Review

Advances in Molecular Diagnosis and Personalized Treatment of Soft Tissue Sarcomas

Abstract

Soft tissue tumors are a diverse range of diagnostic entities including the majority of them benign in nature and behavior. Soft tissue sarcomas are uncommon tumors that represent 1% of all malignancies and are classified as malignant entities. The wide variety of tumor types and pathological overlap across the tumor entities make the diagnosis of soft tissue tumors difficult for pathologists. With the advancement of molecular genetic tools, our understanding of the molecular pathogenesis of soft tissue tumors has been significantly important in diagnosis, treatment, and prognosis. The role of surgery, chemotherapy, radiotherapy, target therapy, and immunotherapy are needed to identify patients who benefit from each type of treatment.

Thisreviewaimstoprovideanupdateonrecentlydescribed diagnostic methods and management of soft tissue sarcomas.

Keywords:softtissuetumor;sarcoma;molecularpathology;immunohistochemistry, target therapy, Immunotherapy

1. Introduction

“In general, soft tissue tumors are classified as connective tissue tumors, which encompass a diverse variety of tumors with varying degrees of differentiation, such as benign mesenchymal tumors and non-osseous sarcomas. Less than 1% of all cancers are soft tissue sarcomas” [1]. The terminology used to characterize these tumors typically refers to their histological origin; for example, malignant tumors originating from fibrous tissue are called fibrosarcomas, whereas malignant tumors originating from bone are called osteosarcomas. Several histological subtypes that may have distinct clinical histories and prognoses are usually present in each sarcoma. The primary focus of treatment for these tumors is pathological diagnosis, much like for

other malignancies. However, because soft tissue tumors are uncommon, diagnosing them can occasionally be challengingdue to the rarity and histological diversity of this group of tumors [2].

“The diagnostic methods for soft tissue tumors using molecular pathology are developing quickly. In recent years, genetic information on tumors has been mostly provided via immunohistochemistry and genetics. A wide range of molecular changes, including growth factors, oncogenes, specific mutations, gene deletions, tumor suppressor genes, and epigenetic changes. Molecular cytogenetics (fluorescence in situ hybridization [FISH]), chromosomal analysis, and molecular assays (RT-PCR and NGS) lead to new insights and approaches in the classification and treatment of these tumors and provide significant diagnostic, prognostic, and even therapeutic information” [3, 4].

According to the most recent classification, sarcomas can be classified into two main groups based on their genetic abnormalities: (1) tumors with a relatively simple karyotype, usually a specific translocation, or tumors with specific activating mutations within oncogenes, or tumors with inactivating mutations within oncogenes, which are tumor suppressor genes. and (2) sarcomas containing several, occasionally intricate chromosomal abnormalities. The subsequent category of these numerous and frequently intricate abnormalities is separated into two groups: (a) soft tissue tumors exhibiting a consistent pattern of genetic imbalances and/or chromosomal breakpoints; these atypical patterns, in conjunction with additional histopathological characteristics, aid in a precise diagnosis; and (b) tumors lacking a distinct pattern, distinguished by a significant level of genomic intricacy and instability (emphasized by an abundance of non-specific marker chromosomes). The use of many common clinical genetic techniques as a differentiation tool is precluded by identifiable heterogeneity, fluctuating copy number variations, and intra- and intratumoral mutations (heterogeneity and chromosomal divergence among others) [5,6].

2. Methods of Soft Tissue Tumor Diagnosis

The new WHO classification of bone and soft tissue tumors, which was just published, is a significant advancement in the field of development and sufficiently processed tissue and extensive clinical data are necessary for the diagnosis of a soft tissue lesion [7]. The meticulous inspection of traditionally stained sections under low magnification is the first and most crucial step in making an accurate diagnosis. Generally speaking, the most important method for diagnosing soft tissue sarcomas is still a light microscopic examination of morphology. Using the reagents in panels and taking an algorithmic approach is necessary for the most economical and efficient use of immunostains [7]. Based on a particular differential diagnosis and pertinent pretest probability, a specific molecular test should be chosen [8]. Given that numerous malignancies contain the same gene or possibly the same translocation, pathologists must take caution when assessing cases [3]. “A coordinated interpretation of a reasonable morphological impression, clinical and radiologic data, and immunohistochemical and molecular discoveries that corroborate the morphological impression should form the basis of the final diagnosis” [8].

3. Molecular tests

“The techniques used to diagnose soft tissue sarcomas and the results of molecular testing have grown more and more vital in increasingly critical investigations and the diagnosis of soft tissue sarcomas” [9,10]. The most popular molecular techniques include reverse transcriptase-polymerase chain reaction (RT-PCR), immunohistochemistry (IHC), fluorescence in situ hybridization (FISH), conventional cytogenetics, and next-generation sequencing (NGS). Traditional cytogenetics requires fresh tissue and assesses the entire karyotype. However, FISH and RT-PCR identify specific translocations or amplifications linked to a particular tumor type [11,12]. Immunohistochemistry is the most often utilized indirect (alternative) approach among practicing pathologists (e.g., MDM2 and STAT6). Although FISH and RT-PCR are complementary methods, the choice of method mostly depends on the experience of the laboratory. FISH is a highly desirable test for well-differentiated lipomas, mucous tumors, spindle cell tumors, and round cell sarcomas [11,13]. Molecular testing has a direct and potentially crucial role when examining soft-tissue sarcomas. Fusion genes arising from chromosomal rearrangements, including

inversions, translocations, deletions, and insertional or tandem duplications, serve as highly effective indicators for the classification of tumors. Fusion gene sarcomas typically lack a benign or premalignant phase. Testing for chromosomal translocations/fusion genes has distinct advantages as a diagnostic tool because these molecular aberrations are usually present from the earliest stages of the disease and continue to exist in lesions that have been treated and metastasize, as well as in neoplasms as they become less differentiated [14]. Table1

Table 1: Abnormal genes in soft tissue sarcomas

Tumor	Abnormal genes
Alveolar rhabdomyosarcoma	PAX3-FKHR/PAX7-FKHR
Embryonal rhabdomyosarcoma	IGF2, ATR, PTCH, CDKN2A , and TP53
Congenital fibrosarcoma	ETV6-NTRK3
Desmoplastic small round cell tumors	EWS-WT1
Ewing sarcoma/PNET	EWS-FLI1
GIST	Lacking KIT, PDHFR mutations
Myxoid/roundcelliposarcoma	EWSR1-DDIT3
Malignant peripheral nerve sheath tumor	NF1, CDKN2A
Kaposi sarcoma	Complex karyotypes
Leiomyosarcoma	Complex karyotype
Synovial sarcoma	SYT-SSX1/SYT-SSX2
Dermatofibrosarcoma protuberans	COL1A1-PDGFB

