Annals of Oncology 16 (Supplement 1): i69–i70, 2005
doi:10.1093/annonc/mdi830

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 1.0–3.0/100 000 per year, the mortality 0.6–0.8/100 000 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)
IA	$T_{1a \text{ or } b}$	$N_{0 \text{ or } x}$	M_0	G_{1-2} (or G_1 or low)
IB	$T_{2a \text{ or } b}$	$N_{0 \text{ or } x}$	M_0	G_{1-2} (or G_1 or low)
IIA	$T_{1a \text{ or } b}$	$N_{0 \text{ or } x}$	M_0	G_{3-4} (or G_{2-3} or high)
IIB	T_{2a}	$N_{0 \text{ or } x}$	M_0	G_{3-4} (or G_{2-3} or high)
III	T_{2b}	$N_{0 \text{ or } x}$	M_0	G_{3-4} (or G_{2-3} or high)
IV	Any T	N_1	M_0	Any G
	Any T	Any N	M_1	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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Approved by the ESMO Guidelines Task Force: August 2003, last update December 2004.

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