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ESMO Minimum Clinical Recommendations for diagnosis, treatment and follow-up of soft tissue sarcomas

Incidence

• The crude incidence of soft tissue sarcoma in the European Union is 1.0-3.0/100000 per year, the mortality 0.6-0.8/100000 per year. They are diagnosed at any age but are more frequent in older patients with a peak incidence at the age of 50 years.

Diagnosis

- Histological diagnosis and evaluation of grades are preferentially made on an incisional surgical biopsy or on the completely resected tumor. Tru-cut biopsies are also used but should be restricted to experienced centers.
- Gastrointestinal stromal tumors should be confirmed by staining for CD117.
- Specific types of small round cell tumors (extra-osseous Ewing's sarcoma, embryonal rhabdomyosarcoma) should be identified by immunohistochemistry and cytogenetics and be treated accordingly.

Staging and risk assessment

- Staging is performed by physical exam and the appropriate radiological techniques. To exclude lung metastases a CT scan is recommended in operable patients.
- For staging according to the UICC/AJCC 2002 system, tumor size is categorized as small (≤5 cm, T1) or large (T2) and is complemented by information about location (superficial: Ta or deep: Tb) and histological grade (using either of the grading systems G1-4 or G1-3 or low/high) as further parameters that are required for the stage grouping are shown in Table 1.

Treatment plan

• Soft tissue sarcoma requires a multidisciplinary approach by an experienced team.

Surgery

- Surgery is the main treatment for localized disease. The tumor should be removed by wide excision or by compartmental resection including the cutaneous scar and tractus of a previous biopsy. The width of the resection might be decreased in case of resistant anatomic planes such as muscular fasciae, periostium, perineurium, if not infiltrated.
- After wide excision of high-grade sarcomas, adjuvant radiation therapy is recommended [II, B].

- In case of radical surgery obtained by compartmental excision or amputation at a large distance from the primary tumor, adjuvant radiation therapy is not necessary.
- Re-operation is recommended in case of previous marginal or intralesional resection [III, B].
- In case of completely resectable lung metastases, surgery has to be considered [III, B].

Radiation therapy

- Radiation therapy should be administered postoperatively at a dose of 60–65 Gy with a shrinking field technique in case of wide resection [II, B].
- In selected patients preoperative radiotherapy may be an option [III, B].

Chemotherapy

Localized disease:

- Preoperative chemotherapy is not standard practice for operable patients [III, B]. It can be considered together with radiotherapy in patients with borderline resectable tumors.
- Adjuvant chemotherapy is not standard practice even though it might improve distant and local control. Its impact on overall survival is still debated [II, A]. It may be considered in younger patients with large and high-grade tumors [II, C].
- In non-resectable tumors confined to an extremity, chemotherapy with or without radiotherapy or isolated hyperthermic limb perfusion with chemotherapy and/or cytokines offers an alternative to amputation [III, B].

Metastatic disease:

Chemotherapy is the standard treatment for metastatic disease. Doxorubicin with or without ifosfamide is commonly

Table 1.

| Stage | Primary tumor | Lymph nodes | Distant metastases | Grading G_{1-4} (or G_{1-3} or low / high) |
|-------|----------------------|-------------------------|------------------------------------------|------------------------------------------------|
| ΙA | T _{1a or b} | N _{0 or x} | M_0 | G ₁₋₂ (or G ₁ or low) |
| IB | T _{2a or b} | $N_{0\ {\rm or}\ x}$ | M_0 | G_{1-2} (or G_1 or low) |
| IIA | T _{1a or b} | $N_{0\ or\ x}$ | M_0 | G_{3-4} (or G_{2-3} or high) |
| IIB | T_{2a} | $N_{0\ or\ x}$ | M_0 | G_{3-4} (or G_{2-3} or high) |
| III | T_{2b} | $N_{0\ or\ x}$ | M_0 | G_{3-4} (or G_{2-3} or high) |
| IV | Any T Any T | N ₁ Any N | $\begin{matrix} M_0 \\ M_1 \end{matrix}$ | Any G Any G |

- used. Doxorubicin alone seems to be equivalent to its combinations with other agents with regard to survival, despite a higher response rate with combination regimens [II, B].
- Imatinib (STI 571, a tyrosine kinase receptor inhibitor) is the treatment of choice for gastro-intestinal stromal tumors (GIST).

Response evaluation

 Response evaluation of chemotherapy for metastatic disease should be performed after 2 or 3 cycles with the radiological exams that were positive before treatment.

Follow-up

• Early detection of recurrence might influence the possibility of a curative therapy. The patients should be followed every 3 months with history and physical examination. MRI of the site of resection of the primary tumor is proposed twice a year for the first 2–3 years and then once a year. For patients with high-grade tumors a chest X-ray is recommended every 3 to 4 months in the first 2–3 years, twice a year up to the 5th year, and once a year thereafter [IV, B].

Note

Levels of Evidence [I-V] and Grades of Recommendation [A-D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the experts and the ESMO faculty.

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Coordinating authors for the ESMO Guidelines Task Force: S. Leyvraz¹ & S. Jelic²

¹Invited author, Fondation du Centre Pluridisciplinaire d'Oncologie, CHUV, Lausanne, Switzerland; ²Assigned task force member, Institute of Oncology and Radiology of Serbia, Department of Medical Oncology, Pasterova 14, 11000 Belgrade, Serbia

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Correspondence to:
ESMO Guidelines Task Force
ESMO Head Office
Via La Santa 7
CH-6962 Lugano
Switzerland