BC Cancer Protocol Summary for First-Line Treatment of Advanced Non-Small Cell Lung Cancer Using 6-Weekly Pembrolizumab

Protocol Code	*LUAVPMBF6*
Tumour Group	*Lung*
Contact Physician	*Dr. Barb Melosky*

ELIGIBILITY:

Patients must have:
- Squamous *or* non-squamous advanced non-small cell lung cancer,
- Previously untreated in the advanced setting, and
- Tumour characteristics confirmed by an accredited laboratory:
    - PD-L1 expression positive (>50%)
    - If non-squamous carcimona:
        - EGFR sensitizing mutation-negative
        - ALK mutation-negative

Patients should have:
- ECOG 0-1,
- Adequate hepatic and renal function, and
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of pembrolizumab

Note:
- CAP approval is not required to switch between LUAVPMBF6 and LUAVPMBF.
- Use of first-line pembrolizumab precludes the use of nivolumab and atezolizumab as any subsequent line of therapy in the same patient.
- Prior adjuvant treatment with either durvalumab or atezolizumab allowed if last durvalumab dose was > 6 months. Not eligible if progressed on adjuvant durvalumab or atezolizumab.
- *NOTE*: Consideration should be given to a standard platinum-based doublet as second-line therapy after progression or failure with pembrolizumab.

EXCLUSIONS:
- ECOG performance status > 2
- Active, known or suspected autoimmune disease
- Use with caution in patients with long term immunosuppressive therapy or systemic corticosteroids (requiring more than 10 mg predniSONE/day or equivalent)

TESTS:

- Baseline: CBC & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH, morning serum cortisol, chest x-ray
  - 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, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH
- 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:

- 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:

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

- Repeat every **6 weeks** until disease progression, unacceptable toxicity, or a maximum of 2 years of treatment (including doses given as ULUAVPMBF)

DOSE MODIFICATIONS:

No specific dose modifications. Toxicity managed by treatment delay and other measures (see SCIMMUNE protocol for management of immune-mediated adverse reactions to checkpoint inhibitors immunotherapy, http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Supportive%20Care/SCIMMUNE_Protocol.pdf).

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, http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Supportive%20Care/SCIMMUNE_Protocol.pdf).
2. **Infusion-related reactions:** isolated cases of severe infusion reactions have been reported. Discontinue pembrolizumab with severe reactions (Grade 3 or 4). Patients with mild or moderate infusion reactions may receive pembrolizumab with close monitoring and use of premedication.

Contact Dr. Barb Melosky or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

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