

## ONCOLOGY KNOWLEDGE HUB · FOR HEALTH PROFESSIONALS

# Bone 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

### Dr. Haritha Chiramana

MD (Internal Medicine), DM (Medical Oncology)

Senior Medical Oncologist & Hemato-Oncologist

C.R. Reddy Cancer Center, C.R. Reddy Superspeciality Hospital

17/406, Old Post Office Road, near Leela Mahal Road, Nellore, Andhra Pradesh 524003

Phone 0861 232 5344 · WhatsApp +91 79896 42272

info@drharitha.co.in · drharitha.co.in

Dr. Haritha teaches oncology to postgraduates and medical students. Colleges and departments may write to info@drharitha.co.in for teaching sessions.

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**Cite as:** Chiramana H. Bone Sarcoma: a mini review for clinicians. Oncology Knowledge Hub [Internet]. Nellore (India): drharitha.co.in; 2026 [updated 2026 Oct 11]. Available from: <https://drharitha.co.in/professionals/sarcoma> · Free for education with attribution (CC BY-NC-ND 4.0).

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.

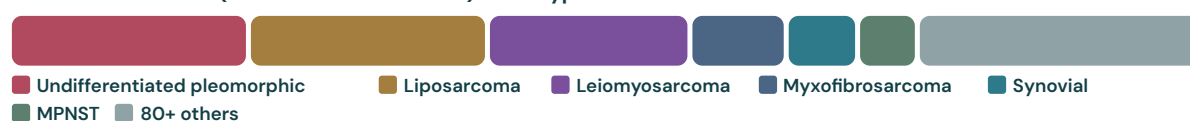
# Bone Sarcoma

From the Sarcoma module · osteosarcoma, Ewing sarcoma and chondrosarcoma · 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<sup>\[1\]</sup>](#)).
- 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 ( <a href="#">Mery 2009<sup>[2]</sup></a> ). |
| 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                                                                                                                 |
|----------------------------|--------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Bone (limb)                | Pain for weeks to months, worse at night, then swelling and limp; pathological fracture in a few | Plain X-ray of the whole bone; MRI of the whole bone; refer before biopsy                                                  |
| Bone (pelvis, spine, ribs) | Deep ache, sciatica, back pain with neurological signs; large soft tissue mass at diagnosis      | MRI ± CT; spinal cord compression is an emergency                                                                          |
| Ewing sarcoma              | Pain and swelling; fever, raised ESR and anaemia in 10–20%, so it is mistaken for osteomyelitis  | If a "bone infection" does not settle or the X-ray shows a permeative lesion with a mass, biopsy for histology and culture |

- **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.
- **Osteosarcoma or osteomyelitis?** Both cause pain and periosteal reaction; send biopsy material for both histology and culture, and never curette a suspected sarcoma as if it were infection.

#### 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)

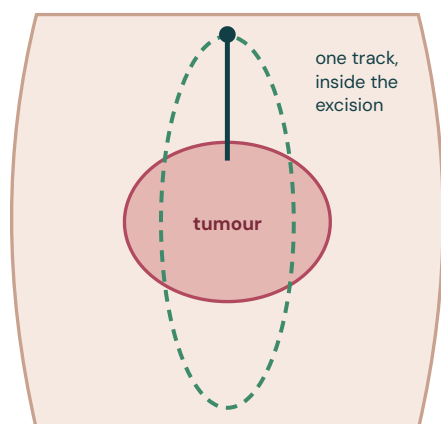
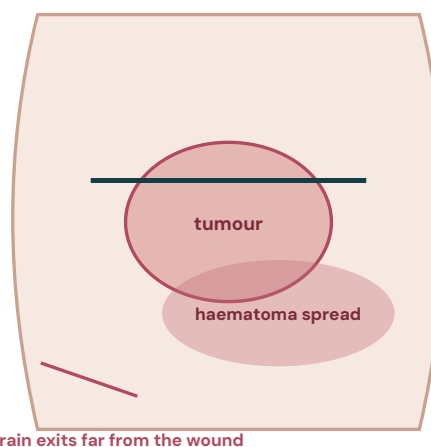
### 5 Sarcoma MDT

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                                                                                                     |
|--------------------------------|-----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|
| Lung metastases (all patients) | CT chest                                                                                      | The lung holds about 80% of metastases; a chest radiograph is acceptable only for small low-grade tumours |
| Bone lesion                    | Plain X-ray in two planes → MRI of the whole bone (skip lesions) → CT for cortical detail     | Recognisable fat in a bone lesion usually means benign                                                    |
| Bone sarcoma staging           | CT chest + PET–CT (or bone scan); bone marrow biopsy in Ewing sarcoma if PET is not available | PET–CT also sets a baseline for response                                                                  |
| 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.

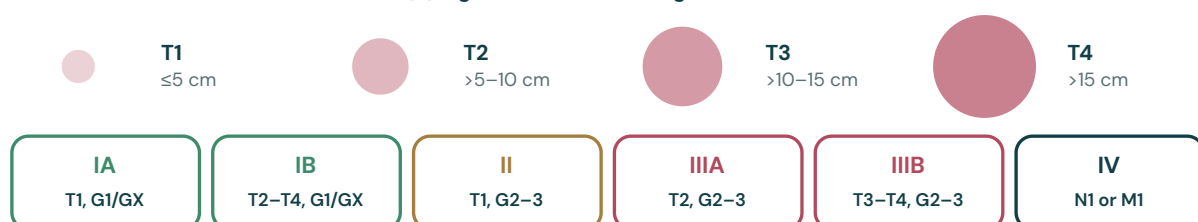
Figure 4. The biopsy decides the operation. A single longitudinal track inside the future excision (left) is removed with the tumour. A transverse cut, haematoma or distant drain (right) contaminates more tissue, enlarges the resection or RT field, and can cost a limb.

