

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, [electrolytes panel](#), 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 8 mg PO/IV 30 to 60 minutes pre-chemotherapy and then 8 mg PO/IV every 8 hours
- dexamethasone 8 mg PO/IV 30 to 60 minutes pre-chemotherapy and then 4 mg PO/IV bid for 4 days
- [aprepitant 125 mg PO 30 to 60 minutes pre-chemotherapy on day 1, then 80 mg PO daily on day 2 and 3](#)
- If intolerable nausea and vomiting develops, add nabilone 1 mg PO 30 to 60 minutes pre-chemotherapy to next cycle
- 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](#) 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:

Drug	Dose	BC Cancer Administration Guideline
DOXOrubicin	75 mg/m ² (consider 60mg/m ² for age greater than 65)	IV push (may give during pre-hydration)
CISplatin	100 mg/m ²	IV in 1 litre of NS with mannitol 30 g/L and potassium chloride 10 mEq/L to infuse over 2 hours

Repeat every 21 days x 6 cycles (THREE cycles usually given pre-operatively and THREE cycles given post-operatively)

HYDRATION:

Pre-CISplatin:	D5W-1/2NS 1000 mL with potassium chloride 20 mEq and magnesium sulphate 2 g IV over 3 h. 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.
Post-CISplatin:	D5W-1/2NS with potassium chloride 20 mEq/L and 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

ANC (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	Dose
greater than equal to 1.5	and	greater than equal to 100	100%
1.0 to less than 1.5	or	70 to less than 100	80%
less than 1.0	or	less than 70	Delay 1 week

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 Cr_{Cl} changes to less than 60 mL/min

If serum creatinine done next day after hydration remains elevated, consider dose reduction for CISplatin:

Creatinine (micromol/L)	CISplatin
less than 135	100%
136 to 180	50%
greater than 180	Delay 1 week

- Mucositis:** Grade 3 or 4, reduce DOXOrubicin to 80%
- Nausea & Vomiting:** Grade 4 despite optimal use of antiemetics, reduce dose of all drugs to 80% or QUIT
- Neurotoxicity:** If patient experiences hearing loss or clinically/functionally significant neuropathy, discontinue CISplatin
- 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:

- Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
- 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.