Introduction

Sarcoma is an uncommon and heterogeneous family of cancers, with more than 50 clinicopathologically distinct subtypes representing 1% of all malignancies. Although ubiquitous in presentation, a significant proportion arises from the extremities. Data from our large sarcoma database which comprise 1029 unique patients demonstrates that 35% of all sarcomas arise from the extremities with soft tissue sarcomas (STS) accounting for 87% of these cases. The 3 most common STS histotypes include liposarcoma, unclassified pleomorphic sarcoma (UPS) formerly termed malignant fibrous histiocytoma (MFH), and myxofibrosarcoma. In the remaining 13% of extremity bone sarcomas, osteosarcomas account for half of the cases.

While several international guidelines exist for the treatment of extremity sarcomas, due to unique geographical differences, patient population, presentation, healthcare resources, and reimbursement issues, direct application of these international guidelines to our local patients may not always be possible. In addition, unique differences in our patient population as well as acceptance and tolerance of various treatment modalities exist. Therefore, there is a need to develop a set of local clinical practice guidelines which would address our own patient population and sarcoma practice within our healthcare context.

In this article, we aim to provide an evidence-based consensus approach to the initial evaluation, diagnosis, and management of an extremity sarcoma, described in close parallel to a patient’s journey. Because patients with limb sarcomas, be it from a soft tissue or bone primary, may present similarly with a painless enlarging mass and physical examination alone may not adequately distinguish them, the initial evaluation of an extremity mass follows the same initial diagnostic paradigm but quickly dichotomises once a bony tumour is differentiated from a soft tissue mass. This article first describes the radiological, diagnostic, and pathological management of an extremity mass and once diagnosis is confirmed, separately discusses the specific management guidelines of limb STS and osteosarcoma.

The SCAN Guidelines for the Initial Evaluation, Diagnosis, and Management of Extremity STS and Osteosarcoma

The SCAN Guidelines are clinical practice guidelines...
for the initial evaluation, diagnosis, and management of extremity STS and osteosarcoma.

These first edition guidelines are intended to serve as treatment recommendations by members of this working group reflecting their views on the management of extremity STS and osteosarcoma. While it hopes to harmonise the management of this disease, it is not intended to serve as the standard of care or to replace good clinical judgment and the individualisation of treatments.

**Target Users of the Guidelines**

The guidelines will be of interest to oncologists, oncology nurse specialists, pharmacists, allied health workers and general practitioners involved in the management of extremity STS and osteosarcoma.

**Guideline Recommendations/Development**

The SCAN Sarcoma Working Group comprises a panel of 14 members with special interests in the management of sarcoma. Members come from diverse specialities including orthopaedic surgery, pathology, diagnostic radiology and medical, radiation, surgical, paediatric and musculoskeletal oncology. Membership of the workgroup was by invitation. The workgroup elected its own chairperson and decided on its own scope. Guideline selection was conducted through workgroup consensus. Potential conflicts of interest were declared by the International Committee of Medical Journal Editors (ICJME) guidelines. Secretarial support for the overall guideline development effort was provided by Annals, Academy of Medicine Singapore. No other financial support was obtained. Guideline searching was conducted by the cancer network team. The group met once in person, and completed guideline development through email communication.

A consensus approach was used to develop guidelines streamlined to the Singapore context. First, available resources were considered. High quality guidelines\(^2\)-\(^5\) were selected for review and structured approaches developed for guideline evaluation. This involved the extraction of data on source guideline development, the setting up of mechanisms for selecting recommendations and also recognising possible dissent amongst panel members. The SCAN guidelines were then written with consensus from workgroup members for each recommendation. Calibration of guidelines to the local context based on available Singapore data was encouraged. The final phase involved writing, external review, stakeholder feedback, and the setting up of a mechanism for regular updating. International measures of cost-effectiveness for each recommendation were obtained where available but not used to inform the recommendations.

These guidelines set out to address the 4 main management issues which were selected for this topic:

1. Radiological Imaging
2. Pathologic Assessment
3. Treatment of Osteosarcoma
4. Treatment of STS

The following international guidelines were selected for review:

- “Improving Outcomes for People with Sarcoma” by the National Collaborating Centre for Cancer (National Institute for Health and Clinical Excellence, London 2006)\(^3\)
- “Soft Tissue and Visceral Sarcomas: EMSO Clinical Practice Guidelines for Diagnosis, Treatment and Follow-up” by the European Sarcoma Network Working Group (2012)\(^4\)
- “UK Guidelines for the Management of Bone Sarcomas” by Grimer RJ et al (Sarcoma, 2008)\(^5\)

These guidelines will be reviewed or updated every 2 years. If there are significant new developments that impact the management of sarcoma, it will be reviewed earlier.