- **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<sup>\[3\]</sup>](#)).
- **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<sup>\[4\]</sup>](#)).
- **Bone biopsy** should be done at, or planned with, the centre that will operate: a poorly placed track can turn limb salvage into amputation. Specimens for Ewing sarcoma need fresh or frozen tissue for molecular confirmation.

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



**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

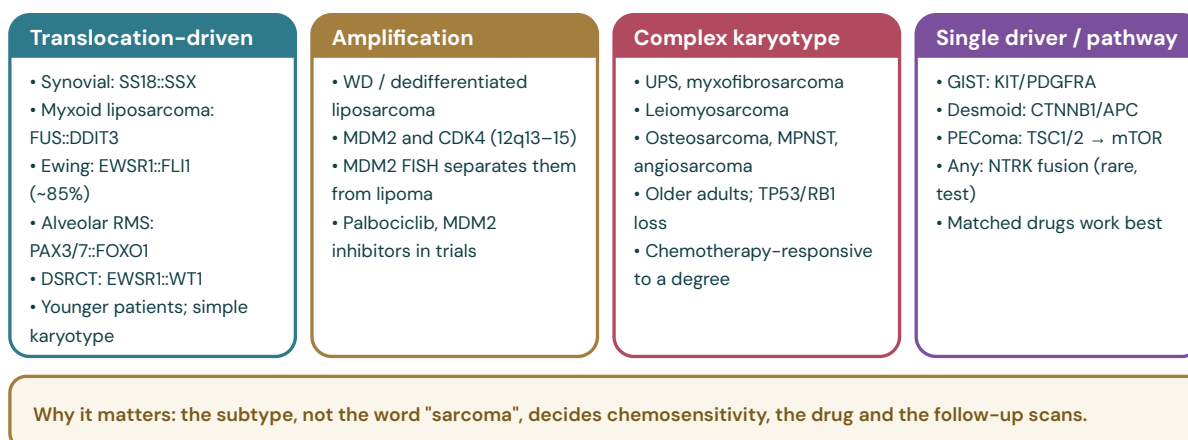


Figure 6. Four families by genetics. Translocation sarcomas affect younger people and carry diagnostic fusions; amplified MDM2/CDK4 marks well-differentiated and dedifferentiated liposarcoma; complex-karyotype sarcomas dominate in older adults; a few have one targetable driver.

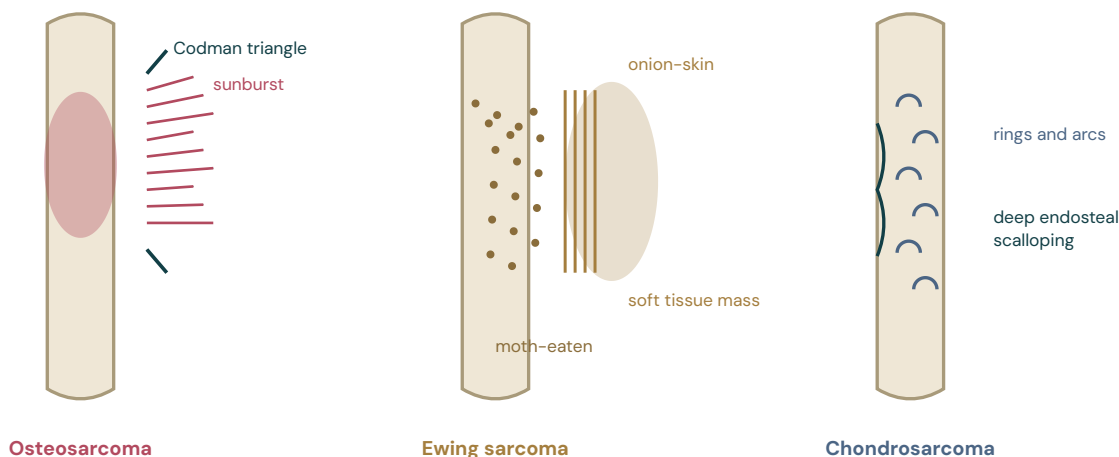
- **Molecular testing is diagnostic first:** in sarcoma the fusion or amplification usually confirms the subtype rather than selecting a drug. Use FISH or RT-PCR for a suspected fusion, or an RNA-based NGS panel that detects many fusions at once.
- **MDM2 amplification** (FISH) separates atypical lipomatous 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](#)<sup>[5]</sup>, [Doebele 2020](#)<sup>[6]</sup>). Screen with pan-TRK IHC and confirm with RNA NGS.
- **Ewing sarcoma:** *EWSR1::FLI1* in about 85% and *EWSR1::ERG* in about 10%; fusion type does not change prognosis with modern therapy ([Le Deley 2010](#)<sup>[7]</sup>). Round cell sarcomas with *CIC* or *BCOR* rearrangement are separate, more aggressive entities.
- **Osteosarcoma** has no routine predictive biomarker; the strongest prognostic factor after metastasis status is **histological necrosis after preoperative chemotherapy** (≥90% = good response).
- **Chondrosarcoma:** *IDH1/2* mutations in most conventional central tumours (diagnostic support; IDH inhibitors in trials).

| Fusion or alteration                            | Tumour                                             |
|-------------------------------------------------|----------------------------------------------------|
| <i>SS18::SSX1/2/4</i>                           | Synovial sarcoma                                   |
| <i>FUS::DDIT3</i> (rarely <i>EWSR1::DDIT3</i> ) | Myxoid liposarcoma                                 |
| <i>MDM2/CDK4</i> amplification                  | Well-differentiated / dedifferentiated liposarcoma |
| <i>EWSR1::FLI1</i> ,<br><i>EWSR1::ERG</i>       | Ewing sarcoma                                      |
| <i>CIC::DUX4</i> ,<br><i>BCOR::CCNB3</i>        | Undifferentiated round cell sarcomas               |

| Fusion or alteration       | Tumour                                                |
|----------------------------|-------------------------------------------------------|
| <i>PAX3/7::FOXO1</i>       | Alveolar rhabdomyosarcoma                             |
| <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

### Bone sarcoma: surgery and local control



Aggressive signs on any film: wide zone of transition, cortical breach, interrupted periosteal reaction, soft tissue mass.

