

BC Cancer Protocol Summary for Treatment of Locally Advanced Non-Small Cell Lung Cancer using CARBOplatin and PACLitaxel with Radiation Therapy

Protocol Code
Tumour Group
Contact Physician

LULACATRT
Lung
Dr. Christopher Lee

ELIGIBILITY:

- Stage IIIA or IIIB NSCLC
 - T1 –T3 with N2 disease if medically inoperable
 - T4 with any node size and extent
 - N3 disease with any tumor involvement
- Unfit for LULAPERT or LULAPE2RT (e.g., elderly or frail, poor renal function)
- Measurable disease
- ECOG performance status 0 – 2
- Suitable candidate for thoracic radiation
- Weight loss less than or equal to 10% in the 3 months before diagnosis

EXCLUSIONS:

- Significant pleural effusions

TESTS:

- Baseline: CBC & differential, platelets, creatinine, total bilirubin, ALT, camera nuclear renogram for GFR (optional)
- Before each treatment: CBC & differential, platelets, creatinine
- If clinically indicated: bilirubin, ALT, magnesium

PREMEDICATIONS:

- **PACLitaxel must not be started unless the following drugs have been given:**
 - 45 minutes prior to PACLitaxel:
 - dexamethasone 10 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)
- **NOTE:** If no PACLitaxel hypersensitivity reactions occur on cycle 1, no hypersensitivity premedications may be needed for subsequent doses and may be omitted at physician's discretion (dexamethasone 8 to 12 mg PO may be given in place of the regimen in the first bullet point above).
- If hypersensitivity reactions occur, premedications for re-challenge include dexamethasone 20 mg PO given 12 hours and 6 hours prior to treatment, plus IV premedications given 30 minutes prior to PACLitaxel: dexamethasone 10 mg, diphenhydrAMINE 25 mg, and H₂-antagonist (e.g., famotidine 20 mg). If no hypersensitivity reactions occur, standard premedications (see above) will be used for subsequent PACLitaxel doses.
- ondansetron 8 mg PO 30 minutes prior to CARBOplatin.

TREATMENT:

Chemotherapy (give PACLitaxel first)

Concurrent with radiation therapy: starting the first day of radiation therapy (**note: lower drug doses with weekly dosing schedule**)

Drug	Dose	BC Cancer Administration Guideline
PACLitaxel	45 mg/m ²	IV in 100 to 250 mL NS over 1 hour (use non-DEHP bag and non-DEHP tubing with 0.2 micron in-line filter)
CARBOplatin	Dose = AUC 2 x (GFR* + 25)	IV in 100 to 250 mL NS over 30 minutes

Repeat weekly x 6 weeks concurrent with radiation therapy

Optional consolidation chemotherapy: starting about 4 weeks after completion of concurrent chemoradiation therapy (**note: regular drug doses with 3-weekly dosing schedule**)

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	Dose = AUC 6 x (GFR* + 25)	IV in 100 to 250 mL NS over 30 minutes

Repeat every 3 weeks x 2 cycles

**Measured GFR* (e.g. nuclear renogram) is preferred in circumstances of co-morbidity that could affect renal function (third-space fluid accumulations, hypoproteinemia, potentially inadequate fluid intake, age greater than 70, etc.). The lab reported GFR (MDRD formula) may be used as an alternative to the Cockcroft-Gault estimate of GFR; the estimated GFR reported by the lab or 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.

Cockcroft-Gault Formula

$$\text{CrCl} = \frac{N (140 - \text{age}) \times \text{weight (kg)}}{\text{serum creatinine (micromol/L)}}$$

Where N = 1.04 for females, and 1.23 for males

Note: The same method of estimation should be used throughout the treatment course (i.e. if lab reported GFR was used initially, this should be used for dosing in all subsequent cycles and not the Cockcroft-Gault estimate).

NOTE: If creatinine increases by greater than 20% or rises above the upper limit of normal, recalculate GFR and recalculate CARBOplatin dose using new GFR. (See Dose Modifications 4. Renal Dysfunction)

RADIATION THERAPY:

60 Gy external beam thoracic radiotherapy in 30 fractions over 6 weeks

DOSE MODIFICATIONS:

1. Hematology:

On treatment days:

ANC (X 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Dose
greater than or equal to 1.0	and	greater than or equal to 50	100%
less than 1.0	and/or	less than 50	Delay chemotherapy for 1 week until recover above these values

2. **Arthralgia and/or myalgia:** If arthralgia and/or myalgia of grade 2 (moderate) or higher was not adequately relieved by NSAIDs or acetaminophen with codeine (e.g., TYLENOL#3®), a limited number of studies report a possible therapeutic benefit using:
 - predniSONE 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 5 to 15 days (based on duration of arthromyalgia)
3. **Neuropathy:** Dose modification or discontinuation may be required (see BC Cancer Drug Manual).
4. **Renal dysfunction:** If significant increase (greater than 20% or rises above the upper limit of normal) in creatinine, recheck/recalculate GFR 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

<u>Mild</u> symptoms (e.g., mild flushing, rash, pruritus)	<ul style="list-style-type: none"> ▪ complete PACLitaxel infusion. Supervise at bedside ▪ no treatment required
<u>Moderate</u> symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension)	<ul style="list-style-type: none"> ▪ stop PACLitaxel infusion ▪ give IV diphenhydRAMINE 25 to 50 mg and hydrocortisone IV 100 mg ▪ after recovery of symptoms resume PACLitaxel infusion at 20 mL/h for 5 minutes, 30 mL/h for 5 minutes, 40 mL/h for 5 minutes, then 60 mL/h for 5 minutes. If no reaction, increase to full rate. ▪ if reaction recurs, discontinue PACLitaxel therapy
<u>Severe</u> symptoms (i.e. <u>one</u> or more of respiratory distress requiring treatment, generalized urticaria, angioedema, hypotension requiring therapy)	<ul style="list-style-type: none"> ▪ stop PACLitaxel infusion ▪ give IV antihistamine and steroid as above ▪ Add epinephrine 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.
4. **Drug Interactions:** PACLitaxel is a CYP 2C8/9 and CYP 3A4 substrate. Drug levels may be increased by inhibitors of these enzymes and decreased by inducers of these enzymes.

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:

1. Santana-Davila R, Devisetty K, Szabo A, et al. Cisplatin and etoposide versus carboplatin and paclitaxel with concurrent radiotherapy for stage III non-small-cell lung cancer: An analysis of Veterans Health Administration data. *J Clin Oncol* 2015;33:567-74.
2. Belani CP, Choy H, Bonomi P, et al. Combined chemoradiotherapy regimens of paclitaxel and carboplatin for locally advanced non-small-cell lung cancer: A randomized phase II locally advanced multi-modality protocol. *J Clin Oncol* 2005;23:5883-91.
3. HK Young, Mishima M. Consolidation chemotherapy after concurrent chemoradiotherapy in patients with stage III non-small-cell lung cancer. *J Clin Oncol* 2016;34(7):767.