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

***Protocol Code**:* *LUMMPG*

***Tumour Group**:* *Lung*

***Contact Physician**:* *Dr. Christopher Lee*

ELIGIBILITY:
- Malignant mesothelioma
- ECOG performance status 0, 1 or 2
- Protocol **NOT** to be delivered with concurrent radiotherapy
- To continue after 6 cycles, BC Cancer Compassionate Access Program (CAP) approval must be obtained.
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EXCLUSIONS:
- Patients with poor renal function (creatinine clearance less than 60 mL/min by GFR measurement or Cockcroft formula)

TESTS:
- Baseline: CBC & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH
- Before each treatment:
  - Day 1 – CBC & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH
  - Day 8 – CBC & differential, platelets, creatinine

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

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
(Administer gemcitabine first)		
gemcitabine	1250 mg/m^2/day on days 1 and 8 (total dose per cycle = 2500 mg/m^2)	IV in 250 mL NS over 30 min
CISplatin	75 mg/m^2/day on day 1	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

- Repeat every 21 days x 6 cycles

DOSE MODIFICATIONS:

1. **Hematology**:

For gemcitabine day 1 of each cycle

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose
greater than or equal to 1.0	and	greater than or equal to 100	100%
0.5 to less than 1.0	or	75 to less than 100	75%
less than 0.5	or	less than 75	**Delay***
Platinum also delayed			

For gemcitabine day 8 of each cycle

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose**
greater than or equal to 1.0	and	greater than or equal to 100	100%
0.5 to less than 1.0	or	75 to less than 100	75%
less than 0.5	or	less than 75	**Omit**
****Dose adjustment only for the day of treatment the CBC is drawn**			

2. **Renal Dysfunction**:

Calculated Cr Clearance (mL/min)	CISplatin dose	Gemcitabine dose
greater than or equal to 60	100%	100%
45 to less than 60	80% CISplatin or go to CARBOplatin option (same prehydration as 75 mg/m^2 dose)	100%
less than 45	Hold CISplatin or delay with additional IV fluids or go to CARBOplatin option	75%
less than 30	Omit	Omit

3. **Other Toxicities**: for gemcitabine only

Grade	Stomatitis	Diarrhea	Dose
1	Painless ulcers, erythema or mild soreness	Increase of 2 to 3 stools/day	100%
2	Painful erythema, edema, or ulcers but can eat	Increase of 4 to 6 stools, or nocturnal stools	Omit until toxicity resolved then resume at 100%
3	Painful erythema, edema, or ulcers and cannot eat	Increase of 7 to 9 stools/day or incontinence, malabsorption	Omit until toxicity resolved then resume at 75%
4	Mucosal necrosis, requires parenteral support	Increase of greater than or equal to 10 stools/day or grossly bloody diarrhea requiring parenteral support	Omit until toxicity resolved then resume at 50%

Alternatively, CARBOplatin may be used instead of CISplatin:

DRUG	DOSE	BC Cancer Administration Guidelines
CARBOplatin	AUC 5 or 6 on DAY 1 Dose = AUC† x (GFR* + 25)	IV in 250mL NS over 30 minutes.
When CARBOplatin is used, gemcitabine dose should be reduced:		
gemcitabine	1000 mg/m^2/day on days 1 and 8 (total dose per cycle = 2000 mg/m^2)	IV in 250 mL NS over 30 min

† determined at discretion of the attending medical oncologist

- 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:

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

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:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare) with gemcitabine. Use caution with pre-existing renal dysfunction.
3. **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue treatment if drug-induced pneumonitis is suspected.

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:

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2. Van Haarst JM, Baas P, Manegold C, et al. Multicentre Phase II Study of Gemcitabine and Cisplatin in Malignant Pleural Mesothelioma. Br J Cancer 2002;86(3):342-5.
3. Favaretto AG, Aversa SM, Paccagnella A, et al. Gemcitabine Combined with Carboplatin in Patients with Malignant Pleural Mesothelioma: A Multicentric Phase II study. Cancer 2003;97(11):2791-7.
4. Van Moorsel CJA, Peters GJ, Pinedo HM. Gemcitabine: Future Prospects of Single-Agent and Combination Studies. *The Oncologist* 1997;2:127-34.
5. Marilyn Bain, Medical Information Specialist. Personal Communication. Eli Lilly Canada Inc; 30 June 2005.