Figure 7. The plain X-ray is still the first and most useful bone test. Schematic only: osteosarcoma (metaphysis, bone-forming, sunburst), Ewing sarcoma (diaphysis or flat bone, permeative, onion-skin, large soft tissue mass), chondrosarcoma (adults, cartilage calcification).

- **Wide resection** removes the tumour en bloc with its reactive zone and a cuff of normal tissue, including the biopsy tract. A microscopic margin under 1 mm raises local recurrence; positive margins are sometimes accepted in pelvis and spine.
- **Limb salvage** is possible in most extremity bone sarcomas after preoperative chemotherapy; survival equals amputation when margins are adequate. Response to chemotherapy and margin both predict local recurrence ([Bielack 1996<sup>\[8\]</sup>](#)).
- **Ewing sarcoma local control:** surgery when an adequate margin is achievable with acceptable function; definitive RT (about 55 Gy) when the tumour is unresectable or resection would be mutilating (spine, much of the pelvis, skull base). Postoperative RT for positive margins, gross residual disease or high-risk chest wall tumours. Isolated lung metastases: whole-lung RT; solitary bone metastases can also be treated locally.
- **Osteosarcoma** is relatively radioresistant: RT only for unresectable or incompletely resected tumours (high dose; protons or carbon ions where available).
- **Chondrosarcoma:** surgery is the only effective treatment. Grade 1 limb lesions (atypical cartilaginous tumour): intralesional curettage with adjuvant (cement, phenol, cryotherapy); grade 2–3, pelvic and axial tumours: wide resection. Skull base and spine: high-dose particle RT after surgery.
- **Enneking/MSTS staging** (grade, compartment, metastasis) still guides surgical planning ([Enneking 1986<sup>\[9\]</sup>](#)).

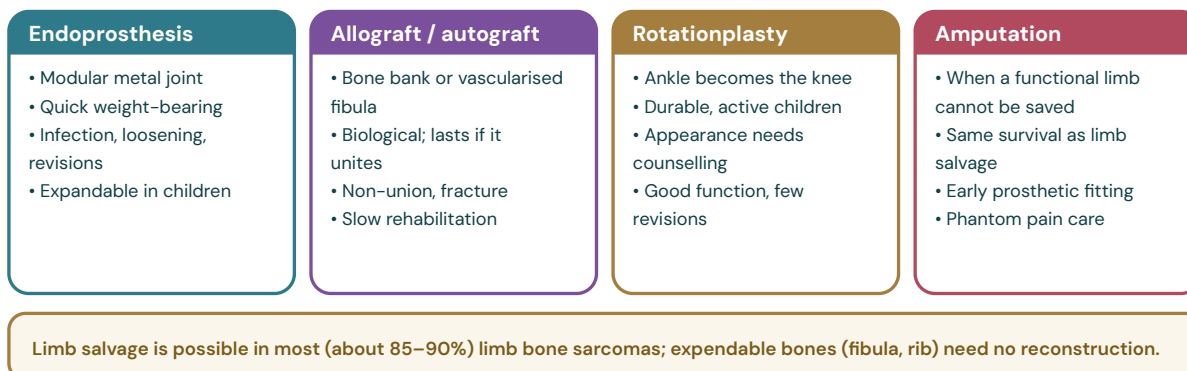


Figure 8. Reconstruction is chosen for durability, age and function. The oncological goal (a wide margin) comes first; the reconstruction is planned around it, never the other way round.

## o6 Systemic therapy: indications & options

### Bone sarcoma: chemotherapy

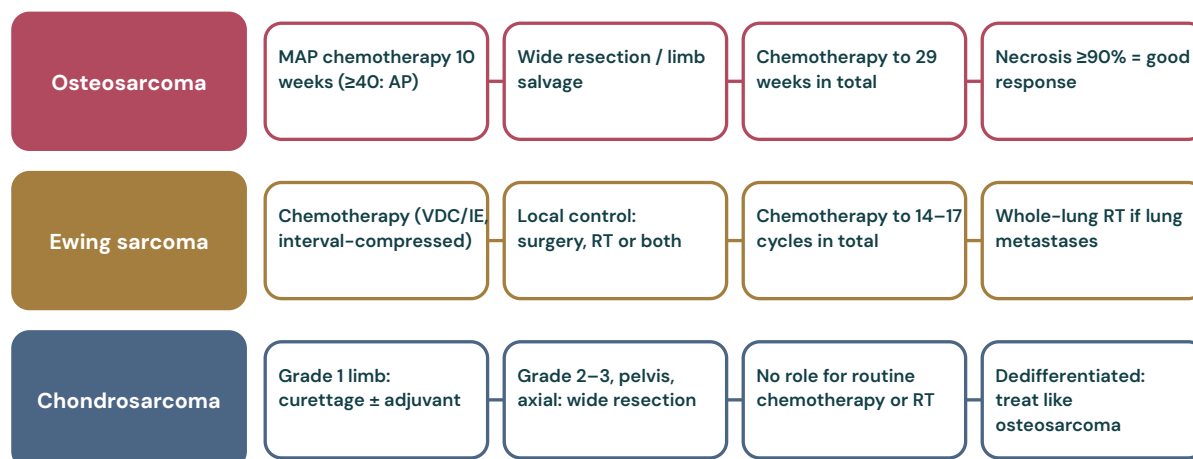


Figure 9. Three bone sarcomas, three strategies. Osteosarcoma and Ewing sarcoma are systemic diseases at diagnosis (micrometastases) and need chemotherapy around local treatment; conventional chondrosarcoma is cured, if at all, by surgery.

