BC Cancer Protocol Summary for the Treatment of Relapsed or Refractory Hodgkin Lymphoma Using 6-Weekly Pembrolizumab

Protocol Code	*LYPEM6*
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) and brentuximab vedotin,
- Relapsed or refractory cHL who are not candidates for ASCT, or
- Relapsed or refractory cHL with contraindication to brentuximab vedotin (e.g. peripheral neuropathy)

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

Patients are funded to receive either nivolumab (LYNIVO) 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 & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH, morning serum cortisol, chest x-ray
- Before each treatment: CBC & differential, platelets, 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
- 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:

If HBsAg or HBcoreAb positive, start lamiVUDine 100 mg PO daily for the duration of chemotherapy and continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive. .

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** until disease progression, unacceptable toxicity or a maximum of 2 years of treatment (including doses given as LYPEM)

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:

- **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,** http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Supportive%20Care/SCIMMUNE_Protocol.pdf).
- **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**: All lymphoma patients should be tested for both HBsAg and HBcoreAb. If either test is positive, such patients should be treated with lamiVUDine 100mg PO daily during therapy and continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive. Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA at least every two months. If the hepatitis B virus DNA level rises during this monitoring, management should be reviewed with an appropriate specialist with experience managing hepatitis and consideration given to halting therapy.

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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3. Lala M, Li M, Sinha V, et al. A six-weekly (Q6W) dosing schedule for pembrolizumab based on an exposure-response (ER) evaluation using modeling and simulation. Poster presented at: 2018 American Society of Clinical Oncology (ASCO) Annual Meeting; 2018 Jun 1-5; Chicago, IL.
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5. Weber JS, et al. Management of adverse events following treatment with anti-programmed death-1 agents. Oncologist 2016;21:1-11.

6. Merck Canada: KEYTRUDA (pembrolizumab) product monograph. Kirkland, Quebec: 15 January 2019.