4. Immunohistochemistry

"A key component in the diagnosis of soft tissue sarcomas is immunohistochemistry"[15]. Over the past ten years, advances in molecular genetics have resulted in the creation of quick, low-cost, and novel immunohistochemistry stain-based diagnostic procedures [15]. Using tissue sections, monoclonal or polyclonal antibodies are used to identify antigens present in a particular tumor. Three broad categories can be applied to recently identified immunohistochemistry markers: (1) proteins associated with molecular genetic alterations (e.g. β-catenin, SMARCB1 [INI1], MDM2, SDHB, CDK4, RB1, H3K27me3, PDGFRA MYC, SMARCA4); (2) pro-protein products of gene fusions (e.g. ALK, FOSB, CIC-DUX4, BCOR, DDIT3,

CCNB3, TFE3, CAMTA1, SS18:SSX and pan-TRK) and (3) diagnostic markers identified by gene expression Profiles (e.g. DOG1, ETV4, MUC4, NKX2-2, NKX3.1, SATB2 and TLE1).

5. Classificationof Soft Tissue Sarcoma

A notable accomplishment in the field of research and standardization of diagnosis based on contemporary genetic approaches is the publishing of the new WHO classification of soft tissue and bone tumors. Furthermore, the WHO classification of 2020 has broadened the range of oncologists and other specialists who can patterns (e.g., rearrangement of the SYT gene in synovial sarcoma; amplification of the MDM2 gene in well-differentiated liposarcoma). While many other anomalies (especially fusion genes) seem to represent non-driving (random) molecular events and their detection has been enhanced by the extensive use of molecular diagnostic tools, this represents a significant advancement in the treatment of sarcoma[16].

Based on histology, STS is classified into more than 50 kinds. The presentation, imaging, differential diagnosis, and course of treatment for all STS are the same. To differentiate between distinct types, histologic findings, and molecular markers are employed. Frequently examined soft tissue sarcomas comprise

- Leiomyosarcoma
- Liposarcoma
- Fibrosarcoma
- Ewing sarcoma
- Follicular Dendritic Cell Sarcoma (FDC sarcoma)
- Gastrointestinal Stromal Tumors (GIST)
- Malignant Peripheral Nerve Sheath Tumor (MPNST)
- Rhabdomyosarcomas
- Synovial sarcomas
- Undifferentiated Pleomorphic Sarcoma
- Dermatofibrosarcoma Protuberans
- Epithelioid Sarcoma
- Angiosarcoma
- Clear Cell Sarcoma

6. Leiomyosarcoma (LMS)

“Leiomyosarcomas (LMSs) are soft tissue tumors that arise mostly from smooth muscle in nonvisceral structures like large to mid-sized veins and/or dermal pillar smooth muscle in the trunk or extremities and from smooth muscle in visceral organs like the uterus or the gastrointestinal tract. With a peak incidence at age 70, the incidence of LMS rises with age. However, within the perimenopausal age range, uterine LMS (uLMS) manifests at a younger age, with a growing frequency from 30 years of age and a peak at 50 years of age. Overall, depending on the location of the tumor, the incidence of LMS differs by sex. In contrast to cutaneous and other LMS locations, retroperitoneal leiomyosarcomas (RP-LMSs), especially of the inferior vena cava (IVC), are more common in women, whereas cutaneous and other LMS sites have a slightmale predominance” [17].

LMSs are tumors derived from smooth muscle, and well-differentiated tumors have the characteristic architecture of plump spindle cells intersected at right angles in broad fascicles. Tumors can exhibit different levels of hyalinization. Neoplastic spindle cells have defined cell boundaries, cigar-shaped nuclei, and an abundance of strongly eosinophilic fibrillary cytoplasm. Additionally, "monster cells" with sporadic, pleomorphic, and hyperchromatic nuclei are frequently found in conventional LMSs. In cases where the diagnosis of LMS is unclear, diagnostic immunohistochemical studies can help confirm the diagnosis. Generally, the presence of at least two of the following muscle markers—desmin, smooth muscle actin, muscle actin HHF-35, h-caldesmon, smooth muscle myosin, or calponin—or their patchy expression is used to confirm smooth muscle differentiation.LMSs are smooth muscle differentiation tumors, and well-differentiated tumors have the characteristic architecture of the portion of the tumor that appears to be the most well-differentiated and should always be assessed using immunohistochemistry, since pleomorphic or dedifferentiated areas may not express any myogenic markers at all. Up to 40% of these tumors, especially high-grade tumors, have keratin and epithelial membrane antigens, which are not specific to LMS. Although it is frequently lost in high-grade

illness, estrogen receptor (ER) and progesterone receptor (PR) expression can be observed in uLMS, certain nonuterine-retroperitoneal-LMS developing in women, and infrequently in malignancies of the extremities in both sexes [18].

Target therapy is difficult due to the complex pathophysiology of LMS. Significant mutational heterogeneity, including recurrent whole-genome duplication, extensive DNA copy-number alterations, and chromothripsis, are the defining characteristics of LMS rather than a single, defining genomic alteration [19]. Mutations or deletions in the tumor suppressors RB1, PTEN, and TP53 are the most frequently seen genomic changes across several investigations.Surgical resection combined with or without adjuvant or neoadjuvant radiation and/or chemotherapy is considered the gold standard for localized disease. The accepted standard of care for localized extremities LMS is neoadjuvant radiation. The most widely prescribed first-line treatment for advanced LMS is anthracycline doxorubicin, which is also among the first medications to show significant improvement in individuals with advanced disease.

