

ONCOLOGY KNOWLEDGE HUB · FOR HEALTH PROFESSIONALS

Soft Tissue Sarcoma

A mini review for clinicians (from the Sarcoma module)

For postgraduate residents (medical, radiation, surgical and paediatric oncology, orthopaedics, general and plastic surgery, radiology, pathology), practising clinicians and medical students

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CONTENTS

01 At a glance

02 Clinical presentation, common traps & genetic causes

03 Screening, workup & staging essentials

04 Biomarkers that change treatment

05 Local therapy: surgery & radiotherapy

06 Systemic therapy: indications & options

07 Management algorithms

08 Survivorship, follow-up & reducing recurrence

09 Landmark trials

10 Practice pearls & pitfalls

11 Case vignettes: lines of management

12 References & guidelines

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Updated 11 October 2026. Educational summary written in our own words from current guidelines and primary trials; no drug doses; not advice for an individual patient. Verify current guidelines and Indian regulatory approvals before treatment decisions. Patients and families: please see the patient guides at drharitha.co.in.

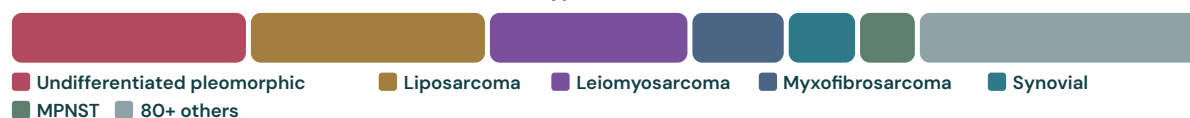
Soft Tissue Sarcoma

From the Sarcoma module · limb, trunk, retroperitoneal and metastatic soft tissue sarcoma · Key points for clinicians · Last updated 11 October 2026

01 At a glance

- Sarcomas are rare: about **1% of adult cancers** but roughly **1 in 7 to 1 in 10 childhood and adolescent cancers**. There are more than 100 subtypes; soft tissue sarcoma outnumbers bone sarcoma about four to one. GLOBOCAN does not report soft tissue sarcoma separately, so reliable Indian figures are lacking; hospital series suggest patients here present younger and with larger tumours.
- **Soft tissue sarcoma** (STS) arises most often in the thigh and limbs (about half), then the retroperitoneum and viscera, trunk, and head and neck. The commonest adult types are undifferentiated pleomorphic sarcoma (UPS), liposarcoma and leiomyosarcoma. Retroperitoneal STS is 10–15% of all STS and is usually about 15 cm at diagnosis.
- **Bone sarcoma**: osteosarcoma (teenagers, around the knee; a second peak after 60, often post-Paget or post-radiation), Ewing sarcoma (children and young adults; long bones, pelvis, ribs; also soft tissue) and chondrosarcoma (adults over 40; pelvis, femur, shoulder girdle).
- Outcome is decided early: **the first operation and the first biopsy** in the right hands give the best chance of cure and of keeping the limb. Treatment in a sarcoma reference centre (or with its input) is linked to better survival ([Blay 2024^{\[1\]}](#)).
- The commonest avoidable harm in India is the **unplanned excision** of a lump presumed benign ("lipoma", "cyst", "fibroma") without imaging, followed by bone pain in teenagers labelled growing pains, injury, osteomyelitis or tuberculosis.

Soft tissue sarcoma (about 80% of sarcomas): main types in adults



Bone sarcoma (about 20%): main types



Limb and trunk soft tissue

- Painless enlarging lump
- >5 cm or deep = image before cutting
- Surgery ± RT; lung is the usual metastatic site

Retroperitoneum and viscera

- Silent until large (median ~15 cm)
- Liposarcoma and leiomyosarcoma
- Local relapse is the main threat

Bone (teens and young adults)

- Night pain, swelling, limp
- Osteosarcoma and Ewing need chemotherapy
- Chondrosarcoma: surgery

Figure 1. Sarcoma is more than 100 diseases. Soft tissue sarcomas outnumber bone sarcomas about four to one; in adults, undifferentiated pleomorphic sarcoma, liposarcoma and leiomyosarcoma lead. Proportions are approximate (WHO 2020 and hospital series).

02 Clinical presentation, common traps & genetic causes

Who is at risk

Factor	Sarcoma risk	Clinical note
Prior radiotherapy	Absolute risk low (well under 1%), but persists for decades; higher with higher dose, younger age and alkylating agents	Latency usually 7–16 years (shorter for angiosarcoma after breast RT, about 4–8 years). Commonest types: UPS, angiosarcoma, leiomyosarcoma, osteosarcoma of bone (Mery 2009^[2]).
Chronic lymphoedema	Lymphangiosarcoma (Stewart–Treves) in a long-standing swollen arm after mastectomy and axillary surgery ± RT	Purple nodules or bruise-like patches on a lymphoedematous limb need a punch biopsy.
Li-Fraumeni syndrome (germline TP53)	Very high lifetime cancer risk; sarcoma at young age	Osteosarcoma, rhabdomyosarcoma, any sarcoma under 46 with family cancers: test TP53; avoid RT where possible.
Neurofibromatosis type 1	MPNST lifetime risk about 8–13%	A plexiform neurofibroma that becomes painful, grows or hardens needs MRI ± PET and biopsy.
Hereditary retinoblastoma (RB1)	Osteosarcoma and soft tissue sarcoma, especially in irradiated fields	Lifelong vigilance for bone pain.
Other syndromes	FAP (desmoid), Werner, Rothmund–Thomson, Gorlin, DICER1, Ollier/Maffucci (chondrosarcoma), Paget disease of bone	Ask about family cancers and skin and bone signs.
Chemicals and infection	Vinyl chloride and arsenic (hepatic angiosarcoma); HHV-8 with HIV (Kaposi sarcoma)	Kaposi sarcoma is managed differently from other sarcomas.
Not causes	A single injury or fall, ordinary implants	Injury often draws attention to a tumour already present.

Soft tissue lump: refer before any cut if

- Larger than 5 cm (a golf ball)
- Deep to the fascia (fixed, under muscle)
- Growing, or recurred after excision
- Painful, or new in an irradiated field
- Firm, irregular or rapidly enlarging
- Any of these: ultrasound then MRI

Bone: image urgently if

- Pain at night or at rest, not settling
- Swelling or a limp in a teenager
- Fracture after trivial injury
- Fever with a bone mass (Ewing mimics infection)
- Back pain with neurological signs
- First test: plain X-ray of the whole bone

Common traps in Indian practice

- "Lipoma" or "cyst" shelled out in a minor theatre, with no imaging: the commonest route to a spoiled limb.
- Bone pain in a teenager called "growing pains" or a sports injury; Ewing sarcoma treated for weeks as osteomyelitis or TB.
- FNAC used to "rule out" sarcoma: a benign or inconclusive cytology report does not close the question.

Figure 2. When to suspect sarcoma. A deep or large lump, a lump that grows, and persistent bone pain in a young person are imaging questions, not excision or reassurance questions. Most soft tissue lumps are benign, which is why the few sarcomas are missed.

How sarcomas present

Site	Typical story	What to do
Limb or trunk soft tissue	Painless, slowly or rapidly enlarging lump; often noticed after minor trauma; pain is uncommon until large	Ultrasound triage; MRI if >5 cm, deep, growing or painful; refer before excision
Retroperitoneum	Silent until large: fullness, early satiety, leg oedema or groin/leg pain from nerve compression; incidental CT finding	CT abdomen–pelvis and chest; testicular examination in men; core biopsy unless classic well-differentiated liposarcoma for upfront surgery
Breast, after RT	Bruise-like violet patch, nodules or thickening in the irradiated breast or chest wall years after treatment (angiosarcoma); often called a haematoma or cellulitis	Punch biopsies of the darkest area; reassess any "bruise" that persists beyond 2 weeks
Uterus, gut, other viscera	Bleeding, mass or obstruction; uterine leiomyosarcoma often found after a presumed fibroid is removed	Avoid power morcellation of fibroids when there are suspicious features

- **A painless lump can be malignant.** Pain does not separate benign from malignant soft tissue masses; size, depth and growth do.
- **Lymph nodes** are rarely involved (under 5%), except in clear cell sarcoma, epithelioid sarcoma, angiosarcoma, rhabdomyosarcoma and (less so) synovial sarcoma: examine the regional basin in these.
- **Retroperitoneal mass differential:** lymphoma (widespread nodes, raised LDH), germ cell tumour (testis, AFP, β -hCG), schwannoma and paraganglioma (paraspinal or para-aortic), retroperitoneal fibrosis, Castleman disease, and primaries of kidney, adrenal or pancreas (which arise from the organ).

SHARE WITH PATIENTS: PRESENTATION AND MYTHS

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

A soft tissue lump is harmless if it doesn't hurt?

Any surgeon can remove a suspicious lump first and test it later?

Persistent leg pain in children is always growing pains?

Every bone swelling is an infection or tuberculosis?

If an X-ray looks normal, bone cancer is completely ruled out?

Bone cancer develops because a child fell or had a sports injury?