1. **Radiological Imaging**

The initial investigation for anyone presenting with a mass in the extremity is a plain radiograph done in 2 planes.\(^5\)\(^7\) This helps to differentiate between STS and bone tumours. Additional oblique radiographs of the bone tumours may help evaluate cortical continuity and joint involvement.

Magnetic resonance imaging (MRI) is used for local staging.\(^2\)\(^4\)\(^8\) An MRI allows for the evaluation of tumour size, the extent (including involvement of contiguous structures), and involvement of the neurovascular bundle. For bone tumours, an additional sequence of the entire long bone is done to look for skipped intramedullary lesions. If the tumour is close to a joint, the joint should be included in the images to check for contiguous involvement. The use of gadolinium contrast is optional for initial staging scans (but is required for follow-up scans post-therapy) and is generally administered unless there is a contraindication. An MRI provides details of the anatomical structures adjacent to the tumour and detects any distortion or involvement. A computed tomography (CT) scan of the local area is generally used for problem solving—to visualise calcification, periosteal bone formation, and subtle cortical erosion.\(^5\)\(^7\) If the MRI is contraindicated, a CT scan (with iodinated contrast) or CT angiogram can be performed.\(^8\)
A biopsy for histological diagnosis is pivotal in the investigation and subsequent management of bone and STS. This biopsy should be performed by the same surgeon who will be performing the surgical resection.

A biopsy should be kept as minimally invasive as possible, while still yielding sufficient tissue to obtain a diagnosis, as more immunohistochemistry and genomic tests are being done to classify sarcoma than previously. Fine needle aspiration cytology is, however, not appropriate as the pathologist needs sufficient tissue for analysis. A percutaneous trucut core needle biopsy, under ultrasound or computed tomogram guidance if necessary, is preferred. Open biopsy may still be indicated if the anatomy precludes percutaneous core needle biopsy or if percutaneous core needle biopsy is unsuccessful.

A biopsy should be performed only after detailed imaging of the lesion has been completed. This allows for careful planning of the biopsy tract. A poorly performed biopsy can compromise treatment outcomes, especially those of possible limb salvage surgery.

The biopsy skin incision should be kept to the minimum required for access. Planning ahead for possible future surgical resection, the biopsy skin incision should be orientated longitudinally, allowing for an extensile surgical approach to the limb.

In general the most direct route is taken to the lesion, avoiding neurovascular structures and traversing of joints. The biopsy should ideally be kept to a single compartment and should minimise the opening of fascial planes. Meticulous haemostasis throughout the biopsy is critical. A muscle splitting approach whenever traversing muscle planes is advised.

If a bone window is required to be made for access, attention should be paid to its size and shape. The bone window should only be made as large as necessary for access and sharp edges are to be avoided as they act as stress risers.

Sampling of the lesion should be directed by the prebiopsy imaging which would identify the part of the lesion with the greatest suspicion for sarcomatous tissue. Intraoperative frozen section analysis to confirm lesional tissue is advised. It is important to take adequate amounts of representative tissue for the pathologist. These samples should ideally be sent to a pathologist with an interest in musculoskeletal oncology. A detailed clinical and radiological patient history in the accompanying histology request form would be helpful to the pathologist and should be included.

Samples should also be taken for cultures by the microbiologist to exclude infection, such as tuberculosis and fungal cultures.

2. Pathologic Assessment

Principles of Biopsy
Principles of Pathologic Assessment

The diagnostic approach of limb sarcomas is highly complex and labour intensive due to the sheer volume of differential diagnoses to consider covering bone, STS, and sometimes carcinomas and melanomas, and therefore requires a multidisciplinary approach. This is especially relevant for bone tumours where input by the clinicians and radiologists are critical to avoid well-known diagnostic pitfalls.

Before interpreting the biopsy, pathologists need to be furnished with relevant clinicoradiological information and radiological images. This information should include at least:

a) site of the tumour (for instance, bone versus soft tissue-centred, anatomical region of the bone),
b) characteristics of the tumour (for instance, benign versus aggressive, homogenous versus heterogeneous, bone or cartilage forming) and
c) tumour relationship with other structures such as nerves, bone, muscle, vessels, etc.

