy-five patients were analyzed (40 were men and 35 were women) with a mean age of 7.7 years (0.6-17 years). The main clinical symptoms were headache (43 patients, 57.3%), vomiting (42 patients, 56%), difficulty walking (36 patients, 48%), and visual disturbances (21 patients, 28%). The most frequent clinical signs were hydrocephalus (32 patients, 42.6%), cerebellar signs (28 patients, 37.3%), visual abnormalities (19 patients, 25.3%), and focal motor signs (18 patients, 24%). The median time to diagnosis was 24 weeks. Tumor resection was performed in 68 patients (90.6%), and 37 patients (49.3%) received postoperative radiotherapy. The most frequent histological subtypes in our study were low-grade gliomas (33.7%) and medulloblastomas (29.7%). Overall survival at 1 and 5 years of disease in our series were 78% (CI 95%, 0.67- 0.86) and 74% (CI 95%, 0.62-0.82) respectively and 5-year EFS was 62% (CI 95% 0.47-0.73).
Conclusions: Headache associated with vomiting, hydrocephalus, and cerebellar signs were the most frequent presenting symptoms and signs in patients analyzed. The diagnosis was late; despite that, survival was higher than other Latin American countries.

EP350 / #1268

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

INCIDENTAL FINDING OF AN ASYMPTOMATIC BRAINSTEM TUMOUR IN A RETINOBLASTOMA PATIENT

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Background and Aims: Incidental findings (IF) are previously undiagnosed abnormalities that are discovered unintentionally during an examination obtained for a different indication. A recent prospective observational study published in the United States in a large cohort of children found that 21.1% presented an IF during a brain magnetic resonance imaging scan (MRI), of which 3.9% required referral for further study or intervention.
Methods: In this report, we present a 3-year-old patient who was diagnosed with a bilateral retinoblastoma with de novo germline RB1 mutation at 2 months of age. She underwent treatment with systemic and intra-arterial chemotherapy as well as cryotherapy and laser therapy, achieving complete control of the disease. When the patient was 30 months old, she had a follow up brain MRI scan showing an expansive lesion in the pons and bulbopontine junction with important exophytic component suggesting a brainstem glioma. Review of previous scans showed that the lesion had been present a year prior, albeit smaller. The patient was asymptomatic and had a normal neurological examination.
Results: Due to the slow growing trend of the lesion and the excellent performance status of the patient, it was decided to continue with clinical and imaging surveillance. To this date, she continues to be asymptomatic and the lesion has not changed significantly in follow up scans although this IF adds an extra concern to the patient due to her cancer predisposition.
Conclusions: Patients with germline RB1 mutations are at risk of developing tumours outside but also within the central nervous system (CNS), most commonly pineoblastomas and tumours of the suprasellar or parasellar regions. We have not found any published association between bilateral retinoblastoma and a brainstem tumour in these patients. The association of the RB1 germline mutation with this second tumour remains to be elucidated.

EP351 / #1283

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

ACTIVATION OF THE TGFB1/ERK/MKNK1 SIGNALING PATHWAY DESENSITIZES MYC-DRIVEN MEDULLOBLASTOMA CELLS TO ENTINOSTAT

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Background and Aims: Resistance to chemotherapy is a common cause of treatment failure in cancer patients and a major problem facing current cancer research. Targeted modulation of oncogenic signaling pathway may be used to systematically characterize drug resistance mechanisms across tumor entities and may help to identify new therapeutic strategies. Since the transcription factor MYC is aberrantly activated in many cancers including pediatric malignant brain tumors, like medulloblastoma (MB), our study focused on MYC-related drug resistance.
Methods: We used high-throughput drug screening and genome-wide dCas9-based transcriptional activation screening.
Results: We performed high-throughput drug screening using our in-house semi-automated platform and identified the HDAC inhibitor Entinostat as a drug that shows promising effects in MYC-driven MB. Investigating genome-wide dCas9-based transcriptional activation screening, potential drug response modulators, mainly TGFB1/Erk/MKNK1 signaling including neural EGFL like 2 (NELL2), were discovered. For further validation, we stably overexpressed NELL2 in MYC-driven MB cells and treated overexpressing cells and the corresponding control cells with Entinostat. Using PI staining, cell cycle status was tracked. Entinostat treatment led to modest induction of cell death in MYC-driven MB control cells, and significant reduced cell death in MYC-driven MB cells with NELL2-overexpression.
Conclusions: We report that the combination of genetic and pharmacological approaches is a powerful approach to study drug resistance. Our data suggest that activation of the TGFB1/Erk/MKNK1 signaling pathway desensitizes MYC-driven MB cells to Entinostat. Synergistic targeting of TGFB1/Erk/MKNK1 signaling and MYC could therefore provide a novel therapeutic option in this aggressive MB subtype.

EP352 / #1802

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

PINEOBLASTOMA – THE EXPERIENCE IN A BRAZILIAN PEDIATRIC ONCOLOGY HOSPITAL

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Background and Aims: Pineoblastomas are rare, malignant embryonal tumors that account for <1% of all pediatric brain tumors. The study aim is to report the experience of a Brazilian pediatric oncology hospital over 30 years.
Methods: Twenty-nine children with pineoblastoma were treated between 1991 to 2021. After maximal surgical resection, the treatment was performed according to the patient's age: under 3 to 5-years the treatment consisted of a modified Head Start backbone protocol followed by myeloablative chemotherapy with autologous hematopoietic stem cell rescue (AuHSCR). Focal Irradiation after AuHSCR was reserved for children with residual tumors at the end of consolidation. For older children, the protocol consisted of 36Gy craniospinal irradiation followed by conventional chemotherapy with cisplatin, cyclophosphamide, and vincristine. We recorded pathological, radiological, surgical, and clinical follow-up data.
Results: Eighteen (62%) patients were female. The median age was 7.23 years (range 0.39 – 17.68). Six (20.6%) patients had metastatic disease at diagnosis. The extent of resection was biopsy in six patients (treated before 2009), subtotal in 14 (48.2%), Near-total in 2 (6,8%), and Gross total resection in 6 (20.6%). Neoadjuvant chemotherapy was administered in one patient, who died before definitive resection. Six patients underwent chemotherapy alone and twenty-two received chemotherapy + radiotherapy. Six patients underwent AuHSCR. Twelve (41.3%) patients experienced tumor relapse or progression and died (5y-PFS 49,7%). As of April 2022, 14 patients (48.2%) had succumbed to their tumor at a median follow-up of 1.9 years. The 3-year and 5-year Overall Survival (OS) was 57.7% and 43.6% respectively. The 5y-OS stratified by age was 37,3% vs 53,7% (<5years vs >5years; p=.47). Patients submitted to GTR and NTR had greater OS (5y-OS Biopsy: 33,3%, STR 25,6%, NTR 100%, GTR 100%, P= .08).
Conclusions: In our series, unfavorable prognostic, as in the literature, seems to be related to age and extent of resection.

EP353 / #1345

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

ENHANCEMENT OF CHEMOTHERAPY DELIVERY AND OUTCOME IN PAEDIATRIC RHABDOMYOSARCOMA USING SMART POLYMERIC NANOCONTAINERS

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Background and Aims: Paediatric rhabdomyosarcoma is the most common type of soft-tissue cancer in children. It originates in the head/neck area in 40% of cases. Despite the progress made in the diagnosis and the treatment of moderate cases with 75% five-year survival rate, severe cases of rhabdosarcoma have lower survival rate (20%) and poor treatment outcome. Also, current chemotherapeutic agents lack in specificity and selectivity, resulting in unpleasant side-effects for the child. Encapsulating the chemotherapy drugs within nanocontainers (NCs) is one approach to improve drugs' efficacy and their therapeutic outcome. Due to their nano-size and suitable modified surface, polymeric NCs can cross the blood-brain-barrier without causing any damage. The aim was to synthesize polymeric NCs capable of delivering chemotherapy drugs at the tumour site to increase their efficacy and reduce their side effects.
Methods: Hollow NCs were synthesised following three steps: 1) PMAA core synthesis, 2) Coating it with P(MAA-co-EGDMA-co-NIPAM) copolymers, and 3) Removal of the PMAA core to obtain hollow NCs. Throughout the synthesis steps, polymeric NCs were characterized structurally by Fourier-Transform-Infrared-Spectroscopy and Dynamic-Light-Scattering, and morphologically by Scanning-Electron-Microscopy. Daunorubicin -as gold-standard drug- and cisplatin were loaded in the nanocontainers. The NCs were used for the following biological evaluations and rabdomysarcoma-TE671 cell-line: haemolysis assay, MTT assay, and fluorescence microscopy.
Results: The NCs' compatibility and loading capacity were investigated. The haemolysis assay showed <10% haemolysed RBCs for the concentrations of nanocontainers tested. Daunorubicin and cisplatin were loaded in NCs by 50-65%. Free NCs were shown to be non-cytotoxic in MTT assay and loaded NCs showed good cellular uptake in fluorescence microscopy.
Conclusions: Re-synthesis of the polymeric NCs will take place to further optimise their loading capacity for a sustained drug release and prolonged drug biodistribution, whilst additional experiments will be performed to evaluate their efficacy in other paediatric brain tumour cell cultures and mouse-models using different drugs.

EP354 / #1367

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

ARE TARGETED THERAPIES CHANGING THE OUTCOME IN PATIENTS WITH HGG?

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Background and Aims: High-grade-gliomas (HGGs) are aggressive neoplasms with dismal prognosis. Their treatment is based on maximal safe surgical resection followed by radiation therapy and alkylating drugs. Recent molecular discoveries are leading to new therapies as promising strategies. The goal of our study is to evaluate the clinical impact of a biological approach on the outcome of children with HGG.
Methods: We performed an institutional retrospective study including patients with histologic diagnosis of HGG. Rradiologic diagnosis alone was used in unequivocal diffuse intrinsic pontine gliomas (DIPG). Clinical and biological data were analyzed. Survival was estimated by the Kaplan-Meier method and compared by the logrank test.
Results: A total of 103 children diagnosed with HGG between 0 and 18 years were studied. Fifty-seven patients were female. Biological studies (TP53/Histones/other; sequencing/immunohistochemical determinations), were performed in 85 patients (83.4%). The most frequent diagnosis was Diffuse-midline-gliomas (DMG) in 66.7% patients (56-DIPG, 12-other-K27M-DMG), followed by WT-HGG (12, 11.8%); bithalamic, G34R and NTRK account for 2/2/1 patients (all 3%). No histomolecular data was available in 17 patients (16.7%). Surgery was performed in 71 patients (70.3%), only biopsy in 49. Radiotherapy was received by 86 patients, mainly focal (90%). Sixty-eight (67.3%) patients received chemotherapy. Biological agents (Bevacizumab or Tyrosine-kinase inhibitors) were given empirically to 38.6% of patients. Targeted therapy was administered in 13 patients (12.9%). Re-irradiation at progression was performed in 23 patients (22.8%). The median OS was 12.9 months (95% CI, 11.7 to 17.0). Targeted therapies did not significantly influence OS or PFS.
Conclusions: In our series biological/targeted therapy did not translate into improved outcomes for patients with HGG. Broad span of time and therapies are limitations of this study. The poor prognosis of these patients encourages to find new therapies to change their dismal outcome.

EP355 / #1382

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

METHYLATION PROFILE CONFIRMS NON-CLONAL ORIGIN OF METACHRONOUS TUMORS IN RTPS PATIENTS.

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Background and Aims: Rhabdoid Tumor Predisposition Syndrome (RTPS) is characterized by increased risk of development of rhabdoid tumors in individuals with germ line mutation of SMARCB1 and SMARCA4 genes. RTPS are prone to develop synchronous and metachronous tumors during lifetime but limited knowledge still exists regarding molecular findings in different tumors of an individual patient with RTPS.
Methods: Retrospective review of 23 rhabdoid tumor patients diagnosed within 2001-2020 was performed with the focus on RTPS and occurrence of the metachronous tumors. Clinical data was collected and molecular analysis of SMARCB1 status and methylation profiling were performed.
Results: Four patients out of 7 with confirmed RTPS were diagnosed with metachronous rhabdoid tumor with a median 469 days (176 -2311) from the primary diagnosis. Two patients (age 6 and 39 months) were initially diagnosed with ATRT, one of them subsequently developed rhabdoid tumor of the kidney (RTK) and one extracranial rhabdoid tumor (eMRT) of the bladder. Two patients diagnosed with eMRT of paravertebral soft tissue and RTK respectively later developed ATRT. The tumors in all 4 patients showed a different pattern of genome-wide DNA methylation and copy number aberrations suggestive of non-clonal origin between primary tumor and metachronous malignancy. Patient diagnosed with eMRT (group ATRT- MYC) was confirmed to develop brain ATRT (ATRT–SHH). Patients with brain tumors (ATRT-SHH, ATRT–TYR) developed RTK and eMRT with methylation profile of ATRT-MYC. One patient is long term survivor, 19 years and 12 years from the diagnosis of her ATRT and bladder MRT, respectively.
Conclusions: Conclusion: Patients with RTPS are at risk of developing metachronous rhabdoid tumor. Methylation profile of tumors differs in single patient suggesting non-clonal origin of metachronous tumours. Supported by Grant of Czech Ministry of Health NU21-07-00419

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Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

USE OF COMPASSIONATE MEDICATION IN CHILDREN WITH BRAIN TUMORS IN ISRAEL

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Background and Aims: Molecular testing of pediatric brain tumors (PBT) is becoming more common, but few biological agents are licensed for PBT. Correspondingly, there has been an increasing off-label use of medications obtained compassionately (CM) from drug companies. We aimed to investigate the scale of use of CM for PBT in Israel and the associated challenges.
Methods: We surveyed all seven pediatric oncology centers in the country from January 2016- March 2022. We collected data on number of patients receiving off-label medications/year, medication class, tumor type, frequency of drug re-orders, staff responsible for orders/re-orders, & whether adverse events (AE) or responses were reported to the sponsor.
Results: Number of patients on CM/year was as follows: 2016-2, 2017-4, 2018-20, 2019-33, 2020-55, 2021-76 and 2022-73. The majority of requests were for BRAF/MEK inhibitors(i) for low grade gliomas. Less frequent requests included NTRK/ROS/ALKi (9), immune checkpoint inhibitors (6), multiple TKi (2), SHHi (1), EGFRi (2), MTORi (4) & thalidomide (1) . In 2 centers a study coordinator assisted with ordering/ re-ordering since 2021; in all the others this was managed by the neuro-oncologist. Re-orders were placed every 2-3 months. Only serious AEs were reported to the IRB & supplier, and no response data were requested by drug companies. Some patients remain on CM for >5 years. During this period only 1 medication (Larotrectinib) entered the Israeli Health Basket for PBT.
Conclusions: There has been an exponential increase in the use of CM for PBT over the last 7 years; this has not been reflected by licensing of these drugs. The burden of managing the ordering and re-ordering is falling on physicians. Collection of data from these patients is sporadic or non-existent. A paradigm shift in the administration of CM using unified protocols that collect safety and efficacy data could expediate the licensing of drugs for PBT.

EP357 / #489

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

MOLECULAR CHARACTERIZATION OF UNIQUE BIOLOGICAL SUBGROUPS AMONG H3 WILD-TYPE HIGH-GRADE GLIOMAS

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Background and Aims: Paediatric high-grade gliomas (HGG) are characterised by the aggressive biological behaviour with dismal prognosis of long-term survival 10-15%. Current molecular-biological diagnostic approaches allow for more precise characterization and determination of new unique subgroups of HGG. Our aim was to identify novel and rare HGG subgroups within our institution cohort.
Methods: Our reference centre patients´ cohort consisted of 97 clinically annotated patients with HGG diagnosed between 2000 and 2021. Sanger sequencing was used for screening of the most common HGG-related oncogenic drivers; furthermore we employed whole genome methylation array (Illumina Infinium MethylationEPIC BeadChip) and for selected samples RNA sequencing and expression profiling.
Results: Based on H3 status and previous radiotherapy we separated our HGG cases into the RIG (radiation-induced glioma), H3mut and H3wt groups. In contrast to H3mut(n=35) and RIG(n=11) that were uniformly fatal, H3wt group contained a proportion of long-term survivors. In the H3wt group we found patients carrying driver mutations in IDH1/2 (n=2) and BRAFV600E (7). Five young patients (under 3) consisted of 3 infant hemispheric gliomas (with NTRK and ROS1 fusions), one gliomatosis cerebri and one brainstem anaplastic astrocytoma with MYB/QKI fusion. We also identified a rare EWSR1-PATZ1 gene fusion in one patient. Importantly, long-term survivors recruited from these subgroups. On the contrary, four cases of MYCN GBM with poor prognosis presented in various locations: one disseminated, one gliomatosis cerebri and two with hemispheric tumour. We identified one patient with “hypermutated” glioblastoma and used targeted therapy with Nivolumab. In three samples of our patients with thalamic glioblastomas, we detected “loss of H3K27-trimethylation” caused by EZHIP overexpression. These tumours proved to be very aggressive with early metastatic recurrence and dismal prognosis.
Conclusions: Detailed characterization of H3 wild-type HGG is important for further understanding of their biological behaviour, diagnostics, prognostication and identification of therapeutic targets.

EP358 / #1817

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

PARENT-REPORTED DIAGNOSTIC PATHWAYS IN CHILDREN AND ADOLESCENTS WITH A CNS TUMOR IN DENMARK

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Background and Aims: Tumors of the central nervous system (CNS) are the second most common tumors among children with cancer. Diverse initial presenting symptoms complicate the diagnostic process, which might result in a diagnostic delay leading to higher mortality and a long-term morbidity. Our aim is to map out the diagnostic intervals in Danish children and adolescents with CNS tumors to identify in which interval, the lag is present and where to aim interventions, thus accelerating diagnostics and enhance timely diagnosis.
Methods: We identified all Danish patients aged 0-17 years, who had survived a CNS tumor diagnosed from 2015–2019 through the Danish Cancer Registry and the Danish National Patient Register. The custody-holding parent(s) at time of diagnosis, completed a web-based questionnaire, consisting of questions on time (date) of first registered symptoms, first contact to a physician and the date of diagnosis with a CNS tumor. In this preliminary study 24 parents participated (N=24).
Results: The parent-reported timeline showed a Total Interval (TI, time from symptom onset to diagnosis) of median: 109.5 days, interquartile range (IQR): 132,5 days. The Patient Interval (PI, time from symptom onset to contact to a physician) of median: 28.5 days, IQR: 53,5 days; and a Diagnostic Interval (DI, time from first contact to a physician to diagnosis) of median: 54.5 days, IQR: 115 days. Males tended to experience shorter TI than females, and patients under the age of 3 years had a longer DI than patients above the age of 3 years.
Conclusions: Parent-reported diagnostic pathways showed varying ranges in the PI as well as the DI. The intervals ranged from hours to years, and varied by gender and age, supporting the fact that symptoms that occur in children with a CNS tumor vary as well as an urgent need of better knowledge to recognize these tumors more timely.

EP359 / #854

Topic: *AS05 SIOP Scientific programme / AS05.m Brain Tumours*

COMPARATIVE ANALYSIS OF AUTOPHAGY IN DRUG RESPONSES AND AGGRESSIVE BEHAVIOR OF ADULT VERSUS PEDIATRIC GLIOMA CELL LINES

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Background and Aims: Pediatric diffuse gliomas are the most challenging pediatric CNS tumors with therapy resistance and poor prognosis. Emerging evidence suggests that the molecular pathway deregulated in pediatric glioma (p-GM) is different from that of adults. Autophagy, a cellular clearance system, has been implicated in glioma progression, yet its role in pediatric patients is not well documented. In this study, we compared the autophagic capacity of adult versus p-GM cell lines. The contribution of autophagy to the aggressive phenotype was evaluated.
Methods: The autophagic capacity of adult glioma cell lines T98, U87, and LN2229 were compared to pediatric cell lines SF-188 and SF-8628 using qPCR and immunoblotting of autophagy-related genes and proteins. The dynamics of autophagy in these cells were evaluated using LC3-I to LC3-II conversion and autophagy receptor p62 degradation assays. Then, key autophagy genes were knocked out by CRISPR/Cas9 gene-editing method. Responses to commonly used chemotherapy drugs of wild-type and knock-out cells were analyzed in detail and compared. In order to document migration and invasion patterns of these autophagy competent and defective cells, scratch assay and transwell invasion assays were performed.
Results: Autophagy has been evaluated and compared in pediatric and adult glioma cell lines. Results showed that adult and pediatric cell lines respond differently to a set of chemotherapy drugs. Chemical inhibition of autophagy resulted in different responses in adult and pediatric cell lines. Changes in drug efficacies were noted in autophagy competent versus deficient cells. Migration and invasion capacity of pediatric and adult glioma cells were compared. Autophagic activity correlated with aggressive behavior in glioma cells.
Conclusions: p-GMs have poor prognosis and new treatment approaches are needed. Manipulation of drug resistance- and tumor aggressivity-related pathways, such as the autophagy pathway, might lead to the development of novel combinatory drug regimens affecting tumor growth and invasion.

EP360 / #440

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

ENTRECTINIB IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS WITH EXTRACRANIAL SOLID OR PRIMARY CNS TUMOURS HARBOURING NTRK1/2/3, ROS1, OR ALK FUSIONS: UPDATED DATA FROM STARTRK-NG

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Background and Aims: Entrectinib, a CNS-penetrant oral TRK/ROS1/ALK tyrosine kinase inhibitor, has demonstrated rapid and durable responses in children and adolescents with extracranial solid or primary CNS tumours harbouring target NTRK1/2/3, ROS1 or ALK fusions from the STARTRK-NG trial (NCT02650401; phase 1/2). We present updated safety and efficacy data from this study.
Methods: Patients aged <22 years with relapsed/refractory extracranial solid or primary CNS tumours were enrolled. Endpoints assessed include: safety, in all patients who received ≥1 dose of entrectinib; blinded independent central review of objective response rate (ORR), duration of response (DoR), time to response (TtR) and progression-free survival (PFS), in patients harbouring NTRK1/2/3, ROS1, or ALK fusions who received ≥1 dose of entrectinib and had ≥6 months of follow-up (enrolment cutoff: 03 June 2021; data cutoff: 03 December, 2021). Patients were classed as having complete/partial responses (CR/PR) or stable disease using RECIST (solid tumours) or RANO (CNS tumours).
Results: The safety-evaluable population comprised 59 patients; median age: 6.0 years (range: 2.0 months to 20 years). Fifty-five of 59 patients (93%) experienced ≥1 treatment-related adverse event

(TRAE), the most frequent being weight gain (37%); thirty-one patients (53%) had a Grade 3/4 TRAE. Thirteen patients experienced ≥1 fracture. There were no AE-related deaths, and no new safety signals were detected. In patients with fusion-positive tumours (n=36), ORR was 61% (95% CI 43.5–76.9; 9 CR and 13 PR), median DoR was 25.4 months (95% CI 16.2–NE), median TtR was 1.9 months (95% CI 1.8–1.9) and median PFS was 27.2 months (95% CI 18.1–NE).
Conclusions: Entrectinib continues to demonstrate rapid and durable responses in paediatric patients with extracranial solid or primary CNS tumours harbouring target gene fusions. Acknowledgments: Medical writing support, under the authors' direction, was provided by Lietta Nicolaides, PhD, of Ashfield MedComms, an Ashfield Health company, and funded by F. Hoffmann-La Roche Ltd.

EP361 / #492

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

THE NEDDYLATION INHIBITOR MLN4924 ALTERS RING1B ACTIVITY IN EWING SARCOMA

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Background and Aims: Ewing sarcoma (EwS) is a highly aggressive bone and soft tissue tumor affecting children, adolescents, and young adults. The fusion oncoprotein EWSR1-FLI1 is the dominant oncogenic driver that acts as an aberrant transcription factor. EWSR1-FLI1 binds GGAA microsatellites causing enhancer remodeling and genome reprogramming. Targeting the degradation of fusion oncoproteins or elements cooperating with EWSR1-FLI1 represent novel therapeutic approaches under current investigation. E3 ubiquitin ligases (E3) culminate the final steps of the ubiquitin transfer cascade to a protein substrate to promote its degradation by the proteasome. The activation of some E3 require the post-transcriptional modification neddylation. MLN4924 is a small molecule inhibitor of neddylation that is highly active in EwS cellular models. We have described the E3 RING1B is among the proteins cooperating with the oncogene at enhancers. Here, we explore the effects of MLN4924 treatment beyond E3 in EwS.
Methods: Human Gene 2.0 ST microarray was used to characterize transcriptional changes upon MLN4924 treatment in EwS cells. In depth expression and functional studies were performed to characterize the drug activity in vitro and in vivo. Chromatin-immunoprecipitation technique (ChIP) was additionally used to validate the effects of the drug on EWSR1-FLI1 targets.
Results: We present the transcriptional effects of MLN4924 treatment on EwS cells, with DNA damage response and interferon signaling among the most significantly altered pathways. We further show RING1B among the E3 deregulated by the drug at a transcript and protein level. Our results indicate that the lack of neddylation caused by the drug is behind the in vitro and in vivo degradation of RING1B. Moreover, treatment of EwS cell lines with the inhibitor promotes RING1B loss from EWSR1-FLI1-activated targets as well as eviction of EWSR1-FLI1, causing transcriptional defects.
Conclusions: MLN4924 deregulates E3, including RING1B, with critical consequences on EWSR1-FLI1 activity, partially explaining the vulnerabilities of EwS cells to the drug.

EP362 / #328

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

THE USE OF CANNABIS DERIVED MEDICAL PRODUCTS IN THE TREATMENT OF CHILDREN'S CANCER: A SYSTEMATIC REVIEW

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Background and Aims: Legislative change to cannabis use has prompted significant interest into the therapeutic utility of cannabis-derived medical products, particularly in the field of oncology. However, much of this research has focused on adults, leaving physicians and caregivers uncertain as to the safety and efficacy of cannabinoids amongst the paediatric demographic. To this end, the aim of this review is to examine the scope of pharmaceutical cannabis in treatment of paediatric cancer, evaluating its utility as an anti-cancer therapeutic as well as symptom relief agent.
Methods: This systematic review was conducted following the PRISMA guidelines. Key words were contrived and deployed, along with all synonyms, across four electronic databases (PubMed, Web of Science, Embase, CINAHL). Initial searches yielded 2217 results. After de-duplication, title and abstract screening, full text review and application of outlined exclusion and inclusion criteria, 30 papers were identified and included.
Results: The 30 articles comprised of 16 clinical and 14 pre-clinical studies. The most frequently reported clinical outcomes were for nausea and vomiting (n = 11), pain (n =4) and anorexia (n = 3). Clinical data regarding the anti-cancer effects were limited to just 2 case studies reporting 3 patients. Pre-clinical research described use of cannabinoid therapy in models of leukaemia (n = 7), osteosarcoma (n = 2), and neuroblastoma (n = 2) among other paediatric cancers (n = 3). 4 studies provided evidence of increase cannabinoid receptor (CBR) expression in the tumour cell lines and 8 studies utilised CBR's successfully as a therapeutic target to induce apoptosis.
Conclusions: There is conclusive evidence for the effectiveness of cannabis-derived medical products in chemotherapy-induced vomiting, with inconclusive but plausible utility for other facets of symptomatic relief. While there was a paucity of literature documenting anti-cancer effects in human patients, in vitro studies utilising paediatric cancer cell models provide sufficient evidence to prompt in vivo studies.

EP363 / #553

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

COMPARISON OF POST INDUCTION MRD OUTCOMES OF PEDIATRIC B-ALL TREATED WITH PEG-ASPARAGINASE VERSUS NATIVE E.COLI ASPARAGINASE

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Background and Aims: L-Asparaginase is one of the main components of the multi-agent treatment regimen for childhood Acute Lymphoblastic Leukemia(ALL). Conventional E. coli L-Asparaginase or Pegylated Asparaginase can be used for the treatment of ALL. Native E. coli L-asparaginase is being used at The Indus Hospital but debate remains regarding its efficacy due to the high rate of positive post-induction minimal residual disease (MRD) and localized hypersensitivity reactions despite being used in the regimen that is internationally followed. Over the period of the last three years, out of 410 cases of pediatric B lymphoblastic leukemia (BALL), 154 (38 %) showed positive MRD results at post-induction. This frequency of MRD positivity is relatively higher than in reported studies using a similar treatment protocol.
Methods: A retrospective study includes pediatric patients diagnosed with B lymphoblastic leukemia. Peg asparaginase which is internationally manufactured given through an intramuscular route to 55 patients during the induction phase instead of L-asparaginase which is conventionally used in childhood leukemia regimens. MRD results of this cohort were compared with those who received locally manufactured E. coli asparaginase through the intramuscular route
Results: A total of 111 patients were included, 55 patients received intramuscular peg-asparaginase and 56 patients received intramuscular conventional E.coli asparaginase. 31 (56.4%) patients in the peg-asparaginase cohort versus 29(51.8%) patients in the E.Coli asparaginase cohort show positive MRD results(p=0.628).Only one patient in each cohort shows l-asparaginase induced adverse effects. The Peg-Asparaginase group had more positive MRD outcomes in high-risk patients(26.8% vs 54.5%:p=0.009)
Conclusions: No significant differences in MRD were identified between the two groups. This study suggests that both forms of L-Asparaginase do not have a significant impact on MRD outcomes. Further prospective, randomized control trials are needed to identify factors that impact treatment outcome negatively and assess the optimal treatment that reduces the rate of positive MRD outcomes

EP364 / #389

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

A PILOT RANDOMIZED CONTROLLED TRIAL OF VIRTUAL REALITY DISTRACTION TO REDUCE PROCEDURAL PAIN DURING SUBCUTANEOUS PORT ACCESS IN YOUTH WITH CANCER

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Background and Aims: Despite numbing with a topical anesthetic, youth with cancer have reported pain and distress during needle insertion into a subcutaneous port (SCP). Virtual reality (VR) has been shown to reduce acute pain in youth. However, research is limited surrounding the use and safety of VR for procedural pain management specifically for youth with cancer. This study aimed to determine the feasibility of implementing a randomized controlled trial (RCT) of VR for SCP needle insertion in youth with cancer and estimate preliminary treatment effects.
Methods: A single-site pilot RCT comparing VR to iPad distraction was conducted in youth aged 8-18 years undergoing cancer treatment. Feasibility (e.g., accrual rate, reasons for non-participation, safety) was reported descriptively. Intervention acceptability was evaluated by youth, parent, and nurse self-report. Preliminary intervention effectiveness for youth-reported pain intensity, distress, and fear was determined using logistic regression models with outcomes compared between groups using preprocedural scores as covariates.
Results: Twenty participants were randomized per group, with an average age of 12 years. The most common diagnosis was ALL. Most eligible participants (62%) participated, and one withdrew after randomization to the iPad group. Participants cited “not interested”, or “comfortable without distraction” as reasons for non-participation. No safety issues were reported. Nurses, parents, and youth found both interventions to be acceptable, with the VR participants reporting significantly higher immersion in the distraction environment (P=0.0318). Although not statistically significant, more VR group participants indicated no pain (65% vs. 45%) and no distress (80% vs. 47%) during the procedure compared with the iPad group. Fear was similar across groups.
Conclusions: VR was feasible and acceptable to implement as an intervention during paediatric SCP access. Preliminary effectiveness results indicate that VR may reduce pain and distress compared with iPad distraction. These data will inform design of a future full-scale RCT.

EP365 / #289

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

DRUG ACCESS REQUESTS FOR INNOVATIVE THERAPIES FOR PEDIATRIC ONCOLOGY PATIENTS IN CANADA

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Background and Aims: Innovative therapies are needed to alleviate the burden of pediatric cancer despite the constant expansion of their indications in the era of precision medicine. The lack of clinical trials or approved indications in children for developed therapeutic agents is a significant barrier for access. This is the first analysis of an extensive Canadian review of innovative drug requests and focuses on drugs requested and their indications.
Methods: We conducted a retrospective review of access requests for anti-cancer therapies (not Health Canada-approved for pediatric indications at the time of application) from 2013 to 2020. Patient, disease characteristics, drug information and request details were collected. We excluded cytotoxic chemotherapy, cellular therapies, and cytokines.
Results: We included 312 drug access requests from nine Canadian tertiary care pediatric oncology centers. Requests increased from 7 in 2013 to 90 in 2020. Forty-nine different agents were requested: most commonly, targeted agents (including multi tyrosine-kinase inhibitors (n=67), inhibitors of MEK (n=64), BRAF (n=25), mTOR (n=24)), immuno-therapy (37) and antibody-drug conjugates (22). Combination therapies accounted for 33% (n=103) of the requests with n=42 for combinations of two innovative therapies. Requests were made for patients with solid tumors (39%), CNS tumors (31%), leukemias/lymphomas (20%), plexiform neurofibromas (7%) and Langerhans cell histiocytosis (3%). Actionable targets were identified by molecular profiling in 41% of cases. Most common targetable alterations were RAS/MAPK pathway activations (42%, defined as clinical diagnosis of NF1 or tumor harboring BRAF fusion or mutations). Other common actionable genomic alterations included ALK/ROS alterations (7%), defects in DNA repair deficiency pathways and alterations in PIK3CA, SWI-SNF subunits, JAK1/2, FLT3, CDK and FGFR genes.
Conclusions: There is an increasing number of drug access requests for pediatric cancers and non-malignant diseases that are not approved for children or available in clinical trials in Canada. Agents targeting the RAS/MAPK pathways were the most frequently sought after.

EP366 / #988

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

DEGRADATION OF XIAP AS A NOVEL TREATMENT STRATEGY IN HIGH-RISK NEUROBLASTOMA

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Background and Aims: XIAP, the most potent mammalian inhibitor of apoptosis protein (IAP), critically restricts developmental culling of sympathetic neuronal progenitors through apoptotic inhibition, and is correspondingly overexpressed in 64% of MYCN-amplified neuroblastoma tumors. ARTS is the only XIAP-antagonist that directly binds XIAP and promotes its degradation via the ubiquitin-proteasome system (UPS). We therefore hypothesized that XIAP antagonism via ARTS mimetics may be an effective treatment for high-risk neuroblastoma.
Methods: Pan-IAP (SMAC mimetics) and XIAP-specific inhibitors (ARTS mimetics) were screened against commercial and patient-derived neuroblastoma cell lines, and ranked by efficacy. IAP protein expression and cell death were assessed via Western blot, clonogenic and biochemical apoptosis assays. Following CRISPR/Cas9-mediated XIAP knock-in, XIAP-compound interaction was evaluated using NanoBRET™ target-engagement, degradation and ubiquitination assays, and NMR spectroscopy. Pharmacokinetics and survival studies were performed with orthotopic patient-derived xenografts. Drug-interaction indices were computed using Chou-Talalay method.
Results: Antagonism of XIAP (but not other IAPs) with ARTS mimetics, triggered apoptotic death in neuroblastoma cells. XIAP silencing induced apoptosis and over-expression conferred protection from drug-induced apoptosis. Among IAP antagonists tested, ARTS mimetic A4 was most effective against high XIAP-expressing neuroblastoma cells (BE(2)-C, KELLY), and least toxic towards liver and bone marrow-derived control cells. NanoBRET™ and MG132 assays showed XIAP engagement and degradation via UPS within 15 minutes of A4 exposure, in a dose-dependent manner. NMR analysis on ^{1}H-^{15}N-HSQC spectra of XIAP showed moderate binding with A4, supporting degradation rather than binding inhibition of XIAP by A4. In MYCN-amplified neuroblastoma xenografts, A4 10mg/kg twice-weekly was well-tolerated and significantly prolonged survival. A4 also showed synergism with second-line agents vincristine and topotecan, with 3- and 6.5-fold effective dose-reduction in BE(2)-C and KELLY, respectively.
Conclusions: Engagement and degradation of XIAP by ARTS mimetics is a novel and effective therapeutic strategy against MYCN-amplified neuroblastoma with intrinsically high XIAP, either alone or in combination with current standard-of-care agents.

EP367 / #994

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

TARGETING MUTANT DICER TUMORIGENESIS IN PLEUROPULMONARY BLASTOMA VIA INHIBITION OF RNA POLYMERASE I WITH CX-5461

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Background and Aims: Development of novel therapeutics for pleuropulmonary blastoma (PPB) has been limited by a lack of actionable molecular targets and biologically and physiologically-representative disease models, so outcomes for these Dicer-mutated malignancies remain poor. With recent evidence of Dicer-mediated RNA polymerase I (Pol I) regulation as a synthetic lethal target in mutant Dicer cells, we hypothesized that Pol I inhibition could abrogate mutant Dicer-mediated accumulation of stalled polymerases to induce p53-mediated cell death in PPB tumor cells. Thus, we sought to test the utility of Pol I antagonism with first-in-class inhibitor CX-5461 as a treatment strategy for PPB.
Methods: From a type III PPB tumor sample, an orthotopic patient-derived xenograft (PDX) model was developed using a novel sub-pleural implantation method in NOD-scid mice. Models were characterized with micro-magnetic resonance imaging and histopathology, and DICER1 variants were profiled in patient and PDX tumors via targeted next-generation sequencing. Tolerance of dosing regimens were compared in tumor-bearing animals using Kaplan-Meier method, and treatment response evaluated with immunoblotting and immunohistochemistry for apoptotic markers.
Results: PDX tumors retained allele frequency of RNaseIIIa and IIIb hotspot loss-of-function mutations over serial passages, and recapitulated the microenvironment and cardiorespiratory impact of intrapleural PPB tumors. In PDX tumors, 24-hours' exposure to CX-5461 significantly reduced H3K9 di-methylation associated with silencing of rDNA repeats (P=0.005), and significantly increased nuclear p53 expression (P=0.04) in treatment versus control groups (n=4 each). At the optimum tolerated dosing regimen of 30mg/kg CX-5461 3 times/week, PDX mice treated with CX-5461 had significantly smaller and less hemorrhagic tumors than controls, with significantly reduced frequency of nuclear Ki67 staining (P=0.03) (n=5 per group).
Conclusions: CX-5461-mediated Pol I inhibition induced regression of PPB PDX tumors, decreased H3K9 methylation, and enhanced p53-mediated cell death. Together, this evidence supports the efficacy of Pol I inhibition as a tolerable and feasible treatment approach for Dicer-mutated PPB.

EP368 / #282

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

PROSPECTIVE IDENTIFICATION OF EXCEPTIONAL RESPONDERS IN HIGH-RISK PEDIATRIC PATIENTS WITH CANCER

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Background and Aims: Despite a high cure rate for most childhood cancers, relapsed and high-risk disease have a much worse prognosis. In adults, genomic tumor profiling can significantly improve poor patient response rates following relapse by identifying gene alterations which can be effectively treated with targeted drugs. These patients are often characterized as “exceptional responders”. We report that tumor genomic profiling can prospectively identify exceptional responders in pediatric patients with cancer.
Methods: Patients with relapsed or aggressive solid tumors were enrolled into the Precision Oncology program at Riley Hospital for Children. DNA and RNA samples were obtained from FFPE preserved tumor samples and sequenced using NexGen techniques in CLIA-certified laboratories. The presence of actionable DNA variants or proto-oncogene mRNA over-expression was used to qualify each patient for consideration to use a matched, FDA-approved targeted agent.
Results: To date, 104 patients have received Riley Precision Oncology-recommended targeted therapy. A subset of these patients has met the Exceptional Responders Initiative definition: tumor regression of at least 30% for six months or more, with an agent that typically results in responses in <10% of individuals on the same treatment. Exceptional responses were observed in patients with sarcomas and CNS tumors with the following biomarker-drug pairings: ALK mutations/gene fusions/over-expression – Crizotinib; CDK4 pathway mRNA – Palbociclib; MET gene fusions / over-expression – Cabozantinib; PMS2 gene loss / high tumor mutational burden – Pembrolizumab; BRAF mutations – Dabrafenib + Trametinib; BRAF gene fusions – Trametininb; NF1 mutations – Selumetinib; NTRK3 gene fusions – Larotrectinib.
Conclusions: Pediatric exceptional responders were predicted by the presence of FDA recognized Level 1-3 DNA/RNA biomarkers in the patients’ tumor genome. These results demonstrate conclusively that many high-risk pediatric patients with solid tumors can benefit from a Precision Oncology approach.

EP369 / #536

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

A PHASE I STUDY OF NAB-PACLITAXEL COMBINED WITH GEMCITABINE FOR PEDIATRIC RELAPSED/REFRACTORY SOLID TUMORS

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Background and Aims: The maximum tolerated dose (MTD) of nab-paclitaxel in children with relapsed/refractory solid tumors is 240 mg/m^2 given weekly three out of four weeks, which is significantly higher than adult dosing. We aimed to determine the MTD of nab-paclitaxel combined with gemcitabine in this population.
Methods: Patients with relapsed/refractory solid tumors outside the central nervous system enrolled on a Phase I multicenter trial. Eligibility included age 6 months to 30 years old, measurable or evaluable disease, and adequate bone marrow, kidney, and liver function. Three dose levels of nab-paclitaxel were evaluated, 180 [dose level (DL) 1], 210 (DL2), and 240 (DL3) mg/m^2, using a rolling six design, and were administered alongside fixed-dose gemcitabine intravenously on days 1, 8, and 15 of 28-day cycles.
Results: Nineteen patients were enrolled and received treatment; 17 were evaluable for dose-limiting toxicity (DLT). The median age was 14 years (range: 3-21). Common tumor diagnoses included osteosarcoma (N=10) and rhabdomyosarcoma (N=4). The median number of cycles received was 2 (range: 1-6). Initially gemcitabine was given at 1000 mg/m^2; however, 2/5 patients evaluable at DL1 had hematologic DLTs including thrombocytopenia and epistaxis, and neutropenia. The study was amended to reduce gemcitabine to 675 mg/m^2/dose. No DLTs were seen on post-amendment DL 1 and 2. One of 6 patients enrolled on DL3 experienced a DLT, a malignant pleural effusion present at enrollment that worsened to grade 3 during cycle 1. Dose level 3 was declared the MTD. Common cycle 1 drug-related toxicities were mainly hematologic in nature, though post-cycle 1 toxicities leading to treatment discontinuation included elevated transaminases, peripheral neuropathy, and paclitaxel-associated acute pain syndrome. One patient remains on active treatment.
Conclusions: The MTD was determined to be nab-paclitaxel 240 mg/m^2 with gemcitabine 675 mg/m^2 on days 1, 8 and 15 of 28-day cycles. An expansion study at the MTD is underway.

EP370 / #1701

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

USE OF ROMIPLOSTIM® IN THERAPY-RELATED THROMBOCYTOPENIA IN PATIENTS WITH HIGH-RISK NEUROBLASTOMA.

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Background and Aims: Therapy-related thrombocytopenia (TRT) is a major problem in children receiving chemo/radiotherapy and frequently causes delays of treatments and/or dosage reduction. Romiplostim® is a thrombopoietin receptor agonist approved by the Food and Drug Administration (FDA) for the treatment of primary immune thrombocytopenia (ITP) in pediatric and adult patients. Reports about Romiplostim® in pediatric cancer patients are scarce. We aim to analyze the effectiveness and safety of Romiplostim® in patients with persistent TRT and high-risk neuroblastoma (HR-NB).
Methods: We conducted a single-institution retrospective analysis of the whole cohort of HR-NB and TRT patients treated with Romiplostim® between July 2017 and June 2021. Romiplostim® was administered as the recommended dose in ITP 1-10mcg/kg/weekly subcutaneously. Platelet increase was measured at 3, 6 and 12 weeks. An increase >50,000/mm3 platelets was considered a response.
Results: We included eighteen patients. Eleven (61.1%) had received autologous stem cell transplant and three (16.6%) craniospinal radiotherapy. Four (22.2%) had morphological bone marrow infiltration by NB cells before starting Romiplostim® and seven (38.8%) minimal residual disease (MRD) positive by PHOX2B. The whole cohort was able to continue chemotherapy, immunotherapy or chemo-immunotherapy. Before start treatment twelve (66.6%) patients had <50,000/mm3 platelets (9,000-85,000/mm3). The mean starting dose of Romiplostim® was 4.84 mcg/kg/week (2.7-7.5) and the maximum dose during was 8.14 mcg/kg/week (4.3-10). Five patients (27,7%) showed >50,000/mm3 platelets on week 3, eight (44.4%) on week 6 and 11 out of 17 patients (64.7%) patients achieved platelets >50,000/mm3 on week 12. The mean duration of treatment was 4,69 months. We did not observe any adverse effects limiting the use of Romiplostim®.
Conclusions: Romiplostim® was effective and safe in the treatment of TRT. The use of Romiplostim® in heavily pre-treated patients with HR-NB may be crucial for access to salvage therapies.

EP371 / #599

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

LIPID REPLACEMENT THERAPY FOR THE TREATMENT OF DIFFUSE MIDLINE GLIOMA

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Background and Aims: Thus far, genomic, proteomic and epigenetic analyses have failed to identify new effective therapies for H3K27M-mutant diffuse midline gliomas (DMG). Lipids are generally not exploited for therapy approaches, even if glycosphingolipids (GSL) are altered in brain tumours and GSL metabolic reprogramming drives neural differentiation. Here we determined the composition of DMG compared to healthy pontine tissue and exploited the altered composition to inhibit DMG growth.
Methods: Lipids were analysed by thin layer chromatography followed by chemical staining or immune overlay as well as by liquid chromatography-coupled tandem mass spectrometry from DMG primary cells, from a DMG cell line and from post-mortem pontine tissue of 3 patients without evidence of brain cancer. The DMG cell line was treated with a lipid extract and proliferation was measured in comparison to a neuroblastoma cell line.
Results: The neutral fraction of pons is rich in cholesterol, sphingomyelin and cerebroside (GalCer), while the same fraction of DMG contains less of these, but does express globoside (Gb4Cer). The acidic fraction of normal pons is rich in sulfatides and complex gangliosides, while the same fraction of DMG is devoid of sulfatide and contains less gangliosides, which are not as complex. Treatment with a complex gangliosides extract reduced proliferation of DMG but not of neurablostoma cells.
Conclusions: GSL composition may control cell behaviour. Non-proliferating adult brain cells contain complex gangliosides, while the globo-series of glycolipids is necessary for the maintenance of an undifferentiated stem cell phenotype during embryogenesis. The addition of complex gangliosides may counteract the effect of globoside in DMG. Lipid replacement therapy has been used in the 80s to treat chronic neuromuscular diseases, but was not effective. However, this therapy has been not evaluated in the context of brain cancer, and our results warrant further analysis to translate these data into a new therapy for DMG

EP372 / #454

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

UNEXPECTED SEVERE TOXICITY OF CRIZOTINIB IN COMBINATION WITH VINBLASTINE: THE CRISP OPEN-LABEL PHASE 1B TRIAL IN PEDIATRIC PATIENTS WITH ANAPLASTIC LARGE CELL LYMPHOMA (ALCL) (ITCC-053)

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Background and Aims: Crizotinib and vinblastine monotherapies have shown promising results in ALK-positive ALCL. The combination was expected to result in a deeper remission status. Here we describe the unexpected severe toxicity in two patients treated with crizotinib and vinblastine in an international prospective study.
Methods: The CRISP trial (EudraCT: 2015-005437-53), is an ITCC international multicentric open-label, non-randomized, two-stage phase 1b dose finding study, with dose escalation according to the escalation with overdose control (EWOC) method. Based on pre-clinical data, the vinblastine starting dose was reduced to 75% of the single-agent dose (dose level 1; 4.5 mg/m^2). Two patients were included in stratum I and treated with crizotinib (fixed dose; 150 mg/m^2 BID) and weekly i.v. vinblastine.
Results: Patient 1, diagnosed with early relapsed ALK-positive ALCL with bone marrow involvement, was assigned to dose level 1. The patient developed a dose limiting toxicity (DLT) on Cycle 1 Day 10 (C1D10); namely, grade 3 nausea unresponsive to anti-emetics, lasting 7 days. On C1D10 the patient also developed neutropenic fever (grade 3) and died 17 days after starting treatment because of liver failure. Autopsy revealed a fungal infection (Lichtheimia species) and a suspected secondary hemophagocytic lymphohistiocytosis. Due to this toxicity, patient 2 (relapsed ALK-positive ALCL) was assigned to dose level -1 (3.0 mg/m^2). This patient developed a DLT on C1D22; neutropenia grade 4 (>7 days). Treatment was stopped and neutropenia resolved. Vinblastine was administered to both patients despite not fulfilling starting criteria (neutropenia grade 4). Both patients were taken off study before scheduled pharmacokinetic sampling. The steering committee decided to terminate stratum 1, assuming further de-escalation of vinblastine was not clinically meaningful.
Conclusions: The unexpected severe toxicity described here is probably due to a stronger than anticipated CYP3A4 interaction, and possible additional pharmacodynamic interactions. This study emphasizes the importance of (pre-)clinical pharmacological evaluation in trials investigating drug combinations.

EP373 / #517

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

IDENTIFICATION OF KDM3A AS A PROMISING PROGNOSTIC MARKER AND THERAPEUTIC CANDIDATE IN PEDIATRIC ADRENOCORTICAL TUMORS

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Background and Aims: Adrenocortical tumors (ACT) are neoplasms that affect the adrenal glands. ACT are rare in children, but with an incidence in Brazil around 10 times higher than worldwide. Treatment options for patients with advanced ACT are limited and little effective. In a previous study using RNASeq, our group identified the KDM3A gene as a possible central player in ACT pathology. KDM3A is a histone demethylase enzyme that acts on the modeling of histones and several studies have associated its hyperexpression with the occurrence and worse prognosis in several other tumors. Thus, this study aimed to evaluate the clinical value of the expression of KDM3A and the effect of its inhibition in vitro.
Methods: The expression of KDM3A was evaluated and correlated with ACT clinical features in two different datasets of pediatric ACT cases (GSE76021, n=34, and GSE76019, n=29) using log-rank and Mann-Whitney tests. The effects of KDM3A inhibition in the viability, migration, and invasion of NCI-H295R cells were evaluated after treatment with 500uM of the KDM3A inhibitor JIB-04 for 48h.
Results: We identified that a higher expression of KDM3A was associated with lower 5-year overall survival in the GSE76021 dataset ($p=0.027$), and event-free survival in both cohorts GSE76019 and GSE76021 ($p=0.031$ and $p=0.045$ respectively). In both datasets, the overexpression of KDM3A was also associated with death ($p=0.009$ and 0.003, respectively) and relapse ($p=0.009$ and 0.005, respectively). In NCI-H295R cells, KDM3A inhibition was confirmed by both mRNA and protein levels and resulted in significant decrease in cell viability, invasion, migration, and colony formation compared to control cells ($p<0.05$).
Conclusions: Our results suggest that KDM3A could be a promising treatment candidate for the pediatric ACT, since its overexpression was associated with poor ACT prognosis, and its pharmacological inhibition limited ACT progression in vitro. (Grant FAPESP: 2014/20341-0)

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Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

COMBINATION OF EEF2K INHIBITION AND CISPLATIN AS A PROMISING COMBINED THERAPEUTIC APPROACH FOR HIGH-RISK MEDULLOBLASTOMA PATIENTS

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Background and Aims: Medulloblastoma (MB) is the most common pediatric cancer of the central nervous system and it has been classified in 4 main molecular subgroups: SHH, WNT, Group 3, and Group 4. The group 3 MB (Grp3-MB) presents the lower survival rates among them. The high-risk tumors frequently regulate protein translation mediated by eEF2K, an essential gene activated to hold energy intake and survive under unfavorable conditions.Thus, this study aimed to evaluate the association of eEF2K expression with Grp3-MB, prognosis features, and therapeutic potential.
Methods: Associations between clinical features and eEF2K expression were evaluated by using public datasets of pediatric MBs (GSE85217, n = 763). Genes coregulated with eEF2K were identified and considered significant when p < 0,001. We also tested an eEF2K inhibitor (NH125) in combination with Cisplatin in two Grp3-MB cell lines (USP-13-Med and D283).
Results: We identified that eEF2K is upregulated in Gr3-MB compared to other molecular subgroups and its overexpression was associated with lower overall survival (P < 0,001) and metastatic disease (p < 0,001). Among genes positively correlated with eEF2K in MB, we found USP2 (r=0.8) and OTX2 (r=0.72), both associated with a unfavorable prognosis in Grp3-MB; DOCK9 (r=0.581) and EPHA8 (r=0.55), involved in invasion in MB; and PCBP4 (r=0.592), reported as a cisplatin-resistance gene in other tumors. Results obtained from two independent experiments of combined therapy showed that the addiction of the eEF2K inhibitor NH125 decreased cell viability to a greater extent than Cisplatin alone, lowering up to four times the necessary dose to ensure cell death (p < 0,005).
Conclusions: Our results reveal that eEF2K is associated with poor prognosis in high-risk MB. Its inhibition decreased cell viability and enhanced the Cisplatin effect in vitro, suggesting this gene as a promising therapeutic target in patients of Grp3-MB (Grant FAPESP: 2014/20341-0).

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PERSONALISED MEDICINE - TARGETED THERAPY USAGE IN PAEDIATRIC ONCOLOGY –WHEN, HOW AND AT WHAT COST IN A MEDIUM SIZED PAEDIATRIC AND ADOLESCENT ONCOLOGY UNIT.

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Background and Aims: Targeted therapy usage is increasing, more so in adults, than in paediatric and adolescence oncology. With limited open studies, these medications can only be accessed individually, at significant expense in cost and resources. The aim of this paper is to review aspects of the usage in a medium-sized paediatric cancer centre based in Melbourne, Australia that annually treats over 75 new oncology patients from 0-19 years.
Methods: Data acquired was patient numbers, reason for targeted therapy, access to clinical trials, how the medications were obtained and cost, and any issues, side effects or benefits.
Results: Data was difficult to obtain, with no tracked record of patients on targeted therapy. Some patients were identified from the nationwide Precision Medicine Program (PRISM). Over twenty patients were identified from October 2018 to December 2021. Of twenty-five patients enrolled on PRISM, twenty had recommendations of a single target, and three had multiple targets. There were over eighteen targets identified. Fifteen different medications were recommended. Fifteen of the twenty-three patients had accessible medications, and eleven commenced on the recommended agent. Eight of these patients remain on the medication with stable disease or better. Other patients on targeted therapies are on agents with more established indications, which are Government funded, and others are on newer agents suggested by pathology, biology and/or clinical course. Most patients were discussed at a multidisciplinary meeting. Most needed individual access to the medication, through hospital drug usage committee or special and compassionate access from drug companies. Parents did not pay for the medications.
Conclusions: Targeted therapies are being increasingly used in paediatric and adolescent oncology, with potentially improved outcomes, but at significant resource and financial costs. Recommendations include improved records of patients on newer/ novel agents. Better systems will track usage, cost, access and outcomes and allow more cost/benefit analysis.

EP376 / #1231

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

VINCRISTINE-INDUCED PERIPHERAL NEUROPATHY IN PEDIATRIC ONCOLOGY: LONG-TERM FOLLOW-UP DATA OF A RANDOMIZED CONTROLLED TRIAL COMPARING PUSH INJECTIONS WITH ONE-HOUR INFUSIONS (THE VINCA TRIAL)

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Background and Aims: Vincristine is one of the mainstays of treatment in children with cancer. Its main side-effect is vincristine-induced peripheral neuropathy (VIPN), a sensory-motoric neuropathy. Therapeutic strategies are limited to pain management and dosage adaptations. The VINCA trial is a randomized controlled trial in which participants were randomized to receive vincristine via push injections or one-hour infusions. We report on the long-term effect of administration duration on VIPN.
Methods: VIPN was measured 1-7 times in 1.5-2.0 years with the Common Terminology for Criteria for Adverse Events (CTCAE) and the pediatric-modified Total Neuropathy Score (ped-mTNS). Poisson mixed model analysis and logistic generalized estimating equation analysis for repeated measures were performed.
Results: Ninety patients were included (n=45 randomized to push- and n=45 to one-hour administration group), of which 58 were diagnosed with acute lymphoblastic leukemia. Overall, the number of participants developing VIPN did not significantly differ between the randomization groups. In participants receiving concurrent azole treatment (n=7 per randomization group), the total CTCAE score was significantly lower and the risk of severe VIPN was borderline significantly lower in the one-hour group compared with the push group (rate ratio 0.52, 95% confidence interval (CI) 0.33-0.80, p=0.003, and odds ratio 0.26, 95% CI 0.06-1.20, p=0.09, respectively). These results were similar in a multivariable analysis. Moreover, if the cumulative vincristine dosage increased, the difference in the total ped-mTNS score between the randomization groups increased in favor of the one-hour group (p=0.006). Of note, findings were not consistent across different VIPN measurement tools.
Conclusions: The development of VIPN over 1.5-2 years among children who receive vincristine was not associated with administration duration. However, in participants receiving concurrent azole treatment and in those receiving higher cumulative vincristine dosages, one-hour administration resulted in less VIPN compared with push administration. Therefore, one-hour administration of vincristine may benefit at least some of the children.

EP377 / #957

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

APPLICATION OF THE COMIK PRECISION MEDICINE PROGRAMME FOR CHILDREN AND ADOLESCENTS WITH ULTRA-RARE TUMOURS

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Background and Aims: Massive sequencing techniques have made possible to identify new therapeutic targets for patients with cancer. However, paediatric patients' access to new therapies in trials remains limited, even more for uncommon (ultra-rare) cancers. We have analysed the somatic alterations identified in the COMIK (Cancer OMIcs for Kids) precision medicine programme and the potential access to targeted therapies.
Methods: Paediatric patients with ultra-rare high-risk solid tumours at diagnosis, relapse or progression (excluding neuroblastoma, Ewing sarcoma, osteosarcoma, rhabdomyosarcoma, glioma, medulloblastoma), who underwent whole exome sequencing of DNA from tumour and germline for the detection of copy number variants, point mutations, small insertions and deletions, tumour mutational burden and mutational signatures.
Results: Thirty-two patients were included from December 2015 to May 2021. Median age was 9 years (range 3 months - 17 years). Genomic somatic alterations were identified among 62% (20/32) of patients, with two or more alterations in nine of them. Thirty-four alterations were described: 32% in epigenetic genes, 15% in receptor tyrosine kinases and 12% in genes involved in transcription regulation. The median rate of mutations was low, 0.97 mutations/Mb (range 0.31–4). Fifty-six per cent of the alterations are directly or indirectly druggable with targeted therapy. This means we can propose therapy based on molecular findings in 50% of patients. In none of these are approved therapies in paediatrics, and although in almost all cases the drug is under development in paediatric clinical trials, in only 20% there is a trial available in our country.
Conclusions: COMIK precision medicine programme identified actionable genomic somatic alterations leading to a targeted therapy recommendation in, at least, half of the patients with an ultra-rare tumour. However, patients did not finally receive a targeted therapy, due to lack of available clinical trials or drugs ready to use, demonstrating the limited access to new drugs for this group of patients.

EP378 / #119

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

APATINIB, IRINOTECAN AND TEMOZOLOMIDE (AIT) REGIMEN IN RELAPSED AND REFRACTORY PAEDIATRIC SOLID TUMOR

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Background and Aims: While irinotecan and temozolomide remains an essential backbone for treatment of paediatric relapsed/refractory solid tumors, the addition of apatinib (tyrosine kinase inhibitor, targeting VEGFR-2) is a potentially beneficial approach. Its efficacy and safety were retrospectively evaluated.
Methods: This territory-wide study included patients age <19 with relapsed/refractory sarcoma, who received AIT regimen during the 3-year period (April 2019-March 2022) in Hong Kong. Starting dose of apatinib was based on body surface area:125mg (<0.6m^2), 250mg (≥0.6-<1m^2), 375mg (≥1-<1.5m^2), 500mg (≥1.5m^2) PO. Irinotecan (50mg/m^2 for 5 days IV) and temozolomide (100mg/m^2 for 5 days PO) were given at a 3-weekly interval. Baseline characteristics, outcome and adverse events (AEs) were analyzed.
Results: Eleven patients received AIT regimen (M:F 7:4) with median age 8.5 years (0.4-16.1 years). They received a median of 6 cycles (2-26) of irinotecan and temozolomide and 6.7 months (0.8-22.5 months) of apatinib. Disease control rate could reach 91% whereas overall response rate was 45%. Best overall response was observed as follows: Ewing sarcoma – 2 partial response(PR), 2 stable disease(SD); BCOR-ITD – 1 SD; rhabdomyosarcoma – 1 PR, 1 SD; clear cell sarcoma – 1 SD; undifferentiated sarcoma – 1 complete response(CR), 1 PR, 1 progressive disease(PD). Median duration of response was at least 4.1 months (0.8-27.3 months), while median overall survival and progression-free survival were 10.6 months (1-27.3 months) and 5.9 months (0.8-27.3 months) respectively. AEs mostly limited to CTCAE grade 1-2, including hair hypopigmentation(27%), palmar-plantar erythrodysthesia syndrome(18%), hypothyroidism(27%), adrenal insufficiency(9%), hypertension(9%), anorexia(18%), malaise(18%). Grade 3 AEs were observed in 4 patients (3 proteinuria, 1 gastrointestinal bleeding with pneumatosis intestinalis), which usually responded to treatment interruption/dosage adjustments. The addition of apatinib did not seem to significantly increase hematological toxicities.
Conclusions: AIT regimen is a potentially effective regimen with manageable AE profile, and is worthwhile for further study in children with relapsed/refractory sarcoma.

EP379 / #559

Topic: *AS05 SIOP Scientific programme / AS05.n New Drugs/Experimental Therapeutics*

EFFICACY AND SAFETY OF LAROTRECTINIB IN PAEDIATRIC PATIENTS WITH TROPOMYOSIN RECEPTOR KINASE (TRK) FUSION CANCER: AN EXTENDED FOLLOW-UP

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Background and Aims: Neurotrophic tyrosine receptor kinase (NTRK) gene fusions are oncogenic drivers in various tumour types. Larotrectinib is a highly selective tropomyosin receptor kinase (TRK) inhibitor approved for treating paediatric and adult patients with TRK fusion cancer. Larotrectinib demonstrated an objective response rate (ORR) of 88% across 78 pediatric pts with non-CNS cancers (van Tilburg et al, SIOP 2021). To better determine the efficacy outcomes in a more mature dataset with a longer follow-up, we report here on the first 70 paediatric patients enrolled as of December 2019 with a data cut-off of July 2021.
Methods: Patients aged <18 years with TRK fusion cancer in larotrectinib clinical trials were included. Responses were investigator-assessed (RECIST v1.1).
Results: Tumor types included infantile fibrosarcoma (57.1%), other soft tissue sarcoma (35.7%), congenital mesoblastic nephroma (2.9%), thyroid cancer (2.9%) and melanoma (1.4%). With longer follow-up, the ORR was 87% (95% CI 77–94): 31 (44%) complete response (CR; including two pending confirmation and nine pathological CR), 30 (43%) partial response (PR), seven (10%) stable disease, one (1%) progressive disease and one (1%) not determined. Median time to response was 1.8 months; one patient converted from PR to CR after ≥2 years on treatment. Treatment duration ranged from 1.0 to 62.6+ months. Medians for duration of response and progression-free survival (PFS) were 43.3 (95% CI 23.2–non estimable [NE]) and 45.1 months (95% CI 22.1–NE); median follow-ups were 34.0 and 33.3 months, respectively. Median overall survival (OS) was not reached; median follow-up was 35.2 months. The 36-month OS rate was 92%. Treatment-related adverse events were mostly Grade 1–2.
Conclusions: With this extended follow-up, larotrectinib demonstrated durable responses and prolonged PFS (medians >3.5 years), and a favourable long-term safety profile in paediatric patients with TRK

fusion cancer. This demonstrates the importance of identifying NTRK gene fusions in paediatric solid tumours.

EP380 / #1881

Topic: *AS05.o Tumor Biology, Immunology and Immunotherapy*

CLASSIFICATION OF PEDIATRIC EXTRACRANIAL SOLID TUMORS USING LOW-COST NANOPORE RNA SEQUENCING OF FORMALIN-FIXED PARAFFIN-EMBEDDED SPECIMENS

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Background and Aims: The accurate diagnosis of childhood cancers requires multiple costly techniques and is unavailable for many low- and middle-income countries (LMIC). We aimed to demonstrate the feasibility of a single, widely available and low-cost molecular sequencing platform (Oxford Nanopore Technologies) to accurately diagnose pediatric extracranial solid tumors.
Methods: We performed multiplex nanopore mRNA sequencing on MinION flow cells for 61 formalin-fixed and paraffin-embedded (FFPE) diagnostic specimens from children and young adults with solid tumors (23 Burkitt lymphoma, 13 diffuse large B-cell lymphoma, 8 Wilms tumor, 6 Ewing sarcoma, 5 neuroblastoma, 5 rhabdomyosarcoma) and 8 non-malignant lymph nodes. Most specimens were originally processed in LMIC hospitals for clinical purposes. To train a classifier from gene expression profiles, we used a set of pairwise and one-vs-all partial least-squares regressions and a support vector machine classifier.
Results: FFPE derived nanopore mRNA sequencing averaged 408,097 reads per sample, with a mean read length of 163 base pairs, median read length 137 base pairs, and an average of 53,868 confidently mapped reads per sample. Three of the 68 (4.4%) cases failed a quality control parameter of > 5,000 mapped reads. Of the cases that passed quality control, 95.6% of specimens (62/65) were correctly classified into tumor type. The three incorrect cases each had a predicted probability of less than 0.6. Within the rhabdomyosarcoma subgroup, samples were classified into FOXO1 fusion status indirectly using gene expression profiling. Each rhabdomyosarcoma sample (n=5) was correctly classifed into FOXO1 status with a predicted probability of greater than 0.7.
Conclusions: We report that it is feasible to use FFPE specimens to diagnose childhood cancers using unbiased nanopore mRNA sequencing. We are now extending this approach to an expanded range of tumor types, defining optimal sequencing depth, testing additional computational approaches, and field testing the assay within multiple LMIC contexts.

EP381 / #311

Topic: *AS05.o Tumor Biology, Immunology and Immunotherapy*

DNA DAMAGE RESPONSE PATHWAY ALTERATIONS AND DEFICIENCY IN SARCOMAS IN CHILDREN AND YOUNG ADULTS

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Background and Aims: Clinically significant alterations in DNA damage response (DDR) pathways contribute to genomic instability and malignant progression in several carcinomas and solid tumors. While ostensibly pathogenic variations have been identified in known and novel cancer genes, we evaluated comprehensive molecular profiles to investigate the role of DDR pathway alterations in sarcomas arising in pediatric, adolescent, and young adult (AYA) patients.
Methods: Sarcoma samples from pediatric and AYA patients aged 0-39 years (N=777), representing 25 histologic subtypes, underwent NGS of DNA (592-gene panel or whole exome, N=777) and RNA (whole transcriptome sequencing, N=475) at a CLIA-certified laboratory (Caris Life Sciences, Phoenix, AZ). Homologous recombination deficiency (HRD) scores were calculated as a composite of loss of heterozygosity, telomeric allelic imbalance, and large-scale transitions, using a positive threshold of 42 (N=261).
Results: A pathogenic DDR pathway mutation was noted in 68 (8.8±1.9% [95%CI]) of the total samples. DDR pathway alteration rates were highest in angiosarcomas (AS;N=6,30.0±17.6%) and alveolar soft part sarcomas (N=3,30.0±24.9%) with >10% mutation rate in 5 other subtypes: spindle cell sarcoma, not otherwise specified, epithelioid sarcoma (ES), solitary fibrous tumor (SFT) of CNS, osteosarcoma and leiomyosarcoma (LMS). ATRX was the most frequently altered DDR gene (4.3±1.8% of all samples), with mutations observed across 9 sarcoma histologic subtypes (range 2.4-15.8%). ERCC2 was mutated in ES (N=1,6.3±11.9%), AS (N=1,5.0±9.6%), and rhabdomyosarcoma (N=1,1.5±3.0%). Median HRD scores ranged between 20-58.5 across all sarcoma subtypes. High rates of deficient HRD (HRDd ≥ 42) were observed in pleomorphic sarcoma(N=4,100%), MPNST(N=10,66.7±23.9%), LMS(N=16,61.5±18.7%) and epithelioid hemangioendothelioma(N=3,60.0±42.9%), while no HRDd tumors were observed in clear cell(N=0/3), Ewing sarcoma(N=0/4), and SFT(N=0/3).
Conclusions: DDR pathway alterations are present in numerous histologic subtypes of sarcomas, particularly those that display nuclear pleomorphism and lack characteristic translocations/fusions. Further research will evaluate the clinical implications of these known and novel mutations to guide risk stratification and potential therapeutic options.

EP382 / #323

Topic: *AS05.o Tumor Biology, Immunology and Immunotherapy*

IMPLEMENTATION OF LIQUID BIOPSY ANALYSIS IN THE SCREENING OF CANCER PREDISPOSITION PATIENTS

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Background and Aims: Individuals with cancer predisposition syndromes (CPS) have a significant higher risk of developing cancer and treatment outcome often improves with early diagnosis. Thus, there is an urgent need for early and precise tumor detection methods. Current standard cancer surveillance measures often rely on radiologic imaging. Complementing surveillance with Liquid Biopsy (LB) blood samples to analyze cell-free DNA (cfDNA) may improve the detection of tumors at early stages and thereby allow for early intervention. Our study explored the potential of LB analysis as a sensitive and minimal-invasive complementary cancer surveillance tool for CPS patients.
Methods: Our cohort comprised plasma samples of 172 CPS patients (n=256 samples) and 10 healthy controls. After cfDNA isolation according to standardized protocols, we performed low-coverage whole-genome-sequencing (lcWGS). Bioinformatic analyses were adapted to computationally enhance somatic copy number variations (CNVs).
Results: In comparison to healthy controls, lcWGS data derived from CPS patients revealed elevated levels of somatic CNVs in 33 percent of hitherto analyzed individuals (n=81). Ongoing clinical follow-up and re-evaluation of medical imaging recorded simultaneously to the blood collection could confirm the LB result in exemplary cases.
Conclusions: These findings indicate the feasibility of cfDNA analysis in early detection of somatic CNVs in CPS affected individuals. Further validation of LB results by comparative analysis with radiological data and long-term surveillance are ongoing in order to evaluate the sensitivity. Altogether our study aims to increase specificity of established methods and to integrate additional sensitive techniques for early cancer detection in patients at high cancer risk.

EP383 / #1574

Topic: *AS05.o Tumor Biology, Immunology and Immunotherapy*

MICRORNA-196A SENSITIZES B CELL LYMPHOMA CELLS TO DAUNORUBICIN THROUGH FOX01

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Background and Aims: MicroRNAs (miRNAs) are small regulatory RNAs that repress gene expression by directly binding to the target mRNA's 3' untranslated region. miRNAs are critical regulators in cellular processes, including stress responses. Thus we were interested in the potential roles of miRNAs in the pathogenesis of B cell leukemia and lymphoma. miR-196a was known to be reversed drug resistance in non-small cell lung cancer and gastric cancer. Daunorubicin is one of the standard therapeutics for various leukemia and lymphoma.
Methods: MiR-196a was overexpressed in SU-DHL-6 cells, a human diffuse large B cell lymphoma cell line, by transfection of a lentiviral vector. Cell viability was measured by CCK8 assay (Dojindo), and apoptosis was assessed with Caspase3/7 assay (Promega). The cell cycle was investigated with flow cytometry using propidium iodine after fixation. The target gene of miR-196a was predicted by TargetScan, and the expression of FOXO1 was assessed by Q-PCR and Western blotting.
Results: We found that overexpression of miR-196a reduced the viability of SU-DHL-6 cells upon daunorubicin treatment. The reduced cell viability was a result of increased apoptosis. The expression of FOXO1 was directly regulated by miR-196a, which was shown by Q-PCR and Western blotting.
Conclusions: We found that miR-196a could sensitize B cell lymphoma cells to daunorubicin through FOX01. We further plan to investigate the underlying mechanism and clinical impact using clinical samples.

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Topic: *AS05.o Tumor Biology, Immunology and Immunotherapy*

SARS-COV-2 INFECTIONS IN PEDIATRIC AND YOUNG ADULT (YA) RECIPIENTS OF CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY: AN INTERNATIONAL REGISTRY REPORT

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Background and Aims: Immunocompromised patients have increased risk from SARS-CoV-2 infections. Patients receiving CAR-T for relapsed/refractory B-cell malignancies are uniquely immunosuppressed due to B-cell aplasia. While SARS-CoV-2 mortality rates of 33% have been reported in adults post-CAR-T, outcomes in pediatric/YA CAR-T recipients are poorly described. We describe outcomes of pediatric/YA CAR-T recipients with SARS-CoV-2 infections.
Methods: We created an international registry of CAR-T recipients aged 0-30 years infected with SARS-CoV-2 within 2 months prior to or any time after CAR-T infusion. Nine centers contributed 78 infections in 75 patients. Suspected US omicron infections were defined as those after December 12, 2021.
Results: Of 70 SARS-CoV-2 infections occurring 20 to 3180 days (median 435 days) post-CAR-T, 13 (18.6%) were classified as asymptomatic, 37 (52.9%) mild, 11 (15.7%) moderate, 6 (8.6%) severe COVID-19 and three (4.3%) were classified as multisystem inflammatory syndrome in children (MIS-C). Twenty (28.6%) infections resulted in admission, with 8 (11.4%) ICU admissions. Median admission length was 13 days (IQR 5-29.8). Prior to the emergence of the omicron variant, 19/47 (40.4%) infections resulted in hospital admission and 7/47 (14.9%) required ICU admission, while after, only 1/23 (4.3%) infections required admission. Death occurred in 3/70 (4.3%); each had ≥1 coinfection or life-threatening condition. Factors associated with severe COVID-19 or MIS-C included: >1 comorbidity (OR 27.0 [95% CI 5.36-208], p<0.0001), coinfection (OR 17.5 [3.46-103], p<0.0001), and absolute lymphocyte count (ALC) <500 cells/uL (OR 21.6 [3.37-428], p=0.006). No patients with severe COVID-19 or MIS-C had a suspected omicron infection. In the 8 patients infected with SARS-CoV-2 pre-CAR-T, infections delayed CAR-T infusions in 4 patients by 15-30 days.
Conclusions: In a large international cohort of pediatric/YA CAR-T-recipients, SARS-CoV-2 infections resulted in high rates of hospital and ICU admissions. Patients with comorbidities, coinfections, and low ALC were more likely to experience severe illness. Suspected omicron infections were associated with milder disease.

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Topic: *AS05.o Tumor Biology, Immunology and Immunotherapy*

PRECISION MEDICINE REVEALS A HETEROGENOUS TUMOUR IMMUNE MICROENVIRONMENT IN PAEDIATRIC GLIOMAS

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Background and Aims: Glioma is one of the most common subtypes of brain tumours in children and includes low-grade glioma (LGG) and high-grade glioma (HGG). Patients with HGG have a poor outcome and desperately need new therapeutic options. Whilst immune checkpoint blockade (ICB) is one option, this has not been successful to date in patients with HGG. HGG tumour immune microenvironment (TIME) could be not permissive to response to ICB. Thus we aimed to investigate paediatric glioma TIME by (1)multiplex IHC to reveal immune cell density, their spatial relationships, and MHC-I expression(2) to investigate immune network signalling and immune suppression pathways by RNA-sequencing.
Methods: We have analysed 15 samples (9 HGG and 6 LGG) with a combination of techniques: digital spatial profiling on $CD45^+$, $CD45^+CD3^+$, and $CD45^-$ regions; Multiplex OPAL-IHC using a pan-immune and T-cell panel (CD68, TMEM119, CD11C, PD1, PDL1, CD3, CD4, CD8, FOXP3, GFAP); MHC Class-I IHC; RNA-sequencing to deconvolute the immune cell mixtures, assess T-cell infiltrative lymphocyte signatures and identify immune suppressive pathways.
Results: Spatial profiling revealed all LGG and a subset of HGG were immune-inflamed, either hot-clustered or hot-diffuse. There was a higher proportion of $CD4^+PD1^+$ than $CD8^+PD1^+$T-cells. All T-cell subset densities were directly associated, as were T-cells and macrophage densities. However, T-cell and microglia were inversely correlated. Double-negative T-cells and T helper cells were significantly spatially diverse, and we saw a significant increase in $CD4^-CD8^-PD1^+$T-cells and $CD11c^+$APC in LGG and HGG that were hot compared to immune-cold HGG.
Conclusions: The paediatric glioma TIME is heterogeneous and the TIME phenotypes do not separate according to low vs high-grade tumours. Importantly, in this study, we identified a subset of immune ‘hot’ HGG that could benefit from ICB. This work stresses the need for a personalised immune-profiling approach and, with the integration of RNA-sequencing, can identify biomarkers to classify patients into immune-altered or -inflamed.

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Topic: *AS05.o Tumor Biology, Immunology and Immunotherapy*

IMPROVING PEDIATRIC MEDULLOBLASTOMA STRATIFICATION THROUGH THE LENS OF TUMOR ASSOCIATED IMMUNE MICROENVIRONMENT

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Background and Aims: The understanding of immune tumor microenvironment and its role in medulloblastoma progression and immune escape is still far from complete. The immune microenvironment of medulloblastoma subgroups has distinct immune profiles, and such differentiation of immunological characteristics suggests that immune profiling these subgroups can add information to improve diagnostic and supports the development of subtype-specific immunotherapeutic strategies. In this study we aimed to identify the immune expression profile of molecularly characterized pediatric Brazilian medulloblastomas, and associated it with their clinical-pathologic features.
Methods: A series of 22 previously molecularly characterized pediatric medulloblastoma from the Barretos Cancer Hospital were evaluated. The medulloblastoma panels were carried out using the NanoString nCounter PanCancer Immune Profiling. The CodeSet had been previously developed by NanoString Technologies comprising 730 genes and 40 housekeeping genes. All procedures regarding sample preparation, hybridization, detection, scanning and data analysis were performed according to manufacturer's instructions.
Results: Classic histology was found for 68.2% of the cases and 72.7% not presented metastasis at diagnosis. Additionally, 59.1% of the patients underwent total surgical resection. The OS for MB_{WNT} samples was 76.15 months, followed by 44.84 months in the MB_{SHH} samples and 43.2 and 36.4 months in the MB_{GPR3} and MB_{GPR4}, respectively. Our results showed that MB subgroups have distinct immuno-oncology-profile. Related to this signatures immune populations, the MB_{SHH} showed that several genes were differentially expressed when compared with other molecular subgroups, and the modulations found in these genes suggested the involvement of myeloid cell populations in an inflammatory tumor microenvironment. In the MB_{GPR4}, differentially expressed genes were implicated in the dysregulation of T cells, and were associated with poor prognosis.
Conclusions: Our study illustrates the robustness of the nanoString for immune profiling, which can contribute for further subgroup classification, and can add information in assessment of specific immunotherapeutic targeting strategies to mediate antitumor immunity in patients with medulloblastoma.

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Topic: *AS05.o Tumor Biology, Immunology and Immunotherapy*

EXPLORING THE ROLE OF INDIGENOUSLY DEVELOPED NOVEL HUMANIZED CD19-DIRECTED CHIMERIC ANTIGEN RECEPTOR(HCAR19) T-CELLS FOR RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA- A PILOT OPEN-LABEL SINGLE-ARM PHASE-I STUDY

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Background and Aims: Emerging and approved Chimeric Antigen Receptor(CAR) T-cell therapies for relapsed-refractory(r/r) B-cell Acute Lymphoblastic Leukaemia (B-ALL) are prohibitive for developing countries due to high-costs and limited expertise. We designed and developed a novel Humanized CD19-directed CAR(HCAR19) meeting regulatory requirements for a Phase-I trial- the first of its kind in India and developing countries(CTRI/2021/05/033348).
Methods: R/r B-ALL patients aged 3-25 years ineligible for Allogenic-Stem Cell Transplant(AlloSCT) and no prior CD19-immunotherapy were included if CD19-expression exceeded 99% blast-population. Those with major comorbidities were excluded. Lymphocyte-collection protocol on FreseniusKabi-Com.Tec™ was used for product-manufacture. Bridging-chemotherapy was physician-determined. HCAR19 cells would be infused to 6 patients at two dose-levels: Dose-1:1x10^6/kg; Dose-2:3-5x10^6/kg body-weight after Lymphodepletion (Fludarabine-Cyclophosphamide), and observed for toxicity, HCAR19 in-vivo dynamics, and effects on tumor burden. Disease-response was assessed on Day-30 bone-marrow.
Results: To-date 6 patients were enrolled, 3 received Dose-1, 1 Dose-2, 2 withdrawn pre-infusion (rapid-progression:1;consent-withdrawl:1). Three patients at Dose-1 were assessable for end-points. Median age was 16-years(range:11-18), M:F-1:2, median previous therapy-lines 3(2-3), 2 with high-risk mutations(IKZF-del/PAX-5-JAK2 fusion-One; T315-mutated BCR-ABL-One). Median pre-infusion bone-marrow blasts were 28.2%(0.09-37.1%). Product-manufacture was sucessful in all. Toxicities included Grade-2 febrile-neutropenia(66%), thrombocytopenia(66%), leukopenia(66%), which recovered. Product-related toxicities were Grade-2 Cytokine release syndrome(CRS)-1(33%) Tocilizumab-responsive, and B-cell aplasia-1(33%) managed with Intravenous-Immunoglobulin. No other toxicities were noted. CRS correlated with peak IL-6 levels on Day-8/11, range:4.8-342 pg/ml. HCAR19 appeared in circulation by Day-7(median-3.6%;range-2.7-6.3%/circulating T-cells) and peaked Day-11-14(15.7%-88%/circulating T-cells). One patient had no expansion in week-2. Of 3 evaluable patients on Day-30, overall response-rate(ORR) was 67%. At last follow-up 2 patients were alive (one post-AlloSCT, one CD19-negative relapse), while one patient with no-response at Day-30 expired subsequently.
Conclusions: Autologous-HCAR19 was safe at starting-level Dose-1:1x10^6/kg with low-toxicities, robust in-vivo dynamics, correlating well with pre-clinical studies, and sufficient responses to proceed with dose-escalation, establishing the feasibility and pathway for CAR T-cell therapy in India and developing countries.

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Topic: *AS05.o Tumor Biology, Immunology and Immunotherapy*

FLOW CYTOMETRY FOR DIAGNOSIS, CLASSIFICATION AND MONITORING OF PEDIATRIC SOLID TUMOR BASED ON THE EUROFLOW SOLID TUMOR ORIENTATION TUBE - STOT

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Background and Aims: Pediatric cancer is the leading cause of death in children, being fundamental the early diagnosis for a better outcome. Neoplastic cells characterization together with the recognition of the tumor-immune system interaction can guide a risk-adapted treatment. The multiparameter flow cytometry (MFC) application to non-hematopoietic solid tumors (NHST) remains limited. Here we designed and prospectively validated a new single 8-color antibody combination- solid tumor orientation tube, STOT- for diagnostic screening, classification and tumor-infiltrating immune cells of pediatric cancer by MFC.
Methods: A total of 476 samples from 296 patients with diagnostic suspicion of pediatric cancer were analyzed by MFC vs., conventional diagnostic procedures. STOT was designed after several design-test-evaluate-redesign cycles based on a large panel of monoclonal antibody combinations tested in 301 samples.
Results: Based on the immunophenotypic pattern of those 301 samples, final version of STOT consisted of a single 8-color-12 marker antibody combination (CD99-CD8/$_{nu}$myogenin/CD4-EpCAM/CD56/GD2/$_{sm}$CD3-CD19/$_{cy}$CD3-CD271/CD45). Prospective validation of STOT in 149 samples showed concordant results with the patient WHO/ICCC-3 diagnosis in 138/149 cases (92.6%). These included: 63/63 (100%) reactive/disease-free samples, 43/44 (98%) malignant and 4/4 (100%) benign NHST and 28/38 (74%) leukemia/lymphoma cases, being Hodgkin lymphomas not diagnosed by STOT tube. STOT allowed accurate discrimination among the four most common subtypes of CD45^{-} CD56^{++} NHST: 13/13 (GD2^{++}CD271$^{-/+}{}_{nu}$MyoD1$^{-}{}_{nu}$myogenin^{-}CD99^{-}EpCAM^{-}) neuroblastoma samples, 2/2 (GD2$^{-/+}$CD271$^{+}{}_{nu}$MyoD1$^{-}{}_{nu}$myogenin^{-} CD99^{+}EpCAM^{-}) Ewing sarcoma family of tumors, 5/5 (GD2^{-} CD271$^{++}{}_{nu}$MyoD1$^{++}{}_{nu}$myogenin^{++}CD99$^{-/+}$EpCAM^{-}) rhabdomyosarcomas and 7/7 (GD2^{-}CD271$^{-/+}{}_{nu}$MyoD1$^{-}{}_{nu}$myogenin^{-}CD99^{-}EpCAM^{+}) Wilms tumors. Among 63 tissue samples, the immune cell infiltrate was composed mostly by T-lymphocytes in neuroblastic tumors and hematopoietic tumors (p=0.003) while granulocytes predominate in germ cell and soft tissue tumors (p<0.001).
Conclusions: In summary, here we designed and validated a new standardized antibody combination and MFC assay for diagnostic screening of pediatric solid tumors that might contribute to fast and accurate diagnostic orientation and classification of pediatric cancer together with a tumor-immune cell profile description in routine clinical practice.

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DEPLETING TUMOR-INFILTRATING MYELOID CELLS TO ENHANCE BISPECIFIC ANTIBODY-DRIVEN T CELL INFILTRATION AND ANTI-TUMOR IMMUNE RESPONSE

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Background and Aims: T cell immunotherapy has emerged as one of the most promising therapeutic modalities for refractory or relapsed cancers. However, the efficacy has been limited by the immunosuppressive tumor microenvironment (TME). TME impedes bispecific antibody (BsAb) or chimeric antigen receptor (CAR)-driven T cell infiltration, survival, and cytotoxic efficacy. We explored the effects of tumor-infiltrating myeloid cells (TIMs) depleting strategies on BsAb-driven T cell infiltration, persistence, and in vivo anti-tumor activity.
Methods: Anti-GD2 BsAb and anti-HER2 BsAb built on IgG-[L]-scFv platform were tested against human cancer xenografts using BALB-Rag2−/−IL-2R-γc-KO (BRG) mice as a stand-alone or as EATs (T cells ex vivo armed with BsAb). Depleting antibodies specific for polymorphonuclear myeloid-derived suppressor cells (PMN-MDSCs), monocytic MDSCs (M-MDSCs), and tumor-associated macrophages (TAMs) were used to study the role of each TIM component. Dexamethasone, an established anti-inflammatory agent, was tested for its effect on TIMs and BsAb-based T cell immunotherapy. The effects of TIM depletion were examined by flow cytometry and IHC of tumors, bioluminescence imaging, and in vivo tumor growth analyses.
Results: BsAb-driven T cells recruited myeloid cells into human tumor xenografts. Each TIM targeting therapy depleted cells of interest in blood and in tumors. Depletion of PMN-MDSCs, M-MDSCs, and particularly TAMs was associated with increased BsAb-driven T cell infiltration into tumors, significantly improving tumor control and survival in multiple cancer xenograft models. Dexamethasone premedication depleted monocytes in circulation and TAMs in tumors, also enhancing BsAb-driven T cell infiltration and persistence, contributing to improved anti-tumor response with survival benefits.
Conclusions: Depleting TIMs significantly improved the anti-tumor efficacy of BsAb-based T cell immunotherapy by increasing intratumoral T cell infiltration and their persistence. TAM depletion was more effective than PMN-MDSC or M-MDSC depletion at boosting the anti-tumor response of BsAb. Dexamethasone premedication also enhanced the anti-tumor response of EATs against varieties of cancer xenografts in the presence of IL-2.

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Topic: *AS05.o Tumor Biology, Immunology and Immunotherapy*

FINE-TUNING OF CHIMERIC ANTIGEN RECEPTORS VIA BARCODED POOLED SCREENING IMPROVES EFFECTOR CELL PERSISTENCE AND ANTI-NEUROBLASTOMA ACTIVITY

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Background and Aims: Chimeric antigen receptor (CAR) T cell-based immunotherapy is an effective treatment for hematologic malignancies but has shown only modest efficacy for solid tumors such as neuroblastoma. Our goal is to improve the efficacy of CAR-based cancer immunotherapies by developing novel barcoded pooled screening methodology to generate CARs with improved function.
Methods: We developed a combinatorial barcoded cloning strategy in which each CAR has a unique DNA barcode sequence corresponding to its serially assembled domains. This barcode allows simultaneous quantification of CAR frequencies in pooled populations via next-generation sequencing (NGS). Using this method, we simultaneously generated 180 CARs based on the 14G2a single-chain variable fragment that targets neuroblastoma antigen GD2. We transduced this library into T cells and performed serial tumor challenges with CHLA255 neuroblastoma cells, assessing proliferation and relative expansion by quantifying changes in CAR barcodes via NGS.
Results: The top two performing CARs from the screen both contained the 4-1BB costimulatory domain. Further characterization revealed these constructs had lower cell surface expression, which correlated with decreased TRAIL expression (p-value <0.0001). Tested individually, these CARs mediated improved cell expansion and anti-neuroblastoma activity compared to a GD2-CAR construct with the CD28 costimulatory domain that is currently being evaluated in phase I studies.
Conclusions: These findings show that our barcoded pooled screen can generate CARs that mediate more potent anti-neuroblastoma activity. This improved activity could be due to optimized surface expression of the CAR, leading to decreased apoptosis that is characteristic of cells that retrovirally-transduced to express 4-1BB-based CARs. This screening method is readily scalable to test thousands of new CAR designs, providing unparalleled insights into how different CAR constructs lead to improved phenotypes. This approach has the potential to revolutionize CAR development and to become a new paradigm for the development of CAR-based cancer immunotherapy.

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Topic: *AS05.o Tumor Biology, Immunology and Immunotherapy*

INTERLEUKIN-15 CO-EXPRESSION INDUCES ROBUST EXPANSION AND ANTITUMOR EFFECT OF GPC3-CAR T CELLS AND TOXICITIES CAN BE MITIGATED WITH THE INDUCIBLE CASPASE-9 SAFETY SWITCH.

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Background and Aims: Glypican 3 (GPC3) is an attractive immunotherapeutic target given its preferential expression in several solid cancers. We previously treated 12 patients with T cells expressing a GPC3-CAR at two doses (DL1: 1 x 10^7; DL2: 3 x $10^7/m^2$). No dose limiting toxicities occurred, but there was minimal CAR T cell expansion; antitumor responses were limited to stable disease by RECIST criteria. Further pre-clinical studies demonstrated that GPC3-CAR T cells co-expressing IL-15 (15.GPC3-CAR) had superior in vivo expansion and antitumor activity in mice with hepatocellular carcinoma (HCC) xenografts compared to T cells expressing GPC3-CAR alone. Thus, we hypothesized that 15.GPC3-CAR would induce higher CAR T cell expansion and boost antitumor activity in patients with GPC3+ solid tumors.
Methods: The AGAR (NCT04377932) study is a phase 1 clinical trial to define the safety and antitumor activity of 15.GPC3-CAR in children with relapsed/refractory solid tumors. Toxicity is assessed using CTCAE v5. Persistence is evaluated by RT-PCR and flow cytometry; anti-tumor effect is measured by standard 3D imaging and serum AFP.
Results: We infused 3 x $10^7/m^2$ 15.GPC3-CAR into 3 patients with HCC. Two patients experienced modest T cell expansion and progressive disease without dose limiting toxicity. In one patient, however, we observed robust expansion of lymphocytes that peaked at week 2, ($9.7x10^9$ CAR transgene copies /ml by QPCR and 2935.6 CAR+ T cells/µL by flow cytometry). This patient had grade 4 cytokine release syndrome which rapidly resolved after the activation of the inducible caspase 9 (iC9) safety switch with rimiducid. At week 4 post-infusion, the primary liver mass and multifocal lung metastases showed marked decrease in size corresponding with a 94% decrease in serum AFP.
Conclusions: 15.GPC3-CAR T cells can induce robust expansion and antitumor activity and toxicities can be mediated with rimiducid.

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Topic: *AS05.o Tumor Biology, Immunology and Immunotherapy*

CLINICALLY RELEVANT GERMLINE VARIANTS DETECTED BY NEXT-GENERATION SEQUENCING IN PATIENTS WITH CHILDHOOD CANCER AT KING HUSSEIN CANCER CENTER

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Background and Aims: Cancer predisposition syndromes (CPSs) are reported in 8-10% of children with cancer. We sought to study genetic predisposition to cancer in children treated at King Hussein Cancer Center.
Methods: This is a retrospective review of patients who were referred to our CPS clinic that was established in June2019. Referred patients were screened using Jongmans' and McGill Interactive Pediatric OncoGenetic Guidelines (MIPOGG) for cancer predisposition. Next-generation sequencing of germline DNA was performed using panels of genes suited for patients' diagnosis and family history.
Results: Forty patients were screened; all were under age of 18-years and of Arab ancestry. All patients fulfilled Jongmans' and/or MIPOGG criteria. Thirty patients (75%) had family history of cancer. Twenty patients had neoplasm indicating CPS (e.g., adrenocortical carcinoma, …). Congenital or other phenotypic anomalies were detected in 7 patients. Five patients were referred due the diagnosis of two malignancies. Excessive toxicity related to cancer treatment was reported in one patient. Primary cancers were hematological malignancy(n=21), brain tumor (n=11), solid tumor (n=8), and LCH (n=1). Pathogenic/Likely pathogenic germline mutations were identified in 14(35 %) patients across ten known cancer predisposition genes: NF1, TP53, MUTYH, SMARCB1, MSH6, CBL, FANCA, DCLRE1C, RB1, DICER1. VUS variants were detected in 17(40%) patients in the following genes: GATA2, PTCH1, ATM, TP53, PMS2, MSH6, ALK, POT1, BRCA1, BRIP1, POLE, RECQL4, CASR, DIS3L2, PALB2, TERT, MET, RET, BPTF, DUT. Ten patients (25%) had negative testing despite harboring clinical features of CPS. Genetic counseling encountered many challenges, mainly performing the testing for extended families and suggesting the proper future surveillance for affected family members.
Conclusions: By screening our patients carefully, we were able to identify a significant number of patients with CPS. Further refinement of our testing may require WES to detect structural variations and collaboration with research centers to perform functional testing for patients with VUS.

EP393 / #1406

Topic: *AS05.o Tumor Biology, Immunology and Immunotherapy*

HARMONIZING GENETIC DATA ELEMENT MODELING ACROSS CANCER TRIALS

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Background and Aims: The Pediatric Cancer Data Commons (PCDC) has facilitated the creation and data modeling work of 9 pediatric oncology consortia with members from 31 data-contributing sites across 13 countries. This modeling involves pooling case report forms, extracting concepts, and harmonizing those concepts into common data dictionaries for each of our currently-supported 11 diseases. Since the data come from trials that span the past several decades, there are many differences in conceptual granularity, nomenclature, and concept organization.
Methods: The PCDC has extracted genetic data elements from over 125 international case report forms. Along with subject matter experts from across the spectrum of pediatric oncology, we have gone through several iterations of a model that would appropriately suit the needs of each disease type. The format of this model consists of variables and sets of coded permissible values.
Results: One of the main principles learned was the appropriate balance of conceptual granularity. For example, meaningful harmonization requires accommodating a “common name” for mutations that may include non-standardized descriptors (hotspot, splice site, etc.) and accommodating the oft-conflated concepts of “type” and “effect” of a mutation. The PCDC “Genetic Analysis” model currently consists of 30 variables and 15 value sets.
Conclusions: The design of clinical trials is a critical recurring task for some clinicians. While these investigators are experts in their oncological domain, they understandably draw from nomenclature and jargon common to that domain. This can make data harmonization across domains a daunting task–with genetic concepts being particularly difficult. This PCDC “Genetic Analysis” model is the result of extensive harmonization efforts and represents international consensus from key stakeholders from across the pediatric oncology landscape. It can be a valuable guide to clinicians who will be tasked with the design of future clinical trials. This is especially timely as genetic analyses play an increasingly vital role in cancer research.

EP394 / #1813

Topic: *AS05.p Supportive Care and Palliative Care*

USE OF QUALITY IMPROVEMENT METHODOLOGY TO IMPROVE TIMELY PLACEMENT OF TOTALLY IMPLANTABLE VENOUS-ACCESS PORTS IN CHILDREN WITH CANCER IN A RESOURCE-LIMITED SETTING

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Background and Aims: Central venous access to provide chemotherapy is the standard of care in children receiving cancer treatment. Totally implantable venous-access ports (TIVAP) are the preferred method for most children and constitute a routine procedure in high-income countries. However, in resource-limited settings, timely TIVAP placement represents a complex and multifactorial challenge due to supply shortages, surgical time delays, and lack of standardized processes. We used quality improvement (QI) methodology from the Institute for Healthcare Improvement to improve timely TIVAP placement at the General Hospital-Tijuana, Mexico.
Methods: Of the 60 children with cancer diagnosed annually, 29 patients were candidates for TIVAP and were included in our QI initiative. Baseline data was collected from September 2020 to January 2021. Our SMART goal was to decrease the TIVAP placement to <42 days from diagnosis. Plan-Do-Study- Act (PDSA) cycle 1 was completed from February 2021 to December 2021. TIVAP placement waiting time (WT) was defined from Day of Diagnosis to Day of Placement. The QI strategy included multimodal interventions that combined system change guided by fishbone and key driver diagrams. Interventions included the establishment of the TIVAP team, ensuring supplies and surgical time, development and application of guidelines/flowhcharts, systemization of communication and processes, and hospital leadership support for implementation.
Results: Baseline overall WT mean was 57 days (12-106 days). Mean WT for children with leukemia and solid tumors were 77 days (57-106 days) and 32 days (12-53 days), respectively. After PDSA1, overall WT mean decreased by 44% to 25 days (3-65 days). WT for leukemia patients decreased by 42% to 32 days (6-65 days) and for solid tumor patients decreased by 53% to 17 (3-29 days).
Conclusions: By using QI methodology, we significantly decreased time to TIVAP placement. We will continue to implement interventions based on future PDSA cycles to ensure sustainability of the results over time.

EP395 / #23

Topic: *AS05.p Supportive Care and Palliative Care*

KETAMINE INFUSION FOR NEUROPATHIC PAIN IN CHILDREN WITH CANCER: KING HUSSEIN CANCER CENTER EXPERIENCE

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Background and Aims: Pain control can be challenging to achieve in children with terminal cancer. Neuropathic and somatic pain sensations may form a complex of symptoms that do not respond to conventional pain medications.
Methods: We identified patients managed in our pediatric department who received ketamine during a 4-year period. Their demographics, pain scores, medication lists and response to ketamine were recorded.
Results: Fifteen patients (5 females; median age 14 years; range, 4.2 to 24) were included in this analysis. Seven patients had bone sarcoma; 4 of them had phantom pain following limb amputation. Patients were on high doses of narcotics and other adjuvant medications. The median pain score at time of starting ketamine infusion was 8 (range, 7 to 10). Ketamine was started at 0.1mg/kg/hour in all patients and increased to a median of 0.2mg/kg/hour (range, 0.1 to 0.5). The lowest pain score achieved was 2 (range, 0 to 4). Narcotics were tapered after a median of 5 days (range, 2 to 13). Ketamine was stopped successfully in 10 patients while 5 died of their disease while receiving ketamine. The 4 patients with phantom pain benefited the most and were all discharged with controlled pain after stopping ketamine.
Conclusions: Ketamine resulted in dramatic pain relief in our patients. Those with phantom pain benefited the most, indicating potency against neuropathic pain. It deserves further evaluation in treating cancer pain in patients with advanced disease.

EP396 / #754

Topic: *AS05.p Supportive Care and Palliative Care*

TIMELY REFERRAL TO PEDIATRIC PALLIATIVE CARE SERVICE DECREASES UTILIZATION OF HOSPITAL RESOURCES IN CHILDREN DYING WITH CANCER

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Background and Aims: Demand for services increases towards the end-of-life in children with terminal cancer. This may be stressful to patients and their families while exhausting hospital limited resources.
Methods: We identified patients who died at our unit over the study period (Jan2016-Dec2021) using our palliative care service database. Service utilization was queried using our medical records. A sheet that includes all encounters was then analyzed and utilization was compared for the 2 months that preceded palliative care referral and the period after referral. Paired t-student's test was used for statistical comparison.
Results: We identified 352 patients who died during the studied period. Most patients (N=328, 90%) had an active DNR order by the time of death. Four families had reversed DNR orders before death. The average timing of referral to palliative care service was of 51 days (+/-88) before death. Forty-seven patients (13%) died at home, while the rest died in hospital units (N=227, 64%), ER (N=9, 3%) or ICU (N=38, 10%). Leukemia patients were more likely to die without DNR orders (26%) than other patients (6.7%, P<0,001). Service utilization decreased after palliative care service referral as follows: Number of admissions (average,1.2 per patient before referral to 0.8 after referral, P<0.001), number of ER visits (8.7 vs 2.6, P<0.001) and outpatient visits (4.0 vs. 3.2, P=0.038). Total inpatient days (10.8 vs. 3.7 day per patient, P<0,001) and ICU days (2.2 vs. 0.1, P<0,001) were significantly less after palliative care referral. Home visits were infrequent and represented a small percentage of all encounters recorded (0.8%, N=198 visits).
Conclusions: Service utilization decreased significantly after referral to palliative care service. Most of our patients died with a DNR order in place and approximately 1 out of 8 died at home. Improving our home care program may help in better utilization of services.

EP397 / #352

Topic: *AS05.p Supportive Care and Palliative Care*

RISK STRATIFICATION TO AID MANAGEMENT OF FEBRILE NEUTROPENIA IN PAEDIATRIC ONCOLOGY PATIENTS: A SINGLE CENTRE STUDY

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Background and Aims: Febrile Neutropenia (FN) is the commonest fatal complication of anticancer treatment in paediatric oncology patients with a mortality rate of 2-21%. Risk stratification can be used to identify children and young people (CYP) at low risk of a life-threatening cause of FN in whom FN treatment could be stepped down to out-patient oral antibiotic treatment. In Nottingham Children's Hospital, CYP admitted with FN were risk stratified using the Swiss Paediatric Oncology Group (SPOG) score. This study aims to determine whether stepping down treatment to oral antibiotics was associated with any adverse outcomes.
Methods: Data was collected from CYP admitted with FN from September 2016 to September 2020. Fever neutropenia episodes were defined according to the SPOG scoring tool and NICE guideline. Admitted CYP with FN were stratified into low and standard risk groups using the SPOG score. Data was collected on duration of admission, culture results and any adverse outcomes.
Results: 227 FN episodes were reviewed. Mean age at admission was 7.17 years (range 0-18). 55% (125) had acute lymphoblastic leukaemia and 59% (74) of these were in their maintenance treatment. 41% (93) of FN admissions were classified as low-risk (LR), and 59% (134) as standard risk (SR). In the SR group 57% (71) of CYP had a positive blood culture. In the LR group, there were 4 positive blood cultures, all subsequently shown to be a contaminant rather than true infection. 27% (25) in the LR group had a positive respiratory viral swab. There were no episodes of sepsis, intensive care admissions or deaths in the LR group.
Conclusions: This study demonstrates the safety of treatment with oral antibiotics in CYP with low-risk FN stratified after admission using the SPOG risk stratification tool. Stepping down treatment to oral antibiotics allows earlier discharge which is beneficial for CYP well-being and reduces healthcare costs and bed utilisation.

EP398 / #163

Topic: *AS05.p Supportive Care and Palliative Care*

GUIDING PRINCIPLES FOR CARE OF ADOLESCENT AND YOUNG ADULT PATIENTS WITH CANCER IN LATIN AMERICA

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Background and Aims: Most adolescents and young adults (AYAs: ages 15-39) with cancer live in low- and middle-income countries (LMIC), including Latin America (LA). However, the majority of what is known about this unique group is from high-income countries, including guidelines for care. To fill this gap, we developed an expert panel endorsed list of guiding principles for AYA cancer care in LA.
Methods: We used the modified Delphi method to gather expert opinion on guiding principles for the care of AYAs with cancer in LA. The expert panel consisted of 25 pediatric and medical hematologist/oncologists from 15 countries (12 in LA). The panelists were electronically presented with 18 proposed guiding principles obtained from literature review and surveys and interviews conducted previously with LA physicians. The panelists scored each proposed guiding principle's importance on a 9-point scale. Panelists were able to modify or recommend additional guiding principles. After the 1st and 2nd round, the study team modified and added guiding principles based on panelist's comments. In each round (3 total), guiding principles were considered endorsed if they had a median score of ≥ 7 (with no participant marking it as <3).
Results: The twenty endorsed guiding principles fell into 4 categories: Clinical Care (e.g., patients should be able to continue care where they started), Support Services (e.g., support group of peers), Education for Physicians (e.g., education on presentation of cancer in AYAs), and Advocacy (e.g., AYA specific foundations). Unendorsed statements included where patients should receive treatment (pediatric vs adult center) based on age.
Conclusions: This study identified 20 guiding principles for AYA cancer care in LA, which can be incorporated into cancer control programs. This study serves as a framework for developing guiding principles for other LMIC with the goal of improving AYA cancer care globally.

EP399 / #778

Topic: *AS05.p Supportive Care and Palliative Care*

INCIDENCE AND FACTORS ASSOCIATED WITH TUMOUR LYSIS SYNDROME AMONG PAEDIATRIC ONCOLOGY PATIENTS AT THE KORLE BU TEACHING HOSPITAL, ACCRA, GHANA

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Background and Aims: Tumour lysis syndrome (TLS) is an oncological emergency associated with high morbidity and mortality especially in centres with limited resources. It is a metabolic disorder characterized by hyperuricaemia, hyperkalaemia, hyperphosphataemia, and hypocalcaemia, with or without renal insufficiency. TLS usually follows chemotherapy but can occur prior to any cancer-related treatment. Prevention, early detection, and management of TLS help improve the survival of children with cancer. The aim of this study was to determine the incidence and factors associated with TLS among children between 0 to 17 years of age, newly diagnosed with cancer, admitted at the Department of Child Health of the Korle Bu Teaching Hospital, Accra, Ghana
Methods: Hospital-based prospective study conducted from September 2020 to February 2021 on 55 children newly diagnosed with cancer. Patients were followed and the socio-demographic, physical diagnosis, imaging, laboratory and treatment data were collected. Serum uric acid, creatinine, potassium, phosphate, and calcium were measured before chemotherapy (Day 0/baseline), then after initiation of chemotherapy on Day + 1 & Day + 3 in all patients. Data was entered and analysed by SPSS version 25.
Results: Among 55 oncology patients, 33(60.0%) were male. Median age was 3.8[IQR 1.9 - 7.1] years. Cancer types were solid tumours 38(69.1%), acute leukaemia 9(16.4%) and lymphoma 8(14.6%). Most cancers 38(69.1%) were high-risk. The overall incidence of TLS was 10/55(18.2%), with one case of spontaneous clinical TLS, and 70% cases by Day+1. Metabolic abnormalities were hyperphosphataemia-10/10(100%), hyperuricaemia-8/10(80%), hyperkalaemia-4/10(40%) and hypocalcaemia-0/10(0%). TLS was present in 2/8(25%) and 8/38(21%) participants with lymphoma and solid tumours respectively. Factors associated with TLS were high-risk disease ($p = 0.020$) and LDH ≥ 1000 IU/L ($p = 0.030$). There was no TLS-related mortality.
Conclusions: incidence of TLS in solid tumours was comparable to lymphoma due to advanced disease at presentation. TLS prophylaxis should be more aggressive in patients with high-risk disease and LDH >=1000 IU/L.

EP400 / #240

Topic: *AS05.p Supportive Care and Palliative Care*

INCLUSION OF PHARMACISTS IN THE MULTIDISCIPLINARY TEAM DEVELOPING EMERGENCY CHEMOTHERAPY PROTOCOLS IMPROVES CHEMOTHERAPY PRESCRIBING AND ADMINISTRATION

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Background and Aims: Uganda Cancer Institute (UCI) is a centralised facility accepting approximately 600 paediatric oncology patients annually. Chemotherapy medication errors at UCI are partially ascribed to unstandardised chemotherapy prescription and administration practices. Key challenges include 4-6 weeks' delay in obtaining confirmed histologic diagnoses and low staffing levels. Objective: to determine whether the introduction of four standardised "emergency" protocols improved the accuracy of prescription and administration, and staff acceptance thereof.
Methods: A multidisciplinary team devised four "emergency" protocols: 1) cyclophosphamide, vincristine, prednisolone for suspected lymphoid malignancies, 2) vincristine, dactinomycin, cyclophosphamide for suspected soft tissue sarcomas, 3) vincristine, carboplatin, etoposide, cyclophosphamide for suspected neural tumours, and 4) carboplatin, etoposide, bleomycin for suspected germ cell tumours. A pilot project assessed impact of the new protocols on medication errors.
Results: Twenty-Four Files were evaluated. Sixteen (8 doctors, 8 nurses) assessed the usefulness of the new protocols. Presence of a filed histologic diagnosis was unchanged before and after project implementation (9/12 to 10/12). Reasons included insufficient pathologists, one immunohistochemistry machine, stock-outs of reagents. Rates of sign-off of chemotherapy prescriptions by qualified medical doctors did not change noticeably (4/12 to 6/12) because of unchanged high patient volumes with few doctors. There was improvement in prescription of supportive fluids (2/12 to 12/12) and antiemetics (9/12 to 12/12), attributed to clear protocol guidance. Majority of doctors (7/8) felt that the tool increased accuracy in prescribing process, and 2/2 ward nurses and 0/8 outpatient nurses felt that the tools improved chemotherapy administration process.
Conclusions: Emergency protocol prescription has enabled a systematic method to treat patients before histologic results are available. Inclusion of a pharmacist in the MDT facilitated standardisation of prescription and administration. Supportive care improved and errors decrease, but nursing acceptance and satisfaction are currently low, which warrants further exploration. Such interventions are low cost and have high impact in LMIC settings.

EP401 / #1416

Topic: *AS05.p Supportive Care and Palliative Care*

DEDICATED PHARMACISTS IN AFRICAN PAEDIATRIC ONCOLOGY UNITS: A SIOP GLOBAL MAPPING PROGRAMME REPORT

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Background and Aims: An oncology clinical pharmacy, part of a multidisciplinary approach to curing and managing paediatric cancer, is a patient-centered, drug-focused, and outcome-oriented process of drug therapy management. Three main barriers to a pharmacist's presence in paediatric oncology units (POUs) in low- and middle-income countries previously reported include: a) health system structural constraints; b) low level/quality of community pharmacy services and c) educational and professional factors. Aim: identify African POUs with dedicated pharmacists and describe facilitators and barriers for dedicated POU pharmacists.
Methods: SIOP Global Mapping Programme data extracted from a survey of African paediatric oncology facilities (2018-2020) documented dedicated pharmacists in POUs. Expert opinion was sought from the pharmacist authors to summarise barriers and facilitators for POU pharmacists.
Results: Mapping data indicated that of 47 African countries surveyed, 91/109 responding POUs had a dedicated pharmacist (don't know=1; missing data=9). Barriers for a dedicated pharmacist include funding, lack of trained staff, and lack of career guidance. Facilitators include resource allocation, acknowledgment of pharmacist expertise, international non-governmental organisation and professional association support, mentors, and increased data to advocate for more staff.
Conclusions: Most reporting African POUs have a dedicated pharmacist. The scope of service should be documented and standardised. Barriers should be systematically analysed using a standardised oncology pharmacy scope approach and facilitators exploited to ensure that all POUs have the essential services of a dedicated pharmacist. The SIOP Global Health Network OncoPharmacy Working Group has initiated coordination with 91 African POUs, to assist other units to establish clinical pharmacy services. It is critical to produce an essential requirements guideline to document minimum competencies for paediatric oncology pharmacists, detailing the space, equipment, and tools required to treat children with cancer. Future directions include documenting the impact of dedicated POU pharmacists and how they support childhood cancer treatment, nursing occupational safety, and parent/caregiver medication education

EP402 / #1649

Topic: *AS05.p Supportive Care and Palliative Care*

GLOBAL CHALLENGES IN PEDIATRIC ONCOLOGY CRITICAL CARE IN RESOURCE-VARIABLE SETTINGS: A ONE-YEAR EXPERIENCE

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Background and Aims: Over 80% of children with cancer reside in low- and middle-income countries which face multiple challenges delivering high-quality pediatric onco-critical care (POCC). The PediatRic Oncology cApaCity Assessment Tool for IntensiVe CarE (PROACTIVE) was launched in 2021 to help organizations evaluate strengths and limitations in POCC services. In this study, we describe common global challenges in POCC services in resource-variable settings identified using PROACTIVE.
Methods: PROACTIVE is an electronic assessment tool divided into 2 English-language surveys for intensivists and oncologists managing critically ill pediatric hematology-oncology patients. The tool is arranged into 8 domains and 22 subdomains with answer options in the dichotomous, numerical, and Likert scale. Aggregated data from 28 centers that completed PROACTIVE between January 2021 and March 2022 were retrospectively analyzed and summarized. Indicators with a mean score ≤ 75% in accessibility or performance across all centers were classified as common global challenges in POCC.
Results: Aggregated data across 28 centers from 19 different countries of varying economic levels and pediatric critical care services were analyzed for performance comparison. Identified common challenges

included: 1) shortage of pediatric intensivists resulting in inability to provide coverage 24 hours a day/7 days a week, 2) lack of updated guidelines to direct the care of critically ill PHO patients such as chemotherapy-related toxicities, 3) absence of abstinence and withdrawal symptoms monitoring, 4) inability to obtain blood products emergently within 1 hour, and 5) lack of collaborative work with other institutions to benchmark outcomes.
Conclusions: PROACTIVE is a contextually appropriate diagnostic tool that can help clinicians and organizations identify challenges in POCC services and prioritize among multiple quality improvement initiatives. Aggregated PROACTIVE data identified common organizational challenges in POCC services that can be used to develop global interventions to improve outcomes for critically ill children with cancer.

EP403 / #840

Topic: *AS05.p Supportive Care and Palliative Care*

EPIDEMIOLOGY OF CENTRAL VENOUS LINE (CVL) DYSFUNCTION IN CHILDREN WITH CANCER: RESULTS OF A PROVINCIAL PROSPECTIVE COHORT STUDY

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Background and Aims: CVL dysfunction (CVL-D) is a common, yet not well described complication in children undergoing cancer therapy. Hence, we undertook a provincewide prospective cohort study to define the epidemiology and risk factors predisposing to CVL-D and its outcome.
Methods: Children (<18 yrs.) with newly diagnosed non-CNS cancer and no history of TE or anticoagulation therapy, were recruited at diagnosis from 5 tertiary-care pediatric oncology centres in Ontario (n=519). Details of demography, cancer diagnosis and therapy, CVL insertion and removal, CVL complications (CVL-D [defined as persistent or recurrent difficulty in infusion, blood draw or both], thrombosis and infection) while on primary cancer therapy, cancer-outcome and survival were collected. Analyses were performed to evaluate the impact of patient and CVL-related factors on the risk of CVL-D.
Results: Of 486 evaluable patients (median age 6.27yrs.; 212 (44%) females), 182 (37.4%) had CVL-D during cancer-therapy. Of 141 (29%) patients that developed CVL-D with first CVL, median time to CVL-D was 47 days; 93 (66%) patients had difficult blood draw and 21(15%) had more than one type of dysfunction. Seventy-eight of 141 patients (55%) had at least one investigation for CVL-D; 28 (20%) had mechanical cause and 5 (3.5%) had thrombotic etiology. Eighty-seven of 141 (62%) patients received some CVL-D-directed therapy; tPA in 58 (41%), anticoagulation in 3(2%) and 33 (23%) required surgical intervention. Patients with CVL-D had significantly more catheter days (median 756 vs. 387; p=0.008). On multivariable analyses, younger age, hematologic malignancies, number of CVLs and CVL care-bundle were significantly associated with CVL-D.
Conclusions: CVL-D occurred in 37% of children during cancer-therapy; younger patients and those with hematological malignancies were at higher risk for CVL-D. Over 20% patients with CVL-D required either revision or removal of CVL underscoring the need for adequate evaluation and management of CVL-D. Efforts also need to be directed at prevention of CVL-D.

EP404 / #1336

Topic: *AS05.p Supportive Care and Palliative Care*

CHEMOTHERAPY-INDUCED NAUSEA AND EMESIS CONTROL IN CHILDREN WITH CANCER: SINGLE-CENTER EXPERIENCE

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Background and Aims: Chemotherapeutics have varying degrees of emetogenic potential. This study aimed to document the emetogenic potential of chemotherapeutics and evaluate the effectiveness of antiemetic treatment.
Methods: All patients receiving intermediate, high or very high emetogenic chemotherapy for 6 months (May to December 2021) were included in the study. Chemotherapy-induced nausea and vomiting (CINV) was defined as acute (<24h) and delayed (24-120h), and overall (0-120h). Emesis was graded according to NCI CTCAE (Version 4.03).
Results: In total, 167 children with a median age of 6.7 years (ranged 0.6-17 years), M/F=1.6) were included in the study. The frequency of emesis was 33% in cyclophosphamide-based regimens, 30% in cisplatin-based regimens, 25% in anthracycline-based regimens and 14% in ifosfamide-based regimens. Emesis was found to be significantly increased in patients receiving cyclophosphamide-based chemotherapy regimen (p=0.014). The combination of cyclophosphamide with anthracycline (74%) and cyclophosphamide with cisplatin (69%) had the highest emetogenic potential. Changes in appetite were found in 81%, 74%, 73% and 69% in ifosfamide-based, anthracycline-based, cyclophosphamide-based and cisplatin-based regimens, respectively. Complete protection rates to antiemetic treatment, in acute, delayed, and overall phases were 91%, 81%, and 76% respectively. The complete protection rate was significantly worse in children older than 6 years (p=0.032). Aprepitant, 5HT3 antagonist and dexamethasone were given for prevention of CINV for high and very high-risk emetogenic chemotherapy (n=82). But 47 children could not receive aprepitant due to insurance or economic reasons, they only received 5HT3 antagonists and dexamethasone. No significant protective effect on appetite was found in children received aprepitant compared to the others (23% vs 31%, p=0.3). But aprepitant provided greater complete control rate of vomiting (84% vs 61%, p=0.004).
Conclusions: Cyclophosphamide-based regimens especially with doxorubicin or cisplatin have higher potential for CINV. Although aprepitant was reported as a potent antiemetic drug for CINV, its effect on appetite was mild in our group.

EP405 / #1988

Topic: *AS05.p Supportive Care and Palliative Care*

DEVELOPMENT OF A GLOBAL PALLIATIVE CARE PROGRAM

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Background and Aims: Disparities in access to pediatric palliative care (PPC) and pain management remain an under-addressed global health issue, especially in low- and middle-income countries (LMICs). Although integration of palliative care (PC) is currently considered a quality standard in children with cancer, very few hospitals, countries and regions have achieved this standard. The St Jude Global Palliative Care Program was created to define the current state of PC in underserved communities worldwide and drive collaborative interventions with our global partners to relieve the suffering of patients and families facing the challenges of pediatric cancer. We describe the program's developmental processes and the challenges and success.
Methods: The St Jude Global Palliative Care program was established in 2018 under the leadership of an interdisciplinary team of experts in PPC. It has been developed through 4 fundamental pillars: Research, Education, Capacity Building, and Advocacy. Activities in these areas have been developed in each of the WHO regions.
Results: From December 2018 to March 2022, the St Jude Global Palliative Care Transversal program has developed 16 educational projects, 7 advocacy activities, 4 projects in capacity building and 4 large research studies. These activities have been conducted in 99 countries from 5 continents. Collaborative work with World Health Organization (WHO), Pan American Health Organization (PAHO), International Children's Palliative Care Network (ICPCN), and the Worldwide Hospice Palliative Care Alliance (WHPCA) has been essential for developing activities. The program has developed a provider network of 1,280 members from every continent of the world.
Conclusions: The development of regional activities based on a needs assessment is essential to promote the development and prioritization of PPC according to their locoregional needs and resources. We are currently in the process of developing a global PPC strategic plan that we will share at the SIOP meeting.

EP406 / #1298

Topic: *AS05.p Supportive Care and Palliative Care*

PREVALENCE AND PERCEPTION REGARDING COMPLEMENTARY AND ALTERNATIVE MEDICINE USE IN CHILDHOOD CANCER PATIENTS

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Background and Aims: Complementary and alternative medicine (CAM) use in childhood cancer patients is less explored. We estimated prevalence of CAM use among children with cancer and analysed the role of demographics, disease characteristics and parents'/caregivers' beliefs on CAM use.
Methods: A cross sectional study was carried out between December 2020 and October 2021 where parent/caregiver of children (≤18 years) on active treatment of malignancy were included. A draft interview schedule was prepared to capture the socio-demographics, clinical details, details of CAM use, and reasons for use/non-use. A 29-item interview schedule was finalized after expert review for content validation and pilot testing among 30 participants for clarity/relevance. Binary logistic regression was used to assess impact of socio-demographic variables, malignancy type (haematological/solid), disease status (newly diagnoses/relapse), treatment intent (curative/palliative), delay in seeking treatment (above/below median symptom duration) on CAM use.
Results: Total 450 patients (median age 9 years) were included (68.9% males; 64% haematological malignancies), with 391 (86.9%) newly diagnosed cases and 402 (89.3%) patients on curative-intent therapy. Median symptom duration was 1 month. Non-prescribed remedies/therapy was used by 162 (36%) patients, of which 62 (13.7%) patients used CAM and 125 (27.7%) patients used home-based remedies alone/concomitantly. The most common system of CAM used was Ayurveda (41/62; 66.1%) followed by Homoeopathy (20/62; 32.2%). Median duration of CAM use was 30 days with median expense of INR 1750 (USD 23). The most common reason of CAM use was suggestion by family member (27/62; 43.5%) while that of non-use of CAM was belief in efficacy of modern medicine (152/388; 39.1%). CAM use was more common in patients on palliative-intent therapy (OR:2.33; p=0.021) and those with delay in seeking care (OR:2.35; p=0.003).
Conclusions: Ayurveda is the most commonly used system of CAM in children with cancer. It is more common in palliative-intent therapy and may contribute to treatment delay.

EP407 / #940

Topic: *AS05.p Supportive Care and Palliative Care*

IMPACT OF SARS-COV-2 PANDEMIC ON TREATMENT INITIATION AND DELIVERY IN CHILDREN WITH CANCER

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Background and Aims: The SARS-CoV-2 pandemic has hindered timely access to paediatric cancer care. Infected children with cancer have a mild clinical course. Less well described is the impact of infection on cancer care on children. Here we report experience at a tertiary cancer centre in India.
Methods: Beginning with the first infection wave, national/institutional protocols required periodic mandatory testing for patients (and where applicable, caregivers) including at first presentation, prior to procedures/admissions, with fever or contact with an infected person. Infected patients were advised mandatory quarantine (2-3 weeks), Infected patients and family contacts were monitored by telephone and in some cases, were prescribed bridging oral chemotherapy. Due to logistic issues, only symptomatic or febrile children were hospitalised in the dedicated Covid-19 ward.
Results: Over 23 months (March'20-Feb'22), 262 children with cancer or non-malignant haematological disorders (median age, 7 years; interquartile, 4·3-11·7 years) were diagnosed with SARS-CoV-2 infection, including 206 (79%) with haemato-lymphoid cancers and 53 (20%) with solid tumours. In 46 (17.5%), infection was diagnosed at first presentation, resulting in either delay (21/46, 46%) or failure to initiate treatment (18/46, 39%). Infection delayed intensive cancer treatment in 148 (56%), with 96 (65%) experiencing treatment delays of ≥ 14 days (median, 20 days, interquartile, 16-24 days). Infection less commonly affected maintenance chemotherapy (31/89, 35%). Eighteen children (3%) required hospitalisation (median 4.5 days; interquartile, 3-7 days), 2 (11%) with symptomatic Covid-19 and the rest for treatment/disease-related toxicities. One died due to probable SARS-CoV-2-related multisystem inflammatory syndrome.
Conclusions: The SARS-CoV-2 pandemic and the associated restrictions delayed initiation of cancer treatment and disrupted cancer treatment intensity in infected children, the impact of which may become apparent with time. Given the protracted pandemic course, institutions will need to develop dedicated facilities and services to ensure that infected children with cancer continue to receive appropriate-intensity treatment.

EP408 / #1992

Topic: *AS05.p Supportive Care and Palliative Care*

MEDICAL PERCEPTION ON PALLIATIVE CARE, THERAPEUTIC OBSTINACY, AND END OF LIFE, IN A PEDIATRIC ONCOLOGICAL HOSPITAL, IN SÃO PAULO STATE, BRAZIL

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Background and Aims: Cancer is not a unique disease, with a unique cause. It is a group of distinct diseases, with different causes, symptoms, treatments, and prognoses. In childhood and adolescence, cancer is the first cause of death by disease in all regions of Brazil. Despite the technical and scientific advancements achieved by oncology and the effort of healthcare professionals, many diseases still threaten the continuity of life and the aim of the treatment is not only to cure, but also to improve the quality of life, prevent and alleviate the suffering of the patient and her/his family. JUSTIFICATION: The medical staff is familiar with dealing with the disease, however there is great difficulty in dealing with the particularities of individuals who cannot be cured; along with the disease, the patients bring with them their fears, doubts, expectations, as well as those of their families. Treating these patients as a whole, tending to their needs, goes beyond care, it becomes a challenge. AIM: To understand the medical perception on palliative care, therapeutic obstinacy, and end of life, in a pediatric oncological hospital in São Paulo State, Brazil.
Methods: This is a descriptive, qualitative exploratory study. The reference framework used to the analysis of qualitative data is the Method of Content Analysis proposed by Bardin.
Results: The data collected were organized according to the following themes: Palliative Care in academic training; The lack of knowledge and the search for information; Conceptions on Palliative Care; Obstacles faced to reach Palliative Care; Therapeutic obstinacy; End of life and a peaceful death
Conclusions: It is evident that issues as palliative care, therapeutic obstinacy, and end of life are not sufficiently addressed in the training of healthcare professionals, turning into a difficulty to them, when facing certain situations during their professional lives.

EP409 / #1996

Topic: *AS05.p Supportive Care and Palliative Care*

PALLIATIVE CARE IN PEDIATRIC ONCOLOGY: CONCEPTIONS OF ADOLESCENTS UNDERGOING CANCER TREATMENT.

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Background and Aims: Considering the scarcity of research addressing palliative care in adolescents with cancer diagnosis and treatment in the Brazilian context. It is necessary to investigate the conceptions and meanings attributed to palliative care for adolescents with a Malignant diagnosis, in order to support the development of educational materials that clarify the main issues related to the topic.
Methods: This is an exploratory descriptive study with a qualitative approach. The sample consisted of adolescent patients, aged between 12 and 19 years, diagnosed with cancer for at least six months and undergoing treatment at the institution. Data collection was divided into two stages. Initially, data were collected to characterize the sociodemographic and clinical profile of the participants. Sequentially, a semi-structured individual interview was carried out based on 5 guiding questions.
Results: Fifteen adolescents participated in this study, among which 46.7% were male, 53% of the sample had solid tumors, with a predominance of the characteristic histological type for osteosarcoma, while 47% presented with hematological neoplasms, thus for acute lymphoid leukemia. Only 1 participant had evolved palliative status in the medical record, another 11 had poor prognostic factors. Of the 15 respondents, 7 reported never having heard the word “Palliative care”. Those who said they knew and understood the word “Palliative Care” demonstrated an association between the term and the distance from cancer treatment. As the main factors for elucidating the theme for this audience, most highlighted the importance of differentiating the term palliative care and its association with end-of-life care. The need for accessibility for clear and effective communication was also highlighted.
Conclusions: Understanding the perceptions of adolescents undergoing cancer treatment on aspects of PC allows health providers to establish not only better and appropriate strategies for communication, but also the development of a care plan aligned with the perspective of the patient and his family.

EP410 / #2001

Topic: *AS05.p Supportive Care and Palliative Care*

ASSESSMENT OF PAIN MANAGEMENT KNOWLEDGE BY THE NURSING TEAM OF A CHILDREN'S CANCER HOSPITAL IN A CITY IN THE INTERIOR OF SÃO PAULO.

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Background and Aims: In view of the difficulties in pain management and assessment, this research seeks to identify the level of assessment of pain management by nursing professionals: nurses and nursing technicians from a Children's Oncological Hospital, in a city in the interior of São Paulo .
Methods: It consists of a longitudinal study with prospective data collection through a questionnaire prepared by the researcher, developed at the Children's Hospital, with 125 nursing staff collaborators, 62 technicians and 63 nurses. The questionnaire and the informed consent were handed by the researcher to the professionals in their respective sectors.
Results: A number of 100 professionals were obtained in the research, being 47 nurses and 53 nursing technicians. The sector with the highest number of professionals is the Infirmary. The FACES and Numerical scales were the most used (86). Most professionals had a period of experience between five and 10 years (40). Most did not receive any teaching about pain during training and do not have extracurricular training (36). Regarding the assessment of patients with cognitive impairment, the vast majority reported having doubts (46). The most common side effect was dependence (35) and respiratory failure (36). When starting laxatives and using opioids, they responded at the same time (62), but reported having doubts (16). Regarding the use of morphine in sedation (63) reported being used,
Conclusions: There is a lack of knowledge regarding the assessment of pediatric pain, from the use of scales to their management. There is also a fear of professionals regarding the use of opioids in the pediatric population, as well as a lack of knowledge of pharmacokinetics, side effects and their correct use for the treatment and management of pain.

EP411 / #595

Topic: *AS05.p Supportive Care and Palliative Care*

THE FIRST YEARS: AN EMBEDDED PEDIATRIC PALLIATIVE ONCOLOGY CLINIC

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Background and Aims: Children with cancer have significant illness burden, suffering, and familial stress. Pediatric palliative care (PPC) improves quality of life and improves end-of-life outcomes, but often occurs late in the disease course. Expanding PPC to the outpatient clinic improves PPC access and timing. The aims are to describe the inaugural four years (2017-2021) of one of the U.S's first academic, consultative, embedded pediatric palliative oncology (PPO) clinics, reviewing patient demographics, disease-based and treatment information, visit data, and palliative and end-of-life outcomes.
Methods: This is a single-institution prospective cohort study of pediatric oncology patients aged 0 – 27 years seen in a PPO clinic from June 2017 through June 2021. Demographics, disease-based data, PPC visit data, and end-of-life outcomes were collected prospectively. Descriptive statistics and changes over time were calculated.
Results: During the first four years, 248 patients (51.6% male; 58.1% White; 35.5% Black; 13.7% Hispanic/Latino) were seen in PPO clinic, totaling 1,665 clinic visits (median 5, IQR 3, 9). Primary diagnosis was brain tumor (42.3%), solid tumor (37.1%), and leukemia/lymphoma (17.3%). The first point of PPC contact was PPO (70.6%) for most patients versus inpatient consult. Over four years, the proportion of PPO consults occurring greater than 90 days from death increased from 39.1% to 85.0%, and median time from PPO consultation to death increased from 74 to 226 days ($p<0.0001$). Among the 136 deceased patients (54.8%), 77.9% had a do-not-resuscitate, and 72.8% received hospice care. When known (n=112), 89.3% died in their preferred location. Early PPO (<12 weeks from diagnosis) and advance care plan documentation ($p=0.03$ and $p=0.02$, respectively) were associated with family identification of a preferred location of death
Conclusions: Embedded PPO clinics can be successful, achieve steady growth, and improve end-of-life outcomes through improved access and timing of PPC delivery. Pediatric cancer centers should work collaboratively to include PPO outpatient services.

EP412 / #686

Topic: *AS05.p Supportive Care and Palliative Care*

MICAFUNGIN TWICE-A-WEEK IS EFFECTIVE FOR PROPHYLAXIS OF INVASIVE ASPERGILLUS INFECTIONS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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Background and Aims: Invasive fungal disease is frequently diagnosed during the early phase of childhood acute lymphoblastic leukaemia (ALL) treatment and is associated with morbidity and mortality. Prophylactic strategies might be beneficial, but first-line azole prophylaxis is hampered by the interaction with vincristine. A twice-a-week micafungin regimen for Aspergillus prophylaxis was therefore evaluated in this study.
Methods: Paediatric patients with ALL (09/2018-07/2020) received micafungin twice-a-week (9 mg/kg/dose [max. 300 mg]) during the first five weeks of treatment (i.e. induction course), as part of routine care. A historical control cohort (04/2012-09/2018) was used without fungal prophylaxis during this induction course. After the first five weeks (i.e. first consolidation course), standard mould-active prophylaxis was used in both groups. The percentage of proven and probable Aspergillus infections at the end of the first consolidation course (i.e. at the end of week 10) was compared between the cohorts.
Results: A total of 169 and 643 paediatric patients with ALL were included in the micafungin (median age, 4 years [range 1-17]; 43.2% female) and historical cohort (median age, 5 years [range 1-17]; 40.4% female), respectively. The percentage of proven and probable Aspergillus infections was 1.2% (2/169) in the micafungin cohort versus 5.6% (36/643) in the historical cohort (p=0.013; Fisher’s exact test).
Conclusions: Twice-a-week micafungin prophylaxis during the induction course significantly reduced the occurrence of proven and probable Aspergillus infections in the early phase of childhood ALL treatment.

EP413 / #253

Topic: *AS05.p Supportive Care and Palliative Care*

FEASIBILITY OF THREE TIMES WEEKLY SYMPTOM SCREENING IN PEDIATRIC CANCER PATIENTS

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Background and Aims: We created the Symptom Screening in Pediatrics Tool (SSPedi) to enable pediatric cancer symptom screening. However, the ability of pediatric patients to self-report symptoms longitudinally was uncertain. Primary objective was to determine the feasibility of three times weekly symptom reporting by pediatric cancer patients for eight weeks.
Methods: We included English-speaking patients 8-18 years of age with cancer. Patients were sent reminders by text or email to complete SSPedi three times weekly for eight weeks. If patients reported at least one severely bothersome symptom, a symptom report was emailed to the primary healthcare team. Patient-reported outcomes were obtained at baseline, week 4±1 and week 8±1. Symptom documentation, intervention provision for symptoms and unplanned healthcare encounters were determined by chart review at weeks 4 and 8. Feasibility threshold was 75% patients achieving compliance with at least 60% of SSPedi evaluations. We planned to initially enroll 20 participants and, if feasibility metrics were not met, to enroll successive cohorts of 10 participants until feasible metrics were met or a maximum of 60 participants had been enrolled.
Results: Two cohorts consisting of 30 patients (cohort 1 (n=20) and cohort 2 (n=10)) were required to meet feasibility metrics. In cohort 1, 11/20 (55%) met SSPedi completion threshold. Interventions applied after cohort 1 included engaging parents to facilitate pediatric patient self-report, providing mechanisms to remember username and password and highlighting potential benefits of symptom feedback to clinicians. In cohort 2, 9/10 (90%) met SSPedi completion threshold and thus feasibility was met. Patient-reported outcomes and chart abstracted outcomes were obtained for all participants in cohort 2.
Conclusions: Three times weekly symptom reporting by pediatric patients with cancer for eight weeks was feasible. Mechanisms to enhance three times weekly symptom reporting were identified and implemented. Future studies of longitudinal symptom screening can now be planned.

