Sarcoma Advisory Group Chemotherapy Guidelines – Bone Sarcomas

These guidelines do not include specific clinic trials, but is assumed that clinical trials should always be considered when available and clinically appropriate. In the guidelines, when several options exist, then the choice will be based on individual patient circumstances, treatment intent, co-morbidities and patient preference, and decisions will frequently be informed by MDT discussion.

Sarcoma Type	Category	1st Line	2nd Line	3rd Line and Other
Osteosarcoma	Resectable < 30 years	Doxorubicin, cisplatin methotrexate[1]+/- mifamurtide[2]	Ifosfamide and etoposide[3]	Gemcitabine and docetaxel[4] **or** Oral etoposide[5]
	Other	Doxorubicin, cisplatin ± methotrexate[1, 2]	Ifosfamide, etoposide ± methotrexate	Gemcitabine and docetaxel[4] **or** Oral etoposide[5]
Ewing's family of tumours	Localised or metastatic disease with lung or pleural metastases only	VIDE x 6 cycles → VAC or VAI x 8 cycles[6, 7]	High dose ifosfamide[8] **or** Ifosfamide and etoposide **or** Cyclophosphamide and topotecan[9] **or** Irinotecan and temozolamide[10] **+/-** High dose chemotherapy (busulphan/lmelphalan or treosulphan/melphalan) with peripheral blood stem cell rescue[11] N.B. Choice of 2nd line therapy will depend on patient/disease specific factors (e.g. if chemotherapy being given with curative intent) and/or patient choice	Cyclophosphamide and topotecan[9] **or** Irinotecan and temozolamide[10] **or** Gemcitabine and docetaxel[12, 13] **or** Oral etoposide[5] **or** Cisplatin and etoposide[14]
	Metastatic disease with bone or bone marrow involvement	VIDE x 6 cycles → VAC or VAI x 8 cycles[6, 15] **or** VDC/IE interval compressed regimen x 14 cycles[16]		
Other high grade bone		Doxorubicin, cisplatin ±	Ifosfamide, etoposide ±	Gemcitabine and docetaxel[4]

sarcomas including malignant fibrous histiocytoma, leiomyosarcoma, angiosarcoma, spindle cell sarcoma, dedifferentiated chondrosarcoma		methotrexate[1, 2]	methotrexate[3]	**or** Oral etoposide[5]
Pigmented villonodular synovitis	Locally advanced unresectable/metastatic	Imatinib*[17]		
Giant cell tumour	Locally advanced unresectable/metastatic	Denosumab[18]		
Chordoma	Locally advanced, unresectable or metastatic: Non-dedifferentiated Dedifferentiated	 Imatinib*[19, 20] Doxorubicin **or** Doxorubicin and cisplatin[21]	 Addition of sirolimus[22]	

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Sarcoma Advisory Group Chemotherapy Guidelines – Soft Tissue Sarcomas

These guidelines do not include specific clinic trials, but is assumed that clinical trials should be always be considered when available and clinically appropriate. In the guidelines, when several options exist, then the choice will be based on individual patient circumstances, treatment intent, co-morbidities and patient preference, and decisions will frequently be informed by MDT discussion.

Sarcoma Type	Category	1st Line	2nd Line	3rd Line and Other
All	Adjuvant (in selected high risk patients)	Doxorubicin and ifosfamide[23]	NA	NA
	Neoadjuvant	Doxorubicin and ifosfamide	NA	NA
	Metastatic/Locally advanced	Doxorubicin[24] +/- ifosfamide[25] (consider combination chemotherapy for fit patients e.g. PS 0/1, age ≤60 years) **or** Oral cyclophosamide and prednisolone[26] (consider for elderly patients of good PS but not suitable for doxorubicin) **or** Caelyx™ (for patients with cardiac impairment requiring an anthracycline in1st or 2nd line indication) (funding via CDF); (for patients with cardiac or intimal sarcomas who may require radiotherapy to the primary site – no current funding)* *N.B. Cardiac or intimal sarcomas who may require radiotherapy to the primary site can receive dexrazoxane with doxorubicin as cardio-protection.	Ifosfamide (bolus or infusional[27, 28]) **or** Trabectedin[29] **or** Oral cyclophosamide and prednisolone[26] **or** Gemcitabine and docetaxel[30] **or** Pazopanib[31] (no current funding) N.B. Choice of chemotherapy will depend on disease factors (histological subtypes) and patient factors (PS, patient choice)	Ifosfamide (bolus or infusional[27]) **or** Trabectedin[29] **or** Oral cyclophosphamide and prednisolone[26] **or** Gemcitabine and docetaxel[30] **or** Pazopanib[31] (no current funding) **or** Dacarbazine[32] N.B. Choice of chemotherapy will depend on disease factors (histological subtypes) and patient factors (PS, patient choice)

