SOFT TISSUE SARCOMA

CLINICAL CASE DISCUSSION

Silvia Stacchiotti
Dipartimento di Oncologia Medica
Fondazione IRCCS Istituto Nazionale dei Tumori
Milan, Italy

MUNICH 2018 ESMO congress

FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI

DISCLOSURES

Personal financial interests (honoraria, consultancy or advisory role):
Adaptimmune, Bayer, Epizyme, Eli Lilly, Daiichi Sankyo, Immunedesign, Karyopharm, Maxivax, Pharmamar, Takeda

Institutional financial interests:
Amgen Dompè, Bayer, Epizyme, Eli Lilly, Daiichi Sankyo, Novartis, Pfizer, Pharmamar

Annals of Oncology 0 (Supplement 0): iv1–iv17, 2018
doi:10.1093/annonc/mdy096

CLINICAL PRACTICE GUIDELINES

Soft tissue and visceral sarcomas: ESMO–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up†

P. G. Casali[1], N. Abecassis[2], S. Bauer[3], R. Biagini[4], S. Bielack[5], S. Bonvalot[6], I. Boukovinas[7], J. V. M. G. Bovee[8], T. Brodowicz[9], J. M. Broto[10], A. Buonadonna[11], E. De Álava[10], A. P. Dei Tos[12], X. G. Del Muro[13], P. Dileo[14], M. Eriksson[15], A. Fedenko[16], V. Ferraresi[17], A. Ferrari[18], S. Ferrari[19], A. M. Frezza[1], S. Gasperoni[20], H. Gelderblom[21], T. Gil[22], G. Grignani[23], A. Gronchi[1], A. Hannu[24], B. Hassan[25], P. Hohenberger[26], R. Issels[27], H. Joensuu[28], R. L. Jones[29], I. Judson[30], P. Jutte[31], S. Kaal[32], B. Kasper[26], K. Kopeckova[33], D. A. Krákorová[34], A. Le Cesne[35], I. Lugowska[36], O. Merimsky[37], M. Montemurro[38], M. A. Pantaleo[39], R. Piana[40], P. Picci[19], S. Piperno-Neumann[6], A. L. Pousa[41], P. Reichardt[42], M. H. Robinson[43], P. Rutkowski[36], A. A. Safwat[44], P. Schöffski[45], S. Sleijfer[46], S. Stacchiotti[47], K. Sundby Hall[48], M. Unk[49], F. Van Coevorden[50], W. Van der Graaf[29], J. Whelan[51], E. Wardelmann[52], O. Zaikova[53] & J. Y. Blay[54], on behalf of the ESMO Guidelines Committee and EURACAN*

[1]Fondazione IRCCS Istituto Nazionale dei Tumori and University of Milan, Milan, Italy; [2]Instituto Portugues de Oncologia de Lisboa Francisco Gentil, EPE, Lisbon, Portugal; [3]University Hospital Essen, Essen, Germany; [4]Department of Oncological Orthopedics, Musculoskeletal Tissue Bank, IFO, Regina Elena National Cancer Institute, Rome, Italy; [5]Klinikum Stuttgart-Olgahospital, Stuttgart, Germany; [6]Institut Curie, Paris, France; [7]NORDIC, Athens, Greece; [8]Department of Pathology, Leiden University Medical Center, Leiden, The Netherlands; [9]Vienna General Hospital (AKH), Medizinische Universität Wien, Vienna, Austria; [10]Hospital Universitario Virgen del Rocio-CIBERONC, Seville, Spain; [11]Centro di Riferimento Oncologico di Aviano, Aviano, [12]Ospedale Regionale di Treviso "S.Maria di Ca Foncello", Treviso, Italy; [13]Integrated Unit ICO Hospitalet, HUB, Barcelona, Spain; [14]Sarcoma Unit, University College London Hospitals, London, UK; [15]Skane University Hospital-Lund, Lund, Sweden; [16]N. N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation; [17]Institute of Scientific Hospital Care (IRCCS), Regina Elena National Cancer Institute, Rome; [18]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan; [19]Istituto Ortopedico Rizzoli, Bologna; [20]Azienda Ospedaliera Universitaria Careggi Firenze, Florence, Italy; [21]Department of Medical Oncology, Leiden University Medical Centre, Leiden, The Netherlands; [22]Institut Jules Bordet, Brussels, Belgium; [23]Candiolo Cancer Institute, FPO IRCCS, Candiolo, Italy; [24]Turku University Hospital (Tuun Yliopistollinen Keskussairaala), Turku, Finland; [25]Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [26]Mannheim University Medical Center, Mannheim; [27]Department of Medicine III, University Hospital, Ludwig-Maximilians-University Munich, Munich, Germany; [28]Helsinki University Central Hospital (HUCH), Helsinki, Finland; [29]Royal Marsden Hospital, London; [30]The Institute of Cancer Research, London, UK; [31]University Medical Center Groningen, Groningen; [32]Radboud University Medical Center, Nijmegen, The Netherlands; [33]University Hospital Motol, Prague; [34]Masaryk Memorial Cancer Institute, Brno, Czech Republic; [35]Gustave Roussy Cancer Campus, Villejuif, France; [36]Maria Sklodowska Curie Institute, Oncology Centre, Warsaw, Poland; [37]Tel Aviv Soutasky Medical Center (Ichilov), Tel Aviv, Israel; [38]Medical Oncology, University Hospital of Lausanne, Lausanne, Switzerland; [39]Azienda Ospedaliera, Universitaria, Policlinico S Orsola-Malpighi Università di Bologna, Bologna; [40]Azienda Ospedaliero, Universitaria Cita della Salute e della Scienza di Torino, Turin, Italy; [41]Fundacio de Gestio Sanitaria de L'hospital de la SANTA CREU I Sant Pau, Barcelona, Spain; [42]Helios Klinikum Berlin Buch, Berlin, Germany; [43]YORC Department of Clinical Oncology, Weston Park Hospital NHS Trust, Sheffield, UK; [44]Aarhus University Hospital, Aarhus, Finland; [45]Leuven Cancer Institute, Leuven, Belgium; [46]Department of Medical Oncology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands; [47]Fondazione Istituto di Ricovero e Cura a Carattere Scientifico, Istituto Nazionale dei Tumori, Milan, Italy; [48]Department of Oncology, Oslo University Hospital, The Norwegian Radium Hospital, Oslo, Norway; [49]Institute of Oncology of Ljubljana, Ljubljana, Slovenia; [50]Netherlands Cancer Institute Antoni van Leeuwenhoek, Amsterdam, The Netherlands; [51]University College Hospital, London, UK; [52]Gerhard-Domagk-Institut für Pathologie, Universitätsklinikum Münster, Münster, Germany; [53]Oslo University Hospital, Norwegian Radium Hospital, Oslo, Norway; [54]Centre Leon Berhard and UCBL1, Lyon, France

*Correspondence to: ESMO Guidelines Committee, ESMO Head Office, Via Ginevra 4, 6900 Lugano, Switzerland. E-mail: clinicalguidelines@esmo.org
†Approved by the ESMO Guidelines Committee and EURACAN: December 2017.

Soft tissue sarcomas (STSs) gather over 80 histological entities, with even more molecular subsets, characterised by a low to very low incidence in all populations. The majority of sarcomas arise from the soft tissue (close to 75%), with ~15% gastrointestinal stromal tumours (GISTs) and 10% bone sarcomas. These ESMO–EURACAN (European Society for Medical Oncology–European Reference Network for rare adult solid cancers) Clinical Practice Guidelines cover STSs, while GISTs are covered by dedicated ESMO–EURACAN Clinical Practice Guidelines [1]. Kaposi's sarcoma is not considered in the present document. Extraskeletal Ewing and Ewing-like sarcoma is covered by ESMO Clinical Practice Guidelines on bone sarcomas [2]. In general, the same principles for these tumours in children apply to adults. This is also the case for embryonal and alveolar rhabdomyosarcomas,

Primary localised Soft Tissue Sarcoma (STS)

MUNICH 2018 ESMO congress

ESMO

Annals of Oncology 0 (Supplement 0): iv1–iv17, 2018
doi:10.1093/annonc/mdy096

CLINICAL PRACTICE GUIDELINES

Soft tissue and visceral sarcomas: ESMO–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up†

P. G. Casali[1], N. Abecassis[2], S. Bauer[3], R. Biagini[4], S. Bielack[5], S. Bonvalot[6], I. Boukovinas[7], J. V. M. G. Bovee[8], T. Brodowicz[9], J. M. Broto[10], A. Buonadonna[11], E. De Álava[10], A. P. Dei Tos[12], X. G. Del Muro[13], P. Dileo[14], M. Eriksson[15], A. Fedenko[16], V. Ferraresi[17], A. Ferrari[18], S. Ferrari[19], A. M. Frezza[1], S. Gasperoni[20], H. Gelderblom[21], T. Gil[22], G. Grignani[23], A. Gronchi[1], A. Hannu[24], B. Hassan[25], P. Hohenberger[26], R. Issels[27], H. Joensuu[28], R. L. Jones[29], I. Judson[30], P. Jutte[31], S. Kaal[32], B. Kasper[26], K. Kopeckova[33], D. A. Krákorová[34], A. Le Cesne[35], I. Lugowska[36], O. Merimsky[37], M. Montemurro[38], M. A. Pantaleo[39], R. Piana[40], P. Picci[19], S. Piperno-Neumann[6], A. L. Pousa[41], P. Reichardt[42], M. H. Robinson[43], P. Rutkowski[36], A. A. Safwat[44], P. Schöffski[45], S. Sleijfer[46], S. Stacchiotti[47], K. Sundby Hall[48], M. Unk[49], F. Van Coevorden[50], W. Van der Graaf[29], J. Whelan[51], E. Wardelmann[52], O. Zaikova[53] & J. Y. Blay[54], on behalf of the ESMO Guidelines Committee and EURACAN*

