BC Cancer Protocol Summary for the Treatment of dMMR/MSI-H Solid Tumours using 6-Weekly Pembrolizumab

***Protocol Code*:**	*UTAAVPEM6*
***Tumour Group*:**	*Tumour-Agnostic*
***Contact Physician*:**	*Dr. Theresa Chan* *Dr. Cheryl Ho*

ELIGIBILITY:

Patients must have:

- Unresectable or metastatic solid tumors,
- dMMR or MSI-H mutation (tested on primary or metastatic tumour),
- At least one prior therapy,
- No satisfactory alternative treatment options, and
- BC Cancer Compassionate Access Program (CAP) approval prior to treatment

Patients should have:

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

Note:

- At time of subsequent disease progression, retreatment is allowed for an additional 1 year of therapy if:
  - Patient completed 2 years of therapy without progression, or
  - Patient stopped pembrolizumab before 2 years due to toxicity (not progression)
  - Additional CAP approval not required for retreatment
- 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:

- Active central nervous system metastases (unless asymptomatic and/or stable)
- Previous progression on an immune checkpoint inhibitor

CAUTIONS:

- Concurrent autoimmune disease
- Patients with long term immunosuppressive therapy or systemic corticosteroids (requiring more than 10 mg predniSONE/day or equivalent)

TESTS:

- Baseline: CBC & Diff, creatinine, ALT, alkaline phosphatase, total bilirubin, albumin, sodium, potassium, TSH, morning serum cortisol, appropriate imaging
- Baseline if clinically indicated: creatine kinase, troponin, free T3 and free T4, GGT, lipase, LDH, random glucose, serum or urine HCG (required for women of childbearing potential if pregnancy suspected), serum ACTH levels, testosterone, estradiol, FSH, LH, ECG
- Prior to each cycle: CBC & Diff, creatinine, ALT, total bilirubin, sodium, potassium, TSH
- If clinically indicated: morning serum cortisol, lipase, LDH, random glucose, serum or urine HCG (required for women of childbearing potential if pregnancy suspected), free T3 and free T4, serum ACTH levels, testosterone, estradiol, FSH, LH, alkaline phosphatase, albumin, GGT, creatine kinase, troponin, 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

Repeat **every 6 weeks** until disease progression, unacceptable toxicity or a maximum of 18 cycles or 2 years of treatment (including doses given as UTAAVPEM)

Retreatment may be allowed (refer to 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).

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, reduced rates of administration and use of premedication.

Contact Dr. Theresa Chan at 604-930-2098 or Dr. Cheryl Ho 604-877-6000 with any problems or questions regarding this treatment program.

References:

1. Marabelle A, O'Malley D, Hendifar A, et al. Pembrolizumab in microsatellite-instability-high and mismatch-repair-deficient advanced solid tumors: updated results of the KEYNOTE-158 trial. Nat Cancer. 2025 Feb;6(2):253-258.
2. Le D, Diaz L Jr, Kim T, et al. Pembrolizumab for previously treated, microsatellite instability-high/mismatch repair-deficient advanced colorectal cancer: final analysis of KEYNOTE-164. Eur J Cancer. 2023 Jun;186:185-195.
3. Kang YJ, O'Haire S, Franchini F, et al. A scoping review and meta-analysis on the prevalence of pan-tumour biomarkers (dMMR, MSI, high TMB) in different solid tumours. Sci Rep. 2022 Nov 28;12(1):20495.
4. Raghav K, Overman M. Small bowel adenocarcinomas--existing evidence and evolving paradigms. Nat Rev Clin Oncol. 2013 Sep;10(9):534-44.
5. Pembrolizumab (Keytruda) CADTH Reimbursement Recommendation. Canadian Journal of Health Technologies, February 2025; 5(2):1-37.