



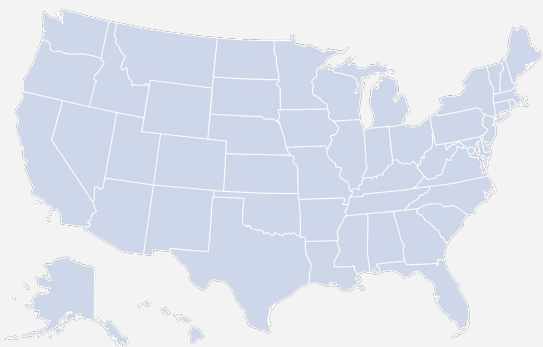
Sarcoma

Soft Tissue & Bone Sarcoma

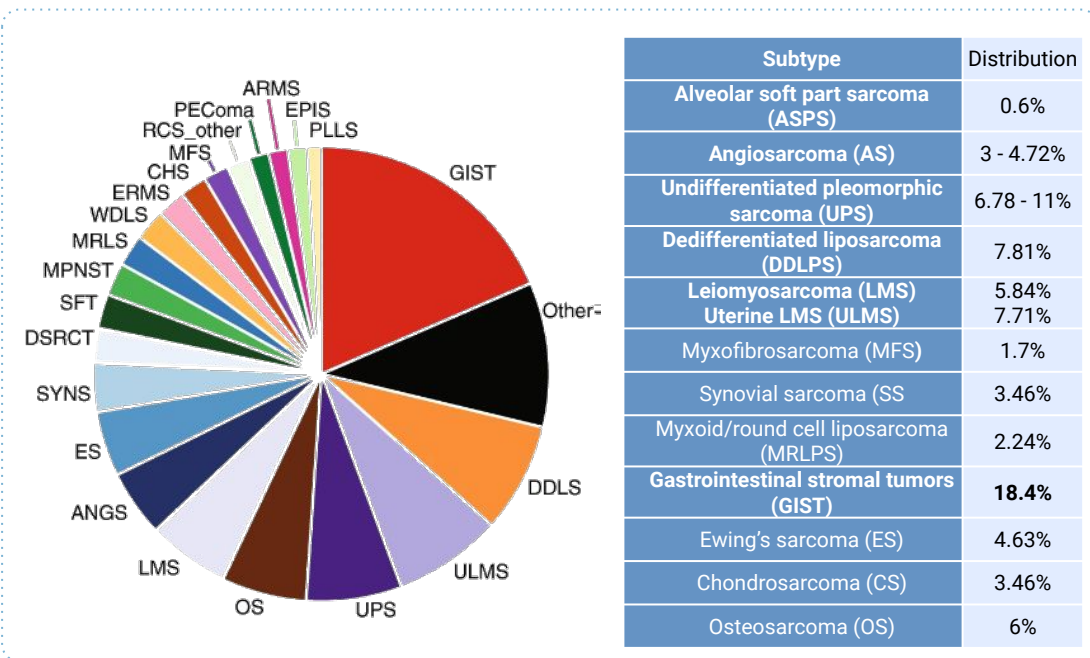
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- ✓ Sarcoma Subtypes
 - ✓ Potential Response to I/Os
 - ✓ Recommended Treatments

SARCOMAS REPRESENT <1% OF DIAGNOSED CANCERS IN THE US; ~13,190 NEW CASES EXPECTED IN 2024 IN THE US

American Cancer Society estimates for soft tissue sarcomas in the United States for 2024



- Highly heterogeneous with more than 50 histologic subtypes of soft tissue sarcoma (STS) and bone sarcoma
- Most common type of STS are GIST, undifferentiated pleomorphic sarcoma, liposarcoma & leiomyosarcoma
- 3 major subtypes of bone sarcoma are osteosarcoma, chondrosarcoma & Ewing's sarcoma



13,590 new soft tissue sarcomas will be diagnosed (7,700 in males and 5,890 in females)

5,200 people (2,740 males and 2,390 females) are expected to die of soft tissue sarcomas



