4.06 Protocol name: Subcutaneous Alemtuzumab (MabCampath®)

Indication
• Treatment of CLL refractory to fludarabine (either primary i.e. 17p deletion, or secondary i.e. following previous fludarabine treatment), and without bulky disease

Pre-treatment Evaluation
• Document histological sub-type of lymphoproliferative disorder according to WHO Classification.
• Document FBC (with film), U&E, creatinine, LFTs, calcium, glucose, serum protein electrophoresis, immunoglobulin levels and a direct antiglobulin test (DAT).
• If staging is relevant this should include documentation of B symptoms, CT of chest, abdomen & pelvis and bone marrow aspirate & trephine.
• Document WHO performance status of patient.
• Document height, weight and body 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.
• If appropriate, discuss the possibility of pregnancy with female patients of child-bearing age and the need for contraception with both male and female patients.
• If appropriate, discuss potential risk of infertility with patient and relatives.
• Consider intravenous hydration in patients with bulk disease.
• Allopurinol should be given for the first month of treatment
• All cellular blood components should be irradiated to prevent the rare occurrence of transfusion associated graft versus host disease.
Drug Regimen (OPCS code: X71.5)

If each dose is well tolerated (i.e. < grade 2 acute, infusion-related toxicities) escalate doses as below

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Alemtuzumab</td>
<td>3mg</td>
<td>If grade 3 adverse events occur (hypotension, rigors, fever or bronchospasm) at 3mg dose repeat 3mg dose daily until it is well tolerated with pre-medication as below, then escalate to 10mg.</td>
</tr>
<tr>
<td>2</td>
<td>Alemtuzumab</td>
<td>10mg</td>
<td>If grade 3 adverse events occur at 10mg dose repeat 10mg dose daily until it is well tolerated with pre-medication as below, then escalate to 30mg.</td>
</tr>
<tr>
<td>3</td>
<td>Alemtuzumab</td>
<td>30mg</td>
<td></td>
</tr>
</tbody>
</table>

**Maintenance dose (week 2 onwards, weekly, up to 12 weeks)**

| 3 times a week | Alemtuzumab | 30mg |

Pre-medication required 30 minutes before each dose:
- Paracetamol 1g PO
- Chlorphenamine 10mg IV or 4mg PO
- may add hydrocortisone 100mg IV if needed

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Administration</th>
<th>Comments</th>
<th>Patient monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alemtuzumab</td>
<td>S/C</td>
<td>Use 30mg/ml solution</td>
<td>May give dose using intravenous</td>
<td>For 1st dose and at each dose increase:</td>
</tr>
</tbody>
</table>
Dose Modifications

**Haematological toxicity:**

<table>
<thead>
<tr>
<th>Toxicity (grade or $10^9$/l)</th>
<th>1st Occurrence</th>
<th>2nd Occurrence</th>
<th>3rd Occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelets &lt;25 and Neutrophils &lt;0.5</td>
<td>Hold; restart at full dose (30mg) when recovered to Platelets &gt;50 and Neutrophils &gt;1.0</td>
<td>Hold; restart at reduced dose (10mg) when recovered to Platelets &gt;50 and Neutrophils &gt;1.0</td>
<td>Discontinue permanently</td>
</tr>
</tbody>
</table>

May use G-CSF to support neutrophil count.

**Infection:**

- If serious infection develops during therapy, stop alemtuzumab until complete resolution.
- May reinstitute alemtuzumab at the previous dose.
- May give prophylactic therapy to prevent recurrence of the diagnosed infection, if clinically indicated.

**Investigations prior to subsequent cycles**

- FBC and differential at least once a week
• Full response assessment every 6 weeks (including BM)
• CMV analysis once a week. If positive, confirm with PCR. If confirmed CMV infection, stop alemtuzumab and treat with ganciclovir or foscarnet (seek specialist advice from Infectious Diseases Specialists). Monitor response to treatment

Treatment Duration

See CAMFLUD protocol.

To maximal response in BM up to 12 weeks as single therapy

If complete remission (CR), stop alemtuzumab and continue to monitor patient without therapy

If evidence of disease progression, serious infection or unacceptable toxicity, discontinue alemtuzumab.

Concurrent Medication

• Oral systemic PCP prophylaxis should be given according to local protocol; start with the first course and continue for at least 2 months after treatment is discontinued. Pentamidine may be used as an alternative.
• Allopurinol 300mg od PO (100mg if creatinine clearance <20mls/min) for D1 to D28 if WBC high, or bulky disease.

References

• UKCLL 02 CAMFLUD trial
• SPC

Patient Information

http://www.cancerbackup.org.uk/Treatments/Biologicaltherapies/Monoclonalantibodies/Alemtuzumab#1577