

BC Cancer Protocol Summary for the First-Line Treatment of Unresectable or Metastatic Melanoma Using Ipilimumab

Protocol Code

SMAVFIPI

Tumour Group

Skin and Melanoma

Contact Physician

Dr. Vanessa Bernstein

ELIGIBILITY:

Patients must have:

- Unresectable stage IIIC or stage IV melanoma, and
- No prior systemic therapy for advanced disease with the exception of BRAF and/or MEK inhibitors for BRAF mutant metastatic melanoma

Note:

- For patients previously treated with pembrolizumab or nivolumab for metastatic disease, see SMAVFIPI protocol.

Patients should have:

- Adequate hepatic and renal function,
- Life expectancy of at least 4 months, and
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of ipilimumab.

EXCLUSIONS:

Patients must not have:

- Active central nervous system metastases (unless asymptomatic and/or stable)

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 & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH, serum morning cortisol, [creatinine kinase](#)
- Baseline, if clinically indicated: [BNP](#), [troponin](#), [ECG](#), [echocardiogram](#)
- Before each treatment: CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH, [creatinine kinase](#)
- If clinically indicated: 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, [troponin](#), ECG
- Weekly telephone nursing assessment for signs and symptoms of side effects while on treatment (Optional but recommended).

PREMEDICATIONS:

- Antiemetics are not usually required.
- Antiemetic protocol for low emetogenicity (see SCNAUSEA).
- If prior infusion reactions to ipilimumab: 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 |
|------------|--------------------------|---|
| ipilimumab | 3 mg/kg IV every 3 weeks | IV in 50 to 250 mL NS over 30 minutes using a 0.2 micron in-line filter |

- Repeat every 3 weeks for 4 cycles

If stable disease (more than 3 months) or complete / partial response, consider repeating treatment course (reinduction) at disease progression

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)

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**).
- **Infusion-related reactions:** isolated cases of severe reaction have been reported. In case of a severe reaction, ipilimumab infusion should be discontinued and appropriate medical therapy administered. Patients with mild or moderate infusion reaction may receive ipilimumab with close monitoring. Premedications with acetaminophen and anti-histamine may be considered.

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

References:

1. Robert C, et al. Ipilimumab plus dacarbazine for previously untreated metastatic melanoma. *N Eng J Med* 2011;364:2517-26.
2. Weber JS, et al. Management of Immune-related adverse events and kinetics of response with ipilimumab. *J Clin Oncol* 2012;30(21):2691-7.
3. Pan-Canadian Oncology Drug Review. Expert Review Committee final recommendation on ipilimumab (Yervoy) for the first-line treatment of adult patients with advanced (unresectable or metastatic) melanoma. 22 December 2014.
4. Bristol-Myers Squibb: YERVOY (ipilimumab): Serious and fatal immune-mediated adverse reactions - YERVOY Risk Evaluation and Mitigation Strategy (REMS). www.hcp.yervoy.com/pages/rem.s.aspx (Accessed in 4 June 2015)
5. Bristol-Myers Squibb: YERVOY (ipilimumab) product monograph. Montreal, Quebec: 4 Dec 2018.
6. Maio M, et al. Efficacy and safety of ipilimumab in patients with pretreated, ocular melanoma: experience from Italian clinics participating in the European Expanded Access Programme (EAP). *ESMO* 2012 abstract 2844.
7. Khattak MA, et al. Ipilimumab activity in advanced uveal melanoma. *Melanoma Res* 2013;23:79–81.
8. Rubin, K. Managing immune-related adverse events to ipilimumab: a nurse's guide. *Clin J Oncol Nurs* 2012; 16(2):E69-E75.
9. Momtaz P, Park V, Panageas KS, et al. Safety of infusing ipilimumab over 30 minutes. *J Clin Oncol* (ePub 29 June 2015).
10. Weber JS, et al. Management of adverse events following treatment with anti-programmed death-1 agents. *Oncologist* 2016;21:1-11.