ASPS, AS & UPS HAVE SHOWN THE HIGHEST ORRs WITHIN STS FOR ICIs; TMB SLIGHTLY HIGH IN AS, UPS & LMS

	Tumor types arranged in the order of response to immunotherapy (highest to lowest)	% of Sarcoma	Median TMB (Mut/MB)	MSI H/ MMR Deficiency (MSISensor Score>10)	PD L1 expression (>1%)	Known ICI response/Off-label usage*	I-O therapies in development	Potential ICI response
Bone sarcoma	Alveolar soft part sarcoma (ASPS)	0.6%	<1		?	Atezolizumab approved on Dec 9, 2022 (ORR: ~24%) Pembrolizumab+Axitinib is already recommended in NCCN . Highest responding subtype (ORR: 25%)	Many basket trials are ongoing for broader sarcoma; No specific trial	
	Angiosarcoma (AS)	3- 4.72%	2 - 3		29%	Pembrolizumab (ORR: Various ~71%) & nivolumab + ipilimumab are already recommended by NCCN	Phase 1 ISS ongoing for mRNA vaccine (dendritic cells)	
	Undifferentiated pleomorphic sarcoma (UPS)	6.78 - 11%	2 - 3		33%	Pembro and nivo have shown response (ORR: 23-66%), also recommended in NCCN	Many anti-PD-1s in development	
	Dedifferentiated liposarcoma (DDLPS)	6 - 7.81%	<1		10%	Responded to pembrolizumab and nivo+ipi (lesser extent than UPS, ORR:10-40%)	Phase 2 ISS ongoing for retifanlimab (PD-1) + pemigatinib (FGFR1i)	
	Leiomyosarcoma (LMS) Uterine LMS (ULMS)	5.84% - 12% 7.71%	2 - 3		11%	The response observed with pembrolizumab is usually lesser than UPS and LPS (ORR: 0-30%)	Many basket trials detected	
	Myxofibrosarcoma (MFS)	1.7 - 3%	<1		18%	Pembrolizumab & nivolumab + ipilimumab recommend in NCCN	Many basket trials detected	
	Synovial sarcoma (SS)	3 - 3.46%	<1		0%	This subtype seems to be responding with nivolumab, but the response is lesser than others	Many cellular therapy and vaccines are under development (some targeting NY-ES01)	
	Myxoid/round cell liposarcoma (MRLPS)	2.24%	<1		0%	?		
	Gastrointestinal stromal tumors (GIST)	7 - 18.4%	<1		?	In not many ICI studies, ORR reported with nivo is very low. GIST is driven by KIT & PDGFR mutations; hence, kinase inhibitors are widely used	Only basket trial detected	
Bone sarcoma	Ewing's sarcoma (ES)	3 - 4.63%	<1		0%	Pembrolizumab failed to show benefit in SARC028 trial	mAb & CARTs in development (some targeting GD2)	
	Chondrosarcoma (CS)	3 - 3.46%	<1		?	BS: Nivolumab+Sunitinib ORR:5%		
	Osteosarcoma (OS)	6%	<1		?	Osteosarcoma: Pembrolizumab ORR:4.5%	TQB2928 (anti-CD47) in Phase 1 & CAR-T are in development	

Source: Secondary sources, Vuyhgenics analysis

*Clinical data

NCCN GUIDELINES: ANTHRACYCLINE-BASED CHEMO USED IN 1L; PD-(L)1s PREFERRED IN CERTAIN SUBTYPES



NCCN guidelines	Resectable disease		Metastatic disease		
	Stage 1 and Stage 2	Stage 3		Stage 4	
		Neoadjuvant	Adjuvant	1L	2L
Soft tissue sarcomas (STS)	Surgery → RT OR Neoadjuvant RT → Surgery	AIM (Doxorubicin + Ifosfamide + Mesna)	Doxorubicin	Pazopanib	
		Ifosfamide + Epirubicin + Mesna	Epirubicin	Eribulin	
			AD/AIM	Trabectedin	
			Ifosfamide + Epirubicin + Mesna	Pembrolizumab*	
			Larotrectinib	Nivolumab +/- Ipilimumab*	
			Entrectinib		
			Repotrectinib		
Bone cancer (Referencing Ewing's sarcoma)	Surgery → RT OR Neoadjuvant RT → Surgery	VDC/IE (Vincristine + Doxorubicin + Cyclophosphamide/ Ifosfamide + Etoposide)	VDC/IE	Pembrolizumab	
			VAIA (Vincristine + Doxorubicin + Ifosfamide + Dactinomycin)	Nivolumab/Ipilimumab	
			VIDE (Vincristine + Ifosfamide + Doxorubicin + Etoposide)	Cyclophosphamide and topotecan	
			VDC (Vincristine + Doxorubicin + Cyclophosphamide)	Irinotecan + Temozolomide ± Vincristine	

 Anthracycline based chemotherapy
 Other chemotherapies
 Kinase inhibitors
 Checkpoint inhibitors
 NTRK fusion +ve
 MSI-H/dMMR and TMB-H tumors
 TMB-H tumors
 ★ New update