# BC Cancer Protocol Summary for First-Line Treatment of dMMR/MSI-H Metastatic Colorectal Cancer using Pembrolizumab

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| ***Protocol Code*:** | *UGIAVPEM* |
| ***Tumour Group*:** | *Gastrointestinal* |
| ***Contact Physician*:** | *GI Systemic Therapy* |

## ELIGIBILITY:

Patients must have:

- Measurable metastatic colorectal adenocarcinoma, de novo or relapsed,
- dMMR/MSI-H (tested on primary or metastatic tumour),
- No prior treatment for metastatic disease, and
- BC Cancer Compassionate Access Program (CAP) approval

Patients should have:

- ECOG performance status 0 to 2
- Life expectancy 3 months or more
- Adequate hepatic and renal function
- Access to a treatment center with expertise to manage immune-mediated adverse reactions of pembrolizumab

Note:

- Patients who were started on, or had completed first-line chemotherapy prior to 1 February 2022 may receive pembrolizumab (UGIAVPEM) if all other eligibility criteria are met
- At time of subsequent disease progression, retreatment is allowed for an additional 1 year of therapy (17 cycles) if:
  - Patients have completed 2 years of therapy without progression
  - Patients have stopped pembrolizumab 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:

- Prior immunotherapy for metastatic colorectal cancer

## 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 & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, albumin,sodium, potassium, TSH, morning serum cortisol, chest x-ray or CT chest
- Baseline if clinically indicated: CEA, CA19-9, creatine kinase, troponin, free T3 and free T4, GGT, lipase, 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: CEA, CA19-9, morning serum cortisol, lipase, 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 |
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| pembrolizumab | 2 mg/kg<br>(maximum 200 mg) | IV in 50 mL NS over 30 minutes<br>using a 0.2 micron in-line filter |

Repeat **every 3 weeks** until disease progression, unacceptable toxicity or a maximum of 35 cycles or 2 years of treatment (including doses given as UGIAVPEM6)

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, 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 the GI Systemic Therapy physician at your regional cancer centre or the GI Systemic Therapy Chair Dr. Theresa Chan at (604) 930-2098 with any problems or questions regarding this treatment program.**

**References**:


1. Andre T, Shui KK, Kim TW, Jensen BV, et al. Pembrolizumab in Microsatellite-Instability-High Advanced Colorectal Cancer. N Engl J Med. 2020;383(23):2207-2218.
2. Andre T, Amonkar MA, Norquist JM, Shui KK, et al. Health-related quality of life in patients with microsatellite instability-high or mismatch repair deficient metastatic colorectal cancer treated with first-line pembrolizumab versus chemotherapy (KEYNOTE-177): an open-label, randomised, phase 3 trial. The Lancet Oncology 2021;22(5), 665-677.