

BCCA Protocol Summary for Treatment of Thymoma with Platinum, Doxorubicin, and Cyclophosphamide

Protocol Code: ULUOTPAC

Tumour Group: Lung

Contact Physician: Dr. Barb Melosky

ELIGIBILITY:

- Unresected thymoma or thymic carcinoma, histologically-proven, limited stage or metastatic. Adjuvant and neoadjuvant treatment may be considered in some cases.
- Adequate hematologic, hepatic, and renal function:
 - WBC greater than $4 \times 10^9/L$
 - platelets greater than or equal to $125 \times 10^9/L$
 - bilirubin less than or equal to 36 micromol/L
 - calculated creatinine clearance greater than 60 mL/min
- ECOG performance status 0, 1 or 2.
- Protocol **NOT** to be delivered with concurrent radiotherapy.
- NOTE: A BCCA CAP request with appropriate clinical information for each patient must be submitted and approved prior to treatment.

EXCLUSIONS:

- History of congestive heart failure

TESTS:

- Baseline: CBC & differential, platelets, creatinine, bilirubin.
- Before each treatment: CBC & differential, platelets, creatinine.
- If clinically indicated: bilirubin.

PREMEDICATIONS:

Antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA).

TREATMENT:

Drug	Dose	BCCA Administration Guideline
Doxorubicin	50 mg/m ²	IV push (may be given during prehydration)
Cisplatin	50 mg/m ²	Prehydrate with 1000 mL NS over 1 hour, then cisplatin IV in 500 mL NS with 20 mEq potassium chloride, 1 g magnesium sulfate, 30 g mannitol over 1 hour
Cyclophosphamide	500 mg/m ²	IV in 100 to 250* mL NS over 20 to 1 hour (*use 250 mL for doses greater than 1000 mg)

- Repeat every 21 days x 6-8 cycles.

DOSE MODIFICATIONS:

1. HEMATOLOGY

For cyclophosphamide and doxorubicin:

ANC (x 10⁹/L)		Platelets (x 10⁹/L)	Cyclophosphamide and Doxorubicin Dose
greater than or equal to 1.5	and	greater than or equal to 100	100%
1-1.4	or	75-99	50%
less than 1	or	less than 75	Delay

2. HEPATIC DYSFUNCTION

For doxorubicin:

Bilirubin (micromol/L)	Doxorubicin Dose
25-36	50%
greater than 36	Delay

3. RENAL DYSFUNCTION

For cisplatin:

Calculated Creatinine Clearance (mL/min)	Cisplatin dose
greater than or equal to 60	100%
45-59	75% (same prehydration as full dose)
less than 45	hold cisplatin or delay with additional IV fluids

For cyclophosphamide:

Calculated Creatinine Clearance (mL/min)	Cyclophosphamide dose
greater than or equal to 10	100%
less than 10	75%

PRECAUTIONS:

1. **Extravasation:** Doxorubicin can cause pain and tissue necrosis if extravasated. Refer to BCCA Extravasation Guidelines.
2. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
3. **Renal Toxicity:** Nephrotoxicity is common with cisplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Use caution with pre-existing renal dysfunction.
4. **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 if lifelong dose of 450 mg/m² to be exceeded. Refer to the BCCA Cancer Drug Manual for more information.
5. **Neuropathy:** Dose modification or discontinuation may be required. Refer to the BCCA Cancer Drug Manual for more information.

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

Date activated: 1 Apr 2009 (replacing ULUPAC)

Date revised: 01 June 2011 (Infusion section revised)

REFERENCES:

1. Loehrer PJ, Sr., Chen M, Kim K, et al. Cisplatin, doxorubicin, and cyclophosphamide plus thoracic radiation therapy for limited-stage unresectable thymoma: an intergroup trial. *J Clin Oncol* 1997;15(9):3093-9.
2. Loehrer PJ, Sr., Kim K, Aisner SC, et al. Cisplatin plus doxorubicin plus cyclophosphamide in metastatic or recurrent thymoma: final results of an intergroup trial. The Eastern Cooperative Oncology Group, Southwest Oncology Group, and Southeastern Cancer Study Group. *J Clin Oncol* 1994;12(6):1164-8.