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 glioblastoma multiforme with MGMT promoter methylation, and
- Age 60 to 70 and not candidates for CNAJTZRT, or
- Age over 70 with adequate performance status to recommend post-surgical treatment

Patients should have:
- Karnofsky Performance Status greater than 50
- Adequate renal and hepatic function

CAUTION:
- 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:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose*</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>temozolomide</td>
<td>150 mg/m² once daily x 5 days (days 1 to 5)</td>
<td>PO</td>
</tr>
</tbody>
</table>

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

- Dose can start at 200 mg/m² for chemo-naïve patients
- Dose may be increased to 200 mg/m² 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:

<table>
<thead>
<tr>
<th>ANC (x10⁹/L)</th>
<th>Platelets (x10⁹/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.5</td>
<td>and</td>
<td>greater than or equal to 100</td>
</tr>
<tr>
<td>less than 1.5</td>
<td>or</td>
<td>less than 100</td>
</tr>
</tbody>
</table>

   * Follow CBC weekly and re-institute temozolomide at 100 mg/m² if ANC recovers to greater than 1.5 x 10⁹/L and platelets recover to greater than 100 x 10⁹/L within 3 weeks

   Day 22:

<table>
<thead>
<tr>
<th>ANC (x10⁹/L)</th>
<th>Platelets (x10⁹/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.0</td>
<td>and</td>
<td>greater than or equal to 50</td>
</tr>
<tr>
<td>less than 1.0</td>
<td>or</td>
<td>less than 50</td>
</tr>
</tbody>
</table>

   **Dose levels are 200 mg/m², 150 mg/m² and 100 mg/m²

   - Note: Dose reductions below 100 mg/m² are not permitted. Temozolomide should be discontinued for repeat grade 3 or 4 hematologic toxicity (ANC less than 1 x 10⁹/L, platelets less than 50 x 10⁹/L) at the 100 mg/m² 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

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**Warning:** The information contained in these documents are a statement of consensus of BC Cancer Agency professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient’s care or treatment. Use of these documents is at your own risk and is subject to BC Cancer’s terms of use available at www.bccancer.bc.ca/legal.htm
3. **Hepatic Dysfunction**

<table>
<thead>
<tr>
<th>Bilirubin (micromol/L)</th>
<th>AST +/- or ALT</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 25</td>
<td>or less than or equal to 2.5 x ULN</td>
<td>100%</td>
</tr>
<tr>
<td>25 to 85</td>
<td>or 2.6 to 5 x ULN</td>
<td>Reduce one dose level**</td>
</tr>
<tr>
<td>greater than 85</td>
<td>or greater than 5 x ULN</td>
<td>Delay***</td>
</tr>
</tbody>
</table>

** 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/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 x 10⁹/L should be monitored at least twice weekly until recovering. Platelet counts less than 20 x 10⁹/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:**