[1]Fondazione IRCCS Istituto Nazionale dei Tumori and University of Milan, Milan, Italy; [2]Instituto Portugues de Oncologia de Lisboa Francisco Gentil, EPE, Lisbon, Portugal; [3]University Hospital Essen, Essen, Germany; [4]Department of Oncological Orthopedics, Musculoskeletal Tissue Bank, IFO, Regina Elena National Cancer Institute, Rome, Italy; [5]Klinikum Stuttgart-Olgahospital, Stuttgart, Germany; [6]Institut Curie, Paris, France; [7]NORDIC, Athens, Greece; [8]Department of Pathology, Leiden University Medical Center, Leiden, The Netherlands; [9]Vienna General Hospital (AKH), Medizinische Universität Wien, Vienna, Austria; [10]Hospital Universitario Virgen del Rocio-CIBERONC, Seville, Spain; [11]Centro di Riferimento Oncologico di Aviano, Aviano; [12]Ospedale Regionale di Treviso "S.Maria di Ca'Foncello", Treviso, Italy; [13]Integrated Unit ICO Hospitalet, HUB, Barcelona, Spain; [14]Sarcoma Unit, University College London Hospitals, London, UK; [15]Skane University Hospital-Lund, Lund, Sweden; [16]N. N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation; [17]Institute of Scientific Hospital Care (IRCCS), Regina Elena National Cancer Institute, Rome; [18]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan; [19]Istituto Ortopedico Rizzoli, Bologna; [20]Azienda Ospedaliera Universitaria Careggi Firenze, Florence, Italy; [21]Department of Medical Oncology, Leiden University Medical Centre, Leiden, The Netherlands; [22]Institut Jules Bordet, Brussels, Belgium; [23]Candiolo Cancer Institute, FPO IRCCS, Candiolo, Italy; [24]Turku University Hospital (Tuun Yliopistollinen Keskussairaala), Turku, Finland; [25]Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [26]Mannheim University Medical Center, Mannheim; [27]Department of Medicine III, University Hospital, Ludwig-Maximilians-University Munich, Munich, Germany; [28]Helsinki University Central Hospital (HUCH), Helsinki, Finland; [29]Royal Marsden Hospital, London; [30]The Institute of Cancer Research, London, UK; [31]University Medical Center Groningen, Groningen; [32]Radboud University Medical Center, Nijmegen, The Netherlands; [33]University Hospital Motol, Prague; [34]Masaryk Memorial Cancer Institute, Brno, Czech Republic; [35]Gustave Roussy Cancer Campus, Villejuif, France; [36]Maria Sklodowska Curie Institute, Oncology Centre, Warsaw, Poland; [37]Tel Aviv Sourasky Medical Center (Ichilov), Tel Aviv, Israel; [38]Medical Oncology, University Hospital of Lausanne, Lausanne, Switzerland; [39]Azienda Ospedaliera, Universitaria, Policlinico S Orsola-Malpighi Università di Bologna, Bologna; [40]Azienda Ospedaliero, Universitaria Cita della Salute e della Scienza di Torino, Turin, Italy; [41]Fundacio de Gestio Sanitaria de L'hospital de la SANTA CREU I Sant Pau, Barcelona, Spain; [42]Helios Klinikum Berlin Buch, Berlin, Germany; [43]CRUK Department of Clinical Oncology, Weston Park Hospital NHS Trust, Sheffield, UK; [44]Aarhus University Hospital, Aarhus, Finland; [45]Leuven Cancer Institute, Leuven, Belgium; [46]Department of Medical Oncology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands; [47]Fondazione Istituto di Ricovero e Cura a Carattere Scientifico, Istituto Nazionale dei Tumori, Milan, Italy; [48]Department of Oncology, Oslo University Hospital, The Norwegian Radium Hospital, Oslo, Norway; [49]Institute of Oncology of Ljubljana, Ljubljana, Slovenia; [50]Netherlands Cancer Institute Antoni van Leeuwenhoek, Amsterdam, The Netherlands; [51]University College Hospital, London, UK; [52]Gerhard-Domagk-Institut für Pathologie, Universitätsklinikum Münster, Münster, Germany; [53]Oslo University Hospital, Norwegian Radium Hospital, Oslo, Norway; [54]Centre Leon Berriard and UCBL1, Lyon, France

*Correspondence to: ESMO Guidelines Committee, ESMO Head Office, Via Ginevra 4, 6900 Lugano, Switzerland. E-mail: clinicalguidelines@esmo.org
†Approved by the ESMO Guidelines Committee and EURACAN December 2017.

Soft tissue sarcomas (STSs) gather over 80 histological entities, with even more molecular subsets, characterised by a low to very low incidence in all populations. The majority of sarcomas arise from the soft tissue (close to 75%), with ~15% gastrointestinal stromal tumours (GISTs) and 10% bone sarcomas. These ESMO–EURACAN (European Society for Medical Oncology–European Reference Network for rare adult solid cancers) Clinical Practice Guidelines cover STSs, while GISTs are covered by dedicated ESMO–EURACAN Clinical Practice Guidelines [1]. Kaposi's sarcoma is not considered in the present document. Extraskeletal Ewing and Ewing-like sarcoma is covered by ESMO Clinical Practice Guidelines on bone sarcomas [2]. In general, the same principles for these tumours in children apply to adults. This is also the case for embryonal and alveolar rhabdomyosarcomas,

Staging and risk assessment

Available staging classifications have limited relevance and should be improved. The Union for International Cancer Control (UICC) stage classification system, 8th edition (Table 1) stresses the importance of the malignancy grade in sarcoma [7]. In general, in addition to grading, other prognostic factors are tumour size and tumour depth for limb sarcomas. Of course, site, tumour resectability and presence of metastases are also important. Nomograms are available, which can help personalise risk assessment and thus clinical decision making, especially on adjuvant/neoadjuvant treatments [8, 9].

A chest spiral CT scan is mandatory for staging purposes. Regional lymph node metastases are rare, with the exception of some histologies, e.g. epithelioid sarcoma and clear cell sarcoma, for which regional assessment through CT/MRI may be added to the usual staging procedures. Likewise, an abdominal CT scan may be added for limb myxoid liposarcoma. The brain CT scan may be added for alveolar soft part sarcoma, clear cell sarcoma and angiosarcoma.

Bone scan, whole-body MRI and PET scan are optional. Cost-effectiveness studies on their incorporation into the staging procedures are required. The surgical report, or patient chart, should provide details on:

- preoperative and intraoperative diagnosis;
- surgical conduct, including possible contaminations (i.e. it should mention whether the tumour was opened and was 'seen' during the excision, etc.); and
- surgical actual completeness vis-a-vis planned quality of margins.

Management of local/locoregional disease (see Figures 1 and 2)

Surgery is the standard treatment of all patients with an adult type, localised STS. It must be carried out by a surgeon specifically trained in the treatment of this disease. The standard surgical procedure is a wide excision with negative margins (no tumour at the margin, R0). This implies removing the tumour with a rim of normal tissue around it [II, A] [10]. The minimal margin on fixed tissue to be considered adequate may depend on several factors, including histological subtype, preoperative therapies and the presence of resistant anatomical barriers, such as muscular fasciae, periosteum and epineurium. As an individualised option, marginal excision can be acceptable in carefully selected cases, in particular for extracompartmental atypical lipomatous tumours [IV, B].

DIAGNOSIS

- Patients with an unexplained deep mass/superficial lesion of soft tissues of > 5 cm
- Sarcoma reference center/network

European Reference Networks

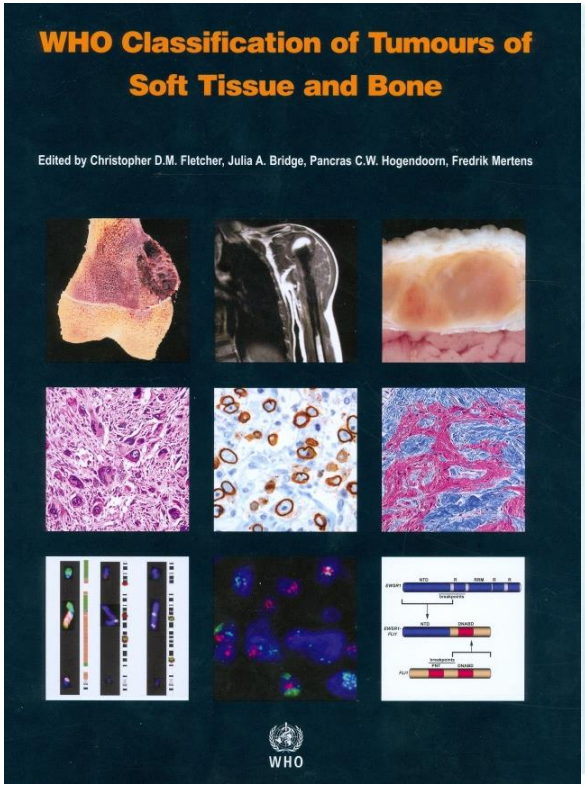
MUNICH 2018 ESMO congress

DIAGNOSIS

- Patients with an unexplained deep mass/superficial lesion of soft tissues of > 5 cm
- Sarcoma reference center/network

- MRI (CT in calcified lesion and for staging; bone scan)
- Biopsy (core needle biopsies, possibly ≥ 14–16G needles; excisional biopsy may be the most practical option for < 3 cm superficial lesions; Open biopsy option in selected cases, as decided within reference centres)

- Multidisciplinary approach



ADIPOCYTIC TUMOURS

Benign	
Lipoma	8850/0
Lipomatosis	8850/0
Lipomatosis of nerve	8850/0
Lipoblastoma/lipoblastomatosis	8881/0
Angiolipoma	8861/0
Myolipoma	8890/0
Chondroid lipoma	8862/0
Extra-renal angiomyolipoma	8860/0
Extra-adrenal myelolipoma	8670/0
Spindle cell/pleomorphic lipoma	8857/0
Hibernoma	8880/0
Intermediate (locally aggressive)	
Atypical lipomatous tumour/ well differentiated liposarcoma	8850/1 8850/3
Malignant	
Dedifferentiated liposarcoma	8858/3
Myxoid liposarcoma	8852/3
Pleomorphic liposarcoma	8854/3
Liposarcoma, not otherwise specified	8850/3

