



Preface

The Ever-Evolving Landscape of Sarcomas: A 2022 Update on This Complex Family of Diseases



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Sarcomas are a heterogeneous family of rare neoplasms comprising over 100 histologies. They arise in virtually every part of the body and every type of tissue. As such, management strategies must be tailored to the specific histologic type and adapted to the site of origin. The scope of surgery and efficacy of radiation therapy, chemotherapy, targeted therapy, and immunotherapy vary considerably for each sarcoma. Incremental progress has been made broadly, warranting this updated primer. Herein, we highlight recent advances in sarcoma care with attention to details relevant to surgical oncologists. To reflect the global collaborative efforts required to make the progress featured here, we have invited a panel of international experts to work together for a balanced discussion about treatment options.

This series starts with an overview on changes in histopathologic classification by Schaefer and Gronchi. In particular, new types of lipomatous tumors and undifferentiated round cell sarcomas of bone and soft tissue are discussed. In addition, new translocation-based classifications are described, which emphasize that different morphologic phenotypes may harbor similar molecular alterations, which in turn lead to similar treatment options neurotrophic tyrosine kinase receptor (NTRK). Other novel molecular classifications are identifying subsets of histologic types with varying prognoses (CIC-rearranged, BCL-6 transcriptional corepressor [BCOR]).

Contemporary clinical trials for localized disease are summarized for gastrointestinal stromal tumors (GIST) and for sarcomas arising in the extremities and retroperitoneum in a review by Callegaro and colleagues. These trials cover neoadjuvant chemotherapy, neoadjuvant immunotherapy, neoadjuvant radiation therapy, and adjuvant targeted therapy.

Similarly, Thirasastr and colleagues describe newly approved drugs for advanced disease. These include new targeted agents for both fourth line and beyond for GIST and GIST with mutations insensitive to prior tyrosine kinase inhibitors (TKIs), new agents approved for a variety of histologic types (eribulin), and newly approved targeted molecular inhibitors (larotrectinib, tazemetostat, sorafenib, nab-sirolimus).

Moreno Tellez and colleagues authored a comprehensive overview of immunoncology for sarcomas. While immune checkpoint inhibition has not had the extent of success in sarcomas as noted in other malignancies, the authors focus on areas of success, including its combination with chemotherapy as a means to change the tumor microenvironment. The utility of adoptive cell therapies in selected histologic types is reviewed. Possible predictive biomarkers are identified.

Siew and colleagues describe newer information in the management of primary retroperitoneal and mesenteric liposarcoma. This includes liposarcoma-specific data drawn from the STRASS phase 3 trial and nomograms, which enable better prognostication. Importantly, the authors emphasize the differences in outcomes for well-differentiated and dedifferentiated liposarcoma (including different grades of the latter entity).

Crago and colleagues shed light on the overlap and differences between myxofibrosarcoma and undifferentiated pleomorphic sarcoma. Sensitivity to chemotherapy is discussed.

Sharma and colleagues provide an update on GIST molecular profiling and provide a detailed overview on surgical management of primary and advanced GIST. They also discuss the current state of targeted therapy for localized and advanced disease, including new drug approvals and future directions.

Spolverato and colleagues recapitulate recent evidence about spontaneous regression of desmoids on active surveillance and discuss various active management strategies, including new drugs and cryoablation. Management of desmoids is constantly evolving, and this article is a must-read for anyone who cares for individuals with desmoid.

Kazazian and colleagues review solitary fibrous tumors, with emphasis on differences based on site of origin (head/neck, central nervous system, thoracic, abdominal/pelvic/retroperitoneum, and extremity/trunk), radiation and chemotherapy options, molecular data, and recent studies on risk stratification.

Subramaniam and colleagues provide an overview of the broad spectrum of rare vascular sarcomas, including the well-described types hemangioendothelioma and angiosarcoma. Importantly, they also address a third distinct type, Kaposi sarcoma, which is often not discussed in general studies or reviews of sarcoma.

Messina and colleagues describe the four most common skin sarcomas: dermatofibrosarcoma protuberans, cutaneous angiosarcoma, pleomorphic dermal sarcoma, and cutaneous leiomyosarcoma.

Devaud and colleagues focus on leiomyosarcomas, highlighting new studies that have distinguished different molecular subtypes. Surgical management of localized disease for leiomyosarcoma of retroperitoneal and uterine origin is discussed as are standard and emerging systemic therapy options.

Hindi and Haas discuss localized and systemic therapy for both synovial sarcoma and myxoid liposarcoma. One important highlight is the neoadjuvant radiation therapy dose reduction trial for the latter, with a unique endpoint of pathologic response.

Finally, The Cancer Genome Atlas sarcoma project is detailed in an article by Burns and colleagues.

The rarity of sarcomas means identifying efficacious treatments can be challenging. Nonetheless, the authors for each of these sections, together with other investigators around the globe, have made remarkable progress over the last 5+ years.

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