03 Screening, workup & staging essentials

1 Examine and image

Ultrasound triage; MRI with contrast for limb, trunk, head and neck; CT for abdomen and retroperitoneum

2 Plan the biopsy

Core needle biopsy AFTER MRI, along the line of the future incision, decided with the operating surgeon

3 Expert pathology

Subtype by IHC ± molecular test; FNCLCC grade; review by a sarcoma pathologist

4 Stage

CT chest for all; extra by subtype (abdomen–pelvis, spine MRI, PET-CT, bone marrow)

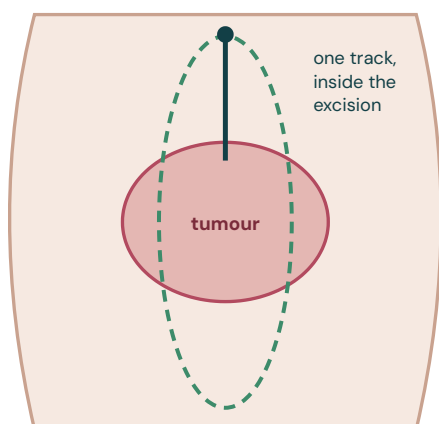
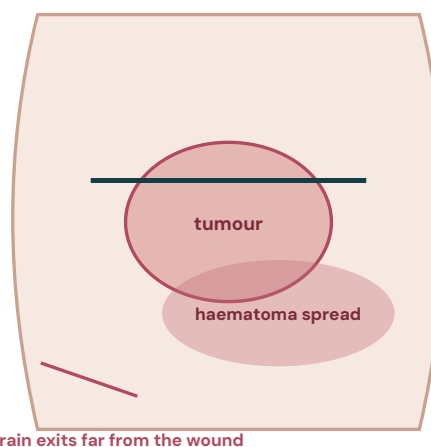
5 Sarcoma MDT

Surgeon, radiation and medical oncologist, radiologist, pathologist decide the sequence

Figure 3. Image first, biopsy second, operate last. MRI before biopsy avoids post-biopsy oedema confusing the picture; the biopsy track is removed with the tumour, so its position is a surgical decision.

Imaging: what to ask for

Question	Test	Notes
Is this soft tissue lump suspicious?	Ultrasound by an experienced operator	Superficial, small, homogeneous fatty lesions can be watched; anything else goes to MRI
Extent of a limb, trunk or head and neck mass	MRI with contrast (T1, T2/STIR, fat-suppressed post-gadolinium)	Shows compartments, neurovascular bundle, bone and peritumoural oedema; do it before biopsy
Abdominal or retroperitoneal mass	Contrast CT abdomen and pelvis	Fat with thick septa or nodules = well-differentiated liposarcoma; a solid non-fatty nodule within fat = dedifferentiation; MRI if muscle, foramen or vessel involvement is unclear
Lung metastases (all patients)	CT chest	The lung holds about 80% of metastases; a chest radiograph is acceptable only for small low-grade tumours
Myxoid/round cell liposarcoma	CT abdomen–pelvis + whole-spine MRI	Spreads to soft tissue, retroperitoneum and bone marrow without lung disease; PET misses it
Angiosarcoma, leiomyosarcoma, epithelioid/clear cell sarcoma, rhabdomyosarcoma	Add CT abdomen ± nodal assessment ± brain MRI (alveolar soft part sarcoma, angiosarcoma)	Subtype-driven staging
Role of PET-CT in STS	Not routine	Useful for high-grade or ambiguous cases, MPNST in NF1, rhabdomyosarcoma and Ewing sarcoma

Planned: core needle along the future incision**Unplanned: transverse cut, haematoma, contamination**

Core needle (image-guided, several cores, 14–16 G) is the default; avoid FNAC as the only test; incisional biopsy only by the treating team.

Figure 4. The biopsy decides the operation. A single longitudinal track inside the future excision (left) is removed with the tumour. A transverse cut, haematoma or distant drain (right) contaminates more tissue, enlarges the resection or RT field, and can cost a limb.

- **Biopsy rules:** image-guided core needle biopsy with several cores is the default; incisional biopsy only by the team that will operate; never a transverse incision on a limb; no drains far from the wound; avoid FNAC as the sole test (low accuracy for subtype and grade, and a false negative delays care). Tract seeding after core biopsy is rare ([TARPSWG 2021](#)^[3]).
- **Pathology:** diagnosis rests on morphology plus immunohistochemistry and, for many subtypes, a molecular test (FISH, RT-PCR or NGS). Ask for review by a sarcoma pathologist; discordance with the first report is common. Grade with FNCLCC (differentiation + mitoses + necrosis) on adequate tissue; grade predicts metastasis in most subtypes ([Coindre 2001](#)^[4]).
- **Retroperitoneal mass:** percutaneous posterior (retroperitoneal) core biopsy is safe and does not raise local recurrence; open or laparoscopic biopsy is avoided. Upfront surgery without biopsy is acceptable for a classic well-differentiated liposarcoma when no preoperative therapy is planned.
- **Prognostic tools:** AJCC 8th edition stage for limb and trunk; for individual risk use nomograms (Sarculator for extremity STS, [Callegaro 2016](#)^[5]; histology-specific retroperitoneal nomogram, [Gronchi 2013](#)^[6]). A 10-year metastasis risk of about 40% or more marks "high risk" for perioperative chemotherapy discussions.

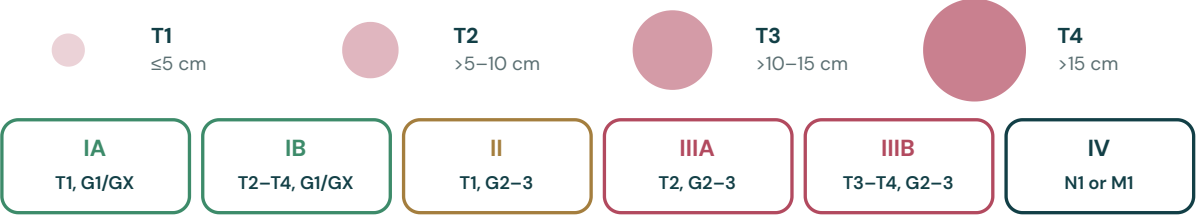
FNCLCC grade = differentiation (1–3) + mitoses (1–3) + necrosis (0–2)

G1
score 2–3

G2
score 4–5

G3
score 6–8

AJCC 8th edition, limb and trunk: size (T) + grade decide the stage



Retroperitoneum: same T sizes, but N1 is stage IIIB, and a histology-specific nomogram predicts better than TNM.
Bone: separate AJCC system (appendicular/trunk 8 cm cut-off; spine and pelvis by segments); grade is low or high.

Figure 5. Grade and size are the stage. Grade predicts metastasis better than any other single factor in most subtypes; nodal spread is rare and makes limb/trunk sarcoma stage IV. Nomograms such as Sarculator add age, subtype and site.

04 Biomarkers that change treatment

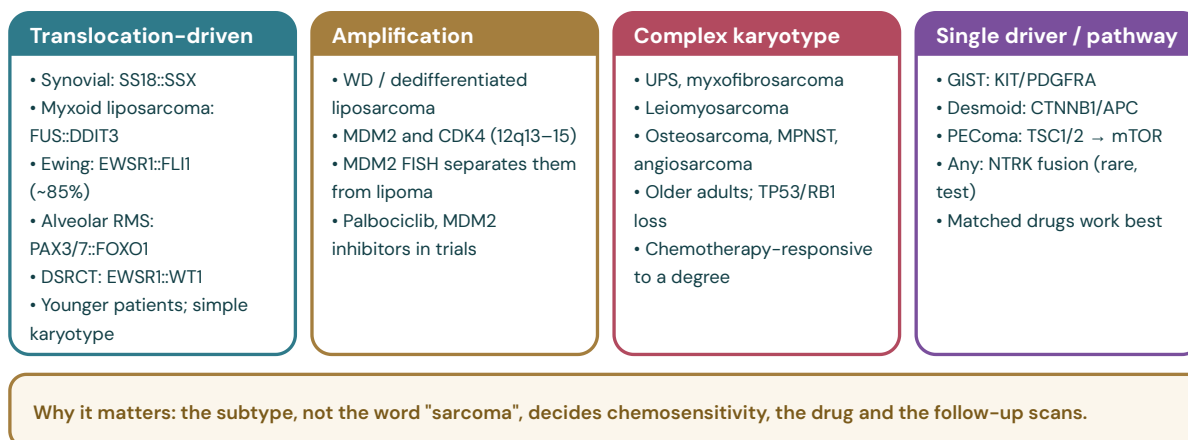


Figure 6. Four families by genetics. Translocation sarcomas affect younger people and carry diagnostic fusions; amplified MDM2/CDK4 marks well-differentiated and dedifferentiated liposarcoma; complex-karyotype sarcomas dominate in older adults; a few have one targetable driver.

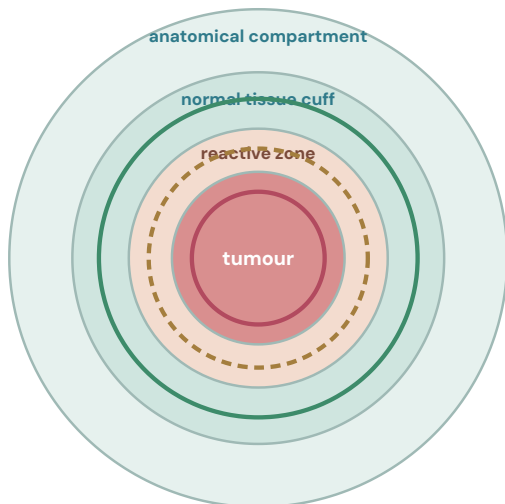
- **Molecular testing is diagnostic first:** in sarcoma the fusion or amplification usually confirms the subtype rather than selecting a drug. Use FISH or RT-PCR for a suspected fusion, or an RNA-based NGS panel that detects many fusions at once.
- **MDM2 amplification** (FISH) separates atypical lipomatous tumour / well-differentiated liposarcoma from lipoma, and dedifferentiated liposarcoma from UPS; any "UPS" in the retroperitoneum should be tested.
- **NTRK fusions** are rare in adult sarcoma but common in infantile fibrosarcoma; TRK inhibitors give high, durable response rates in any tumour type ([Drilon 2018](#)^[7], [Doebele 2020](#)^[8]). Screen with pan-TRK IHC and confirm with RNA NGS.
- **HLA-A*02 and MAGE-A4:** required for afamitresgene autoleucel (engineered T cells) in synovial sarcoma and myxoid/round cell liposarcoma ([SPEARHEAD-1](#)^[9]). Not yet available in India; relevant for trial referral.
- **Grade, not just subtype:** a few entities are not graded (angiosarcoma, epithelioid sarcoma, alveolar soft part, clear cell), and grade from a small core can under-call; the resection specimen re-grades the tumour.
- **PD-L1 is not a useful selector;** response to checkpoint inhibitors is seen mainly in UPS, dedifferentiated liposarcoma, alveolar soft part sarcoma and cutaneous angiosarcoma ([SARCO28](#)^[10], [Alliance A091401](#)^[11]).

