BC Cancer Protocol Summary for the Treatment of Relapsed or Refractory Hodgkin Lymphoma using Pembrolizumab

Protocol Code	*LYPEM*
Tumour Group	*Lymphoma*
Contact Physician	*Dr. Kerry Savage*
Contact Pharmacist	*Louisa Pang*

ELIGIBILITY:

Patients must have:
- Relapsed or refractory classical Hodgkin lymphoma (cHL) who have progressed after autologous stem cell transplantation (ASCT), or
- Relapsed or refractory (cHL) and are not eligible to receive ASCT

Patients should have:
- Good performance status,
- Adequate hepatic and renal function, and
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of pembrolizumab

Note:
- Pembrolizumab is the preferred agent over brentuximab vedotin due to superior progression free survival and better tolerability
- Patients are funded to receive either nivolumab (LYNIV) or pembrolizumab (LYPEM), but not both.
- 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 autoimmune disease,
- Clinically active CNS involvement, or
- Received prior therapy with an anti-PD-1, anti-PD-L1, anti-PD-L2 or anti-cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody

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 & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH, morning serum cortisol, chest x-ray
- Baseline (required, but results do not have to be available to proceed with first treatment; results must be checked before proceeding with cycle 2): HBsAg, HBsAb, HBcoreAb
- Before each treatment: CBC & Diff, 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), creatinine kinase (CK), troponin
- If clinically indicated: HBV viral load (see protocol SCHBV)
- 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

SUPPORTIVE MEDICATIONS:

Moderate risk of hepatitis B reactivation. If HBsAg or HBcoreAb positive, follow hepatitis B prophylaxis as per SCHBV.

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
pembrolizumab	2 mg/kg (maximum 200 mg)	IV in 50 mL NS over 30 minutes 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 LYPEM6)

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:

- **Serious immune-mediated reactions**: 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**).
- **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.
- **Hepatitis B Reactivation**: See SCHBV protocol for more details.

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

References:

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2. Merck Canada: KEYTRUDA (pembrolizumab) product monograph. Kirkland, Quebec: 24 November 2021.
3. CADTH Technology Review: Optimal Use 360 Report. Dosing and timing of immuno-oncology drugs. November 2019. Accessed online: https://www.cadth.ca/ 25Jan 2022.
4. CADTH. In Brief: Dosing and timing of Immuno-Oncology Drugs. Jan 2020. Accessed online: https://www.cadth.ca/ 25Jan 2022.
5. Chen et al. Phase II Study of the Efficacy and Safety of Pembrolizumab for Relapsed/Refractory Classic Hodgkin Lymphoma. JCO 2017: 35(19): 2125-2132.
6. Moskowitz et al. PD-1 Blockade with the Monoclonal Antibody Pembrolizumab (MK-3475) in Patients with Classical Hodgkin Lymphoma after Brentuximab Vedotin Failure: Preliminary Results from a Phase 1b Study (KEYNOTE-013). Blood 2014: 124(21): 290. https://doi.org/10.1182/blood.V124.21.290.290
7. Weber JS, et al. Management of adverse events following treatment with anti-programmed death-1 agents. Oncologist 2016;21:1-11.