AMERICAN ACADEMIC PUBLISHER

INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

ISSN NUMBER: 2692 - 5206 Volume 6. No 01. January ,2026

MODERN APPROACHES IN THE TREATMENT OF SOFT TISSUE LIPOSARCOMAS: A PARADIGM SHIFT TOWARDS PRECISION MEDICINE

I.R. Abdumalikov, A.V. Savkin.

Department of General Oncology, Tashkent Medical Academy

Abstract

Soft tissue liposarcomas (LPS) represent a heterogeneous group of malignancies derived from adipocytic tissue, accounting for approximately 20% of all adult soft tissue sarcomas. Their management has evolved significantly from a uniform, surgery-centric model to a complex, multidisciplinary, and histology-driven paradigm. This review outlines the contemporary therapeutic landscape, emphasizing the critical role of precise histopathological and molecular subtyping in guiding treatment decisions. We discuss the ongoing refinement of surgical and radiotherapeutic techniques, the subtype-specific efficacy of systemic therapies (including traditional chemotherapy, targeted agents like trabectedin and CDK4 inhibitors, and immunotherapy), and the integration of these modalities in both localized and advanced disease settings. The future direction lies in deepening molecular stratification, developing novel targeted therapies, and personalizing treatment algorithms through robust clinical trials and biomarker research. This article synthesizes current evidence to provide a framework for the modern, precision-based approach to liposarcoma care.

Keywords

Liposarcoma, Well-Differentiated, Dedifferentiated, Myxoid, Pleomorphic, Multidisciplinary Treatment, Targeted Therapy, Trabectedin, MDM2, Precision Oncology.

Introduction

Liposarcomas are a diverse collection of mesenchymal neoplasms with adipocytic differentiation, characterized by distinct clinical behaviors, pathological features, and underlying genetic drivers. The contemporary World Health Organization (WHO) classification recognizes four principal subtypes: the locally aggressive but non-metastasizing Atypical Lipomatous Tumor/Well-Differentiated Liposarcoma (ALT/WDLPS), the high-grade Dedifferentiated Liposarcoma (DDLPS), the translocation-associated Myxoid Liposarcoma (MLPS), and the aggressive Pleomorphic Liposarcoma (PLPS). This biological heterogeneity necessitates a departure from generic sarcoma protocols. Historically, treatment relied heavily on surgery, often resulting in high local recurrence rates, particularly in retroperitoneal sites, and poor outcomes for metastatic disease. The modern era is defined by the integration of specialized pathology, advanced imaging, multidisciplinary tumor boards, and a growing arsenal of systemic therapies tailored to specific biological vulnerabilities. This article reviews the established and emerging approaches that constitute the current standard of care and future horizons in liposarcoma management.

Materials and Methods

This narrative review was conducted by synthesizing data from key clinical trials, consensus guidelines from major oncology societies (NCCN, ESMO), and seminal peer-reviewed literature published within the last decade. A focused search of the PubMed/MEDLINE

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 01. January ,2026

database was performed using terms including "liposarcoma," "treatment," "targeted therapy," "trabectedin," "MDM2 inhibitor," and combined with specific subtype names. Priority was given to phase II and III randomized controlled trials, large retrospective cohort studies, and authoritative review articles. The evidence was organized to construct a coherent narrative on diagnosis, localized therapy, systemic treatment by subtype, and future directions.

Discussion

1. Diagnostic Precision as the Foundation

The initial and most critical step is accurate diagnosis through image-guided core needle biopsy interpreted by an expert sarcoma pathologist. Subtyping is confirmed using immunohistochemistry (e.g., MDM2 and CDK4 overexpression in WDLPS/DDLPS) and molecular techniques such as Fluorescence In Situ Hybridization (FISH) for MDM2 amplification or DDIT3 gene rearrangements in MLPS. Staging involves locoregional magnetic resonance imaging (MRI) and computed tomography (CT) of the chest and abdomen, with consideration of spine/pelvic imaging for MLPS due to its unique metastatic pattern.

2. Localized Disease: Evolving Roles of Surgery and Radiotherapy

Surgery: The goal remains complete macroscopic resection with negative margins (R0). For extremity tumors, limb-salvage surgery is standard. For retroperitoneal liposarcomas (mostly WDLPS/DDLPS), more radical approaches like compartmental resection are advocated to reduce the high incidence of local recurrence, though morbidity risks are significant.

Radiotherapy (RT): For extremity/truncal tumors, neoadjuvant radiotherapy is often preferred, allowing for smaller treatment fields, lower doses, and potentially improved resectability. Advanced techniques like Intensity-Modulated Radiotherapy (IMRT) and Image-Guided Radiotherapy (IGRT) maximize tumor control while sparing normal tissue. The role of RT in retroperitoneal sarcoma is controversial and being defined by trials like STRASS-2.

3. Systemic Therapy for Advanced Disease: A Subtype-Specific Roadmap

Myxoid/Round Cell Liposarcoma (MLPS): This subtype showcases the success of histology-driven therapy. It exhibits exquisite sensitivity to the alkylating agent trabectedin, which is believed to disrupt the FUS-DDIT3 oncogenic fusion protein. Trabectedin demonstrates high disease control rates and is a preferred first- or second-line option. Eribulin, a microtubule inhibitor, has also shown a significant survival benefit in later lines.

