BC Cancer Protocol Summary for Adjuvant CISplatin and Pemetrexed Following Resection of Non-Small Cell Lung Cancer

***Protocol Code**:* *LUAJPP*

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

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

ELIGIBILITY:

Patients must have:
- Fully resected stage II or IIIA non-small cell lung cancer, or
- Fully resected stage 1B non-small cell lung cancer, if considered high-risk for relapse, but uncertainty of benefit must be discussed with individual patient,
- *Non-squamous histology*, and
- Lobectomy or pneumonectomy preferred; segmentectomy or wedge resection permitted.

Patients should have:
- Treatment initiated within 60 days of definitive surgery (preferred),
- ECOG performance status 0 or 1,
- Adequate renal function (creatinine clearance greater than or equal to 45 mL/minute),
- Adequate hepatic function, and
- Prior to treatment, consideration for Pneumococcal vaccine and influenza vaccine, if appropriate for season

Note:
- In patients whose tumours are found to have an EGFR mutation, consider CISplatin/vinorelbine

EXCLUSIONS:

Patients must not:
- Require CARBOplatin substitution for CISplatin; if CISplatin is contraindicated or relatively contraindicated, consider treatment with LUAJPC

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 high 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†
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)** **†Pemetrexed may be given anytime during the pre-hydration period**[2]		

- **Repeat every 21 days x 4 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

Calculated Cr Clearance (mL/min)	CISplatin Dose	Pemetrexed Dose
greater than or equal to 60	100%	100%
45 to less than 60	80%	100%
less than 45	**Hold**	**Hold**

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

PRECAUTIONS:

1. **Vitamin supplements**: Appropriate prescription of Folic Acid and Vitamin B12 is important. 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. Kenmotsu H, Yamamoto N, Yamanaka T, et al. Randomized Phase III study of pemetrexed plus cisplatin versus vinorelbine plus cisplatin for completely resected Stage II to IIIA non-squamous non-small cell lung cancer. J Clin Oncol. 2020; 38(19): 2187-2196.
2. 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 randomized, double-blind, phase 3 study. Lancet 2009; 374:1432-40.
3. Kenmotsu H, Yamamoto N, Misumi T, et al., Five-Year Overall Survival Analysis of the JIPANG Study: Pemetrexed or Vinorelbine Plus Cisplatin for Resected Stage II-IIIA Nonsquamous Non–Small-Cell Lung Cancer. J Clin Oncol. 2023; 41, 5242-5246.