Besides influencing the diagnosis, this information may help the pathologist decide whether the biopsies are likely to be diagnostic or representative.

Assessment of Biopsy Specimen

A preliminary investigation of limb sarcomas usually involves obtaining multiple core biopsies (at least 4 to 5 cores) or incisional biopsies from the patient. Excision biopsies may be considered for STS that are small, superficial, and easily resectable. However, fine needle aspiration is not recommended as a primary diagnostic modality, except for confirming disease recurrence or obtaining material for ancillary tests. For bone tumours or specimens, it is likely that the tissue will undergo decalcification, potentially affecting immunohistochemical results or genomic analyses. The frozen-section technique for immediate diagnosis should be avoided in bone tumours due to suboptimal histological interpretation, sampling issues, and lack of immediate ancillary support.

Assessment of Resection Specimen

Histological evaluation of limb sarcomas usually involves a description of the tumour in the resected specimens which should at least include its site, size, gross characteristics and relationships with surrounding structures and margins. A detailed description of the margins (such as intrallesional, marginal, or wide) with close communication between the clinician and pathologist is important since the margin status often determines the tumour recurrence rate.

For post-treated osteosarcoma specimens, there is an additional requirement of detailed tumour mapping and estimation of the amount of tumour necrosis by percentage. Detailed discussions on the gross handling and tumour reporting datasets for resected limb sarcoma specimens are covered comprehensively in the websites of various pathology organisations and colleges.20-22

Histological Diagnosis

Histological diagnosis of limb sarcomas should be made according to the latest (2013) World Health Organisation (WHO) classification for bone and STS. For STS, grading should be provided following the Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system, which is based on tumour differentiation, mitotic count, and necrosis. Malignancy grading may be underestimated in small biopsies particularly in heterogeneous tumours.

The histological assessment of both STS and osteosarcoma requires a combination of careful morphological examination complemented by ancillary investigations especially immunohistochemistry and molecular diagnostic tests to determine the subtype. Morphological examination involves a systematic pattern-based approach taking into consideration the architecture, cytomorphological features and matrix of tumours. The diagnosis of osteosarcoma requires the identification of osteoid forming cells or matrix for both low- and high-grade osteosarcoma variants. However, diagnostic difficulties may arise where the presence of osteoid cannot be confirmed (for instance, sampling problem related to small biopsies, osteoid-poor osteosarcoma variants) or in low-grade tumours.

Ancillary Investigations

A panel of immunohistochemistry stains is often required for the diagnosis of most STS and more rarely in bone sarcoma. Comprehensive discussions of the appropriate immunohistochemistry panels with the corresponding differential diagnoses can be found in most specialised pathology textbooks.

Molecular diagnostic tests play a critical role in determining the final diagnosis of many sarcomas particularly in those with recurrent chromosomal translocations (for instance, Ewing sarcoma, synovial sarcoma, alveolar rhabdomyosarcoma, etc.). Recent studies have also shown that these tests can be utilised to diagnose certain types of low-grade osteosarcoma23 and benign bone tumours (for instance, aneurysmal bone cyst). Molecular tests are often employed in problematic tumours that demonstrate unusual clinical presentation, atypical morphology, encompass numerous differential diagnoses (for instance, small round cell tumours) and overlapping immune-phenotype.
In summary, the diagnostic algorithm of limb sarcoma is a highly specialised and complex process that often requires a sarcoma pathologist with clinical and morphological expertise and a deep familiarity with modern ancillary techniques.

3. Treatment of Osteosarcoma

Once the diagnosis of sarcoma is made and staging completed, treatment of osteosarcoma and STS follows a divergent paradigm. In the following sections we outline the optimal management strategies of limb osteosarcoma and STS.

Surgery in Osteosarcoma

The decision for surgery, including whether the osteosarcoma is resectable, the timing, and type of surgery, should be made by the multidisciplinary oncology team caring for the patient.

Patients with high-grade osteosarcoma of the limbs will typically receive several rounds of preoperative, neo-adjuvant chemotherapy before surgical resection. Postoperative, adjuvant chemotherapy often follows resection. Details on optimal chemotherapy in osteosarcoma will be discussed in the following section.

