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

Protocol Code	*LUNAPGPMB*
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),
- Squamous cell 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 LUNAPGPMB 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, known or suspected 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, TSH, morning serum cortisol, chest x-ray
- Before each treatment:
    - Day 1 – CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH
    - Day 8 – CBC & Diff, creatinine
- If clinically indicated: chest x-ray, morning serum cortisol, lipase, glucose, 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, ECG
- Weekly telephone nursing assessment for signs and symptoms of side effects while on treatment (Optional).

PREMEDICATIONS:

- 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* on Day 1 (maximum 200 mg)	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter
gemcitabine	1000 mg/m^2/day on Days 1 and 8 (total dose per cycle = 2000 mg/m^2)	IV in 250 mL NS over 30 minutes
CISplatin	75 mg/m^2/day on Day 1	IV in 500 mL NS over 1 hour**

*Select dose per Dosing Banding Tables (appendix).

** 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)

- Repeat every 3 weeks x 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 gemcitabine and CISplatin:

a. Hematological:

For gemcitabine Day 1 of each cycle

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%
0.5 to less than 1.0	or	75 to less than 100	75%
Less than 0.5	or	Less than 75	Delay*
* Platinum also delayed			

For gemcitabine Day 8 of each cycle

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%
0.5 to less than 1.0	or	75 to less than 100	75%
Less than 0.5	or	Less than 75	Omit
**Dose adjustment only for the day of treatment the CBC is drawn			

3. Renal Dysfunction:

Creatinine Clearance (mL/min)	CISplatin Dose	Gemcitabine Dose
Greater than or equal to 60	100%	100%
45 to less than 60	80% CISplatin or go to CARBOplatin option (same prehydration as 75 mg/m^2 dose)	100%
Less than 45	Hold CISplatin or delay with additional IV fluids or go to CARBOplatin option	75%
Less than 30	Omit	Omit

Alternatively, CARBOplatin may be used instead of CISplatin:

Drug	Dose	BC Cancer Administration Guideline
CARBOplatin	Dose = AUC 5 x (GFR* + 25) on Day 1	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:

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

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.

4. **Other Toxicities**:

For gemcitabine only:

Grade	Stomatitis	Diarrhea	Dose
1	Painless ulcers, erythema or mild soreness	Increase of 2 to 3 stools/day	100%
2	Painful erythema, edema, or ulcers but can eat	Increase of 4 to 6 stools, or nocturnal stools	Omit until toxicity resolved then resume at 100%
3	Painful erythema, edema, or ulcers and cannot eat	Increase of 7 to 9 stools/day or incontinence, malabsorption	Omit until toxicity resolved then resume at 75%
4	Mucosal necrosis, requires parenteral support	Increase of greater than or equal to 10 stools/day or grossly bloody diarrhea requiring parenteral support	Omit until toxicity resolved then resume at 50%

PRECAUTIONS:

1. **Serious immune-mediated reactions**: can be severe to fatal and usually occur during the treatment course with pembrolizumab, 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 pembrolizumab. Discontinue pembrolizumab with severe reactions (Grade 3 or 4). Patients with mild or moderate infusion reactions may receive pembrolizumab with close monitoring, reduced rates of administration and use of premedication.
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 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**