A retrospective analysis revealed that ifosfamide had no effect in LMS and that there was no discernible difference in OS between ifosfamide and doxorubicin as first-line treatment and the combination. Dacarbazine plus doxorubicin showed a better response rate of 30.9% in advanced LMS patients when compared to doxorubicin monotherapy (25.6%) and doxorubicin plus ifosfamide (19.5%) [20]. Combining gemcitabine with the taxane docetaxel has been suggested as a potentially beneficial regimen due to their complementing mechanisms of action. In a separate phase III trial, eribulin was found to have an OS advantage over dacarbazine in both liposarcoma and LMS populations (median OS 13.5 vs. 11.5 months; P =.0169). However, this benefit is not retained when examining the treatment impact in the LMS group only. Further therapeutic possibilities for LMS include liposomal doxorubicin, dacarbazine, and gemcitabine as a single agent[21]. FDA-approved targeted treatments for LMS are nonexistent. The FDA has approved pazopanib, a tyrosine kinase inhibitor, for the treatment of advanced soft tissue sarcomas, including LMS, that have undergone previous chemotherapy. It has a high affinity for VEGFR, PDGFR, KIT, and FGFR [22]. Based on the PALETTE trial results, pazopanib was found to significantly prolong the median progression-free survival (PFS, 4.6 vs. 1.6 months for placebo). Additionally, 73% of patients with pazopanib (6% had a partial

response and 67% had stable disease) compared to 38% with placebo (stable disease only) experienced a clinical benefit[23]. Pazopanib had a median PFS of 3.0 months, OS of 17.5 months, and an objective response rate (ORR) of 11% about ULMS [24]. The only approved targeted therapies for LMS, other than pazopanib, are those that have approvals that are independent of tissue type. Pembrolizumab and dostarlimab for tumors with high microsatellite instability or TMB [25], dabrafenib plus trametinib for tumors with BRAF V600E mutations, selpercatinib, the RET inhibitor, for tumors with RET fusions [26], and NTRK tyrosine kinase inhibitors (TKIs) like entrectinib and larotrectinib for fusions involving NTRK [27]. To treat LMS, especially ULMS, hormone therapy that targets the estrogen and progesterone receptors (ER and PR) has also been used [28]. These were predicated on research showing that 25–60% and 35–65%, respectively, of ULMS express ER and PR. Improved survival was correlated with higher expression of ER and PR.

7.Liposarcomas

"The most prevalent subtypes of liposarcoma are well-differentiated (WD) and dedifferentiated (DD) liposarcomas" [29]. "The amplification of several hundred genes, including MDM2, an inhibitor of the tumor suppressor p53, and CDK4, a crucial regulator of cell cycling, is seen in both WD and DD tumor cells on chromosome 12q13–15"[30]. The second most prevalent subtype of liposarcoma is called myxoid/round cell (MRC) liposarcoma. The translocation of chromosomes 12 and 16 (t12;16)(q13;p11), which results in a fusion gene arrangement between FUS and CHOP/DDIT3, is one of the genetic anomalies that characterize MRC liposarcoma. Rather than affecting the retroperitoneum, MRC liposarcoma typically affects the proximal lower limbs in younger patients. The third, rarest, and least understood subtype of liposarcoma is called pleuromorphic liposarcoma. Chromosome duplications, gains, losses, and rearrangements are among the complicated modifications observed; a single distinctive genetic defect has not yet been found.

The efficacy statistics from trials covering all subtypes of soft tissue sarcoma are the basis for the current cytotoxic chemotherapy drugs used for unresectable/metastatic liposarcoma. For patients with advanced disease, anthracycline-based combinations or single-agent anthracyclines (mostly doxorubicin) are regarded as the standard for first-line therapy [31].Ifosfamide and dacarbazine are two more drugs with single-

agent activity that are commonly used in combination with doxorubicin. A common non-anthracycline combination utilized in the second-line context for liposarcomas is gemcitabine plus docetaxel. As second-line treatments, ifosfamide, dacarbazine-gemcitabine, and docetaxel-gemcitabine meet these criteria for disease stabilization, according to a recent analysis of published series [31]. Many of the novel systemic therapy for soft tissue sarcoma has the potential to be effective in liposarcoma. Most of these new treatments target a particular, aberrant genetic or molecular pathway, and are based on the knowledge of disease biology intrinsic to a particular sarcoma histology. (Table 2)

Table 2: Novel systemic therapy of liposarcoma

Novel Therapy	Mechanism of Action	Liposarcoma Histologic Subtype	Reference
Trabectedin	Binding of DNA minor groove; direct interaction w/FUS-CHOP	MRC	32
Nelfinavir	SREBP-1 inhibitor	WD/DD	33
Pazopanib, Sorafenib, Sunitinib	Tyrosine kinase receptor Inhibitor	all	34
PD 0332991	CDK4/6 inhibitor	WD/DD	30
Eribulin	Microtubule inhibitor	DD	35
RG7112	MDM2 antagonist	WD/DD	33
Troglitazone, Rosiglitazone, Efatutazone	PPAR-gamma agonist	all	36

Multiple major genetic and molecular aberrations are frequently detected in the same tumor within each histologic subtype of liposarcoma (e.g., MDM2 and CDK4 amplification in WD/DD liposarcoma). Thus, like that of traditional cytotoxic chemotherapy, combinations of innovative medicines may have synergistic effects that improve disease stability and potentially even yield an objective response. Immunotherapy and molecular-based therapy together may improve response rates over time and boost overall survival [37].

8.Fibrosarcoma

Fibrosarcoma is an uncommon, extremely aggressive tumor originating from mesenchymal cells. It comes from spindle-shaped fibroblasts that have undergone pathological transformation and have an abnormally high rate of division. [38]. Fibrosarcoma can be classified into two categories: the adult type and the infantile/congenital type. Deep soft tissue is a common location for fibrosarcoma[39]. The tumor mass has an average size of 3–8 cm, a spherical shape, a strong demarcation from the surrounding tissue, and a hard firmness [40].

A biopsy's guidance, diagnosis confirmation, tumor size assessment, and disease stage determination are all aided by radiological imaging [41]. Confirming a tumor's suspicion, determining its local extent, staging the illness, evaluating post-treatment alterations, and identifying tumor recurrences all depend on radiologic imaging. A less invasive technique like a core needle biopsy or fine needle aspiration (FNA) biopsy may be employed. The majority of soft tissue sarcomas belong to one of the following five histomorphologic groups: spindle cell pattern [42], tiny round cell pattern, myxoid pattern, pleomorphic pattern, and epitheloid cell pattern.

To distinguish fibrosarcoma from other spindle-cell neoplasms, histopathology is insufficient on its own. Using particular antibody reagents, immunohistochemistry (IHC) is used in the diagnosis of fibrosarcoma to identify tumor markers that are crucial for differential diagnosis [43].

Vimentin is frequently the only positively stained marker in fibrosarcoma [43]. As an indicator of myofibroblastic differentiation, muscle-specific antigen (MSA) and/or smooth muscle actin (SMA) may occasionally be found [10, 3]. Sometimes CD34 can be found in fibrosarcomas that develop secondary to either dermatofibrosarcoma or solitary fibrous tumor (SFT). Specific miRNAs that may affect tumor growth, cell cycle regulation, apoptosis, differentiation, and invasion are aberrantly expressed by malignant cells.

