**BC Cancer Protocol Summary for Therapy of Advanced Osteosarcoma Using DOXOrubicin and CISplatin**

**Protocol Code**  
SAAVAP

**Tumour Group**  
Sarcoma

**Contact Physician**  
Dr. Christine Simmons

**ELIGIBILITY:**
- Patients with advanced osteogenic sarcoma
- Normal renal, cardiac and hepatic function

**TESTS:**
- Baseline and before each treatment: CBC & diff, platelets, sodium, potassium, creatinine, calcium, magnesium, albumin, bilirubin, alk phos, ALT, LDH, and GGT.
- If clinically indicated: chest x-ray or other imaging to monitor response

**PREMEDICATIONS:**
- Ondansetron 16 mg PO/IV pre-chemotherapy and then 8 mg PO/IV q8h
- Dexamethasone 8 mg PO/IV pre-chemotherapy and then 4 mg PO/IV bid for 4 days
- If intolerable nausea and vomiting develops, add Nabilone 1 mg PO pre-chemotherapy to next cycle OR Aprepitant 125 mg PO pre-chemotherapy and 80 mg PO post-chemotherapy daily for 2 days
- At discharge continue Ondansetron 8 mg bid and Dexamethasone 4 mg bid for 3 days

**PRN'S:**
- Lorazepam 1 mg SL q 4 to 6 h PRN nausea, sleep or restlessness
- Prochlorperazine 10 mg PO/IV q 4 to 6 h PRN nausea
- DiphenhydramINE 25 to 50 mg PO/IV q 4 to 6 h PRN
- Nabilone 1 to 2 mg PO q 6 to 8 h PRN nausea

**TREATMENT:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
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</thead>
<tbody>
<tr>
<td>DOXOrubicin</td>
<td>75 mg/m² (consider 60mg/m² for age greater than 40)</td>
<td>IV push (may give during pre-hydration</td>
</tr>
<tr>
<td>CISplatin</td>
<td>100 mg/m²</td>
<td>IV in 1 litre of NS with mannitol 30 g/L and potassium chloride 10 mEq/L to infuse over 2 hours</td>
</tr>
</tbody>
</table>

Repeat every 21 days until progression or toxicity
HYDRATION:

<table>
<thead>
<tr>
<th>Pre-CISplatin:</th>
<th>1 L 2/3 D5W 1/3 NS with potassium chloride 20 mEq + magnesium sulphate 2 g over 3 h.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prior to beginning CISplatin, urine output must be greater than or equal to 300 mL in 3 h. May repeat prehydration x 1 L to ensure urine output greater than 300 mL in 3 h. If urine output not adequate after 2 L, notify MD.</td>
</tr>
</tbody>
</table>

| Post- CISplatin: | 2/3 D5W 1/3 NS with potassium chloride 20 mEq/L + magnesium sulphate 2 g/L at 200 mL/h for 12 h. Measure every 3 h in/output while on IV. If output less than 300 mL during a 3 h period, increase IV to 300 mL/h for 3 h. If urine output still less than 300 mL in a subsequent 3 h period, give furosemide 20 mg IV x 1. If output still not adequate, notify MD. May discontinue IV and discharge after post hydration if urine output adequate and patient not vomiting. |

DOSE MODIFICATIONS:

1. **Hematological**: Reduce dose of DOXOrubicin only

<table>
<thead>
<tr>
<th>ANC (x10⁹/L)</th>
<th>Platelets (x10⁹/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.5 and greater than or equal to 100</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>1.0 to less than 1.5 or 70 to less than 100</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>less than 1.0 or less than 70</td>
<td>Delay 1 week</td>
<td></td>
</tr>
</tbody>
</table>

2. **Renal dysfunction**: Calculate creatinine clearance with each cycle using the following formula:

\[
\text{Creatinine clearance} = \frac{N^* \times (140 - \text{Age}) \times \text{Weight (kg)}}{\text{Serum creatinine}}
\]

* For males N= 1.23; For females N=1.04

Dose reduction for CISplatin should be considered if creatinine clearance changes to less than 60 mL/min
If serum creatinine done the next day after hydration remains elevated, consider dose reduction for CISplatin:

<table>
<thead>
<tr>
<th>Creatinine (micromol/L)</th>
<th>CISplatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 135</td>
<td>100%</td>
</tr>
<tr>
<td>136 to 180</td>
<td>50%</td>
</tr>
<tr>
<td>greater than 180</td>
<td>Delay 1 week</td>
</tr>
</tbody>
</table>

3. **Mucositis**: Grade 3 or 4, reduce DOXOrubicin to 80%
4. **Nausea & Vomiting**: Grade 4 despite optimal use of antiemetics, reduce dose of all drugs to 80% or QUIT
5. **Neurotoxicity**: If patient experiences hearing loss or clinically/functionally significant neuropathy, discontinue CISplatin
6. **Neutropenic Fever** (with ANC less than 0.5 x 10⁹/L): Once counts have recovered, reduce dose of DOXOrubicin to 80% (CISplatin may be given at 100%) and continue with these dose revisions for future cycles

**PRECAUTIONS:**

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
2. **Extravasation**: DOXOrubicin causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Cardiac Toxicity**: DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction. Cardiac assessment recommended at 5 years (see TESTS for details)
4. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside

Call Dr. Christine Simmons or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.