# BC Cancer Protocol Summary for First-Line Treatment of Advanced Non-Small Cell Lung Cancer with Platinum and Pemetrexed

***Protocol Code**:* *LUAVPP*

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

***Contact Physician**:* *Dr. Barb Melosky*

**ELIGIBILITY**:
- Advanced non-small cell lung cancer
- Restricted to disease of *non-squamous cell* histology
- May be used as second- or third-line therapy if prior treatment with immunotherapy or targeted agents
- ECOG performance status 0, 1 or 2
- NOTE: Use of LUAVPP as induction therapy precludes the use of second-line pemetrexed in the same patient

**EXCLUSIONS**:
- Prior chemotherapy for advanced non-small cell lung cancer
- Patients who have relapsed within *12 months* of completing adjuvant chemotherapy with LUAJPP

**TESTS**:
- Baseline: CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH
  - C-reactive protein and albumin (optional, and results do not have to be available to proceed with first treatment)
- 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 mcg 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$^2$ | IV in 100 mL NS over 10 minutes$^{\dagger}$ |
| CISplatin | 75 mg/m$^2$ | IV in 500 mL NS over 1 hour* |
| ***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)**<br>**$^{\dagger}$Pemetrexed may be given anytime during the pre-hydration period[3]** | | |

- **Repeat every 21 days x 4 to 6 cycles**

**DOSE MODIFICATIONS**:

1. **HEMATOLOGY**

**Based on day 1 counts:**

| ANC (x $10^9$/L) | | Platelets (x $10^9$/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$^2$ | IV in 100 mL NS over 10 minutes |
| CARBOplatin | Dose = AUC 5 x (GFR* + 25) | IV in 100 to 250 mL NS over 30 minutes |

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

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

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.

- Repeat every 21 days x 6 cycles

**PRECAUTIONS**:

1. **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.
2. **NSAIDs**: Concurrent nonsteroidal anti-inflammatory agents should be avoided as they may decrease the renal clearance of pemetrexed.
3. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
4. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Use caution with pre-existing renal dysfunction.
5. **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.
6. **Ototoxicity**: CISplatin is ototoxic and its use must be cautioned in individuals with existing hearing loss.

**Contact 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. Scagliotti GV, Parikh P, von Pawel J, et al. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naive patients with advanced-stage non-small-cell lung cancer. J Clin Oncol 2008;26(21):3543-51.
2. Syrigos KN, Vansteenkiste J, Parikh P, et al. Prognostic and predictive factors in a randomized phase III trial comparing cisplatin-pemetrexed versus cisplatin-gemcitabine in advanced non-small-cell lung cancer. Ann Oncol 2010;21(3):556-61.
3. Ciuleanu T, Brodowicz T, Zielinski C, et al. Maintenance pemetrexed plus best supportive care versus placebo plus best supportive care for non-small-cell lung cancer: a randomised, double-blind, phase 3 study. Lancet 2009;374:1432-40.