BC Cancer Protocol Summary for Therapy for Malignant Brain Tumours Using Metronomic Dosing of Temozolomide

**Protocol Code**

**CNTEMOZMD**

**Tumour Group**

**Neuro-Oncology**

**Contact Physician**

**Dr. Brian Thiessen**

**ELIGIBILITY:**

- Recurrent malignant glioma
- Progression during or post-completion of CNAJTZRT protocol
- WHO PS greater than or equal to 2
- Adequate renal and hepatic function

**EXCLUSIONS:**

- Creatinine greater than 1.5X normal
- Significant hepatic dysfunction
- Pregnant or breast feeding women
- Patient has received more than 6 cycles of adjuvant temozolomide in the past
- Significant hematologic or other toxicity associated with temozolomide in the past

**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 first dose of temozolomide
- prochlorperazine 10 mg PO q6h prn or dimenhyDRINATE 25 to 50 mg PO q6h prn

**TREATMENT:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose*</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>temozolomide</td>
<td>50 mg/m² once daily x 28 days (d 1 to 28)</td>
<td>PO</td>
</tr>
</tbody>
</table>

* round dose to nearest 5 mg

- Repeat every 28 days to a maximum of 24 cycles.
- Discontinue for clinical or radiographic progression.
DOSE MODIFICATIONS:

1. Hematological

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.5</td>
<td>greater than or equal to 100</td>
<td>100%</td>
</tr>
<tr>
<td>less than 1.5</td>
<td>or less than 100</td>
<td>Delay x 1 week*</td>
</tr>
</tbody>
</table>

* Follow CBC weekly and re-institute temozolomide at 35 mg/m² 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:

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.0</td>
<td>greater than or equal to 50</td>
<td>100%</td>
</tr>
<tr>
<td>less than 1.0</td>
<td>or less than 50</td>
<td>Reduce next cycle to 35 mg/m² once daily</td>
</tr>
</tbody>
</table>

- **Note:** Dose reductions below 35 mg/m² 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 35 mg/m² dose.

2. Renal dysfunction: Dose modification required for creatinine greater than 2 x upper limit of normal. Reduce to 35 mg/m² and discontinue if no resolution of renal dysfunction at this dose.

3. Hepatic Dysfunction

<table>
<thead>
<tr>
<th>Bilirubin (micromol/L)</th>
<th>ALT</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 25</td>
<td>or</td>
<td>less than or equal to 2.5 x ULN</td>
</tr>
<tr>
<td>25-85</td>
<td>or</td>
<td>2.6 – 5 x ULN</td>
</tr>
<tr>
<td>greater than 85</td>
<td>or</td>
<td>greater than 5 x ULN</td>
</tr>
</tbody>
</table>

*** Follow LFTs weekly and re-institute temozolomide at 35 mg/m² if Bilirubin recovers to less than 85 micromol/L and ALT recovers to less than 5 x ULN

- **Note:** Dose reductions below 35 mg/m² 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.

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:


