

# BC Cancer Protocol Summary for Concomitant (Dual Modality) and Adjuvant Temozolomide for Newly Diagnosed Malignant Gliomas with Radiation

**Protocol Code**

CNAJZRT

**Tumour Group**

Neuro-Oncology

**Contact Physician**

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## ELIGIBILITY:

- Patients with newly diagnosed [glioblastoma all variants](#), [Grade 2-4 astrocytoma IDH wild type](#), and [Grade 4 astrocytoma IDH mutant](#)
- Karnofsky Performance Status greater than 50, ECOG 0-2
- Adequate renal and hepatic function
- Age less than 70

## EXCLUSIONS:

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

## TESTS:

- Baseline and before starting adjuvant temozolomide: CBC and differential, platelets, ALT, Bilirubin, serum creatinine, random glucose (patients on dexamethasone)
- During concomitant temozolomide with RT (dual modality):
  - Weekly CBC and differential
  - Before week 1 and before week 4: ALT and bilirubin
- Before each treatment of adjuvant temozolomide:
  - Day 1: CBC and differential, platelets, serum creatinine, ALT and bilirubin
  - Day 22: CBC and differential, platelets
- Before cycles #3 and 5 and at completion of adjuvant temozolomide: neuroimaging
- If clinically indicated: sodium, potassium, magnesium, calcium, random glucose

## PREMEDICATIONS:

- For concomitant temozolomide with RT (dual modality): ondansetron 8 mg given 30 minutes prior to first dose of temozolomide, then prochlorperazine 10 mg po 30 minutes prior to each subsequent dose of temozolomide
- For adjuvant temozolomide: ondansetron 8 mg po 30 minutes prior to each dose of temozolomide

**TREATMENT:**

Drug	Dose*	BC Cancer Administration Guideline
temozolomide	<p>Concomitant with RT: 75 mg/m<sup>2</sup> po daily preferably 1 h prior to RT especially in the first week of treatment, and in A.M. on days without RT until completion of RT (usual duration 6 weeks)</p> <p>Adjuvant treatment starting 4 wks after RT: 150 mg/m<sup>2</sup> once daily x 5 d (d 1 to 5) every 28 d x 6 cycles</p>	PO

\* refer to [Temozolomide Suggested Capsule Combination Table](#) for dose rounding

- Dose may be increased to 200 mg/m<sup>2</sup> for the second cycle of adjuvant therapy if no significant hematologic, hepatic or other toxicity is noted (see below)
- Trimethoprim/sulfamethoxazole DS one tablet po q Monday, Wednesday and Friday is recommended for patients on concomitant or adjuvant temozolomide if requiring dexamethasone for longer than 4 weeks
- Discontinue for clinical or radiographic progression.

**DOSE MODIFICATIONS:****1. Hematological****For Concomitant Temozolomide with RT**

Weekly CBC:

ANC (x10 <sup>9</sup> /L)		Platelets (x10 <sup>9</sup> /L)	Dose
greater than or equal to 1.5	and	greater than or equal to 100	100%
1.0 to less than 1.5	or	75 to less than 100	Delay temozolomide until counts recover
less than 1.0	or	less than 75	Discontinue temozolomide

## For Adjuvant Temozolomide

Day 1:

ANC (x10 <sup>9</sup> /L)		Platelets (x10 <sup>9</sup> /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 one dose level lower (150 mg/m<sup>2</sup> or 100 mg/m<sup>2</sup>) if ANC recovers to greater than 1.5 x 10<sup>9</sup>/L and platelets recover to greater than 100 x 10<sup>9</sup>/L within 3 weeks

Day 22:

ANC (x10 <sup>9</sup> /L)		Platelets (x10 <sup>9</sup> /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<sup>2</sup>, 150 mg/m<sup>2</sup> and 100 mg/m<sup>2</sup>

- Note: Dose reductions below 100 mg/m<sup>2</sup> are not permitted. Temozolomide should be discontinued for repeat grade 3 or 4 hematologic toxicity (ANC less than 1 x 10<sup>9</sup>/L, platelets less than 50 x 10<sup>9</sup>/L) at the 100 mg/m<sup>2</sup> dose.
2. **Renal dysfunction:** Dose modification required for creatinine greater than 2 x upper limit of normal. Reduce to 100 mg/m<sup>2</sup> and discontinue if no resolution of renal dysfunction at this dose.

### 3. Hepatic Dysfunction

#### For Concomitant Temozolomide with RT

Bilirubin (micromol/L)		ALT	Dose
less than 25	and	less than or equal to 2.5 x ULN	100%
greater than or equal to 25	or	greater than 2.5 x ULN	Delay***

\*\*\* Follow LFTs weekly and re-institute temozolomide at 75 mg/m<sup>2</sup> if Bilirubin recovers to less than 25 micromol/L and ALT recovers to less than or equal to 2.5 x ULN

Note: Dose reductions below 75 mg/m<sup>2</sup> are not permitted. Radiation Therapy to continue without temozolomide until recovery of LFTs.

#### For Adjuvant Temozolomide

Bilirubin (micromol/L)		ALT	Dose
less than 25	and	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/m<sup>2</sup>, 150 mg/m<sup>2</sup> and 100 mg/m<sup>2</sup>

\*\*\* Follow LFTs weekly and re-institute temozolomide at 100 mg/m<sup>2</sup> 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<sup>2</sup> 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  $50 \times 10^9/L$  should be monitored at least twice weekly until recovering. Platelet counts less than  $20 \times 10^9/L$  and falling should be treated with platelet transfusion.
3. **Pneumocystis Jiroveci (previously Carinii) pneumonia (PJP):** Occasional reports of PJP in patients receiving concomitant or adjuvant Temozolomide have occurred. Prophylaxis as described above is recommended for patients receiving Temozolomide.

**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<sup>1</sup>:**

1. Stupp R, Mason WP, van den Bent MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. *N Engl J Med* 2005;352(10):987-96.