BC Cancer Protocol Summary for Adjuvant Therapy for Osteosarcoma Using DOXOrubicin and CISplatin

**Protocol Code**  
SAAJAP

**Tumour Group**  
Sarcoma

**Contact Physician**  
Dr. Christine Simmons

**ELIGIBILITY:**
- Well patients with an operable osteosarcoma with no metastases other than 1 or 2 operable lung metastases
- 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.
- Chest x-ray: every 6 – 8 weeks for 2 years, then every 3 months for 1 year, then every 6 months for 2 years, then yearly for 5 years (if CT scan of lungs due, chest x-ray not necessary)
- CT scan of lungs: every 3 months for 2 years, then every 6 months for 2 years
- Bone scan: baseline and repeat every 6 months for 4 years
- Echocardiogram: at 5 years or if pregnant

**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:**
- LORazapem 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>
</tr>
</thead>
<tbody>
<tr>
<td>DOXOrubicin</td>
<td>75 mg/m² (consider 60 mg/m² for age greater than 65)</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 x 6 cycles (THREE cycles usually given pre-operatively and THREE cycles given post-operatively)

### 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>
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</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 (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than equal to 1.5 and greater than 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>
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</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 CrCl changes to less than 60 mL/min

If serum creatinine done 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 10^9/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.