BC Cancer Protocol Summary For Modified PCV Chemotherapy Of Brain Tumours Using Procarbazine, Lomustine (CCNU) and vinCRISTine

Protocol Code  
CNMODPCV

Tumour Group  
Neuro-oncology

Contact Physician  
Dr. Rebecca Harrison

ELIGIBILITY:

Patients must have:
- Embryonal tumours (adjuvant therapy for adults over age 40), or
- Grade 2 oligodendroglioma or astrocytoma

Patients should have:
- Adequate hematological, renal and hepatic function

Note: Patients with Grade 2 oligodendroglioma IDH mutant who are ineligible for or intolerant of CNMODPCV, or poor performance status, can use CNAJTZRT

TESTS:
- Baseline: CBC and diff, platelets, creatinine, ALT, bilirubin, serum glucose (for patients on dexamethasone), anticonvulsant levels
- Before each cycle: CBC and diff, platelets, creatinine, ALT, bilirubin
- Day 22: CBC and diff, platelets (results not required to proceed with vinCRISTine)
  - CBC and diff, ALT, bilirubin, creatinine before last cycle.
- Imaging: CT or MR every 2nd cycle

PREMEDICATIONS
- ondansetron PO 8 mg q12h for 36 hours (starting 30 min before lomustine), then prochlorperazine PO or dimenhydrinate PO prn
- dexamethasone PO 8 mg q12h for 36 hours (starting 30 min before lomustine), then prochlorperazine PO or dimenhydrinate PO prn
- if patients are nauseated with procarbazine, may divide procarbazine dose or add regular prochlorperazine
TREATMENT:

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>vinCRIStine</td>
<td>1.4 mg/m² (see below for maximum cap dose)*</td>
<td>IV in 50 mL NS over 15 mins</td>
</tr>
<tr>
<td>1</td>
<td>lomustine</td>
<td>110 mg/m² at bedtime</td>
<td>PO</td>
</tr>
<tr>
<td>2</td>
<td>procarbazine</td>
<td>60 mg/m²/day, days 2 to 15</td>
<td>PO</td>
</tr>
<tr>
<td>22</td>
<td>vinCRIStine</td>
<td>1.4 mg/m² (see below for maximum cap dose)*</td>
<td>IV in 50 mL NS over 15 mins (Day 22 counts not required to proceed with vinCRIStine)</td>
</tr>
</tbody>
</table>

- Adjuvant chemotherapy for primitive neuroectodermal tumour (PNET):
  - Repeat every 6 weeks x 4 to 6 cycles as tolerated
- Recurrent oligodendrogliomas and mixed gliomas not previously exposed to PCV or with a prior good response to PCV
  - Repeat every 6 weeks x 4 to 6 cycles based on response and tolerability
- Low grade gliomas, to start two weeks post radiation therapy
  - Repeat every 6 weeks x 6 cycles as tolerated

*For planned treatment greater than 4 cycles, cap vinCRIStine at 2 mg

DOSE MODIFICATIONS:

1. **Hematological**: modify lomustine and procarbazine, not vinCRIStine.

For **Day 1/Beginning Cycle counts**:

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose (lomustine, procarbazine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.5</td>
<td>and greater than or equal to 100</td>
<td>give 100%</td>
</tr>
<tr>
<td>1.0 to less than 1.5</td>
<td>and/or 70 to less than 100</td>
<td>give 80%*</td>
</tr>
<tr>
<td>less than 1.0</td>
<td>and/or less than 70</td>
<td>Delay until ANC greater than or equal to 1.5 <strong>AND</strong> platelets greater than or equal to 100. Resume both drugs at 60%*</td>
</tr>
</tbody>
</table>

*For lomustine and procarbazine, this dose becomes the new 100% dose for subsequent treatments If more than 2 delays, CONSULT contact physician.
For **Day 22** counts
- modify Day 1 dosing for the rest of the treatment.
- If Day 22 counts and Day 1 counts are low, the reduction is based on the lowest of
  the two counts (i.e., if Day 22 counts dictated a 60% dose reduction and the Day 1
  counts dictated an 80% dose reduction, then the dose should be lowered to 60%)
- If dose modification is required for the first treatment cycle, reconsider the program's
  advisability as severe myelosuppression is common in future cycles.
- In patients with low grade gliomas, for undue toxicity switch to CNTEMOZ for
  remaining cycles

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<td>greater than or equal to 1.5</td>
<td>and</td>
<td>greater than or equal to 100</td>
</tr>
<tr>
<td>1.0 to less than 1.5*</td>
<td>and/or</td>
<td>75 to less than 100*</td>
</tr>
<tr>
<td>less than 1.0*</td>
<td>and/or</td>
<td>less than 75*</td>
</tr>
</tbody>
</table>

*NOTE: Patients with these variables should have careful monitoring (at least twice a week) of
WBC and platelet counts. Trimethoprim/sulfamethoxazole DS one tablet po q Monday,
Wednesday and Friday is recommended for patients requiring dexamethasone for longer than 4
weeks. Platelet TRANSFUSIONS for platelet less than 40 x10^9/L and downward trend. Consult
contact physician if any questions.

2. **Renal dysfunction**: If creatinine clearance less than 50 mL/min, reconsider
treatment program
3. **Hepatic dysfunction**: hold lomustine if ALT greater than 5 x ULN or bilirubin greater
   than 25 micromol/L until ALT less than or equal to 1.5 x ULN or bilirubin less than 25
   micromol/L, then reinstitute at 60% dose.
4. **Respiratory**: Review case
5. **Intolerable side effects**: Re-evaluate treatment. For patients with low grade
   gliomas, switch to CNTEMOZ for remaining cycles.

**PRECAUTIONS:**
1. **Peripheral neuropathy**: Numbness and tingling of fingers and toes; distal
   weakness, foot drop; constipation; jaw pain; mild to moderate nausea/vomiting.
2. **Psycho-neurological complaints**: including drowsiness
3. **Pancytopenia**: often prolonged thrombocytopenia; possible renal damage
4. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and
   treated aggressively
5. **Extravasation**: vinCRISTine causes pain and tissue necrosis if extravasated. Refer
to BC Cancer Extravasation Guidelines
6. **Hypersensitivity**: Reactions are common with procarbazine. Refer to BC Cancer
   Hypersensitivity Guidelines. *Hypertensive crisis* if taking MAO-like drugs or foods
high in tyramine - diet sheet to be given while on procarbazine. Infrequent allergy to procarbazine includes cough.

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