Indication: Relapsed / refractory acute myeloid leukaemia

Confirm local funding for clofarabine is agreed before commencing treatment. Clofarabine is not licensed for this indication.

Regimen details:

- **GCSF**
  - SC
  - Days 1 to 6

- Clofarabine
  - 25mg/m\(^2\) IV
  - Days 2 to 6

- Cytarabine
  - 2000mg/m\(^2\) IV
  - Days 2 to 6

  Cytarabine infusion is administered 4 hours after the start of the clofarabine infusion

- *GCSF preparation as per local practice, e.g.*
  - Filgrastim
    - 480micrograms SC
    - Days 1 to 6
  - Lenograstim
    - 47million units SC
    - Days 1 to 6

Administration:

- Clofarabine: IV infusion in sodium chloride 0.9% over 1 hour
- Clofarabine is to be administered via a 0.22micron terminal filter
- Cytarabine: IV infusion in sodium chloride 0.9% over 4 hours
- GCSF: subcutaneous injection

Premedication: None required

Frequency: 1 or 2 cycles.

Proceed with cycle 2 when the response to the first cycle has been assessed i.e. bone marrow aspirate and there is neutrophil and platelet count recovery (i.e. neutrophils ≥ 1.0x10\(^9\)/L and platelets ≥ 100x10\(^9\)/L)

Extravasation: Clofarabine and cytarabine are not vesicants

Anti-emetics: Clofarabine and cytarabine are highly emetogenic

Follow local anti-emetic policy

Supportive medication: Rasburicase or allopurinol for prevention of tumour lysis syndrome as per local policy for cycle 1 only.

Mouthcare

Antimicrobial prophylaxis whilst neutrophil count < 0.5 x 10\(^9\)/L as per local policy.

GCSF to be given daily until neutrophil recovery (i.e. until neutrophils > 1.0 x 10\(^9\)/L for 2 consecutive days). Preparation and dose as per local practice.

Corticosteroid eye drops as per local formulary (e.g. prednisolone (Predsol\(^®\)) 0.5% or dexamethasone (Maxidex\(^®\)) 0.1%), during and for 3 days after completion of chemotherapy.
Prior to each clofarabine dose: hydration with 500ml sodium chloride 0.9% over 2 hours

Regular investigations: Prior to day 1:
- FBC
- LFTs
- U&Es

Daily during chemotherapy:
- SeCr to be checked each day prior to administering clofarabine.

Bone marrow aspirate and trephine at day 18 – 21.

Dose Modifications

Haematological Toxicity

Blood counts do not have to be normal prior to cycle 1 GCLAC

Cycle 2 can go ahead after the response to the first course has been assessed i.e. bone marrow aspirate and neutrophil and platelet count recovery. See under frequency.

Renal Impairment

<table>
<thead>
<tr>
<th>Clofarabine – Days 2 to 6</th>
<th>% dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine clearance (mL/min)</td>
<td></td>
</tr>
<tr>
<td>&gt; 60</td>
<td>100% dose</td>
</tr>
<tr>
<td>&lt; 60</td>
<td>Discuss with Consultant</td>
</tr>
</tbody>
</table>

NB if daily trend is increasing serum creatinine even if within normal range discuss with Consultant

Cytarabine

<table>
<thead>
<tr>
<th>Creatinine clearance (mL/min)</th>
<th>% dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60</td>
<td>100% dose</td>
</tr>
<tr>
<td>46 - 60</td>
<td>60% dose</td>
</tr>
<tr>
<td>31 - 45</td>
<td>50% dose</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>Discuss with Consultant</td>
</tr>
</tbody>
</table>

Confirm any dose reductions with the Consultant because in some circumstances 100% dose may be appropriate.

Hepatic Impairment

Reason for Update: Network Protocol Development
Approved by Consultant: K Raj 23/07/12
Version: 1
Approved by Chair Haem TWG: M Kazmi
Supersedes: All other versions
Date: 30/08/12
Prepared by: Laura Cameron
Checked by (Network Pharmacist): J Turner 15/08/12
There is no information on the use of clofarabine in hepatic impairment (bilirubin > 1.5 x ULN plus AST & ALT > 5 x ULN). Use in caution in patients with mild – moderate hepatic impairment and withhold in severe hepatic impairment.

<table>
<thead>
<tr>
<th>Bilirubin (mmol/L)</th>
<th>% dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytarabine</td>
<td></td>
</tr>
<tr>
<td>&lt; 34</td>
<td>100% dose</td>
</tr>
<tr>
<td>&gt; 34</td>
<td>50% dose</td>
</tr>
</tbody>
</table>

Confirm any dose reductions with the Consultant because in some circumstances 100% dose may be appropriate.

Toxicities:
- Clofarabine: headache, peripheral neuropathy, flushing, hypotension, dermatitis, pruritis
- Cytarabine: ocular pain, foreign body sensation, photophobia and blurred vision. Dizziness, headache, confusion, cerebellar toxicity.
- Skin freckling, itching, cellulites at injection site, rash, skin sloughing of the palmar and plantar surfaces. Myalgia and bone pain

Drug interactions: None applicable

Comments: Blood and platelet transfusion according to unit guidelines. Products must be irradiated as patients are at risk of transfusion-associated graft versus host disease - ensure blood transfusion is notified and patient has received a PIL Information for patients needing irradiated blood and Alert Card

References: