Multi-Agent Chemotherapy for Surgically-Treated Soft Tissue Sarcomas Arising from Bone is Not Associated with Improved Survival Versus Surgery Alone: A Propensity-Matched, National Cancer Database Study.

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Background
- Soft tissue sarcomas arising from bone are rare cancers with unestablished treatment protocols.
- Surgery is standard of care for soft tissue sarcomas.
- Multi-agent chemotherapy (MAC) decreases soft tissue sarcoma progression compared to single-agent chemotherapy.
- **Primary objective**: Is the addition of MAC with surgical resection associated with improved survival in treatment of soft tissue sarcomas arising from bone?
- **Secondary objectives**: What factors influence the decision to treat with MAC? Is response histology-specific?

Materials and Methods

Data
- National Cancer Database (NCDB), years 2004-2014
- **Included**: Adults with primary malignant sarcomas of bone who underwent surgical tumor resection
- **Excluded**: Primary bone tumors (e.g. osteosarcoma), single-agent chemo, incomplete survival data
- Control group = surgery only; Treatment = surgery + MAC

Statistics
- Propensity scores used to identify probability of receiving MAC for each subject, ranging from 0-1.
- An optimal, 1:1 match algorithm (using R) was used to match treatment and controls based on propensity scores
- Survival analyzed by Kaplan-Meier curves and the log-rank test. Survival was defined as time to death or censor.
- Subgroup analysis compared histology-specific survival
- Bonferroni correction was used, with resulting significance level set at p<0.001.

Results

Table 1. 10 most common histologic diagnoses of soft-tissue sarcomas arising from bone, identified in the NCDB using ICD-03 codes.

<table>
<thead>
<tr>
<th>Histologic subtypes</th>
<th>Total: 902</th>
<th>% Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrous histiocytoma, malignant</td>
<td>178</td>
<td>20</td>
</tr>
<tr>
<td>Sarcoma, NOS</td>
<td>135</td>
<td>15</td>
</tr>
<tr>
<td>Giant cell sarcoma</td>
<td>107</td>
<td>12</td>
</tr>
<tr>
<td>Spindle cell sarcoma</td>
<td>99</td>
<td>11</td>
</tr>
<tr>
<td>Leiomyosarcoma subtypes</td>
<td>97</td>
<td>11</td>
</tr>
<tr>
<td>Hemangioma sarcoma</td>
<td>84</td>
<td>9</td>
</tr>
<tr>
<td>Fibrosarcoma NOS</td>
<td>61</td>
<td>7</td>
</tr>
<tr>
<td>Undifferentiated sarcoma</td>
<td>43</td>
<td>5</td>
</tr>
<tr>
<td>Synovial sarcoma subtypes</td>
<td>34</td>
<td>4</td>
</tr>
<tr>
<td>Liposarcoma subtypes</td>
<td>27</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 2. Comparison of demographic and disease characteristics of patients with soft tissue sarcoma of bone between those receiving surgery alone versus those receiving surgery plus multi-agent chemotherapy (MAC). Results of propensity matching between treatment and controls are shown, demonstrating decreased differences between groups. CH-squared and Mann-Whitney tests were used for analysis with significance level set at p<0.001.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Surgery + MAC</th>
<th>Control (before propensity match)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery alone</td>
<td>183</td>
<td>0.105</td>
<td>0.099</td>
</tr>
<tr>
<td>Control (after propensity match)</td>
<td>183</td>
<td>0.105</td>
<td>0.099</td>
</tr>
</tbody>
</table>

Figure 1. Propensity-matched survival, multi-agent chemo vs surgery alone. Kaplan-Meier survival analysis of matched cohort of patients with soft tissue sarcoma of bone receiving surgery alone versus surgery with multi-agent chemotherapy. Data shown with 95% CI. * indicates censored points. Dotted lines indicate 50% survival. P-value by log-rank test. 0=no MAC, 1=MAC.

Key Findings
- Addition of MAC to surgery for soft tissue sarcomas arising from bone is not associated with a survival benefit.
- MAC may contribute to worse overall survival, although a statistically significant survival difference was not identified.
- Select tumor types may benefit from MAC, although more investigation and larger samples are needed.
- MAC is more likely given for younger patients with high-grade tumors and axial lesions, despite unclear survival benefit

Considerations
- First study to examine the association of MAC with survival among patients with soft tissue tumors arising from bone
- Propensity matching reduced, but did not eliminate, differences between the treatment and control groups
- NCDB does not include data on progression-free survival, disease-specific mortality, and other important outcomes

Figure 2. Unmatched survival associated with multi-agent chemotherapy based on histologic type. Data shown for 4 most common histologic sarcoma types with 95% CI. * indicates censored points. Dotted lines indicate 50% survival. P-value by log-rank test. 0=no MAC, 1=MAC.

Discussion
- Addition of multi-agent chemotherapy to surgical treatment of soft tissue sarcomas arising from bone is not associated with a survival benefit in this retrospective, propensity score-matched analysis.

Conclusion