BC Cancer Protocol Summary for the Second-Line Treatment of Recurrent or Metastatic Merkel Cell Carcinoma Using Avelumab

Protocol Code	*SMMCCAVE*
Tumour Group	*Skin and Melanoma*
Contact Physician	*Dr. Christopher Lee*

ELIGIBILITY:

Patients must have:

- Recurrent or metastatic Merkel cell carcinoma following progression of disease after first-line chemotherapy with SMMCCPE
  - Unless contraindicated to receive SMMCCPE

Patients should have:

- Adequate hematologic and biochemical laboratory test results
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of avelumab

EXCLUSIONS:

Patients must not have:

- HIV positive status
- Hematologic malignancy

CAUTIONS:

- Concurrent solid organ transplant or autoimmune disease
- Clinically significant comorbidities such as active cardiovascular disease or inflammatory bowel 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, random glucose
- Before each treatment: CBC & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH, random glucose
- If clinically indicated: chest x-ray, CT scan, 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, ECG, fasting blood glucose
- Weekly telephone nursing assessment for signs and symptoms of side effects while on treatment (Optional).

PREMEDICATIONS:

- **For first 4 cycles**: diphenhydrAMINE 50 mg IV in 50 mL NS over 20 minutes and acetaminophen 650 mg PO given 30 minutes prior to treatment
- If prior infusion reactions to avelumab: diphenhydrAMINE 50 mg IV in 50 mL NS over 20 minutes, acetaminophen 650 mg PO, or other based on severity of reaction
- Antiemetics are not usually required.
- Antiemetic protocol for low emetogenicity (see SCNAUSEA).

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
avelumab	10 mg/kg	IV in 250 mL NS over 1 hour using a 0.2 micron in-line filter

- Repeat every 2 weeks until confirmed disease progression or unacceptable toxicity

DOSE MODIFICATIONS:

No dose reductions or escalations recommended. Toxicity managed by treatment delay and other measures (see **SCIMMUNE** protocol for Immune-mediated Adverse Reaction Management Guide).

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 Immune-mediated Adverse Reaction Management Guide).
- **Infusion-related reactions:** isolated cases of severe reaction have been reported. In case of a severe reaction, avelumab infusion should be discontinued and appropriate medical therapy administered. Patients with mild or moderate infusion reaction may receive avelumab with close monitoring. Premedications with acetaminophen and anti-histamine may be considered if there is a history of reaction.

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

References:

1. Kaufman HL, Russell J, Hamid O, et al. Avelumab in patients with chemotherapy-refractory metastatic Merkel cell carcinoma: a multicentre, single-group, open-label, phase 2 trial. Lancet Oncol 2016; 17: 1374-1385.
2. D'Angelo SP, Russell J, Hassel JC, et al. First-line (1L) avelumab treatment in patients (pts) with metastatic Merkel cell carcinoma (mMCC): Preliminary data from an ongoing study. J Clin Oncol 2017; 15 suppl: abstr 9530.
3. EMD Serono Canada. BAVENCIO® (avelumab) product monograph. Mississauga, Ontario; 4 May 2018.