BC Cancer Protocol Summary for the Treatment of Locally Advanced or Metastatic Urothelial Carcinoma Using 6-Weekly Pembrolizumab

Protocol Code *UGUAVPEM6*

Tumour Group *Genitourinary*

Contact Physician *Dr. Christian Kollmannsberger*

ELIGIBILITY:

- Locally advanced or metastatic urothelial carcinoma
- Second-line therapy for disease progression on or after platinum-based chemotherapy or within 12 months of completing adjuvant or neoadjuvant platinum-based chemotherapy
- ECOG performance status 0-2
- Adequate hepatic and renal function
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of pembrolizumab
- *BC Cancer Compassionate Access Program (CAP) approval must be obtained. CAP approval is not required to switch between 3-weekly and 6-weekly dosing of pembrolizumab.*

EXCLUSIONS:

- 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
- 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, glucose, serum ACTH levels, testosterone, estradiol, FSH, LH, ECG, C-reactive protein (CRP), creatine kinase (CK), troponin
- 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 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

*Keep final concentration to 1 to 10 mg/mL

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

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).
- **Infusion-related reactions:** Isolated cases of severe reaction have been reported. In case of a severe reaction, pembrolizumab infusion should be discontinued and appropriate medical therapy administered. Patients with mild or moderate infusion reaction may receive pembrolizumab with close monitoring. Premedications with acetaminophen and anti-histamine may be considered if there is a history of reaction.

Call Dr. Christian Kollmannsberger 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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