REGIMEN TITLE: PCV (Procarbazine, Lomustine, Vincristine) Oral/IV therapy

Indication: Adjuvant and palliative treatment of malignant gliomas. Recurrent oligodendrogliiomas and mixed gliomas not previously exposed to PCV, or with a prior good response to PCV. Eligible for patients able to tolerate and comply with oral dosage forms.

Regimen details: Procarbazine 100mg/m² PO D1 to D10  
Lomustine (CCNU) 100mg/m² PO D1  
Vincristine 1.5mg/m² IV D1 (Max 2mg dose)

Administration: Vincristine in 50 ml 0.9% Sodium Chloride IV over 5-10 minutes  
Procarbazine and Lomustine capsules to be taken once a day  
Lomustine - available as 40 mg capsules  
Procarbazine - available as 50mg capsules

Frequency: 6 weekly cycle  
Total of 4 - 6 cycles

Extravasation: Vincristine is Vesicant

Anti-emetics: Day 1. Highly emetogenic  
Day 2-10. Moderately emetogenic  
Procarbazine induced nausea usually disappears after 3-4 days. If patients are nauseated during the course of procarbazine, the daily dose may be divided or course of antiemetics extended.  
Note- additional dexamethasone anti-emetic cover is not required if patient is already taking dexamethasone to reduce cerebral oedema.

Regular investigations: FBC D1  
LFTs D1  
U&Es D1  
Clinical toxicity assessments including pulmonary toxicity  
Pulmonary functions tests with prolonged therapy

Comments: Procarbazine is supplied to the patient for oral self-administration. Ensure that the patient has an information pack and the treatment plan.  
Adequate contraceptive methods should be used during therapy, and for 6 months after.

Toxicities: Peripheral neuropathy and neuropathy induced constipation, Neurotoxicity, Nausea and vomiting, Alopecia, Mucositis, Myelosupression (cumulative), increased transaminases, Rash, Hypersensitivity reactions (rare), Infertility, GI symptoms
Dose Modifications

Haematological Toxicity

Modify lomustine and procarbazine, not vincristine

<table>
<thead>
<tr>
<th>Neutrophils x 10^9/l</th>
<th>Platelets x 10^9/l</th>
<th>Lomustine and Procarbazine doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1.5 and/or &lt;70</td>
<td>&gt;150 and/or &lt;70</td>
<td>100% delay one week, then resume at 60%</td>
</tr>
<tr>
<td>1.0-1.5 and/or 70-150</td>
<td>70-150</td>
<td>80%</td>
</tr>
</tbody>
</table>

Renal Impairment

Vincristine Dosage adjustment not required
Procarbazine If Serum creatinine >177 micromols/L, reduce to 50% dose
Not recommended in severe renal impairment

CrCl (ml/min) Lomustine dose

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>60</th>
<th>45</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lomustine dose</td>
<td>75%</td>
<td>70%</td>
<td>not recommended</td>
</tr>
</tbody>
</table>

Hepatic Impairment

Lomustine No dose reduction information available

<table>
<thead>
<tr>
<th>AST/ALT (IU/L)</th>
<th>Bilirubin (micromol/L)</th>
<th>Vincristine Dose</th>
<th>Procarbazine dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-180 or &gt;180</td>
<td>normal and/or &gt;51</td>
<td>Give 50%</td>
<td>100%</td>
</tr>
<tr>
<td>normal</td>
<td>&gt;51</td>
<td>Give 50%</td>
<td>100%</td>
</tr>
<tr>
<td>&gt;180</td>
<td>&gt;51</td>
<td>Omit</td>
<td>consider reduction</td>
</tr>
<tr>
<td>&gt;180</td>
<td>&gt;85</td>
<td>Omit</td>
<td>Contra-indicated</td>
</tr>
</tbody>
</table>

Other toxicities

MAO inhibition Procarbazine is a weak inhibitor of MAO, and can cause CNS side-effects (somnolence, hallucinations, ataxia, headache, insomnia), especially when administered with tyramine rich foods, alcohol or interacting medications.

Disulfiram effect Procarbazine has weak disulfiram-like effect and can lead to alcohol intolerance.

Pulmonary dysfunction Lomustine can cause pulmonary problems after high cumulative doses (lifetime cumulative dose 1100-1400mg/m^2). Onset of these can be from 6 months to 15 years after treatment. Procarbazine can cause acute pulmonary toxicity, pneumonitis. Discontinue Procarbazine treatment if symptoms develop.
Drug interactions:

- Aprepitant- increased vincristine plasma levels
- Phenytoin and similar anti-epileptics- decreased plasma levels (vincristine interaction)
- Itraconazole- increased risk of neurotoxicity with vincristine- do not co-administer
- Posaconazole, voriconazole- potentially increased vincristine plasma levels
- Digoxin- potentially decreased levels (vincristine interaction)
- Nifedipine-increased vincristine toxicity
- Tricyclic antidepressants- potential MAOI interaction with procarbazine
- Barbiturates- increased CNS depression with procarbazine
- Multiple potential drug-drug interactions associated with MAO inhibition by procarbazine

References:

- [www.medicines.org.uk](http://www.medicines.org.uk), accessed April 08
- CCO Formulary: PCV. Revised Oct 05
- BCCA Protocol summaries, CNMODPCV, Revised Dec 07
- ASWCS Chemotherapy Handbook, Jan 05 Update
- Micromedex review, accessed April 08
- Discussions with Dr L.Brazil