- **Osteosarcoma** (high-grade): chemotherapy before and after surgery raised long-term survival from under 20% to about 65–70% for localised disease ([MIOS 1986](#)<sup>[10]</sup>). Standard up to age 40: MAP (high-dose methotrexate, doxorubicin, cisplatin), 10 weeks before surgery and continued from 1 week after surgery to complete about 29 weeks. Preoperative and postoperative timing give similar survival; preoperative chemotherapy is preferred because it eases limb salvage. Age 40 and over: doxorubicin–cisplatin alone is usual (benefit of high-dose methotrexate unproven). Where methotrexate cannot be monitored safely, carboplatin–ifosfamide–doxorubicin is an alternative (more second leukaemias).
- **Poor responders** (necrosis under 90%): changing postoperative chemotherapy does not help; adding ifosfamide–etoposide only added toxicity ([EURAMOS-1](#)<sup>[11]</sup>), and interferon maintenance for good responders was also negative ([EURAMOS-1 good response](#)<sup>[12]</sup>). Zoledronate added nothing ([OS2006](#)<sup>[13]</sup>). Mifamurtide with MAP is used where licensed ([INT-0133](#)<sup>[14]</sup>); it is not available in India.
- **No adjuvant RT** after complete resection of osteosarcoma; RT is for incomplete resection, inoperable sites or palliation. **Metastatic at diagnosis**: same chemotherapy plus resection of all sites; up to about half with isolated lung metastases can be long-term survivors.
- **Osteosarcoma subtypes**: low-grade central and parosteal osteosarcoma need surgery alone; periosteal is intermediate (chemotherapy debated).
- **Ewing sarcoma**: adding ifosfamide and etoposide to VDC improved 5-year event-free survival in localised disease (69 vs 54%; [INT-0091](#)<sup>[15]</sup>). Giving cycles every 14 instead of 21 days (with growth factor) improved 10-year EFS (70 vs 61%) and OS (76 vs 69%) without more toxicity ([AEWS0031](#)<sup>[16]</sup>), whereas higher doses per cycle did not help ([Granowetter 2009](#)<sup>[17]</sup>) and adding vincristine–topotecan–cyclophosphamide did not either ([AEWS1031](#)<sup>[18]</sup>). VDC/IE beat VIDE (3-year EFS 67 vs 61%, OS 82 vs 74%; [Euro Ewing 2012](#)<sup>[19]</sup>).
- **Ewing sequence**: 12 weeks of VDC/IE (every 14 days under 18; every 14 or 21 days from 18) → local control → chemotherapy to a total of 14–17 cycles. If RT is the local treatment, chemotherapy continues during RT with doxorubicin omitted. Adults should receive the same protocol at full intensity.

- **Metastatic Ewing sarcoma:** lung-only disease has a better outlook (whole-lung RT after chemotherapy); bone or marrow metastases fare poorly; high-dose busulfan–melphalan is used in some protocols.
- **Relapsed bone sarcoma:** resect lung metastases where possible (still curative in some osteosarcomas); chemotherapy options include ifosfamide-based, irinotecan–temozolomide and topotecan–cyclophosphamide (Ewing), and multitarget TKIs in osteosarcoma ([REGOBONE<sup>\[20\]</sup>](#), [CABONE<sup>\[21\]</sup>](#)); trials preferred. Relapse more than a year after treatment with a few resectable lung nodules can still be cured by surgery.
- **Chondrosarcoma:** conventional chondrosarcoma is chemoresistant; mesenchymal chondrosarcoma is treated like Ewing sarcoma and dedifferentiated like osteosarcoma.

## 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)                  | <i>MYC</i> 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                                                       |

| Subtype                                                               | Key IHC                            | Molecular test                                          | What it changes                                                                      |
|-----------------------------------------------------------------------|------------------------------------|---------------------------------------------------------|--------------------------------------------------------------------------------------|
| 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 $\beta$ -catenin | <i>KIT/PDGFR<math>\alpha</math></i> ; <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, $\leq 5$ cm, low grade                  | Wide excision alone                                                                                                 | Re-excise if margin positive                                                                 | <a href="#">NCI 1998</a> <sup>[22]</sup>                                                                                                  |
| 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                                 | <a href="#">NCIC SR2</a> <sup>[23]</sup> , <a href="#">Folkert 2014</a> <sup>[24]</sup>                                                   |
| Stage III limb UPS (or DD/pleomorphic liposarcoma)                   | Preoperative RT + pembrolizumab → surgery → adjuvant pembrolizumab (shared decision)                                | Survival data immature; not tested with chemotherapy                                         | <a href="#">SU2C-SARCO32</a> <sup>[25]</sup>                                                                                              |
| 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                        | <a href="#">ISG-STS 1001</a> <sup>[26]</sup> , <a href="#">Pervaiz 2008</a> <sup>[27]</sup> , <a href="#">EORTC 62931</a> <sup>[28]</sup> |
| Myxoid liposarcoma, preoperative                                     | RT 50 Gy (36 Gy de-escalation in trials)                                                                            | Very radiosensitive                                                                          | <a href="#">DOREMY</a> <sup>[29]</sup>                                                                                                    |
| 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 | <a href="#">STRASS</a> <sup>[30]</sup> , <a href="#">TARPSWG 2021</a> <sup>[3]</sup>                                                      |
| Unplanned excision ("whoops")                                        | MRI then re-excision of the scar and bed ( $\pm$ RT)                                                                | Residual tumour found in about half                                                          | <a href="#">Noria 1996</a> <sup>[31]</sup>                                                                                                |
| Oligometastatic lung disease                                         | Metastasectomy (VATS) if all disease removable and interval long                                                    | SBRT or ablation if unfit                                                                    | <a href="#">Chudgar 2017</a> <sup>[32]</sup> , <a href="#">Dhakal 2012</a> <sup>[33]</sup>                                                |
| 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  | <a href="#">EORTC 62012</a> <sup>[34]</sup> , <a href="#">LMS-O4</a> <sup>[35]</sup> , <a href="#">ANGIOTAX</a> <sup>[36]</sup>           |
| Osteosarcoma, localised (high grade)                                 | Age $< 40$ : MAP 10 weeks → wide resection → MAP to 29 weeks; $\geq 40$ : doxorubicin–cisplatin                     | Poor necrosis: no change of regimen; no adjuvant RT after complete resection                 | <a href="#">MIOS</a> <sup>[10]</sup> , <a href="#">EURAMOS-1</a> <sup>[11]</sup>                                                          |
| Ewing sarcoma, localised                                             | VDC/IE every 14 days ( $< 18$ ; 14 or 21 days $\geq 18$ ) $\times$ 12 weeks → surgery or RT → 14–17 cycles in total | RT with chemotherapy (no doxorubicin during RT); adults: same protocol at full intensity     | <a href="#">INT-0091</a> <sup>[15]</sup> , <a href="#">AEWS0031</a> <sup>[16]</sup> , <a href="#">Euro Ewing 2012</a> <sup>[19]</sup>     |