Fusion or alteration	Tumour
SS18::SSX1/2/4	Synovial sarcoma
FUS::DDIT3 (rarely EWSR1::DDIT3)	Myxoid liposarcoma
MDM2/CDK4 amplification	Well-differentiated / dedifferentiated liposarcoma
EWSR1::FLI1, EWSR1::ERG	Ewing sarcoma
CIC::DUX4, BCOR::CCNB3	Undifferentiated round cell sarcomas
PAX3/7::FOXO1	Alveolar rhabdomyosarcoma

Fusion or alteration	Tumour
<i>EWSR1::WT1</i>	Desmoplastic small round cell tumour
<i>ASPSCR1::TFE3</i>	Alveolar soft part sarcoma
<i>EWSR1::ATF1</i>	Clear cell sarcoma
<i>COL1A1::PDGFB</i>	Dermatofibrosarcoma protuberans (imatinib-responsive)
<i>NAB2::STAT6</i>	Solitary fibrous tumour
<i>ETV6::NTRK3</i>	Infantile fibrosarcoma
<i>MYC</i> amplification	Radiation-associated angiosarcoma
<i>SMARCB1</i> (INI1) loss	Epithelioid sarcoma
<i>TSC1/2</i> loss	PEComa

05 Local therapy: surgery & radiotherapy

Soft tissue sarcoma: surgery



Intralesional

Through tumour: gross residual; local relapse very likely. Avoid.

Marginal

Through the reactive zone (shelling out a "lipoma"): satellites left; relapse common.

Wide

Whole tumour en bloc with a cuff of normal tissue: the standard, usually with RT.

Radical

Whole compartment or amputation: rarely needed today.

Figure 7. Margins (Enneking/MSTS). A wide margin through normal tissue is the aim; fascia, periosteum and adventitia are good barriers, so a thin margin against an intact fascial plane may be adequate. Re-excision after an unplanned "shell-out".

- **Wide en bloc excision** through normal tissue, never through the tumour or its pseudocapsule, is the cornerstone. Limb-sparing surgery with RT gives the same survival as amputation ([Rosenberg 1982^{\[12\]}](#)); amputation is now needed in under 5–10%.
- **Adequate margin** is not one number: about 1 cm of fat or muscle, or an intact fascial plane, periosteum or vessel adventitia, is usually enough with RT. Planned close margins next to a preserved nerve or vessel are acceptable after preoperative RT.
- **Unplanned excision:** re-image with MRI and re-excise the scar and bed; residual tumour is found in about half ([Noria 1996^{\[13\]}](#)). If re-excision would cost function, RT can secure control in many.
- **Surgery alone** is reasonable for superficial, ≤ 5 cm, low-grade tumours with clear margins, and for selected small intramuscular tumours resected with a wide cuff ([Yang 1998^{\[14\]}](#)).
- **Lymph nodes:** dissect only clinically or radiologically involved nodes; sentinel node biopsy is not routine, even in higher-risk subtypes.
- **Reconstruction:** plan flaps with plastic surgery up front, especially after preoperative RT; vascular grafts and nerve repair are part of limb salvage.

Soft tissue sarcoma: radiotherapy

Feature	Preoperative RT (preferred)	Postoperative RT
Dose	50 Gy in 25 fractions	60–66 Gy (higher if margin positive)
Volume	Smaller: tumour seen on MRI	Larger: operative bed, scar, drains
Wound complications	More: ~35% (mostly lower limb)	Fewer: ~17%
Late fibrosis, oedema, stiffness	Less: grade ≥2 fibrosis ~32%	More: ~48%, permanent
Surgery	4–6 weeks after RT	RT starts 4–6 weeks after surgery
Best for	Most grade 2–3 or large tumours	Infiltrative myxofibrosarcoma; wound risk

Figure 8. Timing trades early wound problems for late limb function. In the NCIC SR2 trial local control and survival were the same; preoperative RT caused more wound complications, postoperative RT more permanent fibrosis, oedema and joint stiffness. IMRT reduces both.

Question	Answer	Evidence
Does RT add to surgery?	Yes for local control in most tumours >5 cm or deep, grade 2–3; no survival gain	Yang 1998 ^[14] , Beane 2014 ^[15] , Pisters 1996 ^[16]
Before or after surgery?	Preoperative preferred for most: same control and survival, fewer permanent late effects; more wound complications	NCIC SR2 ^[17]
Technique	IMRT with daily image guidance; better local control and less dermatitis than 3D-conformal RT	Folkert 2014 ^[18]
Volume	Preoperative: tumour + about 1.5 cm radially and 3–4 cm along the muscle, including T2 oedema where feasible	RTOG 0630 ^[19]
Dose	Preop 50 Gy/25; postop 60 Gy (negative margin), 66 Gy (positive margin), up to 75 Gy (gross residual). No routine boost after preoperative RT with a positive margin	ASTRO 2021 guideline
Shorter courses?	Moderate hypofractionation (15 fractions) and 5-fraction schedules show promising control with acceptable wound rates; still investigational	HYPORT-ST5 ^[20] , Kalbasi 2020 ^[21]
Myxoid liposarcoma	Exceptionally radiosensitive; 36 Gy gave 91% extensive pathological response and no local failures in a phase 2 trial	DOREMY ^[22]
Brachytherapy	Short overall time; lower local control than IMRT in series; reserved for selected cases with expertise	Pisters 1996 ^[16]
Definitive RT	For medically inoperable or unresectable tumours when amputation is declined	Lower control; higher doses

Retroperitoneal sarcoma

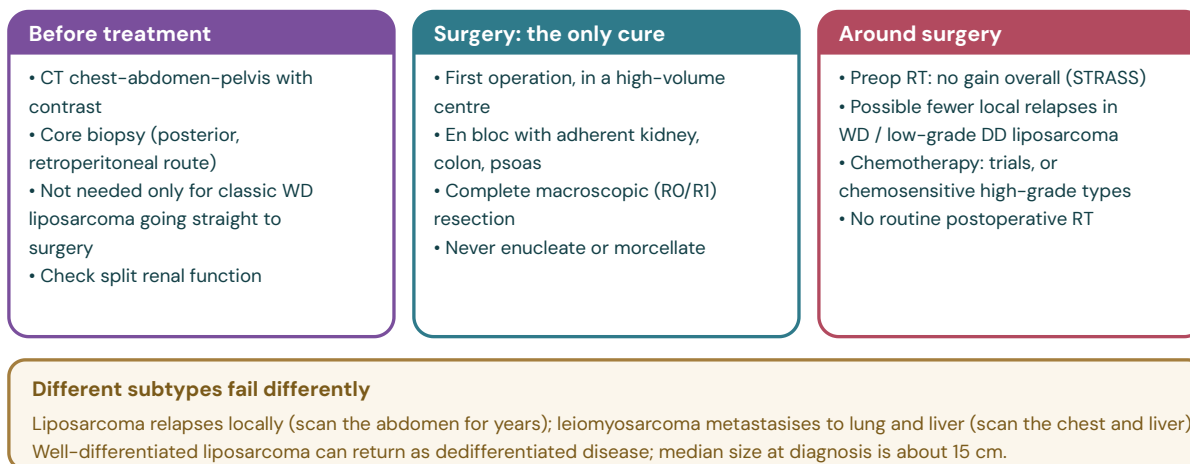


Figure 9. Retroperitoneal sarcoma is a surgical disease that is won or lost at the first operation. A compartmental, organ–inclusive resection by an experienced team gives the best local control; outcomes are better in reference centres.

- **Complete macroscopic resection at the first operation** is the only curative treatment; RO is rarely possible, R1 is acceptable. Extended (compartmental) resection with adherent organs improves local control in liposarcoma ([Bonvalot 2009](#)^[23]).
- **Preoperative RT** did not improve abdominal recurrence–free survival overall in [STRASS](#)^[24]; a possible benefit in well–differentiated and low–grade dedifferentiated liposarcoma makes it an option there, decided at a sarcoma MDT. Postoperative RT is avoided (bowel falls into the bed).
- **Patterns of failure differ by subtype**: liposarcoma recurs locally (often late), leiomyosarcoma metastasises ([Gronchi 2016](#)^[25]). Re–resection of an R2 residuum is considered when morbidity is low.

Head and neck sarcomas

- **Workup**: MRI (with CT for bone detail) and a biopsy planned with the operating surgeon; the narrow spaces make wide margins harder than in limbs.
- **Soft tissue sarcomas**: resect with as wide a cuff as anatomy allows; adjuvant RT for most high–grade tumours and for low–grade tumours with close or positive margins that cannot be re–excised.
- **Osteosarcoma of the jaw**: wide en bloc resection; re–excise positive margins; RT (± chemotherapy) if margins stay positive. High–grade tumours usually get cisplatin–based chemotherapy as for limb osteosarcoma; low–grade do not.
- **Chondrosarcoma**: often low grade (larynx, skull base); wide excision or voice–sparing partial laryngectomy; protons or carbon ions for unresectable skull–base disease.
- **Rhabdomyosarcoma**: 35–40% of childhood primaries are in the head and neck; chemotherapy with RT is standard for parameningeal sites rather than radical surgery.
- **Angiosarcoma of the scalp and face** (older adults): bruise–like plaques wider than they look; surgery with wide margins and RT to a generous field, taxanes for unresectable disease; checkpoint inhibitors are active.