FIBROBLASTIC / MYOFIBROBLASTIC TUMOURS

Benign	
Nodular fasciitis	8828/0*
Proliferative fasciitis	8828/0*
Proliferative myositis	8828/0*
Myositis ossificans	
Fibro-osseous pseudotumour of digits	
Ischaemic fasciitis	
Elastofibroma	8820/0
Fibrous hamartoma of infancy	
Fibromatosis colli	
Juvenile hyaline fibromatosis	
Inclusion body fibromatosis	
Fibroma of tendon sheath	8813/0
Desmoplastic fibroblastoma	8810/0
Mammary-type myofibroblastoma	8825/0
Calcifying aponeurotic fibroma	8816/0*
Angiomyofibroblastoma	8826/0
Cellular angiofibroma	9160/0
Nuchal-type fibroma	8810/0
Gardner fibroma	8810/0
Calcifying fibrous tumour	8817/0*
Intermediate (locally aggressive)	
Palmar/plantar fibromatosis	8813/1*
Desmoid-type fibromatosis	8821/1
Lipofibromatosis	8851/1*
Giant cell fibroblastoma	8834/1
Intermediate (rarely metastasizing)	
Dermatofibrosarcoma protuberans	8832/1*
Fibrosarcomatous dermatofibrosarcoma protuberans	8832/3*
Pigmented dermatofibrosarcoma protuberans	8833/1*
Solitary fibrous tumour	8815/1*
Solitary fibrous tumour, malignant	8815/3
Inflammatory myofibroblastic tumour	8825/1
Low-grade myofibroblastic sarcoma	8825/3*
Myxoinflammatory fibroblastic sarcoma/ Atypical myxoinflammatory fibroblastic tumour	8811/1*
Infantile fibrosarcoma	8814/3
Malignant	
Adult fibrosarcoma	8810/3
Myxofibrosarcoma	8811/3
Low-grade fibromyxoid sarcoma	8840/3*
Sclerosing epithelioid fibrosarcoma	8840/3*

SO-CALLED FIBROHISTIOCYTIC TUMOURS

Benign	
Tenosynovial giant cell tumour	
localized type	9252/0
diffuse type	9252/1*
malignant	9252/3
Deep benign fibrous histiocytoma	8831/0
Intermediate (rarely metastasizing)	
Plexiform fibrohistiocytic tumour	8835/1
Giant cell tumour of soft tissues	9251/1

SMOOTH MUSCLE TUMOURS

Benign	
Deep leiomyoma	8890/0
Malignant	
Leiomyosarcoma (excluding skin)	8890/3

PERICYTIC (PERIVASCULAR) TUMOURS

Glomus tumour (and variants)	8711/0
Glomangiomatosis	8711/1*
Malignant glomus tumour	8711/3
Myopericytoma	8824/0
Myofibroma	8824/0
Myofibromatosis	8824/1
Angioleiomyoma	8894/0

SKELETAL MUSCLE TUMOURS

Benign	
Rhabdomyoma	8900/0
Adult type	8904/0
Fetal type	8903/0
Genital type	8905/0
Malignant	
Embryonal rhabdomyosarcoma (including botryoid, anaplastic)	8910/3
Alveolar rhabdomyosarcoma (including solid, anaplastic)	8920/3
Pleomorphic rhabdomyosarcoma	8901/3
Spindle cell/sclerosing rhabdomyosarcoma	8912/3

VASCULAR TUMOURS OF SOFT TISSUE

Benign	
Haemangioma	9120/0
Synovial	
Venous	9122/0
Arteriovenous haemangioma/malformation	9123/0
Intramuscular	9132/0
Epithelioid haemangioma	9125/0
Angiomatosis	
Lymphangioma	9170/0
Intermediate (locally aggressive)	
Kaposiform haemangioendothelioma	9130/1
Intermediate (rarely metastasizing)	
Retiform haemangioendothelioma	9136/1*
Papillary intralymphatic angioendothelioma	9135/1
Composite haemangioendothelioma	9136/1
Pseudomyogenic (epithelioid sarcoma-like) haemangioendothelioma	9136/1
Kaposi sarcoma	9140/3
Malignant	
Epithelioid haemangioendothelioma	9133/3
Angiosarcoma of soft tissue	9120/3

CHONDRO-OSSEOUS TUMOURS

Soft tissue chondroma	9220/0
Extraskeletal mesenchymal chondrosarcoma	9040/3
Extraskeletal osteosarcoma	9180/3

GASTROINTESTINAL STROMAL TUMOURS

Benign gastrointestinal stromal tumour	8936/0
Gastrointestinal stromal tumour, uncertain malignant potential	8936/1
Gastrointestinal stromal tumour, malignant	8936/3

NERVE SHEATH TUMOURS

Benign	
Schwannoma (including variants)	9560/0
Melanotic schwannoma	9560/1*
Neurofibroma (incl. variants)	9540/0
Plexiform neurofibroma	9550/0
Perineurioma	9571/0
Malignant perineurioma	9571/3
Granular cell tumour	9580/0
Dermal nerve sheath myxoma	9562/0
Solitary circumscribed neuroma	9570/0
Ectopic meningioma	9530/0
Nasal glial heterotopia	
Benign Triton tumour	
Hybrid nerve sheath tumours	9563/0*
Malignant	
Malignant peripheral nerve sheath tumour	9540/3
Epithelioid malignant peripheral nerve sheath tumour	9542/3*
Malignant Triton tumour	9561/3
Malignant granular cell tumour	9580/3
Ectomesenchymoma	8921/3

TUMOURS OF UNCERTAIN DIFFERENTIATION

Benign	
Acral fibromyxoma	8811/0
Intramuscular myxoma (including cellular variant)	8840/0
Juxta-articular myxoma	8840/0
Deep ("aggressive") angiomyxoma	8841/0*
Pleomorphic hyalinizing angiectatic tumour	8802/1*
Ectopic hamartomatous thymoma	8587/0
Intermediate (locally aggressive)	
Haemosiderotic fibrolipomatous tumour	8811/1*
Intermediate (rarely metastasizing)	
Atypical fibroxanthoma	8830/1
Angiomatoid fibrous histiocytoma	8836/1
Ossifying fibromyxoid tumour	8842/0
Ossifying fibromyxoid tumour, malignant	8842/3*
Mixed tumour NOS	8940/0
Mixed tumour NOS, malignant	8940/3
Myoepithelioma	8982/0
Myoepithelial carcinoma	8982/3
Phosphaturic mesenchymal tumour, benign	8990/0
Phosphaturic mesenchymal tumour, malignant	8990/3
Malignant	
Synovial sarcoma NOS	9040/3
Synovial sarcoma, spindle cell	9041/3
Synovial sarcoma, biphasic	9043/3
Epithelioid sarcoma	8804/3
Alveolar soft-part sarcoma	9581/3
Clear cell sarcoma of soft tissue	9044/3
Extraskeletal myxoid chondrosarcoma	9231/3
Extraskeletal Ewing sarcoma	9364/3
Desmoplastic small round cell tumour	8806/3
Extra-renal rhabdoid tumour	8963/3
Neoplasms with perivascular epithelioid cell differentiation (PEComa)	
PEComa NOS, benign	8714/0*
PEComa NOS, malignant	8714/3*
Intimal sarcoma	9137/3*

UNDIFFERENTIATED/UNCLASSIFIED SARCOMAS

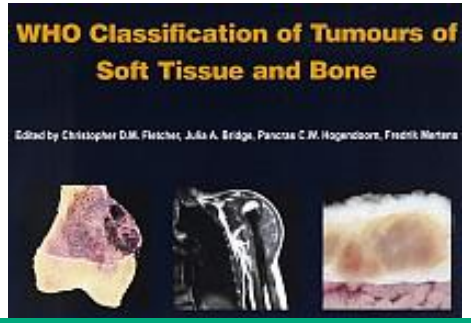
Undifferentiated spindle cell sarcoma	8801/3
Undifferentiated pleomorphic sarcoma	8802/3
Undifferentiated round cell sarcoma	8803/3
Undifferentiated epithelioid sarcoma	8804/3
Undifferentiated sarcoma NOS	8805/3

* The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) (9thEA). Behaviour is coded /0 for benign tumours, /1 for unspecified, borderline or uncertain behaviour, /2 for carcinoma in situ and grade III intraepithelial neoplasia, and /3 for malignant tumours. † The classification is modified from the previous WHO histological classification of tumours [870A] taking into account changes in understanding of these lesions. ‡ These new codes were approved by the IARC/WHO Committee for ICD-O in 2012.

MUNICH 2018 ESMO congress

Fletcher C et al, WHO 2013

Path report



Histology

Grading

Expert pathologist

Path response

MUNICH 2018 ESMO congress

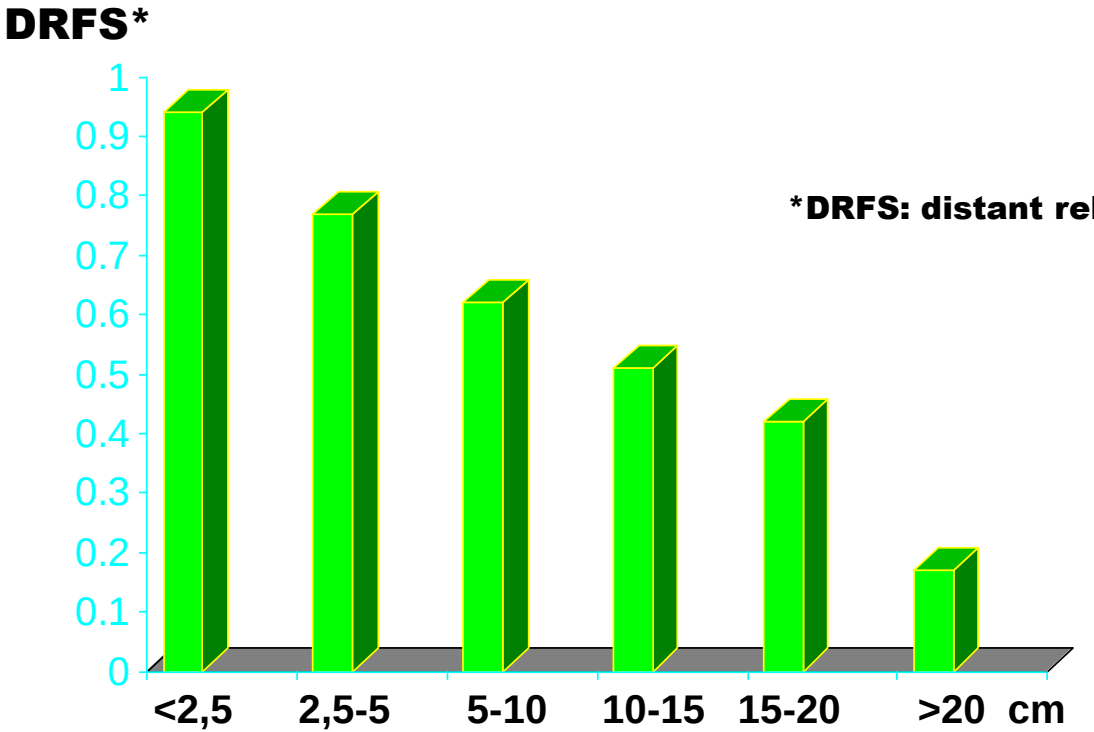
Fletcher C et al, WHO 2013

RISK CLASSIFICATION
(primary, localised, resectable STS)

