BC Cancer Protocol Summary for First-Line Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with CARBOplatin and PACLitaxel

Protocol Code: *LUAVPC*

Tumour Group: *Lung*

Contact Physician: *Dr. Christopher Lee*

ELIGIBILITY:

- Previously untreated patients with Stage IIIB or IV disease.
    - May be used as second- or third-line therapy if prior treatment with immunotherapy or targeted agents
- 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

TESTS:

- Baseline: CBC & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, chest X-ray, camera nuclear renogram for GFR (if available)
    - C-reactive protein and albumin (optional, and results do not have to be available to proceed with first treatment)
- Before each treatment: CBC & differential, platelets, creatinine, any initially elevated tumor marker
- If clinically indicated: alkaline phosphatase, ALT, total bilirubin and LDH prior to each cycle

PREMEDICATIONS:

- **PACLitaxel must not be started unless the following drugs have been given**:

  45 minutes prior to PACLitaxel:
    - dexamethasone 20 mg IV in 50 mL NS over 15 minutes

  30 minutes prior to PACLitaxel:
    - diphenhydrAMINE 50 mg IV in NS 50 mL over 15 minutes and famotidine 20 mg IV in NS 100 mL over 15 minutes (Y-site compatible)

Warning: The information contained in these documents are a statement of consensus of BC Cancer professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is at your own risk and is subject to BC Cancer's terms of use available at www.bccancer.bc.ca/legal.htm

- Antiemetic protocol for High emetogenic chemotherapy (see protocol SCNAUSEA)

TREATMENT: (Give PACLitaxel first)

Drug	Dose	BC Cancer Administration Guideline
PACLitaxel	200 mg/m^2	IV in 250 to 500 mL NS over 3 hours (use non-DEHP bag and non-DEHP tubing with 0.2 micron in-line filter)
CARBOplatin	AUC 6 Dose = AUC x (GFR* + 25)	IV in 100 to 250 mL NS over 30 minutes

- Repeat every 21 days x 4-6 cycles

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

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

The estimated GFR calculated using the Cockcroft-Gault equation 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.

DOSE MODIFICATIONS:

1. **Hematology (on treatment day):**

ANC (x 10^9/L)		Platelets (x 10^9/L)	Doses (both drugs)
greater than or equal to 1.0	and	greater than or equal to 100	100%
less than 1.0	or	less than 100	delay until recovery

2. **Arthralgia and/or myalgia**: If arthralgia and/or myalgia of grade 2 (moderate) or higher is not relieved by adequate doses of NSAIDs or acetaminophen with codeine (e.g., TYLENOL #3®), a limited number of studies report a possible therapeutic benefit using:
   - predni SONE 10 mg PO bid x 5 days starting 24 hours post-PACLitaxel
   - gabapentin 300 mg PO on day before chemotherapy, 300 mg bid on treatment day, then 300 mg tid x 7 to 10 days

   If arthralgia and/or myalgia persists, reduce subsequent PACLItaxel doses to 175 mg/m^2.
3. **Neuropathy**: Dose modification or discontinuation may be required (see BC Cancer Drug Manual).

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4. **Renal dysfunction**: If significant increase (greater than 20%) in creatinine, repeat nuclear renogram (if available) and recalculate CARBOplatin dose using new GFR.
5. **Hepatic dysfunction**: Dose reduction may be required for PACLItaxel (see BC Cancer Drug Manual)

PRECAUTIONS:

1. **Hypersensitivity**: Reactions are common. See BC Cancer Hypersensitivity Guidelines

mild symptoms (e.g. mild flushing, rash, pruritus)	▪ complete PACLitaxel infusion. Supervise at bedside ▪ no treatment required
moderate symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension	▪ stop PACLitaxel infusion ▪ give IV diphenhydrAMINE 25-50 mg and IV hydrocortisone IV 100 mg ▪ after recovery of symptoms resume PACLitaxel infusion at 20 mL/hr for 5 minutes, 30 mL/hr for 5 minutes, 40 mL/hr for 5 minutes, then 60 mL/hr for 5 minutes. If no reaction, increase to full rate. ▪ if reaction recurs, discontinue PACLitaxel therapy
severe symptoms (i.e. *one* or more of respiratory distress requiring treatment, generalized urticaria, angioedema, hypotension requiring therapy)	▪ stop PACLitaxel infusion ▪ give IV antihistamine and steroid as above. Add epinephhrine or bronchodilators if indicated ▪ discontinue PACLitaxel therapy

2. **Extravasation**: PACLitaxel causes pain and may, rarely, cause tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.

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.

References:

1. Kelly K, Crowley J, Bunn PA, et al. Randomized phase III trial of paclitaxel plus carboplatin versus vinorelbine plus cisplatin in the treatment of patients with advanced non-small-cell lung cancer: A Southwest Oncology Group Trial. J Clin Oncol 2001;19:3210-18.
2. Socinski MA, Schell MJ, Peterman A, et al. Phase III trial comparing a defined duration of therapy versus continuous therapy followed by second-line therapy in advanced-stage IIIB/IV non–small-cell lung cancer. J Clin Oncol 2002;20:1335-43.

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