Radiation–associated and breast sarcomas

- **Criteria**: sarcoma in a previously irradiated field, a different histology from the first cancer, and a latency of more than a few years (at least 3; classically over 5). These sarcomas are usually high grade and carry a

worse outlook, but are curable with wide resection.

- **Radiation-associated breast angiosarcoma:** skin-led, multifocal, often wider than imaging suggests. Treatment is radical resection of all irradiated skin where possible, with reconstruction; re-irradiation (often hyperfractionated) and taxanes are used in selected cases. After breast-conserving therapy, the 10-year incidence is around 0.16% ([Wiener 2023](#)^[26]): no reason to withhold breast RT.
- **Primary breast sarcomas** are treated like limb STS (wide excision; axillary surgery only for involved nodes). Phyllodes tumours and desmoids are separate diseases.

o6 Systemic therapy: indications & options

Soft tissue sarcoma: chemotherapy and immunotherapy around surgery

- **Paediatric-type sarcomas** (rhabdomyosarcoma, Ewing sarcoma of soft tissue, extraskeletal osteosarcoma) always receive chemotherapy as part of a protocol.
- **Adult-type STS**: perioperative chemotherapy is controversial; offer it only to fit patients with high-risk tumours (>5 cm, deep, grade 2–3, ideally chemosensitive types such as synovial sarcoma, myxoid/round cell liposarcoma, UPS, high-grade myxofibrosarcoma), after shared decision-making.
- **Evidence**: the meta-analysis of 18 trials showed fewer recurrences and an 11% absolute survival gain with doxorubicin + ifosfamide ([Pervaiz 2008](#) ^[27]); the largest single trial was negative ([EORTC 62931](#) ^[28]; [pooled analysis](#) ^[29]), partly because it included small, low-grade and non-limb tumours. Three cycles of epirubicin + ifosfamide were as good as five ([Gronchi 2016](#) ^[30]), and beat "histotype-tailored" regimens ([ISG-STS 1001](#) ^[31], [final report](#) ^[32]), except trabectedin in high-grade myxoid liposarcoma.
- **Sequence**: if given, 3 cycles before surgery (often before or alongside RT) allow response assessment and may ease limb salvage; postoperative chemotherapy is an alternative when surgery came first.
- **Immunotherapy**: in stage III limb UPS (and dedifferentiated/pleomorphic liposarcoma), adding pembrolizumab before, during and after preoperative RT and surgery improved 2-year disease-free survival (67 vs 52%; [SU2C-SARCO32](#) ^[33]). Overall survival is not yet known and grade ≥3 toxicity rose (56 vs 31%); offer after shared decision-making where access allows.
- **Regional approaches** (isolated limb perfusion with TNF-α and melphalan, regional hyperthermia with chemotherapy) can save limbs in selected locally advanced tumours at specialised centres; rarely available in India.

Advanced or metastatic soft tissue sarcoma

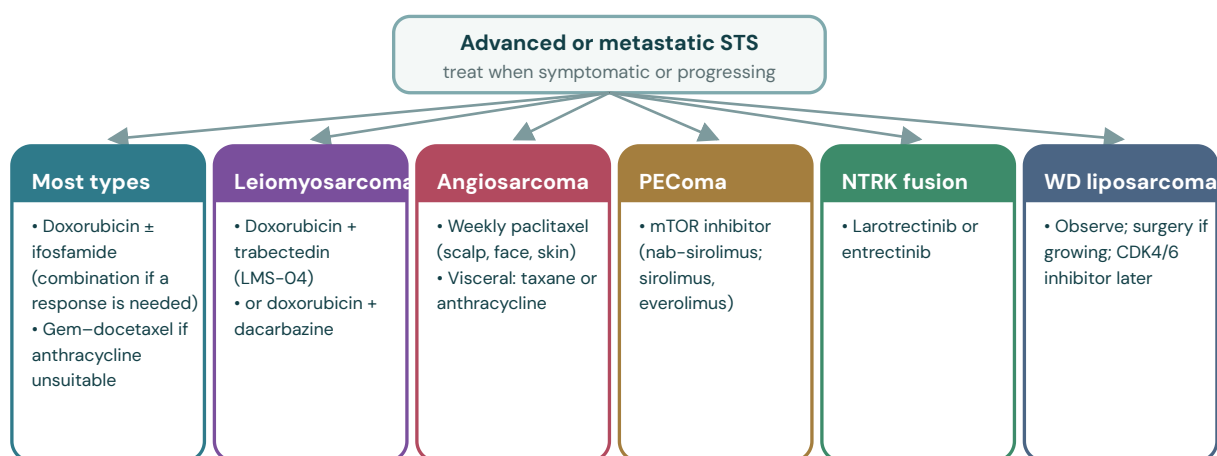


Figure 10. Histology chooses the first drug. Anthracyclines remain the backbone; combinations raise response but not clearly survival (EORTC 62012), except doxorubicin–trabectedin in leiomyosarcoma (LMS-O4). No doses are given here.

- **When to start**: metastatic STS is, with few exceptions, incurable; start systemic therapy for symptoms, substantial burden or clear progression. Slow, low-volume disease (especially well-differentiated liposarcoma, some solitary fibrous tumours) may be watched with scans.

- **First line:** doxorubicin alone remains the reference. Adding ifosfamide doubled response (26 vs 14%) and lengthened PFS (7.4 vs 4.6 months) without a significant survival gain ([EORTC 62012](#)^[34]): use the combination when shrinkage is the goal (symptoms, borderline resectable). Gemcitabine–docetaxel was not better and was more toxic ([GeDDis](#)^[35]). Olaratumab was positive in phase 2 but negative in phase 3 ([Tap 2016](#)^[36]): a lesson in confirming phase 2 signals.
- **Leiomyosarcoma:** doxorubicin + trabectedin then trabectedin maintenance improved PFS (12 vs 6 months) and overall survival (33 vs 24 months) but grade ≥3 toxicity was 97% ([LMS-04](#)^[37], [LMS-04 OS](#)^[38]); doxorubicin + dacarbazine is an alternative.
- **Angiosarcoma:** weekly paclitaxel first for cutaneous, scalp and face disease ([ANGIOTAX](#)^[39]); doxorubicin and paclitaxel have similar activity ([Italiano 2012](#)^[40]). Checkpoint inhibitors work particularly in cutaneous head and neck angiosarcoma.
- **PEComa:** mTOR inhibition (nab–sirolimus, [AMPECT](#)^[41]; sirolimus or everolimus where unavailable).
- **Later lines:** pazopanib (non–adipocytic STS; PFS 4.6 vs 1.6 months, no OS gain; [PALETTE](#)^[42]), trabectedin (L–type sarcomas; [Demetri 2016](#)^[43], [T-SAR](#)^[44]), eribulin (overall survival gain in liposarcoma; [Schöffski 2016](#)^[45]), gemcitabine–docetaxel ([SARC 002](#)^[46]), CDK4/6 inhibitor for indolent dedifferentiated liposarcoma ([Dickson 2016](#)^[47]), checkpoint inhibitors for UPS and selected others.

Leiomyosarcoma	Gem–docetaxel → trabectedin, pazopanib, eribulin, dacarbazine
Liposarcoma (DD, pleomorphic)	Gem–docetaxel → eribulin (OS gain); CDK4/6 inhibitor if indolent; no pazopanib
Myxoid / round cell liposarcoma	Trabectedin (targets FUS::DDIT3); eribulin; afami–cel if HLA/MAGE–A4 fit
Synovial sarcoma	Ifosfamide → pazopanib, trabectedin; afami–cel (HLA–A*02, MAGE–A4)
UPS, myxofibrosarcoma	Gem–docetaxel → pazopanib; pembrolizumab or nivolumab–ipilimumab
Angiosarcoma	Taxane ↔ anthracycline; then gemcitabine, pazopanib, checkpoint inhibitors (scalp/face)
MPNST	Ifosfamide/anthracycline → pazopanib; trials
Alveolar soft part, clear cell	Checkpoint inhibitors (atezolizumab in ASPS); chemotherapy rarely works

Figure 11. After the first line, the subtype map matters even more. Trial enrolment is preferred at every step; pazopanib is not used for adipocytic sarcomas, and responses to later lines are modest, so quality of life leads the decision.

Uncommon subtypes that behave differently

Subtype	Who and where	Key point
Alveolar soft part sarcoma (<i>ASPSCR1::TFE3</i>)	Adolescents and young adults, more often women; thigh, head and neck; brain metastases	Indolent: observe limited stable disease; atezolizumab (Chen 2023 ^[48]) or pembrolizumab if progressing; pembrolizumab + axitinib if bulky or symptomatic (Wilky 2019 ^[49]); brain MRI at staging
Epithelioid sarcoma (<i>SMARCB1/INI1</i> loss)	Young adults; distal (hand, forearm) or proximal type	Nodal spread; mimics granuloma or ulcer; anthracycline first if unresectable; tazemetostat (EZH2 inhibitor) where approved

Subtype	Who and where	Key point
Clear cell sarcoma (<i>EWSR1::ATF1</i>)	Young adults; tendons and aponeuroses of foot and ankle	Melanoma-like (S100, HMB45) but no BRAF; nodal spread; chemotherapy rarely works: trials
Extraskeletal myxoid chondrosarcoma (<i>NR4A3</i> fusion)	Middle-aged men; thigh	Indolent; resect primary; observe limited metastases; VEGFR TKIs (sunitinib, pazopanib) if progressing
Epithelioid haemangioendothelioma (<i>WWTR1::CAMTA1</i>)	Liver, lung, bone; any age	Often multifocal and slow; surveillance first; systemic therapy only for progression or symptoms
Inflammatory myofibroblastic tumour (ALK fusion in about half)	Children and young adults; lung, abdomen	Resect; ALK inhibitors (crizotinib) for unresectable ALK-positive disease
Desmoplastic small round cell tumour (<i>EWSR1::WT1</i>)	Adolescent and young men; abdominal and pelvic peritoneum	Ewing-type chemotherapy, debulking surgery and whole-abdomen RT in selected; poor prognosis

Local treatment of metastases

Favours lung metastasectomy

- All disease removable (RO likely)
- Few nodules (generally under 5)
- Disease-free interval >12–18 months
- Primary controlled; no extrathoracic disease
- Fit for surgery; VATS often possible

Argues against

- Many or bilateral diffuse nodules
- Short interval or rapid growth
- Pleural effusion or bulky nodes
- Uncontrolled primary or other sites
- Option: SBRT, ablation, systemic therapy

In selected patients about a third are alive at 5 years after pulmonary metastasectomy.