| Setting                     | Standard                                                       | Alternatives / notes                                            | Evidence              |
|-----------------------------|----------------------------------------------------------------|-----------------------------------------------------------------|-----------------------|
| 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                                                   |
| 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 |

| Drug                                            | Main problems                                                                                   | Check / prevent                                                                                | Act on                                           |
|-------------------------------------------------|-------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|--------------------------------------------------|
| 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                     |
| 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

### Suspected bone sarcoma

**Persistent bone pain, swelling or aggressive X-ray** → MRI whole bone · CT chest · PET-CT or bone scan → **biopsy at the treating centre** (core, track excisable) → histology + molecular (EWSR1) + culture if infection possible

#### OSTEOSARCOMA

**High grade, <40 y** → MAP 10 weeks (≥40: doxorubicin–cisplatin)

Wide resection / limb salvage → necrosis assessed

Same chemotherapy to 29 weeks; no change for poor response

*Lung metastases: resect all if possible, with chemotherapy*

#### EWING SARCOMA

**VDC/IE** every 14 days (<18 y; 14 or 21 days if ≥18) × 12 weeks

**Adequate margin possible** → surgery (RT if margin positive or chest wall high risk)

**Unresectable or mutilating** → definitive RT with chemotherapy

Complete 14–17 cycles in total

*Lung metastases: whole-lung RT; bone/marrow metastases: protocol or trial*

#### CHONDROSARCOMA

**Grade 1, limb** → curettage + adjuvant

**Grade 2–3, pelvis, axial** → wide resection

*Dedifferentiated* → osteosarcoma-type chemotherapy; *mesenchymal* → Ewing-type

All patients: no curettage of a suspected sarcoma as "infection" · fertility preservation · audiometry and echo · TP53 testing if young with family cancers · rehabilitation and school or work support.

## o8 Survivorship, follow-up & reducing recurrence

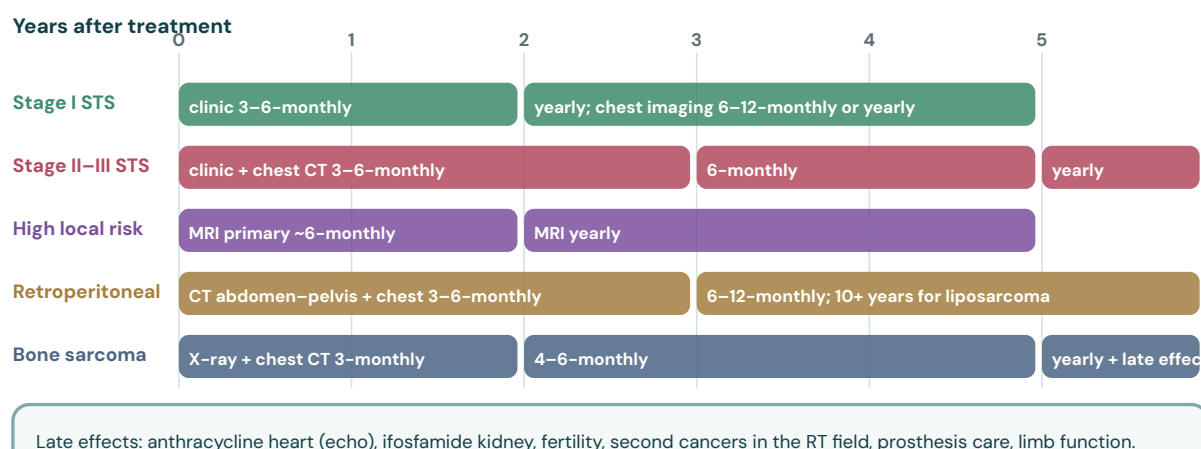


Figure 10. Surveillance is front-loaded because most relapses occur in the first 2–3 years; the aim is to catch lung metastases and local relapses while still resectable. Intervals are approximate (UpToDate, ESMO, NCCN); MRI is preferred for the primary site.

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

| Group        | Visits and imaging                                                                                                  | Notes                                                   |
|--------------|---------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------|
| Bone sarcoma | Clinic, X-ray of the primary and chest CT every 3 months for 2 years, 4–6-monthly to year 5, then yearly to year 10 | Prosthesis surveillance; late relapses in Ewing sarcoma |

- **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 treated for bone cancer will never walk or play normally again?

