

# BC Cancer Protocol Summary for Palliative Therapy for Malignant Melanoma with Brain Metastases using Temozolomide

**Protocol Code**

**SMAVTMZ**

**Tumour Group**

**Melanoma**

**Contact Physician**

**Dr. Vanessa Bernstein**

## ELIGIBILITY:

- Malignant melanoma with brain metastasis
- ECOG less than or equal to 3
- Adequate renal function
- Life expectancy of 12 weeks or longer

## EXCLUSIONS:

- Pregnant or breast feeding women
- Significant hepatic dysfunction (based on physician discretion)

## TESTS:

- Baseline: CBC and differential, platelets, ALT and bilirubin, creatinine, glucose (patients on corticosteroids)
- Before each treatment: CBC and differential, platelets, ALT and bilirubin.
- If clinically indicated: creatinine, glucose

## PREMEDICATIONS:

- ondansetron 8 mg given 30 minutes prior to each dose of temozolomide at the discretion of the treating physician.

## TREATMENT:

Drug	Dose*	BC Cancer Administration Guideline
temozolomide	200 mg/m <sup>2</sup> **once daily x 5 days (d 1-5)	PO at bedtime

\* refer to [Temozolomide Suggested Capsule Combination Table](#) for dose rounding

\*\* For patients who had received prior chemotherapy for metastatic melanoma, start with dose level -1 and then increase to dose level 0 if tolerable (see Dose Levels table below).

- Repeat every 28 days to a maximum of 8 cycles
- Discontinue for clinical or radiographic progression.

## DOSE MODIFICATIONS:

### Dose Levels

Drug	Temozolomide
<b>Dose Level 0 (Starting Dose)</b>	200 mg/m <sup>2</sup> *once daily x 5 days (d 1-5)
<b>Dose Level –1</b>	150 mg/m <sup>2</sup> *once daily x 5 days (d 1-5)
<b>Dose Level –2</b>	100 mg/m <sup>2</sup> * once daily x 5 days (d 1-5)
<b>Dose Level –3</b>	Discontinue temozolomide

\* round dose to nearest 5 mg

### 1. Hematological

ANC (x10 <sup>9</sup> /L)		Platelets (x10 <sup>9</sup> /L)	Dose
greater than or equal to 1.5	and	greater than or equal to 100	100%
less than 1.5	or	less than 100	Delay*

\* Perform weekly CBC, maximum of 3 times.

- If ANC recovers to greater than or equal to 1.5 x 10<sup>9</sup>/L and platelets recover to greater than or equal to 100 x 10<sup>9</sup>/L, re-start temozolomide at one level reduced dose.
- If the hematologic toxicity developed at 100 mg/m<sup>2</sup>, re-start with 100 mg/m<sup>2</sup> upon recovery.
- Dose reductions below 100 mg/m<sup>2</sup> are not permitted. Temozolomide should be discontinued for repeated grade 3 or 4 hematologic toxicity (ANC less than 1 x 10<sup>9</sup>/L, platelets less than 50 x 10<sup>9</sup>/L) at the 100 mg/m<sup>2</sup> dose.

## 2. Hepatic Dysfunction (based on physician discretion)

Bilirubin (micromol/L)		ALT	Dose
less than 25	or	less than or equal to 2.5 x ULN	100%
25-85	or	2.6 – 5 x ULN	Reduce one dose level**
greater than 85	or	greater than 5 x ULN	Delay***

\*\* Dose levels are 200 mg/m<sup>2</sup>, 150 mg/m<sup>2</sup> and 100 mg/m<sup>2</sup>

\*\*\* Follow LFTs weekly and re-institute temozolomide at 100 mg/m<sup>2</sup> if Bilirubin recovers to less than 85 micromol/L and ALT recover to less than 5 x ULN

- Note: Dose reductions below 100 mg/m<sup>2</sup> are not permitted. Temozolomide should be discontinued for repeat Bilirubin greater than 85 micromol/L and repeat AST/ALT greater than 5 x ULN

### PRECAUTIONS:

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.

**Call Dr. Vanessa Bernstein or tumour group delegate at 250-519-5570 or 1-800-519-5500 with any problems or questions regarding this treatment program.**

### References:

1. Quirt I, Verma V, et al. Temozolomide for the treatment of metastatic melanoma: A systemic review. *Oncologist* 2007;12:1114-23.
2. Agarwala SS, Kirkwood, JM, et al. Temozolomide for the treatment of brain metastases associated with metastatic melanoma: A phase II study. *J Clin Oncol* 2004;22(11):2010-7.
3. Agarwala SS, Kirkwood J. Temozolomide, a novel alkylating agent with activity in the central nervous system, may improve the treatment of advanced metastatic melanoma. *Oncologist* 2000;5:144-51.
4. Middleton MR, Aaronson GN, Fierbeck G, et al: Randomized phase III study of temozolomide versus dacarbazine in the treatment of patients with advanced malignant melanoma. *J Clin Oncol* 2000;18(1):158-66.