If unsure, rescan after 6–8 weeks and let the biology declare itself before operating.

Figure 12. Oligometastatic sarcoma can still be cured. Selection, not surgery alone, explains much of the benefit; there is no randomised trial, and adjuvant chemotherapy after metastasectomy is unproven for adult-type sarcomas.

- **Pulmonary metastasectomy** for selected patients: complete resection possible, few nodules, long disease-free interval, controlled primary, no extrathoracic disease. Five-year survival after resection is about 30–40% in series ([Chudgar 2017^{\[50\]}](#)); repeat resection is reasonable for isolated lung recurrence ([Weiser 2000^{\[51\]}](#)).
- **Alternatives:** SBRT gives high local control of lung metastases ([Dhakal 2012^{\[52\]}](#)); radiofrequency ablation, cryoablation; liver resection for isolated leiomyosarcoma metastases.
- **No routine chemotherapy** after complete metastasectomy for adult-type STS outside trials; a 6–8-week rescan or brief chemotherapy can be used to test the tempo of disease before surgery. After resection, chest CT about every 4 months; repeat CT about 6 weeks after a suspected recurrence before re-operating, as more nodules often declare themselves.

Quick reference: tests, treatment by setting, drugs by subtype and side effects

Table A. Subtype tests and what they change

Subtype	Key IHC	Molecular test	What it changes
Well-differentiated / dedifferentiated liposarcoma	MDM2, CDK4 (nuclear)	<i>MDM2</i> amplification (FISH)	Separates atypical lipomatous tumour from lipoma; DD liposarcoma: CDK4/6 inhibitor option later; retroperitoneal follow-up for life
Myxoid liposarcoma	DDIT3 (some labs)	<i>FUS::DDIT3</i> or <i>EWSR1::DDIT3</i>	Very radiosensitive (36 Gy studied in DOREMY); spine MRI and CT abdomen for extrapulmonary spread; trabectedin works
Synovial sarcoma	TLE1, SS18-SSX fusion-specific antibody	<i>SS18::SSX1/2/4</i>	Chemosensitive (ifosfamide); afami-cel if HLA-A*02 and MAGE-A4 positive; may arise anywhere, at any age
Leiomyosarcoma	Desmin, SMA, h-caldesmon	Complex karyotype (no single test)	Doxorubicin + trabectedin first line if fit; scan liver as well as lung
Undifferentiated pleomorphic sarcoma	Diagnosis of exclusion (panel negative)	Exclude dedifferentiated liposarcoma (MDM2), melanoma, carcinoma	Most immunotherapy-responsive common STS; neoadjuvant pembrolizumab + RT option in stage III limb UPS
Angiosarcoma	CD31, ERG, CD34	<i>MYC</i> amplification (radiation-associated)	MYC helps separate post-RT angiosarcoma from atypical vascular lesion; taxane first; immunotherapy for scalp/face
MPNST	Loss of H3K27me3; S100/SOX10 patchy	NF1 (germline in half)	Genetics referral; poorly chemosensitive; pazopanib later
Ewing sarcoma	CD99 (membranous), NKX2.2	<i>EWSR1::FLI1</i> (~85%) or <i>ERG</i> ; FISH or RT-PCR/NGS	Paediatric-type chemotherapy at any age; CIC- and BCOR-rearranged sarcomas are now separate entities
Rhabdomyosarcoma	Desmin, myogenin, MyoD1	<i>PAX3/7::FOXO1</i> (alveolar)	Fusion-positive = higher risk; multimodality protocol with chemotherapy
Osteosarcoma	SATB2 (osteoid matrix on H&E)	Complex karyotype; MDM2 in low-grade central and parosteal types	Low-grade parosteal: surgery alone; conventional high-grade: MAP chemotherapy
Chondrosarcoma	S100	<i>IDH1/2</i> mutation (most conventional)	Surgery; IDH inhibitors in trials; dedifferentiated: osteosarcoma-style chemotherapy
PEComa	HMB45, melan-A + SMA/desmin	<i>TSC1/2</i> loss; <i>TFE3</i> fusion subset	mTOR inhibitor (nab-sirolimus) for advanced disease
Any advanced sarcoma, especially infantile fibrosarcoma, young adults	pan-TRK	<i>NTRK1-3</i> fusions (RNA NGS)	Larotrectinib or entrectinib: high and durable response rates
GIST and desmoid (separate diseases)	KIT/DOG1; nuclear β -catenin	<i>KIT/PDGFR</i> A; <i>CTNNB1/APC</i>	Not treated like sarcoma: imatinib for GIST; observation first for desmoid

Table B. Treatment by setting (no doses)

Setting	Standard	Alternatives / notes	Evidence
Limb/trunk STS, superficial, ≤5 cm, low grade	Wide excision alone	Re-excise if margin positive	NCI 1998 ^[14]
Limb/trunk STS, >5 cm or deep, grade 2–3	Preoperative RT 50 Gy/25 → wide excision 4–6 weeks later	Postoperative RT (60–66 Gy) if surgery first; IMRT preferred	NCIC SR2 ^[17] , Folkert 2014 ^[18]
Stage III limb UPS (or DD/pleomorphic liposarcoma)	Preoperative RT + pembrolizumab → surgery → adjuvant pembrolizumab (shared decision)	Survival data immature; not tested with chemotherapy	SU2C-SARC032 ^[33]
High-risk limb/trunk STS (large, deep, grade 3, chemosensitive type)	Consider 3 cycles of anthracycline + ifosfamide (neoadjuvant or adjuvant), fit patients	Benefit modest and uncertain; synovial and myxoid LPS most responsive	ISG-STS 1001 ^[31] , Pervaiz 2008 ^[27] , EORTC 62931 ^[28]
Myxoid liposarcoma, preoperative	RT 50 Gy (36 Gy de-escalation in trials)	Very radiosensitive	DOREMY ^[22]
Retroperitoneal sarcoma, resectable	Complete en bloc resection in a reference centre	Preoperative RT only for selected WD / low-grade DD liposarcoma; no routine adjuvant therapy	STRASS ^[24] , TARPSWG 2021 ^[3]
Unplanned excision ("whoops")	MRI then re-excision of the scar and bed (± RT)	Residual tumour found in about half	Noria 1996 ^[13]
Oligometastatic lung disease	Metastasectomy (VATS) if all disease removable and interval long	SBRT or ablation if unfit	Chudgar 2017 ^[50] , Dhakal 2012 ^[52]
Metastatic STS, first line	Doxorubicin (single agent if palliation is the goal; + ifosfamide if a response is needed)	LMS: doxorubicin + trabectedin; angiosarcoma: paclitaxel; PEComa: mTOR; NTRK: TRK inhibitor	EORTC 62012 ^[34] , LMS-O4 ^[38] , ANGIOTAX ^[39]
Osteosarcoma, localised (high grade)	Age <40: MAP 10 weeks → wide resection → MAP to 29 weeks; ≥40: doxorubicin–cisplatin	Poor necrosis: no change of regimen; no adjuvant RT after complete resection	MIOS ^[53] , EURAMOS-1 ^[54]
Ewing sarcoma, localised	VDC/IE every 14 days (<18; 14 or 21 days ≥18) × 12 weeks → surgery or RT → 14–17 cycles in total	RT with chemotherapy (no doxorubicin during RT); adults: same protocol at full intensity	INT-0091 ^[55] , AEWS0031 ^[56] , Euro Ewing 2012 ^[57]
Conventional chondrosarcoma	Surgery (curettage for grade 1 limb; wide resection otherwise)	RT for unresectable skull base/axial (high dose, often protons)	ESMO–EURACAN–GENTURIS

Table C. Drugs by subtype in advanced soft tissue sarcoma (no doses)

Subtype	First line	Later lines	Avoid / note
Most anthracycline-sensitive types (UPS, synovial, pleomorphic LPS, myxofibrosarcoma)	Doxorubicin ± ifosfamide	Gemcitabine–docetaxel; pazopanib; trabectedin; immunotherapy (UPS)	Combination only when a response is needed (more toxicity, no clear OS gain)
Leiomyosarcoma (uterine and non-uterine)	Doxorubicin + trabectedin, or doxorubicin + dacarbazine	Gemcitabine–docetaxel, trabectedin, pazopanib, eribulin	Check liver as well as lung on scans

Subtype	First line	Later lines	Avoid / note
Liposarcoma, dedifferentiated/pleomorphic	Doxorubicin	Gemcitabine–docetaxel → eribulin; CDK4/6 inhibitor if indolent	No pazopanib in adipocytic sarcoma
Liposarcoma, myxoid/round cell	Doxorubicin (± ifosfamide)	Trabectedin; eribulin; afami–cel if eligible	Image spine and abdomen
Synovial sarcoma	Doxorubicin ± ifosfamide	Ifosfamide; pazopanib; trabectedin; afami–cel	HLA–A*02 typing and MAGE–A4 IHC to check cell–therapy eligibility
Angiosarcoma	Weekly paclitaxel (cutaneous/scalp); taxane or doxorubicin (visceral)	Switch class; gemcitabine; pazopanib; checkpoint inhibitors	Radiation–associated breast angiosarcoma: surgery is the main treatment when localised
MPNST	Doxorubicin + ifosfamide	Pazopanib	NF1 genetics; low response rates
PEComa	nab–sirolimus (or sirolimus/everolimus)	Chemotherapy has little activity	Hyperglycaemia, stomatitis, pneumonitis
NTRK fusion–positive (any)	Larotrectinib or entrectinib	Repotrectinib for resistance	Test with RNA NGS where possible
Alveolar soft part sarcoma	Observe if limited and stable; atezolizumab or pembrolizumab if progressing; + axitinib if bulky	Pazopanib, sunitinib	Chemotherapy ineffective; brain MRI