EP414 / #1393

Topic: *AS05.p Supportive Care and Palliative Care*

SUPPORTING CHILDHOOD CANCER SURVIVOR QUALITY OF LIFE AND EDUCATIONAL ATTAINMENT: PILOTING THE HOSPITAL EDUCATION LIAISON PROGRAM

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Background and Aims: Childhood cancer survivors often experience learning difficulties. Schooling supports can ameliorate impacts but difficulties with family-school-clinician communication and shared knowledge are barriers to access. Hospital-school liaison programs can provide helpful consultation and facilitate communication. These services, however, can be costly and inaccessible to low-income families. We piloted a grant-funded liaison program to provide no-cost supports and evaluate impacts.
Methods: The Hospital Education Liaison Program (HELP) was established in 2020. Coordinated by a special educator, HELP provides consultation and facilitates communication among patients' families, medical teams, and school teams. Clincian referrals to HELP document patient demographics, diagnoses, and education-related concerns. AT HELP intake, the liaison provides psycho-social education regarding education policies and potential schooling supports. The liaison and family set goals for HELP services engagment. Data regarding parent satisfaction, changes to patient educational services following HELP intervention, and school team feedback are collected.
Results: Since fall 2020, 34 patients have been referred to HELP (27.3% in treatment, 29.4% recently completed treatment, 45.5%> 1 year post-treatment). Nearly half (48%) of patients are from low-income families. Most common reasons for referral were family concerns that educational needs were not being met (21.4%) and family confusion about the academic support eligibility process (19.1%). All patients who engaged with HELP increased their formalized school supports. School teams reported benefiting most from the liaison's translation of medical information into educatinoal language and actionable recommendations.
Conclusions: This education liaison program has, thus far, improved patient access to educational supports. HELP offers just-in-time supports while simultaneously building family, clinician, and educator capacity. The program is a potential low-cost/ high-yield intervention for improving childhood cancer survivors' educational attainment and quality of life. Further research is needed to determine which aspects of the program characteristics are most impactful for families and schools.

EP415 / #1942

Topic: *AS05.p Supportive Care and Palliative Care*

EFFICACY OF EMPIRICAL TREATMENTS USED DURING EPISODES OF FEBRILE NEUTROPENIA IN PEDIATRIC PATIENTS RECEIVING CHEMOTHERAPY: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Background and Aims: Febrile neutropenia (FN) is the first cause of hospitalization due to chemotherapy complications and is the second diagnosis in children with cancer visiting the emergency room. Thus, the aim of this systematic review was to synthesize the evidence of the efficacy of empirical treatments used during episodes of febrile neutropenia in pediatric patients receiving chemotherapy, as well as to compare them through a network meta-analysis (NMA).
Methods: A systematic literature review was carried out in MEDLINE, Scopus, Cochrane Library (CENTRAL), Epistemonikus and LILACS without restrictions. In addition, a gray literature was searched in Scopus Conference and TESIUNAM. Randomized clinical trials (RCT) evaluating the efficacy of empiric treatments for resolution of FN in pediatric patients receiving cytotoxic chemotherapy were included. Odds ratios (OR) 95% confidence intervals (95%CI) were estimated between the comparisons of the different treatments employing cefepime as reference. Direct, indirect, and mixed comparisons were performed using a frequentist-type NMA with a random effects approach using the NETMETA package of the statistical program R 4.0.5.
Results: One thousand and thirty-six studies were identified as potentially relevant. After analyzing titles, abstracts, and full titles, 18 studies with 1547 FN episodes in 1006 pediatric patients were included in the review. The most frequently used treatment was cefepime alone or in combination (11 RCT), followed by piperacillin/tazobactam (9 RCT) and ceftazidime (7 RCT). NMA results showed no difference in efficacy between cefepime and piperacillin/tazobactam (OR= 1.15, [95%CI, 0.72 to 1.83]); results were similar when other antibiotics were compared.
Conclusions: This systematic review with NMA shows that empiric treatment for febrile neutropenia in pediatric cancer patients treated with cytotoxic chemotherapy are similar in efficacy.

EP416 / #428

Topic: *AS05.p Supportive Care and Palliative Care*

INVOLVING CHILDREN TREATED FOR CANCER IN DEVELOPING A SERIOUS GAME ABOUT RADIOTHERAPY

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Background and Aims: Children can experience anxiety and fear in conjunction with radiotherapy (RT). A serious game could prepare children for the procedure, teach them about the treatment and plausibly reduce their anxiety. A serious game is screen-based and can influence the player's view of the displayed phenomenon in the game. To include children with experiences of RT in the developmental process increases the likelihood that the game will be appropriate for children. The aim was to describe the contributions made by children through participatory action research during the developmental process of a serious game about RT.
Methods: Nine children (7-10 years old) with firsthand experience of RT were included. Through interviews and participant observations of the children playing the game, a list of proposed changes was presented to the game designers to make changes. During the iterative process six meetings were held, either face to face or online, in groups or individually.
Results: The children expressed opinions about the RT content and wanted more content about RT to be displayed in the game, which was implemented accordingly. The children conveyed the coping strategies they had used during RT which then was implemented in the game. Through the children's play the investigators could come up with ideas to make the game more amusing following the children's wishes of developing a fun game. The children's ability to participate was affected by the severity of their disease, consequently the prior plan of participation had to be modified.

Conclusions: Through the children's participation the game changed in several ways. Researchers within healthcare could use similar methods to co-create serious games together with children affected by a disease. Since the severity of the children's disease varies, it is necessary to adjust in accordance with the children's needs.

EP417 / #1038

Topic: *AS05.p Supportive Care and Palliative Care*

AN EDUCATIONAL INTERVENTION TO IMPROVE LEUCOVORIN ADHERENCE IN CHILDREN RECEIVING HIGH-DOSE METHOTREXATE IN LILONGWE MALAWI

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Background and Aims: Leucovorin rescue is essential in reducing the risk of high-dose methotrexate toxicity. In our center, all patients receiving high-dose methotrexate (>/=1000 mg/m^2) are given 12 scheduled doses of oral leucovorin rescue, administered to the patient by their guardian. As part of multidisciplinary rounds, we observed a high rate of non-compliance to leucovorin (<30%). We aimed to improve adherence through a quality improvement project focused on guardian education and tracking of leucovorin administration.
Methods: We developed targeted education as the first intervention in our quality improvement project. All patients were counseled on appropriate dosing and administration by nurses and provided with a leucovorin tracking sheet. This sheet contains 12 check boxes for each of the doses of leucovorin, scheduled time of administration, and prescribed dose (number of tablets). Guardians were educated on the number of tablets to administer, dose timing, and ticked a check box after each dose was administered.
Results: Forty-eight patients received high-dose methotrexate between April 2021 and January 2022. Guardians of 23 patients were given the form and tablets as scheduled. Wall clocks were provided in each room to help guardians monitor the correct administration time. Following implementation of the intervention, 64% of patients had no missed doses and used the form correctly, while 36% had at least 1 missed dose and did not complete the form correctly. Mucositis was observed in 25% of those who adhered, vs. 50% of those who didn't. Most guardians are illiterate and required assistance from a nurse to help complete the form.
Conclusions: The leucovorin tracking form was helpful in assessing leucovorin adherence. Additional challenges were uncovered, such as literacy levels of guardians. We are following up with a study to assess the impact of this intervention on the rate of methotrexate toxicity in our patient population.

EP418 / #770

Topic: *AS05.p Supportive Care and Palliative Care*

PILOT STUDY OF NON-ADHERENCE AND TREATMENT DROPOUT IN PEDIATRIC CANCER PATIENTS IN A TERTIARY HOSPITAL IN A LOW- AND MIDDLE-INCOME COUNTRY

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Background and Aims: Background and Objectives: The survival rate for pediatric cancer in low- to middle-income countries (LMIC) can vary from 35 to 60%. Among the factors that may be responsible of this are the lack of adherence and/or treatment dropout. In addition to limitations in the health care system, other causes of dropout and/or non-adherence to treatment in pediatric cancer that are directly related to the patients. Among these factors are gender, refusal of certain treatments and distance to the treatment center. With the purpose of knowing which of these factors influence the lack of adherence and/or dropout in our patients, we decided to carry out this study.
Methods: Cross-sectional study of a random sample of newly admitted patients treated between 2015-2019. Children were grouped into three groups: Patients without Dropout or Non-Adherence (PDA), Patients with Non-Adherence (patients who were absent between 15 and 29 days from their treatment, PNA) and Patients with Dropout (PD). $\chi 2$ and one-way ANOVA were used.
Results: During the study period, 600 new cases were registered, of which a sample of 318 patients was analyzed, 56.65% being boys. The 68.87% were PDA, 26.42% PD and 4.72% PNA. Of all PNA, 53.3% were boys and 26.7% were diagnosed with leukemia. Of all PD, 54.4% were boys and 32.1% were diagnosed with leukemia. A difference with p=0.051 was found between the three groups in terms of time from their house to the hospital in minutes, PDA: 122.12(+107.19), PNA: 113.27(+101.66) and PD: 156.77 (+128.35).
Conclusions: One factor that influences both non-adherence and treatment dropout in pediatric oncohematologic patients is the time to move to the hospital. This indicates factors directly associated with the primary caregivers possibly are elements that favor the lack of adherence and/or dropout of pediatric cancer patients.

EP419 / #1993

Topic: *AS05.p Supportive Care and Palliative Care*

USE OF BEDSIDE ULTRASOUND AND ANTHROPOMETRY TO EVALUATE SARCOPENIA IN CHILDREN WITH CANCER

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Background and Aims: Children with cancer are vulnerable to sarcopenia but defining the condition in this population is difficult due to the inconsistency in concepts and limited studies which assess the potential impact of sarcopenia on clinical outcomes. However in the last decade sarcopenia has been recognized as a negative impact of anticancer therapy in pediatric patients. This study assesses muscle wasting using bedside ultrasound and anthropometry in hospitalized children at pediatric oncology hospital.
Methods: Single-center, prospective cohort study, including consecutive children, admitted to the pediatric oncology ward. Quadriceps muscle thickness (QMT) and anthropometrics measurements were performed at admission, day-1, day-3, day-5, day-7, and then weekly until the 14th day of the ward stay.
Results: 56 children with cancer were evaluated at all time points of this study. 57% had hematologic malignancy, and 87% were hospitalized with an active infection under treatment. According to the Pairwise comparison method, longitudinally, no differences were found in the QMT from day-0 until day-7. However, between day-7 and day-14, a distinction was found but no statistically significant (p-value 0.09). Arm anthropometry (Triceps skinfold thickness, mid-upper arm circumference, and upper arm muscle area) presented similar results. However, when considering the hospitalization between D1 and D5, we did not find differences in quadriceps femoral thickness. This can be considered by the nutritional support offered during this period and the recovery that occurs in D7. In contrast, the measurement reduction in D14 may reflect the pathology, clinical severity, and/or intolerance to nutritional support.
Conclusions: Compared to other body composition assessment techniques, using this tool in children with cancer reduces the use of other tests and avoids additional exposure to ionizing radiation. Therefore, advancing our understanding of bedside ultrasound evaluation of QMT in children with cancer may lead to low-cost clinical interventions, such as optimizing protein intake following specific guidelines aimed at this population.

EP420 / #1994

Topic: *AS05.p Supportive Care and Palliative Care*

HAND-GRIP STRENGTH: A WAY TO ENHANCE BODY COMPOSITION EVALUATION IN CHILDREN WITH CANCER?

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Background and Aims: Much has been discussed about the parameters to identify malnutrition in pediatric cancer patients. Considering the different social issues that guide decision making, anthropometry is an easily accessible, fast and low-cost tool. Hand grip strength, to evaluate the muscle function is well stablished in adult literature and has been suggested as a promising parameter to evaluate the muscle compartment in children. This study aims to describe the use of Hand-grip strength in hospitalized pediatric oncology patients and the correlation of this technique between another anthropometric measurements.
Methods: A cross-sectional study with prospective data collection, which included patients over 1 year of age up to 18 years of age who were hospitalized in the inpatient unit of a developing country, diagnosed with childhood cancer within 3 months. Anthropometric and related signs and symptoms data were collected, and the patients were evaluated and questioned about the signs and symptoms 48 hours after admission.
Results: 114 children with cancer, with an median age of 11 years were included. Average strength observed was 14.4 kg (95% IC: 12.5-16.4). When correlated to Z-scores of weight/age (PCC:0.016), height/age (PCC:0.226), BMI/age (PCC:0.176), and triceps skinfold (PCC:0.252) a very low Pearson correlation coefficient were found, however muscle upper arm circunference was moderately correlated (PCC:0.580, $p<0.001$) with Hang-grip strength. No difference were found in Hand-grip strength between malnutrition and obesity groups.
Conclusions: In adult-cancer population, Hand-grip strength is a good tool to assess functionality, sarcopenia and cachexia both transversally and longitudinally. Being able to apply this tool in children as part of nutritional monitoring can help in selected cases and older children, but it is still necessary to understand its real benefits in pediatric patients.

EP421 / #761

Topic: *AS05.p Supportive Care and Palliative Care*

MOTOR PERFORMANCE ASSESSMENT IN PRESCHOOL CHILDREN AFFECTED BY CANCER: A LONGITUDINAL STUDY

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Background and Aims: Cancer during childhood causes various developmental difficulties. Rehabilitation is widely accepted to offer the best opportunity to optimize the neurodevelopmental outcome of children. However, the literature in pediatric rehabilitation oncology to guide clinical practice is scarce. The purpose of this study is to investigate the feasibility of conducting standardized developmental assessments and to describe motor performance during and after treatment in children affected by cancer.
Methods: A longitudinal design was used with two time points; shortly after diagnosis and two years after diagnosis. Feasibility was evaluated by determining the percentage of eligible participants who were assessed at each time point. Motor performance was assessed using the Peabody Developmental Motor Scales 2nd edition [PDMS-2] for children > three years old and the Movement ABC 2nd edition [M-ABC2] for children ≥ three years old. Motor performance was measured at the two time points and compared to age-specific norms.
Results: Twenty-five children (range 17 months - five years old at diagnosis, 60% male, 88% Caucasian) with various cancer diagnosis (60% leukemia) enrolled on a larger trial were eligible for our study. Shortly after diagnosis, 88% of children were assessed and 76% were able to complete all subtests. Two years after diagnosis, 91% completed the full-assessment. Motor performance decreased significantly from baseline to two years post-diagnosis ($p \leq 0.05$) and children had results significantly lower than the norms at both time points ($p \leq 0.01$). The proportion of children with a result under the 15thpercentile was 50% at both time points, indicating a high risk of motor impairments.
Conclusions: Preschool children affected by cancer are at high-risk of developing motor impairments. Early rehabilitation services are therefore essential to minimize long-term impacts on motor development. This early management of motor development would help to avoid the double punishment that these children suffer: cancer itself and the associated reduction of motor development.

EP422 / #1433

Topic: *AS05.p Supportive Care and Palliative Care*

EVALUATION OF ICPCN'S PALLIATIVE CARE EDUCATION PROGRAMMES

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Background and Aims: ICPCN's mission is to achieve the best quality of life and care for children and young people with life-threatening or life-limiting conditions, their families, and carers worldwide. The ICPCN's overall strategic goal for education is to provide high-quality CPC education which meets an identified global need and to support and empower the ICPCN network to train from their own localities. Since 2011, both online and face-to-face education and training programmes have been offered and in keeping with the spirit of the above goal, an evaluation of the education programme needed to be done. To assess the impact of CPC courses and to shape future improvements in course content and presentation.
Methods: An evaluation questionnaire was distributed via Survey Monkey to all 5165 participants who had been on the ICPCN education programme - this included those who had enrolled on face to face as well as the e-learning training programmes over a period of 10 years (2011 – 2021).
Results: 612 (11.8%) participants responded (490 female, 122 male). 33.95% of respondents were aged 35 to 44 years, 24.8% 45 to 54 years and 20.2% 25 to 34 years. Most respondents (40%) were from Europe, followed by Sub -Saharan Africa (21.04%) and Asia (16.80%). Online courses scored higher than face-to-face sessions in terms of clarity of information. In relation to usefulness to participants practice and overall course ratings face-to-face and online scores were similar. The majority of respondents (91%) reported an increase in their knowledge of CPC, skills improvement (88%), positive change in attitude (86%), and a change in clinical practice (84%).
Conclusions: The evaluation showed that there was a considerable knowledge gain. The main outcome of both the online and face to face education initiatives was a positive impact in terms of developing further support services in CPC.

EP423 / #14

Topic: *AS05.p Supportive Care and Palliative Care*

THE EFFICACY OF NEUTROPENIC DIET IN PREVENTING NEUTROPENIA RELATED INFECTIONS AMONG PEDIATRIC PATIENTS UNDERGOING CHEMOTHERAPY: A META-ANALYSIS

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Background and Aims: Neutropenic diet is still being used among cancer patients despite the lack of evidence of its benefit. Several studies showed lack of effectiveness of this regimen. However, most of these studies were done among adult patients. This meta-analysis analyzes the available data involving pediatric cancer patients who were placed on a neutropenic diet during chemotherapy.
Methods: A systematic search for randomized controlled trials investigating the effect of neutropenic diet versus regular diet among pediatric patients undergoing chemotherapy was done. Outcomes of interest were incidence of febrile neutropenia and bacteremia. A fixed-effects meta-analysis was doe to pool the effect of intervention.
Results: A total of 269 patients were included. There was no statistically significant difference in the incidence of febrile neutropenia (RR 1.16, 95% CI 0.78 to 1.71) and bacteremia (RR 1.57, 95% CI 0.62 to 3.96) between the neutropenic diet and regular diet groups.
Conclusions: This meta-analysis showed that there is no evidence supporting the use of neutropenic diet in preventing febrile neutropenia and bacteremia among pediatric patients undergoing chemotherapy.

EP424 / #658

Topic: *AS05.p Supportive Care and Palliative Care*

TRANSLATION AND VALIDATION OF THE CHICHEWA PEDIATRIC PATIENT-REPORTED-OUTCOME-CTCAE TOOL TO MEASURE TREATMENT-RELATED ADVERSE EVENTS AMONG ADOLESCENT AND YOUNG ADULT LYMPHOMA PATIENTS IN MALAWI

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Background and Aims: Internationally, patient-reported outcome (PRO) tools to assess health-related quality of life (HRQoL) and adverse events (AE) are available, but efforts to translate and culturally validate such tools in sub-Saharan Africa (SSA) are limited.
Methods: The Pediatric PRO version of the Common Terminology Criteria for Adverse Events (Ped-PRO-CTCAE) includes a core 15 AE symptoms. Each symptom has 2-3 questions, a 4-point Likert-type scale, and a 7-day recall period. The Ped-PRO-CTCAE was translated into Chichewa and culturally validated for use in Malawi using the FACIT translation guidance. Psychometric validation was assessed using Spearman's correlation for convergent and discriminant validity, Wilcoxon rank-sum for known group validity, and T-test for responsiveness.
Results: Fifty-Two adolescent and young adult (AYA) patients, with lymphoma completed the Ped-PRO-CTCAE survey. When compared to the translated and validated Patient-Reported Outcomes Measurement Information System (PROMIS) Pediatric tool, there were stronger correlations when symptoms matched (ie pain interference r=0.57, fatigue r=0.73, depression r=0.62, and anxiety r=0.75). Known group validity testing showed that patients with poor performance status (ECOG≥2) had higher pain frequency ($p<0.001$) and pain prevalence ($p=0.005$); and patients with anemia (hgb<9g/dL) had worse fatigue severity ($p<0.001$). Ped-PRO-CTCAE when compared to home symptom diary (ie nausea, constipation, pain, mucositis, insomnia and abdominal pain) were correlated across all matching PRO-CTCAE domains ($p<0.001$). Responsiveness was supported when comparing Ped-PRO-CTCAE scores at T0 and T1 (+5 to < 21 days from T0); T1 exhibited higher mean scores associated with expected worse symptoms after chemotherapy across all fifteen PRO-CTCAE symptom AEs ($p<0.001$).
Conclusions: This study found supporting evidence for the validity of the Chichewa-translated version of the Ped-PRO-CTCAE for Malawi. This emphasizes an urgent need to address symptomatic AEs experienced by children and AYA undergoing cancer treatment in SSA using PRO instruments validated within the local context.

EP425 / #71

Topic: *AS05.p Supportive Care and Palliative Care*

THE ROLE OF CLINICAL PHARMACIST IN PARENTERAL NUTRITION FOR PEDIATRIC CANCER PATIENTS IN 57357 CHILDREN CANCER HOSPITAL EGYPT (CCHE)

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Background and Aims: Parenteral nutrition (PN) therapy is a high alert medication, complex and critical therapy that requires nutrition support pharmacist knowledge, skills, and practice experience to avoid errors in prescribing, compounding, and clinical management of patients. Aims: Evaluate the role of clinical pharmacist to monitor PN therapy in 57357 CCHE to deliver it in safe and effective way.
Methods: A retrospective study over 12-month period conducted in 57357 (CCHE) from 2018 till 2019 . Interventions of clinical pharmacy for order review were documented and divided into categories . The data that be collected were patient anthropometric measurements, PN indication, PN prescription, fluids and electrolytes calculation, monitoring daily laboratory test, calculating caloric requirements, route of administration (central or peripheral line), calculating osmolarity, daily oral intake and other medication-related problems. However, each of these practice helps to support the delivery of safe and effective PN therapy to patients.
Results: The total number of pharmacist interventions were 2240 of PN-related problems. The total number of PN orders were 8892 prescribed to 754 patients. The highest number of interventions were incomplete order element 792 (35.3%), low caloric intake 534 (23.8%), drug -lab interaction 274 (12.2%), wrong volume 155 (6.9%), wrong stopping date 114 (5%), optimize drug monitoring 83 (3.7%), wrong transcription 79 (3.5%), dose calculation error 61 (2.7%), optimize route 55 (2.5%), medication conversion 32 (1.4%),nurse error 23 (1%), medication not written on cerner 22 (0.98%) and therapeutic duplication 16 (0.71%).
Conclusions: Clinical pharmacist role is an important pivot in providing an accurate PN order and follow up of the nutritional status of children suffering from cancer in 57357 CCHE. Many points for order revision is a must for patient safety and avoid health hazards related to parenteral nutrition in the hospital. Inter-disciplinary collaboration between clinical nutrition department and the pharmacy provides parenteral nutrition interventions in an ideal safe way.

EP426 / #1320

Topic: *AS05.p Supportive Care and Palliative Care*

INTEGRATION OF DENTAL HYGIENE CARE FOR PEDIATRIC ONCOLOGY PATIENTS, EXPERIENCE AT A TERTIARY CARE HOSPITAL IN LMIC. A QUALITY CARE IMPROVEMENT INITIATIVE.

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Background and Aims: Cancer therapy leads to oral complications which when left untreated can affect the patient's quality of life, lead to serious systemic infections that can complicate cancer treatment. Early comprehensive oral care measures by a trained dental hygienist can minimize the risk of these oral and associated systemic complications.
Methods: From January 2021 to February 2022, a dental hygienist visited patients in the pediatric oncology unit at the Aga Khan University Hospital Karachi, Pakistan. All patients were examined for cancer therapy related oral complications including mucositis based on the World Health Organization (WHO) Mucositis scale. After initial screening, dental hygienist provided an oral care regimen. Interventions included a combination of mouthwashes (anesthetic, analgesic, anti-microbial) and oral gels with teaching on the prescribed oral care regimen.
Results: A total of 197 pediatric patients were examined by the dental hygienist. This included 126 (64%) males with the age range of 9 months to 20 years. Almost half of the patients had leukemia 93 (48%), followed by lymphomas 22 (12%), and sarcomas 16 (8%). Other diagnoses included Neuroblastoma 5 (2.5%), Medulloblastoma 7 (3.5%), Thalassemia Major 8 (4%), Wilms's tumor 4 (2%). Out of 197 patients 99 (50.25%) had mucositis, Grade I in 17 (17%), Grade II - 50(51%), Grade III - 25 (25%), and Grade IV - 7 (7%) of patients . Grade II and IV mucositis were common in leukemia patients while Grade III was common in sarcoma patients. Continuous monitoring, interventions, and oral hygiene education resulted in improved oral feeding, compliance, and early discharge.
Conclusions: Early oral care measures provided by a dental hygienist can significantly decrease complications, improve diet and compliance with medications leading to early recovery. Further studies are needed to measure the level of satisfaction and effectiveness of care in patients receiving therapeutic care by a dental hygienist.

EP427 / #1523

Topic: *AS05.p Supportive Care and Palliative Care*

ASSOCIATION OF CVC AND NON-CVC RELATED VTE WITH SURVIVAL IN PEDIATRIC ONCOLOGY PATIENTS

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Background and Aims: Venous thromboembolism (VTE) has been associated with inferior survival outcome in pediatric oncology patients. Little is known about how CVC-related and non-CVC-related VTE differ and their corresponding impact on outcome.
Methods: This is a retrospective population-based study from Atlantic Canada (Prince Edward Island, New Brunswick, Nova Scotia, and Newfoundland). Patient demographics, diagnosis, and thrombosis information was collected from 2000-2019. Patients were divided into a CVC-related (CVC-VTE), non-CVC related VTE (N-VTE), and patients without a VTE (non-VTE) groups. Patients with both a CVC and non-CVC related VTE were classified as N-VTE patients. Descriptive analysis was run on the population. Kaplan-Meier was run for survival analysis. ANOVA was performed for analysis of ITR-3 scores.
Results: 1342 patients were included in the study. Of this, 91 patients were diagnosed with a VTE and 57% (n=52) were associated with a CVC. The M:F ratio for non-VTE patients was 54:47, 62:38 for N-VTE, and 62:38 for CVC- VTE. The most common diagnosis for Non-VTE and CVC-VTE was leukemias (30% and 50% respectively). The most common diagnosis for N-VTE patients was sarcoma (33%). When comparing treatment intensity through ITR-3 scores, the results were significant across groups ($p<0.001$). Post-hoc tests showed that non-VTE patients and CVC-VTE differed significantly ($p=0.008$). CVC-VTE and N-VTE patients as well as CVC-VTE and no-VTE patients were similar ($p=0.956$ and $p=0.066$ respectively). When looking at survival curves , N-VTE had significantly inferior survival in comparison to CVC-VTE ($p<0.001$) and non-VTE ($p<0.001$) patients. CVC-VTE and non-VTE patients were similar ($p=0.496$).
Conclusions: N-VTE patients were associated with inferior survival outcome as compared CVC-VTE and non-VTE patients, suggestive that disease related VTE may be prognostic of worse survival outcome. More research looking into the cause of decreased survival in non-CVC related VTE patients is necessary.

EP428 / #631

Topic: *AS05.p Supportive Care and Palliative Care*

COLLECTING SOCIAL DETERMINANTS OF HEALTH DATA AND MEASURING HEALTH LITERACY IN PEDIATRIC ONCOLOGY CAREGIVERS: A CROSS-SECTIONAL COHORT STUDY

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Background and Aims: Despite advances in childhood cancer outcomes, disparities among socially vulnerable populations persist. Associations between educational attainment, parent age, English proficiency and cancer outcomes suggest that factors impacting communication and comprehension may contribute. Health literacy is the degree to which individuals can process and act on health information. While reports from general pediatrics identify associations between low literacy and inferior outcomes, few studies have evaluated potential associations in pediatric oncology. We assessed health literacy among a diverse cohort of pediatric oncology parents, and assessed associations with self-reported demographics.
Methods: English or Spanish-speaking parents of children (1 – 18 years) receiving chemotherapy or stem cell transplantation participated in a cross-sectional survey study. Sociodemographics were collected by parent-report, and health literacy was measured via bilingual interview using the Newest Vital Sign™ screening tool. Scores indicating low (0 -1), moderate (2 – 3) or high (4 – 6) literacy were calculated; logistic regression measured associations between literacy and sociodemographic factors.
Results: Thirty-five parents (100%) completed demographic surveys, 34 (97%) completed literacy screening. Participants were 34% Hispanic, 17% non-Hispanic Black, 23% Spanish-speaking; 50% were publicly insured, 17% had less-than high-school education. Mean literacy score was 3.26 (+/- 2.00); 26% scored 0-1 (low literacy). In univariate models, time from diagnosis was not associated with odds of low or high-literacy; parents who were unemployed, who preferred Spanish, and who did not complete high school however, had increased odds of low literacy. Across all participants, 69% sought additional teaching about their child's illness from providers as well as from supplemental information online.
Conclusions: Over 25% of our pediatric oncology parents/caregivers are at risk of limited health literacy. Univariate analyses suggest associations between parent educational attainment, occupation, primary language and literacy level; ongoing analyses are measuring adjusted associations between sociodemographics and literacy, as well as between literacy and adverse cancer-related outcomes.

EP429 / #1172

Topic: *AS05.p Supportive Care and Palliative Care*

INTRATYMPANIC INJECTION OF SUSTAINED-EXPOSURE DEXAMETHASONE THERMOSENSITIVE GEL (OTO-104) FOR PREVENTION OF CISPLATIN-INDUCED HEARING LOSS IN CHILDREN IS FEASIBLE AND SAFE.

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Background and Aims: This study's purpose was to evaluate the feasibility, safety, and efficacy trends of intratympanic sustained-exposure dexamethasone thermosensitive gel (OTO-104) for preventing cisplatin-induced hearing loss (CIHL).
Methods: This IRB-approved, randomized phase 2 trial was conducted at 8 centers in the United States (January-September 2017). Eligibility criteria were age 0.5-21 years; new diagnosis of neuroblastoma, hepatoblastoma, osteosarcoma, or extracranial germ cell tumor; planned cumulative cisplatin dose ≥ 200 mg/m^2; normal baseline hearing and otoscopy. Participant ears were randomized for intratympanic injection of 0.2 ml OTO-104 6% in one and no treatment in the other. OTO-104 was administered through a 25-27 gauge needle by an otolaryngologist during other procedural sedation within 72 hours before cisplatin cycles (including multiday regimens). Feasibility was assessed by successful administration of intended OTO-104 doses. Adverse events (AEs) were monitored by physical examination, otoscopy, tympanometry, concurrent medications, and audiometry.
Results: Eighteen doses of OTO-104 were administered to 11 evaluable participants at 5 centers (median age 3 years, range 1-14; 6 female; 9 neuroblastoma, 2 osteosarcoma). Five participants received 1 dose, five received 2 doses, and one received 3 doses. OTO-104 was administered via intratympanic injection (9) or tympanostomy tubes (2). Sixteen injections were done during other procedural sedation; 2 were done awake. The median interval between OTO-104 and cisplatin was 14 hours (range 7-64). OTO-104 injection was successful in all 18 procedures. At end of study, clinically insignificant tympanic membrane scabs developed in 5 participants, but no pinna, external canal, or middle-ear changes were noted. No tympanogram shifts were noted. There were 5 otologic treatment-emergent AEs (2 transient mild-moderate otalgia [related] and 1 hypoacusis [unrelated]) and no related non-otologic treatment-emergent AEs. Sensorineural CIHL developed similarly in treated and untreated ears.
Conclusions: Intratympanic administration of OTO-104 to young children is feasible and safe. Further investigation using this route for preventing CIHL is warranted.

EP430 / #1191

Topic: *AS05.p Supportive Care and Palliative Care*

CHANGES IN NUTRITIONAL STATUS AND IMPACT ON OUTCOMES: A REPORT

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Background and Aims: We analyzed the trajectories in nutritional status and impact on outcomes in children with cancer.
Methods: Children (<18 years) with cancer at our center were classified as undernourished (UN), well nourished (WN) and overnourished (ON), based on weight-for-height or body-mass-index-for-age z-scores (WHO classification) and mid upper-arm circumference, at diagnosis and 3-months and 6-months follow-up. Trends in nutritional status (NS), and impact of changes in NS on outcomes (event-free survival, EFS and overall survival, OS) were analyzed.
Results: Data was available in 2,086 children at diagnosis, and 1,245 at follow-up treated between January-2018 and December-2019, median age 6.5 years (IQR 3.3-11 years) with 68.6% boys, all diagnoses included. At diagnosis and follow-up, 643(30.8%) and 511(41%) were WN, 1,360(65.2%) and 663(53.3%) UN and 80(3.8%) and 71(5.7%) ON. During the course of treatment 566(45.5%) gained weight, 145(11.6%) lost weight and 254(20.4%) improved NS. At median follow-up of 28 months, 1,445(69.2%) children were well, 390(18.7%) relapsed/progressed, 173(8.3%) expired, and 73(3.3%) abandoned treatment. At 12, 24 and 36 months, EFS was 82.5%, 72.6% and 63% and OS 96%, 86.5% and 76.7%. Weight gain during treatment was associated with improved EFS at 12, 24 and 36 months (96.5%, 86.6%, 76.4%) vs no weight gain (91.1%, 80.3% and 67.7%, $p<0.001$). Similarly, children with improved NS had higher EFS (96%, 86.5%, 76.7%) vs stable or deteriorated NS (92.9%, 82.3%, and 70.3%, $p<0.001$).
Conclusions: This large single-center cohort confirms the positive prognostic impact of weight gain and improved nutritional status in children with cancer, with beneficial effects lasting for upto 3 years from diagnosis.

EP431 / #478

Topic: *AS05.p Supportive Care and Palliative Care*

MANAGEMENT AND OUTCOME OF CHILDHOOD SUPERIOR CAVA SYNDROME WITH MEDIASTINAL MALIGNANCY: ANALYSIS OF 42 CONSECUTIVE CASES IN A SINGLE CENTER

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Background and Aims: To delineate clinical characteristics, diagnostic modalities and outcome of superior vena cava syndrome (SVCS) secondary to mediastinal malignancy in children through consecutive case analysis.
Methods: Consecutive patients diagnosed with SVCS (ICD-10 I87.106) from 2015 to 2021 at Shanghai Children's Medical Center (SCMC) according to International Classification of Disease 10th Revision were analyzed. Patient demographics, baseline characteristics, systemic work-up, imaging findings and pathological reports were reviewed through hospital electronic medical record system. Outcome were collected from oncology center database. The data were censored on 1st February 2022 for survival analysis.
Results: Consecutive 42 children (31 males and 11 females) with SVCS secondary to newly diagnosed mediastinal malignancy were treated at SCMC from 2015 to 2021. The median age was 8.5 years . T-cell lymphoblastic lymphoma (T-LBL) followed by T-cell acute lymphoblastic leukemia (T-ALL) was the most frequent malignancy in this group (25 cases, 59.5% and 7 cases, 16.7%, respectively). Pathological diagnosis was confirmed by bone marrow aspiration or thoracentesis in 14, peripheral lymph node biopsy in 6, and mediastinal biopsy in 22. Twenty-seven patients (64.3%) had local anesthesia. Respiratory complications due to mediastinal mass developed in 3 of 25 patients (20%) who received general anesthesia. Of all 62 patients with T-LBL treated during the study time period in our hospital, the 3-year event free survival and overall survival of patients who presented with SVCS at diagnosis (n=25) were significantly lower than that of those who had not (n=37) (41.4% vs 79.5% $p<0.001$ and 43.9% vs 87.5%, $p=0.001$; respectively).
Conclusions: T-LBL is the most common primary cause of SVCS in pediatric patients with mediastinal mass. Immediate preoperative team planning and multidisciplinary emergency management strategies are the fundamental for successful clinical management. Diagnosis should be made in the least invasive manner after an initial stabilization.

EP432 / #195

Topic: *AS05.p Supportive Care and Palliative Care*

AT THE END OF LIFE: PEDIATRIC PALLIATIVE CARE CAN MAKE A DIFFERENCE IN CARING FOR THE CHILD AND FAMILY

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Background and Aims: WHO defines pediatric palliative care as the active total care of the child's body, mind and spirit, which also involves giving support to the family, the aim of this study is to describe the end-of-life care of children with cancer during the end-of-life period who receive general palliative care or pediatric palliative care in low- and middle-income countries.
Methods: We conducted a retrospective quasi-experimental study between January 2013 and December 2020 with deceased pediatric cancer patients. Demographic and clinical variables were collected to describe end-of-life care received before (2013–2017) by general palliative care team and after (2018–2020) the creation of a pediatric palliative care team
Results: A total of 180 pediatric patients were evaluated at the end of life (100 between 2013–2017 and 80 between 2018–2020). The median age was 11 years, regardless of sex. Half of the patients had a diagnosis of leukemia (49.8%), 52.7% receive palliative treatment for their oncological condition. Regarding symptoms, 72 hours before death, pain treatment was documented for 52.2% of the patients. Other signs and symptoms, such as dyspnea, seizures, agitation, and irritability, were present, with no differences between groups; however, it was noted that during PPC interventions, there was a significant reduction in anxiety or fear of end of life, we observed a greater number of interventions by the psychosocial professionals and also there was an increase in the number of patients who died in the hospital ward and a decrease in the number of patients who died in the intensive care unit.
Conclusions: Pediatric palliative care requires special knowledge and skills, the provision of PPC for children with cancer allows patients and their families to receive support that alleviates the physical, emotional and social needs that arise from a life-limiting illness and finally receive high-quality end-of-life care.

EP433 / #1158

Topic: *AS05.p Supportive Care and Palliative Care*

LEVERAGING A PALLIATIVE CARE EDUCATIONAL SERIES TO CREATE A GLOBAL NETWORK

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Background and Aims: The mission of the St. Jude Global Palliative Care Transversal Program is to define the current state of palliative care (PC) in underserved communities worldwide and drive collaborative interventions with our global partners to relieve suffering of patients and families facing the challenges of pediatric cancer. A key feature of this mission is to improve educational offerings within pediatric palliative care (PPC) for healthcare professionals providing care for children with cancer. We aim to describe the creation of a global PC network through a series of monthly educational meetings where topics of interest in pediatric palliative oncology are discussed.
Methods: An expert panel selected PPC topics focused on PC integration in childhood cancer that highlighted interdisciplinary and multicultural perspectives. The educational sessions were held through an electronic platform with simultaneous interpretation available. Recordings were available after completion of the session for viewing.
Results: The St. Jude Global Palliative Care Transversal Program held a monthly series between December 2021 and March 2022. In each session, renowned experts in PC from 12 different countries led enriching educational sessions on topics such as quality improvement, research, psychosocial standards, and advocacy in PPC. An average of 212 participants from 99 countries across 5 continents joined 4 virtual sessions. Simultaneous translation in Spanish and English was available and the recordings have been viewed 436 times. These series led to the creation of an educational PPC network that now has 1,280 members from every continent.
Conclusions: The Global Educational Series in PC has been successful in sharing knowledge and as a strategy to create a global PPC network among healthcare professionals caring for children diagnosed with cancer. This educational series will also be used in the future to discuss complex clinical cases, improve patient care, and promote clinician resilience.

EP434 / #1120

Topic: *AS05.p Supportive Care and Palliative Care*

THE EFFICACY OF FIBRE AND PREBIOTIC INTERVENTIONS ON CLINICAL OUTCOMES IN CANCER AND HAEMATOPOIETIC STEM CELL THERAPIES: SYSTEMATIC LITERATURE REVIEW

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Background and Aims: Cancer treatments cause a range of toxicities that impact treatment adherence and patient wellbeing. Dietary fibre/prebiotics characteristically improve the gastrointestinal-microenvironment, which consequently benefit downstream effects pertinent to treating and preventing treatment-related toxicities. This systematic review aimed to evaluate the clinical efficacy and side effects of fibre/prebiotic-based interventions on outcomes in children and adults being treated with cancer or undergoing haematopoietic stem cell therapies.
Methods: This study was conducted in adherence to PRISMA guidelines, and the protocol was published prospectively with PROSPERO (CRD42022299428). Four databases (MEDLINE (Ovid), CINHAL, EMBASE Cochrane CENTRAL) until February 2022 were searched. All articles were assessed for bias using the Cochrane risk-of-bias tool RoB 2.0 (for RCTs) and ROBINS-I (for non-RCTs).
Results: A total 13449 articles were identified, of these, 13 (paediatrics [n= 1], adults [n=12]) met the inclusion criteria (randomised controlled trials (RCT) [n = 10], observational or non-RCTs [n = 3]). The risk-of-bias was graded to be serious/high (n=3); moderate/some concerns (n=7); low (n=3). Interventions included prebiotic supplement (n=8), dietary modification (n=3) and nutrition supplement with added fibre/prebiotic (n=2) with prescribed fibre difference ranging from 2.4-30g/day. Substantial heterogeneity was identified across a range of outcomes including gastrointestinal-side effects; gastrointestinal-microbiome; clinical (including pathology); nutrition status and body composition; and quality-of-life.
Conclusions: The scientific rationale for fibre/prebiotics-based interventions for the prevention or management of cancer treatment-related toxicities is compelling. Despite this, our study highlights the paucity of relevant research, and of which, is highly heterogeneous and is lacking in quality. This is especially pertinent for studies conducted in the paediatric setting (n=1), which was exclusively the initial study scope. This incomplete understanding is at the detriment of clinical care. High-quality interventions studies translatable to clinical practice are now evidently crucial to determine if and how fibre/prebiotics should be used to support people undergoing cancer therapy, especially children.

EP435 / #1438

Topic: *AS05.p Supportive Care and Palliative Care*

IDENTIFYING CHALLENGES IN DELIVERY OF PEDIATRIC ONCO-CRITICAL CARE IN LATIN AMERICA

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Background and Aims: Hospitalized pediatric hematology-oncology (PHO) patients are at high risk for critical illness, especially in resource-limited settings. PROACTIVE (PediatRic Oncology cApaCity Assessment Tool for IntensiVe CarE) is a diagnostic tool designed to evaluate strengths and limitations in global pediatric onco-critical care (POCC) services. In this study, we use PROACTIVE results to describe common challenges to POCC in Latin America.
Methods: PROACTIVE is an English-language electronic assessment tool developed from 119 consensus-derived quality and capacity indicators arranged into 8 domains and divided into 2 surveys for intensivists and oncologists managing critically ill PHO patients. PROACTIVE was administered using REDCap between January 2021 and March 2022. Aggregated data from 15 hospitals in Latin America were analyzed and indicators scoring ≤75% across centers were classified as common challenges in delivery of POCC in the region.
Results: We analyzed aggregated data from 15 hospitals located in 8 Latin American countries with a wide variety of resources, income-levels, and POCC services. The Personnel domain was identified as presenting most common challenges with 15/18 indicators (83%) scoring ≤75% for availability or performance. Challenges in this domain included: 1) inability to provide multidisciplinary care to critically ill PHO patients due to lack of trained nurses and specialists (oncologists, intensivists, neurosurgeons), 2) Limited training and access to educational resources in pediatric critical care for nurses and healthcare providers, 3) Insufficient team participation in quality improvement projects. Other limitations were found in Supportive Services (48%), Service Capacity (44%) and Outcomes (40%) domains, while the Medication and Equipment domain (14%) was considered a relative strength having <20% of low-scoring indicators.
Conclusions: Training and lack of specialists are major limitations to high-quality POCC in Latin America. Awareness of common challenges and improvement efforts focusing on the low-scoring indicators can help stakeholders tailor interventions to improve POCC services and outcomes for PHO patients.

EP436 / #392

Topic: *AS05.p Supportive Care and Palliative Care*

KETAMINE AND MIDAZOLAM FOR SEDATION IN THE PEDIATRIC ONCOLOGY UNIT: SAFETY PROFILE IN THREE CENTERS IN LATIN AMERICA

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Background and Aims: Pediatric cancer patients frequently undergo painful minor procedures, such as spinal tap/ intrathecal chemotherapy, bone marrow aspirate, bone marrow biopsy and central line placement. Although deep sedation is ideal for these procedures, this is not widely available, particularly in limited-resource settings, so dissociative sedation is frequently used as an alternative. Our aim was to describe the safety profile of sedation with Ketamine and Midazolam when administered to pediatric cancer patients for painful minor procedures.
Methods: This was a consecutive case series of 239 events of sedation on pediatric cancer patients in 2 hospitals over a 6-month period. Protocol for sedation included ketamine and midazolam at a starting dose of 1mg/kg and 0.1mg/kg respectively. Records were reviewed for final ketamine/ midazolam dosing, adverse effects, use of adjunctive drugs and perception of sedation.
Results: Our series included 209 events from Mexico, and 30 from Argentina; 131 were male (54.8%), and 108 were female (45.2%). Procedures included Spinal tap/ intrathecal chemotherapy 150 (62.7%), Bone marrow aspirate 14 (5.9%), Bone marrow biopsy 4 (1.7%), Central line placement 18 (7.5%), Bone marrow aspirate + Spinal tap 51 (21.3%) and others 2 (0.8%). Average final dose was 1.2mg/kg for Ketamine, and 0.13mg/kg for Midazolam. Adjunctive drugs used were Atropine (20, 8.4%), supplementary Oxygen (10, 4.2%), and Albuterol (8, 3.3%). Adverse effects included desaturation <94% (10, 4.2%, Bradycardia (1, 0.4%), Emesis (4, 1.7%). 213 events (89.1%) were uneventful. Sedation was adequate (no need for restraint) in 229 events (95.8%). Perception of sedation, final Ketamine/ Midazolam dose, need for adjunctive drugs and adverse effects did not differ significantly when analyzed for gender, procedure or age.
Conclusions: Sedation with ketamine and midazolam can be administered safely for pediatric cancer patients at the oncology ward to facilitate minor procedures in settings where an anesthesiologist or alternate methods for deep sedation are unavailable.

EP437 / #1752

Topic: *AS05.p Supportive Care and Palliative Care*

INTERDISCIPLINARY DECISIONS AND COMMUNICATION PRACTICES: A SURVEY OF PEDIATRIC ONCOLOGY CLINICIANS IN CENTRAL AMERICA AND THE CARIBBEAN

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Background and Aims: Interdisciplinary care is a core attribute of high-quality cancer care and is associated with improved patient outcomes. However, we know little about the role of interdisciplinary pediatric cancer care in low- and middle-income countries. The purpose of this study was to explore communication and decision-making among interdisciplinary clinicians in Central America and the Caribbean.
Methods: We conducted a cross-sectional survey of interdisciplinary clinicians at five pediatric hematology-oncology centers in Central America and the Caribbean (Guatemala, Honduras, Panama, El Salvador, Haiti). The survey included items adapted from previously validated tools investigating frequency of interdisciplinary communication and interdisciplinary decision-making.
Results: 174 interdisciplinary team members completed the survey: nurses (n=60), medical subspecialists (n=35), oncologists (n=22), psychosocial providers (n=20), surgeons (n=12) pathologists (n=9), radiologists (n=9), radiation oncologists (n=5). Oncologists reported daily communication with nurses (95%), other oncologists (91%), psychosocial providers (82%), and pharmacists (81%). While 90% of surveyed nurses reported daily communication with other nurses, only 66% reported daily communication with oncologists and >50% of nurses reported never talking to pathologists, radiologists, radiation oncologists, or surgeons. Most clinicians described interdisciplinary discussion of cancer treatment goals and prognosis (84%), patient preferences (81%), and determination of first treatment modality (80%). Providers who described more interdisciplinary care had higher job satisfaction (p=0.04) and perceived a higher level of overall quality of care (p=0.004).
Conclusions: Clinicians in Central America and the Caribbean describe strong interdisciplinary collaboration contributing to higher job satisfaction and perceived quality of care. However, nurses in these settings experienced more limited interdisciplinary communication and may be left out of important team care. Additional studies are necessary to further define clinical roles on interdisciplinary care teams in LMICs as well as their association with patient outcomes.

EP438 / #430

Topic: *AS05.p Supportive Care and Palliative Care*

PROMOTING POSITIVE PHYSICAL ACTIVITY BEHAVIOURS IN CHILDREN AND ADOLESCENTS UNDERGOING ACUTE CANCER TREATMENT: FEASIBILITY OF THE CANMOVE INTERVENTION

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Background and Aims: Supporting children/adolescents with cancer to be more physically active has the potential to improve short- and long-term health outcomes. The objective of this study was to assess the feasibility of CanMOVE, a complex, theoretically-informed, behaviour change intervention to promote participation in physical activity for children/adolescents undergoing acute cancer treatment.
Methods: A feasibility study using single-group, repeated measures, mixed methods design was completed. Participants completed the 10-week CanMOVE intervention, which involved structured assessment and support from a physiotherapist, and provision of a Fitbit (child and parent) to achieve a daily steps goal. Feasibility domains demand, acceptability, implementation, practicality, limited efficacy, and integration were evaluated. Objective assessment of physical activity, physical function, and health-related quality of life (HRQOL) were completed. Qualitative data were collected via semi-structured interviews with participants (parents and children/adolescents) and focus groups with clinical staff.
Results: Twenty families completed CanMOVE, including children/adolescents (median age 12yrs, range 5-16) with a mix of cancer diagnoses. There was high demand for CanMOVE with 95% enrolment rate. CanMOVE was acceptable for participants, families and staff. All implementation feasibility thresholds were met, with intervention attendance at 93%, and adherence to wearing Fitbit 79%. There were no serious adverse events. For limited efficacy, data indicated CanMOVE was associated with increased child/adolescent physical activity. Positive impacts were seen in parent and staff behaviour towards physical activity promotion. Pre/post physical function and HRQOL assessments improved.
Conclusions: CanMOVE is feasible and safe to implement in the paediatric oncology setting and positively associated with changes in physical activity behaviour of children/adolescents.

EP439 / #465

Topic: *AS05.p Supportive Care and Palliative Care*

PREVALENCE, SEVERITY, TRAJECTORY, AND PREDICTORS OF SYMPTOM BURDEN AMONG ADOLESCENTS AND YOUNG ADULTS WITH CANCER: A POPULATION-BASED COHORT STUY

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Background and Aims: Adolescents and young adults (AYA) with cancer are a population at risk of experiencing outcome disparities. Symptom burdens in this population are not well characterized but are a significant contributor to poor quality of life.
Methods: All Ontario, Canada AYA aged 15-29 years at diagnosis between 2010-2018 were linked to population-based healthcare databases. Symptom burden was determined through linkage to Edmonton Symptom Assessment System-Revised (ESAS) scores, an 11-point scale routinely obtained at the time of cancer-related outpatient visits and collected provincially. Multistate models estimated mean duration of severity states [none (0) vs. mild (1 vs. 2 vs. 3) vs. moderate (4-6) vs. severe (7-9)], trajectories, and associations with death. Patient, disease, and treatment-related variables associated with severe symptoms were also determined.
Results: 4,296 AYA with >=1 ESAS score within a year of cancer diagnosis were included (median age 25 years). The most prevalent moderate/severe symptoms were fatigue and anxiety (59% and 44% of AYA). Across symptom type, AYA reporting moderate symptoms were more likely to subsequently experience improvement vs. worsening. Risk of death within 6 months increased with increasing symptom burden and was highest in AYA with severe dyspnea (9.0%), pain (8.0%), or drowsiness (7.5%). AYA living in the poorest urban neighborhoods were more likely to experience severe symptoms than in the wealthiest areas, with twice the odds of reporting severe depression [adjusted odds ratio (OR) 1.95, 95th confidence interval (95CI) 1.37-2.78], pain (OR 1.94, 95CI 1.39-2.70), and dyspnea (OR 1.96, 95CI 1.27-3.02).
Conclusions: AYA with cancer experience substantial symptom burden. Risk of death increased with symptom severity. Interventions targeting cancer fatigue and anxiety, and targeting AYA in lower-income neighborhoods, are likely to improve quality of life in this population.

EP440 / #280

Topic: *AS05.p Supportive Care and Palliative Care*

ETHNIC-SPECIFIC PREDICTORS OF NEUROTOXICITY AMONG PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) PATIENTS FOLLOWING HIGH-DOSE METHOTREXATE (HD-MTX): A REDUCING ETHNIC DISPARITIES IN ACUTE LEUKEMIA (REDIAL) CONSORTIUM REPORT

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Background and Aims: HD-MTX (≥1 g/m^2) is an important component of curative therapy in many treatment regimens for high-risk pediatric ALL. MTX therapy can result in dose-limiting neurotoxicity. There is growing evidence that neurotoxicity disproportionately affects Latino children. Thus, we evaluated risk factors for neurotoxicity following HD-MTX in an ethnically diverse population of patients with ALL.
Methods: We evaluated patients aged 0-21 years diagnosed with de novo ALL from 2010-2017 in the REDIAL Consortium. Time to MTX clearance, serum creatinine elevations from baseline, supportive care, and sociodemographic factors were abstracted from medical records. MTX neurotoxicity was defined as a neurologic episode (e.g., seizures or stroke-like symptoms) occurring within 21 days of HD-MTX and resulting in subsequent MTX treatment modifications. Mixed effects multivariable logistic regression was used to estimate the odds ratios (OR) and corresponding 95% confidence intervals (CI) for the association between clinical factors and neurotoxicity, both overall and stratifying on ethnicity.
Results: Overall, 417 patients (54.8% Latino) with 1,560 HD-MTX infusions were evaluated. Thirty-six patients experienced neurotoxicity (8.6%), 72% of whom were Latino. Neurotoxicity odds increased with older age at diagnosis (OR = 1.29, 95% CI: 1.12-1.49) and following a creatinine elevation of ≥50%, compared to those with normal creatinine (i.e., <25% elevation) (OR = 3.82, 95% CI: 1.01-14.38). Predictors of neurotoxicity differed by ethnicity. In non-Latinos, longer time to MTX clearance was the only clinical factor associated with neurotoxicity (OR = 1.03, 95% CI: 1.01-1.05). Among Latinos, time to MTX clearance was not associated with neurotoxicity, while creatinine elevations ≥50% were associated with a five-fold increase in neurotoxicity odds (OR = 5.29, 95% CI: 1.41-19.90), compared to normal creatinine.
Conclusions: Serum creatinine increase ≥50% may be associated with an increased risk for neurotoxicity, specifically among Latino children with ALL, and thus may identify candidates for therapeutic and/or supportive care interventions.

EP441 / #1803

Topic: *AS05.p Supportive Care and Palliative Care*

COST ANALYSIS OF INCREASED USE OF PEG-GCSF PRIMARY PROPHYLAXIS DURING THE COVID-19 PANDEMIC

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Background and Aims: During the pandemic, UK guidance recommended prophylactic granulocyte-colony stimulating factor (G-CSF) or biosimilar pegylated G-CSF to reduce hospital admissions with febrile neutropenia (FN). PEG-GCSF offers the advantage of stat dosing over daily G-CSF injections thereby reducing potential virus exposure by avoiding home visits by community nurses. This project aimed to review GCSF prescribing patterns, cost analysis and impact of PEG-GCSF on hospital admissions with febrile neutropenia.
Methods: A drug spend audit compared annual spend of daily GCSF and PEG-GCSF between September 2019-2020 and September 2020-2021 at Southampton Children's Hospital, UK. The average number of patients on active treatment over a one-year period is 126. Dispensing records were reviewed for 6 months from May 2021. Chemotherapy cycle dates were interrogated for delays caused by low counts.
Results: Annual spend on daily GCSF between September 2019-2020 was £8,206 and between September 2020-2021 £5,594 (32% reduction). The pre-pandemic annual spend over the same time period for PEG-GCSF was £27,087 and this increased to £44,160 (63% increase). Within the review period, 18 patients received PEG-GCSF prophylaxis and no patients were discharged with prophylactic daily GCSF. Of the eleven patients (61%) previously ineligible to receive PEG-GCSF, 36% of chemotherapy cycles were delayed (average 5.2 days).
Conclusions: Our results show a significant increase in annual spend of £14,460 in GCSF prophylaxis from pre-pandemic times. This may offset the bed days cost saving for fewer hospital admissions for FN. We plan to ascertain the impact of primary PEG-GCSF prophylaxis use on hospital admissions for FN and evaluate patient and parent preference regarding GCSF choice. More directive GCSF prescribing guidance should include restricting primary prophylaxis to more intensive chemotherapy regimens and those at higher risk of FN admissions. It will be important to evaluate whether other centres have adopted different GCSF prescribing practice since the pandemic and impact on spend.

EP442 / #298

Topic: *AS05.p Supportive Care and Palliative Care*

A CROSS SECTIONAL SURVEY TO EXPLORE BARRIERS AND FACILITATORS TO IMPLEMENTATION OF PHOTOBIOMODULATION FOR MUCOSITIS MANAGEMENT IN CHILDREN RECEIVING CHEMOTHERAPY IN THE UNITED KINGDOM

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Background and Aims: Oral mucositis affects up to 80% of children and young people (CYP) receiving chemotherapy. This can result in pain and reduced oral intake. Hospitalisation may be required for parental nutrition and pain relief which may result in delays to scheduled cancer treatment. Photobiomodulation therapy is recommended by NICE and other international bodies to prevent and treat mucositis. This cross sectional survey aimed to explore existing paediatric photobiomodulation practices in the United Kingdom (UK), and the barriers and facilitators to implementation of this recommended, evidence-based therapy.
Methods: Ethical approval was granted by the University of Leeds. An online mixed-methods survey was administered to representatives from all UK Children's Cancer and Leukaemia Group (CCLG) centres between October 2021-March 2022. Quantitative data underwent descriptive statistics. Qualitative data relating to barriers and facilitators was analysed by two researchers (CH & KG-B) using the Theoretical Domains Framework (TDF).
Results: A 100% (n=20) response rate was achieved. Two units in Scotland were delivering photobiomodulation for CYP receiving chemotherapy prior to haemopoietic stem cell transplant, for osteosarcoma, non-Hodgkin's lymphoma, and those with previous or established mucositis. Four units had plans to implement a service. In TDF analysis, five domains were most frequently populated: knowledge, skills, environmental context and resources, social influences and professional roles of Paediatric Dentists and Paediatric Oncologists.
Conclusions: Despite being a recommended supportive care therapy, photobiomodulation is only available in two CCLG units. Lack of knowledge and skills, and environmental context and resources were identified as barriers. Collaboration with paediatric dental services was identified as a facilitator in implementation. National networks of Paediatric Dentists and Oncologists could be established to standardise protocols and training. Additionally, these networks would promote collaboration to address identified barriers and support wider implementation of this supportive care therapy.

EP443 / #596

Topic: *AS05.p Supportive Care and Palliative Care*

COMPARISON OF CARE IN THE LAST MONTH OF LIFE OF PEDIATRIC CANCER PATIENTS BASED ON THE PROVISION OF PEDIATRIC PALLIATIVE CARE

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Background and Aims: Cancer patients constitute an important group in pediatric palliative care (PPC). Amongst the aims of PPC is to reduce the practice of futile interventions. Comparative data based on the provision of PPC is scarce.
Methods: Retrospective analytical study based on the clinical records of deceased cancer patients from at a tertiary hospital in a 10-year-period (2010-2019). Patients were classified considering if they were attended or not by the hospital PPC Unit (PPCU). We compared baseline characteristics and support and invasive measures applied in the last month of life (LMoL).

Results: Of 198 patients, 99 (50.0%) were attended by the PPCU. No differences were found regarding sex, age at death, disease duration or lines of treatment. Patients with hematological malignancies were less prone to receive attention by the PPCU (21.6%) than patients with CNS cancer (75.0%) or solid tumors (71.0%; $p<0.01$). As for interventions performed in the LMoL patients attended by the PPCU were significantly less prone to receive surgery (15.1% vs 4.0%), red blood cell (77.8% vs 33.3%) and platelet transfusions (74.8% vs 29.3%), invasive procedures (58.6% vs 7.1%), palliative sedation (57.6% vs 17.2%) and died significantly more at home (0% vs 65.7%). Patients attended by the PPCU stayed a mean of 16.8 days less at hospital (CI: 13.9-18.7), 8.6 days less in the ICU (CI: 6.1-11.3) and of 4.4 days less in hospital in their last week of life (CI: 3.5-5.2).

Conclusions: Though adjustment for possible confounding variables should be made our data supports that PPC provision leads to a decrease in medical procedures in the LMoL.

EP444 / #613

Topic: *AS05.p Supportive Care and Palliative Care*

NEUROPATHIC PAIN IN PATIENTS WITH CANCER ATTENDED BY A PEDIATRIC PALLIATIVE CARE UNIT

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Background and Aims: Neuropathic pain (NP) supposes a problem for pediatric patients in palliative care being its management often complex. We aim to describe the prevalence, characteristics and treatments used for the management of neuropathic pain in a cohort of pediatric patients with cancer attended by a pediatric palliative care unit (PPCU).
Methods: Retrospective review of clinical records of patients with cancer attended by a PPCU in a 10-year period (2010-2019). We collected general epidemiological characteristics, presence and pattern of NP and the pharmacological treatments used for its management. We compared baseline characteristics using classic parametrical tests and calculated 95% confidence intervals (CI) for the estimation of parameters. Statiscal significance was established at $p<0.05$.
Results: The records of 171 patients were analyzed with 50.7% presenting NP. Patients were followed for a median of 1.6 months (interquartile range 0.7-4.7). No differences were found regarding sex or age at the first consult with the PPCU. NP was significantly more frequent in patients with solid cancer (68.1%) than in those with CNS cancer (44.6%) and in this group from those with hematological malignancies (15.4%). The most frequent treatments used for managing NP were gabapentinoids (84.6%; CI: 76.4-92.8). Other treatments included parenteral ketamine (28.2%; CI: 18.0-38.4), tricyclic antidepressants (12.8%; CI:5.2-20.4), methadone (11.7%; CI:4.3-19.0), nerve blockage (7.7% CI:1.7-13.7) transdermic 5% lidocaine (3.9%; CI:0-8.2) and transcutaneous electrical nerve stimulation (1.3%; CI:0-3.8). In 5 patients (6.4%; CI:0.8-11.9) NP was considered refractory indicating palliative sedation.

Conclusions: In our cohort, NP was present in half of the patients, being especially frequent in patients with solid tumors. Further studies regarding the best therapeutical strategies are needed to study the best approach for these patients.

EP445 / #615

Topic: *AS05.p Supportive Care and Palliative Care*

NURSING INTERVENTIONS IN DECEASED PEDIATRIC PATIENTS WITH CANCER

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Background and Aims: Patients with cancer in pediatric palliative care (PPC) present complex needs of care. As a part of the interdisciplinary team nurses participate in several aspects of care but little is known of the interventions that they apply.
Methods: Retrospective review of clinical records of deceased patients with cancer attended by a PPC unit (PPCU) in a 10-year period (2010-2019). We collected general epidemiological characteristics and nursing interventions (health education, use of medical devices, symptom management and postmortem care). For each intervention we calculated the estimated 95% confidence interval (CI).
Results: The records of 159 patients were analyzed, 58.5% being male a median age of 9.4 years (interquartile range-IQR: 5.8-14.1) at the first consultation and a median follow-up of 1.4 months (IQR: 0.5-2.8). Considering the type of cancer, 44.0% had a solid tumor, 37.1% CNS cancer and 18.9 hematological cancer; 61.6% of the patients died at their home. Nursing interventions were registered in 87.4% of the patients (CI: 82.2-92.6). The most common intervention was providing health education (85.6%; CI: 79.7-91.5). Nurses managed respiratory devices (69.1%; CI: 61.3-76.8), parenteral devices (68.3%; CI: 60.5-76.2), nutritional support devices (36.0%; CI: 27.9-44.0) and urinary catheters (18.7%; CI: 12.1-25.3). The main symptoms in which nurses were implicated were pain management (68.3%; CI: 60.5-76.2), respiratory distress (64.0%; CI: 56.0-72.1), skin problems (46.0%; CI: 37.7- 54.4), bleeding (21.6%; CI: 14.7-28.5) and seizures (17.3%; CI: 10.9-23.6). In 80.6% of the cases, nurses participated in the postmortem care of the patient´s body (CI: 73.9-87.2).
Conclusions: Nurses participated in different aspects of care regarding the use of medical devices and symptom management, as well as providing health education and postmortem care. These aspects should be correctly tackled in their training curriculum.

EP446 / #906

Topic: *AS05.p Supportive Care and Palliative Care*

HEMODIALYSIS IN METHOTREXATE INTOXICATION.

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Background and Aims: High-dose methotrexate(HDMTX) induced acute kidney injury is a rare but life-threatening complication. Methotrexate is a highly nephro- and hepatotoxic drug used in cancer protocols, in children and adults. High dose methotrexate therapy may lead to kidney injury and decrease of methotrexate clearance, followed by an increase of its serum concentration. As a result, systemic intoxication may develop. Prophylaxis based on intensive fluid therapy and urine alkalization may not be sufficient to prevent the formation of methotrexate crystals in kidney tubules. The aim of the study was to present 12 cases with toxic methotrexate levels treated with hemodialysis at the Hospital Infantil de México Federico Goméz between January 2015– December 2020
Methods: Clinical data and outcomes of all patients who received hemodialysis after HDMTX administration were reviewed.
Results: Of 737 patients who received HDMTX, 12(1.6%) patients received hemodialysis because acute kidney injury and delayed methotrexate clearance. Six were males, median age was 12.2(SD 3), Ten patients had osteosarcoma and 2 acute lymphoblastic leukemia, the doses of MTX were 12-10 grm2sc and 5 grm2sc respectively. At the time of toxicity (hour 24), the median plasma methotrexate concentration was 173.7 µM(SD 73.2) and 3.32 (3.9) at hour 120. The median peak serum creatinine level during these HDMTX courses was 1.86mg/dL(SD 0.75 mg/dL). Despite intensive fluid therapy, urine alkalization and administration of high doses of folinic acid (leucovorin)were indicated, methotrexate serum concentration remained toxic. Reduction of methotrexate concentration (<1.0 µM) was achieved after 5 events of hemodialysis in 4 patient, 3 events in 1, 2 events in 4 and 3 required 2 hemodialysis. Renal function eventually returned to baseline in all patients, and no patient died because of methotrexate toxicity.
Conclusions: Hemodialysis is an effective supportive method in methotrexate elimination in patients with severe intoxication. We use this strategy because Carboxypeptidase is not available in Mexico.

EP447 / #204

Topic: *AS05.p Supportive Care and Palliative Care*

RESEARCH INTEREST OF GLOBAL INFECTIOUS DISEASE TRAINING PARTICIPANTS AND OPPORTUNITIES FOR BUILDING AND STRENGTHENING RESEARCH CAPACITY IN LOW- TO MIDDLE-INCOME COUNTRIES

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Background and Aims: Building research capacity for healthcare professionals (HCPs) in low- and middle-income countries (LMICs) is essential to generating local evidence for infection care and prevention (ICP) interventions to improve outcomes. In 2017 we launched an annual Global Infectious Diseases Training Seminar to give HCPs the education and resources to develop as ICP leaders. Here, we share the outcomes of trainees' project proposals.
Methods: HCPs were trained to develop a project proposal, guided through the development of a research question, background/relevance, aims and objectives, methods, and references. We conducted a qualitative document analysis from 4 cohorts' proposals (2018, 2019, 2020, 2022) to describe common themes.
Results: We reviewed 153 proposals from 174 participants representing 50 countries from all 6 World Health Organization regions. Research themes were antimicrobial use / resistance (n=50, 33%), pathogen-specific infections (n=25, 16%), device-associated infections (n=17,11%), ICP measures (n=14,9%), general infectious epidemiology (n=10,7%), fever management (n=10,7%), oral mucositis (n=8, 5%), diagnostics (n=7, 5%), and other topics (n=12, 8%). Proposals targeted patients (n=102, 67%), HCPs (n=32, 21%), caregivers (n=2, 1%), other hospital staff (n=2, 1%), or isolated pathogens (n=15, 10%). Study proposals included healthcare chart reviews to randomized clinical trials, and study designs were cross-sectional (n=6, 4%), retrospective (n=36, 24%), and prospective (n=111, 73%). There was 1 (1%) systematic literature review, 78 (51%) observational studies, and 74 (48%) studies with an intervention (treatment alternatives or modifications, n=16, 22%; ICP, n=21, 28%; prophylaxis, n=10, 14%; education/training, n=9, 12%; clinical decision support tool testing, n=6, 8%; diagnostics, n=5, 7%; miscellaneous topics, n=7, 9%).
Conclusions: We identified varied infection-related research areas of importance to HCPs caring for children with cancer in LMICs. This information will help us focus future GID training to address these needs.

EP448 / #992

Topic: *AS05.p Supportive Care and Palliative Care*

INTERIM ANALYSIS RESULTS OF SAFETY AND EFFICACY OF PEGYLATED RECOMBINANT HUMAN GRANULOCYTE COLONY STIMULATING FACTOR(PEG-RHG-CSF) IN PREVENTING NEUTROPENIA IN CHILDREN WITH TUMOR AFTER CHEMOTHERAPY

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Background and Aims: Data on the use of PEG-rhG-CSF in children is limited. Therefore, the aims of the study were to investigate the safety and efficacy of PEG-rhG-CSF in children with tumor after chemotherapy.
Methods: Pediatric patients with newly diagnosed malignant tumor who received chemotherapy and expected to have grade III/IV neutropenia were enrolled. PEG-rhG-CSF (100ug/kg, with maximum 6mg) was injected subcutaneously once 24 to 48 hours after chemotherapy of first two courses. We evaluated the efficacy and safety of PEG-rhG-CSF in these patients.
Results: A total of 166 pediatric patients were screened, of which 2 failed to meet the inclusion criteria, 4 cases were excluded, a total of 160 patients who completed the study treatment were included in the statistics. Including 58 sarcoma, 33 neuroblastoma, 21 lymphoma, 19 germ cell tumor, 15 brain tumor and 14 other tumor. The median age of the 160 patients was 6.22 years. In the safety evaluation, among the common adverse reactions related to the study drug, the incidence of bone pain, fatigue, muscle soreness, pain at the injection site was 20.0%, 13.13%, 13.13%, 12.50%. Anemia, decreased neutrophil count, decreased white blood cell count, and decreased lymphocyte count occurred in more than 80% patients. The median neutrophil count recovery time per cycle was 5 days. The incidence of FN in total cycles was 29.45% and the median duration was 2 days. There were no dose adjustments and chemotherapy delays due to adverse events; a total of 40.0% of patients received therapeutic antibiotics.
Conclusions: PEG-rhG-CSF appears to be a safe and effective in children with with tumor after chemotherapy. This will become the basis for PEG-rhG-CSF 's medication in children in the future, and we will further analyze the impact of different tumor subgroups and children's immune function.

EP449 / #1864

Topic: *AS05.p Supportive Care and Palliative Care*

CONTROL, ALT, BUT DO NOT DELETE; THE ROLE OF ANTIMICROBIAL LOCK THERAPY (ALT) IN TREATING CENTRAL LINE INFECTIONS IN AN IRISH PAEDIATRIC HAEMATOLOGY/ONCOLOGY PATIENT COHORT

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Background and Aims: Antimicrobial lock therapy (ALT) is used toprevent and treat central line associated blood stream infections (CLABSI) in children receiving systemic anti-cancer therapy (SACT). Although there is a lack of robust evidence with regard to ALT efficacy in this cohort, it has been a component of care at our institution for over 30 years. Considerable variations in practice exist between institutions and ALT is not widely accepted as best practice. The aim of this study was to retrospectively review and analyse the outcomes of CLABSI, which were treated with eithersystemic antimicrobials and ALT or exclusively with ALT
Methods: Retrospective analysis of patients receiving SACT between 2019 and 2021 at Children's Health Ireland (CHI) at Crumlin. Using the microbiology lab system to identify positive cultures, patient records were reviewed to collect clinical and treatment details of the CLABSI and the Central Venous Line (CVL) outcome (i.e. salvaged or removed)
Results: Study included 19 females: 9 males, ages ranging between 1-14 years and the most common diagnosis was Acute Lymphoblastic Leukemia.An indication of fever (>38ºC) prompted CVL cultures in all cases and the most commonly isolated pathogen was coagulase negative staphylococci. There were 52 CLABSI identified in 28 patients. In 49 of these 52 episodes, the line was retained and 25% of these were exclusively treated with ALT.
Conclusions: This is the first Irish paediatric study of ALT in tertiary care. It cannot be stated with certainty that ALT is wholly responsible for the retention of these CVLs; however, we hypothesise that it contributes to successful treatment of CLABSI in our population and permits ambulatory care as opposed to inpatient care. This study has highlighted the need for more formal, robust research into the use of ALT in this high-risk Irish population

EP450 / #1418

Topic: *AS05.p Supportive Care and Palliative Care*

OUTCOMES OF GRAM-NEGATIVE BACTERIAEMIA IN ONCOHEMATOLOGIC PEDIATRIC PATIENTS IN THE ERA OF MULTIDRUG-RESISTANT MICROORGANISMS

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Background and Aims: Bacteriaemia caused by multi-drug resistant (MDR) gram-negative bacteria (GNB) entail high morbidity and mortality rates among paediatric cancer and hematopoietic stem cell transplant (HSCT) patients. The aim is to describe the characteristics and outcomes of GNB episodes occurring in these patients at a referral hospital in southern Europe.
Methods: Retrospective observational study of all GNB episodes occurring in patients <18 years of age with cancer or having received HSCT, admitted in a childrens' hospital in Barcelona (Spain) between January 2019-December 2021. During this period, the empirical antimicrobial local protocol for febrile neutropenia included piperacillin-tazobactam plus amikacin. Meropenem (+/- aminoglycoside and/or glycopeptide) was first choice drug for patients with known MDR colonization or clinically unstable.
Results: Overall, 87 positive blood cultures for GNB were identified from 73 different patients (30 in patients with solid tumours, 34 with leukaemia-lymphoma and 9 were HSCT patients). The predominant isolated species were Escherichia coli, Klebsiella spp and Pseudomonas spp. The most frequently observed resistance mechanisms were beta-lactamases hyperproduction (29), extended spectrum beta-lactamase(12) and carbapenemases (4).Seven of the patients presented MDR GNB colonization previously to the episode. Resistance to piperacillin-tazobactam was detected in 13/87 of the isolated microorganisms and carbapenem resistance in 4/87. All patients were initially treated with a correct empirical treatment according to in vitro sensitivity testing except for two (both recovered after targeted treatment). 21 patients required ICU admission and 4 died due to the infection despite adequate antimicrobial treatment according to sensitivity testing. From the latest, all were patients undergoing intensive non-first line or palliative chemotherapy protocols.
Conclusions: Disease related risk factors and patient's previous MDR colonisations knowledge helped to better target treatment and, concurrently, avoid unnecessary broad-spectrum treatments. Poorer outcomes occurred in those patients undergoing non-first line or palliative chemotherapy protocols in this cohort, irrespective to the empirical antimicrobial treatment and microorganism sensitivity profile.

EP451 / #1617

Topic: *AS05.p Supportive Care and Palliative Care*

PROFILE OF RESPIRATORY VIRAL INFECTIONS IN A TERTIARY CARE PEDIATRIC HEMATO-ONCOLOGY UNIT FROM A DEVELOPING COUNTRY

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Background and Aims: Infections remains a challenge in every pediatric hemato-oncology(PHO) unit in developing countries. Prevalence of viral infections is increasing with 1/3rd of children with cancer having viral infection.
Methods: A prospective descriptive study was done in PHO unit at our tertiary care centre between January-2020&August-2021. Children <18 years in PHO unit presenting with fever and/or respiratory symptoms were enrolled with informed consent. Nasal swabs for viral RT-PCR studies were done apart from standard unit protocol with bacterial cultures and antibiotics. Details of demographic data, history, physical findings and lab parameters (CBC/cultures/viral PCR), treatment and patient outcomes were analyzed.
Results: Of the 84 events in 58patients, 16patients had more than 1episode; 52.4%was noted in <5-years. In our population, we had 83.3% post-chemotherapy, 5.9% bone marrow transplant recipients and10.7% with benign hematological conditions requiring immunosuppressive therapies/ primary immunodeficiencies; the most encountered diagnosis in 25% being B-Acute lymphoblastic leukemia (ALL). Fever was noted in 90% followed by respiratory complaints in 21%cases; 53.6% were neutropenic (ANC <1500cells/mm3). Median duration of illness was 6.9days (range:1-42days) with 88% requiring hospitalization,10.7% requiring intensive care and 3.5% succumbing to their illness. In our study population, 57.1% tested positive for viral pathogen, 10.7% had bacterial infection, 7.1% had mixed infection and 35% were negative for any pathogen. Rhinovirus was the most frequently detected followed by SARS-CoV-2. There was no statistically significant difference noted in duration of illness or hospital stay (p=0.106), severity of illness or neutropenia status between those with or without virus PCR positivity; however, there was a significant difference between neutropenic and non-neutropenic children in duration of hospital stay (p=0.010).
Conclusions: Frequency and outcome profile of viral infections were similar in neutropenic and non-neutropenic children. Identification of a viral pathogen in a selected cohort (low risk febrile neutropenia&stable children) might help in rationalised decision making on antibiotics.

EP452 / #1454

Topic: *AS05.p Supportive Care and Palliative Care*

EMPIRICAL ANTIBACTERIAL THEAPY BASED ON COLONIZATION STUDIES IN PEDIATRIC PATIENTS WITH SOLID TUMORS RECEIVING HEMOPOIETIC STEM CELL TRANSPLANTATION

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Background and Aims: The carriage of antibacterial resistant strains by pre-treated patients may be a problem in context of prolonged agranulocytosis after hemopoietic stem cell transplantation (HSCT). The pre-transplant intestinal colonization assessment by CHROMagar method may provide more effective detection of resistant pathogen strains.
Methods: A total of 74 pediatric (median age of 6 years) patients with solid tumors (n=63) or non-malignant conditions (n=11) were included in June 2020 to March 2022 into an empirical antibacterial therapy (EAT) protocol. All patients were assessed prior to autologous (n=56) or allogeneic (n=22) HSCT for resistant bacteria intestinal colonization by CHROMagar method and routine cultures. The EAT was started on Day1 of febrile neutropenia (FN) based on colonization data. If no prior colonization was found the escalation strategy was adopted, otherwise the EAT was de-escalated.
Results: The pre-transplant colonization by resistant bacteria was confirmed in 54 patients. The routine culturing methods were able to reveal colonization in 17(22%) cases, but were ineffective in 37(47%). CHROMagar method have shown higher sensitivity being able to find a pathogen in 52(67%) cases with only 2 cases showing positive cultures, but not CHROMagar results. In 40(51%) cases the pathogens produced extended-spectrum beta-lactamases (ESBL), in 7(9%) carbopenemases (Carbo-R) and in 11(14%) cases the Vancomycin-resistant enterococci (VRE) colonization was confirmed. The FN developed at a median of 4 (-9 to +14) days past transplant. The escalation strategy was employed in 24% of cases achieving a 42% response rate. The de-escalation strategy used in 76% of cases with 27 (46%) patients responding first-line therapy.
Conclusions: The combination of CHROMagar method with routine cultures allows early colonization detection in order to choose a correct EAT strategy.

EP453 / #1139

Topic: *AS05.p Supportive Care and Palliative Care*

NONCOVID-19 VIRAL RESPIRATORY INFECTIONS IN CHILDREN WITH CANCER DURING THE COVID-19 PANDEMIC: A MULTICENTER OBSERVATIONAL STUDY

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Background and Aims: Acute respiratory tract infections (RTI) are a significant cause of morbidity and mortality in children with cancer, most are precipitated by viral infections. The aim of this study is to evaluate the nonCOVID-19 viral RTI during the COVID-19 pandemic in children with cancer.
Methods: In this multicenter (13 centers) retrospective observational study, children and adolescents with cancer who presented with RTI symptoms between January 2020- March 2022, and who had viral RTI confirmed by multiplex polymerase chain reaction were evaluated according to demographic, etiological, clinical data and outcome.
Results: A total of 255 episodes in 212 children were evaluated. The 32.1% of episodes occurred in a 16 month period between January 2020 and May 2021 during lockdowns and online distance learning in Turkey and the remaining 67.8% in a 10 month period after the end of lockdowns and distance learning from May 2021 on. Lower RTI comprised 27.5% of episodes. The most common agents were Rhinovirus - Enterovirus (46.3%), Parainfluenza viruses (22.3%) which were detected throughout the year, Influenza viruses (9.8%) and Respiratory Syncytial Virus (RSV) (9.4%) which showed peaks in winter. Parainfluenza viruses, Adenovirus, RSV and Influenza viruses were substantially associated with lower RTI with ratios 47.3%, 36%, 29%, 28% respectively. Complete recovery was observed in 91.7% of episodes. Complications such as bacterial pneumonia (7.4%), multiple organ dysfunction (1.5%), myocarditis (1.1%), hepatitis (1.1%) and Gullian Barre syndrome (0.7%), occurred in 8.6% of episodes. In 30-day follow-up nine patients died.
Conclusions: In children with cancer, the nonCOVID-19 viral RTI episodes were less frequent in the beginning of the pandemic during the lockdown and distant education period in comparison to later in the pandemic. Viral RTI , albeit in few episodes, may cause morbidity and mortality in children with cancer, infection control and early diagnosis are crucial in preventing the spread of infection.

EP454 / #333

Topic: *AS05.p Supportive Care and Palliative Care*

COVID-19 ASSOCIATED INVASIVE FUNGAL INFECTION AMONG CHILDREN WITH CANCER

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Background and Aims: Patients with COVID19 are at risk for secondary complications like invasive aspergillosis. Our study evaluates prevalence and outcome of COVID19 associated invasive aspergillosis among cancer children at the Children's cancer hospital Egypt 57357.
Methods: This is a retrospective study including all cancer children diagnosed with COVID-19 and admitted to our hospital during the period March 2020 - september 2021. The electronic medical records were revised and data was collected including; demographics, diagnosis, PCR - COVID, antifungal prophylaxis, radiological findings, Galactomannan, antifungal treatment, and COVID severity. patients were classified as possible, probable and proven using the "2020 ECMM/ISHAM consensus criteria".
Results: A total of 200 patients were diagnosed with COVID 19 during the study period . COVID-19 associated invasive pulmonary aspergillosis was found in 22/200 (11%) patients. The primary diagnosis was AML in (10) patients, ALL in (5), post auto-HSCT (2), NHL (1). while solid tumors reported in 4 patients (3 with NB and 1 with brain tumor). CAPA was proven in (2) patients with histopathological diagnosis, probable in (12) with galactomannan marker more than 1 coupled with radiological finding , and possible in (8) patients with only radiological finding suggestive for pulmonary aspergillosis. Although the hematological malignancy patients were already on antifungal prophylaxis, breakthrough CAPA was reported in 9/22 (41%). The overall mortality was reported in 6 patients (27%) while CAPA attributable mortality was reported in 4 patients (18 %).
Conclusions: Clinicians caring for pediatric cancer patients with COVID-19 should consider invasive pulmonary aspergillosis, despite being on antifungal prophylaxis, especially with worsening of the clinical chest condition. A better understanding of risk factors for adverse outcomes may improve clinical management in these patients.

EP455 / #334

Topic: *AS05.p Supportive Care and Palliative Care*

EFFICACY OF LEVOFLOXACIN VERSUS AMOXICILLIN/CLAVULANATE AND CIPROFLOXACIN IN THE OUTPATIENT MANAGEMENT OF LOW-RISK FEBRILE NEUTROPENIA IN CHILDREN; PRELIMINARY RESULTS

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Background and Aims: Outpatient management of low-risk fever and neutropenia should be implemented if close monitoring is accessible and patient compliance is feasible. the use of Amoxicillin/ Clavulanate plus ciprofloxacin, Levofloxacin, and Moxifloxacin for the treatment of low-risk febrile neutropenia. There are not enough studies assessing the tolerance, safety, and efficacy of these agents. In this study, we aim to assess the efficacy of single-agent Levofloxacin versus the Augmentin /ciprofloxacin regimen used in our institute.
Methods: This is a randomized prospective interventional 2 arm study of low-risk febrile neutropenia patients presenting to the emergency department at the National Cancer Institute, Cairo University starting from December 2021 to January 2023. Patients will be randomized to double agent ciprofloxacin and amoxicillin-clavulanic acid in comparison to single-agent levofloxacin. Follow up of the outpatient cases at; Day 1: Start oral antibiotics, obtain guardians contacts, and assure compliance, Day 3: Follow up the patient clinically and follow up count, and Day 7: Resolution of infection and stopping of antibiotics regardless of neutropenia. Primary outcomes include Safe marrow recovery and improvement of fever in all eligible patients as well as Detecting drug-related side effects encountered in both arms of the study.
Results: A preliminary analysis of the first 30 patients (15 in each group) was done. 100% of patients achieved marrow recovery in both arms by D7. Fever subsided in 100% on the Levofloxacin arm compared to 60% in the group receiving Augmentin/Ciprofloxacin. only one patient on the double agent arm was upgraded to HR and admitted to the inpatient. Levofloxacin was tolerable in all patients with no significant side effects apart from insomnia reported by the parents in 1 patient.
Conclusions: Levofloxacin has better efficacy and can be administered safely in children with low-risk FN, however close follow-up for long-term side effects and monitoring of possible emerging bacterial resistance is warranted.

EP456 / #690

Topic: *AS05.p Supportive Care and Palliative Care*

CHANGES IN ANTHROPOMETRICAL STATUS AND BODY COMPOSITION OF PAEDIATRIC CANCER PATIENTS DURING INTENSIVE ONCO-CHEMOTHERAPY

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Background and Aims: Children with cancer require adequate nutritional support to prevent malnutrition. This study investigated the impact of intensive onco-chemotherapy on anthropometrical status and body composition during the first six months of treatment.
Methods: Anthropometrical status and body composition were measured at diagnosis, prior to the initiation of chemotherapy utilising standardised protocols and validated S10 InBody bio-electrical impedance (BIA) mobile unit. Baseline values for all variables were compared to consecutive monthly follow-up measurements to plot changes over time during the first six months. $p < 0.05$ indicated statistical significance.
Results: Forty-three newly diagnosed children (median age 4years, range 0.3–15years; 51% male) participated in the study. There were 53% haematological malignancies (n = 23) and 47% solid tumours (n = 20). Prevalence of malnutrition varied among anthropometrical variables, with under-nutrition 14% (mid-upper arm circumference; MUAC), over-nutrition 9.3% (body mass index; BMI) and stunting 7.1% at diagnosis. MUAC recognised only 14% of patients with actual underlying muscle store depletion as per BIA (41.8%). Chemotherapy exposure acutely exacerbated existing nutritional depletion during the first two months after diagnosis for all variables except fat mass (FM), with contrary effects on cancer type, as haematological malignancies had rapid increases in weight, BMI and FM. All patients had a clinically significant, acute loss of skeletal muscle mass during this period. Catch-up growth was achieved for all cancer types with a significant increase in weight ($chi^2 = 40.43$, $p < 0.001$), height ($chi^2 = 53.79$, $p < 0.001$), BMI ($chi^2 = 16.32$, $p < 0.005$)), fat free mass ($chi^2 = 23.69$, $p < 0.003$) and skeletal muscle mass ($chi^2 = 24.19$, $p < 0.001$) after six months.
Conclusions: Children with cancer are vulnerable for the development of acute malnutrition with body composition alterations during the first two months ofonco-chemotherapy treatment. Monthly anthropometry and BIA (body composition) measurements assist in implementation of timely nutritional interventions to prevent malnutrition.

EP457 / #526

Topic: *AS05.p Supportive Care and Palliative Care*

ANTIBIOTIC AND ANTIFUNGAL USE IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES DISRUPTS COMMUNITY LEVEL MICROBIAL ACTIVITIES THAT NORMALLY ENHANCE COLONIC DEFENSE, INHIBIT INFLAMMATION AND DECREASE OXIDATIVE STRESS

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Background and Aims: Antibiotic and antifungal use is highly prevalent in pediatric patients with hematological-cancers to prevent severe infections and febrile neutropenia. The gut microbiome is impacted by antibiotic use yielding decreased diversity, reduction in “good” bacteria and increases in “bad” bacteria although there is disagreement on exactly which taxa change and limited studies in pediatric oncology patients, whereas the effects of antifungal use are less well-understood and are limited to mouse studies. The composition of the gut microbiome has implications in the clinical management of hematologic malignancies. We investigate how antibiotic and antifungal use shapes the microbiome in pediatric patients with leukemia and lymphoma using both 16SrRNA (16S) and metagenome sequence (MGS) data.
Methods: We investigated 134 stool samples from 47 pediatric patients undergoing treatment for acute lymphoblastic leukemia, acute myeloid leukemia, hodgkin lymphoma and non-hodgkin lymphoma after ethics approval. Antibiotic and antifungal use along with age, and sex was collected. Sequences from 16S and MGS were used to identify microbial taxa. Changes in alpha-diversity were examined using Wilcoxon-test, and multivariable differential abundance analysis (MaAsLin2) was used to assess associated changes in the microbiome with antibiotic and antifungal use, accounting for age differences.
Results: Antibiotic and antifungal use resulted in decreased diversity and was associated with a decline in important butyrate producers (Faecalibacterium, Anaerostipes, Dorea, Coprococcus, Blautia, Fusicatenibacter). Antibiotic use was associated with an increase in Lactobacillales and Actinobacteria taxa while antifungal use increased opportunistic Enterococcus and Gammaproteobacteria taxa.
Conclusions: This study shows evidence of gut dysbiosis in patients with hematological malignancies. Butyrate is important for gastrointestinal integrity; it inhibits inflammation, reinforces colonic defense, mucosal immunity and decreases oxidative stress. We find that this patient population, which could benefit from butyrate’s functions, has increased antimicrobial and antifungal use, which is associated with a significant decline in the microbial community responsible for beneficial butyrate production.

EP458 / #105

Topic: *AS05.p Supportive Care and Palliative Care*

FERTILITY PRESERVATION AFTER A CANCER DIAGNOSIS: A STUDY ON KNOWLEDGE, AWARENESS AND READINESS AMONG PARENTS OF PAEDIATRIC CANCER PATIENTS IN MALAYSIA

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Background and Aims: Infertility is one of the most common long-term effects experienced by childhood cancer survivors. The concept of fertility preservation (FP) among paediatric oncology patients is still relatively new in developing countries. This study aimed to assess the knowledge, awareness and readiness for FP among parents of paediatric cancer patients in Malaysia.
Methods: A total of 65 parents participated in this single-centre, cross-sectional study. Validated questionnaires consisting of 10 true/false questions were used to determine their oncofertility knowledge; each correctly answered question contributed one point to the total score (maximum 10 points). Another 12 multiple-choice questions were used to assess the parents' awareness and readiness for their child to undergo FP before cancer treatment.
Results: Most of the children in this study were diagnosed with leukaemia (n=49, 75.4%), followed by brain tumour (n=4, 6.2%), neuroblastoma and lymphoma (n=3, 4.6% each). Majority of them (n=62, 95.4%) were receiving at least one gonadotoxic agent in their treatment protocol. Half of the parents (n=29, 44.6%) were unaware that cancer treatment may potentially affect a child's fertility and almost all (n=61, 93.8%) have not heard of FP before. Mean score for oncofertility knowledge was only 1.31 (SD±1.64), most likely due to lack of information given to them by the healthcare providers. Despite being introduced to the possible option of FP for their child, only half of them expressed their interest to discuss this further with their clinicians due to uncertainty about the procedure as well as concerns regarding the cost and complications.
Conclusions: The present study demonstrated a lack of knowledge and awareness about FP among parents of paediatric cancer patients in our centre. With the increasing number of childhood cancer survivors, efforts should be made to promote dialogue between providers and the parents to increase their knowledge and awareness on FP.

EP459 / #1481

Topic: *AS05.p Supportive Care and Palliative Care*

SARS-COV-2 INFECTION IN CHILDREN UNDERGOING ONCOLOGIC TREATMENT IN HONG KONG – A POPULATION-BASED COHORT DURING THE OMICRON WAVE

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Background and Aims: SARS-CoV-2 virus (COVID-19) led to a global pandemic disrupting all aspects of healthcare. After a period of limited local transmission, emergence of Omicron subvariant BA.2 resulted in rapid surge of cases in Hong Kong. Here we report the features and outcome of COVID-19 infection during the Omicron wave in children undergoing anti-cancer treatment.
Methods: Hong Kong Children's Hospital is the only referral center for Pediatric Oncology and Hematopoietic Stem Cell Transplantation (HSCT) in Hong Kong. Based on this population-wide cohort, we studied the clinical features of children on active anti-cancer therapy or <12-month of HSCT infected with COVID-19 from February-March 2022.
Results: Among 210 patients fulfilling the above criteria, 47 patients (22%) were diagnosed with COVID-19 infection (M:F=35:12). The median age at infection was 10.1years (range: 2.1-20.2). Only 2 patients received ≥1 dose of COVID-19 vaccine ≥2 weeks before documented infection. Thirty-three were diagnosed using RT-PCR, while 14 were diagnosed using rapid antigen test. Forty-two (89%) patients were symptomatic, with the most common symptoms being fever and cough. None developed neurological symptoms. Twenty-seven (57%) patients required hospitalization, and the median duration of admission was 5 days (range 1-43). Forty patients had mild symptoms, while 2 were considered to have moderate symptom severity (lower respiratory tract infection in 1, systemic inflammation in 1); remdesivir was used in 4 patients. None required intensive-care and there was no mortality. COVID-19 infection resulted in interruption of therapy in 83%. Serial COVID-19 testing indicated persistent positivity in some as long as 40 days, including symptomatic re-activation/re-infection in 1.
Conclusions: SARS-CoV-2 virus resulted in high incidence but mostly mild infection during the Omicron wave for unvaccinated children undergoing anti-cancer treatment. Treatment interruption was common, persistent viral detection observed and re-activation/re-infection was possible, encouraging vaccination before and after infection. (A.P.Y.L. & G.K.S.L. contributed equally)

EP460 / #1037

Topic: *AS05.p Supportive Care and Palliative Care*

MOURNING THEMES IN YOUNG CHILDREN AFTER THE DEATH A CLASSMATE: A HYBRID APPROACH FOR THE DEVELOPMENT OF AN EVIDENCE-BASED PICTURE BOOK

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Background and Aims: Although cure rates of children with cancer have increased dramatically, a portion of children with cancer will not survive their disease. When a child dies, classmates are left behind who have to cope with this loss and the emotions involved. We aimed to explore the variety of emotions felt by children aged four to eight years, after the death of a classmate. We used this to develop and publish a picture book aimed at supporting these children (and their teachers).
Methods: First, we commenced a dual appraised systematic literature review in multiple databases. Findings from the review formed the thematic basis for a semi-structured interview study among experts working with bereaved children. These interviews were transcribed, coded and analyzed qualitatively to determine which emotions had been mentioned. These formed the basis of the picture book we developed in collaboration with children's authors and illustrators.
Results: After appraisal of 3,247 citations, no studies were identified describing emotions after the loss of a classmate. We did however include six studies concerning the bereavement of siblings. Fifteen experts participated in the interview study. Identified as the most important emotion was sadness, followed by anger, fear and guilt. The experts also noted that young children express their emotions in a more physical way than older children. Subsequently the picture book entitled "De Klas Neemt Afscheid" ("The Class Says Farewell") was developed, which also includes tools for teachers.
Conclusions: When young children lose a classmate, sadness is prominent, although emotions differ per child, according to age, sex, and relationship with the deceased. We developed an evidence-based picture book to support children in dealing with this loss. After winning a science/art-grant, we managed to get this picture book freely available for schools in which a child has died or is terminally ill. An English translation is currently being developed.

EP461 / #1116

Topic: *AS05.p Supportive Care and Palliative Care*

UNCOVERING THE BARRIERS TO EARLY INTEGRATION OF PALLIATIVE SERVICES IN THE CARE OF CHILDREN WITH CANCER IN BRAZIL USING THE ADAPT SURVEY

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Background and Aims: Multiple studies have demonstrated that early integration of palliative care (PC) in pediatrics helps with pain and symptom management, quality of life, alleviates suffering, and improves communication with families. To understand the structural barriers and underlying stigma preventing effective delivery of PC to children with cancer in Brazil, the “Assessing Doctor’s Attitudes on Palliative Treatment” (ADAPT) survey was implemented.
Methods: Survey questions were updated and translated into Portuguese. A panel of experts from Brazil went through iterative review rounds to improve content validity and cultural sensitivity. Questions evaluate physician perceptions regarding timing of PC integration, the scope of palliative treatment, physician responsibility, and ethical issues. The survey was electronically distributed to doctors from any specialty and residents who treat children with cancer in Brazil. Responses were anonymous.
Results: Providers (228) from 16 hospitals from all the 5 regions in Brazil participated in the survey with a mean alignment to WHO guidelines of 91%. Although 75% have access to a palliative expert in their hospital, 48% feel that PC is integrated too late. Over half (54%) stated that physicians continue recommending curative treatment even when it has little probability of prolonging life. Most (75%) felt that families see the decision to integrate PC as “giving up”. The main barriers to early integration of PC were limited physician knowledge on the topic (81%), discomfort in raising the topic with families (81%), and lack of home-based services (77%). Few participants felt confident addressing the emotional (30%), spiritual (22%), and grief and bereavement (30%) needs of patients and families
Conclusions: Formal education in PC is an important gap to its early integration in the care of children with cancer in Brazil. There is an opportunity to build capacity focused on different patient needs and to work with families to demystify the role of PC in cancer treatment.

EP462 / #1824

Topic: *AS05.p Supportive Care and Palliative Care*

GUIDE BASED ON EVIDENCE OF MULTIPROFESSIONAL GUIDANCE FOR FLUID OVERLOAD IN PEDIATRIC ONCOLOGICAL PATIENTS

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Background and Aims: BACKGROUND: Excessive use of fluids can cause tissue edema and organ dysfunction, which can result in high levels of morbidity, prolonged length of stay and mortality in pediatric cancer patients. The multiprofessional team assists in the recognition of this clinical condition, bringing an important contribution to this scenario, which impacts on improving patient care and reducing admission to the Pediatric Intensive Care Unit. Thus, the present study is justified for the recognition and early approach of these patients, aiming to reduce the morbidity and mortality related to fluid overload, through the construction of an evidence-based multiprofessional guidance flowchart. AIM: To create a multiprofessional guidance guide based on evidence of fluid overload in pediatric cancer patients.
Methods: MATERIALS AND METHODS: Review of articles, for integrative study, selected by research in PubMed- MEDLINE, BVS and Cochrane, looking for articles on fluid overload in pediatric patients.
Results: A bibliographic search was carried out in PubMed, Cochrane and VHL databases for studies on water overload in pediatric patients, from 1932 to September 2020. A total of 3692 articles, after removing articles such as those in the Pediatrics area, resulted in general themes: diarrhea, pneumonia and in areas of specialties. Other topics were evaluated: neonatology, burns, cardiac surgery, but they did not contribute to this work, review of duplicate articles and 76 articles were selected for data extraction according to my inclusion criteria.
Conclusions: CONCLUSION: FO is an important and current topic, as, reported in the studies found, it is a factor of morbidity and mortality. In pediatric oncology, the literature is scarce, so further studies are needed, since excess fluids may be related to reduced survivorship in these patients, and should therefore be detected earlier if present and avoided.

EP463 / #642

Topic: *AS05.p Supportive Care and Palliative Care*

CLINICAL COURSE AND EVOLUTION OF CHILDREN WITH CANCER AND SARS-COV-2 INFECTION IN A PEDIATRIC ONCOLOGY UNIT OF A DEVELOPING COUNTRY (MEXICO).

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Background and Aims: Children with cancer have a higher risk of severe Sars-Cov-2 infection, hospitalization and death, compared to healthy children. In low- and middle-income countries, the likelihood of severe, critical illness or death from COVID-19 is significantly higher than in high-income countries. Aims Describe the clinical course and evolution of children with cancer and Sars-Cov-2 infection in the pediatric oncology unit of a developing country: Hospital Materno Infantil Issemym, Toluca México
Methods: We included in a cohort children with cancer and Sars-Cov-2 infection corroborated by a positive PCR test. We evaluated clinical, demographic, paraclinical characteristics, oncological diagnosis, stage of treatment and variables related to the treatment of Sars-Cov-2, complications and critical interventions during the event, as well as related to the outcome. Descriptive statistics were performed.
Results: 54 patients on cancer had criteria for suspected Sars-Cov-2. PCR test was positive in 18, 10 men and 8 women, 44% > 12 years, 61% with acute lymphoblastic leukemia . 3 patients debuted with cancer and Sars-Cov-2 infection, One patient with relapse of myeloid leukemia. 16.6% asymptomatic. The most frequent symptoms were fever in 62%, cough 40% and diarrhea in 30%. (28%)severe neutropenia, 55% lymphopenia < 300/mm3. 2 patients developed multisystem inflammatory syndrome. Mechanical ventilation and other critical interventions merited 16%, oxygen therapy and pronation required 27% . The most frequent complication was septic shock. A patient in relapse acute myeloid leukemia died, The hospital stay was 6. All patients continued their cancer treatment , without clinical complications.
Conclusions: Most of our patients presented moderate disease, 16% severe and 5% died. Comorbidities, co-infection, and severe neutropenia increase the risk of severe disease, as well as complications related to cancer treatment. Our data is small but could be useful for other oncology units in countries with limited resources, no screening programs and a limited number of tests.

EP464 / #1872

Topic: *AS05.p Supportive Care and Palliative Care*

CHANGES IN ANTHROPOMETRY AND NUTRITIONAL STATUS IN CHILDHOOD CANCER SURVIVORS IN NEW ZEALAND: A LONGITUDINAL STUDY

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Background and Aims: Childhood cancer survivors (CCS) are at risk of malnutrition (over and undernutrition) during treatment and have an increased burden of chronic disease. This study aimed to explore longitudinal changes in anthropometry and determine the prevalence of malnutrition during and after treatment.
Methods: Retrospective longitudinal study of CCS in Auckland, NZ, who entered the Late Effects Assessment Programme (LEAP) between January 2018 and December 2020 (N=67). Data were assessed at diagnosis, months 3 and 6 of treatment, treatment completion, survivorship, and LEAP. Standardised anthropometric data were assessed according to Intensity of Treatment Rating (ITR). A mixed-effects model was used to account for repeated measures on the same patient for anthropometric variables according to ITR.
Results: Sixty-one percent of patients had some dietetic input. Of those, 43% (n=29) saw a dietitian within the first month of diagnosis. The frequency of dietetic contact varied depending on diagnosis, with most patients (39%) receiving nutrition support as an inpatient only. Over 50% of patients had an ITR of 3 or 4. There was a significant interaction effect between ITR and time since diagnosis for mean zweight and zheight. Patients with an ITR of 2 had a significant increase in zweight at treatment completion compared to diagnosis and patients with an ITR of 3 had a significant decrease in zweight at months 3 and 6 of treatment and a significant decrease in zheight at month 6, which persisted into survivorship. The prevalence of undernutrition (z-score: $^{-}$1.0 - $^{-}$2.99) and overnutrition (z-score ≥ 2.0) was 2% and 10%, respectively at diagnosis, increasing nearly six-fold to 11% and four-fold to 18% at LEAP.
Conclusions: CCS experience significant changes in standardised anthropometry and nutritional status during treatment and into survivorship. Dietetic input only occurred ‘on treatment’, however, these data highlight the need for continued input in survivorship.

EP465 / #608

Topic: *AS05.p Supportive Care and Palliative Care*

TREATMENT OUTCOMES IN CHILDREN WITH RELAPSED/REFRACTORY SOLID TUMORS: A SINGLE-CENTER STUDY

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Background and Aims: Relapsed or refractory (R/R) solid tumors remain a significant cause of mortality for children. While upfront therapies have been well-studied, the cumulative effect of multiple relapses and salvage regimens is unknown. We describe the disease trajectory in patients with R/R solid tumors, from the time of first relapse to time of death or last follow-up.
Methods: We reviewed data from electronic medical records for patients with primary, malignant R/R solid tumors treated at Texas Children's Hospital between 2002-2022. Descriptive analysis was performed along with univariate chi-square and independent sample t-tests. Cox regression analysis was used to evaluate time from relapse to death for each variable described. Analysis was performed with SPSS v24.
Results: We reviewed 337 patients with R/R solid tumors (female: 48%; mean age: 8.33 years; median follow-up after first relapse: 14.0 months). Most common diagnoses were neuroblastoma (25.8% of cases), osteosarcoma (16.6%), and rhabdomyosarcoma (15.7%). Patients had a median of 3.03 (IQR: 1-4) progressions or relapses. Deceased patients (n=218) had a median of 287 (IQR: 145-583) days from first relapse to death, and were more likely to have had bone or soft tissue sarcoma ($p<0.001$). Prolonged survival from first relapse to death was associated with specific salvage approaches; increased number of relapses; increased time between diagnosis and first relapse; and increased time between first and second relapse ($p<0.05$). In a multivariable Cox regression model, the presence of a >21 day break in salvage therapy was significantly associated with increased time from first relapse to death ($p<0.05$), while tumor type had no significant effect ($p=0.41$).
Conclusions: The prognosis for children with R/R solid tumors is poor. Delay of salvage therapy did not negatively impact survival after first relapse, implying that this option could reasonably be offered to some patients to promote quality of life and explore goals of care between treatment regimens.

EP466 / #737

Topic: *AS05.p Supportive Care and Palliative Care*

ASSESSMENT OF BARRIERS TO PEDIATRIC PALLIATIVE CARE INTEGRATION FOR CHILDREN WITH CANCER IN LATIN AMERICA

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Background and Aims: Early integration of pediatric palliative care (PPC) for children with cancer is critical for the quality of life of both patient and family. To improve access to PPC in resource-limited settings we must understand perceived barriers to early integration. Our aim is to understand physician perspectives on ideal versus actual timing of PPC integration for children with cancer and uncover barriers to early integration as identified in Latin America.
Methods: The Assessing Doctors' Attitudes on Palliative Treatment (ADAPT) survey was developed to evaluate physician knowledge of, beliefs around, and perceived barriers to palliative care integration for children with cancer globally. We translated the survey into Spanish and contextually adapted the tool for use in Latin America. Descriptive statistics were used to summarize survey data. The McNemar test was used to assess responses regarding the actual versus ideal timing of palliative care consultation. Analysis of variance was used to compare means for perceived barriers.
Results: A total of 831 physicians from 17 countries in Latin America participated, with a median country response rate of 51.4%. Most respondents (68.8%) felt palliative care should be involved from cancer diagnosis, but only 14.1% stated that this occurred at their institution ($P<0.001$). The highest ranked barriers to early integration of PCC were lack of services, personnel, and knowledge about PPC, along with physician and family discomfort about PPC involvement. Respondents from lower-middle income countries described identified barriers as more challenging to overcome than those from upper-middle and high-income countries ($P<0.001$).
Conclusions: These findings highlight the need for interventions to improve access to resources, didactic training, and clinical education on PPC for physicians in Latin America. Each intervention should be tailored to the needs and opportunities specific to each country to improve quality of life for children with cancer.

EP467 / #1255

Topic: *AS05.p Supportive Care and Palliative Care*

EMPOWERING PATIENTS, FAMILIES, CLINICIANS AND TEACHERS ON MANAGING OTOTOXCITY AS AN ADVERSE EVENT OF CHILDHOOD CANCER TREATMENT

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Background and Aims: Ototoxicity is an early, irreversible adverse event occurring in children treated with platinum agents and cranial irradiation. It can have a severe negative impact on speech-language development and quality of life, especially in very young children. Therefore, it is important to provide information on cancer treatment-related ototoxicity on a global level.
Methods: Three efforts were established to develop practical knowledge on several aspects of

ototoxicity, including 1) the Ototoxicity Task Force (International Society of Pediatric Oncology Supportive Care Committee) consisting of audiological and pediatric oncology experts, 2) a multi-disciplinary team including pediatric oncologists, audiologists, a psychologist, a health scientist, and a parent of a child with hearing loss, and 3) a Public Advisory Group. Target groups included childhood cancer patients, survivors, their families, treating clinicians and teachers (of the Deaf and Hard of Hearing). The knowledge obtained can be used upfront, during cancer treatment and for several years thereafter during survivorship.

Results: Standardized surveillance recommendations were developed for age-appropriate testing, timing and frequency of monitoring during childhood cancer therapy, based on literature and consensus. Furthermore, an evidence-based open access book chapter was established to inform the target groups on a global level. Topics included the impact of ototoxicity on the young person, and ways to mitigate or reduce ototoxicity. In addition, the Children's Liver Tumour European Research Network developed educational videos on how to properly support children with ototoxicity in school, along with personal stories of affected childhood cancer survivors and their families.

Conclusions: The ultimate goal of ototoxicity education is to have patients and families more involved in the process of cancer treatment and ototoxicity monitoring, and eventually to implement shared decision making in clinical practice. Furthermore, it emphasizes the need for clinicians and teachers to support the patient and family who have to deal with the long-term consequences of cancer treatment.

EP468 / #1636

Topic: *AS05.p Supportive Care and Palliative Care*

MICROBIOLOGICAL PROFILE OF BLOODSTREAM INFECTIONS IN PEDIATRIC CANCER PATIENTS: A DEVELOPING COUNTRY EXPERIENCE

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Background and Aims: Bloodstream infection (BSI) is the most important cause of morbidity and mortality in pediatric cancer patients. There is a paucity of microbiological data regarding BSIs in pediatric cancer patients in India. Knowledge of prevailing microbiological profiles will help guide empirical antibiotic therapy in patients with febrile neutropenia. This study aimed to analyze the microbiological profile and sensitivity pattern of the BSIs with underlying risk factors in children with cancer.
Methods: Blood culture reports of all the pediatric cancer patients at the treating center between February 2019 and January 2022 were collected retrospectively. The microbiological profile and sensitivity pattern were analyzed.
Results: There were 137 positive blood cultures during the study period. Gram-positive organisms accounted for 54 (39.4%) of all positive cultures. Growth of gram-negative organisms was detected in 72 (52.5%) cultures. Candida species were isolated from the rest 11. Twenty-three episodes of culture positivity were detected in samples from central venous catheters. Staphylococcus aureus was the most common gram-positive isolate accounting for 48 cases, whereas Pseudomonas aeruginosa was the most common gram-negative organism. Methicillin resistance was detected in 32% of Staphylococcus aureus isolates while they remained universally sensitive to vancomycin. Among the gram-negative organisms, sensitivity to anti-pseudomonal penicillins, aminoglycosides, third-generation cephalosporins, and carbapenems were 50%, 52%, 50%, and 60%, respectively. Colistin was sensitive in 92% of isolates, and the rest showed intermediate sensitivity. Antimicrobial resistance was higher in Klebsiella pneumoniae and Pseudomonas aeruginosa.
Conclusions: Gram-negative organisms were the most commonly isolated microbes in the study group. A significantly higher incidence of resistance to the first-line antimicrobial agents was prevalent among gram-negative organisms, particularly with Klebsiella pneumoniae. Similarly, a high incidence of methicillin resistance was also observed. It highlights the importance of hand hygiene practices and aseptic barriers with judicious use of antibiotics.

EP469 / #79

Topic: *AS05.p Supportive Care and Palliative Care*

"YOU DON'T HAVE ANY CHOICE. IF YOU LEAVE WITH THE CHILD, THE DISEASE WILL WORSEN": THEORETICAL APPROACH OF A CLINICAL ETHICS IN AN AFRICAN ONCOPEDIATRICS

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Background and Aims: In a context of medical pluralism, weak universal health coverage, lack of health insurance, and where the death of the child is not always accepted, any decision about the patient, while respecting a moral code that binds everyone everywhere, becomes a real challenge. Thus, the authors of this article engage in a field that does not yet receive the attention of researchers in Cameroon: clinical ethics. The authors lay here the groundwork for a clinical ethics.
Methods: The present study is based on five cases of paediatric cancers, observed in the Mother and Child Centre of the Chantal Biya Foundation in Cameroon. The selection was based on ethnicity, patient's relationship with the warden and stage of the disease. The data collected were analyzed and interpreted on the basis of the interpretative anthropology of Clifford Geertz.
Results: There is no specific profile of caregiver, let alone a known respondent, who should act as a mediator between the health care team and the patient's family. The emergency of clinical ethics in Cameroon lies in its codification. Socio-cultural factors linked to the status of the child in the African culture, the endogenous accounts on the disease and medical pluralism are all major challenges to be met.
Conclusions: While in the countries of the North, the situations with high ethical stakes are those involving the choice of a therapy, the suspension of a protocol, assisted death, euthanasia, etc., in the countries of the South, these situations are crucially dependent on the socio-economic and cultural context and on the good faith of the child's parents. In any case, clinical ethics must be thought of in terms of the realities specific to the groups that make up Cameroon.

EP470 / #1869

Topic: *AS05.p Supportive Care and Palliative Care*

COVID-19 IN CHILDREN WITH CANCER: EXPERIENCE AT THE INSTITUTO NACIONAL DE ENFERMEDADES NEOPLASICAS IN PERU

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Background and Aims: Peru, an upper-middle-income country, according to the World Bank, was severely affected by the COVID-19 Pandemic. Pediatric cancer patients were significantly impacted, because of frequent delays in their access to diagnosis, treatment, and follow-up. Main contributors included economic and social issues, but also the high viral transmission among these special population
Methods: The Instituto Nacional de Enfermedades Neoplásicas (INEN) is the first referral center for pediatric cancer in Peru. All pediatric patients attended from May/20 to Mar/22 have been tested for COVID- 19 at admission, in case of respiratory symptoms or fever during hospitalization or previous to any procedure. A prospective database registry was conducted with data from all patients with a positive SARS-COV2 test including sociodemographic, clinical, and outcome characteristics.
Results: From the early phase of the COVID-19 pandemic, we registered 292 pediatric cancer patients with COVID-19 infection. 217 patients (74.3%) had hematological neoplasms, mainly acute lymphoblastic leukemia, and 75 patients had solid tumors. 188 (64.3%) were male and 104 patients were females. Thirty percent of patients were neutropenic at diagnosis. We registered 8 deaths: 6 patients with progressive disease, 1 female patient with advanced osteosarcoma and pneumonia that had a positive test at admission, and 1 female patient with hepatoblastoma and severe pneumonia. Three patients needed intensive support, of which two of them completely recovered from the COVID-19 infection. Overall, the cohort mortality was 2.9%.
Conclusions: At INEN, we registered the largest cohort of pediatric cancer patients with COVID-19 in Peru. Our results showed that only a few patients developed severe respiratory disease, being most of them asymptomatic. Neutropenia was not a risk factor for severe disease. Future research is needed to determine the long-term outcome for pediatric cancer patients in developing countries.

EP471 / #1975

Topic: *AS05.p Supportive Care and Palliative Care*

IS A 3-POINTS CUTOFF AT SCAN IDEAL TO SCREEN FOR NUTRITIONAL RISK IN CHILDREN WITH CANCER FROM LMIC?

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Background and Aims: Nutritional screening aiming at the early detection of malnutrition in hospitalized pediatric patients has been strongly recommended for children with cancer. Murphy et al (2016) developed and validated the SCAN (Nutrition Screening Tool for Childhood Cancer) tool specifically for pediatric oncology and recently translated Brazilian-Portuguese. This study aims to evaluate the validity and reliability of the translated version (SCAN pt-BR) at a UMIC pediatric oncology hospital.
Methods: SCAN is based on six questions specific to identifying the nutritional needs of children with. Scores higher than 3-points indicate a risk of malnutrition. The original tool was validated comparing with SGNA in a HIC country. To validate the SCAN pt-BR, we compared to STRONGkids, the only pediatric screening tool translated and validated to Brazilian-Portuguese. The reliability was observed through a test-retest assay. Significance was set at $p < 0.05$
Results: 267 children with cancer were evaluated in this study, 35 of whom took part in the test-retest essay. The reliability phase identified a substantial inter-rater agreement of translated SCAN (ICC=0,77). 188 children (70.4%) had a SCAN pt-BR score ≥3. Although, by anthropometric evaluation, 11,4% of patients presented malnourished (Z-score ≤-2). According to the ROC curve analysis, the SCAN pt-BR showed excellent accuracy with an AUC of 0.86 (95% CI:0.819,0.911). Using standard cut-off≥3, a sensitivity of 77.5% and specificity of 83.5% were found. Considering the ideal sensitivity of 100% for a screening tool when the cut-off was set to ≥2 raised the sensibility to 96% and decreased specificity to 49.4%
Conclusions: Validated against the STRONGkids, SCAN pt-BR showed good reliability and accuracy with higher specificity than the original scale (Se100%, Sp39%) in our pediatric oncology population even when the cut-off was decreased to ≥2.However specific conditions and populations especially those from UMIC or LMIC countries particular tools are more sensitive than generic tools and need be adapted for socio-economic reality.

EP472 / #1999

Topic: *AS05.p Supportive Care and Palliative Care*

IS STRONG-KIDS A GOOD NUTRITIONAL SCREENING TOOL FOR BRAZILIAN CHILDREN WITH CANCER?

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Background and Aims: Although a significant number of pediatric nutritional screening tools have been developed, only a few are available (and validated) in languages other than English. For example, the Screening Tool for Risk Of impaired Nutritional status and Growth (STRONGkids) is one of the most frequently used instruments in assessing the malnutrition risk among pediatric inpatients and one of the few translated and validated to Brazilian-Portuguese. Malnutrition in children with cancer can significantly affect outcomes, so nutritional screening aiming at the early detection of malnutrition in hospitalized pediatric patients has been strongly recommended for children with cancer. This study aims to evaluate the effectiveness of using STRONGkids to identify pediatric cancer patients at nutritional risk.
Methods: The anthropometric assessment was used as the reference standard in evaluating the effectiveness of using STRONGkids to identify pediatric cancer patients at nutritional risk.
Results: 267 hospitalized children with cancer were evaluated in this study and submitted to the STRONGkids tool within 48 hours of admission. The median score obtained in our sample was 3 points, corresponding to medium nutritional risk. In this cohort, 70.7% of children were eutrophic by BMI Z-score. The analysis of the correlation of anthropometric and body composition measurements found that 56.6% of patients with adequate arm-circumference were classified as medium/high nutritional risk, and 59.4% with adequate triceps skinfold (p-value 0.043).
Conclusions: STRONGkids seems not to have parameters that guarantee sensitivity for this population by overestimating the nutritional risk, which can be a problem in UMIC and LMIC countries where nutrition assessment and management are readily available in all situations.

EP473 / #2003

Topic: *AS05.p Supportive Care and Palliative Care*

ADDUCTOR POLLICIS MUSCLE THICHNESS (APMT) A EASY WAY TO ENHANCE BODY COMPOSITION EVALUATION IN CHILDREN WITH CANCER

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Background and Aims: Much has been discussed about the parameters to identify malnutrition in pediatric cancer patients. Considering the different social issues that guide decision making, anthropometry is an easily accessible, fast and low cost tool. APMT has been suggested as a promising parameter to evaluate the muscle compartment. Evaluate the behavior in pediatric oncology patients with the APMT and the correlation between MUAC and another antrhopometrics measure with z score de peso, estatura, (MUAC and tricipal skinfold).
Methods: Cross-sectional study with prospective data collection, which included patients aged 0 to 18 years old who were hospitalized in the inpatient unit of a developing country, diagnosed with childhood cancer within 3 months. Anthropometric and body composition data were collected within 48h of their hospitalization.
Results: 135 patients were included with a mean age of 11 years who underwent evaluation of the APMT and objective anthropometric data. They had a mean APMT of 10.79 mm, 95% CI (11.6 - 9.93). When correlating the thumb measurement with weight z score, height z score, BMI z score, MUAC and triceps skinfold. They showed low correlation. When performed the comparison between groups by ANOVA test, the data showed normal distribution, After Bonferroni post hoc test it was observed difference between the averages of thumb of malnourished and obese group ($P<0.001$) and adequate and obese according to MUAC ($P=0.011$). For triceps skinfold had a difference between the averages of the thumb in the malnourished and obese groups ($P=0.002$), averages of the risk group of malnourished and obese ($P=0.039$) and between the averages of the adequate and obese groups ($P<0.001$).
Conclusions: The correlation between APMT measurements with the anthropometric data did not show a good correlation, not even with the arm circumference which shows to be sensitive for pediatric cancer patients, thus, can the EMAP be a tool for early diagnosis of malnutrition?

EP474 / #2024

Topic: *AS05.p Supportive Care and Palliative Care*

RELEVANCE OF CLINICAL SIGNS AND SYMPTOMS OF MALNUTRITION IN CHILDREN WITH CANCER

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Background and Aims: Nutritional status is classically assessed by using anthropometric parameters although changes usually only appear when malnutrition is already installed. In this sense identifying early signs and symptoms that indicate the risk of malnutrition could ensure an early intervention to prevent this undesirable outcome.This study aims to characterize signs of malnutrition and gastrointestinal symptoms in children with cancer undergoing the first four months of treatment at a UMIC pediatric oncology hospital.
Methods: A cross-sectional study with prospective data collection which included patients over 0 to18 y.o of age who were hospitalized in the inpatient unit of a developing country, diagnosed with childhood cancer less 4 months. Anthropometric and related signs and symptoms data were collected and the patients were evaluated and questioned about the signs and symptoms 48 hours after admission.
Results: The vast majority of the 81 participants did not show any early signs of malnutrition(79%) nor symptoms of the upper(66.7%)and low(59.3%) gastrointestinal tracts(GIT).Whether children identified malnourished (or at risk of malnutrition) presented more clinical signs and symptoms than normal-weight children correlation analysis was performed between the nutritional profile and the frequency of clinical signs of malnutrition and symptoms of upper and low GIT.Significant correlations were found between the nutritional status identified by the BMI by age and the presence of clinical signs of malnutrition(p=0.026)and upper GIT symptoms(p=0.008).In addition correlation was found between the nutritional status obtained through the measurement of MUAC and the occurrence of clinical signs of malnutrition.The other parameters used for nutritional assessment(Weight-for-ageHeight-for-age AMC and subscapular and triceps skinfold thicknesses) did not present a correlation with the signs and symptoms presented by the children.
Conclusions: The clinical signs and symptoms of malnutrition should´nt be underestimated in hospitalized children since the presence of these signs correlates directly with their nutritional status and can be identified early during daily assessments during the hospitalization period.

EP475 / #1188

Topic: *AS05.p Supportive Care and Palliative Care*

LEGACY BUILDING; A WAY OF COPING AMONGST PARENTS OF CHILDREN ON QUALITY OF LIFE CARE IN PAKISTAN

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Background and Aims: Losing a loved one to a terminal disease can forever change one's life, and the emotional toll it takes on families is immeasurable. Research has shown that the grief related to losing a child can be more severe than that of a spouse or any other family member. Given the intensity of grief faced by bereaved parents, the need for a multidimensional approach is essential in aiding parents and families through their process of grieving. Legacy building has proven beneficial to the parents and their loved ones in various different ways from aiding conversations about remembrance of the child to even helping them come to terms with the child's mortality. This exploratory study based at Indus Hospital & Health Network (IHHN) looks at how grieving parents get help from legacy building.
Methods: To better understand the impact of legacy making on bereaved parents, this study assessed feelings and thoughts of parents and their recommendations for its utilization. Photos captured with a polaroid camera and hand prints through oil paints. Parents' details were obtained through electronic medical records. A survey form was created to explore parents experiences regarding legacy projects. A total of 6 parents were interviewed over the phone to fill the survey.
Results: All respondents said they would suggest the Legacy building program to other families facing end-of-life decisions. Parents expressed that these souvenirs helped them significantly with their grieving process and with focusing on positive memories of their child. The frequency with which respondents observed or touched their child's memory varied among subjects. Most of the parents were from underprivileged backgrounds and did not have any other souvenirs of their child.
Conclusions: The legacy building program is an efficient, hassle free and cost-effective interventions for bereaved parents and their families. This model if adopted widely can greatly support bereaved parents.

EP476 / #1189

Topic: *AS05.p Supportive Care and Palliative Care*

DEVELOPMENT AND IMPLEMENTATION OF BEREAVED PARENT MENTOR PROGRAM MODEL IN NOT-FOR-PROFIT HEALTH CARE SETUP, LMIC PAKISTAN

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Background and Aims: Parents of childhood cancer patients significantly benefit from emotional support following their child's loss in the long run. Using adaptable and diversified supporting services that change as the grieving process progresses is crucial to coping and mental health of grieving parents. The bereavement program at the Indus Hospital & Health Network (IHHN) was adopted and developed in collaboration with grieving parents by the Palliative care team of the Psychosocial Department to improve and increase institutional services offered to families during and after a child's death.
Methods: The St. Jude's Bereaved Parent Program Mentorship program was contacted for material and permission was granted for replication and translation of their material under copyright of St. Jude Hospital and Research Center. A total of 4 bereaved parents from IHHN consented to participate in the bereavement Program, only 3 participants completed the program. Parents were trained on different skills including, communication, boundary making, confidentiality, spiritual care and self-care to provide secured emotional support to mentees. Seven sessions were conducted with the participants, including a focus group discussion. Pre-training, a detailed interview to assess their availability, readiness and understanding of the program.
Results: The developed program was piloted and ran through smoothly, with parents comprehending, understanding and inculcating the values and training provided to them. The mentors have begun to build their mentor-relationships with the mentees and are on-going with the program.
Conclusions: This Comprehensive Program can be used as a model for the development of bereavement programs in other Pakistani institutes to aid bereaved parents overall, leading to enhanced awareness of grief, parental grief and support systems.

EP477 / #1838

Topic: *AS05.p Supportive Care and Palliative Care*

RESULT OF THE IMPLEMENTATION OF A PEDIATRIC EARLY WARNING SYSTEM (PEWS) IN A HEMATO-ONCOLOGY HOSPITALIZATION AREA IN MEXICO.

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Background and Aims: Pediatric Early Warning Systems (PEWS) are clinical assessment tools that use patient vital signs and symptoms to detect and respond to clinical deterioration events (CDE). Many hospital settings in developing countries, such as Mexico, lack systems for the early identification of cancer patients at risk of clinical deterioration. Objective: Show results after implementing a modified PEWS (EVAT) in the Pediatric Hemato-Oncology area at the Hospital para el Niño de Toluca IMIEM.
Methods: A modified PEWS was implemented in July 2020 in the Pediatric Hemato-Oncology area at the Hospital para el Niño de Toluca IMIEM. In addition, a retrospective cohort was used to evaluate indicators of clinical deterioration in the previous year (2019) and in the following year (2021) the implementation of PEWS.
Results: Before implementing the modified PEWS, 32 EDCs with a mean of 20.4 days of hospitalization were recorded, and in the subsequent period, 28 EDCs and a mean of 24.03 days were observed. When comparing the periods, a 46% reduction in mortality was observed. In addition, the rate of clinical deterioration events decreased after implementing the modified PEWS (1.69 vs 1.46 per 1,000 inpatient days). A 3.6% increase in total hospital patient-days was observed; however, PICU (Pediatric Intensive Care Unit) days of stay decreased from 5.7 to 4.6.
Conclusions: The implementation of PEWS is an effective tool for early identification of clinical deterioration of patients during hospitalization, allowing interventions leading to a decrease in childhood cancer morbidity and mortality. It is expected that the implementation of the modified PEWS will grow over time, with multidisciplinary collaboration in order to be integrated into the quality improvement strategy of hospital care.

EP478 / #1790

Topic: *AS05.p Supportive Care and Palliative Care*

INTERNAL EVALUATION OF RISK STRATIFICATION TOOL USING SERIAL PROCALCITONIN AND CLINICAL RISK FACTORS IN PEDIATRIC FEBRILE NEUTROPENIA: NON-INTERVENTIONAL, SINGLE INSTITUTION EXPERIENCE PRIOR TO CLINICAL IMPLEMENTATION

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Background and Aims: Risk stratification of pediatric febrile neutropenia (FN) is an established concept, yet clinical decision rules (CDR) tools misclassify up to 5% of clinical standard-risk (CSR) episodes with severe outcomes. The clinical discriminatory performance of a CDR observed in one region cannot be inferred to a different region and patient population. The internal evaluation of a CDR before implementation has not been well-described.
Methods: This non interventional cohort study of FN episodes evaluated a CDR alone then prospectively with serial procalcitonin before implementation. The study decision rules (SDR) incorporated serial procalcitonin with a modified, more restrictive CDR (Alexander, et al.) recommended by the Children's Oncology Group. Median time from fever onset for each procalcitonin value was 2 and 16 hours, respectively. The study standard-risk (SSR) group met CSR criteria with serial procalcitonin <0.4 ng/mL. The study high-risk (SHR) group met clinical high-risk (CHR) criteria or CSR with a procalcitonin ≥0.4 ng/mL. Severe events were defined as blood stream infection (BSI), intensive care unit (ICU) admission, or death. Descriptive and bivariate statistics compared the groups and outcomes.
Results: In 608 FN episodes, the CDR alone identified 39.1% (238/608) CSR episodes; 5.9% (14/238) had severe events. Prospectively using the SDR, the SHR group included 76.6% (92/120) of episodes; severe events occurred in 20% (3/15) of CSR episodes included in the SHR group due to elevated procalcitonin ≥0.4 ng/mL. The SHR group had significantly more BSI [21.7% (20/92) vs. 0% (0/28); P= 0.007] and ICU admissions [13% (12/92) vs. 3.6% (1/28); P= 0.158]. This group also had significantly fewer short hospital stays < 3 days [17.4% (16/92) vs. 60.7% (17/28); P= <0.001].
Conclusions: The SDR with serial procalcitonin aided in identifying severe events in CSR episodes, but analysis was limited. Institutions may consider similar internal evaluation methodology before FN episode risk stratification.

EP479 / #855

Topic: *AS05.p Supportive Care and Palliative Care*

PREVALENCE AND OUTCOMES OF CARBAPENEM RESISTANT BLOODSTREAM INFECTION IN CHILDREN WITH CANCER

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Background and Aims: Carbapenem-resistant (CR) infections cause major morbidity and mortality.Data on CR infections in children with cancer are scarce,especially from developing world.The aim of this study was to evaluate characteristics and outcomes of bacteremia with CR organisms (CRO) compared to bacteremia with Carbapenem sensitive organisms (CSO) in children with cancer.
Methods: This retrospective observational study was conducted in a tertiary pediatric oncology centre in South India. Data on all bloodstream infections with Gram negative organisms (CRO and CSO) in children with malignancy aged ≤14 years, from August 2017 to July 2021 were retrieved. The final outcome was determined as survival and all-cause death at 28 days after the date of Bloodstream infection (BSI) onset.
Results: Sixty four patients with gram negative BSI were identified, with 23.4% (n=15) in the Carbapenem Resistant Bloodstream Infection (CR-BSI) group and 76% (n=49) in the CS-BSIgroup. The patients included 39 males (61%) and 25 females (39%), with age ranging from 1 year to 14 years (median age: 6.2 years). The most common underlying disease was hematologic malignancy (92.2%, n=59). Children with CR-BSI had higher incidence of prolonged neutropenia, septic shock, pneumoniae, enterocolitis, altered consciousness and acute renal failure and were associated with 28 day mortality in univariate analysis. The most common carbapenem resistant gram negative bacilli isolates were Klebsiella species (47%) and E.coli (33%).All carbapenem resistant isolates were sensitive to colistin and 33% were sensitive to Tigecycline. The case-fatality rate was 14% (9/64) in our cohort. The overall 28 days mortality was significantly higher in patients with CR-BSI than in those with CS-BSI (28-day mortality: 43.8% vs. 4.2%, P = 0.001).
Conclusions: Bacteremia with CRO has higher mortality in children with cancer. Prolonged neutropenia, pneumoniae, septic shock, enterocolitis, acute renal failure and altered consciousness were predictors of 28-day mortality in carbapenem resistant septicemia.

EP480 / #1478

Topic: *AS05.p Supportive Care and Palliative Care*

BASELINE ASSESSMENT FOR FACILITY READINESS FOR PEDIATRIC CANCER SHARED-CARE SERVICES IN GREATER KUMASI, GHANA

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Background and Aims: Experts generally recommend patient/family-centered care for pediatric cancer treatment in centers with suitable facilities, specialized skills, and multidisciplinary team capacity. In Ghana access to comprehensive treatment centers is limited. Decentralizing some aspects of care may improve the quality of care. A collaborative project by the Komfo Anokye Teaching Hospital, KATH, and the City Cancer Challenge, C/CAN implemented in February 2022 aimed to train hospital staff within Greater Kumasi on pediatric cancer early warning signs and referral. We aimed to assess the personnel, capabilities, and facilities available to provide pediatric cancer shared-care services among participating hospitals.
Methods: We conducted a cross-sectional survey among hospital managers, HM and healthcare providers, HCP using a structured questionnaire including a 5-point Likert scale rating by HCPs on their hospitals' readiness. Data were analyzed with Microsoft Excel.
Results: There were 31 HMs and 63 HCPs from 17 hospitals including 1 Tertiary; 1 Regional; 5 Private; and 10 Secondary (4 Quasi-Government and 6 District). All hospitals had dedicated pediatric wards. Most hospitals had on-site blood banks 15/17(88%); Ultrasound 13/17(76%); Automated Full Blood Count Analyser 12/17(71%); Blood Chemistry Analyser 10/17(59%); and X-ray services 10/17(59%). No hospital had Pediatric Intensive Care facilities, while 16/17(94%) had pharmacists and laboratory scientists, 13/17(76%) hospitals had pediatricians and surgeons. Only 2 hospitals had any palliative care services. Although 10/17(59%) could dispense parenteral morphine, only 7/17(41%) dispensed oral morphine. Among the 63 HCP trainees, at least 43(68%) and 23(37%) agreed that their hospitals could provide "some basic aspects of pediatric cancer care" and "palliative and end-of-life care respectively, while 39(62%) and 46(73%) agreed to being "highly confident in identifying a child with suspected cancer" and providing "initial care for children receiving chemotherapy with fever or intercurrent illness" respectively.
Conclusions: Participating hospitals within Greater Kumasi demonstrated adequate readiness to provide pediatric cancer shared-care services. Palliative care requires specific attention.

EP481 / #1066

Topic: *AS05.p Supportive Care and Palliative Care*

GRANULOCYTE TRANSFUSIONS AS A LIFESAVING TREATMENT FOR PEDIATRIC PATIENTS WITH NEUTROPENIA AND SEPSIS

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Background and Aims: Severe neutropenic sepsis (SNS) caused by multi-drug resistant (MDR) bacteria is a leading cause of mortality in patients with hemato-lymphoid malignancies and hematopoietic stem cell transplantation (HSCT) recipients. Granulocyte transfusion (GTX) is a therapeutic option for SNS with limited data on its efficacy. Our aim was to study the effectiveness of GTX administered to patients with SNS at our institution.
Methods: Patients who received GTX between April 2017 to March 2022 were included.
Results: Out of the 25 patients who received GTX, 11 were <18 years old. A total of 22 transfusions happened with 9 patients receiving >1 transfusion for the same episode of neutropenia. The median age was 5 years. Male to female ratio was 2.6. Nine patients were undergoing HSCT while two were receiving induction for acute leukemia. Patients were on an average of five anti-microbials, with positive bacterial blood culture (BC) in only 9 patients. Six (54.5%) patients had MDR Klebsiella pneumoniae in BC, one each had Escherichia coli and Pseudomonas aeruginosa and, one patient grew Staphylococcus aureus (methicillin sensitive); the latter had evidence of fungal pneumonia. The mean granulocyte dose was 2.65 x 10^8 neutrophils per kilogram body weight. No patient experienced any transfusion-related adverse effects. Nine patients (81.8%) showed response; 2 patients progressed and died of sepsis. The average time to resolution of fever and stopping of therapeutic anti-microbials from the last GTX was 1.45 and 4.68 days respectively. A paired t-test showed an improved mean WBC count from 65.45/uL before to 963.63/uL 24 hours after the last GTX ($p=0.03$) and C-reactive protein from 21.05 mg/L to 13.16 mg/L ($p=0.0008$).
Conclusions: GTX offers a safe and effective treatment for our patients with SNS, especially in the era of MDR bacterial infections.