A child cured of sarcoma will never develop another cancer?

Osteosarcoma always needs amputation?

## 09 Landmark trials

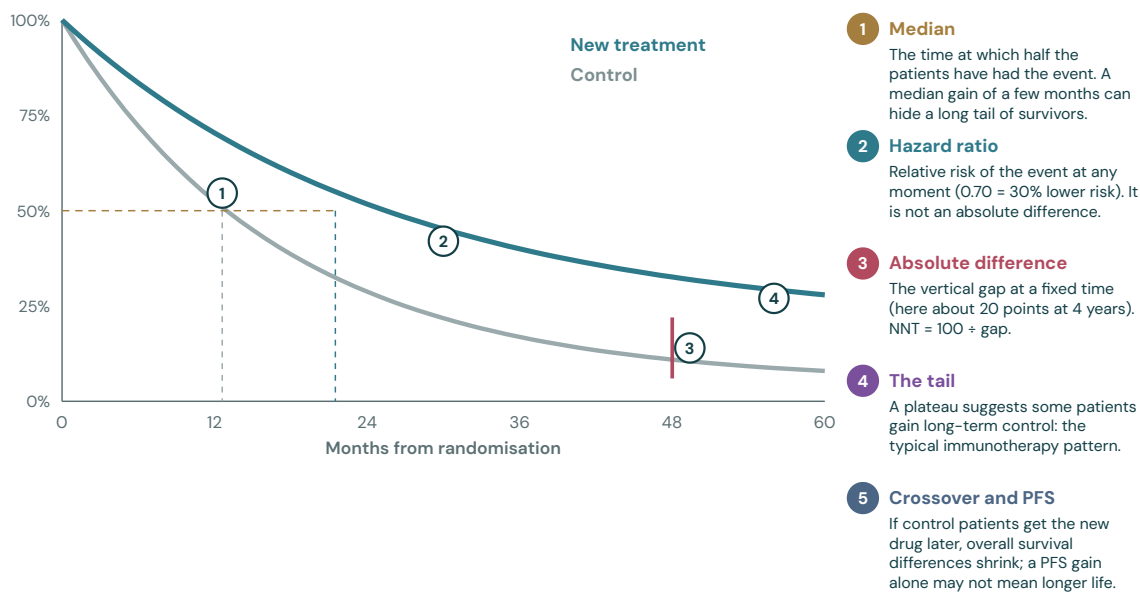


Figure 11. How to read a survival curve (illustrative). Use the absolute gap at a fixed time and overall survival, not the median or PFS alone, when weighing benefit against toxicity and cost.

- [MIOS \(Link 1986\)](#)<sup>[10]</sup>: adjuvant chemotherapy vs observation after surgery for osteosarcoma → relapse-free survival about 65 vs 17% → chemotherapy is standard.
- [EURAMOS-1](#)<sup>[11]</sup>: adding ifosfamide–etoposide for poor responders → no gain, more toxicity → MAP throughout.
- [INT-0091](#)<sup>[15]</sup>: VDC ± IE in Ewing sarcoma → 5-year EFS 69 vs 54% in localised disease → VDC/IE backbone.
- [AEWS0031](#)<sup>[16]</sup>: VDC/IE every 14 vs 21 days → 10-year EFS 70 vs 61%, OS 76 vs 69%, no extra toxicity → interval compression.
- [Euro Ewing 2012](#)<sup>[19]</sup>: VDC/IE vs VIDE → 3-year EFS 67 vs 61%, OS 82 vs 74%, less febrile neutropenia → one international standard.

## 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.
- Night pain in a teenager is not growing pains. X-ray the whole bone.
- Fever, raised ESR and a bone lesion can be Ewing sarcoma: send biopsy for culture and histology together.
- In osteosarcoma, response is judged on the resection specimen (necrosis), not on how much the mass shrinks.
- Adults with Ewing sarcoma or osteosarcoma should receive paediatric-style protocols in experienced units; under-dosing is a common cause of failure.
- 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

Two 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 Osteosarcoma · teenager

#### Knee pain in a 15-year-old cricketer

15 years, boy

Distal femur

No metastases

A 15-year-old boy has had knee pain for 3 months, blamed on a cricket injury and treated with painkillers; now it wakes him at night and there is a firm swelling above the knee. X-ray: a mixed lytic-sclerotic distal femoral metaphyseal lesion with a Codman triangle and sunburst periosteal reaction.

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

1

#### IMAGE AND STAGE

MRI of the whole femur (no skip lesion), CT chest (clear), PET-CT (no bone metastases); baseline audiometry, echo, renal function.

2

#### BIOPSY

Core biopsy at the treating centre, track placed where it will be excised: high-grade conventional osteosarcoma.

3

#### BEFORE CHEMOTHERAPY

Sperm banking.

4

#### TREATMENT

MAP chemotherapy for 10 weeks → wide resection with modular endoprosthesis → necrosis 95% (good response) → MAP resumed a week after surgery to complete 29 weeks in total.

5

#### FOLLOW-UP

Chest CT and limb X-ray 3-monthly for 2 years; physiotherapy; late-effects clinic (heart, hearing, kidneys).

#### TEACHING POINTS

- Night pain in a teenager is a red flag: X-ray the whole bone.
- Biopsy where the definitive surgery will be done.
- Necrosis after preoperative chemotherapy is the key prognostic factor.

**See:** Sections 02, 05, 06 · Algorithm 4 · [MIOS](#)<sup>[10]</sup>, [EURAMOS-1](#)<sup>[11]</sup>

### CASE 2 Ewing sarcoma · pelvis · adult

#### Hip pain treated as tuberculosis

24 years, man

Iliac wing + soft tissue mass

EWSR1::FLI1

A 24-year-old man has 4 months of right buttock pain, fever and weight loss. ESR is raised. He was started on antituberculous treatment for a "lytic lesion" of the ilium without a biopsy. Pain is worse and a mass is now palpable.