The expression profile of miRNA seems to vary depending on the kind of cancer. Additionally, fibrosarcoma can be distinguished from other spindle-cell sarcomas using this method [44].

First-line treatment for patients with advanced-stagefibrosarcomas involves chemotherapy, with anthracyclines serving as the basis. The most commonly used chemotherapy in this situation is doxorubicin. In addition to doxorubicin, ifosfamide, and actinomycin D can also provide response rates of more than 15% [45].
Mesna, doxorubicin, ifosfamide, and dacarbazine a presurgical treatments that can be beneficial for patients with high-grade fibrosarcomas [46].

9.Ewing sarcomas

A FET gene family member (usually EWSR1) and an ETS gene family member fuse to form Ewing sarcoma (EWS) [47]. Additional mutations may arise in TP53 (7%) [1,2], CDKN2A (12%), and STAG2 (15–22%). Chimeric transcription factors, encoded by FET::ETS fusion genes, act as master regulators, activating and repressing thousands of genes. To create EWS, these atypical transcription factors must express themselves. The most frequent translocation, t(11;22)(q24;q12), which yields the EWSR1:FLI1 fusion mRNA and protein, occurs in 85–90% of cases.
The MIC2 gene produces CD99, a glycoprotein found on the cell surface. About 95% of EWS have strong, diffuse membranous expression [48]. With a somewhat lower .sensitivity, FLI1 immunohistochemical detection is more specific for ES than CD99 EWSR1-FLI1 fusions are found in about 85% of ES patients; EWSR1-ERG fusions are found in 10% of cases, while fusions between EWSR1 and additional transcription factors from the ETS family, namely FEV1, are found in 3% of cases. A small group of ESs has the FUS gene rearranged with an ERG or FEV gene partner, as opposed to the EWSR1 gene; these tumors are immunohistochemically and morphologically .identical to EWSR1-positive ES
The results of the imaging constitute the basis for the initial staging, the biopsy, the .local and systemic therapies, and the post-treatment care
Before beginning treatment, comprehensive imaging is essential for determining both distant metastasis (M-staging) and locoregional expansion (T-staging). The staging of EwS patients can be reliably performed with 18F-FDG-PET/CT with a diagnostic chest CT, or with either 18F-FDG-PET/MRI or whole-body MRI in conjunction with a thorax CT.
Open biopsies have been claimed to be nearly 100% accurate in certain publications. The range of CNB-reported biopsy success rates for patients with sarcoma is 50% to 98%. In particular, for EwS patients, the success rate of needle biopsy may be lower

than that of open biopsy [49].Unless urgent surgery is required at the time of diagnosis, neoadjuvant chemotherapy is usually followed by definitive surgery. Treatment: Surgery and/or radiation therapy are often used after the first course of chemotherapy, which usually consists of vincristine, ifosfamide, doxorubicin, and etoposide (VIDE). The treatment may subsequently be finished with further chemotherapy using VIA (vincristine, ifosfamide, and actinomycin D) and VAC (vincristine, actinomycin D, and cyclophosphamide). Following two to three months of chemotherapy (VIDE), the primary tumor will be treated with either surgery or radiation therapy. The goal will be to administer a total dose of 50–60 Gy in 5–6 weeks for the majority of patients.

EWSR1/FLI1 and EWSR1/ERG, the two most prevalent fusion proteins, are implicated in several regulatory and cell signaling pathways [50]. In most cases, these fusion proteins function as transcription factors. For example, Boulay et al. [51] discovered a chromatin-binding factor (BAF) that interacts with EWSR1/FLI1 to induce phenotypic alterations and gene expression in ES tumor cells.

Although tyrosine kinase inhibitors (TKIs) frequently target receptors from different tyrosine kinases, the inhibitors of the vascular endothelial growth factor receptor (VEGFR), pazopanib, regorafenib, and cabozantinib, have drawn particular attention because of the volume of information that has been gathered about the role of angiogenesis in Ewing sarcoma [52]. Stable disease was observed for 6 and 13 months on pazopanib therapy in a retrospective series that included two ES patients[53].Talazoparib exhibits substantial PARP trapping, is a highly strong inhibitor of PARP1 and PARP2, and is active in cancer cell lines with impairments in DNA damage repair. Studies on PARP inhibitors both in vivo and in vitro showed significant efficacy against ES [54].The only VEGFR2 tyrosine kinase inhibitor with specific MET receptor inhibitory effect is Cabozantinib (XL184), which has demonstrated anti-tumor activity in vitro and in vivo in several osteosarcomas and Ewing sarcoma tumor models [55].

10.Follicular dendritic cell sarcoma (FDC sarcoma)

In 1986, Monda et al1 reported the first description of follicular dendritic cell sarcoma (FDCS), a tumor with follicular dendritic cell differentiation. Despite being an uncommon tumor, FDCS typically affects lymph nodes, most frequently the cervical, mediastinal, or axillary lymph nodes. Less than one-third of cases also had

extranodallocations (tongues, nasopharynx, pancreas, liver, and peritoneal and peripancreatic tissues) with FDCS [56,57].Pathology**:** Histologic patterns of spindle cells in the tumor include diffuse sheets, fascicles, bundles, meningioma-like (whorled), storiform (the most common type), and heterogenicity in growth patterns. Tumor cells exhibit fibrillary, somewhat eosinophilic cytoplasm and are plump with syncytial, unclear cell boundaries. Tumor cells feature vesicular nuclei that contain nucleoli, thin chromatin, and occasionally intranuclear pseudoinclusions; binucleate cells are also seen. It is possible to see perivascular B or T cells.

Immunohistochemistry: Cells exhibit membrane responses to CD21, CD23, and CD35, which is the C3d complement receptor. The most sensitive marker in FDCS that exhibits diffuse high cytoplasmic positivity is clusterin. In other dendritic cell tumors, this marker is negative. Podoplanin (D2-40) is an additional highly responsive marker with a robust membrane response. Another novel and practical diagnostic that is effective in the diagnosis of FDCS is c-synuclein, which stains follicular dendritic cells significantly.