1. Tumour grade
2. Tumour size (5 cm)
3. Tumour site (superficial/deep)

Status of surgical margins
(tumour rupture)

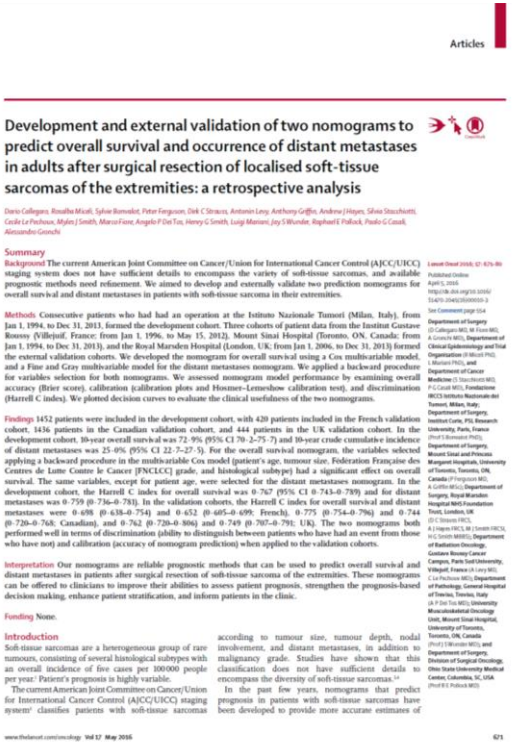
High grade STS, diameter



*DRFS: distant relapse free survival

Suit HD et al. J Clin Oncol 1988

SARCULATOR
(extremities/retroperitoneum)



Articles

Development and external validation of two nomograms to predict overall survival and occurrence of distant metastases in adults after surgical resection of localised soft-tissue sarcomas of the extremities: a retrospective analysis

Dario Callegaro, Rosalba Miceli, Sylvie Bonvalot, Peter Ferguson, Dirk C Strauss, Antonin Levy, Anthony Griffin, Andrew J Hayes, Silvia Stacchiotti, Cecile Le Pechoux, Myles J Smith, Marco Fiore, Angelo P Dei Tos, Henry G Smith, Luigi Mariani, Jay S Wunder, Raphael E Pollock, Paolo G Casali, Alessandro Gronchi

Summary

Background The current American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) staging system does not have sufficient details to encompass the variety of soft-tissue sarcomas, and available prognostic methods need refinement. We aimed to develop and externally validate two prediction nomograms for overall survival and distant metastases in patients with soft-tissue sarcoma in their extremities.

Methods Consecutive patients who had had an operation at the Istituto Nazionale Tumori (Milan, Italy), from Jan 1, 1994, to Dec 31, 2013, formed the development cohort. Three cohorts of patient data from the Institut Gustave Roussy (Villejuif, France; from Jan 1, 1996, to Mar 15, 2012), Mount Sinai Hospital (Toronto, ON, Canada; from Jan 1, 1994, to Dec 31, 2013), and the Royal Marsden Hospital (London, UK; from Jan 1, 2006, to Dec 31, 2013) formed the external validation cohorts. We developed the nomogram for overall survival using a Cox multivariable model, and a Fine and Gray multivariable model for the distant metastases nomogram. We applied a backward procedure for variables selection for both nomograms. We assessed nomogram model performance by examining overall accuracy (Brier score), calibration (calibration plots and Hosmer–Lemeshow calibration test), and discrimination (Harrell C index). We plotted decision curves to evaluate the clinical usefulness of the two nomograms.

Findings 1452 patients were included in the development cohort, with 420 patients included in the French validation cohort, 1436 patients in the Canadian validation cohort, and 444 patients in the UK validation cohort. In the development cohort, 10-year overall survival was 72·9% (95% CI 70·2–75·7) and 10-year crude cumulative incidence of distant metastases was 25·0% (95% CI 22·7–27·5). For the overall survival nomogram, the variables selected applying a backward procedure in the multivariable Cox model (patient's age, tumour size, Fédération Française des Centres de Lutte Contre le Cancer [FNCLCC] grade, and histological subtype) had a significant effect on overall survival. The same variables, except for patient age, were selected for the distant metastases nomogram. In the development cohort, the Harrell C index for overall survival was 0·767 (95% CI 0·743–0·789) and for distant metastases was 0·759 (0·736–0·781). In the validation cohorts, the Harrell C index for overall survival and distant metastases were 0·698 (0·638–0·754) and 0·652 (0·605–0·699; French), 0·775 (0·754–0·796) and 0·744 (0·720–0·768; Canadian), and 0·762 (0·720–0·806) and 0·749 (0·707–0·791; UK). The two nomograms both performed well in terms of discrimination (ability to distinguish between patients who have had an event from those who have not) and calibration (accuracy of nomogram prediction) when applied to the validation cohorts.

Interpretation Our nomograms are reliable prognostic methods that can be used to predict overall survival and distant metastases in patients after surgical resection of soft-tissue sarcoma of the extremities. These nomograms can be offered to clinicians to improve their abilities to assess patient prognosis, strengthen the prognosis-based decision making, enhance patient stratification, and inform patients in the clinic.

Funding None.

Introduction

Soft-tissue sarcomas are a heterogeneous group of rare tumours, consisting of several histological subtypes with an overall incidence of five cases per 100 000 people per year.[1] Patient's prognosis is highly variable.

The current American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) staging system[2] classifies patients with soft-tissue sarcomas according to tumour size, tumour depth, nodal involvement, and distant metastases, in addition to malignancy grade. Studies have shown that this classification does not have sufficient details to encompass the diversity of soft-tissue sarcomas.[3,4]

In the past few years, nomograms that predict prognosis in patients with soft-tissue sarcomas have been developed to provide more accurate estimates of

Lancet Oncol 2016; 17: 671–80

Published Online April 5, 2016 http://dx.doi.org/10.1016/S1470-2045(15)00515-3

See Comment page 614

Department of Surgery (D Callegaro MD, M Fiore MD, A Gronchi MD), Department of Clinical Epidemiology and Trial Organisation (R Miceli PhD, L Mariani PhD), and Department of Cancer Medicine (S Stacchiotti MD, P G Casali MD), Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Department of Surgery, Institute Curie, PSL Research University, Paris, France (Prof S Bonvalot PhD); Department of Surgery, Mount Sinai and Princess Margaret Hospitals, University of Toronto, Toronto, ON, Canada (P Ferguson MD, A Griffin MSc); Department of Surgery, Royal Marsden Hospital NHS Foundation Trust, London, UK (D C Strauss FRCS, A J Hayes FRCS, M J Smith FRCS, H G Smith MRCP); Department of Radiation Oncology, Gustave Roussy Cancer Campus, Paris Sud University, Villejuif, France (A Levy MD, C Le Pechoux MD); Department of Pathology, General Hospital of Treviso, Treviso, Italy (A P Dei Tos MD); University Musculoskeletal Oncology Unit, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada (Prof J S Wunder MD), and Department of Surgery, Division of Surgical Oncology, Ohio State University Medical Center, Columbia, SC, USA (Prof R E Pollock MD)

Callegaro D et al, Lancet 2015

TREATMENT, LOCALIZED DISEASE

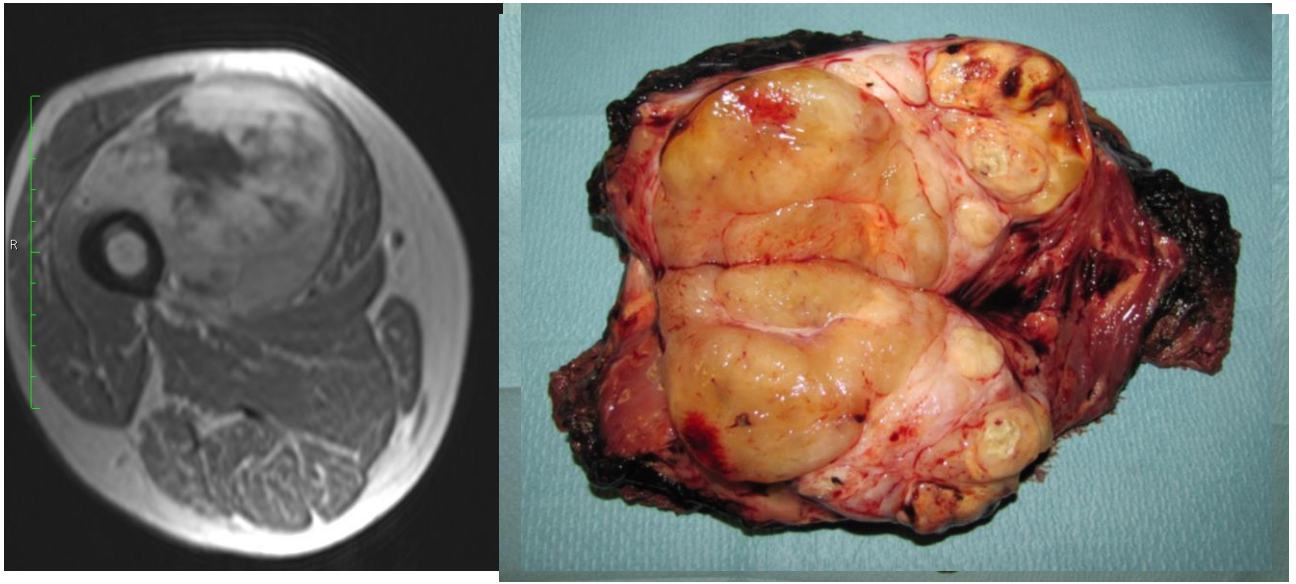
1. **Surgery:** wide excision with negative margins (R0)

(i.e. removing the tumour with a rim of normal tissue around; cut-off of the minimal margin depends on several factors, including histological subtype, preoperative therapies, presence of resistant anatomical barriers, such as muscular fasciae, periostium and epineurium)

2. **Radiotherapy** (+ wide excision; adjuvant/neo-adjuvant):
   high-grade (G2–3), deep, >5 cm lesions
   high grade, deep, <5 cm lesions