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

1

#### RECOGNISE

Permeative lytic lesion with a large soft tissue mass in a young adult with fever and raised ESR: Ewing sarcoma until proven otherwise.

2

**DIAGNOSE**

CT-guided core biopsy (histology, molecular test and culture): small round blue cells, CD99 membranous, EWSR1::FLI1. TB cultures negative; stop antituberculous drugs.

3

**STAGE**

PET-CT and CT chest: localised. Fertility preservation.

4

**TREATMENT**

VDC/IE every 14 or 21 days (he is 24) with growth factor; local control after 12 weeks: resection if an adequate margin is possible without disabling loss of function, otherwise definitive RT with chemotherapy continuing (doxorubicin omitted); 14–17 cycles in total.

**TEACHING POINTS**

- Fever and raised ESR do not exclude Ewing sarcoma.
- Do not start empirical antituberculous treatment for a bone lesion without tissue.
- Adults need the full paediatric-style protocol.

**See:** Sections 02, 05, 06 · Algorithm 4 · [INT-0091<sup>\[15\]</sup>](#), [AEWS0031<sup>\[16\]</sup>](#), [Euro Ewing 2012<sup>\[19\]</sup>](#)

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- **NCI amputation vs limb-sparing (Rosenberg 1982):** Rosenberg SA, Tepper J, Glatstein E, et al. The treatment of soft-tissue sarcomas of the extremities: prospective randomized evaluations of limb-sparing surgery plus radiation therapy compared with amputation and the role of adjuvant chemotherapy. *Ann Surg* 1982;196:305. [PubMed](#)  
Local therapy for limb and trunk soft tissue sarcoma
- **NCI adjuvant EBRT 20-year (Beane 2014):** Beane JD, Yang JC, White D, et al. Efficacy of adjuvant radiation therapy in the treatment of soft tissue sarcoma of the extremity: 20-year follow-up of a randomized prospective trial. *Ann Surg Oncol* 2014;21:2484. [PubMed](#) Local therapy for limb and trunk soft tissue sarcoma
- **MSKCC brachytherapy trial (Pisters 1996):** Pisters PW, Harrison LB, Leung DH, et al. Long-term results of a prospective randomized trial of adjuvant brachytherapy in soft tissue sarcoma. *J Clin Oncol* 1996;14:859. [PubMed](#)  
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- **RTOG 0630:** Wang D, Zhang Q, Eisenberg BL, et al. Significant reduction of late toxicities in patients with extremity sarcoma treated with image-guided radiation therapy to a reduced target volume: results of RTOG 0630. *J Clin Oncol* 2015;33:2231. [PubMed](#) Local therapy for limb and trunk soft tissue sarcoma
- **HYPOT-STs:** Guadagnolo BA, Bassett RL, Mitra D, et al. Hypofractionated, 3-week, preoperative radiotherapy for patients with soft tissue sarcomas (HYPOT-STs): a single-centre, open-label, single-arm, phase 2 trial. *Lancet Oncol* 2022;23:1547. [PubMed](#)  
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- **5-fraction preoperative RT (Kalbasi 2020):** Kalbasi A, Kamrava M, Chu FI, et al. A phase II trial of 5-day neoadjuvant radiotherapy for patients with high-risk primary soft tissue sarcoma. *Clin Cancer Res* 2020;26:1829. [PubMed](#)  
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- **RPS reference-centre surgery (Bonvalot 2009):** Bonvalot S, Rivoire M, Castaing M, et al. Primary retroperitoneal sarcomas: a multivariate analysis of surgical factors associated with local control. *J Clin Oncol* 2009;27:31. [PubMed](#)  
Retroperitoneal, radiation-associated and breast sarcoma
- **RPS recurrence patterns (Gronchi 2016):** Gronchi A, Strauss DC, Miceli R, et al. Variability in patterns of recurrence after resection of primary retroperitoneal sarcoma (RPS): a report on 1007 patients. *Ann Surg* 2016;263:1002. [PubMed](#)  
Retroperitoneal, radiation-associated and breast sarcoma
- **RPS nomogram (Gronchi 2013):** Gronchi A, Miceli R, Shurell E, et al. Outcome prediction in primary resected retroperitoneal soft tissue sarcoma: histology-specific overall survival and disease-free survival nomograms. *J Clin Oncol* 2013;31:1649. [PubMed](#)  
Retroperitoneal, radiation-associated and breast sarcoma
- **Sarcoma after breast-conserving RT (Wiener 2023):** Wiener AA, Schumacher JR, Hanlon B, et al. Incidence of radiation-associated sarcoma after breast-conserving surgery plus radiation. *J Surg Oncol* 2023;127:535. [PubMed](#)  
Retroperitoneal, radiation-associated and breast sarcoma
- **EORTC pooled adjuvant analysis (Le Cesne 2014):** Le Cesne A, Ouali M, Leahy MG, et al. Doxorubicin-based adjuvant chemotherapy in soft tissue sarcoma: pooled analysis of two STBSG-EORTC phase III clinical trials. *Ann Oncol* 2014;25:2425. [PubMed](#) Perioperative systemic therapy

