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

Protocol Code	*CNTEMOZ*
Tumour Group	*Neuro-Oncology*
Contact Physician	*Dr. Rebecca Harrison*

ELIGIBILITY:

Patients must have:

- Newly diagnosed malignant gliomas, or
- Recurrent malignant gliomas (Note: If previously treated with CNAJTZRT, CNTEMOZMD is preferred)

Patients should have:

- Karnofsky Performance Status greater than 50
- Adequate renal and hepatic function

EXCLUSIONS:

- Pregnant or breast feeding women

CAUTION:

- Significant hepatic dysfunction

TESTS:

- Baseline: CBC & Diff, ALT, total bilirubin, creatinine, random glucose (patients on dexamethasone)
- Before each treatment:
  - Day 1: CBC & Diff, ALT, total bilirubin, random glucose
  - Day 22: CBC & Diff
- Neuroimaging:
  - every 2 cycles for malignant glioma
  - every 3 cycles for low-grade oligodendrogliomas.
- If clinically indicated: electrolytes, magnesium, calcium, creatinine

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 (days 1 to 5)	PO

* refer to Temozolomide Suggested Capsule Combination Table for dose rounding

- Dose can start at 200 mg/m^2 for chemo-naïve patients
- 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)
- 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/m^2 if ANC recovers to greater than 1.5 x 10^9/L and platelets recover to greater than 100 x 10^9/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/m^2, 150 mg/m^2 and 100 mg/m^2

- Note: Dose reductions below 100 mg/m^2 are not permitted. Temozolomide should be discontinued for repeat grade 3 or 4 hematologic toxicity (ANC less than 1 x 10^9/L, platelets less than 50 x 10^9/L) at the 100 mg/m^2 dose.

2. **Hepatic Dysfunction**

Bilirubin (micromol/L)		ALT	Dose
less than 25	or	less than or equal to 2.5 x ULN	100%
25 to 85	or	2.6 to 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/m^2 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 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.
3. **Renal Dysfunction:** Renal impairment is not expected to affect temozolomide clearance. Caution should be exercised when treating patients with creatinine clearance less than 36 mL/min.

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. 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.
3. Sandhu G, Adattini J, Armstrong Gordon E, O'Neill N. On behalf of the ADDIKD Guideline Working Group. International consensus guideline on anticancer drug dosing in kidney dysfunction. 2022. eviQ, Cancer Institute NSW. St Leonards, Australia