Low-grade osteosarcoma, such as low-grade central and parosteal osteosarcoma, can however sometimes be treated by wide surgical resection alone. Updated imaging of the osteosarcoma should be carefully reviewed by the multidisciplinary oncology team to determine the optimal surgical procedure for each individual patient, i.e. whether limb salvage or amputation surgery is indicated.

Any surgery performed should be by the same surgeon who performed the initial biopsy procedure. This surgeon should ideally be an orthopaedic oncologist who is familiar with both sarcoma resection, as well as the subsequent reconstructive surgery.

The primary aim of surgery is en-bloc resection of the osteosarcoma (including the biopsy tract, if any) with adequately clear surgical margins. Intraoperative frozen section is helpful in evaluating operative margins. Close surgical margins should be marked with MRI compatible titanium surgical clips for postoperative surveillance and the possible need for adjuvant radiotherapy.

If limb salvage surgery is to be performed, wide resection has to be thoughtfully executed, with surgeons mindful of the need to preserve as much limb function as possible. Reconstruction can involve the use of autografts, allografts, endoprostheses, or combinations of the above. A multidisciplinary team of surgeons may need to be involved in the reconstructive phase of the surgery, for example, plastic surgeons to assist with skin and soft tissue coverage and vascular surgeons for vessel reconstruction.

Primary solitary or oligometastatic osteosarcoma, especially in cases with completely resectable lung metastases only, strongly merits consideration for curative treatment intent along the principles of localised osteosarcomas. Of note, there are subsets of patients who may have a very similar prognosis to that of localised disease provided surgical removal of all known metastatic disease is achieved.

In the management of recurrent osteosarcoma, one needs to consider the timing of the recurrence, as well as the number and site of any metastases. If surgery is to be performed, complete removal of all recurrent and metastatic tissue must be attempted otherwise the prognosis is very poor.25,26

Radiotherapy in Osteosarcoma

In general, there is no indication for the role of radiotherapy in the adjuvant management of osteosarcoma. However, in clinical and anatomical situations where complete surgical excision is not possible, e.g. spine or skull base, radiotherapy may be an option to delay disease recurrence and extend progression-free survival.6

Systemic Chemotherapy in Osteosarcoma

High-grade osteosarcoma, which accounts for the majority of osteosarcoma in children and adolescents, is predominantly treated by chemotherapy and surgery.27,28 The advantages of preoperative chemotherapy include:

1. providing symptom relief,
2. reducing size of primary tumour and therefore improving resectability and chance of limb salvage,
3. treating metastatic disease as well as micrometastases, and
4. allowing the assessment of response to chemotherapy.

The histological response to preoperative chemotherapy predicts survival outcome. Tumours with over 90% necrosis following preoperative chemotherapy are associated with a more favourable outcome.29 Metastatic disease is also strongly prognostic. However, the optimal chemotherapy regimen and schedules are yet to be determined. High-dose methotrexate, adriamycin (doxorubicin), and cisplatin (MAP) form the backbone in most chemotherapeutic regimes for high-grade osteosarcoma, especially in children and young adults.6,7 In older adults, doxorubicin and cisplatin alone without methotrexate is a reasonable option in view of poor tolerance to high-dose methotrexate in this patient population.6,7,30 The addition of ifosfamide to the traditional MAP backbone for osteosarcoma did not improve survival,
and thus is not employed in the adjuvant setting.³¹ At this moment, it remains unclear if switching or adding other drugs to the postoperative chemotherapy for patients with poor response to preoperative chemotherapy will improve survival outcome.

The European and American Osteosarcoma Study Group (EURAMOS)-1 randomised poor responders (defined as patients with >10% viable tumour after preoperative chemotherapy) to continue with the same chemotherapy (MAP), or to receive additional drugs (ifosfamide and etoposide, MAPIE). The results of this large study are eagerly awaited. Patients with metastatic disease (mainly to the lungs) have a significantly poorer outcome than those with non-metastatic disease. Thoracotomies with removal of all lung metastases should be considered. Options for salvage chemotherapies include high-dose ifosfamide with etoposide (IE), and gemcitabine with docetaxel. The role of interferon or muramyl tripeptide, either upfront or in salvage setting, remains unclear.³¹,³² Although the addition of muramyl tripeptide to standard chemotherapy in patients with completely resected osteosarcoma significantly improved overall survival in a large phase III randomised study, this finding was not associated with a significant corresponding improvement in the event free survival.³¹ Muramyl tripeptide is not available in Singapore.