EP482 / #153

Topic: *AS05.p Supportive Care and Palliative Care*

RESULTS OF AN EDUCATIONAL COMPONENT OF DECREASING TIME TO THERAPY (DOTT) IN PEDIATRIC CANCER PATIENTS WITH FEBRILE NEUTROPENIA IN PERU

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Background and Aims: In low-and middle-income countries, a limitation for optimal treatment of children with cancer and febrile neutropenia (FN) is the delay in administering the first dose of antibiotics. DoTT is a quality improvement project implemented in Peru and aligned to the WHO Global Initiative of Childhood Cancer
Methods: This study was performed in a Peruvian tertiary care center. We defined TTA as the time elapsed between patient's arrival to ER and administering the first dose of antibiotic. PTA is the time elapsed between the onset of symptoms and arrival to the hospital. The intervention consisted of a synchronous and asynchronous educational course for pediatricians and pediatric residents on managing FN in children with cancer. We compared the TTA between 22 patients admitted from October to November 2020 (after educational intervention) and baseline data of 99 patients admitted from 2020 January to 2021 August (before intervention).
Results: The median age was 5 years, 55 patients were female and 66 were male. 104/121 patients had leukemia, and 17/121 patients had solid malignant tumors. No patients required admission to ICU or died of sepsis in the pre-intervention group, in the post-intervention group one patient required admission to ICU and one patient died of sepsis. In the pre-intervention group (97 patients), the median TTA was 171 minutes (IQR: 102–293), and in the post-intervention group, the median TTA was 60 minutes (IQR: 35–73). Early results indicate a statistically significant decrease in the TTA (p=0.001). A long PTA was observed in both groups (before intervention, median= 1483 minutes) and (post-intervention, median=1290 minutes) (p=0.06).
Conclusions: This study suggests the potential impact of an educational intervention in pediatric health care professionals to decrease the TTA in pediatric patients with cancer and FN. The PTA was very long in both groups demonstrating the need for an additional intervention to improve these results.

EP483 / #1711

Topic: *AS05.p Supportive Care and Palliative Care*

CONCORDANCE IN SYMPTOM REPORTS AMONG YOUTH WITH ADVANCED CANCER

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Background and Aims: Youth with pediatric cancer may have high symptom burden, and pain is nearly universal near end-of-life. However, few studies have examined child-report of symptoms and distress relative to other reports. Thus, we examined concordance between child- and proxy-report of the three most common symptoms in the context of advanced cancer.
Methods: As part of a longitudinal study, families of youth with advanced cancer (physician estimated prognosis of <60%, relapse, or refractory disease), ages 5-25, were recruited from a large U.S. children's hospital. Parents and youth completed the Memorial Symptom Assessment Scale (MSAS). Average symptom scores based on child-report (n=41), mother-report (n=55), and father-report (n=30) were compared using paired and independent samples t-tests. Pearson correlations explored associations between symptom scores.
Results: Youth reported fatigue (73%), drowsiness (73%), and pain (66%) as their most common symptoms. Mothers reported their child's top symptoms were fatigue (73%), lack of appetite (71%), and drowsiness (65%), while fathers reported pain (80%), nausea (67%), and fatigue (66%). The mean child-reported MSAS was 1.93 (SD=0.46), mother-reported MSAS was 1.98 (SD=0.46), and father-reported MSAS was 1.95 (SD=0.51). These scores were correlated between mother-child, $r(29)=0.58$, $p<0.001$; father-child, $r(17)=0.63$, $p=0.01$; and mother-father reports, $r(20)=0.73$, $p<0.001$. Symptom scores did not differ across mother-child, $t(28)=-1.27$, $p=0.92$; father-child, $t(16)=-0.11$, $p=0.21$; and mother-father reports, $t(19)=0.84$, $p=0.41$. Mothers reported higher symptom burden in girls than boys, $t(53)=-2.44$, $p=0.01$; Child age was unrelated to symptom scores ($p's>0.05$).
Conclusions: Although the most frequent symptoms varied by informant, fatigue, drowsiness, and pain were common among youth with advanced cancer, and there was general agreement on overall symptom burden. Future work should examine other factors associated with symptom communication and concordance, as well as ways to improve symptom management. Clinicians should solicit multiple perspectives of the symptom experience for optimal care.

EP484 / #433

Topic: *AS05.p Supportive Care and Palliative Care*

PAEDIATRIC PALLIATIVE ONCOLOGY ACROSS EUROPE: A CROSS-SECTIONAL SURVEY

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Background and Aims: Despite substantial improvements in 5-year survival rates, almost every fifth child diagnosed with cancer dies. It is increasingly recognized that palliative care (PC) should be an integral part of comprehensive paediatric oncology care. The availability of PC services in paediatric oncology settings is currently unknown. Aim: To describe the availability of PC services in paediatric oncology centres across Europe.
Methods: We contacted paediatric oncology centres across Europe and invited one health care professional per centre with experience in PC to complete an online questionnaire.
Results: We included 151 paediatric oncology centres from 27 European countries in our analyses. Most centres (97.3%) offer either general (32%) or specialized paediatric palliative care (PPC) services (65.3%). The majority have multidisciplinary care teams (79.5%) and offer PC at home (69.5%). Current service capacity is reported lower than demand in 39.1% centres. In most centres (82.1%) PC consultation is initiated in case of a refractory neoplasm, or high symptom burden (60.3%). Very few centres (7.3%) offer PC consultation at the time of a new cancer diagnosis. Bereavement services including phone calls by team members after the child's death (68.2%), on-site psychological counselling (62.9%) and medical debriefing (61.6%) were reported to be an integral part of PC.
Conclusions: Although caution is warranted due to potential self-report bias, results indicate that while PPC are available in most paediatric oncology centres, many cannot completely fulfil the demand. Distinguishing between common paediatric oncology services and more individualized PPC ones is difficult. Reducing suffering throughout the disease process should remain the standard of care for all children with cancer regardless of disease outcome. Identification of children and families with the highest symptom burden and early referral to PC could help meet this standard. Funding: SSPH+ GlobalP3PH Programme (Marie Curie Grant Agreement Number 801076), Swiss Cancer League: KFS-4995-02-2020.

EP485 / #646

Topic: *AS05.p Supportive Care and Palliative Care*

THE MANAGEMENT OF PAIN FOR CHILDREN HOSPITALISED DURING HAEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background and Aims: Children hospitalised following Haematopoietic Stem Cell Transplantation (HSCT) experience complex and prolonged pain in response to the intensity of this treatment. The aim of this study is to describe how pain is managed for children during HSCT therapy and how contextual factors related to the clinical environment influenced the pain management practices of healthcare providers and parents.
Methods: A longitudinal qualitative study was conducted and involved naturalistic observations of pain-related care provided to children (n=29) during HSCT therapy by their healthcare providers (n=10). Semi-structured interviews were conducted with healthcare providers (n=14) and parents (n=10) participated in semi-structured interviews at two timepoints following transplantation (30 and 90 days).
Results: The effectiveness of pain management interventions was hindered by the multifactorial nature of pain children experienced and a lack of evidence-based guidelines for the sustained, and often long-term, administration of opioids and adjuvant medications with analgesic properties. Misconceptions were demonstrated about escalating pain management according to pain severity and differentiating between opioid tolerance and addiction. Parents had an active role to play in the management of pain for children, especially the provision of non-pharmacological interventions. Collaboration with external pain services and the impact of caring for children in protective isolation delayed the timely management of pain.
Conclusions: There is a pressing need for the creation of evidence-based supportive care guidelines for the management of pain post-transplantation to optimise children’s relief from pain. If parents and children are to be involved in how pain is managed, then greater efforts need to be directed towards building their capacity to make informed decisions.

EP486 / #498

Topic: *AS05.p Supportive Care and Palliative Care*

CARBAPENEM RESISTANT ENTEROCOCCI (CRE): AN IMPEDIMENT IN THE CARE OF PAEDIATRIC HEMATOLOGY ONCOLOGY AND HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) RECIPIENTS.

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Background and Aims: Gram-negative bacteria including CRE, are an important cause of life-threatening infections in children with haematological malignancies and HSCT recipients.The prevalence of CRE related infections is increasing worldwide.This study assesses prevalence and outcomes of CRE septicaemia in children undergoing treatment in our unit.
Methods: A retrospective observational study was conducted in the department of Paediatric Haematology Oncology & HSCT at SRCC Children's Hospital, managed by Narayana Health. Stool samples for CRE screening were sent for all high risk patients [Pre HSCT, high risk Acute Leukaemia(AL), AL in relapse]. The samples were processed on MacConkey's agar as per standard microbiological methods. Identification of organisms and antimicrobial susceptibility (AS) testing were performed as per CLSI guidelines. AS was used as a guideline to start antibiotics during febrile neutropenic (FN) episodes.
Results: A total of 422 stool samples from 126 patients (M: F- 76:50), mean age 7.68 years (2-17years) were sent from January 2019 to December 2021. Stool samples were positive for CRE in 57/126(45.2%). Both stool and blood cultures were positive for CRE in 24/57(42.1%) children during febrile neutropenia suggesting translocation from gut. There were 19(79.1%) deaths in the CRE- positive group- 7 patients had CRE positivity in both stool and blood (6-post HSCT and 1-ALL). 10 deaths were non CRE related infectious reasons, mainly fungal/Methicillin Resistant Staphylococcus Aureus(MRSA) and 2 were disease related. The mean duration after initiation of antibiotics till death in CRE positive blood cultures was 46 hours (SD ± 25.5 hours). There were 18 deaths in the CRE- negative group- 6 deaths were due to sepsis and 12 were disease related conditions, usually relapse.
Conclusions: CRE infections are potentially fatal especially in post HSCT conditions. Those with both stool and blood cultures positive are at a higher risk. Aggressive escalation to higher antibiotics and other supportive measures may help to decrease mortality.

EP487 / #1537

Topic: *AS05.p Supportive Care and Palliative Care*

EFFECT OF BUFFY COAT DERIVED GRANULOCYTE TRANSFUSIONS IN CHILDREN WITH POST CHEMOTHERAPY HIGH RISK FEBRILE NEUTROPENIA IN DECREASING MORTALITY –AN OPEN LABEL RANDOMISED CONTROL TRIAL

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Background and Aims: Background: Granulocyte transfusion (GT) in febrile neutropenia (FN) may help in marrow recovery and reduce morbidity and mortality by replenishing the deficient granulocytes to combat infection. Aims: To study the effect of addition of irradiated buffy coat derived GT to the standard of care in reducing the 28d mortality in children with chemotherapy associated high risk FN.
Methods: Design: Randomised Control trial Duration: Jul'20- Mar'22 Setting: Tertiary care teaching institute in northern India Participants: Children ≥18y with malignancy and chemotherapy induced high risk FN. Palliative care, hematopoietic stem cell transplantation, recovery phase and non-availability of group specific granulocyte, were exclusions. Interventions: Irradiated buffy coat derived GT at 10ml/kg every 48h till afebrile for >24h and Absolute neutrophil count(ANC)≥500/mm^3. Standard therapy(ST) included antimicrobials, blood components and G-CSF. Outcome measures: 28d mortality, duration of hospital stay, antibiotic days, day of defervescence and adverse events
Results: Sixty children were enrolled (GT, n=30; ST, n=30). Demographic characteristics and baseline investigations were comparable. There was no significant difference in mortality [8(26.7%) v/s 2(6.7%); p=0.08], duration of hospital stay [11d(8-15) v/s 9d(6-14.2); p=0.51] and antibiotic days [23d(15.7-30.5) v/s 19d(12.7-28); p=0.18] between the 2 groups. Total febrile period before admission [3d(1-5.25) v/s 3d(1-7)] and day of defervescence were similar [8d(5-12) v/s 8d(5-11), p=0.86]. However, days to achieve ANC >500/mm3 was significantly lower in the GT arm [4.5d(3-6.5) v/s 8d(4-11); p=0.01]. Microbiologically documented infection [9(30%) v/s 7(23%); p=0.77], radiologically defined pneumonia [10(33%) in each], volume overload (4(13.3%) v/s0; p=0.11] and Transfusion related adverse events [1(3.3%) v/s 0, p=1] did not differ significantly.
Conclusions: Granulocyte transfusion helped in early neutrophil recovery but survival benefit could not be attained. Lesser efficacy of GT may be secondary to prolonged febrile period prior to admission. Buffy coat derived GT is safe to administer in children with high risk FN.

EP488 / #875

Topic: *AS05.p Supportive Care and Palliative Care*

PERFORMANCE OF THE GOLDEN HOUR PROTOCOL IN FEBRILE NEUTROPENIC PATIENTS AS AN INDICATOR OF THE QUALITY OF CARE; CHANGE AND ADAPTATION DURING THE COVID-19 PANDEMIC.

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Background and Aims: The COVID-19 pandemic posed extraordinary challenges to emergency departments (ED) worldwide. These challenges could have jeopardized previously developed quality indicators, mainly time-dependent outcomes. This study aimed to analyze whether pandemic-related time constraints and the use of personal protective equipment (PPE) affected golden hour adherence for febrile neutropenic patients.
Methods: In 2019, we implemented a quality improvement methodology to improve outcomes in pediatric oncology patients with febrile neutropenia. This methodology fosters multidisciplinary collaboration that enhances results and increases staff awareness of the importance of this protocol to patient prognosis. For this analysis, we included all febrile neutropenic patients treated in the ED from June 2020 to December 2021 to compare the outcomes of patients who required wearing PPE due to suspected covid-19 and those who did not require the use of special equipment.
Results: The study population consisted of 92 febrile neutropenic patients. Of these, 21 patients (22.8%) came from their homes and were treated as suspects of COVID-19; 71 patients (77.2%) came from the hospital's hospice and were not suspected due to the installed isolation. Global adherence was reported in 91.3% (84). The adherence in suspected patients was 85.7% (18) and 92.9% (66) in the control group. The mean time from triage to antibiotic was 49.9 min and 42.1 min, respectively. In patients who had a delayed antibiotic administration time in the suspicious group (3 patients), the leading cause for delay was difficult intravenous access.
Conclusions: Despite challenges and time constraints with suspected COVID-19 patients, global adherence to the golden hour was maintained in our patients. The quality improvement methodology helped create lasting staff awareness and collaboration on the importance of the protocol, and even in difficult times, this made a difference for our patients.

EP489 / #413

Topic: *AS05.p Supportive Care and Palliative Care*

MICRONUTRITION EVALUATION AT TIME OF A PEDIATRIC CANCER DIAGNOSIS AND DURING CHEMOTHERAPY

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Background and Aims: Many children with cancer undergoing chemotherapy experience adverse events that could be exacerbated due to micro-nutrient abnormalities. We conducted a prospective pilot study to evaluate micro-nutrient and body mass at diagnosis and after 6 months of chemotherapy.
Methods: Informed consent/assent were obtained. Height and weight were measured and body mass index (BMI) and corresponding Z-scores were calculated. Blood samples were collected as part of routine blood work and analyzed for vitamins A, D, E and trace elements copper (Cu), selenium (Se) and zinc (Zn).
Results: Twenty-nine patients (16 male, 55%) with a median (range) age of 8.2 (1.7-17.6) years participated. Diagnoses included AML (n=1), Alveolar Rhabdomyosarcoma (n=1), Astrocytoma (n=1), B-Cell ALL (n=7), Burkitt Lymphoma (n=3), Ependymoma (n=1), Epithelioid Sarcoma (n=1), Ewing Sarcoma (n=4), Germinoma (n=1), Hodgkin Lymphoma (n=1), LCH (n=1), Medulloblastoma (n=2), Neuroblastoma (n=2), Osteosarcoma (n=1), T-Cell ALL (n=1), and Wilms Tumour (n=1). The median BMI was 17.2 (14.4-26.4) kg/m^2 and 16.6 (14.0-27.7) kg/m^2 at diagnosis and after 6 months of chemotherapy, respectively. Fifty-nine and 52% of patients had BMI Z-scores of -1 or lower or +1 or greater at diagnosis and at 6 months. Micronutrient deficiencies were found in 26/29 (90%) patients. Vitamins A, D, and E were low in 6 (21%), 13 (45%) and 0 patients at diagnosis and in 6 (21%), 11 (38%) and 1 (3%) patients at 6 months. Cu, Se and Zn were abnormal in 4 (14%), 5 (17%) and 13 (45%) patients at diagnosis and in 2 (7%), 8 (28%) and 15 (52%) patients at 6 months. Albumin was abnormal in 6/16 (38%) patients at diagnosis and 4/7 (57%) of patients at 6 months.
Conclusions: These results suggest that micro-nutrient abnormalities are common throughout chemotherapy. This provides insight on the potential worsening of short and long-term adverse events associated with chemotherapy.

EP490 / #1023

Topic: *AS05.p Supportive Care and Palliative Care*

THE IMPACT OF FERTILITY GUIDELINES AND EDUCATION ON THE RATE OF PRE-THERAPY FERTILITY RISK DISCUSSIONS IN PEDIATRIC ONCOLOGY: A RETROSPECTIVE COHORT STUDY

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Background and Aims: Pediatric cancer patients undergoing treatment are often at risk for infertility or subfertility. Healthcare providers do not consistently deliver fertility information prior to therapy. Our objective was to assess if development and implementation of a fertility guideline improves the frequency of pre-treatment fertility discussions with pediatric cancer families.
Methods: This retrospective cohort study analyzed all consecutively eligible patients over two time periods. The pre-guideline time period was 18 months prior to implementation and the post-guideline time period was 12 months after implementation. Guideline implementation included education with oncology staff. Eligible patients were < 19 years old at cancer diagnosis and received chemotherapy and/or radiation therapy. Pre-guideline rate of pre-treatment fertility discussions was estimated at 40%. An estimated 40 participants in the post-guideline cohort can detect a 30% increase in fertility discussions with β 0.8 and α 0.05. Exploratory analysis assessed factors associated with fertility discussions.
Results: Ninety-five patients were included. Fifty-seven percent were < 10, 26% were 10-15, and 17% were ≥ 16 years old. Pre- and post-guideline cohorts are compared in table 1. In the pre-guideline cohort, 41% of patients had a discussion about risks of fertility impairment documented, while post-guideline cohort had 49% documented (p = 0.531). Exploratory assessment of combined cohorts found males (OR 0.2.7, 95% CI 0.1.2-6.3-0.87) and patients ≥ 10 years old (OR 5.0, CI 2.1-12.1) were more likely to receive fertility discussions prior to therapy. Radiation and cancer type did not influence whether fertility discussions occurred.
Conclusions: Implementation of a fertility guideline did not increase fertility discussions, and less than half of patients had a documented fertility discussions. Male patients and age ≥ 10 years old were more likely to have documented fertility discussions. Effective strategies are needed to improve the rate of discussions regarding fertility risk to ensure families receive this information prior to therapy.

EP491 / #1556

Topic: *AS05.p Supportive Care and Palliative Care*

TO PREMEDICATE OR NOT? A LOOK AT PREMEDICATIONS FOR BLOOD PRODUCT TRANSFUSIONS AT MSK KIDS

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Background and Aims: Blood product transfusions are given often in pediatric oncology patients. Transfusion-related reactions, though uncommon, range in severity from mild, allergic to severe, anaphylactic. Though lacking robust evidence, many patients receive prophylactic premedications to prevent transfusion reactions, leading to practice variability, unnecessary treatments, and additional costs. We analyzed blood product premedication practices at MSK Kids.
Methods: Our retrospective, single-institution review included all pediatric patients who received a blood product transfusion at MSK Kids from January to April 2021, excluding patients with a complex transfusion reaction history. Data extracted included: demographics, transfusion type (platelet and/or red blood cell (RBC)), reaction history, premedication(s) administered (acetaminophen, antihistamine, and/or hydrocortisone), and signs/symptoms of reactions.
Results: 112/116 patients who received a blood product transfusion met inclusion criteria. Median age at transfusion was 8.2 years (range 0.6 – 17.8). A total of 603 transfusions were given with a median of 3 transfusions per patient (IQR 2-7). This included 315 (52.2%) platelets and 288 (47.7%) RBCs. Premedications were given for 434 (72.0%) transfusions: acetaminophen monotherapy (n=77), diphenhydramine monotherapy (n=11), or combination therapy (n=346). Of the 34 patients with a transfusion reaction history, 212/217 (97.7%) of their transfusions were premedicated. 78 patients had no history of a transfusion reaction, yet 222/386 (57.5%) of their transfusions were premedicated. 19/603 (3.2%) transfusions resulted in a reaction including: rash/pruritus (n=17), fever (n=6), respiratory symptoms (n=3), and/or hypotension (n=1). No transfusions caused anaphylaxis. There was no difference in the incidence of transfusion reactions between premedicated (3.2%) and not premedicated patients (3.0%). No severe sequelae or intensive care unit admissions occurred.
Conclusions: Our cohort experienced a low incidence of transfusion reactions. Most patients received premedication(s), despite no history of transfusion reactions, with no clear benefit. An evidence-based algorithm and provider education are needed for blood product transfusion premedication in pediatric oncology patients.

EP492 / #695

Topic: *AS05.p Supportive Care and Palliative Care*

PEDIATRIC ONCOLOGY SUPPORTIVE CARE IN INDIA DURING PANDEMIC TIMES: WHAT WE LIVED WITH AND WHAT WE LEARNT?

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Background and Aims: We conducted a survey among practicing pediatric oncologists to assess the modifications made in supportive-care during the pandemic, specifically if any of those were safe and effective enough to be practice-changing.
Methods: A survey-questionnaire with 27 questions was circulated through the emailing list and WhatsApp/Telegram groups of Indian pediatric oncology group in January 2022. Responses were accepted till 31st March 2022. The questions focused on disruptions in continuation of patient-care over past two years, strategies to minimize the impact of such disruptions, and the potential, if any, for incorporating these modifications into standard practice.
Results: Of seventy-one responses from approximately 250 active members contacted, 39(55%) were from public hospitals and 23(32%) from centers seeing >200 new cases/year. Decline in new patient registration, funding shortage, increase in treatment abandonment and delay in maintenance/follow-up visits were reported by 7(9.8%), 37(52%),44 (62%), and 52(73%). In (25)35.2% centers, scarcity of ICU beds during COVID waves resulted in higher non-COVID mortality/morbidity. Several centers reduced transfusion cut-offs (23,33%), used granulocyte stimulating factors more often (21, 30%), increased use of oral antibiotics in low-risk febrile neutropenia(FN) (29,40%), and stopped intravenous antibiotics earlier (11,15%). Strategies to curtail abandonment and drug default included tracking phone calls (50,72%), couriering medicines to patients' homes (27,39%) and teleconsultation (43,62%). Post–treatment follow-up frequency and investigations were reduced in 50(70%) centers and 54(76%) started teleconsultations; respondents considered these strategies likely to be incorporated into routine practice. While 35(49%) respondents supported increased use of outpatient chemotherapy, most(70,99%) respondents chose to revert to pre-pandemic policies for transfusion and FN. Establishment of sustainable shared-care networks was considered a priority by 44(62%).
Conclusions: Pediatric oncology services were remarkably compromised during the pandemic. Of the many adaptations made to tackle the pandemic conditions, virtual follow-up of selected patients and rationalizing post-treatment follow-up and investigations are likely to continue into the post-pandemic period.

EP493 / #1658

Topic: *AS05.p Supportive Care and Palliative Care*

DEVELOPMENT OF A FACILITY REPORT HIGHLIGHTING STRENGTHS AND LIMITATIONS IN PEDIATRIC ONCO-CRITICAL CARE SERVICES IDENTIFIED USING THE PROACTIVE ASSESSMENT

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Background and Aims: PROACTIVE is an electronic assessment tool arranged into 8 modules, each divided into 2 surveys for intensivists and oncologists managing critically ill pediatric hematology-oncology (PHO) patients. The tool was designed to evaluate strengths and limitations in pediatric oncology critical care (POCC) services in resource-limited settings. Our objective is to describe the development of a center-specific report to facilitate interpretation of PROACTIVE results.
Methods: The PROACTIVE pilot (January 2021 – June 2021) was conducted in 10 centers from 10 different countries with a wide range of POCC services. Surveys were administered in English using REDCap. Collected data were used to create center-specific score-based and descriptive reports highlighting areas of strengths and opportunities for improvement in POCC services. The clarity, user-friendliness, and format of the reports were assessed in 2 focus group meetings with pilot center PROACTIVE leads. Adjustments were made to the reports based on feedback to improve the presentation of PROACTIVE results.
Results: A total of 20 surveys from 10 centers were analyzed and used to develop the PROACTIVE reports. Recommended adjustments to the reports resulted in a combined score for each module, including the results from both the intensivist and oncologists' surveys. A separate area highlights the top 5-highest and lowest scored areas to allow easier interpretation of a center's strengths and weaknesses. In focus groups, PROACTIVE reports were described as practical and were used by several pilot centers to advocate for additional resources to improve intensive care and POCC capacity.
Conclusions: Center-specific reports facilitated interpretation of PROACTIVE results and allowed organizations to prioritize multiple improvement opportunities and benchmark their performance against others. Global implementation and use of PROACTIVE reports highlighting challenges in POCC services can help improve the quality of care and outcomes for critically ill PHO patients in resource-limited settings.

EP494 / #1551

Topic: *AS05.p Supportive Care and Palliative Care*

FACTORS CONSIDERED BY PEDIATRIC ONCOLOGISTS GLOBALLY WHEN APPROACHING TREATMENT DECISION-MAKING AT DIAGNOSIS

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Background and Aims: Global childhood cancer outcomes are inextricably linked with available local healthcare infrastructure and cultural environments. Yet existing guidelines and resources inconsistently account for specific contextual factors that physicians consider when making decisions about cancer-directed therapy. Importantly, treatment misaligned with local capacity can lead to patient harm and compromise health system efficiency and effectiveness. In this study, we sought to understand factors considered by physicians in low- and middle-income countries (LMICs) when deciding to offer curative treatment versus non-curative treatment to children presenting with advanced or incurable cancer at the time of diagnosis.
Methods: To identify and define factors impacting decision-making, we used a community-engaged research approach, inviting a global panel of pediatric oncology experts to participate in sequential focus groups. In two initial focus groups, physicians were asked to list factors related to the disease, the decision-maker, and other contextual factors. Content analysis of focus group data informed the development of a visual model and semi-structured interview guide, which the global panel reviewed together in the subsequent two focus group sessions.
Results: 11 pediatric oncologists representing all WHO regions participated, comprising 11-21+ years of medical experience. Participants identified a broad range of factors influencing decision-making, including variables unique to LMIC settings such as ability to access diagnostic tools and interventions, unclear referral pathways, and effects of war or political instability. Physicians often defaulted to offering curative therapy even when they recognized that intensive treatment would result in excess toxicities and poor outcomes. Member-checking yielded consensus development of a semi-structured interview guide to further probe these critical topics with LMIC physicians in future work.
Conclusions: Physicians in LMICs face unique factors and challenges that influence treatment decision-making. Treatment guidelines should account for these factors and offer direction for treatment pathways supporting curative and non-curative therapies.

EP495 / #2043

Topic: *AS05.p Supportive Care and Palliative Care*

FACTORS INFLUENCING PEDIATRIC ONCOLOGISTS' DECISION-MAKING WHEN BALANCING CURATIVE AND NON-CURATIVE TREATMENT OPTIONS AT DIAGNOSIS IN LOW- AND MIDDLE-INCOME COUNTRIES (LMICS)

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Background and Aims: Global childhood cancer outcomes are inextricably linked to local and regional economic and social contexts, including available healthcare infrastructure and psychosocial support. Treatment misaligned with local capacity can lead to patient harm and compromise health system efficiency and effectiveness. In this study, we sought to understand factors considered by physicians in LMICs when deciding how to balance curative and non-curative treatment options for children presenting with advanced or incurable cancer at the time of diagnosis.

Methods: To identify and define factors impacting decision-making, we used a community-engaged research approach, inviting a global panel of pediatric oncology experts to participate in four sequential focus groups. In two initial focus groups, participants were asked to identify factors related to the disease, the decision-maker, and additional contextual factors impacting care. Content analysis of focus group data informed the development of a visual model and semi-structured interview guide to further probe these topics with LMIC physicians, which the working group reviewed together in the subsequent two focus group sessions.

Results: Eleven pediatric oncologists representing all WHO regions participated. Participants identified numerous factors influencing decision-making, confirmed these major categories, and identified numerous additional factors such as the ability to access diagnostic tools and treatment interventions, lack of established referral pathways, and financial compromises to treat their child at expense of the health of the family. Participants recognized that intensive treatment often resulted in excess toxicities and poor outcomes, yet they defaulted to offering curative therapy due to perceived lack of alternatives and lack of direction from available guidelines. Member-checking with the working group yielded consensus on semi-structured interview prompts for future work.

Conclusions: Physicians in LMICs face unique factors and challenges that influence treatment decision-making. Findings from future interviews may inform development of educational interventions and shape guideline development to better support oncologist treatment decision-making in LMICs.

EP496 / #1705

Topic: *AS05.p Supportive Care and Palliative Care*

PROSPECTIVE EVALUATION OF OTOTOXICTY DURING PLATINUM CHEMOTHERAPY AMONG PAEDIATRIC PATIENTS.

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Background and Aims: The platinum chemotherapy agents, cisplatin and carboplatin are widely used in the treatment of paediatric cancers. Cisplatin causes hearing loss in at least 60% of paediatric patients. In a young child, this will have a detrimental effect on speech, language, and social development. The study aims to identify the risk of ototoxicity associated with platinum compounds and to assess the risk factors associated with them.
Methods: Prospective hospital based observational study of 22 patients who received platinum based chemotherapy for newly diagnosed malignancies between 01.03.2020 and 31.08.2021. Children were assessed with audiometry at baseline and middle of chemotherapy if feasible and after completion of treatment. Cases with normal baseline hearing were included in the study. Ototoxicity was diagnosed and graded according to SIOP- Boston Ototoxicity Scale.
Results: Twenty two cases were included in the study. Seventeen children received cisplatin (77.3%) while 4 received carboplatin (18.2%) and one (4.5%) received both. Median cumulative dose of cisplatin was 540 mg/m^2 while median cumulative carboplatin dose was 2400 mg/m^2. Eighteen cases (81.8%) had ototoxicity [Grade 1: n= 3 (16.6%), Grade 2: n=6 (33.3%), Grade 3: n= 5(27.2%), Grade 4: n= 4(22.2%)]. All 9 children who received radiation to head developed ototoxicity and all children with acute malnutrition developed ototoxicity, however, these associations were not significant. Univariate binary logistic regression revealed significant association of ototoxicity with cumulative cisplatin dose, cisplatin dose per cycle, cumulative cisplatin dose > 400 mg/m^2. Carboplatin, use of vinca alkaloids, hypomagnesemia were not associated with ototoxicity.
Conclusions: Cumulative cisplatin dose, especially dose >400 mg/m^2 is associated with ototoxicity. Close audiological monitoring of children on cisplatin based chemotherapy is warranted.

EP497 / #1062

Topic: *AS05.p Supportive Care and Palliative Care*

MUSCLE STRENGTH, CARDIORESPIRATORY FITNESS AND PHYSICAL PERFORMANCE IN CHILDREN AND ADOLESCENTS WITH NEWLY DIAGNOSED CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims: Anti-cancer treatment impairs muscle strength, cardiorespiratory fitness, and physical performance in children with cancer throughout the treatment trajectory. However, it is sparsely investigated how early these impairments occur. We aimed to provide an overview of current evidence regarding muscle strength, cardiorespiratory fitness, and physical performance status of children with newly diagnosed cancer compared with healthy controls.
Methods: We performed a systematic search in five scientific databases, for scientific literature published before January 3, 2021. Studies were eligible if they contained objective measures of muscle strength, cardiorespiratory fitness, or physical performance of children and adolescents (age 6-18) diagnosed with cancer within the first 31 days from treatment initiation and reported a comparative analysis to norm-values and/or a study group of healthy sex and aged-matched controls. When possible, random-effects meta-analyses were used to synthesize the results.
Results: The search identified 9,036 unique study references. Five studies; two RCTs, two quasi-experimental, and one cross-sectional study, embodying 330 participants, were included for preliminary analysis. Of these studies, three reported muscle strength, one reported measures of cardiorespiratory fitness, and all reported physical performance. The meta-analysis showed a lower muscle strength within the first 31 days of treatment initiation compared with either healthy controls or reference values (mean difference -2.42 kg [95% CI -3.94 to -0.89]; I^2 = 44%, p = 0.002). All studies reported a reduction in all parameters compared with matched healthy controls, except for two sub-measures of upper body muscle strength and reaction time. Regarding physical performance, studies reported reduced motor development, walking distance, and balance.
Conclusions: This systematic review indicates that the deterioration in cardiorespiratory fitness, muscle strength, and physical performance occurs early and may already be impaired before the clinical diagnosis is given and treatment is initiated. Consequently, physical rehabilitation is needed from treatment initiation to ameliorate further deterioration in general physical performance.

EP498 / #259

Topic: *AS05.p Supportive Care and Palliative Care*

A COLLABORATIVE EDUCATION MODEL FOR ADVANCING NUTRITIONAL CARE IN AFRICA

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Background and Aims: The SIOP Global Health nutrition committee (2017) administered a survey among Pediatric Oncology Units (POUs), located in Africa, to determine the existing nutritional services and unmet needs. The most common reported barrier was a lack of education in nutritional assessment and intervention. A 2022 survey of Ghanaian POUs found that 90% of POUs were merely at levels 1-2 in terms of nutrition capacity. A partnership between World Child Cancer (WCC) and the International Initiative for Nutrition and Paediatrics (IIPAN) aims to increase nutritional knowledge among clinicians caring for children with cancer in Ghana.
Methods: WCC and IIPAN held a five-day nutritional workshop in Accra, Ghana from 7 to 11 March 2022. Attendees included paediatric oncologists, paediatricians, dieticians, nutritionists, nursing staff and WCC personnel. The first three days addressed theory and clinical practice, followed by a two-day practical exercise at Korle Bu Teaching and Greater Accra Regional Hospitals in Accra. A standardised questionnaire was completed by all participants to test pre-training and post-training knowledge.
Results: Seventy-four percent of participants felt they were 'very knowledgeable' after the course; compared to 10% prior and 92% felt they could use the knowledge daily. Participants reported that hospital practical sessions (30%), determining nutritional requirements (23%) and performing anthropometry (18%) were the most beneficial aspects of the training. The mean test grade post-training was 77%. Several barriers were identified that would preclude incorporation into clinical practice namely lack of resources (32%), additional training needs (18%), and non-supporting colleagues (10%). Almost all participants reported they would benefit from longer training, more on-site training, and more opportunities for subsequent/ongoing training.
Conclusions: This workshop successfully improved knowledge about nutrition in pediatric oncology. Future planning with WCC, IIPAN, and SIOP Global Nutrition Committee will involve addressing the barriers to incorporate nutritional assessment and interventions into clinical practice in pediatric oncology units.

EP499 / #361

Topic: *AS05.p Supportive Care and Palliative Care*

IMPACT OF MALNUTRITION ON PHARMACOKINETICS OF CHEMOTHERAPY IN CHILDREN WITH CANCER: A SYSTEMATIC REVIEW

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Background and Aims: The majority of children with cancer in low- and middle-income countries (LMICs) are at risk for severe malnutrition. Malnutrition might affect the pharmacokinetics of chemotherapeutic agents and understanding this impact is crucial to better understand the impact of nutrition on toxicity and survival. Therefore, a systematic review on the effect of malnutrition on pharmacokinetics of chemotherapy in children with cancer was conducted.
Methods: PubMed, Embase and Cochrane were searched in October 2021 to identify eligible studies. Inclusion criteria were studies on chemotherapy pharmacokinetics in children with cancer, assessing the effect of malnutrition referring to undernutrition. Risk of bias assessment was performed using the Quality Assessment Tool for Quantitative Studies. Malnutrition was defined by the World Health Organization (WHO) criteria and the Gomez' classification.
Results: Four eligible studies with a total of 668 children were included, containing 18% (n=121) malnourished children. One study reported a significantly prolonged mean clearance rate and increased logAUC for vincristine among malnourished versus non-malnourished children ($p<0.05$). Clearance rates and volume of distribution of methotrexate, doxorubicin and etoposide even incline to be lower in malnourished children, although not significant.
Conclusions: Decreased clearance rates, increased logAUC, and decreased volume of distribution among children with malnutrition and cancer are suggestive for significant pharmacokinetic alterations of chemotherapy. However, data is scare, groups are small, and 75% of the studies were performed in high-income countries where nutrition status is less compromised compared to LMICs and no children with severe acute malnutrition were included. This systematic review highlights the urge for further pharmacokinetic research among severely malnourished children with cancer in order to ultimately improve their outcome by adapted dosing of anticancer agents.

EP500 / #490

Topic: *AS05.p Supportive Care and Palliative Care*

SATISFACTION WITH TELECONSULTATION DURING THE COVID-19 PANDEMIC

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Background and Aims: The pandemic taught us to manage patients via teleconsultation (TC), previously not a part of routine patient care. This study aimed to assess parental satisfaction with TC services provided during the COVID-19 pandemic.
Methods: A survey questionnaire containing 6 parts with 35 questions in the vernacular was provided to the participants who were families of children diagnosed with cancer from July 2019 to March 2020. The survey took 20-30 minutes to complete.
Results: Eighty three families consisting of 66 patients with haematolymphoid malignancies and 17 with solid tumors (median age: 7.13 [2-14] years), 60 on active treatment and 23 having completed therapy participated. Two-thirds belonged to rural areas and 40% were from the upper-lower socioeconomic strata. Seventy-one percent of the participants did not encounter any difficulty in contacting the doctors, 19% had occasional problems and 10% reported major difficulties in contacting by TC. Most (75/83) families expressed ease in communicating problems by TC. Respondents were satisfied with the time (81/83), explanation (82/83), thoroughness (82/83), and courtesy (78/83) extended to them during TC. The positive impact of TC was: time-saving (93%), cost-saving (87%), decreased physical exertion (82%), and availability of daily access to care providers (63%). Nearly 75% of the respondents concurred to TC being as good as face-to-face consultation and wanted TC to be a part of routine care. Seventy-one (85%) families were very satisfied/satisfied with TC and 13% were somewhat satisfied. Patients off therapy preferred physical visits vis-a-vis those on therapy (p=0.0018). Availability of a local physician and socioeconomic status had no bearing on the satisfaction/continuation of TC (p=0.74 & .09)
Conclusions: Creative adaptation of technology has resulted in revisiting patient care delivery methods during the pandemic. High satisfaction levels (85%) among patients indicate the usefulness of these applications and the feasibility of a hybrid method of care in pediatric oncology.

EP501 / #1408

Topic: *AS05.p Supportive Care and Palliative Care*

NEUTROPENIC ENTEROCOLITIS DURING ACUTE MYELOID LEUKEMIA THERAPY IN CHILDREN

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Background and Aims: Neutropenic Enterocolitis(NE)/Typhlitis is a necrotizing inflammation involving the caecum and the terminal part of ileum having 24%incidence and 44.8%mortality in paediatric Acute Myeloid leukemia(AML). The aim was to study the clinical profile and the treatment outcome of NE during paediatric AML therapy.
Methods: Seventeen newly diagnosed AML children aged 0-14 years were prospectively analyzed between 1st May 2021 and 31st March 2022.NE was defined by the presence of the clinical triad of abdominal pain, fever and neutropenia(Absolute neutrophil count less than 500 /mm3)or imaging signs (thickened bowel wall) plus two of the clinical features. AML treatment consisted of 2 induction courses with Cytosine arabinoside and Daunorubicin and3 consolidation courses with high dose Cytosine arabinoside.
Results: Among 49 chemotherapy cycles(induction-26, consolidation-23) administered in 17 children, there were 23(46.9%) episodes of febrile neutropenia and 8(16.3%) episodes of NE. Six(75%)of these NE episodes occurred in 1st induction. The clinical triad of fever, abdominal pain and loose stools were seen in 5 (62.5%) patients. NE was radiologically diagnosed in 5(62.5%) children(2 in ileocaecal junction and 1 each in caecum, descending colon with rectum and rectosigmoid). The mean wall thickness was 7 mm. Four of the 5 children(80%) with a positive blood culture had Gram-Negative(GN) bacteremia and septic shock. Of the 6 chemotherapy cycles that had GN bacteremia 4 were associated with NE(P-value=0.005). All children were treated with meropenam and colistin. Six children required oxygen support and 3 required Total parenteral nutrition. Six children recovered while 2 expired(both were in 1st induction). GN bacteremia was associated with mortality in NE(P-value-0.039).
Conclusions: Neutropenic enterocolitis was seen in 16.3% of children during AML therapy with majority of these occurring in 1st induction. With supportive care the recovery rate was 75% and mortality rate was 25%.

EP502 / #245

Topic: *AS05.p Supportive Care and Palliative Care*

THE DEVELOPMENT AND EVALUATION OF A NATIONAL CHILDREN'S & YOUNG PERSON'S CANCER VIRTUAL TRAINING PROGRAMME FOR PHYSIOTHERAPISTS AND OCCUPATIONAL THERAPISTS

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Background and Aims: Physiotherapy (PT) and Occupational Therapy (OT) are essential specialities in the management of children and young people with cancer (CYPC). Function and quality of life of CYPC on treatment, survivors, and those at end of life, can be enhanced with access to appropriately trained PTs and OTs. No national programmes previously existed in the UK. We aimed to bring professionals together to share knowledge and training to enhance care for CYPC.
Methods: Through national bodies, professional networks, and social media, we identified PTs and OTs working in services for CYPC in the UK. An organisational committee was formed, and services were invited to contribute and participate. A diverse training programme was organised, including training and speakers arranged from CYPC Principal Treatment Centres (PTC) across the UK. Over the period of one year, feedback was gained from attendees every session, and a one-year evaluation was performed.
Results: The training programme is 18 months old and is delivered virtually to optimise access. 18 of 19 PTCs in the UK plus five associated centres participate in the programme. Over 100 PT & OTs who work exclusively or partly with CYPC participate, and the average attendance is 36. 93% were satisfied with the training and all participants reported gaining knowledge and new information from attending. 73% rated the programme 5/5 stars and 87% believed the sessions were relevant to their roles.
Conclusions: Through virtual technology, the development and delivery of national training programmes is highly achievable. These programmes can elicit high levels of participant satisfaction and be rated highly by attendees. They have the potential to enhance collaboration and professional development and consequently improve the care of CYPC. If done on a global setting, virtual PT & OT programmes have the potential to help bridge the gap between different income/resource settings with supportive care and rehabilitation interventions.

EP503 / #467

Topic: *AS05.p Supportive Care and Palliative Care*

PERCEPTIONS OF PHYSIOTHERAPY & REHABILITATION SERVICES FOR CHILDREN & YOUNG PEOPLE (0-25 YEARS) WITH CANCER & THEIR PHYSICAL ACTIVITY LEVELS DURING THE COVID-19 PANDEMIC

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Background and Aims: During the COVID-19 pandemic, many healthcare settings worldwide prioritised COVID over other areas such as paediatric oncology rehabilitation. Physical outcomes for children and young people (CYP) with cancer and their physical activity levels may have been compromised by these changes and the pandemic in general. Through this exploratory pilot survey, we aimed to understand physiotherapists perspectives of physiotherapy and rehabilitation services and the physical activity levels of CYP during the pandemic.
Methods: A survey was used to understand the experience and perspectives of physiotherapists working with CYP with cancer across the world. Questions were structured around the local effects of the pandemic, the impact on physiotherapy and rehabilitation services, and effects on physical activity levels of CYP. The survey was distributed to a convenience sample of physiotherapists in low, middle, and high-income settings.
Results: 60% of responses were from high-income, 27% from middle income and 13% from low-income settings (n=23). All worked with CYP with cancer. 91% reported some/major disruption to their healthcare establishment and 83% reported physiotherapy and rehabilitation services for CYP with cancer were affected in their countries. Factors which caused this included service closure, restrictions, staff redeployment and staff sickness. Only 48% felt that services had returned to pre-pandemic levels. 83% reported that physical activity levels of CYP were affected during the pandemic. Factors which caused this were identified as being lockdown, restrictions, shielding and isolation. 61% felt that physical activity had not yet returned to pre-pandemic levels.
Conclusions: Physiotherapy, rehabilitation, and physical activity are essential to optimise function and quality of life for CYP with cancer. These domains were affected during the pandemic, potentially compromising outcomes for CYP with cancer. Physiotherapists and rehabilitation professionals must find strategies to adapt their intervention and optimise physical activity of CYP with cancer to mitigate the effects of future COVID-19 related disruption.

EP504 / #25

Topic: *AS05.p Supportive Care and Palliative Care*

MORPHINE GAP IN CAMEROON: MORE ADMINISTRATIVE FACILITATION REQUIRED TO REDUCE SUFFERING

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Background and Aims: Many patients in Low- and middle-income countries lack access to the opioid medicines that the World Health Organization designates as essential for pain control. Disparities in opioid consumption are partly related to policies affecting opioid access. Pain associated with cancer can significantly influence an individual's morbidity and quality of life. Therefore, Pain relief is fundamental to quality of life and palliative care.
AIM: To evaluate the availability of oral Morphine in relation to pain control need in Cameroon and national opioids regulation policies.
Methods: Analysis of opioid consumption data for Cameroon as published by the international narcotic control board (INCB), followed by a descriptive literature review of publicly available documents on pain control needs and opioid regulations for Cameroon using PubMed, Medline, Google Scholar, Google, Ministry of Public Health Website and National Institute of Statistics Cameroon.
Results: The annual consumption of morphine in Cameroon has steadily increased from 0.07 mg/capita in 1985 to 0.35 mg/capita (7.6 kg) in 2012. About 55.3 % of cancer and HIV related deaths are associated with moderate/severe pain. Almost all (98%) of patients dying of HIV or Cancer have untreated moderate /severe pain. An average annual import of 3.4kg of Morphine was recorded between 20011 and 2013, while a minimum of about 183Kg is required for HIV and cancer patients only. Importation of morphine is subject to signed authorization signed by the minister of public health.
Conclusions: There is a huge unmet need for pain relief with oral morphine in Cameroon. Limited access is at least in part from unduly strict national narcotic drug policies and regulations. Continuous advocacy with the ministry of health is essential to reduce the suffering of many

EP505 / #1174

Topic: *AS05.p Supportive Care and Palliative Care*

UNMET PALLIATIVE CARE NEEDS OF A CHILD WITH CANCER

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Background and Aims: In low and middle-income countries, palliative care has received little or no attention. When children with incurable cancer continue aggressive treatment, they may suffer unnecessarily from pain, discomfort, and low quality-of-life. Families are often not allowed to participate in decision-making whether they want to extend the life of their children or focus on relieving pain and discomfort.
Methods: A single case study was conducted to highlight the challenges facing families of children who die of cancer in Indonesia. Investigators identified a child with acute lymphoblastic leukemia and studied her medical records. A home visit was conducted in December 2019 to interview the mother. Two independent interviewers used a semi-structured questionnaire. Informed consent was obtained.
Results: A nine-year-old Indonesian girl suddenly suffered from fever episodes and paleness. Her mother brought the child first to a local shaman. When symptoms persisted, she was referred to a tertiary care referral hospital, where a bone-marrow puncture confirmed the diagnosis of acute lymphoblastic leukemia, and treatment was started. The mother experienced a lack of openness in communication about her daughter's treatment and prognosis. She reported that her child received intensive chemotherapy during the first two years despite a poor prognosis and severe side effects. She was not informed about the child's treatment choices during their final illness. Palliative treatment was ultimately started without informing the family. The mother emphasized that, in retrospect, the family would have preferred to participate in decision-making and opt for a shorter, more comfortable life without so much needless pain and suffering.
Conclusions: This study highlights the importance to start palliative care immediately at diagnosis. Both the physical and psychosocial well-being of patients needs to be closely monitored. Training on open communication in palliative care is required in universities and hospitals to enable shared decision-making and improve quality-of-life of children and their families.

EP506 / #798

Topic: *AS05.p Supportive Care and Palliative Care*

SAFETY OF PROCALCITONIN GUIDED DISCONTINUATION OF ANTIBIOTIC THERAPY AMONG CHILDREN RECEIVING CANCER CHEMOTHERAPY AND HAVING LOW RISK FEBRILE NEUTROPENIA: A RANDOMIZED NON-INFERIORITY TRIAL (PROFEN-C STUDY)

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Background and Aims: Febrile neutropenia (FN) is one of the most common oncological emergencies. There is no consensus regarding the optimal duration of empirical antibiotics. The safety of early discontinuation of antibiotics without marrow recovery is not well established. In this study we explored the safety of early discontinuation of empirical antibiotics in low-risk FN (LR-FN) without marrow recovery, utilising procalcitonin (PCT) guided protocol.
Methods: In this randomised non-inferiority trial, the children with LR-FN with afebrile period of at least 24 hours, sterile blood culture and negative/normalised PCT, were randomised at 72 hours into intervention and standard arm. The empirical antibiotics were stopped at 72 hours for those in intervention arm regardless of their absolute neutrophil count (ANC). The patients in standard arm continued to receive antibiotics for at least 7 days or until ANC >500/mm^3. The primary objective was to compare the treatment failure rates between the two arms. The secondary objectives were to compare the duration of antibiotics and all-cause mortality between the two arms.
Results: Between February 2020 and October 2021, 46 children with LRFN were randomised to intervention arm (n=23) or standard arm (n=23). Treatment failure was observed in 2/23 (8.7%) of patients in intervention arm compared to 1/23 (4.3%) in the standard arm [RR: 2 (95% CI: 0.19 to 20.55); p value = 0.550]. The patients in the intervention arm had significantly lesser days of antibiotic exposure compared to those in standard arm (3 days vs 7 days; [p value < 0.001]). None of the study subjects died due to any cause during the study follow up.
Conclusions: Early discontinuation of antibiotics at 72 hours did not result in significantly increased risk of treatment failure. The total duration of antibiotic exposure was significantly lesser among intervention arm. Further, multicentre randomised control studies are needed to throw some light on this subject.

EP507 / #279

Topic: *AS05.p Supportive Care and Palliative Care*

IMPLEMENTATION OF A PRACTICE GUIDELINE FOR THE MANAGEMENT OF RESPIRATORY DISTRESS FOR HOSPITALIZED CHILDREN WITH CANCER IN A RESOURCE CONSTRAINED SETTING THROUGH VIRTUAL COLLABORATION

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Background and Aims: Gains in survival in programs treating pediatric cancer in sub-Saharan Africa have been modest. Improvements in the quality of supportive care may be impactful. Global HOPE in Uganda is a high-volume referral center with seriously ill patients and limited pediatric critical care resources. Respiratory distress occurs commonly. We implemented a symptom-based management algorithm for respiratory distress on the hospital ward using quality improvement methodology and virtual mentoring.
Methods: Stakeholder interviews and focus groups identified two key drivers: access to equipment/medication (E/M) and healthcare worker (HCW) skills. E/M interventions included identifying gaps in the restocking process and improving organization of E/M. PDSA cycles, an E/M checklist, and run charts evaluated, measured, and analyzed effectiveness of the intervention. For HCW skills, acute care experts at Texas Children's Hospital virtually trained and mentored local champions to deliver training. We used before and after assessment of HCW knowledge acquisition and self-efficacy to evaluate improvement.
Results: Baseline data were collected for E/M using the checklist. As the result of a restocking process implemented by nursing and pharmacy team members, E/M have been consistently available. An organization system using a wall hanging with pockets was well-received. However, the ward soon moved to a new location that did not have a suitable location for it. To support HCW training, the clinical team leader identified trainers and a training schedule. Two training sessions have been well-received. However, scheduling training sessions has been challenging due to HCWs' clinical responsibilities.
Conclusions: HCWs and program leadership have been enthusiastic about the project. Contextual factors (change in location and the busy clinical environment) have impacted success. Next steps for the E/M intervention include developing a new organizational system and ensuring sustainability of the restocking process. For HCWs, a flexible training schedule is needed to accommodate clinical responsibilities.

EP508 / #376

Topic: *AS05.p Supportive Care and Palliative Care*

PLATELET AND RED BLOOD CELL TRANSFUSIONS IN CHILDREN WITH CANCER: A CLINICAL PRACTICE GUIDELINE

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Background and Aims: Both platelet and red blood cell transfusions play an important role in supportive care in children with cancer. In current clinical practice, recommendations regarding thresholds for administering platelet or red blood cell transfusions are often not evidence-based. Therefore, a clinical practice guideline (CPG) was developed to establish an overview of the available evidence and provide recommendations for clinicians.
Methods: A systematic literature review was performed, including dual appraisal of all citations. The GRADE methodology was used to assess, extract and summarize the evidence. When evidence in children with cancer was limited, additional evidence was extracted from adult cancer guidelines. A comprehensive multidisciplinary panel was assembled, comprising 24 professionals and patient representatives. Multiple in-person meetings were held to discuss evidence, complete evidence-to-decision frameworks and formulate recommendations.
Results: In total, eight studies including almost 2,000 children with cancer formed the evidence base for the recommendations. The expert panel assessed all evidence and translated it, transparently, into recommendations. In total, more than 38 recommendations were made regarding platelet transfusions and red blood cell transfusions in children with cancer. Thresholds for prophylactic platelet transfusions were recommended for children with cancer undergoing for example a lumbar puncture or line insertion or for children with cancer and sepsis. Also, thresholds for red blood cell transfusions were recommended for children with cancer and for example cardiac or pulmonary comorbidities, sepsis or undergoing radiotherapy. Some of these recommendations have a great impact already as they result in changes in current policy and standard of practice.
Conclusions: In this clinical practice guideline, we provide evidence-based recommendations regarding platelet and red blood cell transfusions in children with cancer. With these recommendations we aim to provide guidance for clinicians and contribute to improving outcomes for children with cancer.

EP509 / #378

Topic: *AS05.p Supportive Care and Palliative Care*

SOCIAL RESTRICTIONS IN CHILDREN WITH CANCER: A CLINICAL PRACTICE GUIDELINE

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Background and Aims: In current clinical practice, recommendations regarding social restrictions for children with cancer are often not evidence-based. Critically reviewing the evidence and recommendations is therefore of great importance as these social restrictions (e.g. swimming, school attendance, sports) can impair the quality of life of these children severely. Therefore, a clinical practice guideline (CPG) was developed to establish an overview of the available evidence and provide recommendations for clinicians, children and their parents.
Methods: A systematic literature review was performed, including dual appraisal of all citations. The GRADE methodology was used to assess, extract and summarize the evidence. A comprehensive multidisciplinary panel was assembled, comprising 21 professionals and patient representatives. Multiple in-person meetings were held to rank outcomes, discuss evidence, complete evidence-to-decision frameworks and formulate recommendations.
Results: Nine studies, including more than 1,400 children, with various study designs formed the evidence base for the recommendations. Considering the limited amount of studies in children with cancer, additional evidence was also extracted from adult guidelines. Our experts assessed all evidence and translated it, transparently, into recommendations. In total, 14 recommendations were made regarding social restrictions in children with cancer. For example, recommendations were made on swimming, having pets, visiting the zoo or farm, performing sports or high-velocity events, attending school or kindergarten, use of public transport and more. Some of these recommendations have a great impact already as they result in changes in current policy and standard of practice.
Conclusions: In this clinical practice guideline, we provide both evidence-based recommendations and best practice statements regarding social restrictions in children with cancer. With these recommendations we provide guidance for clinicians, children and their parents and contribute to improving quality of life for children with cancer.

EP510 / #373

Topic: *AS05.p Supportive Care and Palliative Care*

COMPLICATIONS OF CENTRAL VENOUS AND PERIPHERAL INSERTED CENTRAL LINE CATHETERS IN PEDIATRIC ONCOLOGY PATIENTS. A SINGLE CENTER EXPERIENCE

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Background and Aims: Studies comparing types of central venous catheter (CVC) and their associated complications are particularly limited and contradictory in children diagnosed with malignancy and receiving chemotherapy. Due to the ease of insertion and overall usability as well as the site of insertion, the PICC line seems an appealing choice specially for older children.
Methods: This is a ten-year retrospective study, comparing the complication rates among the most commonly applied types of CVCs in a Pediatric Hematology-Oncology Unit. Data was mainly collected from the patients' medical records.
Results: In total 192 CVCs were placed in 137 children (119 Hickman/73 PICC lines) with a median age of 8.3±5.6 years(0.4-20.7 years). In children <10 years of age, the most prevalent choice was Hickman line (68%), while for those >10 years PICC line (77.85%). The percentage of patients with Hickman catheters who experienced an infection at the first catheter insertion was 34.5% while with PICC line 23.3% (p = 0.102). The median time of infection (95% CI) was 339 days for Hickman and 288 for PICC line type catheters (1,68 episodes / 1000 catheter days for Hickman type catheters and 1.70 / 1,000 for PICC lines). The incidence of a thrombotic episode was 22.1% for Hickman and 33.8% for PICC line catheter (p=0.073), with a median time (95% CI) of 126 and 130 days respectively (p=0.430) (0,63 episodes / 1,000 catheter days for Hickman type catheters and 1.51 / 1000 catheter days for PICC lines). The overall perforation and accidental removal/displacement rate was 16.8% for Hickman and 12.3% for PICC line type catheters (p = 0.400).
Conclusions: The occurrence of complications does not seem to be affected by the type of catheter inserted. The age of the patient and the duration of the catheter placement rather predispose for an infectious or thrombotic incident.

EP511 / #864

Topic: *AS05.p Supportive Care and Palliative Care*

TREATMENT AND OUTCOMES OF CENTRAL VENOUS CATHETER (CVC) - ASSOCIATED CANDIDEMIA AMONG CHILDREN WITH CANCER: KING HUSSEIN CANCER CENTER EXPERIENCE

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Background and Aims: The best treatment for CVC associated candidemia remains obscure. Mainly, the indications for line removal and duration of treatment are not well defined.
Methods: A retrospective chart review of children treated at our center over a 5-year period. Cases were identified via microbiology lab records in patients having CVC between Jan2016-Dec2020. Data collected included demographics, diagnosis, CVC type, species identity and sensitivity, modes of treatment, and outcomes, defined as 30-day mortality and CVC removal.
Results: There were 25 candidemia episodes in 24 patients with CVC (median age, 2.4 years; range, 0.2-18.8; males, 72%). These lines were ports (37%), CVP (33%), and Hickman (22%). Candidemia occurred at a median of 1.7 months after cancer diagnosis (range,0-180), which was mainly leukemia (32%), solid tumors (24%), and lymphomas (8%). Fourteen patients (56%) had an absolute neutrophil count <100/microL at first positive culture. A positive bacterial culture coincided in 44%, and 92% had received broad-spectrum antibiotics within the prior 2 weeks. Lung infections were detected in 9 patients (36%). Fever was present at initial diagnosis in 89% of patients, and 52% suffered hemodynamic instability. Non-albicans Candida comprised 64% of cultures. Antifungal resistance to fluconazole and voriconazole was present in 2 and 1 cases, respectively. Amphotericin was the most commonly used initial agent (44%). An antifungal switch was needed for different reasons in 17 patients (67%) after a median of 5 days (range,1-27). Most used second-line agents were caspofungin (26%), and fluconazole (19%). Median time to clearing culture was 2 days (range,1-26), and to fever resolution was 3 days (range,0-33). Sixteen CVCs (63%) were removed. Overall 30-day mortality was 18.7%±7.5%.
Conclusions: CVC-associated candidemia occurred mainly in suppressed patients. With optimal supportive care, we successfully treated most of these infections. Lines were removed in approximately two-thirds of our patients.

EP512 / #879

Topic: *AS05.p Supportive Care and Palliative Care*

UNMET SUPPORTIVE CARE NEEDS OF FAMILIES OF CHILDREN WITH CANCER AND OTHER CHRONIC ILLNESS: A SYSTEMATIC REVIEW

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Background and Aims: Childhood chronic health conditions (CHC), like cancer can be complex and challenging with parents expressing many needs relating to caring for their child. However, whether the needs of families with a child with cancer differ from families with children with other CHC is not clear as there has been no systematic synthesis of available evidence in this area. To address this gap, this systematic review examines the unmet Supportive Care Needs (SCN) of families with common pediatric CHC to identify similarities and differences in needs and characterise assessment tools.
Methods: Electronic searches were performed among the databases of Medline complete, PsycINFO, CINHAL, and Embase and screened articles published between 1990- April 2021. Qualitative and quantitative studies involving children aged between 0-18 years, diagnosed with cancer and other CHC reporting unmet needs were eligible. Studies focusing on children with genetic or developmental conditions were excluded. Study characteristics, sample demographics, outcome measures were extracted from eligible papers.
Results: Of the 5061 papers identified 34 studies were eligible. Cancer was the focus of 25 studies and other work focused on heart disease, asthma, diabetes, renal problems and mixed CHC (n=9). Parents of children with cancer reported gaps in information, emotion, and psychosocial support. However, practical/caretaking, informational and health care service needs were higher for other conditions. There was a lack of a consistent need assessment across conditions and most studies (n=11) used a non-validated tool.
Conclusions: While families of children with cancer seem to have fewer practical and caretaking needs, there is still a gap in the emotional and psychosocial support they would like and the support they receive. Work is needed to develop a valid and reliable measure of need across CHC to all comparison and thereby ensure all families with children with CHC received the support they need.

EP513 / #723

Topic: *AS05.p Supportive Care and Palliative Care*

VALIDATION OF A MODIFIED BEDSIDE PEDIATRIC EARLY WARNING SYSTEM SCORE FOR DETECTION OF CLINICAL DETERIORATION IN HOSPITALIZED PEDIATRIC ONCOLOGY PATIENTS: A PROSPECTIVE COHORT STUDY

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Background and Aims: Hospitalized pediatric oncology patients are prone to clinical deterioration. Pediatric early warning system (PEWS) scores have not been prospectively validated for these patients. We determined the predictive performance of a modified BedsidePEWS score for clinical deterioration during an inpatient ward admission in pediatric oncology patients.
Methods: This prospective cohort study was conducted in hospitalized pediatric oncology patients aged 0 to 18 years at the 80-bed Dutch pediatric oncology national referral center. The association between PEWS score and unplanned PICU admission or cardiopulmonary resuscitation (CPR) was estimated by a Cox proportional hazard model. The predictive performance (discrimination and calibration) of the model was assessed by bootstrapping.
Results: We included 1137 patients, of which 103 patients experienced 130 primary outcome events (127 unplanned PICU admissions and 3 CPRs). The modified BedsidePEWS score was significantly associated with time to unplanned PICU admission or CPR (hazard ratio 1.65 (95%CI 1.59–1.72) per point increase). Discriminative ability was moderate, considering a discrimination-index close to zero and concordance-index of 0.83. Calibration was excellent (index-corrected slope of 0.99). Positive and negative predictive values at score cut-off 8, at which escalation of care is required, were 1.4% and 99.9%, respectively.
Conclusions: The modified BedsidePEWS score is a strong prognostic factor for time to unplanned PICU admission or CPR in pediatric oncology patients. The score may aid in clinical decision making for timing of escalation of care.

EP514 / #1610

Topic: *AS05.p Supportive Care and Palliative Care*

PEDIATRIC ONCOLOGY: A DATA ANALYSIS OF PATIENTS USING OPIOIDS DURING THEIR HOSPITALIZATION IN PERU

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Background and Aims: Pain in hospitalized children with cancer may be unrecognized and undertreated. This study aimed of this study was to determine the use of opioids and evaluate the differences according to sex, age, pathology, and the occurrence of side effects in pediatric cancer inpatients in a Peruvian hospital.
Methods: Retrospective, observational, monocentric study. All infants and children younger than 14 years who initiate opioids in emergency or hospitalization at the National Institute of Neoplastic Diseases (INEN) between December 2021 and February 2022 were reviewed. Statistical analysis was descriptive and analytic.
Results: A total of 134 children were identified, 73 patients (54.5.7%) were male and 61 (45.3%) female. Tramadol (81%) followed by morphine (19%) were the most used opioids for pain management. The median age that used tramadol was 8 years. (IQR 4.12) and morphine was 8 years. (IQR 5-10). In the multivariate analysis, the use of tramadol treatment ($P<0.001$) did not significantly affect the occurrence of side effects. Conversely, the use of morphine ($P<0.001$) was statistically significant for the occurrence of side effects. There were no significant differences in the appearance of side effects between the use of tramadol and morphine according to the type of diagnosis, whether they were hematological or solid neoplasms, nor the reason for starting the opioid or the place where treatment was started (emergency or hospitalization). The median time of opioid use was 6 days for both tramadol (IQR 2-10) and morphine (IQR 4-12). The Kruskal Wallis test showed that the duration of opioid use was not significant for the development of side effects.
Conclusions: The use of morphine is still restricted in developing countries, so the use of tramadol is preferred. Although there are restrictions on the use of tramadol, there was no evidence of greater development of side effects.

EP515 / #741

Topic: *AS05.p Supportive Care and Palliative Care*

USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) REMEDIES IN CHILDHOOD CANCER PATIENTS - A SURVEY REPORT FROM CHILDREN CANCER CENTRE OF CAA-NICH,KARACHI

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Background and Aims: In children; complementary and alternative medicine (CAM) including herbal remedies, homeopathic medicines, hikmat medicines, diet changes, nutritional supplements, vitamins, spiritual therapy,use of massage, acupuncture, and aromatherapy have been used for a variety of chronic illnesses including asthma, arthritis, cancer, gastrointestinal diseases, and neurological or developmental disorders.[1, 2] This study aims to investigate the prevalence of the use of CAM among pediatric cancer patients in a tertiary care teaching hospital.
Methods: Caregivers of 287 pediatric cancer patients receiving conventional treatment including chemotherapy for various types of cancer were enrolled at pediatric oncology department from January 1, 2021 till March 31, 2021.Data was recorded in a Performa with relevant questions to assess parents' perspectives about CAMs and their use.
Results: 211 (73.5%) caregivers agreed to give response to the survey.Among them,126 (59.7%) replied in affirmation regarding use of complementary and alternative remedies. Acute Leukemia (n=66) was the most common diagnosis getting CAM. Of them, (79.4%) were receiving curative intent treatment. M: F ratio was 1.4:1 and 69.8% patients were from outside Karachi. Only 28.5 %(n=36), caregivers informed about CAM use to their physician. Common reasons of using CAM in order of frequency were; feeling of un-wellness with chemotherapy (n=27), loss of appetite (n=25), repeated episodes of fever (n=24) and repeated hospitalization (n=15). Natural health products, herbal medicines, appetite stimulants, weight gain products, use of vitamins and minerals were reported by 45% (n=56) caregivers as alternative remedies, followed by spiritual healing in another 39% patients. The reasons for not using CAM were concern for side effects and doubt of its effectiveness in two-third patients.
Conclusions: Caregivers are hesitant of talking about the use of CAM in our survey. To ensure patient safety, healthcare providers including doctors and nurses, pharmacists and psychosocial team need to include CAM use in their data registry and counseling sessions.

EP516 / #157

Topic: *AS05.p Supportive Care and Palliative Care*

CENTRAL VENOUS CATHETER ASSOCIATED COMPLICATIONS IN PEDIATRIC PATIENTS DIAGNOSED WITH HODGKIN LYMPHOMA: IMPLICATIONS FOR CATHETER CHOICE

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Background and Aims: The purpose of this study was to determine the most optimal central venous catheter (CVC) for pediatric patients with Hodgkin lymphoma (HL) in terms of complications.
Methods: A retrospective study including patients diagnosed with HL from 2015-2021 at the Princess Máxima Center. Patients were followed from CVC insertion until removal or 06-2021, whichever came first. The primary outcome was the CVC-related complication incidence rate (IR) per 1 000 CVC-days. Furthermore, the incidence rate ratio (IRR) was calculated by comparing complication IRs between peripherally inserted central catheters (PICC) and totally implantable venous access ports (TIVAP). Additionally, risk factors for central venous thrombosis (CVT) were identified.
Results: A total of 98 patients were included. The most frequently observed complications were local irritation/infections (18%;IR0.93), malfunctions (15%;IR0.88), and CVC-related CVTs (10%;IR0.52). Single lumen PICCs were associated with a higher risk of complications (49% vs. 26%; IRR5.12, CI95%2.76-9.50), severe complications (19% vs. 7%; IRR11.96, CI95%2.68-53.42), and early removal (16% vs. 7%; IRR8.97, CI95%1.94-41.50). A single lumen PICC, was identified as a risk factor for CVC-related CVT when compared to TIVAPs (12% vs. 7%, IRR6.98, CI9%1.45-33.57).
Conclusions: The insertion of a TIVAP rather than a PICC should be recommended for pediatric patients with HL, especially in the presence of CVT-related risk factors. Future trials should evaluate the efficacy and safety of direct oral anticoagulants for the primary prevention of CVT in pediatric patients with a PICC and other CVT-related risk factors.

EP517 / #495

Topic: *AS05.p Supportive Care and Palliative Care*

THE IMPACT OF TASTE AND SMELL CHANGES IN CHILDREN WITH CANCER UNDERGOING CHEMOTHERAPY: A QUALITATIVE STUDY

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Background and Aims: Children receiving chemotherapy often report taste changes. Although this is a bothersome symptom, it is still unclear what the essence of these taste changes are, to what degree concomitant smell changes qualify this symptom and how much of an impact it has on the life of children with cancer.
Methods: Semi-structured interviews were used to explore characteristics and impact of taste and smell changes in 27 children with cancer (6-18 years) receiving chemotherapy. Thematic analysis of interview data was performed.
Results: Interview data could be grouped into three main themes, namely changes in 1) taste, 2) smell, and 3) eating behavior. As expected, most children reported experiencing taste and smell changes just after start of treatment, but changes varied greatly; that is, some reported increased taste and smell function, whereas others reported a decrease. Taste and smell changes (regardless of direction) negatively impact quality of life, with these changes commonly described as “disappointing” or “frustrating”. Interestingly, particular chemotherapeutic agents appear strongly associated with taste and smell changes (e.g., methotrexate), prompting sensory-specific coping strategies.
Conclusions: Both taste and smell changes are common in children with cancer. The essence of these changes varies widely, but are generally considered bothersome symptoms. Ways to cope with taste or smell changes were described by the children, warranting further research and offering the opportunity for enhancing patient-centred care.

EP518 / #72

Topic: *AS05.p Supportive Care and Palliative Care*

DEVELOPMENT OF A QUESTIONNAIRE TO EVALUATE FEMALE FERTILITY CARE IN PEDIATRIC ONCOLOGY, A TREL INITIATIVE.

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Background and Aims: Currently the five-year survival of childhood cancer is up to 80% due to improved treatment modalities. However, the majority of childhood cancer survivors develop late effects including infertility. Survivors describe infertility as an important and life-altering late effect. Fertility preservation options are becoming available to pre- and postpubertal patients diagnosed with childhood cancer and fertility care is now an important aspect in cancer treatment. The use of fertility preservation options depends on the quality of counseling on this important and delicate issue. The aim of this manuscript is to present a questionnaire to determine the impact of fertility counseling in patients suffering from childhood cancer, to improve fertility care and evaluate what patients and their parents or guardians consider good fertility care.
Methods: Within the framework of the EU-Horizon 2020 TREL project, a fertility care evaluation questionnaire used in the Netherlands was made applicable for international multi-center use. The questionnaire to be used at least also in Lithuania, incorporates patients' views on fertility care to further improve the quality of fertility care and counseling.
Results: evaluate and will be used to improve current fertility care in a national specialized pediatric oncology center in the Netherlands and a pediatric oncology center in Lithuania.
Conclusions: An oncofertility-care-evaluation questionnaire has been developed for pediatric oncology patients and their families specifically. Results of this questionnaire may contribute to enhancement of fertility care in pediatric oncology in wider settings and thus improve quality of life of childhood cancer patients and survivors.

EP519 / #442

Topic: *AS05.p Supportive Care and Palliative Care*

THE DUTCH MULTIDISCIPLINARY CLINICAL PRACTICE GUIDELINE FOR PEDIATRIC PALLIATIVE CARE

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Background and Aims: Pediatric palliative care is concerned with relief of suffering of all children with a life threatening disease and their families in all domains (physical, psychological, social and spiritual). This includes pediatric oncology patients. In 2013, the first Dutch multidisciplinary clinical practice guideline for pediatric palliative care was developed, providing recommendations on relief of symptoms, decision-making and organization of care. Evaluation of the guideline revealed a need for revision of the recommendations and inclusion of new recommendations on topics such as psychosocial and bereavement care, advance care planning and shared decision-making. The aim of this research is to improve provision of pediatric palliative care in the Netherlands by developing an updated version of the Dutch Pediatric Palliative Care guideline.
Methods: A multidisciplinary guideline panel reviewed literature on pediatric palliative care by systematic literature searches. The GRADE methodology was used to grade the evidence and to formulate recommendations. Recommendations were formulated and refined based on the evidence, clinical expertise, and patient values. For those topics where no evidence was available, recommendations were based on other guidelines, clinical expertise and patient values.
Results: The updated systematic literature search identified 14 randomized controlled trials and 15 systematic reviews that prompted refinement of recommendations. For 27 out of 42 formulated clinical questions, no evidence was found. This revealed major gaps in knowledge on pediatric palliative care. Based on evidence (if available), clinical expertise and patient values, more than 100 recommendations on various topics in pediatric palliative care were generated.
Conclusions: The updated guideline uses existing evidence and national expertise to develop transparent and easy-to-use recommendations to facilitate provision of high quality pediatric palliative care. The guideline promotes interdisciplinary collaboration and opens opportunities for international research into the identified knowledge gaps to further improve pediatric palliative care.

EP520 / #963

Topic: *AS05.p Supportive Care and Palliative Care*

A STITCH IN TIME SAVES NINE: TIMELY USE OF N-ACETYL CYSTEINE (NAC) FOR CHEMOTHERAPY INDUCED VENO-OCCLUSIVE DISEASE (VOD), IS IT A COST-EFFECTIVE ALTERNATIVE?

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Background and Aims: Defibrotide, the conventional antidote for chemotherapy induced veno-occlusive disease(VOD) is costly and not accessible to majority getting treated at resource constrained settings. We describe the successful management of chemotherapy induced VOD with timely administration of N-acetyl cysteine(NAC).
Methods: A total of 4 children developed chemotherapy induced VOD during the study period (2019-2021). All these patients received NAC at a dose of 100mg/kg loading followed by 50mg/kg over 4hours then 100mg/kg continuous infusion till complete resolution of clinical and laboratory features of VOD.
Results: First case was a 10-year-old boy,with non-metastatic right kidney Wilms tumor with renal vein thrombus who received 3-drug neo-adjuvant chemotherapy regimen. Post-week-6 of Vincristine/Dactinomycin chemotherapy, he developed clinico-radiologic features suggestive of VOD. Second case was a 4-year-old girl with B-cell acute lymphoblastic leukemia (B-ALL) on modified BFM-95 ALL protocol. She presented with clinical and laboratory features suggestive of VOD during phase-1b consolidation. Ultrasound imaging and histopathology biopsy of liver confirmed underlying hepatic VOD. Third and fourth cases were of a 2-year girl and an 8-year boy with non-metastatic biliary and bladder rhabdomyosarcoma(RMS) respectively. Both of them developed clinical and laboratory features suggestive of VOD post 1st and 2nd cycle of Vincristine, Actinomycin D,Cyclophosphamide (VAC) regimen respectively. In all these cases, NAC was promptly infused on 2nd admission day and was continued for a median of 4days(range:3-6days) following which VOD resolved completely. Dactinomycin was implicated as the causative agent in cases-1,3 and 4 and oral 6-mercaptopurine and cyclophosphamide in case-2.
Conclusions: Timely NAC infusion at the earliest clue of VOD in a resource constrained setting, may prevent irreversible hepatic damage as well as mortality. Besides being cheap, availability and excellent safety profile make NAC an attractive option in chemotherapy induced VOD.

EP521 / #400

Topic: *AS05.p Supportive Care and Palliative Care*

DEVELOPMENT OF NEW PREDCITIVE EQUATION FOR RESTING ENERGY EXPENDITURE IN PEDIATRIC PATIENTS WITH ONCOLOGY DIAGNOSIS

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Background and Aims: Accurate resting energy expenditure (REE) predictive equations are crucial for designing nutritional strategies for patients with cancer diagnoses. The REE is the most widely used measure to estimate energy requirements in the nutritional context; the most accurate method to measure it is indirect calorimetry (IC), however, this method is expensive and not as feasible in clinical settings. Our aim was to develop an equation for predicting resting energy expenditure in pediatric patients diagnosed with oncology based on easily obtained anthropometric predictive variables.
Methods: Cross-sectional study, including pediatric patients (6-18y) with cancer diagnoses, the REE is measured by IC, anthropometric, clinical and body composition variables are measured by impedance. Predictive equation proposals were derived using multiple linear regression analyses.
Results: One hundred patients with an average age of 12±2.9y have been evaluated, according to the diagnostic stratum, 20% had a diagnosis of leukemia, 65% solid tumor and 15% brain tumor. Two model proposals were derived: the basic model that considered the variables of weight, age, sex ($r=0.565$, $p<0.001$), and the morphofunctional model with the variables: weight, age, sex, FFM, ($r=0.596$, $p<0.001$). When comparing the average calories vs IC (1179±387kcal), no significant differences were observed with the basic model (1115±197kcal, $p=0.132$), nor with the morphofunctional model (1101±223, $p=0.129$). The basic model presented an average bias of 90 (-479, 660) and the morphofunctional model 73 (-553, 679), compared to the existing equations: Harris and Benedict -174 (-75, 446), IOM -231 (-911, 449), FAO -207 (-830,414).
Conclusions: The proposed equations had the highest predictive accuracy in pediatric patients diagnosed with oncology compared to the existing equations.

EP522 / #337

Topic: *AS05.p Supportive Care and Palliative Care*

LEGACY-MAKING: EXPLORING CULTURAL DIFFERENCES

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Background and Aims: Background: Legacy-making is an intervention psycho-oncology and palliative care professionals use to help people living with cancer and their families prepare for end-of-life. Legacy-making includes activities to preserve memories. There is a dearth of research on how legacy practices may differ by culture. This study explores legacy practices that pediatric psycho-oncology and palliative care professionals of different cultures and countries offer to children, adolescents, and young adults (AYAs) with cancer, and perceived barriers to legacy-making.
Methods: An interdisciplinary study team designed an anonymous survey on legacy practices in different countries and cultures. The study instrument contained questions on respondent discipline, legacy practices for pediatric patients, and barriers to discussing legacy creation. Questions provided space for open-ended responses. The IPOS Palliative Care Special Interest Group and the St. Jude Global Palliative Care Transversal Program listserv were sent a survey link inviting interested providers to participate.
Results: 25 participants from 17 countries on 6 continents completed the online survey. Responses were representative of the multidisciplinary team, including psychologists, occupational therapists, social workers, and physicians from multiple specialties. 57% of participants reported discussing creating a legacy with their pediatric and AYA patients. Meaningful legacies included creative and expressive art making, creating special moments and memories, photo portraits, forming memorial foundations/charities, and participating in advance care planning. Barriers to legacy creation included provider discomfort, family reticence, timing, and lack of clinical staff and resources. Various cultural processes/considerations were noted, including the role of family beliefs and lack of familiarity with the concept of legacy.
Conclusions: This study is a first step towards understanding cultural differences in legacy-making practices with youth living with cancer. Findings indicate that while many providers discuss legacy making with their pediatric patients, ‘legacy’ may be an unfamiliar term in some cultures and can have different meanings within and across cultures

EP523 / #295

Topic: *AS05.p Supportive Care and Palliative Care*

OUTCOME OF VARICELLA EXPOSURE IN PEDIATRIC PATIENTS WITH CANCER AT A TERTIARY HOSPITAL: A THREE-YEAR EXPERIENCE

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Background and Aims: Background/Significance: In the Philippines, Varicella vaccine immunization is not included in the national immunization program. Annual outbreaks occur during summer months. For children with cancer, Varicella infection is associated with disseminated disease and high mortality rates. Exposures may also cause treatment interruptions impacting survival rates. Objectives: To describe the outcome of pediatric cancer patients exposed to varicella infection.
Methods: Retrospective, medical chart review of patients exposed to varicella from January 2018 to December 2020. Chi-square test was used to examine the risk factors for breakthrough infection.
Results: A total of 380 patient exposures were identified in 301 patients. The most common diagnosis was leukemia (N=195, 51%) followed by brain tumor (N=38, 10%), retinoblastoma (N=33, 9%) and sarcomas (N=33, 9%). Exposures occurred at the outpatient clinic (N = 262, 69%), halfway house (N = 62, 16%), home (N= 11, 3%), hospital party (N= 45, 12%). Majority were unvaccinated N = 374 (98%). Post exposure prophylaxis administered were: Acyclovir (N = 314, 95%), Valacyclovir (N = 11, 3%), and IVIG (N = 6, 2%). Breakthrough infection occurred in only N=6, 1.6%, all recovered. Only household exposure was significantly associated with infection. Chemotherapy was discontinued in N= 107, 42% of cases for 21-28 days. At the time of this study, 70% of the exposed were alive, wherein 60% were in remission, 10% in relapse and 30% expired from disease progression or other causes.
Conclusions: Post exposure prophylaxis with oral antivirals is effective in preventing infection among pediatric cancer patients. Breakthrough infections were few and occurred among close household contacts. Cessation of chemotherapy during the incubation period was significant cause of treatment delay. Findings from the study will improve institutional varicella guidelines. Future studies will explore benefits of varicella vaccination among low risk pediatric cancer patients.

EP524 / #1932

Topic: *AS05.p Supportive Care and Palliative Care*

THE NUTRITIONAL STATUS OF CHILDREN IN THE PEDIATRIC HEMATO-ONCOLOGY DEPARTMENT IN NOUAKCHOTT DESCRIPTIVE OBSERVATIONAL STUDY AIMED AT ANALYSIS WITH COLLECTION OF PROSPECTIVE DATA

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Background and Aims: Context: in mauritania one in ten children is malnourished, the malnutrition of children with cancer limits the therapeutic possibilities. the objective of this work is to take stock of the nutritional status of our patients in order to prepare a nutritional management integrated into the care of children with cancer
Methods: Our study is a nutritional survey at the pediatric hemato-oncology consultation at the Center National Oncology allowing the recruitment of 100 children including 64 with cancer and 36 with benign blood diseases over a period of 3 months.
Results: The average age was 8 years The sex ratio is 2.03 in favor of boys. 74% of our patients live in urban areas 78% of our patients had a low socio-economic level 42% of children were in school 58% of parents were illiterate This study showed the frequency of undernutrition in our sick children regardless of the etiology. According to the HAS criteria, 50% of children with cancer were malnourished, 3.1% overweight and 4.7% were obese, 52.8% of non-cancer children were malnourished 20% of children had localized tumors, 16% had locally advanced tumors and 11% had metastases. children with metastases were undernourished at 63%, and those with localized tumors at 45%. The cancers that were most associated with malnutrition were Leukemia at 21.9%, nephroblastoma at 15.6%, retinoblastoma, germ cell tumors, and osteosarcoma at 9.37%. 32% of children with cancer were under chemotherapy, of which 59% were malnourished. 50% of children were anorexic 28% of children had pain 64% of morbid children were malnourished and cancerous.
Conclusions: the nutritional status of our patients justifies the integration of nutritional support in the daily care of our patients.

EP525 / #1719

Topic: *AS05.q Psychosocial (PPO)*

THE IMPACT OF SOCIAL DETERMINANTS OF HEALTH ON QUALITY OF LIFE AND PSYCHOSOCIAL OUTCOMES FOR CHILDREN WITH CANCER

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Background and Aims: Social determinants of health (SDH), such as income, race/ethnicity, and population density influence health-related quality of life (HRQL) in the context of chronic pediatric conditions. There is a need to understand SDH's impact on HRQL and psychosocial outcomes for children with cancer. To evaluate the impact of SDH on HRQL and psychosocial outcomes, hypothesizing that more social vulnerability, less access to care (e.g., further from hospital, lower population density), and identification with a racially underrepresented group would be associated with poorer HRQL and psychosocial functioning. An exploratory aim was to determine whether diagnosis type or treatment intensity moderated these associations.
Methods: Participants were youth ages 7-14 who completed treatment within six months for either brain tumor (BT; n=42) or non-central nervous system solid tumor (ST; n=29). The Total Problems subscale of the Child Behavior Checklist (CBCL) assessed psychosocial difficulties. Youth completed the Pediatric QOL Inventory (PedsQL 4.0) to assess HRQL. The Pediatric Neuro Oncology Rating of Treatment Intensity measured treatment intensity. Population density, rural status, and socioeconomic status (SES) were determined via the U.S. Census Bureau. Social vulnerability was calculated using the CDC/ATSDR Social Vulnerability Index (SVI), which captures household composition/disability, minority/language, and housing/transportation. Analyses included partial correlations and moderation models using the SPSS PROCESS macro.
Results: For the BT group, distance from the hospital was significantly associated with CBCL, ($r=0.35$, $p=.02$) with a trend for HRQL ($r=-0.29$, $p=.059$). Neither treatment intensity nor diagnosis significantly moderated the association between distance and CBCL/HRQL. Other SDH were not related to outcomes.
Conclusions: Increased distance from the hospital may be associated with worse HRQL and psychosocial outcomes for BT patients. Future work should investigate the cumulative impact of SDH longitudinally with a larger sample, as the cumulative impact of multiple risk factors may be more substantial than any single factor.

EP526 / #316

Topic: *AS05.q Psychosocial (PPO)*

HOUSEHOLD MATERIAL HARDSHIP AND FOOD INSECURITY IN CHILDREN WITH NEWLY DIAGNOSED CANCER: ASSOCIATIONS WITH SOCIAL DETERMINANTS OF HEALTH

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Background and Aims: Poverty is associated with poorer health outcomes. Research on household material hardship (HMH) and food security and associations with social determinants of health (SDoH) in diverse populations is lacking in pediatric cancer. To fill this gap, we conducted cross-sectional and longitudinal assessments of HMH and food security in families of children with cancer.
Methods: We prospectively enrolled parents of children with newly-diagnosed cancer at Rady Children's Hospital-San Diego, a large children's hospital with high representation of Hispanics. Assessments of HMH (food, housing, energy insecurity), food security, and SDoH (health literacy, acculturation (if Hispanic), socio-demographics) were conducted at 0, 3, 6, 12, and 24 months after diagnosis. Univariate and multivariate analyses were used to determine associations at each timepoint and longitudinally.
Results: Of 107 parents included, 55% were Hispanic and 74% married. At baseline, 52% reported HMH and 24% reported food insecurity. In univariable analysis, public insurance was associated with HMH ($P=0.007$) and food insecurity ($P<0.001$); associations remained in multivariable analysis of HMH ($P=0.046$) and food insecurity ($P=0.008$). In univariable analysis, unmarried status was associated with HMH ($P<0.001$) and food insecurity ($P<0.001$); in multivariable analysis, associations with HMH ($P=0.004$) and food insecurity ($P=0.001$) remained. In longitudinal analysis, unmarried individuals and those with public insurance had higher likelihood of HMH (OR 3.399, $P<0.001$; OR 2.705, $P=0.014$) and food insecurity (OR 5.423, $P<0.001$; OR 4.091, $P=0.011$).
Conclusions: HMH and food insecurity were highly prevalent in our sample and associated with unmarried status and public insurance. These associations persisted over time. Our findings contribute to the scant literature in diverse populations, emphasizing the importance of financial hardship screening and resources, particularly to underserved individuals. Future directions include systematic assessments of HMH and food insecurity in children with cancer, including those enrolled in clinical trials, and development and implementation of effective interventions targeting HMH and food insecurity.

EP527 / #1388

Topic: *AS05.q Psychosocial (PPO)*

EVALUATION OF THE PSYCHOLOGICAL SUPPORT PROJECT FOR CHILDREN TREATED FOR CANCER IN THE PAEDIATRIC ONCOLOGY UNIT OF ARISTIDE LE DANTEC HOSPITAL (SENEGAL)

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Background and Aims: The pediatric oncology unit was created since 2000. In a holistic approach, a psycho-oncology team has been integrated into the unit since July 2018 thanks to the support of the Sanofi-Espoir Foundation. After one year of implementation (from July 1, 2020 to December 31, 2021), the Foundation wanted to evaluate the project. We conducted a survey. The general aim was to evaluate the perceptions by stakeholders of psychological support activities.
Methods: A qualitative approach was used. It was based on individual interviews and stories of illnesses order to capture the discourse and points of view regarding the perceived effects. The targets of the surveys were the project implementation teams, the authorities, the patients/families, and the associations of the patients' families concerned.
Results: The presence of the psychooncology team was positively appreciated. Their contribution was considered satisfactory. The activities mentioned were support during announcements (diagnosis, relapse, palliative care, end of life), skill building on verbal and non-verbal communication techniques, weekly psychological interviews of the oncopediatric team. They fostered a better ability to manage negative emotions and deal with families or children's emotional distress. These statements were confirmed by the decrease in anxiety scores (Spielberg Anxiety Scale). The feeling of being psychologically supported was verbalized by team members and was seen as motivation to continue their work. The alternative psychotherapy activities offered were a great source of satisfaction for children and parents. They included art therapy, story therapy and psychomotricity. Free play groups for children were organized. These sessions allowed families to see their children in a new light. This was reflected in the quality of life measures (AUQUEI). A decrease of dropouts was noted. The families raised communication problems.
Conclusions: The integration of a multidisciplinary psychooncological team was one of the foundations of the success of this experiment, which is unique in West Africa.

EP528 / #1825

Topic: *AS05.q Psychosocial (PPO)*

STRUCTURED PSYCHOLOGICAL SUPPORT MODEL IN PEDIATRIC ONCOLOGY ONCOLOGY : SENEGALESE EXPERIENCE

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Background and Aims: Psychological support in paediatric oncology aimed to accompany patients, families and oncopediatri team. The originality lies in the fact that it was the first experience of a paediatric onco unit with an integrated psycho-oncology team in West Africa.
Methods: We carried out a retrospective, descriptive study. An evaluation from 1 July to 31 December 2020. Individual interviews, group activities, psychomotricity, art therapy and story therapy were carried out. Used tools were genogram, quality of life scale for children and Spielberg anxiety test for team.
Results: 172 (115 children and 57 families) were consulted. Psychological support for children consisted of individual psychological interviews, psychotropic drugs'prescription (delirium, anxiety-depression), and "alternative" psychotherapy activities (art-therapy, story therapy and psychomotricity). The assessement of children quality of life (Auquei) showed 73% of children with an alteration in one or more areas. 69 familial interviews and 39 post-diagnostic consultations were carried out. 14 specific accompaniments were set up for parents with children at the end of life. 34 families were supported in the grief by calls. 57 accompanying persons received individual psychological support. Their families' emotional distress was high (7.8/10 sd = 3.44). Three focus groups were conducted. Regular psychological monitoring was provided for oncopediatric team. The focus groups were very safe spaces, where the team was invited to share their emotions and all the weight generated by the care and/or deaths of patients. The cohesion activity was also a group activity bringing together all team members (oncology and psycho-oncology), the framework was expressly more flexible and even almost playful.
Conclusions: It has also enabled the first multidisciplinary paediatric psycho-oncology team to be set up. Indeed, childhood cancers cause profound psychological upheavals in the child and his or her entourage and are the cause of real systemic changes that must necessarily be considered in a holistic care approach.

EP529 / #468

Topic: *AS05.q Psychosocial (PPO)*

SOCIAL AND COMMUNICATION BEHAVIORS IN PEDIATRIC BRAIN TUMOR SURVIVORS COMPARED TO HEALTHY CONTROLS USING THE AUTISM DIAGNOSTIC OBSERVATION SCHEDULE (ADOS-2) DURING THE COVID-19 PANDEMIC

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Background and Aims: Pediatric brain tumor survivors (PBTSs) experience significant impairments in social competence. Impairments in discrete social behaviors of PBTSs were previously identified using the ADOS-2. Here we compared social behaviors assessed with the ADOS-2 during the Covid-19 pandemic in PBTS and healthy controls (HCs), and examined cognitive and social adjustment correlates.
Methods: PBTSs (at least one year post treatment) and HCs, aged 8-16 years and English speaking, were recruited. Participants completed the ADOS-2, WASI-II (Full Scale IQ), WISC-V's subscales digit span (working memory) and coding (processing speed). Caregivers completed the CBCL. The ADOS-2 is a semi-structured interactive interview to code thirty-two behavior items during social interaction, with higher scores reflecting higher impairment. Recruitment took place during the pandemic (March, 2021-March, 2022). Participants and examiners wore a surgical face mask during all assessments.
Results: 16 PBTSs (mean age 13.24; 56% female) and 16 HCs (mean age 14.8; 75% female) participated. Diagnoses in PBTSs included low-grade glioma, ependymoma, medulloblastoma and germinoma (19% each). Compared to HCs, PBTSs presented with more social problems (p=.03), lower FIQ (p=.07), and lower processing speed (p=.005). ADOS-2 overall scores for PBTS were higher (.08) than for HC (.03) (p=.07) and were correlated with CBCL social problems (r=.41, p=.056), FSIQ (r=-.48; p=.03) and processing speed (r=-.34, p=.11). Items showing higher impairment in PBTSs compared to HCs included: comments on other's emotions (44% vs. 0%), using imagination (44% vs. 19%), insight into social situations/relationships (19% vs. 0%), offering information (19% vs. 6%), conversation (38% vs. 25%), and reciprocal social communication (33% vs. 23%).
Conclusions: Compared to HCs, PBTSs showed impairments in social-communication behaviors, as well as cognitive and social adjustment. These findings bear important implications for understanding social interactions in the context of the pandemic and the development of targeted social skills programs for PBTSs.

EP530 / #619

Topic: *AS05.q Psychosocial (PPO)*

PEDIATRIC PATIENTS CHECK IN: A LOOK AT SELF-REPORTED PSYCHOSOCIAL SYMPTOM INTERFERENCE

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Background and Aims: Youth with serious illnesses often experience medically related emotional and behavioral stressors that can impact quality of life. Routine screening and assessment of psychosocial factors is a well-documented and evidence-based Standard of Care, that can provide opportunities for appropriate referrals. Following a larger study examining feasibility of Checking IN, an e-screening measure, this study describes patient-reported psychosocial symptom interference.
Methods: Pediatric outpatients aged 8-21 and their caregiver completed Checking IN. Participants were receiving outpatient treatment for cancer (66%) or another chronic illness at 1 of 4 hospital centers. Checking IN is a brief and interactive screening measure designed to assess psychosocial symptom interference across the domains of anxiety, depression, anger, attention, body image, sleep disturbance, fatigue, pain, medication adherence, family relationships, peer relationships, faith, and school.
Results: One hundred (100) participants aged 8 to 21 (M=14.27, SD=3.81) completed Checking IN and their caregiver completed the proxy screener. Generally, patients endorsed low level impact ("a little bit" or "sometimes") versus high ("often" or "almost always") of distress domains. The symptoms most frequently endorsed by youths were Fatigue ((Low: n=50, 50%; High: n=21, 21%), Paying Attention (Low: n=45, 45%; High: n=16, 16%), Sleep Difficulty (Low: n=46, 46%; High: n=13; 13%), and Worry (Low: n=46, 46%; High: n=8, 8%). Caregiver proxy responses were concordant with those of youth, evidenced by absence of significant differences between them on any domain.
Conclusions: This study suggests that Checking IN identifies areas of psychosocial distress in youth with serious medical illnesses in the outpatient setting across 4 hospital centers. Symptoms of fatigue, sleep, attention, and worry were endorsed most frequently in these youth with a serious illness, as well as on caregiver proxy report. Use of Checking IN may expand opportunities for providers to appropriately address problematic symptoms of psychosocial distress.

EP531 / #704

Topic: *AS05.q Psychosocial (PPO)*

ADOLESCENT AND YOUNG ADULT (AYA) CANCER SURVIVORS IN SWITZERLAND: FOCUS ON POSSIBLE POSITIVE OUTCOMES

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Background and Aims: Adolescents and young adults (AYAs) are diagnosed with cancer during a unique and challenging period of their life. This experience may result in positive changes called posttraumatic growth (PTG) later on. We aimed to 1) describe PTG and illness perception in Swiss AYA cancer survivors and 2) determine the association between PTG and sociodemographic and cancer-related characteristics as well as illness perception.
Methods: We conducted a population-based questionnaire survey in AYA cancer survivors diagnosed 1990-2005 at age 16-25 years, registered in the Cancer Registry Zurich and Zug, Switzerland, who had survived at least five years. PTG was assessed using the German version of the Posttraumatic Growth Inventory (PTGI), and illness perception using the Brief illness Perception Questionnaire (BIPQ). We further assessed sociodemographic characteristics, while cancer-related information was obtained from the Cancer Registry. Data were analyzed using descriptive statistics and univariable and multivariable linear regressions.
Results: Among 469 eligible survivors, 389 could be contacted, and 160 were included in the analysis (61.3% male; mean age=34 years, SD=5.8). The average PTG score was 54.63 (SD=20.24; range: 8-101) and they reported PTG especially in the scales Appreciation of life (mean=3.23; 95% confidence interval [CI], 3.05-3.40), followed by Personal strength (2.94; 2.77-3.12), Relating to others (2.57; 2.40-2.74), New possibilities (2.35; 2.35-2.54), and Spiritual change (1.46; 1.21-171). Neither sociodemographic nor clinical characteristics were associated with PTG. AYA cancer survivors who perceived follow-up care as helpful ($p<0.001$) and those with high concern about consequences of the illness ($p<0.001$) reported higher PTG.
Conclusions: The majority of Swiss AYA cancer survivors reported to have developed some PTG, and thus experienced some positive outcomes. Finding ways to promote PTG and to identify and address maladaptive illness perceptions throughout the illness course may help survivors transforming their experience of life-threatening disease into something meaningful for their future life.

EP532 / #767

Topic: *AS05.q Psychosocial (PPO)*

PREVALENCE AND CORRELATES OF SUICIDAL IDEATION REPORTED BY CHILDREN AND ADOLESCENTS DURING TREATMENT FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: Physical side effects of childhood acute lymphoblastic leukemia (ALL) therapy are well-described; however, less is known about mental health outcomes. The objectives of this study were to describe the prevalence of suicidal ideation (SI) during ALL therapy and investigates whether SI is influenced by clinical factors or physical symptoms.
Methods: Patients age 7-18 years with newly-diagnosed ALL were recruited from three U.S. childhood cancer treatment centers (2012-2017). The Children's Depressive Inventory (CDI-2) was administered at start of consolidation, delayed intensification (DI), maintenance cycle 1 (MC1), and maintenance cycle 2 (MC2). SI was considered present if patients endorsed the "I want to kill myself" item. Logistic regression models evaluated associations between SI and sociodemographic factors; depressive symptoms; and symptom clusters identified using latent class analysis (LCA) of patient-reported pain, nausea, fatigue, and sleep also assessed at the start of each phase of therapy.
Results: Participants (n=175) were 51% male, 75% high-/very high-risk, with a median age of 11.2 years at diagnosis. LCA identified three symptom clusters characterized by individuals with a below average (n=49), average (n=82), and above average (n=44) symptom burden throughout treatment. Overall, 26 patients (14.9%) endorsed SI at least once during treatment, including 4% at consolidation, 9% at DI, 8% at MC1, and 4% at MC2. In adjusted models, non-Hispanic others were 10.9-times more likely than non-Hispanic whites to endorse SI (p=0.003). The frequency of SI was also higher in patients reporting above average symptoms (53.3%) than those with below average symptom severity (4.1%, p=0.003). Depressive symptoms were consistently associated with SI.
Conclusions: SI occurring during the initial year childhood ALL therapy is associated with increased physical symptom severity, depressive symptoms and certain sociodemographic features. Findings highlight the need for improved screening of mental health problems to mitigate or alleviate symptoms of distress in this at-risk population.

EP533 / #114

Topic: *AS05.q Psychosocial (PPO)*

INFLUENCE OF ETHNICITY AND PARENTS' EATING HABITS ON DIET QUALITY IN PEDIATRIC CANCER SURVIVORS

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Background and Aims: Pediatric cancer survivors (PCS) exhibit poor adherence to dietary guidelines and have an increased risk of obesity and endocrine complications. As family and culture play important roles in shaping children's eating behaviors, research is needed to investigate the impact of these factors on children's diet quality to tailor nutrition interventions for PCS. The aims of this study were to examine associations in diet quality (1) between Hispanic vs. non-Hispanic PCS and (2) between PCS and their parents.
Methods: This is a cross-sectional analysis of data collected from 46 PCS with overweight/obesity (off treatment for ≥ 6 months; mean age 10 years; 40% Hispanic) and their parents. Participants completed a 1-day 24-hour dietary recall. The Healthy Eating Index-2015 (HEI-2015) was calculated to assess diet quality. T-tests were performed to examine differences in HEI overall and component scores between Hispanic vs. non-Hispanic PCS, and associations in HEI scores between parents and PCS were examined with Pearson correlations.
Results: The mean HEI score was 50.2 for children and 51.9 for parents out of 100. Ethnicity was not associated with overall HEI score, but Hispanic PCS had significantly lower total vegetable and fatty acid scores ($p=0.02$) compared to non-Hispanic PCS. Significant correlation was found between child and parent overall HEI scores ($r=0.56$, $p<0.0001$). Children's and parents' component scores were correlated for added sugar ($r=0.45$, $p=0.005$), sodium ($r=0.42$, $p=0.005$), greens and beans ($r=0.33$, $p=0.02$), whole grains ($r=0.39$, $p=0.007$), and fatty acids ($r=0.31$, $p=0.04$). Other findings were not significant.
Conclusions: Findings indicated poor diet quality scores in PCS with overweight/obesity and their parents. Significantly high correlations between parent and child diet quality justifies using parents as change agents in nutrition interventions for PCS. Cultural factors and parent role modeling should be considered in future interventions to promote healthy eating in this population.

EP534 / #1429

Topic: *AS05.q Psychosocial (PPO)*

BEHAVIOURAL AND PSYCHOLOGICAL EFFECTS OF CHILDHOOD SOLID MALIGNANT TUMORS AND ITS MANAGEMENT

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Background and Aims: A large number of survivors of paediatric solid tumours experience significant disease or treatment related sequelae. These adverse health outcomes can be both physiological, psychological, and behavioural. The aim of the present study was to assess the long-term psychological and behavioural effects faced by the survivors of solid malignant tumours.
Methods: Survivors were assessed for behavioural problems with help of Child Behaviour Checklist (6-18 years). They were also screened for post-traumatic stress disorder (PTSD) with the help of Children Impact of Event Scale (CRIES-13).
Results: Seventy-nine survivors with a median age of 10 years (6-18 years) were included. There were 57 males (72.15%) and 22 females (27.85%). The evaluation was done at a median age of 5 years (2 to 13 years) after treatment completion and the median age of time since diagnosis was 6 years (2 to 16 years). One or more behavioural problems were found in 35 (44.30%) patients. Out of these 35 patients, parents of 23 (65.71%) patients had an awareness prior to the assessment that their child has some behavioural issue(s). Internalizing problems were found in 10/79 (12.66%) patients (attention problems (n=12, 15.18%), anxiety issues (n=3, 3.79%) and depression (n=2, 6.32%). Externalizing problems were found in 19 (24.05%) patients (conduct problems (n=12, 15.18%) and oppositional-defiant behaviour (n=2, 2.53%)). Gender and time since treatment completion & evaluation had no significant effect on the patient having internalizing and externalizing problems. PTSD was screened in 8/79 (10.12%) patients while taking cancer as the event of trauma.
Conclusions: About half (44.30%) of the childhood cancer survivors experience significant long-term behavioural and psychological consequences. Because psychological health is a significant factor in person's quality of life, survivors must be closely monitored for co-morbid behavioural and psychological consequences.

EP535 / #1005

Topic: *AS05.q Psychosocial (PPO)*

MINDFULNESS AND INTERNALIZING SYMPTOMS AS PREDICTORS OF FEAR OF RECURRENCE IN CAREGIVERS OF PEDIATRIC CANCER SURVIVORS

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Background and Aims: Despite being common, caregiver fears of their child's cancer recurrence (FCR) after the transition off treatment (TOT) are associated with negative health outcomes. Patient demographic and medical factors have been linked to FCR, yet little is understood about modifiable psychological mechanisms that may be linked to FCR in caregivers. The goal of this research was to explore psychological risk (e.g., anxiety, depression) and protective factors (e.g., mindfulness) associated with FCR at TOT.
Methods: Participants were 84 caregivers (M_{age}=41.18, SD_{age}=8.01, 90.7% mothers, 72% white) recruited from a pediatric oncology outpatient clinic as part of a study examining psychosocial factors associated with TOT among pediatric cancer survivors and their caregivers. Caregivers completed the four-item versions of the PROMIS Anxiety and Depression scales. FCR was examined via three items from the Pediatric Quality of Life – Cancer Module. Mindfulness was examined via the Five Facets of Mindfulness Questionnaire. Regression analyses were used to explore associations between FCR with caregiver internalizing symptoms and mindfulness, while controlling for relevant demographic and medical variables. Non-significant variables were removed from the final models.
Results: Demographic and medical variables were not significantly associated with FCR and were removed from the model. Model two included depression, anxiety, and mindfulness as predictors of FCR and was significant (R^2=.375, F(3,80)=16.032, p<.001). Mindfulness was negatively associated with FCR (b=-.045, p<.05), and anxiety was positively associated with FCR (b=.518, p<.001). When exploring similar models with FCR predicting depression and anxiety, the models were non-significant.
Conclusions: Elevated anxiety, but not depression, was significantly associated with FCR, but the reverse was not true (FCR predicting anxiety). This suggests interventions targeting caregiver anxiety at TOT may be of benefit in reducing FCR. Interventions that focus on building mindfulness skills may also serve to reduce FCR. These will be important avenues to explore in future research.

EP536 / #691

Topic: *AS05.q Psychosocial (PPO)*

THE BALINT GROUP AS A RESOURCE FOR EMOTIONAL CARE IN A PAEDIATRIC ONCOLOGY UNIT OF A TERTIARY HOSPITAL

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Background and Aims: Working in Paediatric Oncology entails high emotional demands and daily exposure to intense affective burden for which it is not easy to cope with. This paper describes and evaluates the operation of a Balint Group as an emotional protection factor, provider of emotional coping resources, and generator of psychosocial well-being in the professionals.
Methods: We evaluated the functioning of a Balint Group in Paediatric Oncology of the Cruces University Hospital through the observation of the topics addressed in sessions and the analysis of a questionnaire filled out by the participants. The group began in 2019 with 17 participants (doctors, nurses, psychologists and a psychiatrist leading the group) who meet weekly. Every session a participant raises emotional difficulties related to his work and all together try to understand such difficulties, overcome them and learn how to cope with them.
Results: The most frequently addressed topics have been team's communication, personal involvement at work, relational difficulties with families, bereavement coping, adequacy of the diagnosis information and emotional support of patients. Those that have been of most interest have to do with team's communication and management of complex relational situations with families. Participants significantly value being able to share and understand feelings or experiences derived from work, as well as feeling supported and understood by the group. There is evidence of an improvement in greater personal and group care, understanding and support in emotional issues, and better ability to express concerns.
Conclusions: The Balint Group is serving as support for health professionals as a space to share concerns, as an engine of communication and group cohesion, as a facilitator of the understanding of the emotional universe, and as a promoter of better care of patients and families. The participants recommend this resource and wish to continue participating considering that it is a medium and long-term aid resource.

EP537 / #581

Topic: *AS05.q Psychosocial (PPO)*

THE NEEDS OF FAMILIIES DURING THE 1ST MONTH AFTER THEIR CHILD IS DIAGNOSED WITH CANCER

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Background and Aims: Through World Child Cancer's psychosocial support work, we strive to improve quality of life and wellbeing for families and to reduce treatment abandonment. We provide financial support to families, along with emotional, practical, and educational support. Previous studies have shown that treatment abandonment mainly happen in the first few weeks or months after a child in a low and middle-income country, is diagnosed with cancer. Following these previous studies, we used the results of a psychosocial support survey to analyse the needs of families during this initial stage after diagnosis.
Methods: A semi-structured beneficiary feedback survey was used. The survey focused on 5 key areas: About you, Quality, Impact, Future improvements, Support provided by nursing team. The survey was conducted at different stages of treatment: within 1st month of diagnosis, currently receiving treatment, recently finished treatment, and post treatment. For the purpose of this research, we analysed data from families who were within the 1st month after diagnosis.
Results: Of the 115 surveys completed in 2021, 17% were completed by families in the 1st month of their child's treatment. Respondents were asked, 'How important was the financial support you received in being able to treat your child?' The majority (90%) responded 'Critical - without it, we would never have been able to treat our child'. When asked 'What was the most important type of support you received?' 65% said financial support for drugs and diagnostic and 25% said financial support for transport costs. 95% of respondents said they would have liked access to a professional to talk to, about how they were feeling.
Conclusions: The survey highlights the critical needs of families during the first month after their child was diagnosed and the importance of financial and psychosocial support being available for families, in order for them to continue with their child's treatment.

EP538 / #1274

Topic: *AS05.q Psychosocial (PPO)*

UNDERSTANDING AND IMPROVING FEEDING AND EATING PRACTICES IN CHILDREN WITH CANCER IN INDIA: DEVELOPING A MANUALIZED PSYCHOLOGICAL FAMILY INTERVENTION

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Background and Aims: Paediatric cancers affect up to 400,000 children yearly worldwide(WHO, 2021). Almost half of the paediatric patients undergoing cancer treatment experience malnutrition(Bauer et al., 2011). In low- and middle income(LAMI) countries this number is estimated to be even as high as 59%(Sharma et al., 2015). It is therefore important to improve the nutritional status of patients throughout cancer treatment as malnutrition negatively affects disease related outcomes(Sala et al., 2004). The aim of the current study was therefore to better understand factors affecting feeding and eating practices during paediatric cancer treatment.
Methods: Nurses, doctors, nutritionists, mental-health-care professionals, parents, and children(n=46) in a paediatric cancer hospital in India were asked to provide inputs on feeding and eating related challenges and strategies using both qualitative focus group interviews and quantitative questionnaires.
Results: In all six groups(n=46),feeding and eating related strategies and challenges could be categorized into being cognitive, behavioural, parental, or nutritional factors. Children were capable of identifying what works for them and wanted to be included in decisions around feeding and eating. Parents could benefit from psychoeducation about cancer and all aspects of its treatment as misconceptions around feeding, eating and nutrition were common. Time pressure and patient volumes often did not allow medical teams to focus on eating practices with parents and children as disease and treatment was a priority. Instead, nurses and nutritionists could play a central role here, as they spend most time caring for patients, and have experience with feeding and eating. General mental health professionals could also play a role, but may need additional training in dealing with this specific patient population.
Conclusions: Including various stakeholders in designing psychological interventions in LAMI countries is practically challenging yet relevant and necessary.Information from phase 1 will further be used to design and test a new manualized psychological family to address FEP’s in India.

EP539 / #1683

Topic: *AS05.q Psychosocial (PPO)*

SOCIAL SUPPORT TO DECREASE ABANDONMENT RATE IN LMICS : EXPERIENCE OF MY CHILD MATTERS PROGRAM IN THE GFAOP PEDIATRIC UNIT IN SENEGAL

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Background and Aims: Pediatric oncology services are very costly for low and middle income countries(LMICS). The pediatric oncology unit(UOP) in Dakar, Senegal, receives approximately 200 new cases yearly. The major contributors to treatment failure are poverty, lack of social insurance, and abandonment. In order to promote early diagnosis, rapid initiation of treatment and reduce abandonment, My Child Matters(MCM) program of the Sanofi Espoir Foundation has been supporting the UOP since 2007. We describe the social support from June 2020 to December 2021 and its impact.
Methods: Monthly financial support was given to families by the social worker for biological and radiological exams, chemotherapy adjuvants and transportation costs. A total amount of 37591,46 euros allowed the implementation of the program. Data were collected from the social worker register, and GFAOP-Registry.
Results: During the period, 369 children were supported. The mean age was 6.8 years. The most common cancers were leukemia (26%), nephroblastoma (21%), retinoblastoma (6%), Burkitt lymphoma (6%), Hodgkin lymphoma (4%). 75% of patients lived outside of Dakar, where the UOP is located. The average distance from the UOP was 200 kilometers, 43% of families had no accommodation during treatment. The socio-economic level was low in 80%, fathers being involved in informal activities with irregular income. 82% of mothers were unemployed, and 90% of the families had no medical insurance. Financial support for adjuvant chemotherapy was preponderant, followed by biological, radiological exams and transportation. Abandonment decrease from 20.3% in 2018 to 2.7% in December 2021.
Conclusions: MCM social support of Sanofi Espoir Foundation showed its effectiveness. It demonstrated that strong political willingness and sustainable funding initiatives are needed for better management of children with cancer, and their families, in Senegal.

EP540 / #1736

Topic: *AS05.q Psychosocial (PPO)*

BEREAVED PARENTS' PERSPECTIVE ON COMMUNICATION OF TRANSITION TO PALLIATIVE CARE IN PEDIATRIC ONCOLOGY - HUNGARIAN EXPERIENCE

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Background and Aims: Transition to palliative care (PC) is a critical aspect of pediatric oncology requiring a high level of communication skills from doctors, which could be best judged by parents of children died in cancer. Our aim was to explore parents' perspectives regarding the timing of the consultation on implementing PC, as well as facets of verbal and non-verbal communication in Hungary.
Methods: Semi-structured interviews were conducted with parents who had lost their child to cancer within the past 1-5 years. Interview transcripts (n=23) were scrutinized with Interpretative Phenomenological Analysis.
Results: Parents frequently associated palliation with end-of-life care and clearly delimited the transition to PC after curative treatments had been exhausted. Parents were ambivalent regarding using the word "death" during this consultation and often did not receive information on what to expect (e.g., regarding symptoms) and who to turn to for further information or support (e.g., concerning bereavement).
Conclusions: Although significant progress could be observed in the organization of pediatric palliative care in Hungary, there is still no widely accepted communication method for communication of transition to sole PC. There is a need for a culturally-sensitive approach to refining recommendations on word-use and communication protocol in pediatric PC also in Hungary.

EP541 / #1985

Topic: *AS05.q Psychosocial (PPO)*

DEVELOPMENT OF A CULTURALLY ADAPTED INTERVENTION TO IMPROVE QUALITY OF LIFE IN SPANISH-SPEAKING FAMILIES IMPACTED BY CHILDHOOD CANCER

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Background and Aims: Caregivers of children with cancer experience significant psychological distress and cancer-health disparities experienced by marginalized populations further exacerbate disparities among children with cancer and their caregivers. Efforts to reduce health disparities have illuminated the need to unite researchers with communities in the development and utilization of culturally relevant and appropriate health care interventions. Participatory research approaches, such as community-based participatory research (CBPR) methods can meet needs for patient-centered methodological approaches that engage patients in healthcare improvement and decision-making. The purpose of the present study is to describe the use of CBPR to develop a culturally adapted intervention to improve quality of life in Spanish-speaking families impacted by childhood cancer.
Methods: Two community advisory boards (CABs) were formed, including a group of n = 6 Spanish-speaking parents of children who had completed cancer treatment and a group of n = 5 Spanish-speaking parents whose children had begun treatment for cancer in the previous 16 weeks. Following CBPR principles, multiple meetings with the CABs and academic researchers were held over a period of four years. All meetings were audio recorded and transcribed to identify barriers to optimal quality of life during cancer treatment in the target community as well as culturally-informed intervention components that would ameliorate disparities in psychosocial outcomes in Spanish-language families
Results: Four domains of barriers were identified that impacted treatment experience and cancer health outcomes: healthcare system, healthcare providers, family, and parent/caregiver. A twelve-session family-focused intervention was developed that included three targets: health literacy, culturally competent care, and caregiver wellness. Specific intervention components included complementary and alternative medicine, psychoeducation, fitness, gardening, culinary medicine, and multiple strategies to improve health literacy
Conclusions: The use of CBPR is an effective approach to develop culturally relevant interventions that may reduce cancer health disparities in Spanish-language families impacted by childhood cancer.

EP542 / #203

Topic: *AS05.q Psychosocial (PPO)*

UNDERSTANDING THE INFLUENCES OF HCP-PATIENT INTERACTIONS IN CANCER CARE FOR LGBTQ+ CHILDREN AND YOUNG PEOPLE

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Background and Aims: The lesbian, gay, bisexual, transgender, queer or questioning (LGBTQ+) population experience inequalities throughout the continuum of cancer care. These are compounded for children, adolescents and young adults who may be at a critical time for exploring their gender identity and sexual orientation, as well as facing a cancer diagnosis. Previous studies have examined knowledge, attitudes and behaviours of oncologists treating LGBTQ+ adults and how these might contribute to those inequalities. However, there is limited research on those treating LGBTQ+ children and adolescents with cancer. We investigated knowledge, attitudes and behaviours of paediatric, teenage and young adult oncology healthcare professionals (HCPs) treating and supporting LGBTQ+ patients in the UK with the aim of identifying ways to improve care for this group.
Methods: We carried out semi-structed interviews with HCPs in paediatric, teenage and young adult oncology at a UK specialist cancer centre. Questions centred around participants' knowledge, attitudes and behaviours regarding management of LGBTQ+ patients in oncology. Interview transcripts were analysed by inductive thematic analysis.
Results: We identified 13 themes and subthemes, of which 12 were mapped to a new framework for improving HCP-patient interactions in LGBTQ+ Cancer Care. This framework highlights the cyclical nature of knowledge acquisition, attitude shifts and behavioural change. We identified needs around cultural and organisational change and individual HCP education. As an enabler of tailored care, disclosure of identity was a major theme and we identified multiple barriers to, and facilitators of, HCP enquiry and patient disclosure.
Conclusions: Knowledge, attitudes and behaviours of HCPs are interdependent. Our framework, with a particular focus on disclosure, can be used to support HCP education and organisational change. The resulting increase in disclosure and provision of tailored care has the potential to improve the patient experiences, engagement with healthcare and later outcomes for LGBTQ+ young people with cancer.

EP543 / #19

Topic: *AS05.q Psychosocial (PPO)*

PARENTS' AND PATIENTS' UNDERSTANDING OF A PRECISION MEDICINE TRIAL FOR HIGH-RISK CHILDHOOD CANCER

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Background and Aims: Precision medicine is projected to become the mainstay of childhood cancer care. As such, it is essential that we develop resources to support patients' and families' understanding. We aimed to explore patients' and families' information needs, and potential gaps for intervention.
Methods: One-hundred-and-eighty-two parents and 23 adolescent patients participated in a psychosocial sub-study to PRISM, an Australian precision medicine clinical trial for children with high-risk cancer, completing questionnaires after study enrolment (Time 0, T0). Parents also completed a questionnaire and an interview following return of their child's precision medicine results (Time 1, T1). We used validated measures and purpose-designed items to explore families' perceptions of the PRISM participant information sheet and consent form (PISCF), understanding of the information, and factors associated with understanding.
Results: Most parents were satisfied with the PISCF information, saying it was at least somewhat clearly presented (n=160/175, 91%) and informative (n=158/175, 90%). Many parents expressed a desire for additional information presented in a more accessible and visually engaging format. On average, parents' actual understanding scores increased between T0 and T1 (55.8/100 to 60.0/100, p=0.012). At T0, parents from culturally and linguistically diverse backgrounds (n=42/177, 25%) had lower actual understanding scores (p=0.010). Parents' perceived and actual understanding scores were not associated (p=0.794). Most adolescent patients read the study information sheet either 'briefly' or 'not at all' (n=16/23; 70%) and on average had a perceived understanding score of 63.6/100 (n=23, SD=21.7).
Conclusions: Our research reinforces the challenge of communicating complex information to families about precision medicine for childhood cancer. Our findings have informed the development of animated videos which explain childhood cancer precision medicine processes and convey key themes of parents' experiences of the journey.

EP544 / #1344

Topic: *AS05.q Psychosocial (PPO)*

PSYCHOSOCIAL ISSUES, COPING STRATEGIES AND PSYCHIATRIC DISORDERS IN ADOLESCENT CANCER PATIENTS REFERRED TO PSYCHO-ONCOLOGY SERVICES: AN OBSERVATIONAL STUDY IN A LOW MIDDLE INCOME COUNTRY

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Background and Aims: Diagnosis of cancer and treatment both are challenging for adolescent cancer patients. Adolescent patients cognition, knowledge and awareness differ from young children and adults, resulting in different coping strategies. There are few reports of psychosocial concerns and coping strategies in adolescent cancer patients in low resource settings. Our study aims to determine psychosocial problems, coping strategies and psychiatric disorders in adolescent cancer patients referred to a specialist Psycho-oncology service in a metropolitan tertiary cancer hospital in a low middle income country.
Methods: We conducted a retrospective analysis of psycho-oncology case records of adolescents with cancer referred to Psycho-Oncology services from Jan 2019 to Dec 2021. Patients on best supportive care alone and incomplete documentation were excluded. We noted sociodemography, cancer diagnosis and psychosocial problems according to clinical interview and mental status examination as documented in psycho-oncology assessment records. Coping strategies were documented according to Brief COPE. Psychiatric diagnosis was done using International Classification of Disease-10.
Results: A total of 194 adolescents with cancer were included in the analysis of whom 128 (66%) were male and. 106 (55%) were outpatients. Almost half the patients had solid tumours (bone and brain). The most common issues reported were distress, physical 140 (72%) and emotional 111 (57%). 154 (79%) were aware of their diagnosis. Adolescents used various coping strategies 168 (86%) of the used active coping and 130 (67%) coped by seeking emotional/instrumental support. A psychiatric diagnosis of adjustment disorder was present only in 41 (21%), situational distress in 21%, emotional and behavioural disorder in (12%) and delirium in 11(6%) of the patients.
Conclusions: There is a need for evidence-based, age appropriate interventions to address the psychological issues to enhance coping strategies and mental health of adolescent cancer patients. Limitations Small sample size, group with heterogeneous diagnosis. Lack of standard measures due to diversity of language and culture.

EP545 / #1745

Topic: *AS05.q Psychosocial (PPO)*

DETERMINANTS OF QUALITY PATIENT-CENTERED COMMUNICATION IN PAKISTAN

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Background and Aims: Communication is a fundamental aspect of patient- and family-centered care. Unfortunately, there is a dearth of evidence regarding pediatric cancer communication in low- and middle-income countries, where approximately 80% of all children with childhood cancer live. The purpose of this study was to explore determinants of quality communication within two pediatric cancer centers in Pakistan.
Methods: Semi-structured interviews were conducted with 20 multidisciplinary pediatric cancer clinicians at Children's Hospital of Lahore and Indus Hospital in Pakistan. Interviews were conducted in English or Urdu and audio recorded. All interviews were transcribed, with simultaneous translation to English as necessary. Two independent coders used inductively derived codes to code each transcript. Thematic content analysis focused on barriers and facilitators of high-quality communication.
Results: Pakistani clinicians identified factors that affected the quality of patient-centered cancer communication. These included characteristics related to the clinician such as communication training, clinician distress, and the availability to have recurrent conversations. Patient or family characteristics impacting communication included education, literacy level, income status, geography, language, social support systems, and empowerment. Finally, factors related to the institution including setting, available interpreters, documentation, patient volume, and teamwork, affected communication. Clinicians perceived certain determinants, such as patient volume or the income status of a family, as immutable. Other determinants, including clinician communication training or interpreter services, provided opportunities for improvement.
Conclusions: Multilevel factors serve as either barriers or facilitators for pediatric cancer communication in Pakistan. Identification of these determinants of communication is an essential step toward interventions aimed at improving patient and family-centered care in resource limited settings.

EP546 / #568

Topic: *AS05.q Psychosocial (PPO)*

FATIGUE MEDIATES THE RELATIONSHIP BETWEEN EMOTIONAL AND COGNITIVE FUNCTIONING IN CHILDREN POST-CANCER TREATMENT

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Background and Aims: Children treated for cancer are at risk to develop health-related quality of life problems, including cognitive problems. To allow optimizing of interventions, underlying associations with other domains such as emotional functioning and fatigue need to be clarified. We therefore aim to study emotional functioning, fatigue and cognitive functioning in children post-cancer treatment and investigate whether fatigue mediates the relationship between emotional and cognitive functioning.
Methods: Children aged 8-18 years who were post-cancer treatment filled out questionnaires to measure emotional functioning, fatigue and cognitive functioning using subscales of the Pediatric Quality of Life Inventory (PedsQL) generic core scales and PedsQL multidimensional fatigue scale. Student's t-test was used to compare with peers of the general population and mediation analysis to address the effect of fatigue on the relationship between emotional and cognitive functioning. Moderation of relapse of the primary tumor and tumor type (central nervous system tumor/other) was evaluated. The mediation model was adjusted for sex, age, relapse, tumor type and sleep if they were relevant confounders.
Results: A total of 137 children (62.4%, mean age: 13.6, SD +/- 3.3 years) participated. Lower scores on emotional functioning (Cohen's d [D]: 0.4), fatigue (D: 0.8) and cognitive functioning (D: 0.6) were found ($P < 0.001$) in children post-cancer treatment. A medium association was found between emotional and cognitive functioning (standardized regression coefficient [β]: 0.27, $P < 0.001$), which was fully mediated by fatigue ($\beta = 0.16$), in a model adjusted for sleep. No significant moderation effect on the model was found.
Conclusions: Outcomes on emotional and cognitive functioning are decreased and fatigue is increased in children post-cancer treatment. Fatigue mediates the relationship between emotional and cognitive functioning. Our results underscore the need to include monitoring and intervening on fatigue in clinical interventions to improve cognitive functioning.

EP547 / #1840

Topic: *AS05.q Psychosocial (PPO)*

STUDY ON THE EMOTIONAL RESPONSE TO MUSIC THERAPY IN ONCOLOGY AND INTENSIVE CARE PEDIATRIC UNITS

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Background and Aims: The objective of music therapy in pediatrics is to promote the humanization of hospital health care and help in adaptation to illness on admission. This study evaluate the emotional response of pediatrics patient to music therapy, taking into account the variables of valence (joy), activation, relaxation and dominance (feeling of self-control).
Methods: Patients (77), up to 16 years of age, admitted to pediatric oncology units and pediatric intensive care unit of Son Espases Hospital (Palma). Quasi-experimental, longitudinal, intrasubject design, with one pre-session music therapy measure and two post-session measures. The self-assessment Manikin (SAM) scale of measurement of emotional variables is completed before, after the session and 3 hours after. Trait anxiety is measured with the STAI or STAIC questionnaires to check if its values influence the results of the session. The groups are analyzed by age (0-8 years and 9-16 years) and type of unit. Questionnaire on satisfaction and usefulness of the session were completed by families.
Results: Music therapy has an influence with an increase in valence, dominance and activation, between the moments before and after the session ($p \leq 0.001$) in both age groups and, in the case of relaxation, $p = 0.041$ for the group of younger patients and $p = 0.011$ for the older ones. The feeling of relaxation is maintained 3 hours after the session with $p = 0.382$, in the case of children < 9y ($p = 0.343$), in > 8y. It is considered a positive and useful intervention by users .
Conclusions: Music therapy has effects on the emotional variables studied increasing self-control of pediatric patients and places them at the center of treatment. The relaxation variable remains the longest in time after the session. Music therapy could be a complementary therapy to provide resources to cope with disease in pediatric cancer patients and in intensive care units

EP548 / #1026

Topic: *AS05.q Psychosocial (PPO)*

AN EXPLORATION OF THE EMOTIONAL SUPPORT NEEDS OF GRANDPARENTS WHOSE GRANDCHILD HAS HAD A CHILDHOOD CANCER DIAGNOSIS

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Background and Aims: Wakefield et al. (2014) note that little research has been conducted on the psychological impact on grandparents of children with cancer despite evidence to suggest that this can be challenging. This research explores the lived experiences of grandparents whose grandchild has had a childhood cancer diagnosis, taking specific interest in narrative relating to symptoms of distress, coping mechanisms, perceived emotional support needs, potential barriers to support and signs of post-traumatic growth. The impact of COVID-19 is also explored.
Methods: Twelve grandparents were interviewed using a qualitative methodology that focuses on hermeneutic phenomenology. Semi-structured questions were asked. Interviews were transcribed verbatim and analysed using Interpretative Phenomenological Analysis, an approach that is understood via examination of meanings people impress upon their experience. Group experiential themes and sub themes are presented.
Results: Grandparents, without question, resume their parental role as their adult children retreat towards their childhood 'nest' to be protected and cared for. They also change their 'hat' to that of 'parent' to siblings of their poorly grandchild. This becomes a dominant role, often without warning, impacting greatly on their normal routine. Their own suffering is intentionally suppressed to give full attention to their child and family. Grandparents struggle to articulate their own needs as they automatically place themselves second, however, when pushed, there is a sense of wishing to be acknowledged as taking an active, primary care-giving role within their family, together with permission to process their own emotions in a way that suits their needs.
Conclusions: A grandchild's childhood cancer diagnosis can lead to signs of traumatic stress for grandparents, yet they suppress their emotional support needs as their 'parental nest' is temporarily filled again. It is suggested that cancer support services work with parents to ensure that grandparents are also included in support-offers as a matter of course.

EP549 / #1240

Topic: *AS05.q Psychosocial (PPO)*

SCREENING FOR MENTAL HEALTH PROBLEMS IN CHILDHOOD CANCER SURVIVORSHIP: A SYSTEMATIC REVIEW

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Background and Aims: A childhood cancer diagnosis can be followed by severe psychological sequalae. This is why annual psychological evaluations and continuous monitoring is recommended for childhood cancer survivors. However, these recommendations are rarely implemented in clinical practice. Reasons are: lack of institutional resources, health professionals' uncertainty in dealing with mental health problems or their unfamiliarity with available screening tools. We aimed to systematically review the evidence on screening for mental health problems in childhood cancer survivors: a) which screening instruments should be used, b) by whom screening should ideally be conducted, and c) what time frame is recommended.
Methods: The databases PubMed, PsycINFO, and CINAHL were systematically searched for publications concerning childhood cancer, mental health problems, survivorship and screening. The search yielded 1729 potentially relevant articles, out of which 24 were included in the narrative data analysis.
Results: We found a wide variety of common (e.g., the Distress Thermometer) and newly developed screening tools for psychological distress, depression, expressed suicidal ideation or behavior, attention deficit hyperactivity disorder, and post-traumatic stress disorder recommended for screening. Depending on the age of the survivor, type of cancer, and mental health area, it can be advantageous to involve caregivers, teachers, medical professionals, but also research staff in the screening process in addition to self-report. Most tools are designed for regular use, with many aiming to detect mental health problems as early as possible.
Conclusions: Contrary to the described obstacles, most tools can be easily administered and evaluated without training and take only a few minutes to complete. The overview of screening tools for various mental health problems hopefully helps facilitating the transition from recommendations to practice.

EP550 / #1293

Topic: *AS05.q Psychosocial (PPO)*

(NEURO)COGNITIVE CHILD DEVELOPMENT AT 9 YEARS AFTER PRENATAL EXPOSURE TO MATERNAL CANCER AND ITS TREATMENT: REPORT BY THE INTERNATIONAL NETWORK ON CANCER, INFERTILITY AND PREGNANCY.

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Background and Aims: Limited evidence exists on the long-term effects of prenatal exposure to maternal cancer and its treatment on the (neurocognitive) development of the offspring. The aim of the current study was to determine the impact of this antenatal exposure on children at the age of nine years.
Methods: In an international, multicentre (n=5) cohort study (Belgium, the Netherlands, Italy, USA) children were prospectively assessed using a comprehensive neuropsychological battery, examining intelligence (IQ), attention and memory. Behaviour was assessed using parental behavioural questionnaires. Results were compared with test-specific normative data by country and age using ANCOVA. Sub-analyses with gestational age at birth were performed using linear regression. Children with and without a deceased mother were compared using independent-samples t-tests.
Results: Overall, 142 children (mean age, 9.2 years; range, 7.8 to 10.6 years) were included. During pregnancy, 100 children (70.4%) were exposed to chemotherapy (only or in combination with other treatments), 18 (12.7%) to surgery only, 17 (12.0%) to radiotherapy (only or in combination), 16 (11.3%) to no treatment and 1 to trastuzumab (0.7%). No significant differences in intelligence, attention, memory, and behavioural outcomes were found. Gestational age at birth predicted Total IQ ($F(1,135)=12.075$, $p<0.001$, $R^2=0.083$), Verbal IQ ($F(1,135)=9.665$, $p=0.002$, $R^2=0.067$), Performance IQ ($F(1,125)=6.814$, $p=0.010$, $R^2=0.052$), Verbal Memory Span ($F(1,123)=11.888$, $p<0.001$, $R^2=0.089$), Verbal Working Memory ($F(1,64)=6.654$, $p=0.012$, $R^2=0.096$), and Visual Memory Span ($F(1,122)=5.217$, $p=0.024$, $R^2=0.041$). Children with a deceased mother obtained lower scores on Total IQ ($t(134)=1.892$, $p=0.030$), Processing Speed ($t(124)=1.712$, $p=0.045$) and Visual Memory Span ($t(121)=2.861$, $p=0.002$).
Conclusions: Children born after a pregnancy complicated by maternal cancer seem to have a normal neurocognitive development at the age of 9 years. These are reassuring results. However, caution is indicated and surveillance of the neurocognitive development is needed in children born preterm and in children whose mothers are deceased due to her disease.

EP551 / #1544

Topic: *AS05.q Psychosocial (PPO)*

HEALTH-RELATED QUALITY OF LIFE OF INDONESIAN CHILDREN WITH SOLID TUMORS

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Background and Aims: Advances in childhood cancer treatment have improved survival rates in low and middle-income countries (LMIC), such as Indonesia, in recent years. However, not only curing children with cancer, but also ensuring a good health-related quality of life (HRQOL) during treatment is of utmost importance. Particularly because childhood cancer treatment can be aggressive and adversely affect children's well-being due to side-effects. Few studies focused on HRQOL in LMIC, where supportive care is limited. About 30% of all childhood cancers consist of solid tumors. This study aims to investigate HRQOL among children with solid tumors in Indonesia.
Methods: A cross-sectional study was conducted among children with solid tumors in Dr. Sardjito General Hospital, Indonesia. The HRQOL data were obtained from patients and their guardians using Pediatric Quality of Life Inventory™ (PedsQL™) 4.0 Generic Core Scale and Pediatric Quality of Life Inventory™ (PedsQL™) 3.0 Cancer Module (Indonesian version).
Results: Sixteen children aged 5-18 years and 41 guardians of children aged 2-18 years participated in this study. Twenty-six (63%) children were boys. Of all children, 9 children (22%) were diagnosed with nephroblastoma, 8 children (20%) with neuroblastoma, 6 (15%) with retinoblastoma, and 18 (44%) with other solid tumors. In PedsQL™ 4.0 Generic Core Scale, children reported worse total HRQOL-scores than parents (66 vs. 72). By contrast, in PedsQL™ 3.0 Cancer Module, parents and children reported equal total HRQOL-scores (80 vs. 80). Procedural anxiety had the worst score of all subscales for both groups (58 vs. 70). Although not statistically significant, parents of boys reported worse total HRQOL-scores than girls.
Conclusions: Indonesian children with solid tumors had most problems in procedural anxiety. To improve HRQOL during cancer treatment, special attention and care is required during intervention procedures to reduce stress and improve coping of these children.

