# 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. Brian Thiessen*

## ELIGIBILITY:

- Recurrent malignant glioma
- Progression during or post-completion of CNAJTZRT protocol
- WHO PS greater than or equal to 2
- Adequate renal and hepatic function

## EXCLUSIONS:

- Creatinine greater than 1.5X normal
- Significant hepatic dysfunction
- Pregnant or breast feeding women
- Patient has received more than 6 cycles of adjuvant temozolomide in the past
- Significant hematologic or other toxicity associated with temozolomide in the past

## 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
- If clinically indicated: electrolytes, magnesium, calcium, glucose

## 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 (d 1 to 28) | PO |

* round dose to nearest 5 mg

- 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 x 1 week* |

* Follow CBC weekly and re-institute temozolomide at 35 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 next cycle to 35 mg/m$^2$ once daily |

- 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.

2. Renal dysfunction: Dose modification required for creatinine greater than 2 x upper limit of normal. Reduce to 35 mg/m² and discontinue if no resolution of renal dysfunction at this dose.

**3. 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 | 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 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 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.

**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. 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.