Multiple Myeloma

3.04 Protocol name: Melphalan +/- Prednisolone

Indication

- Initial treatment of choice for most patients in whom high dose therapy is not planned. The evidence of benefit from steroids in standard doses is controversial. It is therefore reasonable not to include prednisolone, particularly in patients at risk of steroid-related side effects.

Pre-treatment Evaluation

- Document FBC (with film), plasma viscosity, U&E, creatinine, LFTs, calcium, glucose, serum free light chain measurements, serum protein electrophoresis and paraprotein quantitation, CRP, β₂-microglobulin and immunoglobulin levels.
- Urine for BJP (and formal evaluation of 24 hour urinary BJP excretion if light chain only myeloma).
- Bone marrow aspirate ± trephine (and cytogenetics if part of local protocol).
- Skeletal survey.
- Document height and weight and surface area.
- Consider ECG ± echocardiogram if clinical suspicion of cardiac dysfunction.
- Give adequate verbal and written information for patients and relatives concerning patient’s disease, treatment strategy and side effects.
- Obtain written consent from patient or guardian.
- Discuss issues relating to contraception and potential risk of infertility with patient and relatives (if applicable).

Drug Regimen (OPCS code: X70.1)

<table>
<thead>
<tr>
<th>Days</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Administration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 4</td>
<td>Melphalan</td>
<td>7mg/m²/d</td>
<td>PO</td>
<td>Oral</td>
<td>on an empty stomach</td>
</tr>
<tr>
<td>1 – 4</td>
<td>Prednisolone</td>
<td>40mg/m²/d</td>
<td>PO</td>
<td>Oral</td>
<td>MAX. 60mg/d</td>
</tr>
</tbody>
</table>

Cycle Frequency

Repeat every 4 – 6 weeks, as the counts permit
Dose Modifications

**Melphalan:**

<table>
<thead>
<tr>
<th>Creat. (µmol/L)</th>
<th>dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;200</td>
<td>5mg/m2/d</td>
</tr>
</tbody>
</table>

**Prednisolone:**

- Prednisolone may be omitted in patients intolerant of steroids.
- Patients with bone pain, hypercalcaemia or cytopenias may however benefit from retaining the prednisolone for the first 3 courses.

**Haematological toxicity:**

- Monitor FBC 14 days after melphalan in the first cycle
- If this shows marked thrombocytopenia or neutropenia adjust melphalan as below

<table>
<thead>
<tr>
<th>Platelets x 10⁹/l</th>
<th>Neuts x 10⁹/l</th>
<th>No. of days of Melphalan on subsequent courses</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-75 Or 0.5-1.0</td>
<td>0.5-1.0</td>
<td>3 days</td>
</tr>
<tr>
<td>&lt;25 Or &lt;0.5</td>
<td>&lt;0.5</td>
<td>2 days</td>
</tr>
</tbody>
</table>

- Neutropenia and/or Thrombocytopenia - neutrophil count should be >1.3 x 10⁹/l and the platelet count > 75 x 10⁹/l before any drugs are given, and treatment may be delayed for up to 2 weeks from the last chemotherapy.
- If the requisite counts have been reached within 2 weeks, ie 6 weeks from the start of the previous course, the next course should be given without dose modification unless this is required by the day 14 counts (see above).
- If neutrophils <1.3 x 10⁹/l and/or platelets < 75 x 10⁹/l 6 weeks after the last chemotherapy was given, change the patient to weekly cyclophosphamide or other alternative therapy.

**Investigations prior to subsequent cycles**

- FBC, U&E, creatinine, LFTs, paraprotein level or urinary protein/BJP excretion, plasma viscosity.
- Reassess disease response after each cycle and then 6 weekly during plateau phase.

**Treatment Duration**

- Until plateau phase achieved.
- Maximum of 12 courses.
Concurrent Medication

- Consider oral systemic anti-bacterial, anti-viral and/or anti-fungal prophylaxis if patient is neutropenic - refer to local protocol.
- Consider Allopurinol 300mg (or 100mg if creatinine clearance <20mls/min) od po during the first month.
- Bisphosphonates

Anti-emetics

- This regimen has mild emetic potential - refer to local protocol.

Adverse Effects

See patient information

References


Patient Information