EP552 / #76

Topic: *AS05.q Psychosocial (PPO)*

FATIGUE TRAJECTORIES DURING PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA THERAPY IS ASSOCIATED WITH FATIGUE AFTER TREATMENT: A DUTCH NATIONAL LONGITUDINAL COHORT STUDY

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Background and Aims: Fatigue is one of the most prevalent and distressing symptoms reported by survivors of childhood cancer. There is currently a lack of longitudinal studies on cancer-related fatigue, and especially on the relationship between the course of fatigue during treatment and fatigue at follow-up. The aim of the current study was therefore to investigate if the course of fatigue during treatment, treatment intensity, serious adverse events, sex, or age at diagnosis are associated with cancer-related fatigue after treatment.
Methods: Participants were 92 children and adolescents diagnosed with acute lymphoblastic leukemia (mean age at diagnosis was 6.26 years). Fatigue was measured with PedsQL Multidimensional Fatigue Scale proxy-reports 5 months after diagnosis, 12 months after diagnosis, 24 months after diagnosis, and at follow-up 12 months after end of treatment. The course of fatigue was defined as the fatigue reported during treatment. The effect of patient and treatment characteristics on the fatigue reported at follow-up was tested through logistic regression analyses.
Results: At follow-up, 26% reported general fatigue, 16% sleep-rest fatigue, and 22% cognitive fatigue. The course of fatigue during treatment significantly predicted fatigue reported at follow-up for general fatigue ($p=0.036$, OR=9.26), sleep/rest fatigue ($p= 0.011$, OR=15.03), and cognitive fatigue ($p<0.001$, OR=10.54). Age at diagnosis, serious adverse events, sex, or risk group were not associated with fatigue at follow-up for any of the subscales.
Conclusions: The findings demonstrate that fatigue reported during treatment can predict fatigue at follow-up. Healthcare professionals need to be aware that pediatric patients who are fatigued during treatment need to receive additional attention and timely interventions since cancer-related fatigue will not resolve by itself in the first year after end of treatment. Furthermore, these results stress the need for multiple assessments during treatment and longitudinal studies focusing on following the participants for a longer time-period after end of treatment.

EP553 / #232

Topic: *AS05.q Psychosocial (PPO)*

COGNITIVE AND ADAPTIVE FUNCTION IN INFANTS AND TODDLERS BEING TREATED FOR ACUTE LEUKEMIA

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Background and Aims: Survivors of childhood acute leukemia are at risk for neurocognitive difficulties that emerge during therapy. Younger age at diagnosis is a risk factor for poorer outcomes. Few studies have examined early cognitive and adaptive function in infants and toddlers during cancer-directed therapy.
Methods: In this retrospective study, data on cognitive and adaptive function were abstracted from the medical record for 41 infants and toddlers who completed neurodevelopmental evaluations in our Early Childhood Clinic (53.6% male; mean±SD age at diagnosis = 20.3±9.5 months; age at assessment = 23.6±9.4 months). Patients were evaluated during treatment for acute lymphoblastic leukemia (ALL; n=30; 73.2%) or acute myeloid leukemia (AML; n=11; 26.8%). Results are age-standardized Z scores (normative mean = 0, SD = 1).
Results: Compared to age expectations, patients had significantly lower scores in global cognitive ($Z=-1.07$, $p<0.001$) and adaptive function ($Z=-0.70$, $p<0.001$). Patients were significantly below age expectations in adaptive subdomains of social ($Z=-0.49$, $p<0.001$), practical ($Z=-0.40$, $p=0.008$), motor ($Z=-0.76$, $p<0.001$), and communication ($Z=-0.44$, $p=0.006$), and in cognitive subdomains of fine motor ($Z=-0.53$, $p=0.036$), gross motor ($Z=-1.41$, $p<0.001$), and receptive and expressive communication ($Z=-0.84$, $p=0.006$; $Z=-0.75$, $p=0.014$). There were no significant group differences by diagnosis (ALL v. AML). Among children treated for ALL (53.3% male; age at assessment = 24.7±9.3 months; time since diagnosis = 2.5±2.3 months), females demonstrated significantly worse adaptive motor function than males ($Z=-1.18\pm0.75$ v. -0.52 ± 0.73; $p=0.041$). Among the ALL group, females had lower global cognitive scores than males, with moderate effect size (Hedge's $g=0.93$; $p=0.119$).
Conclusions: Infants and toddlers treated for acute leukemia show developmental delay during cancer directed therapy, which highlights the need for early intervention and supportive care to promote developmental gains. Consistent with studies in long-term survivors of ALL, findings suggest that females may be at greater risk for treatment-related cognitive difficulties.

EP554 / #1868

Topic: *AS05.q Psychosocial (PPO)*

ADAPTATION AND ACCEPTABILITY OF TOKEN ECONOMY SHOWN TO IMPROVE ADHERENCE TO ACTIVITIES OF DAILY LIVING IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT

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Background and Aims: Pediatric patients face health risks while undergoing hematopoietic stem cell transplant (HSCT) including oral complications (Elad et al., 2015), deconditioning (Lago et al., 2021), and bloodstream infections (Dandoy et al., 2016). These risks were significantly reduced by engagement in activities of daily living (ADL): oral care, physical activity, and bathing via a token economy during inpatient admission (Best et al., 2016; Hickey et al., 2018). We adapted and implemented this program with comparable findings, and utilized acceptability and feasibility (AF) data to guide quality improvement (QI).
Methods: Our BMT Bucks Program, adapted from ADL 1-2-3 (Hickey et al., 2018) targeted 3 daily ADL and added a 4th, daily weights. Percent of completed ADL over 21 days was compared across 8 pilot patients and matched comparisons using an independent samples t-test. Caregivers and patients rated 7 AF items via 5-point Likert scale from 1 (strongly disagree) to 5 (strongly agree). This survey was also completed by 26 bedside nurses, and later by 19 additional pediatric patients undergoing HSCT after implementing initial QI feedback.
Results: Pilot patients completed approximately 20% more ADL than comparison group $t(14) = 2.77$, $p = 0.021$*. Initial AF mean rating by bedside nurses was 3.8, whereas patient/caregiver combined AF mean was 4.5. Specifically, QI ratings suggested we increase patient and caregiver engagement in tracking ADL and increase nursing awareness of results supporting program efficacy. After QI-informed adjustments, mean acceptability and feasibility rating was 4.8 for caregivers and 4.7 for patients. The highest rating for both caregivers (mean = 5.0) and patients (mean = 4.9) was for the item indicating they would recommend BMT Bucks to others.
Conclusions: Patients participating in the token economy demonstrated significantly increased adherence to ADL, which has been shown to correlate with improved health outcomes. AF ratings suggest the BMT Bucks Program is acceptable and feasible in our setting.

EP555 / #1377

Topic: *AS05.q Psychosocial (PPO)*

EDUCATION NEEDS OF CAREGIVERS OF CHILDREN WITH CANCER IN TANZANIA

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Background and Aims: Caregivers play the main role in the support of children with cancer, influencing presentation and treatment completion. Therefore, caregiver knowledge about childhood cancer must be understood to address the challenges and facilitators for the initiation and completion of pediatric cancer care in Tanzania.
Methods: A descriptive qualitative study was conducted at Bugando Medical Center in Northwest Tanzania. Caregivers of children receiving cancer care completed a focus group discussion to understand their knowledge about childhood cancer, and education needs at diagnosis and during treatment. Data was transcribed, coded, and analyzed by thematic content-analysis with the support of NVIVO software.
Results: A total of 9 caregivers were in the focus group, 7 female and 2 male participants. The analysis was conducted by the first two authors with an inter-rater agreement score of 94.8%. Caregiver knowledge on pediatric cancer was low with many believing prior to their child's diagnosis that children could not get cancer, cancer is caused by witchcraft and that it was an incurable disease. Pediatric cancer education at diagnosis by patient navigators lessened their worries and gave them hope that their children could be cured. When asked what key education topics should be provide for caregivers, suggestions included the cause of cancer, duration of their child's cancer and treatment, and the side effects of treatment, and future impact on fertility. To improve baseline community knowledge, caregivers recommended going into rural communities and using media-based education programs including the radio for greater reach, regardless of literacy rates.
Conclusions: Low caregiver knowledge about pediatric cancer led to delayed presentation. Cancer education programs had a positive impact in caregiver understanding and hopefulness of their child's diagnosis. Educational interventions should be prioritized in rural communities, to increase cancer knowledge and improve pediatric cancer outcomes.

EP556 / #63

Topic: *AS05.q Psychosocial (PPO)*

PSYCHOSOCIAL FUNCTIONING OF PARENTS OF DUTCH LONG-TERM SURVIVORS OF CHILDHOOD CANCER

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Background and Aims: Childhood cancer has a major impact on psychosocial functioning of parents. The aim of the current study is to describe psychosocial functioning of parents of long-term survivors of childhood cancer and to study associated factors.
Methods: Parents of survivors of the Dutch Childhood Cancer Survivor Study LATER cohort (diagnosed 1963-2001) were invited to complete the TNO-AZL Questionnaire for Adult's HRQoL, General Health Questionnaire (psychological distress), Self-Rating Scale for Post-traumatic Stress Disorder, Post-traumatic Growth Inventory, and Illness Cognition Questionnaire (acceptance, helplessness and disease benefits). HRQoL domain scores (e.g. vitality, aggressive emotions) were compared to references using Mann-Whitney U tests with effect size r. Associations of post-traumatic stress and growth with other outcomes were studied with Pearson's r. Child disease variables and parent illness cognitions were studied as associated factors of HRQOL, distress, post-traumatic stress and post-traumatic growth using multivariable linear regression analyses. Level of significance was $p<.05$.
Results: Parents (n=661, 56% female, time since child's diagnosis: 21.3 [SD: 3.3] years) reported less aggressive emotions than references (r=.10–.14). Mothers reported better HRQoL in social functioning, daily activities and vitality than references (r=.10–.14). Other HRQoL domains were not different from references. Post-traumatic stress was symptomatic in 3% and was associated to worse HRQoL and distress (r=-.27–.48). Post-traumatic growth was associated to post-traumatic stress and better HRQoL (r=.09-.12). Recurrence was associated to better HRQoL (β=.30–.47). Acceptance was associated to better (β=.12–.24), and helplessness to worse outcomes (β=.11–.38).
Conclusions: On the long run parents of survivors of childhood cancer appear to have limited psychosocial difficulties and HRQoL similar to the general population. Only a small proportion experiences symptomatic post-traumatic stress, and post-traumatic stress symptoms are associated to other psychosocial outcomes. Illness cognitions may provide treatment targets in interventions for parents with psychosocial problems.

EP557 / #99

Topic: *AS05.q Psychosocial (PPO)*

DIAGNOSIS RELATED INFORMATION PREFERENCES OF ADOLESCENTS WITH CANCER IN ARMENIA

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Background and Aims: According to the legislation of the Republic of Armenia, health-related information of adolescents under 18 years old, should be provided to their parents or legal representatives. Parents' opinion on informing an adolescent about a cancer diagnosis is decisive. There is less evidence about health-related information preferences of adolescents with cancer. This study aims to explore parents' and adolescents' preferences on disclosure of a cancer diagnosis related information among the population of Armenia
Methods: This qualitative study was conducted through semi-structured in-depth interviews with 15 adolescents with cancer aged 12-18, had been receiving chemotherapy at least one month before the interview and 15 mothers aged 37-53. Two study instruments were developed based on the literature review, respectively for adolescents and parents. A qualitative content analysis with inductive approach was used for data analysis.
Results: The results of the research indicated that the 15 interviewed adolescents preferred to be properly informed about their diagnosis and treatment specifics. According to the adolescents, coping with the disease, handling difficulties, fighting cancer becomes easier when they are informed appropriately. In comparison with adolescents, 13 out of 15 interviewed parents stated that awareness of the diagnosis would negatively affect treatment process and mood of adolescents. Moreover, in their opinion, adolescents would not be able to handle the information. However,6 parents changed their non-disclosure attitudes at the end of the treatment. The other important study finding was related to the source of the diagnosis information; adolescents mentioned that they would prefer to receive information from doctors, since they would provide detailed information in an empathetic, but non-emotional manner, while parents stated that it should be them providing diagnosis information.
Conclusions: Conducted study results indicate that adolescents with cancer need to be involved in diagnosis related communication, which can be led by the doctor and conducted in the presence of parents.

EP558 / #1133

Topic: *AS05.q Psychosocial (PPO)*

UTILIZATION OF THE AYA PSYCHO-ONCOLOGY SCREENING TOOL IN A PEDIATRIC HOSPITAL AYA PROGRAM

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Background and Aims: The AYA Psycho-Oncology and Survivorship Screening Tools were developed to assess distress and concerns of AYA cancer patients during and after treatment. We report on the use of the distress thermometer and areas of concern reported by AYAs age 15+ at our pediatric hospital.
Methods: AYAs are typically given assessment within 1 month of diagnosis, and every 2, 4, or 6 months depending on their previous distress score (DT). For off-treatment patients, assessments are typically given every 6 months. Findings are shared with AYA team, medical team, and other treatment services as needed and entered into EMR.
Results: Between 1/21 and 3/22, we completed 108 DTs in 62 AYAs on-treatment and 37 in 24 AYAs off-therapy. Thirty-two individuals completed one screen, 33 have completed two and 10 have completed 3 or 4.The average and median age was 18 (range 15-30). The average distress score was 3.3 for on-therapy and 3.5 off-therapy AYAs. Thirty-two percent on treatment and 27% off-treatment DT scores were 5+ . Among patients on therapy, the most commonly endorsed concerns were "Missing doing 'normal stuff' with friends" (51%), "Boredom" (44%), "Isolated from friends" (39%) and "Education" (38%). The off-therapy assessment has 76 possible areas of concern; AYAs marked an average of 10 items. The most commonly endorsed concerns were "Trouble remembering things", "Worry about cancer coming back", "Short attention span or concentration", and "Feeling like missed out on life because of cancer" (each 4%).
Conclusions: Most AYAs age 15-30 in a pediatric hospital report low levels of distress. However, the DT identified 30% with high levels of distress and areas of concern allowing for targeted support. Anecdotally there was a sense among clinicians that the tool uncovered concerns that the team was not aware of; we intend to study the added value of the tool to clinicians in future research.

EP559 / #1877

Topic: *AS05.q Psychosocial (PPO)*

IMPLEMENTATION OF PSYCHOSOCIAL STANDARDS OF CARE. WHAT HAVE WE LEARNED ABOUT BARRIERS AND SUPPORTING FACTORS?

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Background and Aims: The consensus- and evidence-based guideline "Psychosocial care in pediatric oncology and haematology" (Schröder et al., 2019) defines standards for basic principles of psychosocial care, framework and structures, psychosocial assessment, and interventions. However, the issue of translation into clinical practice remains critical.
Methods: As part of the second update of the guideline, supporting and hindering factors regarding implementation were explored in a transnational online survey. Thirty-five questions related to knowledge about the guideline, comprehensibility, feasibility, relevance to overall treatment concept, benefits, and barriers to implementation were developed and agreed upon by the guideline development steering group. The online questionnaire was distributed to psychosocial staff in the D-A-CH region in a two-month period. A total of 76 respondents completed the survey (43% Clinical Psychology, 20% Social Work, 16% Psychotherapy, 9% School, 4% Art therapy, 8% others). Responses were given on a visual analogue scale, with 0 being the lowest and 100 being the highest.
Results: Knowledge (M=81.15, SD=20.75) and comprehensibility (M=83.86, SD=19.43) of the guideline were rated high, feasibility significantly lower (M=62.01, SD=29.56). Experienced benefit of the guideline was mainly explained by the own evaluation of knowledge, feasibility, and comprehensibility (regression analysis: F (3; 65) = 20.91; r2 = 0.49; p = 0.00). Within the psychosocial team, the guideline was regarded integrated into the overall treatment concept by 44% of the respondents, considered or accepted to be a standard by 42%, for 14% it was not considered a standard. The experienced importance of the guideline in the own institution was indicated on average with 60.55, with a broad distribution (SD=33.71).
Conclusions: A clear discrepancy between defined standards and practical use of the guideline became apparent. From the factors analyzed, an action plan was developed with the goal of higher awareness, changes in structures and frameworks, and targeted interdisciplinary training.

EP560 / #418

Topic: *AS05.q Psychosocial (PPO)*

IDENTITY FUNCTIONING AND PERSONALITY IN ADOLESCENT AND EMERGING ADULT SIBLINGS OF SURVIVORS OF PEDIATRIC CANCER

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Background and Aims: The psychological long-term impact of childhood cancer on siblings is poorly understood, especially concerning important self-related constructs such as identity and personality. The objectives of this study were: 1) to compare siblings with control participants on identity functioning, personality traits, and general well-being (depression, self-esteem, satisfaction with life) and to investigate associations of identity functioning and personality with demographic, and clinical characteristics and general well-being in siblings.
Methods: Siblings (n=80; mean age: 19.13; 49% male) were matched on age and gender with healthy controls (2:1). Identity synthesis and confusion were measured with the identity subscale from the Erikson Psychosocial Stage Inventory. The Dimensions of Identity Development Scale was used to measure five identity dimensions. Personality traits were measured using the Quick Big Five questionnaire.
Results: Siblings had significantly lower scores than community youth on agreeableness, openness to experience, and conscientiousness, but they did not differ on any of the identity constructs. Siblings reported lower self-esteem and satisfaction with life. For siblings, age of sibling at diagnosis was positively associated with the identity dimension of exploration in breadth. Sisters reported more identity confusion, less identity synthesis, more neuroticism, and openness to experience than brothers. Identity synthesis, the identity dimension of identification with commitment, and the personality trait of agreeableness related to better well-being in siblings. Exploration in depth was positively related to satisfaction with life. Extraversion was positively related to satisfaction with life and self-esteem. In contrast, identity confusion, the identity dimension of ruminative exploration, and neuroticism were associated with worse well-being.
Conclusions: The finding that siblings are at risk of having low self-esteem and satisfaction with life is in line with existing literature. Our findings suggest that identity functioning and personality can be important constructs to consider in relation to general well-being in siblings of survivors of pediatric cancer.

EP561 / #1247

Topic: *AS05.q Psychosocial (PPO)*

RELIABILITY, VALIDITY AND APPLICABILITY OF THE FLEMISH ADAPTATION OF THE PAT: A MULTICENTER STUDY

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Background and Aims: The Psychosocial Assessment Tool (PAT) is a tool to screen for psychosocial risk factors in families confronted with a child with cancer. We translated the PAT for the Flemish speaking part of Belgium using the forward-backward procedure. The aim of the present study was to investigate the reliability, validity, usability, and clinical added value of the PAT.
Methods: In two pediatric oncological centers in Belgium (UZGent/UZLeuven) families confronted with a new diagnosis of childhood cancer were asked to complete the PAT and additional questionnaires (e.g., usability of PAT). The multidisciplinary team rated these families in one of the three risk categories (universal, targeted and clinical). A Spearman rank correlation was used to investigate agreement between PAT and team scores.
Results: A total of 106 families participated in the study. The completion of the PAT was on average 37 days after diagnosis. The reliability of the total PAT score (α=.86) and most of the subscales was adequate to good (α=.64-.88). One subscale was inadequate (Family Beliefs, (α=.45)). Content validity was adequate (r=.30-.62), except for the 'social support' subscale. The usability of the PAT, as rated by the parents was adequate to good. Based on the total PAT score 68%, 26% and 6% of the families were classified in the universal, targeted and clinical group, respectively. A modest correlation between the PAT and the team's assessment was found (r= .38, p<.001). According to the assessment of the team, 36%, 48% and 17% were classified in the universal, targeted and clinical group, respectively.
Conclusions: Our study demonstrates the reliability, validity, and applicability of the Flemish adaptation of the PAT. More research is required to evaluate the added clinical value of combining different assessments (i.c. PAT and multidisciplinary evaluation) of psychosocial risk factors in order to optimize psychosocial support of families confronted with a child with cancer.

EP562 / #576

Topic: *AS05.q Psychosocial (PPO)*

LACK OF POST COMPULSORY EDUCATION PREDICTS UNEMPLOYMENT IN TEENAGERS AND YOUNG ADULTS TREATED FOR BRAIN TUMOURS IN CHILDHOOD

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Background and Aims: It is well recognized that there is a high risk of late complications after a brain tumour in childhood, which may affect academic performance. The aim of this study is to explore participation in post compulsory education and its impact on employment for Swedish teenagers and young adults treated for brain tumours in childhood. Differences due to sex, age at diagnosis, and tumour type will also be explored.
Methods: Nationwide registry data about 452 individuals, born 1988–1996 and diagnosed with a brain tumour before their 15th birthday, are compared with five times as many controls matched by birth year, sex, and place of living. Data were obtained from The Swedish Childhood Cancer Registry and Statistics Sweden.
Results: Preliminary results show that the number of individuals not attending any post compulsory education was significantly higher within the group treated for brain tumours compared with controls (8.2% vs. 4.2%; $p<0.001$). Significantly fewer individuals treated for brain tumours attended high schools (83.6% vs. 90%; $p<0.001$) or universities (36.5% vs. 45.6 %; $p<0.001$) compared with controls, while they to a larger extent attended the Swedish folk high schools (15.3% vs. 8.8%; $p<0.001$), educational institutions which focus on providing an accessible learning environment. Other preliminary analyses showed that individuals without post compulsory education, treated for a brain tumour, had been significantly less employed compared with individuals treated for brain tumours with post compulsory education (40.5% vs. 24.8%; $p=0.040$). This was the same for controls (28.6% vs. 10.7%; $p<0.001$).
Conclusions: Participation in post compulsory education seems to prevent unemployment. Hence, results indicate a need for more knowledge about post compulsory education tailored to the specifics needs of the group to compensate for often-experienced late complications after a brain tumour treatment.

EP563 / #930

Topic: *AS05.q Psychosocial (PPO)*

ANXIETY AND DECISION-MAKING AMONG PARENTS COPING WITH CHILDHOOD CANCER DURING THE FIRST YEAR OF TREATMENT

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Background and Aims: Parents of children with cancer face a high level of distress. One contributing factor to this is their need to make life-altering treatment decisions. In order to understand specific variables that may contribute to parents' distress and decision-making preferences, we assessed correlations between parent anxiety, decision-making preferences, personal variables (gender, age, religion, education, socioeconomic, occupational status), cancer characteristics (type, stage, time since diagnosis), existing support system, and trust in the medical staff.
Methods: Sixty-nine parents of children with cancer during the first year after diagnosis were recruited to the study during their child's hospitalization, and answered the State-Trait Anxiety inventory, the Control (decision-making) Preferences Scales for Pediatrics and questions about their environmental support and trust in the medical staff.
Results: Parents' anxiety level was significantly higher than the general population, especially for state anxiety. Arab parents had higher trait anxiety comparing to Jewish parents, and less environmental support. Higher socioeconomic status and greater extent of employment of the spouse related to higher levels of state anxiety. Anxiety did not relate to any of the cancer properties, nor to the amount of support the parents had or their trust in the medical staff. Parents' level of education positively related with willingness to take part in decision-making, as well as with trust in the medical staff.
Conclusions: The results emphasize the importance of trust in and the support of the medical and psychosocial staff and to the need to be attuned to different parents' needs to increase this trust

EP564 / #1866

Topic: *AS05.q Psychosocial (PPO)*

THE INTRODUCTION OF A ROBOTICS PROGRAMME TO SUPPORT SCHOOL ABSENCE: WHAT HAVE WE LEARNT FROM FAMILIES SO FAR?

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Background and Aims: Children with cancer may experience prolonged disruptions to their school attendance due to symptoms of illness, health risks associated with the illness, and effects of treatment. National reports on childhood cancer survivors indicate that this population is at increased risk of long-term social outcomes, which include reduced educational attainment and feelings of loneliness (Gurney et al., 2009). The Robotics programme, associated with The Children's Cancer Unit Charity (CCUC) at the Royal Belfast Hospital for Sick Children (RBHSC), involves the use of telepresence robots as an alternative form of education provision. The robots support students to remain linked in academically and connected to their classmates from their hospital bedside and/or home. This qualitative quality improvement study aimed to explore the practicalities of implementing the robots into families' lives. It also explored any barriers to engagement from a service-delivery perspective.
Methods: Semi-structured interviews were conducted with ten parents (eight mothers and two fathers) of ten children under the care of the paediatric cancer service at RBHSC who had been invited to take part in the Robotics programme. All children had a minimum of two months absence from school at the time of the family's introduction to the robot. Thematic analysis was used to explore the data.
Results: Five main themes emerged; 1 (Hearing about the robot), 2 (Acquiring the robot), 3 (Family introduction), 4 (School introduction) and 5 (Incorporating into school day).
Conclusions: The results of this study highlight the practical considerations and obstacles for families' when telepresence robots are introduced as a way of supporting school absence in the paediatric cancer population. Using the data from this quality improvement study, resources have been developed to support and assist families and schools when a child is enrolled onto the Robotics programme.

EP565 / #218

Topic: *AS05.q Psychosocial (PPO)*

MOTHERS´ AND FATHERS´ PERSPECTIVES ON HEALTH-RELATED QUALITY OF LIFE OF CHILDREN WITH CANCER

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Background and Aims: Evaluation of patient-reported outcome measurements (PROMs) in pediatric cancer remains controversial, as parent-proxy reports significantly differ from child self-reports. The specific aim of this study was to examine agreement between mother and father proxy report on health-related quality of life (HRQOL) in a sample of pediatric cancer patients.
Methods: Based on the Pediatric Quality of Life (PedsQL) 4.0 Generic Core Scales and PedsQL 3.0 Cancer Module, patients and parents completed monthly HRQOL reports following the diagnosis of cancer. Intraclass correlations (ICCs) between child self-report and reports of mother and father were analyzed at the domain level.
Results: Within the first seven days following cancer diagnosis, 32 dyads of mother-child and 19 dyads of father-child were included in this prospective longitudinal study. Shortly after diagnosis, mother-child dyads showed moderate and good agreement on all domains of PedsQL Generic, except for social, whereas father-child dyads showed only moderate agreement on physical and school domain. With ongoing therapy, moderate agreement remained only on the physical domain, as both mothers and fathers overestimated impairments. The PedsQL Cancer Module showed moderate and good agreement not only for the observable domains (e.g. pain and hurt, nausea) but also for worry (0.77 [95% CI, 0.52-0.89, P<0.001]) in case of mother-child dyads. Fathers tended to overestimate the child's symptom burden and achieved only moderate agreement for the domain procedural anxiety (0.56 [95% CI, 0.04-0.86, P=0.02]), whereas mother-child dyads reached excellent agreement (0.92 [95% CI, 0.81-0.97, P<0.001]).
Conclusions: The results suggest that both parent proxy-reports can provide valid information about the HRQOL of the child. However, mothers and fathers provide significantly different information, suggesting that proxy data should be used with caution.

EP566 / #142

Topic: *AS05.q Psychosocial (PPO)*

COGNITIONS AND ATTITUDES OF CHILDREN WITH CANCER DURING LONG-TERM CANCER TREATMENT: IMPLICATIONS FOR SHARED DECISION MAKING IN PEDIATRIC ONCOLOGY

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Background and Aims: Cancer treatment for children is typically long-term and difficult. Understanding children's thoughts and attitudes when they are informed about cancer, while receiving cancer therapy, and while speculating regarding the consequences of treatment, may be valuable for informing treatment approaches. Children's thinking should be considered in cases of shared decision making in pediatric oncology.
Methods: To examine this question, we conducted long-term observation and interviews with seven children with hematologic cancer, aged 5 to 10 years, in a Japanese pediatric ward and two outpatient clinics. The data collection took a total of 211 days, from 2016 to 2020. This study dealt with a large amount of data on observation narratives and children's discourses using a qualitative analysis that combined thematic data analysis with longitudinal process analysis.
Results: We identified five main themes that encompassed children's thoughts and attitudes: making promises with doctors, learning about the treatment procedures, taking care of oneself, increasing the range of activities they can perform, and living an ordinary life. Children participated in decision making by engaging in pediatric cancer therapy, taking care of their own bodies, and increasing their range of activities. Children perceived the therapeutic course as a path to living an ordinary life, such as going to school, playing with friends, and living without wearing a mask. These expectations were maintained from the start of cancer treatment to the follow-up period. Children developed cognitively and socially during these processes.
Conclusions: A forward-looking attitude toward understanding cancer, accepting treatment, and looking forward to the future were observed in children with cancer. In addition, children developed throughout the processes of cancer treatment. These findings have implications for shared decision making in pediatric oncology.

EP567 / #1714

Topic: *AS05.q Psychosocial (PPO)*

META-ANALYSIS WITH ALARMING FINDINGS OF PSYCHOSOCIAL INTERVENTIONS ON PHYSICAL, MENTAL AND SOCIAL WELLBEING FOR CHILDREN WITH CANCER AND THEIR FAMILIES IN LOW- AND MIDDLE-INCOME COUNTRIES.

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Background and Aims: The greatest proportion of children at risk for cancer reside in Low- and Middle-Income Countries (LAMICs). Psychosocial care is essential to care in most developed settings seeking to address stressors accompanying a cancer diagnosis. However, the evidence on psychosocial interventions in LAMICs remains unexplored. This meta-analysis aimed to synthesize findings on psychosocial interventions for children with cancer and their families in LAMIC settings.
Methods: Systematic searches of five databases were conducted to identify appropriate studies. Data were extracted and ANOVAs and meta-regression analyses were performed.
Results: Out of 3,501 hits, 334 full texts were screened, with 17 studies eligible for inclusion. All interventions had a combined sample size of 3,140 and covered 7 countries. Interventions comprised families/parents of children with cancer, only children or both, and were art, play music-based, spiritual, religious, financial, logistic support, counselling psychotherapy-based, sleep, breathing, relaxation, and solution-focused trainings. Primary outcomes were anxiety, depression, fatigue, distress, burnout, quality of life, treatment completion and pain reduction. All showed significant relationships between the interventions and outcomes ($p < 0.05$). The overall log odds ratio was 1.773 ($p < 0.0001$), implying not providing a psychosocial intervention increases the likelihood for poorer health and wellbeing outcomes in children with cancer and their parents. Additional analysis showed the outcomes were statistically significant on all domains: emotional, physical, health, and social wellbeing. There is a large heterogeneity in samples and research methodology, and a gross under-representation of LAMICs.
Conclusions: Over the last decade, an alarming note to the childhood oncology community was observed. Our meta-analysis points at the lack of psychosocial interventions for children with cancer and their families. This study presents an opportunity for SIOP to direct member countries and outreach teams to develop, adapt, and empirically evaluate more psychosocial interventions in the chosen population.

EP568 / #1469

Topic: *AS05.q Psychosocial (PPO)*

FAMILY MATTERS: THE INTERACTION BETWEEN FAMILY FUNCTIONING AND TREATMENT INTENSITY IN CONTEXT OF PEDIATRIC CANCER

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Background and Aims: Background: Children with cancer have lower quality of life (QOL) compared to peers, yet heterogeneity underscores a need to understand how risk and resilience factors interact. Children diagnosed with brain tumors (BT), those with higher intensity treatments (i.e., cranial radiation and intensive chemotherapies), and those with more maladaptive family functioning (i.e., lower cohesiveness/communication) have lower QOL. Aim: To evaluate how risk factors interact to determine if family functioning impacts QOL differentially depending on diagnosis and treatment intensity. It was hypothesized that diagnostic group and treatment intensity would moderate the relationship between family functioning and QOL, such that family functioning would be more predictive of QOL for BT with higher treatment intensity.
Methods: Participants included school-aged children (ages 7-14) who completed cancer treatment within six months for either BT (n=42) or non-central nervous system solid tumor (ST; n=29). Caregivers completed the Pediatric QOL Inventory (PedsQL 4.0) to assess their child's health-related QOL. Children completed the Family Assessment Device-General Functioning Scale (FAD-GF) to assess family functioning. Treatment intensity was rated following chart review using the Pediatric Neuro Oncology Rating of Treatment Intensity to divide the sample into low, moderate, and high intensity groups. Moderation models were tested using the SPSS PROCESS macro, covarying for executive functioning.
Results: Diagnosis type was a significant moderator between family functioning and QOL, such that more maladaptive family functioning was associated with reduced QOL for the BT group, p=.01. Similarly, treatment intensity was a significant moderator, such that family functioning was associated with QOL for the high intensity treatment group, p=.04.
Conclusions: The current findings indicate that maladaptive family functioning is a risk factor for children with BT and higher treatment intensities, highlighting a high-risk group to target for screening and family-level intervention to improve QOL. Future work should examine these relationships longitudinally with larger samples.

EP569 / #605

Topic: *AS05.q Psychosocial (PPO)*

SOCIAL DETERMINANTS OF COGNITIVE OUTCOMES AMONG SURVIVORS OF PEDIATRIC BRAIN TUMORS FOLLOWING RADIOTHERAPY

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Background and Aims: Social determinants of health such as parental occupation, household income, and neighborhood environment have been used to predict cognitive functioning among healthy and ill children; however, few pediatric oncology studies have investigated this relationship. The primary study aim was to use the Economic Hardship Index (EHI) to measure neighborhood-level social and economic conditions to predict cognitive outcomes among children treated for brain tumors with radiotherapy (RT).
Methods: 241 children treated on a prospective, longitudinal, phase II trial of conformal photon RT (54-59.4 Gy) for ependymoma, low-grade glioma, or craniopharyngioma (52% female, 79% White, age at RT= 7.76±4.97 years) completed serial cognitive assessments (intelligence quotient [IQ], reading, math, adaptive behavior) for ten years. Six US census tract-level EHI scores were calculated for an overall EHI score: unemployment, dependency, education, per capita income, crowded housing, and poverty. Socioeconomic measures in the existing literature (i.e., Barratt Simplified Measure of Social Status [BSMSS] based on parental income and occupation, and insurance type- no insurance, public, private) were also derived.
Results: Spearman correlations revealed EHI overall score and 3 of 6 subscores associated with the BSMSS ($r=-.22$ to $.37$; $p< .005$), and Kruskal-Wallis Tests indicated EHI overall score and 2 of 6 subscores associated with insurance type ($p< .05$). Linear mixed models adjusted for age at RT and sex indicated a significant impact of EHI (overall, unemployment, per capita income, poverty) on baseline cognitive performance (IQ, reading, math, adaptive behavior, $p< .05$), as well as change in cognition over time (IQ, math, $p< .05$).
Conclusions: Neighborhood-level measures of social and economic conditions such as the EHI are associated with easily-derived socioeconomic status measures but also account for unique variance in cognitive outcomes. Research is needed to isolate modifiable factors within these social and economic conditions to develop interventions that improve cognitive outcomes for childhood cancer survivors.

EP570 / #1198

Topic: *AS05.q Psychosocial (PPO)*

IS MENTORING HEALING? AN ANALYSIS OF MENTORS EXPERIENCES AS PART OF THE BEREAVED PARENT MENTORSHIP PROGRAM IN PAKISTAN

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Background and Aims: Bereaved Individuals providing support to others in need of support find this connection meaningful and helpful. A parent-to-parent program that involves training bereaved parents learn from their loss to support those recently bereaved. Providing emotional support to families going through similar experiences could be healing for mentors. This study is conducted to explore parents' experiences and factors involved in the role of mentorship. Their experiences were explored in four domains 1) Their feelings as part of program 2) Their expectation as mentor3) Their feelings and expectation related to interactions with mentee 4) To explore difficulty faced at personal level associated with mentorship.
Methods: Parents serving as Bereaved mentors at TIH were interviewed to explore in four different areas. Their experiences were explored using semi structured interviews. Interviews were held on zoom and were recorded. Thematic analysis was used to analyze data.
Results: Overall parents reflected positive experiences and self-satisfaction on becoming a part of BPP. Self-learning, self-growth, and self-healing were major driven forces at mentors level as a source of satisfaction and participation. Parents shared a positive attitude towards training as well and it helped them explore their emotions and helped them achieve better communication. Overall analysis reflects mentorship and training as an aided tool to their grief journey.
Conclusions: Participating in bereaved parent program serves as positive experience for parents. Mentorship not only gives meanings of life to mentors but actually provide them with driving force to continue legacy of their child and aid them in their grief journey. Because of first batch of mentors, few participants were interviewed , which lower generalizability, to overcome this limitations next study can be done more objectively.

EP571 / #189

Topic: *AS05.q Psychosocial (PPO)*

EXPERIENCES OF CHILDHOOD CANCER SURVIVORS AND THEIR PARENTS WITH A PHYSICAL AND SOCIAL INTERVENTION DURING CANCER TREATMENT - A RESPECT STUDY

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Background and Aims: Physically inactivity during treatment results in children with cancer remaining inactive post-treatment. Furthermore, recurrent hospitalizations often cause prolonged absences from school and a dramatic reduction in peer interactions. The combination of school absence, being physically impaired, and lacking peer interactions negatively impact quality of life for the child with cancer. What these children and their parents consider to be barriers to physical activity during treatment is pivotal. This study explores experiences of childhood cancer survivors and their parents with a combined physical and social activity intervention during treatment, including the program's impact on survivors' physical activity post-treatment.
Methods: We designed a phenomenological-hermeneutic qualitative interview study. Using a criterion-sampling strategy, 18 childhood cancer survivors (aged 11-18 years) and their parents were interviewed from September 2019 through May 2020. Data analysis used a deductive thematic approach focused on meaning.
Results: Three themes emerged: 1) being physically active during hospitalization; 2) peers as motivators; and 3) physical activity post-treatment. During hospitalization, daily motivation to do physical activity was dependent on the well-being, i.e., the presence of the child's treatment side effects. Healthy classmates provided a distraction, reduced loneliness, and promoted normality for those hospitalized. When surplus energy was lacking, some children preferred doing physical activity alone with a professional. Those who were physically active in the hospital sustained being physically active post-treatment while their parents continued seeking advice about appropriate activity levels.
Conclusions: Childhood cancer survivors and their parents benefited from the intervention which also provided guidance to remain physically active post-treatment. This was particularly true for the participants with leukaemia.

EP572 / #322

Topic: *AS05.q Psychosocial (PPO)*

EXPERIENCES WITH ONLINE PEER VISITS AT THREE DANISH PEDIATRIC ONCOLOGY WARDS DURING THE COVID-19 PANDEMIC – A QUALITATIVE STUDY

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Background and Aims: During the COVID-19 pandemic, children with cancer were at higher risk of social isolation since visits were strictly reduced to parents' visits only. To carry on an existing intervention of peer visits during hospitalization, we moderated the intervention to an online version during COVID-19. The online visits were provided during school hours. Research nurses and the children's teachers facilitated the online visits. This study explores how children with cancer, their peers, teachers, and nurses experienced online visits.
Methods: Using purposive sampling, children with cancer aged 7-15 years (n=15), their peers (n=15), nurses (n=4), and teachers (n=4) participated in semi-structured interviews from January 2022 through March 2022. The interviews were analyzed using an inductive thematic approach.
Results: In total, 70 online visits were facilitated from March 2020 through March 2022. The online visits varied from 15 minutes to 90 minutes. We suggest two central themes: maintaining social attachment through online interaction and facilitating online visits based on a preliminary analysis. Preliminary findings indicate that the children are overall pleased with online visits to maintain their social relations during the COVID-19 pandemic. Regardless, online visits cannot replace face-to-face interaction between the children as the content and quality may change during the online visits. Findings indicate that technical shortcomings with equipment, e.g., computers, internet connection, and online meetings platform, negatively impacts the children's experiences with the online visits. Furthermore, the nurses and teachers experience that the online visits need facilitation, e.g., suggesting games, participating in the games, or introducing conversations topics to get an experience of flow.
Conclusions: During hospitalization, online visits from peers may support children with cancer in maintaining contact with their school and classmates.

EP573 / #775

Topic: *AS05.q Psychosocial (PPO)*

FACTORS ASSOCIATED WITH CAREGIVER STRAIN AMONG MOTHERS AND FATHERS OF CHILDREN WITH ADVANCED CANCER

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Background and Aims: While parents of children with cancer are at-risk for elevated stress and caregiver strain, they must also manage other responsibilities both inside and outside of the hospital. These challenges may be magnified when the child has advanced disease. Thus, we examined how mothers' and fathers' stress, family roles and satisfaction, and social support relate to caregiver strain in the context of advanced pediatric cancer.
Methods: Data were from a longitudinal study of families of children (aged 5-25) with advanced cancer (i.e., physician-estimated prognosis<60%, relapsed, or refractory disease). At enrollment, mothers (n=55; M_{age}=41.41 years; 87% White) and fathers (n=30; M_{age}=43.95 years; 83% White) reported on the division of 7 family roles (e.g., medical care of ill child, caring for others, household chores) and their satisfaction with each role. Parents also reported on their cancer-specific stress, general stress, social support, and caregiver strain.
Results: Parents reported moderate caregiver strain (Scale: 1-5; Mothers: M=2.88, SD=0.67; Fathers: M=2.59, SD=0.59). Fathers reported family roles were shared equally, whereas mothers reported either sharing roles or completing them independently. Parents were highly satisfied with their roles (Scale: 0-3; Mothers: M=2.45, SD=0.70; Fathers: M=2.65, SD=0.46). Accounting for income and marital status, multiple regression analysis, $F(7,42)=7.41$, $p<0.001$, $R^2=0.55$, revealed that greater caregiver strain for mothers was associated with greater general stress ($\beta=0.45$, $p=0.001$), greater satisfaction with family roles ($\beta=0.25$, $p=0.04$), and lower social support ($\beta=-0.25$, $p=0.04$). For fathers, $F(5,22)=4.34$, $p=0.01$, $R^2=0.50$, greater caregiver strain was only associated with greater cancer-specific stress ($\beta=0.48$, $p=0.02$).
Conclusions: In the context of advanced pediatric cancer, fathers may experience caregiver strain as cancer-specific stress increases, whereas mothers' strain may depend on broader family and social factors. Psychosocial providers should address general and cancer specific stress within families, in addition to social support (especially for mothers). Additional research regarding the family impact of advanced pediatric cancer is needed.

EP574 / #999

Topic: *AS05.q Psychosocial (PPO)*

PSYCHOMETRIC PROPERTIES AND EXPLORATORY ANALYSIS OF THE CANCER WORRY SCALE IN YOUTH SURVIVORS OF CHILDHOOD CANCER AND THEIR PARENTS

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Background and Aims: Forty three percent of pediatric cancer survivors experience fear of cancer recurrence (FCR); yet, no brief measures have been validated for youth survivors. The aim of this study was to evaluate the psychometric properties of the 6-item Cancer Worry Scale (CWS) in pediatric cancer survivors.
Methods: Survivors [n=146; 49.3% male, M_{age}=16.7 years (Range=8-25)] were recruited from Canada. Participants completed the CWS, Benefit-Burden Scale, Pain Catastrophizing Scale, Patient Reported Outcome Measurement Information System – Anxiety and Depression scales, Child Posttraumatic Stress Scale, Pediatric Quality of Life Inventory, Intolerance of Uncertainty Scale, and the Posttraumatic Stress Disorder Checklist for the Diagnostic Statistical Manual of Mental Disorders (Version 5). Internal consistency was calculated using Cronbach's alpha (Good = α>0.8). Fit indexes were calculated using confirmatory factor analysis (target values: X^2, p>.05; GFI>.95; RMSE<.06; CFI>.95; TLI>.95). Pearson correlations were used to calculate associations between the CWS and other outcomes.
Results: Internal consistency was good (α=.906). Confirmatory factor analysis yielded pattern coefficients relating the latent variable with the items (Range=.54-.92). Fit indexes for the model revealed a statistically significant chi square test, 29.16 (9, N=146), p=.001. The GFI (.94), RMSEA (.12), CFI (.97), and TLI (.94) suggest that the model was an adequate fit. The CWS was significantly correlated to anxiety (r=.50, p<.001) and depressive symptoms (r=.38, p<.001), posttraumatic stress symptoms (r=.50, p<.001), intolerance of uncertainty (r=.25, p=.008), quality of life (r=-.36, p<.001), disease burden (r=.53, p<.001), and pain catastrophizing (r=.32, p<.001); but not benefit finding (p=.126).
Conclusions: Results showed that the 6-item CWS is a good option to briefly assess FCR in youth, but based on the fit indexes, does not appear to be a robust measure of FCR. Future research should create a FCR measure from the ground up to better elucidate this construct in younger populations.

EP575 / #1125

Topic: *AS05.q Psychosocial (PPO)*

A MIXED-METHODS, CAREGIVER-ORIENTED APPROACH IS FEASIBLE TO EXPLORE THE IMPACT OF THE CHILDREN'S ONCOLOGY GROUP KIDSCARE APP ON EDUCATION/SUPPORT OF PEDIATRIC ONCOLOGY PARENTS/CAREGIVERS

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Background and Aims: The Children's Oncology Group (COG) recently launched the COG KidsCare App, which contains educational materials for parents/caregivers. Studies on the impact of Apps in pediatric oncology are limited and there is no published standard method for evaluation. Although data suggests the benefit of patient/caregiver-oriented research, few pediatric oncology studies have been identified that include caregivers as authors. This study assesses the feasibility of a mixed-methods, caregiver-oriented approach to explore the impact of the COG KidsCare App on the education/support of pediatric oncology patients/families in Atlantic Canada.
Methods: A questionnaire with 23 multiple-choice questions was developed using OPINIO software and disseminated to parents/caregivers via email. Parents/caregivers were invited to participate in a virtual, one-hour semi-structured interview (13 open-ended questions), hosted by a parent/caregiver on the study team. All participants were identified by investigators using convenience sampling. Data was analyzed using descriptive statistics. Participants were invited to share their feedback on the questionnaire and interview.
Results: This pilot study was fully implemented as planned within six weeks. Five parents/caregivers completed the questionnaire. There were no missing responses. Two participated in the semi-structured interview; both were engaged and spoke freely for over one hour. All participants agreed that the COG KidsCare App provided helpful educational materials and made them feel better supported. Minor wording changes were made to one questionnaire item and two interview questions to provide better clarity for future participants.
Conclusions: A mixed-methods approach that includes a parent/caregiver on the study team is a novel and feasible method of exploring the impact of Apps in pediatric oncology. Having a parent/caregiver host a semi-structured interview facilitated honest and open discussion. Preliminary results suggest that the COG KidsCare App improves education and support of parents/caregivers.

EP576 / #1882

Topic: *AS05.q Psychosocial (PPO)*

COMMUNITY STIGMA TOWARDS CHILDREN WITH CANCER IN TANZANIA

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Background and Aims: In Tanzania, prior research with caregivers of children with cancer and expert health care providers explored how misbeliefs and perceived community reaction and fears lead to delays in health seeking behavior and increased treatment abandonment. To target this internalized stigma and improve outcomes, tailored interventions are needed at the community level. However, the community perspective on stigma towards childhood cancer has not been evaluated, a critical knowledge gap.
Methods: This was a descriptive qualitative study conducted in the Mwanza region. Community members aged ≥18 years from 1 rural and 1 urban community were purposively selected to participate in three focus group discussions (each with 8-12 respondents) in April 2021. Data were transcribed, coded and analyzed by thematic content with the support of NVIVO software.
Results: A total of 28 participants were interviewed. Individual and health system level stigma was expressed by FGD participants, including avoidance, severity, public stigma and health practitioner stigma. In each focus group, participants mentioned the belief that cancer was incurable. Public stigma was also highly referred to, with some believing that childhood cancer was due to bewitchment and seeking treatment at the hospital will not help. Structural level stigma was not discussed by participants, including policy opposition, financial discrimination, and employment stigma.
Conclusions: Individual level stigma towards children diagnosed with cancer is present within the Tanzanian community. The common belief that childhood cancer is incurable and may be due to the child being bewitched likely contributes to delayed health seeking behaviour, especially in rural areas. Additional evaluation of organizational level stigma is needed, but may be better perceived and evaluated by caregivers and patients directly. Cultural and contextually relevant awareness interventions are needed to decrease stigma towards childhood cancer and increase cancer health-seeking behaviour in Tanzanian communities.

EP577 / #1244

Topic: *AS05.q Psychosocial (PPO)*

"I CAN DO IT"—A QUALITATIVE STUDY ON HOW REHABILITATION INCLUDING STRUCTURED ACTIVE PLAY IMPACTS PERSONAL AND SOCIAL DEVELOPMENT IN PRESCHOOLERS DIAGNOSED WITH CANCER.

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Background and Aims: Development of gross motor skills (i.e., jumping, running, hopping, throwing, and kicking), as well as personal and social competencies, are affected by cancer treatment in preschool children — with long-term implications. This study aims to explore how a structured active play intervention impacts the development of preschoolers' (1-5 years old) social and personal skills expressed by their behavior, body language, and verbal expressions.
Methods: Using convenience sampling, the project team conducted 12 months of participant observations of the structured active play intervention sessions. The observations focused on situations with social interaction, joy of movement, and confidence in movement. Observations were written as narrative scenic descriptions and analyzed with an inductive approach using thematic analysis.
Results: Observations were carried out during 50 group- and individual structured active play sessions (37 hours), resulting in 83 different scenic descriptions relating to 15 children (aged 1 to 5, 7 girls, and 8 boys). Preliminary findings indicate three overarching themes: 1) Wanting to play; 2) Playing together; 3) Gaining confidence. When given the opportunity, children willingly participate in active play regardless of being perceived as unwilling or unable by parents or caregivers. In the structured active play, children, parents, and exercise professionals play together as equals, teaching the children to take charge, take turns and be inclusive. With the support of exercise professionals and parents, the children can gain confidence in their movement abilities even when struggling with treatment-related side-effects — showing themselves and their parents that they can do it.
Conclusions: Preschool children with cancer want to play and can be their own best gatekeepers in activities and play. Their participation in structured active play during hospitalization may positively impact personal and social development.

EP578 / #1822

Topic: *AS05.q Psychosocial (PPO)*

EXECUTIVE FUNCTIONING IN A MULTI-ETHNIC SAMPLE OF PEDIATRIC SURVIVORS OF ACUTE LYMPHOBLASTIC LEUKEMIA (ALL): EXPLORING THE BILINGUAL ADVANTAGE

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Background and Aims: Deficits in executive functioning (EF) are common cognitive late effects of treatment for childhood acute lymphoblastic leukemia (ALL). Latino children are at increased risk of neurotoxic events during treatment, which may predispose them to EF difficulties post-treatment. Bilingualism has been shown to correlate with better EF in healthy children and may provide some protection against therapy-related neurological deficits. The primary objective of this study was to extend the investigation of a “bilingual advantage” in EF to childhood ALL.
Methods: Performance-based and parent report measures of EF were examined at a single time-point in survivorship among monolingual English-speaking (n = 44) and bilingual Spanish-English-speaking (n = 22) survivors of childhood ALL. Aspects of performance-based EF include concept formation, inhibition, and visual and verbal working memory. Parent ratings on the behavioral regulation index and the metacognitive index of the Behavior Rating Inventory of Executive Function were also collected.
Results: Participants (56% male) were diagnosed with standard risk ALL (64%) at a mean age of 5.40 years. Survivors were evaluated an average of 6 years post-diagnosis. Bilingual children performed better than monolingual children on performance-based tasks of inhibition ($p < .05$) and verbal working memory ($p < .01$), and parent ratings of metacognitive aspects of EF ($p < .05$). The observed effect of bilingualism on parent ratings of metacognitive aspects of EF remained after accounting for SES and was marginally significant for performance-based inhibition ($p = .053$). Parent ratings completed by Spanish-speaking parents correlated with performance-based testing ($r = -.69$ for inhibition and $-.70$ for verbal working memory).
Conclusions: This study presents preliminary evidence of a bilingual advantage for specific aspects of EF, namely inhibitory control. Bilingual language exposure and fluency may act as a protective factor against commonly observed weaknesses in EF among survivors of childhood ALL.

EP579 / #1652

Topic: *AS05.q Psychosocial (PPO)*

ACCESS TO PSYCHO-ONCOLOGY SERVICES FOR CHILDHOOD CANCER PATIENTS IN PAKISTAN

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Background and Aims: The burden of cancer in children is increasing globally. Improvement and access to services are needed to treat this disease as well as enhancing mental well-being, highlighting the need for dedicated pediatric psycho-oncology services for patients and their families. Cancer treatment is a long and difficult journey that becomes exponentially harder without psycho-social support. This study explored the availability and existing gap of paediatric-oncology services in paediatric-oncology units across Pakistan.
Methods: An online survey was created on google forms and circulated to unit heads and psychologists across all childhood cancer facilities. A total of 11 participants completed the online questionnaire containing nine open-ended and eleven multiple-choice questions.
Results: Out of the 13 units surveyed, 11 centers responded, and (54.5%) have a psycho-social department existing in their facility of which 4 are dedicated to paediatric oncology. Play area for children was present in 8(72%) of facilities. There are only 5(45%) centers that have psychologists, 3(27%) only social workers and 3(27%) have none of them. All of the dedicated psycho-social departments had required NGO and welfare support for hiring psychosocial personnel since state allotted positions did not exist. The psycho-social worker has always been involved in inpatient counseling, particularly in enucleation and amputation cases in most centers. The majority of the centers' psycho-social departments don't conduct training sessions for other staff members regarding counseling techniques and the mental health of patients. A vast majority of units did not have a full-time dedicated resource for psychosocial services and no immediate plans to appoint one.
Conclusions: Paeds-Oncology centers of Pakistan are lacking in psycho-oncology services for the mental well-being of children battling cancer. Additional research can be conducted to explore the factors causing constraints in the availability of Paeds-Psycho-Oncology services in Pakistan.

EP580 / #997

Topic: *AS05.q Psychosocial (PPO)*

QUALITY OF LIFE FOR ADOLESCENT AND YOUNG ADULT HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS AND HEALTHCARE PROVIDERS: A MIXED METHODS STUDY

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Background and Aims: Previous research in adolescent and young adult (AYA) patients suggests an association between hematopoietic stem cell transplantation (HSCT) and physical dysfunction, resulting in physiological stress impairing quality of life. However, few studies have examined both patients and healthcare providers' perceptions of quality of life while undergoing HSCT. This study aims to address this gap in research by 1) gathering information from quantitative surveys at three-time points and 2) completing qualitative semi-structured interviews with HSCT health care providers
Methods: This mixed-methods study assessed AYA HSCT patients (5 females, 6 males[MS1] [MS2]; mean age = 28, range from 23 to 38 years) on quality of life (QOL) using the PROMIS® HealthMeasures survey at three-time points: before, directly after, and 3-months post-HSCT. Responses ranged on a Likert scale from 1-5, lower scores indicating greater QOL. T-tests and repeated measures ANOVA were used to determine statistical significance across time points using SPSS v.27 ($p=0.05$). Healthcare providers (n=10) participated in semi-structured interviews post-transplantation. Qualitative themes were identified and integrated with quantitative data.
Results: Patients reported higher fear levels before as compared to directly after and 3-months post-HSCT ($p<0.05$). Patients reported higher fatigue directly after HSCT as compared to before and 3-months post-HSCT ($p<0.05$). Health care providers described "stress," "anxiety," and "physical complications" as common patient reactions during the HSCT trajectory. When asked about the utility of mindfulness-based interventions, HPs indicated that they would likely be "effective," "helpful," and "beneficial" for patients to reduce stress.
Conclusions: Patients reported the highest fear before HSCT and greatest fatigue immediately following HSCT. These findings are supported by qualitative interviews conducted with HPs regarding stress and anxiety observed in clinic. All health care providers agreed that a mindfulness-based intervention for their patients would improve their quality of life, such an intervention is currently being designed.

EP581 / #1232

Topic: *AS05.q Psychosocial (PPO)*

FACILITATORS AND BARRIERS THAT INFLUENCE ENGAGEMENT IN EXERCISE INTERVENTION DURING THE FIRST SIX MONTHS OF TREATMENT IN CHILDREN AND ADOLESCENTS WITH CANCER: A QUALITATIVE STUDY

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Background and Aims: Early initiation of physical exercise programs is needed to limit the physical deterioration caused by inactivity and treatment-induced toxicities during anti-cancer treatment in children and adolescents with cancer. We aimed to identify facilitators and barriers that influence engagement in an exercise intervention during the first six months of treatment.
Methods: By using a qualitative study design and purposely sampling, we generated data from semi-structured interviews with children diagnosed with cancer (n=9) (6-17 of age) and their parents (n=10). The interviews were conducted from December 2021 through February 2022. Deductive thematic analysis was used based on three components of self-determination theory: autonomy, competence, and relatedness.
Results: A preliminary analysis suggests three central themes: 1) Clinical versus household environment (autonomy); Children and parents described that they (children) in general, were motivated for exercise when hospitalized if supervised by exercise professionals, despite feeling less capable of exercise due to presence of side effects. However, their home environment often lacked the equipment and presence of exercise professionals, and therefore, some children and their parents experienced being unmotivated and sedentary. 2) Keeping side effects at bay (competence); Exercise was described to ameliorate certain side effects, creating confidence in keeping some degrees of fatigue and nausea at bay. However, structure and age-appropriate communication on physical activity and exercise were sought-after by some parents. 3) Confidentiality with exercise professionals (relatedness); trust and confidentiality with the exercise professionals during hospitalization are described as crucial for children to engage in the exercise sessions.
Conclusions: Although exercise interventions may be challenging to conduct in children during the first six months of anti-cancer treatment, with fluctuating side effects and hospitalization, children and parents describe exercise as relevant, motivating, and engaging. Methods for engaging children in exercise in their household should be explored further.

EP582 / #486

Topic: *AS05.q Psychosocial (PPO)*

IMPACT OF COVID-19 PANDEMIC ON FAMILIES OF CHILDREN WITH CANCER

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Background and Aims: The pandemic affected the continuum of care in patients & had a harsh effect on the makeup of society disrupting life. This study assessed the impact of the pandemic on families with children with a malignancy.
Methods: A survey questionnaire, taking 20-30 minutes (6 parts; 35 questions) was provided to the participants (families of children diagnosed with cancer from July 2019 to March 2020).
Results: Families of sixty patients on therapy and 23 who had completed therapy (median age: 7.13 [2-14] years) participated. Two-third families belonged to rural areas and 40% were from the upper-lower socioeconomic strata. Social media (n=74, 89%) and medical professionals (n=61, 73.5%) were main sources of COVID-19 information. Fifty-three percent school going patients transitioned to virtual learning and 22% quit school. One fourth children became less physically active. Information received about COVID-19 specific to cancer was perceived adequate by 25% families. Major factors which took a toll on the psychological wellbeing of the families were (i) risk of child contracting SARS-Cov-2 infection [n=64, 77%], (ii) greater morbidity/mortality owing to underlying cancer& lack of definitive therapy for COVID 19 [n=58;70%] (iii) fiscal hardship [75%](iv) adequacy of virtual schooling (40%) . Seventy six percent participants reported a negative impact on employment, 25% losing jobs entirely. Handwashing and wearing face masks were the most adhered behavioural modifications (100% and 97%). Most families avoided public places (96%) and using public transport (52%) with 76% avoiding contact outside home. Twenty percent families experienced problems with regards to delay in diagnosis, appointments and therapy.
Conclusions: 'Coronaphobia' psychological stress was observed in 75% families with a child with a malignancy. Economic loss (75%), modification/absence of schooling (75%) and delayed theranostics (20%) resulted owing to an unprecedented dismantled community & social network and disruption of health care facilities.

EP583 / #1047

Topic: *AS05.q Psychosocial (PPO)*

PSYCHO SOCIAL PROBLEMS OF CHILDREN AND CAREGIVERS REFERRED TO THE PEDIATRIC PSYCHO ONCOLOGY SERVICES IN A TERTIARY CARE CANCER CENTER IN A DEVELOPING NATION

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Background and Aims: Childhood cancer is considered a crisis not only for young patients but also for his/her entire family and social environment. The period of disease and treatment is physically and emotionally stressful for children and family who must adapt to a hospital environment with not only physical but also psychosocial challenges. The aim of this study is to evaluate psychosocial problems of children with cancer and caregivers.
Methods: A retrospective analysis of all new referrals of children with cancer and caregivers of pediatric cancer patients referred to a specialist Psycho-Oncology service in a tertiary cancer care center over the period of 3 years (January 2019 to December 2021) was done. Children up to 12 years of age and on active oncology treatment were included in the present study.Caregivers were independently referred for psycho social issues by pediatric oncology unit and they were not related to the pediatric patients included in this study. Socio demographic and clinical details of all referrals were noted. Clinical interview details as noted in Psycho-Oncology case record forms.
Results: We analyzed records of 99 children who met the eligibility criterion .Sixty three (64%) were male. The median age of patients was 9 years. The most common cancers were bone and soft tissue sarcomas 35 (32%) and hematolymphoid 30 (29 %). Majority of psycho social problems reported by children were emotional 68 (69 %) and physical 65 (66%).Few problems reported by children were practical 12(12%) and family 10 (10%). Among all referred caregivers (83) majority were both the parents in which 36 were mothers (43%) and 37 were fathers (45%). Most caregivers reported emotional problems 61 (73%) followed by practical problems 27(33%) and family problem (24%) during their children's treatment.
Conclusions: Pediatric patients and caregivers undergo mostly emotional, physical and practical problems. Findings support the need for tailor-made psychological intervention.

EP584 / #112

Topic: *AS05.q Psychosocial (PPO)*

IMPROVING HEALTH BEHAVIORS OF PEDIATRIC CANCER SURVIVORS WITH OBESITY DURING THE COVID-19 PANDEMIC: BARRIERS, OPPORTUNITIES, AND MEASUREMENT CONSIDERATIONS

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Background and Aims: Prevalence of overweight/obesity in pediatric cancer survivors (PCS) is 40-50%, yet few programs target this high-risk population. Little research is available on lifestyle interventions for PCS during the pandemic. This study examines the impact of COVID-19 on participants and research staff in our multi-site randomized controlled trial, NOURISH-T+; and whether an intervention targeting parents as role models for change can promote healthy eating and exercise in PCS.
Methods: Thus far, n=80 dyads of PCS (M=10 years) and their parents have been randomly assigned to NOURISH-T+ or comparison, Enhanced Usual Care (EUC). This cross-sectional analysis included descriptive statistics of baseline demographics, COVID-19-related factors, and lifestyle behavior changes from post-assessment surveys. Preliminary thematic analysis was conducted for qualitative feedback from research staff.
Results: Participants were ≥ 6 months off-treatment, and 20% had received cancer treatment during the COVID-19 pandemic. Mean baseline child BMI%ile was 95th. At baseline, many participants reported engaging in more home cooking (61%), snacking (50%), and eating out (37%) and less exercise 63%) since the pandemic began. COVID-19 created barriers related to participant recruitment and engagement, technology access and literacy, and data collection and management, as well as COVID-related challenges (e.g., Zoom fatigue). Strategies used to overcome these challenges included developing trust and rapport with participants, providing support through multiple routes of dissemination, and using data management applications for automation and project management. Post-assessments have indicated that those who participated in the 6-week intervention plus two PCS sessions and one dietitian session reported positive changes in eating and exercise behaviors.
Conclusions: Results suggest that the COVID-19 pandemic has impacted participant lifestyle behaviors, recruitment, and engagement. Nevertheless, preliminary findings suggest that PCS and their caregivers are making positive health behavior change. COVID-19 should be considered at multiple timepoints throughout the analysis due to its unique effects on trial implementation and participant experiences.

EP585 / #1532

Topic: *AS05.q Psychosocial (PPO)*

PREDICTION OF POST-TRAUMATIC SYMPTOMS 1 YEAR AFTER DIAGNOSIS AMONG CHILDREN WITH CANCER

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Background and Aims: Children with cancer are at heightened risk of stress and distress during treatment. Multiple factors may predict long-term post-traumatic stress symptoms (PTSS) in children, such as demographic and family factors, as well as survivor's stress. However, limited research has examined factors involved in PTSS during treatment or early survivorship. Therefore, we examined the association between demographic factors, cancer-related stress, and family communication near diagnosis and survivors' PTSS approximately 1 year later.
Methods: Data were from a longitudinal study of families (N=100) of children newly diagnosed with cancer; mothers and children (M_{age}=13.44; 50% Female; 90% White) completed surveys near diagnosis (T1) and at 1 year (T2). Mothers reported on sociodemographic background and attitudes about cancer communication with their child. Children self-reported on cancer-related stress and PTSS. Hierarchical regression examined T1 demographic factors, PTSS, cancer-related stress, and attitudes regarding cancer communication as predictors of T2 PTSS.
Results: At T1 and T2, 24.3% and 25.7% of children, respectively, met clinical cutoffs for PTSS. PTSS scores were not significantly associated with any demographic factors. The regression model predicting PTSS at T2 was significant, $F(5,94)=10.05$, $R^2=0.31$, $p<0.001$. T1 cancer-related stress ($b=0.36$, $p=0.001$) and mother attitudes preferring less communication with their child about cancer ($b=0.23$, $p=0.01$) predicted higher levels of PTSS at T2, beyond the impact of T1 PTSS ($b=0.16$, $p=0.13$).
Conclusions: Children were more likely to exhibit increases in PTSS 1 year following diagnosis when they had greater cancer-related stress, as well as mothers who were less inclined to share information with them about cancer. Providers should encouragement more open attitudes about cancer communication with children to reduce PTSS over the first year of treatment. Future research should include more diverse samples, especially fathers, and examine other predictors of PTSS.

EP586 / #549

Topic: *AS05.q Psychosocial (PPO)*

INTERNET-ADMINISTERED, LOW-INTENSITY COGNITIVE BEHAVIORAL THERAPY FOR PARENTS OF CHILDREN TREATED FOR CANCER: A FEASIBILITY TRIAL (ENGAGE)

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Background and Aims: A sub-group of parents of children treated for cancer report mental health difficulties, such as depression and anxiety. There is a lack of evidence-based psychological interventions for parents, with psychological support needs unmet. An internet-administered, guided, low-intensity cognitive behavioural therapy-based (LICBT) self-help intervention may provide a solution. The aim of this study was to examine methodological, procedural, and clinical uncertainties of such and intervention, and related study procedures, to prepare for the design and conduct of a future pilot RCT and subsequent superiority RCT.
Methods: The feasibility and acceptability of the intervention and study procedures was examined using a single-arm feasibility trial (ENGAGE). Primary objectives examined: 1) estimates of recruitment and retention rates; 2) feasibility and acceptability of data collection instruments and procedures; and 3) intervention feasibility and acceptability. Clinical outcomes were collected at baseline, post-treatment (12 weeks), and follow-up (6 months).
Results: The following progression criteria were met: sample size was exceeded within 5 months, with 11.0% enrolled of total population invited, study dropout rate was 24.0%, intervention dropout was 23.6%, missing data remained at ≤10% per measure, and no substantial negative consequences related to participation were reported. Intervention adherence was slightly lower than progression criteria (47.9%).
Conclusions: Findings suggest an internet-administered, guided, LICBT self-help intervention may represent a feasible and acceptable solution for parents of children treated for cancer. With minor study protocol and intervention modifications, progression to a pilot randomized controlled trial (RCT) and subsequent superiority RCT is warranted.

EP587 / #1260

Topic: *AS05.q Psychosocial (PPO)*

PARENTAL EXPERIENCES AND MENTAL HEALTH CONCERNS OF PEDIATRIC ONCOLOGY CARE DURING COVID-19 PANDEMIC: A CROSS SECTIONAL STUDY

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Background and Aims: Onset of the COVID-19 pandemic posed high demands on health care systems and introduced modifications to the delivery of care. In Australia, changes include shift to telehealth appointments, restricting procedures, and limiting the number of people attending appointments. There is limited evidence on how these changes impacted parents and children during oncology care. This study aimed to examine parental experiences during child's oncology care amidst pandemic in Australia.
Methods: Cross-sectional online survey conducted with parents of children diagnosed with cancer in the past 5 years when aged between 0-12 years. Participants completed the DASS-21, 17 items assessing the impact of COVID-19 on the child's medical care, and hospital care experience.
Results: Forty parents participated (Response rate 48%; 98% mothers). Children were under different phases of treatment (25%-active treatment, 30%-maintenance therapy, 42.5%- follow-up). DASS-21 scores indicated on average parents experience mild depression (M=13.3, SD=11.0), and moderate anxiety (M=11.0, SD=10.2)/stress (M=19.6, SD=10.2). Majority (88%) maintained face-to-face appointments and felt safe at appointments (M=8.2, SD=2.7). However, 30% reported delays booking appointments, 15% were not able to ask all their questions about COVID-19, 13% did not feel safe from COVID-19 during hospital visits and 20% were moderately to highly anxious about possible impact of COVID-19 on child's health. The majority (53%) reported that they did not receive information about the risk of COVID-19 virus on their children. Lack of information was associated with feeling unsafe at appointments ($r = -.445$, $p<0.05$), feeling anxious about the impact of COVID on their child's heath ($r=.443$, $p<0.01$) and higher scores on DASS-Anxiety ($r=.325$, $p<0.05$).
Conclusions: While many parents experiences of their child's health care during the pandemic were positive, there was a need for greater information and support in asking questions. Understanding family experiences of pediatric oncology care during pandemic is important for developing better health care practices.

EP588 / #884

Topic: *AS05.q Psychosocial (PPO)*

PARENTAL BURNOUT IN PARENTS OF CHILDREN UNDER THERAPY FOR LEUKEMIA: FACTORIAL ANALYSIS OF THE QUESTIONNAIRE AND POSSIBLE ASSOCIATIONS WITH BEHAVIORAL SYMPTOMS IN THEIR CHILDREN

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Background and Aims: Parental burnout is a global exhaustion of the role of parent, an emotional detachment from children and a loss of self-perception as a good parent (Roskam & Mikolajczak, 2020). Parental chronic oppressive stress affects not only the parent but also the child. This study aims to identify the possible dimensions of Parental burnout in parents of children with leukemia and its possible associations with emotional and behavioral symptoms in their children.
Methods: Participants who signed the informed consent were principally mothers (N = 47; 92.2%) while there were only 4 fathers (7.8%) recruited at the Pediatric Onco-Hematology Clinic, University of Padua. Their average age was 40.5 years (SD = 7.15; range 22-54) and they mostly were married or cohabitants (91.1%). Their children, aged between 3 and 10 years (average age = 6.5 years; SD = 2.07), underwent the first month of hospitalization for leukemia. They were 26 males and 27 females, 83% were Caucasian and 17% non-Caucasian. They filled in questionnaires on their Parental Burnout and Child Behavior Check List about their children.
Results: A Varimax factor analysis found that the best model explained 44.4% of variance with two identified factors: "Parental inefficacy perception" and "Parental Exhaustion and Emotional Distance", with their Cronbach alphas greater than 0.75. A series of Spearman's correlations were run, and significative associations were found between parental burnout and children's internalizing (rho = 0.46; $p = 0.01$) and externalizing (rho = 0.57; $p < 0.001$) symptoms but limited to schooling age children.
Conclusions: Some aspects of Parental burnout such as exhaustion and emotional distance could be related to children's negative symptoms. The onco-hematological diagnosis is considered as familiar disease and for this reason the psychological interventions should be focused also on parental well-being, reducing their stress, and ameliorating their parenting role.

EP589 / #889

Topic: *AS05.q Psychosocial (PPO)*

VOLUNTEERING AT PEDIATRIC ONCOHEMATOLOGY: AN ANALYSIS OF THE NARRATIVES CONCERNING THE MOTIVATION AND PSYCHOLOGICAL WELL-BEING DURING THE COVID-19 EMERGENCY

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Background and Aims: The phenomenon of volunteering is very widespread in the world and in Italy with ever-growing numbers (6.63 million in 2013). The possibility of volunteers to continue their activities in the hospitals have blocked during the Covid19 pandemic. The aims of this study are to assess the psychological well-being and motivation associated with volunteering in pediatric oncohematology during the March 2020 lockdown.
Methods: Participants were twenty-five volunteers (8 males and 17 females) at Pediatric Oncoematology Clinic, University of Padua. They had an average age of 54.52 years (SD=15.59; range: 26-73), 12 with a current job and 13 not working. A socio-demographic questionnaire and a semi-structured interview consisting of twenty-five questions were administered online using video calls with Skype. After obtaining the participant's consent, the entire interviews were audio-recorded and fully transcribed.
Results: A word cloud analysis of the interviews adopting software QRS N-vivo identified as the main volunteers' characteristics the more recurrent words belonging to Empathy (N=21), Relational skills and Discretion / Flexibility (N = 19). The main reasons for the volunteers' choice were Expression of values (N=18), Growth (N=16) and Social (N=10). A Wilcoxon test (Z= -4.207; p= 0.0001) found that the volunteers' experience was significantly reported as Good (Mean=7.76) than Bad (Mean=2.60). Most of the volunteers reported the possibility to do online activities with children during lockdown (60%), even if the majority perceived this option as difficult to do (90.47%). They used more negative words (Mean = 2.36) than positive ones (Mean = 1.20) when speaking about isolation (Z= -1.94; p= 0.05).
Conclusions: Volunteers reported more adoption of positive words during their activities with the children in the hospitals and they identified empathy as the most important characteristic of the volunteer profile. Online activities with children during lockdown were considered difficult and they adopted more negative words related to the isolation.

EP590 / #891

Topic: *AS05.q Psychosocial (PPO)*

SIBLINGS IN PEDIATRIC ONCOHEMATOLOGY COMPARED WITH HEALTHY PEERS: PSYCHO-SOCIAL WELL-BEING AND ASSOCIATED FACTORS

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Background and Aims: Siblings in pediatric oncohematology could have negative sequelae such as somatic complaints (Lane & Mason, 2014) and psycho-social problems (Wallin et al., 2016), but also positive social and personal growth (Sloper, 2000). This study aims to: 1. screen possible emotional and psycho-social difficulties in siblings; 2. study the relationship between siblings along patient's and sibling's perceptions.
Methods: Participants were 21 siblings with a mean age of 9.61 years (SD= 2.28; range: 5.8-13), 62% females and 76% firstborn recruited at the Onco-Hematology Clinic, University of Padua. Pediatric patients were 21 with a mean age of 7.7 (SD = 3.35; 1.06-15), 86% with leukemias. After the signature of informed consent by parents, several self and proxy questionnaires were given to patients and their siblings during the first four months from the diagnosis., i.e. Child Behavior Check List (CBCL), Strengths Difficulties Questionnaire (SDQ) and Siblings Inventory of Behavior (SIB). The same questionnaires were filled in also by matched siblings of healthy peers.
Results: A Wilcoxon test showed no significative differences between clinical and control group along CBCL scores, even if 50% of siblings in the clinic group showed clinical levels in the internalizing symptomatology. Siblings' age was positively associated with emotive (rho=0.6; p=0.009) and conduct problems (rho=0.61, p=0.007) and their birth order was negatively associated with social problems (rho=-0.51, p=0.03). Siblings' age was negatively associated with Empathy (rho=-0.55; p=0.01) and their birth order was negatively associated with the total mean of feelings in the fraternal relationship (rho=-0.47; p=0.05). A Wilcoxon test found that Empathy (Z= -1.93; p= .05) was distributed differently between patients (Mean ranks = 8.55) and their siblings (Mean ranks = 6.5).
Conclusions: No differences were found in the behavioral symptoms' frequency comparing clinical and control groups. Older and first birth siblings reported more emotive and social problems and have lower empathy.

EP591 / #902

Topic: *AS05.q Psychosocial (PPO)*

A PARTICIPATIVE PROCESS TO ADAPT AND IMPLEMENT PSYCHOSOCIAL STANDARDS OF CARE IN CHILDHOOD CANCER IN PERU

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Background and Aims: Since 2019, the WHO Global Initiative for Childhood Cancer (GICC) has been implemented in Peru. As a formal collaboration between the Pan American Health Organization, the Ministry of Health, Childhood-Cancer-International, and La Roche-Posay, a nation-wide project was initiated to improve the psychosocial care (PC) of children with cancer in Peru. The aim of this study was to conduct a national situational assessment, determine the level of compliance of the international PC standards and finally, to develop and implement local standards, including activities and tools to implement them.
Methods: A pilot mix-method study was conducted for two years involving several stakeholders, including project managers, local experts, regional partners and pediatric oncology providers in Peru. A psychosocial GICC committee was formed to design activities and tools to implement the PC standards in Peruvian institutions. Six standards were proposed: psychosocial assessment, psychoeducation and support, mental health care, reintegration and survival resources, competences and self-care in health professionals, and transversal approaches.
Results: Between Jul/19 and Mar/22, X professionals from 15 Peruvian institutions and regional collaborators were involved in the pilot study. After a national PC assessment, we determined that international psychosocial standards were poorly provided at most Peruvian centers. The development of the conceptual framework of the PC local standards involved the participation of national and international professionals in a think-tank meeting, 98 online meetings and a webinar. Four technical products

(national psychosocial assessment tool; PC guide for parents, PC screening tool, and 4 educational documents), and one national meeting were developed to improve PC in childhood cancer in Peru. **Conclusions:** In the present study, we propose a conceptual framework defining relevant phases to develop and implement PC local standards in pediatric cancer, through transdisciplinary collaboration. The ongoing work of professionals throughout the country has been relevant to develop materials to implement the PC standards in Peru.

EP592 / #1755

Topic: *AS05.q Psychosocial (PPO)*

STANDARDS FOR THE PSYCHOSOCIAL CARE OF CHILDREN AND ADOLESCENTS WITH CANCER: AN ADAPTED PROPOSAL IN LATIN AMERICA COUNTRIES

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Background and Aims: The World Health Organization Global Initiative for Childhood Cancer (GICC) aims to improve outcomes for children with cancer around the world guided by the CureAll framework. The development of the conceptual framework of the standards of psychosocial care (PC) began in Peru in 2019. The proposal is aligned with the CureAll objectives, in specific the first pillar for centers of excellence and care of children and adolescents diagnosed with cancer, including quality of care. Expanding and implementing PC standards in Latin American Countries (LAC) is relevant for reducing psychosocial risks and promoting coping strategies for patients and their families.
Methods: A Latin American GICC psychosocial working group was established focused on improving PC for children and adolescents with cancer through the implementation of standards of care in LAC. Between Jun/21 and Dec/21, monthly online meetings were scheduled to review background documents and materials related to the standards and conduct regional discussions about four questions related to each PC standard, entitled: “what we know”, ”what we propose”, “what works”, and “how we can apply it”.
Results: Fifteen professionals from six LAC attended 6 online meetings and revisited previous educational materials about PC standards. Six (6) technical fact sheets about psychosocial standards of care were developed with relevant information to improve the quality of care in LAC childhood cancer institutions. An operative plan has been designed to validate the strategies to implement each standard at different levels according to short, medium, and long-term goals and available resources.
Conclusions: Implementing psychosocial standards contribute not only to LAC children and adolescents with cancer but also may allow other low and middle-income countries to replicate this process and improve PC.

EP593 / #1410

Topic: *AS05.q Psychosocial (PPO)*

LONG-TERM FUNCTIONING OF CHILDHOOD CANCER SURVIVORS AND THEIR PARENTS: LONGITUDINAL RELATIONS WITH PARENTAL INCOMPETENCE AND PARENTING DIMENSIONS

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Background and Aims: Most childhood cancer survivors tend to be resilient in the long term, with benefit finding being frequently reported. However, some survivors suffer from depressive symptoms and cancer-related worries as well. As cancer is considered a 'family disease', investigating the role of parental functioning and parenting may provide insight into why some youth experience growth and others struggle. The current study examined the directionality of effects among parental incompetence, parenting dimensions (i.e., responsiveness, psychological control, and overprotection), and survivor functioning (i.e., depressive symptoms, cancer-related worries, and benefit finding). Additionally, we investigated if parenting mediates the effect of parental incompetence on survivor functioning.
Methods: Our three-wave longitudinal questionnaire study included 125 Dutch-speaking survivors (14-25 years at baseline) who completed their treatment, 114 mothers and 82 fathers. Survivors reported (SR) about mothers' and fathers' parenting and their own functioning. Mothers (MR) and fathers (FR) reported about their parenting and sense of incompetence. Cross-lagged panel models were estimated for each informants' perspective on parenting separately.
Results: Primarily unidirectional relations were found, i.e., from parental incompetence to parenting, and from parenting to survivor functioning. Different relations were obtained for each informant. First, parental incompetence positively predicted maladaptive parenting SR, MR and FR. Second, maternal responsiveness SR positively predicted benefit finding SR and negatively predicted depressive symptoms SR, whereas responsiveness MR positively predicted cancer-related worries SR. Overprotection MR positively predicted depressive symptoms SR. Finally, one reversed pathway emerged, responsiveness SR negatively predicted parental incompetence. Also, correlated changes indicated co-development among these variables. There was no evidence of mediation, as there were no significant pathways linking parental incompetence to parenting which, in turn, predicted survivor functioning.
Conclusions: Results support parent-driven processes in survivors' long-term functioning and a need to consider parents' sense of incompetence in research and clinical practice. Additionally, our findings stress considering multiple perspectives when investigating family dynamics.

EP594 / #721

Topic: *AS05.q Psychosocial (PPO)*

IDENTITY FORMATION AND GENERIC AND ILLNESS-SPECIFIC FUNCTIONING IN ADOLESCENT AND EMERGING ADULT CANCER SURVIVORS: A LONGITUDINAL INVESTIGATION INTO DIRECTIONALITY OF EFFECTS

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Background and Aims: Youth who survived childhood cancer generally adjust well psychologically and achieve important developmental milestones through life similar to their peers. Nevertheless, some survivors are at greater risk for developing psychological and physical problems. To shed light on these individual differences, identity formation and its interplay with psychosocial functioning need to be investigated. The aim of the present study was to examine the longitudinal associations linking personal identity formation and generic and illness-specific functioning in adolescent and emerging adult childhood cancer survivors using three-wave data over a two-year period.
Methods: Dutch-speaking survivors (14 - 25 years) who were treated at the pediatric oncology department of the University Hospitals Leuven (Belgium) completed self-report questionnaires addressing identity formation, depressive symptoms, life satisfaction, physical functioning, cancer-related worries, posttraumatic stress symptoms, and benefit finding. A total of 125 survivors participated at baseline, 100 survivors at T2, and 93 survivors at T3. Directionality of effects was examined using cross-lagged structural equation modeling.
Results: Regarding generic functioning, bidirectional effects occurred. Life satisfaction positively predicted identity synthesis and both life satisfaction and good physical functioning negatively predicted identity confusion over time. Identity synthesis, in turn, positively predicted life satisfaction and identity confusion negatively predicted good physical functioning over time. Regarding illness-specific functioning, mainly unidirectional effects occurred. Posttraumatic stress symptoms negatively predicted identity synthesis and positively predicted identity confusion over time, whereas the reverse pattern of associations was found for benefit finding. Several correlated changes were found linking identity formation and psychosocial functioning as well, attesting to co-development.
Conclusions: The current study focused on clarifying the longitudinal associations linking identity synthesis and confusion to both generic and illness-specific functioning in youth who survived childhood cancer. Several significant pathways emerged that can substantially inform both clinical practice and future research.

EP595 / #313

Topic: *AS05.q Psychosocial (PPO)*

RISK OF ALTERATIONS IN NEURODEVELOPMENT IN INFANTS AND PRESCHOOLERS WITH CANCER IN A REFERENCE HOSPITAL IN MEXICO

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Background and Aims: Systemic and intrathecal chemotherapy can cause cognitive impairments in the form of lowered concentration, attention, and memory power in cancer survivors. However, there is no information on the effect of cancer treatment on neurodevelopment in cancer patients under five years of age. Therefore, the aim was to evaluate neurodevelopment in cancer patients under five years of age through the Infant Development Assessment test.
Methods: A cross-sectional study was carried out from February 2018 to March 2019. Patients with cancer diagnoses outside the central nervous system in any phase of cancer treatment were included.
Results: A total of 45 patients were included. Regarding the areas of development, the following was the result: In the gross motor area, 31 (68.8%) patients were green, while 35 patients (77.7%) were in the fine motor area. In the fine motor area, 28% of patients with retinoblastoma and 23% of patients with leukemias and lymphomas were found in red (delay) compared to 0% of patients with solid tumors (P = 0.025).The final result of the test found that 19 (42.2%) patients were in the green with normal neurodevelopment, 7 (15.5%) in the yellow with a lag in neurodevelopment, and 19 (42.2%) in the red with a risk of delay in the development. Of the patients with developmental delay, 52% were from the leukemia and lymphoma group, 71% from the retinoblastoma group, and 23% from the solid tumor group (P = 0.06).
Conclusions: The risk of delay and lag in neurodevelopment is frequent in cancer patients under five years of age undergoing treatment. However, more studies are required to evaluate the effect of treatment in this group of patients since various factors may influence them.

EP596 / #696

Topic: *AS05.q Psychosocial (PPO)*

EXPECTATIONS OF CHILDREN WITH CANCER, NEUROMUSCULAR DISEASES OR ANXIETY, AND TEACHERS FOR TELEPRESENCE ROBOTS AS A TOOL TO REDUCE ABSENCE IN EDUCATION

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Background and Aims: School absence negatively influences children's academic advancement and psychosocial wellbeing. This study explores expectations for telepresence robots as a tool to reduce absence in education.
Methods: A qualitative semi-structured interview study. Using convenience sampling, we interviewed 11 children aged 8–17 years with cancer (n=4), neuromuscular diseases (n=3) or anxiety (n=4) who had a high level of school absence (more than 15 days' absence in a school year), and who had recently encountered a telepresence robot; and eight of their teachers. A thematical analysis and a deductive approach based on the theory of Technological frames were used.
Results: The children's and teachers' expectations of how telepresence robots could support them in reducing their school absence were identified and structured in three categories and five main themes: 1) Nature of technology: a) Learning, b) Sociality, c) Additional supportive resources; 2) Technology strategy: a) Flexible school day; 3) Technology in use: a) New workflows. Children and their teachers had positive expectations regarding telepresence robots as being a flexible tool to support children with high absence in re-integrating in the school environment, both socially and academically. However, in relation to inclusion, the expectations across diagnostic groups varied from an opportunity of creating friendships to maintaining existing friendships. Teachers expected that the telepresence robot implementation requires additional supportive resources from them such as establishing blending learning situations, new workflows in education and coordination between family and school. However, the teachers were willing to allocate the resources because they saw potential in the new technology as a tool to reduce the high level of absences.
Conclusions: The organization around telepresence robots in school settings is lacking because the implementation process is still in an explorative stage. It is a simple technology, but it requires new workflows and structures in the organization and school environment.

EP597 / #1656

Topic: *AS05.q Psychosocial (PPO)*

RESULTS OF FEASIBILITY - WHAT DOES IT TAKE TO IMPLEMENT STANDARDIZED PSYCHOSOCIAL TOOLS: "MEIN LOGBUCH – ICH KENNE MICH AUS!" („MY LOGBOOK")

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Background and Aims: Psychosocial care and research are well-documented essential components in pediatric oncology care. Hence, guidelines and standards offer evidence-based framework for quality assurance. Nevertheless, actual care is quite heterogenous and reveals a care gap. Highly complex, system-wide interventions represent considerable challenges for operationalization of relevant factors and evaluation of psychosocial processes compared to single interventions. To bridge the gap from need to implementation literature reveals specific demands and research methods as well as successful implementation strategies. Quality improvement (QI) is an iterative process designed to make controlled changes within the health care delivery system to provide patients with high-quality care.
Methods: PDSA cycles were applied in all steps of a multilevel, interdisciplinary conceptualization and implementation. We present a protocol of a mixed methods observational study to gain more insight on sustainability, implementation and its determinants. Therefore we observed communication levels (face-to-face discussions, telephone conferences, e-mail exchange) combined with regular online Surveys (D-A-CH region). Participants are associated HCP in regular research meetings by the local expert-research group (N=11), expert groups with multidisciplinary HCP and stakeholders (N=28) for the development and expert validation of 18 theme booklets, monitoring group (quality assurance group/PSAPOH), N=47 Experts in a delphi-survey and N=48 Study coordinators/Collaborators in the multicenter pilot phase.
Results: Implementation factor "Characteristics of the intervention" reached an overall consensus above 80% and include predominantly design quality, cost and evidence strength/quality. However, "inner setting", despite acceptable implementation climate due to high response (sites N=27), highlights major obstacles: structural framework, funding, research culture, improvement on networks and communication, personnel resources and pandemic. Hence, we derived and realized expert trainings/training videos, manual, regular meetings (exchange, mutual support), FAQs, and organizational assistance.
Conclusions: Implementing standards demands the establishment of research & care networks, concrete methods/tools for good scientific and clinical practice, adaptation of structural framework conditions of the health care system.

EP598 / #127

Topic: *AS05.q Psychosocial (PPO)*

SOCIAL PARTICIPATION AMONG SURVIVORS OF PEDIATRIC BRAIN TUMORS AS MEASURED THROUGH A DAILY DIARY

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Background and Aims: Pediatric brain tumor survivors (PBTS) experience difficulties with social functioning. Social participation - the frequency of social interactions and the maintenance of relationships - is associated with emotional health. This paper aims to describe the social participation of PBTS to better understand their social functioning.
Methods: PBTS (n=64, 54.7% female, 85.9% white, 40.6% medulloblastoma) were enrolled on a study assessing social functioning. Youth were 10.58 (SD=1.37) years old and 5.24 (SD=2.46) years off-therapy. Youth completed a daily diary which asked participants to record the social interactions experienced daily for seven days across five categories: social victimization, physical victimization, exclusion, positive social interactions, and participation in social activities. Parents provided information about their child's overall social participation (e.g., number of outside school peer interactions).
Results: Three-quarters of participants (n=47) completed the Daily Diary at least five of seven days. Participants most frequently identified positive social interactions, with an average of 11.38 interactions endorsed (SD=7.9). Physical victimization (M=0.79, SD=2.23) was infrequently reported. Twenty-six survivors (40%) indicated experiencing one or more negative social interactions during the five-to-seven-day diary period. Of these 26, 53.8% of children engaged in no clubs or out-of-school activities. Frequencies of social interactions indicate generally low participation for a large subset of survivors, especially when including data from parents: 25% of survivors (n=16) recorded less than ten interactions for the entire week and 46.9% of parents (n=30) reported their child having less than one social interaction outside of school per week.
Conclusions: The use of daily diaries revealed a wide range of social experiences for PBTS. There appears to be a notable number of survivors who are engaging in little to no social participation during the average week. Lack of participation in regular social interactions may contribute to PBTS difficulties with social functioning; however, further work to assess this is needed.

EP599 / #590

Topic: *AS05.q Psychosocial (PPO)*

PERCEPTIONS OF PARENTING AMONG CAREGIVERS AND SCHOOL-AGED SURVIVORS OF RETINOBLASTOMA

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Background and Aims: Retinoblastoma is the most common intraocular childhood cancer and is typically diagnosed in young children. With increasing numbers of survivors and improved medical outcomes, long-term adjustment and psychosocial impacts merit exploration. The current study examines both caregiver- and patient-reported perceptions of parenting among school-aged survivors.
Methods: Sixty-nine survivors of retinoblastoma underwent an assessment of psychosocial functioning. Survivors (age=10.89±1.07 years; 49.3% male; 56.5% unilateral disease, 68.1% treated with enucleation, years since diagnosis=9.37±1.16) completed the Parental Bonding Instrument to assess perception of one's parenting relationship with one's primary caregiver. Caregivers completed the Parenting Relationship Questionnaire, a complementary assessment of a parent's view of their relationship with their child across multiple domains.
Results: Survivors' report indicated that parenting was perceived as high on the care dimension (M=30.32) and within the low range for overprotection (M=14.87). Perceptions of parental care and overprotection did not vary by disease laterality or enucleation status (all $p>0.05$). Caregiver report indicated that perceptions of parenting fell in the average range across assessed domains including attachment (M=50.25), communication (M=53.26), discipline practices (M=49.19), involvement (M=52.53), parenting confidence (M=53.82), and relational frustration (M=45.47). Caregiver perspective of the parent-child relationship did not differ by disease laterality or enucleation status (all $p>0.05$). Child-reported perceptions of parental caring were positively correlated with parental report of attachment ($r(52)=.32$, $p=0.02$) and involvement ($r(52)=.33$, $p=0.02$).
Conclusions: Results indicate that survivors of retinoblastoma report an optimal parenting experience, with parents who are caring without being overly protective. Similarly, parental perspective of the parent-child relationship indicated parenting within the average range across multiple domains. Disease- and treatment-related factors do not appear to impact this relationship. Overall, results suggest that survivors of retinoblastoma experience appropriate, responsive parenting from caregivers. Future research should continue to examine illness-related aspects of adjustment to characterize long-term functioning of survivors.

EP600 / #1286

Topic: *AS05.q Psychosocial (PPO)*

QUALITY OF LIFE OF CHILDREN AND ADOLESCENTS WITH CANCER BEFORE AND DURING THE WAR IN UKRAINE

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Background and Aims: Oncology, COVID-19, war... what is the biggest impact on a child's mental health? May be all three factors at once? Can we talk about the quality of life in such conditions? Turning to the famous works of Victor Frankl, let's try to assume our capabilities. We prioritize understanding the assessment of quality of life in children with cancer, as the idea that it is primarily the disease affects human life. The war in Ukraine has significantly changed the medical services for children with cancer, so it is important now to investigate how the quality of life of a child with cancer has changed.
Methods: The Pediatric Quality of Life Inventory (PedsQL 3.0 Cancer Module) questionnaire was used for 131 people (children aged 5 to 18 and their parents) and divided on two groups:before war in Ukraine (n1 = 64) and another during war (n2 = 67).
Results: Indicators of the average value according to the scales of the group n1 and n2, respectively (where Xnorm.=100): pain (55.2/79.8); nausea (51.9/79); anxiety associated with procedures (42.8/32.3); anxiety associated with treatment (65.2/56.8); general anxiety (39.6/32.5); cognitive problems (63.9/42.1); physical perception of appearance (68/74,2); communication (71/40). The overall quality of life index x group n1 is the lowest in children/adolescents 13-18 years (x = 52.26) compared to 5-7 years (x = 58.3) and 2-4 years (x = 63.5). In group n2, in general, the quality of life in all age groups of children decreased significantly: 5-7 years (x = 47.7), 8-12 years (x = 54.3), 13-18 years (x = 45.9).
Conclusions: Self-assessment of health is a more powerful predictor of mortality and morbidity than many objective indicators of health. A structured assessment of the quality of life of children with cancer during the war is an important final point for further correct treatment and rehabilitation.

EP601 / #412

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

MICROORGANISM PATHOGEN PATTERN IN PEDIATRIC ONCOLOGY PATIENTS WITH FEBRILE NEUTROPENIA ADMITTED TO TERTIARY REFERRAL HOSPITAL DURING PANDEMIC CORONAVIRUS-19

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Background and Aims: Almost 700,000 deaths attributable to multidrug-resistance (MDR) occurring each year with Enterococcus spp., Staphylococcus aureus, K. pneumonia, Acinetobacter baumanii, P. aeruginosin, and Enterobacter spp. (ESKAPE) pathogens became main concern mainly because of risk to became resistence pathogen, while COVID-19 pandemic presents an unprecedented global threat to the safe and effective care for children with cancer, one of the reason they were more prone to be infected and treated with antibiotic irrationally. Aim of this study to discribe the incidence of MDR, extensively drug-resistant (XDR) and pan drug-resistant (PDR) in febrile neutropenia patient that admitted during pandemic period that could be present many difficulties come to hospital to seek treatment.
Methods: All pediatric oncology patients diagnose with febrile neutropenia from January 2020 to Februari 2022 were retrospectively studied. Data consists of demography pattern, underlying disease, number of drawn blood culture and positive results, type of bacteria, sensitivity pattern. International standard definitions for acquired resistance by ECDC and CDC was used as definitions for MDR, XDR and PDR bacteria
Results: Most of patient came to hospital in severe neutropenia stage (74,6%). Main underlying oncology cases are ALL (38,1%), from 153 speciment collected out of 189 subjects, there were 26 (17%) growth founded from culture. 13, 6, 6, 1 founded in blood, urine, pus, sputum respectively. ESKAPE pathogen dominantly founded in blood with E. Coli is the most (46,2%), 11 (84,6%) of them are MDR pathogen while 1(7,6%) is XDR pathogen, there were not any possible PDR pathogen founded.
Conclusions: The prevalence of MDR pathogens is quite high, but the XDR and PDR pathogen is still low, antibiotic for treatment based on guideline and local antibiogram pattern could be rationally use, however, despite the low number, antibiotic resistance remains one of the main challenging issues demanding for further attention expecially in pandemic era.

EP602 / #1827

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

LEVERAGING THE PROFILE TOOL TO IDENTIFY NATIONAL PRIORITIES AND SUPPORT GLOBAL INITIATIVE FOR CHILDHOOD CANCER (GICC) COUNTRY STATUS IN CAMEROON

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Background and Aims: Paediatric oncology professionals must work together with civil society and government to improve childhood cancer survival in low- and middle-income countries. The Cameroon National Strategic Plan for the Fight Against Cancer (NSPFAC) aims to improve survival by 25% for all cancers by 2024. To identify priority actions towards this goal, the Cameroon Paediatric Oncology Group and National Committee for the Fight Against Cancer led a national priority-setting initiative.
Methods: The St Jude Global Paediatric Oncology Facility Integrated Local Evaluation (PrOFILE) tool was used to identify opportunities for improvement. A baseline assessment was conducted by institutional representatives at two hub centres and one shared care centre. Data was analyzed centrally at St. Jude. Using these data as evidence to guide discussion, a hybrid national stakeholder workshop was organized and led by the Ministry of Health. Using a co-design methodology, four exercises were completed by 49 in-person stakeholders in order to identify 12 priorities.
Results: From baseline data analysis, strengths and weaknesses were identified and recommendations made for six domains including: national context, workforce, diagnostics, chemotherapy and supportive care, surgery and radiotherapy, and patients and outcomes. The priority action areas identified were training at all levels; strengthening cancer registry; and increasing funding for care and research. Next steps identified included: develop an action plan in line with the NSPFAC; organize working groups to address the identified priorities; engage the World Health Organization to support activities that align with the CURE ALL Framework.
Conclusions: By leveraging technical support from St Jude Global, the Cameroon MoH leadership and civil society stakeholders have identified key priorities to support childhood cancer activities nationally. In addition, the workshop report was shared with World Health Organization officials to demonstrate ongoing work and request additional support through the GICC.

EP603 / #687

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

EPIDEMIOLOGY OF PEDIATRIC CENTRAL NERVOUS SYSTEM TUMORS: A SINGLE-CENTER EXPERIENCE FROM 2013 TO 2019

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Background and Aims: Pediatric central nervous system (CNS) tumors are the most common solid tumors during childhood, but few epidemiological studies in this group. We aimed to characterize the epidemiological profile of pediatric patients with CNS tumors at Barretos's Children and Young Adults Cancer Hospital, a reference for the treatment and management of children with CNS tumors in Brazil.
Methods: This study retrospectively evaluated patients treated at Barretos's Children and Young Adults Cancer Hospital from September 2013 to December 2019. 313 patients were collected from the REDCap platform and included: histopathology reports, patient demographics, symptoms/signs at the time of diagnosis, symptom interval, and anatomical site of the tumor. Patients were divided into groups 1 (less than or equal to 2 years of age) and group 2 (greater than two years of age).
Results: Of the 313 cases reviewed, 53.7% were males, and 46,3% were females. The average age was 8.5 years. The interval between the onset of signs and symptoms until diagnosis was three months. Approximately 5.1% of cases are associated with genetic syndromes. The number of patients younger than two years was 35 (11.2%), and those ≥ 2 years 278 (88.8%). The most frequent symptoms/signs recorded at presentation were: headache (59.7%), nausea/vomiting (39.6%), cranial nerve palsy (27.2%), seizures (17.9%), limb weakness (16.6%), cerebellar syndrome (15.7%), visual changes (15.3%). Patients in Group 1 presented different frequencies of signs and symptoms concerning Group 2, prevailing: vomiting (40%), developmental delay (25.7%), cranial nerve palsy (17.1%), and limb weakness (17.1%).
Conclusions: We report important epidemiological information for Brazilian pediatric CNS tumors. We identified differences in diagnostic range, signs, symptoms, histological types, and regions affected in children younger than or equal to 2 years of age and children older than two years.

EP604 / #527

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

IMPACT OF COVID-19 PANDEMIC TOWARDS PEDIATRIC CANCER CARE: A SYSTEMATIC REVIEW

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Background and Aims: Cancer, when identified early, is more likely to respond to effective treatment. COVID-19 pandemic causes reduction in services therefore patients experience significant delay in diagnosis and treatment. In particular, pediatric cancer patients are considered vulnerable subjects despite encompassing around only 5-10% of total cancer cases. Herewith we perform a systematic review to determine the extent of changes in healthcare and the outcome in pediatric cancer cases during the COVID-19 pandemic and postpandemic.
Methods: PubMed, EBSCO Host, the Cochrane Library, and Proquest were searched up to March 2022 using concepts including COVID-19, pediatric cancer, and impact. Inclusion criteria were: 1) Studies describing timing of diagnosis and treatment of pediatric cancer in COVID-19 pandemic period in children; 2) reporting of at least one of the following outcomes: delay in diagnosis, treatment. We excluded letters and editorials. Risk of bias was assessed by using the ROBINS-I tool. Primary outcome was delayed diagnosis and treatment, with secondary outcome was change in hospital visit compared with telemedicine.
Results: Fifteen studies out of 12.466 hits were identified reporting from > 10 different countries. There are reported delays in diagnosis varying from 3.5% - 62%, delays in treatment varying from 3.5% - 64.6% (including chemotherapy, radiotherapy), and also a shifting trend into preferring telemedicine over hospital visits. Reasons for delay include limited service, risk of infection, and COVID-19 infection. Reported positive impacts include higher appointments via telemedicine, and receiving cancer care closer to home/decentralized care. There are no differences between solid and hematological cancers.
Conclusions: The COVID-19 pandemic has negative impacts in the already vulnerable subjects that are pediatric cancer patients ranging from delays in diagnosis into treatment. Even so, the pandemic has shown us the possibility of employing telemedicine in pediatric cancer healthcare utilization to help in postpandemic recovery and future pandemics.

EP605 / #1965

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FACTORS ASSOCIATED WITH DELAYED DIAGNOSIS OF CANCER IN CHILDREN UNDER 15 YEARS OF AGE IN THE ONCOHEMATOLOGY UNIT OF HOSPITAL DEL NIÑO OVIDIO ALIAGA URIA

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Background and Aims: Early diagnosis of childhood cancer is essential, since it allows treatment in early stages, which results in a better prognosis and a positive effect on quality of life. First contact physicians seldom interpret symptoms in a timely manner and this implies a delay in diagnosis; Parents do not always give importance to symptoms, which also causes delay. By virtue of knowing these data, the objective of this research was proposed: Identify the factors associated with the delay in cancer diagnosis in children under 15 years of age treated at the Oncohematology Service of the Ovidio Aliaga Uria Children's Hospital.
Methods: It is a non-experimental, retrospective, analytical work, the information was obtained in direct interviews with the parents and review of clinical records applied to 104 patients; subsequently analyzed by calculating the mean and statistical significance for the different non-parametric variables using the Kruskal Wallis and Whitney's Mann U test.
Results: A mean delay by parents of 39.44 days (63.7 SD) was obtained (minimum 1 day and maximum 360 days); the mean delay of health personnel, also called diagnostic delay, was 26.84 (38.8 SD), (minimum 1 day and maximum 210 days); and a mean total delay of 66.28 days (77.3 SD), minimum of 5, maximum of 376. The factors associated with paternal delay with statistical significance were age (p 0.021); the smaller the child, the less delay time; the type of tumor, having a longer delay in bone tumors (mean of 112 days), and retinoblastoma with a mean delay of 104 days. The factors associated with diagnostic delay by medical personnel were diagnostic certainty, having less delay time in the event of early suspicion of oncological pathology (p 0.01)
Conclusions: The factors associated with total delay are age, type of cancer and educational level of the parents. Greater delay attributed to parents

EP606 / #1763

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

HEREDITARY CANCER SYNDROMES, THE FORGOTTEN OF LONG-TERM FOLLOW-UP CARE OF PEDIATRIC ONCOLOGY: NEUROFIBROMATOSIS TYPE 1, EPIDEMIOLOGICAL OVERVIEW OF A SINGLE INSTITUTION IN MEXICO.

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Background and Aims: Neurofibromatosis type 1 (NF1), autosomal dominant disorder, heterozygous loss-of-function mutation in the NF1 gene. It is part of hereditary cancer syndromes (HCS). Patients with NF1 have a decrease in life expectancy of about 15 years compared with the general population, Cancer is a leading cause of death, these patients are susceptible to some type of screening and follow-up care. Objective: to know the epidemiological panorama of NF1 in our institution, and to establish the need for an HCS clinic for multidisciplinary follow-up.
Methods: Cross-sectional retrospective cohort study in <25 years with a diagnosis of NF1, between January 2011 and September 2021, National Medical Center "20 de Noviembre", we obtained demographic variables, details of the multidisciplinary follow-up care, we evaluated the multidisciplinary follow-up care according to the number of medical specialty that provided follow-up care: good(>7 physician specialties), regular(4-6 physician specialties) and bad(<3 physician specialties).
Results: During the study period, 115 patients were diagnosed, we eliminated 13, leaving 102 patients, 52 female and 50 male; age range from 1 month to 23 years; mean age: 8.8 years; 62% had no family history of NF1, 25% development of plexiform neurofibroma: 35% abdominal, 27% head and neck, 19% chest, 19% extremities, 52% had bad multidisciplinary follow-up care, 15% regular and 28% good. The first contact medical specialty was Medical genetics 45%, and only 14% presented follow-up care by Pediatric Oncology, 10% course with diagnosis of cancer: tumors of the central nervous system 55%; sarcomas 18%, and hematological neoplasms 27%; 36% abandoned follow-up care and 5% were reported as deaths.
Conclusions: The care of patients with NF1 requires the teamwork of multiple medical specialties, in order to establish screening and health education programs, to improve timely detection of cancer and their life expectancy.

EP607 / #2004

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

INFECCIONES ASOCIADAS A LA ATENCIÓN DE SALUD EN PACIENTES PEDIÁTRICOS CON INMUNOSUPRESIÓN POR VIRUS DE INMUNODEFICIENCIA HUMANA Y CÁNCER

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Background and Aims: RESUMEN Infecciones Asociadas a la Atención de Salud (IAAS) incrementan estancia hospitalaria, morbilidad y mortalidad en inmunocomprometidos. Objetivo: Evaluar evolución clínica y pronóstico de pacientes pediátricos con VIH (Virus de Inmunodeficiencia Humana) y cáncer que presentan eventos de IAAS hospitalizados.
Methods: MÉTODOS Método: estudio observacional, descriptivo, prospectivo del Hospital de Niños JM de los Ríos en pacientes entre 1 mes - 18 años, durante 2014 – 2017; formulario incluyó demografía, tipo de infección, estancia hospitalaria, tratamiento recibido y evolución; registrándose base de datos Google drive, analizándose con Epi-Info 7 y STATA12 análisis descriptivo general, frecuencias relativas, porcentajes para variables nominales y medidas de tendencia central (media y desviación estándar para variables cuantitativas).
Results: Resultados: 5.224 pacientes, 652 presentaron IAAS 12,48% (652/5224), 100 eventos de IAAS en 70 pacientes. Tasa de IAAS: 12,64%, Densidad de Incidencia: 0,04 día, Sexo: 51% femenino y 49% masculino; 36% adolescentes, 26% procedencia Estado Miranda, edad decimal 8,83 (DE=7,71). Estancia hospitalaria 65,6 días. IAAS más frecuentes 22% en Leucemia Linfocítica Aguda, 12% Neuroblastoma y pacientes VIH estadío C3; IAAS más reportada con 24% bacteriemia. Eventos por paciente de 1 - 4. En 99% tratamientos antibióticos estuvieron combinados. Microorganismos aislados: 13,5% Pseudomonas aeruginosa, 9,6% Candida parapsilosis y S. aureus, 7,7%. Klebsiella pneumoniae y Staphylococcus coagulasa negativo. Causas de muerte: 31,8% insuficiencia respiratoria, 26,3% Bacteriemia Asociada a Catéter Vascular, 21% Sépsis bacteriana y 10,5 % falla multiorgánica. Mortalidad relacionada con IAAS 89,5%.
Conclusions: Conclusión: IAAS modifican evolución y pronóstico en pacientes pediátricos con inmunosupresión por VIH y Cáncer, primera descripción en Venezuela y Latinoamérica.

EP608 / #501

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

SHARING PERSONAL DATA IN INTERNATIONAL HEALTH RESEARCH: A SCOPING REVIEW

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Background and Aims: Representative, accurate, accessible, and timely data are the cornerstone of cancer research and care. Implementation of the General Data Protection Regulation (GDPR) of the European Union (EU) in 2018 led to increased individual control of personal data and inhibited health research. We reviewed the reported impediments and proposed solutions to maintain international data sharing.
Methods: Three independent reviewers searched PubMed for articles in English published in 2011-2021 addressing topics like GDPR, data sharing, information dissemination, health research, and cancer research. Papers focusing only on biobanks or genomic research were excluded.
Results: Out of 643 identified publications, 43 met criteria for inclusion. All papers originated in high income countries. The barriers identified through qualitative synthesis were: scarcity of qualified personnel and infrastructure, uncertainty over key definitions, poor interpretation of rules, fear of penalties, and lack of fit of GDPR for scientific research. Specific to data sharing within the EU, the implementation of GDPR was obstructed by fragmentation and insufficient harmonization. Interpretation of crucial terms, such as ‘personal data’, ‘informed consent’ and ‘data anonymization’ depended on the application of national laws and local expertise. Transfer of data outside the EU was hampered by the absence of workable legal transfer mechanisms. To improve the availability of data for international research, the proposed solutions included: control of the interpretation of the GDPR, more explicit definitions of terms and processes, and harmonized application of the regulations.
Conclusions: Our review confirmed that GDPR affects cancer surveillance and research, jeopardizing thus the public interest in learning from contributed data. Data sharing is indispensable, especially in research of rare diseases like childhood cancer. Using these data, the ChildGICR programme (https://gicr.iarc.fr/childgicr) will develop policy briefs to support global cancer surveillance.

EP609 / #934

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

THE CUDDLES FOUNDATION MODEL FOR ADDRESSING MALNUTRITION IN PEDIATRIC ONCOLOGY PATIENTS IN INDIA

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Background and Aims: Malnutrition at diagnosis or/and during treatment in pediatric oncology patients can result in poor outcomes and survival. Children from a lower socioeconomic group, in particular, are at a higher risk of being malnourished. This study highlights the model which Cuddles Foundation (CF) uses to provide nutritional support to such children in government hospitals throughout India.
Methods: In collaboration with government hospitals, CF first places specially trained nutritionists in the pediatric oncology departments and then onboards children who are in need of nutrition support. The CF nutritionist assesses the clinical condition and nutritional status of the patient, designs a nutrition intervention program, monitors progress and supports the family through parent support meetings. Nutrition aid if required is provided in the form of ration bundles, nutritional supplements, nutritious snacks and hot meals. Patient data is maintained in the internal CF FoodHeals® app, which enables the tracking of nutritional status and ensures uniformity of care across the various CF centres.
Results: Over the last 5 years, CF nutritionists have provided over 630,000 counsels. In the year 2020-2021, despite the COVID-19 pandemic, CF provided 101,805 counsels including teleconsultations to 6,123 patients. Nutrition supplements worth USD 218,623, ration bundles worth USD 368,139, nutritious snacks worth USD 62,616 and hot meals worth USD 15,886 were distributed to the recipients. Using data from the FoodHeals® app, CF was able to assess that 80% of patients improved or maintained their nutritional status during treatment and 94% of patients counselled, returned for a second visit or continued treatment.
Conclusions: Children were able to maintain or improve their nutritional status with support from CF. This study demonstrates that the CF model is effective in providing essential nutrition support and counselling to help address malnutrition in children during cancer treatment.

EP610 / #405

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

FORECASTING POPULATION-BASED MEDICINE NEEDS AND COSTS FOR CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA TREATMENT IN ARGENTINA

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Background and Aims: Lack of access to essential medicines has limited improvements in global childhood cancer survival. FORxECAST is a pediatric cancer-specific model that predicts future drug quantity and cost using modelled or user-inputted data including resource-adapted treatment regimens (ATRs), incidence, and local drug pricing. We used FORxECAST to predict the drug needs and costs for treating acute lymphoblastic leukemia (ALL) in Argentina.
Methods: FORxECAST was modified to incorporate Argentine treatment protocols. Sensitivity analyses were conducted using in-built consensus ATRs and 2015 international reference pricing from the Management Sciences for Health (MSH) International Medical Products Price Guide, adjusted for inflation. Incidence data from the Argentinean Oncopediatric Registry (ROHA) and domestic pharmacy retail price data, represented as median cost per drug, were incorporated.
Results: Using MSH prices and modelled disease incidence, the annual median cost of treating ALL in Argentina was 1.20 million (M) USD with Argentine-specific protocols and 1.16 M USD with ATRs. The difference in aggregate cost was driven by increased use of IV methotrexate in Argentina protocols compared to ATRs (3.6 vs. 0.1 M mg); however, the total volume of chemotherapy drugs required remained broadly similar. When adjusting for incidence per ROHA, the cost with Argentine-specific protocols increased to 1.26 M USD. The largest difference was seen when MSH prices were replaced by Argentina-specific prices with overall cost increasing to 4.73 M USD.
Conclusions: FORxECAST can be readily adapted to develop accurate estimates of drug quantities and prices in the treatment of paediatric cancer using modelled and user-inputted data. Our results highlight the significant impact of local pricing on drug costs in comparison to international references; local prices are essential for accurate forecasting of domestic drug budgets. In Argentina, innovative procurement strategies, regulation of drug pricing, and health technology assessment processes are needed to improve sustained and affordable supply of quality-assured childhood cancer medicines.

EP611 / #920

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

IMPACT OF COVID-19 INFECTION IN CHILDREN WITH CANCER: EXPERIENCE IN A HOSPITAL IN LATINAMERICA

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Background and Aims: While cancer is an established risk factor for severe COVID-19 in adults, it has thus far not been considered so in children. The aim of this study is to describe the epidemiological characteristics, histological type, clinical evolution and repercussions in the treatment of patients with cancer infected by COVID-19.
Methods: Epidemiological and retrospective study. We reviewed the medical records of patients (p) with COVID-19 treated in the oncology pediatric department of a Hospital from latinamerica from march 2020 to march 2022.
Results: During that period 52p were diagnosed with solid tumors. Median age: 7 years (2 month -17 years). Male: 30p (58%). Female 22p (42%). Eighteen p (34%) underwent surgery only, 34p (65%) received intensive chemotherapy and/or radiotherapy. Seventeen p (32%) were infected by COVID-19. Histology: medulloblastoma 5p, ependymoma 1p, high-grade glioma 1p, Wilms tumor 4p, osteosarcoma 1p, Ewing's sarcoma 1p, germ cell tumor 1p, rhabdomyosarcoma 1p, cavum carcinoma 1p, angiosarcoma 1p. Clinical manifestations: 11p (58%) asymptomatic, 4p (21%) mild symptoms (no hospitalization requirement), 1p (5%) severe respiratory symptoms, mechanical respiratory assistance requirement, was the only one who delayed his treatment. None have risk factors. No multisystem inflammatory syndrome associated. No deaths
Conclusions: In our cohort, Children with cancer have not generally had increased incidence or severity of COVID-19 infection. The COVID-19 infection did not interfere with the oncological treatment of the patients except for one case that began with severe symptoms after surgery. These results are similar to those published in international reports.

EP612 / #910

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

RACIAL AND ETHNIC DISPARITIES IN PEDIATRIC CANCER INCIDENCE AMONG CHILDREN AND ADOLESCENTS IN HAWAI'I FROM 1990 TO 2014

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Background and Aims: Racial and ethnic differences in cancer incidence have been reported for many pediatric cancers and have been attributed to genetic ancestry, infection exposure, and socioeconomic status. As a "minority-majority" state, Hawai'i provides a unique opportunity for close examination of these differences among underrepresented groups and to isolate the distinct contributions of environment and ancestry. We aim to characterize the incidence of common pediatric cancer types between different races and ethnicities within Hawaii and compared to mainland US using the SEER 9 API data.
Methods: Incidence rates (per 100,000) were age adjusted by the direct method, among children and adolescents (aged 0 to 19 years old), using SEER 9 API data from 1990-2014. Standardized incidence ratios (SIR) and 95% confidence intervals were calculated comparing Hawaii to US rates.
Results: Within Hawaii, age adjusted incidence rates of leukemia, lymphoma, neuroblastoma, hepatic tumors, and germ cell tumors were similar across all races. Compared to White children, incidence of CNS tumors was lower in Filipinos, Japanese, and Native Hawaiians (NH) ($P<.01$, $P<.05$, $P<.01$), incidence of neuroblastoma was lower in Filipinos ($P<.05$), incidence of renal tumors was lower in Japanese and NH ($P<.01$), and incidence of bone tumors was higher in Japanese ($P<.01$). Relative to the mainland US, incidence rates were similar for leukemia, hepatic tumors, and germ cell tumors in Hawaii. Incidence rates were lower than the US for lymphomas for Japanese and NH (SIR0.57, 0.67); for CNS tumors in Japanese, Filipino, and NH patients (SIR0.56, 0.45, 0.75); for renal tumors in Japanese and NH patients (SIR0.15, 0.15); and for bone tumors in White patients (SIR0.46).
Conclusions: Racial and ethnic differences are seen in incidence of pediatric cancer subtypes within Hawaii and compared to mainland US. Our findings provide an important foundation for future studies to better understand the genetic, immune and socioeconomic factors underlying these differences.

EP613 / #1208

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

INVASIVE FUNGAL DISEASE IN PEDIATRIC ONCOLOGY

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Background and Aims: Invasive fungal infections are a major cause of death in pediatric oncology, especially among patients under chemotherapy. This study aims to identify risk factors for invasive fungal infections in pediatric oncology.
Methods: We conducted a monocentric retrospective case-control multi-cohort study on a population of 30 patients with malignant hemopathies or solid cancers under chemotherapy, admitted in the Pediatric Oncology unit of Nafissa Hammoud Hospital in Algiers, amongst which 24 patients were controls, and 6 patients were cases.
Results: In a total of 30 patients (53.3 % male), 13 patients developed a fever, from which 6 patients on 13 were identified as invasive fungal infection cases according to the EORTC/MSG guidelines, with an incidence of 20 %. The mean age was 7.47 years old at the admission date. 04 statistically significant risk factors were identified (p-value < 0.05, CI 95 %) : mucositis with an odds ratio (OR) at 10 (1,34 – 74,51), the most aggressive chemotherapy protocol according to the ITR2 with an OR at 115 (6,10 – 2165,95), severe prolonged neutropenia with an OR at 7,6 (1,07 – 54,09) and severe prolonged lymphopenia with an OR at 25 (2,27 – 275,71).
Conclusions: Many conditions were identified as risk factors for invasive fungal infections in pediatric oncology, especially severe lymphopenia and aggressive chemotherapy. These patients may have to receive close monitoring or even antifungal prophylaxis.

EP614 / #1742

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

INFLUENCING FACTORS IN THE DELAY OF INTIAL DIAGNOSIS OF CHILDHOOD CANCER

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Background and Aims: Being the leading worldwide cause of non-communicable death in minors, low- and mid-income countries have more than 80% of the oncological burden and almost 90% of the paediatric population. The opportune diagnosis is important because of its progression without treatment, contrasting its curability rate at early stages. Paediatric cancer´s recognition is tougher because of unspecific symptoms which can be confused with more common diseases, patients age, and many other factors.
Methods: A retrospective study was made through 406 electronic files of 0–17-year-olds, admitted to our hospital through December 2013-February 2020 with a high suspicion of cancer.
Results: Mean age was 7 years 10 months old, with a 1:1.3 M:F ratio. In average, patients went to 2.3 physicians (2-8 total) before the cancer diagnosis, 37.93% took 0 to 31 days for that diagnosis, 20.69% took 32 to 61 days, 12.07% took 61 to 90 days and 29.31% took longer. For 259 patients, their first physician was a general practitioner, 80 consulted a paediatrician and 67 a subspecialist. Sociodemographic factors were analysed using multivariate analysis to determine their influence on the diagnosis delay, such as age, type of cancer, initial symptoms, religion, socioeconomic strata, academic degree of first physician, insurance and academic degree of parents without finding a significant difference. Survival in patients diagnosed within the first 30 days was significantly better than the rest.
Conclusions: We identified a delay in the referral from the first physician to a level 3 hospital, not determined by its specialty, or factors like parental academic degree, religion, socioeconomic strata, etc. Diagnosis before 30 days is associated with a better overall survival. The opportune detection signs and symptoms of childhood cancer are well known, it´s important that first contact healthcare workers know the exams that can help rule out that diagnosis.

EP615 / #1076

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

CREATION OF A PROGRAM-SPECIFIC FORECASTING APPROACH FOR ESSENTIAL CHEMOTHERAPY: A GLOBAL HOPE PERSPECTIVE

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Background and Aims: Texas Children's Global HOPE is a collaboration focused on advancing pediatric cancer care in sub-Saharan Africa. A major barrier to improving outcomes is the availability and affordability of chemotherapy and supportive care. The purpose of this project was to create a tool with program-specific inputs to help forecast medication needs of our programs.
Methods: This was an operational and quality improvement initiative to reduce stock-outs and improve access to medications. We performed semi-structured interviews with program medical directors at each clinical site to better understand treatment practices. Historical patient data were collected from program records. Treatment details were abstracted from treatment protocols and guidelines identified from semi-structured interviews. A customizable tool was designed to incorporate these inputs and forecast immediate and long-range medication needs.
Results: We identified 24 disease states and 28 distinct treatment protocols through semi-structured interviews and database review. Within these protocols, we identified 32 chemotherapy agents for initial forecasting. Excel workbooks were created for each disease state with customized inputs (median patient age, body surface area, risk stratification, survival estimates, patient attrition, anticipated program growth) and fixed inputs (drug doses, frequency, and cycle details; vial/tablet sizes). Each workbook generates a forecasted number of vials/tablets for a single disease state. These tools have been used to forecast medication needs for 6 programs in 5 countries for the past 2 years. Since March 2020, this approach has allowed us to work with donors to receive an equivalent of over $10 million in medications. Challenges using the tool include changing clinical practices, practice outside of guidelines, and unanticipated patient fluctuations such as responses to Covid19.
Conclusions: Forecasting medication needs is an essential component of program planning. Program-specific forecasting allows for tailored inputs and more sensitive analysis of needs, enabling a program to anticipate medication-related costs and strategize approaches to prevent medication shortages.

EP616 / #1169

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

SUSTAINED GROWTH OF A GLOBAL CLOUD-BASED HOSPITAL-BASED CANCER REGISTRY (HBCR): A REPORT FROM THE SJCARES REGISTRY COLLABORATIVE NETWORK

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Background and Aims: The SJCARES Registry Collaborative network was designed to provide a standardized mechanism for HBCR data collection and support institutional quality improvement. We report the network growth from the first 18 months of operation.
Methods: Data captured between 9/24/2020 and 3/7/2022 are included. Procedures to join the network are provided on our website (https://www.stjude.org/global/sjcares/registry.html). Participating institutions are onboarded on a rolling basis. Case registrations are also rolling, starting with essential information and demographics (presentation date), diagnosis/staging (3-months later), frontline treatment (6-months later) and follow-up/outcomes (annually). Data entered are identifiable only to the local team. De-identified data are available to all Collaborative members for quality control and loco-regional-global analyses.
Results: 108 institutions have signed data use agreements to join the network. 51/108 network members established local teams and 23/51 completed the onboarding process. 11/23 have prospectively entered >20 patients' data into the network. 12/23 either recently onboarded or are finalizing operating procedures. 127 individuals have completed HBCR training. Essential information for 2612 patients across all sites are included, an increase of 1974 new patient registrations over a one year period. Complete demographic and diagnostic data are available for 94.3% (2462/2612) and 92.4% (2413/2612) of patients, respectively, with the remainder pending data entry. 96.3% (2325/2413) of registered patients have a confirmed cancer diagnosis, with 79.7% (1854/2325) microscopically verified. Median age is 6.5 years [interquartile range 3-10 years]; 58.0% are male (1516/2612). Lymphoid leukemias are the most common malignancy among registered cases (835/2325, 35.9%), followed by acute myeloid leukemias (202/2325, 8.7%) and nephroblastoma (148/2325, 6.3%).
Conclusions: The SJCARES Registry Collaborative network is sustainable and provides a foundation for collaborative research. The number of new members and patient registrations in the network have more than tripled over the past year. Next steps involve deploying quality control procedures, identifying implementation strategies to support network growth and analyzing patient outcomes.

EP617 / #1590

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

A RAPID ASSESSMENT COSTING TOOL TO ESTIMATE PUBLIC SECTOR CHILDHOOD CANCER SPECIFIC BUDGET NEEDS FOR NATIONAL CANCER CONTROL PLANS (NCCPS) IN LOW-AND MIDDLE-INCOME COUNTRIES (LMICS)

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Background and Aims: The need to present budget forecasts for NCCPs is often challenging, due to urgent time constraints. Using an accepted costing framework, we piloted a rapid assessment budget tool using excel, to estimate the specific public sector needs associated with childhood cancer control.
Methods: Publications with data from nine institutions in LMICs classified costs into eleven categories. Primary costing data for four categories (medical personnel, non-medical personnel, hoteling, outpatient) were collected in Zambia, Zimbabwe, and Uganda. Pharmacy costs were calculated using country-specific modeled data (https://chemoglobe.stjude.org/). The remaining six categories (pathology, radiation, imaging, surgery, blood services and administration) were estimated using proportions of the overall budget, bounded by ranges from previous publications. Scale-up scenarios are included based on goals collaboratively defined by the local planning teams.
Results: An average of three weeks were required to generate a preliminary budget, currently under revision. For Zambia, Zimbabwe and Uganda, we estimated a baseline budget of $640,000, $1,100,000, and $1,600,000, respectively. The two largest baseline cost categories were medical personnel (43%-49%) and pharmacy (16%-31%). Forecasted year-five budgets were $2,200,000, $4,000,000, and $6,600,000. Over the five-year period, pharmacy costs had the highest growth (average 10%) driven mostly by assumed improvements in case-finding and intensifying treatment protocols. Medical personnel were assumed to be understaffed in year-one, therefore, in addition to accounting for the rising number of patients, an increase of 10% was applied between years one and two, tapering off to 8%, 6% and 4% in the following years.
Conclusions: The Global Initiative for Childhood Cancer has increased interest in incorporating childhood cancer into NCCPs. By leveraging published real-world data from LMICs, we designed a collaborative budget tool that ensures NCCPs will not exclude childhood cancer in their budgeting. Our tool offers a feasible solution to meet urgent needs while providing a bridge for more comprehensive, and time-consuming, costing initiatives.

EP618 / #1799

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

TUMORS IN NEONATES, EPIDEMIOLOGICAL PROFILE AND MANAGEMENT. WHAT IS THE PROGRESS IN ALGERIA?

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Background and Aims: Background Discovery of neoplasia in neonates often poses a diagnostic and therapeutic problem because of age of onset, organs functional immaturity and therapeutic procedures related risks. Objectives This study aims to analyze the epidemiological profile and to evaluate the outcome.
Methods: Material and methods A retrospective study is conducted between January 2003 and December 2021 at the pediatric unit “Pédiatrie A” of CHU Béni Messous, including all patients diagnosed with neonatal tumor. Patients are evaluated according to neoplasia nature by biochemical studies and imaging exploration, with a follow up time varying from 6 months to 18 years.
Results: We identified 80 patients (43 girls and 37 boys) aged between 0 and 28 days. 20% were diagnosed in utero. Patients presented with solid tumor in the vast majority, with leukemia in only two patients. The histologic diagnoses were, neuroblastoma (n = 47, 58.7%), teratoma/germ cell tumor (n = 17, 21.2%), angioma 6.5%, kidney tumor in 3.8%. Two patients were diagnosed with hereditary retinoblastoma through screening (2.5%). There was no patient with primary central nervous system. Sixty patients(75%) underwent treatment including chemotherapy or/ and surgery whereas 25% of them were just observed. Overall survival is 82.5%.
Conclusions: Conclusion Tumoral pathology in neonatal period is dominated by solid tumors, particularly neuroblastoma. Management has significantly improved in Algeria thanks to advances in imaging and the adoption of the observational strategy concept.

EP619 / #1619

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

CHARACTERISTIC OF CHILDREN ATTENDING PEDIATRIC ONCOLOGY UNITS IN 7 SUB-SAHARAN AFRICAN COUNTRIES.

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Background and Aims: In sub-Saharan Africa, data concerning pediatric oncology are collected by few regional population based registries. In January 2016, the French African Pediatric Oncology Group (GFAOP) working in 18 countries set up an international hospital based cancer registry collecting data on line. Here we report on the characteristics of children attending 7 units from 2017 to 2019 to document needs of dedicated pediatric oncology units.
Methods: Units that registered at least 120 new cases from 2017-2019 were selected. Units included Abidjan, Bamako, Dakar, Kinshasa, Ouagadougou, Tananarive, and Yaoundé. Diagnosis was confirmed on radiological, histological or hematological examination, stage was examined according to the Toronto Guidelines. Information concerning resources was provided by the GFAOP, or given by units.
Results: Data for 2715 children with a cancer attending the units over the 3 years was analyzed. The mean age was 6.6; the most frequent age group was 1-4 age group. The annual number of registered cancers ranged from 42 in Tananarive to 217 in Ouagadougou. Doctor patient ration was above 1 doctor to 75 children in 6 of the units. The most common malignancies were Burkitt lymphoma (BL) N=563, retinoblastomas (RB) N=438, nephroblastoma N=433, and acute lymphoid leukaemia (ALL) N=349. Ouagadougou had the largest proportion for both LB and RB with 37% and 27% respectively. ALL represented 63% of all leukemias. Thirty-four brain neoplasms were registered. Data concerning stage was available for 91% of cases.
Conclusions: The small number of brain tumors reflects the difficulties of countries to diagnose, often due to lack of essential equipment. We are aware that the presented pattern may be a skewed representation of childhood cancer incidence, as the data come from hospital registries. Our data highlights the need for development of pediatric oncology services, including both diagnostic and human resources and the development of hospital and regional population-based cancer registries.

EP620 / #1885

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

IMPLEMENTING AND OPTIMIZING THE CLINICAL RESEARCH COORDINATOR ROLE IN SIXTEEN PEDIATRIC HEMATOLOGY AND ONCOLOGY UNITS IN MEXICO

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Background and Aims: Clinical research coordinators (CRC) play a pivotal role in research study implementation. The CRC role was incorporated in 2017 into Mexico in Alliance with St. Jude's multidisciplinary pediatric hematology and oncology (PHO) teams. It replaced the existing data manager role as a strategy to address the medical staff's lack of protected time for research. We describe the process of implementing and optimizing the CRC role in sixteen MAS collaborating centers.
Methods: The MAS operational team and local PHO team lead led the recruitment process for each institution. CRCs were gradually incorporated to assist research and quality improvement (QI) project implementation. In December 2021, we used the Institute for Healthcare Improvement Model as a strategy to optimize the CRC role. Virtual meetings were conducted with an expert panel, core team, and CRC regularly (biweekly, weekly, and monthly respectively). We developed a measurement strategy, a driver diagram and carried out several Plan-Do-Study-Act (PDSA) cycles. A de-identified survey assessed CRCs and stakeholders' satisfaction after 14 months of implementation.
Results: Sixteen healthcare facilities in Mexico have adopted the CRC role. Each CRC supports an average of 3 (range 1-5) projects; only 50% have a full-time position. We have conducted a total of 48 virtual meetings and implemented 40 change ideas targeting five primary drivers: effective documentation systems (32%), defined processes and responsibilities (28%), effective study management (20%), teamwork & communication (12%), and empowerment (8%). CRC's project data completion and accuracy have been above 94.1%. Ninety-two percent of CRCs agreed that the training provided and change ideas implemented had improved their performance as CRCs. All stakeholders were satisfied with the outcomes of the project.
Conclusions: We have demonstrated the feasibility of incorporating the CRC role in PHO units in Mexico. This role may serve as a valuable model for other countries and clinical departments.

EP621 / #623

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

EFFECT OF DISTANCE TO TERTIARY CENTRE ON ENROLMENT OF PAEDIATRIC PATIENTS WITH RELAPSED/REFRACTORY/PROGRESSIVE CANCER ON PHASE I/II TRIALS IN BRITISH COLUMBIA

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Background and Aims: Survival outcomes are poor for paediatric oncology patients with relapsed, refractory or progressive disease (RRPD.) Access to early phase clinical trials in Canada is limited. Distance as a factor for enrolment on phase I/II trials in RRPD remains unexplored. Our primary aim was to determine if distance from home residence to study site predicted odds of local phase I/II trial enrolment among eligible patients on univariate analysis. Secondary aims included multivariable analyses for impact of distance adjusted for other variables.
Methods: Paediatric oncology patients with RRPD followed at the only tertiary paediatric cancer centre in British Columbia were identified retrospectively from a relapse registry. Distance was calculated using postal code and geocoding software (CDXZipStream v5.1.0.3, CDX Technologies, Randolph, NJ) and analyzed as a categorical variable.
Results: Between January 2015 and July 2021, 266 patients experienced 396 RRPD events: 75 (28.2%) were eligible for a local phase I/II trial at least once; 191 (71.8%) were never eligible. Of 61 patients offered enrolment at first eligible RRPD event, 69% were male, 46% had a primary CNS tumour, and median age was 11.8y (range 2.3-22.8y.) There was no difference in distance category between those who enrolled and those who declined (p=0.86.) Males were more likely to enrol (p=0.016). Two-year event-free survival (EFS) and overall survival were 39.8%±13.3% and 52.6%±13.6%, respectively. EFS/OS did not differ with enrolment status, but varied dramatically by disease group (p=0.0002; p<0.0001.) Fourteen (5.3%) patients were not offered enrolment per physician preference. Fifteen patients were treated on phase I/II trials at outside centres, and half (47%) enrolled on trials that we subsequently opened locally.
Conclusions: In British Columbia, 22.9% of patients with RRPD were offered, and 11.3% enrolled on local early phase trials. Distance from home did not impact enrolment, suggesting that patients and families make difficult choices to access limited early phase trials.

