BC Cancer Protocol Summary for Therapy for Malignant Brain Tumours using Metronomic Dosing of Temozolomide

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

ELIGIBILITY:

Patients must have:
- Recurrent malignant glioma, or
- Progression during or post-completion of CNAJTZRT protocol

Patients should have:
- WHO PS greater than or equal to 2
- Adequate renal and hepatic function

EXCLUSIONS:

Patients must not:
- Have received more than 6 cycles of adjuvant temozolomide in the past
- Be pregnant or breast feeding

CAUTION:

- Significant hematologic or other toxicity associated with temozolomide in the past
- Significant hepatic dysfunction

TESTS:

- Baseline: CBC & Diff, ALT, total bilirubin, creatinine, random glucose (patients on dexamethasone)
- Before each treatment: CBC & Diff, ALT, total bilirubin, random glucose
- Neuroimaging: every 2 cycles
- If clinically indicated: electrolytes, magnesium, calcium, creatinine

PREMEDICATIONS:

- ondansetron 8 mg given 30 minutes prior to first dose of temozolomide
- prochlorperazine 10 mg PO q6h prn or dimenhyDRINATE 25 to 50 mg PO q6h prn

TREATMENT:

Drug	Dose*	BC Cancer Administration Guideline
temozolomide	50 mg/m^2 once daily x 28 days (days 1 to 28)	PO

*refer to Temozolomide Suggested Capsule Combination Table for dose rounding

- Repeat every 28 days to a maximum of 24 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 until ANC is greater than 1.5 x 10^9/L and platelets are greater than 100 x 10^9/L • Follow CBC weekly • If counts recover within 3 weeks, restart temozolomide at 35mg/m2 • If recovery takes more than 3 weeks, discontinue treatment

- Note: Dose reductions below 35 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 35 mg/m^2 dose.

3. Hepatic Dysfunction

Total 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	35 mg/m^2
greater than 85	or	greater than 5 x ULN	Delay***

*** Follow LFTs weekly and re-institute temozolomide at 35 mg/m² if total bilirubin recovers to less than 85 micromol/L and ALT recovers to less than 5 x ULN

- Note: Dose reductions below 35 mg/m^2 are not permitted. Temozolomide should be discontinued for repeat total 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:** 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. Perry JR, Mason WP, Belanger K, et al. The temozolomide RESCUE study: A phase II trial of continuous (28/28) dose-intensive temozolomide (TMZ) after progression on conventional 5/28 day TMZ in patients with recurrent malignant gliomas (abstr). J Clin Oncol 2008;26(15S):91s.
2. Tolcher AW, Gerson SL, Denis L, et al. Marked inactivation of O6-alkylguanine-DNA alkyltransferase activity with protracted temozolomide schedules. Br J Cancer 2003;88(7):1004-11.
3. Neyns B, Chaskis C, Joosens E, et al. A multicenter cohort study of dose-dense temozolomide (21 of 28 days) for the treatment of recurrent anaplastic astrocytoma or oligoastrocytoma. Cancer Invest 2008;26:269-77.
4. Yung WKA, Albright RE, Olson J, et al. A phase II study of temozolomide vs. procarbazine in patients with glioblastoma multiforme at first relapse. Brit J Cancer 2000;83:588-93.
5. 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