



## Soft Tissue Sarcomas

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### Editorial

Soft tissue sarcomas are rare tumors with an incidence less than 6/100,000/year. The soft tissue sarcomas include various histologies characterized by different prognosis and different treatment response. The histological diagnosis might be difficult due to the peculiarity and rarity of these tumors and therefore it is strongly recommended to consult reference centers. Indeed the literature reports that 30-40% of sarcoma histological diagnoses that are revised by expert pathologists are then modified. Soft tissue sarcomas can arise in the limbs and trunk but also in the viscera and retroperitoneum. The localization of the tumors influences the prognosis with retroperitoneal sarcomas showing a worse prognosis than sarcomas of the trunk and limbs. Moreover retroperitoneal sarcomas are very difficult to treat with radical surgery, thus increasing the aggressiveness of these tumors. All masses greater than 5 cm in diameter in the limbs, in the extremities and in the retroperitoneum should be biopsied when there is a suspicion of sarcoma.

In the case of localized disease, the standard treatment is represented by surgery because it is the only approach that can potentially lead to healing. There is still no consensus regarding adjuvant treatment after surgery in soft tissue sarcomas. The literature shows indeed very conflicting data; the available clinical trials include very different populations in terms of histologies and localization thus providing confusing data. The adjuvant treatment of soft tissue sarcomas is so far optional and it needs to be personalized considering the following factors: diameter, grade and localization. A standard adjuvant treatment, represented by anthracycline and ifosfamide, can be proposed in the case of lesions greater than 5 cm in diameter, G3 or non-superficial localization. Generally sarcomas of the extremities benefit from more than one adjuvant treatment compared to visceral or retroperitoneal sarcomas. Nevertheless adjuvant treatment does not determine an improvement in Overall Survival (OS) but only in Relapse Free Survival (RFS).

Neoadjuvant treatment is recommended before conservative surgery; in this case, chemotherapy can be administered before surgery, thus avoiding administered up after surgery.

In the metastatic disease chemotherapy is considered the standard treatment. If the disease has spread to other organs, chemotherapy is intended as a palliative treatment. In this case it is preferred a single-agent chemotherapy with anthracycline. Otherwise a poly-chemotherapy is preferable in case of single localization of the metastatic disease, e.g. pulmonary localization from limbs sarcomas. It is also known that combination chemotherapy achieve better results in terms of Objective Responses Rate (ORR) compared to single-agent chemotherapy. For this reason chemotherapy with two drugs is preferred in neoadjuvant and adjuvant setting, when Response Rate (RR) is the primary end point.

In metastatic disease the treatment is histology-driven, although the anthracycline and/or ifosfamide represents the standard treatment.

Leiomyosarcoma is very sensitive to anthracycline, dacarbazine, gemcitabine but not to ifosfamide. For this reason ifosfamide is not used in the treatment of this tumor type. The liposarcomas respond to anthracycline and ifosfamide. Angiosarcomas respond very well to taxanes, anthracycline and gemcitabine. Trabectedin is very active in mixoid liposarcomas and in different translocated sarcomas. Pazopanib is indicated in second line treatment of soft tissue sarcomas but not in liposarcomas. In this setting pazopanib determine an improvement in Progression Free Survival (PFS) but not in OS.

Recently eribulin has shown good activity in liposarcomas in a Phase III study compared with dacarbazine. Eribulin improve OS in this setting. Finally olaratumab was effective in increasing survival in association with anthracycline in soft tissue sarcomas and phase III studies are still ongoing.