HLA-DR, fascin, EGFR, vimentin, and other markers are typically positive in tumors. The range of the MIB-1/Ki-67 index is 1% to 25%. The tumor cells do not stain positively for CD1a, lysozyme, myeloperoxidase, HMB-45, desmin, CD30, CD34, CD79a, CD3, or high-molecular-weight cytokeratins[58,59]**.**

Treatment: Although FDCS usually progresses slowly, there is a 40% to 50% chance of local recurrence, and an aggressive clinical course, including metastases to the liver, lungs, or lymph nodes, is conceivable[60]. For both initial and recurrent cases, the preferred course of treatment is complete surgical excision. Chemotherapy and radiation have not yet been shown to have advantages and benefits. If a patient has a BRAF V600 mutation, vemurafenib, an inhibitor of the BRAF enzyme, may be an option. EGFR inhibitors provide a further treatment option, particularly for patients with moderate-to-strong EGFR expression.

11.Gastrointestinal Stromal Tumors (GIST)

With an annual incidence of roughly 10–15 cases per million, gastrointestinal stromal tumors (GISTs) are the most prevalent mesenchymal neoplasms of the gastrointestinal tract [61,62]. They replicate the Cajal (ICC) lineage/differentiation's interstitial cells. GISTs rarely affect the colon/rectum or the esophagus, usually occurring in the

stomach, small intestine (including the duodenum), and finally, the stomach. The liver and peritoneum are the primary sites of metastases [63].

Three distinct morphologic patterns are generally visible based on cytomorphology [62]. About 70% of GISTs have spindle cell morphology, which is made up of cells with ovoid nuclei, palely eosinophilic fibrillary cytoplasm, and often ill-defined cell boundaries that resemble syncytial growths.

According to immunohistochemistry, 95% of "classic" GIST express KIT overall [64]. Furthermore, it has been observed that 60–70% express CD34, 30–40% express smooth muscle actin (SMA), 5% express S-100 protein, and 1-2 percent express desmin or keratin [65].

GISTs were subclassified using an SDHB IHC into two groups: one that was SDH-competent and the other that was SDH-deficient. The GISTs with KIT and PDGFRA mutations, GISTs with mutations in BRAF, NF1, HRAS, and NRAS, and (iii) GISTs with extremely uncommon reported mutations in ARID1A, ARID1B, CBL, FGFR1, ATR, LTK, SUFU, PARK2, ZNF217, KRAS, MEN1, and PIK3CA are all included in the SDH-competent tumor category. Furthermore, GISTs that possess structural chromosomal alterations, such as those found in FGFR1-HOOK3, FGFR1-TACC1, ETV6-NTRK3, KIT-PDGFRA, and PRKAR1B-BRAF, are classified as SDH-competent GISTs [66]. The group of tumors deficient in SDH comprises wt-GISTs linked to CT, CSS, or intermittent pediatric and so-called "young adult" GISTs [63,66].

Options for GIST Treatment:For non-metastatic wt-GIST, surgical resection is thought to be the primary therapeutic option. If a druggable targetcannot be found, surgical management should also be taken into consideration as a therapy option in the metastatic context, in the group known as wt-GIST [67]. Systemic treatment for metastatic wt-GIST had a better response to sunitinib, particularly in the juvenile GIST group, but no objective tumor response to imatinib [68].

12.Malignant peripheral nerve sheath tumor (MPNST)

Malignant peripheral nerve sheath tumor (MPNST) is the sixth most common soft tissue sarcoma, approximately 5–10% of all soft-tissue sarcomas are malignant

peripheral nerve sheath tumors (MPNSTs), which are a very uncommon malignancy [*69,70]*. It does not include epineurium or nerve vasculature; it refers to malignant tumors of peripheral nerves or nerve sheath cells even though Schwann cells or neural crest-origin pluripotent cells are often the sources of MPNSTs [71].
Malignant triton tumor, glandular MPNST, and epithelioid MPNST subtypes were also described. In the general population, MPNST affects one in 100,000 people, equally affecting both sexes [72].Etiology and Risk Factors: Several risk factors have been linked in the past to the beginning of MPNST. For 50% of MPNST patients, NF1 is the most significant component. An additional factor that may raise the risk of MPSNT is a history of therapeutic radiation. The malignant potential of PN and ANNUBP can lead to the development of MPNST.

Diagnosis: Peripheral nerve sheath tumor that is malignant (MPNST). The most recent techniques for detecting MPNST include molecular detection during the pathogenesis of the condition, gene mutation studies, and conventional imaging and pathology approaches. Improved diagnosis and grading of MPNST will be possible with the application of novel molecular targets. It is highly advised to do a biopsy to diagnose and grade soft tissue sarcomas. There isn't a single pathogenic criterion for MPNST, especially sporadic MPNST, because gene mutation locus and immunohistochemistry symptoms vary so much. As such, it is difficult to differentiate it from other soft tissue sarcomas.At the moment, exclusion is the main basis for MPNST diagnosis. There are no unique molecular markers for MPNST. As mentioned earlier, the diagnosis of exclusion also forms the basis of the immunohistochemistry analysis. (Table 3)

Table 3. Immunohistochemical markers for MPNST.

Markers	Positive %	References
Nestin	94	73
H3K27me3	30–90%	74
S-100	50–60%	75
p16	45%	76
p27	33%	77
SOX-10	27%	78
p53	21%	79

The frequently used markers and the MPNST expression rate are shown in this table.

Treatment: Complete surgical resection to achieve negative margins is the only successful treatment for MPNST, and there are few other choices [80]. For those with metastatic or incurable MPNST, chemotherapy represents an alternate course of treatment. When it comes to high-grade lesions or tumors bigger than 5 cm, radiation therapy is frequently advised [81]. Radiation therapy produces great local control over the long term [82]. The pathways of NF1-Ras, Raf-MEK-ERK (Sorafenib), PI3K-AKT-mTOR (Selumetinib/Sirolimus), Wnt signaling, and abnormal expressions of apoptotic proteins, the general loss of polycomb repressive complex 2 (PRC2), upregulation of the HDAC family, abnormal expressions of receptor tyrosine kinases (Imatinib, Dasatinib), expressions of programmed cell death ligand (PD-L1), aurora kinase (Alisertib), and various microRNAs have all seen a rapid development of translational research on the driving factors and therapeutic targets of MPNST in recent years.

For MPNST that is incurable or metastatic, doxorubicin-based cytotoxic chemotherapy continues to be the recommended course of treatment. Depending on the study, RR for incurable or metastatic disease can vary from 20% to 60%. When one considers stable disease, the CBR is close to 80%.[83] Although regimens incorporating ifosfamide show the highest RR, adding this medication has no overall survival benefit.

