BC Cancer Protocol Summary for Treatment of Advanced Non-Small Cell Lung Cancer Using 4-Weekly Nivolumab

Protocol Code	*LUAVNIV4*
Tumour Group	*Lung*
Contact Physician	*Dr. Christopher Lee*

ELIGIBILITY:

Patients must have:
- Advanced non-small cell lung cancer, irrespective of histology, and
- Disease progression on or after prior platinum-based chemotherapy requiring second- or subsequent-line therapy

Note:
- In the advanced setting, patients are eligible to receive nivolumab, atezolizumab ***or*** pembrolizumab, but not sequential use of these agents
- CAP approval is not required to switch between LUAVNIV4 and LUAVNIV.

Patients should have:
- Good performance status (ECOG 0-2)
- Adequate hepatic and renal function
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of nivolumab

EXCLUSIONS:

Patients must not have:
- Relapsed on or within 6 months of completing adjuvant durvalumab or atezolizumab, or
- Prior use of first-line nivolumab and ipilimumab or pembrolizumab

CAUTION:
- 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 & 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
- Antiemetic protocol for low emetogenicity (see SCNAUSEA)
- If prior infusion reactions to nivolumab: 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
nivolumab	6 mg/kg (maximum 480 mg)	IV in 50 to 100 mL NS over 30 minutes Using a 0.2 micron in-line filter

- Repeat **every 4 weeks** until disease progression or unacceptable toxicity
- If pseudo progression on imaging is suspected, may continue treatment for another 8 weeks. Discontinue treatment if confirmatory progression on subsequent scan (8-12 weeks)

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 nivolumab with severe reactions (Grade 3 or 4). Patients with mild or moderate infusion reactions may receive nivolumab with close monitoring and use of premedication.

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.

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