

## SOFT TISSUE SARCOMA TREATMENT REGIMENS (Part 1 of 2)

**Clinical Trials:** The National Comprehensive Cancer Network recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced health care team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are provided only to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data become available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

### Systemic Therapy With Activity in Soft Tissue Sarcoma Subtypes With Non-specific Histologies<sup>1,a,b,c</sup>

**Note:** All recommendations are Category 2A unless otherwise indicated.

#### Combination Regimens

REGIMEN	DOSING
<b>Doxorubicin + dacarbazine (AD)<sup>2-5</sup></b>	<b>Days 1-4:</b> Doxorubicin 60mg/m <sup>2</sup> + dacarbazine 750mg/m <sup>2</sup> as a continuous IV infusion over 96 hours. Repeat cycle every 3 weeks.
<b>Doxorubicin + ifosfamide + mesna (AIM)<sup>4-7</sup></b>	<b>Days 1 and 2:</b> Doxorubicin 30mg/m <sup>2</sup> /day IV + ifosfamide 3,750mg/m <sup>2</sup> /day IV + mesna 750mg/m <sup>2</sup> IV immediately preceding and then 4 and 8 hours after ifosfamide administration. Repeat cycle every 3 weeks.
<b>Mesna + doxorubicin + ifosfamide + dacarbazine (MAID)<sup>4,5,8,9</sup></b>	<b>Days 1-3:</b> Doxorubicin 20mg/m <sup>2</sup> /day + ifosfamide 2,500mg/m <sup>2</sup> /day + dacarbazine 300mg/m <sup>2</sup> /day as continuous IV infusion over 72 hours, <b>plus</b> Mesna 2,500mg/m <sup>2</sup> /day IV for 84 to 96 hours. Repeat cycle every 3 weeks.
<b>Ifosfamide + epirubicin + mesna<sup>10</sup></b>	<b>Days 1 and 2:</b> Epirubicin 60mg/m <sup>2</sup> /day IV <b>Days 1-5:</b> Ifosfamide 1.8g/m <sup>2</sup> /day IV over 1 hour + mesna at 20% of the ifosfamide dose IV immediately preceding and then 4 and 8 hours after ifosfamide administration. Repeat cycle every 3 weeks for 5 cycles.
<b>Gemcitabine + docetaxel<sup>11,12</sup></b>	<b>Days 1 and 8:</b> Gemcitabine 900mg/m <sup>2</sup> IV <b>Day 8:</b> Docetaxel 100mg/m <sup>2</sup> IV. Repeat cycle every 3 weeks.
<b>Gemcitabine + vinorelbine<sup>13</sup></b>	<b>Days 1 and 8:</b> Vinorelbine 25mg/m <sup>2</sup> IV over 10 minutes + gemcitabine 800mg/m <sup>2</sup> IV over 90 minutes. Repeat cycle every 3 weeks.
<b>Gemcitabine + dacarbazine<sup>14</sup></b>	<b>Day 1:</b> Gemcitabine 1,800mg/m <sup>2</sup> IV + dacarbazine 500mg/m <sup>2</sup> IV. Repeat cycle every 2 weeks for a total of 12 cycles; continuation of treatment after 24 weeks was allowed at investigator discretion.
<b>Doxorubicin + olaratumab<sup>15,e</sup></b>	<b>Day 1:</b> Doxorubicin 75mg/m <sup>2</sup> IV <b>Days 1 and 8:</b> Olaratumab 15mg/kg IV. Repeat cycle every 3 weeks for up to 8 cycles.

#### Single Agents

<b>Doxorubicin<sup>4,5,16</sup></b>	Doxorubicin 60-75mg/m <sup>2</sup> IV every 3 weeks.
<b>Ifosfamide<sup>10,17</sup></b>	Ifosfamide 2,000-3,000mg/m <sup>2</sup> /day IV for 3 to 4 days + mesna at 20% of the ifosfamide dose IV immediately preceding and then 4 and 8 hours after ifosfamide administration every 3 weeks. <b>OR</b> Ifosfamide 5,000mg/m <sup>2</sup> + mesna 5,000mg/m <sup>2</sup> as a continuous IV infusion over 24 hours followed by additional mesna 400-600mg/m <sup>2</sup> IV over 2 hours after completion of ifosfamide administration. Repeat every 3 weeks.
<b>Epirubicin<sup>18</sup></b>	Epirubicin 160mg/m <sup>2</sup> IV every 3 weeks.
<b>Gemcitabine</b>	<b>Days 1 and 8:</b> Gemcitabine 1,200mg/m <sup>2</sup> IV over 90 to 120 minutes. Repeat cycle every 3 weeks.
<b>Dacarbazine</b>	Dacarbazine 250mg/m <sup>2</sup> /day IV for 5 days every 3 weeks. <b>OR</b> Dacarbazine 800-1,000mg/m <sup>2</sup> IV every 3 weeks.
<b>Liposomal doxorubicin<sup>19</sup></b>	Liposomal doxorubicin 30-50mg/m <sup>2</sup> IV every 4 weeks.
<b>Temozolomide<sup>20,d</sup></b>	<b>Day 1:</b> Temozolomide 200mg/m <sup>2</sup> oral bolus dose once <b>followed by</b> temozolomide 90mg/m <sup>2</sup> after 12 hours. <b>Days 2-5:</b> Temozolomide 90mg/m <sup>2</sup> orally twice daily. Repeat cycle every 4 weeks.

*continued*

## SOFT TISSUE SARCOMA TREATMENT REGIMENS (Part 2 of 2)

### Systemic Therapy With Activity in Soft Tissue Sarcoma Subtypes With Non-specific Histologies<sup>1abc</sup> (continued)

#### Single Agents (continued)

REGIMEN	DOSING
Vinorelbine <sup>21,d</sup>	Vinorelbine 30mg/m <sup>2</sup> IV weekly for 6 weeks during an 8-week interval.
Pazopanib <sup>22,d,f</sup>	Pazopanib 800mg orally once daily without food until disease progression or unacceptable toxicity.
Eribulin <sup>23,d,g</sup>	<b>Days 1 and 8:</b> Eribulin mesylate 1.4mg/m <sup>2</sup> IV. Repeat every 3 weeks until disease progression or unacceptable toxicity.
Trabectedin <sup>24-26,d,h</sup>	Trabectedin 1.5mg/m <sup>2</sup> as a 24-hour continuous IV infusion every 3 weeks.

<sup>a</sup> Alveolar soft part sarcomas (ASPS), well-differentiated liposarcoma/atypical lipomatous tumor, and clear cell sarcomas are generally non sensitive to cytotoxic chemotherapy.

<sup>b</sup> Anthracycline-based regimens are preferred in the neoadjuvant and adjuvant setting.

<sup>c</sup> Regimens appropriate for pleomorphic rhabdomyosarcoma.

<sup>d</sup> Recommended only for palliative therapy.

<sup>e</sup> For use in STS histologies for which an anthracycline-containing regimen is appropriate.

<sup>f</sup> Pazopanib should not be used for lipogenic sarcomas.

<sup>g</sup> Category 1 recommendation for liposarcoma.

<sup>h</sup> Category 1 recommendation for liposarcoma and leiomyosarcoma (L-types).

#### References

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