EP622 / #1017

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

THE UNIVERSITY OF CAPE TOWN PAEDIATRIC CANCER DATABASE: RESULTS FROM THE FIRST YEARS 2019-2021

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Background and Aims: The paediatric oncology multidisciplinary team at the University of Cape Town (UCT) developed a research-ready database to describe epidemiological profiles, biology, treatment and outcomes, and determine factors associated with presentation and outcome.
Methods: A REDCap database was developed with a Cancer Association of South Africa grant, which employed an administrator to consent all new patients, record demographic and social information, and capture clinical information in real time.
Results: There were 212 children consented from 2019 to 2021: 109 girls and 103 boys. Ages ranged from 1 day to 15.98 years. Only 15% of these families had medical insurance, 16% lived in informal housing and 12% did not have access to piped water. Seventy-four families (35%) reported a relative with cancer, including seven first degree relatives (one each from a retinoblastoma and a DICER family) and two cousins with acute myeloid leukaemia (AML). There were no specific or strong correlations between incident and associated cancers. Patient diagnostic groups included leukaemia (33%), lymphoma (11%), CNS tumours (14%), embryonal tumours (20%), sarcomas (12%) and germ cell tumours (6%). Most patients with solid tumours (72%) had advanced disease at diagnosis. The estimated 2-year overall survival was significantly different (p=0.013) by disease group: acute lymphoblastic leukaemia (78%), acute myeloid leukaemia (55%), lymphoma (96%), central nervous system tumours (60%), neuroblastoma (89%), retinoblastoma (75%), Wilms tumour (100%), hepatoblastoma (86%), rhabdomyosarcoma (52%) and germ cell tumours (100%). Outcomes were poorer for children living in informal housing (61% vs 80%; p=0.04) and without piped water (61% vs 79%; p=0.058). Children with a family history of malignancy did not have significantly poorer outcomes.
Conclusions: Active inclusion of children and families in a robust database maintained in real time can provide a research-ready platform for interrogating cohort-specific factors impacting childhood cancer outcomes, and generate new areas for research.

EP623 / #1897

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

THE FIGHT JUST BORN- NEONATAL CANCER: RARE OCCURRENCE WITH A FAVORABLE OUTCOME BUT CHALLENGING MANAGEMENT

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Background and Aims: The occurrence of cancer in newborns within the first 28 days of life is uncommon with different clinical presentation from other age groups.
Methods: Data were obtained through a retrospective chart review of patients admitted at Bambino Gesù Children's Hospital from 1st January 2006 to 31st December 2021. All children histologically diagnosed with a tumor within 28 days of life were included. The medical records of patients were reviewed.
Results: We describe the first Italian series over 15-year period of patients affected by neoplastic disease diagnosed within the first 28 days of life; 74 newborns were diagnosed with neonatal tumor representing 1,5 % of the cancer population in the same period: a prevalence of germ cell tumor (55%) and neuroblastoma (16%) was observed. Surgery was performed in 80% of patients while chemotherapy was necessary in about 20%. The 5 years OS exceeded 90%; to underline that deaths related to treatment is the major concern representing 80%. A genetic/syndromic condition was detected in 16% of population, and a cancer predisposition syndrome (CPS) was identified in 7 patients.
Conclusions: This series represents the first and largest Italian case series of patients with cancer in the neonatal period. Although it is a retrospective evaluation, it provides many insights for prospective studies. Neonatal tumors represent a rare occurrence with a complex genetic landscape considering both CPS and syndromic condition; extensive genetic studies should be addressed in all cases in order to achieve a better management in term of treatment and for family counselling. The management should be considered with caution and in experienced centers considering the impressive 5% mortality rate related to treatment; in our experience the treatment related mortality rate is mainly due to infective complications.Above all, the outcome is favorable with an excellent OS survival that exceeded 90%, while relapse or progression is rare.

EP624 / #1845

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

THE CRITICAL ROLE OF ACADEMIC CLINICAL TRIALS IN PEDIATRIC CANCER DRUG APPROVALS: CONSIDERATIONS FOR FIT FOR FILING TRIALS

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Background and Aims: Despite changes in both the European and American legislation aiming to promote drug development for children, availability of approved or licensed new drugs for the treatment of cancer in children still lags significantly compared to cancer drug approval in adults. Therapeutic innovation is traditionally dependent upon the pharmaceutical industry who own the assets, while in paediatric oncology, academic consortia dominate the trials landscape. Data repurposing from these academic trials to obtain regulatory approval of a drug has historically not been a smooth process.
Methods: We convened a Fit for Filing Working Group, under the auspices of the multi-stakeholder platform ACCELERATE. The group included representatives from academia, pharmaceutical industry, EMA, FDA and patient advocacy. Via interactive case discussions on trial data repurposing, surveys and expert consultation we defined the challenges and formulate recommendations to facilitate academic-sponsored trial design and conduct to address the expectations of pharmaceutical companies and Regulatory Authorities.
Results: We propose a set of recommendations that would facilitate more effective academic-industry partnerships and enable the results of academic-sponsored trials to satisfy a regulatory obligation or contribute to a submission for marketing authorisation by EMA or approval by FDA. These recommendations cover the collaboration itself but also the specific aspects of trial documentation, essential data, data management and trial resources. The recommendations will result in an educational resource for the community.
Conclusions: To expedite the process of bringing novel treatments to children we should grasp the opportunities presented by recent legislation changes. Successful collaboration between industry and academic investigators with early input from regulatory agencies is necessary and should include advocate engagement to ensure patient-centric focus is encouraged. The recommendations of our working group should help all stakeholders achieve the end goal of marketing authorisation of a product for children with cancer sooner, resulting in better access to innovation for children with cancer.

EP625 / #12

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

IMPACT OF THE SOCIAL DEPRIVATION ON THE PSYCHOSOCIAL DIFFICULTIES OF PEDIATRIC CANCER SURVIVORS: A PROSPECTIVE MULTICENTRIC STUDY

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Background and Aims: The posttreatment period is a key part of the management of pediatric cancer care. At this period, psychosocial effects (scholarly and psychological difficulties) have been described in pediatric cancer patients and can be prognostic for the success of social reintegration. Psychosocial effects and their impact may be related to the household’s socioeconomic background. The aim of this study was to estimate psychosocial difficulties during the posttreatment period based on a social deprivation score.
Methods: This study is based on a prospective multicentric study database, and focused on the children who had received psychosocial evaluation during their follow-up after cancer treatment since 2013 to 2020. We retrieved data on their learning and psychological difficulties. Socioeconomic status of the household was estimated by a social deprivation score.
Results: 1003 patients were analyzed. Learning difficulties at school were noted in 22% of patients. A greater social deprivation was significantly associated with learning difficulty (OR=1.09 per unit of the deprivation score). Tumor relapse, treatment with hematopoietic stem cell transplantation, and diagnosis of a CNS tumor remained significant risk factors. In the subgroup analysis of children with CNS tumors, learning difficulties were increased and associated with greater social deprivation. By contrast, psychological difficulties were not associated with the deprivation score.
Conclusions: There is a link between SE status and learning difficulties in survivors of childhood cancer. Further investigations should be carried out to confirm these results for children with CNS tumors, which is the population of the greatest concern.

EP626 / #948

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

REVIEW ON THE FIRST 2 YEARS OF OPERATION OF THE CRDCE

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Background and Aims: The Reference Center for the Diagnosis of Childhood Cancers (CRDCE) founded in 2020, aimed to centralize and complete histological results for pediatric cancers as needed with immunohistochemistry.
Methods: It was a retrospective study collecting epidemiological aspects of pediatric tumors within the first two years of activity. We used standard histopathologic method and immunochemistry if necessary, to confirm the diagnostic.
Results: During the period of study, 231 samples from children aged 0 to 16, recorded over a period of time from January 2020 to December 2021, including 126 boys (54.55%) and 105 girls (45.45%) with a gender ratio of 1.2. The number of tumor lesions was 171, with 135 cancers as in 78.95%, and 36 benign tumors as in 21.05%. As for the rest of the lesions that were non-tumor, a number of 60 as in 25.97% of the total samples. The distribution of cancers by gender was leaning towards boys (73) with a gender ratio of 1.18. Kidney cancer was the most common, with nephroblastoma as the predominant histological type in 41 cases (30.37%) followed by retinoblastoma in 27 cases (20%) and lymphomas in 6 cases (4.44%). The immunohistochemical study was necessary on 32 samples as in 13.85%. Immunohistochemistry was performed with the available antibodies and was conclusive in 26 cases. Although, this study could not determine the diagnosis for the rest yet, which was particularly due to insufficient antibody panel.
Conclusions: The results were obtained within a maximum of 10 days, a review concluded during a local anatomo-pathological staff along with difficult cases, were sent to the i-PATH network for advice. Thanks to the GFAOP network.

EP627 / #1359

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

IMPLEMENTATION OF EARLY DIAGNOSIS PROGRAM FOR FIVE CHILDHOOD CANCERS IN SUB-SAHARAN AFRICA. A FINAL REPORT FROM GFAOP

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Background and Aims: This presentation is an update of the oral presentation given during SIOP AFRICA 2022 in Sub-Saharan Africa, like in other low-income countries, delayed diagnosis is the first cause of death by cancer in children. Developing early diagnosis tools, trainings healthcare givers (HCG) as well as raising awareness among populations is paramount to improve survival rates.
Methods: two workshops on designing and validating childhood cancer education and awareness tools were conducted in 2019 with pediatric oncology experts and health authorities from Senegal. Educational modules on detection of early signs leading to the diagnosis of five main children's cancers (Retinoblastoma, Acute Lymphoblastic Leukemia, Wilms Tumor, Burkitt and Hodgkin Lymphoma) were developed and harmonized. These modules (manuals, flyers, posters), intended for general practitioners, nurses and other healthcare givers have been used to train trainers and then to train healthcare givers. In 2022, these modules have been digitalized for online teaching.
Results: during the 2019-2022 campaign in eight countries in sub-Saharan Africa, 1110 HCG were trained, including general practitioners, pediatricians, nurses, midwives, and other health technicians, as part of 33 training workshops. Seventy-six HCG will be participating in a remote teaching program in April-May 2022. Post formative onsite evaluation in two pilot districts in Senegal including 44 HCG showed the referral of 21 patients. Experimental digital technology is under development to support HCG in swiftly referring patients to services for children with cancer in two countries (Senegal and Burkina Faso).
Conclusions: the implementation of effective tools to enhance early diagnosis may improve the survival of children with cancer in Sub-Saharan Africa. Demonstrating such an impact will need further development in additional regions and countries in the coming years to demonstrate its impact on survival.

EP628 / #1959

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

CHILDHOOD CANCER AT KINSHASA: SITUATION IN THE ONLY CHILDHOOD CANCER CENTRE IN THE CONTEXT OF WHO 2030 OBJECTIVES

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Background and Aims: Cancer is one of the leading causes of death among children and adolescents in high-income countries. In sub-Saharan Africa, there is lack of data about childhood cancer and its burden is not well known. We describe a single childhood cancer centre situation in Kinshasa from January 2018 and June 2021.
Methods: This is a cross-sectional and descriptive retrospective study conducted at the pediatric hematology-oncology unit of the Department of Pediatrics of the university hospital of Kinshasa.
Results: We managed 285 children (163 boys and 122 girls) with median age of 5.74 years (0.15 and 18 years). Retinoblastoma, leukemia, non-Hodgkin's lymphoma and nephroblastoma were the most frequent cancers with respectively 74 cases (25.96%), 47 cases (16.49%), 45 cases (15.79%) and 42 cases (14 .74%). In addition, 137 (48.07%) had access to treatment, 148 (51.93%) abandonned, 4 (1.40%) were lost to follow-up and 87 (30.53%) died. Remission and relapse rates were 8.07% and 2.81% respectively.
Conclusions: Childhood cancers remain a public health threat in the DRCongo. Sufficient knowledge of its epidemiological situation may help to develop effective policies that can improve its cure rate in line with WHO 2030 objectives.

EP629 / #782

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

GEOGRAPHIC AND SOCIOECONOMIC ANALYSIS OF PEDIATRIC CANCER CASES IN TANZANIA

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Background and Aims: The Tanzanian National Childhood Cancer Network (NCCN) includes eleven hospitals, each with individual clinical databases. To determine the geographic variation of presenting patients and potential regional socioeconomic influences, it is important to merge this data into a single National registry.
Methods: Demographic data, diagnosis, and home region was extracted for all patients presenting to the Tanzanian NCCN in 2019. Regional socioeconomic data was extracted from published sources. Geographic distribution of pediatric cancer was determined and retrofitted against regional socioeconomic data to determine correlation.
Results: In 2019, a total of 826 patients aged <19 presented to the NCCN. 58.7% were male and mean age was 6.45 +/- 4.47 Yr. The most common diagnoses were Wilms Tumor (n=134), retinoblastoma (n=133), and ALL (n=125). The regions patients most commonly presented from were Dar es Salaam (n=107), Mwanza (n=73), and Mara (n=44), coinciding with the location of the three comprehensive childhood cancer treatment hospitals. Regional variations were noted, with hotspots for CNS tumors in Arusha (0.34/100,000) and retinoblastoma in Geita (1.0/100,000). Regions with the highest overall rates of cancer positively correlated to the National census reported literacy rate, mobile phone ownership, cement flooring, and percent unemployment.
Conclusions: There is a regional variation among pediatric cancer diagnoses in Tanzania. Regional cancer incidence positively correlated with urban designation, likely due to increased diagnostic testing in larger cities. However, an inverse correlation with incidence was seen with regional percent employment, which will need to be evaluated on an individual basis to confirm this finding. This study further delineated the regional disparities in pediatric cancer presentation in Tanzania, highlighting the need for research into potential environmental and socioeconomic influences on the observed distribution, and the need for increased knowledge and diagnostic capacity in regions further away from major treatment centers.

EP630 / #1288

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

ADAPTED RESOURCE AND IMPLEMENTATION APPLICATION (ARIA) GUIDELINES: AN APPROACH TO BETA TESTING OF THE WEB-BASED PLATFORM

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Background and Aims: Resource adapted clinical guidelines such as ARIA (Adapted Resource and Implementation Application) have the potential to improve global pediatric cancer care and close the cancer survival gap. User feedback is a critical preimplementation strategy to overcome barriers related to design quality and packaging, and to improve innovation, utilization, and dissemination. We hypothesized that systematic involvement of end-users in the design process will lead to a better design and superior usability of the ARIA platform.
Methods: Beta-testing was conducted with multidisciplinary global collaborators including a 60-minute tutorial followed by a 45-question electronic survey. The survey was developed to evaluate the functionality, visual design, and content language of the platform and included 10 close-ended questions from the System Usability Scale, a simple tool that assesses high level need for training, complexity, and usability of a system. Responses included a combination of Likert-type scale responses and open-ended questions.
Results: Seventy-eight collaborators attended the introductory tutorial with 1,019 unique page views during the test period. Fifty-five respondents completed the survey (71% response rate), including 50% early career professionals (< 45 years old) with diverse geographic representation (15% Africa, 29% Central and South America, 11% Eurasia, 5% Middle East, 13% North America, 27% Southeast Asia/Oceania). Themes from real-time feedback during the tutorial and 58 submitted comments were categorized. Users found the platform interesting (93%), easy to learn how to use (89%), and 98% would recommend ARIA to other providers. Ninety-six percent of respondents agree that ARIA is likely to increase awareness of the importance of guidelines in pediatric cancer management.
Conclusions: Diverse user will improve the effectiveness and platform satisfaction of the ARIA platform. This is an important consideration for clinical guideline development as it helps tailor the design, and increase utilization, and impact of these tools on a global scale.

EP631 / #1547

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

THE ROLE OF TIMELY INTERVENTIONS FOR PATIENT ABANDONMENT IN A COHORT OF PEDIATRIC CANCER PATIENTS IN PAKISTAN

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Background and Aims: Abandonment of childhood cancer treatment compromises the survival of approximately one in seven children worldwide annually. Socio-demographic determinants include affordability issues, long distances, lack of public transport, malnourishment, parental education, daily wage dependency and perceived poor prognoses. Despite free of cost treatment and specialized pediatric oncology centres in Pakistan, over 20% children still abandon therapy. Early interventions for accommodation support, parental counselling and education, nutritional evaluation, monitoring missed appointments and psychosocial involvement are effective ways to improve abandonment rates in low-middle income countries.
Methods: A prospective one-year study was initiated by the[DR1] Pediatric Oncology Department at Indus Hospital and Health Network (IHHN). Newly registered patients (0 to 16 years) who presented to IHHN in December 2021 were enrolled. Non-malignant, palliative treatment, expired and referred patients were excluded. Weekly meetings were conducted with stakeholders involved in patient care (physicians, data managers, clinical coordinators, oncology nurses, psychosocial and welfare workers). Data was collected using a comprehensive case report form and recorded on password protected digital files.
Results: Eighty nine children were included. A large majority presented with leukemia and lymphoma. Over 70% resided outside Karachi, and 12% were from Afghanistan. Average monthly household income was PKR 24,608 (USD 133) and average number of siblings was 4. Most common paternal profession was labourer. Residence was provided to 12 families and translators to 19. Three children were enrolled in IHHN's school. Eight were called for missed appointments, 2 of whom returned. Nutritional consults were provided to 14 and psychosocial counselling sessions to 30. Thirteen families (7 solid tumours, 6 hematologic malignancies) abandoned treatment, mainly due to fear of surgery and denial of disease. All abandoned families resided outside Karachi or Pakistan.
Conclusions: Despite interventions to curb abandonment rates, pediatric oncology patients often refuse or discontinue treatment. Further efforts are required to understand and address more specific determinants of patient abandonment.

EP632 / #1603

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

AN ETHNOGRAPHIC EVALUATION OF PROVIDER'S AND PATIENT'S CONCEPTUALIZATION OF QUALITY OF LIFE IN A PAEDIATRIC HEMATOLOGY/ONCOLOGY FACILITY OF AN LMIC

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Background and Aims: Despite improvement in 5-year survival (79.6%) of childhood cancer patients in high-income countries, it remains a leading cause of disease-related death. In the developing world, survival stands under 35%, reflecting shortfalls greater than just availability of treatment. Discussions surrounding quality of life (QoL) are key in treatment decisions, physician-patient relationship and patient abandonment. Unfortunately, a holistic evidence-based pediatric QoL measure does not exist for the South Asian context
Methods: Four trained volunteers conducted observations in five patient areas (in-patient wards, out-patient clinics, ER, day-care and play area) at Department of Paediatric Hematology/Oncology in Indus Hospital & Health Network (IHHN), one of the largest facilities for childhood cancer in Pakistan. Semi structured interviews of providers and patients were conducted to assess perceptions of treatment experience on QoL.
Results: Observations in each area related to environment (hygiene, temperature, equipment, overcrowding, ambience, waste disposal and use of technology), providers (demeanour, approachability, tone, eye contact, body language, level of engagement and expressions), patients (clinging to parents, physical appearance, confidence, eye contact, answering and inquiring, mood and expression) and their parents (demeanour, mood, interaction with provider and child, self-expression, body language). Provider interviews showed awareness of social, financial and disease related domains of patient QoL, however, emotions, body image and self-esteem were not identified. Providers also categorised mental and emotional wellbeing exclusively as a domain of psychologists. All providers identified guidance and counselling as their main tool in improving QoL of children. Parent responses were focused on social and financial issues and feelings of illness, reflecting limited prioritisation of emotions and relationships, especially in those from lower socioeconomic backgrounds.
Conclusions: As useful as measures of morbidity and mortality rates are, the need of the hour are outcome measures reflecting the patient's overall well-being and subjective evaluation of QoL and experience to create holistic policies and processes.

EP633 / #1623

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

IMPACT OF THE MY CHILD MATTERS GRANT ON HOLISTIC CARE IN PEDIATRIC ONCOLOGY UNITS IN PAKISTAN

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Background and Aims: Paediatric oncology in LMICs faces several challenges while attempting to improve overall survival. Lack of public awareness, inaccessible specialised or quality care, delayed diagnosis and treatment, patient abandonment and absence of an all-encompassing national action plan. The My Child Matters (MCM) Grant by the Sanofi Espoir Foundation aimed at holistic improvement of childhood cancer in 8 paediatric oncology units in Pakistan was re-awarded to the Indus Hospital & Health Network (IHHN) in 2019. As a leading tertiary childhood cancer facility in Pakistan, IHHN worked with stakeholders to improve and build capacity for paediatric oncology services.
Methods: The IHHN team visited partnered units in March and December 2021. A detailed performa was filled regarding the facility, patient care, data management, human resources, baseline nursing standards, infection control standards and hand hygiene. Chemotherapy preparation was observed and feedback taken from focal persons regarding local challenges. Between both visits, educational initiatives were launched with goals and timelines created for each unit with constant communication and mentoring through nursing, physician and data managers.
Results: Out of eight POU's, six showed drastic improvement in baseline nursing standards. Each center now had a dedicated infection control nurse enrolled in a diploma sponsored by the grant. Regular tumor boards and case presentations were initiated through IHHN shared telemedicine equipment. Three units now have full time psychologists available for patients and families, two of which are supported by the grant. Childhood cancer registry data is maintained by grant appointed data operators, however, hospitals lack organized medical recordkeeping systems leading to constant challenges. Shortage of chemotherapeutic and pain medications persisted across all public hospitals along with increasing patient volumes.
Conclusions: Establishment of a widespread partnership model is essential for the promotion and sustainability of childhood cancer services in Pakistan. A rounded national action plan is needed to implement and coordinate these efforts.

EP634 / #366

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

ANALYSIS OF COVID19 PANDEMIC AND THE EARLY DIAGNOSIS PROGRAM FOR CHILDHOOD CANCER IN THE WEST OF PARANÁ- BRAZIL

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Background and Aims: In 2020, Brazil and the world faced an outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The early childhood cancer diagnosis program has been developed since 2008, training health professionals in the early recognition and referral of suspected cases and was interrupted in 2019 for restructuring. OBJECTIVE- To analyze the number of cases referred to the referral service with a diagnosis of cancer and the degree of staging of patients and compare with the last 5 years before the pandemic.
Methods: Medical records of children under 19 years of age were retrospectively evaluated from January 2014 to December 2021. Low Risk (LR) (stage I and II) and High Risk (HR) (stage III and IV) criteria for solid tumors. Leukemias followed the LR and HR criteria, according to age and leukemia, with HR < 12 months and > 10 years, and leukocytos number >50,000/mm3. The early diagnosis program was administered online, from October to December/2021.
Results: 534 patients were treated from 2014 to 2021, of these 276 (52%) were considered HR and 258 (48%) were LR. There was a predominance of HR over LR in the years 2019, 2020 and 2021, different from the values found in the last five years from 2014 to 2018, where there was a predominance of LR over HR.
Conclusions: Children and adolescents with cancer during this period of the COVID19 Pandemic have been diagnosed with advanced disease. These data allow us to say that the Covid 19 Pandemic associated with the interruption of actions aimed at the guidance and training of health professionals may be related to the change in the presentation and severity of the disease in children and adolescents with cancer in the western region of Paraná, Brazil.

EP635 / #583

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

THE PROFILE TOOL JOURNEY: RESULTS FROM THE SECOND PEDIATRIC HEMATOLOGY AND ONCOLOGY(PHO) FACILITIES BETA TESTERS COHORT

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Background and Aims: The Pediatric Oncology Facility Integrated Local Evaluation (PrOFILE) has been developed and validated in four phases: consolidation, pre-alpha, alpha, and beta testing. The Full Version PrOFILE underwent Beta-1 testing in five PHO facilities in 2019. Twelve institutions participated in Beta-2 from July 2021 to May 2022. Beta-2 aimed to assess the feasibility and utility of short-interval reports, co-design descriptive reports, improve data visualization, and gather feedback on the benefits and challenges of completing the tool.
Methods: During the preparation phase, 12 local assessment teams were enrolled in three online platforms and identified three individuals per team to enroll in basic quality improvement (QI) certification. During the assessment phase, teams completed 12 modules, 26 electronic surveys, 14 educational modules, 6 QI exercises, and 33 weekly online mentoring sessions. A short interval report was generated by PrOFILE component (n=5) two weeks after data entry if the team's data completion rate was ≥ 60%. Participants received final score-based and descriptive reports during the interpretation and action phase to assist local workshop and action plan development.
Results: A total of 191 healthcare providers from twelve healthcare facilities located in five global regions participated. Teams varied in size (7-32). The final form completion rate was 100% for site coordinators and 89% for point of care staff. Only one team was not able to review the educational modules. Teams conducted an average of 5 QI exercises (range 0-6). A total of 29 providers completed the basic QI certification. All facilities received two short interval reports (range 2-5). Participants agreed that it was preferable (88%) and valuable (89%) to review results immediately after data collection.
Conclusions: Beta testing confirmed the feasibility and utility of the short interval reporting. The approach will be permanently incorporated into PrOFILE. The descriptive report and data visualization will continue evolving to optimize data visualization and benchmarking.

EP636 / #611

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

UPDATES ON THE IMPACT OF THE IMPLEMENTATION OF THE ST. JUDE PROFILE TOOL: APPLICATION OF THE RE-AIM FRAMEWORK

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Background and Aims: The Pediatric Oncology Facility Integrated Local Evaluation (PrOFILE) tool has two versions. The Full Version takes a “look within” a Pediatric Hematology and/or Oncology (PHO) facility to define and generate consensus on an institutional improvement strategy. The Abbreviated Version provides a “looking across” institutions to identify national, subnational, and regional opportunities for collaboration. PrOFILE implementation occurs in three phases: preparation, assessment, and interpretation and action (I&A). We evaluate implementation for the Full and Abbreviated versions of PrOFILE utilizing the RE-AIM framework.
Methods: Each RE-AIM element is defined as follows: Reach: the number of facilities completing the assessment phase. Effectiveness: the outcomes obtained from the I&A phase. Adoption: the number of St. Jude Global regional directors, local regional teams, and third parties willing to implement PrOFILE and the additional assessment tools developed using PrOFILE as the backbone (“sibling tools”). Implementation: the fidelity or extent to which PrOFILE was delivered as intended. Maintenance: the institutionalization or autonomously delivery of PrOFILE as part of the routine practices of St Jude Global regional programs.
Results: Reach: 136 PHO facilities (119 Abbreviated & 17 Full versions) in 34 countries completed data collection activities from the assessment phase. Effectiveness: 14/15 cohorts conducted prioritization workshops during the I&A phase (Abbreviated), and 16/17 institutions are expected to complete the I&A phase (Full). Adoption: 5/7 St. Jude Global Regions implemented PrOFILE, and it has been delivered in four languages (English, Russian, Spanish, and Portuguese). Six additional assessment tools were designed using PrOFILE as the backbone. Implementation: Adaptations occurred in the I&A phase, but fidelity has been preserved. Maintenance: 9/15 cohorts delivered the I&A phase autonomously by regional programs.
Conclusions: PrOFILE implementation has been successfully conducted in diverse healthcare settings. Data obtained through PrOFILE has allowed facilities, countries, and regions to define a strategy to improve childhood cancer outcomes.

EP637 / #1893

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

COACHING FOR IMPROVEMENT: THE MEXICO IN ALLIANCE WITH ST. JUDE GOLDEN HOUR QUALITY IMPROVEMENT COLLABORATIVE EXPERIENCE

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Background and Aims: Coaching is a key element to the success of Quality Improvement Collaboratives (QIC) in low- and middle-income settings where QI capacity and knowledge are limited. In the Mexico in Alliance with St. Jude Collaborative (MAS Collaborative), we used coaching to help teams achieve and sustain their local aim and build local capability.
Methods: From May 2019 to November 2020, 23 institutions participated in the MAS "Golden Hour" Collaborative, aimed at reducing time to antibiotic administration in children with cancer and febrile neutropenia to <=60 minutes. A 1-5 score was used to assess progress over time (1=interest in participating; 5=sustained improvement). Two coaches with quality improvement and clinical expertise were assigned to each team. Coaching was delivered through one-hour monthly virtual sessions and included: 1) reviewing project's status (run charts and Plan-Do-Study-Act cycles); 2) providing feedback; 3) conducting team building activities, and 4) exploring challenges and facilitators.
Results: Teams received an average of 12 (8-16) coaching sessions. For the teams with >=12 coaching sessions, 63% (10/16) achieved the Collaborative aim and had an average progress score of 4.0; compared with 57% (4/7) and an average score of 3.43 for those with less <=12. The frequency of calls was variable due to the lack of availability of team members, competing schedules, and the COVID-19 pandemic. Teams reported an overall positive experience with the coaching process, and that it helped them to achieve and sustain progress over time.
Conclusions: Providing coaching as part of the MAS Collaborative contributed not only to helping teams achieve their aim for the Golden Hour but also to building local capability for improvement and transferring knowledge and skills for future projects. Based on the experience and learnings from the first MAS Collaborative, we have refined the coaching model for the second larger-scale MAS Collaborative (ongoing).

EP638 / #326

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

STORYTELLING STRATEGY FOR POLICY CHANGE IN GLOBAL CHILDHOOD CANCER: IMPLEMENTING A PAN-AMERICAN HEALTH ORGANIZATION WORKSHOP

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Background and Aims: Storytelling has been used to highlight health disparities and mobilize awareness for critical global pediatric oncology issues. This study explored how effective and ethical storytelling can be a valuable policy-change and advocacy tool. The aim was to describe the strategic planning process to design and implement a Pan-American Health Organization (PAHO) workshop using storytelling to engage stakeholders with national cancer control plan implementation for Central America, Dominican Republic and Haiti, and ensure uptake of policy impact.
Methods: We developed a five-step process to strategize and implement the virtual PAHO workshop: a) define audience: country, type of institutions, positions, and backgrounds of healthcare and policy professionals; b) define storytelling goal: emotionally engage participants and provide a compelling action toolkit; c) build appropriate storyline: platform, content, group dynamics, length of film; d) present theoretical frameworks: Theory of Change, Socioecological Model, CureAll framework: WHO Global Initiative for Childhood Cancer; United Nations Sustainable Development Goals, and WHO Health Systems Building Blocks; e) design interactive exercises; f) disseminate workshop results.
Results: The day-long workshop included 8 PAHO countries and 80 participants representing pediatric oncology, hospital administration, ministries of health, foundations, scientific community, and public health organizations. Outputs of the workshop included: a) summary report, b) empathy word cloud with live reactions, c) qualitative responses (quotes); d) stakeholders analysis, and e) a prioritization matrix of country strategic activities. The workshop report included a practical how-to guide to replicate workshops in other PAHO or World Health Organization regions. Participants shared lessons learned and action plans on how to incorporate storytelling in their local settings.
Conclusions: Evidence-based policy making may be informed by effective storytelling, guide decision-making, and contribute to dissemination of scientific data to build emotional engagement and trust. Next steps include testing the strategic roadmap in other regions and examine the role of storytelling using Narrative Policy Framework.

EP639 / #1884

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

TIMELINE FOR THE CARE AND OUTCOMES OF 10 CHILDREN WITH CANCER AT HÔPITAL SAINT-DAMIEN

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Background and Aims: Most of the world's children with cancer live in low- and middle-income countries (LMICs), where many childhood cancers are not diagnosed or reported, or encounter delays to diagnosis. Late diagnosis decreases the survival in childhood cancer. We report the timeline of clinical events and the healthcare outcome of ten children with cancer in Haiti.
Methods: We selected children with cancer diagnosed between 2019 and 2020 representing the most frequent type of cancer at our institution. We obtained time intervals between clinical events including appearance of cancer signs and symptoms, first time consultation with a healthcare provider, referral to a pediatric cancer center, evaluation by pediatric oncologists, and the definitive diagnosis of cancer. We extracted the time intervals of the clinical events, the demographics, and the clinical data from the participants' medical records; we complemented the data with the information obtained from available parents.
Results: We included 10 patients, with ages ranging from 2 to 16 years. They represented malignant diseases typically seen and treated at our institution: acute lymphoblastic leukemia, acute myeloid leukemia, Hodgkin lymphoma, Wilms tumor, retinoblastoma, rhabdomyosarcoma, Ewing sarcoma, bone tumor and nasopharyngeal carcinoma. We found that there was a delay time of 68.5 weeks, with delays longer in patients with solid tumors than hematologic malignancies. The median delay to obtain pathology's report was 7 weeks. Causes of delays were multifactorial, including socioeconomic and health system factors, as well as communication and speed of diagnostics.
Conclusions: Despite limited data, our report shows an important delay for the cancer diagnosis at our institution that should be improved for better outcomes for children with cancer.

EP640 / #1042

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

PEDIATRIC MALIGNANT TUMORS: DIAGNOSTIC EXPERIENCES FROM KAMUZU CENTRAL HOSPITAL PATHOLOGY LABORATORY IN MALAWI 2011-2013

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Background and Aims: In regions where reliable population-based pediatric cancer data is scarce, histopathological diagnosis and classification is crucial for both patient care and surveillance. In 2011, diagnostic pathology services became available in Malawi's capital for the first time when the University of North Carolina-Kamuzu Central Hospital (UNC-KCH) pathology laboratory was established. The pathology laboratory is one of two in the country, serving roughly half of 19 million population.
Methods: This is a retrospective case series of tumors diagnosed at UNC-KCH pathology laboratory between 2011-2020 for ages 0-18 years. Until 2013, pathologic diagnoses from the laboratory were based on morphology alone. After this, services expanded to include cytology, histology, and immunohistochemistry.
Results: 12,761 specimens were received between 2011-2020 from 5,137 pediatric patients. 1,498 (29%) patients received a malignant diagnosis, median age was 10 (IQR 5-14) and 810 (54%) were male. The most common malignancy was lymphoma (574 [38%]: including [WKD1] Non-Hodgkin's lymphoma (387 [67%], of which 301 (78%) were Burkitt lymphoma), Hodgkin's lymphoma (125 [21%]), and lymphoma-not otherwise specified (NOS) (57 [10%]). Next most common were sarcomas (325[WKD2] [22%]: including Kaposi's sarcoma (111 [34%]), rhabdomyosarcoma (68 [21%]), osteosarcoma (61 [19%]), and sarcoma-NOS (61 [19%]); and carcinomas (139 [9%]: including squamous cell carcinoma (73 [53%] and carcinoma-NOS (27 [19%]). Then, leukemias (95 [6%]): including acute lymphoblastic leukemia (63 [66%]) and acute myeloblastic leukemia (30 [32%]). Followed by Wilm's Tumor (90 [6%]), small round blue cell tumors (SRBCT) (77 [5%]), retinoblastoma (66 [4%]), neuroblastoma (32 [2%]), hepatic tumors (31 [2%]), and germ cell tumors (22 [1%]). 45 (3%) of tumors could not be classified. The proportion of lymphoma-NOS and malignant-NOS decreased post-2013, while SRBCT increased ($p<0.01$).
Conclusions: The most common pediatric tumors in UNC-KCH laboratory are haematolymphoid of which Burkitt's is the commonest. Services need to be expanded further to aid in the diagnosis of SRBCTs, carcinomas, and sarcomas.

EP641 / #1583

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

IDENTIFYING CONTEXTUAL FACTORS INFLUENCING THE SUCCESS OF FUTURE QUALITY IMPROVEMENT PROJECTS IN TWELVE PROFILE BETA TESTING INSTITUTIONS.

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Background and Aims: The Pediatric Oncology Facility Integrated Local Evaluation (PrOFILE) helps institutions define an improvement strategy. During the past nine months, twelve pediatric hematology and oncology (PHO) institutions joined the second beta testing cohort and implemented PrOFILE. Post-PrOFILE activities will include implementing quality improvement projects (QI) as part of their 3-year institutional action plan. The Model for Understanding Success in Quality (MUSIQ) framework identifies contextual factors necessary for successful quality improvement (QI) projects implementation and outcomes. We aimed to identify contextual factors that institutional teams should consider during future QI project implementation.
Methods: The site coordinator (SC) and physician lead (PL) from each institution completed the MUSIQ 35-item questionnaire before starting PrOFILE data collection. We averaged SC and PL scores to generate the final institutional scores for five domains: QI team, microsystem, QI support and capacity, organization, environment, and miscellaneous. Each domain includes between 3-9 contextual factors. A maximum of 7 points are assigned to each factor. The highest possible MUSIQ score was 168. A reasonable chance of success is suggested when scores range from 120 to 168. Each participant center received a 3-page score-based report that invited them to identify areas of opportunity and next steps.
Results: The average MUSIQ score was 127 (range 82-142). Seventy-five percent (9/12) of the institutions have a reasonable chance of success when implementing a QI project. The domains with the lowest scores were QI support and capacity, and external environment. Contextual Factors with the lowest scores included: external QI motivators (3, range 1-5), external project sponsorship (3, 1-7), team prior QI experience (4, range 1-6), and QI capability (4, range1-7). The domains with the highest scores include QI team and organization.
Conclusions: MUSIQ assisted us in recognizing contextual barriers that exist among PrOFILE beta testing institutions. Post-PrOFILE activities will target some of the identified barriers.

EP642 / #1914

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

UNDERSTANDING THE ROLE OF CONTEXTUAL FACTORS IN DETERMINING SUCCESS OF QUALITY IMPROVEMENT COLLABORATIVES: EXPERIENCE FROM THE MAS GOLDEN HOUR COLLABORATIVE

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Background and Aims: A series of contextual factors contribute to the variation in the success of Quality Improvement Collaboratives (QIC) in real-world settings. Between May 2019 to November 2020, 23 Mexican institutions engaged in conducting the first Mexico in Alliance with St. Jude Golden Hour Collaborative (MAS Collaborative), improving the percentage of children with cancer and febrile neutropenia who presented to the emergency department and received the first dose of antibiotics in ≤60min from 39% to 78%, with varying results across institutions. This study aimed to assess the role of contextual factors in determining the success of the MAS Collaborative.
Methods: This QIC followed the Breakthrough Series Model coupled with a QI capability-building program. We used the Model for Understanding Success in Quality (MUSIQ) to assess 24 contextual factors organized around six dimensions (external environment, organizational factors, QI support and capacity, microsystem, QI team; and miscellaneous) using baseline and end-line surveys. Factors were assessed using a 1 to 7 scale (1=totally disagree; 7=totally agree), for a total score from 25 to 168, where a score >120 means the project has a reasonable chance of success.
Results: Seventeen (73.9%) teams reported MUSIQ scores for both reporting periods. The average total score was 128 (83-156) at baseline and 135 (100-161) at the end of the QIC. The dimensions with the lowest average score were environment (3.6; 3.0-4.2) and QI support and capacity (4.8; range 3.9-5.3). Eighty-two percent (14/17) of the teams had an increase in their overall MUSIQ score and their QI support and capacity scores.
Conclusions: MUSIQ scores provided a foundation for understanding the context and specific needs and gaps of participating institutions that are key to the success of a QIC. Including structural and QI supports is key to achieving and sustaining results in real-world settings.

EP643 / #817

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

IMPLEMENTING THE PEDIATRIC ONCOLOGY FACILITY INTEGRATED LOCAL EVALUATION (PROFILE) TOOL AT A TERTIARY CARE HOSPITAL IN PAKISTAN

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Background and Aims: The Pediatric Oncology Facility Integrated Local Evaluation (PrOFILE) tool was developed by St. Jude Global to define improvement strategies for increasing childhood cancer survival rates. It provides a dynamic 360-degree evaluation of health service delivery over 5 components (context, workforce, diagnostics, therapy, and patients & outcomes).
Methods: The IHHN participated in PrOFILE Beta-2 testing from August 2021 to May 2022, conducted in three phases: (i) preparation, (ii) assessment, and (iii) interpretation and action. The preparation phase entailed leadership engagement and recruitment of assessment teams. Twelve modules, 26 electronic forms, and 6 quality improvement exercises were completed during the assessment phase. After approval of the physician lead, the reports' feedback was recorded on the Cure4Kids online portal by the site coordinator. Weekly mentoring sessions with the St. Jude Global PrOFILE team were continued throughout this period. During the interpretation and action phase, an institutional report was generated to develop a three-year action plan and a 2-day workshop was scheduled.
Results: Twenty-eight employees from various disciplines were enrolled. The overall form completion rate was 55%. A polar graph was generated with scores <50% for the national context. Radiation therapy, surgery, personnel, patients and outcomes, service capacity, and chemotherapy were scored between 50% and 75%. Scores >75% were given for finances and resources, facility and local context, service integration, supportive care, and diagnostics. Institutional insights highlighted the need for a national cancer control plan, enhancement of referral systems, increasing availability of drugs, strengthening of core Pediatric Hematology and Oncology (PHO) teams, and improving nurse to patient ratios.
Conclusions: Team-building activities and a dedicated patient-care assessment team are needed to effectively integrate multidisciplinary approach to childhood cancer. PrOFILE feedback reports helped identify areas of improvement in local and national contexts and involved institutional and national leadership. Similar healthcare assessment programs must be initiated locally for continuous improvement.

EP644 / #1351

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

GLOBAL PROBLEM OF PHYSICIAN DUAL PRACTICES: A LITERATURE REVIEW

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Background and Aims: Physician dual practices (PDP) is a term used to describe physicians who combine work in the public and private health-care sector. This study aimed to find evidence of PDP worldwide, investigate reasons and consequences of PDP, and compare PDP in high-income (HIC) versus low and middle-income countries (LMIC).
Methods: In this literature review, the search for PDP evidence was conducted in the English language. PubMed and Google were searched for relevant publications up to September 30, 2020.
Results: Of 195 countries, PDP-reports were found in 157 countries (81%). No significant difference in prevalence of PDP was found between HIC (77%) and LMIC (82%). Most common reason for working in private sector was low government salaries in public hospitals (55%). This was more reported in LMIC (65%) than HIC (30%; P<0.001). Most common reason for working in public sector was patient recruitment for private practice (25%). This was more reported in HIC (45%) than LMIC (16%; P<0.001). PDP were described as detrimental to the public health-sector in 58% of country-reports. Most common adverse consequence was lower quality-of-care in public hospitals (27%). LMIC with PDP-reports had more severe corruption (P<0.001), lower current health-expenditure (P<0.01), and higher out-of-pocket expenditure (P<0.001) than HIC. The scale of PDP was common in more LMIC (92%) than HIC (60%; P<0.001). Government policies to address PDP did not differ significantly between HIC and LMIC.
Conclusions: We conclude that PDP were present in most HIC and LMIC. In the majority of reports a detrimental effect of PDP on public health-care was described.

EP645 / #1575

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

CURING SAFELY: CO-DEVELOPING A REGIONAL RESOURCE GUIDE WITH THE WORLD HEALTH ORGANIZATION TO EMPOWER COMMUNITY-BASED CLINICIANS CARING FOR CHILDREN WITH CANCER

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Background and Aims: A context-sensitive practical guide is key to empowering community-based physicians and nurses who play critical roles in the initial diagnosis, referral, and treatment maintenance for pediatric hematology/oncology (PHO) patients, but who often have limited time and variable backgrounds. Building on engagement with the Myanmar National Childhood Cancer Network in 2019, St. Jude Children's Research Hospital and WHO South-East Asia Regional Office launched Curing Safely in 2021 as a regional Resource Guide project, recognizing the amplified need for clinicians to access point-of-care practice recommendations during the pandemic.
Methods: Initial co-design needs assessments with collaborators across nine disciplines identified content, format, and target audiences. Guided by the Kirkpatrick Model, a toolkit was structured to encompass evaluation and implementation support, including: 1) a scoring matrix measuring accuracy, applicability, comprehensiveness, and clarity; 2) feedback forms assessing local relevance and incorporating CDC's Clear Communication index; 3) a prioritization survey; 4) a pre/post quiz measuring clinicians' comfort in managing PHO patients; and 5) an adaptation guide and introductory materials for co-designers and end-users.
Results: Collaborators from 8 core institutions across 6 countries and 23 Myanmar network sites provided initial feedback. Eight national ministry-selected teams, including 35 volunteer physicians and nurses from 15 tertiary and shared care institutions constituted an expanded regional Working Group. Three guide components integrating local provider practices and patient safety considerations are in phased development: 1) Summaries to Safely Administer 31 Essential Medicines (testing underway in English/Burmese); 2) Chapters on 4 prioritized topics (Chemotherapy and Supportive Care Medications; PHO Overview; Pain and Palliative Care; Fever and Neutropenia); and 3) Poster job aids.
Conclusions: The Curing Safely Resource Guide co-development illustrates a collaborative approach in disseminating regionally tailored best practices to safely manage PHO patients, meeting pressing needs to empower community-based providers where specialists remain scarce, and access further constrained by COVID-19.

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DEPLOYMENT OF A HYBRID WORKSHOP FOR NATIONAL CHILDHOOD CANCER PRIORITY SETTING IN THE SUB-SAHARAN AFRICAN REGION DURING THE COVID-19 PANDEMIC

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Background and Aims: In-person multinational stakeholder workshops during the COVID-19 pandemic were not feasible. To ensure sustained progress toward the World Health Organization Global Initiative for Childhood Cancer (GICC) targets, we designed a blended virtual and in-person hybrid workshop for national priority setting.
Methods: Three hybrid workshops were conducted in Cameroon, Ethiopia, and Tanzania during 2021. Prior to the workshops, 3-5 webinars were held with country teams to build national engagement, engage ministries of health and support completion of the St. Jude PrOFILE tool. PrOFILE data was entered locally, shared electronically, analyzed at St. Jude, and returned as reports to each center. To support the co-design workshop, local facilitators were identified, a curriculum was developed, and online trainings were conducted using Zoom video conferencing and MURAL online collaboration platforms.
Results: A total of 3, 5, and 5 hospitals agreed to participate in PrOFILE in Cameroon, Ethiopia, and Tanzania, respectively: all but one completed data entry. Six local and 8 global facilitators were trained in Cameroon; 5 local and 8 global in Ethiopia; and 11 local and 2 global in Tanzania. There were 59 participants in Cameroon (49 in-person, 10 virtual); 64 (50 in-person, 14 virtual) in Ethiopia; and 63 (53 in-person, 10 virtual) in Tanzania. 17 small groups across all 3 hybrid workshops successfully completed 4 co-design exercises to identify 12 childhood cancer priorities. Iterative design improvements occurred based on feedback. Training evolved from lecture-based presentations to practice exercises using MURAL. Instant messaging (WhatsApp) rather than video conferencing (Zoom) became the preferred method of communication for real-time remote support.
Conclusions: Using web-based services, three countries successfully hosted hybrid workshops. Data from these workshops reflect inputs from key loco-regional-global stakeholders and provide basis for GICC status. The hybrid approach also substantially reduced costs and allowed more rapid engagement with new regional partners.

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PET-CT VS CECT FOR RESPONSE ASSESSMENT IN CHILDHOOD HODGKIN LYMPHOMA- SUBSET ANALYSIS OF INPOG HL-15-01 STUDY- NEED FOR A POLICY CHANGE

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Background and Aims: The InPOG-HL-15-01 used a risk-stratified and response-based approach with an ABVD backbone to treat children with Hodgkin Lymphoma(HL). Children with bulky disease or inadequate response at early response assessment(ERA) after 2 cycles of chemotherapy were assigned to receive radiation. For ERA, PET-CT was recommended but not mandatory in view of limited access. Although the developed world has moved away from CECT, in many LMIC, it is still the easily available and preferred modality and this lead to a natural randomisation. We aimed to compare the impact of using CECT vs PET-CT for ERA in treatment decisions and outcomes.
Methods: 396 children were enrolled and 382 had an ERA at the assigned time point. Satisfactory response was defined as Deauville score 3 or less for patients undergoing PET-CT and CR/VGPR for patients undergoing CT.
Results: At ERA, satisfactory response was observed in 277/382(72.5%) and this was significantly more in PET-CT(151/186, 81.2%) as compared to CT based assessments(126/196, 64.3%) respectively($p<0.001$). In 203 patients with non-bulky disease (in whom the indication for radiation was entirely dependent on ERA), 96/114(84.2%) and 61/89(68.5%) patients achieved a satisfactory response based on PET-CT and CT based ERA($p=0.008$) and hence a lesser proportion of patients in the PET-CT arm had radiation. The 5 year EFSa for children undergoing CECT vs PET-CT was 85.1% +/- 2.6% vs 84.6% +/- 2.7%($p=0.969$). The 5 year EFS and OS for children undergoing CECT vs PET-CT was 86.6% +/- 2.4% vs 85.1% +/- 2.7%($p= 0.725$) and 91.5 +/- 2% vs 94.1% +/- 1.7%($p=0.407$) respectively.
Conclusions: Use of PET-CT for ERA is more likely to indicate satisfactory response reducing the need for radiation. Lesser use of radiation did not have negative impact on outcomes. An urgent need of policy change and advocacy measures to use PET-CT is likely to reduce late effects in children with HL.

EP648 / #612

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MAPPING THE TERRITORY OF INNOVATIVE DRUG THERAPY ACCESS FOR PEDIATRIC ONCOLOGY PATIENTS IN CANADA

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Background and Aims: Lack of funding for innovative drugs in pediatric oncology impacts drug access in Canada with marked variation by disease and geography. Each province controls its own health care funding. For unfunded marketed agents, pharmaceutical companies may have compassionate access programs to obtain access to expensive, unlicensed therapies. This extensive Canadian review of innovative drug requests focuses on understanding the impact of funding and process in the time to drug access.
Methods: We conducted a retrospective review of access requests for anti-cancer therapies (not Health Canada-approved for pediatric indications at the time of application) from 2013 to 2020. Patient characteristics, drug information and request details were collected. We excluded cytotoxic chemotherapy, cellular products, and cytokines.
Results: Of 312 requests, 95% (N=295) were approved; 17 were rejected or abandoned prior to approval and 276 led to drug administration. Forty-nine different agents were requested from 18 different companies. Provincial health insurance funding was approved in 28% (n=87) cases, with disparities between provinces. Compassionate access from a pharmaceutical company was approved in 57% (n=169) of cases. Other requests were either paid out-of-pocket, by patient's private health insurance or from hospital funds). The median time to approval was 6 days (range: 0-190 days). Bridging therapy was required while waiting for approval for 28 cases; treatment plan was delayed in 22 cases and patient's disease status or outcome was impacted in 15 cases.
Conclusions: In Canada, inconsistency in provincial funding models for drugs affects the equity of access to novel cancer treatments for children. Complex application processes, and the rarity of most pediatric cancer indications may cause treatment delays and impact clinical outcomes. The need to understand and help surmount barriers in access to novel cancer therapies spurred the establishment of a National Drug Access Navigator.

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SCOPES AND FIRST ANNUAL RESULTS OF THE NATIONAL REGISTRY OF PAEDIATRIC PATIENTS WITH NEOPLASTIC DISEASES IN GREECE

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Background and Aims: National registries are significant tools to determine incidence and prevalence of rare diseases, like pediatric cancer, and enable optimal health resources allocation and respective therapeutic and diagnostic strategies. The aim of this study is to describe the structure of the newly-established national registry for pediatric cancer in Greece and its first annual results.
Methods: The Greek Ministry of Health, in collaboration with the Hellenic Society of Pediatric Hematology-Oncology, along with representatives from all the Pediatric Hematology/Oncology units and parents' and patients' support groups developed the new national registry for pediatric cancer.
Results: The registry uses the digitalized operating platform 'IDIKA', that has initially been developed to unify and digitalize the prescription system. The registry structure follows the patient journey starting from the diagnosis of the disease. The data captured include 4 sections: demographics, disease characterization, treatment and follow up. Disease is reported based on ICD-10 and ICD-O-3 (Toronto classification) systems. Treatment section describes the different modalities used (chemotherapy along with the protocol name, radiation therapy, etc), with description of the respective health care provider. The follow up section focuses on sequential update of the patient's condition and includes data on remission, relapse, therapy continuation, mortality and second malignancy. The registry was established in early 2021. After one year there were 501 registrations, involving 441 patients. Data were registered by 14 different health care providers from all the Pediatric Hematology/Oncology Units in Greece. The number of registered patients that were diagnosed during 2021 was 178. The majority of registered patients were diagnosed and followed in Athens.
Conclusions: Initial registry use and acceptance is promising. Further data analysis will help delineate the prevalence of different types of cancer in pediatric population in Greece, the complexity of patient journey and the evolving needs. Improvements in platform structure and registering process will optimize registry's use and outcomes.

EP650 / #1524

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HISTORY AND CHALLENGES OF A YOUNG PEDIATRIC ONCOLOGY UNIT IN SUB-SAHARAN AFRICA IN A CONTEXT OF UNSAFETY AND COVID-19 PANDEMY

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Background and Aims: The Bobo-Dioulasso pediatric oncology unit was born in the difficult context of unsafety due to terrorism in Burkina Faso and of Covid19 pandemic. Nevertheless, local initiatives and external support allowed its creation and the care of over one hundred children affected. The aim of this work was to report the obstacle course of this unit, its victories and challenges.
Methods: Description of the different steps that led to the creation of the Pediatric Oncology Unit (POU) of Bobo-Dioulasso ; mention of several impediments linked to unsafety and covid-19 ; description of the care activities since their beginning in January 2019 ; point of challenges and perspectives.
Results: The regular admissions of children with cancers motivated the initiation of a study making the inventory of fixtures in 2012. The main feature was the refusal of treatment by families, since they were almost systematically referred to Ouagadougou, 365 km away. Formalized activities were started in 2019, with the support of the POU of Ouagadougou. However, in the context of terrorism and Covid-19, the development of the new unit was not a priority for local authorities. The unit joined GFAOP in December 2020 : two nurses from CHUSS participated in a online training organized by the GFAOP. A collaboration with a local women LIONS club led to the renovation and equipment of the unit. Since January 2019, 143 children with cancers have been treated in the pediatric oncology unit of Bobo-Dioulasso, with a predominance of Burkitt lymphoma followed by leukemia and nephroblastoma.
Conclusions: Several challenges of which, supply of anti-cancer drugs and fight against dropout from treatment are remaining. Nevertheless, the perspectives are good, with a better involvement of the highest health authorities in the battle against cancers and other non-communicable diseases.

EP651 / #1566

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

LYMPHOMA AND SOLID TUMORS AMONG ADOLESCENTS 15-19 YEARS OF AGE: SINGLE CENTER EXPERIENCE

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Background and Aims: AYA (Adolescents and Young Adults) includes 15 to 39 years of age. Over 70000 AYAs are diagnosed with cancer each year in United States. Adolescent cancers are defined as cancers between 15-19 years of age and only this group can be treated and followed in pediatric oncology. We aimed to present our adolescent patients in this study.
Methods: A retrospective review of 209 patients between 15-19 years of age at diagnosis was done. Medical files were evaluated for distribution of cancer types, clinical features, treatment courses, survival rates and follow-up times.
Results: Two hundred and nine patients between 15-19 years, who diagnosed with lymphoma and solid tumors at our department in the last 34 years evaluated. The median age at diagnosis was 16.3 yrs. M/F: 1.2 (115/94). Cancer type distribution was as follows: Hodgkin lymphoma (20.6%), NHL (16.3%), CNS tm (13.4%), nonrhabdo sarcoma (10%), germ cell tm (9.6%), Ewing sarcoma (7.2%), osteosarcoma (6.7%), others (%16.2). Treatment details as follows: Chemotherapy (22%), chemotherapy+radiotherapy (24.4%), chemotherapy+radiotherapy+surgery (19.1%), chemotherapy+surgery (19.1%), radiotherapy+surgery (5.8%), surgery (9.6%). Median follow-up time was 36 mos (1mos-28yrs). Non-compliance to treatment was observed in 8% of patients. Overall survival was 71% and event-free survival was 51% for 5 years.
Conclusions: Adolescent cancer patients are different from younger group. Their treatment begins in pediatric oncology department but after 18 years of age, it continues in adult clinics. As solution, treatment centers special for AYA patients should be considered.

EP652 / #1173

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PEDIATRIC CANCER TREATMENT ON THE VERGE OF COLLAPSE IN SOUTH KOREA: REPORT OF THE KOREAN SOCIETY OF PEDIATRIC HEMATOLOGY-ONCOLOGY FOR IMPLEMENTING BETTER POLICY

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Background and Aims: South Korean pediatric cancer patients have an 85 percent five-year survival rate, demonstrating world-class cancer treatment. However, decreasing birth rates, low medical costs, and a shrinking pediatrician population raise concerns regarding future pediatric cancer therapy. This study aims to analyze the current situation of pediatric cancer treatment from the Korean Society of Pediatric Hematology-Oncology (KSPHO).
Methods: KSPHO has been conducting the research since April 2021. The study included extensive data searches, big data analyses on national health insurance claim, in-depth interviews, and reviews on medical systems of pediatric cancer care from the US, Japan, and the Netherlands .
Results: Although cancer is the leading cause of mortality in children, less social, medical, and political attention has been paid to pediatric cancer patients than to adult counterparts in Korea. In 2018, 1,275 children aged 0-17 years were diagnosed with cancer. The Age-Standardized Rate (ASR) was 146.9, below the global ASR of 151.5. A decrease in new pediatric cancer specialists accompanied by low birth rates (0.84 by 2020) has increased the burden of present pediatric hemato-oncologists. Additionally, investments in pediatric cancer resources are relatively limited because pediatricians are seeing less number of cancer patients than adult oncologists with current medical expenses of minimum consideration of age and severity in Korea. Worsening eccentric centralization of patients to the capital city, Seoul jeopardizes equal and fair supply of quality medical services to people. Patients in the regional areas will face compromised patient care because of the lack of skilled human resources and facilities.
Conclusions: Based on the data collected regarding the current situation and future obstacles, we are proposing the evidence-based recommendation from KSPHO. Furthermore, we anticipate that those concerns should be discussed in-depth in public hearings and incorporated into national policy for the sake of pediatric cancer patients in Korea.

EP653 / #1305

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

HEALTH WORKFORCE NEEDS FOR OPTIMAL CANCER CARE IN RESOURCE-LIMITED SETTINGS: FACTORS AFFECTING EMPLOYEE PRODUCTIVITY IN UGANDA

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Background and Aims: Uganda Cancer Institute (UCI) registers about 6000 new cancer cases a year. As the numbers continue to overwhelm the healthcare systems, cancer patients face more challenges in obtaining cancer care services, partly due to human resource needs. This study was conducted to identify the staff needs that affect the delivery of efficient cancer care services at UCI.
Methods: We conducted a cross-sectional study in May-July 2019. One hundred and five (105) health workers were randomly selected using proportionate random sampling. Data was collected using a face-to-face interview-administered questionnaire. We collected data on demographics, contractual terms, and workplace issues (physical, psychosocial and administrative) affecting employee productivity. Data was analyzed using Excel and Stata Version 14.0.
Results: Fifty-three percent (53%) were males and 92.6% were between 20-50 years of age. The majority (82.6%) were clinicians. Although many indicated that the workspace is adequate (81%) with suitable facilities and equipment (78%), 34-36% lacked adequate protective gear and handwashing facilities and 42% had no Standard Operating Procedures in their departments. Ninety-two percent (92%) did not have all the required skills to perform their responsibilities and 88% indicated that there are no career development and on-job training opportunities to bridge the skills gap for staff. The majority (70-85%) did not have good working relationships with their supervisors and lacked adequate support/feedback/communication from their immediate supervisors. Eighty-eight (88%) indicated that there is no robust employee performance appraisal system and 74% said that there are no policies to promote experienced/skilled staff. Other challenges included a lack of flexible working arrangements to balance work and family (53.6%); colleagues interfering with their work (77.6%); and lack of teamwork (70%).
Conclusions: The limited supply of competent and motivated workforce is a great challenge to the provision of optimal cancer care. Developing dynamic human resource management/development strategies/systems should remain a top priority for UCI.

EP654 / #1766

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

ANALYSIS OF THE IMPLEMENTATION OF THE GOLDEN HOUR PROGRAM AT A CHILDREN'S HOSPITAL IN A MIDDLE-INCOME COUNTRY

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Background and Aims: Mexico in Alliance with Sj Jude (MAS) is an initiative that seeks to improve the survival of pediatric cancer patients in Mexico. The "Golden Hour" program aims to administer antibiotics in less than 60 minutes in these patients with febrile neutropenia (FN) to reduce the risk of life-threatening bacterial infection. Since May 2019, our hospital has implemented the "Golden Hour" program. This study aims to determine the benefits of this implementation regarding mortality, admission to the intensive care unit, and days of in-hospital stay.
Methods: We determined the percentage of pediatric cancer patients with FN event who received antibiotics <60 min, percentage of patients who required intensive care admission, mortality per event, and days of hospital stay in the pre-implementation and post-implementation phases.
Results: A total of 293 events were analyzed, of which 53 correspond to the pre-implementation and 240 to the post-implementation phase. The percentage of patients receiving antibiotics in <60 min increased from 16.9% to 71.6% from the implementation. In-hospital stay reduces from 12.67 (3-49) to 9.82 (2-62) days. Finally, the intervention reduced the percentage of patients who required critical care admission from 11.5% to 5.4% and the mortality per event from 5.6% to 2.1%.
Conclusions: The implementation of the "Golden Hour" program reduced the days of in-hospital stay, admission to the intensive care unit, and mortality of pediatric cancer patients with febrile neutropenia in our hospital.

EP655 / #1778

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GEOSPATIAL ANALYSIS OF GAPS IN ACCESS TO CARE IN THE PHILIPPINES USING SJCARES COUNTRY VITAL SIGNS

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Background and Aims: The National Integrated Cancer Control Act (NICCA) and the Universal Health Care (UHC) Act were enacted in the Philippines in 2019, the same year Philippines was established as Western Pacific region (WPR)'s first focus country for the WHO Global Initiative for Childhood Cancer. In an archipelago of over 7000 islands, access for children with cancer is a recognized concern.
Methods: Geospatial, health systems and childhood cancer data were collated as part of the St. Jude SJCARES Systems tool, Country Vital Signs. Additional geospatial data was obtained from Google Maps, Malaria Atlas Project and publicly available facility and road network travel datasets. Data on cancer and health systems for children (age 0-19) were compiled from national datasets and World Bank, WHO World Cancer Report 2020, UN population data and GLOBOCAN 2020.
Results: Only 28% of children in the Philippines are within one-hour travel to a public cancer facility. Disparities were noted between regions, with children in Luzon having 1.6-fold increased likelihood of being near a public cancer facility compared to children in the Visayas and Mindanao ($p < 0.05$). In context, the number of public cancer facilities per 10,000 cancer patients, a metric previously associated with cancer outcomes, is 0.4 for the Philippines, and maximum of 700 for WPR.
Conclusions: Baseline assessment of access to care in the Philippines prior to full implementation of NICCA and the UHC Act shows gaps in access to any health facility as well as to public cancer facilities, with disparities across regions. This approach can serve as a template for use of geospatial mapping for health systems analysis, especially as governments consider strategies to scale-up investments for children with cancer. Data generated can support national cancer control planning and population-sensitive allocation of resources.

EP656 / #830

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

HEALTH-INSURANCE INFLUENCE ON TREATMENT OUTCOMES OF CHILDHOOD CANCER IN WESTERN KENYA

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Background and Aims: Only few government leaders in low and middle-income countries have responded favourably to the international plea for Universal Health Coverage by the UN, WHO and over 500 health-organisations. Survival of childhood cancer in low and middle-income countries is often less than 20%. Limited health-insurance coverage may contribute to these poor survival rates. Our study explores the influence of health-insurance status on childhood cancer treatment in a Kenyan academic hospital.
Methods: Medical records of all children diagnosed with cancer between 2010 and 2016 were reviewed retrospectively and data on treatment outcomes (absolute values at time of analysis) and health-insurance status at diagnosis and during treatment were collected.
Results: Of 763 patients, 28% abandoned treatment, 23% died and 17% had progressive or relapsed disease resulting in 32% event-free survival. In total 280 patients (37%) had health-insurance coverage at diagnosis and 483 patients (63%) did not. Of patients without health-insurance coverage, 299 patients (62%) enrolled during cancer treatment leading to a total health-insurance registration level of 579 patients (76%). Treatment outcome of patients differed per health-insurance status (P<0.001). The most likely treatment outcome in uninsured patients was death (49%) whereas in those with health-insurance at diagnosis and those who enrolled during treatment it was event-free survival (36% and 41% respectively). The overall survival (P<0.001) and event-free survival (P<0.001) was significantly higher for patients with health-insurance compared to those without. Hazard-ratio for treatment failure was 0.30 (95% CI: 0.22-0.39; P<0.001) for patients insured at diagnosis in relation to those without health-insurance and 0.32 (95% CI: 0.24-0.4,1; P< 0.001) for patients insured during treatment in relation to those without insurance.
Conclusions: Our study findings underline the need for Universal Health Coverage in low and middle-income countries. Children without health-insurance had significantly lower chance of event-free and overall survival. Childhood cancer treatment outcomes can be ameliorated by strategies that improve health-insurance access.

EP657 / #907

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

NON-TRANSPLANT HEPATIC SINUSOIDAL OBSTRUCTION SYNDROME IN PEDIATRIC ONCOLOGY: A SYSTEMATIC REVIEW

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Background and Aims: Hepatic sinusoidal obstruction syndrome (SOS) is a rare and potentially fatal liver disease often seen in pediatric patients. SOS is a common sequelae of conditioning regimens for hematopoietic stem cell transplantation with well-described epidemiology and pathophysiology. However, there is a paucity of literature examining SOS secondary to chemotherapy. We conducted a systematic review of pediatric non-transplant SOS and examined etiology, management, and outcomes.
Methods: Four databases were searched for non-transplant SOS in pediatric cancer patients between 2000–2021. Two reviewers each performed screening and full text review before data abstraction. Articles were retained if they included pediatric patients with cancer who experienced non-transplant SOS.
Results: We screened 2301 records and reviewed 195 full-texts. Of these, 80 articles were included, yielding preliminary data from 546 patients with SOS: 41 (8%) female, 48 (9%) male, and 457 (84%) patients of unknown sex. Mean age was 5.15 years with a range of one month to 17 years. Underlying diagnoses included ALL (61%), Wilms tumour (WT) (18%), AML (2%), medulloblastoma (2%), and other malignancies (17%). Most common inciting chemotherapy agents included 6-thioguanine (55%), actinomycin-D (21%), vincristine (17%), and cyclophosphamide (10%). SOS was predominantly managed with supportive measures, however, 98 (20%) patients also received defibrotide. The overall SOS survival rate was 90%, with recurrence of SOS in three patients. Twenty-five patients died due to SOS and nine as a result of underlying diagnoses or infection. In patients with ALL and WT, survival rates were 99% and 86%, respectively.
Conclusions: This review demonstrates trends in non-transplant SOS. ALL is a frequent underlying cancer diagnosis in SOS, along with WT. Conventional chemotherapies, such as 6-thioguanine, actinomycin-D, vincristine, and cyclophosphamide have been observed as common offending agents. Notably, non-transplant SOS resolves in most patients, largely due to supportive care and novel treatments, such as defibrotide.

EP658 / #1370

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

THE ST. JUDE PEDIATRIC ONCOLOGY FACILITY INTEGRATED LOCAL EVALUATION (PROFILE) BETA 2 TESTER EXPERIENCE IN A TERTIARY CENTRE AT KUALA LUMPUR, MALAYSIA

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Background and Aims: Biological and non-biological factors contribute to pediatric cancer outcomes. Most non-biological factors are amenable to improvement through quality improvement interventions. The Universiti Kebangsaan Malaysia Medical Centre (UKMMC) joined the second PrOFILE beta testing cohort to assess actionable non-biological factors and identify opportunities for improvement in pediatric hematology-oncology (PHO) care delivery.
Methods: We conducted PrOFILE between August 2021 and March 2022. The site coordinator (SC) and physician lead (PL) participated in weekly online mentoring sessions. A multidisciplinary team was invited to complete the 12 PrOFILE modules. Twenty-six electronic forms collecting objective and subjective data were entered in DatStat. The SC and PL completed 12 asynchronous educational PrOFILE modules, six quality improvement (QI) exercises, a basic certificate in QI methods, and provided feedback on preliminary reports. A 2-day prioritization workshop to define the institutional 3-year action plan was conducted using PrOFILE results.
Results: Thirteen PHO providers formed the assessment team. The form completion rate was 100%. All the 12 modules scored between 50 - 75%. Service capacity and facility and local context scored above 70%, while national context and service integration scored lowest. We found an important discrepancy between the SC/PL and the point of care staff's awareness of institutional planning (100% vs. 27%). An average of 13 opportunities per PrOFILE module were identified; the personnel module had the highest number. Opportunities prioritized during the workshop include but are not limited to creating a dedicated ambulatory area for PHO patients, improving the overall nurse: patient ratio and nurse skill mix, promoting access to written protocols/guidelines for safe chemotherapy handling, implementing multidisciplinary care meetings for all patients, and a non-punitive standard process to track major adverse patient events.
Conclusions: PrOFILE allowed UKMMC relevant stakeholders and the PHO team to systematically capture the impact of non-biological factors and generate consensus and momentum for addressing them.

EP659 / #1530

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

USING THE PEDIATRIC ONCOLOGY FACILITY INTEGRATED LOCAL EVALUATION (PROFILE) TOOL: EXPERIENCE AT BARRETOS CHILDREN'S CANCER HOSPITAL IN BRAZIL

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Background and Aims: Both biological and non-biological factors determine overall survival in pediatric oncology. Systematic evaluation of non-biological factors allows identification of opportunities for improvement. PrOFILE, created by the St. Jude Global Metrics and Performance Unit, is a dynamic 360° assessment of health services that helps teams and institutions define quality improvement strategies. The main objective is to gather data needed to understand care delivery and develop an action plan prioritizing the areas that most require attention.
Methods: PrOFILE was implemented from August 2021 to May 2022 at Barretos Children's Cancer Hospital (BCCC) with guidance from the St. Jude team. The internal assessment team included a lead physician, a local coordinator, and 31 local multidisciplinary staff. The 12 modules of the tool were completed using DATSTAT (26 electronic forms). Six quality improvement exercises were conducted. A final report was produced by PrOFILE team with quantitative and qualitative data. Tables and graphs for each module identified opportunities for improvement that will be discussed at a local workshop in May 2022. Five opportunities will be identified that will guide action plans for the next three years.
Results: The form completion rate for the objective data (collected by the site coordinator and approved by the lead physician) and for the subjective data (31 participants) was 100%. In the score calculation for each module, BCCC scored > 75 % in eleven modules and 71% in the facility and local context. Finances and resources and radiation therapy modules scored the highest (98% and 92%, respectively). In the impressions section, 146 opportunities for improvement were highlighted.
Conclusions: Conducting PrOFILE provided the local team with insight on how to collect and use our data, promote change and a culture of quality locally, plan new projects and disseminate our experience.

EP660 / #718

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

THE BENCHISTA PROJECT: INTERNATIONAL BENCHMARKING OF CHILDHOOD CANCER SURVIVAL BY TUMOUR STAGE

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Background and Aims: Variation in stage at diagnosis of childhood cancers (CC) may explain variations in survival rates observed between countries. This project aims to understand these differences and to encourage the application of the Toronto Staging Guidelines (TG) by Population-Based Cancer Registries (PBCRs) to the most common solid paediatric cancers.
Methods: PBCRs within and outside Europe have been invited to participate in the BENCHISTA Project. PBCRs will identify all cases of Neuroblastoma, Wilms tumour, Medulloblastoma, Ewing Sarcoma, Rhabdomyosarcoma, and Osteosarcoma diagnosed in a consecutive three-year period within 2014-2017 and apply the TG at diagnosis. Other non-prognostic factors, treatment and recurrence/progression will be collected. A minimum of 3-year follow-up has to be assured.
Results: Sixty-four PBCRs from thirty countries have committed to participate and have agreed a maximally depersonalised, patient-level data collection format. Forty-four require a Data Transfer Agreement (DTA) to comply with data protection regulations; for twenty PBCRs the data format and ethical approval are sufficient for data transfer. Due to heterogeneity encountered in legal aspects, fifteen months were spent on finalising the DTA; data transfers started in March 2022. To standardise TG application by cancer registries, three on-line training workshops led by six tumour-specific clinical experts were held (https://www.ucl.ac.uk/child-health/research/developmental-biology-and-cancer/benchista/training-and-workshops). Based on the pilot study, a total of >8,000 staged cases are expected; stage distribution and survival analyses will be conducted by large geographical regions comparable to prior EUROCARE studies.
Conclusions: Despite efforts to harmonise General Data Protection Regulations across Europe, multiple differences in interpretation and required processes were encountered, causing delays to data transfer. The Benchista project has achieved a large-scale collaboration across PBCRs and with their clinical data sources to assign stage at diagnosis according to international consensus guidelines. This is a key aspect for improving patient outcomes and stimulating research.

EP661 / #1662

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

INTERVENTIONS IN FIRST VERSUS SUBSEQUENT FULL BODY SCREENING IN LI-FRAUMENI SYNDROME

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Background and Aims: Li-Fraumeni Syndrome is a hereditary cancer predisposition syndrome caused by pathogenic changes in the TP53 gene. Lifetime cancer risk is between 80-90%, with up to 40% risk of cancer in childhood. Screening protocols which include annual whole body and brain MRI have been effective in improving survival through early cancer detection. Several studies have shown a high rate of cancer detection on baseline screening, but as yet none has compared rate of detection on first versus subsequent screenings.
Methods: Through an IRB-approved protocol, the LFS cohorts at a pediatric (CHOP) and adult (UPenn) tertiary-care institution were reviewed to identify individuals who had undergone two or more whole-body imaging screenings. For each screening, clinical response was recorded (no intervention needed, imaging follow up either immediately or in the short term, biopsy, or surgery), and analyzed on initial vs subsequent scans. Cancers were identified as related to first vs subsequent screening.
Results: A total of 68 adult patients (28% male) and 50 pediatric patients (42% male) were identified as having undergone multiple full-body screenings. On initial screening, a total of 38% of the adult cohort and 20% of the pediatric cohort required intervention. On subsequent screening, a total of 19% of both cohorts required intervention. The most frequent intervention after screening was short-term follow up imaging. A total of 13 cancers were detected (6 pediatric, 7 adult); cancer detection rate was similar between first and subsequent screenings.
Conclusions: Rate of intervention after screening was lower in subsequent screenings for adult patients, and remained similar for subsequent screenings for pediatric patients. Rate of cancer detection on annual screening was consistent with prior studies and was similar between first and subsequent screenings. Next steps to include analysis of screening to include other modalities, especially ultrasound and colonoscopy.

EP662 / #1593

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

CURRENT STATUS OF PEDIATRIC CANCER TREATMENT SYSTEM IN JAPAN EVALUATED BY THE QUALITY INDICATORS (QI) FOR CORE AND AFFILIATED HOSPITALS

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Background and Aims: In Japan 15 core hospitals (CHs) for pediatric cancer treatment were elected by the Ministry of Health, Labour and Welfare and they designated affiliated hospitals (AHs) in seven regional blocks. We established two quality indicators (QI) to evaluate separately 15 CHs and 105 AHs categorized as local main hospitals for pediatric cancer treatment. The aim of this study was to analyze the current status of pediatric cancer treatment system in Japan and to verify the QIs for CHs and AHs.
Methods: Thirty-one indicators for CHs (11 structure, 15 process and 5 outcome index) and 21 indicators for AHs (10 structure, 8 process and 3 outcome index) were developed in 2015 and 2020 respectively. Data from 15 CHs (100%) and 105 AHs (96.3%) were collected in 2021 and the common indicators were compared.
Results: For structure indicators, the average number of pediatric cancer specialists differed significantly (CHs 5.2, AHs 1.74, $p<0.0001$). Similarly, the average number of certificated surgeons in pediatric oncology and certified Child Life Specialists (including the Hospital Play Specialists and Child Care Staffs) differed significantly (CHs 1.93, 2.33; AHs 0.52, 0.53, respectively. $p<0.0001$). For process indicators, hospital days of ALL patients were 58.1 for CHs and 72.6 for AHs ($p=0.3815$) and the intervention rates by palliative care team were 5.3% for CHs and 11.0% for AHs ($p=0.3311$). Outpatient follow-up system of pediatric cancer survivors was equipped in 100% of CHs but only 51.4% for AHs ($p=0.0001$).
Conclusions: There existed obvious difference between CHs and AHs in structure indicators, which would reflect the number of pediatric cancer patients. To the contrary, difference in process indicators, such as palliative care or hospital days of ALL, was small, which could partly be interpreted as treatment of ALL is almost equalized by JCCG in Japan.

EP663 / #1086

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

COVID-19 INFECTION IN CHILDREN WITH CANCER IN ARMENIA: REPORT FOR THE WHOLE PANDEMIC PERIOD

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Background and Aims: As pediatric patients with cancer are frequently immunocompromised, they may be more vulnerable to severe COVID-19 infection than other children. In a global registry study of COVID-19 in childhood cancer including 1500 patients, 20% had severe or critical infection, and mortality equal to 4% was higher than that in the general pediatric population. Data about development of COVID-19 complications in children with cancer are limited and variable worldwide. The study aimed at describing the incidence of COVID-19 infection in children with cancer in Armenia.
Methods: Prospective analysis of PCR confirmed cases of COVID-19 infection in children with cancer aged 0-18 years during 2020-2022 were performed in the Pediatric Cancer and Blood Disorders Center of Armenia created in 2019 as a result of the union of three medical units. Based on the fact that it is the only center treating children with cancer, this is the first report involving all children with cancer infected with COVID-19 during this entire period.
Results: Between June 2020 and March 2022 of 201 children with cancer 35 cases of COVID-19 infection were confirmed in Armenia. Median age was 8.4, male/female ratio was 1.3. Acute lymphoblastic leukemia was diagnosed in 15, neuroblastoma-4, lymphoma-5, medulloblastoma-2, Ewing sarcoma-2, rhabdomyosarcoma-2, osteosarcoma-1, acute myeloid leukemia-1, malignant peripheral nerve sheath tumor-1. Twenty patients (57%) were asymptomatic, the rest of the patients had fever, sore throat and cough. Four patients with hematological malignancies developed pneumonia, followed by cancer progression in two of them. Pancytopenia/thrombocytopenia was found in 4 patients probably infected with Omicron variant during the last three months. Overall, the incidence of COVID-19 complications was 11%, mortality was 0.
Conclusions: This analysis showed that the rate of severe COVID-19 infection and mortality among children with cancer in Armenia was lower than global estimates and further studies to explore these differences are emerging.

EP664 / #1040

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

COVID-19 IN CRITICALLY ILL ONCOLOGY PEDIATRIC PATIENTS: EXPERIENCE IN A LIMITED-RESOURCE SETTING

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Background and Aims: Background: From the beginning of COVID-19 pandemic pediatric oncology patients (POP) have been considered at considerable risk of develop severe disease and mortality. The risk becomes even higher in a limited resource setting. Previous reports have described the experience of COVID-19 in general population, however there is not enough evidence of COVID-19 in POP requiring critical care. The aim of this work is to describe the experience with critically ill POP infected with COVID 19 in a limited resource oncology hospital in Guatemala, Central America.
Methods: We perform a review of our internal data base, identifying POP with COVID-19 diagnosed (by PCR-RT) at PICU admission. Demographic (age, sex), epidemiology (oncological diagnosis, treatment phase), laboratory [Ferritin, Pro-BNP, D dimer (DD)] data and critical interventions [mechanical ventilation (VM), sequential organ failure assessment score (SOFA)] were reviewed and compared between survivors and non-survivors.
Results: From 371 POP diagnosed with COVID-19 and admitted, 66 required PICU between June 2020 and December 2021, oncology diagnosis was acute lymphoblastic leukemia (ALL) in 39 POP (59%) and 62% were receiving induction chemotherapy. The overall mortality was 18%, non survivors (n= 21) had an older median age (12.5 vs 8) in years and required MV more frequently (57% vs 9%). The median values of ferritin (1,492ng/mL), Pro-BNP (4,450pg/mL) and DD (2,717ng/mL) were higher in the non-survivor's group, although these tests were not performed in every patient. Non survivors also had more organ failure with a median pSOFA/SOFA score of 10 points and 2 patients received high frequency oscillatory ventilation.
Conclusions: Patients with ALL in induction phase tend to be more likely to develop severe COVID-19 disease. Non-survivors group required more MV, had more organ failure and higher values of Pro-BNP, DD and ferritin than survivors. Further studies are needed to determine the statistic significance of these findings.

EP665 / #1161

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

COVID-19 INFECTION IN CHILDREN AND ADOLESCENTS WITH CANCER DURING THE SECOND AND THIRD WAVE OF THE PANDEMIC IN INDIA: A TERTIARY CENTER EXPERIENCE

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Background and Aims: Children with cancer are at greater risk for COVID-19 infection than their healthy counterparts. We had reviewed 68 pediatric cancer patients with COVID-19 in the first wave of the pandemic. This study evaluates an additional 52 children and adolescents with COVID-19 during the second and third waves in India.
Methods: Data of 52 (37 and 15 in second and third waves, respectively) children and adolescents with cancer and under treatment at our center with RT-PCR confirmed COVID-19 between April-2021 and February-2022 were analyzed. Results were compared with the first wave.
Results: The median age was 4.7 years with a male to female ratio of 1.6:1. The most common (80.7%) cancer type was acute leukemia. Forty (77%) patients were on myelosuppressive chemotherapy, and 23% were on less intense maintenance chemotherapy. COVID-19 was asymptomatic/mildly symptomatic in 48 (92.3%) patients and severe/critical in only 1 (1.9%) patient. Coryza/cough was the commonest symptom, and fever was observed in only 40% of cases. One patient with Acute Myeloid Leukemia (AML) and severe/critical COVID-19 and associated neutropenic-enterocolitis succumbed. There was a delay in treatment in 63% of patients, and the median duration of delay was 21-days. Three (5.8%) patients were repeat positives, and the median time to achieve negative RT-PCR was 13 days.
Conclusions: Despite the apprehension of more severe diseases in children with cancer, our study found that the number of cases and COVID-19 related mortality (4.4% vs. 1.9%) has decreased after the first wave. We observed a change in clinical symptoms with more children having coryza/cough than fever. However, there was no change in the cancer types and severity of COVID-19. Patients with AML and COVID-19 and concurrent neutropenic sepsis may be at increased risk of morbidity/mortality. Though there was a decrease in the median duration of delay in treatment (28-days vs. 21-days), it remains a concern.

EP666 / #924

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

ROLE OF SOCIOECONOMIC STATUS IN MALNUTRITION IN PEDIATRIC ONCOLOGY PATIENTS IN GOVERNMENT HOSPITALS IN INDIA

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Background and Aims: Malnutrition at diagnosis in paediatric oncology patients can result in poor outcomes and treatment abandonment. Children from lower socioeconomic statuses (SES) are at a higher risk of being malnourished and therefore, Cuddles Foundation (CF) supports them by providing nutritional aid and supplements. This study explores the association between SES and nutritional status (NS) in paediatric oncology patients in government hospitals in India.
Methods: Self-reported data of CF beneficiaries across 23 hospitals were collected in June 2021 and beneficiaries were categorised into different SES groups basis three parameters; total household income of all earning members, education level and occupation of the head of household. The Kuppuswamy scale, an established tool used to determine SES in hospital patients in India, was used. The beneficiary's NS at diagnosis available on the FoodHeals® app was then correlated to their SES. The NS was determined using MUAC or BMI for age indices and beneficiaries were then categorised as undernourished, well-nourished, or overnourished.
Results: A total of 667 patients participated in this study. The majority of beneficiaries (75%) were categorised into the lower and upper-lower SES. With regard to NS, our findings indicate that patients in the lower SES category had the highest percentage of undernourishment (66%) as compared to the upper-lower (58%), middle (55%) and upper-middle classes (47%). As expected, the upper-middle class had the highest percentage of well-nourished (52%) compared to the other classes, in particular the lower class (33%). The strongest negative correlation was found between SES and undernutrition based on the Pearson correlation test ($r = -.64$).
Conclusions: This study indicates that there is a negative correlation between SES and undernutrition in pediatric oncology patients. This emphasises the urgent need for nutrition interventions to address the health disparities experienced by children from a lower SES.

EP667 / #1398

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

INTRODUCTION TO PEDIATRIC ONCOLOGY BLENDED CURRICULUM: PILOTING A TIERED APPROACH IN SUB-SAHARAN AFRICA

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Background and Aims: Training of future professionals is crucial for the care of children with cancer. However, workload and competing responsibilities in low- and middle-income countries (LMICs) can limit structured approaches to training. This blended curriculum was conceived to complement institutional education programs for the management of children with cancer.
Methods: A curriculum development group was formed between sub-Saharan African institutional educators and North American pediatric hematologists/oncologists. The curriculum was developed based on the needs of local institutions, level of trainees, and pediatric oncology rotation timeframe.
Results: The curriculum identified 3 levels of learners: a) pediatric residents in training (Level 1); b) physicians, (community- or hospital-based) caring for children with cancer (Level 2); c) fellows or professionals committed to pediatric oncology (Level 3). The curriculum for Level 1 learners was piloted at two sites in sub-Saharan Africa to evaluate the feasibility, acceptance, and appropriateness of the blended curriculum. Overview of the topics was provided by online pre-recorded lectures delivered by experts in the field through the Cure4Kids platform. This was complemented by high-yield self-paced reading material and context-relevant case-based discussions by an in-person moderator to consolidate the concepts using problem-based learning. Supervision of delivery of the curriculum and monitoring the progress of learners was the responsibility of local preceptors. The curriculum has been delivered to two groups of pediatric residents (n=7) at two sites simultaneously allowing educational collaboration. The blended curriculum allowed continuation of structured learning experience during the COVID pandemic.
Conclusions: It is feasible to develop and implement a tiered pediatric oncology curriculum combining in-person and asynchronous learning. This curriculum was well accepted by local learners and teachers; quantitative and qualitative data are being collected for evaluation of the program for modifications prior to broader use. Such curriculums maybe helpful educational resources for programs in LMICs to provide training opportunities.

EP668 / #1571

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

OPTIMIZATION OF WORKFORCE IN PEDIATRIC CANCER UNITS IN LOW- AND MIDDLE-INCOME COUNTRIES: THE EVALUATION OF TASK SHARING

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Background and Aims: Task sharing has been implemented as a response to the shortage of healthcare professionals caring for children with cancer in low- and middle-income countries (LMICs). This study sought to describe the tasks assigned to non-oncologists caring for children with cancer and evaluate their comfort level in providing care.
Methods: This multicenter study was undertaken at 10 institutions in 5 countries. Two surveys were employed to: 1) identify the models used to implement task sharing, and 2) evaluate the confidence of non-specialists working in pediatric cancer units.
Results: Of the professionals that are engaged in task sharing at these institutions, general physicians and pediatricians were the most commonly mentioned. Most hospitals have task sharing professionals cover the inpatient (90%) and outpatient (80%) units. These professionals participate in many tasks, including cancer diagnosis and risk-stratification (40%), selecting initial chemotherapy plans for new diagnosed patients (50%), and modifications of chemotherapy based on toxicities (60%). These professionals can prescribe chemotherapy (80%). Furthermore, they can perform common procedures in pediatric oncology (90%). These professionals usually discuss patients with pediatric oncologists (90%). For the individual survey, 15 physicians and 2 nurses provided responses. Most respondents were very comfortable or comfortable with the responsibilities of the scope of practice. Defining the initial treatment plan and staging of cancers (24%) had the greatest number of respondents who felt uncomfortable or very uncomfortable with these tasks. Respondents mentioned that the hardest part of their jobs included the number of patients need to be seen and their complexity and the emotional toll of their job.
Conclusions: Capable non-oncologists are frequently responsible for essential steps in the pediatric cancer care continuum. These data can provide insight into the implementation strategies for task sharing as a generalizable approach to scale up pediatric cancer care in LMICs.

EP669 / #1055

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

SIGNIFICANT IMPROVEMENT IN SURVIVAL AND STABLE INCIDENCE RATE IN CHILDHOOD CANCER IN ARGENTINA: ARGENTINE ONCOPEDIATRIC REGISTRY-INC (ROHA-NET). 2000-19

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Background and Aims: To present incidence and survival trends in childhood cancer in Argentina in the period 2000-19.
Methods: ROHA is a population-based hospital registry that has been active since 2000 and is part of the National Pediatric Program at the Ministry of Health's National Institute of Cancer. ROHA's network data comes from different sources; most are reported by pediatric oncology units from all regions in the country. Estimated coverage is 91%. .
Results: In the period 2000-19, 27,016 new cases of cancer were recorded with a ASR 131.6. Between 2000 and 2019, a modest or no change in ASR was observed for all common pediatric cancer diagnoses (APC: 0.25%; 95% CI [0.2; 0.5]; p=0.0), except for a descent in Lymphomas. In the period 2005-2014 (n:13597), the five-year OS for all tumors was 67.6% (66.8-68.4). A three-year OS was observed in 2000-05 (n:7689); 2006-11 (n:7969); and 2012-16 (n:7211). 64.0% (63.0-65.1); 69.7% (68.7-70.7); and 72.7% (71.7-73.7). Lymphoblastic Leukemia: (n:2254) 76.0% (74.1-77.7); (n:2237) 69.0% (67.1-70.8); and (n:2175) 76.1% (74.2-77.8).
Conclusions: Incidence rates are comparable to Latin American ones and lower than those in USA and European countries. There is no substantial change in incidence for the major pediatric cancers, and rates have remained relatively stable. Survival is inferior to what was observed in more developed countries. There were many initiatives developed by the National Cancer Institute, the scientific community, cooperative groups, and non-governmental organizations such as early diagnosis programs, standardization of clinical support practices, and continuing nursing education that may have contributed to improving survival.

EP670 / #1084

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

DEVELOPMENT OF A STRATIFICATION TOOL FOR PEDIATRIC ONCOLOGY UNIT TO IDENTIFY LOCAL CAPACITY TO ACHIEVE ADEQUATE, TIMELY AND QUALITY CARE. NATIONAL CANCER INSTITUTE, ARGENTINA.

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Background and Aims: The National Cancer Institute of the Ministry of Health promotes the process of stratification of Pediatric Oncology Units (POU). This process aims to identify the POU's capabilities to manage different conditions. This will allow to formalize share care processes according to levels of increasing complexity.

Methods: The Stratification tool (ST) was prepared by consensus including scientific societies, and 74 specialists, working on scientific rounds and 15 focus meetings.
A pilot was carried out in 8 POU to assess the validity, reliability and sensitivity of the questionnaire. Finally, the ST is self-administrated and had 224 questions online.
Results: The ST evaluates four dimensions (Human Resources, Infrastructure, Equipment, and Comprehensive Care) according to the type of tumor: Leukemia and Lymphomas, CNS Tumors, Bone Tumors, Retinoblastoma, Liver Tumors and Other Solid Tumors. The level of complexity is stratified by tumor type. There are 4 categories: Basic complexity and Follow-up Units, Standard, Complex and Maximum Complexity Patient Treatment Centers. The answers were categorized as "Desirable", "Mandtory" or "Priority", each one with its respective power for each tumor, and according to the combination of answers and their pre-established cut-off points, allowing defined capacity and category of POU by tumor. The document has to be completed by hospital authorities and a multidisciplinary team. All 30 public POUs were invited to participate with the ST.
Conclusions: The ST was carried out by consensus and is a feasible tool to identify the local capacity for each tumor in the POUs, allowing a stratification of the Argentine oncopediatric public network to achieve adequate, timely and quality care.

EP671 / #739

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

DEPLOYMENT OF RESONANCE PATIENT CENTER FOR DATA MANAGEMENT IN A NATIONAL PEDIATRIC CANCER UNIT IN URUGUAY

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Background and Aims: Introduction: There are many challenges for the data management in pediatric oncology in countries with limited resources. In Uruguay, there is a single national referral center for pediatric cancer and a national cancer registry but no dedicated electronic pediatric oncology resource capable of detecting and analyzing specific data or performing subgroup analysis or outcome measures such as BMT. So, we aimed to create a single electronic data base to generate comprehensive data to address this limitation.
Methods: An agreement was signed with Resonance Inc to create a dedicated site at Resonance Patient Center (RPC). The deployment process was divided into 3 phases: 1) Design of the database and training of personnel. 2) Import of historical registry data from the national registry data base, 3) Real-time registration of cases.
Results: First phase: 34 data capture forms were created for each of the most common diagnosis and clinical situations. All medical, administrative and psychosocial staff (n=34) was trained. Second phase: 6008 cases were imported from the national registry database on October 2021 including demographic, diagnostic and mortality data. Survival data was updated from institutional databases and consultations in the long-term follow-up clinic for 1973 patients, including all cases undergoing stem cell rescue (n=367). One hundred fifty-five new cases were added on real time in the third phase. The 3-year overall survival of 1320 patients (7 incomplete data) with cancer diagnosed from 2010-2019 (n=1320) was 0.82 (SE= 0.02). A future 4th phase is envisioned to include enhancement of collected data including surgery, radiotherapy and pathology as well as nursing and pharmacy reports.
Conclusions: Safe and comprehensive data management in a country with limited resources is feasible with RPC. However, barriers include time-intensive human resources and the need of effective inter-operability of available data systems to enhance the quantity and quality of data recorded.

EP672 / #1366

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

UNIDOS PELA CURA GUIDE: PATHS FOR IMPLEMENTATION OF A POLICY OF EARLY CHILDHOOD CANCER DIAGNOSIS

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Background and Aims: In Brazil, cancer is the leading cause of death by disease amongst children and adolescents and late diagnosis is still a concern. In this context, Unidos pela Cura (UPC) a policy to promote early diagnosis, was developed in Rio de Janeiro. Based on the success of the experience, the Desiderata Institute prepared a guide for replicating this strategy in other territories, with the objective of promoting the same chances of cure for all children.
Methods: The development of the Guide involved two stages: an exploratory descriptive study of the main UPC's results achieved between 2007 and 2021 and the systematization of the paths for the implementation of an Early Diagnosis Policy in other cities.
Results: The UPC enabled 91% of suspected cases to reach diagnostic centers within three days and trained 4378 Primary Care Professionals to identify the symptoms of childhood cancer. The systematization of this experience identified eight important steps to an early diagnosis policy: (1) Identification and awareness of key actors; (2) Creation of a Strategic Committee; (3) Knowledge enhancement about the local scenario (epidemiological profile and existing services); (4) Preparation of a term of commitment signed by all interested parties; (5) Organization of an referral flow; (6)Definition of education strategies; (7) Monitoring of the referred cases and evaluation of the strategy and (8)Consolidation of the Policy to guarantee its continuity even with changes in public management.
Conclusions: Access to early diagnosis is essential to increase the chances of cure for children and adolescents with cancer. However, there are still few instruments that help managers to organize the referral flow of suspected cancer cases. The elaboration of the UPC Guide aimed to fill this gap by systematizing ways to reduce the time needed for the diagnosis of childhood cancer. It can also be used as a reference for national public policies.

EP673 / #1928

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

GUIDELINE DEVELOPMENT FOR MANAGEMENT OF FEVER IN CHILDHOOD CANCER PATIENTS: A COMPARISON OF REGIONAL PRIORITIES

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Background and Aims: Lack of process standardization contributes to poor infectious outcomes in children treated for cancer in low- and middle-income countries. We aimed to test a standardized cooperative education and adaptation framework to create evidence-based guidelines for fever management in diverse regional groups.
Methods: A multidisciplinary guideline development group was convened in parallel to develop priority questions for a febrile neutropenia guideline in three regions: Eurasia, South Africa, and non-South Africa Sub-Saharan Africa. Regional stakeholders were surveyed to identify priority topics for guideline inclusion.
Results: Guideline development groups created and disseminated prioritization surveys that addressed up to 37 topics but encompassed 26 questions in common. Question categories included: definitions of fever and neutropenia, initial management, modifications to therapy, management of prolonged fever and discharge parameters. Topics identified only by specific regional groups included: tuberculosis diagnostics, Pneumocytis jirovecii pneumonia; endemic parasitic diseases. 151 and 52 responses were obtained from Eurasia and South Africa, respectively. Sub-Saharan African responses are pending. More than 80% of respondents ranked 23/26 (88%) of questions as "important/very important" in both regions. Agreement to prioritize a particular question between the two regions was low [kappa (95% CI)= -0.054 (-0.130, 0.022)][BN1] .[BN2] [TR3] [BN1]This is awkward so I rewrote. Check its true. [BN2]This is weird. Basically you are saying that of the 3 questions excluded, they did not agree? [TR3]For the 3 questions, one group included and the other excluded. No questions were excluded by both groups. Kappa is a very poor statistic when inclusion rate is over 80%. Here it is 96% for one group and 92% for the other group.
Conclusions: Best practice for guideline adaptation remains an open research question. Stakeholders identify many of the same priorities in fever management but differences underscore the importance of interrogating local priorities. Next steps include training regional groups in evidence-based guideline development, proficiency testing, and voting on recommendations.

EP674 / #1613

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

TRANSFORMING TRAINING STRATEGY FOR GLOBAL SCALE OF A QUALITY IMPROVEMENT (QI) INTERVENTION

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Background and Aims: Quality improvement (QI) in healthcare has gained considerable momentum in recent years, yet there are significant barriers to adopting effective teaching approaches to successfully implement QI initiatives in clinical settings. Our work describes educational strategies and key interventions used in the implementation of the QI project, Proyecto EVAT.
Methods: In 2017, Proyecto EVAT was stated by St Jude Children´s Research Hospital in collaboration with 17 pediatric oncology centers in Latin America. Currently, the project has successfully trained 5 cohorts, encompassing 73 centers in 19 countries. A comparative analysis was conducted to evaluate the evolution of Proyecto EVAT training material content, delivery, and teaching strategies used for the successful scale-up of Proyecto EVAT over the last 5 years.
Results: The original project curriculum (designed in 2017) was established to deliver core project concepts using a teaching-feedback-learning process, where materials were adapted on a weekly basis which resulted in lack of structure and slow/inadequate learning. Lessons learned from this first cohort led to adopting a proactive teaching approach, with structured lesson plans, setting clear expectations, and promoting active learning to incite curiosity and higher order thinking. Our modules include topics in creating baseline data, defining problems, identifying, and engaging with stakeholders and implementation of QI initiatives. Iterative review of learning materials resulted in the use of a teach-practice-apply model to develop training materials and employ interactive virtual practices for content delivery.
Conclusions: Creative strategies using innovative tools for teaching and practice, while promoting collaborations between physicians and nurses can lead to fostering a cultural change in the clinical setting. To date, training for Proyecto EVAT has been conducted in 73 hospitals across Latin America. We believe we have created a highly adoptable model that can be tailored to any QI intervention for successful implementation of the initiative.

EP675 / #1439

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

DEVELOPMENT OF A FEBRILE NEUTROPENIA GUIDELINE FOR SOUTH AFRICAN CHILDREN WITH CANCER

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Background and Aims: Febrile neutropenia (FN) is a common cause of interruptions to childhood cancer treatment. Lack of guidance and inconsistent management of FN may contribute to poor patient outcomes. We hypothesize that creating an evidence-based guideline for FN management across South African institutions is feasible and may optimize patient outcomes across centres.
Methods: A multi-centre, cross-discipline guideline development panel was convened. A guideline prioritisation survey was designed to identify topics that should be considered for development of a guideline tailored to the South African context. The survey, which consisted of 51 questions inclusive of 37 practice points, was distributed to colleagues working in child health disciplines across South Africa in December 2021 through February 2022.
Results: Fifty-two (74.3%) complete responses were obtained from the 70 clinicians surveyed. Twenty-eight (53.9%) of the respondents were paediatric haematologist-oncologists and 12 (23.1%) were general paediatricians, mostly (48/52, 92.3%) based at tertiary/academic centres. Eight (88.9%) of the nine South African provinces were represented. Topics deemed "very important" (according to >75% of respondents) included: 1) to define fever; 2) to define neutropenia; 3) to describe how to modify antimicrobial therapy in unstable patients; 4) to define patients at high risk for invasive fungal disease; and 5) to define when to remove indwelling lines in paediatric patients with FN. A further 19 questions were considered either "important" or "very important" for inclusion in the guidelines, according to >90% (47/52) of respondents.
Conclusions: Twenty-four topics were considered important for inclusion in a South African FN guideline. Future steps will be to apply the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach to develop recommendations for the prioritized questions. This work will facilitate research to evaluate the use and impact of the completed guidelines on outcomes of FN in South African children with cancer.

EP676 / #1743

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

COVID-19: COLLATERAL DAMAGE IN CHILDHOOD CANCER IN A SOUTH AFRICAN CENTRE

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Background and Aims: Introduction
Studies from high-income countries predominantly reporting on adult patients, demonstrated detrimental effects of the COVID-19 pandemic on cancer care, including marked reductions in new cancer diagnoses. There is comparatively little evidence about the effect of the pandemic on paediatric cancer care, especially in low-and middle-income countries.
Methods: Retrospective clinical data from medical records was extracted for paediatric cancer patients (age ≤ 19) admitted to the paediatric oncology department, Chris Hani Baragwanath Academic Hospital, for two time periods: the first from March 2018 to February 2020, and the second from March 2020 to February 2022.
Results: Data for 518 newly diagnosed patients was extracted over the four years (248 pre-Covid [group 1] and 270 [group 2] during Covid). The male: female ratio was 1.67 and 1.23, while 6% and 4% were living with HIV. The mean ages of diagnoses were 7.5 and 6.7 years for groups 1 and 2 respectively. Haematological malignancies accounted for 34.67% and 37.78% for groups 1 and 2, respectively. Hodgkin lymphoma accounted for a total of 8.1% of diagnoses in group 1 and 4.4% in group 2, a decrease by 50%. Similarly, the number of children with brain tumours decreased by 48.2% between group 1 and group 2. In group 1, 36.6% of solid tumours presented with localized disease and 28.3% with advanced disease, while in group 2, 28.2% and 33.3% presented with localized and advanced disease respectively (p=0.04).
Conclusions: Significant decreases in the number of children presenting with Hodgkin lymphoma and brain tumours, and children with solid tumours presenting with advanced disease during the pandemic is worrying. The WHO Global Initiative for Childhood Cancer to improve outcomes of children with cancer living in low- and middle-income countries by 2030 implies that strengthening of campaigns for early diagnosis and referral in children with cancer is therefore needed.

EP677 / #1925

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

PAEDIATRIC CANCER TRENDS IN A TANZANIAN TERTIARY HOSPITAL IN DURING THE COVID-19 PANDEMIC

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Background and Aims: Drastic measures to curb the spread of COVID-19 in Tanzania led to disruptions in essential services that compounded the already limited access to peripheral and national paediatric oncology clinics. The study aimed to describe the incidence of childhood cancers at Muhimbili National Hospital during the pandemic, with the overall aim to estimate potential gaps in the continuum of paediatric cancer care.
Methods: In this descriptive study, we analyzed hospital medical records to identify children aged 10-18 years newly diagnosed with paediatric cancers between January 2020 and December 2021. Diagnosis was established by histopathology, flow cytometry and immunohistochemistry where applicable. For all children with a confirmed diagnosis, we retrieved demographic and treatment data, as well as the outcome of treatment (dead/alive) at the time of their last available medical record during the study period.
Results: Of the 745 diagnosed with paediatric cancer, the mean age at diagnosis was 6.69±6.34 years. Extracranial solid tumours were the commonest 404/745 (54%) with Nephroblastoma 135/745 (18%) and Retinoblastoma 109/745 (14.6%) diagnosed most frequently. By December 2021, 213/745 (29%) had died.
Conclusions: The incidence of paediatric cancers during the COVID pandemic were lower than in pre-pandemic years. A comprehensive assessment of systemic and socioeconomic bottlenecks is warranted to improve overall access to paediatric cancer care in Tanzania.

EP678 / #1837

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

THE IMPLEMENTATION OF A WORKSHOP FOR ADAPTED MANAGEMENT GUIDELINES AND QUALITY IMPROVEMENT SCIENCES IN AFRICA

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Background and Aims: The capacity to develop resource-based management guidelines amongst African paediatric oncology teams is limited. SIOP Africa and St. Jude Global members developed a workshop to build interest in quality improvement and implementation science, related to adapted management guidelines (AMG) based on the WHO 2030 Global Initiative for Childhood Cancer (GICC). We describe implementation and participant feedback of the workshop.
Methods: Four theory-based lectures on Adapted Resource and Implementation Application (ARIA) guides, implementation science, quality improvement and guideline methodologies were pre-recorded by content experts as requested viewing for participants prior to the workshop. The one-day in-person workshop consisted of three sessions drawing on the participants' experience. Sessions included: (1) facilitated small group discussions on guideline development and research; (2) a hybrid, expert panel discussion on real-world experience of multidisciplinary teams; (3) facilitated small group discussions to identify barriers and enablers to implementing guidelines for the six GICC index cancers. Feedback was captured through an online survey in English and French.
Results: There were 62 participants (75% Anglophone, 25% Francophone) and 14 facilitators, from 22 African countries, 4 European countries and United States. Stakeholders were recruited from radiotherapy, oncology, surgery and nursing. Final outputs included two worksheets summarising implementation factors for each participant's setting and the six GICC index cancers. The post-workshop survey was completed by 38/62 (61.3%) of participants: all felt that the workshop will influence their practice and 30/38 (79%) reported that >75% material was new to them. At least 71% of Francophone participants reported minimal trouble in comprehension of the content, which increased to 86% with the aid of translation.
Conclusions: This workshop demonstrates potential for continental partnerships in developing AMGs to improve management practices and outcomes. Future activities will be developed to strengthen resource-based management of childhood cancers in Africa, and consideration must be given to measuring impact of these processes.

EP679 / #1051

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

IMPROVEMENT OF CHEMOTHERAPY COMPOUNDING VIA EDUCATION AND IMPLEMENTATION OF A CLOSED SYSTEM TRANSFER DEVICE IN UGANDA

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Background and Aims: In high income countries, pharmacy professionals compound hazardous agents such as chemotherapy using aseptic technique in controlled environments with engineering controls, such as certified biosafety cabinets in pharmacy cleanrooms. In Low and Middle Income countries (LMICs), chemotherapy is often reconstituted in an open environment due to costs associated with constructing and maintaining compounding rooms and equipment. Closed system transfer devices (CSTDs) may be an alternate approach to minimizing occupational exposure, in the absence of these engineering controls. The purpose of this project was to improve the safety of chemotherapy compounding and to demonstrate the utility of CSTDs to reduce surface contamination and thus minimize occupational exposure.
Methods: This was an education-focused, quality improvement project of aseptic technique and safe handling of hazardous medications. The educational intervention was conducted in a blended classroom with online coursework, case-based virtual discussions, recorded simulations, manufacturer's training materials, and hands-on training and validation. Hands-on validation was completed using traditional compounding supplies, CSTDs, soy-broth test kits, and fluorescein dye test.
Results: All staff completed the training course and passed the final exam. Initial hands-on validation revealed visual confirmation of the efficacy of CSTDs to reduce hazardous drug exposure. The traditional syringe and needle method revealed visual spillage (via fluorescein dye) on the operator's gloves, as well we on the exterior of the vial, syringe, needle, and preparation surface. When using the same approach with CSTDs, no visual spillage was detected. A recent re-validation of practice revealed that out of 15 simulations, the traditional method produced 14/15 with surface contamination vs a 0/15 when using the CSTD.
Conclusions: CSTDs may be a suitable approach to minimizing surface contamination and occupational exposure in the absence of highly-controlled pharmacy compounding. We recommend consideration of CSTDs in this setting and encourage further research in the cost-utility of CSTDs in LMICs.

EP680 / #362

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

A REGIONAL VIRTUAL CASE DISCUSSION FORUM IN PEDIATRIC ONCOLOGY: EXPERIENCE OF THE PEDIATRIC ONCOLOGY EAST AND MEDITERRANEAN GROUP

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Background and Aims: The Pediatric Oncology East & Mediterranean (POEM) group aims to share expertise among pediatric oncology providers across the Middle East, North Africa, and East Asia region. In 2013, POEM initiated a fortnightly virtual Case Discussion forum, for peer input on clinical management. Here, we evaluate its scope and impact.
Methods: Meeting records from September 2013 till June 2021 were reviewed. Detailed minutes were available starting August 2016; accordingly, case data between August 2016 and June 2021 were analyzed including diagnoses, purpose of presentation and recommendations.
Results: A total of 140 cases from 14 countries were presented, respecting patient anonymity. After August 2016, 65 cases were presented, with a mean of 14 attendees per meeting (range 5 - 49) from 21 countries. Reasons for presentation included questions regarding histopathologic/molecular diagnosis in 23%, imaging interpretation in 18%, chemotherapeutic options in 18%, and surgery in 8%. Therapeutic challenges were related to treatment planning in 14%, resource limitations in 12%, surgical difficulties in 9%, and expertise availability in 6%. Peer recommendations included specific chemotherapy regimens in 40%, imaging in 29%, same management in 29%, surgery in 26%, radiation therapy in 17%, molecular testing in 17%, and pathology review in 15%. Discussion of stem cell transplant indications occurred in 22%. Other recommendations were related to anticoagulation, infection control, clinical trials, and child protection laws. Surgical management of locally advanced hepatoblastoma accounted for 20% of solid tumor cases discussed, which has now spurred a retrospective multi-institutional regional study to better understand the regional needs for this malignancy. Similarly, histopathologic diagnostic limitations were common in one country, resulting in a twinning project between two centers in the region for improving diagnostic infrastructure.
Conclusions: The POEM case discussion forum allows sharing expertise and sheds light on resource limitations in pediatric cancer management across the region, directing efforts for capacity building.

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STANDARD OPERATING PROCEDURES PROMOTES SAFETY AND EFFICIENCY IN PAEDIATRIC ONCOLOGY- WESTERN KENYA ONCOLOGY PHARMACIES BENEFITS

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Background and Aims: Good policies and procedures are a prerequisite to efficiency in hospitals. Oncology centers are at higher risk of harmful incidents due to chemotherapy exposure, toxicity and radiation. This article reports on the measures taken to ensure safety and efficiency at work.
Methods: AMPATH Oncology Pharmacy in Moi Teaching and Referral Hospital collaborated with Takeda Pharmaceuticals to develop standard operating procedures to promote safety. Policy implementation in paediatric oncology clinic was through ECHO Pharmacy online participation model during the pandemic. Peadiatric pharmacovigilance reporting protocol promoted reduced medication errors and CINV among inpatients. The focus points included the chemotherapy compounding area, waste incineration area, paediatric inpatient pharmacy, chemotherapy administration, main pharmacy dispensing point, cytotoxic drug store and inpatient pharmacovigilance. Manuals and protocols were developed on safe handling of cytotoxic products, pharmacovigilance reporting, inter and intra facility drug movement, patient education and counselling, and sterile chemotherapy preparation in aseptic cyto-cabinets.
Results: There has been improved documentation of chemotherapy spills in the log sheet with appropriate combatting measures, reduced exposure of staff to cytotoxic molecules and comprehensive waste segregation and incinerations of 1200 ° C for chemotherapy exposed materials. Patient compliance to medication and hospital visits also increased because of better advice and counselling by the pharmacy team. There were reduced incidences of chemotherapy compounding and dispensing errors in the paediatric oncology pharmacy due to intensified SOP based patient care. This initiative also had an unintended positive effect of generating other standard operating procedures across the unit that facilitated improved both vertical and horizontal forms of communication. These SOPs have steered to newer oncology facilities benchmark on operations.
Conclusions: SOPs should be considered an essential component of service delivery and safety in paediatric oncology centres. Proper implementation will not only improve staff safety but also patient welfare and promote equity, efficiency and standard of care.

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THE IMPACT OF A PROJECT ECHO TELEHEALTH EDUCATION PROGRAM ON THE REGIONAL DIAGNOSTIC RATES OF PEDIATRIC CANCER IN KENYA

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Background and Aims: Despite recent advances, childhood cancer remains under-diagnosed in low-middle-income countries (LMICs). In Kenya, less than 25% of pediatric patients with cancer receive a diagnosis. Project ECHO, a telehealth education platform, is recognized for its capacity to address disparities in medically underserved communities. At Moi Teaching and Referral Hospital (MTRH), the only tertiary care center in Western Kenya, an ECHO program was piloted to provide instruction and mentorship to providers at county hospitals to recognize and evaluate pediatric patients with new malignancies.
Methods: In January 2020, a pediatric cancer ECHO was implemented. Sessions occurred twice monthly and continued through the COVID-19 pandemic. Sessions lasted 75 minutes and included case-based discussion supplemented with a rotating didactic curriculum. Counties were found to have high attendance if averaging at least one participant per session, moderate attendance if 0.5-1 participant per session, and low attendance if <0.5 per session. In addition to the ECHO program, the total new cancer diagnosis from each country was tracked starting in 2018 and continuing through the entire duration of the ECHO.
Results: A total of 37 sessions over 2 years occurred with participants from Western Kenya. There were 4 counties with high participation, 6 with moderate participation, and 19 counties with low participation. Among counties with high attendance, an average of 10.5 additional cases per county were diagnosed during the program, compared to 3 additional cases in the moderate group and 1.3 additional cases in the low attendance group (p=0.014).
Conclusions: The implementation of Project ECHO led to a significant increase in pediatric cancer diagnoses in Western Kenya despite the global pandemic. The greater increase in counties with high participation suggest consistent involvement in this educational program is one mechanism to improve care in medically underserved communities, further validating Project ECHO as a mechanism to reduce disparities in LMICs.

EP683 / #1019

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

PROFILE OF PEDIATRIC ONCOLOGY PATIENTS FROM PUERTO RICO AND HISPANICS FROM UNITED STATES

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Background and Aims: Childhood cancer is still a significant public health issue. Nowadays, there is a large data gap on Puerto Rico (PR) childhood cancer epidemiology. This small island in the Caribbean has a genetically unique population that continues to be poorly understood in the scientific community. Genetic admixture had a big impact in this population and there is not updated data regarding pediatric cancer incidence. In the United States (US), approximately 13,500 pediatric patients per year are diagnosed with cancer. In PR, the most recent statistics from 2010-14 showed, a total of 783 children corresponding to an average of 157 cases/year. Cancer remains the second most common cause of death among children in the US and the sixth leading cause in PR. The primary goal of this study is to create an epidemiological profile of the island pediatric oncology patients. This database will identify cancer incidence in the island and compare it with Hispanic children in the US.
Methods: The two main pediatric cancer hospitals in Puerto Rico participated in this descriptive cross-sectional study. Data was collected from the electronic medical record in PR and from SEER for Hispanics in the US. Classification was done based on the ICCC-3 system. Inclusion criteria was restricted to patients within 0-21 years-old with pathology results confirming the presence of malignancy between 2016-2018. Data was adjusted per 100,000 habitants and evaluated using ANOVA analysis.
Results: Cancer incidence between 2016-18 was 30.5%/30.4% for leukemias, 17.6%/11.8% for CNS malignancies and 16.2%/14.4% for lymphomas in PR/US respectively. This study showed variability among two Hispanic populations that were statistically significant between sex, cancer diagnosis and age group.
Conclusions: There are differences in pediatric cancer incidence among Hispanic populations. This information provides an opportunity to explore other factors such as genetic variability in the role of cancer development among Hispanic populations.

EP684 / #1118

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

CATEGORIZING DIVERGENT CLINICAL PHENOTYPES AMONG CHILDREN AND ADOLESCENTS WITH KAPOSI SARCOMA IN A PEDIATRIC-SPECIFIC CLASSIFICATION

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Background and Aims: The Kaposi sarcoma (KS) T0 versus T1 staging classification does not address the unique clinical features of pediatric KS in human herpesvirus-8 endemic regions of Africa. This study seeks to define patterns of childhood KS using a pediatric-specific approach.
Methods: The Lilongwe Pediatric KS Staging Classification categorizes disease based on clinical phenotype: stage 1=mild/moderate KS limited to cutaneous/oral involvement, stage 2=primarily lymphadenopathic, stage 3=woody edema KS, stage 4=visceral and/or severe/disseminated mucocutaneous disease. Characteristics and outcomes were evaluated from tertiary care pediatric centers in Lilongwe, Malawi, and Mbeya, Tanzania. Event-free survival (EFS) is defined as sustained complete remission (CR), while progression-free survival (PFS) includes patients with sustained CR plus partial response.
Results: Among 171 patients, median age was 9.3 years, 37% (n=63) were female, 87% (n=149) were HIV-positive, and 49% (n=84) were histologically-confirmed. Breakdown by stage was: 18% (n=31) stage 1, 33% (n=56) stage 2, 19% (n=33) stage 3, and 30% (n=51) stage 4. Stage 4 categorization consisted of pulmonary KS (n=24), GI involvement (n=10), and disseminated mucocutaneous KS without visceral disease (n=17). Age (younger stage 2 and older stage 3), severe CD4 count suppression (lower CD4 for stages 1 and 4), and presence of severe anemia and thrombocytopenia (worse for stages 2 and 4) differed across stages. Estimated 2-year EFS/PFS/overall survival (OS) by stage were as follows: stage 1–81%/81%/87%, stage 2–50%/50%/63%, stage 3–24%/49%/81% and stage 4–29%/34%/54%. Excluding five deaths within the first week of diagnosis, sub-analysis of stage 2 lymphadenopathic KS demonstrated superior long-term 6-year EFS of 70% (95% CI: 49-83) for younger children (<7 years old) versus 27% (95% CI: 8-51) for older children.
Conclusions: This pediatric-specific staging classification categorizes patients with distinct characteristics and patterns of treatment response. It may serve as a platform for risk-stratified treatment with the hope of improving survival.

EP685 / #1280

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

INCIDENCE OF BRAIN TUMORS IN AN ITALIAN REGIONAL COHORT FROM 2012 TO 2021: AN EPIDEMIOLOGICAL STUDY

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Background and Aims: Brain tumors are the second most common cancer in childhood. The purpose of this study was to estimate the incidence of primary central nervous system (CNS) tumors in a regional cohort of children under 16 years from 2012 and 2021.
Methods: We conducted a retrospective epidemiological study of primitive lesions, all revised by Central Pathological Review, from our regional database of CNS tumors in children < 16 years. Relapses were excluded. We calculated the incidence per 100.000 children per year and analyzed the incidence trend of low- vs high-grade tumors in 2-5 years subgroups (2012-2016 vs 2017-2021). Descriptive statistic with mean +/- standard deviation (DS) and frequencies were used. Indipendent Student t-test and Chi-square test were used when appropriate (p= .05).
Results: In the studied decade, 93 CNS tumors have been diagnosed with a mean age of 9,2 years +/- 4,7 (44 males, 47,3%) with a mean incidence of 5,41 cases +/- 1,22 (range 3,9-8,5) per 100.000 inhabitants under 16 years per year. We also documented a reversal of the trend with a rising number of high grade diagnosis compared to low-grade. Although homogeneus by age (9,3 vs 9,1 years, p=.83) and sex (48,8% vs 58,4 of males, p=.38), the second 5-years group (2017-2021) showed a rising rate of high-grade cases (60% vs 21,95%, p=.000493), compared to the first group (2012-2016). In particular, in the last two years (2020-2021) there was a 2.65 (95%CI 1.39-9.1) higher probability to diagnose a high grade brain tumor than in the previous period (2012-2019).
Conclusions: In childhood, CNS tumors incidence has been fairly stable in the last ten years in our regional cohort, but a recent concern of an increased rate of high-grade diseases emerged according to our data. In case of a confirmation of this trend, a further analysis aiming to understand the reason is needed.

EP686 / #1853

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

EXPERIENCE OF RADIATION TREATMENT INTERRUPTIONS AND IDENTIFICATION OF MEASURES TO IMPROVE CARE AT A TERTIARY CARE UNIVERSITY HOSPITAL IN LMIC

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Background and Aims: Radiation therapy is an essential local control modality of many pediatric solid and brain tumors and shall be completed withoug unscheduled gaps to achieve optimum outcomes. Here we look into the reasons and patterns of gaps in radiation treatment for children at our institute.
Methods: Children treated from January 2009-March2021 with RT with or without GA at Aga Khan University were included. Patients having treatment gap of one or more days during radiotherapy were identified and data for demographic details, diagnosis, region of treatment, duration of gap and reason for treatment interruption was recorded and analyzed.
Results: There were 178 events of treatment gap in 118 out of 511 patients treated during study period with mean age 8.2years[±4.95) and 71(60%)male. Most of patients(75%) were referred from another hospital after discussion in tumor board. All RT plans were peer reviewed. Most common diagnoses were sarcomas 57%(67 patients), CNS 15%(16 patients), lymphomas 14%(16 patients) and renal tumors 10%(12%) patients. There was a gap of 1-2days in 40(34%)patients, 2-7days in 42(36%)patients and ≥8days in 36(30%)patients. Major reasons included in-patient admission due to fever, neutropenia or diarrhea in 53 patients, machine breakdown in 29 patients, refusal of anesthesia fitness due to chest congestion in 24patients, patients' social reason in 14 and RT re-planning in 10 patients. Out of 118 patients, 45(38%) were being treated under GA and 73(62%) without GA. 24 of 45 patients treated under GA had treatment interruption because of being unfit for GA before RT. Longer interruption was noted in children treated under GA with 3-7 days gap in 36%patients and ≥8days gap in 42%patients.
Conclusions: The demonstrated prospecte factors which could minimize treatment interruptions including improvement in supportive care, prevention of infections, maintenance of equipment. Local control can be improved by working on these things, specifically in shared care tertiary care setting.

EP687 / #237

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IMPACT ON CHILDHOOD CANCER CARE DUE TO COVID-19 PANDEMIC IN NATIONAL REFERRAL HOSPITAL IN INDONESIA

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Background and Aims: Cipto Mangunkusumo Hospital (CMH) is the national referral hospital in Indonesia. Following the COVID-19 pandemic, many problems occurred due to lockdown areas, increased suspected cases, and limitation of non-urgent visits to the hospital. This study analysed the difference in the number of visits for new oncology patients and associated outcomes before and during the COVID-19 pandemic.
Methods: A retrospective review of pediatric oncology patients was conducted in CMH from January 2015 to December 2021. Data of all newly diagnosed oncology patients were collected. Each patient was counted once and changed in diagnosis when appropriate was not listed as a new patient. A total number of new cases were registered, and data during the pandemic (2020-2021) were compared with previous years (2015-2019). Outcomes were also collected and analysed.
Results: This study included 2142 new cases across seven years of observation, with 551 patients (25.7%) from the COVID-19 pandemic and 1591 patients (74.2%) from the baseline period. Acute lymphoblastic leukemia is still the most common type of cancer, with 171 (31%) and 484 (30.4%) patients. The ratio between leukemia and the solid tumor was 1.0: 1.14. Outcomes were worse than in previous years, with a higher number in diagnosis and treatment, mortality rate, readmission rate, relapse, and a lower number of remissions. Associated factors include delayed treatment due to isolation, COVID-19 co-infections, and severe clinical conditions.
Conclusions: There was no significant decrease in the yearly number of childhood cancer cases during the COVID-19 pandemic. But delay in diagnosis and treatment led to worse clinical outcomes. Therefore, despite the ongoing pandemic, solutions and extra attention from families, health care workers, and stakeholders must be given to our oncology patients to prevent delays in diagnosis and treatment.

EP688 / #1795

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

PEDIATRIC SOLID TUMOR MANAGEMENT IN A NATIONAL REFERRAL HOSPITAL IN INDONESIA: CHANGES BEFORE AND DURING COVID-19 PANDEMIC

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Background and Aims: In lower-middle-income countries, advanced investigations for solid tumours are often incomplete and inaccessible. Patients usually come to our centre with advanced stages and make it difficult to manage. Delays in diagnosis (including elective surgeries) and treatment interruptions increase complications and mortality. This study aims to determine pediatric solid tumours management changes due to the COVID-19 pandemic in Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
Methods: This was a retrospective study. Data were obtained from the clinical records of pediatric patients with solid tumours treated in our oncology unit before the pandemic (January 2015 - December 2019) and during the pandemic (January 2020 - December 2021). Histology reports were obtained from the histopathology unit. Procedures waiting times and any treatments disruptions were analysed.
Results: There were 862 and 273 new solid tumour cases treated at our hospital before and during the pandemic, respectively. The mean age of all subjects was 6.9±5.5 years. The differences in the proportion of five most common solid tumor observed in our study before and during COVID-19 pandemic: retinoblastoma (23.2% vs 23.4%, p=0.934), osteosarcoma (12.2% vs 10.6%, p=0.487), neuroblastoma (7% vs 9.9%, p=0.11), rhabdomyosarcoma (8.5% vs 5.1%, p=0.07), and non-Hodgkin lymphoma (8.6% vs 4.4%, p=0.02). We found delays in elective surgeries and disruptions to chemotherapy and radiotherapy during the pandemic, especially during the high wave period. Associated factors include reduction in health care services, staff shortages, waiting time for COVID-19 test results and treatment disruption due to COVID-19 infection.
Conclusions: Our centre's most common pediatric solid tumour was retinoblastoma, osteosarcoma, neuroblastoma, rhabdomyosarcoma, and non-Hodgkin lymphoma. There was no significant decrease in the total case number of the solid tumour during the COVID-19 pandemic. Varieties of diagnostic delays and treatment disruptions were observed. Strategies are needed to mitigate the significant delays and disruptions in cancer care.

EP689 / #1673

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

ANNUAL DISEASE BURDEN OF PEDIATRIC ONCOLOGY PATIENTS PRESENTING TO A TERTIARY CARE HOSPITAL IN PAKISTAN

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Background and Aims: Over 90% of children at risk of developing cancer reside in low to middle income countries (LMICs) such as Pakistan. Unfortunately, overall survival rates fall far below high income countries at 35%. For adequate resource allocation and improvement of patient outcomes, accurate documentation and analysis of the numbers and presentations of childhood cancer is essential. Moreover, registry data is essential for hospitals to effectively manage caseloads and streamline patient care, and contributes significantly to local policy making. Due to the absence of a national cancer registry, tracking systems and trained data operators, scarce information is available regarding childhood cancer incidence and outcomes in Pakistan.
Methods: Supported by the My Child Matters grant, Indus Hospital and Health Network (IHHN) established a comprehensive multi-institutional hospital-based childhood cancer registry in 2016. Seven other pediatric oncology units across Pakistan also enter data into the web-based IHHN registry via trained officers. Annual IHHN data from January to December 2021 was extracted and analyzed.
Results: A total of 1,073 childhood cancer cases registered at IHHN in 2021. Gender distribution showed a male predominance of 63.7%, with females constituting only 36.3%. Mean age was 8.37 ± 4.41 years. A large majority of patients (58.4%) presented from various cities across Pakistan, followed by residents of Karachi (38.4%) and Afghanistan (3.2%). The most notable malignancies were leukemias, lymphomas (18.7%), abdominal tumours (12.3%), CNS tumors (6.4%), soft tissue sarcomas (6.0%), retinoblastoma (5.8%), bone tumours (5.0%), epithelial neoplasms and melanoma (2.9%), histiocytic disorders (1.0%) and others (0.6%).Over 15% patients were on palliative care, and the rest on curative treatment. Abandonment rate was observed to be 15%, whereas 10% of patients expired following registration.
Conclusions: Documentation of pediatric oncology cases at a national level in the form of a comprehensive cancer registry is essential to establish disease incidence, prevalence and final outcomes.

EP690 / #1684

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AN ACCOMMODATION SUPPORT MODEL FOR PEDIATRIC ONCOLOGY PATIENTS OF A TERTIARY CARE HOSPITAL IN KARACHI, PAKISTAN

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Background and Aims: Abandonment of cancer treatment compromises the survival of approximately one in seven children worldwide annually. Despite free of cost treatment facilities and availability of specialized centers, over 20% oncology cases in Pakistan abandon therapy, leading to overall survival of under 35% compared to 80% in high income countries. To promote social support systems in healthcare, Indus Hospital & Health Network (IHHN) initiated Madina Residency, a one-of-a-kind facility for pediatric oncology patients on curative treatment.
Methods: With the help of donors, IHHN acquired a 25 bedroom residence building in Karachi in 2019. This residence was offered to patients originating from remote areas with severely underprivileged backgrounds and on active curative treatment. The accommodation, food, transportation to the hospital and treatment offered was completely free of cost.
Results: Of the total 126 patients accommodated up to December 2021, 90(71.4%) were male, with mean age of 8.2 ± 4.1 years. Distribution of diagnoses displayed highest burden of leukemias 69(54.7%), followed by solid tumors 28(22.2%) and lymphomas 12(9.5%). The average stay of Pakistani patients was 96 ± 86 days and neighboring countries was 105 ± 85 days, with the longest stays ranging between 6 months to 1 year, in leukemia and bone tumor patients. Forty three (34.1%) patients were from Afghanistan and 83(65.9%) from various far flung areas of Pakistan. Average monthly household income was PKR 14,721 (USD 79.68), with an average of 7.3 ± 3.1 family members per household. On feedback at checkout, each of these patients stated that the residence facility directly prevented them from abandoning treatment.
Conclusions: Further studies and cost analysis of accommodation support models is essential for childhood cancer budgets to be invested in effective preventive strategies. In order to improve overall survival, early presentation and compliance to recommended treatment in safe and hygienic environments is crucial, especially in low-middle income countries.

EP691 / #1699

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

DEVELOPMENT OF MULTIDISCIPLINARY PEDIATRIC ONCOLOGY TUMOUR BOARDS: PERSPECTIVE FROM A LOW-MIDDLE INCOME COUNTRY

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Background and Aims: Multidisciplinary tumour boards (MTBs) are essential for provision of high quality, comprehensive cancer care. Establishment of MTBs enables the thorough discussion of patient diagnoses, tumour staging and management by an expert committee, thus improving clinical management and outcomes. In countries such as Pakistan, where a national cancer plan is lacking and healthcare systems are plagued with administrative and managerial gaps, MTBs allow formation of strong multidisciplinary teams to address various problems. Moreover, tumour boards provide postgraduate trainees with an opportunity to present cases, enhance knowledge and interact with national and international faculty and residents from different specialties.
Methods: The Pediatric Hematology/Oncology (PHO) Department at Indus Hospital and Health Network (IHHN) has organized and participated in multiple MTBs for various pediatric malignancies since 2015. Two solid tumour MTBs, twice a month in conjunction with international faculty and once a month on a multi-institutional level have been conducted. In collaboration with international specialists, a retinoblastoma and neuro-oncology tumor board each have occurred once a month. On a local, multi-institutional level, IHHN faculty have conducted monthly leukemia, lymphoma, Wilm's tumor and pediatric sarcoma MTBs. Due to the COVID-19 pandemic, in-person MTBs were shifted to virtual Zoom meetings.
Results: Over 30 IHHN faculty members have attended and presented cases at various MTBs, ranging from oncologists, hematologists, radiologists, histopathologists, pediatric surgeons (orthopedic, cardiothoracic, head and neck), radiotherapists and ophthalmologists. PHO fellows and residents in training from hematology, histopathology, radiology, general pediatrics and radiotherapy also participated. Over three thousand cases have been discussed thus far.
Conclusions: Within the realm of pediatric oncology, a patient-centered multidisciplinary approach through the establishment of MTBs is essential to improve patient outcomes and survival.

EP692 / #176

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EQUIVALENT DOSES FOR ANTICANCER AGENTS USED IN PAEDIATRIC ONCOLOGY: A SCOPING REVIEW AND EVALUATION OF A NOVEL APPROACH

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Background and Aims: Subsequent neoplasms are one of the severest late effects of the therapy of childhood cancer. In epidemiological research on this relevant topic, it can be necessary to aggregate chemotherapy agents into substance classes, as in our study on Second Tumours after Tumour Therapy (STATT). Cumulative doses are calculated using conversion factors by substance classes.
The aim of the review was to identify conversion factors from the literature and to compare them to our novel approach.
Methods: First, a scoping review was performed in PubMed in August 2021 to compile conversion factors used in previous studies. Second, based on a comprehensive list of treatment protocols used in German paediatric oncology, we derived alternative conversion factors from “typical doses” per substance with a novel approach. Finally, the conversion factors were compared on a log scale using Pearson correlation coefficients and linear regression. Substances were grouped according to the Anatomical Therapeutic Chemical Code (ATC).
Results: The literature search identified 23 studies in which conversion factors were used or defined as described above. Mostly, the factors were presented as based on the relative toxicity or potency of the drugs, though usually without a specific reference. Conversion factors were available for 49 substances, either from the literature (n = 38) or from typical doses (n = 41).
The Pearson correlation coefficient for the 18 substances (excluding the 12 reference substances) with available factors based on both principles was r = 0.84 with a slope in linear regression of 0.75.
Conclusions: The conversion factors from the two approaches were highly correlated and on average very similar. Hence, for substances for which no conversion factor has been published so far, a factor based on a “typical doses approach” may be used in epidemiological research. Funding: Deutsche Krebshilfe, grant number: 70112099

EP693 / #1180

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INTERNATIONAL ACCREDITATION OF A PEDIATRIC HEMATOLOGY/ONCOLOGY FELLOWSHIP PROGRAM IN GUATEMALA

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Background and Aims: Graduate medical education programs in pediatric hematology/oncology are necessary to train specialists to provide future quality care for children with cancer. The Unidad Nacional de Oncología Pediátrica (National Pediatric Oncology Unit, UNOP) is Central America's only hospital solely dedicated to pediatric cancer and was founded in Guatemala City in 2000. In 2003, UNOP, together with the Universidad Francisco Marroquin Medical School and St. Jude Children's Research Hospital, created a fellowship program in pediatric hematology/oncology. Our aim is to describe the accreditation process for the pediatric hematology/oncology program at UNOP.
Methods: The Accreditation Council for Graduate Medical Education - International (ACGME-I) accreditation process includes two main steps: the accreditation of the institution overseeing a training program; and the accreditation of the program itself of the trainees, the faculty, and the program itself.
Results: After ACGME-I's initial visit to UNOP in January of 2019 confirmed the areas of improvement, institutional and program level changes were embarked upon. ACGME-I accredited UNOP as a sponsoring institution on August 25, 2021. To apply for accreditation of the pediatric hematology/oncology fellowship program, multiple modifications were also required. The didactics schedule and rotations schedules were updated, and a system to support fellows' research programs was designed, with a Scholarly Oversight Committee. Also, web-based evaluations were designed to provide structured evaluations. The accreditation of the fellowship program was obtained on January 22, 2022. The process of accreditation has already improved the educational infrastructure and fellowship program educational organization, enabling a better training environment.
Conclusions: UNOP is the first pediatric hematology/oncology fellowship program in the world accredited by ACGME-I. The UNOP fellowship program should be considered a model for future regional workforce training programs in pediatric hematology/oncology, as well as in other specialties.

EP694 / #1013

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

TELEO PROGRAMME: TELE-EDUCATION IN PEDIATRIC ONCOLOGY AS A TOOL TO SUPPORT TRAINING PROGRAMMES IN LATIN AMERICA

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Background and Aims: Experts in most pediatric oncology areas are scattered among many centers in Latin America and there are limited opportunities for trainees to be exposed to their experience. Therefore, TeLeo was created under the premise that academic excellence could be shared among centers by a virtual learning program to favor networking and share context-sensitive high-quality content.
Methods: TeLeo was created with the support of a My Child Matters grant and promoted by Hospital Sant Joan de Déu, Foundations Messi and Flexer and the Latin American Society of Pediatric Oncology (SLAOP). A digital platform was created to allow participants to access the learning activities, stored educational content and interact through social networking tools. Healthcare professionals involved in childhood cancer care can freely access content at TeLeo after registration.
Results: A board was appointed including representatives from the major programs in Latin America. A two-year virtual training program (144 hours) based on the SLAOP educational curriculum was launched to support fellowship programs. Weekly sessions in Spanish and Portuguese, given by local and international experts were scheduled. In its first edition beginning in 2021, 185 fellows from 40 centers (12 countries) were enrolled. Additional courses were produced to further support the program such as an interactive bone marrow morphology (40 students, 10 hours), imaging for pediatric oncologists (310 attendees, 12 hours), essential drugs for leukemia treatment (235 assistants, 9 hours), as well as a two-day pediatric psycho-oncology meeting (440 attendees). The platform also hosted the 2020 and 2021 SLAOP virtual congresses and overall, more than 3,000 professionals registered.
Conclusions: TeLeo is a successful program to offer a free online educational tool for healthcare professionals related to oncology in Latin America highlighting the importance of a collaborative network to provide free and high-quality contents for the future generations of pediatric oncologists and other professionals related to cancer care.