- **ISG/GEIS short adjuvant (Gronchi 2016):** Gronchi A, Stacchiotti S, Verderio P, et al. Short, full-dose adjuvant chemotherapy in high-risk adult soft tissue sarcomas: long-term follow-up of a randomized clinical trial. *Ann Oncol* 2016;27:2283. [PubMed](#)  
**Perioperative systemic therapy**
- **ISG-STES 1001 final:** Gronchi A, Palmerini E, Quagliuolo V, et al. Neoadjuvant chemotherapy in high-risk soft tissue sarcomas: final results of a randomized trial from Italian, Spanish, French, and Polish sarcoma groups. *J Clin Oncol* 2020;38:2178. [PubMed](#)  
**Perioperative systemic therapy**
- **GeDDiS:** Seddon B, Strauss SJ, Whelan J, et al. Gemcitabine and docetaxel versus doxorubicin as first-line treatment in previously untreated advanced unresectable or metastatic soft-tissue sarcomas (GeDDiS). *Lancet Oncol* 2017;18:1397. [PubMed](#)  
**Advanced soft tissue sarcoma**
- **Olaratumab phase 2 (Tap 2016):** Tap WD, Jones RL, Van Tine BA, et al. Olaratumab and doxorubicin versus doxorubicin alone for treatment of soft-tissue sarcoma: an open-label phase 1b and randomised phase 2 trial. *Lancet* 2016;388:488. [PubMed](#)  
**Advanced soft tissue sarcoma**
- **LMS-O4:** Pautier P, Italiano A, Piperno-Neumann S, et al. Doxorubicin alone versus doxorubicin with trabectedin followed by trabectedin alone as first-line therapy for metastatic or unresectable leiomyosarcoma (LMS-O4). *Lancet Oncol* 2022;23:1044. [PubMed](#) **Advanced soft tissue sarcoma**
- **SARC 002 gemcitabine-docetaxel:** Maki RG, Wathen JK, Patel SR, et al. Randomized phase II study of gemcitabine and docetaxel compared with gemcitabine alone in patients with metastatic soft tissue sarcomas (SARC 002). *J Clin Oncol* 2007;25:2755. [PubMed](#) **Advanced soft tissue sarcoma**
- **PALETTE:** van der Graaf WT, Blay JY, Chawla SP, et al. Pazopanib for metastatic soft-tissue sarcoma (PALETTE): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet* 2012;379:1879. [PubMed](#) **Advanced soft tissue sarcoma**
- **Trabectedin vs dacarbazine (Demetri 2016):** Demetri GD, von Mehren M, Jones RL, et al. Efficacy and safety of trabectedin or dacarbazine for metastatic liposarcoma or leiomyosarcoma after failure of conventional chemotherapy. *J Clin Oncol* 2016;34:786. [PubMed](#) **Advanced soft tissue sarcoma**
- **T-SAR:** Le Cesne A, Blay JY, Cupissol D, et al. A randomized phase III trial comparing trabectedin to best supportive care in patients with pre-treated soft tissue sarcoma: T-SAR. *Ann Oncol* 2021;32:1034. [PubMed](#) **Advanced soft tissue sarcoma**
- **Eribulin vs dacarbazine (Schöffski 2016):** Schöffski P, Chawla S, Maki RG, et al. Eribulin versus dacarbazine in previously treated patients with advanced liposarcoma or leiomyosarcoma. *Lancet* 2016;387:1629. [PubMed](#) **Advanced soft tissue sarcoma**
- **Palbociclib in liposarcoma (Dickson 2016):** Dickson MA, Schwartz GK, Keohan ML, et al. Progression-free survival among patients with well-differentiated or dedifferentiated liposarcoma treated with CDK4 inhibitor palbociclib. *JAMA Oncol* 2016;2:937. [PubMed](#) **Advanced soft tissue sarcoma**
- **Doxorubicin vs paclitaxel in angiosarcoma (Italiano 2012):** Italiano A, Cioffi A, Penel N, et al. Comparison of doxorubicin and weekly paclitaxel efficacy in metastatic angiosarcomas. *Cancer* 2012;118:3330. [PubMed](#) **Advanced soft tissue sarcoma**
- **AMPECT (nab-sirolimus):** Wagner AJ, Ravi V, Riedel RF, et al. nab-Sirolimus for patients with malignant perivascular epithelioid cell tumors. *J Clin Oncol* 2021;39:3660. [PubMed](#) **Advanced soft tissue sarcoma**
- **SPEARHEAD-1:** D'Angelo SP, Araujo DM, Abdul Razak AR, et al. Afamitresgene autoleucel for advanced synovial sarcoma and myxoid round cell liposarcoma (SPEARHEAD-1). *Lancet* 2024;403:1460. [PubMed](#) **Advanced soft tissue sarcoma**
- **SARCO28:** Tawbi HA, Burgess M, Bolejack V, et al. Pembrolizumab in advanced soft-tissue sarcoma and bone sarcoma (SARCO28). *Lancet Oncol* 2017;18:1493. [PubMed](#) **Advanced soft tissue sarcoma**
- **Alliance A091401:** D'Angelo SP, Mahoney MR, Van Tine BA, et al. Nivolumab with or without ipilimumab treatment for metastatic sarcoma (Alliance A091401). *Lancet Oncol* 2018;19:416. [PubMed](#) **Advanced soft tissue sarcoma**
- **Repeat lung metastasectomy (Weiser 2000):** Weiser MR, Downey RJ, Leung DH, Brennan MF. Repeat resection of pulmonary metastases in patients with soft-tissue sarcoma. *J Am Coll Surg* 2000;191:184. [PubMed](#) **Advanced soft tissue sarcoma**
- **Atezolizumab in ASPS (Chen 2023):** Chen AP, Sharon E, O'Sullivan-Coyne G, et al. Atezolizumab for advanced alveolar soft part sarcoma. *N Engl J Med* 2023;389:911. [PubMed](#) **Advanced soft tissue sarcoma**
- **Axitinib-pembrolizumab in ASPS (Wilky 2019):** Wilky BA, Trucco MM, Subhawong TK, et al. Axitinib plus pembrolizumab in patients with advanced sarcomas including alveolar soft-part sarcoma: a single-centre, single-arm, phase 2 trial. *Lancet Oncol* 2019;20:837. [PubMed](#) **Advanced soft tissue sarcoma**

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.