BC Cancer Protocol Summary for Treatment of Metastatic Breast Cancer using 6-Weekly Pembrolizumab

Protocol Code	*BRAVPEM6*
Tumour Group	*Breast*
Contact Physician	*Dr. Nathalie LeVasseur*

ELIGIBILITY:

Patients must have:

- Locally recurrent unresectable or metastatic triple negative breast cancer*,
- PD-L1 expression with combined positive score (CPS) greater than or equal to 10, and
- Completed or discontinued chemotherapy portion of either BRAVPPN, BRAVPP, or BRAVPGC

* Patients are eligible if:

1. HER2 negative:
   - HER2 IHC 0 to 1, or
   - HER2 IHC 2 with FISH negative,

   and
2. ER negative:
   - Less than 1% of ER positive cells, and
   - ER Allred score 0 to 2 out of 8

- Regardless of PR results
- All other cases including ER-low requests require approval via BC Cancer Compassionate Access Program (CAP)

Patients should have:

- ECOG 0 to 2,
- Adequate hematological, hepatic and renal function,
- Asymptomatic/stable brain metastases (if applicable), and
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of pembrolizumab

Notes:

- Patients are eligible if greater than or equal to 6 months since completion of prior neoadjuvant or adjuvant immunotherapy
- At time of subsequent disease progression, pembrolizumab retreatment (with chemotherapy per BRAVPPN, BRAVPP, or BRAVPGC or without chemotherapy per BRAVPEM or BRAVPEM6) is allowed for an additional 1 year of therapy if:
  - Patients have completed 2 years of therapy without progression
  - Patients have stopped pembrolizumab for reasons other than progression (e.g. toxicity or complete response)
  - Additional CAP approval not required for retreatment

EXCLUSIONS:

Patients must not have:

- Relapsed on or within 6 months of completing neoadjuvant or adjuvant pembrolizumab

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, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, sodium, potassium, TSH
- Before each treatment: CBC & Diff, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, sodium, potassium, TSH
- If clinically indicated:
  - Morning serum cortisol, creatine kinase, lipase, GGT, LDH, random glucose, free T3 and free T4, serum ACTH levels, testosterone, estradiol, FSH, LH, CA15-3, serum or urine HCG (required for women of child bearing potential if pregnancy suspected)
  - ECG, chest x-ray
- Weekly telephone nursing assessment for signs and symptoms of side effects while on treatment (Optional)

PREMEDICATIONS:

- Additional anti-emetics not usually required
- 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 pembrolizumab

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

- Repeat every **6 weeks** for a maximum of 18 cycles or 2 years of treatment, including doses given with chemotherapy as BRAVPPN, BRAVPP, or BRAVPGC, and doses given as BRAVPEM
- Retreatment may be allowed (refer to eligibility)

DOSE MODIFICATIONS:

No specific dose modifications for pembrolizumab. 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 to pembrolizumab**: 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).
2. **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 antihistamine may be considered if there is a history of reaction.

Call Dr. Nathalie LeVasseur or tumour group delegate at 604-877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

REFERENCES:

1. Cortes J, Cescon DW, Rugo HS, et al. Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer (KEYNOTE-355): a randomised, placebo-controlled, double-blind, phase 3 clinical trial. Lancet 2020;396(10265):1817-1828.
2. Pembrolizumab (Keytruda) CADTH Reimbursement Recommendation. Canadian Journal of Health Technologies 2023; 3 (1):1-20.