

BCCA Protocol Summary for Palliative Therapy for Malignant Melanoma with Brain Metastases Using Temozolomide

Protocol Code

SMAVTMZ

Tumour Group

Melanoma

Contact Physician

Dr. Richard Klasa

ELIGIBILITY:

- Malignant melanoma with brain metastasis
- ECOG less than or equal to 3
- Adequate renal function
- Life expectancy of 12 weeks or longer
- A "Class II Drug Registration Form" must be submitted at the time of initiation of treatment.

EXCLUSIONS:

- Pregnant or breast feeding women

TESTS:

- Baseline: CBC and differential, platelets, creatinine, glucose (patients on corticosteroids)
- Before each treatment: CBC and differential, platelets
- 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*	BCCA Administration Guideline
Temozolomide	200 mg/m ² **once daily x 5 days (d 1-5)	PO at bedtime

* round dose to nearest 5 mg

** 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
Dose Level 0 (Starting Dose)	200 mg/m ² *once daily x 5 days (d 1-5)
Dose Level -1	150 mg/m ² *once daily x 5 days (d 1-5)
Dose Level -2	100 mg/m ² * once daily x 5 days (d 1-5)
Dose Level -3	Discontinue Temozolomide

* round dose to nearest 5 mg

1. Hematological

ANC (x10 ⁹ /L)		Platelets (x10 ⁹ /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 10⁹/L and platelets recover to greater than or equal to 100 x 10⁹/L, re-start temozolomide at one level reduced dose.
- If the hematologic toxicity developed at 100 mg/m², re-start with 100 mg/m² upon recovery.
- Dose reductions below 100 mg/m² are not permitted. Temozolomide should be discontinued for repeated grade 3 or 4 hematologic toxicity (ANC less than 1 x 10⁹/L, platelets less than 50 x 10⁹/L) at the 100 mg/m² dose.

PRECAUTIONS:

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

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

Date activated: 1 July 2010

Date revised: 1 Jan 2012 (Eligibility revised)

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, Fierlbeck G, et al: Randomized phase III study of temolozomide versus dacarbazine in the treatment of patients with advanced malignant melanoma. *J Clin Oncol* 2000;18(1):158-66.