

# 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. Rebecca Harrison

## ELIGIBILITY:

Patients must have:

- Newly diagnosed **malignant gliomas** with MGMT promoter methylation

Patients should have:

- Karnofsky Performance Status greater than 50
- Adequate renal and hepatic function

## 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 <sup>2</sup> once daily x 5 days (days 1 to 5)	PO

\* refer to Temozolomide Suggested Capsule Combination Table for dose rounding

- Dose can start at 200 mg/m<sup>2</sup> for chemo-naïve patients
- Dose may be increased to 200 mg/m<sup>2</sup> 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 <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 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

Bilirubin (micromol/L)		AST +/-or ALT	Dose
less than 25	or	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 x 10<sup>9</sup>/L should be monitored at least twice weekly until recovering. Platelet counts less than 20 x 10<sup>9</sup>/L and falling should be treated with platelet transfusion.

**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. 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).