
Protocol Code: ULUAVNIV

Tumour Group: Lung

Contact Physician: Dr. Christopher Lee

ELIGIBILITY:
- Advanced non-small cell lung cancer, irrespective of histology
- Second- or subsequent-line therapy for disease progression on or after prior platinum-based chemotherapy
- Good performance status
- Adequate hepatic and renal function
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of nivolumab
- \textit{BC Cancer Compassionate Access Program (CAP) approval must be obtained} for nivolumab
- Patients are eligible to receive nivolumab, atezolizumab or pembrolizumab, but not sequential use of these agents
- CAP approval is not required for switch to ULUAVNIV if prior approval is in place for ULUAVNIV4

EXCLUSIONS:
- Patients who have relapsed on or within 6 months of completing adjuvant durvalumab
- Prior use of first-line pembrolizumab (ULUAVPMBF)
- ECOG performance status > 2
- Active 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
- 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:

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<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
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<tr>
<td>nivolumab</td>
<td>3 mg/kg (maximum 240 mg)</td>
<td>IV in 100 mL* NS over 30 minutes</td>
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<td>Using a 0.2 or 0.22 micron in-line filter</td>
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* Keep final concentration to 1-10 mg/mL

- Repeat every 2 weeks until disease progression or unacceptable toxicity
- If pseudo progression on imaging is suspected, may continue treatment for another 6 weeks. Discontinue treatment if confirmatory progression on subsequent scan (6-10 weeks)

DOSE MODIFICATIONS:

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.
REFERENCES: