BC Cancer Protocol Summary for Palliative Therapy for Malignant Melanoma with Brain Metastases using Temozolomide

Protocol Code
SMAVTMZ

Tumour Group
Melanoma

Contact Physician
Dr. Vanessa Bernstein

ELIGIBILITY:
- Malignant melanoma with brain metastasis
- ECOG less than or equal to 3
- Adequate renal function
- Life expectancy of 12 weeks or longer

EXCLUSIONS:
- Pregnant or breast feeding women
- Significant hepatic dysfunction (based on physician discretion)

TESTS:
- Baseline: CBC and differential, platelets, ALT and bilirubin, creatinine, glucose (patients on corticosteroids)
- Before each treatment: CBC and differential, platelets, ALT and bilirubin.
- If clinically indicated: creatinine, glucose

PREMEDICATIONS:
- ondansetron 8 mg given 30 minutes prior to each dose of temozolomide at the discretion of the treating physician.

TREATMENT:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose*</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>temozolomide</td>
<td>200 mg/m² **once daily x 5 days (d 1-5)</td>
<td>PO at bedtime</td>
</tr>
</tbody>
</table>

* refer to Temozolomide Suggested Capsule Combination Table for dose rounding
** For patients who had received prior chemotherapy for metastatic melanoma, start with dose level -1 and then increase to dose level 0 if tolerable (see Dose Levels table below).

- Repeat every 28 days to a maximum of 8 cycles
- Discontinue for clinical or radiographic progression.
DOSE MODIFICATIONS:

Dose Levels

<table>
<thead>
<tr>
<th>Drug</th>
<th>Temozolomide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose Level 0</td>
<td>200 mg/m² * once daily x 5 days (d 1-5)</td>
</tr>
<tr>
<td>(Starting Dose)</td>
<td></td>
</tr>
<tr>
<td>Dose Level –1</td>
<td>150 mg/m² * once daily x 5 days (d 1-5)</td>
</tr>
<tr>
<td>Dose Level –2</td>
<td>100 mg/m² * once daily x 5 days (d 1-5)</td>
</tr>
<tr>
<td>Dose Level –3</td>
<td>Discontinue temozolomide</td>
</tr>
</tbody>
</table>

* round dose to nearest 5 mg

1. Hematological

<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 and greater than or equal to 100</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>less than 1.5 or less than 100</td>
<td>Delay*</td>
<td></td>
</tr>
</tbody>
</table>

* Perform weekly CBC, maximum of 3 times.

- If ANC recovers to greater than or equal to 1.5 x 10⁹/L and platelets recover to greater than or equal to 100 x 10⁹/L, re-start temozolomide at one level reduced dose.
- If the hematologic toxicity developed at 100 mg/m², re-start with 100 mg/m² upon recovery.
- Dose reductions below 100 mg/m² are not permitted. Temozolomide should be discontinued for repeated 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. **Hepatic Dysfunction (based on physician discretion)**

<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>100%</td>
</tr>
<tr>
<td>25-85</td>
<td>2.6 – 5 x ULN</td>
<td>Reduce one dose level**</td>
</tr>
<tr>
<td>greater than 85</td>
<td>or</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 recover 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 AST/ALT greater than 5 x ULN

**PRECAUTIONS:**

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.

Call Dr. Vanessa Bernstein or tumour group delegate at 250-519-5570 or 1-800-519-5500 with any problems or questions regarding this treatment program.

**References:**