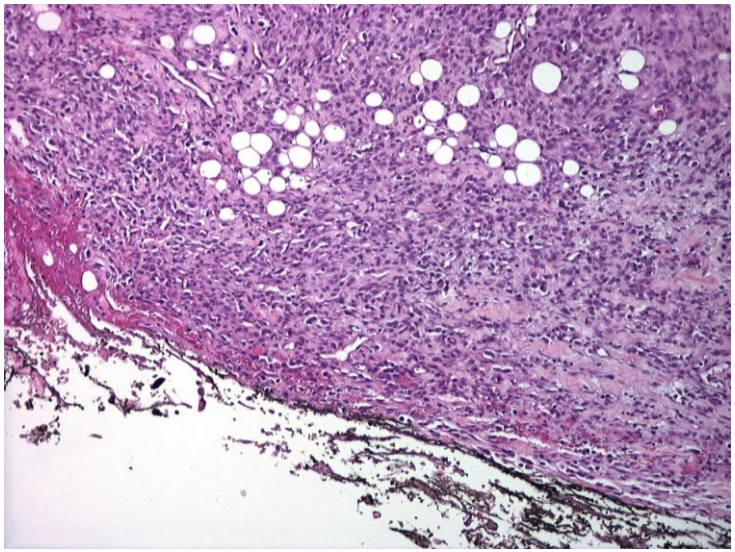
3. ***Chemotherapy*** *(adjuvant/neoadjuvant)*

Basic principles of surgery



Every attempt should be made to avoid positive microscopic surgical margins

Basic principles of surgery



Tumour edge at the inked surface
(within 1 mm)


(neo)adjuvant
→ resectable tumour
cytoreductive
→ unresectable tumour

(Neo)Adjuvant chemotherapy

Annals of Oncology 0 (Supplement 0): iv1–iv7, 2018
doi:10.1093/annonc/mdy096

CLINICAL PRACTICE GUIDELINES

Soft tissue and visceral sarcomas: ESMO–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up†

P. G. Casali[1], N. Abecassis[2], S. Bauer[3], R. Biagini[4], S. Bielack[5], S. Bonvalot[6], I. Boukovinas[7], J. V. M. G. Bovee[8], T. Brodowicz[9], J. M. Broto[10], A. Buonadonna[11], E. De Álava[10], A. P. Dei Tos[12], X. G. Del Muro[13], P. Dileo[14], M. Eriksson[15], A. Fedenko[16], V. Ferraresi[17], A. Ferrari[18], S. Ferrari[19], A. M. Frezza[1], S. Gasperoni[20], H. Gelderblom[21], T. Gil[22], G. Grignani[23], A. Gronchi[1], A. Hannu[24], B. Hassan[25], P. Hohenberger[26], R. Issels[27], H. Joensuu[28], R. L. Jones[29], I. Judson[30], P. Jutte[31], S. Kaal[32], B. Kasper[26], K. Kopeckova[33], D. A. Krákorová[34], A. Le Cesne[35], I. Lugowska[36], O. Merimsky[37], M. Montemurro[38], M. A. Pantaleo[39], R. Piana[40], P. Picci[19], S. Piperno-Neumann[6], A. L. Pousa[41], P. Reichardt[42], M. H. Robinson[43], P. Rutkovski[36], A. A. Safwat[44], P. Schöffski[45], S. Sleijfer[46], S. Stacchiotti[47], K. Sundby Hall[48], M. Unk[49], F. Van Coevorden[50], W. Van der Graaf[29], J. Whelan[51], E. Wardelmann[52], O. Zaikova[53] & J. Y. Blay[54], on behalf of the ESMO Guidelines Committee and EURACAN*

[1]Fondazione IRCCS Istituto Nazionale dei Tumori and University of Milan, Milan, Italy; [2]Instituto Portugues de Oncologia de Lisboa Francisco Gentil, EPE, Lisbon, Portugal; [3]University Hospital Essen, Essen, Germany; [4]Department of Oncological Orthopedics, Musculoskeletal Tissue Bank, PO, Regina Elena National Cancer Institute, Rome, Italy; [5]Klinikum Stuttgart-Olgahospital, Stuttgart, Germany; [6]Institut Curie, Paris, France; [7]NORDIC, Athens, Greece; [8]Department of Pathology, Leiden University Medical Center, Leiden, The Netherlands; [9]Vienna General Hospital (AKH), Medizinische Universität Wien, Vienna, Austria; [10]Hospital Universitario Virgen del Rocío-CIBERONC, Seville, Spain; [11]Centro di Riferimento Oncologico di Aviano, Aviano; [12]Ospedale Regionale di Treviso "S.Maria di Ca Foncello", Treviso, Italy; [13]Integrated Unit ICO Hospitalet, HUB, Barcelona, Spain; [14]Sarcoma Unit, University College London Hospitals, London, UK; [15]Skane University Hospital-Lund, Lund, Sweden; [16]N. N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation; [17]Institute of Scientific Hospital Care (IRCCS), Regina Elena National Cancer Institute, Rome; [18]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan; [19]Istituto Ortopedico Rizzoli, Bologna; [20]Azienda Ospedaliera Universitaria Careggi Firenze, Florence, Italy; [21]Department of Medical Oncology, Leiden University Medical Centre, Leiden, The Netherlands; [22]Institut Jules Bordet, Brussels, Belgium; [23]Candiolo Cancer Institute, FPO IRCCS, Candiolo, Italy; [24]Turku University Hospital (Turun Yliopistollinen Keskussairaala), Turku, Finland; [25]Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [26]Mannheim University Medical Center, Mannheim; [27]Department of Medicine III, University Hospital, Ludwig-Maximilian-University Munich, Munich, Germany; [28]Helsinki University Central Hospital (HUCH), Helsinki, Finland; [29]Royal Marsden Hospital, London; [30]The Institute of Cancer Research, London, UK; [31]University Medical Center Groningen, Groningen; [32]Radboud University Medical Center, Nijmegen, The Netherlands; [33]University Hospital Motol, Prague; [34]Masaryk Memorial Cancer Institute, Brno, Czech Republic; [35]Gustave Roussy Cancer Campus, Villejuif, France; [36]Maria Sklodowska Curie Institute, Oncology Centre, Warsaw, Poland; [37]Tel Aviv Sourasky Medical Center (Ichilov), Tel Aviv, Israel; [38]Medical Oncology, University Hospital of Lausanne, Lausanne, Switzerland; [39]Azienda Ospedaliera, Universitaria, Policlinico S.Orsola-Malpighi Università di Bologna, Bologna; [40]Azienda Ospedaliero, Universitaria Citta della Salute e della Scienza di Torino, Turin, Italy; [41]Fundacio de Gestio Sanitaria de l'hospital de la SANTA CREU i Sant Pau, Barcelona, Spain; [42]Helios Klinikum Berlin Buch, Berlin, Germany; [43]CRC Department of Clinical Oncology, Weston Park Hospital NHS Trust, Sheffield, UK; [44]Aarhus University Hospital, Aarhus, Finland; [45]Leuven Cancer Institute, Leuven, Belgium; [46]Department of Medical Oncology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands; [47]Fondazione Istituto di Ricovero e Cura a Carattere Scientifico, Istituto Nazionale dei Tumori, Milan, Italy; [48]Department of Oncology, Oslo University Hospital, The Norwegian Radium Hospital, Oslo, Norway; [49]Institute of Oncology of Ljubljana, Ljubljana, Slovenia; [50]Netherlands Cancer Institute-Antoni van Leeuwenhoek, Amsterdam, The Netherlands; [51]University College Hospital, London, UK; [52]Gerhard-Domagk-Institut für Pathologie, Universitätsklinikum Münster, Münster, Germany; [53]Oslo University Hospital, Norwegian Radium Hospital, Oslo, Norway; [54]Centre Leon Berrard and UCBL1, Lyon, France

*Correspondence to: ESMO Guidelines Committee, ESMO Head Office, Via Ginevra 4, 6900 Lugano, Switzerland. E-mail: clinicalguidelines@esmo.org
†Approved by the ESMO Guidelines Committee and EURACAN: December 2017.

Soft tissue sarcomas (STSs) gather over 80 histological entities, with even more molecular subsets, characterised by a low to very low incidence in all populations. The majority of sarcomas arise from the soft tissue (close to 75%), with ~15% gastrointestinal stromal tumours (GISTs) and 10% bone sarcomas. These ESMO–EURACAN (European Society for Medical Oncology–European Reference Network for rare adult solid cancers) Clinical Practice Guidelines cover STSs, while GISTs are covered by dedicated ESMO–EURACAN Clinical Practice Guidelines [1]. Kaposi's sarcoma is not considered in the present document. Extraskeletal Ewing and Ewing-like sarcoma is covered by ESMO Clinical Practice Guidelines on bone sarcomas [2]. In general, the same principles for these tumours in children apply to adults. This is also the case for embryonal and alveolar rhabdomyosarcomas,

There is no consensus on the current role of adjuvant ChT. Study results are conflicting, in the presence of negative results from the largest studies, though data are available from smaller studies suggesting that adjuvant ChT might improve, or at least delay, distant and local recurrence in high-risk patients [18, 19]. A meta-analysis on published data found a statistically significant limited benefit in terms of both relapse-free survival (RFS) and overall survival (OS) [20]. Gain in OS was not significant on the only meta-analysis using source data [21]. Given the conflicting results of trials included in the meta-analyses, adjuvant ChT is not standard treatment in adult-type STS. It can be proposed as an option to the high-risk individual patient (high-grade, deep, >5 cm tumour) for a shared decision making with the patient [II, C]. ChT was used as neoadjuvant treatment, aiming at a local benefit facilitating surgery, in addition to the systemic one. A randomised trial showed no differences between three (preoperative) and five (pre- and postoperative) courses of full-dose ChT in high-risk STS patients [22]. A subsequent trial compared preoperative ChT with full-dose epirubicin plus ifosfamide versus a histology-driven ChT. This trial was closed slightly in advance because three interim analyses showed a statistically significant benefit in terms of both RFS and OS in favour of neoadjuvant therapy with epirubicin and ifosfamide. Since there is no obvious evidence lesions >5 cm, deep, of a high-grade histology including undifferentiated pleomorphic sarcoma, liposarcoma, LMS, malignant peripheral nerve sheet tumour and synovial sarcoma). However, this evidence currently corresponds to an interim planned analysis within a trial statistically conceived to test the superiority of a histology-driven ChT [23]. The trial has been amended to test the superiority of epirubicin plus ifosfamide over the histology-driven therapy at the time of the final analysis. While awaiting these results, neoadjuvant ChT with anthracyclines plus ifosfamide for at least three cycles can be viewed as an option in the high-risk individual patient, for shared decision making [II, C[a]] (see note [a] in Table 2).

