BC Cancer Protocol Summary for First-Line Treatment of Advanced Non-Small Cell Lung Cancer with PACLitaxel, CARBOplatin and Cemiplimab

Protocol Code	*LUAVPCCEM*
Tumour Group	*Lung*
Contact Physician	*Lung Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Stage IIIB or IIIC non-small cell lung cancer (NSCLC) not amenable to curative intent therapy, or stage IV NSCLC, and
- No prior treatment in the advanced setting

Patients should have:

- Good performance status,
- Adequate hematologic, hepatic and renal function, and
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of cemiplimab

Note:

- Use of first-line cemiplimab precludes the use of nivolumab, pembrolizumab and atezolizumab as any subsequent line of therapy
- At time of subsequent progression, retreatment (with or without chemotherapy) is permitted for an additional 1 year (17 cycles) if:
  - Patient completed 108 weeks (36 cycles) of therapy without progression, or
  - Patient stopped treatment due to toxicity (not progression)
  - CAP approval not required for retreatment

EXCLUSIONS:

Patients must not have:

- Presence of EGFR, ALK or ROS1 mutations
- Progression on or within 6 months of completing adjuvant or neoadjuvant treatment
- Active central nervous system metastases (unless asymptomatic and/or stable)

CAUTIONS:

- Concurrent autoimmune disease
- Patients with long term immunosuppressive therapy or systemic corticosteroids (requiring more than 10 mg predniSONE/day or equivalent)
- Received prior treatment with idelalisib, regardless of indication

TESTS:

- Baseline: CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH, morning serum cortisol
- Baseline, if clinically indicated: BNP, troponin, creatine kinase, ECG, echocardiogram, chest x-ray
- Before each treatment: CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH
- If clinically indicated: chest x-ray, morning serum cortisol, lipase, serum or urine HCG (required for women of child bearing potential if pregnancy suspected), free T3 and free T4, serum ACTH levels, testosterone, estradiol, FSH, LH, random glucose, troponin, creatine kinase, ECG
- Weekly telephone nursing assessment for signs and symptoms of side effects while on treatment (optional).

PREMEDICATIONS:

Cycles 1 to 6:

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

- If no prior infusion reactions to cemiplimab: administer premedications as sequenced below

  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)

- If prior infusion reactions to cemiplimab: administer PACLitaxel premedications prior to cemiplimab

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

  30 minutes prior to cemiplimab:
  - 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)

  acetaminophen 325 to 975 mg PO prior to cemiplimab

- Antiemetic protocol for highly emetogenic chemotherapy (see SCNAUSEA)

Cycle 7 onwards:

- Antiemetics are not usually required.
- If prior infusion reaction to cemiplimab: diphenhydrAMINE 50 mg PO, acetaminophen 325 to 975 mg PO, and hydrocortisone 25 mg IV 30 minutes prior to treatment

TREATMENT:

Cycles 1 to 6:

Drug	Dose	BC Cancer Administration Guideline
cemiplimab	350 mg	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter*
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 5 Dose = AUC x (GFR** + 25)	IV in 100 to 250 mL NS over 30 minutes

* use separate infusion line and filter for each drug

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

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

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 3 weeks for up to 6 cycles, then proceed to maintenance treatment ycle 7 onwards).

Cycle 7 onwards:

Drug	Dose	BC Cancer Administration Guideline
cemiplimab	350 mg	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter

- Repeat every 3 weeks until disease progression, unacceptable toxicity, or a maximum of 108 weeks (total of 36 cycles including those given with chemotherapy), whichever comes first.
- Retreatment may be allowed (refer to Eligibility section, above).

DOSE MODIFICATIONS:

1. **For cemiplimab**:
   No specific dose modifications for cemiplimab. Toxicity managed by treatment delay and other measures (see SCIMMUNE protocol for management of immune-mediated adverse reactions to checkpoint inhibitors immunotherapy).

2. **Hematological:**
   Cycles 1 to 6:

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose
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

3. **Arthralgia and/or myalgia related to PACLitaxel**: 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:
   - 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 7 to 10 days
   - If arthralgia and/or myalgia persists, reduce subsequent PACLItaxel doses to 175 mg/m^2.

4. **Neuropathy**: Dose modification or discontinuation may be required (see BC Cancer Drug Manual).

5. **Renal dysfunction**: If significant increase (greater than 20%) in creatinine, repeat nuclear renogram (if available) and recalculate CARBOplatin dose using new GFR.

6. **Hepatic dysfunction**: Dose reduction may be required for PACLItaxel (see BC Cancer Drug Manual)

PRECAUTIONS:

1. **Serious immune-mediated reactions**: can be severe to fatal and usually occur during the treatment course with cemiplimab, but may develop months after discontinuation of therapy. They may include enterocolitis, intestinal perforation or hemorrhage, hepatitis, dermatitis, neuropathy, endocrinopathy, pneumonitis, as well as toxicities in other organ systems. Early diagnosis and appropriate management are essential to minimize life-threatening complications (see **SCIMMUNE** protocol for

management of immune-mediated adverse reactions to checkpoint inhibitors immunotherapy).

2. **Infusion-related reactions:** isolated cases of severe infusion reactions have been reported with cemiplimab. Discontinue cemiplimab with severe reactions (Grade 3 or 4). Patients with mild or moderate infusion reactions may receive cemiplimab with close monitoring, reduced rates of administration and use of premedication.
3. **Hypersensitivity**: Reactions are common with PACLitaxel. 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

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

Contact the LU Systemic Therapy physician at your regional cancer centre or LU Systemic Therapy Chair with any problems or questions regarding this treatment program.

REFERENCES:

1. Gogishvili M, Melkadze T, Makharadze T, et al. Cemiplimab plus chemotherapy versus chemotherapy alone in non-small cell lung cancer: a randomized, controlled, double-blind phase 3 trial. Nat Med. 2022 Nov;28(11):2374-2380.
2. Cemiplimab (Libtayo) CADTH Reimbursement Recommendation. Canadian Journal of Health Technologies, May 2024; 4(5).