BC Cancer Protocol Summary for the Adjuvant Treatment of Resected Urothelial Carcinoma using Nivolumab

Protocol Code	*UGUAJNIV*
Tumour Group	*Genitourinary*
Contact Physician	*Dr. Jean-Michel Lavoie*

ELIGIBILITY:

Patients must have:

- Urothelial carcinoma,
- Muscle invasive disease at diagnosis,
- High-risk disease after radical surgical resection (R0 with negative margins) within the past 120 days, defined as either:
    - residual ypT2 to ypT4a or ypN+ if they received prior CISplatin-based neoadjuvant chemotherapy, or
    - pT3 to pT4a or pN+ if they received no prior CISplatin-based neoadjuvant chemotherapy, and not eligible for or decline adjuvant with CISplatin chemotherapy, and
- BC Cancer “Compassionate Access Program” request approval prior to treatment

Patients should have:

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

Note:

- This protocol is for nivolumab monotherapy only. Combination therapy is not funded.
- CAP approval is not required to switch between 2-weekly and 4-weekly dosing of nivolumab
- PD-L1 status and CPS score not required
- Patients with partial cystectomy or partial nephrectomy are eligible if negative surgical margins, and if all other criteria are met

EXCLUSIONS:

Patients must not have:

- evidence of recurrence prior to initiation of UGUAJNIV
- metastatic disease
- concurrent treatment for urothelial carcinoma
- post-operative chemotherapy for urothelial carcinoma (UGUAJNIV is funded after prior neoadjuvant chemotherapy)

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 & 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 & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH
- If clinically indicated: chest x-ray, morning serum cortisol, lipase, glucose, 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, ECG
- 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 nivolumab: 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
nivolumab	3 mg/kg (maximum 240 mg)	IV in 50 to 100 mL NS over 30 minutes using a 0.2 micron in-line filter

- Repeat **every 2 weeks** for 52 weeks (26 doses), unless disease progression or unacceptable toxicity. *Includes doses given as UGUAJNIV4 to total 52 weeks treatment

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, nivolumab infusion should be discontinued and appropriate medical therapy administered. Patients with mild or moderate infusion reaction may receive nivolumab with close monitoring. Premedications with acetaminophen and anti-histamine may be considered if there is a history of reaction.

Call Dr. Jean-Michel Lavoie or tumour group delegate at 250-519-5500 or 1-800-670-3322 with any problems or questions regarding this treatment program.

References:

1. Bajorin DF, Witjes JA, Gschwend JE, et al. Adjuvant nivolumab versus placebo in muscle-invasive urothelial carcinoma. N Engl J Med 2021;384(22):2102-2114.
2. CADTH. CADTH reimbursement recommendation nivolumab (Opdivo). Canadian Journal of Health Technologies. 2022 October;2(10).