

BC Cancer Protocol Summary for Therapy for Malignant Brain Tumours using Temozolomide

Protocol Code

CNTEMOZ

Tumour Group

Neuro-Oncology

Contact Physician

Dr. Brian Thiessen

ELIGIBILITY:

- Recurrent gliomas not previously treated with CNAJTZRT
- Newly diagnosed Glioblastoma, MGMT methylated, not considered a candidate for CNAJTZRT
- Karnofsky Performance Status greater than 50
- Adequate 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, ALT and bilirubin
 - Day 22: CBC and differential, platelets
- Every second (ie, odd-numbered) treatment cycle (BEFORE #1, 3, 5, etc): creatinine
- Neuroimaging:
 - every 2 cycles for malignant glioma
 - every 3 cycles for low-grade oligodendrogliomas.
- If clinically indicated: electrolytes, magnesium, calcium, glucose

PREMEDICATIONS:

- ondansetron 8 mg given 30 minutes prior to each dose of temozolomide

TREATMENT:

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

* round dose to nearest 5 mg

- Dose can start at 200 mg/m² for chemo-naïve patients
- Dose may be increased to 200 mg/m² for the second cycle if no significant hematologic, hepatic or other toxicity is noted (see below)
- For recurrent malignant gliomas and anaplastic oligodendrogliomas:
 - Repeat every 28 days x **6** cycles, to a maximum of 24 cycles.
- For low grade oligodendrogliomas:
 - Repeat every 28 days x **12** cycles
- Discontinue for clinical or radiographic progression.

DOSE MODIFICATIONS:

1. Hematological

Day 1:

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*

* Follow CBC weekly and re-institute temozolomide at 100 mg/m² if ANC recovers to greater than 1.5 x 10⁹/L and platelets recover to greater than 100 x 10⁹/L within 3 weeks

Day 22:

ANC (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	Dose
greater than or equal to 1.0	and	greater than or equal to 50	100%
less than 1.0	or	less than 50	Reduce one dose level**

**Dose levels are 200 mg/m², 150 mg/m² and 100 mg/m²

- Note: Dose reductions below 100 mg/m² are not permitted. Temozolomide should be discontinued for repeat 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.

2. Renal dysfunction: Dose modification required for creatinine greater than 2 x upper limit of normal. Reduce to 100 mg/m² and discontinue if no resolution of renal dysfunction at this dose

Hepatic Dysfunction

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/m², 150 mg/m² and 100 mg/m²

*** Follow LFTs weekly and re-institute temozolomide at 100 mg/m² if Bilirubin recovers to less than 85 micromol/L and ALT recovers to less than 5 x ULN

- Note: Dose reductions below 100 mg/m² are not permitted. Temozolomide should be discontinued for repeat Bilirubin greater than 85 micromol/L and repeat ALT greater than 5 x ULN

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 10⁹/L should be monitored at least twice weekly until recovering. Platelet counts less than 20 x 10⁹/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. Bower M, Newlands ES, Bleehan NM et al. Multicentre CRC phase II trial of temozolomide in recurrent or progressive high grade glioma. *Cancer Chemother Pharmacol* 1997;40:484-8.
2. Yung WKA, Prados MD, Yaya-Tur R et al. Multicenter phase II trial of temozolomide in patients with anaplastic astrocytoma or anaplastic oligoastrocytoma at first relapse. *J Clin Oncol* 1999;17:2762-71.