(Neo)Adjuvant chemotherapy

A Systematic Meta-Analysis of Randomized Controlled Trials of Adjuvant Chemotherapy for Localized Resectable Soft-Tissue Sarcoma

Nabeel Pervaiz[1]
Nigel Colterjohn, MD[2]
Forough Farrokhyar, MPhil, PhD[2]
Richard Tozer, MD, PhD[3]
Alvaro Figueredo, MD[3]
Michelle Ghert, MD[2]

[1] University of Waterloo, Waterloo, Ontario, Canada.

[2] Department of Surgery, McMaster University and Hamilton Health Sciences, Juravinski Cancer Center, Hamilton, Ontario, Canada.

[3] Department of Medicine, McMaster University and Hamilton Health Sciences, Juravinski Cancer Center, Hamilton, Ontario, Canada.

Absolute Risk Reductions and 95% Confidence Intervals for Local Recurrence, Distant Recurrence, Overall Recurrence, and Survival

	Local recurrence		Distant recurrence		Overall recurrence		Survival	
Treatment	ARR	95% CI	ARR	95% CI	ARR	95% CI	ARR	95% CI
Doxorubicin	3%	1%-7%	9%	4%-14%	9%	4%-14%	5%	6%-21%
Doxorubicin with ifosfamide	5%	1%-12%	10%	1%-19%	12%	3%-21%	11%	3%-19%
Combined	4%	0%-7%	9%	5%-14%	10%	5%-15%	6%	2%-11%

ARR indicates absolute risk reduction, 95% CI, 95% confidence interval.

6%, 10%, 4% absolute benefit
local disease-free survival, distant metastasis-free, overall survival
not statistically significant

Pervaiz N et al, Cancer 2008

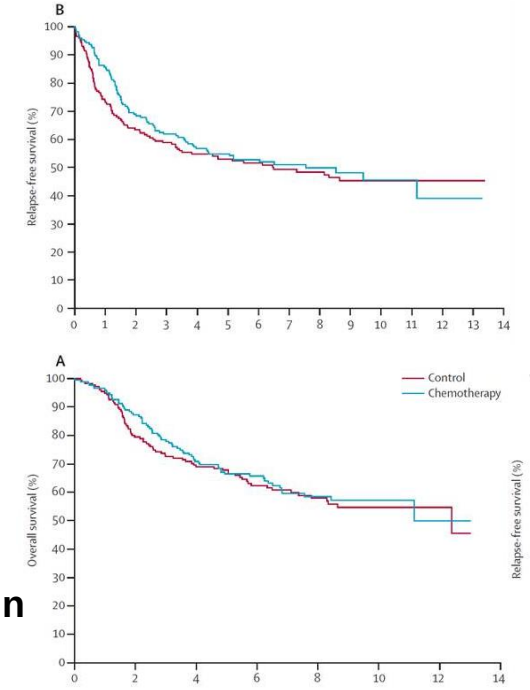
(Neo)Adjuvant chemotherapy

Adjuvant chemotherapy with doxorubicin, ifosfamide, and lenograstim for resected soft-tissue sarcoma (EORTC 62931): a multicentre randomised controlled trial

Penella J Woll, Peter Reichardt, Axel Le Cesne, Sylvie Bonvalot, Alberto Azzarelli†, Harald J Hoekstra, Michael Leahy, Frits Van Coevorden, Jaap Verweij, Pancras C W Hogendoorn, Monia Ouali, Sandrine Marreaud, Vivien H C Bramwell, Peter Hohenberger, for the EORTC Soft Tissue and Bone Sarcoma Group and the NCIC Clinical Trials Group Sarcoma Disease Site Committee

- 1995-2003
- 351 patients
- Median Follow-Up = 8 years

- G2 and G3 (G3 = 46% after central path review)
- Any size (median 8 cm)
- Any site (extremity and girdle: 278)
- Any histology: 90 patients affected by “other” histotypes + DD liposarcoma in the liposarcoma group
- Adriamycin (ADM) 75 mg/m^2 + Ifosfamide (IFX) 5 g/sqm
- **A trend for better Relapse Free survival/ Overall Survival in larger tumours and G3**

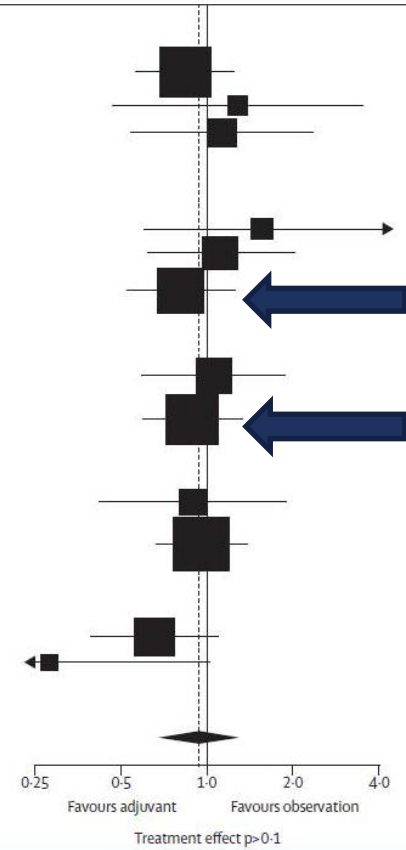


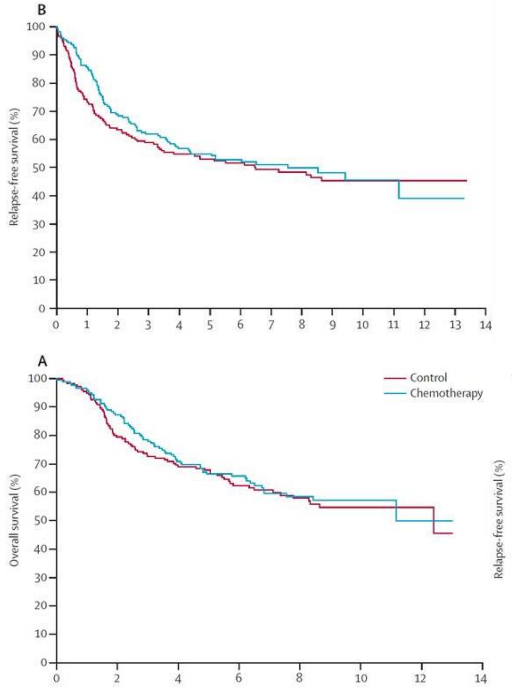
Woll PJ et al. Lancet Oncol 2012

STS, soft tissue sarcoma; G, grade

(Neo)Adjuvant chemotherapy

	Events/patients		Statistics		HR (95% CI)
	Adjuvant	Control	O–E	Variance	
Tumour site					
Limb	45/118	52/118	−4·1	24	0·84 (0·56–1·26)
Trunk	8/24	7/27	0·9	3·7	1·29 (0·47–3·55)
Central	15/33	14/31	0·9	7·1	1·13 (0·54–2·36)
Test for heterogeneity df=2; p>0·1					
Tumour size					
<5 cm	10/41	8/44	1·9	4·2	1·56 (0·60–4·05)
5–9 cm	26/70	18/54	1·2	10·8	1·12 (0·61–2·03)
≥10 cm	32/64	47/78	−4·1	19·6	0·81 (0·52–1·26)
Test for heterogeneity df=2; p>0·1					
Local grade					
II	24/71	22/69	0·6	11·5	1·06 (0·59–1·89)
III	44/104	51/107	−2·8	23·6	0·89 (0·59–1·33)
Test for heterogeneity df=1; p>0·1					
Post-operation radiotherapy					
No	12/33	15/37	−0·8	6·7	0·89 (0·42–1·90)
Yes	56/142	58/139	−1·2	28·2	0·96 (0·66–1·38)
Test for heterogeneity df=1; p>0·1					
Isolated limb perfusion					
No	24/91	34/92	−6·2	14·5	0·65 (0·39–1·09)
Yes	3/6	7/8	−2·9	2·3	0·28 (0·08–1·02)
Test for heterogeneity df=1; p>0·1					
Total	**68/175 (40%)**	**73/176 (41%)**	**−2·1**	**35·1**	**0·94 (0·68–1·31)**





Woll PJ et al. Lancet Oncol 2012

STS, soft tissue sarcoma

(Neo)Adiuvant chemotherapy

Histotype-tailored neoadjuvant chemotherapy versus standard chemotherapy in patients with high-risk soft-tissue sarcomas (ISG-STS 1001): an international, open-label, randomised, controlled, phase 3, multicentre trial

Alessandro Gronchi, Stefano Ferrari, Vittorio Quagliuolo, Javier Martin Broto, Antonio Lopez Pousa, Giovanni Grignani, Umberto Basso, Jean-Yves Blay, Oscar Tendero, Robert Diaz Beveridge, Virginia Ferraresi, Iwona Lugowska, Domenico Franco Merlo, Valeria Fontana, Emanuela Marchesi, Davide Maria Donati, Elena Palassini, Emanuela Palmerini, Rita De Sanctis, Carlo Morosi, Silvia Stacchiotti, Silvia Bagué, Jean Michelle Coindre, Angelo Paolo Dei Tos, Piero Picci, Paolo Bruzzi, Paolo Giovanni Casali

High-risk population
(high-grade, deep, > 5 cm)

Epirubicin (epiADM) 120 mg/m²
+
Ifosamide (IFX) 9 g/m² @3week

R

histology-driven chemo x 3

- **leiomyosa:** **gemcitabine + dacarbazine**
- **myxoid lipo:** **trabectedin**
- **synovial sa:** **HD-IFX**
- **malignat schwannoma:** **IFX + VP16**
- **pleomorphic sa (UPS):** **gemctabine + docetaxel**