13.Rhabdomyosarcomas

Rhabdomyosarcomas (RMS) are a class of soft tissue tumors related to the skeletal muscle lineage that are generally found in youngsters, however, they are relatively uncommon in adults. Based on histopathologic characteristics, two subgroups—embryonal (ERMS) and alveolar (ARMS)—were identified and associated with particular clinical characteristics and genetic alterations. ARMS is associated with the chromosomal translocations 2;13 and 1;13,)(p36;q14). which produce the PAX3-FKHR and PAX7-FKHR fusion products, respectively. Chimeric proteins, which are produced when PAX3 or PAX7 combines with FOXO1, are present in most ARMS. The resulting chimeric protein induces abnormal transcription, which in turn triggers the start of a myogenesis pathway and unchecked cellular division [84]. Based on

these data, Downing et al. [85] created a molecular diagnostic test in 1995 that used reverse transcriptase–polymerase chain reaction (RT-PCR) to identify this abnormality. These proteins seem to be the direct cause of the adverse outcome associated with this subtype, and they also induce a distinct pattern of downstream protein expression. These translocations, as opposed to those involving wild-type proteins, impact the processes of development, differentiation, and apoptosis, which subsequently influences the fusion products' expression, functionality, and subcellular localization. Ultimately, oncogenic activity is supported by these changes.

Young children are more likely to have the embryonal and botryoid subtypes, young adults are more likely to have the alveolar subtype, and older individuals are more likely to have the pleomorphic subtype . (Table 4)

A biopsy is used to make the diagnosis. Myoglobin, desmin, myosin, and vimentin MyoD1 are all positive for immunostains.

Table 4 Classifications of Rhabdomyosarcomas [86]

Horn-Enterline	**National Cancer Institute NCI**	**International**
Embryonal	Embryonal	Embryonal
Botryoid	Botryoid	Botryoid
Alveolar	Alveolar	Alveolar
Pleomorphic	Pleomorphic	Pleomorphic

Treatment: A multimodal strategy that includes chemotherapy, surgical resection, and/or radiation therapy is currently the first line of treatment for all RMS risk groups. Vincristine, actinomycin D, and cyclophosphamide (VAC) make up the conventional chemotherapy backbone in North America [87], whereas isofasfamide, vincristine, and actinomycin D (IVA) make up the chemotherapy backbone in Europe [88]. VAC and IVA have remained in use in their respective regions since a randomized trial found no discernible difference in patient outcomes between the two therapy combinations [89]. With frontline multi-modality therapy, children with low-risk RMS (located in favorable anatomical areas, grossly resected ERMS) are now seeing great outcomes, with 90% of them not experiencing a relapse. Patients with metastatic disease continue to have poor survival rates (event-free survival <20%, excluding

patients less than 10 years old diagnosed with ERMS), and there has been no progress in frontline treatment in the past 30 years [90]. A third of juvenile RMS patients may either relapse or develop progressive disease; the median interval between relapse and progression is 13 months from the date of initial diagnosis [91]. Generally, chemotherapy and local control (RT or surgery) are used to treat most recurrent RMS patients. Generally, chemotherapy and local control (RT or surgery) are used to treat most recurrent RMS patients.Salvage chemotherapy, such as irinotecan/vincristine or alternating vincristine/doxorubicin/cyclophosphamide, and etoposide/ifosfamide, may be beneficial for patients who show relapse following low-risk disease [92]. Phase II trials for children with relapsed RMS have sadly failed to show significant, single-agent effectiveness of targeted inhibitors like sorafenib [93] and a monoclonal antibody targeting IGF-1R (R1507).

14.Synovial sarcomas

Young adults are more likely to develop synovial sarcomas than other soft tissue sarcoma subtypes. The pathognomonic t(X;18) translocation, which causes the fusion of the SS18 (formerly SYT) gene on chromosome 18 with an SSX gene on chromosomal X (SSX1, SSX2, or infrequently SSX4), is present in the majority of synovial sarcomas.[94] The disease has been determined to have a relatively stable genome and few further mutations, with this genetic trigger being the only consistent cytogenetic aberration[95]. The histological overlap with various tumor forms makes the pathologic diagnosis of synovial sarcoma difficult. A panel of immunohistochemical markers, conventional morphology, and the discovery of the chromosomal t(X;18) translocation should all be taken into consideration when diagnosing the condition. There are three recognized subtypes: (1) monophasic, which is primarily composed of spindle cells; (2) biphasic, which is composed of spindle and epithelial-like cells, with areas recapitulating gland formation; and (3) poorly differentiated, which can be characterized by nuclear atypia, high cellularity, necrosis, and unusual mitoses, but is probably more commonly observed as a proliferating population of small, round cells[96].

Cytogenetic diagnosis: Only synovial sarcoma has been found to harbor the translocation t(X;18), and both its sensitivity and specificity have been demonstrated[94].

Immunohistochemical Markers: A few immunomarkers that may be useful are cytokeratins, vimentin, calponin, TLE1, Bcl2, CD34, CD99, and S100 protein. Epithelial membrane antigen (EMA) and carcinoembryonic antigen (CEA) are also included[97]. In the spindle cell component, cytokeratins and EMA exhibit a distinctive patchy pattern, while the epithelial component exhibits a more consistent staining. In some circumstances, strong, diffuse nuclear TLE1 reactivity could be a useful result.A number of genes and pathways, including RTKs (FGF2, FGF3, EGFR, PDGFR, and IGFBP3), Wnt (LEF1, TCF7, ZIC2, WNT5A, and FZD10), Hedgehog (PTCH1), NY-ESO-1 (CTAG1A), and Notch (JAG1, JAG2, and HES1), are disrupted in synovial sarcoma.

Treatment: Depending on the stage and prognostic variables, several therapeutic techniques are used. The surgical therapy of soft-tissue sarcomas generally follows similar principles. Wide surgical excision may be the only course of treatment for patients with nonmetastatic, T1 (<5 cm), superficial cancers at favorable extremities regions. Radiation and surgery may be necessary for larger tumors located in deeper, less advantageous locations.

Multimodal therapy, which includes systemic chemotherapy, radiation therapy, and surgery, may be necessary for more advanced diseases[98]. In front-line therapy for synovial sarcoma, doxorubicin (60–75 mg/m2) and ifosfamide (7.5–9 g/m2) are administered[99]. When combined, the medicines outperform other chemotherapy regimens, producing superior results in advanced disease. Gemcitabine and docetaxel combined is an alternate treatment that might be considered for patients who are resistant to or cannot handle regular chemotherapy. One patient with advanced synovial sarcoma showed a partial reduction of bilateral lung metastases, suggesting that Trabectedin is a potential treatment [100].

