DHAX +/- R (dexamethasone, cytarabine, oxaliplatin +/- rituximab) for relapsed / refractory Lymphoma

Indication: Relapsed / refractory lymphoma, for patients that cannot tolerate DHAP because of renal impairment or tinnitus.

NB. The use of oxaliplatin for this indication is not licensed.

Regimen details:
- Dexamethasone 40mg PO Days 1 to 4
- Oxaliplatin 130mg/m² IV Day 1
- Cytarabine 2000mg/m² BD IV Day 2

If rituximab is indicated:
- Rituximab 375mg/m² IV Day 1

Administration:
- Dexamethasone Oral
- Oxaliplatin IV infusion in 500ml glucose 5% over 2 hours
- Cytarabine IV infusion in 500ml sodium chloride 0.9% over 3 hours
- Rituximab IV infusion in 500ml sodium chloride 0.9%. Rate as per rituximab administration guidance. Administer rituximab before DHAX.

Premedication: Calcium gluconate 1g and Magnesium sulphate 1g in 100ml Glucose 5% over 15-30 minutes prior to oxaliplatin administration.

For patients receiving rituximab:
- 30 minutes prior to rituximab
  - Paracetamol 1000mg PO
  - Chlorphenamine 10mg IV
  - Hydrocortisone 100mg IV

Frequency:
- 21 day cycle
- Suitable for autograft: up to 2 cycles
- Not suitable for autograft: up to 2 - 4 cycles

Extravasation: Oxaliplatin is an irritant and should be administered with appropriate precautions to prevent extravasation.

If there is any possibility that extravasation has occurred, contact a senior member of the medical team and follow local protocol for dealing with cytotoxic extravasation of irritant and non-vesicant drugs.

Anti-emetics: Moderate emetogenic potential (30% - 90%). Anti-emetics as per local policy.
Supportive medication: Allopurinol 300mg od orally (100mg if renal impairment) for prevention of tumour lysis syndrome for first cycle only. Predsol 0.5% eye drops (or equivalent steroid eye drops), 1 drop, both eyes, every 2 hours whilst the patient is awake and for 3 days after cytarabine infusion. Calcium gluconate 1g and Magnesium sulphate 1g in 100ml Glucose 5% over 15-30minutes before and after oxaliplatin chemotherapy. Care in patients with known hypercalcaemia or already treated with thiazidic diuretics or digoxin. GCSF support as per local policy.

Regular investigations: Baseline & regular FBC LFTs U&Es Prior to each cycle

Dose Modifications

Haematological Toxicity

Prior to every cycle of DHAX:

<table>
<thead>
<tr>
<th>Neutrophils (x 10⁹/L)</th>
<th>Platelets(x 10⁹/L)</th>
<th>DHAX</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1.0 x 10⁹/L &amp; ≥ 100 x 10⁹/L</td>
<td>100% dose</td>
<td></td>
</tr>
<tr>
<td>&lt;1.0 x 10⁹/L &amp; / or &lt; 100 x 10⁹/L</td>
<td>Delay 7 days until neutrophils ≥1.0 x 10⁹/L and platelets ≥ 100 x 10⁹/L</td>
<td></td>
</tr>
</tbody>
</table>

Renal Impairment

No dose reductions required for creatinine clearance > 50 ml/min. Creatinine clearance ≤ 50 ml/min discuss treatment with Consultant (for consideration of dose cytarabine dose reduction).

Hepatic Impairment

Bilirubin > 34umol/L, discuss with Consultant and consider 50% dose reduction for cytarabine.

Toxicities: Oxaliplatin and Neurotoxicity

- **Acute Cold-related Dysaesthesia (CRD):**
  Many patients experience transient paraesthesia of hands & feet. Onset is during or within hours of infusion, and resolves within minutes to a few days. Symptoms are exacerbated by cold, so patient should be well advised on precautions to be taken. Does not require treatment or dose reduction.

- **Acute laryngopharyngeal dysaesthesia:**
  Some patients experience laryngopharyngeal dysaesthesia (unpleasant sensations in the throat). Onset is during or within hours of infusion, and resolves within minutes to a few days.
DHAX +/− R (dexamethasone, cytarabine, oxaliplatin +/- rituximab)
for relapsed / refractory Lymphoma

Symptoms are exacerbated by cold, so patient should be well advised on precautions to be taken. Does not require treatment or dose reduction.

<table>
<thead>
<tr>
<th>Clinical symptoms</th>
<th>Laryngopharyngeal dysesthesia</th>
<th>Platinum hypersensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnoea</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>O2 saturation</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
<tr>
<td>Difficulty swallowing</td>
<td>Present (loss of sensation)</td>
<td>Absent</td>
</tr>
<tr>
<td>Pruritus</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Cold induced symptoms</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Normal or increased</td>
<td>Normal or decreased</td>
</tr>
<tr>
<td>Treatment</td>
<td>Anxiolytics; observation in a controlled clinical setting until symptoms abate or at clinician’s discretion</td>
<td>Oxygen, steroids, adrenaline, bronchodilators, antihistamine; Fluids and vasoressors if appropriate</td>
</tr>
</tbody>
</table>

Following treatments to be initiated only after discussions with the consultant:

**Subsequent infusions** after episode of laryngopharyngeal dysesthesia oxaliplatin should be given over 6 hours.

**Cumulative Dose related peripheral sensory neuropathy**
Usually occurs after a cumulative dose of 800mg/m². It can occur after treatment with oxaliplatin is completed, and is usually reversible, taking approx 3 – 5 months to recovery.

**Allergic reactions to oxaliplatin during infusion**
Immediate intervention is to stop the infusion and call for medical help. Treat with IV corticosteroid and antihistamine. At Consultant discretion, the patient may be re-challenged with oxaliplatin on the next cycle, with the following premedication prescribed:
Dexamethasone 4mg po 6hrly x 3 doses, starting 24hrs pre-treatment, plus 8mg IV 30 minutes pre dose and Chlorphenamine 10mg IV and Ranitidine 50mg IV 30 minutes pre-dose.

**Patients who have severe reactions should not be re-challenged, as per SPC.**

**Drug interactions:** Aminoglycoside antibiotics- increased risk of ototoxicity with oxaliplatin

**References:**

Dose modifications as per UCLH Dosage Adjustment for Cytotoxics January 2009.

| Reason for Update: Review of haematological parameters, anti-emetic and GCSF comments updated to state as per local policy | Approved by Consultant: P Fields |
| Version: 2 | Approved by Chair Haem TWG: M Kazmi |
| Supersedes: Version 1 | Date: 30/08/12 |
| Prepared by: Laura Cameron | Checked by (Network Pharmacist): J Turner 15/08/12 |