4. Treatment of STS

Surgery in STS

Surgical resection, with appropriate negative margins, is the mainstay of treatment for STS. There is no universally agreed margin, but generally 1 cm of soft tissue, or an appropriate anatomic layer like fascia, is accepted.³³ Closer margins can be accepted in order to preserve uninvolved critical neurovascular structures.

Preoperative radiotherapy and/or chemotherapy can be considered to downstage large high-grade tumours to enable effective surgical resection. However, there is a risk of tumour progression on treatment and higher wound infection rates with preoperative radiotherapy. Postoperative radiotherapy should be considered following resections with close margins, or microscopically positive margins on bone, critical nerves, and vessels (see following section on Radiotherapy in STS).

The biopsy tract should be excised en bloc together with the main tumour during the definitive resection. Dissection should be done through grossly normal tissue that is not contaminated by tumour. Critical vessels and nerves can be preserved if they are not grossly involved by the tumour, by dissecting through the adventitia or epineurium. Radical resection of the entire anatomic compartments is not routinely required. In some situations, amputations may be required in order to achieve adequate local control. These are situations where complete resection of the tumour will result in a non-functional limb.

If positive microscopic or gross margins are suspected, surgical clips should be used to mark the site to facilitate subsequent radiotherapy planning or surgical resection. If surgical drains are used, they should be placed close to, preferably in line with, the surgical incision, to facilitate subsequent radiotherapy or repeat surgical resection.

The margins should be marked by the surgeon and reviewed with the pathologist. Should there be a positive gross margin, repeat resection to negative margins should be strongly considered. Microscopic positive margins may be acceptable in situations where wide excisions would result in severe morbidity (e.g. when sacrifice of major vessels or nerves is required) in which case, postoperative radiation treatment should be discussed.

Radiotherapy in STS

Good limb conservation surgery combined with postoperative radiotherapy is standard treatment for limb STS and achieves a high rate of local control while maintaining optimal function. Radiotherapy may be avoided in patients with low-grade tumours that have been completely resected or those with small and superficial high-grade tumours resected with adequate wide margins.

Postoperative radiotherapy is considered to be the standard of care for intermediate and high-grade STS as well as deep and large lesions. This allows preservation of function with similar local control rates and survival to radical resection.³⁴ The majority of patients with low-grade tumours will not require radiotherapy, however it should be considered for those with large, deep tumours that are incompletely resected, especially if adjacent to vital structures that could limit further surgery in the future.³⁵,³⁶ Patients who have undergone a compartmental resection or amputation do not require adjuvant irradiation assuming that the margins are clear.

The recommended postoperative radiation dose is 60-66 Gy in 1.8-2 Gy fractions. A 2-phase technique using a shrinking field is commonly used; 50 Gy to the initial larger volume followed by 10-16 Gy to a smaller volume.³⁵,³⁶ This dose may need to be reduced if the field includes critical structures (for instance, the brachial plexus). Dose to the skeletal bone should be avoided if possible, to prevent risks of fractures in future, and the volume should take into consideration natural tissue plane/compartments and fascia.

There is a VORTEX randomised clinical trial for extremity STS in the United Kingdom. It compares the standard 2-phase conventional radiotherapy technique with a single phase to a smaller tissue volume, in an attempt to
spare normal tissue and hence improve subsequent limb function without compromising local control. The study has completed accrual and results are pending.

Comparing pre versus postoperative radiation in limb sarcoma, preoperative radiation has been shown to be associated with increased postoperative wound complications compared to the standard postoperative treatment but less late toxicity and better limb function. The standard regimen for preoperative radiotherapy is 50 Gy, in 1.8-2 Gy fractions, followed by surgery approximately 6 weeks following completion of radiotherapy. Further radiotherapy (10-16 Gy) may be given postoperatively if tumour margins are positive. Preoperative radiation dose is lower compared to postoperative radiation and the treatment volumes are also smaller. Preoperative radiotherapy is not used routinely, but may be preferred in certain situations where the size of the radiation field required for postoperative treatment is likely to be associated with significant late morbidity, or when the tumour is of borderline operability and preoperative radiotherapy is judged to be capable of rendering the tumour operable. In such situations, more radiosensitive histological types like myxoid liposarcoma may benefit from this approach.

