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

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

ELIGIBILITY:

Patients must have:

- Newly diagnosed malignant gliomas

Patients should have:

- Karnofsky Performance Status greater than 50, ECOG 0-2
- Adequate renal and hepatic function
- Age less than 70 (see CNELTZRT for patients 70 or older)

EXCLUSIONS:

- Pregnant or breast feeding women

TESTS:

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

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	Concomitant with RT: 75 mg/m^2 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) Adjuvant treatment starting 4 wks after RT: 150 mg/m^2 once daily x 5 d (d 1 to 5) every 28 d x 6 cycles	PO

* refer to Temozolomide Suggested Capsule Combination Table for dose rounding

- Dose may be increased to 200 mg/m^2 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 (x10^9/L)		Platelets (x10^9/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 ($x10^9$/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 one dose level lower (150 mg/m^2 or 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

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^2 if Bilirubin recovers to less 25 micromol/L and ALT recovers to less than or equal to 2.5 x ULN

Note: Dose reductions below 75 mg/m^2 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/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. **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.
4. **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]:

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.