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. Brian Thiessen*

ELIGIBILITY:

- Recurrent embryonal tumours such as medulloblastoma
- Recurrent gliomas in temozolomide naïve patients
- Karnofsky Performance Status greater than 50
- Adequate bone marrow, cardiac, renal and hepatic function

EXCLUSIONS:

- Creatinine greater than 1.5X normal
- Significant hepatic dysfunction
- Pregnant or breast feeding women

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^2 once daily x 5 days (d 1-5)*	PO
etoposide	50 mg/m^2 once daily x 12 days (d 1-12)**	PO

* round dose to nearest 5 mg
** round dose to nearest 50 mg

Repeat every 28 days x 12 cycles

- Temozolomide dose may be increased to 200 mg/m^2 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 (x10^9/L)		Platelets (x10^9/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^2, 150 mg/m^2 and 100 mg/m^2

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

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

*For **repeat** grade 3 or 4 hematologic toxicity (ANC less than 1 x 10^9/L, platelets less than 50 x 10^9/L), discontinue etoposide and continue temozolomide at the 100 mg/m^2 dose.*

Day 22:

ANC (x10^9/L)		Platelets (x10^9/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^2

Dose levels for temozolomide are 200 mg/m^2, 150 mg/m^2 and 100 mg/m^2

Note: Temozolomide dose reductions below 100 mg/m^2 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^2
greater than 85		greater than 5 x ULN	delay*	delay*

Dose levels for temozolomide are 200 mg/m², 150 mg/m² and 100 mg/m²
*Follow LFTs weekly and re-institute temozolomide at 100 mg/m² and etoposide at 35 mg/m^2 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^2 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/m² and etoposide to 35 mg/m^2. Discontinue both drugs if no resolution of renal dysfunction at this dose.

PRECAUTIONS:

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

Call Dr. Brian Thiessen 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.