Systemic Chemotherapy in STS

The value of adjuvant chemotherapy in STS, as with any malignancy, is predicated upon 2 fundamental issues—the rates and patterns of recurrence and the efficacy of any therapy in modifying them. Factors like age, size, depth, histology, and anatomical site have been incorporated into validated nomograms to yield recurrence estimations for sarcomas based upon the cumulative datasets of several specialised sarcoma centres. Despite the greater accuracy in predicting recurrences using these tools, data directly addressing the benefit of adjuvant chemotherapy is patchy and inconsistent.

A European study involving 468 patients between 1977 and 1988 revealed no significant benefit of multi-agent combination adjuvant chemotherapy. However, a subsequent meta-analysis evaluating 18 trials revealed absolute risk reductions in recurrence and death of 12% and 11%, respectively, with the use of adjuvant doxorubicin in combination with ifosfamide. Despite this, the most recently reported large randomised trial using a modern day sarcoma combination chemotherapy regimen of doxorubicin and ifosfamide in 351 patients, two-thirds of whom had extremity sarcoma, revealed no benefit in recurrence free and overall survival. Concerns have been raised regarding certain aspects of this trial, including the relatively low dose intensity of ifosfamide used, the inclusion of a substantial number of patients with clinicopathological lower risk disease, and the heterogeneity of diagnoses studied. Nonetheless, it remains the largest randomised clinical trial of adjuvant doxorubicin-based chemotherapy in recent years.

Beyond the uncertainty surrounding absolute efficacy, there is also little data to guide the choice and duration of the regimen to be used in adjuvant therapy. A European randomised trial revealed no differences in outcomes between 3 and 5 cycles of neoadjuvant epirubicin in combination with ifosfamide for STS with high-risk clinicopathological features, suggesting that, if and when adjuvant chemotherapy is used, more dose intensive regimens may not always be superior. A large criticism of most studies in STS is the inappropriateness of treating disparate histologies, with unquestionably differing biologies and chemosensitivities, in an identical manner. An ongoing randomised trial is thus evaluating a histologically adapted approach (using agents with known preferential activity in particular histologies) in comparison with 3 cycles of epirubicin and ifosfamide. At the time of this writing, the role of adjuvant chemotherapy in completely resected STS remains controversial, and must be discussed on a case-by-case basis. In addition, we do not recommend the routine use of adjuvant chemotherapy as standard of care in resected extremity STS.

Extremity sarcomas are predisposed to both local and distant recurrence, with disease-associated mortality predominantly contributed by the latter. Doxorubicin has been used in the systemic treatment of advanced sarcomas for the last 40 years and remains the most broadly active agent. Ifosfamide is another commonly used drug in first-line therapy, with a more pronounced disparity in activity across different histologic subtypes.

A landmark randomised controlled trial compared single-agent doxorubicin against the combination of doxorubicin and ifosfamide in advanced STS with more than 200 patients evaluated from 2003 to 2010. While combination therapy doubled objective response rates (26% versus 14%) and improved progression-free survival (7.4 versus 4.6 months), overall survival was no different in the 2 arms. In second-line therapy, there are several active agents, either as single agents or in combination. The combination of gemcitabine with either docetaxel or dacarbazine has demonstrated salutary improvements in overall survival in pretreated advanced STS in 2 large randomised phase II studies. Single agent gemcitabine is also reported to be effective in leiomyosarcoma.

Pazopanib, a multi-targeted tyrosine kinase inhibitor directed against the receptors of vascular endothelial growth factor, platelet derived growth factor, fibroblast growth factor and KIT, is approved for the treatment of advanced pretreated non-adipocytic STS, following demonstration of a significant progression-free survival benefit when compared

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against a placebo in a large randomised phase III trial. Several histological subtypes are often treated based upon observed preferential sensitivity to specific agents, such as trabectedin in myxoid liposarcoma and weekly paclitaxel in angiosarcoma, emphasising again the crucial need for appreciating the clinicobiological diversity of sarcomas in order to select appropriate therapy.

**Conclusion**

In conclusion, extremity sarcoma is a complex and heterogeneous group of diseases best managed in a high volume sarcoma centre experienced in the management of these diseases. The initial efforts are aimed at securing an accurate diagnosis leading to a disease-stratified approach in terms of surgery and adjunctive therapies comprising chemotherapy and radiotherapy as appropriate (Figs. 1 and 2). Clinical practice guidelines contextualised to the local patient and unique healthcare setup in Singapore will hopefully streamline care and improve clinical outcomes for our sarcoma patients.
Conflicts of Interest

All the authors have nothing to disclose.

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