BC Cancer Protocol Summary for Treatment of Microsatellite Instability-High or Mismatch Repair Deficient Endometrial Cancer using 6-Weekly Pembrolizumab

***Protocol Code*:**	*UGOENDAVP6*
***Tumour Group*:**	*Gynecology*
***Contact Physician*:**	*Dr. Aalok Kumar*

ELIGIBILITY:

Patients must have:

- Advanced or metastatic endometrial cancer,
- Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), tested on primary or metastatic tumour,
- Progression following at least one prior line of treatment or intolerant to prior line of treatment,
- No alternative systemic treatment options, and
- BC Cancer “Compassionate Access Program” request approval prior to treatment

Patients should have:

- ECOG performance status 0 to 2
- Adequate hepatic and renal function
- Access to a treatment center with expertise to manage immune-mediated adverse reactions of pembrolizumab.

Notes:

- At time of subsequent disease progression, retreatment is allowed for an additional one year of therapy (18 cycles of pembrolizumab at 3-weekly dosing or 9 cycles at 6-weekly dosing, or a combination of both if:
  - Patients have completed 2 years of therapy without progression
  - Patients have stopped pembrolizumab due to toxicity (not progression)
- BC Cancer Compassionate Access Program (CAP) approval is not required to switch between 3-weekly and 6-weekly dosing of pembrolizumab.

EXCLUSIONS:

Patients must not have:

- Prior immunotherapy,
- Combination treatment. This protocol is monotherapy only, or
- Active central nervous system (CNS) metastases. Treated or stable CNS metastases are eligible.

CAUTIONS:

- 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 and differential, platelets, creatinine, ALT, alkaline phosphatase, total bilirubin, sodium, potassium, TSH, glucose, morning serum cortisol, chest x-ray or CT chest if not previously done.
- Prior to each treatment: CBC and differential, platelets, creatinine, ALT, alkaline phosphatase, total bilirubin, sodium, potassium, TSH
- If clinically indicated: morning serum cortisol, lipase, glucose, creatine kinase, 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, chest x-ray
- Weekly telephone nursing assessment for signs and symptoms of side effects while on treatment (Optional).

PREMEDICATIONS:

- Antiemetics are not usually required.
- If 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:

A cycle equals -

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

- Each cycle is 42 days (6 weeks).
- Duration of treatment:
  - Initial pembrolizumab therapy: Maximum 36 cycles for 3-weekly dosing or 18 cycles for 6-weekly dosing (or a combination of both), including doses given as GOENDAVP and GOENDAVP6, to a maximum of 2 years of treatment.
  - Retreatment may be permitted (see eligibility)

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).
2. **Infusion-related reactions:** isolated cases of severe infusion reactions have been reported. Discontinue pembrolizumab with severe reactions (Grade 3 or 4). Patients with mild or moderate infusion reactions may receive pembrolizumab with close monitoring and use of premedication.

Call Dr. Aalok Kumar or tumour group delegate at (604) 930-2098 or 1-800-523-2885 with any problems or questions regarding this treatment program.

References:

1. Marabelle A, Fakih M, Lopez J, et al. Association of tumour mutational burden with outcomes in patients with advanced solid tumours treated with pembrolizumab: prospective biomarker analysis of the multicohort, open-label, phase 2 KEYNOTE-158 study. Lancet Oncol. 2020 Oct;21(10):1353-1365.
2. Pembrolizumab (Keytruda) CADTH Reimbursement Recommendation. Canadian Journal of Health Technologies 2023; 3(2):1-20.