Bone Metastases in Soft Tissue Sarcoma: Natural History, Prognostic Factors, and Genomic Characterization in a Modern Cohort

Rieker MG, Patt ON, Voskuil RT, Jagosky MH, Patt JC

Significance & Hypothesis: Bone metastases are a clinically significant but understudied site of metastasis for soft tissue sarcoma (STS). Prior literature is limited to small, predominantly non-U.S. cohorts studied before the era of modern systemic therapy and advanced imaging surveillance. Reported median survival following skeletal disease diagnosis has historically been poor, and the genomic landscape of bone-metastatic STS remains poorly characterized. This study aims to report patient and tumor characteristics, treatment, and survival for a single-institution cohort of patients with bone metastases from STS. We hypothesized that a contemporary cohort would demonstrate improved survival compared to historical benchmarks, and that genomic profiling could identify potentially actionable molecular targets in this population.

Innovation: This represents the largest dedicated study of bone metastases across all STS subtypes from a North American center and the first to incorporate molecular profiling data in this clinical context. Additionally, this is one of few studies to report race, ethnicity, and insurance data, adding a health equity dimension to the existing literature on skeletal disease in STS.

Approach: We performed a retrospective review of 80 patients with radiologically confirmed bone metastases from STS at a single academic institution. Demographics, tumor characteristics, bone metastasis details, treatment, and available genomic profiling data were collected.

Results: The cohort included 41 males (51.3%) and 39 females (48.8%) with a median age of 59.5 years (range 17–85). The racial and ethnic distribution was 72.2% White, 12.7% Black, 11.4% Hispanic or Latino, and 1.3% Asian. Insurance status included Medicare (45.0%), private (42.5%), Medicaid (7.5%), and uninsured (5.0%). The most common histologic subtypes were leiomyosarcoma (22.5%), angiosarcoma (11.3%), and undifferentiated pleomorphic sarcoma (8.8%). The most common primary tumor sites were lower extremity (30.8%), retroperitoneal (20.5%), trunk (15.4%), and upper extremity (15.4%). Among patients with available staging data, 68.1% presented with stage 3 disease. Primary tumor resection was performed in 82.5% of patients. Bone metastases were present at initial diagnosis in 15.0%. Initial imaging modalities most frequently included MRI (58.0%), CT (53.6%), and PET (42.0%). Treatment of bone metastases included palliative radiotherapy (71.6%), palliative surgery (35.1%), and palliative chemotherapy (9.5%). Genomic reports were available for 38.8% (31/80), with targetable mutations identified in 11 patients. The most frequently identified mutations were TP53 (36.4% of those with targetable mutations), RB1 (18.2%), and NOTCH1 (18.2%), with additional alterations in CDK4, NF1, ATRX, KMT2D, PI3KCA, ARID1A, and TSC2.

Discussion & Impact: This study provides a comprehensive characterization of bone-metastatic STS in a modern, diverse North American cohort. The predominance of leiomyosarcoma and angiosarcoma is consistent with their known propensity for hematogenous spread. The high rate of primary tumor resection (82.5%) and frequent use of palliative radiotherapy (71.6%) reflect current multimodal management strategies. Genomic profiling identified potentially targetable alterations, supporting the integration of molecular profiling into management of this population. The inclusion of race, ethnicity, and insurance data adds important health equity context. Survival analysis and univariate prognostic factor assessment are ongoing and will further define the natural history of this disease. Limitations include the retrospective single-institution design.