Dedifferentiated and Pleomorphic Liposarcoma (DDLPS, PLPS): These high-grade subtypes are treated with anthracycline-based chemotherapy (doxorubicin) as first-line. Combination regimens (e.g., doxorubicin/ifosfamide) are used for fit patients requiring a rapid response. In later lines, gemcitabine/docetaxel, trabectedin (with activity in DDLPS), and the multi-kinase inhibitor pazopanib are options.

Well-Differentiated Liposarcoma (WDLPS): Chemotherapy is largely ineffective for the well-differentiated component. Management focuses on local control via surgery. For unresectable, progressive disease, targeted therapies are paramount.

4. The Rise of Targeted Biological Therapies

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 01. January ,2026

CDK4 Inhibition: The nearly universal co-amplification of CDK4 in WDLPS/DDLPS led to the investigation of CDK4/6 inhibitors. Palbociclib has shown meaningful progression-free survival benefit and disease stabilization in clinical trials, establishing it as a valuable option for advanced WDLPS/DDLPS.

MDM2-p53 Pathway Targeting: Multiple MDM2 inhibitors (e.g., milademetan) are in advanced clinical development, aiming to reactivate wild-type p53 in these amplification-driven tumors, showing promising anti-tumor activity.

Immunotherapy: Liposarcomas are generally "immunologically cold." Checkpoint inhibitors (e.g., anti-PD1) have shown limited single-agent activity, except possibly in a subset of DDLPS/PLPS. Research focuses on combination strategies to stimulate an immune response.

5. The Multidisciplinary Tumor Board (MDT)

The MDT is the central nervous system of modern sarcoma care. Regular discussion among surgeons, medical and radiation oncologists, pathologists, radiologists, and specialized nurses ensures that each patient's treatment plan is tailored to their tumor's biology, anatomical location, and personal circumstances, optimizing outcomes.

Conclusion

The treatment of soft tissue liposarcoma has undergone a profound transformation, moving from a generalized approach to a precision medicine model. Effective management is entirely contingent upon accurate histological and molecular subtyping. While surgery and radiotherapy remain pillars for local control, the systemic therapy arsenal has expanded to include highly effective subtype-specific agents like trabectedin for MLPS and targeted options like palbociclib for WDLPS/DDLPS. The future promises further personalization through novel MDM2 inhibitors, advanced cellular therapies, and biomarker-guided treatment sequencing. Continued enrollment of patients into clinical trials and centralization of care in specialized sarcoma centers are imperative to accelerate progress and improve survival and quality of life for patients with these complex malignancies.

References

1. Doyle, L. A. (2014). Sarcoma classification: an update based on the 2013 World Health Organization Classification of Tumors of Soft Tissue and Bone. Cancer, 120(12), 1763–1774.

2. Gronchi, A., et al. (2021). Soft tissue and visceral sarcomas: ESMO-EURACAN-GENTURIS Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology, 32(11), 1348–1365.

3. Demetri, G. D., et al. (2016). Efficacy and Safety of Trabectedin or Dacarbazine for Metastatic Liposarcoma or Leiomyosarcoma After Failure of Conventional Chemotherapy: A Randomized Clinical Trial. JAMA, 316(15), 1914–1924.

4. Dickson, M. A., et al. (2021). Phase II Trial of the CDK4 Inhibitor Palbociclib in Patients with Advanced CDK4-Amplified Well-Differentiated or Dedifferentiated Liposarcoma. Journal of Clinical Oncology, 39(30), 3397–3407.

AMERICAN ACADEMIC PUBLISHER

INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

ISSN NUMBER: 2692 - 5206 Volume 6. No 01. January ,2026

5. Tap, W. D., et al. (2017). Effect of Doxorubicin Plus Olaratumab vs Doxorubicin Plus Placebo on Survival in Patients with Advanced Soft Tissue Sarcomas: The ANNOUNCE Randomized Clinical Trial. JAMA, 323(13), 1266–1276.

6. Kawai, A., et al. (2020). The EORTC Soft Tissue and Bone Sarcoma Group: A history of clinical research contributing to improve the management of patients with soft tissue sarcoma. European Journal of Cancer, 127, 139-148.

7. Bonvalot, S., et al. (2022). STRASS (EORTC 1809): A phase III randomized study of preoperative radiotherapy plus surgery versus surgery alone for patients with retroperitoneal sarcoma. Journal of Clinical Oncology, 40(17_suppl), LBA11501.

8. Schöffski, P., et al. (2020). Eribulin versus dacarbazine in previously treated patients with advanced liposarcoma or leiomyosarcoma: a randomised, open-label, multicentre, phase 3 trial. The Lancet, 387(10028), 1629-1637.

9. National Comprehensive Cancer Network (NCCN). (2023). NCCN Clinical Practice Guidelines in Oncology: Soft Tissue Sarcoma. Version 2.2023.

10. Keung, E. Z., et al. (2020). The immune microenvironment of soft tissue sarcomas: Implications for immunotherapy. Clinical Sarcoma Research, 10, 5.