15.Undifferentiated pleomorphic sarcoma

Undifferentiated pleomorphic sarcoma (UPS), once termed malignant fibrous histiocytoma, is one of the most frequent soft tissue sarcomas [101]. Myxofibrosarcoma (MFS), histologically similar to UPS, was segregated from UPS and re-classified as an individual entity in 2002 on the grounds of its clinic pathology [102].Although non-specific, the genetic changes, such as mutation, deletion, and

epigenetic modifications, may be significant for the onset and course of UPS/MFS. TP53, ATRX, H3F3A, ZFHX3, CSMD3, PRPRT, TRIO, CLTC, PDGFRB, ALK, PTCH1, RET, ERBB4, JAK3, GATA1, PIK3CG, RARA, and MYH9 were identified as "cancer driver genes" after additional research [103].

Treatment: It is acknowledged that surgery remains the mainstay of treatment for all patients with localized UPS/MFS. However, the infiltrative growth pattern of UPS/MFS is a negative factor for prognosis after surgery. It is usually advised to perform wide excision and radiotherapy for deep lesions; however, post-radiation UPS/MFS may require less radiation. A negative margin has a substantial impact on local control and overall survival (OS), as postoperative radiation therapy may not be able to recover inadequate excision of UPS/MFS [104].

In general, neoadjuvant/adjuvant chemotherapy improved OS in subsets of UPS/MFS, with first-line treatment being anthracyclines plus ifosfamide (A + I), well recognized as the most utilized regimen. However, the clinical response is limited and varied, which might be ascribed to the nature of high heterogeneity [105]. found an improved response to combined agents of doxorubicin-ifosfamide compared to doxorubicin alone (42.5% versus 6.9%) and better OS after combination chemotherapy in subsets of UPS. Clinicians also conducted randomization trials of Gemcitabine plus docetaxel (G + D) for UPS, which showed that G + D is not superior to A + I [106]. Trabectedin is one of the hot-button drugs that has shown cytotoxic activity in UPS/MFS. Better still, Trabectedin might be the alternative option or subsequent therapy after A + I failure for UPS/MFS. [106] Pazopanib and Anlotinib are novel tyrosine kinase inhibitors targeting multiple factors involving VEGF/VEGFR signaling and fibroblast growth factor receptor.

Programmed cell death ligand 1 (PD-L1) is variably expressed by STS, especially undifferentiated pleomorphic sarcomas (UPSs) [107]. Responses to pembrolizumab monotherapy have been seen in STS, particularly UPS, and some, though not all, combination therapies may be associated with improved programmed cell death 1 (PD-1) blockade[108].

16.Dermatofibrosarcoma protuberans (DFSP):

Dermatofibrosarcoma protuberans (DFSP), which are formed from cutaneous fibroblasts, were identified as keloid sarcoma.Hoffman gave it the term DFSP in 1925 [109]. Clinically, it is a low- to intermediate-grade malignant sarcoma that grows slowly and usually affects adults in their middle years. By using an incisional biopsy or, less commonly, an excisional biopsy, the final diagnosis of DFSP is established. The dermis and subcutaneous fat often exhibit diffuse infiltration when stained with hematoxylin and eosin. From a histopathological perspective, it consists of homogeneous spindle cell fascicles that exhibit a storiform growth pattern, strong and diffuse CD34 staining, and numerous variations. Its spindle cell shape and CD34 immunostaining pattern, however, need to be distinguished from other benign and malignant lesions because they overlap. Stellate or spindle cells with long, slender, ramified cell processes connected by primitive connections, resembling dermal dendrocytes, are the ultrastructural hallmarks of DFSP [110]. Cytogenetically, t(17; 22) (q22; q13) is present in over 90% of DFSP, resulting in the production of COL1A1-PDGFB fusion transcripts. Not only is it useful for diagnosing cases lacking conventional morphology, but it can also be used to screen patients who may benefit from the use of imatinib mesylate, a tyrosine kinase inhibitor that inhibits PDGFβR.More than 90% of DFSPs are identified by chromosomal translocation t(17; 22) (q22; q13) or supernumerary ring chromosomes derived from chromosomes 17 and 22, according to cytogenetic and molecular studies. This leads to the fusion of the genes for platelet-derived growth factor beta (PDGFB at 22q13) and collagen type 1-alpha 1 (COL1A1 at 17q22). The fusion of the genes places the PDGFB gene under the COL1A1 promoter [111], which causes PDGFβ to be overexpressed and dimerized. This, in turn, causes the PDGF receptor β protein-tyrosine kinase to be continuously activated [112].

Treatment:Surgical excision is the standard treatment of DFSP including stage I and II, even III and IV whenever feasible.Advanced-stage tumors, recurrent tumors that cannot be removed further because of their size, location, or potential for significant functional or cosmetic abnormalities as well as multiple organ metastases are

examples of DFSPs that are not resectable. Targeted therapy or adjuvant radiation should be used to treat these cancers. Adjuvant radiation therapy has been demonstrated in numerous studies to be successful in reducing the incidence of postoperative recurrence and regulating the growth of DFSP, a tumor that responds to radiotherapy [113,114].

The use of imatinib mesylate (IM) as a targeted therapy interferes with the phosphorylation and activation of the PDGF receptor β, which is constitutively activated as a result of translocation and fusion between the PDGFB and COL1A1 genes. Other multikinase inhibitors, such as sunitinib [115], sorafenib [116], and pazopanib [117], can be taken into consideration in cases of imatinib mesylate resistance since treatment with these inhibitors proved beneficial in IM-resistant DFSP patients.Expression of the programmed cell death 1 ligand (PD-L1) was found in metastatic FS-DFSP but not in the original tumor, indicating a potential role for PD-L1 in FS-DFSP metastasis [118].

17.Epithelioid sarcoma

Epithelioid sarcoma is a very rare (less than 1% of all soft tissue sarcoma) high-grade soft tissue sarcoma (STS) with a knownpropensity for locoregional recurrence and dissemination [119]. Spindled and epithelioid cells that encircle regions of central hyalinization and necrosis are typically responsible for the construction of ES tumors. ESs have a mesenchymal origin, however, it might be difficult to differentiate them histopathologically because of their mixed differentiation. The expression of sarcoma markers, such as vimentin, and carcinoma markers, such as cytokeratin and EMA, along with CD34, are indicative of epithelioid sarcoma; S-100 and CD31 are not [120]. Other changes observed in ES cells include overexpression of EGFR, activation of MET, and activation of PI3K/AKT/mTOR. It has been demonstrated that SMARCB1 adversely regulates the expression of AURKA, E2F, and cyclin D1 in ES cells. These cancers have lost SMARCB1, which causes cyclin D1, E2F, and AURKA to become overexpressed and stimulate the cell cycle.

