BC Cancer Protocol Summary for Treatment of Thymoma with Platinum, DOXOrubicin, and Cyclophosphamide

***Protocol Code**:* *LUOTPAC*

***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 x 10^9/L
  - platelets greater than or equal to 125 x 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.

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	BC Cancer Administration Guideline
DOXOrubicin	50 mg/m^2	IV push (may be given during prehydration)
CISplatin	50 mg/m^2	Prehydrate with NS 1000 mL over 1 hour, then CISplatin IV in NS 500 mL with potassium chloride 20 mEq, magnesium sulfate 1 g, mannitol 30 g over 1 hour
Cyclophosphamide	500 mg/m^2	IV in NS 100 to 250* mL over 20 min to 1 hour (*use 250 mL for doses greater than 1000 mg)

- Repeat every 21 days x 6 to 8 cycles.

DOSE MODIFICATIONS:

1. HEMATOLOGY

For cyclophosphamide and DOXOrubicin:

ANC (x 10^9/L)		Platelets (x 10^9/L)	Cyclophosphamide and DOXOrubicin Dose
greater than or equal to 1.5	and	greater than or equal to 100	100%
1.0 to less than 1.5	or	75 to less than 100	50%
less than 1.0	or	less than 75	**Delay**

2. HEPATIC DYSFUNCTION

For DOXOrubicin:

Bilirubin (micromol/L)	DOXOrubicin Dose
25 to 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 to less than 60	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 BC Cancer 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/m^2 to be exceeded. Refer to the BC Cancer Drug Manual for more information.
5. **Neuropathy**: Dose modification or discontinuation may be required. Refer to the BC 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.

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.