BC Cancer Protocol Summary for Concomitant (Dual Modality) and 12 Cycles of Adjuvant Temozolomide for Newly Diagnosed Astrocytomas and Oligodendrogliomas with Radiation

Protocol Code	*CNAJ12TZRT*
Tumour Group	*Neuro-Oncology*
Contact Physician	*Dr. Rebecca Harrison*

ELIGIBILITY:

Patients must have:

- Newly diagnosed grade 3 gliomas (astrocytomas and oligodendrogliomas) with IDH mutant or IDH status unknown tumours

Patients should have:

- Karnofsky Performance Status greater than 50, ECOG 0-2
- Adequate renal and hepatic function
- Age less than 70

EXCLUSIONS:

- Pregnant or breast feeding women

CAUTION:

- Creatinine greater than 1.5X normal
- Significant hepatic dysfunction

TESTS:

- Baseline and before starting adjuvant temozolomide: CBC and differential, platelets, ALT, Bilirubin, serum creatinine, 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 cycle #3 and every second cycle thereafter, and at completion of adjuvant temozolomide: neuroimaging
- Before Cycle 7: assess response to treatment and continue adjuvant temozolomide for responding measurable disease up to 12 cycles
- If clinically indicated: sodium, potassium, magnesium, calcium, 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	Concomitant with RT: 75 mg/m^2 PO once 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 weeks after RT: 150 mg/m^2 PO once daily x 5 d (d 1 to 5) every 28 d x 12 cycles**	PO

* refer to Temozolomide Suggested Capsule Combination Table for dose rounding

- **Dose should 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)
- **Assess after 6 cycles to determine duration of treatment
- 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%
less than 1.5	or	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 to100	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 1.0 x 10^9/L, platelets less than 50 x 10^9/L) at the 100 mg/m^2 dose.

2. **Renal dysfunction**: Dose modification required for creatinine greater than 2 x upper limit of normal. Reduce to 100 mg/m^2 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/m² 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.

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. van den Bent MJ, Baumert B, Erridge SC, et al. Interim results from the CATNON trial (EORTC study 26053-22054) of treatment with concurrent and adjuvant temozolomide for 1p/19q non-co-deleted anaplastic glioma: a phase 3, randomized, open-label intergroup trial. Lancet Oncology 08;2017 (published online)