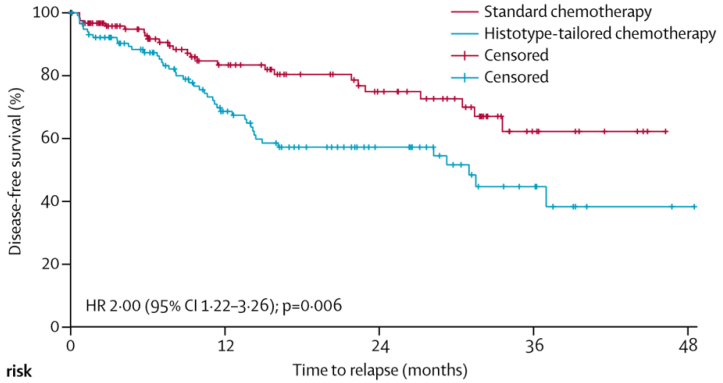
epiADM + IFX x 3

Gronchi A et al. Lancet Oncol 2017

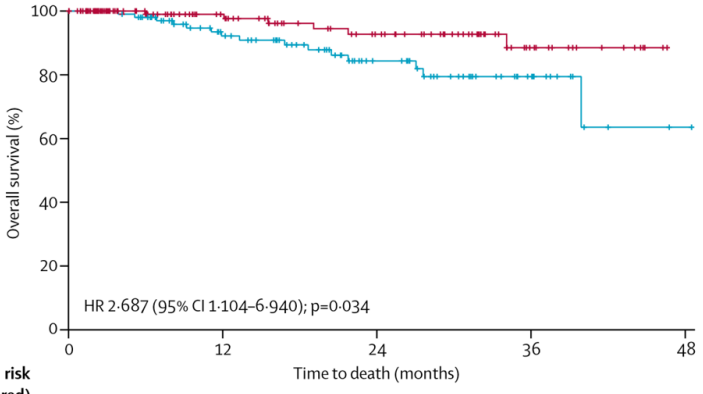
(Neo)Adiuvant chemotherapy

Histotype-tailored neoadjuvant chemotherapy versus standard chemotherapy in patients with high-risk soft-tissue sarcomas (ISG-STS 1001): an international, open-label, randomised, controlled, phase 3, multicentre trial

Alessandro Gronchi, Stefano Ferrari, Vittorio Quagliuolo, Javier Martin Broto, Antonio Lopez Pousa, Giovanni Grignani, Umberto Basso, Jean-Yves Blay, Oscar Tendero, Robert Diaz Beveridge, Virginia Ferraresi, Iwona Lugowska, Domenico Franco Merlo, Valeria Fontana, Emanuela Marchesi, Davide Maria Donati, Elena Palassini, Emanuela Palmerini, Rita De Sanctis, Carlo Morosi, Silvia Stacchiotti, Silvia Bagué, Jean Michelle Coindre, Angelo Paolo Dei Tos, Piero Picci, Paolo Bruzzi, Paolo Giovanni Casali



Number at risk (number censored)					
Standard chemotherapy	144 (0)	63 (65)	37 (72)	9 (103)	0 (119)
Histotype-tailored chemotherapy	142 (0)	57 (54)	28 (70)	9 (87)	1 (95)



Number at risk (number censored)					
Standard chemotherapy	144 (0)	75 (68)	48 (83)	15 (89)	0 (138)
Histotype-tailored	142 (0)	72 (63)	40 (74)	13 (91)	1 (125)

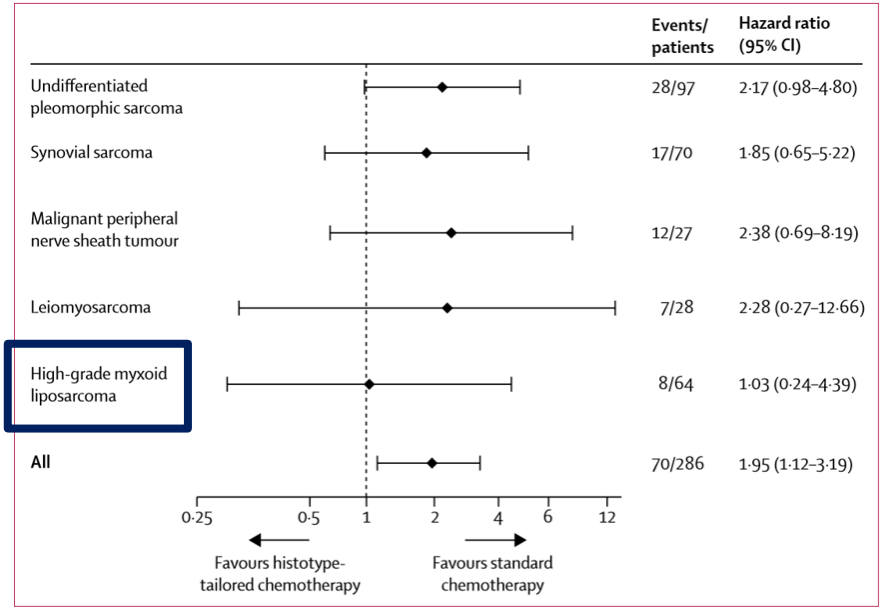
Median Follow-up 12.3 months

Gronchi A et al. Lancet Oncol 2017

(Neo)Adjuvant chemotherapy

Histotype-tailored neoadjuvant chemotherapy versus standard chemotherapy in patients with high-risk soft-tissue sarcomas (ISG-STS 1001): an international, open-label, randomised, controlled, phase 3, multicentre trial

Alessandro Gronchi, Stefano Ferrari, Vittorio Quagliuolo, Javier Martin Broto, Antonio Lopez Pousa, Giovanni Grignani, Umberto Basso, Jean-Yves Blay, Oscar Tendero, Robert Diaz Beveridge, Virginia Ferraresi, Iwona Lugowska, Domenico Franco Merlo, Valeria Fontana, Emanuela Marchesi, Davide Maria Donati, Elena Palassini, Emanuela Palmerini, Rita De Sanctis, Carlo Morosi, Silvia Stacchiotti, Silvia Bagué, Jean Michelle Coindre, Angelo Paolo Dei Tos, Piero Picci, Paolo Bruzzi, Paolo Giovanni Casali

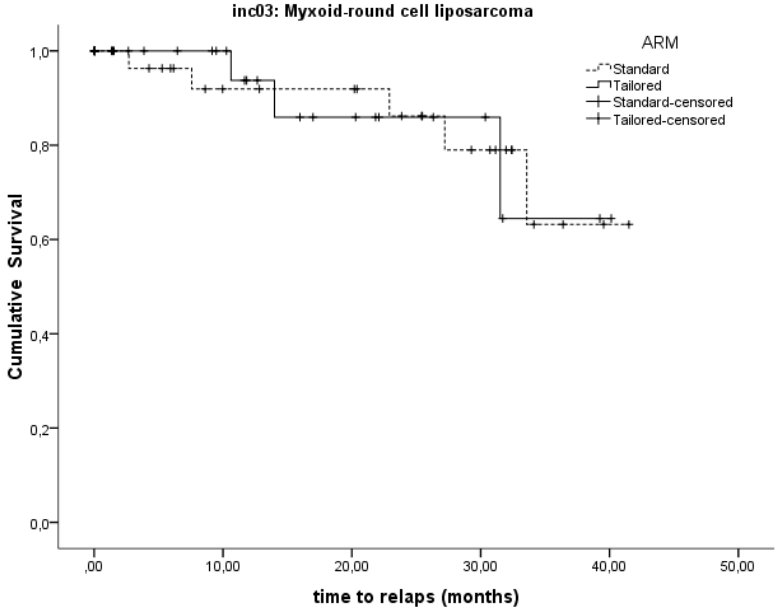


Gronchi A et al. Lancet Oncol 2017

(Neo)Adiuvant chemotherapy

Histotype-tailored neoadjuvant chemotherapy versus standard chemotherapy in patients with high-risk soft-tissue sarcomas (ISG-STS 1001): an international, open-label, randomised, controlled, phase 3, multicentre trial

Alessandro Gronchi, Stefano Ferrari, Vittorio Quagliuolo, Javier Martin Broto, Antonio Lopez Pousa, Giovanni Grignani, Umberto Basso, Jean-Yves Blay, Oscar Tendero, Robert Diaz Beveridge, Virginia Ferraresi, Iwona Lugowska, Domenico Franco Merlo, Valeria Fontana, Emanuela Marchesi, Davide Maria Donati, Elena Palassini, Emanuela Palmerini, Rita De Sanctis, Carlo Morosi, Silvia Stacchiotti, Silvia Bagué, Jean Michelle Coindre, Angelo Paolo Dei Tos, Piero Picci, Paolo Bruzzi, Paolo Giovanni Casali



Gronchi A et al. Lancet Oncol 2017

(Neo)Adiuvant chemotherapy

Histotype-tailored neoadjuvant chemotherapy versus standard chemotherapy in patients with high-risk soft-tissue sarcomas (ISG-STS 1001): an international, open-label, randomised, controlled, phase 3, multicentre trial

Alessandro Gronchi, Stefano Ferrari, Vittorio Quagliuolo, Javier Martin Broto, Antonio Lopez Pousa, Giovanni Grignani, Umberto Basso, Jean-Yves Blay, Oscar Tendero, Robert Diaz Beveridge, Virginia Ferraresi, Iwona Lugowska, Domenico Franco Merlo, Valeria Fontana, Emanuela Marchesi, Davide Maria Donati, Elena Palassini, Emanuela Palmerini, Rita De Sanctis, Carlo Morosi, Silvia Stacchiotti, Silvia Bagué, Jean Michelle Coindre, Angelo Paolo Dei Tos, Piero Picci, Paolo Bruzzi, Paolo Giovanni Casali

- Short follow-up (12.3 months medium follow-up)
- One-sided test
- Lack of control arm

- Selected histologies
- Selected tumour site
- Neoadjuvant setting

Gronchi A et al. Lancet Oncol 2017

(Neo)Adjuvant chemotherapy

ESMO

Annals of Oncology 0 (Supplement 0): iv1–iv7, 2018
doi:10.1093/annonc/mdy096

CLINICAL PRACTICE GUIDELINES

Soft tissue and visceral sarcomas: ESMO–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up†

P. G. Casali[1], N. Abecassis[2], S. Bauer[3], R. Biagini[4], S. Bielack[5], S. Bonvalot[6], I. Boukovinas[7], J. V. M. G. Bovee[8], T. Brodowicz[9], J. M. Broto[10], A. Buonadonna[11], E. De Álava[10], A. P. Dei Tos[12], X. G. Del Muro[13], P. Dileo[14], M. Eriksson[15], A. Fedenko[16], V. Ferraresi[17], A. Ferrari[18], S. Ferrari[19], A. M. Frezza[1], S. Gasperoni[20], H. Gelderblom[21], T. Gil[22], G. Grignani[23], A. Gronchi[1], A. Hannu[24], B. Hassan[25], P. Hohenberger[26], R. Issels[27], H. Joensuu[28], R. L. Jones[29], I. Judson[30], P. Jutte[31], S. Kaal[32], B. Kasper[26], K. Kopeckova[33], D. A. Krákorová[34], A. Le Cesne[35], I. Lugowska[36], O. Merimsky[37], M. Montemurro[38], M. A. Pantaleo[39], R. Piana[40], P. Picci[18], S. Piperno-Neumann[6], A. L. Pousa[41], P. Reichardt[42], M. H. Robinson[43], P. Rutkovski[36], A. A. Safwat[44], P. Schöffski[45], S. Sleijfer[46], S. Stacchiotti[47], K. Sundby Hall[48], M. Unk[49], F. Van Coevorden[50], W. Van der Graaf[29], J. Whelan[51], E. Wardelmann[52], O. Zaikova[53] & J. Y. Blay[54], on behalf of the ESMO Guidelines Committee and EURACAN*

[1]Fondazione IRCCS Istituto Nazionale dei Tumori and University of Milan, Milan, Italy; [2]Instituto Portugues de Oncologia de Lisboa Francisco Gentil, EPE, Lisbon, Portugal; [3]University Hospital Essen, Essen, Germany; [4]Department of Oncological Orthopedics, Musculoskeletal Tissue Bank, IFO, Regina Elena National Cancer Institute, Rome, Italy; [5]Klinikum Stuttgart-Olgahospital, Stuttgart, Germany; [6]Institut Curie, Paris, France; [7]NORDIC, Athens, Greece; [8]Department of Pathology, Leiden University Medical Center, Leiden, The Netherlands; [9]Vienna General Hospital (AKH), Medizinische Universität Wien, Vienna, Austria; [10]Hospital Universitario Virgen del Rocío-CIBERONC, Seville, Spain; [11]Centro di Riferimento Oncologico di Aviano, Aviano; [12]Ospedale Regionale di Treviso 'S.Maria di Ca Foncello', Treviso, Italy; [13]Integrated Unit ICO Hospitalet, HUB, Barcelona, Spain; [14]Sarcoma Unit, University College London Hospitals, London, UK; [15]Skane University Hospital-Lund, Lund, Sweden; [16]N. N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation; [17]Institute of Scientific Hospital Care (IRCCS), Regina Elena National Cancer Institute, Rome; [18]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan; [19]Istituto Ortopedico Rizzoli, Bologna; [20]Azienda Ospedaliera Universitaria Careggi Firenze, Florence, Italy; [21]Department of Medical Oncology, Leiden University Medical Centre, Leiden, The Netherlands; [22]Institut Jules Bordet, Brussels, Belgium; [23]Candiolo Cancer Institute, FPO IRCCS, Candiolo, Italy; [24]Turku University Hospital (Turun Yliopistollinen Keskussairaala), Turku, Finland; [25]Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [26]Mannheim University Medical Center, Mannheim; [27]Department of Medicine III, University Hospital, Ludwig-Maximilians-University Munich, Munich, Germany; [28]Helsinki University Central Hospital (HUCH), Helsinki, Finland; [29]Royal Marsden Hospital, London; [30]The Institute of Cancer Research, London, UK; [31]University Medical Center Groningen, Groningen; [32]Radboud University Medical Center, Nijmegen, The Netherlands; [33]University Hospital Motol, Prague; [34]Masaryk Memorial Cancer Institute, Brno, Czech Republic; [35]Gustave Roussy Cancer Campus, Villejuif, France; [36]Maria Skłodowska Curie Institute, Oncology Centre, Warsaw, Poland; [37]Tel Aviv Sourasky Medical Center (Ichilov), Tel Aviv, Israel; [38]Medical Oncology, University Hospital of Lausanne, Lausanne, Switzerland; [39]Azienda Ospedaliera, Universitaria, Policlinico S.Orsola-Malpighi Università di Bologna, Bologna; [40]Azienda Ospedaliero, Universitaria Città della Salute e della Scienza di Torino, Turin, Italy; [41]Fundacio de Gestio Sanitaria de l'hospital de la SANTA CREU I Sant Pau, Barcelona, Spain; [42]Helios Klinikum Berlin Buch, Berlin, Germany; [43]CRC Department of Clinical Oncology, Weston Park Hospital NHS Trust, Sheffield, UK; [44]Aarhus University Hospital, Aarhus, Finland; [45]Leuven Cancer Institute, Leuven, Belgium; [46]Department of Medical Oncology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands; [47]Fondazione Istituto di Ricovero e Cura a Carattere Scientifico, Istituto Nazionale dei Tumori, Milan, Italy; [48]Department of Oncology, Oslo University Hospital, The Norwegian Radium Hospital, Oslo, Norway; [49]Institute of Oncology of Ljubljana, Ljubljana, Slovenia; [50]Netherlands Cancer Institute-Antoni van Leeuwenhoek, Amsterdam, The Netherlands; [51]University College Hospital, London, UK; [52]Gerhard-Domagk-Institut für Pathologie, Universitätsklinikum Münster, Münster, Germany; [53]Oslo University Hospital, Norwegian Radium Hospital, Oslo, Norway; [54]Centre Leon Bernard and UCBL1, Lyon, France

*Correspondence to: ESMO Guidelines Committee, ESMO Head Office, Via Ginevra 4, 6900 Lugano, Switzerland. E-mail: clinicalguidelines@esmo.org
†Approved by the ESMO Guidelines Committee and EURACAN: December 2017.

Soft tissue sarcomas (STSs) gather over 80 histological entities, with even more molecular subsets, characterised by a low to very low incidence in all populations. The majority of sarcomas arise from the soft tissue (close to 75%), with ~15% gastrointestinal stromal tumours (GISTs) and 10% bone sarcomas. These ESMO–EURACAN (European Society for Medical Oncology–European Reference Network for rare adult solid cancers) Clinical Practice Guidelines cover STSs, while GISTs are covered by dedicated ESMO–EURACAN Clinical Practice Guidelines [1]. Kaposi's sarcoma is not considered in the present document. Extraskeletal Ewing and Ewing-like sarcoma is covered by ESMO Clinical Practice Guidelines on bone sarcomas [2]. In general, the same principles for these tumours in children apply to adults. This is also the case for embryonal and alveolar rhabdomyosarcomas,

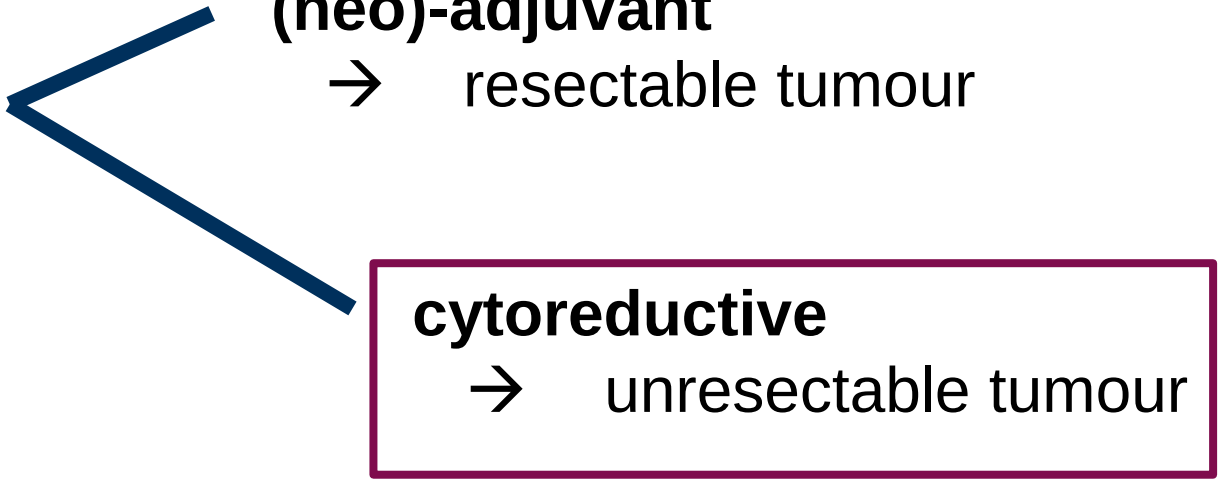
(Neo)adjuvant chemotherapy
not standard

high-risk

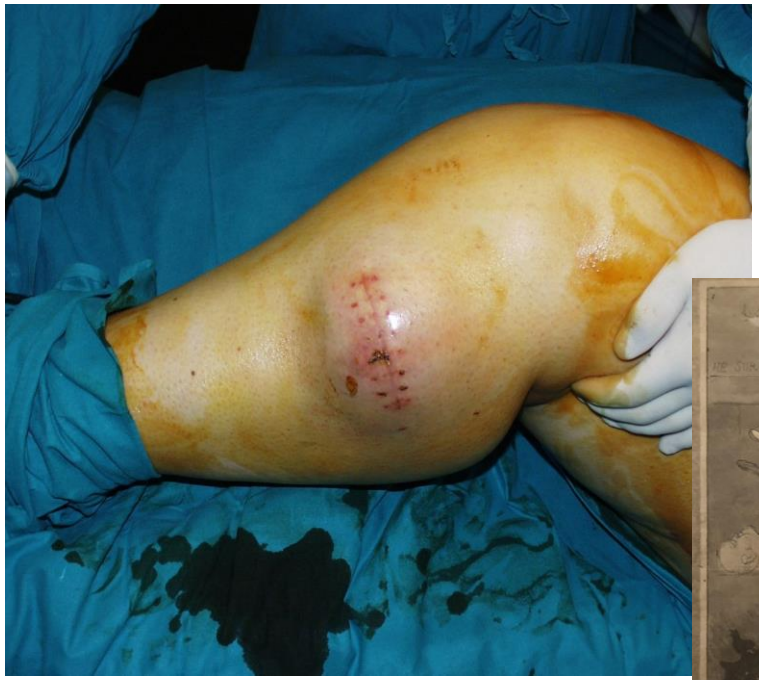
…waiting for the final analysis of the ISG-STS 1001 study*

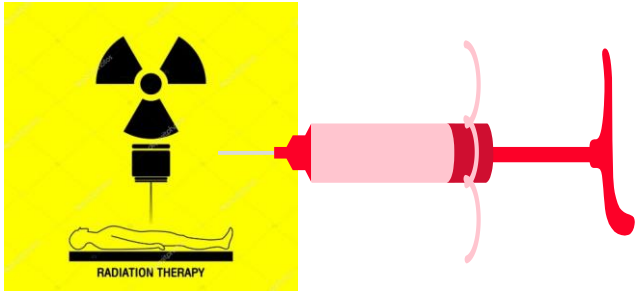
MUNICH 2018 ESMO congress

*ISG, Italian Sarcoma Group; STS, soft tissue sarcoma


(neo)-adjuvant
→ resectable tumour
cytoreductive
→ unresectable tumour

Treatment, locally advanced disease





Silvia Stacchiotti, MD
silvia.stacchiotti@istitutotumori.mi.it