Treatment: Radical excision with large R0 margins is the curative treatment for ES. Enbloc excision is often the best course of treatment for ES in the extremities. Amputation is frequently required in cases involving big tumors to achieve radical

resection with tumor-free margins. Dissection of lymph nodes may occur concurrently with primary tumor excision. In high-risk individuals, adjuvant chemotherapy and/or radiation therapy may be given after MDT [121].For ES patients, the MDT ought to take into account neoadjuvant chemotherapy in accordance with prognostic classification using a Sarculator nomogram for STS. In comparison to conventional ES, the proximal subtype of ES is more aggressive, has greater rates of metastases and recurrence, and generally has a worse prognosis and higher mortality [122].

The lungs or pleura are where epithelioid sarcoma metastasizes most commonly. Patients with big tumors, high tumor grade, insufficient tumor excision, and metastatic disease are considered to have high-risk epithelioid sarcomas, which is associated with a poor prognosis [123]. In these circumstances, objective responses were recorded for patients receiving doxorubicin in combination with ifosfamide, pazopanib (ORR: 100% – 2/2), or trabectedin (33.3% – 1/3), but not for patients receiving doxorubicin alone. For patients receiving first-line treatment, the median progression-free survival (PFS) was 4.04 months. Anlotinib, a different TKI, combined with PD-1 inhibitors is a further treatment that has demonstrated some efficacy in case series [124]. Immunocheckpoint inhibitor treatments may be a possibility for ES sarcoma because of its comparatively high mutation rate. Patients with PD-L1 positive, advanced, refractory, or refractory solid tumors were enrolled in a KEYNOTE-051 research involving pembrolizumab, although no subgroup ORR has been published as of yet [125].

18. Angiosarcoma

Angiosarcomas are complex andaggressive soft-tissue sarcomas that typically involve blood and lymph vessels and are derived from malignant endothelium origins. Approximately 2 % of soft tissue sarcomas and 5 % of cutaneous sarcomas are diagnosed as angiosarcomas [126]. The incidence of angiosarcoma has risen over the last several decades with a higher prevalence in older Caucasian males with average age at diagnosis of 65–70 [127]. Angiosarcomas have a poor prognosis; less than 40% of patients survive for five years.

The most frequent chromosomal abnormalities were on chromosomes 8q, 10p, and 5q [128]. Additionally, MYC amplification is a recurrent genetic mutation in secondary angiosarcoma.

This highly aggressive tumor spreads widely through the skin, recurs locally, and metastasizes early. It is well known that this tumor frequently metastasizes to the lung, often inducing repeated pneumothorax and/or hemothorax as a result of rupture of enlarged cystic tumors arising in the peripheral lung field

Diagnosis: Due to disease rarity and non-specific clinical presentations, it is difficult to differentiate angiosarcomas from other malignant tumors. As a result, diagnostic imaging is crucial to the first diagnosis. MRI, CT, and ultrasound are frequently used diagnostic methods for angiosarcoma.

Angiosarcomas can occur in a variety of ways histologically, from well-differentiated variations to poorly differentiated forms. Endothelial cells lining a multitude of irregular vascular channels are seen in well-differentiated angiosarcoma. Additionally, Spindle-shaped, polygonal, epithelioid, and primitive round cells, with increased mitotic activity and poorly formed vascular spaces, can be found in tissues of poorly differentiated angiosarcoma [129].

Immunohistochemistry: useful in the diagnosis of less-differentiated types of angiosarcomas. Angiosarcomas typically express endothelial markers including Factor-VIII-related antigen (Factor-VIIIRA), CD31, CD34, and vascular endothelial growth factor (VEGF)[130].

Cytogenetically, angiosarcoma is defined by the overexpression of receptor tyrosine kinases that are unique to blood vessels, including TEK, TIE1, KDR, and FLT1. Despite this, the majority of primary angiosarcomas' genetic alterations are still unknown. It has been established that angiogenesis genes, such as phospholipase C gamma 1 mutation, MYC gene amplification, and protein tyrosine phosphatase receptor type B (PTPRB), play important roles in secondary angiosarcomas [131].

Treatment: Although previous reports have emphasized the poor prognosis of this disease, effective treatment strategies have yet to be elucidated. Surgery was the

mainstay of treatment, but the high frequency of local recurrence of this strategy is discouraging [132,133]. Radiotherapy was generally performed in cases of widely spread and unresectable tumors, but the outcomes were also unsatisfactory [132,1126]. Therefore, several authors advocated a combination of surgery and radiotherapy for these tumors [126,134]. Recently, chemotherapy and immunotherapy using recombinant interleukin-2 (rIL-2) have been studied as potential treatments [135]. Taxanes, doxorubicin, liposome doxorubicin, and ifosfamide were the four main chemotherapeutic drugs used overall. Targeted intervention In targeted therapy for angiosarcomas, tyrosine kinase inhibitors (TKI), particularly sorafenib and pazopanib, have been used to block the VEGF/VEGFR signaling pathway.In the description of the phase II clinical trial by Penel et al., Sorafenib, a small molecule B-RAF and VEGFR inhibitor, was confirmed to be useful in the treatment of angiosarcoma [135]. The Programmed death 1 (PD-1) and its receptors including ligand-1 (PD-L1) and ligand-2 (PD-L2) are thought to be another effective therapeutic target for angiosarcomas

19. Conclusions

Soft tissue sarcomas continue to be an uncommon but serious cause of death. Due to the variety of tissues, they affect, it is difficult to diagnose them early on. For radiologists and pathologists among other relevant professions, the diagnosis of soft tissue sarcoma is a major difficulty. The categorization of soft tissue sarcoma is constantly evolving, and accurate diagnosis of multiple subtypes requires the use of advanced molecular diagnostic procedures, with results evaluated by skilled pathologists and geneticists. Planning a course of treatment necessitates close collaboration amongst all relevant disciplines, which are represented by an expert sarcoma team that meets frequently and updates institutional treatment guidelines in response to mounting scientific data.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of manuscripts.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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