Phase I Study of Neoadjuvant Chemoradiation Plus Sorafenib for High Risk Extremity Soft Tissue Sarcomas

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Phase I Neoadjuvant Chemoradiation Plus Sorafenib Background

Sorafenib, a sorafenib inhibitor, is an oral multi-kinase inhibitor of the Raf kinase and the vascular endothelial growth factor receptor tyrosine kinase 2 (VEGFR-2). Sorafenib has shown synergistic effects with chemoradiation therapy.

Methods

Eligibility Criteria

• Histologically confirmed soft tissue sarcoma (excluding rhabdomyosarcoma, Ewing’s, PNET, osteosarcoma, or GIST)
• Age ≥ 15
• Histologically confirmed soft tissue sarcoma (excluding rhabdomyosarcoma, Ewing’s, PNET, osteosarcoma, or GIST)

Surgical Procedure

- R0 (negative)
- R1 (positive)
- Other

Results

Baseline Characteristics (N=16)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54</td>
<td>15-77</td>
</tr>
<tr>
<td>Median size, cm</td>
<td>12</td>
<td>1-80</td>
</tr>
<tr>
<td>Grade</td>
<td>3</td>
<td>1-5</td>
</tr>
</tbody>
</table>

Dose Limiting Toxocities During First 6 Weeks of Treatment

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 mg/m²</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>250 mg/m²</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>300 mg/m²</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
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</tbody>
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Other complicating factors present in patients with pathological necrosis:

- Fatigue
- Rash
- Hand foot syndrome
- Fatigue
- Rash
- Hand foot syndrome

Disease-Free Survival

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
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<tbody>
<tr>
<td>Survival (%)</td>
<td>100</td>
<td>88</td>
<td>88</td>
<td>88</td>
<td>88</td>
<td>88</td>
<td>88</td>
<td>88</td>
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Discussion

The addition of sorafenib to our chemoradiotherapy regimen is safe and will improve outcomes by increasing sorafenib dose using a 3+3 cohort design with dose level escalation based on dose limiting toxicities (DLTs)

References