EP695 / #39

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

IMPACT OF CLINICAL PHARMACIST IN OPTIMIZATION OF DRUG THERAPIES FOR EFFECTIVE OUTCOMES IN HOSPITALIZED PEDIATRIC ONCOLOGY PATIENTS

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Background and Aims: Background Oncology patients especially pediatric patients need special care since they are on multi drug regimens that are complex in nature. These require close monitoring due to potential interactions, precise dosing and adverse reactions. As per CDC, approximately 1.3 million ER visits and 350,000 hospitalizations each year in United States are due to Adverse Drug Events. Being one of the last safety checks, clinical pharmacists are vital in prevention of adverse drug events and near miss prescribing/transcribing errors in clinical practice. Aim Role of clinical pharmacist in improving patient safety and quality of care in hospitalized pediatric oncology patients.
Methods: This is a retrospective observational study analyzing clinical pharmacist interventions from November 2020-November 2021 in pediatric oncology patients at Indus Hospital and Health Network.
Results: Total 1,149 interventions were done. Addition of drug was highest i.e., 242(21%), followed by lab based, 167(14.5%) and inappropriate duration, 126(10.9%). Less frequent were wrong route selection, wrong dosage form selection, switching to alternate, 2(0.17%) each, followed by hepatic dose adjustment, 4(0.34%), IV to PO, 8(0.69%) and CS based interventions 9(0.78%). Other interventions include duplication of class/activity 97(8.4%), supra-therapeutic dose 85(7.39%), sub-therapeutic dose 83(7.22%), wrong frequency selection 80(6.96%), duplication medication order 60(5.2%), unnecessary drug and interaction 35(3%) each, therapy modification 26(2.2%), drug-disease interaction and renal dose adjustment 19(1.6%) each, wrong drug selection and inappropriate dose 17(1.47%) each and contraindicated drug prescribing contributes to 13(1.13%) interventions Considering risk, significant and highly significant were 597(51.95%) and 545(47.43%) respectively while 7(0.6%) were lethal.
Conclusions: Interventions are aimed at improving outcomes. Incorporating pharmacist in clinical practice of specialized area of patient care has great potential to reduce drug related problems to a greater extent thus optimizing therapeutics and improving patient safety. This study also highlights need of more training programs of prescribers in terms of drug use.

EP696 / #95

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

A MODIFIED E-DELPHI CONSENSUS PROCESS FOR THE DEVELOPMENT OF A CLINICAL GUIDELINE FOR SUSPECTED BONE AND ABDOMINAL TUMOURS

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Background and Aims: The incidence of childhood cancer has risen by 15% in the UK and is the leading illness cause of death in children and young people (CYP). Childhood cancer poses a diagnostic dilemma to clinicians due to the non-specificity of symptoms. Although the overall five-year survival is 84%, bone and abdominal tumours still have the lowest survival rates with many experiencing delays to diagnosis. A clinical guideline specifically for bone and abdominal tumours will provide evidence-based guidance to allow prompt diagnosis.
Methods: Emails of invitation were sent to healthcare professionals (HCPs) to join the Delphi panel. 65 statements were derived from evidence review by a multidisciplinary team. Participants were asked to rank their agreement with the statements by means of a 9-point Likert scale (1 = strongly disagree; 9 = strongly agree). Statements reached consensus if 70% or more rated the statement 7, 8 or 9. Rankings for each statement were collated and any statement achieving the pre-determined level of consensus was accepted. Statements not reaching consensus were rewritten and re-issued in a subsequent round.
Results: 133 healthcare professionals took part. All statements achieved consensus at the end of two rounds. 96 of 133 (72%) participants responded to the Round 1 (R1). 62 of 65 (94%) statements achieved consensus in R1 with 29 (47%) gaining more than 90% consensus. Three statements did not reach consensus scoring between 60.9 and 69.1%. All reached numerical consensus at the end of Round 2. One statement was deemed similar to another and so was omitted from the final list.
Conclusions: This consensus process has produced expert guidance for a new clinical guideline for suspected bone and abdominal tumours for use in both primary and secondary care. This evidence base will be translated into awareness tools for the public as part of the Child Cancer Smart national awareness campaign.

EP697 / #688

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

DEVELOPING A HARMONISED FRAMEWORK FOR MONITORING OUTCOMES AND IMPACT OF DONOR INVESTMENT INTO PAEDIATRIC CANCER SERVICES IN LOW- AND MIDDLE-INCOME COUNTRIES

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Background and Aims: Improving the scale and quality of paediatric cancer services in low- and middle-Income countries (LMICs) is often contingent on financial investment from external, institutional donors. Securing longer-term donor investment requires that downstream partners (e.g., clinical services) evidence the health outcomes of this investment. World Child Cancer (WCC), a UK-based Non-Governmental Organisation, set out to determine and pilot a standardised set of indicators to measure the impact of financial investments which would satisfy the requirements of institutional donors whilst being feasible to collect and relevant for health care providers delivering and developing services.
Methods: World Child Cancer reviewed 29 indicators from six programmes across Africa and Asia that had invested in scaling up and/or improving quality of paediatric cancer services. A WCC working party of four, led by the Quality Manager and including the programme coordinator from Cameroon, systematically determined whether: 1. a common approach/structure to programme design was evident across the six programmes 2. a standard set of relevant and feasible outcome indicators could be developed to measure across the different programmes 3. these were suitable to satisfy the requirements of institutional donors whilst relevant and useful to programme managers and providers.
Results: There was a common approach/structure to programme design that was evidenced across different contexts. Twenty-four common indicators could be determined, which were then piloted. These indicators satisfied most donor requirements for demonstrating outcomes and impact and were also relevant for programme managers and clinical practice.
Conclusions: This feasibility study suggests there is scope for a relatively simple, standardised approach to measuring the impact of donor investment in paediatric oncology in low- and middle-income countries. The framework has potential to facilitate increased donor confidence in long-term, sustainable investment whilst also assuring that relevant and useful data is available to service providers to monitor the impact and outcomes of their programmes.

EP698 / #312

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FINANCIAL PLANNING FOR EXPANSION OF PEDIATRIC CANCER SERVICES IN SAN SALVADOR, EL SALVADOR

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Background and Aims: While need for pediatric oncology services exists in low-and-middle-income countries (LMICs), planners have limited access to user-friendly and context-appropriate resources to develop a comprehensive, evidence-based financial plan for the establishment of these services. Leadership at Centro Médico Ayúdame a Vivir (CMAV) and Hospital Nacional de Niños Benjamin Bloom (HNBB) in San Salvador, El Salvador have identified a need to expand their pediatric cancer services. This study aims to explore important internal and external considerations for financial planning for expansion of a pediatric cancer unit at CMAV; use a financial planning tool to determine estimated construction, start-up, and operational costs; and summarize important lessons learned to improve knowledge-sharing globally.
Methods: Key informant interviews were conducted with twenty-three clinical and non-clinical CMAV and HNBB staff members including physicians, nurses, psychosocial providers, administrators, foundation and hospital leadership, and Ministry of Health representatives. Budgeting, what-if scenarios, and SWOT (Strength Weakness Opportunities Threats) exercises were conducted in focus groups. Interviews were transcribed and analyzed for identification of recurrent themes.
Results: Interviewees highlighted the following important considerations for expanding pediatric cancer services that would significantly impact the financial plan: need for incorporation of adolescent patients to the pediatric care model, improvement of palliative care services, and expansion of laboratory capabilities. Barriers and enabling factors to financial planning were also identified. Barriers included difficulties with staff retention, reliance on local donations for operating costs, and medication access and cost. Enabling factors included mission-driven leadership, highly skilled subspeciality nursing and nurse training, multiple national and international partnerships, and focus on future advocacy.
Conclusions: The CMAV/HNBB experience builds on previous analysis of financial planning practices in LMICs, which continues to emphasize the need for systematic and data-driven financial planning, consensus-building, and buy-in for the effective projection of costs and sustainability of new pediatric oncology services.

EP699 / #1902

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

HYPOVITAMINOSIS D IN CHILDREN DIAGNOSED WITH CANCER: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims: Vitamin D is an essential hormone for bone metabolism, growth, immune system regulation, and metabolism. Vitamin D deficiency and insufficiency, also known as hypovitaminosis D, have been associated with the survival of cancer patients, as well as the appearance of adverse reactions to chemotherapy. Therefore, the aim of this systematic review and meta-analysis was to synthesize the evidence on the prevalence of hypovitaminosis D in pediatric patients at the diagnosis of any type of cancer.
Methods: A systematic literature review was carried out in MEDLINE without restrictions. Observational studies that determined hypovitaminosis D at the diagnosis of any type of pediatric cancer were included. Studies where patients received vitamin D supplementation at the time of diagnosis were excluded. The meta-analysis of the prevalence's with 95% confidence intervals (95% CI) was conducted under a random effects approach using the R program. A subgroup analysis was performed to estimate the proportion of vitamin D deficiency and insufficiency.
Results: Thirty-two studies were identified as potentially relevant. After analyzing titles, abstracts, and full titles, 7 studies with 1143 patients were included in the review. The proportion of hypovitaminosis D was 0.37 ([95%CI 0.30 to 0.44], I^2= 83%). In subgroup analysis, the proportion of patients with vitamin D deficiency was 0.45 ([95% CI 0.34 to 0.56], I^2= 85%), while for insufficiency it was 0.30 ([95% CI 0.26 to 0.34], I^2= 0%).
Conclusions: This systematic review with meta-analysis shows that pediatric cancer patients have a high prevalence of hypovitaminosis D. This deficiency can condition patients to suffer long-term adverse reactions such as lower bone mineralization, especially in patients receiving doses high methotrexate or prolonged corticosteroids.

EP700 / #1512

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

SCALE OF CHILDHOOD CANCER INEQUALITIES: NEW WHO EUROPEAN REGION REPORT

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Background and Aims: Strong inequalities remain across the 53 Member States of the WHO European Region. They arise along the whole cancer care continuum, from access to care. Available evidence and information were collated together and analyzed in the first report on childhood cancer inequalities across the Region.
Methods: The report summarized literature in four main areas: the childhood cancer continuum, inequalities across countries, inequalities within countries, and childhood cancer as a driver of inequalities. Where possible, studies from the 53 countries of the WHO European Region were used.
Results: Disparities between countries included: incidence rates varying due to high levels of underdiagnosis/reporting, higher childhood cancer proportion of all cancers in countries with lower HDI scores, wider than for adult cancers disparities in survival rates between higher- (HIC), and lower-and-middle-income (LMIC) countries. Lack of precise and timely universal access to high-quality first-line diagnostics, contemporary therapy, and supportive care result in poorer outcomes. Within individual countries: boys with cancer have poorer outcomes than girls (HIC) but are less frequently underdiagnosed (LMIC); higher socioeconomic status results in higher survival rates; centralized services require patients to travel large distances for care, but dispersed services lack enough expert staff; and data on migrants remain limited. A childhood cancer diagnosis can lead to significant short- and long-term inequalities in the life of the child (vulnerabilities in physical health, well-being and access to follow-up care, worse quality of life and lower academic achievement than peers without cancer) and their entire family (financial difficulties and poorer quality of life), with more frequent reliance on government insurance.
Conclusions: Within the framework of the Global Initiative for Childhood Cancer, the current report proposes recommendations on the key steps that are likely to have the greatest impact in reducing inequalities and is advocating for more data collection to better understand them across the Region and beyond.

EP701 / #1830

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

ANY CONCERN ABOUT DELAYS IN DIAGNOSIS OF CHILDHOOD CANCERS DURING COVID-19 PANDEMIC?

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Background and Aims: Early diagnosis of cancer ensures better prognosis with lower metastasis and higher cure rates. The lock-down precautions during Covid-19 pandemic led to concerns about delayed diagnosis of malignancies. In this study, we aimed to compare the duration of complaint at home and presence of metastasis at diagnosis during pre-pandemic and pandemic period in children with cancer.
Methods: We have 300 patients between 0-18 years of age who have been followed-up in our pediatric oncology clinic, since 2017. In this study, all the children with cancer except leukemia were included. Age, gender, cancer type, duration of complaints and presense of metastasis at diagnosis were recorded. The duration of complaints before admission and the presence of metastasis at diagnosis were compared statistically before and after March 11, 2020, the start point Covid-19 pandemic in our country.
Results: A total of 161 patients diagnosed with cancer except leukemia between 2017-2022 were analyzed retrospectively. 61% of the patients were male, while 39% were female. These patients were diagnosed with brain tumours (23.6%), lymphomas (23%), rhabdo/non-rhabdomyosarcomas (14.3%), neuroblastoma (13.7%), Ewing sarcoma (4.3%), osteosarcoma (3.7%), Wilm's tumor (3.7%), germ cell tumors (3.1%). Distant metastases were present in 42.3% of the patients. The number of patients were 59 and 102 before and after the pandemic, respectively. The duration of complaint was longer (median 45 days) during the pandemic period than before pandemia (median 30 days) ($p<0.05$). The presence of metastases at diagnosis was 45.3% in the pre-pandemic period, while it was 40% during pandemia with no statistical difference ($p>0.5$).
Conclusions: We concluded that the duration of complaint before diagnosis was found to be longer during pandemia while this delay did not affect the metastasis rate at diagnosis in children with cancer.

EP702 / #826

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

ACUTE LEUKEMIAS: DIAGNOSIS AND CLASSIFICATION CHALLENGE IN LOW- MIDDLE INCOME COUNTRY (LMIC)

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Background and Aims: Acute leukemia (AL) seems to be the most common worldwide childhood malignancy, accounting more than 25% of all childhood cancer. In Senegal, an onco-pediatric unit (UOP) has been opened for 20 years, in Dakar, to improve the therapeutic follow up of patients. In order to improve the diagnosis and to deliver a timely accurate diagnosis, a Reference Center for Diagnosis of childhood Cancers (CRDCE) was created in Dakar.
Methods: Hematologists, pathologists, immunologists, specialist for cytogenetics and clinicians were gathered working together for this challenge.
Results: During the year 2021, 226 malignancies (67 acute leukemias (AL), 39 nephroblastoma, 28 retinoblastoma, 18 lymphomas, 16 neuroblastoma, 16 rhabdomyosarcoma) were diagnosed. Children with AL referred in the Pediatric Unit were evaluated by cytology, cytochemical staining and immunophenotyping. The median age of children with AL is 60 months [6 – 228] with the incidence rate of males (55.2%). Peripherical blood and myelogram blasts count performed to confirm and classify AL according to the FAB classification, cytochemical staining was used for some cases. They revealed 44 Acute Lymphoid leukemia (ALL), with 33 new cases and 23 Acute Myeloid Leukemia (AML) with 22 first diagnosis. Relapses were represented by 11 ALL and 1 case of AML. After the setting of flow cytometry, 33 cases of AL were immunophenotyped: 21 cases were classified as ALL (11 B-ALL, 10 T-ALL) and 12 as AML. Immunophenotyping adjusted the cytological diagnosis in 3 cases: 2 patients classified by cytology as ALL, become AML and one AML was really ALL.
Conclusions: The improvement of distinction between lymphoid and myeloid leukemias by flow cytometry is crucially important and actually works in the CRDCE. In fact, cytogenetics abnormalities appear to be most important for identifying entities with prognostic and clinical behavior. This will be the next step of our Reference Center. Acknowledgments: AMCC GFAOP Sanofi Espoir Foundation

EP703 / #1214

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

HOSPITAL-BASED PEDIATRIC CANCER REGISTRIES IN LOW AND MIDDLE-INCOME COUNTRIES: A SCOPING REVIEW

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Background and Aims: In low- and middle-income countries (LMIC), hospital-based pediatric cancer registries are often non-existent or of limited quality. However, these registries are an important tool for improving the quality of patient care within hospitals and allow for multicenter registries and studies. This study on hospital-based pediatric cancer registries in LMIC maps: 1) all existing literature; 2) requirements needed for successful implementation; and 3) its benefits.
Methods: A scoping review, in line with the PRISMA-ScR guidelines (2020) was conducted searching the following databases: Medline, Pubmed, Cochrane and Web of Science. Additionally, reference lists of selected papers were screened for relevance (‘snowballing’ technique). All peer-reviewed literature on hospital-based pediatric cancer registries in LMIC published in English between 1990 and 2021 was considered eligible for inclusion. Three reviewers independently screened all titles and abstracts and consequently the full texts.
Results: In total, 17 articles were included for content analysis. Reports of hospital-based pediatric cancer registries concerned: Africa (n=8), Latin-America (n=4), Asia (n=3), and LMIC in general (n=2). The majority of registries were established through twinning projects around 1990. Most cancer registries were not pediatric specific, were primarily used to provide epidemiological data, and had limited or no clinical follow-up data. Fifteen studies distinguished the following requirements: ownership, availability of technical infrastructure, local leadership, trained data managers, international coding, sustainability, and funding. Thirteen studies described benefits of registries as being vital for: collecting population data on pediatric cancer, evaluating patient care, enabling high quality research, facilitating comparison with other centers (external benchmarking), and planning of appropriate health-services to improve long-term clinical outcomes in LMIC.
Conclusions: Hospital-based pediatric cancer registries are often lacking in LMIC. There is a strong need for easy accessible registries, inclusive of international standards, to evaluate pediatric cancer care. This may ultimately improve survival of children with cancer in LMIC.

EP704 / #250

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

REGIONAL COLLABORATION CAN ACCELERATE SUCCESS: THE EXPERIENCE OF THE GLOBAL INITIATIVE FOR CHILDHOOD CANCER IN LATIN AMERICA AND THE CARIBBEAN

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Background and Aims: The Global Initiative for Childhood Cancer (GICC) aims to increase the cure rate for children with cancer globally by improving healthcare access and quality. In Latin America and the Caribbean (LAC), 29,000 children and adolescents develop cancer, and 10,000 will die yearly. The Pan American Health Organization (PAHO), St Jude Children's Research Hospital (SJCRH), and collaborators have joined efforts to improve outcomes of children with cancer in LAC using the CureAll framework. We report on the LAC Working Groups' plans and activities to accelerate GICC implementation.
Methods: CureAll delineates the childhood cancer pathway, including multidisciplinary and family-centered care. In March 2021, PAHO formed and coordinated regional working groups focusing on core projects aligned to CureAll pillars and enablers in implementing the GICC. Seven working groups emerged from regional dialogues: early detection, treatment abandonment, nursing, palliative care, nutrition, psychosocial, and supportive care. PAHO orchestrated regular online meetings under the mentorship and support of SJCRH's regional/transversal programs and international mentors.
Results: Between Apr/21 and Dec/21, 202 subject matter experts attended 43 online meetings to promote the dialogue between stakeholders to improve childhood cancer outcomes. Twenty four (24) technical outputs were produced in English, Spanish, and Portuguese: 4 regional snapshots (palliative care, abandonment of treatment, early diagnosis, and nutrition), 3 technical guidelines (nutrition, oral care, and early diagnosis of childhood cancer), 1 technical report (pediatric oncology nursing), 6 fact sheets (psychosocial care), and educational and communication materials (2 virtual courses on early diagnosis and palliative care, and 8 modules on pediatric palliative care for caregivers). Countries in LAC engaged in GICC dialogues, activities and implementation have grown to 19.
Conclusions: LAC Working Groups' ongoing dialogue and commitment are essential foundations to successfully accelerate GICC implementation through collaboration among multidisciplinary stakeholders. Thirteen countries entering the implementation phase are being actively helped by this experience.

EP705 / #408

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

MIGRATION OF CHILDREN WITH CANCER IN LATIN AMERICA: A REGIONWIDE CROSS-SECTIONAL SURVEY OF PEDIATRIC ONCOLOGY PROVIDERS

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Background and Aims: This study aims to understand the situation of migrant children and adolescents diagnosed with cancer (MCAC) in Latin America and explore the factors that hamper access to care.
Methods: A regionwide cross-sectional survey among health care workers from pediatric oncology units in Latin America was conducted in March 2022. The self-administered online questionnaire inquired about the respondent's perception of these children's socio-demographic characteristics, migration-related

factors, and access to cancer treatment. Data analysis was done using descriptive statistics, chi-square, and Kruskal-Wallis test.
Results: The majority of the 150 respondents were pediatric oncologists (81%) and pediatricians (6%) from 17 countries. In 2021 respondents cared for a median of 3.5 MCAC (IQR, 1-9) mainly from Venezuela (55%), Bolivia (23%), Nicaragua (17%), Paraguay (12%), and Haiti (11%). Language was an important barrier to access care (17%) as only a quarter of the centers offered interpreter services. Twenty-three percent of cases reported a history of previous treatment. The MCAC's families' socioeconomic status was perceived as slightly lower (40%) or much lower (45%) than non-migrant children. Although most respondents (84%) reported that their country guaranteed health coverage to MCACs, only 38% of respondents reported that their countries have national migrant-inclusive health regulations. MCAC usually required vaccinations (36%), psychosocial (54%), and nutritional support (38%). Their cancer outcomes were perceived as similar (53%), worse (39%), or much worse (8%) than for non-migrant. Respondents from countries spending less than 7% of their GDP on health perceived a significantly higher risk of treatment abandonment (p=0.001), lack of health coverage (p=0.001), and difficult access to treatment during the COVID-19 pandemic (p=0.033) for MCAC.
Conclusions: A considerable proportion of pediatric oncology providers reported MCAC having difficulties accessing healthcare services in Latin America. Countries must work on widespread policies and ensure their implementation to safeguard the well-being of migrant children.

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Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

PREVALENCE OF MALNUTRITION IN CHILDREN WITH CANCER: A STUDY OF 3608 CHILDREN ACROSS INDIA

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Background and Aims: Large scale data on malnutrition prevalence in paediatric cancer across India is lacking as most studies till date have reported centre- or hospital-specific prevalence rates. Hence, the aim of this retrospective study was to analyse the prevalence of malnutrition in paediatric cancers in 33 government hospitals across India that Cuddles Foundation (CF) partners with.
Methods: FoodHeals® is a CF-developed app that collects data from patients who have been counselled by a CF nutritionist. Anthropometric data uploaded between Feb 2021 and Jan 2022 of patients in the induction phase was analysed. The nutritional status of children with solid cancers (SC) and those below the age of 5 years were determined using mid-upper arm circumference. Children with haematological cancers (HC) were graded using the WHO BMI for age index. Children were classified as; mildly-, moderately- or severely-undernourished, well-nourished or overnourished.
Results: A total of 3608 children between 0-18 years were included in the analysis. The overall prevalence of undernourishment was found to be 59.4%. However, when stratified according to cancer type, children with SC had a higher prevalence of undernutrition (71.1%) compared to HC (52.3%). Percentage of mildly-, moderately- and severely-undernourished children suffering from HC was 22.3%, 15.3%, 14.8% and from SC was 18.3%, 20.9%, 31.8%, respectively. The prevalence of well-nourished children was lower in the SC group (26.8%) compared to the HC group (44.0%). Prevalence of overnourished children was higher in the HC group compared to the SC group (3.6% vs 2.1%).There was a statistically significant difference in nutritional status between SC and HC ($p<0.001$).
Conclusions: More than half the children with cancer that CF supports, across India are undernourished in the induction phase of chemotherapy. Children with SC are at a higher risk of being severely undernourished.

EP707 / #1376

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BRAZILIAN NUTRITIONAL REGISTRY OF CHILDREN WITH CANCER

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Background and Aims: Brazil is composed of five geographically diverse regions regarding population density and socioeconomic inequalities. There is a lack of high-quality research on nutritional status of children and adolescents with cancer in Brazil, particularly of multicentric studies. A national nutritional registry was designed with support from IIPAN (International Initiative for Pediatrics and Nutrition) to assess children with cancer from diagnosis through 6 months of treatment.
Methods: This is a prospective multicenter study involving 9 pediatric cancer units in Brazil, representing all geographical regions. Children with cancer (0-19 years old) are enrolled at diagnosis and followed-up for the first 6 months of treatment. Information on clinical data including anthropometry, food security, and socioeconomic status are collected at pre-defined timepoints (diagnosis, 3 and 6 months after start of treatment).
Results: From January 2021 to February 2022, 315 of 619 patients registered have completed 6 months of treatment (59% male, median age at diagnosis 7.2 years). According to region, 6% were from the South, 42% South East, 16% Central West, 20% North, 16% North East. The analysis of nutritional status at diagnosis, defined by mid-upper arm circumference (MUAC) z-score, showed 11% undernutrition and 7% overnutrition; after 6 months of treatment 7% undernutrition and 6% overnutrition ($P<0.001$). Children under 5 years old (n=128) who were undernourished at 6 months had more antimicrobial days per agent in 6 months compared to healthy (117 vs. 37.5, $P=0.028$) and more days on TPN than healthy ($P=0.001$) and overnourished ($P=0.005$) children.
Conclusions: The Brazilian nutritional registry will provide unprecedented data on the nutritional status of children with cancer at a national level and possible interactions of demographic and socioeconomic factors with nutritional and treatment outcomes. These results suggest that undernourished children under 5 years old may have a higher cost of treatment compared to healthy and overnourished patients.

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IMPACT OF COVID-19 IN PEDIATRIC ONCOLOGY CARE IN LATIN AMERICA DURING THE FIRST YEAR OF THE PANDEMIC

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Background and Aims: The ongoing COVID-19 pandemic strained medical systems worldwide. We report on the impact on pediatric oncology care in Latin American (LATAM) during its first year.
Methods: Four cross-sectional surveys were electronically distributed among pediatric onco-hematologist in April/June/October 2020, and April/2021 through the Latin American Society of Pediatric Oncology (SLAOP) email list and St Jude Global regional partners.

Results: 453 pediatric onco-hematologists from 20 countries responded the first survey with subsequent surveys response rates above 85%. More than 95% of participants reported that treatment continued without interruption for new and active on-going patients, though with disruptions in treatment availability. During the first three surveys, respondents reported suspensions of outpatient procedures (54.2%), a decrease in oncologic surgeries (43.6%), radiotherapy (28.4%), stem cell transplants (SCT) (69.3%), and surveillance consultations (81.2%). Logistic regression analysis showed that at the beginning of the first wave, participants from countries with healthcare expenditure below 7% were more likely to report a decrease in outpatient procedures (OR:1.84, 95%C:1.19; 2.8), surgeries (OR:3, 95%CI:1.9; 4.6) and radiotherapy (OR:6, 95%CI:3.5;10.4). Suspension of surveillance consultations was higher in countries with COVID-19 case fatality rates above 2% (OR:3, 95%CI:1.4; 6.2) and SCT suspensions in countries with COVID-19 incidence rate above 100 cases per 100,000 (OR:3.48, 95%CI:1.6; 7.45). Paradoxically, at the beginning of the second wave with COVID-19 cases rising exponentially, most participants reported improvements in cancer services availability.
Conclusions: Our data show the medium-term collateral effects of the pandemic on pediatric oncology care in LATAM, which might help delineate oncology care delivery amid current and future challenges posed by the pandemic.

EP709 / #1073

Topic: *AS05 SIOP Scientific programme / AS05.r Epidemiology, Policy and Advocacy*

FREQUENCY OF CLINICALLY ACTIONABLE TPMT HAPLOTYPES AMONG CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA: THE TEXAS CHILDREN'S HOSPITAL EXPERIENCE

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Background and Aims: The thiopurine-s-methyltransferase (TPMT) enzyme is responsible for catabolizing thiopurines, such as 6-mercaptopurine (6MP), into active and inactive metabolites. Loss-of-function variants in the TPMT gene increase myelosuppression and leukopenia during 6MP treatment, a key component of curative acute lymphoblastic leukemia (ALL) therapy. We conducted a retrospective analysis examining the frequency of clinically relevant genetic haplotypes in TPMT among patients treated at Texas Children's Hospital (TCH) for ALL.
Methods: We performed TPMT genotyping for patients treated for ALL at TCH from September 2009 to January 2021 to determine allele status for 6 haplotypes with evidence of clinical activity in 6MP metabolism. We evaluated the *1 (normal), *1S (synonymous), and *2, *3A, *3B, *3C (pathogenic) haplotypes and classified the patients as normal, intermediate, and poor 6MP metabolizers based on diplotypes according to established guidelines. We stratified results by self-identified race and ethnicity and performed Fisher's exact tests for independence.
Results: Of the 421 patients in the cohort, 392(93.1%) were normal metabolizers, 29(6.9%) were intermediate metabolizers, and none were poor metabolizers. Of the 29 intermediate metabolizers, 26 had the *3A haplotype, 2 had the *3C haplotype, and one was an unknown haplotype due to use of a qualitative assay. Of the 120 non-Hispanic White patients, 7(5.8%) were intermediate metabolizers. Of the 35 Native American patients, 4(11.4%) were intermediate metabolizers. All 31 non-Hispanic Black patients and 25 Asian/Pacific Islander patients were normal metabolizers. Of the 243 Hispanic patients, 21(8.6%) were intermediate metabolizers. There was no clear association between metabolizer status and race (p=0.25) or ethnicity (p=0.12).
Conclusions: Among our cohort, 7% had a clinically actionable TPMT metabolizer status. Higher frequencies of intermediate metabolizers were seen among Native American and Hispanic patients, although the association did not reach significance. Evaluation of the clinical phenotypes of patients with pathogenic haplotypes and their 6MP dosing requirements is ongoing.

EP710 / #986

Topic: *AS05.s Survivorship*

CHARACTERIZATION OF ENDOCRINOPATHIES IN CHILDREN TREATED FOR MEDULLOBLASTOMAS

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Background and Aims: Endocrinopathies are common in survivors of medulloblastoma (MB) especially after radiotherapy (RT). Data comparing outcomes following proton (PRT) and photon radiation therapy (XRT) are scarce. Even less data exist on the association with various chemotherapy regimens for treatment of MB. We aimed to characterize endocrinopathies in children with MB, and to examine the association between RT (dose/type) along with chemotherapy regimens and the development of endocrinopathies.
Methods: Following IRB approval, charts of children with MB seen at Riley Hospital for Children between 2005 and 2022 were reviewed. Analysis of patients' demographics, clinical characteristics, chemotherapy regimen, radiation dose and type, and endocrine sequelae was done.
Results: Seventy- eight patients (70.5% male) with MB were identified. The mean age ± SD at diagnosis was 7.4 ± 3.7 years, and the mean duration of follow-up was 9.8 ± 5.8 years. Seventy of 78 (89.7%) patients received radiation (XRT=25, PRT=45). Endocrinopathies were diagnosed in 60 of 78 (76.9%), with growth hormone deficiency being the most common (44/78, 56.4%). No endocrinopathies were seen in the no RT group. Compared to PRT, a higher proportion of patients with XRT had endocrinopathies (96.0% vs. 80.0%, p = 0.04), central hypothyroidism (68.0 % vs 28.9% P= 0.002) and hypogonadism (40.0% vs 15.6% P=0.012). In the XRT group, 1 patient developed thyroid nodules and 3 were diagnosed with follicular thyroid cancer. No differences were seen in frequency of endocrinopathies for high dose (36-39Gy) versus standard (23Gy) RT dose, or the chemotherapy regimen.
Conclusions: We found a higher frequency of endocrinopathies in children treated with XRT versus PRT. Similarly, thyroid nodules and cancers were more common with XRT. While no difference found in the prevalence of endocrinopathies between those who received high dose vs standard dose RT, RT remains the major risk factor for endocrinopathies in MB highlighting need for long term monitoring.

EP711 / #1301

Topic: *AS05.s Survivorship*

AN AUDIT OF CARDIAC SURVEILLANCE PRACTICES IN PEDIATRIC ONCOLOGY PATIENTS FOR EARLY IDENTIFICATION OF ANTHRACYCLINE ASSOCIATED CARDIOTOXICITY - A PILOT STUDY

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Background and Aims: Anthracyclines can cause serious acute and chronic cardiovascular side effects. Regular echocardiograms based on the treatment regimen for early detection and modification of therapy are recommended for early detection. The audit was designed to assess compliance in establishing cardiac status at diagnosis and monitoring of cardiac function during and after therapy.
Methods: A retrospective review was carried out to determine baseline cardiac surveillance clinical practice in pediatric oncology unit at Aga Khan University Hospital between January and June 2020, and 19 patients were randomly selected. The online medical record system was utilized to search their diagnoses, anthracycline dosages, and surveillance echocardiogram findings. These were recorded in separate forms on REDCap and analysed to assess compliance.
Results: The patients were between the ages of 1 and 19, with a mean of 8.3years. Diagnoses included, ALL(n=4), osteosarcoma(n=3), Ewing's sarcoma(n=3), Wilms' tumor(n=3), AML(n=3), and DLBCL, Hodgkin's and Burkitt's lymphoma(n=1). A total of 79 doses of anthracyclines (doxorubicin, daunorubicin or idarubicin) were administered. Baseline echocardiograms at diagnosis were done for all patients, A total of 64 surveillance echocardiograms were done during treatment, a minimum of one scan while on therapy and 23 echocardiograms after completion of treatment. Out of the 19 patients in this study, 7 were started on cardiac medications (ACE inhibitors, calcium channel blockers or beta blockers); indications included low LVEF in 2 patients and depressed LV strain, pericardial effusion and hypertension.
Conclusions: This pilot project will help in developing a robust system for anthracycline surveillance. Our data indicates that surveillance practices were followed for all new diagnosis and patients on chemotherapy. Timely surveillance allowed for immediate identification of compromised cardiac function and initiation of anti-failure medications. In the LMICs, there is lack of availability of Dexrazoxane for cardio protection. Robust surveillance programs allow for prevention of anthracycline associated cardiotoxicity.

EP712 / #2012

Topic: *AS05.s Survivorship*

ANALYSIS OF SURVIVAL IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA TREATED AT HOSPITAL DEL NIÑO OVIDIO ALIAGA URIA, MANAGEMENT 2014-2019 LA PAZ, BOLIVIA

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Background and Aims: Leukemia represents the main hematological malignancy in pediatrics. The incidence registered in the world context is 20 to 35 annual cases per million inhabitants. In developing countries, survival curves oscillate between 60 and 70%, even when the same original protocols applied in cancer centers in developed countries are reproduced; Considering that statistical data is a powerful tool in decision making, the following objective was set: Estimate the survival rate in pediatric patients diagnosed with acute lymphoblastic leukemia treated at the Ovidio Aliaga Uría Children's Hospital for the 2014-2019 period.
Methods: It is a non-experimental, retrospective, analytical work, of a predictive research level, descriptive tools were applied for numerical and categorical variables, in addition to Kaplan and Meyer actuarial survival analysis methods; the total number of patients diagnosed with ALL in the study period was 147; 122 were selected by means of inclusion and exclusion criteria, of which 30 correspond to patients who completed treatment and began surveillance, on whom the survival analysis was carried out.
Results: The median survival was 48 months, the cumulative disease-free survival was 92% at 5 years and 100% in the first 3 years, since there was only one isolated event of death at 42 months of follow-up. Having an average surveillance time of 38 months (3.1 years). The mean age of the children under surveillance was 68 months, the relapse event occurred in 3 patients, 1 died and 2 abandoned treatment. The dropout rate in the study period was 26%, as was the mortality rate, 26%, of which half died due to causes inherent to the treatment, the majority in the first months, the induction phase, and the rest died due to activity of the treatment. illness and abandonment.
Conclusions: Median overall survival is 54 months. And the median disease-free survival is 52 months

EP713 / #1831

Topic: *AS05.s Survivorship*

LONG TERM PULMONARY AND CARDIAC FUNCTION AFFECTION AMONG NON-HODGKIN LYMPHOMA SURVIOURS

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Background and Aims: The survival outcomes of mature B-cell non-Hodgkin lymphoma (NHL) patients have improved due to advances in treatment. In this study we aim to assess the frequency and trends of the late effects and their impact on quality of life among these survivors at Children Cancer hospital Egypt.
Methods: A retrospective study including all patients diagnosed with Non-Hodgkin's lymphoma "Mature B" at CCHE 57357 in the period between January 2012 till December 2015. All of the patients were examined for: Cognitive functions (by assessing IQ level using (Stanford-Binet Intelligence Scales, Fifth Edition ''SB5''), Cardiac function, Endocrine (Thyroid functions, Growth curves), Pulmonary (pulmonary function test), 5. Quality of life assessment (PedsQL) and Lipid profile (triglyceride, cholesterol, HDL, LDL)
Results: A total of 345 patients were enrolled, 213 were evaluable with a male: female ratio 4:1. Staging: stage I (7.5%), II (14.1%), III (58.7%), IV (19.7%). The total mean QoL score 99 ± 0.058, the order of the affected domains, according to severity: physical functioning 92 ± 0.1, emotional functioning 92 ± 0.15, followed by social functioning 97 ± 0.08, school functioning 99 ± 0.06. IQ scores (low average 24.4%, high average 10.3%, average 63.8%). Pulmonary functions test was evaluated in 123 patients with affection detected in (57.7%) as follows: (mild degree 34.2%, moderate 14%, sever 9.3%). Cardiac reported with early onset 22% (from which 63% resolved, 36% persistent), late onset 10.3% . Lipid profile was significantly affected (high triglycerides 21.6%, low HDL 16%, high LDL 8.9% and high total cholesterol 41.8%)while Growth affection: regarding weight (25.4% dropped 2 or more centiles, height (33.3% dropped 2 or more centiles)
Conclusions: long term NHL survivors , pulmonary and cardiac functions should be followed up for possible affection. Lipid profiles and weight affection should be monitored closely. Survivorship program for NHL is recommended

EP714 / #789

Topic: *AS05.s Survivorship*

OBESITY AND METABOLIC SYNDROME IN CHILDHOOD CANCER SURVIVORS – AN INSTITUTIONAL COHORT ANALYSIS

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Background and Aims: Childhood cancer survivors (CCS) have increased risk of adiposity, metabolic syndrome, diabetes and dyslipidaemia. We analysed the prevalence of obesity, overweight, abnormal triglycerides (TG), high-density cholesterol (HDL-C) and impaired fasting glucose (FPG) in an institutional cohort of CCS.
Methods: CCS (diagnosed ≤21 years), currently ≥ 5 years of age were included from December 2020 to February 2022. Weight, height, waist circumference (WC) and hip circumference (HC) were measured. FPG and lipid profile were also advised ≥10 years of age. For survivors ≥16 years, body mass index (BMI) ≥23 and ≥27 were defined as overweight and obesity respectively; WC of >90cm (males) and >80cm (females) or WC:HC ratio (WHR) ≥0.90 (males) and ≥0.85 (females) were defined as central adiposity as per WHO Asian recommendations. For 5-<16 years, adult BMI of 23 and 27 as per Indian Academy of Pediatrics (IAP) BMI chart were defined as overweight and obesity respectively and WC≥90th percentile as per IAP-WC chart was considered as central adiposity. FPG≥100mg/dl, TG≥150mg/dl and HDL-C<40mg/dl were considered as abnormal as per International Diabetes Federation Recommendation.
Results: Total 367 survivors were included with median age of 16 years (77.4% males; 61.1% haematological malignancies). Median duration from treatment completion was 5 years (4 months-19.5 years). The prevalence of obesity in the cohort was 11.1% (41/367), while another 71 survivors (19.3%) were overweight. Central adiposity based on WC and/or WHR was observed in 31.3% (115/367) survivors. Total 79 and 82 survivors underwent lipid profile and FPG estimation. Abnormal TG, HDL-C and impaired FPG were observed in 16/79 (20.2%), 24/79 (30.3%) and 7/82 (8.5%) survivors respectively. Baseline type of malignancy, duration from treatment completion, and current age of CCS did not predict development of obesity/ overweight metabolic abnormalities.
Conclusions: Obesity/overweight, dyslipidaemia, and impaired FPG are common in CCS in developing country and needs regular multi-disciplinary follow up.

EP715 / #149

Topic: *AS05.s Survivorship*

SELF-PERCEIVED HEARING HANDICAP AND SOCIAL AND BEHAVIORAL OUTCOMES IN ADULT CHILDHOOD CANCER SURVIVORS WITH TREATMENT-INDUCED HEARING LOSS

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Background and Aims: Hearing loss (HL) is a prevalent adverse effect in childhood cancer survivors treated with ototoxic therapy that may negatively impact quality of life. Self-perceived hearing handicap in the general adult population is a stronger predictor of reduced quality of life than measured HL alone. Self-perceived hearing handicap and its association with social and behavioral outcomes have not been examined in childhood cancer survivors.
Methods: Adult survivors previously treated with platinum and/or head and neck radiotherapy with HL in at least one ear documented by audiological evaluation were recruited (N=364). Two hundred thirty-seven survivors (median[range] age at survey 37.0[30.0-45.0] years, 29.1[22.4-35.0] years since diagnosis, 4.0[2.9-7.7] years from last audiogram to survey) completed the Hearing Handicap Inventory for Adults (total score: 0-16=no handicap, 18-42=mild-moderate handicap, ≥44=significant handicap) and questionnaires on social and behavioral outcomes. Survivors were grouped by HL severity according to Chang ototoxicity criteria: grades 1a-2a=mild-moderate HL vs. grades ≥2b=severe HL. Multivariable logistic regression models examined associations between HL, hearing handicap, and social and behavioral outcomes with adjustment for sex, race, age at HL, and age at survey.
Results: Among 237 survivors, 81 (34.2%) had mild-moderate HL and 156 (65.8%) had severe HL. Severe HL was associated with increased likelihood for mild-moderate hearing handicap (odds ratio [OR]=3.40, 95% confidence interval [CI] 1.61-7.18) or significant hearing handicap (OR=7.41, CI 3.14-17.51). Self-perceived hearing handicap was associated with increased likelihood for social isolation (OR=2.79, CI 1.52-5.10), depression (OR=4.95, CI 1.98-12.35), anxiety (OR=11.25, CI 2.51-50.47), somatization (OR=2.85, CI 1.28-6.37), and reduced personal income (OR=2.22, CI 1.23-4.00).
Conclusions: Severe HL following ototoxic therapy is associated with self-perceived hearing handicap. Survivors who reported hearing handicap are at increased risk for adverse social and behavioral outcomes. Assessment of hearing handicap may facilitate access to targeted recommendations and interventions in adult survivors with HL.

EP716 / #383

Topic: *AS05.s Survivorship*

PREDICTION OF VENTILATORY THRESHOLD WITH A 6-MINUTE WALK TEST IN SURVIVORS OF ACUTE LYMPHOBLASTIC LEUKAEMIA

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Background and Aims: Exercise is beneficial for cancer patients. Measurement of oxygen consumption and identification of the heart rate (HR) at ventilatory threshold remain the gold standard for exercise stress test. However, access to this technology is limited. The 6-Minute Walk Test (6MWT) is a valid and safe field test for assessing aerobic capacity in survivors. The aim is to validate a specific 6MWT equation to predict HR at ventilatory threshold.
Methods: Paediatric ALL survivors (n=154) completed a 6MWT and an incremental cardiorespiratory exercise test on an ergogycle with gas exchange analysis. Participants were randomized into 2 groups to predict the equation (n=107 (70%)) and to validate the equation (n=47 (30%)). Backward linear regression analyses were used to determine the prediction equation for HR at ventilatory threshold from the 6MWT. The root mean square error (RMSE) and the Bland and Altman method were used to measure the accuracy of the predicted HR at ventilatory threshold on the validation group.
Results: The equation determined is [HR ventilatory threshold = (0.074 x age) + (0.218 x HR end 6MWT) + (0.016 x cumulative doxorubicin dose) – (0.051 x height) – (0.835 x years since the end of treatment) – (0.115 x physical activity level) + (0.010 x distance 6MWT) + (0.142 x HR rest) – (0.492 x rating of perceived exertion) + 126.79] ($p=0.001$, $R^2=0.271$). The resulting RMSE was 14.5 bpm. Validation with the Bland and Altman method showed that more than 95% of the values fall between the limits of agreement (-28.7 to 28.8) and the mean bias was 0.085 bpm.
Conclusions: The equation with 6MWT data and disease-specific variables could predict an individualized training level for ALL survivors. This study reinforces the utility of assessing the functional capacity of patients with a 6MWT to propose an individualized training programme at ventilatory threshold based on their abilities.

EP717 / #1936

Topic: *AS05.s Survivorship*

LONG-TERM NEUROPSYCHOLOGY DEFICITS IN PEDIATRIC CNS TUMOR: REVIEW OF 20 YEARS OF EXPERIENCE

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Background and Aims: Childhood cancer is the second leading cause of death. Of all neoplasms, Central Nervous System (CNS) tumors account for 30% of cases. Posterior Fossa Tumors (TFP) are the most prevalent and account for about 50% of all tumors. Medical advances have allowed survival to be around 80% after 5 years. Two-thirds of these children will experience some kind of long-term sequelae. 60% of survivors will be at risk for some form of neurocognitive impairment.
Methods: The groups of populations studied are analyzed according to the location of the tumor and the diagnosed neuropsychological profiles. Material and Method. Retrospective review of children assessed between 2001 and 2021. A total of 151 patients were reviewed and analyzed.
Results: The localitzation was in a 35% supratentorial versus 65% infratentorial. Only 2% of the total sample had no neurocognitive deficits, whereas 16% had an intellectual disability and the rest a wide range of neurocognitive focal deficits. All of teh had a scholar support amb more than a half repeat course. The group of infratentorial tumors, teh 75% of children had long-term characteristics typical of Cognitive Affective Cerebellar Syndrome (SCCA).
Conclusions: The need for specialized neuropsychological assessments in the follow-up of these children is demonstrated in order to be able to favor adequate school and adaptive achievements.

EP718 / #1704

Topic: *AS05.s Survivorship*

MANAGING THE AFTERMATH OF RECENT CANCER: A STUDY INVESTIGATING AND EVALUATING A MODEL FOR SUPERVISED INTENSIVE GROUP INTERVENTION FOR PSYCHOSOCIAL REHABILITATION

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Background and Aims: Following diagnosis, young, young adult and adult cancer patients face dealing with the unwanted consequences and the challenges of managing post-treatment life. Rehabilitation after the illness and the anticancer treatment has been established as a vital part of treatment and surveillance. The aim of this study was to implement and evaluate an intensive supervised group model for psychosocial rehabilitation (PSR).
Methods: This pre- and post-assessment intervention study included patients diagnosed with cancer, and for whom treatment was in the final stage or completed, and who were >3 months from diagnosis. The PSR intensive intervention was manual-guided, supervised by experienced qualified leader, and offered two weekly sessions over 10 weeks. The effect of the PSR was assessed pre- and post-intervention regarding anxiety and depression using the Hospital Anxiety Depression Scale (HADS), the Spielberger State-Trait Anxiety Inventory (STAI), and sense of coherence using the Sense of Coherence Scale. Participants were enquired about their subjective experience of the value, usefulness, and efficiency of the PSR program.
Results: Nine out of 11 patients completed the intensive program. A positive effect of involvement in the PSR was reflected in a significant decrease in post-intervention anxiety and depression, i.e., in HADS-anxiety ($P<0.01$), HADS-depression ($P=0.04$), STAI trait anxiety (STAI-T, $P=0.01$). State anxiety showed a decrease tendency (STAI-S, $P=0.07$). Program involvement also resulted a non-significant increase in sense of coherence ($P=0.12$). The program was generally evaluated positively as regards quality, extent, degree to which it had met needs, and overall usefulness of the program.
Conclusions: Time-limited intensive PSR intervention is helpful, and meets needs of help in adjusting to post-treatment life after recent cancer. Intensive face-to-face group rehabilitation intervention can reduce emotional burden, and endorse sense meaningfulness. Findings justify a larger implementation study to further examine the strengths of this rehabilitation model, and usefulness in general clinical after-care.

EP719 / #706

Topic: *AS05.s Survivorship*

CANCER CARE FOR CHILDREN, ADOLESCENTS AND YOUNG ADULTS AND THEIR PATHS TO DIAGNOSIS: AN IRISH EXPERIENCE.

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Background and Aims: Improving survival rates of childhood and adolescent cancer has meant survivorship, and long-term follow-up and care for these patients has been at the forefront of focus in recent years. There is a paucity of literature examining the experiences of young people (YP) with cancer in Ireland. We aimed to explore the Irish experience of cancer care for this group
Methods: Data was collected via anonymous online survey. Inclusion criteria were being over 16 years of age and having been diagnosed with cancer between 0 and 26 years. Data including demographics, path to diagnosis, diagnosis and treatment was collected.
Results: Sixty-one surveys were completed. Disease types reflected incidence patterns nationally. In the 0–14-year cohort, the commonest diagnosis was leukaemia (35.7%, n=10), solid tumour (28.6%, n=8) and CNS tumour (21.4%, n=6). Lymphoma was the commonest diagnosis in the 15–26-year age group (51.5%, n=17 vs 10.7%, n=3 in 0-14yo) (p= 0.009). Most patients (85.2%) attended a general practitioner (GP) prior to diagnosis, with 21.2% reporting >3 GP visits. A statistically significant difference was noted between the groups as to who informed YP they had cancer; 76% of over 15s were told by healthcare professionals compared with 36% of 0-14yo (p=0.16). Participants were invited to leave comments with one respondent quoting “Nobody properly told me I just figured it out from hearing doctors talk around me”.
Conclusions: Multiple visits to GPs reflect data from international studies, demonstrating a change in healthcare utilisation prior to a cancer diagnosis. Differences in communication around diagnosis are somewhat expected but we must endeavour to include children and young people in discussions about their health. Children and YP with cancer require their unique psychosocial needs to be met with age-appropriate communication styles and provision of information which needs to be prioritised by healthcare professionals. No one should overhear their cancer diagnosis.

EP720 / #710

Topic: *AS05.s Survivorship*

NAMED PATIENT PROGRAM USE OF PEDMARK™ TO REDUCE THE RISK OF CISPLATIN-INDUCED OTOTOXICITY IN PEDIATRIC PATIENTS WITH LOCALIZED SOLID TUMORS

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Background and Aims: Background: Cisplatin induced-otoxicity (CIO), with permanent hearing loss is observed in 60%-90% of pediatric patients treated. PEDMARK™ (sodium thiosulfate anhydrous) reduced the proportion of patients with hearing loss by half as observed in two Phase 3 studies (SIOPEL 6 & COG ACCL0431). Aim: Evaluate the safety of the investigational product (PEDMARK™) provided to pediatric patients via a multi-national Named Patient Program (NPP).
Methods: Patients (1 month to <18 years) with a localized solid tumor, treatment plans including a cisplatin-containing regimen, and cisplatin infusion time ≤6 hours were eligible. PEDMARK™ is administered intravenously 6 hours after each cisplatin infusion. Demography, tumor type, and adverse events (AEs) were recorded from APR2018 - DEC2021.
Results: The NPP has been active for 3.6 years as of the data cut-off (31DEC2021). Forty-six hospitals in 14 countries requested PEDMARK™, totaling 106 case requests, of which 105 were fulfilled. The UK encompassed 35% of hospitals and 41% of case requests. The age range was 1 month to 20 years. Most frequent age ranges were 12-18 months and 2-3 years (17% each), 1-6 months and 18-24 months (13% each), and 3-4 years (12%), respectively. Median weight was 12 kg. Localized tumors included hepatoblastoma (HB) in 90% of patients, of those with known staging, 55% were HB Pretext III/IV. Most frequent ages for patients with HB pretext III/IV was 1-2 years (20%) and under 1-year (14%). Other tumors included medulloblastoma (n=4); nasopharyngeal carcinoma (n=3); glioblastoma (n=1), atypical teratoid/ rhabdoid tumor (n=1); and osteosarcoma (n=1). One SAE has been reported, a serious AE of Grade 1 metabolic acidosis, which was reversible and did not lead to PEDMARK™ discontinuation.
Conclusions: PEDMARK™ was supplied multi-nationally via a NPP to reduce the risk of CIO in pediatric patients of varied ages, tumor types, and staging, with minimal safety findings. The NPP is ongoing.

EP721 / #1740

Topic: *AS05.s Survivorship*

LONG-TERM SIDE EFFECTS OF CHILDHOOD CANCER. WHAT ARE PARENTS WORRIES DURING TREATMENT?

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Background and Aims: Most survivors of childhood cancer develop long-term side effects due to their cancer treatment or their disease.These can negatively affect their quality of life. Our objective is to investigate worries and needs about this topic of parents of children receiving cancer treatment in our unit,as well as determine how much information about long-term care they have.
Methods: We performed a 19-question survey about parent's experiences with late effects communication,general worry about late effects,and specific late effect worries.
Results: 32 parents completed the survey(71.9% female).34.4% had University graduate,21.9% Professional graduate and 37.5% had Middle School graduate.Children diagnosis were 43.8% leukemia/lymphoma,31.3% extracranial solid tumor and 25% CNS tumor. 96.9% of children were receiving chemotherapy,21.9% radiotherapy and in 34.4% surgery was performed. 84.4% thought their children would be cured of their cancer. 62.5% of parents referred they were quite or very worried about long-term side effects.They were especially worried about cardiotoxicity and second malignancies(87.5%),followed by neurocognitive impairment(78.2%),growth impairment(62.5%) and infertility(59.4%).75% of parents had received information during treatment about long-term side effects, but 65.6% said they would have preferred to be better informed, and only 56.3% felt prepared to manage those effects. However,68.8% of parents thought long-term side effects should not influence cancer treatment at all, as cure of their children was the main objective.All parents said they would like to receive more information about long-term side effects at the end of treatment and all them thought long-term care and follow up is necessary.
Conclusions: Most parents of children with cancer showed concerns about long-term side effects and demand information from the beginning of treatment.However,during treatment, they think cure is above sequelae.Early information about long-term toxicity during treatment might help parents to solve worries,thoughts and doubts of families of children with cancer.

EP722 / #5

Topic: *AS05.s Survivorship*

ORGANIC AND STRONG: TEAM BUILDING OF HIGH SCHOOL TEACHERS ADVOCATING FOR A STUDENT RETURNING TO SCHOOL AFTER TREATMENT FOR OSTEOSARCOMA

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Background and Aims: When adolescents return to school after treatment for osteosarcoma of lower extremities, they experience a temporary physical disability before they can walk on their own. With significant bodily changes, they are faced with teachers' and peers' questions or misunderstandings regarding their movement, cancer, and health. To add to the body of knowledge of childhood cancer survivors' school reentry and self-advocacy, this qualitative study explores how three high school teachers joined forces with the school nurse in organically developing a successful team to advocate for and empower their student with osteosarcoma.
Methods: A part of a larger qualitative project of teachers' experiences serving students receiving cancer treatment in Taiwan, this study is focused on how a homeroom teacher, a school counselor, and a designated mentor worked together to support a Grade 9 student returning to school after biological reconstruction. Each teacher was interviewed individually 90-120 minutes. The interview transcripts were analyzed using a thematic analytical method.
Results: The findings were: 1. The organically formed student support team was successful. With students' best interest in mind and given teachers' different professional roles, they focused on what they could do for the student and his family in their own capacity. They trusted and relied on one another to perform their individual task. 2. As the student's single father was busy working to support the family, teachers shared a joint parenting role. 3. Teachers trained the student to self-advocate by guiding him to ask physicians relevant questions, participate in school events, and speak about his cancer experience in public. 4. The school nurse (not interviewed) checked student's wound daily and promptly communicated the student's needs with the teachers.
Conclusions: Given the diverse situations of students treated for cancer, teachers need to learn about the students and their family situation to know what is the best for them.

EP723 / #945

Topic: *AS05.s Survivorship*

DESIRE FOR CHILDREN AND USE OF REPRODUCTIVE HEALTH CARE AMONG MALE SURVIVORS OF CHILDHOOD CANCER: A DCCSS-LATER 1 STUDY

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Background and Aims: Gonadal damage leading to fertility problems is a frequently encountered late effect in childhood cancer survivors (CCS). This study evaluated the desire for children and use of reproductive health care among male CCS in comparison to male siblings.
Methods: A nationwide cohort study was conducted as part of the Dutch Childhood Cancer Survivor LATER study part 1; questionnaire & linkage study. A questionnaire addressing desire for children, reproductive health care and reproductive outcomes was completed by 1,317 male CCS and 407 male sibling controls.
Results: After adjustment for age at assessment, the percentage of men who had an overall (previous, current or future) desire for children was significantly lower in male CCS compared to the male siblings (74% and 82%, respectively; OR, 0.61; 95% CI, 0.46 to 0.82; P = 0.001). The association between survivorship status and desire for children was attenuated after adjustment marital status, level of education and employment status (OR, 0.83: 95% CI, 0.61 to 1.14; P = 0.250). A previous or current desire for children was reported by 491 CCS and 185 siblings. Of these CCS, 34% consulted a reproductive specialist compared to 12% of the siblings (P < 0.001). The percentage of CCS who used assisted reproductive techniques (ART) after consulting a reproductive specialist was lower compared to the siblings (41% and 77%, respectively; P < 0.05). Also, the percentage of men who fathered a child after ART was lower in CCS compared to siblings (49% and 94%, respectively; P < 0.05).
Conclusions: The majority of male CCS have a desire for children. More survivors consult a reproductive specialist, both the utilization of and pregnancy rates after ART are lower compared to their siblings. This insight is important for counseling of CCS regarding family planning and fertility issues.

EP724 / #445

Topic: *AS05.s Survivorship*

METABOLIC SYNDROME IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA/LYMPHOMA SURVIVORS: A GLOBAL CAUSE FOR CONCERN

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Background and Aims: Metabolic syndrome, obesity, and insulin resistance are reported late effects in survivors of childhood Acute lymphoblastic Leukemia (cALL). Our objective was to evaluate the prevalence of metabolic syndrome and its components in survivors of cALL, and to assess predictors for its development.
Methods: Between January-2020 and November-2021, 65 cALL survivors, aged 7-18 years, and at least 2 years from treatment completion, were enrolled. Relevant clinical details were recorded, and testing for fasting blood sugar, insulin, and lipid profile were done. Body composition was measured by a Dual-Energy Xray Absorptiometry (DXA) scan.
Results: The mean (SD) age was 12.7 (±3.2) years and median [IQR] time since diagnosis was 6.5 [5.9;8] years. Majority (74%) of our survivors were male. Primary diagnosis was B cell ALL in most survivors (55/65, 85%), remaining were T cell ALL/Lymphoma. A large proportion of patients (43/65, 66%) received prophylactic cranial radiotherapy. Central obesity was seen in 14/65 (21.5%) children, with 30.8% being overweight/obese. Sarcopenic obesity was seen in 21/65 (33.9%) survivors. Eleven survivors (16.9%) had metabolic syndrome, with 37/65 (56.9%) fulfilling atleast 1 criteria of metabolic syndrome. Hypertension and impaired fasting glucose (>100mg/dL) were seen in 12/65 (18.5%) children each. Triglyceride >150mg/dL and HDL <40mg/dL was seen in 16/65 (24.6%) and 24/65 (36.9%) survivors, respectively. Insulin resistance was seen in 32/65 (49.2%) of survivors. On multivariable regression, presence of increased fat mass/Height z-score on DXA-scan, was the only factor associated with an increased risk of metabolic syndrome [OR:11.44 (2.85-45.88), p=0.001]; age at diagnosis/assessment, chemotherapy or radiotherapy, did not have a direct impact.
Conclusions: Metabolic syndrome and its components are frequent late effects in cALL survivors from low middle income countries. DXA scan for body composition assessment, is a cost effective tool, which may be incorporated globally in survivorship guidelines, to steer appropriate preventive and rehabilitative interventions.

EP725 / #556

Topic: *AS05.s Survivorship*

SERUM ADIPOKINES AS BIOMARKERS FOR SURVEILLANCE OF METABOLIC SYNDROME IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA/LYMPHOMA SURVIVORS IN LOW MIDDLE INCOME COUNTRIES: AN EMERGING CONCEPT

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Background and Aims: Serum adipokines (leptin and adiponectin) are dysregulated before development of Metabolic syndrome, an important late effect in childhood Acute Lymphoblastic Leukemia/Lymphoma (cALL) survivors. We compared serum levels of adipokines in cALL survivors and controls, and further studied their role in prediction of metabolic syndrome in our cohort of survivors.
Methods: Forty cALL survivors (aged:10-18 years, and at least 2 years from treatment completion) and 40 controls, similar for age, sex, body mass index, and Tanner stage, were enrolled. Relevant clinical and treatment details were noted. Body composition by Dual-Energy Xray Absorptiometry (DXA) scan, fasting blood sugar, insulin, lipid profile, and adipokines were evaluated.
Results: Compared to controls, cALL survivors had higher prevalence of metabolic syndrome (8/40 vs 2/40, p=0.042), central obesity (11/40 vs 4/40, p=0.042), and hypertension (9/40 vs 2/40, p value=0.024), and had higher median LDL (78.5mg/dL vs 59mg/dL, p=0.008), VLDL (20.5mg/dL vs 16mg/dL, p=0.020) and triglyceride levels (102mg/dL vs 80.5mg/dL, p=0.014). Though not statistically different, trends of Leptin (7.39 vs 4.23ng/mL, p=0.207) and derived Leptin-Adiponectin ratio (LAR; 1.44 vs 0.80, p=0.598) were higher in cALL survivors while adiponectin levels were similar. Receiver Operator Curve analysis revealed largest area under curve (AUC) at 16.3ng/mL for leptin [AUC: 0.887, (0.780-0.934), sensitivity 88%, specificity 78%] and 4.65 for LAR [AUC: 0.910, (0.801-1.000), sensitivity 88%, specificity 91%]. Survivors who were obese/overweight [37.8 (3.78-377.91], or had higher Leptin [1.11 (1.02-1.19), p=0.006], LAR [1.52 (1.12-2.07), p=0.006], percentage fat z-score [4.75 (1.43-15.77), p=0.011] and fat mass/height z-score [7.11 (1.89-26.80), p=0.004], had a statistically significant increased risk of developing metabolic syndrome in univariate analysis but not in the multivariable regression analysis.
Conclusions: Serum adipokines and DXA-scan variables can be used for surveillance of metabolic syndrome in cALL survivors of low middle income countries. This may help in implementing early preventive measures, improving the quality of life of these survivors.

EP726 / #504

Topic: *AS05.s Survivorship*

RISK AND DETERMINANTS OF REDUCED BONE MINERAL DENSITY AND FRACTURES IN A NATIONAL COHORT OF DUTCH CHILDHOOD CANCER SURVIVORS: A DCCSS-LATER STUDY

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Background and Aims: Childhood cancer survivors are at risk of developing skeletal late effects. However, evidence on risk factors for very low bone mineral density (BMD, Z-score ≤-2), as well as on risk and risk factors of (vertebral) fractures is limited. We investigated this in a national cohort of Dutch childhood cancer survivors treated from 1963-2002.
Methods: A total of 2,003 survivors aged 18-45 years at invitation were included (mean age at participation 33.1±7.2 years). BMD was assessed by dual-energy X-ray absorptiometry (DXA, n=1,548). We assessed fractures that occurred >5 years after cancer diagnosis by medical history (n=1,892). Fracture incidence was compared with Swedish normative data by calculating a standardized incidence ratio (SIR). Vertebral fractures were evaluated by DXA-assisted vertebral fracture assessment (n=249). Associations between demographic, treatment-related, endocrine, as well as lifestyle-related factors and reduced BMD and (vertebral) fractures were evaluated using univariable or multivariable logistic regression models.
Results: The SIR of any first fracture was 3.53 (95%CI=3.06-4.06) for male and 5.35 (95%CI=4.46-6.52) for female survivors. Vertebral fractures were prevalent in 13.3% of evaluable survivors. In the models for low (Z-score ≤-1) or very low BMD (Z-score ≤-2), male sex, underweight, shorter follow-up time (continuous), total body irradiation, cranial irradiation, carboplatin (≥2,000 mg/m^2), alkylating agents (≥8,000 g/m^2), hypogonadism, growth hormone deficiency (GHD), hyperthyroidism, low physical activity, severe vitamin D deficiency, vitamin B12 deficiency, and folic acid deficiency were statistically significant. Male sex, obesity, previous/current smoking, and very low lumbar spine BMD were significantly associated with reported clinical fractures. Older attained age, platinum drugs, GHD, and low physical activity were significantly associated with vertebral fractures.

Conclusions: Childhood cancer survivors are at increased risk of any fracture. Reduced BMD at follow-up (especially very low lumbar spine BMD) was associated with fractures. In addition, several modifiable risk factors for reduced BMD and vertebral fractures were identified.

EP727 / #883

Topic: *AS05.s Survivorship*

MAINTAINING GAINS IN SURVIVOR PSYCHOSOCIAL WELLNESS THROUGH VIRTUAL PROGRAMING DURING A PANDEMIC

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Background and Aims: Adult survivors of childhood cancer (LTS) have difficulty adjusting to life. The Periwinkle Foundation (TPF) serves children with cancer with a variety of programs. In 2018, TPF developed programming specifically for LTS over age 18 designed to provide a strong social network through positive peer interactions. The program was in person (IP) 2018-2019 but largely virtual due to COVID in 2020-2021. Our goal was to compare the impact on survivor wellness comparing IP vs. virtual programing.
Methods: Cancer survivors were aged 18-46: pre-pandemic 46; mid-pandemic 30. One third of LTS had significant physical/neuropsychological sequelae. Pre-pandemic, survivors had monthly IP socials and participated in volunteer activities. Mid-pandemic monthly “socials” were largely virtual. To determine the impact of this novel psycho-social wellness intervention, LTS were asked to complete a 5 question SurveyMonkey questionnaire ranking the impact of the program on their lives as: not important; useful but without significant impact; important; extremely valuable; life changing. Forty of 46 LTS pre-pandemic and 20/30 mid-pandemic program responded. Results were compared between pre-pandemic (IP) and mid-pandemic (virtual) programming.
Results: The percent of LTS who rated the impact of this programming as life changing or extremely valuable in response to specific questions follow with pre-pandemic results preceding mid-pandemic results. 1 –Improved sense of well-being: life changing (75/70%); extremely valuable (20/30%). 2-Helped adjust to cancer history: life changing (65/65%); extremely valuable (13/20%) 3-Improved self-confidence: life changing (72/70%); extremely valuable (18/25%) 4-Helped establish meaningful relationships: life changing (70/70%); extremely valuable (20/10%) 5-Helped adjust to/accept ongoing late effects: life changing (68/65%); extremely valuable (15/15%)
Conclusions: The impact of TPF LTS Wellness Interventions were ranked as life changing or extremely valuable in 75-90% of LTS whether IP or virtual.programming. Establishing a social network of LTS in a non-medical environment provides critically important peer support which enhances survivor psychological wellness.

EP728 / #1256

Topic: *AS05.s Survivorship*

NEUROCOGNITIVE OUTCOME IN LONG-TERM, ADULT SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA TREATED WITH CHEMOTHERAPY ONLY

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Background and Aims: Long-term survivors of childhood acute lymphoblastic leukemia (ALL) demonstrate neurocognitive late effects, including impairments in executive functions (EFs). EFs which are cognitive control processes, enable goal-oriented behavior, and are thus essential for adult life success and wellbeing. Still, relatively few studies have examined neurocognitive functioning in long-term survivors in adulthood, treated with modern chemotherapy only protocols, which was the aim of this study.
Methods: Long-term, adult survivors of childhood ALL (N=53, 51% females, mean age=24.40 years, SD=4.41, mean= 14.65 years post-diagnosis, SD=3.42) participated in this study assessing intellectual abilities, performance based and self-reported EFs in daily life. Neurocognitive performance and self-reported EF complaints were compared to population means or medians using one sample t-tests and Wilcoxon signed rank tests.
Results: Survivors demonstrated better general intellectual abilities ($p < 0.001$), but poorer inhibition ($p < 0.001$) than population mean. Performance of shifting and working memory were not significantly different from population medians ($p > 0.05$). Self-reported EF complaints were significantly higher than population mean ($p < 0.001$) with a strong effect size for the index of metacognitive EFs (MI), and 30% scoring above clinical cut-off $T \geq 65$. The index of behavior regulation EFs (BRI) was not significantly different from population mean ($p > 0.05$).
Conclusions: Long-term, adult survivors do not demonstrate poorer performance on most neurocognitive tests compared to the population mean. However, poorer inhibition and higher levels of metacognitive EF complaints was found. The latter suggest daily-life problems with working memory, planning, organization and task monitoring. Cognitive rehabilitation methods addressing these domains should be examined.
Acknowledgements: This study was supported by grants from The Norwegian Cancer Organization and the Norwegian University of Science and Technology (NTNU).

EP729 / #1440

Topic: *AS05.s Survivorship*

EMPLOYMENT STATUS AND OCCUPATIONAL POSITIONS OF CHILDHOOD CANCER SURVIVORS FROM DENMARK, FINLAND AND SWEDEN: A REGISTER-BASED COHORT STUDY FROM THE SALICCS RESEARCH PROGRAMME

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Background and Aims: A childhood cancer diagnosis and late effects of treatment may affect survivors' possibilities of employment or highly skilled occupations later in life. In this study, we compared the employment and occupational status of childhood cancer survivors with population comparisons and siblings.
Methods: In a cohort study based on Nordic registers, we identified 10,461 survivors of childhood cancer diagnosed before age 20 years in Denmark, Finland and Sweden since 1971. Survivors were compared with 48,928 population comparisons matched to survivors by age, sex and geographical region and 12,605 siblings. Annual outcome information on employment, unemployment, health-related unemployment and occupational position was obtained from statistical institutes for the period 1980-2017 and assessed in multivariate logistic regression analyses from age 30 onwards.
Results: By 30 years of age, 9.2% (95% CI, 8.6-9.9%) of survivors were unemployed for health reasons. Although this proportion was slightly smaller for survivors of cancers diagnosed in more recent decades, childhood cancer survivors had considerably higher odds of health-related unemployment at ages 30, 40 and 50 than population comparisons (OR_{age30}, 2.57; 95% CI, 2.35-2.81) and siblings (OR_{age30}, 2.50; 95% CI, 2.15-2.90). Health-related unemployment was particularly pronounced among survivors of central nervous system tumours and survivors diagnosed below 15 years of age. We observed no large differences in unemployment unrelated to health or in occupational position.
Conclusions: Although our study indicates that many survivors are employed and obtain highly skilled occupational positions to the same extent as the general population and their siblings, we revealed that some adult survivors of childhood cancer have a substantial burden of health-related unemployment. These survivors should be offered comprehensive survivorship care and interventions for obtaining and maintaining suitable employment.

EP730 / #1451

Topic: *AS05.s Survivorship*

PARENTHOOD IN MALE SURVIVORS OF CHILDHOOD CANCER IN DENMARK, FINLAND AND SWEDEN: A REGISTER-BASED COHORT STUDY FROM THE SALICCS RESEARCH PROGRAMME

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Background and Aims: A childhood cancer diagnosis, its treatment and possible late effects may impact whether survivors become parents later in life, but the literature on parenthood in male survivors is sparse. In this study, we compared the probability of parenthood and the number of children among male childhood cancer survivors with population comparisons and siblings, and we assessed the risks of congenital malformations in the offspring, as well as the risk of stillbirths.
Methods: In a large Nordic population- and register-based cohort study, we identified 9,488 male survivors of childhood cancer diagnosed before age 20 years in Denmark, Finland and Sweden since 1971. Survivors were compared with 45,253 randomly selected males from the general population, matched by year of birth and geographical region, and 6,541 male siblings of the survivors. Information on parenthood, congenital malformations, and stillbirths was obtained from the Medical Birth Registers for the period 1973-2017.
Results: By age 35 years, 41.4% (95% CI 40.1-42.8%) of childhood cancer survivors, 58.9% (95% CI 58.2-59.5%) of population comparisons and 60.5% (95% CI 58.9-62.1%) of siblings had become parents. Survivors of childhood cancer had a lower probability of becoming parents than population comparisons (HR 0.64, 95% CI 0.61-0.67) and siblings (HR 0.63, 95% CI 0.58-0.69) throughout the follow-up period. Moreover, our findings suggest that survivors have fewer children than population comparisons and siblings. Lastly, we observed no significant differences between childhood cancer survivors, population comparisons and siblings in the probability of fathering a child with a congenital malformation, and in the risk of stillbirths.
Conclusions: Our findings point towards lower probabilities of parenthood among survivors compared with the general population and their siblings. Reassuringly, we found no differences in the risk of congenital malformations in the offspring or risk of stillbirths.

EP731 / #1943

Topic: *AS05.s Survivorship*

A GOAL-DIRECTED INTERVENTION FOR ADOLESCENT CANCER SURVIVORS

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Background and Aims: Adolescence is a critical developmental period that involves negotiating greater independence and autonomy in social, physical, academic, and professional domains. Accordingly, a diagnosis of cancer in this formative period can disrupt achievement of developmental norms and this disruption can continue through survivorship into adulthood. A previously developed psychotherapeutic intervention that targets mechanisms underlying adjustment difficulties in young adult cancer survivors – Goal-focused Emotion-Regulation Therapy (GET) – is relevant to the adolescent cancer population. The purpose of the present study was to gather a rich description of cancer experiences with a particular focus on goal navigation, coping, and health-related quality of life with adolescent survivors in order to adapt GET.
Methods: A total of 15 adolescent survivors aged 15 – 19 years participated in individual interviews focused on the following domains: Unmet psychosocial needs after treatment, relevance of proposed intervention components, and utilization of the intervention (e.g., structure and format of the intervention). Interviews were audio recorded, transcribed, and coded for thematic content.
Results: The following four themes emerged across interviews: academic struggles, social functioning, mental health and emotional challenges, and goal navigation difficulties. All survivors noted disruption of academic achievement and challenges navigating academics post-treatment. Related to this struggle were social challenges where participants reported difficulty making and maintaining friendships, although most survivors noted their family relationships were stronger following their cancer experience. Many adolescents reported struggling with mental health issues, including depression and anxiety, and reported having limited emotion regulation strategies. Finally, many participants noted that the experience of cancer shifted focus to short-term, rather than long-term goal attainment and that ongoing effects of cancer treatment often meant having to reprioritize and shift goal navigation.
Conclusions: Cancer can disrupt the developmental trajectory for adolescent survivors and the adaptation of GET may be an effective means of ameliorating these disruptions.

EP732 / #669

Topic: *AS05.s Survivorship*

FACTORS RELATED TO GROWTH RETARDATION IN LONG-TERM HIGH-RISK NEUROBLASTOMA SURVIVORS TREATED WITH HIGH-DOSE CHEMOTHERAPY

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Background and Aims: High-risk neuroblastoma (HRNB) survivors treated with high-dose chemotherapy followed by autologous stem cell rescue (HDC-ASCR) experience multiple late effects, including endocrine disorders and gonadal endocrine dysfunction.
Methods: We evaluated growth profile after ASCR by using height-for-age (HFA) Z-scores, in a large cohort of 145 five-year disease-free survivors treated for HRNB with HDC-ASCR from 1980-2012 at Gustave Roussy. Association of clinical and therapeutic risk factors with growth curves were evaluated using linear mixed models for repeated measures data.
Results: Heights were available for 138/145 HRNB survivors. Sex-ratio M/F=1.12, median age at diagnosis=2.5y (range=0-13.3), median HFA Z-score at diagnosis=0.41 (-2.6-3.5). With a median follow-up of 14.1 years (range=3.3-27), HFA Z-score at last follow-up had decreased, with a median HFA Z-score of -0.92 (-3.6-2.2) at a median age of 18.1y (5.5-33.6). Growth curve analysis showed progressively decreasing of HFA after ASCR, with no recovery after 15y, resulting in a median HFA Z-score variation of -0.6 (-3.1-2.1) at 15y post-ASCR. Pre-existing small height and young age at HDC were important predicting factors for growth alteration (estimate=0.73 +/-standard-error=0.06, $p<0.0001$ and 0.12 +/-0.002, $p<0.0001$, respectively). Gonadal insufficiency had a negative impact (-0.27 +/-0.05, $p<0.0001$), whereas hormonal replacement therapy (HRT) was beneficial (0.14 +/-0.06, $p=0.02$). After adjustment for gonadal endocrine dysfunction, HDC regimen was not significantly associated with HFA Z-score, whereas negative effects were observed with doxorubicin (cumulative doses ≥250mg/m²) and cisplatin (≥400mg/m²), (-0.92 +/-0.18, $p<0.0001$ and -0.38 +/-0.14, $p=0.006$, respectively). Spinal radiotherapy doses were not associated with growth impairment ($p=0.46$).
Conclusions: In conclusion, we demonstrate for the first time in a large cohort of HRNB survivors a frequent growth alteration after HDC-ASCR, worsening over time, mainly related to gonadal dysfunction. HRT was beneficial, supporting adequate hormonal substitution. The effect of high cumulative doses of doxorubicin and cisplatin before HDC have to be explored.

EP733 / #1709

Topic: *AS05.s Survivorship*

FIVE-YEAR TRAJECTORIES OF SOCIAL AND SCHOOL COMPETENCE AMONG PEDIATRIC CANCER SURVIVORS

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Background and Aims: Pediatric cancer survivors may experience poor social and school competence, but limited work has examined patterns of competence over time or predictors of these trajectories. Thus, we examined trajectories of social and school competence across 5 years following diagnosis. Central-nervous system (CNS) directed treatment, diagnostic categories, age at diagnosis, and child sex were examined as predictors of group trajectories.
Methods: Data (N=326) were from a longitudinal study of children with cancer ($M_{AgeAtDiagnosis}$=10.41, SD=3.91; 47% Female). Mothers completed the Child Behavior Checklist near diagnosis (T1) and at one (T2), three (T3), and five (T4) years post-diagnosis. Children were grouped by whether they received CNS-directed treatment (n=173) within the first year (T2). Group-based trajectory modeling (Nagin, 2005) examined predictors of trajectory membership, separately for social and school competence.
Results: Final models identified two social competence trajectories: stable poorer competence (53.1%; 95% CI, 45%-61%) and delayed increases in competence (46.9%; 95% CI, 39%-55%). Age at diagnosis (X_1^2=14.31 [n=322]; p=0.0002; r^2=0.060) and CNS-directed treatment (X_1^2=5.81 [n=325]; p=0.02; r^2=0.024) individually predicted social competence trajectory membership, with younger age and receipt of CNS-directed treatment predicting greater likelihood of membership in the poorer competence group. When accounting for other predictors, only age at diagnosis predicted trajectory group status (p=.004). Group-based trajectory models also identified three school competence patterns: increasing competence (6.5%; 95% CI, 3.7%-11.1%), decreasing competence (21.4%; 95% CI, 15.7%-28.4%), and stable higher competence (72.2%; 95% CI, 64.9%-78.0%). Variables of interest did not predict trajectory membership.
Conclusions: Children who receive CNS-directed treatment or are younger at diagnosis may experience consistently poorer social competence over the first 5 years after diagnosis. Interventions should target younger children receiving CNS-directed treatment near diagnosis to minimize social difficulties over time. Future research including child and father perspectives should examine other predictors of social and school competence trajectories.

EP734 / #1833

Topic: *AS05.s Survivorship*

OUTCOMES IN PATIENTS WITH SOLID TUMORS WITH STANDAR CHEMOTHERAPY TREATMENT IN A DECENTRALIZED REGION OF SOUTHERN PERU

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Background and Aims: OUTCOMES IN PATIENTS WITH SOLID TUMORS WITH STANDAR CHEMOTHERAPY TREATMENT IN A DECENTRALIZED REGION OF SOUTHERN PERU HENRY GARCIA P.1 1. Assistant Physician of the Pediatric Oncology Service of IREN SUR, Arequipa- Peru BACKGROUND AND OBJECTIVES. cancer in children of Latin America is a public health problem, due to many factors: late diagnosis in advanced stages, cultural socioeconomic difficulties to access oncological services, poor adherence to treatment, access to drugs that complement standard treatment-initiation chemotherapy and second-line options to provide greater benefit. Lack of availability of modern radiotherapy equipment, etc. The aim of the present study was to evaluate the results of standard chemotherapy treatment in patients treated in a region of southern Peru.
Methods: METHODS. A total of 189 children and adolescents from 1 to 18 years old with a diagnosis of solid tumors were evaluated from November 2009 to December 2021. Treated with standard chemotherapy only. Data were extracted from clinical records and grouped among the main and most frequent cancer diagnoses.
Results: RESULTS. 171/189 (90.5%) of the patients were diagnosed in advanced stages III/IV. Being the 66,6% (126/189) most frequent neoplasms: Osteosarcoma, Wilms tumor, Rhabdomyosarcomas, Lymphomas and Hepatoblastoma. Rare neoplasms were not taken into account. Cases that were treated completely in another hospital and came only for control were discarded. It is found that they remain without evidence of the disease (PSEE) in Osteosarcoma 13/35 (37.1%), Wilms tumor (TW) 13/26 (50%), Hepatoblastoma 10/17 (58.82%), Non-Hodgkin lymphoma 11/26 (42.3%), Rhabdomyosarcoma 5/11 (45.45%) and Hodgkin lymphoma 3/11 (27.27%). The patients who died and lost sight were 114/189 (60.31%) y the survivors 63/189 (30.33%)
Conclusions: CONCLUSIONS. The outcomes still remain unsatisfactory with high mortality, It is necessary have public health strategies to make diagnoses in early stages, have drug options to intensify chemotherapy treatments and teach to parents to complete treatments and better results.

EP735 / #528

Topic: *AS05.s Survivorship*

CLINICIAN PERCEPTIONS OF PASSPORT FOR CARE FOR SURVIVORSHIP CARE PLAN DELIVERY TO SURVIVORS OF CHILDHOOD CANCER

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Background and Aims: The Children's Oncology Group evidence-based guidelines provide exposure-based risks and recommendations for late effects screening of survivors of childhood cancer. The Passport for Care (PFC) was developed as a web-based clinical decision support tool to generate a personalized survivorship care plan (SCP), derived from guidelines and user-entered exposures. Over 150 Long-Term Survivor clinics utilize PFC, generating over 47,000 SCPs. Our objective was to assess PFC user practices and perceptions of impact on clinic workflow, guideline application, and survivor shared decision-making.
Methods: In June 2021, a 35-item REDCap™ survey was emailed to 935 PFC users in 145 clinics: 107 active PFC clinics and 38 inactive. Survey results were summarized and compared with prior 2012 survey data using a Chi square test, when applicable.
Results: Valid data were available from 142 respondents, representing 64 clinics and comprising mostly physicians, advanced practice providers (APPs), and nurses. Seventy-one respondents (50%) used PFC to generate an SCP at entry to LTS, and 54 (38%) used PFC at every visit. Data entry was completed by nurses (n=89, 63%), APPs (n=63, 44%), physicians (n=37, 26%), and data managers (n=13, 9%). Sixty-seven respondents (48%) felt data entry was a modest or significant barrier to PFC application; however, the majority were satisfied with PFC (87%): 72% of respondents felt PFC had a high impact on their ability to accurately apply the guidelines, compared with 41% in 2012 ($p<0.001$), and 70% felt PFC had a high impact on fostering conversations with survivors about risk for late effects and screening, compared with 44% from 2012 ($p<0.001$).
Conclusions: PFC facilitates guidelines dissemination and uptake, and supports accurate application of guidelines as well as fostering of conversations regarding survivorship care. The burden of data entry is a limitation, further corroborated by user prioritization of 'exposure data pre-population by treatment protocol' for future PFC modifications.

EP736 / #617

Topic: *AS05.s Survivorship*

DISTRIBUTION AND FREQUENCY OF TYROSINE-KINASE INHIBITOR-ASSOCIATED COMPLICATIONS IN SURVIVORS OF PEDIATRIC LEUKEMIAS

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Background and Aims: Tyrosine kinase inhibitors (TKIs) improve outcomes for Philadelphia chromosome (Ph)-positive chronic myelogenous leukemia (CML), Ph+ acute lymphoblastic leukemia (ALL), and Ph-like ALL. However, little is known about the impact of long-term TKI exposure in pediatric patients. Our objective was to assess the incidence and type of late-onset TKI-related toxicities in children with Ph+/Ph-like ALL or CML.
Methods: We performed a retrospective chart review of patients under 21 years old diagnosed with CML or Ph+/Ph-like ALL at Texas Children's Cancer Center from 2006-2019 and prescribed a TKI. Patients were excluded who received stem cell transplant (SCT) and who never achieved a durable remission. Data capture began on the last day of combination chemotherapy for ALL and one year after diagnosis for CML. Events related to TKI exposure were manually abstracted from the electronic medical record. Descriptive statistics were used to stratify outcomes by diagnosis, exposure to specific TKIs, and TKI use during data capture.
Results: Of the 30 eligible patients, 22 had CML, 7 had Ph+ ALL, and 1 had Ph-like ALL. The median follow-up was 6.3 years (range 2.2-14.3). All pericardial (n=3) or pleural (n=3) effusions occurred in patients that continued on a TKI during data capture. Other observed outcomes included hypertension (n=3), ectopy on electrocardiogram (ECG) (n=3), gastrointestinal bleed (n=2), and growth hormone deficiency (n=1). No differences were noted in outcome incidence by diagnosis or TKI exposure type.
Conclusions: Long-term complications of TKIs are well-characterized in adults, but little is known regarding the long-term impact of these agents in survivors of childhood leukemia. Our results support assessment of pulmonary, cardiac, and endocrine outcomes in larger childhood cancer survivor cohorts that continue on TKIs long-term. This study adds to the growing evidence of long-term TKI-associated toxicities and supports ongoing efforts to evaluate the feasibility of TKI discontinuation in children with CML (NCT03817398).

EP737 / #1800

Topic: *AS05.s Survivorship*

STRUCTURAL BARRIERS TO SURVIVORSHIP CARE IN SURVIVORS OF CHILDHOOD CANCER

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Background and Aims: Consistent long-term follow-up care is important for surveillance and timely treatment of childhood cancer therapy late effects; however, structural barriers may disproportionately affect at-risk populations. Our objective was to evaluate factors associated with loss to follow-up after childhood cancer treatment.
Methods: We electronically extracted and manually curated electronic health records to identify childhood cancer cases diagnosed 2011-2014. Individuals without a cancer diagnosis, treated with surgery or observation alone, treated with allogeneic stem cell transplant, or those that transferred to an outside hospital, relapsed, or died <2 years from end of treatment (EOT) were excluded. Attendance of at least one Long-Term Survivor (LTS) Clinic visit was the primary outcome. Multivariable logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI) for the association between clinical factors and LTS Clinic attendance.
Results: We identified 573 survivors that completed treatment and were eligible for LTS care. Most were male (57.5%) and/or Latino (52.0%). The median age at diagnosis was 6.7 years (range: 0-20). Overall, 178 (31.1%) were never seen in LTS clinic. Compared with leukemia survivors, lymphoma (OR=2.37, CI: 1.23-4.57), central nervous system tumor (OR=7.55, CI: 2.43-23.44), and solid tumor (OR=10.23, CI: 4.26-24.57) survivors were more likely to never attend LTS clinic. Black race and/or older age at EOT were predictive of lower likelihood of an LTS visit ($p<0.001$). Of those never seen in LTS clinic, 48% had no contact with the hospital system 2-5 years after EOT, suggesting loss to follow-up. Seven percent had ongoing non-oncology contact and 45% had ongoing oncology contact, suggesting deficiencies in the LTS referral process.
Conclusions: We identified two barriers to LTS care: unexplained loss to follow-up and issues with LTS referral. Ongoing efforts include establishing practice standards for LTS referrals and investigation of the impacts of payer status and social determinants on LTS attendance.

EP738 / #563

Topic: *AS05.s Survivorship*

A RETROSPECTIVE REVIEW OF FERTILITY PRESERVATION SERVICES IN A LARGE TEENAGE AND YOUNG ADULT CANCER AND BONE MARROW TRANSPLANT CENTRE

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Background and Aims: Infertility, a distressing late effect of childhood cancer, impairs quality of life and contributes to mental health problems. We reviewed our fertility preservation service in a large teenage and young adult (TYA) centre.
Methods: Patients treated by our Haematology, Oncology and Bone Marrow Transplant (BMT) service from 01.01.2020-30.06.2021 were included. Data was collected from electronic patient records (EPR). Patients were categorised into risk-groups using the “Children’s Cancer and Leukaemia Group” (CCLG) Consensus Statement on Oncofertility.
Results: Haematology/Oncology (148) and BMT patients (44) were analysed separately. Median age of the haematology/oncology cohort was 16 years. Male:female ratio was 1:1.14. Diagnoses included sarcoma (34%), lymphoma (26%), leukaemia (18%), head and neck cancers (9%), brain tumours (6%) and others (7%). Fertility risk was classified as low-risk (16.2%), medium-risk (30.0%), medium-high (3%), high-risk (10.1%), very high-risk (33.1%), no-risk (6.76%), unknown (8.11%) and “undocumented” (0.68%). EPR were examined for documentation of discussions at diagnosis occurring in 116/148 (78.4%) cases. Fertility preservation referral was offered to 64/148 patients. Males were offered sperm cryopreservation (39), and testicular tissue cryopreservation (1). Females were offered laparoscopic ovarian transposition (1) and ovarian cryopreservation (2). Thirty percent of males (16/56) declined referral. Reasons for non-referral were not documented (40/56). In the BMT cohort median age was 17 years. Male:female ratio was 1:0.76. Indications for BMT included malignant haematology (64%), non-malignant haematology (30%) and oncology (7%). Patients were classified as low-risk (2.27%), medium-risk (4.55%), medium high-risk (6.82%), high-risk (45.5%) and very high-risk (38.6%). Thirty-four patients were offered fertility preservation and 24 accepted. Sperm cryopreservation (58.3%), testicular tissue cryopreservation (4.2%) and oocyte cryopreservation (37.5%) were offered.
Conclusions: All patients warrant an informed discussion at diagnosis about risk of infertility based on their proposed treatment regimen. This should be clearly documented in the EPR and their consent. Fertility preservation should be offered to all patients where appropriate.

EP739 / #1977

Topic: *AS05.s Survivorship*

AN ASSESSMENT OF YOUNG PEOPLE LIVING BEYOND CANCER AND FACTORS THAT IMPACT THEIR ATTENDANCE OF THEIR AFTERCARE

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Background and Aims: Young people impacted by childhood cancer are at risk for medical, psychological, and social late effects. To screen for their risks, receipt of consistent, cancer-specific aftercare is crucial. Yet, less than 50% of those that live beyond their cancer attend their aftercare and only 35% recognize that they could have a serious health problem. Aftercare knowledge, core health beliefs, and the sociocultural context of young people living beyond their cancer are critical aspects of their outcomes and optimal care. This study 1) examined the effect of aftercare knowledge and core health beliefs on adherence to aftercare and 2) described the sociocultural context in which these young people engage in their aftercare.
Methods: Participants completed a cross-sectional online survey assessing their cancer history, aftercare attendance and knowledge, core health beliefs (perceived susceptibility and seriousness to their late effects), and sociocultural context (defined as cultural background, modified from the Cultural Formulation Interview). Inclusion criteria included those who are currently 18 – 35 years and > 5 years from childhood cancer diagnosis.
Results: Forty-four participants (30 females, 13 males, 1 non-binary) with a mean age of 27.3 years (SD = 4.96) completed the study. Thirty-two participants (73%) reported engaging in their aftercare and indicated a significantly greater perceived susceptibility and seriousness to their late effects, compared than those that did not engage in their aftercare, $t(32) = -2.38$, $p < .05$, $d = .81$. Thirteen participants (29%) reported that their social/cultural background made a difference to understanding their aftercare, including their ethnicity, cultural values, and family.
Conclusions: Core health beliefs of young people living beyond childhood cancer play an important role in their engagement in their care. Consideration of the sociocultural context of these young people may be important to improving their aftercare experience. These findings clarify possible avenues for clinical intervention to improve their adherence to aftercare.

EP740 / #256

Topic: *AS05.s Survivorship*

ANALYSIS OF CHILDHOOD CANCER SURVIVORS RECEIVING HOSPITALIZATION BENEFITS UNDER THE HEART-LINK MUTUAL INSURANCE

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Background and Aims: Heart-link Mutual Insurance was established in June 2005. Since its establishment, it has been providing life insurance coverage for children with cancer. We analyzed data from mutual aid insurance subscribers who received hospitalization benefits.
Methods: Study subjects were 86 who received hospitalization benefits among total of 465 enrolled in the Heart-Link Mutual Aid Plan from 2005 to 2020. We extracted a list of people who received hospitalization benefits, and collected information after acquiring the IRB permission. The extracted data were analyzed statistically using SPSS Ver 26.
Results: The primary diseases were hematologic tumors (n=56), brain tumors (n=5), abdominal tumors (n=8), sarcomas (n=11), and others (n=6). Age at onset of primary disease ranged from 0 to 20 years (median 6.5 years). The number of hospitalizations ranged from 1 to 10 (median 1 year), age at first admission ranged from 12 to 46 years (median 28 years), and the interval between the completion of treatment and the first admission ranged from 3 to 35 years (median 16 years). The accumulated total number of hospitalizations in 86 patients was 178. Reasons for hospitalization were secondary tumors in 47 times (26%), infectious in 26 times (15%), surgical conditions in 25 times (14%), sequelae-related conditions in 20 times (11%), etc. Surgeries were performed in 95 times. A median age at first admission was 21 years in bone-joint related disease; it was 22 years in surgical condition and mental illness; it was 32 years in secondary cancer; and it was 34 years in pregnancy/childbirth, and digestive/liver disease.
Conclusions: The responsible disease conditions varied widely and the age at admission ranged from as young as 12 to as old as 46 years in this study. Relationship between primary diseases and a long-term sequelae should be elucidated in order to provide better benefits for all childhood cancer survivors.

EP741 / #310

Topic: *AS05.s Survivorship*

THE ASSOCIATION OF ENVIRONMENTAL FACTORS WITH NEUROCOGNITIVE OUTCOMES IN SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

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Background and Aims: Survivors of childhood ALL are at risk for treatment-related neurocognitive deficits. The role of environmental factors, including intervention to promote early development and socioeconomic status (SES), is not well understood.
Methods: Participants were 236 children treated on the St. Jude Total Therapy Study 16 who completed neurocognitive assessments at the end of therapy. Neurocognitive outcomes included IQ, attention, processing speed, executive function, memory, fine motor speed, and academics, and caregiver ratings of attention, executive function, and adaptive skills. Participation in rehabilitation services during therapy (yes, no) and patient insurance status (private, public; proxy for SES), were abstracted from the medical record. Results are age-standardized Z-scores (normative mean=0, SD=1).
Results: Nearly half (n=110, 46.4%) of patients received rehabilitation services during therapy. Groups with and without rehabilitation did not differ based on patient sex (47.3% female, p=.399), treatment arm (45.5% low risk, p=.929), insurance type (47.7% private, p=.117), or mean age at diagnosis (7.7 vs. 6.8 years, p=.143). Compared to those without rehabilitation, the rehabilitation group had more difficulties with attention (Z=-0.28 vs. 0.43, p=.022), executive function (Z=-0.50 vs. -0.08, p=.003), and adaptive skills (Z=-0.41 vs. -0.13, p=.031). Among the rehabilitation group, there was no difference in neurocognitive outcomes by insurance. Among those without rehabilitation, patients with public insurance had worse outcomes than those with private insurance in IQ (Z=-0.04 vs. -0.49, p=.012), processing speed (Z=-0.09 vs. -0.64, p=.003), reading (Z=0.20 vs. -0.62, p<.0001), and math (Z=-0.06 vs. -0.61, p=.035).
Conclusions: Developmental intervention during treatment for ALL and SES are associated with end of therapy neurocognitive outcomes. Compared to those without rehabilitation, children who required rehabilitation had worse neurocognitive outcomes at the end of therapy. Participation in rehabilitation may have mitigated the impact of lower SES, as differences by SES were only observed in the group without rehabilitation.

EP742 / #698

Topic: *AS05.s Survivorship*

FEMALE YOUNG ADULT SURVIVORS OF PEDIATRIC CANCER EXPERIENCES OF MENTAL WELL-BEING, SELF-IMAGE, AND FERTILITY: A QUALITATIVE STUDY.

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Background and Aims: Young adult cancer survivors that have gone through childhood cancer treatment often think about their experiences and express concern about the future. They also report need for psychological support and described feeling physically, socially, and mentally marked by their cancer experience. The aim of the present study was to gain in-depth knowledge about how women in their twenties with previous childhood cancer treatment experience their fertility today and the disease's effect on their self-image and mental health.
Methods: A qualitive study with semi-structured interview was carried out during 2016-18. The study was approved by the regional ethics board, University of Gothenburg, Sweden. Fourteen female survivors of pediatric cancer, treated with chemotherapy and/or radiotherapy, were part of the present study. Median age was 27 years (range 25–31) and median age at cancer diagnosis was 7.5 years (range 2–13). The interviews were recorded and analyzed by a thematic approach. The software program ATLAS.ti 8 was used to facilitate the qualitative data analysis.
Results: The analysis resulted in three main themes labeled, An experience for better and worse, An everyday life similar and different from peers and An uncertain fertility. These three main themes contained a total of 11 sub-themes. The women expressed that their experiences of childhood cancer have both strengthened and impaired their everyday life. Result showed that insufficient information about the effects on fertility was given by healthcare staff during the treatment period, and this had led to unnecessary suffering in both practical and psychological aspects.
Conclusions: Although it was over 10 years since cancer diagnosis for all participants it was still present for better and worse. Healthcare workers need to keep this complexity in mind when facing the "cured" young patient. Addressing questions and giving support regarding fertility and mental health are wanted.

EP743 / #950

Topic: *AS05.s Survivorship*

HEALTHCARE UTILIZATION AND FREQUENCY OF PHYSICIAN VISITS AMONG SURVIVORS OF CHILDHOOD AND ADOLESCENT CANCER AND POPULATION COMPARATORS IN BRITISH COLUMBIA (BC), CANADA

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Background and Aims: Healthcare utilization and frequency of physician visits of survivors of childhood and adolescent cancer have not been studied very widely. Many of the existing studies are out of date, often rely on case ascertainment pooled from different institutions or assessment via self-report. The objective of this work is to assess frequency of physician visits and the impact of health status on visit rates among survivors of childhood and adolescent cancer and matched general population comparators.
Methods: The study group consisted of 1,960 survivors diagnosed between 0-19 years from 1970 to 2003, surviving five or more years, alive and resident in BC during the follow-up period (2008-2010) and an age and sex frequency-matched population sample of 7,840. Patient records were linked to provincial physician claims data. Counts of visits to general/family and specialty practitioners were generated. Negative binomial regression with and without adjusting for comorbidity (i.e., the number of unique major aggregated diagnoses groups during the three years of follow-up) was used.
Results: Survivor status itself was associated with higher visit rates to primary (RR=1.22, 95% CI 1.16 1.26) and specialty care (RR=1.60, 95% 1.51 1.70). The number of major aggregated diagnosis groups was a significant independent predictor of visit frequency with a stepwise increase in visit rates with each increase in number of major ADGs. Survivors' health status accounted for a 40% difference in the rate of specialist visits (RR=1.19, 95% CI 1.12-1.26).
Conclusions: Survivors' health status accounted for a sizable portion of estimates, highlighting the importance of taking comorbidity into account to accurately estimate utilization and avoid overestimation. It also highlights increased demand/need for healthcare services among survivors, who after taking comorbidity into account still had higher visit rates than population comparators. Healthcare practitioners and policy makers need to be aware of the increased demand and needs of this population.

EP744 / #1310

Topic: *AS05.s Survivorship*

PREMATURE OVARIAN FAILURE IN CHILDHOOD CANCER SURVIVORS IN GREECE

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Background and Aims: Female childhood cancer survivors (CCS) have increased risk of ovarian dysfunction. Our aim is to assess the incidence of premature ovarian failure (POF) in female CCS and evaluate the AMH in relation to FSH and known single nucleotide polymorphisms (SNPs) related to premature menopause.
Methods: POF was considered if FSH>20. AMH (ng/ml) was estimated into (a) very low: <0.5, (b) low: 0.5–1.0, (c) low normal: 1.0–1.5 and (d) normal: >1.5. The cumulative dose of alkylating agents was calculated using the validated cyclophosphamide equivalent dose (CED) score. All survivors were genotyped for SNPs rs1172822 and rs11668344 in BRSK1 and rs1054875 in FANCI through direct sequencing. Chi-square or Fisher's exact test were applied to test the relationship between clinical and genetic categorical variables with POF. Mann Whitney U test was used to compare the age of cancer diagnosis and POF. All analyses were performed using «STATA» software (Stata Corporation, USA).
Results: 95 female CCS, median age (IQR) at the end of the study 13.2 (10.3-17.6) years, median age at diagnosis 5.3 (2.6-11.8) years were included. Survivors were followed for median 5.4 (2.6-11.8) years. 76.3% received chemotherapy; median CED 2400 (1900–3800) mg/m^2. POF had 9.5% (9/95) CCS. High FSH had 6.3% (6/95) CCS and intermediate 2.1% (2/95). Very low AMH was recorded in 6.3% (6/95) CCS, low in 4.2% (4/95) and low normal in 2.1% (2/9). High FSH was strongly associated with low AMH ($p<0.001$). POF was significantly associated with hematopoietic stem cell transplantation (HSCT) ($p=0.02$) and radiotherapy ($p<0.01$) but not with chemotherapy ($p=0.4$). The allele frequencies of the three SNPs were equivalent to the Gnomad European populations, but none of them did associate with POF ($p>0.5$).
Conclusions: The evaluation of AMH had added value in the screening for ovarian reserve. More data are needed to evaluate the relationship between SNPs and POF development in CCSs.

EP745 / #702

Topic: *AS05.s Survivorship*

IDENTIFYING CHILDHOOD CANCER PATIENTS IN NEED FOR SUPPORT - PSYCHOSOCIAL RISK PREDICTION FROM ELECTRONIC HEALTH RECORDS WITH MACHINE LEARNING

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Background and Aims: Background and aims Childhood cancer survivors require more health monitoring than the average population and they have a higher risk for mental health disorders compared to their siblings. Assessing the need for psychosocial support is essential for prevention. This project aimed to automate the process of identifying childhood cancer patients in need for psychosocial support from electronic health records (EHRs) with supervised machine learning (ML) in the form of text classification models.
Methods: We tested three well-known ML-based models to recognize patients who have received mental health-related care or consultation from EHRs of 2083 patients. EHRs written in mental health-related units were excluded from the data to see if the models can capture hidden signals of psychosocial challenges. We used stratified five-fold nested cross-validation to evaluate the performance of the models in a binary classification task: no need for support or psychosocial support needed. Patients belonging to the latter had received psychiatric-level mental health support or consultation.
Results: The Random Forest classification model performed best in nested-cross validation with 0.79 mean area under the receiver operating characteristics curve. Performance increases when more EHRs are available. Our findings also indicate that nurses with psychosocial support training, who retrospectively read the patient notes, agreed more with the model's predictions than the original recommendations given in psychiatric consultations of the patients.
Conclusions: Automated evaluation of psychosocial conditions may help in the identification of childhood cancer patients who are likely to need mental health-related support later in life.

EP746 / #779

Topic: *AS05.s Survivorship*

LONG-TERM FOLLOW-UP OF CHILDHOOD CANCER SURVIVORS IN AFRICA: A SCOPING REVIEW

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Background and Aims: Introduction: The number of children surviving cancer in Africa is increasing. However, comprehensive knowledge about the physical and psychosocial late effects of survivors is lacking, while this becomes increasingly relevant. Our study maps existing literature regarding the long-term follow-up of childhood cancer survivors in Africa.
Methods: This scoping review follows JBI-guidelines for data extraction, charting and analysis. Databases searched were: OVID Medline, Embase, African Index Medicus (AIM), Web of Science, Elsevier/Scopus, and Psycinfo. All peer-reviewed literature published in English or French between 1978 and 2021 was considered. Screening of titles and abstracts was conducted by two independent reviewers, with a third available in case of doubt, followed by full-text screening involving two reviewers.
Results: In total, 82 studies were included for content analysis. Studies originated from 9 (17%) of 54 African countries: Egypt (n=45), South-Africa (n=11), Tunisia (n=7), Morocco (n=6), Nigeria (n=5), Uganda (n=3), Cameroon (n=2), Malawi (n=2), Kenya (n=1). Studies addressed following diagnoses: lymphoma (n=15), leukemia (n=13), retinoblastoma (n=7), nasopharyngeal carcinoma (n=6), germ-cell tumor (n=6), brain tumor (n=5), sarcoma (n=4), nephroblastoma (n=3), ovary tumor (n=1), mixed diagnoses (n=22). Only 20 studies (24%) concerned survivors with ≥5 years follow-up. Sixty-three studies described physical late effects, which were classified in 16 categories: cardiology, secondary malignancy, infertility, neurological, hormonal, gastroenterology, nutrition, pulmonary, cutaneous, renal, hematological, bone density, otology, oral-dental, ocular, and cosmetic toxicity. Twenty-one studies described psychosocial late effects, which were classified in 5 categories: intelligence, psychological, social reintegration, follow-up adherence, and quality-of-life malfunctions.
Conclusions: Conclusion: Childhood cancer survivors are emerging in Africa. This study reveals that literature concerning knowledge and infrastructure on long-term follow-up of survivors is available from a limited number of African countries. More countries should focus and report on this topic to assist international workgroups with developing adapted follow-up guidelines to prevent, identify and monitor late effects in survivors.

EP747 / #774

Topic: *AS05.s Survivorship*

RESULTS OF THE EARLY NEURO-REHABILITATION IN PATIENTS WITH BRAIN TUMORS.

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Background and Aims: Cognitive functioning requires a constant interaction between different brain areas. This connectivity can be altered by the different co-adjuvant treatments and by the tumor location itself. Due to these aspects, as well as the high vulnerability of a developing brain, an adequate neuropsychological rehabilitation plan is necessary at the sub-acute stage, with the aim of achieving greater functional plasticity.
Methods: Two groups of patients were compared in this study. One group consisted of 26 patients who completed an eight-month neuropsychological rehabilitation program. The other group, a control group, was made up of 23 patients with the same oncological characteristics, but who did not receive this rehabilitation program. For this analysis, the Mann-Whitney test was used. At the same time, from the group of patients who underwent rehabilitation treatment, two subgroups were created and compared: patients who had undergone an early rehabilitation, <1 year post-treatment (n=20, 76.9%) versus patients who underwent a late rehabilitation, >1 year post treatment (n= 6, 23.1%). In this comparison, given the small sample, descriptive measurements, the medians of the different neuropsychological variables for each group, were calculated in order to compare said groups.
Results: After the intervention, a clear improvement in the executive and attentional functioning is reflected. This correlates with a greater functionality and autonomy of the child in their daily life, in comparison to the group that did not perform a cognitive rehabilitation. When we compare the moment of rehabilitation (early versus late), a similar profile is shown in the cognitive variables of both times, but a greater functionality and autonomy in school and family day-to-day life is evidenced when rehabilitation is early.
Conclusions: The improvement in cognitive processing, shows us the validity of these rehabilitation programs in the sub-acute phase, ecological and multidisciplinary program.

EP748 / #537

Topic: *AS05.s Survivorship*

A10! TRANSITION PROGRAM - ROAD TO ADULT CARE FOR CANCER SURVIVORS

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Background and Aims: Background: At Sant Joan de Déu Children´s Hospital Barcelona, more than 300 children and adolescents with newly diagnosed cancer are treated every year. In excess of eighty percent will survive and 30% with serious late effects. The increasing survival rate highlights the importance of transitioning for continued care. A10! is a structured transition-transfer program designed with the participation of patients, families, and professionals to guarantee the continuity of care within the adult healthcare system. Aims: to evaluate the transition process and the satisfaction with the A10! Program.
Methods: We performed a structured interview by phone to 48 patients and/or their families who had finished the transition-transfer A10! Program from June 2020 to February 2022. Additionally, we evaluated the quality of the process through a pre-designed checklist.
Results: Forty-eight patients were transferred during the study period, nine to primary care and 39 to adult hospitals. Forty-four (92%) patients received self-care training and were transferred when they felt ready. Five (10%) patients required an extra year of training. Forty-eight patients had an individualized summary of treatment and plan of care. Inconsistencies with old records doubled the expected time to produce reports. Adult hospitals' network received a digitalized report per patient. Special difficulties were encountered to complete a full summary when more than 4 disciplines were involved. Eight percent of patients did not receive the summary. Periodic clinical sessions with adult physician are performed to improve coordination of patients referred to adult hospitals. Eighty-seven percent of patients and/or families and 98% of adult hospital professionals express satisfaction with the program.
Conclusions: The implementation of the structured transition-transfer A10! Program for children and adolescent cancer survivors to the adult healthcare network provided a high satisfaction level among families, patients, and professionals. Program improvements through continued quality control checks is ongoing.

EP749 / #733

Topic: *AS05.s Survivorship*

SYSTOLIC DYSFUNCTION IN CHILDHOOD CANCER SURVIVORS ON ECHOCARDIOGRAPHY: SEX-SPECIFIC EFFECTS AND RISK BEYOND CARDIOTOXIC EXPOSURES. RESULTS FROM THE DCCSS LATER 2 CARD STUDY.

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Background and Aims: Childhood cancer survivors (CCS) are at risk of cardiotoxicity. Global longitudinal strain (GLS) on echocardiography may improve our understanding of risk factors for cardiac dysfunction.
Methods: In this cross-sectional Dutch Childhood Cancer Survivor Study, we included 1,397 ≥5-year CCS treated with anthracyclines, mitoxantrone, radiotherapy to the heart region (RT^{heart}), vincristine, cyclophosphamide or ifosfamide, and 277 sibling controls. We compared prevalence of sex-specific abnormal ejection fraction (LVEF; men <52%, women <54%) and age-/sex-specific abnormal GLS. In multivariable logistic regression, we assessed demographic, cardiotoxic and traditional cardiovascular risk factors among CCS, and their residual risk for cardiac dysfunction compared to siblings.
Results: CCS were median 27 [range: 14-55] years after diagnosis, 49% were women and 77% received anthracyclines (median dose 180 mg/m^2) while 30% received RT^{heart} (median prescribed dose 12Gy). Among CCS, 24% had an abnormal LVEF versus 5% of siblings (p<0.001). Abnormal GLS occurred in 30% and 11% (p<0.001), respectively. Among CCS with normal LVEF, 20% had abnormal GLS.
Risk factors for abnormal LVEF were female sex (OR 1.5; 95%CI 1.1-2.1), younger age at cancer diagnosis (OR 0.95/year increase; 95%CI 0.91-0.98), anthracycline dose (nonlinear OR), unconventional RT^{heart} fractionation (OR 2.2; 95%CI 1.3-3.9) and, only in women, RT^{heart} dose (p interaction 0.007). Abnormal GLS was associated with female sex (OR 1.8; 95%CI 1.3-2.4), RT^{heart} dose (OR 1.4/10Gy; 95%CI 1.2-1.6), unconventional fractionation (OR 2.7; 95%CI 1.5-4.9), diastolic blood pressure (nonlinear OR) and, only in women, with anthracycline dose (p interaction 0.019).
Independently of these established risk factors, CCS had a residual risk of both abnormal LVEF (OR 2.9; 95%CI 1.4-6.6) and abnormal GLS (OR 2.1; 95%CI 1.2-3.7) compared to siblings.
Conclusions: Using sex-specific thresholds, female CCS have more cardiac dysfunction than male CCS,

with female-sex dependent contributions of cardiotoxic doses. CCS have residual, unexplained risk of cardiac dysfunction compared to their siblings.

EP750 / #606

Topic: *AS05.s Survivorship*

ENDOCRINE SEQUELAE IN FEMALE CHILDHOOD CANCER SURVIVORS AT FOLLOW-UP CLINIC AT A WOMEN'S AND CHILDREN'S HOSPITAL IN URUGUAY

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Background and Aims: Background and aims: There are scarce reports of long-term follow-up (LTFU) and endocrinological impact in female pediatric cancer survivors in Latin America. We report the experience at a referral center for women's and children's health in Uruguay aiming to describe the prevalence of endocrine disorders.
Methods: A dedicated LTFU clinic for women's health was set up including a pediatric oncologist, endocrinologist, psychologist, social worker and gynecologist. We included all female patients who visited the LTFU clinic from 01/2004 to 2011 and thereafter resumed from 2018 to 2020 due to staff availability, who were under 40 years old, with cancer diagnosis before 18 years of age and disease-free for at least 5 years.
Results: We included 216 patients. Mean age at cancer diagnosis was 7.5 ± 0.3 years. Diagnosis included acute leukemias and lymphomas 55.6%; non CNS solid tumors 36.6%; and CNS tumors 8.7%. Almost all patients (94.4%) were treated with chemotherapy, while 43.1% received surgery, 36.6% radiotherapy and 8.8% hematopoietic stem cell transplantation (HSCT). In most cases there had been combinations of treatments. At the last visit, 43.1% of these patients had at least one endocrine dysfunction. Mean time from end of treatment to detection of endocrine disorders was 4.6 ± 0.6 years. Endocrine disorders included: metabolic (24.7%), thyrotropic (17.7%), gonadotropic (15.4%), somatotropic (10.8%),bone (10%) and corticotropic (0.9%). The most common disorders were obesity (13.9%), hypothyroidism (13.4%) and ovarian failure (11.1%), and the main risk factors for endocrine disorders were radiotherapy (P = 0.007, OR = 1.442, 95% CI1.015 – 3.789) and HSCT (P = 0.017, OR = 1.295, 95% CI1.023–2.2115).
Conclusions: Conclusions: There was a high prevalence of endocrine late effects in our population, especially in those receiving radiotherapy and HSCT. A dedicated multidisciplinary team was feasible but there were challenges in sustainability.

EP751 / #155

Topic: *AS05.s Survivorship*

A CROSS-SECTIONAL STUDY ON THE LATE EFFECT OF TREATMENT IN INDONESIA'S CHILDHOOD CANCER SURVIVORS

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Background and Aims: The number of childhood cancer survivors increases every year. Cancer or its various treatments cause late effects that may appear in the future, which also increase the risks of morbidity and mortality. Currently, no research on late effects in childhood cancer survivors has been done in Indonesia. This study aims to determine late effects in childhood cancer survivors.
Methods: The study was conducted as a cross-sectional study. The subjects were childhood cancer survivors who had remission for a minimum of 6 months when the patients were asked to join the research in Cipto Mangunkusumo Hospital.
Results: A total of 107 subjects aged 6 years to 33 years participated in this study. The duration of remission was from 6 months to 366 months. Based on the medical history, we included acute lymphoblastic leukemia (56.0%), acute myeloblastic leukemia (4,6%), non-Hodgkin's lymphoma (8.4%), Hodgkin's lymphoma (2.8%), germ cell tumors (4,7%), retinoblastoma (5,7%), and other tumors (16.8%). Late puberty was found in 24.6% of subjects. Short stature was found in 37.1% of subjects. Obesity, dyslipidemia, and diabetes mellitus were found in 30.0% of subjects, 45.1% of subjects, and 0.15% of subjects respectively. Decreased bone mineral density was found in 34.9% of subjects. The incidence of vitamin D deficiency was 69.8%. Neurocognitive impairment was found in 22.9% of subjects. Peripheral neuropathy was found in 36.4% of subjects. Cardiotoxicity occurred in 5.3% of subjects.
Conclusions: The late effect of treatment in childhood cancer survivors is prevalent. Long-term monitoring using a risk assessment system based on tumor type and treatment history should be carried out to detect late effects in survivors. It is necessary to conduct a cohort study on pediatric cancer patients from the initiation of the treatment to improve the pediatric cancer survivors' quality of life.

EP752 / #1509

Topic: *AS05.s Survivorship*

REMOTE ASSSESSMENT OF PHYSICAL FUNCTION IN ADULT SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE ST. JUDE LIFETIME COHORT (SJLIFE)

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Background and Aims: Childhood cancer survivors have higher rates of impaired physical function than peers; function appears to decline with age. Less is known about the timing and trajectory of, or about specific treatment-related risk factors for, declining function. Addressing these knowledge gaps requires longitudinal assessment of parameters of physical function in large numbers of survivors, many of whom live distant from their cancer treatment center. This study determined feasibility and validity of remote assessment of hand grip strength, cardiopulmonary fitness, and usual walking speed in adult survivors of childhood cancer.
Methods: Adult survivors of childhood cancer participating in SJLIFE completed assessment of physical function using 3 test conditions (in-person, at-home by self-assessment, using remote audio and video technology). Measures included dynamometer ascertained grip strength, peak oxygen uptake using cardiopulmonary exercise testing for in-person assessment and the two-minute step in place test (peak oxygen uptake=26.56+(0.084*leg lifts)-(0.591*body mass index)) for at home assessments, and walking speed measured over four meters. Feasibility was evaluated as percentage of persons able to complete all three assessments, and validity of measures with interclass correlation coefficients (ICC) and Bland Altman methodology. Mean differences between test conditions were compared with analysis of variance.
Results: Of 79 individuals approached, 64 (81.0%) completed the self-assessment and 60 (75.9%) the remote assessment. Means±Standard Deviations for the in-person, self, and remote assessment were: handgrip 39.6±12.9, 38.4±12.7, 38.6±13.6 kilograms (p=0.80, ICC 0.95); peak oxygen uptake 27.7±9.1, 26.1±6.4, 27.8±6.3 milliliters/kilogram/minute (p=0.35, ICC=0.88); and usual walking speed 1.20±0.20, 1.05±0.25, 0.98±0.66 meters/second (p <0.001).
Conclusions: Remote assessment of physical function is feasible, and measures of handgrip strength and cardiopulmonary fitness are valid. Self- and remote assessment of walking speed overestimate laboratory measured values, perhaps because participants have to manage their own stopwatch and may not have adequate reaction time at the start and/or end of the path.

EP753 / #540

Topic: *AS05.s Survivorship*

ONCOLOGY-BASED PARTNERSHIP PROMOTES PATIENT SURVIVAL OUTCOME, A PEDIATRIC BLUEPRINT IN WESTERN KENYA MAY REVEAL.

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Background and Aims: The Academic Model Providing Access to Healthcare (AMPATH) oncology was established with a primary goal to fight the global increase of cancer cases through screening, treatment, education and training, care for cancer patients and other chronic illnesses. The objective was to evaluate the impact of partnership to the patient survival outcome among adults and paediatric patients attending oncology clinics
Methods: A retrospective chart review of patient files was conducted for 33 mixed paediatric and adult consecutive patients with diseases ranging from leukaemia, lymphomas, KS, myeloma, breast and cervical cancers receiving treatment in different AMPATH supported oncology facilities from May 2014 to Oct 2019. Different protocols were used to determine the number of cycles of treatment for each clinical condition. Data was collected at the last cycle of treatment for each file, and at the last follow-up visit and compared to the standard protocol and documented as either lost to follow up (Lf/u), incomplete(Inco) and complete (compd). Lf/u was reported at ≤ 20%, Inco ≤ 25% and compd ≥ 50%.
Results: The population consisted of 17 males (51.52%) and 16 females (48.48%). 23 (69.70%) adults and 10 (30.30%) paediatrics. ≥ 80% of the sample size reached midway through the treatment protocol. 70% of paediatric cases sailed through to completion of treatment to the last cycle. Patients received a mean of 5.4 doses (range: 6–8). The average time between doses was 25.6 days for the 3 weekly protocol. 24 were classified with stable disease while 1 with progressive disease. 3 patients were initiated on second-line chemotherapy and the rest untraced.
Conclusions: Donor collaboration enhanced free medication, healthcare support system and accelerated treatment compliance, reduced dropouts, enhanced patient outcome and promoted high paediatric patient survival outcome. More child cancer treatment- support and further studies are warranted to confirm activity in the same expanse.

EP754 / #1315

Topic: *AS05.s Survivorship*

ASSESSING FATIGUE IN CHILDHOOD CANCER SURVIVORS: PSYCHOMETRIC PROPERTIES OF THE CHECKLIST INDIVIDUAL STRENGTH AND THE SHORT FATIGUE QUESTIONNAIRE ; A DCCSS LATER STUDY

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Background and Aims: With one in four childhood cancer survivors (CCS) reporting symptoms of chronic fatigue, it is important to screen for and monitor fatigue regularly. Early identification of persons with fatigue symptoms and, subsequently, providing a personalized intervention can hopefully help to prevent (severe) fatigue to become chronic. Several instruments to measure fatigue exist, although none are validated for use in CCS specifically. The aim of the current study was to present psychometric properties of an easy to use fatigue screening instrument, the Short Fatigue Questionnaire (SFQ), and a well-known multidimensional fatigue questionnaire, the Checklist Individual Strength (CIS), in a nationwide cohort of CCS.
Methods: We included 2073 participants from the Dutch Childhood Cancer Survivor Study (DCCSS) LATER cohort. Convergent validity (correlation with other fatigue questionnaires), structural validity (confirmatory factor analysis) and internal consistency (Cronbach's alpha) were calculated for the CIS and SFQ. In addition, test-retest reliability (correlation, intraclass correlation coefficient (ICC) and weighted Cohen's kappa item scores (Kw) between two measurements within one week), and a cut-off score to indicate severe fatigue, using the validated CIS-fatigue severity subscale cut-off point of 35 as golden standard, were determined for the SFQ.
Results: Pearson's correlations between CIS/SFQ and other fatigue questionnaires were high (>0.8), indicating good convergent validity. Confirmatory factor analysis resulted in a four-factor solution for the CIS and a one-factor solution for the SFQ with Cronbach's alpha for each (sub)scale showing good to excellent values (>0.8). Test-retest reliability of the SFQ was adequate (Pearson's correlation = 0.88; ICC = 0.946; Kw ranged 0.31-0.50) and a cut-off score of 18 showed good sensitivity and specificity scores (92.6% and 91.3% respectively).
Conclusions: The current study shows that the SFQ and CIS are good instruments to assess fatigue in CCS. A cut-off score of 18 for the SFQ was proposed to easily indicate persons who experience severe fatigue.

EP755 / #771

Topic: *AS05.s Survivorship*

RIGHTFULLY WORRIED? ACTUAL VS. PERCEIVED FERTILITY RISK AND RELATIONSHIP TO PSYCHOLOGICAL FUNCTIONING IN AYA SURVIVORS OF PEDIATRIC CANCER

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Background and Aims: Many survivors of childhood cancer are at risk for infertility, an issue that may become of greater concern to them as they reach adolescence and young adulthood. Perceived infertility (whether accurate or not) may impact survivors' social behavior and psychological functioning. The present study examined the match between perceived and actual risk for infertility among AYA survivors, and its association with psychological function.
Methods: Survivors of childhood cancer (N = 284; Age range 13-26; Mean 18.6 years; 52.1% male; time from diagnosis 5-23 years, Mean 9.1 years) completed measures of reproductive concerns, social functioning/dating status, personality, and symptoms of anxiety and depression. A sample of age/gender matched AYA's completed a similar battery of measures for comparison. Based on review of treatment history, survivors' risk for infertility was rated on a 4-point scale (no increased risk; low, moderate, and high-risk).
Results: As expected, reproductive concerns were greater among survivors than healthy comparisons ($p < .001$). However, within the survivor group, there was only a marginal relationship between perceived and actual fertility risk ($r = .24$, $p < .05$). Among the 130 survivors identified at high risk of infertility, 54 (41.5%) perceived their risk as low. A smaller number of survivors (10.5%) who were at low risk, rated their risk as high. Psychological functioning was significantly related to both perceived and actual fertility risk, but in opposite directions: Those who perceived themselves at high-risk had higher scores on neuroticism, anxiety and depression; whereas those whose actual risk was high, had lower scores on those outcomes.
Conclusions: There is widespread misperception of risk of infertility among survivors, with substantial numbers of those who both underestimate and overestimate their risk. Higher perceived risk (regardless of accuracy) is associated greater psychological distress. Greater attention to educating survivors about fertility risk is necessary, and is an important part of survivorship care.

EP756 / #1565

Topic: *AS05.s Survivorship*

ESTABLISHING A CHILDHOOD CANCER SURVIVOR'S PROGRAM IN A GENERAL HOSPITAL IN MEXICO: INITIAL STEPS AND LESSONS LEARNED

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Background and Aims: Sixty percent of childhood cancer survivors experience at least one late-onset therapy-related complication, requiring long-term follow-up care. Comprehensive programs for cancer survivors are scarce in Mexico. We describe the initial steps to implement a childhood cancer survivors' program (CCSP) at the General Hospital-Tijuana, Mexico aimed at monitoring and treating late-effects, including prevention of chronic diseases.
Methods: A pediatric oncologist (RRG) completed a fellowship in survivorship in 2019. A multidisciplinary team was established: pediatric oncologists(1), social workers(2), and psychologists(1). In 2019, patients at least 5 years off-therapy were identified and scheduled to be seen in the survivorship clinic by the multidisciplinary team in a "one-stop-shop" model. In 2020, due to the COVID-19 pandemic, the in-person clinic was paused and a sub-group of patients were followed-up by video-calls. In 2021, in-person care resumed. In 2022, dieticians(1), neuropsychologists(1) and pediatric endocrinologists(1) joined the team.
Results: One-hundred forty-three cancer survivors have been identified and 70 have received comprehensive care. Initial barriers included: lack of dedicated work space; misinformation regarding CCSP purpose and workflow; incomplete data regarding cancer treatment details in charts; difficulty contacting patients who had been discharged from the hospital after 5 years off-therapy (per the current practice in Mexico); and parents/patients doubts regarding returning to the hospital. Complications have been detected in 50% of patients, including: neurocognitive deficits (35%), obesity (30%), mental health disorders (25%), ototoxicity (12%).
Conclusions: Despite the COVID-19 pandemic and initial barriers, 50% of childhood cancer survivors have received comprehensive care. By establishing the CCSP in a general hospital, patients continue care in our survivorship clinic when transitioning to adults. Future steps include: multidisciplinary team strengthening with continued education, involving pediatric/adult specialists (generalists, cardiologists, psychiatrists, ophthalmologists), advocating for survivors to gather government resources, and expand the CCSP to provide a high-quality care to survivors in Northwestern Mexico.

EP757 / #69

Topic: *AS05.s Survivorship*

SURVIVAL RATE AND ASSOCIATED FACTORS AMONG PATIENTS WITH XERODERMA PIGMENTOSUM AT MUHIMBILI NATIONAL HOSPITAL, TANZANIA

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Background and Aims: Xeroderma pigmentosum (XP) is a rare hereditary disease of defective deoxyribunucleic acid repair defined by extreme sensitivity to sunlight, with a greatly elevated incidence of skin cancers. Mortality mainly occurs from 2nd decade of life Aim was to determine the survival rate and associated factors among pediatric patients with XP at Muhimbili National Hospital (MNH), Tanzania from June 2011 to December 2020
Methods: A retrospective cohort study with a longitudinal follow up of the pediatric patients with XP at MNH from 2011 to 2020. A total of 100 files and database records of registered patients with XP were extracted using a structured data collection tool. Collected patient's information included socio-demographical and clinical characteristics, and whether alive or dead. Patients with available contact information were contacted and consented for a short mobile interview. Analysis was done using SPSS version 23. Kaplan-Meier survival analysis was used to determine the overall survival rate. Independent mortality predictors were assessed in adjusted Cox regression model.
Results: Of 100 enrolled patients, half were male. Mean age was 5.4 ± 4.1 years. Cutaneous squamous cell carcinoma (cSCC) was found in 41% of the patients, ocular squamous cell carcinoma in 25% and oral Squamous cell carcinoma in 14%. At the end of the study, 39% of patients were alive, 35% had been lost to follow up and 26% died. The median survival was 14.1 years (IQR= 11.7 – 17.2). Estimated overall survival rate was 90%, 64% and 46% at 5, 10 and 15 years respectively. Those with cSCC had lower survival rate, 87% and 55% at 5 and 10 years respectively. Only cSCC was found to be a strong predictor of mortality (HR 2.8, 95% CI 1.0-7.3, P= 0.02)
Conclusions: Survival of patients with XP was progressively decreasing. Cutaneous squamous cell carcinoma was found to be a strong predictor of mortality.

EP758 / #1762

Topic: *AS05.s Survivorship*

PREFERENCES OF LATINO AND NON-LATINO SURVIVORS FOR SURVIVORSHIP EDUCATION AND SERVICES

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Background and Aims: There is an unmet need for survivorship education targeting diverse populations of survivors of childhood cancer. Our objective was to assess preferences related to accessing survivorship information, education, and support networks in rural and metropolitan regions of Texas.
Methods: Leveraging the multi-institutional Survivorship and Access to Care for Latinos to Understand Disparities (SALUD) cohort, we administered a 25-item bilingual survey to adult survivors of childhood cancer and parents of younger survivors. All survivors were ≥1 year off-therapy. Responses from survivors vs. parents of survivors and Latinos vs. non-Latinos were compared using a Fisher exact test. Odds ratios (OR) for the outcomes of interest were calculated with 95% confidence intervals (CI).
Results: We received 135 responses from 56 survivors and 79 parents of survivors treated at Texas Children's Hospital (Houston, n=49), Vannie Cook Children's Clinic (McAllen, n=70), and El Paso Children's (n=16). Respondents were 83% White, 75% Latino, and 27% Spanish-speaking. The mean age of survivor respondents was 22 years (range, 16-32), and 14 years (range, 5-20) for survivors with parent respondents. Most survivors (68%) were >5 years off therapy. From a list of 12 topics, both survivors and parents selected 'risk for second cancers' and 'diet, nutrition, and exercise' as highest educational priorities, with no difference by ethnicity. Parents were more likely than survivors to seek survivorship information from other survivor families (OR=7.97, CI 1.77, 35.93) and utilize social networks comprised of survivor families (OR=2.9, CI 1.08, 7.85). Survivors were more likely than parents to prefer short videos as a mode of survivorship education delivery (OR=2.41, CI 1.02, 5.70). Non-Latinos were more likely than Latinos to prefer social media as an educational resource (OR=3.70, CI 1.58, 8.68).
Conclusions: Differing preferences for survivorship education and resource utilization by ethnicity and respondent type suggest a need for adapted content delivery for this vulnerable population.

EP759 / #516

Topic: *AS05.s Survivorship*

PROGNOSTICATION OF PEDIATRIC NASOPHARYNGEAL CARCINOMA PATIENTS USING BASELINE 18F-FDG PET/CT

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Background and Aims: Paediatric Nasopharyngeal Carcinoma (NPC) is a rare form of malignant cancer. Currently there is paucity of data to support and correlation between metabolic parameters and post treatment outcome. Current prognostic indicators are: age of onset, clinical staging and treatment modality used.

Aim: Assess correlation between metabolic parameters derived from baseline FDG-PET/CT with patient outcomes (DFS and OS) in patients with pediatric nasopharyngeal carcinoma (NPC).
Methods: Single centre retrospective observation study, with 64 subjects. Treatment naïve pediatric NPC who underwent baseline FDG PET/CT were included. Metabolic parameters i.e. SUVmax, SUVmean, metabolic tumor volume (MTV) and total lesion glycolysis (TLG) were evaluated from PET/CT data. Univariate analysis of metabolic parameters was done using independent t test. Receiver operating characteristic (ROC) curve was generated to calculate cut-off values. Cut-off was calculated using Youdens-index for significant variables. Survival analysis was done using Kaplan Meier analysis
Results: Out of 64 subjects, 26 had disease relapse and 17 were dead at time of analysis. Univariate analysis using independent t test revealed MTV ($p<0.001$) and TLG ($p<0.003$) i.e. significant predictors of OS and DFS. SUVmax and SUVmean - not significant. ROC curve analysis revealed area under curve of MTV of 0.861 ($p<0.0001$) and TLG of 0.815 ($p<0.0001$) i.e., significant. SUVmax and SUVmean had AUC as 0.498 and 0.449 hence not significant. Cut-off for MTV was 67.14 (Sensitivity 94.1%, Specificity 74.5%, $p<0.0001$) and TLG 366.09 (Sensitivity 92.3%, Specificity 65.8%, $p<0.0001$). Mean survival patients above cut-off of MTV was 41.72 months (OS) and 28.44 months (DFS) ($p<0.0001$), for TLG it was 41.36 months (OS) and 34.55 (DFS) ($p<0.0001$)
Conclusions: MTV and TLG can predict patient adverse outcome independent of other variables (age, stage etc). SUVmax and SUVmean were not significant. MTV and TLG can be used to stratify patients for treatment intensification and should be made a part of clinical trials.

EP760 / #630

Topic: *AS05.s Survivorship*

ASSESSING QUALITY OF LIFE IN CHILDHOOD CANCER SURVIVORS AT RISK FOR HEARING LOSS; A COMPARISON OF THE HEAR-QL AND PROMIS MEASURES

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Background and Aims: Background: Carboplatin and cisplatin can lead to hearing loss (HL) and quality of life (QOL) deficits in childhood cancer survivors (CCS). We compared two QOL measures; one developed for children with HL (HEAR-QL) and a validated measure for CCS (PROMIS). Hypothesis: HEAR-QL would be more sensitive than PROMIS at identifying QOL deficits in CCS with HL.
Methods: Inclusion criteria: 1) 8-17 years of age, 2) cancer diagnosis, 3) history of ototoxic chemotherapy, 4) at least 6 months post therapy, 5) audiogram within 1 year. Exclusion criteria: 1) central nervous system (CNS) malignancy, 2) cranial radiation, 3) CNS surgery, 4) intrathecal chemotherapy. Participants completed the PROMIS and age appropriate HEAR-QL (-26 or -28) after routine appointments.
Results: Fifty individuals were evaluated. Mean age was 12.94 years (range 8-17), and 56% were male. Twenty-two (44.9%) received cisplatin and 30 (61.2%) carboplatin. Participants with HL (30%) had significantly lower scores on the HEAR-QL-26 and HEAR-QL-28 than those with normal hearing (mean = 67.9 + 25.6, verses 88.6 + 9.4, $p = 0.044$, and 82.3 + 8.8 verses 94.8 + 3.6, $p = 0.016$, respectively). Participants with higher SIOP grades (more HL) had lower scores on the HEAR-QL-26 (Grade 0: 88.6 +9.4, Grades 1-2: 77.4 + 10.1, Grades 3-4: 60.4 + 32.8, $p = 0.005$) and HEAR-QL-28 (Grade 0: 94.8 + 3.6, Grade 1-2: 84.4 + 0.6, Grade 3-4: 81.3 + 11.1 $p = 0.001$). Feelings subscale scores on the HEAR-QL-26 and -28 worsened with higher SIOP grades. Significant differences were seen in the Environments (HEAR-QL-26), and Hearing Situations (HEAR-QL-28) subscales. The PROMIS failed to identify any inferior outcomes with worsening HL.
Conclusions: Conclusion: The HEAR-QL is more sensitive than the PROMIS in identifying QOL deficits in CCS at risk for HL. The HEAR-QL should be utilized in studies examining QOL of CCS with HL.