Table D. Managing common side effects of sarcoma drugs

Drug	Main problems	Check / prevent	Act on
Doxorubicin	Cardiomyopathy (cumulative), mucositis, alopecia, myelosuppression, extravasation injury	Echo or MUGA before; track lifetime dose; central line if vesicant risk	Breathlessness, oedema, falling ejection fraction: stop; cardiology
Ifosfamide	Encephalopathy, haemorrhagic cystitis, proximal tubulopathy (Fanconi), myelosuppression	Mesna, hydration, urine for blood; renal function, phosphate, bicarbonate	Confusion or drowsiness: stop infusion; methylene blue per protocol
Trabectedin	Transaminitis, neutropenia, rhabdomyolysis, fatigue	Central line; dexamethasone premedication; LFTs and CK each cycle	Rising CK or bilirubin: delay or reduce
Gemcitabine–docetaxel	Myelosuppression, fluid retention, pneumonitis, nail changes	Growth–factor support; steroid premedication for docetaxel	New cough or breathlessness: exclude pneumonitis
Pazopanib	Hepatotoxicity, hypertension, diarrhoea, hair depigmentation, pneumothorax with lung metastases	LFTs at 3, 5, 7, 9 weeks then monthly; BP; caution with many lung metastases	ALT >3× ULN: interrupt
Eribulin, paclitaxel	Neuropathy, neutropenia	Ask about numbness every cycle	Grade 2 neuropathy: delay/reduce
Pembrolizumab, nivolumab–ipilimumab	Immune–related colitis, hepatitis, pneumonitis, endocrine	TSH, cortisol, LFTs; patient alert card	Steroids by grade; hold drug

Drug	Main problems	Check / prevent	Act on
Afamitresgene autoleucel	Cytokine release syndrome, cytopenias, (rarely) neurotoxicity	Lymphodepletion in a cell-therapy centre	Fever after infusion: CRS protocol (tocilizumab)
High-dose methotrexate (osteosarcoma)	Acute kidney injury, mucositis, hepatitis	Hydration, urine alkalinisation, levels, leucovorin rescue; avoid NSAIDs, PPIs, co-trimoxazole	Delayed clearance: glucarpidase
Cisplatin (osteosarcoma)	Ototoxicity, nephrotoxicity, emesis	Audiometry; magnesium	Hearing loss: discuss modification
Cyclophosphamide, ifosfamide, etoposide (Ewing)	Infertility, second leukaemia, cystitis	Sperm banking or ovarian protection before treatment	Long-term survivorship clinic

07 Management algorithms

These decision paths pull together sections 02–06. Colours: teal for favourable paths, purple for intermediate, rose for high-risk paths.

ALGORITHM 1

Soft tissue mass of the limb or trunk

Lump >5 cm, deep, growing, painful or recurrent → ultrasound → MRI with contrast → **core needle biopsy after MRI**, track planned with the surgeon → sarcoma pathologist (subtype, FNCLCC grade, molecular test) → CT chest → sarcoma MDT

LOW RISK

Superficial, ≤5 cm, low grade
→ wide excision alone

Atypical lipomatous tumour (limb) → marginal excision is acceptable

Positive margin → re-excision; RT only if re-excision would cost function

DEEP OR >5 CM, GRADE 2–3

Preoperative IMRT 50 Gy/25
→ wide excision 4–6 weeks later

Stage III UPS → consider pembrolizumab with RT and after surgery

High-risk, chemosensitive, fit
→ consider 3 cycles anthracycline + ifosfamide

Infiltrative myxofibrosarcoma or wound-risk sites → surgery first, postoperative RT 60–66 Gy

SPECIAL SITUATIONS

Unplanned excision elsewhere
→ MRI → re-excision of scar and bed ± RT

Unresectable without amputation → chemotherapy/RT first; amputation if no functional limb can be saved

Inoperable → definitive RT

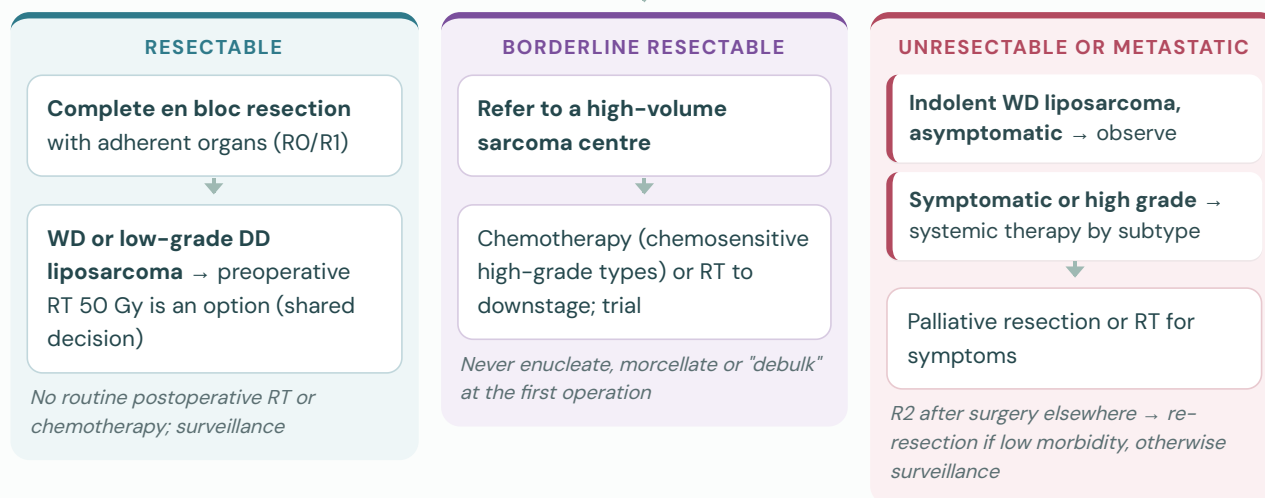
Paediatric-type sarcoma (RMS, Ewing): protocol chemotherapy at any age

All patients: no excision before imaging · no FNAC-only diagnosis · plan flaps up front · physiotherapy and lymphoedema care · fertility counselling before chemotherapy · follow-up by stage (Figure in section 08).

ALGORITHM 2

Retroperitoneal mass

Retroperitoneal mass: CT chest–abdomen–pelvis · testicular examination, AFP, β -hCG, LDH if germ cell or lymphoma possible · **is it extravisceral and unifocal?** → sarcoma likely → percutaneous posterior core biopsy (unless classic WD liposarcoma for upfront surgery) → reference–centre MDT

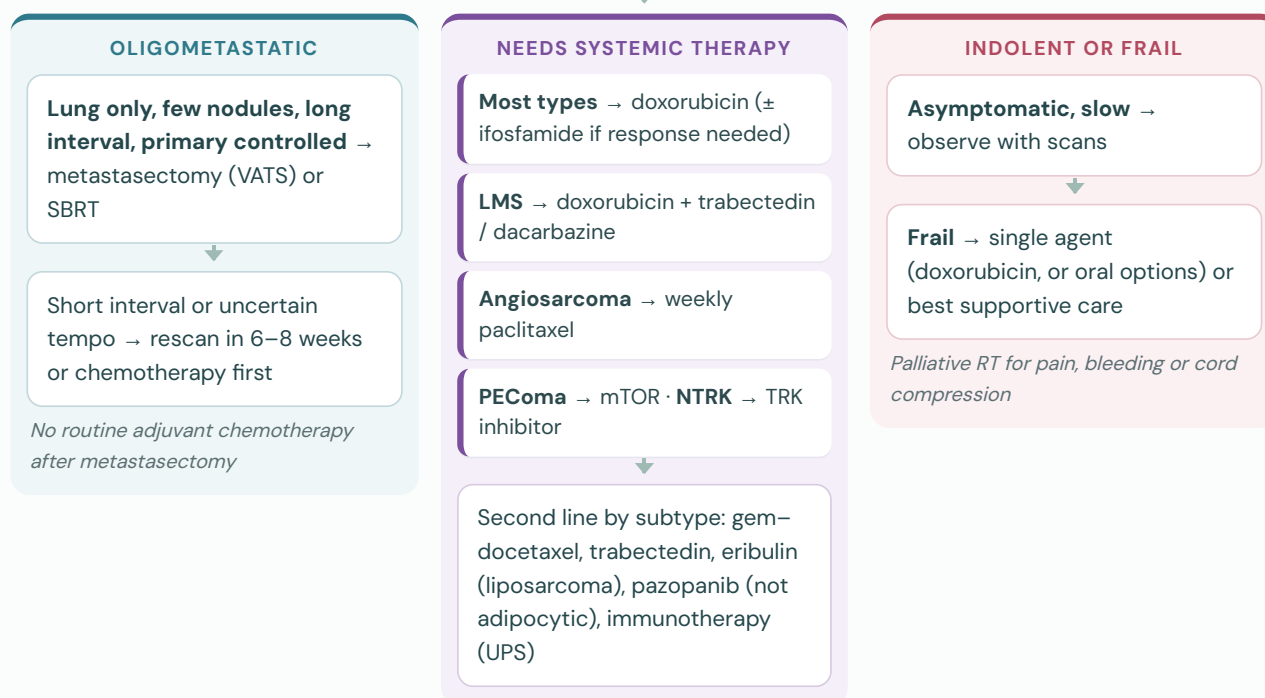


Scan for life in liposarcoma (late local relapse; dedifferentiation can appear years later) · chest and liver imaging in leiomyosarcoma · check renal function before nephrectomy.

