BC Cancer Protocol Summary for the Adjuvant Treatment of Resected Renal Cell Carcinoma using 6-Weekly Pembrolizumab

Protocol Code	*GUAJPEM6*
Tumour Group	*Genitourinary*
Contact Physician	*Dr. Krista Noonan*

ELIGIBILITY:

Patients must have:

- Renal cell carcinoma (RCC) with a clear cell component, with or without sarcomatoid features,
- Previous radical or partial nephrectomy with negative surgical margins,
- No prior systemic therapy for RCC,
- Previous resection of metastatic lesions (if applicable), and
  - Intermediate-high risk for recurrence (pT2, Grade 4 or sarcomatoid, N0, M0 or pT3, any grade, N0, M0), or
  - High risk for recurrence (pT4, any grade, N0, M0, or pT any stage, any grade, N+, M0), or
  - M1 No Evidence of Disease (NED): Primary kidney tumour and solid, isolated, and/or soft tissue metastases which are completed resected. Must have negative surgical margins for resected metastases. Metastases must be resected 4 weeks or greater from start of treatment.
- Initiation of pembrolizumab within 12 weeks of surgery (nephrectomy or metastasectomy). Metastasectomy must be within 12 months from nephrectomy.

Patients should have:

- ECOG 0 to 2,
- Adequate baseline hematological, hepatic and renal function, and
- Access to a treatment centre with expertise in managing immunotherapy mediated toxicities of pembrolizumab.

Notes:

- Patients may have subsequent checkpoint inhibitors-based therapy for advanced disease if last adjuvant pembrolizumab dose was completed 6 months ago or longer
- CAP approval is not required to switch between 3-weekly and 6-weekly dosing of pembrolizumab.

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EXCLUSIONS:
- Patients must not have concurrent treatment. This protocol is for monotherapy only.

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 and differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH, morning serum cortisol, appropriate imaging (at least a baseline CXR if no baseline chest CT)
- Before each treatment: CBC and 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, serum ACTH levels, testosterone, estradiol, FSH, LH, glucose, ECG, C-reactive protein (CRP), creatine 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

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 9 cycles* maximum (approximately 1 year), unless disease progression or unacceptable toxicity.
  *Includes doses given as GUAJPEM.

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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.

Call Dr. Krista Noonan or tumour group delegate at 604-930-2098 or 1-800-523-2885 with any problems or questions regarding this treatment program.

References:

1. KN 564: Choueiri TK, Tomczak P, Park SH, et al. Adjuvant pembrolizumab after nephrectomy in renal-cell carcinoma. N Engl J Med 2021;385(8):683-694.
2. Powles T, Tomczak P, Park SH, et al. Pembrolizumab versus placebo as post-nephrectomy adjuvant therapy for clear cell renal cell carcinoma (KEYNOTE-564): 30-month follow-up analysis of a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol 2022;23(9):1133-1144.
3. Pembrolizumab (Keytruda) CADTH Reimbursement Recommendation. Canadian Journal of Health Technologies 2022;2(10):1-18.
4. CADTH Reimbursement Recommendation. Provisional funding algorithm. Renal cell carcinoma. January 2023.

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