EP761 / #1812

Topic: *AS05.s Survivorship*

FUNCTIONAL CONNECTIVITY AND ATTENTION IN SURVIVORS OF PEDIATRIC BRAIN TUMORS AND HEALTHY CONTROLS

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Background and Aims: Treatment of pediatric brain tumors often impairs social perception (e.g., inhibition, attentional control) in survivors. Children receiving radiation therapy are at a greater risk of impairment in these domains, particularly as the dorsolateral prefrontal cortex (DLPFC) and frontal gyrus may be impacted. This study aimed to identify if DLPFC functional connectivity differences exist between survivors and healthy controls.
Methods: Thirteen survivors (n=5 glioma, n=2 medulloblastoma, n=6 other tumours; n=2 chemotherapy, n=12 surgery, n=5 radiation; mean[SD] diagnosis age 5.8[4.1], assessment age 14.4[2.9] years; 53.8% male) and 19 controls (assessment age 11.7[3.0] years; 57.9% male) completed resting state functional MRI (3T General Electric Healthcare). The FMRIB Software Library (FSL) was used to assess connectivity between the right and left DLPFC as a seed region and the rest of the brain. Parents completed the attentional control index of the Behavioral Assessment System for Children-Third Edition (BASC-3). Higher scores indicate greater distractibility.
Results: Stronger connectivity between the right inferior frontal gyrus and left DLPFC was observed in controls only (voxels n=185, p=0.0105), no differences between groups were noted in right DLPFC connectivity. Scores on the attentional control index of the BASC-3 did not significantly differ between groups (mean[SD] survivors=51.9[15.1], controls=44.9[6.3], p=.149).
Conclusions: Survivors may have worse connectivity in regions of social perception due to the nature of their treatment. Future research should examine other possible seed regions for connectivity related to social perception with an emphasis on the right inferior frontal gyrus, given its role in attention and social cognitive processes.

EP762 / #849

Topic: *AS05.s Survivorship*

IMPACT OF HEARING IMPAIRMENT ON HEALTH-RELATED QUALITY OF LIFE IN EUROPEAN CHILDHOOD CANCER SURVIVORS

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Background and Aims: Hearing impairment can be a late effect of childhood cancer treatment and can lead to impairments in education, social attainment, and health-related quality of life (HRQoL). We assessed the impact of hearing impairment on HRQoL in a large European cohort of childhood cancer survivors (CCS).
Methods: Within the PanCareLIFE consortium, we used the combined dataset from four countries (CH, CZ, DE, FR), including 5-year survivors diagnosed before age 19 years, who were off cancer treatment and aged 25-44 years at study. Questionnaires were used to assess hearing impairment, HRQoL (Short Form 36) and potential confounders including socio-demographic and clinical factors. We performed multivariable linear regression to investigate the role of hearing impairment on HRQoL adjusting for age at survey, sex, education, country, period of cancer diagnosis, tumor type, and cancer treatments.
Results: In total, 6,262 CCS participated, with a mean age at questionnaire survey of 32 years (SD 5). We included 4,627 CCS from Germany, 804 from Switzerland, 579 from Czech Republic, and 252 from France. Fifty-three percent of CCS were female and mean age at diagnosis was 9 years (SD 5). Hearing impairment was associated with a reduced physical component (coef. -3.8, 95% CI: -6.4 to -1.1) and mental component (-2.9, CI: -5.2 to -0.7). Particularly strong associations were with HRQoL domains of physical functioning (-3.9, CI: -7.0 to -0.8), bodily pain (-2.3, CI: -4.0 to -0.5), general health (-4.4, CI: -6.7 to -2.0), vitality (-3.7, CI: -5.9 to -1.6), social functioning (-3.4, CI: -5.8 to -1.0), and mental health (-2.5, CI: -4.5 to -0.6).
Conclusions: This collaborative four-country study suggests that hearing impairment following cancer treatment in childhood may affect HRQoL. Close monitoring of hearing function with early therapeutic support could improve quality of life of young people treated for cancer when they were children.

EP763 / #677

Topic: *AS05.s Survivorship*

THE NUTRITIONAL TRAJECTORY OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA: A 10-YEAR FOLLOW UP STUDY FROM A REFERRAL CENTER IN SOUTH INDIA

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Background and Aims: Overnutrition and undernutrition in children with cancer are associated with adverse events, the risk continuing after completion of treatment.
Methods: A file review of children treated for ALL from 2002 to 2012 was performed. The body mass index (BMI) was calculated at diagnosis, end of treatment, and at 5, 8 and 10-years from diagnosis. BMI-centiles were used to categorize the patients as underweight (<5^{th}-percentile), normal (5^{th}-85^{th} percentile), overweight (85^{th}-95^{th} percentile) and obese (≥95^{th} centile).
Results: The study analyzed 179 children with ALL [median age:59-months (range:24-182), male:female ratio 2:1]. The immunophenotype was B-ALL, T-ALL and B-myeloid in 147(82%), 26(15%) and 6(3%) patients, respectively. Fifty-five(31%) patients received cranial irradiation. Of 66(37%) children who were underweight at diagnosis, 20(31%), 33(51%) and 12(18%) were underweight, normal and overweight/obese after 5-years, respectively (5-year BMI unavailable for one patient). Of the 100(56%) children who were normal, 7%, 55% and 38% were underweight, normal and overweight/obese after 5-years, respectively. Of the 13(7%) children who were overweight/obese, 3(23%) and 10(77%) were normal and overweight/obese after 5-years, respectively. The median (IQR) BMI Z-score at diagnosis was -1.12(-2.40,-0.26). The median (IQR) BMI z-score of the cohort was higher at the end of treatment [-0.04(-1.16,1.03), P<0.001], and remained higher after 5 [0.22(-0.83,1.24), P<0.001] and 10-years [0.30(-0.69,0.99), P<0.001], respectively. The proportion of overweight/obese individuals was higher at the end of treatment (25%, P<0.001) and remained higher after 5 (34%, P<0.001) and 10 (26%, P=0.001) years. There was significant correlation of the baseline BMI Z-score with that observed at the end of treatment (ρ=0.50, P<0.001), after 5-years
Conclusions: In a large cohort of 179 children treated for ALL, a ten-year follow up study showed that more than 25% were overweight/obese. The BMI Z-score at the time of diagnosis continued to correlate with the Z-score after 10-years.

EP764 / #571

Topic: *AS05.s Survivorship*

CELLULAR SENESCENCE IS ASSOCIATED WITH RENAL FUNCTION DECLINE IN CHILDHOOD CANCER PATIENTS WITH KARYOMEGALIC INTERSTITIAL NEPHROPATHY

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Background and Aims: Patients with karyomegalic interstitial nephropathy (KIN) show a clinical picture of interstitial nephopathy with enlarged, irregular and hyperchromatic nuclei of tubular epithelial cells (TECs) on renal biopsy. The histologic pattern was first described in patients with FAN1 mutations with defective DNA damage repair, but has also been infrequently reported in children treated for childhood cancers with the alkylating agent ifosfamide. To evaluate the presence of features of KIN in children with renal function decline and a medical history of childhood cancer, we evaluated their history and renal biopsy results.
Methods: All consecutive children treated for childhood cancer in the Princess Máxima Center for Pediatric Oncology who were biopsied for progressive chronic kidney disease (CKD) with low molecular weight LMW proteinuria of unknown cause between 2018 and 2021 were included.
Results: Karyomegalic interstitial nephropathy could be diagnosed in all six patients.Features of karyomegaly and senescence were identified in TECs of these patients by automated morphometric assessment of nuclear size distribution, and immunohistochemical markers for DNA damage (γH2AX), cell-cycle arrest (p21+, Ki67-), and nuclear lamina decay (loss of lamin B1). The number of p21 positive cells by far exceeded the typically very small numbers of truly karyomegalic cells. P21 positive TECs were found to contain significantly less lysozyme, testifying to defective resorption as an explanation of the consistent finding of LMW proteinuria. Moreover, in the 5 patients with the largest nuclei, the percentage of p21-positive TECs showed strong inverse correlation with change in eGFR from biopsy to last follow-up (R^2=0.93, $p<0.01$).
Conclusions: Karyomegaly and cellular senescence-associated tubular dysfunction appear to be a more prevalent, rather than rare, cause of otherwise unexplained chronic kidney disease and LMW proteinuria in children treated for cancer with ifosfamide. This finding may have important implications for future personalized treatment strategies.

EP765 / #62

Topic: *AS05.s Survivorship*

WHITE PAPER: ONCO-FERTILITY IN PEDIATRIC PATIENTS WITH WILMS TUMOR

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Background and Aims: The survival of childhood Wilms tumor is currently around 90%, with many survivors reaching reproductive age. Chemotherapy and radiotherapy are established risk factors for gonadal damage and are used in both COG and SIOP Wilms tumor treatment protocols. The risk of infertility in Wilms tumor patients is low but increases with intensification of treatment including the use of alkylating agents, whole abdominal radiation or radiotherapy to the pelvis.
Methods: Both COG and SIOP protocols aim to limit the use of gonadotoxic treatment, but unfortunately this cannot be avoided in all patients. Infertility is considered one of the most important late effects of childhood cancer treatment by patients and their families. Thus, timely discussion of gonadal damage risk and fertility preservation options is important. Additionally, irrespective of the choice for preservation, consultation with a fertility preservation (FP) team is associated with decreased patient and family regret and better quality of life.
Results: Current guidelines recommend early discussion of the impact of therapy on potential fertility. Since most patients with Wilms tumors are pre-pubertal, potential FP methods for this group are still considered experimental. There are no proven methods for FP for pre-pubertal males (testicular biopsy for cryopreservation is experimental), and there is just a single option for pre-pubertal females (ovarian tissue cryopreservation), posing both technical and ethical challenges. Identification of genetic markers of

susceptibility to gonadotoxic therapy may help to stratify patient risk of gonadal damage and identify patients most likely to benefit from FP methods.
Conclusions: We summarize the literature regarding fertility risk and preservation in WT and make recommendations regarding the approach to onco-fertility in this young population.

EP766 / #34

Topic: *AS05.s Survivorship*

EXERCISE TOLERANCE AND PHYSICAL ACTIVITY SHORT AFTER INTENSIVE TREATMENT IN PATIENTS WITH CHILDHOOD CANCER

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Background and Aims: Patients with childhood cancer are confronted with exercise intolerance (EI (VO_2peak<85% predicted)) after treatment, with a detrimental effect on quality of life and mortality. Knowledge on the limiting factor(s) for this EI and its relation with physical activity (PA) is essential in order to prescribe individually tailored rehabilitation and to stimulate physical and social reintegration.
Methods: Forty-one patients with childhood cancer (13±3 years; 71% boys; BMI: 20±4 kg/m²), diagnosed with leukemia/lymphoma (61%), solid tumor (32%) or brain tumor (7%) and recently finalized (duration cancer treatment: 216 [168-270] days) their oncology-related treatment were included in the study. Patients performed a maximal symptom-limited cardiopulmonary exercise test (CPET) on a treadmill (4.8 km/h; +2% elevation/min). PA was recorded with a 3-axial accelerometer (Dynaport MoveMonitor, McRoberts, The Hague), that patients wore for 7 consecutive days. Active time (standing and walking), sedentary time and steps were withheld.
Results: The duration of CPET amounted 7 [6-9] minutes, reaching an inclination of 12 [10-16] %. Exercise tolerance (VO_2peak: 29.7±7.8 ml/min/kg (67±16% predicted)) was markedly reduced in patients with childhood cancer compared to healthy peers. Eighty-eight percent of patients were defined as exercise intolerant. The majority of patients were peripherally limited (83%). A cardiac limitation was present in 71% of patients and was predominantly due to a reduced oxygen pulse (97%). Hyperventilation (32%) and a ventilatory limitation (12%) were less prevalent. PA data of 13 patients were available (Active time: 178±67 minutes/day; sedentary time: 515±113 minutes/day; steps: 6411 [4458-6838]).
Conclusions: Exercise tolerance is markedly reduced in patients with childhood cancer short after intensive treatment and mainly caused by deconditioning of peripheral muscles and reduced oxygen pulse. Further research is necessary to study the link with physical activity.

EP767 / #1130

Topic: *AS05.s Survivorship*

CANCER-RELATED WORRY AS A PREDICTOR OF 5-YEAR PHYSICAL ACTIVITY LEVEL IN CHILDHOOD CANCER SURVIVORS

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Background and Aims: Cancer-related worry (CRW) is a prevalent psychological outcome among childhood cancer survivors; 69% of survivors report concerns about health and/or a future cancer diagnosis. Elevated CRW in survivors has been associated with reporting risky health behaviors, such as not meeting recommended guidelines for physical activity (PA). The aim of this investigation was to describe associations between CRW and subsequent level of PA.
Methods: CRW was collected at a baseline clinical assessment using 6 survey items. Using factor analysis, two groups were identified “Body-Focused” and “General Fear”. Total CRW scores were calculated as the sum of the average responses to the “Body-Focused” and “General Fear” items. Moderate and vigorous physical activity (MVPA) minutes were captured 5-years later using accelerometry and categorized for analysis into meeting or not meeting recommended guidelines (150 minutes moderate and/or 75 minutes vigorous/week). Logistic regression determined independent associations between CRW and MVPA adjusting for sex, race, diagnosis, age at baseline, and presence of grade 3-5 chronic conditions at baseline.
Results: Among 1,218 participants (49% female, mean [SD] age at baseline 31.5 [6.87] years, mean [SD] age at follow up 36.8 [7.0] years), 25% met PA guidelines and 8% reported CRW (responses “agree” (score=4) or “strongly agree” (score=5) for individual items, averaged and summed for total CRW score of 8-10). Participants who identified as black race (OR 1.78; 95% CI 1.17-2.73) and those who had neurological conditions (OR 1.75; 95% CI 1.40-2.17) were less likely to meet PA guidelines. Odds of not meeting PA guidelines increased for every one-point increase in total CRW [BTM4] (OR 1.16; 95% CI 1.08-1.25). Findings were similar for both “Body-Focused” (OR 1.34; 95% CI 1.15- 1.56) and “General Fear” (OR 1.22; 95% CI 1.08-1.38) factors.
Conclusions: Conclusion: Interventions to promote PA among adult survivors of childhood cancer should consider CRW during implementation.

EP768 / #542

Topic: *AS05.s Survivorship*

THE ASSOCIATION BETWEEN SOCIAL SUPPORT AND POSTTRAUMATIC GROWTH WITH IDENTITY STATUS AMONG ADOLESCENT AND YOUNG ADULT CANCER SURVIVORS

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Background and Aims: Over 85% of children and adolescents who are diagnosed with cancer survive for at least 5 years. Alongside successful survival rates come various late effects of cancer, such as incomplete identity development, which can impact health-related quality of life. Social support and posttraumatic growth (PTG) may play a significant role in identity development. By exploring these variables as potential drivers of or barriers to identity development among adolescent and young adult (AYA) cancer survivors, we might elucidate mechanisms that lead to identity development, thus influencing future quality of life.
Methods: AYA cancer survivors (n=153) completed the Inventory of Parent and Peer Attachment, the Posttraumatic Growth Inventory, and the Extended Objective Measure of Ego Identity Status, which groups participants into four identity statuses: diffusion, foreclosure, moratorium, and achievement. Moderation models were used to assess the effect of PTG on the relationship between parent and peer attachment and identity status.
Results: Mean age was 21.8 years (SD = 2.55) and 91.5% identified as White, 3.9% as Black/African American, 1.3% each of American Indian/Alaska Native and Asian/Pacific Islander, and 7.2% identified as Hispanic/Latino. Within the sample, 58.2% identified as male and 41.8% as female. Thirty-five (24.6%) participants were identified as identity diffused; 24 (16.9%) as foreclosed; 61 (43%) as in moratorium; and 22 (15.5%) as in achievement. There was a significant interaction effect of PTG on the relationship between peer attachment and foreclosure (B = 0.0050; SE = 0.0019; p = 0.008).
Conclusions: PTG moderated the relationship between peer attachment and the foreclosed identity status. Our data provides preliminary evidence for the role that both social support, particularly peer support, and PTG may affect identity development. Future studies should assess all three constructs over time to ascertain both change and influence.

EP769 / #402

Topic: *AS05.s Survivorship*

MOVING FORWARD IN PEDIATRIC EXERCISE ONCOLOGY: DEVELOPING TRAINING RESOURCES TO SUPPORT EXERCISE PROFESSIONALS

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Background and Aims: Qualified exercise professionals (QEP) are crucial to implement safe and effective physical activity (PA), particularly for children and adolescents affected by cancer. Yet, few training resources are available for QEP working in pediatric oncology, representing a barrier to implementation, and ultimately sustainable PA delivery.
Methods: To equip QEP with the knowledge, skills, and abilities to implement safe and effective PA, an implementation science framework was adopted and we created a comprehensive training protocol (>30 hours) that covers substantive (eg, disease, treatment-related side-effects, role of PA, progression principles) and practical components (eg, tailoring considerations, fostering autonomy). Training is delivered online asynchronously and synchronously via modules, workshops, scenario-based competency sessions, and shadowing of pediatric oncology PA sessions. QEP are audited during PA delivery to ensure safety and effectiveness (eg, PA progression, behaviour modification support) and semi-structured interviews are used to assess training components, instructor confidence, and need for ongoing support.
Results: Within an evidence-based pediatric oncology PA intervention (IMPACT; Trial registration: NCT04956133), QEP onboarding and training commenced 10/2021 (n=7) and PA delivery began 03/2022. Audits will commence 04/2022 and first interviews will occur 05/2022. Data will be analyzed using descriptive statistics and content analysis.
Conclusions: QEP play a vital role in PA implementation and sustainability, yet few resources are available to support QEP in pediatric oncology. By reporting on our training protocol, it is hoped that others will do the same, enhancing transparency in reporting and moving towards standardized QEP training requisites in pediatric oncology.

EP770 / #1159

Topic: *AS05 SIOP Scientific programme / AS05.a Acute Lymphoblastic Leukaemia*

FRECUENCY OF IKZF1 AND IKZF1PLUS DELETIONS IN CHILDREN WITH PATIENTS PEDIATRIC B CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA CHILDREN. AN INTERIM ANALYSIS IN A COLOMBIAN COHORT.

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Background and Aims: Deletions in IKZF1 have been associated with poor prognosis in pediatric B-cell precursor ALL (BCP-ALL). This study aimed to describe the frequency of IKZF1 and IKZF1 plus deletions in a cohort of Colombian patients with BCP- ALL.
Methods: Gene deletions were assessed by multiplex ligation-dependent probe amplification (MLPA), using a commercially available kit (SALSA MLPA P335 ALL-IKZF1 probemix). Between 2018 – 2020, 117 de novo pediatric BCP-ALL patients from Fundación Hospital Pediátrico La Misericordia (Bogotá, Colombia) were enrolled. All the patients were treated according to BFM – ALLIC 2009 protocol.
Results: IKZF1 and IKZF1 plus deletions were detected in 17 (14.5%) patients. In patients with IKZF1 and IKZF1 plus , we found higher age at diagnosis compared with no IKZF1 deletions patients (9,52y vs 6.83y) p=0.01. IKZF1 deletions were detected in 5.98% (n=7) and IKZF1 plus were detected in 8.54% (n=10). In patients with IKZF1 deletions, the median age was 9.15 y, 2 patients had iAMP21, 2 had poor steroid response, 4 were classified as high risk and 2 with residual disease >0,1% at the end of induction. During the follow up, 1 patient had
early relapse. Within the group of 10 patients with IKZF1 plus , the median age was 9,8 y, 2 had CNS 3, 2 had t(9;22), 5 had poor steroid response, 5 were classified as high risk and 3 with residual disease >0,1% at the end of induction. During the follow up, early relapse was observed in
2 patients.
Conclusions: These findings support that this cohort of patients has similar frequency of IKZF1 and IKZF1 plus deletions comparing with reports from other countries. MLPA could help improving risk stratification of BCP-ALL like other investigation groups propose (AEIOP-BFM ALL 2017 and DCOG ALL11). We should follow up this cohort to see the impact of IKZF1 in survival outcomes.

EP771 / #1819

Topic: *AS05 SIOP Scientific programme / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

RELAPSE AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PEDIATRIC PATIENTS WITH ACUTE MYELOID LEUKEMIA OR MYELODYSPLASTIC SYNDROME: SINGLE INSTITUTION RETROSPECTIVE STUDY

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Background and Aims: Introduction: Despite high rates of initial remission (>90%) after the first treatment, 40% of pediatric patients with AML will experience relapse. Allogeneic hematopoietic stem cell transplantation (HSCT) is recommended for children in 1st CR (intermediate- or high-risk cytogenetics or genetic mutations) or in 2nd CR. Risk factors for relapse after transplant include status at the time of transplant (beyond the first CR) and absence of chronic graft versus host disease (GVHD). Overall survival after relapse is poor and there is no standard treatment in these situations. Objective: Describe the outcomes of pediatric patients with AML or MDS who experienced relapse after allogeneic HSCT.
Methods: Methodology: Retrospective analysis of pediatric patients transplanted for AML or MDS who experienced disease relapse.
Results: From January 2015 to September 2021 30 pediatric patients underwent allogeneic HSCT for AML or MDS in our institution. One patient had active extramedullary disease at HSCT and progressed after transplant. Four patients experienced relapse between 55 days and 43 months after transplant. Of these, two patients had MDS (RAEB-T) and 2 patients had AML (1st CR and 3rd CR). Transplant characteristics are described in table 1. One patient with MDS had poor functional clinical status and received exclusive palliative care. Two patients received were refractory to high-dose chemotherapy and died from the disease and infection. One patient relapsed as T-cell ALL de novo, received high dose chemotherapy with multiple agents but progressed just after, and died 18 months after relapse diagnosis.
Conclusions: Conclusion: All patients relapsing after HSCT for AML or MDS in our institution died from disease or toxicity. New agents (with less toxic profile) and cellular immunotherapy may have a role in these very severe situations. Complementary palliative care could be beneficial.

EP772 / #1938

Topic: *AS05 SIOP Scientific programme / AS05.d Stem Cell Transplantation*

OUTCOMES FOLLOWING RELAPSE AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR CHILDREN WITH ALL: A SINGLE-CENTER EXPERIENCE.

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Background and Aims: Acute lymphoblastic leukemia (ALL) represents the most prevalent pediatric cancer. Trough multicentric trials, approximately 90% of all pediatric patients with ALL survive for at least 5 years. In the relapse scenario, allogeneic HSCT is indicated and survival may reach 70% if the disease is in complete remission. However, post–HSCT relapses still represent the major cause of treatment failure, with a dismal prognosis. Objective: Describe the outcomes of patients experiencing relapse after HSCT for pediatric ALL.
Methods: We retrospectively analyzed ALL patients relapsed after HSCT in our institution from January 2015 to September 2021.
Results: In the study period, 46 pediatric patients underwent allogeneic HSCT for ALL in our institution. From these, 17 had relapse after allo-HSCT. Two patients were excluded from the analysis for loss to follow-up. Median time from transplant to relapse was 240 days (range 30-840). Most patients (n=12) relapsing before 1 year after HSCT. Patients' characteristics were divided in two tables for early (before 6 months - table 1) or late (after 6 months - table 2) relapses. Most of the patients (92.8%, n = 13) received classic chemotherapy and 3 also received Donor Lymphocyte Infusion (DLI), and 6 also received target immunotherapy with blinatumomab (n = 5) or inotuzumab (n = 1). Two patients received a 2nd HSCT. Only 1 patient received exclusive palliative care (very early relapse). Three patients are still alive and only one is disease-free with a good quality of life, 14 months after relapse. Twelve patients died, most from disease progression. All patients with early relapse died before 6 months, while patients with late relapses survived at least two years.
Conclusions: Survival after relapsing allogeneic HSCT is dismal, especially before 6 months. New therapeutic agents (immunotherapy) and cellular therapy (CAR-T cells and second HSCT) may change this scenario. These children should receive early comprehensive care.

EP773 / #1835

Topic: *AS05 SIOP Scientific programme / AS05.I Rare Tumours and Histiocytosis*

PRIMARY CARDIAC TUMORS IN CHILDREN: A SINGLE INSTITUTION CASE SERIES

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Background and Aims: Cardiac tumors (CT) are a rare condition in childhood. The majority of primary cardiac tumors (PCT) are benign (60% rhabdomyomas) and about 10% of CT are malignant. Life threatening symptoms (arrhythmia and flow obstruction) and sudden death are described. Treatment should be tailored according to the histological subtype and multiple options are reported. Recently, mTOR inhibitors have been explored in patients diagnosed with rhabdomyomas given its high prevalence and association with Tuberous Sclerosis (TS).
Methods: Retrospective analysis of CT in patients < 18 years old from 2013 to 2021 in a single institution.
Results: 7 patients were diagnosed with PCT. Six female and 1 male. 3/7 were intra-uterine diagnosed, 1/7 at birth, 3/7 after 1 year of age. Clinical presentation was heart failure (3/7) and pericardial effusion/chest pain (1/7).Biopsy was done in 4/7 cases and pathology report was consistent with germ cell tumor (2/7), hemangioma (1/7) and sarcoma (1/7). In 3/7 cases a rhabdomioma diagnosis was assumed and tissue sample was not obtained. TS complex was confirmed in only 1 patient. Cancer specific protocol was offered for patients with malignant diagnosis as appropriated (yok sack tumor and sarcoma). Surgery was the treatment choice for an immature teratoma. Steroids were used for the hemangioma treatment and sirolimus was utilized in 1/3 rhabdomyoma. All patients are alive and no recurrence disease was observed.
Conclusions: CT in childhood are a rare and heterogeneous group of disease. Our small case series do not support a treatment recommendation with respect of malignant tumors, although a disease-specifc approach is encouraged in the literature. Considering that rhabomyomas are largely the most common CT subtype, and commonly associated with TS, mTOR inhibitor approach is a reasonable, non-invasive option and should be considered in prospective studies as an alternative for patients with life-threating cardiac dysfunction rhabdomyoma-related.

P001 / #1707

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

IDENTIFICATION OF REASONS AND ROOM FOR IMPROVEMENT IN TIMELY INITIATION OF RADIATION THERAPY AFTER SIMULATION-A SHARED CARE MODEL FROM TERTIARY CARE HOSPITAL IN LMIC

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Background and Aims: Timely delivery of radiation therapy (RT) is vital to local control in many pediatric tumors. The aim of this study was to review the pattern and reasons of delay in initiating radiotherapy for children treated at our institute and identify the reasons for delayed initiation of treatment.
Methods: Hospital database was reviewed for patients treated with radiation therapy on pediatric treatment protocol from December,2016-May,2021. Patients were identified who had delays in starting RT of more than 10 working days following planning CT scan. Data for demographics, diagnosis, duration and reason for delay in treatment initiation were recorded and analyzed.
Results: Out of 224 patients treated from December,2016-May 2021, 199 events of treatment delay recorded in 175patients. The mean age of patients was 8.6years (± 4.6, 1-19years) and 109(62%) of the patients were male. Most of the patients 145(83%) were referred from another institute for radiotherapy at our hospital. One-fourth of patients were treated under general anesthesia. Most of the patients were being treated for sarcomas 46%(81)patients, lymphomas 26%(45)patients, renal tumors 12%(21)patients, CNS tumors 11%(20)patients, and rare tumors 5%(8 patients). Duration of treatment delay was 11-15days in 73patients,16-20days in 72 patients and 20-40 days in 30patients. Major reason for the delay identified was due to changes recommended in peer review meeting for treatment planning in 102 patients. Other reasons were complex planning in 35patients, treatment machine overbooked in 28patients, equipment breakdown in 19patients and nonavailability of diagnostic imaging in 15patients. Peer review changes was most observed reason in 11-15days delay, imaging unavailability in 16-20days delay, while a combination of complex planning, machine overbooking, and breakdown were most common in delay of greater than 20days.
Conclusions: The study identifies areas working on which could help early initiation of curative local treatment in children. Availability of treatment machine, manpower and coordination with pediatric oncologist are essential.

P002 / #464

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

SHOULD THE CARDIAC SUBSTRUCTURES BE DELINEATED FOR THE RADIATION OF MEDIASTINAL HODGKIN'S LYMPHOMA?

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Background and Aims: Radiation therapy (RT) in mediastinal Hodgkin's disease (MHD) exposes long survivors to late cardiac complications. The aim of this study is to evaluate the doses received by the heart, the left ventricle (LV) and the left anterior descending (LAD) artery in case of mediastinal irradiation of Hodgkin lymphoma.
Methods: Nine patients were treated for mediastinal MHD in the radiotherapy department of the Farhat Hached Hospital, over a period of 6 years (2014 _2020). The LV and the LAD artery were delineated retrospectively as organs at risk in the same simulation scanner on which the RT was planned.
Results: The mean age was 15.3 years; the sex ratio was 4/5. The circumstance of discovery was mostly a cervical adenopathy. The patients were classified as stage II (n=5), stage III (n=2) and stage IV (n=2) respectively. All patients received ABVD or BEACOPP chemotherapy followed by 3D-conformal RT of initial affected sites at a dose of 30Gy in 15 fractions +/- boost of 6 Gy on residual sites for stage II and RT of residual sites at a dose of 36Gy in 18 fractions for stages III and IV. Delineation of cardiac substructures was performed by radiation therapy residents with reference to the Contouring Atlas of Duanes et al. Dosimetric datas were collected from the planning software. Dose averages were for the heart (Mean Dose/Max Dose=8.4Gy/32.13Gy), LAD artery (Mean Dose/Max Dose=3.44/ 18.13 Gy), and LV (Mean Dose/Max Dose= 1.88 Gy/14.54 Gy), respectively. After a mean follow-up of 30 months, none of our patients presented a major cardiac event.
Conclusions: The new RT techniques in the treatment of mediastinal MHD may lead to heterogeneity of dose distribution in the heart; indeed, constraints based on the mean heart dose underestimate the cardiac risk associated with RT; the involvement of cardiac substructures influences the cardiovascular prognosis of the patient.

P003 / #1318

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

RADIOTHERAPY FOR NON-METASTATIC WILMS TUMOR

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Background and Aims: Wilms tumor (WT) is the most common malignant renal tumor in children. Current results aftermultidisciplinary treatment, especially for non metastatic WT, are excellent with long-term cure rates greater than 85%. Our aim is to describe clinical characteristics and therapeutic results of non metastatic WT in a Tunisian population.
Methods: Descriptive study of 14 patients with non metastatic WT treated in the Radiation Oncology Departement of the Farhat Hached Hospital, Sousse, Tunisia between 1995 and 2019.
Results: Of 24 patients with WT treated, 14 patients had localized disease.The median age was 54 months [18 - 216 months], with a slight female predominance [sex ratio =0.55].The stage distribution of the tumors was stage I in1 patient, stage II in 3, and stage III in10 patients. Treatment was based on the SIOP9 and SIOP93-01 protocols. All patients received upfront chemotherapy followed by nephrectomy.The histology was of intermediate risk in10cases and high risk in 4. Radiotherapy(RT) was indicated in13 cases. two patients were lost of sight before RT.The median time between surgeryand RT was 18 weeks. All patients received flank RT, the average dose was 25.9 Gy [14.4-36Gy] with 1.6-1.8Gy/day using two-dimensional RT in 5 cases and three-dimensional conformal RT in 6 cases. RT was delivered within an average time of 22 days. Overall tolerance was good. Local recurrence was observed in 2 patients, those who abondonned treatment,treated by chemotherapy, surgery, and flank RT and metastatic relapse in 1 case treated by chemotherapy and bipulmonary RT. After a median follow-up of 101 months; 12 patients were in complete remission and 2 patients died.The 5 year survival rate was 85%.
Conclusions: In our population, the characteristics of WT are mostly similar to those reported in the literature. Thus, with appropriate treatment, an excellent outcome can be achieved in most cases.

P004 / #1338

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

EWING SARCOMA IN CHILDREN : EXPERIENCE OF A TUNISIAN CENTER

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Background and Aims: Ewing sarcoma (ES) is a rare, aggressive malignant bone tumor that primarily affects children and adolescents. It represents 10 to 15% malignant bone tumors and 40 to 45% pediatric malignant bone tumors.It is part of neuroectodermal tumors with high metastatic potential. The purpose of this study was to investigate patient characteristics, treatment strategies, and outcomes of Ewing sarcoma.
Methods: From January 2005 to June 2021, 12 patients <18 years of age with histologically confirmed Ewing sarcoma were enrolled. Data were collected in the radiation therapy department at the University Hospital Farhat Hached, Sousse, Tunisia.
Results: The median age was 11.25 years. The sex-ratio was 1. Local pain was the initial symptom in 84%.A palpable mass was noted in 33% of patients at the first visit. The diagnosis of ES was confirmed by immunohistochemistry.The most frequent location was in the femur (11.5%). In relation to the axial skeleton, the spine bone was the most common location affected.Initially metastatic disease was observed in only 3 cases.In the majority of our patients therapeutic approach was based on induction chemotherapy followed by surgery and /or radiotherapy followed by consolidation chemotherapy. Euro-Ewing 99 protocol was the most frequently used (91.6%). Nine children underwent 3D (5 patients) or 2D (4 patients) radiotherapy with curative purposes (doses between 45 - 50.4Gy) and three patients with palliative purpose.Overall survival at 5 years was 90% while 5-year progression-free survival was 38%.The prognosis in cases of Ewing's sarcoma was mainly influenced by the presence of metastases at the time of diagnosis
Conclusions: The treatment strategy for ES is characterized by multi-disciplinary collaboration. New approaches include anti-angiogenic therapy, particularly since vascular endothelial growth factor is an apparent downstream target of the ews-fli1 oncogene.

P005 / #1365

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

MANAGEMENT OF PEDIATRIC MEDULLOBLASTOMA IN SOUSSE : ABOUT 26 CASES

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Background and Aims: Medulloblastoma (MD) is the most common malignant brain tumor in children,comprising 40% of all childhood posterior fossa (PF) tumors. It is potentially curable, and prognosis depends of the likehood of disseminated disease at the time of diagnosis. The purpose of this study was to describe clinical characteristics, treatment strategies, and outcomes of MD.
Methods: We retrospectively reviewed 26 patients treated for MD in the Farhat Hached Hospital, Sousse, Tunisia between 1996 and 2020.
Results: Median age was 7.8 years (1-15) with a sex ratio of 1.The main reason for consultation was intracranial hypertension syndrome in 13 patients with an average consultation time of 2 months.Cerebral spinal fluid involvement was detected in 5 children.Overall,25 patients had gross or near-total surgical resection. It was incompleteonly in 5 cases. Histologically, MD subtypes were distributed as follows :4 desmoplasmic,4 classic,2 with extensive nodularity and 1 anaplastic.9 infants were categorized as having high-risk disease.Radiotherapy(RT) was indicated to all patients but only delivered to 24 at a dose of 23.4 to 36Gy (1.8Gy/fraction) to the craniospinal axis with a complement in the PF at a dose of 54 to 56 Gy.21 patients received adjuvant Chemotherapy(CT) and 8 had concomitant RT-CT. 4 patients kept neurological sequelae of which 2 had gait impairment,1 neurocognitive disorders and 1 kept a kineticmutism. Eleven relapses (42.3%) were observed after median time of 11 months (3-76) mostly localized in the PF (87.5%). Reirradiation was performed in one case at a dose of 15 Gy in the PF. After a mean follow-up of 39 months,11 deaths were noted,13 children were in full remission and 2 lost to follow up. Median overall survival was 22.5 months (2-248).
Conclusions: In accordance with the literature data, our study suggest a potential survival benefit from multimodal treatment in pediatric MD but recurrence remains high with a rate exceeding 30%.

P006 / #1409

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

IMAGING CHANGES IN PEDIATRIC EPENDYMOMA PATIENTS TREATED WITH PROTON BEAM RADIATION THERAPY

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Background and Aims: To describe the imaging changes in pediatric ependymomas patients treated by proton therapy and trying to find an explanation by reviewing dosimetry.
Methods: Descriptive study including 4 children with ependymoma treated by proton therapy at the Proton Therapy Center in Orsay between August 2015 and June 2016 and who have developed imaging changes at the MRI of control.For each case a fusion between CT and MRI was performed.
Results: 4 girls, aged between 18 months and 5 years (median 2 ½ years). The tumor was supratentorial in 3 cases and infra tentorial in one case. All children had surgery. The surgical time to proton therapy was 41.25 days (range: 28 - 60 days). All children received proton therapy. The doses varied from 54 to 59.4 GyE (Median, 58 GyE). These 4 children presented imaging changes :T2 Flair hypersignal for all children associated with a T1 hypersignal in one case. The average time to appear for these images was 3.25 months (range 1 month-4 months). Dosimetric analysis of these 4 cases showed that the the variability of RBE were incriminated in 2 patients (cases 1 and cases 4) . In case 3, these images can be explained by the high dose received by the brainstem (average dose: 50Gy).
Conclusions: In our study, the variability of RBE and the high dose received by the brainstem were very likely responsible for these imagingchanges. It is necessary to confirm these data by having more follow-up and important series To carry out prospective studies.

P007 / #1808

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

GONADAL DAMAGE FOLLOWING TREATMENT OF MEDULLOBLASTOMA IN CHILHOOOD

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Background and Aims: Cranio-spinal irradiation (CSI) for medulloblastoma (MB) can impair fertility. Gonadal failure can result from either gonadotropin deficiency, caused by radiation to the brain or direct damage to the gonads following spinal radiation therapy (RT). The objective of the current study is to estimate the gonade dose received during CSI in pediatric MB.
Methods: We studied retrospectively 5 boys and 6 girls treated by postoperative CSI for MB in the radiation oncology department,Farhat Hached hospital,Sousse,Tunisia between 2015 and 2020.
Results: All patients were prepubertal at diagnosis.The mean age was 5.5 years (4-10 years) with a sex ratio of 0.8 (M/F). Tumors were classified into high risk (50%) and standard risk (50%) MB. After total surgical removal of the tumor, each child received three-dimensional conformational RT at a dose of 23.4 Gy to 36 Gy on the cerebrospinal axis with boost in the posterior fossa up to 54 Gy.The maximum average dose delivered to gonads was 0.85 Gy (0.004-2.1 Gy).The maximum mean doses delivered to testes and ovaries were respectively 0,5 Gy (0.1-1.7 Gy) and 1.1 Gy (0.004-2.1 Gy). The pubertal status of each was defined by the staging technique of Tanner and the hormone blood tests.After an average time of 15.5 months (6-29 months),all 5 boys had normal testes and normal testosterone concentrations for their stage of pubertal development.Two boys spontaneously progressed through puberty.For our 6 girls, the ovaries dose estimation enabled us to be counselled about future ovarian function and fertility because they hadn’t yet reached menarche.
Conclusions: The Dmax of gonads is 3 Gy.It was largely respected in our series without impact on gonadal function temporarily.The risk of gonadal failure from CSI should be further reduced and possibly eliminated if proton therapy is used because there is no scatter dose to the gonads.

P008 / #919

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

AN UPDATE OF TREATMENT OUTCOME OF PAEDIATRIC MEDULLOBLASTOMA – A SINGLE INSTITUTION EXPERIENCE IN SABAH WOMEN AND CHILDREN'S HOSPITAL, EAST MALAYSIA

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Background and Aims: Treatment of paediatric medulloblastoma has improved but remains a challenge in low and middle-income countries. This study aims to present the demography and treatment outcome of paediatric medulloblastoma at Sabah Women and Children's Hospital in East Malaysia.
Methods: This is a 7-year retrospective study. Seventeen children were identified between 2015 and 2021. Four were excluded, one due to missing records while three did not fulfil the treatment criteria. The data was analysed using SPSS version 25.
Results: The mean age at diagnosis is 7.6 years (range from 3.1 to 13.2 years). 53.8% are female. Vomiting, headache and ataxia are the commonest presenting symptoms. Median interval between symptom onset and diagnosis was 7 weeks (range from 4 to 24 weeks). Six children presented with metastatic disease. Eleven children (84.6%) were categorized into high risk group. Histological subtype was reported as classic medulloblastoma for all children except for one without record in the histopathological report. Five children (38.5%) received radiotherapy within ≤5 weeks of surgical resection. Four children (30.8%) completed radiotherapy within 45 days. All children received craniospinal irradiation and tumour bed boost with additional spinal boost for two children, followed by chemotherapy with CH 455 Packer Protocol. With a mean follow-up of 33 months (range from 12 to 64 months), the 3 year progression free survival rate is 76.4% ±15.5%. Two children have relapse at 15 and 36 months respectively, including one with delayed maintenance chemotherapy due to logistic issue. As of March 2022, ten children are still living with three lost to follow-up. Hearing impairment and hypothyroidism were noted in 7 (53.8%) and 6 (46.2%) children respectively.
Conclusions: Our study showed good treatment outcome in children treated for medulloblastoma. Optimisation of treatment delivery and logistic support may improve the outcome of paediatric medulloblastoma. However further study is needed to address these challenges as well as to assess overall survival and long term complications.

P009 / #268

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

HEALTH-RELATED QUALITY OF LIFE OUTCOMES FOLLOWING PHOTON AND PROTON RADIATION THERAPY FOR CHILDHOOD CANCER

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Background and Aims: Childhood cancer survivors have a risk of late effects secondary to treatment. Due to its unique dose deposition, proton beam therapy (PBT) has the potential to reduce the incidence and severity of toxicities relative to conventional photon radiation therapy (XRT), which may translate into improvements in Health-Related Quality of Life (HRQoL). This systematic review summarises the evidence of HRQoL in childhood cancer survivors following PBT and XRT.
Methods: Medline, Embase and Scopus were systematically searched. Studies were included if they collected HRQoL data from children diagnosed with cancer, using a validated patient-reported outcome measure, and included patients treated with external beam radiation therapy (PBT or XRT) after the year 2000.
Results: Fourteen cross-sectional, 15 longitudinal and one mixed methods study were analysed to describe 1,986 childhood cancer survivors. There were minimal differences in HRQoL after XRT or PBT. HRQoL for children with a central nervous system tumour treated with XRT or PBT, captured by Pediatric Quality of Life Inventory Generic Core total score, improved with time from treatment delivery. However, the change over time could not be quantified due to many studies including participants at variable time-points following treatment, within a single cohort. No studies analysed the implementation of routine HRQoL assessment during pediatric radiation oncology clinical practice. No studies described actioning severe or declining HRQoL outcomes.
Conclusions: Based on the current available evidence, HRQoL outcomes for children receiving XRT or PBT are similar. HRQoL outcomes for children diagnosed with a central nervous system tumour improve with time from radiation therapy. Recommendations for clinicians and researchers include the routine collection of pre-treatment HRQoL baseline assessments, implementation of HRQoL assessment into clinical practice to action poor patient outcomes, and improved reporting of radiation dosimetry to identify the impact of prescribed dose.

P010 / #356

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

REPORTED DENTAL TOXICITIES AFTER PROTON BEAM THERAPY FOR PAEDIATRIC HEAD AND NECK CANCERS.

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Background and Aims: It is known from the literature that the nature and severity of dental disturbances is inversely related to a patient's age and stage of tooth development at the time of radiotherapy. Despite this, dental toxicities after radiotherapy are often underreported and there is very limited published data following proton beam therapy (PBT). This service development project aimed to establish the reported incidence of tooth development disorders in patients treated with PBT within the Proton Overseas Programme (POP).
Methods: Clinical follow-up data of patients treated with PBT within the POP is stored in a national database and curated by a dedicated outcomes unit at The Christie NHS Foundation Trust. A retrospective service evaluation utilising this data was conducted to evaluate the documented assessment of dental toxicities in paediatric head and neck (H&N) cancer patients treated in the POP.
Results: From 2008-2019, 195 paediatric were treated for H&N malignancies within the POP, and toxicities grade 3+ were prospectively recorded. Tooth development disorders were recorded by clinicians at scheduled outcome appointments in four patients (median follow-up 5 years). Of note, the permanent dentition in one patient aged 3.5 years at the time of treatment has severe abnormal tooth development first observed 3.5 years post-treatment. For this patient, mean doses of 30Gy and 14.1Gy(RBE=1.1) were delivered to the maxilla and mandible respectively, and were correlated to the dental findings.
Conclusions: The dose threshold for tooth development disorders following either PBT or conventional photon radiotherapy remains unknown. It is recommended that the dose to teeth is kept as low as reasonably possible in younger patients, with a proposed restriction of <20Gy in patients <4 years old. The findings in the presented patient suggest that dental disturbances can occur with doses <10Gy(RBE=1.1). Further studies evaluating the long-term effect of PBT on dental development in paediatric H&N patients is encouraged.

P011 / #1979

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

OUTCOMES OF PEDIATRIC EPENDYMOMA TREATED AT A SINGLE TERTIARY CENTER IN MEXICO

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Background and Aims: Ependymoma is one of the most frequent primary brain tumors in children. Gross total resection is associated with improved survival outcomes. Adjuvant radiotherapy (RT) is considered for most cases.
Methods: We performed a retrospective review of pediatric patients treated last decade at our center for intracranial ependymoma with the objective to describe 5-year event free survival (EFS) and overall survival (OS). Variables included on analysis were: Tumor grade, tumor location, extent of resection, time between surgery and RT, RT duration and extent of residual tumor after RT.
Results: Twelve patients were treated with surgery and adjuvant RT between 2011 and 2021. Mean age was 9.2 years (2-20), 50% had tumors grade 2, 58% had supratentorial tumors, only one patient (8%) presented with metastatic disease. Only 33% of the patients had gross total resection (GTR), mean time between surgery and RT was 98 days (34-243), mean time of RT duration was 51 days (41-72). Of the patients without GTR, only in 2 out of 7 the residual tumor disappeared after RT. Five-year EFS was 55% and OS was 71%, no variable was associated with improved outcomes. Two out of 5 patients with residual tumor after radiotherapy had tumor progression.
Conclusions: Survival outcomes of our patients were acceptable compared to what is reported on literature, even with subtotal resections performed in two thirds of our patients.

P012 / #1847

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

DOSE RECEIVED BY THE SCALP AFTER RADIOTHERAPY FOR PEDIATRIC MEDULLOBLASTOMA

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Background and Aims: Medulloblastoma accounts for nearly 10% of all childhood brain tumors. These tumors occur exclusively in the posterior fossa. Radiation therapy (RT) remains a critical component of multimodality treatment for medulloblastoma , wich have largely evolved resulting in better survival rates. Nevertheless, long-term toxicity is a major concern in this setting.
Methods: A retrospective study of 14 patients diagnosed with medulloblastoma in the department of radiotherapy of Farhat Hached hospital between 2013 and 2021.
Results: The average age was 6 years (4-15 years) .There were 4 girls and 10 boys .The most common manifestations were ataxia . Diagnosis was confirmed by characteristic imaging on Magnetic Resonance Imaging. It was commonly presented as midline masses in the roof of the 4th ventricle with associated mass effect and hydrocephalus .The average tumor size was 43 mm (17-55 mm) .Five patients had presented bone marrow enhancement related to metastasis ,wich were confirmed by a lumbar puncture. Nine patients had ventriculoperitoneal shunt placement. All patients underwent surgery. The excision was complete in 73% of cases . Almost all patients were treated with concurrent chemotherapy .All patients were treated with conformal RT.The median RT dose was 54 Grays (30-54Gy) in the posterior fossa , and 36Gy (23.6-36Gy) in the craniospinal axis . The average RT dose received by the scalp was 34 Gy (32-38Gy).Acute alopecia was presented in 50% of cases commonly localized in the occiput.It was grade 3 in half of the cases. After a median follow up of 10 months (4-96 months),10 patients was in complete remission ,with persistent alopecia in 2 cases.Four patients had metastasic progression,3 of them died.
Conclusions: Cranial irradiation for medulloblastoma can causes inevitable alopecia ,wich can affect the survived children’s self image.Therefore we suggest to contour the scalp as an organ at risk to minimize the dose received by it.

P013 / #1957

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

PLACE OF RADIOTHERAPY IN THE TREATMENT OF HIGH RISK NEUROBLASTOMA

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Background and Aims: Neuroblastoma is the most common extracranial solid tumor in children, accounting for approximately 8% of all childhood cancers and 15% of childhood cancer mortality. We shared here our experience, in the treatment of children with high-risk neuroblastoma treated with radiotherapy. This work study is as an overview of the current treatment, for high-risk neuroblastoma and a glimpse at current research for future therapy.
Methods: We carried out an analytical descriptive retrospective study, between January 2008 and September 2019, concerning 165 cases of neuroblastoma, 32 patients had high-risk neuroblastoma indicating radiotherapy, with a minimum of two years of follow-up.
Results: Our patients received an induction phase of intensive chemotherapy according to the national protocol, followed by surgery when possible, then a consolidation phase consisting of high-dose chemotherapy with stem cell transplantation, external radiotherapy, and a final maintenance phase. In our series the radiation dose was 21.6 Gy. All patients were irradiated by conventional fractionation. At the end of the treatment 22 patients were in general response, four patients failed, three patients lost to follow-up at the end of radiotherapy and three patients were in local response but with the persistence of metastases. After a decline of twenty four months, the overall survival rate was fifty eight percent. The median survival of our series was twenty months, and the relapse-free survival at twenty-four months, was ten percent.
Conclusions: Current research is focusing on further intensification of therapy to improve outcomes and evaluating the role of precision medicine in this patient population.

P014 / #941

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

PILOT STUDY OF THE ITALIAN VERSION OF THE PEDSQL™ HEALTHCARE SATISFACTION HEMATOLOGY/ONCOLOGY MODULE WITH PARENTS OF CHILDREN UNDERGOING RADIOTHERAPY.

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Background and Aims: Several studies have shown a significant relationship between healthcare satisfaction and health-related attitudes and behaviours. The assessment of parental satisfaction is assuming an increasingly important role also in paediatric oncology. In our Radiotherapy department a Multi-professional Group (MPG) has been established. MPG aimed to a multidimensional assessment of pediatric patients (PP) and introduced specific action, such as psychological preparation and support, and specific tools (audiovisual, digital, etc.) during radiotherapy care-path. MPG felt the need to measure parents' health satisfaction. After elaborating the Italian translation of the PedsQL™ module for health satisfaction in Oncology/Hematology, they started to administer it to parents during their child's radiotherapy treatment.
Methods: The questionnaire consists in 25 item scale grouped in 6 domains: General Satisfaction, Information, Inclusion of Family, Communication, Technical Skills, Emotional Needs. A 5-point Likert responses scale is utilized, from 1 (Very dissatisfied) to 5 (Very satisfied). Linearly transformed to a 0-100 scale was performed, then mean score was reported by dimension. The questionnaire was delivered in the last radiotherapy week by a physician not involved in MPG.
Results: Fifteen parents were recruited and the return rate of the questionnaire was optimal. For all domains the mean score was very high with a mean value >85: mean score for General Satisfaction was 94, for Information was 85, for Inclusion of Family was 87, for Communication was 88, for Technical Skills was 88 and for Emotional Needs 90.
Conclusions: These preliminary results demonstrate that an assessment of parental satisfaction could provide valuable information on the children's radiotherapy pathway and help clinicians to improve quality standards of care.

P015 / #1387

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

THE DREAMS CHEST PROJECT EXPERIENCE: TOKEN ECONOMY FOR INCREASING COMPLIANCE IN PEDIATRIC RADIOTHERAPY

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Background and Aims: Radiotherapy (RT) has become an important treatment modality in pediatric oncology, but its delivery to young children with cancer is challenging and general anesthesia is often needed. The efficacy of psychoeducational interventions to increase treatment adherence and compliance of the pediatric patient in radiotherapy has now been widely demonstrated in the literature, with a reduction in the need for anesthesia and a consequent significant reduction in costs for the national health system. In our center, a dedicated multidisciplinary team aims to increase children's confidence in radiotherapy staff, space, and procedure, and consequently reduce the frequency of sedation.
Methods: Among the psychosocial interventions carried out, specific for the ages, we started the project "the Dreams Chest". The project involved all the pediatric patients in radiotherapy and offer them the opportunity to choose and receive a present on the last day of their therapy. The project is based on the rationale of the token economy method, where today's radiotherapy session is considered a "token" to reach the treasure.
Results: More than 400 children expressed their dreams through this project, thanks to a large number of donors and large and small companies who paid for the gifts. The project has proved to be a useful tool for engaging patients from the first visit, and also to create a community that supports children and their families. In this way also the value of the gift, even if with a fixed budget of 40 euros, becomes a personal value of a co-created path. This contributed to a 6% reduction in sedation, which corresponds to an average savings of more than 45000€ in 2021.
Conclusions: The token economy project is an economically sustainable method that can help increase adherence to radiotherapy in pediatric patients and reduce the use of anesthesia, resulting in lower healthcare costs.

P016 / #1356

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

EARLY REPORT ON FEASIBILITY AND EFFICACY OF PERCUTANEOUS CT-GUIDED CRYOABLASTION OF PULMONARY METASTASIS IN CHILDREN AND YOUNG ADULTS

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Background and Aims: The lung is a common site of malignancy metastasis; while metastasectomy has long been the standard of care for many tumor types, many patients are not surgical candidates due to disease burden, lesion location, or general patient state. The development of less invasive methods of local therapy has allowed a higher proportion of patients with pulmonary metastases to receive local therapy. However, the use of this approach in pediatric patients has never been documented. The aim of our study was to assess if percutaneous CT-guided cryoablation is technically feasible and clinically effective to treat pulmonary metastasis in children and young adults.
Methods: Patients with lung metastasis treated with CT-guided cryoablation from January 2019 to January 2022 were reported. The procedure was performed with two cycles of 10 minutes each from -20°C to -40°C core temperature, followed by 5 minutes of thawing. Demographic data, radiological and clinical issues were collected.
Results: Five patients (median age: 12.88 years; range 9.43-24.01 years) with pulmonary metastasis treated with CT-guided cryoablation were included in the study. Two Ewing sarcomas (one of the rib and one of the leg), one Wilms tumor, one embryonal sarcoma of the limb, and one clear-cell sarcoma of the foot were the initial malignancies. Three lung metastases were found in the latter patient. Seven total lesions were treated with CT-guided cryoablation. After median 6.53 months follow-up (range 0.77-11.306 months), six lesions presented dimensional reduction (median 40.88%; range 20.92-60.47%). The patient with embryonal rhabdomyosarcoma developed metastasis progression (35.71% of dimensional increase); additionally, unlike all other metastasis, this lesion had a ground-glass halo. No major or minor complications were reported.
Conclusions: Regardless of the histology and clinical features of the primary tumor, percutaneous CT-guided cryoablation is a safe, minimally invasive approach for treating lung metastases in children and young adults.

P017 / #1718

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

DOSIMETRIC IMPACT OF TUMOR TREATING FIELDS TRANSDUCER ARRAYS ON CONCURRENT RADIATION THERAPY FOR PEDIATRIC BRAIN TUMORS

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Background and Aims: Previous results suggest that tumor treating fields (TTF) concurrent with radiotherapy (RT) for glioblastoma yields acceptable dosimetry in adults; the impact of TTF on RT dose distribution in children is unknown. This study was undertaken to evaluate the dosimetric impact of TTF transducer arrays on concurrent photon RT for children with brain tumors.
Methods: CT scans of an anthropomorphic pediatric head phantom (approximately 15-year-old) and an infant-head-sized spherical phantom were acquired with and without the arrays. For an infratentorial tumor, clinical targets and a VMAT treatment plan (54Gy/50Gy to gross tumor volume [GTV]/clinical tumor volume [CTV] in 30 fractions) were transferred to the phantoms CT sets. For a supratentorial tumor, treatment plans were created (60Gy/50Gy to GTV/CTV in 30 fractions) for simulated targets on the phantom CT sets. For each tumor location, dose distributions were computed and compared with and without the arrays. Target coverage metrics were compared, and skin dose was measured with thermoluminescent and film dosimeters when the same plan was delivered with and without the arrays.
Results: For the infratentorial tumor, the arrays reduced CTV D95 by 0.48% and 1.04%, and GTV D95 by 0.31% and 1.41% for the two phantoms respectively; they increased skin Dmean by 1.10% and 4.09% respectively from planning study. For the supratentorial tumor, the reduction in target coverage was all <1.0%. Electrodes under the direct beam path increased skin dose by an average of 43.3% (0.3Gy – 20.7Gy), but all skin dose measurements stayed within tolerance.
Conclusions: The dosimetric impact of TTF on pediatric head phantoms receiving concurrent RT resembles that reported in adult studies. Although the tumor dose is not significantly affected, the skin dose notably increases due to the bolus effect from the TTF electrodes, which may be mitigated by skin-sparing planning and shifting of the device during RT.

P018 / #903

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

THE ROLE OF INTERDISCIPLINARY MANAGEMENT OF CHILDREN WITH CRANIOPHARYNGIOMA

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Background and Aims: An analysis of the outcome of children with craniopharyngioma.
Methods: A retrospective analysis of patients below 21 years old treated due to craniopharyngioma in years 1971-2018 was performed. Standard statistical tests were used
Results: A total number of 41 patients (median age of 12 years old)was evaluated. The most common symptoms were headaches(63%), nausea/vomiting(37%), visual disturbances(44%) and endocrine disorders(20%). Surgery was primary treatment in 40 patients, however only in 20 it was the only one neurosurgical intervention. Two,three and five surgeries were conducted in 12,6&2 cases, respectively. Thirteen children had shunt placed. After the surgery endocrine deficits and visual disturbances were present in 72%&57% patients,respectively. Radiotherapy (RT) was applied in 38 children (in 40% in primary treatment). Stereotactic RT was conducted in 13 cases with median fraction and total dose of 6Gy&15Gy,respectively. Conventional RT was applied in 25 cases (median total dose of 54Gy) combined in 4 patients with 5-6Gy stereotactic boost. Complications after RT were diagnosed in 13 cases with the most common endocrine deficits (in 4),vasculopathies (3) and secondary tumors (in 2 cases). Median follow-up from the date of diagnosis was 13 years. During that time 6 patients died and 5-,10-&15-years overall survival was 97%,92%&92%,respectively. The only factor found to have positive impact on the survival was the lack of endocrine deficits before the first surgery(p=0.006). The outcome of RT was evaluated in 35 cases with stagnation and partial regression observed in 19&16 cases, respectively. Progression after RT was diagnosed in 9 cases and median progression free survival (PFS) was 7.1year. Five-&10-years PFS was 85%&71%, respectively. Repeated RT was applied as part of recurrence treatment in case of 5 children.
Conclusions: Surgery combined with RT provides satisfactory long-term outcome in majority of craniopharyngioma patients. The impact of endocrine deficits and the time of their onset on survival requires further studies.

P019 / #1093

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

MULTIDISCIPLINARY TEAM EXPERIENCE OF 39 VERSUS 13 FRACTIONS OF RADIOTHERAPY FOR TREATMENT OF DIFFUSE MIDLINE GLIOMA AT A NATIONAL REFERRAL CENTRE

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Background and Aims: The prognosis of diffuse midline glioma (previously diffuse intrinsic pontine glioma) remains poor, with a 5-year survival rate of less than 1%. Conventional radiotherapy remains the mainstay of treatment, with a total radiation dosage of 5,400 cGy to the tumour, delivered in 30 fractions (30#) over 6 weeks, considered standard. However, hypofractionated radiotherapy, with 3,900 cGy delivered in 13 fractions (13#) over 2.5 weeks, is increasingly being used. This study aimed to explore the experiences and perceptions of a paediatric oncology multidisciplinary team (MDT) at a national referral centre for radiotherapy and explore opportunities and challenges of the two treatment options.
Methods: A focus group representative of the MDT including medical, nursing, and allied health professionals was formed. The group identified opportunities and challenges of both treatment options from their own professional perspectives. Themes were further identified, and a survey was created to understand the extent of MDT consensus regarding opportunities and challenges of both treatment options using a Likert-type scale.
Results: Survey responses demonstrated strong consensus across the themes identified by the focus group. Respondents felt 30# allowed more opportunities and greater flexibility for MDT input to facilitate quality intervention, and provided opportunities to develop trust and rapport with patients and their caregivers. However, longer hospital admissions had emotional impacts on patients, their families, and health professionals. 13# was felt to result in lesser burden on patients and families. However, it often resulted in reduced opportunities to facilitate adequate rehabilitation and to manage certain aspects of the patient’s holistic care.
Conclusions: Both treatment options offered differing opportunities and challenges. Given it is generally accepted both treatment options have comparable results, decisions regarding which option to take should carefully consider the opportunities and challenges. This study identified only professional perspectives and further research is needed to understand perspectives of children and their caregivers.

P020 / #1497

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

TWO-YEAR EXPERIENCE OF A NEW PROTON FACILITY IN MADRID TREATING PEDIATRIC CANCER PATIENTS DURING THE COVID PANDEMIC

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Background and Aims: We summarize our experience treating Pediatric cancer patients in the Clínica Universidad de Navarra Proton Facility since its opening in May 2020, in the midst of the COVID19 pandemic.
Methods: We retrospectively review the charts of the Pediatric patients treated with proton therapy at our institution.
Results: Between May 2020 and April 2022, 96 patients received treatment (46 males). Median age was 8.4 years (range, 1.2 – 19.4). Forty-nine percent required anaesthesia. The median number of days elapsed between the simulation and the start of the treatment were 13.5 days (range, 6-49). The most frequent tumours were: 66% central nervous system; 23% sarcomas; 4% head and neck tumors, among others. Twenty-five patients received radiation at relapse (7 of them received re-irradiation). Treatment modality consisted in focal radiation (69%), craniospinal (27%), whole ventricular (3%), and holocranial (1%). Median dose was 54 Gy (range, 15-72Gy) focal, and 36 Gy (range, 18- 36 Gy) craniospinal. Thirty-six patients received concomitant chemotherapy. All patients completed their treatment plan. The non-hematological toxicity grade≥3 occurred in 6 patients (radiodermatitis, central venous catheter infection, febrile neutropenia, Clostridioides difficile, sepsis and hypernatremia). The hematologic toxicity grade≥3 was related to concomitant chemotherapy, craniospinal irradiation or both. During the pandemic, 8 COVID19 infections were diagnosed, 6 asymptomatic and 2 mild symptoms. In 3 patients the start of radiation was delayed. However, in 2 patients with high-risk CNS tumors treated with chemotherapy and radiation, treatment was not discontinued. The median follow-up was 6.4 months (range, 0-21.3 months). Current status of the patients: alive without disease 68.8%; active treatment 17.2%; alive with disease 9.7%; deceased 4%.
Conclusions: The opening of the Proton Therapy Unit has allowed access to this type of precision radiotherapy in Spain, favouring communication between Pediatric oncology institutions and avoiding international travel. The COVID19 pandemic did not affect the treatment of these patients.

P021 / #1487

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

CONTRALATERAL LENS DOSE IN CURATIVE RADIATION TREATMENT PLANS FOR ORBITAL AND PARAMENINGEAL RHABDOMYOSARCOMA – A SIGLE CENTER EXPERIENCE

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Background and Aims: Radiation therapy is a curative local treatment for parameningeal rhabdomyosarcoma (RMS) with good outcome but can have long term effects due to radiosensitivity of normal structures like lens. Our aim is to evaluate dose distribution to contralateral lens patients with paramenigeal or orbital RMS treated at our institute.
Methods: Institutional record was searched for children treated with radiotherapy between January,2009 till May,2021 for non-metastatic RMS of orbit or parameningeal primary. Radiation treatment plans were reviewed for dose distribution to contralateral lens. Mean lens dose was reviewed and tolerance dose criteria (<6Gy) was evaluated. All plans were peer reviewed according to departmental protocol. Treatment site, total dose prescribed, treatment volume crossing midline or not and planning technique (3DCRT or IMRT) were reviewed.
Results: A total of 59patients of RMS were identified. The mean age was 6.8years (1–18years) with 41(69%)males. A total of 44patients(75%) were treated for parameningeal RMS with dose ranging from 37Gy-56Gy while 15(25%) patients received RT to orbit only with dose ranges of 36-56Gy. Average Dmax of contralateral lens was 4.7Gy in patients treated for orbital RMS and 5.3Gy for patients with parameningeal RMS. A total of 23(39%) patients were planned with 3DCRT and 36(61%) with IMRT both having average Dmax of 4.7Gy for contralateral lens. Average Mean dose received by contralateral lens in 3DCRT was 1Gy(0.57-3.4Gy) and 6Gy(0.3-45 Gy) with IMRT. Treatment volume was crossing midline in 27(79%) patients with IMRT and 7(21%) patients with 3DCRT. All the patients met tolerance dose criteria except 2 patients whose treatment volume was crossing the midline.
Conclusions: Our study has shown that mean dose distribution to contralateral lens was found to be lower with 3DCRT and depends on treatment volume crossing midline. We recommend each patients plan should be individually evaluated with peer review by physician and physicists for planning with 3DCRT or IMRT technique.

P022 / #1904

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

SERVICE PROVISION GAPS IN PEDIATRIC RADIOTHERAPY DURING COVID 19 PANDEMIC AT A TERTIARY CARE UNIVERSITY HOSPITAL IN PAKISTAN

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Background and Aims: The aim of this study was to review the service provision delays in radiation therapy for children treated at a tertiary care university hospital in a developing country, and identify the reasons for those gaps.
Methods: Hospital database was reviewed for childred irradiated during covid-19 pandemic (March 2020 – October 2021),. Patients who had gap of one or more day in radiation planning and delivery were identified and analyzed.
Results: 128 pts were treated with mean age of 9.25 years(±5.41) of which 68%(n=87) were male and 40%(n=51) were treated under general anesthesia. Most common diagnoses included sarcomas(n=32), lymphomas(n=29), renal tumors (n=24) and CNS(n=14).Simulation was delayed in 27 patients. The commonest reason was fever/neutropenia in 37%(n=10), social reasons in 30%(n=8), anesthesia denied due to chest congestion in 26%(n=7)and covid positivity in 7%(n=2).Planning scan was cancelled in 16patients commonest reason being logistic in 50%(n=8), fever/neutropenia in 25%(n=4), unavailability of laboratory tests in 19%(n=3) and one was lost to follow-up. 45/127 (35%)patientsbeing planned for radiotherapy had cancellation at start of treatment delivery. Majority cancellations were due to fever/neutropenia in 28%(n=13), logistic reasons in 24%(n=11), covid positivity in 23%(n=10), 8%(n=4) each due to covid-PCR not done and anesthesia denied due to chest congestion. On-treatment delays of 125 irradiated patients were recorded.44 patients had treatment gaps of which, 1-2day gap was identified in 7% (n=3), 3-7day gap in 32% (n=14) patients, while a gap of 8days or more occurred in treatment of 57% (n=25) patients. Major reasons were fever/neutropenia in 48%(n=21), anesthesia denied due to chest congestion in 29.5%(n=13), social reasons in 13.6%(n=6), machine breakdown in 4.5%(n=2).
Conclusions: This study identifies barriers to care and identifies areas we need to work upon in this pandemic to provide continuous care to children with cance. Uninterrupted radiaiton treatment is required for achieving adequate local control as part of overall treament plan.

P023 / #394

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

REIRRADIATION (RE-RT) FOR HIGH-GRADE GLIOMA (HGG) IN A 10 YEAR-EXPERIENCE

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Background and Aims: Recurrence rate for paediatric/adolescent HGGs exceeds 80%. Radiotherapy(RT) remains the mainstay of relapse treatment for symptoms palliation and disease progression delay.
Methods: We re-evaluated charts, including MRI and RT plans, of 21 relapsed HGG patients, accrued 2010-2021, not DIPG/not included in open trials/not secondary, aged under 18 years. All had surgery (CR+PR in 14) before RT+chemotherapy(14 temozolomide,5 nimotuzumab+vinorelbine,2 sequential/HD-CT). Two had metastases, 3 gliomatosis, 1 two non-contiguous tumors; 10 glioblastoma,5 grade 3 HGG,5 diffuse-midline-glioma(DMG)H3.3 mutated, 1 not-defined HGG(all centrally reviewed).
Results: Fifteen had first RT on tumor bed(54 Gy), 4 whole brain(34-39.6 Gy), 1 craniospinal-CSI(35.2 Gy) and 1 on two sites(54 Gy). Median time to relapse/death were 11.5/23.5 months: relapse was local in 12(7 marginal),4 disseminated,5 local+disseminated. Re-RT obtained 8 SD,1 PR,1PsPD,1 mix response,10 PD; neurological signs/symptoms improved in 8, were stable in 3. Local reRT was given to 12(19.8-30.6 Gy), followed by 6 local(2 marginal) and 4 local+disseminated second relapses in 10/12 re-evaluated. The 4 with dissemination had 1 whole brain(30 Gy),2 CSI(30.6-39.6 Gy),1 spine(39.6 Gy)RT and further relapsed with dissemination(2) and locally+dissemination(1) in 3/four assessed. Five locally+disseminated tumors had 3 CSI(23.4-39.6), 1 spine(39.6) and 1 extended local(30 Gy) RT, further progressing locally(2),disseminated(1), psPD(1), n.a.(1). Three had a third RT; three were alive at 19.4,29 and 50.3 months after diagnosis. Median times to progression/survival after re-RT were 3.7 months(0.6-16.2 months)/6.9 months(0.6-17.9 months), significantly better for longer interval after 1st RT. Sex, grade and DMG diagnosis did not impact PFS/OS after re-RT. In this selected series of only relapsed patients 4/5 patients with CR vs 3/11 noCR/noM+ after surgery had a component of dissemination at relapse(P 0.038). No radionecrosis was appreciated.
Conclusions: This is the biggest series of re-RT in HGG. A randomized question could answer at reirradiation field extension and better fractionation for efficacy and quality of life improvement.

P024 / #1944

Topic: *AS02 Radiation Oncology - PROS - if accepted, the abstract will be presented in the radiation oncology programme*

HEAD AND NECK RHABDOMYOSARCOMA IN A LOW MIDDLE INCOME COUNTRY

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Background and Aims: Rhabdomyosarcoma (RMS) is a soft tissue mesenchymal tumor that accounts for 5% of all pediatric solid tumors. Thirty percent are head and neck RMS. The treatment is multidisciplinary, it is based on chemotherapy, surgery and radiotherapy. The Treatment depends on the tumor site.Objective: Discuss through the data of our series the clinical and evolutionary profile and the therapeutic results of pediatric RMS in particular in Tunisia wich is a lowmiddle income countris with dificuly acces to radiotherapy.
Methods: This is a retrospective observational series of 32 children with RMS collected and treated between 1993 and 2017 at the Salah Azaiz Institute (ISA) in Tunisia.
Results: There were 32 cases. median age was 5.5 years. The predominant revealing symptoms were: tumor syndrome (62.5%), proptosis (22%) and cranial nerve palsy (15.6%). The diagnosis was confirmed by surgical biopsy in 84.3% of cases. It was an embryonic RMS in 75% and alveolar in 21.9% . The location was orbital in 34.4% of cases and parameningeal in 21.9%. Twelve percent of patients had lymph node involvement. All patients were non-metastatic. 93.5% received chemotherapy. Thirty-one percent of patients had surgery, 60% with a complete resection, 10% with R1 resection and 30 with R2 resection. RT was delivered in 56.3% of cases at a median dose of 52 Gy (40-55Gy) with normfractionation. Forty-six percent of patients experienced a relapse after an average time of 7.3 months, 53.3% with local relapse, both local and distant relapse was noted for 33.3%. . At 8 months, 25% of patients were alive in complete remission, 46.8% alive in progression, 18.8% dead. in univariate and multivariate analysis, the only prognostic factor for survival was the surgical margins.
Conclusions: Surgical margin remains a strong prognostic factor for survival of patients with head and neck RMS espacially in our country with lack of acces to radiotherapy

P025 / #1421

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

PEDIATRIC HEMATOLOGY ONCOLOGY INTEGRATED PRACTICE UNIT (IPU) IN A TERTIARY CARE SETTING – AN INITIATIVE TO FACILITATE UNINTERRUPTED ACCESS TO CARE DURING THE COVID-19 PANDEMIC

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Background and Aims: Cancer patient experience series of events influencing overall well-being of the patient and families. Pediatric Hematology Oncology department at King Faisal Specialist Hospital & Research Centre, Riyadh serve as tertiary care referral center for cancer care and stem cell transplant. Our aim is to ensure access to uninterrupted cancer care during COVID-19 pandemic.
Methods: Integrated Practice Unit (IPU) covering cancer healthcare delivery adjusted during the pandemic and Hospital-metrics analysis and patient satisfaction outcomes comparing year 2020 (COVID-19 outbreak) to 2021 (living with COVID-19) reported
Results: Pediatric oncology IPU adjusted in response to the COVID-19 outbreak in 2020 through daily bed and operating room huddle and weekly interdisciplinary care rounds with prioritization of cases and procedures to facilitate uninterrupted therapy as pandemic evolves. An overall increase in new cases by 15% (544 cases in 2021 vs.471 cases in 2020), with 84% increase in outpatient productivity (16856 visits in 2021 vs. 13133 visits in 2020), while an overall inpatient productivity increased by 26% with admissions increased by 32% (1334 in 2021 vs.1009 in 2020), inpatient days increased by 36% (1366 days in 2021 vs. 1007 days in 2020) and bed occupancy increased by 15% (96% in 2021 vs. 81% in 2020), however Average Length of Stay (ALOS) reduced by 12% (13.6 days in 2021 vs. 15.5 days in 2020). Patient satisfaction improved by 5% with a major difference in inpatient satisfaction score by 8.5% (93.5% in 2021 vs. 85% in 2020). An increase in Stem Cell Transplantations (SCT) by 30% (137 SCT in 2021 vs. 105 SCT in 2020) observed
Conclusions: In our experience an existing oncology IPU, supported our ability to adapt and mitigate through evolving pandemic addressing full cycle of cancer care through comprehensive range of services, IPU demonstrated unexpected prospect in the face of adversity improving integration and communication throughout continuum of care

P026 / #794

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

ASSOCIATIONS BETWEEN SLEEP AND MENTAL HEALTH IN SURVIVORS OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: In North America, acute lymphoblastic leukemia (ALL) is the most common diagnosis for children and adolescents impacted by cancer. With advances in treatment, survival rates of survivors of childhood ALL have improved substantially over the past decade. However, survivors of childhood ALL live with chronic health problems related to their treatment, referred to as late effects. Among these late effects, fatigue, and mental health concerns are particularly prevalent. The current study therefore aimed to examine how mental health (depression and anxiety) is related to sleep in survivors of childhood ALL.
Methods: Survivors of childhood ALL (n = 45, 58% male, average 5 years since diagnosis) and between 8 and 18 years old (m_{age}=11.62, SD=2.62) at evaluation were asked to complete a daily sleep diary for 7 consecutive days to determine their wake after sleep onset (WASO) and total sleep time. Their parents completed questionnaires related to their child's mental health, and demographic information.
Results: Pearson's correlations were conducted to determine the relationship between sleep and mental health. Child anxiety was significantly related to total sleep time ($r=-0.076$, $p< .05$). Multiple regression analysis was conducted to determine predictors of sleep, including participant and clinical characteristics (gender, age at diagnosis) and mental health (child anxiety). The multiple regression was significant for predicting WASO $F(4,33)=140.831$ $p=0.049$ adjusted $r^2=0.153$. Age at diagnosis emerged as a significant positive predictor of WASO (standardized $B=0.400$, $p=0.018$) where older age at diagnosis predicted higher WASO.
Conclusions: Analysis revealed that those who were diagnosed older had more disrupted sleep and those who had higher anxiety had less overall sleep. Information on survivors' mental health and treatment variables may help provide targets for intervention to improve their quality of sleep and well-being.

P027 / #1466

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

UNIDOS PELA CURA: OUTCOMES OF THE CHILDHOOD CANCER EARLY DIAGNOSIS STRATEGY IN RIO DE JANEIRO, BRAZIL

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Background and Aims: In Brazil, childhood cancer is the leading cause of death by disease amongst children between 1 to 19 years old. This paper analyses the main results of the Unidos pela Cura (UPC) strategy, launched in 2005, with the goal to promote early diagnosis of childhood cancer in Rio de Janeiro. The UPC program comprises three strategies: training of primary care professionals to suspect cancer; systematization of a referral flow of suspected cancer cases within 72 hours from Primary Care to Specialized Hospitals; monitoring suspected cases referred to diagnostic confirmation.
Methods: This is a descriptive, cross-sectional, documentary study with a quantitative methodology, based on the results of the 18th publication of the Unidos pela Cura report.
Results: Between 2008 and 2020, two thousand one hundred forty-six cases of suspected cancer cases were referred by the UPC program. 91% of them were referred within 3 working days for the diagnostic confirmation at the Specialized Hospital. One hundred eighty types of cancer were confirmed among the cases evaluated by the hospitals, representing 8% of the referrals. The diagnostic of five hundred seventy-seven other diseases was also possible because of the UPC's referral flow. Another aspect that deserves to be highlighted is the training of health professionals on the signs and symptoms of childhood cancer. Four thousand three hundred seventy-eight primary care professionals were trained in Rio de Janeiro, and 97% of the city's primary care units referred suspected cases through the UPC.
Conclusions: Improving early diagnosis is crucial to increase the chances of cure and the quality of life of children and adolescents with cancer. The UPC produced significant results in Rio de Janeiro by making suspected childhood cancer visible in primary care and ensuring that children with suspected cancer cases reached diagnostic and treatment centers within three working days.

P028 / #1036

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

THE USE OF SOCIAL MEDIA TO WIDEN REACH OF PRACTICAL GUIDANCE FOR UK CHILDREN WITH CANCER AND THEIR FAMILIES DURING THE COVID-19 PANDEMIC

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Background and Aims: The Children's Cancer and Leukaemia Group (CCLG) were one of the first professional groups to develop specific COVID-19 guidance for patients and families internationally. The guidance was based on UK Government and Public Health England advice and was regularly updated as further evidence became available. This was disseminated to families and professionals online, including via the CCLG social media channels. The aim of this study was to analyse the online reach of the CCLG COVID-19 guidance and the primary sources of website traffic.
Methods: The CCLG COVID-19 group convened in March 2020 and included consultant representation from neuro-oncology, oncology, haematology, and bone-marrow transplantation. The group also received input from clinical trial management groups and early phase trial researchers. The first version was published on the CCLG website on 11/03/20. Parents and families provided direct feedback on each revision via CCLG social media channels. Data analytics from the CCLG COVID-19 guidance webpage were collated from 11/03/20 to 03/10/21.
Results: There were a total of 90396 views to the CCLG COVID-19 guidance webpage from 142 countries during the study period. Most views were from the United Kingdom (n=78499, 86.8%), followed by the United States (n=2753, 3.0%), Australia (n=845, 0.9%), Ireland (n=784, 0.8%) and Canada (n=593, 0.7%). Of the total views, 79245 (87.7%) were from unique IP addresses. Peaks in web traffic correlated with release of updated versions of the guidance. The webpage was primarily accessed through Google (38%), directly (29%) or via Facebook (19%).
Conclusions: The CCLG COVID-19 guidance has had a wide reach, both in the UK and internationally. Patients and their families commonly use the internet to seek healthcare information, including via social media platforms. It is therefore important to utilise these channels to disseminate accurate, evidence-based and up-to-date information to the general public.

P029 / #1555

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

ARE CURRENT NUTRITION SUPPORT STRATEGIES EFFECTIVE AT IMPROVING NUTRITIONAL STATUS IN CHILDREN AND ADOLESCENTS WITH OSTEOSARCOMA?

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Background and Aims: Studies investigating the impact of nutritional support (NS) on paediatric osteosarcoma patients' nutritional status are scarce, despite evidence showing optimal nutritional status improves clinical outcomes. We investigated patterns of change in the nutritional status of osteosarcoma patients receiving NS.
Methods: A retrospective study of patients (aged <18 years) diagnosed and treated for osteosarcoma at Bristol Royal Children's Hospital (2015–2020) was performed. Clinical and nutritional data were collected over 30-day periods at defined time points from the start of treatment (days 0 to 270). BMI and weight Z-scores were calculated from WHO (2010) and nutritional status was defined as underweight (BMI -2 SD), over-nourished; overweight [BMI ≥1.05<1.63 SD] and obese [BMI ≥1.63 SD]. Energy (EI) Kcal/day and protein intake (PI) g/day were obtained from medical records, compared against energy (ER) and protein requirements (PR) respectively (DRVs 1991) and presented as a percentage difference from the estimated requirement. NS was defined as oral (ONS), enteral feeding (NG/PEG), parenteral nutrition (PN) and/or complex NS (CNS: NG+PN). Data was analysed using descriptive statistics and correlations.
Results: Eleven patients [mean±SD 13.3±2.8 years old, 72.7% female]. Of these, 3 (27.3) were over-nourished, 7 (63.6%) well-nourished, and 1 (9.1%) was underweight at the start of treatment. NS was prescribed to 9 (82%) patients. Of these, 8 (73%) received ONS, 4 (36%) NG, 3 (27%) TPN and 1 (9%) CNS. EI% of ER and PI% of PR mean±SD were -32.2±30.0 and 26.9±82.1 respectively. Correlation between EI and PI and treatment length were r=-0.6; p=0.06 and r =- 0.32; p=0.36 respectively. Weight change Z-score from the start until the end of treatment was - 0.97±0.36.
Conclusions: We showed high demand for NS in osteosarcoma patients, and current NS strategies did not support weight maintenance probably attributed to reduced EI. Although this appeared to reduce treatment length, larger prospective studies are warranted.

P030 / #219

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

IMPROVED HOME MANAGEMENT OF ORAL PEDIATRIC ANTICANCER DRUGS AS A RESULT OF AN INTERVENTION COMPRISING PRACTICAL TRAINING, WRITTEN INSTRUCTIONS AND MOVIE CLIPS: A PILOT STUDY

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Background and Aims: Background: Long term treatment of pediatric patients with oral anticancer drugs (OADs) requires the parents/caregivers to prepare the drug at home. The handling procedures in the home setting are, however, not regulated by Swedish law and the parents are often left without guidance on how to handle OADs in a safe way. Aim: The aim of this study was to increase understanding of how OADs are handled by parents/caregivers in the home setting before and after an intervention.
Methods: Parents of pediatric cancer patients were observed and videotaped during their handling of OADs in the home setting before and after the intervention. During the intervention, the parents were provided with written instructions, movie clips and practical training on handling the OADs. Four checklists were used to compare and score the four handling procedures (measuring an oral suspension, cutting tablets, dissolving tablets, and opening capsules) for each parent before and after the intervention.
Results: The intervention significantly improved the OAD handling procedures among the studied parents. The median score for correct handling was 19 % (IQR: 3.6 to 30%) before the intervention and 89.5 % (IQR: 71.5 to 94.5%) after the intervention ($p < 0.0001$).
Conclusions: An intervention comprising practical training and information presented in different forms improved the handling of OADs at home by parents. There is an urgent need to implement this method in all oncology centers in Sweden, educate HCPs to standardize the presentation of information. There is also a great need to provide parents with age-appropriate oral drug formulations from the local hospital pharmacies in Sweden.

P031 / #1353

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

EXPRESSIVE ARTS IN BAUH: CASE STUDIES AND REVIEW OF EVIDENCE

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Background and Aims: Pediatric cancer is a leading cause of death for children, with almost 400,000 new cases diagnosed globally and 33 800 new cases estimated among children aged 0-14 years in the Eastern Mediterranean Region (EMR) in 2020. Although childhood cancer is curable for the majority of children when essential diagnostic, therapeutic and supportive care services are accessible. The number of people under the age of 18 in Egypt reached 38 million in 2017, making up 40% of total population, the Central Agency for Public Mobilization and Statistics (CAPMAS) announced. As of January 1, 2021, the Egyptian population was estimated at 101.48 million inhabitants. A population of 17,000,000 is being served by BAUH, roughly speaking 20% or 1/5 of Egypt population. This presentation shall explore the evidence of art therapy and pediatric cancer patients, shall teach pediatric cancer patients/staff how to express their feelings via arts, shall help cancer patient/family to heal from cancer journey, shall highlight the psychological/psychosocialsocial/rehabilitation support program at Burg AlArab University Hospital BAUH.
Methods: Weekly art therapy interventions are carried out with the pediatric patients over the year 2021. These interventions covered fingerprints, oregami, clay, music and drama therapy sessions. A sample of 180 pediatric cancer patients aged 5 to 15 years old were studied for emotional change and psychosocial status. Major Depressive Disorder MDD was used to determine the depression, anxiety levels which caused impairmnet in social and academic behaviours. Also Generalized Anxiety Disorder GAD was used to determine the excessive anxiety and worry.
Results: At least 2 of the symptoms included in MDD were expressed among the pediatric cancer patients at BAUH in the first 2 weeks. The Kubler-Ross change curve was aoolied to determine the emotions of the pediatric cancer patients at BAUH.
Conclusions: Therapeutic art encourages both verbal and non-verbal communications of a person’s perceptions and feelings.

P032 / #284

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

REPORTING OF RACIAL/ETHNIC MINORITY REPRESENTATION IN PHASE I/II PEDIATRIC ONCOLOGY CLINICAL TRIALS

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Background and Aims: Racial/ethnic minorities experience inferior cancer outcomes and face systemic barriers to equitable clinical trial access, but the extent of underrepresentation, particularly among children and in early phase trials, is incompletely understood. We explored patterns of reporting of race/ethnicity to evaluate representation across early phase pediatric oncology studies.
Methods: Phase I/II clinical trials in pediatric oncology from 2012-2018 were previously analyzed in a systematic review by our group to assess for toxicity and response (Cohen et al., The Oncologist 2020). Articles were subsequently screened for reporting of race and/or ethnicity in baseline patient characteristics and outcomes by race and/or ethnicity in the main text, tables, and figures.
Results: In total, 109 articles were included for analysis, 78 (72%) of which incorporated targeted therapies. The total number of patients was 2713 with median age of 11 years (range 3 – 21). Among all articles, only 36 (33%) reported race or ethnicity in baseline patient characteristics, of which 23 (63.9%) provided information on both race and ethnicity of trial participants. Trials published in 2014 reported race/ethnicity most frequently (42%), whereas trials published in 2016 reported race/ethnicity least frequently (18%). No year-on-year reporting trends were identified. Only one study described safety or toxicity outcomes by race/ethnicity.
Conclusions: Reporting of racial/ethnic representation in early phase pediatric oncology clinical trials published between 2012 and 2018 was very limited, inconsistent, and did not improve over time. Additionally, subgroup analyses of safety and efficacy results by race/ethnicity was rarely reported. Reporting of representation and outcomes of racial/ethnic minorities in clinical trials needs to be prioritized to better evaluate the extent of demographic underrepresentation, health disparities, and ultimately improve access to emerging therapies for high-risk groups.

P033 / #1867

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

INVOLVING PARENTS & CARERS IN THE DEVELOPMENT OF NOVEL DEVICES AND PROTOCOLS FOR THERAPEUTIC DRUG MONITORING IN PAEDIATRIC ONCOLOGY

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Background and Aims: ChromaDose is a NIHR (National Institute of Health Research) funded project that is developing a bedside drug monitoring technology to enable safe and effective personalised anthracycline chemotherapy for children. Public and Patient Involvement and Engagement (PPIE) is a core element of the project for feedback and advice on the patient experience with the technology. Various stakeholder groups are actively involved, including the Young Persons Advisory Groups at Great Ormond Street Hospital and North England, and the Paediatric Oncology Reference Team. Herein, we are presenting the outcomes obtained during the initial phase of the project.
Methods: Active involvement of patients and young persons as well as parents and carers was ensured through two separate streams of consultation. For each stakeholder group, an interactive online survey was conducted with embedded videos. Live online sessions were subsequently carried out with an interactive whiteboard as well as individual questionnaires. Participants were shown the data of the survey and asked to respond to follow-up questions for selected topics centred around participation in a clinical trial for therapeutic drug monitoring, confidence in a novel blood testing tool, and different forms of engagement.
Results: Our PPIE activities are planned, carried out and analysed in close collaboration with the engineering team to ensure that findings are directly implemented into the design. Example outcomes from Phase 1 include technical features on displaying the progress of analysing the blood, quality controls, guidance on appropriate terminology, and visual appearance.
Conclusions: Our work has been perceived as a model approach that others should follow (NIHR review). Online and in-person sessions are planned to create patient information resources, provide input on device design and for receiving advice on blood sampling protocols. Outreach events will serve to raise awareness of therapeutic drug monitoring and to highlight our approach of co-creation in product development.

P034 / #59

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

PRIMARY CAREGIVERS EXPERIENCES OF HAVING A CHILD WITH CANCER: A SCOPING LITERATURE REVIEW OF QUALITATIVE STUDIES

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Background and Aims: Having a child diagnosed with cancer greatly affects the lives of the child and his/her primary caregivers. This scoping review aimed at summarizing the qualitative studies in the recent literature on the experiences of primary caregivers living with childhood cancer, identifying key themes and determining the gaps in the extant literature. Knowledge about primary caregivers' individual responses and perceptions of the cancer experience may provide insight into the experiences of the larger family system.
Methods: Following PRISMA-ScR guidelines, a systematic scoping review was conducted. Data sources included PubMed, CINAHL, Medline and Embase (Ovid), Cochrane Library, and AMED. Using key terms "childhood cancer ", "primary caregivers" and "qualitative research"; and then hand searched for the time period 2010-2021. Lastly, reference lists and citations of all identified articles were manually searched. No new articles were identified through this process.
Results: 729 papers were reviewed, 10 met inclusion criteria. This review examined the qualitative research exploring the experiences of primary caregivers' who has children with cancer and discusses common themes across all studies. Qualitative research makes it possible to gather and analyze individualistic data on deeper levels. Five themes were identified which were concerned with the effect a diagnosis of cancer can have on primary caregivers' lives. These were: 'Emotional Roller Coaster',' Pivotal Moment',' Financial Burden',' Effect on Relationships' and 'Valuable Experience'.
Conclusions: It is important for clinicians in this field to understand the experiences of primary caregivers in order to provide effective support. It is hoped that this study may provide healthcare professionals with a useful insight into understanding the unique experiences of being a primary caregiver of a child who is diagnosed with cancer.

P035 / #1164

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

COMMUNICATION CHARACTERISTICS FOR FERTILITY PRESERVATION PATHWAY FOR ADOLESCENT AND YOUNG ADULT CANCER PATIENTS AND THEIR CARE GIVERS IN KOREA

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Background and Aims: Fertility preservation (FP) discussion is a crucial step for adolescent and young adult (AYA) cancer patients; however, it is relatively new to Asian countries. This study highlights the quality of communication during FP discussions in Korea.
Methods: We performed FP clinical pathways and surveyed details on the discussion characteristics and satisfaction scales dufing the FP discussions for AYA cancer patients and their guardians in Yonsei Cancer Center, Seoul, Korea; Quality of FP discussions and the degree of satisfaction of the discussions were measured on a scale of 1-7.
Results: Out of the 34 patients and their 32 guardians completed the survey. Two guardians did not answered the survey. All respondents reported high overall satisfaction, however several factors were related with low satisfaction or information quality. On the type of counsellors, both respondent groups showed high overall satisfaction when their counsellor were physicians rather than other types of care providers. For the information quality, the guardians who were provided with verbal and non-verbal communication tools (pamphlets, internet resources, or others) both were more satisfied with the information quality than the only verbal communications. As for th number of discussion sessions, more than one discussion sessions showed improved understanding of the concept of FP, higher communication and information quality.
Conclusions: In order to improve FP process for AYA cancer patients, we need to adjust the type of counsellors, number of discussion sessions, and types of information. This will be the cornerstone of the effective FP communications in Korea.

P036 / #217

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

UNDERSTANDING HEALTHCARE DATA FOR CHILDREN'S AND YOUNG PEOPLE'S CANCERS: A PARTICIPATORY STUDY.

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Background and Aims: In the United Kingdom, healthcare data is collected on all patients receiving National Health Service care, including children and young people (CYP) with cancer. This data is primarily used to inform service delivery but with special permissions, and without individual consent, can also be reused for research. The use of routinely collected health data in research is an advancing field with huge potential benefit, particularly in CYP where case numbers are small and the impact across the lifecourse can be significant. We aimed to determine what CYP and carers knew about health data collection and their views on its use for research.
Methods: CYP and carers were invited to an interactive 2.5 hours online workshop comprising of presentations from health data experts, case-studies and group discussion. With consent the workshop was recorded, transcribed verbatim and analysed using thematic analysis.
Results: Ten young people currently aged ≥16 years and diagnosed with cancer at age 5-19 years attended. Six carers also participated. Three key themes emerged: Awareness: Participants were surprised at the volume and depth of data collected and reported receiving little information about use of their healthcare data. They reported this could lead to mistrust in healthcare sytems. Value: Participants were happy for their data to be used for research and felt data should be more accessible for the purposes of research. Data sharing: The importance of data sharing in CYP cancers, particularly in rarer tumours, to improve outcomes was recognised by participants. Participants identified numerous barriers to data sharing including mistrust in the media and difficulty accessing their own health records.
Conclusions: Young people and their carers support the idea of data collection and recognise its importance in research to improve outcomes for CYP. However, education and transparency relating to data collection and its uses are required.

P037 / #1473

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

PASSPORT TO GLOBAL HEALTHCARE: ECONOMIC COST TO A HIGH-INCOME NATION

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Background and Aims: Social media communities enable greater awareness of treatments available across borders. Parents/carers of children with poor-prognosis cancers who exhaust options in-country may choose to seek therapies abroad. Child Medical Tourism (CMT) is controversial, ethically challenging, limited to high-income families, or those with responsive networks in high-income countries. The national cost of CMT has not been quantified, nor have the inherent socioeconomic disparities been described. This case study highlights the significant cost to the UK economy when millions of GBP are spent for treatments abroad via support by one disease-specific charity and signals the need for a multistakeholder strategy, to include expert advocates and clinicians, to prioritize and address the challenges of initiating and conducting clinical trials in the UK.
Methods: Five years of expenditure on treatment and travel costs for UK neuroblastoma families are reported, supported by Solving Kids' Cancer UK.
Results: From 3/2017- 3/2022 50 UK families with neuroblastoma children travelled or intended to travel to the US, Germany and Spain for treatments. The therapies included proton beam, surgery, immunotherapy, radio-immunotherapy, chemotherapy regimens, and relapse prevention. The cost of treatment and travel varies for each family and can range from £180,000 to more than £300,000. Campaigns for 66 children raised £10,177,974 with ongoing expenditures. In the 5-year period, £5,102,267 was spent abroad for 50 children.
Conclusions: Economic issues of CMT in UK neuroblastoma children highlight the need for developing a national strategy to prioritize the conduct of clinical trials for innovative therapies at home. This is an opportunity to call for systemic change and could accelerate evaluation of more effective treatments for children with cancer, re-directing the millions of GBP spent abroad. Other countries may benefit from a similar effort to prioritize the support of specific clinical trials within their national health service.

P038 / #532

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

EXPLORING COPING STRATEGIES AMONG CAREGIVERS OF CHILDREN WHO HAVE SURVIVED CANCER IN JORDAN.

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Background and Aims: Children who have survived cancer and their caregivers may deal with residual physical, cognitive or social disabilities. There is little research on caregivers' health and wellbeing after cancer. In addition, there is no specific research about how caregivers cope with everyday stressors after cancer. This study aimed to explore the coping strategies that caregivers of children who have survived cancer utilize to overcome everyday stressors.
Methods: This study utilized a descriptive survey design. The sample consisted of 103 caregivers, visited the clinic at a national cancer center. The study included caregivers of children who were off cancer treatments for at least two years. Caregivers completed the study survey. The survey collected caregiver reported demographic information, and the Brief COPE which measures caregivers' frequency of engaging in certain coping strategies. The Brief COPE consisted of 14 coping sub-scales, which are Self-Distraction, Active Coping, Denial, Substance Use, Use of Emotional Support, Use of Instrumental Support, Behavioral Disengagement, Venting, Positive Reframing, Planning, Humor, Acceptance, Religion, and Self-Blame. Data Analyses included calculating sub-scales' scores for the fourteen coping strategies.
Results: The 103 caregivers were 62% mothers, 80% married, 45% finished high school, 50% don't work outside the house, and 60% have low family income. Result showed that Religious Coping (66%) and Acceptance (60%) were the most utilized coping strategies, followed by Positive Reframing (45%), Active Coping (44%) and Planning (43%). The least utilized coping strategies in our sample were Humor (5%), Behavioral Disengagement (8%), and Substance-Use (10%).
Conclusions: Caregivers mostly utilize religious coping and acceptance in dealing with everyday stressors. Because these coping strategies do not directly solve stressors, it is important to support caregivers in choosing and implementing effective coping strategies. Some caregivers may utilize substance use as a coping strategy, which has negative health effects, there must be direct interventions that targets these caregivers and their families.

P039 / #85

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HEALTH-RELATED QUALITY OF LIFE AND SOCIAL DETERMINANTS OF HEALTH WITHIN CHILDREN WITH BRAIN AND SPINAL CORD TUMORS

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Background and Aims: Social determinants of health (SDOH) have a significant impact on health, well-being, and quality of life (QOL). Validated tools to assess these disparities have been developed but not utilized prospectively in children with central nervous system tumors (CNS). Objective: To establish a baseline assessment of health-related quality of life and associated social determinants of health in children with CNS tumors in Indiana.
Methods: We implemented the Pediatric Quality of Life Inventory™ (PedsQL™) for patients (ages 0-21 years) diagnosed with a CNS tumor evaluated in the neuro-oncology clinic from July 2019-January 2022. A higher score is associated with better quality of life. Patient's address was utilized to obtain Area Deprivation Index (ADI) and Child Opportunity Index (COI). ADI allows for rankings of neighborhoods by socioeconomic disadvantage at state or national level (1-10: 1 is least disadvantaged). COI measures the quality of resources in a patients' community, with five categories ranging from very low- to very high-opportunity.
Results: We assessed 107 patients and their parents. The ADI decile within Indiana ranged 1 to 10 (median 5, mean 5.3); national percentile ranged 7 to 100 (median 71, mean 67.3). Overall COI mean was 3, with sub-scores for education - 2.9, health/environment - 2.6, and social/economic - 3.1. The PedsQL™ was completed by 96 parents and 91 patients. Physical mean was 67.4 and 71.2, psychosocial mean 67.8, 68.9, and total mean 67.7, 69.8, respectively. Simple linear regressions demonstrated a correlation between increasing disparity and decreasing quality of life across all dimensions.
Conclusions: This is one of the first studies to associate a decrease in pediatric quality of life with disparities of social determinants of health. These data demonstrate the need for expanded prospective evaluation to track social determinants of health that may impact on the quality of life in children diagnosed with CNS tumors.

P040 / #1759

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

HOW DOES HAVING A CHILD WITH CANCER AFFECT PARENTS' PSYCHOLOGY?

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Background and Aims: 'Cancer' affects parents as well as children in both physical and psychological aspects. The aim of this study was to evaluate psychological resilience, hopelessness and intolerance of uncertainty in parents of children with cancer.
Methods: Parents of children with cancer of our clinic were asked to fill a personal information form and the Intolerance of Uncertainty Scale (IS), the Resilience Scale for Adults (RSA), and the Beck Hopelessness Scale (BHS). These scales consisted of a total of 79 questions were answered by the volunteer parents. The results of the questionnaire were statistically compared.
Results: Our study group consisted of 84 parents of 84 children. Demographic features were summarized as: 85% of the parents were between ages of 30-49, 94% were married, 81% had 2 or more children, 58% had lost their jobs during treatment period. 78% of their children with cancer were <12 years old, 60% had solid tumors and 40% had leukemia. No significant difference was observed in the scores of the intolerance of uncertainty, hopelessness and resilience scales between the parents of the patients with leukemia and solid tumor($p>.05$). There was no difference in the psychological evaluations of the parents regardless of the cancer type and stage. According to the time elapsed after diagnosis; the resilience scores of the parents during the first month of the treatment were higher than those of the parents during 1-6 months and after one year($p<.05$). According to the BHS; the scores were significantly higher among the parents of children whose treatment had been completed than those who were being actively treated($p<.05$).
Conclusions: Our study showed that the parents' psychological situations were better during treatment period. We suggest that our multi-disiplinary oncologic team including doctors, nurses with a psychologist and a play therapist may strongly impact psychological well-being of both children and parents.

P041 / #1088

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

BELIEFS AS COPING RESPONSE IN PARENTS' ADJUSTMENT TO CHILDHOOD CANCER

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Background and Aims: Parents of children with cancer face high uncontrollability and uncertainty of the situation with few possibilities to regulate events, but they have the ability to regulate the cognitive appraisal of the situation. This study aimed to explore the cognitive beliefs in response to their children being diagnosed with cancer.
Methods: A cross-sectional study was conducted among 55 parents (mostly mothers, n=49) having children with cancer. Pre-adapted Latvian version of Psychosocial Assessment Tool (PAT) was used to collect information about parental beliefs and stress reactions after diagnosis.
Results: Spearman's rank correlation was computed to assess the relationship between parental beliefs and stress reactions whilst controlling for diagnose (leukemia (ALL, CML, AML), lymphoma, brain tumors, sarcoma). There was a negative correlation between the belief in doctors' competencies and depressiveness, $r(53) = -.34$, $p < .05$, as well as positive correlations with the belief in overcoming the illness ("We are going to beat this"), $r(53) = .49$, $p < .001$, and the time since starting treatment, $r(53) = .31$, $p < .05$. Belief in doctor's competencies correlated negatively with belief about child's pain ("My child will be in a lot of pain"), $r(53) = -.28$, $p < .05$. Positive correlations were found between the belief in reason ("Everything happens for a reason") and the belief in strengthening the family ("Our family will be closer because of this"), $r(53) = .36$, $p < .001$, but also with higher level of depressiveness, $r(53) = .27$, $p < .05$, and anxiety, $r(53) = .31$, $p < .05$.
Conclusions: Results suggest that parental beliefs in response to a child's cancer diagnose are comparable to emotion-focused coping strategies (secondary control strategies - predictive, vicarious, interpretative). Some beliefs may simultaneously correlate with anticipation of positive outcomes from disease but also with negative stress reactions (anxiety/depression) in the context of the coping process.

P042 / #1804

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

PRELIMINARY FINDINGS ON PSYCHOLOGICAL SEQUELAE OF PARENTS OF PAEDIATRIC CANCER PATIENTS, DURING AND AFTER THE COVID-19 EMERGENCY

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Background and Aims: Pediatric cancer diagnosis is considered a condition of traumatic risk for patients and parents. In this population, COVID-19 may be considered a stressful event that may exacerbate risk or sequelae. Many studies have investigated parental perceptions during the pandemic, so it is also essential to monitor families over time. During the COVID-19 pandemic we initially studied the psychological impacts on parents of the cancer diagnosis of their children and the epidemic event. Then, after one year, we measured if there were changes in parents' psychological conditions.
Methods: Eighty parents of pediatric cancer patients were enrolled in the study at an early stage. At T1 (during the 2020 COVID-19 emergency) four questionnaires were completed: Impact of Event Scale-Revised - IES-R; Perceived Stress Scale - PSS; State-Trait Anxiety Inventory - STAI-Y; Pediatric Quality of Life Inventory Parent Proxy-report - PedsQL), at T2 (one year later) 3 of the 4 questionnaires (PSS, STAY, and PedsQL) were administered. We analyzed preliminary data from this sample and the evolution of scores over time considering the 36 parents who participated in both T1 and T2 measurements.
Results: In our sample (36/80), the bivariate correlation matrix found a significant positive correlation between IES-R and STAY Y-1 (state) scores ($r = 0.46$; $P < 0.005$) in T1. This correlation was not confirmed in T2. Post-hoc comparison between mothers (18) and fathers (18) showed a significant difference in PSS scores at T2 ($t = 4.62$; $P < 0.001$), with, respectively: mothers 21.28±3.66 and fathers 15.44±3.90. State anxiety levels were maintained high in T2, with 83% of scores exceeding the STAI-Y cut-off.
Conclusions: Results confirm that parents of pediatric cancer patients have high psychological risk and long-term sequelae and that the COVID-19 pandemic likely influenced the maintenance of high levels of anxiety. Psychological interventions for parents are essential in oncology services.

P043 / #1267

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

PREVALENCE OF ALTERNATIVE MEDICINE USE BY CAREGIVERS OF CHILDREN RECEIVING TREATMENT AT KORLEBU TEACHING HOSPITAL ACCRA,GHANA.

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Background and Aims: Socio-cultural practices contribute to health-seeking behaviour in many low and middle-income countries, including Ghana. Parents may ascribe spiritual and other causes to their child's cancer and may seek complementary and alternative treatment approaches. Such practices may however undermine treatment, leading to adverse treatment outcomes. The study aim was to describe the prevalence of alternative medicine use at the Paediatric Oncology Unit (POU) of the Korle Bu Teaching Hospital (KBTH), Accra, Ghana.
Methods: Cross-sectional study using a questionnaire administered to caregivers of children with cancer receiving or recently completed treatment at the POU, KBTH.
Results: Of the 35 caregivers included in the study, majority (68%) were female and about half (53%) were aged between 26-40 years. Less than a third (27%) had no formal education. The children of majority (84%) were still undergoing treatment. The most common diagnoses of the children were acute leukaemia (40%), retinoblastoma (35%) and Wilms tumour (15%). Over two-thirds (70%) of the parents admitted to use of alternative medicine. This included spiritual (60%) and herbal medicine (35%). Some of the spiritual therapies included oils and 'anointed' water from churches, prayer camps and traditional healers. Of those using herbal medicine, 60% were oral, 30% topical and 10% via enema. Of the parents who used alternate medicine, only 20% discussed their use with the medical staff. Worryingly, 15% of the caregivers used these alternative therapies concurrently with chemotherapy. Fourteen caregivers (40%) said they would still recommend alternative medicine to others. Majority (90%) recommended that education be provided to all caregivers on use and effects of alternate medicine.
Conclusions: An overwhelming proportion of caregivers in the POU, KBTH use alternative medicine. Ongoing education on use of alternative medicine is needed for all caregivers of children receiving treatment for cancer to avoid harmful effects.

P044 / #477

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

BARRIERS TO LONG TERM FOLLOW UP IN PEDIATRIC HODGKIN LYMPHOMA SURVIVORS

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Background and Aims: Childhood cancer survivors of Hodgkin Lymphoma are at high risk of late effects following their cancer treatment. Unfortunately, there are numerous barriers at the patient, provider, hospital, and payor level that may adversely affect their adherence to long term follow up care.
Methods: We conducted a retrospective chart review on a cohort of 122 Hodgkin lymphoma survivors diagnosed between 1994 and 2014 and identified patients who were lost to follow up after completing treatment (defined as no visits to Texas Children's Long-Term Survivor clinic for 2 or more years). Structured phone interviews were then conducted to determine contributing factors.
Results: Of the 122 patients, 56 (45%) were lost to follow up and 24 (42%) of these patients were interviewed by phone. 11 (46%) of the patients lost to follow up cited loss of or inadequate insurance as their primary reason for not following up. 8 (33%) of patients indicated a lack of education as another reason for their lack of follow-up. Fewer patients reported following up with adult oncology (21%), moving (21%), Covid-19 pandemic (13%), or not wanting to follow-up (4%).
Conclusions: Lack of or inadequate insurance and lack of education were the two most common reasons for lost to follow-up in LTS clinic in a cohort of pediatic Hodgkin’s Lymphoma survivors. These factors could easily be targeted to improve adherence to care of this vulnerable population who are at risk for late effects from their cancer treatment.

P045 / #1572

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

PALLIATIVE CARE FOR CHILDREN AND ADOLESCENTS WITH CANCER IN ZAMBIA

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Background and Aims: Background Pediatric Palliative care is specialized medical care for children living with serious and chronic illnesses focusing on relief from symptoms/stress to improve the quality of life. Palliative care began in Zambia in 1992. The Cancer Diseases Hospital sees about 160 newly diagnosed children a year. Aims Explore Care givers perspective of pediatric palliative care at Cancer Diseases Hospital.
Methods: Structured interviews were conducted with caregivers at Cancer Diseases Hospital by a palliative care nurse and 4 pediatric nurses using a questionnaire (25 items). Answer choices: yes, no, never and some free text. Interviews conducted in Nyanja (local language) for 32 caregivers and English for 8. Caregivers consent was obtained, and interviews took 20 minutes.
Results: Most caregivers (70%) were aware about pediatric palliative care services, but the rest did not understand the significance of holistic care. Most (60%) were concerned about the limited number of palliative care staff. Most did not want the child to be informed of their diagnosis; mothers complained fathers not participating in the child's care.
Conclusions: Conclusion In Zambia, children are left out of decision-making; caregivers assume they would be devastated. However, teenagers find solace in talking with nurses about their disease. These issues make it difficult for palliative care nurses to render all services. Most Zambians believe cancer is due to witchcraft, although most caregivers expect their children to be cured. Unfortunately, they trust more in traditional medicines than biomedicine, so children are brought late for treatment. There is need for more trained personnel (pediatric palliative care nurses), nurses advocating for children's involvement in their care and sensitization about palliative care and childhood cancer.

P046 / #1734

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

COVID19 INFECTION IN PEDIATRIC HEMATOLOGY/ONCOLOGY PATIENTS IN A DEVELOPING COUNTRY

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Background and Aims: To determine the characteristics of COVID19 infection in pediatric hematology/oncology patients in a developing country.
Methods: Prospective cohort study conducted from January 2021 till March 2022. Pediatric hematology/oncology patients, under 16 years of age, with a positive PCR for COVID19 infection were enrolled.
Results: During the study period 1784 new patients of pediatric oncology,833 new patients of pediatric hematology,and 1821 admissions with febrile neutropenia were registered.Total 38 patients with confirmed COVID19 infection were enrolled.Mean age at presentation was 7.47 years +/- 4.60 SD,with male to female ratio of 4:1.Fifty eight percent of COVID19 infections were community and 42% where hospital acquired.Mean duration of stay in the hospital was 16 days +/- 14 SD.Sixty three percent patients were with hematological malignancies,18.5% with solid tumors,10.5% patients with benign hematological disorders and 8% with Histiocytosis syndromes.Forty percent cases were detected during pre-op screening while 60% were investigated for atypical pneumonia.Thirty one percent patients were asymptomatic,24% had mild,16% moderate and 29% had severe disease.Chest X-ray showed no abnormality in 29% cases,bilateral pulmonary infiltrates in 29%,lobar consolidation in 18.5%,mediastinal widening in 10.5%,ARDS in 10.5% and pleural effusion in 2.5% cases.Delay in the diagnosis of primary disease was observed in 37%,and treatment delay/interuuption was observed in 66% cases.Forty five percent patients were sent to home quarantine,32% patients expired,16% discharged;5% were shifted back to oncology ward for further treatment and 2.5% patients left against medical advice.Supplemental oxygen,mechanical ventilation and absolute neutrophil counts were the statistically significant factors (p-value <0.05) associated with the outcome.Three peaks of infections were observed in 15 months duration and frequency decreased in the second half of study period.
Conclusions: Incidence of COVID19 infection seems to be very low in pediatric hematology/oncology patients. Chemotherapy-induced neutropenia, and respiratory failure is associated with poor outcome. After the provision of vaccination the frequency of COVID19 infections decreased.

P047 / #813

Topic: *AS03 CCI - Childhood Cancer International - focused for parents of children with cancer - if accepted, the abstract will be presented in the parent association programme*

PARENTS' UNDERSTANDINGS AND EXPERIENCES OF PHYSICAL ACTIVITY IN CHILDHOOD CANCER SURVIVORS IN SINGAPORE: A QUALITATIVE STUDY

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Background and Aims: Childhood cancer survivors are more likely to be sedentary and have an increased risk of developing chronic illnesses and reduced quality of life. The current evidence base affirms the efficacy of physical activity to promote health and wellbeing in childhood cancer survivors, but few studies explore the of parents of childhood cancer survivors on physical activity, despite the key role parents could play in encouraging physical activity. This study aims to explore the understandings and role parents of childhood cancer survivors in Singapore may have in regard to physical activity.
Methods: Participants were recruited through the Singapore Children's Cancer Foundation. Semi-structured online interviews were conducted with seven parents. Each interview lasted about an hour. With consent, interviews were recorded, transcribed verbatim and analysed using themati[LW1] c analysis, assisted by QSR NVivo.
Results: Three main themes were identified; 1) understanding and perceived value of physical activity, which describes parental views on the importance of physical activity, 2) influences on physical activity, describing the barriers and enablers of physical activity and 3) impact of cancer, which describes the side-effects of cancer that potentially mediate levels of physical activity in childhood cancer survivors. Parents reported that childhood cancer negatively affects quality of life and participation in physical activity. The determinants of participation in PA are multifaceted and the socio-ecological and health belief models were used to demonstrate how these factors are interlinked.
Conclusions: Participation in physical activity is influenced at an individual, family, community and societal level. Improved understanding acquired through this research can be used to shape paediatric cancer care practices in Singapore. It also paves the way for further research in more diverse groups to inform an intervention study to optimise support for this population.

P063 / #1379

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

PSYCHOLOGICAL FUNCTIONING FOR SIBLINGS OF CANCER CHILDREN : NURSING STUDY

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Background and Aims: Background: The sibling relationship is usually the first, most intense, and longest peer relation that an individual will ever have. Therefore, having a brother/sister with terminal illness like cancer poses a risk to the siblings' mental health because of the stress they are under and insufficient support from others. Aim: This study aimed to assess psychological functioning for siblings of cancer children in Egypt
Methods: Design: descriptivecorrelational design was adopted for this study. Sample: purposeful sample of eighty onesibling of children with cancer and their mothers. Tool of data collection: the data wasgathered through structured interview where the tool was divided into two parts: the first partincludes: demographic characteristics of the studied subject ,and the second part includesthree adopted tools: (I) The Child PTSD Symptom Scale (CPSS), (II) Beck Youth Inventory(BYI) (Second edition), (III) Achenbach's Child Behavior Checklist (CBCL).
Results: Allsiblings of children with cancer in this study have met criteria of post-traumatic stresssymptomatology (PTSS) and nearly half of them had severe symptoms. In addition, thehighest percentage of them had much lower than average self-concept, severe anxiety anddepressive symptoms, average anger and disruptive behavior symptoms, and clinical range ofthe internalized, externalized and total problem. Also, there was a significant relationbetween the siblings' PTSS and their self-concept, anxiety, depression, and internalizing andtotal problems.
Conclusions: Conclusion: Siblings of children with terminal illness are at substantial riskfor PTSS, depression, anxiety, low self-cocept, internalizing, externalizing, and totalproblems. Recommendation: Create supporting groups for siblings as an ongoing servicewhere siblings of children with terminal illness as cancer have an opportunity to meet withothers in a similar situation and share their experiences and feelings.

P064 / #1494

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

INCREASING KNOWLEDGE FOR THE NECESSITY OF LONG-TERM FOLLOW-UP CARE AMONG PEDIATRIC CANCER SURVIVORS: A QUALITY IMPROVEMENT INTERVENTION

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Background and Aims: More than 60 percent of pediatric cancer survivors experience at least one treatment-related late effect while less than half adhere to recommended long term follow-up care. We hypothesized that the majority of caregivers/survivors lack knowledge regarding the need for long term follow-up and risks for late effects.
Methods: Using quality improvement methods we developed an intervention and surveyed solid and brain tumor caregivers or survivors (16 years and older) treated with chemotherapy and/or radiation and 3-24 months off therapy. Survey questions inquired the length of long term follow-up, the reason for life-long follow-up and possible late effects. Subjects were provided with the correct answers. We explored whether the questions triggered any anxiety and rated anxiety on a 10-point scale. We repeated the same process and prospectively assessed percent change from baseline of the following: Correctly acknowledging need for lifelong follow-up care and at least two late effects; How often anxiety is endorsed and rated greater than 5 out of 10 point scale.
Results: To date, we completed two PDSA cycles with 29 patients and 10 with two visits. From first to second visit, correct responses for follow up duration increased from 10 to 60 percent. Those who identified at least two late effects correctly increased from 40to 70 percent. Discussing late effects caused anxiety in 60 percent at the first visit and half of those rated greater than 5 on the 10 point scale. At the second visit, only 20 percent reported any anxiety and none greater than 5 points.
Conclusions: A simple educational intervention led to a significant increase in knowledge regarding need for lifelong follow-up in survivors, their late effects, and a decrease in anxiety associated with late effects. We will assess whether these improvements will be sustained at the next time point.

P065 / #624

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

VALIDATING A QUESTIONNAIRE TO ASSESS THE USE OF COMPLEMENTARY HEALTH APPROACHES IN CHILDREN WITH CANCER: FACE AND CONTENT VALIDITY TESTING (PHASE 2)

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Background and Aims: Complementary health approaches (CHA) such as naturopathy, chiropractic, and yoga are commonly used by children with cancer globally. Discussions between patients/parents and health care providers (HCP) about CHA are often infrequent or superficial and could be facilitated by a standardized questionnaire-based approach. A systematic review by our team showed initial evidence of validity for a paper-based generic questionnaire, the “Which Health Approaches and Treatments are you using?” (WHAT) tool. We are using a sequential approach to adapt and validate the WHAT questionnaire for use by HCP initiating CHA discussions with patients/parents. As part of this approach, this study aimed to test the face and content validity of the WHAT questionnaire for children with cancer.
Methods: Children with cancer, parents, and HCP (n=5-7 from each group per round) were recruited at the Hospital for Sick Children and invited to participate in rounds of individual interviews to determine item relevance, comprehensiveness, and comprehensibility of the WHAT questionnaire. A cognitive interview technique was used.
Results: The first round of cognitive interviews was completed by 19 participants (5 children, 7 parents, 7 HCP). Feedback revealed the following: short completion time was appropriate for clinical use, and items were comprehensive. However, the paper-based format was not user-friendly (limited space with a busy layout); the generic items were vague; and the items should be focused for clinical (as opposed to research) use. Our team modified the questionnaire to address these comments, and changed the current version into an electronic cancer-specific questionnaire for use in clinical settings. Preliminary results of the second round completed by 10 participants (4 children, 5 parents, 1 HCP) revealed no need for further changes.
Conclusions: The WHAT questionnaire has been modified based on children with cancer, parents, and HCP suggestions. The next step is measurement property testing of the modified WHAT questionnaire in pediatric oncology.

P066 / #421

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

CHILDREN'S NARRATIVES OF SUPPORT FROM PARENTS WHEN EXPERIENCING FEAR RELATED TO ACUTE LYMPHOBLASTIC LEUKEMIA

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Background and Aims: Children diagnosed with Acute Lymphoblastic Leukemia (ALL) typically undergo intense treatment with frequent hospitalizations. Medical, as well as existential fears have been identified. It has also been found that children's coping strategies develop during their illness trajectory. The literature on what children with ALL find to be valuable support from parents when experiencing fear is sparse. Thus, the aim of this presentation is to describe what young children find to be important support from their parents when experiencing fear related to ALL.
Methods: The study had a longitudinal descriptive qualitative design. Thirteen children (3 girls and 10 boys), initially 5-9 years old were interviewed once to three times during their treatment period (approximately 2 months after the diagnosis, after 1 year, and at end of treatment). Data were analyzed using a matrix-based qualitative analysis method.
Results: The parents' physical and emotional closeness was the most frequently reported support. It eased the children's medical and existential fears. The children also found it supportive when the parents facilitated for them to participate in their care and when the parents acted as their advocate. Other supportive measures were offering distraction, talking to the child about their fears, assisting the professionals in alleviating pain and fear, being playful and encouraging. Five children also appreciated when their parents restricted them, during medical procedures. The experiences of support varied between children and between different time points during treatment.
Conclusions: Although being quite young, the children were able to describe what they found to be supportive when experiencing fear, or for preventing fear. The parental support had an impact on the child's emotional, social and physical wellbeing. Professionals should encourage parents to stay with their child, and offer support to the parents, so that they in turn can support their child.

P067 / #1233

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

CARING FOR CARER AND CARE PROVIDERS PERSPECTIVE ON COMPASSION FATIGUE: A SHORT VIDEO FROM MCM GRANT

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Background and Aims: Around 8000 new cases of Pediatric Oncology being identified annually in Pakistan. Half of the population coming to pediatric oncology centers are staged with advanced disease. This can be difficult for healthcare workers as well as patient's family.
Methods: With help of Sanofi Espoir My Child Matters grant- training and education of Nurses in palliative care in Pakistan. A video was created on identifying needs of caregiver and carers who had taken care of Pediatric Oncology patients. Psychosocial department 4 Bereaved families were identified along with healthcare providers who frequently took care of these children. Parent and healthcare workers were invited to explain their journey of being an immediate caregiver. Their expression and feeling were recorded to be later turned into educational video as exemplar for other families and healthcare providers.
Results: It was peculiar experience where parents and healthcare workers were invited to share deepest moments of grief on video. During, interview various theme emerged; communication gap, not understanding patient and family's needs, sibling neglect and social support. Parents confronted their children were referred to as degrading metaphors, Parents were not provided social support to take care of their homes and other children, some parents were shouted at for not being able to follow their routine appointments. Healthcare worker shared, they grieved same way; explained their compassion fatigue and ways of dealing with it.
Conclusions: Pediatric Oncology can be strenuous domain for nurses, doctors, support staff, and psychosocial workers. It can be draining physically and emotionally for parents and their families' especially when outcomes are poor. Caregivers and carers need to focus on their mental health during this tough time of caring for pediatric oncology patient. Hospital should provide extra support for individuals that are suffering with compassion fatigue, their mental wellbeing will help improve outcomes of other patients and families.

P068 / #1626

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

IMPROVED QUALITY OF LIFE USING MOLECULAR GUIDED THERAPY: A CASE REPORT

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Background and Aims: Pleomorphic Xanthoastrocytoma (PXA) is a rare type of central nervous system tumor among children. Despite the fact that they have a high cure rate, PXA's remain a significant clinical challenge. Case Study: Patient is a 14-year-old male who presented at 11 years of age with a history of migraines, worsening headaches, nausea, and vomiting. MRI after emergent EVD placement revealed a mixed solid and cystic lesion centered in the right temporal lobe and thalamus.
Methods: Patient underwent two subtotal resections followed by VP shunt placement. Complicated pathology findings required consideration for standard chemotherapy versus proton radiation therapy. At this time, he was referred to our Precision Genomics Neuro Oncology program for tumor molecular characterization. While patient was recovering, he presented with severe headaches. Imaging revealed overshunting and right sided subdural hematoma, evacuation with burr holes was performed.
Results: Somatic tumor testing revealed BRAF V600E mutation and allowed for enrollment in Novartis CDRB436G2201. Patient was assigned to the standard treatment arm and received Carboplatin and Vincristine, per CCG 9952A. Disease burden continued to progress through cycle 7, and per central review patient was transistioned to the Dabrafenib and Trametinib arm of study.
Conclusions: Imaging was performed 5 weeks post treatment transition, which revealed interval reduction of dominate tumoral cyst in the right thalamus and heterogenous solid lesion. Disease burden still continues to decrease with therapy. This case illustrates a clear benefit of using molecular guided therapy for improvemet of patient quality of life in the treatment of PXA's.

P069 / #1920

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

NUTRITIONAL DISORDERS AMONG CHILDREN WITH CANCER RECEIVING CHEMOTHERAPY AT THE PAEDIATRIC ONCOLOGY UNIT, KOMFO ANOKYE TEACHING HOSPITAL, GHANA

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Background and Aims: Background Chemotherapy and its outcomes are potentially detrimental to nutritional status; and as a result, there is increasing confirmation that nutritional status might influence the outcomes of chemotherapy. Mucosal ulceration due to chemotherapy presenting as cheilosis, mucositis, stomatitis, glossitis, and esophagitis painfully obstruct ingestion of nutriments.Nearly all antineoplastic drugs produce nausea and vomiting while several results in diarrhea; constipation may also occur. Adequate nutrition during cancer plays a decisive role in several clinical outcome measures, such as treatment response, quality of life, and cost of care. Objective To assess the nutritional status and treatment outcome of children with cancer receiving chemotherapy at Komfo Anokye Teaching Hospital, Kumasi.
Methods: The study used structured questionnaire as the primary source of data collection to interview key people such as parents, caretakers, and guardians. Secondary data, from hospital folder was also reviewed.Data that were generated was subjected to both descriptive and statistical analyses using stata11.0
Results: Finding showed a significant relationship between anemia and dietary diversity score at three months of chemotherapy ($p = 0.016$). Three months after chemotherapy, participants had moderate anemia (87.4%) and highest poor DDS compared to normal (2.2%), mild (4.1%) and severe anemia (6.3%) children with cancer ($p = 0.016$). This means that poor diet diversity could be associated with prevalence of anemia in children with cancer.
Conclusions: There was high prevalence of wasting and anemia at baseline, one to three months of chemotherapy. Poor diet diversity was found significantly higher among male children with cancer and lymphoma participantThere was significant relationship between anemia status and dietary diversity at three months of chemotherapy.

P070 / #1518

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

THE IMPACT OF THE CORONAVIRUS DISEASE (COVID-19) PANDEMIC ON THE PEDIATRIC ONCOLOGY NURSES MENTAL HEALTH IN RABAT MOROCCO

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Background and Aims: The coronavirus disease (COVID-19) pandemic has caused a major health crisis in most countries, particularly the mental health of health workers.The impact of the pandemic on the care of patients followed at the Department of Hematology and Pediatric Oncology in Rabat has been well documented. However, no study has measured its impact on nurses. Objective: Identify areas of pediatric oncology nurse mental health most impacted and coping strategies.
Methods: Study based on a questionnaire derived from the American Nurses Association Covid-19 impact survey, translated locally to French and distributed to all department nurses. The 14 questions coveredemotional feelings, behavior related to stress experienced and methods of coping.
Results: Nineteen among 22 nurses participated anonymously. Eight were diagnosed withCOVID 19. Most (17/ 19) felt overwhelmed and depressed, but many (17/19) feltoptimistic and confident. The pandemic impacted sleep (10/19) and appetite (8/19).Two nurses experienced domestic abuse. Strategies used to overcome the crisis included spending time with family or nature, entertainment or spiritual practices.
Conclusions: The pandemic (COVID-19) impacted the psychological mental health of pediatric oncology nurses in Rabat. The findingsemphasizes the need of investing in the well-being of nurses, and preparing them to be resilient in the face of future public health emergencies.

P071 / #1919

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

EFFECTS IN EDUCATION COMPETENCY SELF-ASSESSMENT OF A BASIC HEALTH EDUCATION ONLINE COURSE FOR HEALTH PROFESSIONALS IN PEDIATRIC HEMATOLOGY-ONCOLOGY: A PILOT STUDY

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Background and Aims: Patient/family education in childhood cancer care is recognized as one of the most effective strategies for better patient and family outcomes across the childhood cancer continuum; yet health professionals have limited training on the basics of health education. This study aims to: (1) describe participants' current patient/family education practices; and (2) compare their confidence level on relevant education competencies pre- and post-course attendance.
Methods: A 10-hour online training course on basics of health education was implemented for health professionals in childhood cancer care. Participants answered a pre- and post-course self assessment survey to describe their current practices, and measure their confidence level on relevant education competencies. Descriptive statistics were computed, thereafter.
Results: Twenty-two (22) participants included 15 (68%) staff nurses, 4 (18%) out-patient clinic staff, and 3 (14%) nurse navigators. All units in the selected Philippine public end-referral center caring for children with cancer were represented. Majority (77%) implements an individual approach in education. Only 2 (9%) stated that everyone taking care of the child is responsible for education. Most (32%) use teach back method to assess understanding. Confidence level on delivering health education increased from a mean of 3.5 (SD = 0.67) to 4.4 (SD = 0.51). Mean self-assessment increased on all relevant competencies pre- and post-course attendance. Assessment of education needs increased from a mean of 6.05 (SD = 1.91) to 8.33 (SD = 1.83); provision and reinforcement of education on diagnosis, treatment options, side effect management, and post-treatment care and survivorship from 6.18 (SD = 2.06) to 8.33 (SD = 1.87); promotion of autonomous decision making from 6.27 (SD = 2.12) to 7.92 (SD = 2.15); and education and reinforcement of adherence from 6.5 (SD = 2.15) to 8.5 (SD = 2.24).
Conclusions: Targeted training should be continued to increase relevant education competencies of health professionals in pediatric hematology-oncology.

P072 / #1015

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

BEREAVED MOTHERS' AND FATHERS' PERCEPTIONS OF COMMUNICATION ABOUT THEIR CHILD'S CANCER DIAGNOSIS AND WHEN THE ILLNESS BECAME INCURABLE - A POPULATION-BASED NATIONWIDE SURVEY

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Background and Aims: A vast majority of parents and children want honest communication and openness regarding diagnosis and prognosis but conveying bad news to children and their family is a challenging task for healthcare professionals. However, research shows that parents often struggle to grasp such challenging information. The aim of this study was to describe bereaved mothers' and fathers' perceptions of communication of their child's cancer diagnosis and when the illness became incurable.
Methods: This study derives from a population-based nationwide postal survey, including 232 parents (135 mothers and 97 fathers) who had lost a child to cancer 1–5 years earlier. The survey covered sociodemographic characteristics and study-specific questions about the parents' experiences of their child's illness and when the illness became incurable.
Results: Key findings of this study include that almost all (93%) parents want information when their child's illness become incurable. However, analysis revealed that fathers to a lesser extent than mothers reported that they were informed. Furthermore, parents reported that 13% of the children did not receive diagnostic information and 56% of the parents reported that their child never received the information that their cancer was incurable. Fewer children were present when a bad prognosis was communicated to the family than when the family received diagnostic information.
Conclusions: Most parents reported that they would like to know when their child's illness becomes incurable, and more than half of the parents reported that their child never received this information. Yet, it is unknown to what extent parents want their child to be informed and reasons for the child being uninformed remain unclear.

P073 / #1757

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

IMPACT OF THE COVID 19 PANDEMIC ON THE CONTINUITY OF TREATMENT IN PEDIATRIC CANCER IN A UNITY OF ONCOLOGY IN MEXICO

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Background and Aims: The COVID-19 pandemic impacted health systems in unprecedented ways. In Mexico, most third-level hospitals were converted into hybrid hospitals for the care of patients with Sars-Cov-2 infection and at the same time for the care of cancer children. Strategies were designed to reduce the risk of infection however most patients have had contact with infected people. Aims: To know the impact of the covid 19 pandemic in children with cancer of the unit and oncology of the HOSPITAL MATERNO INFANTIL ISSEMYM in Toluca Mexico
Methods: Cross-sectional cohort study. A random representative sample of patients treated in the oncology unit was included . We analized Demographic, clinical, diagnosis and stage of oncological treatment, characteristics, Also the treatment conitnuity, punctuality and compliance were recorded. Reasons for delay and modifications of the treatment were consigned
Results: We included 46 patients , 22 women, 26 men, 23 with leukemias , 26 with solid tumors , indicated treatment was 4 Surgery , 43 chemotherapy , 2 radiotherapy . Treatment continuity decreased from 75-90 % before March 2020 to 25-40 % in the first 6 months of pandemic onset with decrease in punctuality , 36% had delay in treatment with chemotherapy , due to drug shortage that was aggravated by the pandemic and 35% with delay in compliance in febrile neutropenic patients who they had WHO definition of suspected sars cov2. In 80 % the treatment was modified, 21 % due to toxicity, shortage of medications and delay of care in other areas due to infections in health staff
Conclusions: The COVID-19 pandemic has impacted globally, aggravating problems such as shortages of medicines. The multidisciplinary team was insufficient in our hospitals with limited resources , in addition the treatment was interrupted in all patients with respiratory symptoms for 1-3 weeks. Rapid tests have optimized the time of care in our hospital

P074 / #1074

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

APPLYING THE SIOP NURSING BASELINE STANDARDS IN PRACTICE-A NEW NURSE ORIENTATION IN KORLE-BU TEACHING HOSPITAL

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Background and Aims: Pediatric oncology in lower-and middle income- countries (LMIC) lack basic structure and terms of reference for nursing care of children with cancer. The SIOP nursing baseline standards serves as a guide for nurses in developing countries to offer quality nursing care for children with cancer. Empowering new nurses with skills and knowledge will go a long way to improve survival rates. The project was to equip new nurses in pediatric oncology with the requiste skills and knowledge.
Methods: Ten (10) new nurses (100%) were posted to the pediatric oncology unit of the Korle-Bu Teaching Hospital in 2020. The request for additional nurses was made using the SIOP nursing baseline standards as evidence to support more nurses. The nurses completed two weeks of didactic teaching and learning on various topics related to pediatric oncology nursing care using the sub saharan Africa Nursing Network educational pakage (SSANN) A pre and postest was administered. Competency assessment was done for each new nurse three(3)months after working with senior nurse mentors.
Results: Pre and post evaluations revealed that nurses increased their knowledge of early signs of childhood cancer. Increased knowledge occurred regarding tumor lysis syndrome with only 10% knowing about the symptoms before the class and 90% had good understanding afterwards. Evaluations revealed nurses' ability to quickly intergrate essential skills into nursing care.
Conclusions: The SIOP nursing baseline standards is an evidenced based pediatric oncology nursing standards that can help improve nursing care of children with cancer in developing countries. The SSANN educational package also when used in teaching new nurses posted to the units can help boost their confidence and improve survival rates for patients.

P075 / #628

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

BARRIERS IN ACCESS TO PSYCHOSOCIAL SUPPORT FOR YOUNG PEOPLE WITH CANCER

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Background and Aims: Children and adolescents experience cancer at a time of significant developmental transition. Both disease and treatment impact psychosocial well-being in significant, persistent ways. While the impacts are now described, and the need for psychosocial care is increasingly well recognized, to date, the barriers in access to care have not been well delineated. This is essential to understand to facilitate access to appropriate care and improve outcomes.
Methods: This study explored the barriers in access to psychosocial care for young people. Semistructured, audio-recorded interviews were undertaken with 16 young people. Eligible participants were diagnosed within the previous 24 months and recruited through the Queensland Youth Cancer Service (QYCS). Transcribed interviews were analyzed using content analysis.
Results: Barriers in access to support were related to person-centered, service-related, and systemic factors. Barriers experienced at diagnosis and during treatment were less common compared with barriers after treatment; these were significant and largely related to a lack of holistic, multidisciplinary survivorship care.
Conclusions: Barriers in access to psychosocial care are multifactorial, although most can be addressed through health-service responses. Ensuring standardized referral and repeated introduction of psychosocial care for young people is imperative, regardless of location of treatment. Flexible services are especially important for patients treated across different facilities. The development of comprehensive post-treatment survivorship models of care is also essential. Continued evaluation of the experience of young people and the barriers they face is also crucial to ensure responsive service development and promote optimal care.

P076 / #180

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

CHANGES IN BODY SIZE AND BODY COMPOSITION IN SURVIVORS OF CHILDHOOD CANCER: 7 YEARS FOLLOW-UP OF A PROSPECTIVE COHORT STUDY

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Background and Aims: Cancer treatment is known to have impact on nutritional status, and both underweight and overweight have been reported in several studies in survivors. A limitation of most studies is that they relied on retrospective data or were limited to a subgroup of patients. The current study aims to describe changes in body size and body composition prospectively in a heterogeneous sample of childhood cancer survivors and to evaluate associated factors.
Methods: Participants were 66 children diagnosed with heterogeneous malignancies 0-18 y at diagnosis. Data of body size, body composition, and associated factors were collected at diagnosis, one year, and seven years after diagnosis.
Results: In the total cohort mean BMI z-score increased during treatment. In children with hematological and brain malignancies mean zBMI continued to increase after end of treatment leading to quadrupling of the prevalence of obesity at seven years follow up. Low initial zBMI and maternal BMI were associated with increase in mean zBMI. Mean fat mass (FM) z-score, already high at diagnosis, increased during treatment in children with hematological and brain malignancies and evened out during follow-up. Changes in mean FM z-scores were predicted by type of malignancy (hematologic/brain malignancy versus solid tumor). Mean fat free mass (FFM) z-score started low at diagnosis, particularly in patients with brain tumors, increased during treatment in patients with hematological and brain malignancies, though decreased in children with solid tumors. At seven years follow-up a clear increase to normal was seen. Older age and low mean zFFM at diagnosis were found to be significant predictors for increase in mean zFFM.
Conclusions: The once obtained extra weight and fat mass remained in survivors of hematological and brain malignancies. This stresses the importance of life style interventions concurrent with therapy, especially for those who experience substantial gain in weight and fat mass during treatment.

