GEM-P +/- R (Gemcitabine, Cisplatin, Methylprednisolone +/- Rituximab) for relapsed Lymphoma

Indication:
Relapsed Lymphoma
Second-line salvage

NB. Gemcitabine and cisplatin are not licensed for this indication
Rituximab is not licensed in the relapse setting with this combination of chemotherapy; confirm local funding arrangement e.g. via CDF.

Regimen details:
- Gemcitabine $1000mg/m^2$ IV Day 1, 8, 15
- Cisplatin $100mg/m^2$ IV Day 15
- Methylprednisolone $1000mg$ IV Days 1 to 5

If rituximab is indicated:
- Rituximab $375mg/m^2$ IV Day 1

Administration:
- Gemcitabine IV infusion in 250-500ml sodium chloride 0.9% over 30 minutes
- Cisplatin IV infusion in 1000ml sodium chloride 0.9% over 4 hours (starting 4 hours after the gemcitabine infusion). Pre- and post- hydration is required, please see information in supportive medication section below.
- Methylprednisolone IV infusion in 100ml sodium chloride 0.9% over 30 minutes
- Rituximab IV infusion in 500ml sodium chloride 0.9%. Rate as per rituximab administration guidance. Administer rituximab before gemcitabine.

Premedication:
None required for GEM-P
For patients receiving rituximab:
- Paracetamol 1000mg PO 30 minutes prior to rituximab
- Chlorphenamine 10mg IV
- Hydrocortisone 100mg IV

Frequency:
28 day cycle for 2 - 4 cycles

Extravasation:
Cisplatin 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.
Gemcitabine is a non-vesicant.
Anti-emetics: Moderate emetogenic potential (30%-60% incidence) day 1 and day 8. Very High emetogenic potential (> 90%) incidence) day 15. 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. PPI prophylaxis. Mouthcare as per local policy. Pre- and post- cisplatin hydration as per local policy, for example Pre-hydration 1000ml sodium chloride 0.9% + 20mmol potassium chloride + 1g magnesium sulphate over 1 hour Furosemide 40mg orally Commence cisplatin when urine output > 100ml/hour Post-hydration 1000ml sodium chloride 0.9% to run concurrently with the cisplatin 1000ml sodium chloride 0.9% + 40mmol potassium chloride + 1g magnesium sulphate over 4 hours

Regular investigations: Baseline & regular FBC Prior to days 1, 8 and 15 of every cycle LFTs Prior to day 1 of every cycle U&Es Prior to days 1 and 15 of every cycle

Dose Modifications

Haematological Toxicity

Prior to day 1, 8 and 15:

<table>
<thead>
<tr>
<th>Neutrophils (x 10^9/L)</th>
<th>Platelets (x 10^9/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1.0 x 10^9/L</td>
<td>&amp; ≥ 75 x 10^9/L</td>
<td>100% dose</td>
</tr>
<tr>
<td>0.5 – 0.9 x 10^9/L</td>
<td>&amp; / or 50 – 74 x 10^9/L</td>
<td>75% dose gemcitabine and cisplatin</td>
</tr>
<tr>
<td>&lt; 0.5 x 10^9/L</td>
<td>&amp; / or &lt; 50 x 10^9/L</td>
<td>Hold both gemcitabine and cisplatin until recovery. GCSF support if reoccurs and then 75% dose in subsequent cycles.</td>
</tr>
</tbody>
</table>

Doses reduced for haematological toxicity should continue for subsequent cycles.
Renal Impairment

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Cisplatin Dose</th>
<th>Gemcitabine Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60</td>
<td>Give 100%</td>
<td></td>
</tr>
<tr>
<td>50 – 60</td>
<td>Give 75% of the dose</td>
<td></td>
</tr>
<tr>
<td>40 – 50</td>
<td>Give 50% of the dose</td>
<td></td>
</tr>
<tr>
<td>&lt; 40</td>
<td>Omit and discuss with Consultant</td>
<td>Consider dose reduction, clinical decision</td>
</tr>
</tbody>
</table>

Hepatic Impairment

- Bilirubin > 27umol/L, discuss with Consultant and if not thought to be disease related, consider reducing gemcitabine dose to 800mg/m²
- Cisplatin: No dose reduction required

Toxicities:

- In the event of grade 3 or 4 non-haematological toxicity, reduce the gemcitabine dose by 25% and the cisplatin dose by 50%.
- With the first occurrence of transient tinnitus reduce the cisplatin dose to 80mg/m² and with the second occurrence to 60mg/m². Cisplatin should be discontinued in patients with unresolved or recurrent tinnitus.

Drug interactions:

- If possible, avoid any other potentially nephrotoxic drugs.

Comments:

- GFR should be calculated using the Cockcroft & Gault equation in all patients; if the calculated GFR < 60ml/min measure EDTA clearance or creatinine clearance before prescribing. Monitor trends in serum creatinine between treatments: if > 25% from baseline value re-calculate using the Cockcroft & Gault equation.
- Encourage oral hydration during treatment; for instance drink a glass of water every hour during treatment and at least a further 2 litres over the 24 hours following treatment. Weight should be recorded prior to and at the end of cisplatin treatment, and a strict fluid balance chart should be maintained. An average urine output of at least 100ml/hour must be maintained throughout treatment and cisplatin infusion should not be commenced unless this urine output is achieved. For low urine output consider increasing the pre-hydration and diuretic regimen. Consider adding diuretics in weight–gain of 1.5kg or symptoms of fluid overload.

References:

- Chau I et al. Gemcitabine, cisplatin and methylprednisolone chemotherapy (GEM-P) is an effective regimen in patients with poor prognostic primary progressive or multiply relapsed Hodgkin’s and non-Hodgkin’s lymphoma. Br J Haematol 2003; 120: 970-977

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Prepared by: Laura Cameron
Checked by (Network Pharmacist): Jacky Turner
Approved by SELCN DTAC Chair:
Date: 23 Apr 2012
Ng M et al. Gemcitabine, cisplatin and methylprednisolone (GEM-P) is an effective salvage regimen in patients with relapsed and refractory lymphoma. Br J Cancer 2005; 92: 1352-1357

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