What ESMO guidelines could and could not acknowledge

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EORTC

Conticanet, EuroSARC

Clinical practice guidelines

Soft tissue sarcomas: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

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On behalf of the ESMO Guidelines Working Group*

Bone sarcomas: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

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clinical recommendations

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Gastrointestinal stromal tumours: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

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2008 2010 2012 2014

GIST

- Incidence
  - Molecular subtypes becoming better described
- Diagnosis
  - <2cm: endoscopic monitoring (rectum exception)
  - Monitoring frequency: no data
  - If GIST diagnosis: resection advised
  - >2cm : resection
  - Biopsy first including percutaneous biopsy in large abdominal mass.

GIST (2)

- Histology-Phenotype:
  - No changes
  - Expert opinion advised
- Molecular diagnosis
  - Recommended (standard)
  - Predictive and prognostic
  - Tumor banking

GIST (3)

- Risk classification (from 1 to 5 digits)
  - Size, MI, site, rupture, heat-maps
  - Mutations
- Staging
  - Unchanged
  - PET scan for neoadjuvant
- Multidisciplinary management

GIST (4)

- Localized phase
  - Experience center/multidisciplinary assessment
  - Complete surgical excision, without the dissection of clinically negative lymph nodes
  - R0 (programmed R1 if large multivisceral)
  - R1: re resection to be discussed
  - Adjuvant 3 year if high risk
    - Dose of 800mg/d for exon 9 : no consensus
    - WT: no consensus
    - D842V: no treatment
  - Neoadjuvant in expert centers only

GIST (5)

- Advanced phase
  - Imatinib 400/800 (exon 9) indefinitively
  - Surgical removal of the lesions not proven useful
  - Monitoring trough levels still a research question
  - Careful evaluation of “progressions”
  - Compliance
  - Dose escalation up to 800mg/d
  - Sunitinib 50mg/d 4/6w or 37.5mg/d continuous
  - Regorafenib at progression post imatinib, sunitinib
  - Imatinib rechallenge (RIGHT study)
  - Combinations discouraged outside clinical trials
  - Clinical trials

GIST (6)

- Follow-up
  - No standard options
  - Adapted to the risk
  - Frequency increased after end of adjuvant (1-3 y)

STS

- Incidence
  - Unchanged
- Diagnosis
  - Importance of reference centers (to be described)
  - Multidisciplinarity
  - MRI, CT Scan
  - Biopsy : 14-16 gauge
  - WHO 2013 classification, Grade
  - No Bouin

STS (2)

- Pathology report
  - Experienced physician/center
  - Description of the procedure
  - Margins
  - Histological response to neoadjuvant not standardized
- Histological diagnosis
  - Morphology , IHC
  - Molecular diagnosis should complement: if diagnosis is doubtful, unusual presenation, prognostic/predictive

STS (3)

- Staging
  - AJCC/UICC
  - Local staging
  - CT scan thorax
    - (+Abdomen/pelvis, brain if specific histologies)
    - Regional LN assessment for rare histologies

STS (4)

- Treatment of localized disease
  - Specifically trained surgeon
  - Wide excision R0
  - Radiation therapy for G2-3, deep-seated, >5 cm
    - Adaptation to clinical presentation, site, sequelae, histologies
    - 50Gys in 2 Gy fractions, + boost depending on surgery
  - Reoperation to be considered if R1 outside reference center. Mandatory if R2

STS (5)

- Treatment of localized disease
  - Adjuvant CT not a standard/no consensus
    - Subgroups to be identified
    - To be avoided in certain histologies
  - Hyperthermia+CT & ILP as options
  - Neoadjuvant CT not a standard

STS (6)

- Treatment of advanced disease
  - Multidisciplinary assessment
  - Surgical removal of isolated lung metastasis if feasible
  - Chemotherapy as standard otherwise
    - Doxorubicine vs Doxo-ifosfamide
    - Taxanes for Angios, DTIC for LMS, imatinib for DFSP
    - Trabectedine as second line option
    - Pazopanib as 2nd line option but LPS (RCT)
    - Gem Docetaxel, Gem DTIC
    - mTOR, crizotinib, cediranib, sunitinib in selected subtypes

STS (7)

- Follow-up
  - Unchanged as compared to 2012
  - Utility of intense CT scan monitoring not demonstrated in a recent randomized trial (RCT).

STS- RPS

- To be refered in high volume centers
  - Biopsy first
  - Careful preoperative assessment
  - En-bloc multiorgan resections
  - RCT exploring preoperative RT (EORTC, EuroSARC)

STS- Uterine Sarcoma

- Different histological subtypes
  - LMS, HGUS, ESS (exclude CS)
- Total hysterectomy, no lymphadenectomy
- Role of BSO unclear
- Chemotherapy : similar (ifo?)
- LGESS : AI,Pg, aLHRH

STS- Desmoids

- Diagnostic strategy similar to STS
- Watchful waiting
- RT, NSAIDS, hormonal treatments, CT, sorafenib, in a step-wise fashion
- Homonal treatment to be stopped.

STS- Breast sarcomas

- To be refered in sarcoma center centers
  - Post RT vs primary sarcoma
  - Distinguish from skin sarcoma
  - Angiosarcoma: mastectomy
  - Lymphadenectomy not required

Bone Sarcoma

- Histological classification refined
- Introduction of chordoma
- Chondrosarcoma and medical treatment
- Highy structured document

What ESMO guidelines could and could not acknowledge

- Strong recommendation towards centralization of management
- Often expert opinion, more than EBM
- Molecular characterisation
- Large number of novel agents in rare subsets
- Many unsolved questions
  - Most on “molecular subtypes”
- RCT vs “outstanding clinical activity”
- The questions are on the table!