

BCCA Protocol Summary for Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with Platinum and Gemcitabine

Protocol Code:

LUAVPG

Tumour Group:

Lung

Contact Physician:

Dr. Christopher Lee

ELIGIBILITY:

- Previously untreated patients with Stage IIIB or IV disease
 - May be used as second-line therapy if prior first-line treatment with an EGFR tyrosine-kinase inhibitor (eg: ULUAVGEFF)
- Also:
 - Previously untreated stage IIIA disease not amenable to combined modality therapy
 - Inoperable early stage disease
- Recurrent disease, including individuals treated with adjuvant chemotherapy following resection of early stage disease or individuals treated with combined modality therapy for locally advanced disease
- Adequate hematologic, hepatic and renal function.
- Age greater than or equal to 18 years.
- ECOG performance status 0, 1 or 2.
- Protocol **NOT** to be delivered with concurrent radiotherapy.
- A "Class II Drug Registration Form" for gemcitabine must be submitted at the time of initiation of treatment. For other indications, an "Individual Use of Benefit Drug List Medication for an Undesignated Indication" form must be approved.

TESTS:

- Baseline: CBC & differential, platelets, creatinine, liver function tests, bilirubin
- Before each treatment:
 - Day 1 – CBC & differential, platelets, creatinine, liver function tests, bilirubin.
 - Day 8 – CBC & differential, platelets, creatinine.

PREMEDICATIONS:

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

TREATMENT:

Drug	Dose	BCCA 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 KCl, 1 g MgSO ₄ , 30 g mannitol over 1 hour

- Repeat every 21 days x 4-6 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	and	greater than 100	100%
0.5-0.99	or	75-100	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	and	greater than 100	100%
0.5-0.99	or	75-100	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%
45-59	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 2-3 stools/day	100%
2	Painful erythema, edema, or ulcers but can eat	Increase of 4-6 stools, or nocturnal stools	Omit until toxicity resolved then resume at 100%
3	Painful erythema, edema, or ulcers and cannot eat	Increase of 7-9 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 IV support	Omit until toxicity resolved then resume at 50%

Alternatively, carboplatin may be used instead of cisplatin:

DRUG	DOSE	BCCA Administration Guidelines
Carboplatin	AUC 5 or 6 DAY 1 only Dose = $AUC^{\dagger} \times (GFR^* + 25)$	IV in 250mL D5W over 30 minutes.
When carboplatin AUC = 6 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 4-6 cycles

*GFR preferably from nuclear renogram, if not possible use:

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

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:

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.

Call 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.

Date activated: 01 December, 2004 (replacing LUPG)

Date revised: 1 Aug 2011 (eligibility updated)

References:

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2. Non-small Cell Lung Cancer Collaborative Group. Chemotherapy in non-small cell lung cancer: a meta-analysis using updated data on individual patients from 52 randomized clinical trials. *BMJ* 1995;311:899-909.
3. Scagliotti GV, De Marinis F, Rinaldi M, et al. Phase III randomized trial comparing three platinum-based doublets in advanced non-small-cell lung cancer. *J Clin Oncol* 2002;20(21):4285-91.
4. Schiller JH, Harrington D, Belani CP, et al. Comparison of four chemotherapy regimens for advanced non-small-cell lung cancer. *N Engl J Med* 2002;346:92-98.
5. Zatloukal P, et al. Gemcitabine plus cisplatin vs. gemcitabine plus carboplatin in stage IIIb and IV non-small cell lung cancer: a phase III randomized trial. *Lung Cancer* 2003;41(3):321-31.
6. Van Moorsel CJA, Peters GJ, Pinedo HM. Gemcitabine: Future prospects of single-agent and combination studies. *The Oncologist* 1997;2:127-34.
7. Marilyn Bain, Medical Information Specialist. Personal Communication. Eli Lilly Canada Inc; 30 June 2005.