

BCCA Protocol Summary for Adjuvant Therapy for Osteosarcoma Using Doxorubicin and Cisplatin

Protocol Code	<i>SAAJAP</i>
Tumour Group	<i>Sarcoma</i>
Contact Physician	<i>Meg Knowling</i>

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, lytes, creatinine, calcium, magnesium, albumin, bilirubin and LFTs
- 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 12 mg PO/IV pre-chemotherapy and then 8 mg PO/IV q8h
- 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 8 mg bid for 3 days

PRN'S:

- Lorazepam 1 mg SL q 4-6 h PRN nausea, sleep or restlessness
- Prochlorperazine 10 mg PO/IV q 4-6 h PRN nausea
- Diphenhydramine 25-50 mg PO/IV q 4-6 h PRN
- Nabilone 1-2 mg PO q 6-8 h PRN nausea

TREATMENT:

Drug	Dose	BCCA Administration Guideline
Doxorubicin	70 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 30 g/L mannitol and 10 mEq/L potassium chloride 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:	1 L 2/3 D5W 1/3 NS with 20 mEq KCl + 2 g MgSO ₄ 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:	2/3 D5W 1/3 NS with 20 mEq KCl/L + 2 g MgSO ₄ /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 1.5	and	greater than 100	100%
1.0-1.5	or	70-100	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 – 180	50%
greater than 180	Delay 1 week

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 $0.5 \times 10^9/L$): 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 BCCA Febrile Neutropenia Guidelines.
2. **Extravasation:** Doxorubicin causes pain and tissue necrosis if extravasated. Refer to BCCA [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. Meg Knowling or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: N/A

Date revised: 1 Oct 2009 (Cisplatin infusion time reduced)