BC Cancer Protocol Summary of Therapy for Newly Diagnosed Malignant Brain Tumours with MGMT Methylation in Elderly Patients using Temozolomide

Protocol Code *CNTEM60*

Tumour Group *Neuro-Oncology*

Contact Physician *Dr. Brian Thiessen*

ELIGIBILITY:

- Newly diagnosed glioblastoma multiforme with MGMT promoter methylation:
  - Patients age 60 to 70 years who are not candidates for CNAJTZRT
  - Patients age over 70 years who have adequate performance status to recommend post-surgical treatment
- Karnofsky Performance Status greater than 50
- Adequate renal and hepatic function

EXCLUSIONS:

- Creatinine greater than 1.5X normal
- Significant hepatic dysfunction

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 each dose of temozolomide

TREATMENT:

Drug	Dose*	BC Cancer Administration Guideline
temozolomide	150 mg/m^2 once daily x 5 days (d 1-5)	PO

* refer to Temozolomide Suggested Capsule Combination Table for dose rounding

- Dose can start at 200 mg/m^2 for chemo-naïve patients
- Dose may be increased to 200 mg/m^2 for the second cycle if no significant hematologic, hepatic or other toxicity is noted (see below)
- Repeat every 28 days a maximum of 12 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*

* Follow CBC weekly and re-institute temozolomide at 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. Renal dysfunction: Dose modification required for creatinine greater than 2 x upper limit of normal. Reduce to 100 mg/m² and discontinue if no resolution of renal dysfunction at this dose

3. **Hepatic Dysfunction**

Bilirubin (micromol/L)		AST +/or ALT	Dose
less than 25	or	less than or equal to 2.5 x ULN	100%
25-85	or	2.6 – 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.

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. Wick W, et al. Temozolomide chemotherapy alone versus radiotherapy alone for malignant astrocytoma in the elderly: the NOA-08 randomised, phase 3 trial. Lancet Oncol 2012;13:707-15.
2. Malmstrom A, et al. Glioblastoma in elderly patients: A randomized phase III trial comparing survival in patients treated with 6-week radiotherapy versus hypofractionated RT over 2 weeks versus temozolomide single-agent chemotherapy. J Clin Oncol 2010;28:18s (abstr LBA2002).