P077 / #1378

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

LET'S EXERCISE PLAYING MUSIC

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Background and Aims: The Hospital admission of a child or a teenager diagnosed with cancer supposes a limitation of his daily physical activity and his social life. Prevent and improve the lost of fitness and provide well-being on patients in oncology ward are some of the main goals of the physiotherapy in Hospital Sant Joan de Déu.
Methods: A daily exercise program was implemented in September 2018 till it has to stope by the Covid-19 crises. It consists of different type of exercise for each day of the week. “Let’s exercise playing music” is the Tuesday exercise proposal. It is a link of Physiotherapy (aerobic work, strength exercises, coordination, balance and joint and muscle flexibility) with Music Therapy, to transform these practice into a more playful and enjoyable sessions and provide along with the physical benefits emotional and social ones. All patients of the oncology ward allowed to move out from their room were invited to the program, which took place in the ward gym. A “Let’s exercise playing music” was a 30 minutes session, structured in 4 sections: Activation (aerobic warm-up). Stations (work sites provided with an instrument to play while performing a strength exercise). Session ends with stretching and relaxation. According to its musical characteristics special songs were selected to accompany the activity,.
Results: The proposal was followed by 45 patients (17 females and 28 males in an age range between 5 and 16 years old) with a total of 72 interventions. Patients, families and health workers value very positively the program, generating a special, atractive, motivating and very moving atmosphere. It was well tolerated by patients while they enjoyed the sessions.
Conclusions: The program was easily implemented. It provided the patients with physical and emocional benefits and facilitated socialization between them. It will be restarted as soon as Covid allows it

P078 / #1850

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

CHEMOTHERAPY/BIOTHERAPY NURSE EDUCATION – CREATING A GLOBAL PROGRAM

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Background and Aims: The Association of Pediatric Hematology/Oncology Nurses (APHON) has a well-established chemotherapy/biotherapy curriculum which was created to provide nurses with key principles and theoretical knowledge to administer chemotherapy/biotherapy safely and competently. In a collaborative effort, a pilot study was conducted to determine the feasibility of utilizing the APHON provider chemotherapy certification to meet the required standard of practice for accreditation in Australia/New Zealand.
Methods: Members of APHON Global Outreach and Chemotherapy/Biotherapy Committees held meetings via Zoom with the Australia/New Zealand nurse leadership team to establish course structure and content as well as addressing logistics. The pilot course was held over a 4-week period with content for each module presented in 4 hour blocks virtually. Complimentary access to the Curriculum eBook and handouts via the APHON website were provided. Participants were assessed via an exam at the end of the course.
Results: The course was conducted in May 2021. Seventeen nurses from Australia and New Zealand participated in the APHON Chemotherapy/Biotherapy course, representing ten hospitals. All participants were experienced pediatric oncology nurses. There were five instructors, one coordinator and three APHON staff from the United States who taught and coordinated the program. There was 100% participation and attendance, and all nurses passed the exam on first attempt. Weekly debriefings and course evaluations provided feedback on course content and delivery. Challenges included navigating nine time zones, cultural and healthcare system differences, and access to course materials. Both instructors and participants benefited by the exchange of knowledge and clinical practice, teaching strategies, and discussion about advanced clinical nursing roles and responsibilities.
Conclusions: This pilot program highlights the importance of global collaboration and lays the foundation for future development of shared education resources between countries. This international education experience promotes a rich opportunity for nurses to reflect, learn and improve clinical care for patients and families.

P079 / #1561

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

LESSONS LEARNED FROM INNOVATING THE PEDIATRIC CANCER ENGAGING IN EXERCISE FOR RECOVERY (PEER) PROGRAM TO AN ONLINE MODALITY DUE TO COVID-19. USER & NON-USERS PERSPECTIVES

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Background and Aims: The focus of the PEER program is to increase physical literacy, fitness and socialization for children affected by cancer and their siblings. In response to the COVID-19 pandemic, the program transitioned to an online group format for youth (6-11 years and 12-17 years).
Methods: Anonymous surveys were distributed amongst 17 regularly attending families (16 kids and 9 teens) to better understand motivators and barriers of online programming, safety, and satisfaction. Another survey was completed for 25 parents of children that never or occasionally joined the program (N=18,7) to understand non-user barriers.
Results: Families primarily participated in the program to (1) improve fitness and (2) increase peer connections. All felt safe. 95% agreed that the sport kit increased engagement during and after the session. 83% of parents felt program participation increased their child's fitness level and confidence to exercise and 100% would recommend it to other families. Parents whose child/teen rarely attended PEER online recognized that 'physical activity is important for their child/teens recovery', 'helps their child/teen to socialize', and 'improves focus and academics' (80%, 67%, 83% strongly agree, respectively). Some of the key reasons the children/teens occasionally or never participated in PEER online were because day/time did not work and/or nervousness to participate. Fatigue was another frequent reason for not participating, however, 72% of parents indicated an understanding that physical activity decreases cancer-related fatigue. Finally, 84% mentioned that their oncologist recommended an active lifestyle after treatment vs 60% during treatment.
Conclusions: This program was engaging, safe, accessible, and improved confidence to exercise for children affected by cancer. Fun and inclusion of socialization are key elements to increasing enjoyment and adherence. Providing a sport kit is recommended. Education of families and health care teams about exercise benefits and local physical activity programs are important to decrease barriers to participation.

P080 / #1588

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

DETERMINATION OF PAEDIATRIC ONCOLOGY PROVIDER ATTENTION TO CARE-GIVER BURDEN AND STRESS MANAGEMENT-:, ZIMBABWE

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Background and Aims: Approximately 250 children/adolescents a year are diagnosed with cancer in Zimbabwe; all are treated at Parirenyatwa Group of Hospitals (PGH), the largest tertiary and referral hospital. Twenty nurses provide care on Ward A4 Special. Care-givers are key in the delivery of paediatric palliative care, from diagnosis to end of life. The World Health Organisation has acknowledged the significance of family care for sick children, especially in cases of cancer and other chronic diseases.
Aim
Identify the needs of care-givers of children and adolescents with cancer at PGH.
Methods: This cross-sectional study was conducted with care-givers of children with cancer. Eligibility criteria: 20-40 years, speak English, Ndebele or Shona, and no cognitive deficit. A researcher-developed questionnaire based on a topical literature search was created in collaboration with other hospital-based palliative care specialists. The questionnaire included 5 items, scored on a Likert-type scale (1- 5) and was given to the care-givers to complete anonymously at the hospital.
Results: A total of 50 care-givers participated (10 male and 40 female). The majority (80%, n=40) expressed that they were extremely devastated when they heard their child's diagnosis. All participants indicated they were struggling to cope when asked how the child's condition had impacted the family's living conditions and all reported being depressed. Funding of the child's treatment was (60%, n=30) self-funded, and (20%, n=10) social welfare and assistance from a non- governmental organisation.
Conclusions: This study provided evidence that the care-givers of children and adolescents with cancer in Zimbabwe suffer from depression due to the child's illness and the need for funding of the prescribed treatment. As health-care providers, and nurses specifically, we need to cushion the care-givers from the point of diagnosis by providing more effective counselling and support before and during treatment as well as lobbying for financial assistance.

P081 / #936

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

COMPARISION OF NORMAL SALINE AND HEPARINIZED SALINE SOLUTION FOR FLUSING CNTRAL VENOUS CATHETER IN PEDIATRIC PATIENTS

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Background and Aims: We compared the efficacy of normal saline (NS) with heparinized solution (HS) as a method of flushing central venous catheter (CVC) in pediatric patients undergoing hematopoietic stem cell transplantation (HSCT). This was a prospective, randomized, double-blind clinical trial.
Methods: Twenty-two pediatric patients had newly placed CVCs for allogeneic HSCT between February 14, 2018 and December 3, 2018 at our center. All patients were implanted with a triple-lumen 12.5 French tunneled-Hickman catheter through internal jugular or subclavian veins. Of 22 patients, 11 were flushed their CVC with HS and 11 with NS. CVC-related complications including occlusion, exit-site infection, tunnel infection, CVC-related bloodstream infection, mechanical event, and premature removal were assessed.
Results: During a 213-day period (range, 84-420), one CVC partial occlusion occurred in HS at 77 days post-insertion, but no complete occlusion happened in total patients. Eight CVCs (NS and HS in 4 each) were prematurely removed at a median of 226 days (range, 168-420). Reasons for premature removal were documented bacterial infections in 3 (staphylococci in 2 and enterococcus in 1), exit-site infection in 3, tear in the external portion of catheter in 1 and death without catheter-related events in 1 patient. At a median follow-up of 388 days (range, 271 to 563), CVC occlusion-free survival was 96% ± 4.4% (100% for NS versus 91% for HS. CVC occlusion-free survival was not different between two flushing methods ($P>0.05$).
Conclusions: Normal saline seems to be as effective as heparinized solution for maintaining patency of placed CVC in pediatric patients. Further study including more cases is warranted to verify our finding.

P082 / #271

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

TAKING OVER CARE FOR UKRANIAN CHILDREN WITH CANCER: EXPERIENCES AT THE PRINCESS MAXIMA CENTER

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Background and Aims: The war in Ukraine has caused an acute emergency in the care and treatment of children with cancer. It is important that care for Ukrainian children with cancer can be continued, whether in the country itself or elsewhere in Europe.
Methods: The International Office of the Princess Maxima Center is a member of the St. Jude4Ukraine group, which coordinates receiving our target group from Ukraine in order to aid to children with cancer in Ukraine. This is carefully coordinated and attuned with all the affiliated SIOP countries.
Results: All children and family members have been picked up from Poland by plane by our medical team. A medical check has been performed upon arrival in our center; the children were organized by specialty and medical teams (including the pharmacist) were ready to perform a second triage and intake with support of an interpreter. All children have been scheduled for different appointments the next few days. The families have been accommodated by host families, mostly from our center, these families have been instructed in advance by several professionals from our center. The focus is on providing families with daily structure as soon as possible, enabling children to go back to school and giving help from the government (financial, care) they are entitled to. The use of interpreters and other tools to communicate is of great importance.
Conclusions: In order to treat children with cancer from Ukraine, it is important to focus on a number of themes; legal, medical, psychosocial support for families and for professionals, the following topics are important: Transport, capacity management, housing, culture differences (also in care) and communication.

P083 / #1907

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

BEDSIDE ULTRASOUND TO ASSESS MUSCLE MASS IS A FEASIBLE MEASUREMENT TOOL FOR HEALTH PROFESSIONALS FROM DIFFERENT BACKGROUNDS.

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Background and Aims: Ultrasonography can assist in clinical and therapeutic diagnosis; it is a non-invasive and operator dependent method. It is a good tool to assess quadriceps femoris thickness and corroborate nutritional data. A topic of extreme importance for the care of hospitalized children, especially oncological children who present greater loss of lean mass. This study aims to evaluate performance and reliability degree of measuring the Quadriceps Muscle Thickness (QMT), among examiners of different backgrounds (physicians, nurses, dietitians, medical and nutrition students).
Methods: A prospective and observational study was performed with health professionals related to the nutritional care of children with cancer. The standardization of measurements and validation of image collection was performed in an 8-hour training structured course with a practical evaluation at the end. All parameters were compared to the gold standard (radiologist). Pearson correlation coefficient was used to calculate the realibity of the QMT between examiners and gold-standard.
Results: Thirteen individuals from different professional categories participated. The group of participants was heterogeneous in terms of training time, area of expertise, and prior knowledge. In total, 311 images were examined by the trainer and compared to the gold-standard. We observed a substantial (PCC=0.822) correlation between image acquisition using a structured theoretical-practical course. It was also noted, with statistical relevance (p-value=0.03), that individuals over 30 years of age presented better adequacy of the images throughout the various measurements. This fact can be explained that regardless of the contact or not with new technologies, the time spent in the profession may seem to impact this finding positively.
Conclusions: Through specific training, evaluating the student in the different spheres of learning and retention of knowledge, it is possible to reach a substantial correlation between measurements made by different examiners, indicating that QMT is a feasible and easily applicable tool.

P084 / #177

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

AYA ROOMSERVICE: A MORE PLEASANT STAY IN THE HOSPITAL.

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Background and Aims: In University Hospital Leuven (Belgium), more than 200 AYAs (Adolescents and Young Adults) are diagnosed with cancer every year. These AYAs have age-specific health care needs that too easily stay undetected and unanswered in adult wards. A multidisciplinary working group of the Leuven Cancer Institute has taken important steps to promote age-specific care for AYAs in UZ Leuven. One of the initiatives is the optimization of the hospital stay of AYAs in the adult wards.
Methods: It is very important for young people to get on with their lives. One of the objectives of the working group was to bring the normal living environment of young people into their hospital room. The idea was to offer them a box full of possibilities to relax during their stay and to decorate their room with accessories. Through a survey, the AYAs were allowed to decide what exactly should be in the box.
Results: This resulted in the AYA Roomservice: the young patient chooses from the box what he want to use, just like a real roomservice. The purpose of the AYA Roomservice is fourfold: decorating the hospital room, distraction, providing information resources and support. In addition to an information folder with 'Good to Know' tips, there are mood lamps, an aroma dispenser, beautiful sheets and nice crockery to make the room 'AYAproof'. In addition, the box also contains board games and a tablet with a Netflix and Spotify account.
Conclusions: The project started in two departments in 2018. After a positive evaluation by the young people themselves, the project was expanded in 2021 to seven other oncology units, including pediatric oncology. The project was made possible thanks to the support of the Albert Fund and the help of volunteers. More information: AYA@uzleuven.be

P085 / #178

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

MY NEEDZ: A DIGITAL TOOL FOR AYA IN UNIVERSITY HOSPITAL LEUVEN

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Background and Aims: Every year in Flanders (Belgium), slightly less than 1000 'adolescents & young adults' (AYA) are diagnosed with cancer. In Univesity Hospital Leuven, approximately 200 AYA are diagnosed with cancer every year. Due to their age and the stage of life in which they are confronted with cancer, these AYA have age-specific needs that too easily remain undetected and unanswered in adult wards. To meet this, we designed a tool within our digital patient platform mynexuzhealth, called MY NEEDZ.
Methods: By offering information and psycho-education, we want to meet the needs of AYA and empower them to ask their questions. The MY NEEDZ tool invites them to think about their own needs and questions, around age-specific themes. Based on recognizable statements, we explore possible problems and questions typical for AYA. We provide information for a better understanding of what they are experiencing and give suggestions on how to deal with it. In addition, we also advise which healthcare providers they can contact. If they can't find an answer to their question, they are given the opportunity to ask their question inside the tool. A healthcare provider will then contact them to find out how the AYA can be helped.
Results: The tool was co-developed and tested by AYA from our AYA Advisory Group. In a next phase (begin 2022), 30 AYA's will be testing the tool in order to make the necessary adjustments. We expect to offer the tool to every AYA in our hospital at the end of 2022. We hope to capture questions and needs from AYA that have not yet been detecterd or answered.
Conclusions: Thanks to the tool My Needz, available in the app mynexuzhealth, every AYA can consult age-specific information and ask questions during their oncological trajectory and afterwards. It provides a platform where AYA discover answers to their needs, at any time.

P086 / #715

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

TRAINING IN 'CUSTOMIZED CARE FOR AYAS' FOR HEALTHCARE PROVIDERS IN FLANDERS (BELGIUM)

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Background and Aims: In 2017, almost 1000 patients between the ages of 16 and 35 were diagnosed with cancer in more than 50 different hospitals in Flanders (Belgium). Appropriate care for AYAs means multidisciplinary, integrated care for patients who have unique and diverse needs due to their age and stage of life. With this training, the Cédric Hèle Institute (CHi) wants to raise awareness among caregivers from different institutions.
Methods: In 2019, CHi set up a steering group with the aim of developing a (multi-day) training course on AYA-specific care. This steering group is composed of care providers from various centers (doctors, social workers, psychologists, policy makers, ...) and AYAs themselves. In terms of content: good practices from abroad (the Netherlands, UK, Australia, ...), results from research and experiences of care providers and AYAs were examined.
Results: In addition to existing introduction days on AYA-specific themes, a more extensive training module was developed. This first AYA basic training in Flanders took place in 2020 and consisted of a four-day training. Following themes were included: communication with AYAs and their families, medical aspects, palliative care and AYAs, identity development, impact on self-image, revalidation, sexuality, fertility, fear of relapse, ... Given the holistic and interdisciplinary nature of AYA care, we offer this training interprofessionally. In total, across the introduction days and the first AYA basic training, more than 80 care providers (doctors, nurses, social workers, psychologists, moral consultants, nurse specialists, ...) were trained in specific care for AYAs.
Conclusions: In collaboration with its partners, CHi wants to offer healthcare professionals more specialized knowledge and skills related to AYA care. Introduction days and a basic training were developed for this. In the future, further courses, in-depth courses and e-learning will be developed to further stimulate the exchange of knowledge and experience about this target group in Flanders (Belgium).

P087 / #890

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

TELEO: A VIRTUAL TOOL FOR NURSING EDUCATION IN LATIN AMERICA

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Background and Aims: There are scant virtual education tools for Latin American (LATAM) nurses; fewer on pediatric oncology or in Spanish. In 2021, TELEO [Tele-educación en Oncología Pediátrica] was created for educating pediatric oncology professionals through a My Child Matters grant Two free nursing education programs (one orientation and one continuing education in line with the SIOP Baseline Standards for Nurses in low- and middle-income countries) were developed in Spanish.
Methods: The first TELEO program (2021), was a weekly, 2-month online orientation to pediatric oncology nursing. Topics taught by expert LATAM and international nurses included oncogenesis, chemotherapy care, vascular access, pain management, and others. Classes limited to 50 nurses for questions and discussion. Later, this program was on-demand with free access to recorded classes with expert nurse support through the TELEO networking platform. The second TELEO program (2021) was a monthly online 1-hour meeting with no registration requirement. Designed as continuing education for more experienced pediatric oncology nurses, topics included nursing research, medication errors and second victim issues, palliative sedation, and CAR T-cell therapy.
Results: Overall, 293 nurses from 14 countries participated in the two orientation courses: 225 South Americans and 68 Central Americans. 48 completed the synchronous and 83 the on-demand course. Colombia had the most attendees (70 nurses), followed by Uruguay and Argentina.The pass rates were 70% (first edition) and 63% (second edition); total dropout rate was 54%. Ninety-one percent considered the course useful, and 98.8% would recommend it. Future topics indicated educational needs, e.g., bone marrow transplant and palliative care. The second program's monthly meetings were dynamic and interactive; 237 participated.
Conclusions: TELEO virtual education by regional and international expert nurses provides useful training opportunities and a discussion platform for common LATAM nursing problems . Alternative formats may provide an enhanced experience and address formal courses' high drop-out rates.

P088 / #674

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

DEVELOPMENT OF VIDEO CALL IN A FOLLOW-UP PROGRAM FOR CHILDREN NEWLY DIAGNOSED WITH CANCER AND THEIR PARENTS

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Background and Aims: In 2017, we developed a systematic follow-up program at home after the first discharge to ensure that families receive the information, guidance and training they needed to handle care and treatment tasks. Families receive the program if they live within 50 km from the hospital. The program is provided by a nurse from the childhood cancer department. Our survey of the program showed that the great majority of the families found the program very usable and comforting. To give all families access, we want to extend and provide the follow up-program as a video call to families that cannot receive a home visit. As the first step, the aim of this pilot study was to develop the video call technology and determine whether it may be usable if it was an option.
Methods: This is an explorative ongoing pilot study at the childhood cancer department at the university hospital in Copenhagen. We initiated a collaboration with the new Mary Elizabeths Hospital to develop the video call technology and conducted interviews with to families. We asked when the videocall should be after the discharge, how long it could take and which topics they wanted follow-up on.
Results: The video call is developed in the electronic medical journal system ‘EPIC’ but has not yet been tested. The interviews showed that the families would accept a video call if the department offered it. They did not think it could replace the follow-up visit at home, but it would better than no follow-up.
Conclusions: The preliminary results indicate that a video call can be used in the follow-up program instead of a visit at home. More data are needed, and the next step is to test the video call with five families and evaluate with a short questionnaire.

P089 / #60

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

THE LIVED EXPERIENCES OF MOTHERS OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA IN MALTA

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Background and Aims: Acute Lymphoblastic Leukaemia (ALL) is one of the most common cancerous illness amongst the paediatric oncology population. Most patients receive full treatment for ALL within the local oncology centre as patients with other diagonosis require international hospitalisation. The inital induction phase of treatment for ALL is characterised by a lenghty period of hospitalisation which ranges between four and six weeks until medically stable to continue treatment at home. This phase is surrounded by a captivating range of emotions felt by parents upon the return home. The transition of care shifts from a hospital based setting to a home-care approach. Behavioural concerns, fear of the unknown and physical changes of the child along the struggle to deal with oral chemotherapeutic medications and the care management of central lines are some of the main concerns that trouble parents as they try to manage the challenges brought about by the new 'normality'. The aim of this study sought to explore the lived experiences of mothers who strive to adapt to the situation of returning home for the first time with a child diagnosed with ALL.
Methods: For the purpose of this research, a qualitative method to explore the lived phenomenon encountererd by mothers was used. The reseacher followed the approach of an interpretative phenomenological analysis (IPA). Data was collected from in-depth semi-structured interviews, conducted with five mothers.
Results: Six super-ordinate themes emerged which are mixed emotional cycle, relocation, daily struggles of living with ALL, the way forward, shifting perspectives and supportive encounters.
Conclusions: The need of supportive and educational programmes was reflected for health professionals and families along the need for employmnet assistance for parents and a structued home health-care based support. More reserach is essential to explore the father's role and the difficulties encountered, so as to enhance a favrouable quality of life for all the family.

P090 / #1138

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

UTILIZING QUALITATIVE STUDY RESULTS TO INFORM NOVEL EDUCATIONAL INTERVENTIONS AT A PEDIATRIC ONCOLOGY CENTER IN EL SALVADOR

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Background and Aims: El Salvador is a low-middle income country (LMIC) with a 52% overall survival for childhood cancer, compared to 80% in high-income countries. Abandonment and lack of treatment adherence are major barriers to improving the survival rate in children and adolescents with cancer in LMICs. Previous research at Centro Médico Ayúdame a Vivir Fundación (CMAVF) in El Salvador identified common questions and educational needs shared by caregivers and health care providers in the early stages of a new cancer diagnosis. Results were subsequently utilized to inform “Day One” videos to complement the initial discussion following a new diagnosis. Recognizing the need for further tailored, educational interventions, the healthcare team at CMAVF has created a project entitled “Emely’s Suitcase” to provide lighthearted anticipatory guidance at cancer treatment initiation through age-appropriate education aiming to increase treatment adherence.
Methods: The CMAVF healthcare team conducted qualitative, semi-structured interviews with patients, families, and healthcare staff in February 2019 and March 2022 to assess the most important information that patients and families need to know related to the initial diagnosis, self-care and hospital procedures and expectations. After analyzing the interviews' common themes, educational resources were developed for implementation at CMAVF.
Results: Three educational tools were created for different age groups including a coloring book and doll, simple infographics, informational booklets, and a Pop-Up Book. The CMAVF psychology team piloted these materials and solicited feedback from six patients, six families, two nurse educators, and one pediatrician. A training program was created for volunteers to implement the curriculum to ensure sustainability.
Conclusions: Educational needs assessments that are patient- and family-centered can be utilized to develop tailored educational tools that are specific to the context of each clinic and unique patient population. The next steps will assess patient and family knowledge gain and acceptability of the information.

P091 / #225

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

MENTORSHIP: NURSES SUPPORTING NURSES: A PILOT PROJECT IN THE HAEMATOLOGY/ONCOLOGY/ BLOOD AND MARROW/TRANSPLANT/ CELLULAR THERAPY PROGRAM

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Background and Aims: Pediatric oncology comes with many difficulties including challenging patient and family interactions, complex therapies, and palliative management of pediatric patients. Prior literature has shown that novice pediatric oncology nurses are ill-equipped to assess and manage these challenging situations. Coping strategies have not been developed therefore nurses feel overwhelmed and unsupported. These impacts on nursing morale play a significant role in nursing attrition in the early years of a nurses' career. The aim of this pilot project for the haematology/oncology/SCT division at our hospital was to provide support and nurture novice nurses as they navigate their first year as independent clinicians with an eventual goal to measure retention at two and five years.
Methods: Via email, we asked nurses if they would be interested in mentoring new staff. Nurses and advanced practice clinicians were required to have a minimum of five years of Oncology BMT/SCT experience. Mentorship education was provided. We developed a process where a newly hired nurse can choose a mentor from a profile list. Mentorship was a requirement for new hires. The mentor-mentee pair were required to meet four times each year. The mentee prepared objectives and areas for discussion or reflection. Two surveys administered to the mentees six months apart evaluated the relationship, the reflective practice element and the effectiveness of the relationship.
Results: A total of thirty nurses were interested in mentoring. Seventeen novice nurses participated (100 %). Fifty-three percent (9/17) of the mentees completed the survey one year after starting the program. Eighty-nine percent (8/9) of the mentees found the relationship supportive and suggested mentorship beyond the first year.
Conclusions: Mentorship is an effective method of supporting novice nurses in a difficult field as they develop into independent clinicians. The mentorship program will continue at our center, and nursing attrition at two and five years will be evaluated.

P092 / #1058

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

SYMPTOMATIC PRESENTATION OF CANCER PATIENTS WITH ACUTE METHOTREXATE TOXICITY TREATED WITH CARBOXYPEPTIDASE

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Background and Aims: Methotrexate is a common chemotherapy agent used in treatment protocols for pediatric cancers. Acute methotrexate toxicity due to abnormally high methotrexate levels can lead to multiorgan damage and death, and carboxypeptidase is an approved treatment. Presenting symptoms of acute methotrexate toxicity are not well described in the literature. The aim of this study is to describe early clinical signs and symptoms in patients with acute methotrexate toxicity to educate nursing staff, who are often the first care providers to note symptoms.
Methods: A single institution retrospective medical record review of patients who received carboxypeptidase due to methotrexate toxicity from 2006 to present was completed. Data collected on 13 patients included age, gender, dose of methotrexate, methotrexate and creatinine levels at 24, 48, 72, 96, and 120 hours, timing and value of peak methotrexate and creatinine level, presenting symptoms, and timing. Descriptive statistics were utilized.
Results: The 13 patients consisted of 11 osteosarcoma, 1 pleomorphic sarcoma, and 1 lymphoma patient. Five patients had abdominal pain, 3 had back pain, 3 had extremity pain, and 9 had severe nausea/vomiting. Mean 24-hour methotrexate level was 323 uMol/L (range 17.5 – 826.8 uMol/L), mean peak creatinine level 2.1 mg/dL at 44 hours. Mean time to symptom onset from start of methotrexate was 16.5 hours for abdominal pain, 16 hours for back pain, 15 hours for extremity pain. Nausea and vomiting was seen frequently during the infusion of methotrexate. Mean time from first symptom to carboxypeptidase dose was 34 hours.
Conclusions: As bedside nurses are most often the first line, early symptom recognition is crucial for acute methotrexate toxicity. The effectiveness of carboxypeptidase decreases when given more than 60 hours after exposure to methotrexate. Next steps include development of an education module for nurses on methotrexate toxicity.

P093 / #1106

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

INTEGRATIVE THERAPIES: A NON-PHARMACOLOGICAL NURSING INTERVENTION FOR SYMPTOM MANAGEMENT

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Background and Aims: Pediatric patients diagnosed with oncology, hematology and immunology conditions often experience pain, nausea, anxiety and other side effects. In an effort to augment traditional treatments, bedside nurses on the hematology/oncology/ hematopoietic stem cell transplant units at Boston Children's Hospital adopted a holistic approach to their practice by providing Integrative Therapies (IT). IT are nonpharmacological interventions including Reiki, relaxation massage, and yoga. As a result of the positive reports and increasing patient requests, the IT Program was developed in 2019 and serves to enhance a patient's physical, mental, emotional and spiritual well-being. The IT team consists of five specially trained nurses available 30 hours per week providing 30-minute IT sessions.
Methods: The IT team created a data collection tool to be completed before and after patient IT sessions including: a radial pulse and breaths for thirty seconds. Patients completed the Wong-Baker FACES® scale to measure pain, Baxter Animated Retching Faces (BARF) scale to measure nausea, Children's Fear scale to measure fear/anxiety and a visual analog scale to measure fatigue. Demographics are also collected. Qualitative data is obtained through open ended questions about the patient's IT experience. All data was recorded into an Excel spreadsheet.
Results: There were 946 IT sessions from September 23, 2019 – March 5, 2021. Data was obtained from 751 sessions. Results included patients who experienced one of the symptom variables to start and completed a pre and post rating of the variable. Of those patients: 63% reported a decrease in pain, 61% reported a decrease in nausea, 74% reported a decrease in anxiety and 54% reported a decrease in fatigue.
Conclusions: Data driven information was acquired to support the IT program and its benefits to patient care. The program provides valuable nonpharmacological interventions, especially for symptom management.

P094 / #1211

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

ADDRESSING GLOBAL HEALTH ISSUES IN OCEANIA- "CLOSING THE GAP IN OUR NEIGHBOURHOOD"

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Background and Aims: Global disparities for childhood cancer survival rates between high-income (HIC) and low-middle income (LMIC) countries are well documented. The World Health Organisation, St Jude Global, and SIOP share the common goal to improve the survival of all children with cancer – irrespective of where they live. Encompassing land and sea, Oceania is characterized by its vast geography, with a diverse mix of ethnicities and cultures. Comprising 18 countries, only Australia and New Zealand [NZ] are classified as HICs; the remaining 16 are classified as small-island, low-income countries (LIC). Within the Oceania region there is a wide variation in healthcare provision which, together with geographic barriers of distance and limited infrastructure, create challenges to provide support.
Methods: Method The paediatric oncology workforce in LICs within Oceania are supported and strengthened by the establishment of a multidisciplinary group to provide teaching, training and protocol development and implementation.
Results: Since 2014, representatives from Australia and NZ have worked to develop and implement strategies that provide in-country support and capacity building. These include: international observorships and fellowships (nursing and medical), twinning programs and in-country visits. To date, key champions in specific regions (Papua New Guinea, Timor Leste, Laos and Fiji) have been identified to promote and implement oncology nursing education programs. In 2022, the SIOP Oceania Advisory Board was formalised to further promote and consolidate support. The Board consists of multiple expert members from Australia and New Zealand representing medical, nursing, allied health, psychosocial and family support groups.
Conclusions: Conclusion Successful cancer care in these regions requires the Six Baseline Standards for Paediatric Oncology Nursing to be met. Partnering with key stakeholders, SIOP Oceania aims to implement nurse-led training programs that support these international standards of care. Moreover, strategies will continue to be developed to support sustainable in-country care of children with cancer and improve survival.

P095 / #108

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

ASSESSING FEASIBILITY AND FACE VALIDITY OF TWO NAUSEA INSTRUMENTS: A CLINIMETRIC STUDY IN CHILDREN WITH CANCER.

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Background and Aims: Chemotherapy causes distressing side effects such as nausea. However, control of nausea in children remains challenging. Two clinimetric instruments are available for optimizing recognition and management of nausea in children: the Pediatric Nausea Assessment tool (PeNAT) and the Baxter Retching Faces (BARF) scale. Nevertheless, more knowledge regarding practical use and children's preferences is needed. This study aimed to assess feasibility and face validity of both the BARF and the PeNAT according to children aged 4 to 18 years old with cancer treated in a paediatric oncology centre.
Methods: A quantitative clinimetric study (n=34) was conducted. Feasibility and face validity were measured, and scores of the BARF and the PeNAT were compared to each other. Feasibility included three items: understanding, ease of use, and communication. Face validity was studied in terms of: to what extent did faces of both tools correspond with the children's feelings of nausea severity. A Wilcoxon signed rank test was executed to statistically compare outcomes of both tools.
Results: Both tools complied to the feasibility criterium, and the BARF was more feasible than the PeNAT. Scores were lower for children aged 4 to 8 years old in comparison with older children, but not significantly different. The faces of the BARF corresponded significantly more with children's feelings of nausea than the PeNAT, however, the neutral face did not.
Conclusions: Both tools are feasible, however difference between age groups should be taken into account for communication and understanding. Children prefer the BARF's faces, however, they prefer the PeNAT's neutral face. Because most children were not nauseous at the time of this study, different outcomes could have been achieved and should be taken into account for future research.

P096 / #853

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

EXPECTATION ON THE ROLE OF ADVANCED NURSE PRACTITIONERS IN PEDIATRIC HEMATOLOGY ONCOLOGY: A DESCRIPTIVE QUALITATIVE STUDY

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Background and Aims: China ranks among the top five countries in the world with the highest burden of pediatric hematology and oncology. As a vital position of specialized nursing, the advanced practice nurse in pediatric hematology oncology (PHO-APN, as an abbreviation) have been established in developed countries for decades, but there is no such position in China. This study is to explore expectations of stakeholders on the role of PHO-APN in China, under the guidance of Hamric's Advanced Nursing Practice Theory, in order to develop this position in future.
Methods: From November 2020 to April 2021, 18 stakeholders, including advanced nursing practice experts, doctors, nurses, children's families in this specialty, were purposively selected for one-to-one in-depth interviews. The semi-structured interview started with a wide range of questions, and each lasts 60-90 minutes. Then each interview was transcribed word by word and sentence by sentence. The data were analyzed by qualitative content analysis, through transcription, coding, generic analysis, description and organization, in QSR NVIVO12 0 software.
Results: Three themes were extracted as follows. A) Necessity of developing the PHO-APN in China: The PHO-APN in China is necessary, in terms of policy environment, clinical needs and nurses' personal development. B) Position responsibilities of PHO-APN: the responsibility of PHO-APN should be established based on the clinical needs, including three roles, filling gaps, promoting care quality, and training and education. C) Selection of PHO-APN candidate: the possible candidate should be based on capability and quality, including professional competency, physical condition, team communication ability, system-based analysis and decision-making ability, self-learning and research ability.
Conclusions: The position responsibilities of PHO-APN in China should focus on clinical needs, including filling gaps, promoting care quality, and training and education, so as to effectively improve the system efficiency and the prognosis of children. Nurses and doctors had basically the similar expectations, but there were also differences.

P097 / #962

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

RISK FACTORS OF FEBRILE NEUTROPENIA IN CHILDREN WITH ACUTE LEUKEMIA

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Background and Aims: Febrile neutropenia is one of the most common and severe complications associated with chemotherapy. The investigation is to explore the occurrence and risk factors of febrile neutropenia in children with acute leukemia in a tertiary pediatric hospital in Shanghai, China.
Methods: A total of 801 pediatric patients with acute leukemia treated with chemotherapy in the department of pediatric hemantology in a tertiary pediatric hospital from January to December, 2020 were selected. The demographic, disease-related, treatment-related factors were collected. Logistic regression analysis was used to screen out the risk factors of FN, and ROC was used to assess the resulting equation.
Results: There were 268 patients occurring the FN, with an incidence rate of 33.46%. Logistic regression analysis showed that age, damaged oral mucosa in 5^{th} day after chemotherapy, recurrence, first-time chemotherapy, cytarabine-containing regimen, neutropenia in 5^{th} days after chemotherapy were the risk factors of FN. The AUC of this model is 0.884. When the cutpoint was 0.2957, the sensitivity and specificity of the model were 0.881 and 0.822, respectively.
Conclusions: The incidence of FN in pediatric patients with acute leukemia is relatively high, and the established model showed certain clinical value with moderate predictive capability. Prevention of FN should be emphasized from the first-time chemotherapy, especially in pediatric patients with recurrence, young age, early neutropenia. At the same time, nurses should pay attention to assessment of oral mucositis, blood routine test, and vital signs, actively prevent and treat oral mucositis and bone marrow suppression.

P098 / #745

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

STRATEGIES TO PREVENT FALLS IN HEMATOPOIETIC STEM-CELL TRANSPLANT (HSCT) PATIENTS

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Background and Aims: Pediatric falls are complex, as many factors influence both the risk of falls and the likelihood of sustaining injury. Pediatric falls occur less often and have different associated risks than in adult hospitalized patients. Fall prevention requires daily risk screening, education and partnership with families, and ongoing evaluation of fall prevention strategies. Hematopoietic Stem-Cell Transplant (HSCT) patients are at higher fall risk due to factors such as complications of disease and treatment, prolonged hospitalization and deconditioning. On our HSCT unit, staff nurse “fall champions” collaborate with nursing leadership to collect and analyze falls data monthly. In 2019, it was noted that the unit’s fall rate was trending upwards, peaking in 2020 to 9.61 per 1,000 patient days. A goal was established to decrease patient falls on the HSCT unit.
Methods: In 2019, a Fall Prevention group was formed, comprised of staff nurse champions, nursing leadership and physical therapists. The following strategies were implemented over a two year period: •Development of Higher Fall Risk Category •Creation of targeted interventions for patients identified as Higher Fall Risk •Initiation of purposeful rounding every four hours with vital signs, with shared responsibility between nurses and clinical assistants for rounding and documentation •Apparent cause analysis (ACA) reports performed with all falls •Physical Therapy/ HSCT pilot to reduce deconditioning •Nursing Leadership follow up post falls, engaging parents in prevention of recurring falls
Results: The rate of patient falls with injury decreased from 9.61 to 0.95 per 1,000 patient days on the HSCT Unit between January 2020 and January 2021.
Conclusions: Pediatric patients undergoing Hematopoietic Stem Cell Transplant are at increased risk of injury due to falls. Targeted interventions can reduce the risk of falls with injury in this vulnerable patient population. Collaboration between multiple disciplines to achieve shared goals increases likelihood of success.

P099 / #560

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

THE IMPORTANCE OF AN ONCO-FERTILITY PROGRAM FOR PEDIATRIC ONCOLOGY PATIENTS

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Background and Aims: Introduction; In the Netherlands pediatric oncology care is centralized in one hospital since 2018. 600 new patients a year are seen. Of these patients, 25-35 % classify as high risk (HR) for infertility. An onco-fertility program was started navigated by a nurse-practitioner. The program runs with intense collaboration between the different specialties. All new patients are identified according to the international guidelines on fertility care. The fertility-risk is based on the cyclofosfamide equivalent dose, radiotherapy dose and surgery to the gonadal area. Since 2018 awareness was created by teaching sessions among colleagues, nursing staff, and parent association organizations. The onco-fertility program was started as standard of care.
Methods: ; All patients are informed on fertility risk by their oncologist. All HR children are additionally councelled by the onco-fertility nurse-practitioner and referred for further counseling to gynecology for ovarian tissue cryopreservation(OTC) or urology for sperm cryopreservation or testicular biopsy (in research setting). Monthly the onco-fertility working-group members discuss difficult cases and research in the field.
Results: ; In 2019, 29 % cases and in 2020 31% of cases were HR for infertility. In both years 45 % of these cases had fertility preservation performed. In 2021, 30 % cases HR were identified, of these HR patients in 44 % preservation was performed. Reasons for not preserving fertility were diverse.
Conclusions: Conclusion. Awareness of the fertility risk in pediatric oncology patients is necessary. All patients need to be informed and all HR patients need to be counselled on the risk of infertility and offered fertility preservation before start of their treatment. An active onco-fertility program helps to offer the best option for future fertility for these patients.

P100 / #558

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

PILOTING THE DANISH VERSION OF THE "AUSTRALIAN AYA ONCOLOGY SCREENING TOOL" AT THE DEPARTMENT OF CHILDREN AND ADOLESCENTS WITH CANCER AT AARHUS UNIVERSITY HOSPITAL(AUH)

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Background and Aims: It is a known challenge that adolescents and young adults(AYAs) need help and support during and after cancer treatment. Unfortunately, they sometimes experience that their desired topics are not addressed. The Australian AYA Oncology Screening Tool is a validated tool that can be used in consultations with AYAs with cancer and support them identifying, discussing and prioritizing psychosocial issues that need to be addressed in their care. The tool has been translated into Danish following the World Health Organization's process of translating and adapting instruments. The tool has been tested in the Oncology and Haematology department at AUH on AYAs (+18 years) with good experience. The purpose of this study is to investigate whether the tool can be used with AYAs (14-22 years) in the follow-up consultations. Furthermore, we will investigate the use of split visit, where parents only participate for a limited period of the consultation, provide increased opportunity for AYAs to talk about their concerns and challenges after cancer treatment.
Methods: The Department of Children and Adolescents with Cancer AUH began using the tool with AYAs (14-22 years) in the follow-up consultations. The consultations include a physician and a nurse, who incorporate the tool into their consultations with AYAs. After each consultation, the physician and nurse fill out a questionnaire about their experience and feasibility of the tool, while AYAs and parents evaluate their experience of the consultation.
Results: Preliminary results indicate that the tool is promising for AYAs to help them express their concerns. Healthcare professionals describe that AYAs open up topics they have not mentioned before, and the tool helps healthcare professionals get to the point more quickly.
Conclusions: Work continues on the applicability of clinical practice, and the first results point to a promising psychosocial screening tool that Danish healthcare professionals can use with their AYA patients.

P101 / #1562

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

SETTING A NEW RESEARCH AGENDA IN PEDIATRIC CANCER: A JAMES LIND ALLIANCE PRIORITY-SETTING PARTNERSHIP WITH PATIENTS, SURVIVORS, FAMILY MEMBERS, AND CLINICIANS

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Background and Aims: Rigorously conducted and well-implemented pediatric cancer research is needed to improve outcomes for children and their families during and after therapy. We aimed to conduct a Canada-wide Priority Setting Partnership with pediatric cancer patients, survivors, family members, and clinicians, to identify and prioritize research questions to inform the decisions of research funders and guide Canadian researchers.
Methods: A steering group oversaw our phased James Lind Alliance approach and Canadian childhood cancer partner organizations were recruited. First, a national online survey collected research uncertainties that were collated into indicative questions. Questions were systematically checked against published evidence to identify previously answered questions. A second national survey was administered to prioritize questions. A shortlist of these questions was then taken to a consensus-building workshop, where a decision on the top ten priorities was made.
Results: Three hundred and fifty-two respondents submitted over 600 potential questions in English and in French. Following the removal of 'out of scope' questions, question collation, and our evidence check, 50 questions were put forward for prioritization by 201 participants. The top 24 questions underwent final prioritization at a workshop attended by 24 childhood cancer survivors, family members of children who have or had cancer, and multidisciplinary pediatric oncology clinicians. The top ten priorities reflect the breadth of the pediatric cancer continuum, focusing on access to new and innovative therapies; physical, mental, and psychosocial impacts and needed supports; preventing and treating relapsed and refractory cancers; and survivorship issues.
Conclusions: We have identified shared pediatric cancer research priorities in Canada using a rigorous, co-development approach involving stakeholders typically not involved in setting research agendas. The

priorities broadly suggest a call to research action on minimizing barriers to accessing care, improving capacity to implement evidence into practice, and the delivery of holistic and psychosocial care.

P102 / #288

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

TENTATIVE MODEL OF IMPAIRED NUTRITIONAL STATUS AMONG THAI CHILDREN WITH CANCER: THE INTERVENTION MAPPING APPROACH

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Background and Aims: Most children diagnosed with cancer receive chemotherapy that causes gastrointestinal (GI) symptoms, which impair their eating behaviors and nutritional status. Impaired nutritional status lowers children's quality of life (QOL) and places them at risk for febrile neutropenia in the first year following diagnosis and for worse survival. Most studies in this research area were done in Western countries. However, Thai children undergo chemotherapy in cultural and other environmental contexts including the typical Thai diet. Intervention Mapping (IM) uses a 6-step iterative process and a socio-ecological perspective to develop interventions to improve health behaviors and outcomes. This study used IM, step 1 to develop a tentative model of impaired nutritional status among Thai children with cancer during chemotherapy.
Methods: We used IM step 1 and IM core processes (reviewing the literature, collecting data from key stakeholders) to develop a tentative multi-level logic model of impaired nutritional status in children with cancer. We also considered the Thai culture and standard clinical practices.
Results: The tentative model includes QOL as the health outcome; impaired nutritional status as health problem; children's eating and self-management as the behaviors contributing the problem; GI symptoms as modifiable determinants of children's behaviors, and the child's biological sex and treatment intensity as non-modifiable factors contributing the problem. Environmental factors include caregiver and clinician attitudes, beliefs, and behaviors (interpersonal level); and features of the hospital environment (organizational level) that may affect children's eating and self-management behaviors.
Conclusions: Step 1 of the IM approach is useful in understanding complex health problems with influencing factors at multi-levels. This tentative model will be refined through collection of data from children, parents, and pediatric oncology clinicians. The results will inform subsequent IM steps to develop a targeted intervention to reduce impaired nutritional status and improve QOL for Thai children with cancer.

P103 / #574

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

NURSING WORKING GROUP AT SIOP E START; TO SHARE EXPERIENCES AND STRENGTHEN OUR KNOWLEDGE IN A NETWORK

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Background and Aims: SIOPE started a nursing group for nurses specialized in pediatric oncology, to exchange knowledge and experience and to facilitate research in nursing care. The ultimate aim is to bring pediatric oncology nursing care in Europe to a higher level. The official re-start of this group was in November 2021 and currently 15 countries participate. The structure of the nursing working group is very similar to other SIOPE working groups, with an elected steering committee and a chair, developed in accordance with SIOPE guidelines. The aim is to start round table meetings to promote networking between the European centers for all nursing professionals of each participating center.
Methods: A good organization of these meetings makes the threshold low to participate. We propose to work with a rotating system, whereby each time a country is responsible for organizing an online network meeting. The organizing center selects topics for the round table and from each center nurses with expertise or interest on this topic will be invited to join the round table meeting.
Results: The result for the nursing group is to engage members to exchange views and encourage debate to identify areas of common interest and to prioritize ideas for future development of care. As nursing group SIOP E, we will empower and boost the topics that are offered in the network. The nursing professionals of the participating centers will get to know each other better and will benefit of each expertise.
Conclusions: Networking with nurses improves knowledge. Live meetings at international conferences and symposia are good for connection. We would like to plan a round table meeting at SIOP Barcelona to invite other nurses. In the future online meetings is an easy way to continue this collaboration.

P104 / #1194

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

DEVELOPMENT OF A HANDBOOK TO PROMOTE THE RESILIENCE OF JAPANESE PARENTS OF THEIR CHILDREN WITH CANCER

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Background and Aims: As a factor related to recovery from mighty stressors, support to enhance "resilience" has been getting attention in recent years. The purpose of this study was to develop a self-administered handbook to promote resilience among parents of children with cancer.
Methods: Data were obtained through semi-structured interviews and analyzed using a qualitative approach. All interviews were conducted from March to October 2021. Participants were seven parents whose children were undergoing treatment or had completed treatment. The study was approved by the local ethics committee. The analysis revealed the parents' feelings from the time their child was diagnosed to the present, and the external and internal factors that they recognized to help them overcome their adversities. Items for the handbook were generated from the results, and the contents were discussed with experts involved in pediatric oncology.
Results: The handbook's contended begin with "Treatment Schedule," followed by "Points to keep in mind after discharge" and "Preparations for returning to school" after the completion of treatment. In addition, it included not only the sick child but also the family and family life events. The "Stories of Family Members Who Have Fought Disease Before Me" was intended to help parents learn about the experiences of others and promote their own resilience. Free descriptions were provided for parents to organize their emotions and thoughts, and to reflect on their own experiences later. The handbook was ring-file style and can easily hold documents.
Conclusions: The structure of this handbook is designed to help parents become aware of their psychological recovery through visualization of their experiences. However, verification is needed in the future. This work was supported by J SPS KAKENHI Grant Number 17 K 12374.

P105 / #1223

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

KNOWLEDGE, ATTITUDES AND PRACTICES REGARDING PAIN ASSESSMENT AMONGST NURSES WORKING AT PUBLIC-SECTOR PEDIATRIC ONCOLOGY UNITS IN PAKISTAN

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Background and Aims: Pain in pediatric oncology patients is often undertreated due to lack of timely assessment and inefficient communication between healthcare workers. Improper pain assessment is a leading cause of poorly managed pain in children, negatively affecting quality of life. In high-income countries, pediatric oncology nurses play a key role in developmentally appropriate pain assessment measures to identify potential management strategies. However, nurses in low-middle income countries (LMICs) face a deficit of knowledge about pain assessment tools and management. Owing to differences in availability of resources, a disparity exists between health-related quality of life of cancer patients treated at public and private sector hospitals in Pakistan.
Methods: The Indus Hospital and Health Network partnered with nine public-sector hospitals nationwide to improve pediatric oncology practices. Supported by the My Child Matters grant, training sessions were conducted for nurses at each public-sector pediatric oncology unit (POU) from March to December 2021. Pain assessment tools were provided. To assess retention and implementation of practices, a knowledge, attitudes and practices questionnaire was distributed online to nurses at each POU. All responses remained anonymous.
Results: Fifty four responses were recorded, 87% female and most between 26 and 30 years of age. Majority participants held a Diploma in Nursing, were designated Charge Nurses and had over 6 years of experience. Forty nurses reported routinely assessing pain; the most common reason for not doing so was increased workload. Significant correlations were observed between routinely performing pain assessment and maximum patients per nurse, availability of formal credentialing or certifications at institution and routinely performing pain assessment, availability of trainings focused on pain assessment and routinely performing pain assessment, and qualification of nurses and knowledge of non-pharmacological pain assessment methods.
Conclusions: Strategies to improve pain assessment knowledge and practices amongst pediatric oncology nurses in LMICs must be developed to improve patientcare and clinical outcomes.

P106 / #184

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

THE PEDIATRIC ONCOLOGY NURSE AS TRANSPLANT DONOR: THE EMIC PERSPECTIVE

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Background and Aims: Blood/bone marrow donation is an essential part of an allogeneic transplant in pediatric oncology. There is significant literature about donation by clinicians, psychologists, and nurses; however, little written by donors. Objective: A self-reflection and assessment by a pediatric oncology nurse serving as a bone marrow donor, and comparison with other nurse donor experiences—an exploration of role-reversal.
Methods: An autoethnographic retroactive and selective accounting highlights my interactions with the donor experience and makes visible my emotions and thoughts as both “patient” and professional. A medical anthropologist assisted in data and experience analysis. A review and comparison of marrow/stem cell donation process accounts by nurses from grey literature conducted to include additional role-reversal data.
Results: Medical knowledge of bone marrow transplant and donation processes did not provide the mental preparedness required by a donor for this nurse. Like most pediatric oncology nurses with experience caring for patients undergoing a bone marrow transplant, I had not given much thought to the donor’s experience as our focus is on our patients. My donor experience significantly raised my consciousness of the intensity of the donation experience, which now informs my practice.
Conclusions: Through my donor experience, I have developed greater empathy as a nurse. This aligns with the donor experiences of other nurses as documented in grey literature. I believe that all hematology/oncology nurses would benefit from hearing the emic perspective of a nurse donor’s story to raise their awareness of the full scope of donor needs and care. Nurses can provide more holistic care to their donor “patients” and have greater respect and appreciation for the intricate the process leading up to the donation. By sharing my experience of role reversal, nurses will have a unique insight into a complex and so far, under-examined aspect of bone marrow donation.

P107 / #533

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

A MULTIDISCIPLINARY APPROACH TO I-131 MIBG THERAPY FOR THE TREATMENT OF NEUROBLASTOMA

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Background and Aims: MIBG therapy is an effective treatment for stage IV Neuroblastoma, currently being studied as part of up front therapy, and also used for refractory and relapsed MIBG-avid Neuroblastoma. The purpose of this poster is to share lessons learned in managing this unique treatment through a multidisciplinary approach to improving patient care.
Methods: Clinical and operational challenges were identified that contribute to the fluidity of patient care both prior to admission and during the hospitalization for MIBG including: pre-admission coordination and communication, caregiver compliance with radiation safety guidelines, achievement of adequate anxiolysis, successful Foley catheter placement, and nursing discomfort with radiation exposure.
Results: Multidisciplinary team members are engaged in several initiatives to streamline the care of MIBG patients. Prior to admission, education is provided to caregivers from the oncology team, radiation safety, and child life specialists (including handbooks and a video) which is then reinforced by radiation safety and nursing throughout the hospitalization. Prior to admission, email communication and pre-admit huddles occur between the oncology team, pharmacy, pain service, and nursing to review the patient's case and hospital plan. Patient exams and past medical history have been expanded to include a thorough GU physical exam and an in-depth medication history (for patients receiving anxiolysis). In addition, monthly meetings with the multidisciplinary team provide an opportunity to review areas for improvement with past cases and to plan for upcoming treatments. Educational sessions have been provided to nursing focused on radiation safety and Foley catheter placements.
Conclusions: Collaboration between oncology, nursing, radiation safety, pain service, urology, nuclear medicine, and child life specialists is key in the provision of safe and optimal care for patients with Neuroblastoma undergoing MIBG therapy. Educational materials and discussions with patients/caregivers and staff are vital for this complex therapy. Patients, caregivers, and staff are well supported and benefit from using a multidisciplinary approach.

P108 / #905

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

PRACTICES ON PROTEIN PROVISION IN ADOLESCENTS UNDERGOING HAEMATOPOIETIC STEM CELL TRANSPLANT: A LITERATURE REVIEW, INTERNATIONAL BENCHMARKING AND RETROSPECTIVE AUDIT

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Background and Aims: Protein requirements in adolescents undergoing haematopoietic stem cell transplant (HSCT) is unknown. In the absence of specific evidence-based guidelines for HSCT, at the Royal Children's Hospital (RCH) in Melbourne, Australia we use the American Society for Parenteral and Enteral Nutrition (ASPEN) Critically Ill Children Guidelines 2009 for estimated protein requirements (EPR). The aims of our study are to review the literature and to compare current local and international practices in enterally and parenterally-fed HSCT patients.
Methods: Databases CINAHL, Cochrane Central, EMBASE and MEDLINE from 2006-2021 were searched in both paediatrics and adults using the terms "protein requirements", "bone marrow transplant" and " haematopoietic stem cell transplant". To assess international practice, 11 international paediatric oncology centres were contacted. A retrospective audit of 15 HSCT adolescent patients at RCH was performed, to assess provision of protein compared with the ASPEN recommendation of 1.5g/kg/d.
Results: Literature for paediatrics was found to be limited, therefore the adult literature was included. Five review papers and practice guidelines recommended a minimum of 1.5g/kg/d. Three papers recommended up to 2.5 g/kg/d for those with malnutrition or gut-graft-versus host disease (GvHD). Three paediatric oncology centres were found to use the ASPEN Guidelines and five centres aim for a minimum of 1.5g/kg/d. Two centres increased to 2-3g/kg/d or by 20-30% for severe gut GvHD. The audit of RCH HSCT adolescents found that the mean provision of protein was 1.1g/kg/d which is 73% of the EPR.
Conclusions: There is no international consensus on appropriate provision of protein in paediatric HSCT. The provision of protein in RCH HSCT adolescents was found to be suboptimal compared to the ASPEN guidelines. There is limited evidence to understand whether protein intake impacts on HSCT outcomes. Further research is recommended to develop evidenced-based guidelines in this nutritionally vulnerable cohort.

P109 / #1635

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

THE ROLE OF NURSING IN THE 101 TRIAL WITH OMBURTAMAB FOR PATIENTS WITH CENTRAL NERVOUS SYSTEM RELAPSE OF NEUROBLASTOMA.

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Background and Aims: Conventional systemic treatment for newly diagnosed patients with neuroblastoma doesn't adequately treat the central nervous system and leptomeningeal space, which may serve as a sanctuary site leading to relapse. Besides this, there are significant toxicities in those children who reach cure, associated with standard therapies (surgery, radiotherapy and chemotherapy). Consequently, new treatments, as radiolabeled monoclonal antibodies, are emerging.
Methods: Trial 101 (NCT03275402) is a single-arm, international study (4 US and 1 Spain) in patients aged 0-18 years with radiographically and/or histologically confirmed neuroblastoma with CNS/LM metastases. Treatment with 131I-omburtamab consist of a 2 mCi dosimetry dose followed one week later by up to two cycles of administration of 50 mCi activity and 4-week observation period/cycle. Radiolabeled antibody administration requires a formal safety and management training for clinical trial nurses as well as parents. The objectives of this study include the development of the training material for patient/parents and environmental safety in the outpatient setting for Omburatamb treatment.
Results: The developed protocol for patients treated with radiolabeled medications include nursing visit with patient and parents prior to first infusion to focus on techniques and recommendations to deal with expected toxicities; qualifying nursing staff for being capable to face this specific administrations with adequate monitoring strategies; enrolment of supportive care professionals to increase patient well-being before, during and after infusion. Specific monitoring registries and specific nursing care during infusion.
Conclusions: Adopting this treatment to our site required an in-depth analysis of all particular medications and procedures, because as nurses, we must adapt current caring to new therapies requirements and implement appropriate procedures, care and circuits to ensure patients and their families safety as well as health staff and environment safeness.

P110 / #1671

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

THE JOURNEY OF CAR-T CELL THERAPY: PEDIATRIC PATIENT'S PERSPECTIVE

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Background and Aims: Even though the outcomes of pediatric and young adult patients diagnosed with acute lymphoblastic leukemia (ALL) have improved significantly in the past few decades, approximately 2–3% of patients will present with refractory disease and 15–25% of patients will relapse. To improve outcomes of patients with r/r disease, immunotherapies targeting specific B cell antigens are being developed. With the expanding use of CAR-T cell therapy, there is a need to characterize the patient's experience over time to guide patients and their families to face physical and emotional roller coaster experiences. To provide patient-oriented care, it is necessary to gather information about their experience. The patient's perception of the quality of contact with a health professional has a very important subjective component. Communication skills, amount of information provided, treatment and the environment can condition the perception of quality and are factors that decisively determine the patient's experience.
Studies that assess satisfaction with medical care in children treated with CAR-T, either directly or indirectly, through the perception of parents or caregivers, are scarce, even though it is a relevant part in the evaluation of health systems.
Methods: An ambispective and qualitative study based on semi-structured individual interviews and focused on r/r B-ALL patients who benefited from CAR-T cell therapy from 7 years of age at the time of administration of CAR-T therapy.
Results: Knowing the experience and perceived needs regarding the received care and information provided during the process of CAR-T therapy and improving care satisfaction for children and adolescents with B-ALL who undergo CAR-T treatment.
Conclusions: Taking into account that a huge amount of our patients is treated away from their primary oncology team with which they are most familiar, the development of a welcome programme for pediatric patients with B-ALL receiving CAR-T therapy, following already treated patients background, could improve future patient’s experience.

P111 / #82

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

CANCER AND PALLIATIVE CARE IN RURAL SETTINGS IN INDIA

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Background and Aims: In a southern district of West Bengal, India almost 75% of cancer patient die a sad death of neglect due to lack of awareness about palliative care and low economic level. To identify and try to solve to the extent possible the main difficulties in giving palliative care to the terminal cancer patients of the area.
Methods: Home visit by volunteers and enumeration of the problems as discussed by the patient and their families.
Results: Analysis the following data and identify these main problems. Patient problems: Pain, vomiting, respiratory distress, fatigue, etc. Our volunteers visited terminal cancer patients and their families in our areas. Family problems: Inability to match work life with the care of the patients. Adverse attitude of neighbors and local peoples. Social problems: Lack of awareness of the neighbor of local people about cancer and palliative care resulting in isolation of the family. Projected Intervention: Trying to relieve the patient's problems through home based medications and intervention by volunteers and family members. Re-orientating the attitude of family members through discussions and other methods of communication i.e. get-together of cancer survivors. Social effort to raise the awareness of neighbors and local people through discussion and other audio visual method (i.e. poster, leaflet, slide presentation, etc).
Conclusions: We believe that if we are able to continue our program for a long enough period the suffering of the terminal cancer patient and their families might be resolved to a large extent over time.

P112 / #1103

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

IMPLEMENTATION OF A PEDIATRIC EARLY WARNING SYSTEM (PEWS) IN A PEDIATRIC ONCOLOGY UNIT OF A SPANISH HOSPITAL: ADVANTAGES AND LIMITATIONS

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Background and Aims: Hospitalized pediatric cancer patients have high-risk of life-threatening complications. Our aim is to analyze the implementation of validated PEWS in our Pediatric Oncology Unit and the utility for identifying early clinical deterioration.
Methods: Descriptive study of the Onco-PEWS implementation process in one year (December 2017-December 2018), a pilot study (November 2017) and the specific training for Oncology and PICU staff. Review of PEWS numerical values (0-5) assigned by nurses (cardiovascular, respiratory, neurological signs) and family concerns of inpatients below 18 years. The pediatricians performed the clinical evaluation of cases with abnormal scores. Scores were transferred to an actuation algorithm: 0-2(green): nursing assesses every 4 hours, 3-4(yellow): pediatricians notified, and ≥5 (red): mandatory PICU consultation.
Results: Admissions at pediatric oncology ward were 454. Reasons: chemotherapy (50.9%), fever (24.4%), debut (9.7%), surgery (9%), chemotherapy complications (5.3%). Underlying disease: 212 leukemias, 37 lymphomas, 142 solid tumors and 63 brain tumors. Onco-PEWS complete registered: 51.5%. At admission: 94.3% green, 5.3% yellow, 0.4% red. At discharge: 98% green. During the stay: 14.7% deteriorated Onco-PEWS (1.3% yellow to red, 2.2% red). Notice to pediatrician 14.6%. Therapeutic interventions in 13.2%: 4 yellow and 1 red Onco-PEWS required surgery. Transfer to PICU in <1 hour in 9 patients (1yellow, 8 red). Only one death terminal disease.
Conclusions: In our experience, the Onco-PEWS is a feasible and effective tool that helps to identify clinical deterioration and risk to PICU transfer. It empowers nurses to identify clinical changes and allows appropriate response with timely interventions that improves outcomes. However, the full mid-registration can be improved. Rapid PEWS deterioration in younger children suggests that narrower age-specific ranges should be implemented.

P113 / #1112

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

NURSES TRAINING IN MOROCCO : REPORT FROM THE PEDIATRIC ONCOLOGY DEPARTMENT OF RABAT

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Background and Aims: Nursing education in pediatric oncology is the cornerstone of all the actions of the strategies for improving the quality of care. The SIOP Baseline Standard for Pediatric Oncology Nursing in low- and middle-income countries calls for a minimum of 10 hours/year of continuing education. To cope with modern developments, the Children Hospital of Rabat, with 24 pediatric oncology nurses, must therefore ensure the updating and permanent progress of its nurses. Objective: Report our experience during 2 years (2021- 2022) of nursing continuing education activities over 4 scientific days. This training was supported by the Francophone African Group of Pediatric Oncology GFAOP and the Sanofi Espoir foundation
Methods: Collect and evaluate all pediatric oncology nursing continuing education trainings to identify gaps for future programming.
Results: The 1st scientific day (March 06, 2021), with 16 attendees covered line care, cardiopulmonary resuscitation and emergency trolley, and the administration and monitoring of Ifosfamide and high-dose Methotrexate. The 2nd scientific day (October 23, 2021) addressed transfusion and line care, with transfusion experts (16 attendees). The 3rd scientific day (February 15, 2022) On the occasion of International Childhood Cancer Day, the nurses presented their activities by developing posters. The 4th scientific day (February 26, 2022) included cytotoxic process, and patient risk management attended by pharmacy, physician and the nursing staff (26 attendees). We also include our participation in international meetings (SIOP Africa Uganda, virtual conferences, daily trainings, and nursing education sessions).
Conclusions: In reviewing these sessions, the nurses were input sought for improvement, update knowledge, develop skills, exchange experiences, and improve their profession in Morocco. By striving to achieve the SIOP Baseline Nursing Standards, our nursing staff can increase the quality of care and safety of nursing practice. Nursing recommendations: encourage central lines use, reinforce communication, update basics of cardiopulmonary resuscitation, and cart management, transfusion and chemotherapy risk management.

P114 / #1485

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

PEDIATRIC ONCOLOGY NURSING CONTINUOUS CAPACITY BUILDING IN ETHIOPIA

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Background and Aims: As of March 2013, there was no dedicated pediatric oncology units (POUs) or specialized care in Ethiopia. Currently there are active POUs in four cities. Since 2013, >6,100 children with cancer have been treated and Ethiopian physicians, nurses, and pharmacists trained in childhood cancer care in partnership with US-based, non-governmental organization, The Aslan Project (Aslan). International pediatric oncology nurse educators have conducted multiple onsite trainings and select Ethiopian pediatric oncology nurses have attended trainings in Pakistan and India. Capacity-building goals of the Ethiopian pediatric hematology-oncology (PHO) teams and Aslan experts are to address gaps in care and promote local program ownership. Cancellations of planned training programs due to COVID spurred local leadership; thus, the Rising Nurse Project 2021 was created. Objective: Develop a standardized Ethiopian pediatric oncology nursing training curriculum and manual for continuous and sustainable professional development.
Methods: Ethiopian PHO physicians and nurse educators, with consultation from three international experts, wrote the curriculum for a two-week nursing orientation training, in line with the SIOP Nursing Baseline Standards recommendations. Pilot trainings were conducted in two sites with post-training assessment by local and international trainers.
Results: Twenty-two nurses participated. Interest in expanding training to other centers led to creation of a Pediatric Oncology Nursing Task Force (PONTF) including Aslan's international experts. PONTF is working with the Federal Ministry of Health (MOH) to certify the curriculum as a national standard and has directed the development of comprehensive training modules.
Conclusions: Challenges for pediatric oncology nurses include a lack of professional recognition within health system, pay scale that fails to reflect specialized work, frequent rotation of nurses, institutional policies, and mental/emotional burdens of patient care. Three MOH/PONTF workshops are scheduled to complete the curriculum to address the first challenge. Workshops will culminate in trainings at all POUs led by local nurse educators.

P115 / #700

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

INVESTIGATION OF THE USEFULNESS OF THE PROCESS MODEL IN WHICH CHILDHOOD CANCER SURVIVORS BECOME INDEPENDENT WHILE BALANCING HEALTH MANAGEMENT AND SOCIAL LIFE

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Background and Aims: To provide comprehensive long-term support for childhood cancer survivors (CCSs), professionals from various departments need to understand the process of long-term change and its influencing factors from the perspective of CCSs. The authors' previous studies identified "the process of becoming independent while balancing health management and social life in CCSs from adolescence to adulthood" (model-1). The purpose of this study is to clarify the validity and applicability of model-1 from the perspective of professionals who have experience in supporting CCSs and their parents.
Methods: We distributed model-1 and a self-administered, anonymous questionnaire survey to 373 health care professionals working at 20 hospitals treating childhood cancer in some areas of Japan.
Results: The questionnaire was validated for 108 respondents (valid response rate: 29.0%). They were 53 physicians, 26 nurses, 6 psychologists, 5 social workers, and 18 others. The diagram and explanatory text of model-1 were understood or generally understood by 72.2% and 84.2% of the respondents, respectively. The suitability for CCS and utility for the health care professionals of the model were recognized by 76.8% and 80.2% of the respondents, respectively. The most common responses that they could be useful were "predicting what CCSs may experience" and "considering professional support for what CCSs may experience", both at 87.0%. All responses related to understanding model-1 and its possibility for utilization were significantly correlated with Spearman's ρ ($p<0.001$).
Conclusions: These findings suggest that model-1 can be used by health care professionals to anticipate what CCSs might experience and to consider support for them. However, in order to increase the potential use of model-1, the diagram should be more easily understood.

P116 / #712

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

INVESTIGATING THE USEFULNESS OF THE PROCESS MODEL IN WHICH PARENTS SUPPORT CHILDHOOD CANCER SURVIVORS AS THEY BECOME INDEPENDENT WHILE BALANCING HEALTH MANAGEMENT AND SOCIAL LIFE

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Background and Aims: To provide comprehensive long-term support for pediatric cancer survivors (CCSs), it is necessary for professionals in various sectors to understand the process and factors that influence the long-term support of children by parents of CCSs. The authors' previous studies identified "the process of parents' support as CCSs become independent while balancing health management and social life from adolescence to adulthood" (model-2). The purpose of this study is to clarify the validity and applicability of model-2 from the perspective of professionals who have experience in supporting CCSs and their parents.
Methods: We distributed model-1 and a self-administered, anonymous questionnaire survey to 373 health care professionals working at 20 hospitals treating childhood cancer in some areas of Japan.
Results: The questionnaire was validated for 108 respondents (valid response rate: 29.0%). They were 53 physicians, 26 nurses, 6 psychologists, 5 social workers, and 18 others. The diagram and explanatory text of model-2 were understood or generally understood by 87.1% and 91.6% of the respondents, respectively. The suitability for the CCSs and utility for the health care professionals of the model were recognized by 75.9%, and 82.6% of the respondents, respectively. The most common response that they could be useful was "predicting what parents will experience" at 87.9%, followed by "understanding parents' experiences" at 87.0%. All responses related to understanding model-2 and its possibility for utilization were significantly correlated with Spearman's ρ ($p<0.001$).
Conclusions: These findings suggest that model-2 can be used by health care professionals to understand the experiences of parents of CCSs and to predict what they may experience. However, it should be considered that some parents may not suit the model.

P117 / #922

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

PERCEPTIONS OF NUTRITIONAL NEEDS AND SUPPORT OF PEDIATRIC ONCOLOGY PATIENT CAREGIVERS IN GOVERNMENT HOSPITALS IN INDIA

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Background and Aims: Approximately 40% of pediatric oncology patients are malnourished at diagnosis in India. Malnutrition during cancer treatment can lead to greater risk of infections, side effects, complications and treatment delays. Caregivers are integral to preventing and addressing malnutrition in children with cancer. Therefore, caregiver education is crucial to ensure that they have the knowledge required to manage this responsibility. The aim of this study was to therefore understand the knowledge, attitudes and practices of caregivers of pediatric oncology patients belonging predominantly to the lower socioeconomic group.
Methods: We administered a structured questionnaire to caregivers of oncology patients aged 0 to 18 years in March 2021. The study was conducted during the nutrition counselling session that Cuddles Foundation (CF) provides and questions were designed to elicit data on their knowledge and attitudes on nutrition, hygiene and health behaviours. Responses were collected on a 3-point Likert scale (Yes, Somewhat, No).
Results: Caregivers of 754 patients participated across 31 government hospitals in India. The results indicated that 80.1% of caregivers did not know the proper foods to feed their child at cancer diagnosis. The findings also demonstrated that most caregivers (58.5%) were unaware of the proper hygiene practices required to handle their child's food. Unfortunately, even after the caregivers understood the nutritional requirements, 33.9% of caregivers did not have the means to provide that for their child. The majority of caregivers (88.1%) found that the support groups conducted by CF were helpful.
Conclusions: The study indicates that there is a gap in the knowledge base of caregivers of pediatric oncology patients. The findings demonstrate that there is a significant requirement for not just nutritional, health and hygiene counselling but also a necessity for financial and emotional support.

P118 / #653

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

PRACTICAL APPROACH TO HIGH-DOSE METHOTREXATE INTOXICATION: FOCUS ON NURSING ASPECTS

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Background and Aims: High-dose (HD) methotrexate (MTX) is essential in the treatment of many childhood cancers. The use of HD-MTX can be associated with multiple side effects and requires close monitoring and preventive measures to avoid life-threatening toxicities. Although preventive measures have always been in place in our hospital's guidelines, we were recently faced with HD-MTX toxicities, which prompted us to perform a root analysis of our practice. We here focus on the impact on nursing care.
Methods: A root analysis including identification of the contributing factors, interpretation and possible solutions followed by communication to the team were performed.
Results: Root analysis revealed that small inter-individual approaches in follow-up and management of toxicities were uncovered. The infusion setup and number of manipulations were identified as possible causes for misinterpretations. To improve patient safety, we implemented a multidisciplinary follow-up document for closer monitoring of different parameters per time point, including blood sampling (MTX level, creatinine level), hyperhydration volume and infusion time and dose of folinic acid administration based on the MTX level. Second, current instructions on how to handle urine alkalinisation, hyperhydration and folinic acid rescue were written out more detailed in a specific intoxication policy document. Third, we reduced the likelihood of errors during the administration of HD-MTX, by reducing the number of manipulations on the infusion setup based on suggestions of our nursing team. The hyperhydration is only interrupted to administer antiemetics.
Conclusions: Nurses have a key role in the administration of HD-MTX and concurrent follow-up. By implementing the follow-up document, all key factors during HD-MTX administration are now monitored more closely. The more detailed instructions are more comprehensive for all nurses. By using a bottom up insight of the nurses to simplify the infusion setup, nurses feel more confident during HD-MTX administration. A prospective follow up of this change in practice is currently ongoing.

P119 / #1098

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

KNOWLEDGE ON NURSING PREVENTATIVE MEASURES AMONGST ADOLESCENTS IN GANTSI, BOTSWANA

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Background and Aims: THE ABSTRACT Introduction-cancer remains a leading cause of death in many developing countries such as Botswana with adolescents included in the statistics. this study was was carried out to investigate knowledge amongst adolescents in Gantsi, Botswana to find out how much knowledge they have on cancer screening and prevention measures.
Methods: Design-the study was carried out on 6 adolescents, 3 were out of school adolescents who were selected randomly as they come for consultations at Gantsi Primary Hospital (OPD), 3 were schooling adolescents from Gantsi Senior who were also selected randomly from the school, information was gathered through oral interviews.
Results: -My analysis shows that even though there is information on cancer screening and prevention available on different sources, fair number of adolescents in Gantsi know about them, 1 (17%) said he do not know anything about cancer, 2 (33%)said they do not know that cancer could be prevented, they thought it is a natural disease, 1 (17%) metioned that she is aware of pap smear done on females to screen for cervical cancer, she commented that she knows it allows for early detection of the disease, 2 (33%) were highly knowlegeable and even elaborated on factors that can expose one to cancer such as active/passive smoking, use of drugs, and also that cancer can come as an opportunistic infection if a person contact other diseases like HIV/AIDS.
Conclusions: Conclusion-50% of my participants showed complete no knowledge on cancer prevention and screening, that is a large number therefore I conclude that information dissermination is low, a lot needs to be done to sensitize not only the adolescents in my study but also the Gantsi population at large on cancer prevention and screening looking at the fact that my place of study is one of the areas in Botswana with high substance abuse and cancer cases.

P120 / #1275

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

PATIENT AND PUBLIC VIEWS ON INFORMATION, CONSENT AND DATA SHARING IN THE REGISTRY OF STORED OVARIAN AND TESTICULAR TISSUE FOR YOUNG PEOPLE IN THE UK.

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Background and Aims: To generate a resource to support service development, evaluation and research, we are establishing a UK Register of stored ovarian and testicular tissue (UKSTORE). We performed a series of patient and public engagement consultations to determine what aspects of data capture, consent and storage would be acceptable to service users.
Methods: Participants were recruited via useMYdata, DATACAN, Leeds Research Owls, Candlelighters, Children's Cancer and Leukaemia Group and Teenage Cancer Trust. Two 1.5-hour virtual meetings were used to explore views of data capture and data use for UKSTORE. Following an overview of UKSTORE aims and objectives, participants were asked to choose answers to 5 multiple choice questions using Mentimeter web-based technology, the online chat function and/or verbal discussion.
Results: Twelve young people aged 13-18 and seven adults, including three parents of children who had undergone ovarian or testicular tissue preservation attended the consultations. Quantitative data showed a strong preference to data capture without patient informed consent, including data linkage and retention. Adults prefer to receive information about the registry via a printed leaflet and children prefer a mixture of written and web-based materials. Children preferred to speak to their doctor face to face. Qualitative data highlighted the importance of whole population data registries, application of an opt-out approach and the reassurance of robust data for the purposes of learning and understanding patient needs. A registry of young people who have stored tissue for future fertility was deemed necessary and important. The majority of patients consulted would be happy for their data to be captured and used without written informed consent.
Conclusions: Qualitative consultation has generated informative and supportive intelligence ensuring ethical and consent issues are appropriately handled in the development of a new data resource.
Acknowledgements: Thank you to all the participants who kindly attended the meetings.

P121 / #319

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

THE TIMING WHEN THE MOTHER OF A CHILD UNDERGOING EYE ENUCLEATION DUE TO RETINOBLASTOMA STARTS MIGRATING SELF-CARE OF ARTIFICIAL EYE TO CHILD

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Background and Aims: Parents of children who underwent eye enucleation in an early postnatal period due to retinoblastoma (RB) seek a way of migrating self-care of an artificial eye to their children with little support by specialists. We conducted a study to understand the problems arising from such a migration process. The objective of this study was to identify the appropriate shift timing.
Methods: Individual semi-structured interviews were conducted for mothers who have 3- to 10-year-old children with RB under a qualitative descriptive design. Participants were 18 mothers, recruited through RB family liaison groups in Japan. The mean age of mothers at the time of interview was 38.9 years (SD = 3.9). The child's mean age at the time of eye enucleation was 19.8 months (SD = 11.9). This study was approved by the research ethics committee of the author's institution.
Results: To investigate the timing when mothers began to encourage their children to take artificial eye care by themselves, 7 categories and 4 large categories were extracted from 16 subcategories. Some children began to look after their artificial eyes, as suggested by “My child unconsciously began to remove his/her artificial eye by himself/herself” and “My child became able to wear/remove, clean, and adjust the position in his/her way.” Other children were encouraged by their mothers, as suggested by “I encouraged him/her not to miss the timing when my child wanted to imitate me or look after an artificial eye by himself/herself.” The parental intervention began at their own discretion or after “leaning from experience or advice by experts.”
Conclusions: Parents encouraged their children to do self-care when they were interested in looking after their artificial eye, and sought an appropriate migration timing because they wanted their children to learn self-care before entering preschool/school, where children can no longer be under the supervision of their parents.

P122 / #901

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

ACTUAL STATUS OF SELF-CARE ON ARTIFICIAL EYE IN CHILDHOOD AFTER ENUCLEATION DUE TO RETINOBLASTOMA

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Background and Aims: In Japan, no guidelines for migrating self-care of artificial eye to the child undergoing enucleation due to retinoblastoma (RB) have been established. The purpose of this study was to identify actual self-care on an artificial eye of RB children.
Methods: Individual semi-structured interviews were conducted under a qualitative descriptive design. Participants were mothers of 3- to 10-year-old children undergoing enucleation due to RB who have experience of administrating either ongoing or completed migration of artificial eye self-care to their children. Mothers were recruited through RB family liaison groups. This study was approved by the research ethics committee of the author's institution.
Results: The mean infant age was 6.1 years (SD = 2.0). The mean age of enucleation was 19.8 months (SD = 11.9). From 75 subcategories, 26 categories were extracted, including "Parents prepare a space and items for children to facilitate doing self-care," "Encourage children to understand the purpose of self-care," "Wash and wipe to clean the artificial eye used all day," "Wash and wipe to clean in the orbit and around the area that the artificial eye touches," "Hygienically treat an artificial eye," "Devise a way to remove eye discharge," "Open eyelid to wear an artificial eye with fingers," "Take good care of one’s own sense during wear/removal of artificial eye."
Conclusions: At the beginning of children's self-care of artificial eye, parents took initiative to promote children's understanding of the purpose of self-care and increase their motivation in accordance with development of finger dexterity or cognitive function. There were methods for the care of an artificial eye. Parents devised an appropriate procedure according to children's development and condition in the orbit and supported treatment-related care such as techniques that infants had not gained yet or ocular instillation. Caregiver should establish a system to help parents at any time.

P123 / #1287

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

CONTINUOUS NURSING EDUCATION IN UGANDA: A SUSTAINABLE MODEL FOR LOW- AND MIDDLE-INCOME COUNTRIES

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Background and Aims: BACKGROUND The International Society of Pediatric Oncology PODC Baseline Nursing Standards 2 and 3 state formalized orientation and continuing education as critical for a successful pediatric oncology service. Specialized education and clinical training for new nurses and formal mandatory continuing nursing education are rarely available in low-income countries and likely contribute to continued disparity in survival. Uganda has no accredited pediatric oncology nursing program, so nurses learn through mentorship from (and observership) of senior nurses, as well online free courses. The Uganda Cancer Institute (UCI) pediatric department started weekly continuing nursing education (CNE). OBJECTIVE Meet increasing demand for specialized knowledge required for childhood cancer nursing practice.
Methods: METHODOLGY Weekly one-hour CNE sessions are conducted by a senior nurse, and sometimes by a pediatric oncologist, for pediatric nurses caring for approximately 500 children with cancer (received annually). CNE sessions delivered to diploma and bachelor-prepared nurses and occasionally attended by adult oncology nurses, doctors and fellows. Presentations include oncology nursing (e.g., oncologic emergencies, chemotherapy administration and side-effect management), case studies and nursing implications of treatment protocols.
Results: RESULTS A CNE baseline assessment (by questionnaire with Likert scale) in October 2018 showed improvement in nurses' knowledge and attitudes. CNE outcomes include: quality improvement project, successful My Child Matters 2020 Nursing project funding, and nurses' improved confidence in clinical work and active participation in the multi-disciplinary clinical team.
Conclusions: CONCLUSIONS A cornerstone of successful treatment of childhood cancer is the provision of specialized professional care in pediatric oncology units. Ugandan pediatric oncology nurses manage disease-related complications, coordinate care, administer chemotherapy, and educate patients and families. Our CNE program supports all these activities and has proven to be sustainable and cost-effective. CNE has improved nursing care and multi-disciplinary team integration and serves as an education model for nurses in other resource-limited settings.

P124 / #1983

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

ANTICOAGULATION ERROR REDUCTION STRATEGIES

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Background and Aims: Anticoagulation medications are the leading cause of acute serious drug events among hospitalized patients. Since 2008, reducing patient harm from anticoagulation has been a Joint Commission National Patient Safety Goal. A safety event resulted when a patient developed a pulmonary embolism after being discharged with an incorrect enoxaparin prescription. This event led to a nurse-driven initiative to evaluate the processes at Boston Children's Hospital for patients receivng anticoagulation therapy. Aims: The learner will identify potential opportunities for error reduction strategies for patients on high risk medications, specifically anticoagulants.
Methods: A multidisciplinary group was convened and the root cause analysis (RCA) highlighted gaps in practice. These included: the ordering and prescribing of anticoagulation therapy, the understanding of the treatment plan and outpatient follow-up plan. Specific, targeted interventions were implemented to address the three themes that emerged from the gap analysis, these included work flow issues, documentation, and educational consistency in patient/family education. The educational work led to the creation of documents necessary to guide the nurse in caring for a patient receiving anticoagulation therapy.
Results: To evaluate the effectiveness, when nurses discharges a patient, a five question survey is sent determine to determine the usefulness of the created tools. Each educational tool has received a score of > 4 (5 being the highest) on the perceived value of the document.
Conclusions: The incidence of venous thromboembolism (VTE) has been increasing due to the advances in technology and medical care in the pediatric population, especailly hospitalized children, patients with central venous catheters, and patients recovering from surgical procedures (Mahajerin & Croteau, 2017). The vast amount of knowledge nurses need to know has exceeded any one's ability to safely and reliably manage each patient's educational needs. Nurses must be empowered with tools, such as a checklist to provide focused, consistent education and care each and every time.

P125 / #1291

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

OUTREACH PALLIATIVE CARE TO CHILDREN WITH CANCER AT BANSO BAPTIST HOSPITAL (BBH) AND MBINGO BAPTIST HOSPITAL(MBH) NORTH WEST CAMEROON: NINE YEARS (2013-2021) EXPERIENCE

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Background and Aims: Background Annually, about 140 children are diagnosed with cancer, treated and cared for in the the Cameroon Baptist Convention Health Services(CBCHS) Childhood Cancer (CHC) program with approximately 50% chances of been cured. Majority who are not cured and their families need home-based palliative care services. Palliative care (PC) remains an essential component for every comprehensive childhood cancer treatment and management. In 2013, BBH established an outreach PC with the aim of offering palliative care to children with cancer at home. The same services were later established at MBH in 2014 to serve the same purpose. Aim The main aim of the outreach pediatric palliative care(PPC) services is to offer pain management, symptoms management, psycho-social and spiritual care to children with cancer on palliation at their homes.
Methods: PPC nurse spent two weeks at each of the hospitals. Home visits conducted by PC nurse on motorbike every fortnight. Phone contact was maintained with families. A well-documented data base on each patient status was maintained and updated periodically.
Results: Over nine years, a total of 234 children with cancer on palliation(both from BBH and MBH) received PC services with focus on pain and symptom management, psycho-social and spiritual care, 699 home visits were conducted which allowed the families to fully engage in decision making concerning advanced home end of life care plan as wells as breaking of cultural barriers, 52bereavement visits were conducted as part of psycho-social and spiritual care, 1618 phone calls were made to maintain good communication between families and health care team as to offer immediate support that was needed before the next home visit.
Conclusions: Conclusion An outreach PC service has offered and improved holistic care, health-related communication and quality of life for children with cancer and families. It reduced needless hospitalization, promoted rehabilitation, home-based end of life care and relieved burden of care-giving.

P126 / #1450

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

RECRUITING CHILDREN WITH CANCER TO RESEARCH: A QUALITATIVE INTERVIEW STUDY EXPLORING ETHICAL VALUES AND CHALLENGES AMONG SWEDISH HEALTH CARE PROFESSIONALS AND RESEARCHERS

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Background and Aims: Research remains crucial to improve treatment, survival, and quality of life for children with cancer. However, recruitment of children to research raises ethical challenges. This study aimed to explore ethical values and challenges in recruitment of children with cancer to research, among health care professionals and researchers in Sweden. Another aim was to explore health care professionals and researcher's perceptions of ethical competence in the context of recruiting children to research.
Methods: An explorative qualitative design, using semi-structured interviews with seven pediatric oncologists and ten nurses. Interviews were analyzed with inductive qualitative content analysis.
Results: The analysis resulted in five categories: Establishing relationships and trust, Meeting informational needs, Acknowledging vulnerability, Balancing roles and interests, and Ensuring ethical competence. Health care professionals and researchers described care-based, research-based and children's rights-based ethical values in recruitment. Further, they reported ethical challenges related to informed consent, vulnerability, and shared decision-making. They relied on research ethical principles and regulations but also reasoned from ethics of care and virtue ethics perspectives.
Conclusions: Health care professionals and researchers are guided by care- and research ethical values, and report ethical challenges in recruitment. There is a need to highlight ethical aspects of pediatric research. Promoting research ethical competence among health care professionals and researchers may reduce moral distress and ensure ethical quality in pediatric research.

P127 / #1775

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

STATE OF THE PROFESSIONAL TRAINING OF NURSING THAT SERVES PEDIATRIC ONCOLOGICAL PATIENTS IN HEALTH INSTITUTIONS IN MEXICO.

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Background and Aims: Background. The Child Cancer Global Initiative Nurse Specialists point out that specialized education in pediatric oncology is insufficient and one of the main concerns related to nursing practice. In Mexico, as in other middle-income countries, it is necessary to recognize this need, as well as implement actions to resolve it. Objective: To describe the state of education of nurses who treat pediatric patients with cancer diagnosis in different health institutions in Mexico.
Methods: In the period from September to November 2021, a survey was applied to nurses who provide care to pediatric patients with cancer to learn about their professional education and training in pediatric oncology.
Results: Two hundred ninety-one individuals, with an average age of 34.2 years, from different institutions in Mexico, 58% of public and 42% private hospitals, which have 5 and up to 20 beds allocated for onco-care50.9% attended between 2 and 4 patients, 28.9% between 5 and 10 patients hospitalized per day and 20% provided ambulatory, surgical, administrative, or supervisory care. 0.68% have specialty in pediatric oncology, 6.18% specialty in general oncology, 4.4% diploma in pediatric onco, 55% monographic courses in the last 3 years related to pediatric oncology, 33.7% do not have training in pediatric oncology and 98.6% show interest in formal training.
Conclusions: . The World Health Organization aims to increase survival to 60% by 2030 by improving diagnosis and treatment in low- and middle-income countries. Our results confirm that the professionalization needs reach high levels since in the group of 291 respondents only 2 are specialists in pediatric oncological nursing, a large percentage only perform short courses. The imperative challenge to solve is the financing necessary to achieve and make possible in our environment with limited resources the specialization in pediatric oncology supported by technology to achieve the greatest reach in our country.

P128 / #1805

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

COMPETENCIES OF THE NURSING PROFESSIONAL ENTERING A PEDIATRIC ONCOLOGY HOSPITAL: FACING THE REALITY IN MEXICO.

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Background and Aims: Background. Teleton Oncology Children's Hospital receives about 20 newly hired nurses per year. The Task Force on Pediatric Oncology Nursing in Developing Countries in its basic standards for safe and effective nursing care recommends assessing competencies in pediatric oncology patient care from the time of recruitment and then training with a formalized induction program.
Objective: To describe the results of professional nursing competencies on the care of pediatric oncology patients in evaluation prior to the induction course.
Methods: This was an observational, descriptive, cross-sectional and retrospective research, we analyzed results of 64 employees who entered in 2019 to 2021. The initial assessment consisted of 35 multiple-choice items and two additional questions of self-perception of knowledge and clinical skills; the results were concentrated in Excel and descriptive statistics are shown.
Results: The initial theoretical evaluation of 64 nursing admissions, showed a minimum score of 23, a maximum of 78 and an average of 47.2, in education related to pediatric oncology, showed that 3.1% had a specialty in general oncology, 4.6% had a chemotherapy course, 9.3% took a related course, and 82% reported not having any of the above. In self-perception of theoretical and practical knowledge in pediatric oncology, on a scale where 0 is no knowledge or experience and 5 is excellent, 64% were between 0 and 1 in theory, 52% were between 0 and 1 in skill in clinical care.
Conclusions: . The training of nurses in pediatric oncology, a pending task in university programs, our results confirm the need and importance of implementing or maintaining the induction program when starting to work in this type of hospital and developing competencies to ensure the care of this vulnerable group of patients.

P129 / #567

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

EXPERIENCES FROM DIGITAL CLINIC AT A LONG-TERM FOLLOW-UP CLINIC FOR ADULTS AFTER CHILDHOOD CANCER DURING COVID-19

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Background and Aims: In Sweden, there are about 10,000 adult child cancer survivors (ACCS). In 75% of the survivor's late complication is found after 30-40 years of follow-up. In Gothenburg at the long-term-follow up clinic for ACCS from West Sweden, had due to the covid-19 situation change from physical to digital clinic. Aim Explore how a digital visit, by a video clinic was experienced by ACCS.
Methods: Invitation was sent to the patients with an offer of either digital or physical clinic, followed by a telephone call for decision of clinic and instructions for digital visits. The visit was attended by the patient and the health care team, consisting of counselor, nurse, doctor. In the beginning of the covid pandemic patients had a choice of either digital or physical visits, but after a few moths it was no choice, all visits were digital. Since clinical investigation was not possible at the digital visit, referral to local health care was made when needed. After the visit, a webbased evaluation during was sent to 139 patients with a response rate of 47,5 %.
Results: Patients attending the clinic were 67% digitally, 27% physical and 5% a telephone visit. Patients reported the importance of receiving information on their previous cancer diagnosis, treatment, and possible long-term complications, 80% of the patients reported the clinical visit fulfilled their needs. Patients having the digital clinic was 73% satisfied and 80% of them would like to attend another digital clinic.
Conclusions: A digital team-based clinic can be an alternative when a physical meeting is not possible or when the patient has a long journey. In the post-covid era, digital clinical visit is now offered to patients as an option. Acknowledgement - We would like to give special thanks to all the young adult cancer survivors who participated in the evaluation.

P130 / #1109

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

THE USE OF TRADITIONAL AND COMPLEMENTARY MEDICINE AMONG CHILDREN WITH CANCER IN TURKEY: WHAT WE KNOW SO FAR

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Background and Aims: Traditional and Complementary Medicine (T&CM) is widely used by children with cancer globally. T&CM use varies among ethnic groups because it is generally linked to cultural background and health beliefs. In Tukey, T&CM use is rooted in the country's tradition, and it isn't only used to relieve symptoms or treat illnesses. In this study, we reviewed published research articles about T&CM use by children with cancer in Turkey to identify T&CM use prevalence rate, used types, and the factors affecting T&CM use.
Methods: ULAKBIM TR, YÖK thesis center, EBSCO, MEDLINE, Elsevier, ScienceDirect, Psychoinfo, CHINAL, Thomson, and google scholar were searched. The inclusion criteria were primary studies from Turkey involving children with cancer (<18 years) who used any type of T&CM. Data were extracted by two reviewers.
Results: Thirteen studies published between 2000 and 2022 were included. T&CM use prevalence ranged from 26.6% to 99.4% (median=63.5%). All used questionnaires to assess T&CM use prevalence had no evidence of validity. The most common T&CM method was nutritional approaches and herbs (range=44.2%-97%, median=90.7%), including carob, mulberry, grape molasses, honey, and stinging nettle. The most common reasons for the use were treating cancer symptoms (range=4.5%-96.8%, median= 58.8%) and reducing the side effects of cancer treatments (range=5.2%-90.7, median=22.1%). Mostly, patients' relatives recommended using T&CM (range=18%-79.1%, median=%58.8). Most patients/parents do not disclose T&CM use to the health care team (range=25%-67.8%, median=62.4%).
Conclusions: T&CM use is common among children with cancer in Turkey. The reported T&CM use prevalence by children with cancer in Turkey varies widely. This could be explained by the inconsistent methodology used in T&CM studies, and the lack of standardized and validated T&CM questionnaires. Also, the ambiguity in the T&CM definition poses challenges when comparing the results across studies (e.g., some studies included surveys asking about multiple T&CM types while others had a limited number).

P131 / #223

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

THE BENEFITS OF IMPLEMENTING A NURSE PRACTITIONER-LED ONCOLOGY EDUCATION PROGRAM FOR PEDIATRIC RESIDENT PHYSICIANS: THE CHILDREN'S HOSPITAL LOS ANGELES EXPERIENCE

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Background and Aims: Pediatric resident physicians ('residents') often feel unprepared for the complexities and unique challenges of oncology patient care. During their oncology rotation, residents manage care for acutely ill and newly diagnosed oncology patients, frequently doing so without prior exposure or comprehensive oncologic-specific medical education. The aim of our study is to assess residents' comfort and knowledge prior to their oncology rotation and design a nurse practitioner (NP) led educational intervention to address gaps.
Methods: The NP education program consists of a comprehensive didactic lecture on the first day of each resident rotation, a pocket-sized information card, in-depth resource binders, and daily check-ins. Questionnaires are distributed before and after the residents' rotation and contain: a Likert scale-based survey assessing comfort and confidence; oncologic knowledge-based questions aligned with the survey topics; and demographic information. Preliminary data was gathered from April-June 2021. Post-survey data will be compared to preliminary results to analyze the impact of our intervention.
Results: Preliminary data found that as residents began their oncology rotation, they lacked confidence overseeing oncologic emergencies, managing chemotherapy and immunotherapy side effects, and providing supportive care. The education program began in July 2021 and will continue through June 2022. 35 physicians have participated to date. Early findings reveal an improvement in residents' confidence, satisfaction, and knowledge in comfort managing oncologic emergencies (18% increase from baseline) and providing supportive care (28% increase from baseline). The complete data analysis will be available for presentation at the Congress.
Conclusions: A NP-led clinical education program has shown to be beneficial in enhancing residents' confidence and knowledge in caring for oncology patients. Residents are empowered with more knowledge, skills, and support, which may lead to improved patient outcomes for pediatric cancer patients. This program proved feasible to implement and could be replicated in other sub-specialty areas.

P132 / #143

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

INFORMATION PROVISION TO SUPPORT PARENT DECISION-MAKING IN HIGH-RISK NEUROBLASTOMA: THE USE OF ANIMATION AS A METHOD OF INFORMATION GIVING

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Background and Aims: Background and aims The high-risk neuroblastoma clinical trial contains randomisations for induction, consolidation, and radiotherapy treatment. At diagnosis, parents are given detailed information to make an informed decision in relation to the clinical trial. Each stage/component of randomised treatment involves further decision making and consent processes for families. Adaptive and engaging information is needed to help parents understand the complexities and support their decision making for this clinical trial. Health literacy of individuals in information provision is paramount. Information should be provided in a variety of ways to maximise understanding and engagement particularly in decision-making (Sheridan et al, 2011). Visual, verbal, and written information is the 'gold standard' in the provision of information (Sheridan et al, 2011). The aim was to develop animation videos providing concise information on the high-risk neuroblastoma clinical trial. Animated information would complement the verbal and written information given to parents providing an additional layer of information provision to support health literacy, understanding and decision-making.
Methods: The National Neuroblastoma Nursing Group co-produced with parents a script of the different phases of treatment within the high-risk neuroblastoma clinical trial. Animation was created to support the script based on these treatment phases in collaboration with a creative design company. Ethical approval was received.
Results: Eight animated videos with screen captions were created providing information on: introduction to high-risk neuroblastoma, induction chemotherapy, stem cell harvest, surgery, consolidation chemotherapy, radiotherapy, maintenance therapy and end of treatment.
Conclusions: Videos will be available online alongside accessible information on the clinical trial parent/participant information sheets. Charity social media, professional Twitter accounts will support dissemination within the parent community. Future evaluation of this project will be conducted once the videos have been integrated into clinical practice.

P133 / #379

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

THE IMPACT OF A CONTINUED EDUCATION OF NURSES IN PAEDIATRIC ONCOLOGY: A CROSS-SECTIONAL EVALUATION WITH GRADUATED NURSES

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Background and Aims: Research has shown an association between nursing education and patient outcomes. Specialization of nurses has been identified as a nursing priority of the WHO Global Initiative for Childhood Cancer. In Sweden, a national educational program (45 and later 30 credits) in pediatric oncology nursing have been provided since 2003. The aim with the evaluation was to gain knowledge of nurses' perceptions of the impact of the national educational program in pediatric oncology nursing.
Methods: This cross-sectional study used a study-specific questionnaire to explore perceptions of nurses who had completed the national educational program. All participants in three cohorts (2012-2014, 2015-2017, 2017-2019) were invited to participate (30 March-17 May 2021). An electronic study-specific questionnaire with response alternatives yes and no, or a 4-point Likert-type scale (Not at all, to a small extent, to a fairly large extent, to a large extent), was used. Analysis included descriptive statistics and associations.
Results: Eighty nurses were invited to participate and 59 (74%) responded. At the time of the survey, 15 (25%) had left pediatric oncology. Among the remaining 44, 31 nurses (71 %) were working bedside, of which 13 (42%) combined it with a special position. The number of nurses with special positions (manager, consultant-, contact-, coordinating- or research nurse) increased, after the education, from 9 (20%) to 26 (59%). The vast majority (89%) stated that the knowledge from the education to a fairly large/large extent, helped them in their work and contributed to increased confidence in the interaction with the patient and the family.
Conclusions: Education has an impact on the career opportunities in clinical practice and contributes to nurses' confidence and professional work with children, adolescents, and their families. A limitation was the relatively small sample. To meet the demands of highly specialized pediatric oncology care, it is essential to provide continued education to nurses.

P134 / #1228

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

"BASIC PEDIATRIC ONCOLOGY COURSE MCM GRANT" FOR NURSES: IMPLEMENTATION CHALLENGES DUE TO PANDEMIC

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Background and Aims: Only 50 % of the 8000 Pakistani children with cancer are properly diagnosed and treated, and 40% of those who approach to a medical facility comes with advanced disease difficult to treat. Unfortunately, there are no palliative care services available for the 1600 children who have advanced disease in public or private health sectors in Pakistan. There is an urgent need for palliative care, particularly in the training for health workers and improving poor availability and/or accessibility to palliative care in terms of factors such as medication and bereavement support. Delivering palliative care requires a specialized set of skills from experience and training to provide holistic care to the patient and their family. MCM nursing grant was applied for creating and delivering "Basic Pediatric Hematology/Oncology Palliative Care Course "in 2019 for the purpose of training and education of Nurses from all over Pakistan. Primary objective for the grant was to provide Pakistani nurses training in palliative care
Methods: Sanofi Espoir My Child Matters Grant was approved in 2020 and funds were received. Implementation plan included creating a module and conducting workshops in three different cities with goal of training over 200 Nurses which was not possible due to pandemic COVID – 19 travel Restrictions and lockdown. The implementation plan was changed and improvised, new plan included developing two videos and a handbook which can be utilized by Health care workers not only In Pakistan but other countries as well.
Results: Palliative care resource material was developed with grant funds which included two Videos and a Pediatric Palliative Care Handbook.
Conclusions: Pediatric Palliative care educational material for health care professional was developed in local language with keeping in mind resources and cultural aspects. This is now a resource available online for all healthcare workers all over the world to be used in all training

P135 / #1342

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

CHILDREN'S VOICES ON THEIR PARTICIPATION AND BEST INTERESTS DURING A HOSPITAL STAY IN AUSTRALIA

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Background and Aims: The concepts inherent in defining the best interests of a child come from Article 3 of the United Nations Convention on the Rights of the Child (UNCRC). Listening to children's voices is vital to install trust, foster respect, autonomy, self-determination, as well as honour social justice and equity However, there is a lack of information on how children's best interests are upheld and expressed in hospitals globally. This study aims to explore school-aged children's experiences about their best interests and participation in care during a hospital admission.
Methods: A descriptive qualitative design involving in-depth, iterative inductive analysis of child's interviews. The study was guided by the UNCRC's definition of the best interests of the child, Bronfenbrenner's bioecological model and a child centred care approach.
Results: Nine school-aged children (5–15 years old) from one children's ward in Australia participated. Analysis yielded thirteen categories, six sub-themes, and three themes: 1) Relationships with parents were positive when they met their children's physical and emotional needs and advocated for them; 2) Relationships with staff were positive when staff created opportunities for children to have a say in their healthcare, and checked in on the children and 3) Seeking familiarity away from home was facilitated when the environment children found themselves in provided them their own space and various forms of entertainment.
Conclusions: School-aged children were able to verbalize what their best interests were and how participation in care could be facilitated in the hospital setting. The interrelationships of the children with their parents, healthcare professionals, and the immediate environment reflected interactions both within, and between systems. Children in hospital need to be provided with age-appropriate opportunities to participate in shared decision making to support their best interests.

P136 / #2009

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

EXPERIENCES OF THE CAREGIVER OF THE CANCER CHILD, WITH A PERIPHERALLY INSERTED CENTRAL CATHETER (PICC), DURING THEIR TREATMENT AT THE TELETON ONCOLOGY CHILDREN'S HOSPITAL (HITO).

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Background and Aims: Background: Cancer is the disease with the highest prevalence worldwide, affects children and adults, the PICC catheter is used for the oncological treatment of children with cancer, care is important to preserve it properly, training the caregiver and the health personnel who handle it, avoiding complications or untimely loss of the catheter. Hence the importance of sharing the caregiver's experiences and serving as a reference in the use and care of the PICC for the benefit of children with cancer. Objective: To describe the experiences of the caregiver, in the use and care of the PICC, for oncological treatment in pediatrics.
Methods: Material and Methods: It is a descriptive, cross-sectional investigation, a self-applicable questionnaire was used through a social network platform (WhatsApp) to caregivers of patients with PICC, the analysis was carried out through a sampling of finite populations where the margin is 5% and confidence level of 95% the sample size was 49 caregivers of children. Using descriptive statistics with the support of Excel, the permission to carry out this study was authorized by HITO management staff and caregivers.
Results: 49 surveys were conducted, 100% of the sample to caregivers of children with PICC, 90% mothers and 10% fathers. The longest stay of the catheter was 16 months, the average 6.9 months and the shortest 1 month. The medical diagnosis of the patients was: leukemia 45.2%, solid tumors 40.6% and post-transplant treatment 14.2%. The reported experiences were: 38% tolerable without discomfort, 31% uncomfortable at first, 28% no discomfort, 2% reported discomfort.
Conclusions: The experiences reported by the caregivers were less suffering, they avoided multi-tasking, responsibility, courage and affection, with some patients referring to the catheter as: "My tummy, Baby Piccito, Little Pet, Emily and Hose-legs".

P137 / #450

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

IMPACT OF RESILIENCE AND SOCIAL SUPPORT ON LONG-TERM GRIEF IN CANCER-BEREAVED SIBLINGS: AN EXPLORATORY STUDY

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Background and Aims: Background: Bereavement research has mainly explored potential risk factors associated with adverse outcomes, and the role of protective factors has received less attention. More knowledge is needed about factors related to unresolved grief in bereaved siblings. This study aimed to assess grief adjustment and possible gender differences among bereaved young adults 2–10 years after losing a brother or sister to cancer. We also sought to explore how resilience and social support influenced their grief.
Methods: A total of 99 young adults (18-26 years) who had lost a brother or sister to cancer between the years 2009 and 2014 were invited to participate in this Norwegian nationwide study. The study-specific questionnaire was completed by 36 participants (36.4%). Social support during the sibling's illness, after the death, and during the past year, in addition to grief and resilience were measured.
Results: Overall, the prevalence of unresolved grief was 47.2 % among bereaved siblings, whereas 52.8 % had worked through their grief. The level of having worked through grief and resilience was similar between male and female siblings. Bereaved siblings with higher Personal Competence reported lower unresolved grief.
Conclusions: Approximately half of the young adults experience unresolved grief 2-10 years after losing a sibling to cancer. The findings also highlight the need for long-term support for bereaved siblings to help improve their resilience and better have worked through their grief.

P138 / #381

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

DEVELOPMENT OF A NATIONAL NETWORK OF ALLIED HEALTH PROFESSIONALS WORKING WITH CHILDREN WITH CANCER TO IMPROVE PARTICIPATION AND QUALITY OF LIFE (KINDERONCONET).

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Background and Aims: Since 2018 medical care for children with cancer in the Netherlands is concentrated in one dedicated Princess Máxima Center for pediatric oncology. Stakeholder analysis reveals that strengthening and continuity in care by allied health professionals is essential for optimizing care, participation and quality of life.
Methods: Using a mixed methods approach, with quantitative (survey) and qualitative co-creation sessions we determined and identified wishes and needs among parents of children with cancer and pediatric physiotherapists with respect to continuity of care close to home.
Results: A survey among 98 parents of children with cancer and 176 local physiotherapists showed that 96% of parents think it is important that the local therapist is aware of the pediatric oncological condition, the side effects and late effects of treatment affecting exercise, and that 93% of therapists are enthusiastic about developing a national network for collaboration (KinderOncoNet). Moreover, 40% of physiotherapists think that they do not have sufficient knowledge to be able to give a high-quality treatment, and that they lack opportunities for education to gain more knowledge in the field of pediatric oncology in relation to physiotherapy care.
Conclusions: Parents and therapists indicated that a national, multidisciplinary care network specialized in pediatric oncology involving children/parents/survivors and local physiotherapists (and other allied health professionals), in which they entrust each other in providing care, in which knowledge is available at the right time and place and build capacity in pediatric oncological care, would improve the accessibility and continuity of optimal care, participation and quality of life.

P139 / #494

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

AMBIGUOUS EXPECTATIONS OF PARENT CAREGIVING FOR THE CHILD AND ADOLESCENT WITH CANCER AT HOSPITAL AND AT HOME – AN ETHNOGRAPHIC STUDY

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Background and Aims: Over the past three decades, complex care and treatment has increasingly become the responsibility of parents as home-based care providers; yet little is known about parents' caregiving experiences when considering the variety of care tasks. It is imperative to gain insight into the challenges that parents face when managing treatment and care of their child with cancer to ensure optimal parent support and prior to further expansion of home-based parent caregiving. The aim of this study was to explore the experiences of children and adolescents with cancer and their parents in managing different care tasks. It is the first study of the research project 'INTravenous AntiCancer Treatment for children and adolescents at Home (INTACTatHome)', that aims to develop and test an intervention of home-based intravenous anti-cancer treatment.
Methods: An ethnographic fieldwork comprising participant observation and semi-structured interviewing was conducted from July 2020 to December 2020 at the hospital and in the homes of the families. A purposeful maximum variation sampling strategy was applied, and 13 families participated in the fieldwork (13 children and adolescents and 15 parents). Teen of these families were interviewed (five children and adolescents and 16 parents). Data was analyzed using qualitative thematic analysis.
Results: Three main themes were identified: 1) Being a "mini-nurse"; 2) Dividing care; and 3) Managing anxiety and fear, each based on separate sub-themes. These themes were bound together by an overarching theme: 'Ambiguous expectations of parent caregiving'.
Conclusions: This study contributes to a deeper understanding of the varying experiences of parents in managing different care tasks for a child or adolescent with cancer. It underscores the need to establish clear expectations for parents as caregivers throughout the cancer treatment trajectory. This perspective is crucial when developing and implementing future home-based care services.

P140 / #1368

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

DEVELOPING A COMPLEX INTERVENTION OF INTRAVENOUS ANTICANCER TREATMENT FOR CHILDREN AND ADOLESCENTS AT HOME.

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Background and Aims: Studies show that parents of children with cancer are willing to provide a variety of home care tasks to avoid hospitalization. However, intravenous chemotherapy given at home is a complex task that impacts patients, caregivers, and health professionals. The aim of this study was to develop a feasible and safe home chemotherapy intervention for children targeted to parents.
Methods: The study was conducted at the Pediatric Oncology and Hematology Department at Copenhagen University Hospital. This is the second study of the research project INTravenous AntiCancer Treatment for children and adolescents at Home (INTACTatHome). The intervention was developed in a framework of actions for intervention development within the National Institute of Health Research and UK Medical Research Councils guidelines for developing complex interventions in health care. The development was structured in three phases: 1) two workshops with multidisciplinary health professionals (n=12 and n=13) based on the nominal group technique method and focus groups to identify eligible chemotherapy treatments for parent-led home administration, 2) interviews with parents of children with cancer with experiences of intravenous antibiotics at home, on their opinions of chemotherapy administration (n= 9), and 3) pilot test of the developed intervention on three families.
Results: showed that low dose bolus cytarabine was the most eligible chemotherapy for parent-led home administration. The administration procedure, and a parent-education program were developed. The pilot test showed that the parent-led administration procedure was feasible, the parent-education program was manageable and corresponded to parents' needs, and pilot families were satisfied and preferred home-based to hospital-based chemotherapy.
Conclusions: This development study informs the next phase of the research project that aims to test the home chemotherapy intervention in a prospective single-arm intervention study to evaluate feasibility, process, and outcome measures relevant to future larger scale evaluation and implementation.

P141 / #435

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

NURSING ROLE IN THE HEMATOPOIETIC STEM CELL AND BONE MARROW TRANSPLANTATION UNIT IN RABAT, MOROCCO

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Background and Aims: Increase number of allografts to 10 in 2022, and elucidate the nursing role for success. This information can also serve as a training tool for nurses in the pediatric hemato-oncology department SHOP Rabat.
Methods: Data collection performed by participatory observation during my nursing work in transplant from October 2020 until March 2022, 24-hour shift, and review of transplant files and statistics of the transplant unit.
Results: Over 18 months, 17 autografts and 5 allografts were completed. Nursing role by transplant phase presented here. Pre-transplant: perform complete patient biological assessments, HLA typing for the donor and recipient for allograft, mobilization of stem cells for autograft. Transplant hospitalization: welcome and educate the child and caregiver on hygiene and transplant procedures. Administer myelo-ablative and non myelo-ablative conditioning treatment. Reinject of stem cells or bone marrow. Immediately post-transplant: prevent/treat complications of aplasia and early toxicity of conditioning. Recovery from aplasia: prevent graph versus host disease in allograft patients. Exit from hospitalization: prepare child for discharge and educate child/family for home therapeutic care: diet, hygiene, leisure, and school activities.
Conclusions: The nursing role in the pediatric transplant unit is important to prevent and treat transplant complications and to succeed in our department's project of achieving 10 successful allografts per year. Sharing this knowledge will enable nurses working in settings in other limited resource settings to understand the nursing role and scope of practice in a lower-middle-income country transplant unit to ensure a good outcome for the child and family.

P142 / #668

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

DEVELOPMENT OF A FAMILY NAVIGATOR FUNCTION TO ASSIST FAMILIES NAVIGATING THE COMPLEX CANCER TREATMENT

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Background and Aims: Multiple challenges arise in a family when a child or an adolescent is diagnosed with cancer, concerning mental, social, and physical development. The parents are often burdened by numerous care related tasks, in addition to maintaining their work or education. Additionally, siblings may suffer from their parent's preoccupation of the sick child. As part of a national cancer strategy optimising patients' experience of coherent treatment trajectories, management at the children's cancer ward in Rigshospitalet, Copenhagen, Denmark, encouraged the development of a function to support the families navigating the complex cancer treatment, facilitate access to services, and reduce the families experience of psychological distress.
Methods: Through an iterative process of three months, we conducted fieldwork consisting of several interprofessional meetings with medical and nursing specialists, and management to describe and map the family navigators' functions and need for family navigation.
Results: We identified four types of needs for family navigation: 1) Families with particular attention needs (i.e. single parents, families with social challenges, or families with competing illness'), 2)Need identified by one or more healthcare professionals within the first months, 3) Need assessed by the family navigator for assistance at any time during the treatment, and 4) Relapse of disease. All families to children and adolescents diagnosed with cancer are offered structured dialogues identifying areas for assistance throughout the treatment trajectory. The structure entails every-day challenges, concerns, support, and treatment. Three family navigators share between them the patients according to their diagnosis to ensure individually adapted treatment, care, and rehabilitation, in collaboration with the families.
Conclusions: The family navigators work systematically to ensure family-adapted nurse navigation to assist the families navigating the complex cancer treatment and reduce the families experience of psychological distress. An evaluation of families' experience and perception of distress is needed, as well as evaluation of the function.

P143 / #1145

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

INFANT ACUTE LYMPHOBLASTIC LEUKEMIA: RECENT ADVANCES IN RESEARCH AND A REVIEW OF STANDARD THERAPY

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Background and Aims: Infant acute lymphoblastic leukemia (ALL) is a rare, aggressive and distinct subset of pediatric leukemia. Historical 6-year event-free survival was previously 46% for patients with infant ALL. Infant ALL comprises about 4% of all cases of pediatric ALL, therefore advances in treatment of infant ALL require international collaboration. The current standard treatment backbone was developed from Interfant-99, which was the first large-scale international clinical trial for infant ALL. This presentation aims to summarize current standard therapy for infant ALL, including recent advances, as well as highlight upcoming clinical trials.
Methods: Performed literature review of large, international, multi-center trials for treatment of infant ALL. Reviewed treatment protocols and outcomes for Interfant-99, Interfant-06, and a recent phase 2 study using blinatumomab (Van Der Sluis et al, 2021) in addition to upcoming international clinical trials (Interfant-21 and AALL2122).
Results: The current standard treatment backbone was developed from Interfant-99, which was the first large-scale international clinical trial for infant ALL. The last large international study for infant ALL was Interfant-06. The primary aim of this study was to identify if a myeloid-style consolidation chemotherapy regimen was superior to lymphoid style for patients with KMT2A rearrangement. Unfortunately, outcomes did not differ significantly between the lymphoid and myeloid groups. However, recent clinical trial data by Van Der Sluis et al. (2021) has shown dramatic improvement in event-free survival for this patient population with the addition of blinatumomab immunotherapy with a one-year event-free survival of 96.2%.
Conclusions: After advances in treatment had been generally stagnant over the past decade, incorporating targeted therapy with blinatumomab immunotherapy has shown staggering improvement in patient outcomes. This has influenced upcoming international clinical trials for infant ALL (AALL2122 and Interfant-21) to include blinatumomab as part of standard therapy in addition to other novel approaches to treatment for patients with KMT2A-rearrangement.

P144 / #869

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.a Education*

COMPETENCE AND ATTITUDE OF NURSES ON PAIN MANAGEMENT AMONG CHILDREN WITH CANCER IN GANTSI PRIMARY HOSPITAL, BOTSWANA.

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Background and Aims: BACKGROUND: Pain is among the most common effects of cancer and this have been undertreated and under-recognized. WHO have advocated that children with cancer receive pain management based on the WHO analgesics ladder. However, poor pain management remains a common problem in Botswana. The goal of pain management is to reduce pain, distress and anxiety, and nurses are the key player in pediatric cancer pain management and therefore is important to identify nurses competency on pain management. AIM: To generate baseline data on nurses competency and attitude in pediatric pain management among children with cancer.
Methods: A descriptive design using qualitative methods was used to conduct the study. The convenience sample consisted of 20 nurses in Gantsi Primary Hospital who completed a questionnaire designed in English. Data were analyzed using thematic content analysis.
Results: Nurses stated that they rely on parents to report childre"s pain since it is subjective. They demostrate moderate knowledge on pain management but dont follow the WHO pain ladder when managing pain due to no knowledge about the kadder. They had less knowledge on pain assessment methods among children but had a positive attitude towards pain managemnt in children and adolescent. They reported reluctance to give opiods due their side effects such as constiption, respiratory failure and fear of adiction. Nurses had good knowledge on non pharmacological management of pain, they stated to be using distraction most. Inadequate pain management training and guidelines for nurses was reported as the main challenge among children with cancer.
Conclusions: Children with cancer should be pain free hence pain management is a prioritized. however, pain management in children with cancer is still a challenge for nurses due to lack of in-service trainings. A few negative attitudes were still prevalent arising from the side effects of opioids hence reluctant to give.

P145 / #885

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

CHALLENGES EXPERIENCED BY NURSES ON HAND-WASHING WHILE NURSING CHILDREN WITH CANCER IN GANTSI PRIMARY HOSPITAL, BOTSWANA.

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Background and Aims: Background: Hand hygiene remains the cornerstone of infection prevention but often an overlooked aspect in infection control. Children with cancers are already immune compromised hence hand washing should be practiced effectively and consistently inorder to reduce the morbidity and mortality of children with cancers from nosocomial infections. WHO have introduced the Hand washing guidelines even though lower- and middle-income countries like Botswana, still experience challenges with infection prevention and control measures like hand washing. Aim: To describe the challenges related to hand hygiene experienced by nurses working with children with cancer.
Methods: A qualitative study in which convenience sampling was used to select 12 nurses from the pediatric ward who completed a self-administered questionnaire. Thematic data analysis was used for data analysis.
Results: Themes emerged from participant responses and perceived challenges to hand washing included the following themes: unavailability of supplies (especially soap and water, lack of time to do hand washing due to workload, cultural resistance to hygiene practices from parents. Nurses also stated that hand washing have been replaced by hand sanitizing during the COVID-19 era. Nurses also stated that poor infrastructures with no accessibility to sinks and hand washing equipment, which makes hand washing an inconvenient nurses working with cancer children.
Conclusions: The research concluded that the main barrier fo handwashing was lack of supplliers and workload, therefore strategies to improve infection prevention control should focus mainly on the provision of suppliers such as soap, water, sanitazing.In summary, our study shows that interventions and guidelines aimed at improved hand hygiene in oncology pediatric wards shold be supported by nursing managers to have shared effeorts and results.

P146 / #162

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

RELIABILITY AND VALIDITY OF PROXY-SSPEDI AND MINI-SSPEDI IN PEDIATRIC PATIENTS 2-7 YEARS RECEIVING CANCER TREATMENTS

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Background and Aims: Symptom Screening in Pediatrics Tool (SSPedi) and proxy SSPedi were developed for symptom screening by children 8-18 years old. An important gap was that SSPedi did not address the needs of younger children. The objectives were to evaluate the reliability and validity of proxy-SSPedi (2-7 years) and self-report mini-SSPedi (4-7 years).
Methods: This multi-center study enrolled guardians of children 2-7 years receiving cancer treatments (proxy-SSPedi) and their children if they were 4-7 years (mini-SSPedi). The two populations were: (1) More symptomatic group where children were receiving active cancer treatment and were in hospital or clinic for four consecutive days; and (2) Less symptomatic group where children were receiving maintenance therapy for acute lymphoblastic leukemia or had completed cancer therapy. Proxy-SSPedi or mini-SSPedi were completed with measures of mucositis, nausea, pain, quality of life and overall symptoms. Respondents in the more symptomatic group repeated proxy-SSPedi/mini-SSPedi and a global symptom change scale at the second assessment.
Results: There were 402 guardians and 326 children included in the analysis. Test re-test reliability of proxy-SSPedi showed intraclass correlation coefficient (ICC) 0.83 (95% confidence interval (CI) 0.72-0.90). Mean difference in proxy-SSPedi between more and less symptomatic groups was 9.7, 95% CI 8.3-11.1. Proxy-SSPedi was responsive to change and hypothesized relationships between measures were observed. With a priori threshold ≥ 0.6, inter-rater ICC among all dyads and those 6-7 years were 0.54 (95% CI 0.45-0.62) and 0.62 (95% CI 0.50-0.71) respectively. Among participating children, other hypothesized reliability and validity thresholds were met.
Conclusions: We found that proxy-SSPedi (2-7 years) and mini-SSPedi (4-7 years) exhibited test re-test reliability, internal consistency, known groups validity, convergent validity and responsiveness. However, interrater reliability was established only for children 6 and 7 years of age. A dyadic child-guardian approach may be promising for future research.

P147 / #457

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

SYMPTOM DOCUMENTATION AND INTERVENTION PROVISION RELATED TO PROXY-SSPEDI ASSESSMENTS IN PEDIATRIC PATIENTS 2-7 YEARS RECEIVING CANCER TREATMENTS

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Background and Aims: To enable pediatric patient symptom self-report, we previously created Symptom Screening in Pediatrics Tool (SSPedi). However, SSPedi does not address the needs of those who cannot or will not self-report symptoms including some younger children. Therefore, we created proxy-SSPedi, which is aimed at pediatric patients receiving cancer treatments who are 2-18 years of age.
Understanding healthcare professional symptom documentation and intervention provision may provide insight into why symptoms may be poorly controlled.
Objectives were to describe symptom documentation and intervention provision for children 2-7 years of age receiving cancer treatments. Secondary objectives were to determine the relationship between symptom documentation and intervention provision with increasing severity of bothersome symptoms as identified by guardian proxy-SSPedi.
Methods: We included guardians of children 2-7 years of age receiving cancer treatments and seen in hospital or clinic daily for four consecutive days. Guardians reported proxy-SSPedi at study entry and three days later. Chart review was performed between the day prior and the day following proxy-SSPedi completion. Symptom documentation and intervention provision were determined by two independent abstractors.
Results: We enrolled 190 guardians who provided 371 proxy-SSPedi assessments. The most common severely bothersome symptoms were “feeling tired”, “feeling more or less hungry than you usually do” and “feeling cranky or angry”. Among those with increasing severity of bother, documentation was significantly more common for 12 symptoms while intervention was significantly more common for 7 symptoms. Intervention was not significantly more common with increasing severity of “feeling tired”, “feeling more or less hungry than you usually do” and “feeling cranky or angry”.
Conclusions: Symptom documentation was generally more common among those with increasing severity of symptoms. Intervention was not more common among those with increasing severity of fatigue, changes in hunger or anger, which were the most common severely bothersome symptoms. Future efforts should focus on increasing intervention provision.

P148 / #1095

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

ASSESSING THE KNOWLEDGE OF NURSES IN THE PAEDIATRIC ONCOLOGY UNIT AT TAMALE TEACHING HOSPITAL ON FEBRILE NEUTROPENIA AND ITS MANAGEMENT

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Background and Aims: Febrile neutropenia (FN) can cause significant morbidity and mortality in children with cancer if it is not recognised early and treated promptly. The aim of the study was to assess the knowledge of nurses working in the paediatric oncology shared care centre at the Tamale Teaching Hospital on the management of febrile neutropenia.
Methods: A descriptive cross-sectional study with a quantitative data collection method was used. All nurses assigned to the paediatric oncology unit were recruited. A structured questionnaire was used in the data collection.
Results: A total of 18 nurses were recruited. Majority of the respondents 14/18(77.8%) had worked in the unit for less than 2 years. Most of them, 15/18(83.3%) did not have formal training in the management of febrile neutropenia and did not even know it was an emergency. The majority did not know the cause, and children were at risk of the condition. Also, 13/18 (72.2) of respondents did not know the time within which to initiate antibiotics upon triage of patients and 16/18 (88.9) did not know the first-line antibiotics to give.
Conclusions: Most of the respondents had no formal training in the management of FN. The majority of them could not recognize FN as an emergency and when to initiate treatment. Knowledge regarding its management is important among nurses taking care of children with cancer hence in-service training should be organized regularly among nurses.

P149 / #1064

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

DEVELOPMENT OF NOVEL CHILD AND PARENT INFORMATION LINE TO INCREASE EMPOWERMENT AND THE FAMILY'S AUTONOMY; ESTABLISHED IN COOPERATION WITH CHILD AND PARENTS

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Background and Aims: The Princess Máxima Center for Pediatric Oncology has combined innovative care, treatment and state of the art research into one center. With each step taken in treatment, we are committed to ensure continuation of the child's regular development, as natural as possible, with maximum quality of life. Empowerment of child and parents is a key priority. Effective communication as well as coordination with child and family are essential. Better knowledge and understanding about illness and treatment increases the autonomy of child and parents. To accomplish this goal, the aim was to develop reliable and easily comprehensible information, in co-creation with children and parents.
Methods: Together with children and parents, we developed a vision on how to create and implement adequate information. It is crucial that information is understandable, applicable and findable for child and parents. The use of positive and supportive language is essential. Age specific information as well as inclusiveness in cultures and languages are taken into account. Ensuring information to be understandable, this requires visually clear information, developed for a young target audience or illiterate people, using recognizable animations and visual stories. Each type of information uniformly uses the same format, recognizable icons and unambiguous language.
Results: We have developed an entirely new child and parent information line. This uniform line is fully integrated into all types of information provided for children and parents, e.g. website, patient portal, leaflets, consultation support, etc.
Conclusions: A complete and fully uniform way of providing information has been implemented in the patient journey for child and parents. This optimizes decision-making for healthcare professionals in cooperation with child and parents. This way, they will be better prepared for consults, procedures or treatment. Because of this, joint decisions made by child, parents and professionals will be more in line with their personal situation and needs.

P150 / #1184

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.b Research*

"12 YEARS OF LEARNING TO RELIVE EXPERIENCES OF FATHERS AND MOTHERS IN A BEREAVEMENT SUPPORT GROUP."

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Background and Aims: The death of a child from cancer has a great impact on the parents, due to the disease process, unresolved suffering, and because it is considered a "taboo" subject. Twelve years ago, at the Roberto del Río Hospital in Santiago de Chile, an interdisciplinary team formed a self-help group called "Aprendiendo a Revivir", whose objective is "To accompany parents and families who have lost a child to cancer in the mourning process" through two annual meetings. Aims: Understand the experiences of parents who have participated in the meetings auto self group.
Methods: Qualitative descriptive research. All parents who attended the meetings on a voluntary basis were invited to participate. A questionnaire with open-ended questions was used: "What did you find most difficult during the meeting?", "What did you like most about the meeting?" and "What did participate in these meetings mean to you?". This was answered by 30 parents. A content analysis was carried out according to Krippendorf.
Results: Parents are motivated to participate in the meetings because of the opportunity to talk about their children and remember them in a safe environment. The most complex thing is attending for the first time, because of the uncertainty and lack of knowledge about the meeting. What is most difficult for them is to talk about their pain and share it, contain their emotions, and feel guilty about laughing. They liked having a space for reunion and remembrance, sharing their pain in a safe environment, and feeling listened to. For the parents, these meetings have meant: Achieving greater personal and spiritual growth; an instance of reunion with significant people, and feeling understood.
Conclusions: For parents, having a meeting with a focus on self-help provides them with tools to elaborate their grief, in a protected and safe environment, together with people who are significant to them.

P151 / #990

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

IMPACT OF "IN SITU" PEDIATRIC ONCOHEMATOLOGY EMERGENCY SIMULATION: ORGANIZATIONAL AND CARE IMPROVEMENTS

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Background and Aims: To assess the usefulness of the low-complexity simulation carried out "in situ" to promote the competence of professionals in the initial care of pediatric oncohematology emergencies (ICPOE) and to identify aspects for improvement both at the organizational and care levels.
Methods: The material used in the simulation were megacode baby trainer, junior Danny mannequins, and ALSi simulator.
The minutes of the ICPOE simulations were reviewed.

Results: From June 2018 to December 2021, 12 ICPOE simulations have been carried out. They were performed "in situ" in a room on the hospitalization floor and in the procedure area, with the participation of the usual care team in both locations (pediatricians, anesthesiologists, nurses, auxilliaries, ancillaries). They lasted two hours with a basic scheme of briefing, simulation development and debriefing. The assessment of the simulations made it possible to verify that the global method applied and the assistance to the patient's physiological compromises were correct. Even so, aspects of improvement could be detected, especially related to the coordination and communication of the healthcare team. To this end, the use of the mental model was reinforced, work was done on a communication model between teams that led to the creation of a leading nurse in charge of receiving medical indications and transmitting them in an organized manner to the nurses dedicated to airway care, vascular access and medication preparation. Likewise, the need to create a trolley for seriously ill children was detected, locating treatment algorithms available in it, as well as a timer and a record to control medication times.
Conclusions: In situ simulations are a useful instrument to evaluate and improve the competence of professionals in emergency care, reinforcing leadership and teamwork, and also allow to detect weaknesses in oncohaematological emergency care. Carrying out periodic drills is a tool used to assess the impact of improvement actions.

P152 / #194

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

APPLYING THE INITIATIVE OF MEANINGFUL RECOGNITION TO IMPROVE A HEALTHY WORK ENVIRONMENT ON THE HEMATOPOIETIC STEM CELL TRANSPLANT UNIT

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Background and Aims: The work environment is a major focus in healthcare systems across the country due to burnout rates and work-related stressors healthcare providers experience every day. In addition, Hematopoietic Stem Cell Transplant (HSCT) is a complex treatment course and often a fast-paced work environment leading to stress and compassion fatigue. Boston Children's Hospital (BCH) incorporated the American Association of Critical-Care Nurses Six Standards of a Healthy Work Environment (HWE). The six components include skilled communication, true collaboration, effective decision-making, appropriate staffing, meaningful recognition and authentic leadership (AACN Website). The HWE committee was established with representatives, also known as "Champions" from all areas of BCH including the HSCT Program.
Methods: Starting in 2019, each year, the HWE champions from all areas of BCH send a universal survey to selected staff members. To date, the HSCT Program has completed four annual surveys, comprised of nurses, nurse practitioners, nutritionists, clinical assistants and Patient Experience Administrators.
Results: Survey results for 2019, had a completion rate 82%, averaged "excellent", the lowest scoring category being meaningful recognition, 3.74 on a 5.0 scale. The following two years, the HSCT Unit survey response rate was 100% completion with results demonstrating dramatic improvement in meaningful recognition, illustrating a 14% increase in satisfaction.
Conclusions: Through focus groups and brainstorming sessions, led by HSCT nursing leadership the Most Valuable Player (MVP) Program was created. Staff, families, and patients can put nominations into a box, located at a central location. On the first of the month, one name is drawn randomly to select the MVP. All the other nominations are then read aloud with a group of staff members and typed up quarterly to share with staff. When selected for the MVP their picture, name, and comments from the nominees are displayed on a designated board on the unit as well as given a gift card.

P153 / #447

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

REDUCING OUTSIDE LAB MONITORING FOR PEDIATRIC PATIENTS WITH SOLID TUMORS: IMPACT ON SAFETY, COST, AND QUALITY OF LIFE

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Background and Aims: Our institution historically monitored bloodwork twice weekly for patients with solid tumors to establish white blood cell count recovery following receipt of daily filgrastim. This frequency of lab monitoring was heavily taxing on care coordination and required twice weekly central line access. At present, most patients receive peg-filgrastim and require bloodwork to monitor for transfusion needs rather than count recovery. This quality improvement project aimed to identify the minimum number of surveillance labs required, based upon disease and chemotherapeutic regimen, and to provide guidelines to safely reduce the number of home labs for targeted solid tumor diagnoses by 50% over 2 years.
Methods: We sourced data regarding the number of transfusions performed to correlate whether laboratory work was obtained concurrent with transfusion needs or clinical symptoms, or if labs were obtained unnecessarily. We found that only 24% of transfusions were informed by home bloodwork. Based on these findings, we developed new monitoring guidelines categorized by disease and treatment regimen. We conducted educational sessions and longitudinal chart reviews to ensure safety.
Results: Post-implementation data analysis resulted in a 77% reduction in home lab draws, exceeding the 50% goal. There were no adverse events. Estimated cost savings over two years, accounting for oncology provider follow up, price per lab and visiting nurse sessions, was $70,751.
Conclusions: Our findings indicate that there are a cohort of solid tumor diagnoses that do not require twice weekly bloodwork to monitor for transfusion needs. By identifying these patient populations, formulating, and implementing bloodwork guidelines, we have safely reduced the number of labs drawn and, in keeping, optimized resource utilization, cost, and quality of life. Attention to clinical context remains warranted as additional labs, outside of these guidelines, may be required to address clinical status or clinical trial requirements.

P154 / #1917

Topic: *AS04 Nursing - if accepted, the abstract will be presented in the nursing programme / AS04.c Quality Improvement/Practice Project*

DEVELOPMENT OF A MULTI-DISCIPLINARY, MULTI-DEPARTMENTAL QUALITY IMPROVEMENT COUNCIL FOR A LARGE PEDIATRIC ONCOLOGY PROGRAM

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Background and Aims: The Center for Cancer and Blood Disorders (CCBD) at Children's National Hospital (CNH) serves pediatric patients with hematological, immunological, rheumatologic and oncological diseases including 1600 patients with sickle cell disease, 300 new cancer diagnosis/year, 60 hematopoietic stem cell transplants/ year with 1,300 outpatient visits/week and an average inpatient census of 28.5. There was no overall structure to coordinate quality improvement (QI) projects across disciplines and departments, foster a culture of cooperation and develop a metric driven process.
Methods: The CCBD QI Council consists of a multidisciplinary and multi-departmental team of physicians, nurses and leaders from pharmacy, patient safety, laboratory and environmental services, monitors ongoing QI projects, identifies new opportunities to improve safe and timely care delivery and initiates new projects. Projects are required to be rigorous using published QI techniques. Progress is monitored and displayed on a dashboard available to the entire CCBD community.
Results: The council has shown effectiveness through individual projects such as advancing chemotherapy start time on the day of admission from 70% to less than 50% being started after 5PM and reducing chemotherapy preparation and delivery time to clinic patient from a baseline of 150 minutes to 105 minutes, a 30% improvement. The CCBD QI Council identifies partners with ideas to improve care; such as a partnership with anesthesia to decrease anesthesia times during lumbar punctures. Monthly evaluation of data and strong partnerships has led to the identification of trends and opportunities for sustained improvement such as reduction of hospital acquired viral infections during the COVID pandemic, changes in processes to deliver timely antibiotics to febrile neutropenic patients, improvement in timely report of laboratory results and reduction in central line associated blood stream infections (CLABSI).
Conclusions: A multi-disciplinary, multi-department structured QI council can lead to a vigorous safety culture through partnership and data analysis.