

# BC Cancer Protocol Summary for Treatment of Malignant Mesothelioma with Platinum and Pemetrexed

**Protocol Code:**

LUMMPP

**Tumour Group:**

Lung

**Contact Physician:**

Dr. Christopher Lee

## ELIGIBILITY:

- Malignant mesothelioma
- ECOG performance status 0, 1 or 2

## EXCLUSIONS:

- Prior chemotherapy

## TESTS:

- Baseline: CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH
- Before each treatment: CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH

## PREMEDICATIONS:

- Antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA)
- **Vitamin supplementation mandatory** starting at least 7 days prior to the first cycle, and to continue while on treatment, until 21 days after last Pemetrexed dose:
  - Folic Acid 0.4 mg PO OD
  - Vitamin B12 1000 µg IM every 9 weeks
- Prophylaxis for skin rash: dexamethasone 8 to 12 mg PO prior to treatment, then 4 mg PO every 12 hours for 4 doses.

## TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
pemetrexed	500 mg/m <sup>2</sup>	IV in NS 100 mL over 10 minutes <sup>†</sup>
CISplatin	75 mg/m <sup>2</sup>	IV in NS 500 mL over 1 hour*
<b>*Pre- and post-hydration protocol for high-dose CISplatin required according to institutional guidelines (eg, prehydration with 1 L NS over 1 hour, CISplatin in 500 mL NS with potassium chloride 20 mEq, magnesium sulfate 1 g and Mannitol 30 g)</b> <b><sup>†</sup>Pemetrexed may be given anytime during the pre-hydration period<sup>3</sup></b>		

- Repeat every 21 days x 6 cycles

## DOSE MODIFICATIONS:

### 1. HEMATOLOGY

Based on day 1 counts:

ANC (x 10 <sup>9</sup> /L)		Platelets (x 10 <sup>9</sup> /L)	Dose
Greater than or equal to 1.5	and	Greater than or equal to 100	100%
Less than 1.5	or	Less than 100	Delay

### 2. RENAL DYSFUNCTION

Creatinine Clearance (mL/min)	CISplatin Dose	Pemetrexed Dose
Greater than or equal to 60	100%	100%
45 to less than 60	80% CISplatin or go to CARBOplatin option	100%
Less than 45	Hold	Hold regardless of type of platinum

### 3. MUCOSITIS

For next cycle:

Mucositis Grade	CISplatin dose	Pemetrexed dose
0 to 2	100%	100%
3 to 4	100%	50% previous dose*
*Discontinue treatment after two dose reductions		

#### 4. OTHER TOXICITIES

For any other grade 3 or higher toxicity, delay treatment until toxicity resolves, then resume with 25% dose decrease if considered appropriate to resume by attending oncologist

**Alternatively, CARBOplatin may be used instead of CISplatin:**

DRUG	DOSE	BC Cancer Administration Guidelines
Pemetrexed	500 mg/m <sup>2</sup>	IV in 100 mL NS over 10 minutes
CARBOplatin	Dose = AUC 5 x (GFR* + 25)	IV in 250mL NS over 30 minutes

- Repeat every 21 days x 6 cycles

\*GFR may be determined by nuclear renogram or estimated by the Cockcroft formula, at the discretion of the attending physician:

$$\text{GFR} = \frac{N \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{Serum creatinine (micromol/L)}} \quad N = 1.04 \text{ (women) or } 1.23 \text{ (men)}$$

The estimated GFR should be capped at 125 mL/min when it is used to calculate the initial CARBOplatin dose. When a nuclear renogram is available, this clearance would take precedence.

#### PRECAUTIONS:

- Vitamin supplements:** Appropriate prescription of folic acid and vitamin B12 is essential. The incidence of adverse events such as febrile neutropenia related to pemetrexed is higher without vitamin supplementation.
- NSAIDs:** Concurrent nonsteroidal anti-inflammatory agents should be avoided as they may decrease the renal clearance of pemetrexed.
- Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
- Renal Toxicity:** Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Use caution with pre-existing renal dysfunction.
- Neurotoxicity:** CISplatin is neurotoxic and may have to be discontinued if functionally important neuropathy develops. Particular caution must be used in individuals with existing neuropathy.
- Ototoxicity:** CISplatin is ototoxic and its use must be cautioned in individuals with existing hearing loss.

**Contact Dr. Christopher Lee or tumour group delegate at (604) 930-2098 or 1-800-523-2885 with any problems or questions regarding this treatment program.**

#### REFERENCES:

- Volgelzang NJ, Rusthoven JJ, Symanowski J, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. *J Clin Oncol* 2003;21:2636–44.
- Hughes A, Calvert P, Azzabi A, et al. Phase I clinical and pharmacokinetic study of pemetrexed and carboplatin in patients with malignant pleural mesothelioma. *J Clin Oncol* 2002;20:3533–44.
- Thodtmann R, Depenbrock H, Dumez H, et al. Clinical and pharmacokinetic phase I study of multitargeted antifolate (LY231514) in combination with cisplatin. *J Clin Oncol* 1999;17:3009–16.