BC Cancer Protocol Summary for Neoadjuvant-Adjuvant Treatment of Non-Squamous Non-Small Cell Lung Cancer with Pemetrexed, Platinum and Pembrolizumab

Protocol Code	*LUNAPPPMB*
Tumour Group	*Lung*
Contact Physician	*LU Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Previously untreated resectable non-small cell lung cancer (NSCLC),
- Stage II, IIIA or IIIB (T3 to 4N2),
- Non-squamous histology

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 checkpoint inhibitors

Notes:

- PD-L1 status not required
- Patients who started treatment on neoadjuvant immunotherapy with chemotherapy prior to 1 Feb 2026, may switch to LUNAPPPMB provided all eligibility criteria are met and no progression has occurred
- Patients are eligible for subsequent checkpoint inhibitors in the advanced setting, provided progression occurred at least 6 months after treatment completion

EXCLUSIONS:

Patients must not have:

- Known EGFR or ALK genomic tumour mutations
- Prior treatment with any immunotherapy
- Planned neoadjuvant radiotherapy

CAUTIONS:

- Active uncontrolled autoimmune disease
- Patients with long term immunosuppressive therapy or systemic corticosteroids (requiring more than 10 mg predniSONE/day or equivalent)

TESTS:

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

PREMEDICATIONS:

- **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 daily
  - 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.
- Neoadjuvant phase: antiemetic protocol for high emetogenic chemotherapy (see SCNAUSEA)
- Adjuvant phase: Antiemetics are not usually required. If required, antiemetic protocol for low emetogenicity (see SCNAUSEA)
- If prior infusion reactions to pembrolizumab: diphenhydrAMINE 50 mg PO, acetaminophen 325 to 975 mg PO, and hydrocortisone 25 mg IV 30 minutes prior to treatment

TREATMENT:

Neoadjuvant Phase:

Drug	Dose	BC Cancer Administration Guideline
pembrolizumab	2 mg/kg* (maximum 200 mg)	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter**
pemetrexed	500 mg/m^2	IV in 100 mL NS over 10 minutes**
CISplatin	75 mg/m^2	IV in 500 mL NS over 60 minutes†
† pre- and post-hydration protocol for high-dose CISplatin required according to institutional guidelines (e.g., prehydration with 1000 mL NS over 60 minutes, CISplatin in 500 mL NS with potassium chloride 20 mmol, magnesium sulfate 1 g and mannitol 30 g)		

*select dose per Dose Banding Tables (appendix).
** pembrolizumab and pemetrexed may be given during the pre-hydration period

- Repeat every 3 weeks for 4 cycles, followed by surgical resection

then at least 4 weeks but no later than 12 weeks after surgery,

Adjuvant Phase:

Drug	Dose	BC Cancer Administration Guideline
pembrolizumab	2 mg/kg* (maximum 200 mg)	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter

*select dose per Dose Banding Tables (appendix).

- Each cycle is 3 weeks
- Give for a maximum of 13 cycles* post-operatively, unless disease progression or unacceptable toxicity
  * or equivalent, including cycles given on 6-weekly schedule

OR

Drug	Dose	BC Cancer Administration Guideline
pembrolizumab	4 mg/kg* (maximum 400 mg)	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter

*select dose per Dose Banding Tables (appendix).

- Each cycle is 6 weeks
- Give for a maximum of 7 cycles* post-operatively, unless disease progression or unacceptable toxicity
  * or equivalent, including cycles given on 3-weekly schedule

DOSE MODIFICATIONS:

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

2. **For pemetrexed and CISplatin:**

   a. **Hematological:**

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

b. 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 use CARBOplatin option	100%
Less than 45	Hold	Hold regardless of type of platinum

Alternatively, CARBOplatin may be used instead of CISplatin:

Drug	Dose	BC Cancer Administration Guideline
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:

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

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.

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		

PRECAUTIONS:

1. **Serious immune-mediated reactions**: can be severe to fatal and usually occur during the treatment course, 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 reaction have been reported. In case of a severe reaction, pembrolizumab infusion should be discontinued and appropriate medical therapy administered. Patients with mild or moderate infusion reaction may receive pembrolizumab with close monitoring. Premedications with acetaminophen and antihistamine may be considered.
3. **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.
4. **Neutropenia**: fever or other evidence of infection must be assessed promptly and treated aggressively.
5. **NSAIDs**: concurrent nonsteroidal anti-inflammatory agents should be avoided as they may decrease the renal clearance of pemetrexed.
6. **Renal Toxicity**: nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Use caution with pre-existing renal dysfunction.
7. **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.
8. **Ototoxicity**: CISplatin is ototoxic, and its use must be cautioned in individuals with existing hearing loss.

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

REFERENCES:

1. Wakelee H, Liberman M, Kato T et al. Perioperative Pembrolizumab for Early-Stage Non-Small-Cell Lung Cancer. N Engl J Med 2023; 389: 491-503.
2. Pembrolizumab (Keytruda) Canada's Drug Agency (CDA-AMC) Reimbursement Recommendation. Canadian Journal of Health Technologies. April 2025; 5(4): 1-25.

Appendix. Dose Bands

PEMBROLIZUMAB DOSE BANDING TABLE (2 mg/kg capped 200 mg)

Ordered Dose (mg)		Rounded dose (mg)
From:	**To:**	
Less than 70		**Pharmacy prepares specific dose**
70	80.49	**75**
80.5	92.49	**85**
92.5	110.49	**100**
110.5	137.49	**125**
137.5	162.49	**150**
162.5	187.49	**175**
187.5	200	**200**

PEMBROLIZUMAB DOSE BANDING TABLE (4 mg/kg capped 400 mg)

Ordered Dose (mg)		Rounded dose (mg)
From:	**To:**	
Less than 137.5		**Pharmacy prepares specific dose**
137.5	162.49	**150**
162.5	187.49	**175**
187.5	221.49	**200**
221.5	242.49	**225**
242.5	264.49	**250**
265.5	284.49	**275**
285.5	332.49	**300**
333.5	374.49	**350**
374.5	400	**400**