ALGORITHM 3

Metastatic soft tissue sarcoma

Metastatic STS: confirm subtype (expert pathology, molecular test, NTRK if relevant) · count and site of metastases · performance status · goals of care · trial?



All patients: cumulative anthracycline dose and echo · fertility · VTE awareness · early palliative care · trial referral at every progression.

o8 Survivorship, follow-up & reducing recurrence

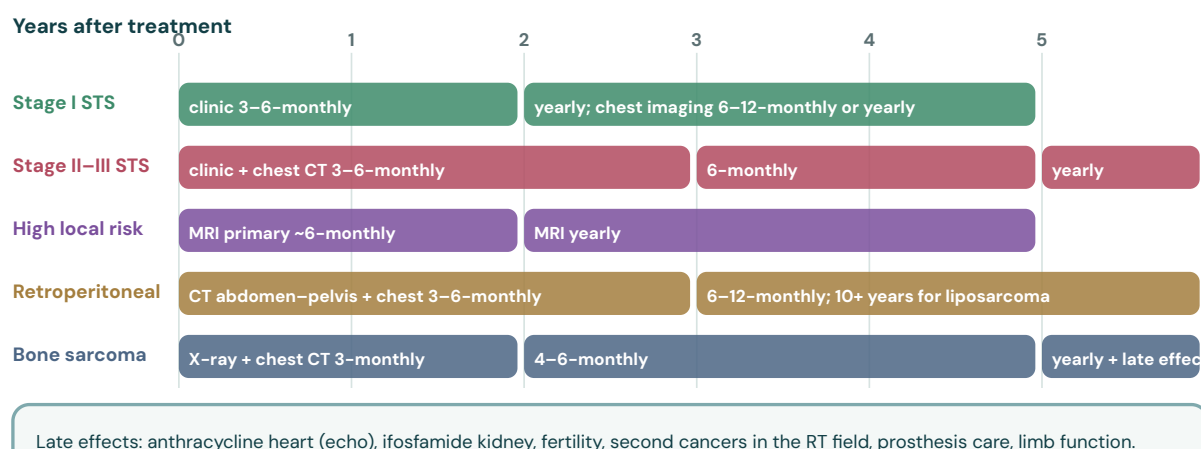


Figure 13. Surveillance is front-loaded because most relapses occur in the first 2–3 years; the aim is to catch lung metastases and local relapses while still resectable. Intervals are approximate (UpToDate, ESMO, NCCN); MRI is preferred for the primary site.

Follow-up protocol (UpToDate, ESMO, NCCN; adapt to resources)

Group	Visits and imaging	Notes
Stage I STS (limb/trunk)	History and examination every 3–6 months for 2 years, then yearly; chest imaging periodically	Patients should report a new lump in or near the scar
Stage II–III STS	Examination and chest CT every 3–6 months for 2–3 years, then 6-monthly to 5 years, then yearly	Most relapses occur within 2–3 years
Positive margins or hard-to-examine sites	MRI of the primary site about 6-monthly for 2 years, then yearly to 5 years	MRI preferred to CT (sensitivity, no radiation)
Retroperitoneal sarcoma	CT abdomen–pelvis and chest 3–6-monthly for 2–3 years, then 6–12-monthly; beyond 10 years for liposarcoma	Liposarcoma recurs late; leiomyosarcoma metastasises early

- **Late effects:** anthracycline cardiomyopathy (echo at the end of treatment and periodically), ifosfamide and cisplatin kidney damage (tubular loss of phosphate and magnesium), hearing loss after cisplatin, infertility and early menopause after alkylators, second cancers (therapy-related leukaemia, sarcoma in RT fields), and RT fibrosis, oedema, fracture and growth disturbance.
- **Function:** physiotherapy from day one after limb surgery; lymphoedema care; prosthetic and orthotic support; return-to-school and work plans. Many young survivors walk, run and play sport.
- **Reducing risk:** no tobacco; maintain weight and activity; avoid unnecessary CT in young survivors; genetic counselling for TP53, NF1 and RB1 families (cascade testing).
- **Psychosocial:** fear of recurrence, body image after amputation or rotationplasty, and financial toxicity (long treatment away from home) are common; involve social workers early.

SHARE WITH PATIENTS: FOLLOW-UP AND LIFE AFTER TREATMENT

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

Once sarcoma treatment is finished, follow-up isn't needed?

A child cured of sarcoma will never develop another cancer?

A child treated for bone cancer will never walk or play normally again?

Osteosarcoma always needs amputation?

09 Landmark trials

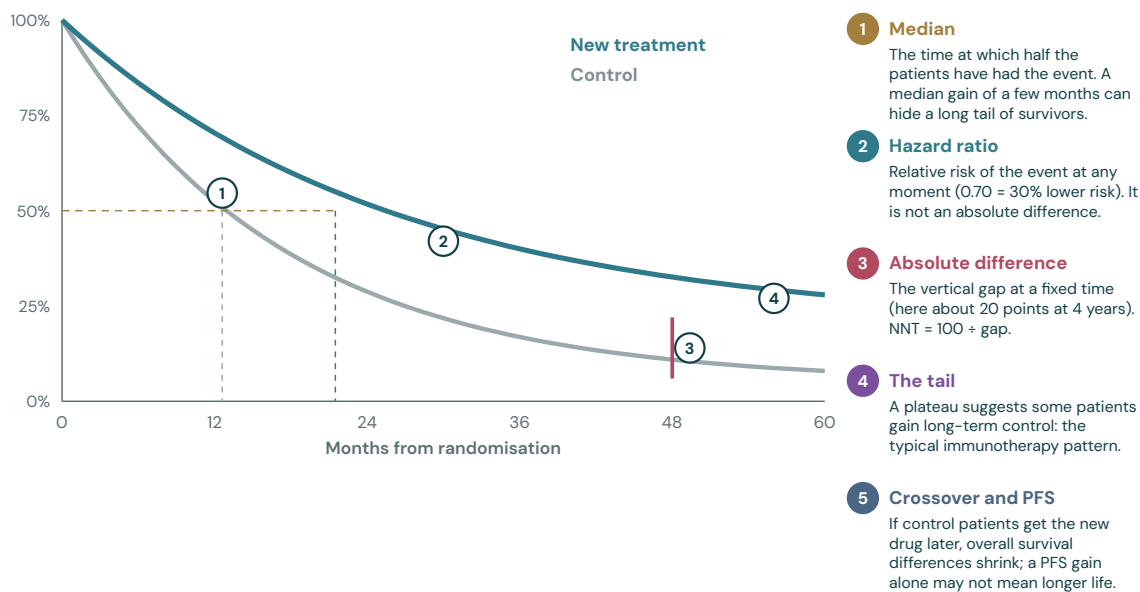


Figure 14. How to read a survival curve (illustrative). Use the absolute gap at a fixed time and overall survival, not the median or PFS alone, when weighing benefit against toxicity and cost.

- [NCI \(Rosenberg 1982\)](#)^[12]: amputation vs limb-sparing surgery + RT → same survival → limb salvage became standard.
- [NCI \(Yang 1998\)](#)^[14] and [MSKCC \(Pisters 1996\)](#)^[16]: RT after limb-sparing surgery → better local control, no survival difference → RT for most large, deep, high-grade tumours.
- [NCIC SR2](#)^[17]: preoperative vs postoperative RT → equal local control and survival; wound complications 35 vs 17%, late fibrosis lower preoperatively → preoperative RT for most.
- [RTOG 0630](#)^[19]: image-guided preoperative RT to reduced volumes → few marginal failures and late grade ≥ 2 toxicity about 10% → smaller margins are safe.
- [STRASS](#)^[24]: preoperative RT + surgery vs surgery for retroperitoneal sarcoma → no overall gain; possible benefit in liposarcoma → not routine.
- [Pervaiz 2008](#)^[27] vs [EORTC 62931](#)^[28]: meta-analysis suggests a survival benefit from doxorubicin + ifosfamide; the largest trial was negative → individualised, high-risk-only use.
- [ISG-ST5 1001](#)^[31]: 3 cycles of epirubicin + ifosfamide beat histotype-tailored regimens in high-risk STS → standard regimen when chemotherapy is used.
- [SU2C-SARCO32](#)^[33]: pembrolizumab with preoperative RT and surgery in stage III limb UPS/liposarcoma → 2-year DFS 67 vs 52% → first immunotherapy for localised sarcoma; OS awaited.
- [EORTC 62012](#)^[34]: doxorubicin ± ifosfamide first line → higher response and PFS, no significant OS gain → single-agent doxorubicin when palliation is the goal.
- [LMS-04](#)^[37]: doxorubicin + trabectedin in leiomyosarcoma → PFS and OS gains → new first-line standard for fit patients.
- [PALETTE](#)^[42], [eribulin trial](#)^[45], [trabectedin trial](#)^[43]: modest later-line gains; histology decides which.
- [Larotrectinib \(2018\)](#)^[7]: tumour-agnostic TRK inhibition → high durable responses → test for NTRK fusions.

10 Practice pearls & pitfalls

- Any lump larger than a golf ball, deep to the fascia or growing deserves an MRI before a knife.
- Do not shell out a "lipoma" in a minor theatre: a well-differentiated liposarcoma in the thigh can be indistinguishable to the hand, and an unplanned excision makes the definitive operation and RT field larger.
- Biopsy after MRI, with a core needle, along the line of the future incision; tell the radiologist where the surgeon will cut.
- A benign FNAC report does not exclude sarcoma.
- Ask for a second opinion from a sarcoma pathologist and a molecular test when the subtype will change treatment; misdiagnosis is common outside reference centres.
- Preoperative RT means more early wound problems but better long-term function; warn the patient and involve plastic surgery.
- Myxoid liposarcoma behaves unlike other sarcomas: very radiosensitive, metastasises to spine, retroperitoneum and soft tissue, and responds to trabectedin. Image the spine.
- In the retroperitoneum, the first surgeon has the best chance: refer before laparotomy, never enucleate.
- A bruise that will not fade on an irradiated breast is angiosarcoma until a punch biopsy says otherwise.
- Doxorubicin alone is a reasonable first line when the aim is palliation; reserve combinations for when a response is needed.
- Pazopanib is not for liposarcoma; eribulin is.
- Bank sperm or consider ovarian protection before alkylators, cisplatin or pelvic RT; it is often forgotten in the rush to start.
- In India, long treatment far from home drives abandonment: plan travel, lodging and financial support (PM-JAY, state schemes) at diagnosis.

