BC Cancer Protocol Summary for Treatment of Metastatic or Advanced Renal Cell Carcinoma Using Nivolumab

Protocol Code	*GUAVNIV*
Tumour Group	*Genitourinary*
Contact Physician	*Dr. C. Kollmannsberger*

ELIGIBILITY:

Patients must have:

- Metastatic or advanced renal cell carcinoma,
- Any histology and IMDC risk group, and
- Failure of first-line tyrosine kinase inhibitor (TKI) therapy (SUNItinib, SORAfenib, or pazopanib), or
- Third-line therapy after failure of first-line (SUNItinib, SORAfenib or pazopanib) and second-line TKI (axitinib or cabozantinib), and
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of nivolumab.

Patients should have:

- Good performance status, and
- Adequate hepatic and renal function

Notes:

- Patients are eligible to receive nivolumab or everolimus, but not sequential use of these agents.
- May receive GUAVNIV if relapsed greater than 6 months after GUAJPEM or GUAJPEM6, if all other eligibility criteria are met.

EXCLUSIONS:

Patients must not have:

- ECOG performance status greater than 2, and
- Active central nervous system metastases (should be asymptomatic and/or stable)

CAUTIONS:

- Active autoimmune disease, and
- 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 (or CT chest)
- 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 women 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 emetogenic chemotherapy protocols (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** until disease progression or unacceptable toxicity.
- If pseudo progression on imaging is suspected, may continue treatment for another 6 weeks. **Discontinue** treatment if confirmatory scan shows an additional 10% tumour burden volume and/or development of new lesions.

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:

1. **Serious immune-mediated reactions**: can be severe to fatal and usually occur during the treatment course, but may develop months after discontinuation of therapy. They may include enterocolitis, intestinal perforation or hemorrhage, hepatitis, dermatitis, neuropathy, endocrinopathy, pneumonitis, 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).
2. **Infusion-related reactions:** isolated cases of severe infusion reactions have been reported. Discontinue nivolumab with Grade 3 or 4 reactions. Patients with mild or moderate infusion reactions may receive nivolumab with close monitoring and use of premedication.

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

References:

1. Motzer RJ, et al. Nivolumab versus everolimus in advanced renal-cell carcinoma. N Engl J Med 2015;373:1803-13.
2. Bristol-Myers Squibb Canada. OPDVIO® product monograph. Montreal, Canada; 26 October 2016
1. Weber JS, et al. Management of adverse events following treatment with anti-programmed death-1 agents. Oncologist 2016;21:1-11.Postow M, Wolchok J. Toxicities associated with checkpoint inhibitor immunotherapy. In: 2015 UpToDate®; Ross,Michael E. (Ed); Waltham, Massachusetts: UpToDate®; Available at www.uptodate.com; updated 6Jan2016; accessed 31Jan2017
2. Weber JS, et al. Management of adverse events following treatment with anti-programmed death-1 agents. Oncologist 2016;21:1-11.
3. Waterhouse D, Horn L, Reynolds C, et al. Safety profile of nivolumab administered as 30-min infusion: analysis of data from CheckMate 153. Cancer Chemother Pharmacol 2018;81:679-86.