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

Protocol Code	*LUAVATZ4*
Tumour Group	*Lung*
Contact Physician	*Dr. Barb Melosky*

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:
- CAP approval is not required to switch between LUAVATZ and LUAVATZ4.
- In the advanced setting, patients are eligible to receive one of atezolizumab, nivolumab ***or*** pembrolizumab, but not sequential use of these agents

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 atezolizumab

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
- Myasthenia gravis or Guillain-Barré syndrome
- 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, calcium, 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 atezolizumab: 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
atezolizumab	1680 mg	IV in 250 mL NS over 1 hour*

* subsequent infusions may be given over 30 minutes if the first infusion is well-tolerated

- Repeat **every 4 weeks** until disease progression or unacceptable toxicity

DOSE MODIFICATIONS:

No specific dose modifications. Toxicity managed by treatment delay and other measures (see SCIMMUNE for management of immune-mediated adverse reactions to checkpoint inhibitor 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. 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 for management of immune-mediated adverse reactions to checkpoint inhibitor 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 atezolizumab for severe reactions (Grade 3 or 4). Patients with mild or moderate infusion reactions may receive atezolizumab with close monitoring and use of premedication.
3. **Infections:** severe infections have been reported. Treat with antibiotics for suspected or confirmed bacterial infections. Hold atezolizumab for Grade 3 or 4 infections. Permanently discontinue for any grade of meningitis or encephalitis.

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.

REFERENCES:

1. Genentech Inc. TECENTRIQ® full prescribing information. South San Francisco, CA, USA; August 2019.
2. Rittmeyer A, Barlesi F, Waterkamp D, et al. Atezolizumab versus docetaxel in patients with previously treated non-small cell lung cancer (OAK): a phase 3, open-label, multicenter randomized controlled trial. Lancet 2017; 389(10066):255-265.
3. Weber JS, et al. Management of adverse events following treatment with anti-programmed death-1 agents. Oncologist 2016;21:1-11.
4. Hoffman-La Roche Limited. TECENTRIQ® product monograph. Mississauga, Ontario, Canada; January 21, 2020.
5. Morrissey KM, Marchand M, Patel H, et al. Alternative dosing regimens for atezolizumab: an example of model-informed drug development in the postmarketing setting. Cancer Chemotherapy and Pharmacology (2019) 84: 1257-1267.