11 Case vignettes: lines of management

Six cases, written for postgraduates and practising clinicians. Read the presentation, decide on diagnosis, workup and plan, then open the line of management. No doses are given.

CASE 1 Unplanned excision · thigh · UPS

A "lipoma" removed in a minor theatre

52 years, man

Thigh, deep, 8 cm

Margins involved

A 52-year-old shopkeeper had an 8 cm painless thigh lump excised under local anaesthesia at a nursing home as a "lipoma". No imaging was done. Histology: high-grade pleomorphic sarcoma, margins involved. A drain was brought out 10 cm away.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

RESTAGE

MRI of the thigh (residual mass and the contaminated field, including the drain site) and CT chest: no metastases.

2

EXPERT PATHOLOGY

Review with IHC and MDM2 FISH (negative): undifferentiated pleomorphic sarcoma, FNCLCC grade 3.

3

PLAN

Preoperative IMRT 50 Gy to the tumour bed, scar and drain track (larger field than the original tumour would have needed); pembrolizumab with RT and after surgery discussed as for stage III UPS.

4

SURGERY

Re-excision of the scar, drain tract and bed with plastic surgical closure 4–6 weeks after RT; residual tumour found; margins clear.

5

FOLLOW-UP

Clinic and chest CT 3–6-monthly; MRI of the thigh 6-monthly for 2 years.

TEACHING POINTS

- Deep or >5 cm lumps need MRI before any excision.
- An unplanned excision enlarges the definitive surgery and RT field.
- The drain site and scar are contaminated and must be treated.

See: Sections O2, O3, O5 · Algorithm 1 · [Noria 1996](#)^[13], [NCIC SR2](#)^[17], [SU2C-SARCO32](#)^[33]

CASE 2 Retroperitoneal liposarcoma

Abdominal fullness in a 58-year-old woman

58 years, woman

24 cm fatty mass

Solid nodule

A 58-year-old woman has 6 months of abdominal fullness and early satiety. CT: a 24 cm predominantly fatty left retroperitoneal mass displacing the kidney and colon, with a 5 cm solid enhancing nodule in its lower part. No metastases on chest CT.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

RECOGNISE

Fat with a solid nodule = well-differentiated liposarcoma with a dedifferentiated component.

2

BIOPSY

Percutaneous posterior core biopsy of the solid nodule: dedifferentiated liposarcoma, MDM2 amplified.

3

MDT AT A REFERENCE CENTRE

Complete en bloc resection including the left kidney, descending colon and psoas fascia; preoperative RT not offered because the dominant risk is the high-grade component (STRASS showed no overall gain).

4

AFTER SURGERY

R1 resection; no adjuvant therapy; CT every 3–6 months for 3 years, then 6–12-monthly for more than 10 years.

TEACHING POINTS

- Image-guided core biopsy of a retroperitoneal mass is safe.
- The first operation decides local control; organ-inclusive resection is standard.
- Liposarcoma recurs locally and late: long follow-up.

See: Sections 03, 05 · Algorithm 2 · [STRASS^{\[24\]}](#), [Bonvalot 2009^{\[23\]}](#), [Gronchi 2013^{\[6\]}](#)

CASE 3 Myxoid liposarcoma · radiosensitive**A soft thigh swelling in a 34-year-old**

34 years, man

Posterior thigh, 12 cm

FUS::DDIT3

A 34-year-old man has a 12 cm soft, deep posterior thigh mass. MRI: well-defined, T2-bright, lobulated, little fat. Core biopsy: myxoid liposarcoma (FUS::DDIT3 fusion), about 10% round cell component.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

STAGE BY SUBTYPE

CT chest, CT abdomen–pelvis and whole-spine MRI (myxoid liposarcoma spreads to bone marrow, retroperitoneum and soft tissue): all clear.

2

LOCAL THERAPY

Preoperative RT (50 Gy; 36 Gy is under study in DOREMY-type protocols) → marked shrinkage → wide excision with sciatic nerve preserved.

3

SYSTEMIC THERAPY?

High-risk (12 cm, round cell component): anthracycline + ifosfamide or trabectedin discussed; he chooses 3 cycles of anthracycline + ifosfamide after fertility preservation.

4

FOLLOW-UP

Chest CT and spine/abdomen imaging at intervals; recurrence can be late.

TEACHING POINTS

- Myxoid liposarcoma is exceptionally radiosensitive.
- Stage the spine and abdomen, not just the lung.
- Trabectedin is particularly active in this translocation sarcoma.

See: Sections 03–06 · Algorithm 1 · [DOREMY^{\[22\]}](#), [ISG–STS 1001^{\[31\]}](#)

CASE 4 Radiation-associated angiosarcoma**A bruise that will not fade**

64 years, woman

Breast RT 7 years ago

Violet patches

A 64-year-old woman treated with breast-conserving surgery and RT 7 years ago has a violet, bruise-like patch on the treated breast for 2 months, now with small nodules. She was given antibiotics for "cellulitis".

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1 BIOPSY

Multiple punch biopsies from the darkest areas: angiosarcoma, MYC amplified (radiation-associated).

2 EXTENT

Breast MRI and CT chest-abdomen: disease confined to the breast skin and parenchyma, wider than visible.

3 TREATMENT

Mastectomy with excision of all irradiated skin and flap reconstruction; weekly paclitaxel before or after surgery is used in some centres; re-irradiation considered in selected cases.

4 FOLLOW-UP

Close skin examination; local recurrence is common.

TEACHING POINTS

- Persistent bruising or nodules in an irradiated breast need a punch biopsy.
- Resect all irradiated skin where possible.
- The tiny risk of angiosarcoma is not a reason to withhold breast RT.

See: Sections 02, 05, 06 · [Mery 2009](#)^[2], [Wiener 2023](#)^[26], [ANGIOTAX](#)^[39]

CASE 5 Metastatic leiomyosarcoma

Lung and liver nodules after a "fibroid"

47 years, woman

Uterine LMS

Lung + liver metastases

A 47-year-old woman had a hysterectomy for a rapidly growing "fibroid" 18 months ago (uterine leiomyosarcoma). She now has a cough; CT shows 6 lung nodules and 2 liver lesions. ECOG 1. Echo normal.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1 GOALS

Not curable; aim for symptom control and survival with acceptable toxicity.

2 FIRST LINE

Doxorubicin + trabectedin then trabectedin maintenance (LMS-04: longer PFS and OS) with growth-factor support and LFT/CK monitoring; doxorubicin + dacarbazine is an alternative.

3 SECOND LINE

Gemcitabine–docetaxel; later trabectedin, pazopanib, eribulin or dacarbazine.

4 SUPPORTIVE

Early palliative care; fertility not relevant; VTE awareness.

TEACHING POINTS

- Leiomyosarcoma spreads to lung and liver; scan both.
- Doxorubicin + trabectedin is the new first-line standard for fit patients.
- Morcellation of a suspicious fibroid can spread disease.

See: Sections 06, 08 · Algorithm 3 · [LMS-04](#)^[37], [LMS-04 OS](#)^[38], [SARC 002](#)^[46]

CASE 6 Oligometastatic synovial sarcoma

Two lung nodules three years later

29 years, woman

Synovial sarcoma, knee

2 lung nodules

A 29-year-old woman treated 3 years ago for a grade 3 synovial sarcoma near the knee (preoperative RT, wide excision) has two new right-lung nodules (8 and 12 mm) on surveillance CT. Nothing else on PET-CT.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1 SELECTION

Long disease-free interval, 2 nodules, controlled primary, fit: a good metastasectomy candidate.

2 TEMPO CHECK

Repeat CT at 6–8 weeks: no new lesions.

3 SURGERY

VATS wedge resections of both nodules: synovial sarcoma, clear margins.

4 AFTER

No routine adjuvant chemotherapy; chest CT 3-monthly. At a later relapse: ifosfamide-based chemotherapy, pazopanib, trabectedin; HLA-A*02 typing and MAGE-A4 testing for cell-therapy trials.

TEACHING POINTS

- Selected lung oligometastases can be cured by resection.
- A short rescan lets the biology declare itself.
- Synovial sarcoma is relatively chemosensitive and a target for MAGE-A4 cell therapy.

See: Sections 06, 08 · Algorithm 3 · [Chudgar 2017](#)^[50], [SPEARHEAD-1](#)^[9]

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- Cross-checked in October 2026 against 24 UpToDate topic reviews (soft tissue sarcoma presentation and staging; pathogenetic factors; uncommon subtypes; head and neck sarcomas; treatment protocols (doses not used); osteosarcoma epidemiology, diagnosis, chemotherapy and radiotherapy; Ewing sarcoma treatment; surgical resection of pulmonary metastases; multimodality treatment, surgery, radiation techniques and perioperative systemic therapy for limb and trunk sarcoma; retroperitoneal sarcoma presentation and initial management; breast and radiation-associated sarcoma; initial and later-line therapy and local treatment of metastatic sarcoma; bone tumour diagnosis and biopsy; bone sarcoma surgery; Ewing sarcoma pathology, molecular genetics, presentation and staging). Facts only, rewritten in our own words; primary studies cited.

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Educational summary for health professionals, written in our own words from current guidelines and primary trials. No chemotherapy doses

are given. Verify current guidelines, Indian regulatory approvals and individual patient factors before treatment decisions.