

# BC Cancer Protocol Summary for Therapy for Recurrent Malignant Brain Tumours using Temozolomide and Etoposide

**Protocol Code**

CNTMZETO

**Tumour Group**

Neuro-Oncology

**Contact Physician**

Dr. [Rebecca Harrison](#)

## ELIGIBILITY:

### Patients must have:

- Recurrent embryonal tumours such as medulloblastoma, or
- Recurrent gliomas in temozolomide naïve patients

### Patients should have:

- Karnofsky Performance Status greater than 50
- Adequate bone marrow, cardiac, renal and hepatic function

## EXCLUSIONS:

- Pregnant or breast feeding women

## CAUTION:

- Creatinine greater than 1.5X normal
- Significant hepatic dysfunction

## TESTS:

- Baseline: CBC and differential, platelets, ALT and bilirubin, creatinine, glucose (patients on dexamethasone)
- Before each treatment:
  - Day 1: CBC and differential, platelets, creatinine, ALT and bilirubin
  - Day 22: CBC and differential, platelets
- Neuroimaging every 2 cycles
- If clinically indicated: electrolytes, magnesium, calcium, glucose

## PREMEDICATIONS:

- ondansetron 8 mg given 30 minutes prior to each dose of temozolomide
- prochlorperazine 10 mg or metoclopramide 10-40 mg PO q4-6 hours prn with etoposide doses
- hydrocortisone and diphenhydrAMINE for history of hypersensitivity to etoposide

## TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
temozolomide	150 mg/m <sup>2</sup> once daily x 5 days (d 1-5)*	PO
etoposide	50 mg/m <sup>2</sup> once daily x 12 days (d 1-12)**	PO

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

\*\* round dose to nearest 50 mg

Repeat every 28 days x 12 cycles

- Temozolomide dose may be increased to 200 mg/m<sup>2</sup> for the second cycle if no significant hematologic, hepatic or other toxicity is noted (see below)
- Discontinue for clinical or radiographic progression.

## DOSE MODIFICATIONS:

### 1. Hematological

Day 1:

ANC (x10 <sup>9</sup> /L)		Platelets (x10 <sup>9</sup> /L)	Temozolomide Dose	Etoposide Dose
greater than or equal to 1.5	and	greater than or equal to 100	100%	100%
1.0 to 1.4	and	75 to 99	delay*	delay*
less than 1	and	less than 75	delay**	delay**

Dose levels for temozolomide are 200 mg/m<sup>2</sup>, 150 mg/m<sup>2</sup> and 100 mg/m<sup>2</sup>

\* Follow CBC weekly and re-institute temozolomide at minus one dose level and etoposide at 50 mg/m<sup>2</sup> if ANC recovers to 1.5 x 10<sup>9</sup>/L and platelets recover to 100 x 10<sup>9</sup>/L within 3 weeks

\*\* Follow CBC weekly and re-institute temozolomide at minus one dose level and etoposide at 35 mg/m<sup>2</sup> if ANC recovers to 1.5 x 10<sup>9</sup>/L and platelets recover to 100 x 10<sup>9</sup>/L within 3 weeks

For **repeat** 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), discontinue etoposide and continue temozolomide at the 100 mg/m<sup>2</sup> dose.

Day 22:

ANC (x10 <sup>9</sup> /L)		Platelets (x10 <sup>9</sup> /L)	Temozolomide dose	Etoposide dose
greater than or equal to 1.0	and	greater than or equal to 50	100%	100%
less than 1.0	or	less than 50	reduce one dose level	35 mg/m <sup>2</sup>

Dose levels for temozolomide are 200 mg/m<sup>2</sup>, 150 mg/m<sup>2</sup> and 100 mg/m<sup>2</sup>

**Note:** Temozolomide dose reductions below 100 mg/m<sup>2</sup> are not permitted.

## 2. Hepatic Dysfunction

Bilirubin (micromol/L)		ALT	Temozolomide dose	Etoposide dose
less than 25	or	less than or equal to 2.5 x ULN	100%	100%
25 to 84	or	2.6 to 5 x ULN	reduce one dose level	35 mg/m <sup>2</sup>
greater than 85		greater than 5 x ULN	delay*	delay*

Dose levels for temozolomide 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> and etoposide at 35 mg/m<sup>2</sup> if Bilirubin recovers to less than 85 micromol/L and ALT recovers to less than 5 x ULN

**Note:** Temozolomide dose reductions below 100 mg/m<sup>2</sup> are not permitted.

For **repeat** Bilirubin greater than 85 micromol/L and repeat ALT greater than 5 x ULN, discontinue both drugs

## 3. Renal dysfunction

Dose modification required for creatinine greater than 1.5 x upper limit of normal. Reduce temozolomide to 100 mg/m<sup>2</sup> and etoposide to 35 mg/m<sup>2</sup>. Discontinue both drugs if no resolution of renal dysfunction at this dose.

### PRECAUTIONS:

- Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
- Thrombocytopenia:** Day 22 platelet counts less than 50 x 10<sup>9</sup>/L should be monitored at least twice weekly until recovering. Platelet counts less than 20 x 10<sup>9</sup>/L and falling should be treated with platelet transfusion.

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

**References:**

1. Korones NK, Smith A, Foreman N, Bouffet E. Temozolomide and oral vp-16 for children and young adults with recurrent or treatment-induced malignant gliomas. *Pediatr Blood Cancer* 2006;47:37-41.
2. Korones NK, Benita-Weiss M, Coyle TE et al. Phase I study of temozolomide and escalating doses of oral etoposide for adults with recurrent malignant glioma. *Cancer* 2003;97(8):1963-8.