Leiomyosarcoma	Metastatic/Locally advanced	As for STS **or** Aromatase inhibitor (if ER/PR positive) (for uterine leiomyosarcoma)[33]	As for STS	As for STS
Endometrial stromal sarcoma	Metastatic/Locally advanced	Aromatase inhibitor[34] **or** As for STS	Medroxyprogesterone[34] **or** As for STS	As for STS
Dedifferentiated liposarcoma	Metastatic/locally advanced	Infusional ifosfamide[27, 28] **or** As for STS	Infusional ifosfamide[27, 28] **or** As for STS	As for STS
Angiosarcoma	Metastatic/Locally advanced Cutaneous angiosarcoma	As for STS **or** Paclitaxel[35, 36] **or** Liposomal doxorubicin[37] (no current funding)	As for STS **or** Paclitaxel[35, 36] **or** Liposomal doxorubicin[37] (no current funding)	As for STS
Desmoplastic small round cell tumour		VDC/IE 2 weekly x 14, maintenance VAC[38] **or** VIDE	Trabectedin[39] **or** Gemcitabine and docetaxel	Pazopanib[40] (no current funding)
Alveolar soft part sarcoma	Metastatic/locally advanced	No standard therapy, clinical trial if available		
Haemangiopericytoma/ Malignant solitary fibrous tumour	Metastatic/Locally advanced	As for STS **or** VEGFR inhibitor e.g. pazopanib (no current funding)	As for STS **or** VEGFR inhibitor e.g. pazopanib (no current funding)	As for STS **or** VEGFR inhibitor e.g. pazopanib (no current funding)
Fibromatosis	Unresectable	Nonsteroidal anti-inflammatory (e.g. sulindac, naproxen)[41] **and/or** Tamoxifen[42]	Tamoxifen[42] **or** Liposomal doxorubicin[43] **(funding via CDF)** **or** Vinblastine and methotrexate[44] or Vinorelbine and methotrexate[45]	Imatinib[46]
PEComa	Locally advanced/metastatic	Sirolimus[47]	As for STS	

	disease			
Gastrointestinal stromal tumour	Adjuvant - high risk of recurrence	Imatinib 400mg[48] (except for KIT exon 9 mutations, PDGFRB mutations and wild type tumours)		
Gastrointestinal stromal tumour	Locally advanced/metastatic disease	Imatinib 400 mg[49, 50] (800 mg for exon 9 mutations[51])	Sunitinib[52]	Regorafenib[53] (funding via CDF)
Inflammatory myofibroblastic tumour	Locally advanced/metastatic disease	Corticosteroids		
Dermatofibrosarcoma protuberans	Locally advanced, unresectable or metastatic	Imatinib 400mg[54]		
Rhabdomyosarcoma (embryonal and alveolar)	Localised non-metastatic: Low risk Standard risk High risk Very high risk Metastatic	 Vincristine, actinomycin Vincristine, actinomycin, ifosfamide Vincristine, actinomycin, ifosfamide +/- doxorubicin Vincristine, actinomycin, ifosfamide +/- doxorubicin +/- maintenance vinorelbine and cyclophosphamide Vincristine, actinomycin, ifosfamide, doxorubicin +/- maintenance vinorelbine and cyclophosphamide	*No previous doxorubicin: Topotecan, vincristine, doxorubicin **or** vincristine, irinotecan **or** vinorelbine, cyclophosphamide **or** vincristine, doxorubicin, etoposide Previous doxorubicin: vincristine, irinotecan **or** vinorelbine, cyclophosphamide *Recommendations from EpSSG phase II committee 07.08.13	

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