BC Cancer Protocol Summary for the Treatment of Unresectable or Metastatic Melanoma Using 4-Weekly Nivolumab

Protocol Code
USMAVNIV4

Tumour Group
Skin and Melanoma

Contact Physician
Dr. Kerry Savage

ELIGIBILITY:
- Unresectable or metastatic melanoma in patients who are previously untreated, regardless of BRAF V600 mutation status
- Patients are eligible to receive pembrolizumab or or nivolumab but not sequential use of these agents
- Good performance status
- Adequate hepatic and renal function
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of nivolumab
- BC Cancer Compassionate Access Program (CAP) approval must be obtained

EXCLUSIONS:
- ECOG performance status > 2
- Active central nervous system metastases (should be asymptomatic and/or stable)
- Active autoimmune disease
- Use with cautions 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
- 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, serum or urine HCG (required for woman 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 1000 mg PO, and hydrocortisone 25 mg IV 30 minutes prior to treatment.

TREATMENT:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
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<tbody>
<tr>
<td>nivolumab</td>
<td>6 mg/kg (maximum 480 mg)</td>
<td>IV in 100 mL* NS over 30 minutes using a 0.2 or 0.22 micron in-line filter</td>
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*Keep final concentration to 1 to 10 mg/mL

- 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:


PRECAUTIONS:

- Serious immune-mediated reactions: these can be severe to fatal and usually occur during the treatment course. They may include enterocolitis, intestinal perforation or hemorrhage, hepatitis, dermatitis, neuropathy, endocrinopathy, 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).
- Infusion-related reactions: isolated cases of severe reaction have been reported. In case of a severe reaction, nivolumab infusion should be discontinued and appropriate medical therapy administered. Patients with mild or moderate infusion reaction may receive nivolumab with close monitoring. Premedications with acetaminophen and anti-histamine may be considered if there is a history of reaction.
Call Dr. Kerry Savage or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References: