**R-GDP: Rituximab, Gemcitabine, Dexamethasone & Cisplatin**

**INDICATION**

Relapsed or refractory Hodgkin and non-Hodgkin lymphoma.

Omit Rituximab for patients with Hodgkin Lymphoma.

**TREATMENT INTENT**

Palliative or curative depending on context.
Can be used for salvage therapy before Autologous Stem Cell Transplantation.

**PRE-ASSESSMENT**

1. Ensure histology is confirmed prior to administration of chemotherapy and document in notes.

2. Record stage of disease - CT scan (neck, chest, abdomen and pelvis) and/or PET-CT, presence or absence of B symptoms, clinical extent of disease, bone marrow aspirate and trephine.

3. Blood tests - FBC, U&Es, LDH, urate, calcium, magnesium, creatinine, LFTs, glucose, Igs, hepatitis B core antibody and hepatitis BsAg, hepatitis C antibody, EBV, CMV, VZV, HIV 1+2 after consent, group and save.

4. Send a "group and save" sample to transfusion and inform patient and transfusion laboratory that they will require irradiated blood products for 7 days before harvest.

   See ‘Guidelines for the use of blood components in adult haematology’ for details.
   Ensure irradiation card is attached to the patient's notes and copy given to the patient.

5. Urine pregnancy test - before cycle 1 of each new chemotherapy course in women aged 12 – 55 years of age unless they have been sterilised or undergone a hysterectomy.

6. ECG +/- Echo - *if clinically indicated*.

7. Record performance status (ECOG).
8. Record height and weight.

9. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent on the day of treatment.

10. Hydration - *in patients with bulky disease* pre-hydrate with sodium chloride 0.9% 1 litre over 4-6 hours. Patients at high risk of tumour lysis refer to tumour lysis protocol.


12. Treatment should be agreed in the relevant MDT.

13. Venous access should be assessed well in advance of collection. Every effort should be made not to use antecubital fossa veins in the run up to harvest.

14. If good antecubital fossa veins, insert Hickman line. Apheresis line to be inserted if poor antecubital veins.

15. Ensure the peripheral stem cell harvest / final donor clearance form (form FRM3721/1) is sent within 30 days of scheduled harvest date, via nhs.net mail to NHSBT STS, to confirm eligibility for PBSCH.

**NB:** Infective agent screen. Peripheral blood stem cells for autologous transplant are cryopreserved in liquid nitrogen. In order to eliminate the risk of transmitting infective agents during the storage of marrow, virology testing is mandatory within 30 days of the harvesting procedure and results must be known before priming. Bottles and consent form provided by NBS Oxford. Please send to the Stem Cell Laboratory, Oxford. Address provided on consent form.

**DRUG REGIMEN**

**Day 1**

**Pre-med** - paracetamol 1g po, chlorphenamine 10 mg iv, hydrocortisone 100 mg iv 30 minutes before rituximab  
*RITUXIMAB* 375 mg/m² iv infusion in 500 ml sodium chloride 0.9%

**Days 1 & 8**  
**GEMCITABINE** 1000mg/m² in 250 ml sodium chloride 0.9% iv infusion over 30 minutes

**Day 1**  
**Pre-Hydration:**  
1L sodium chloride 0.9% + 20 mmol KCl + 8 mmol MgSO4 infusion over 2 hours.
200 ml Mannitol 10% intravenous infusion over 30 minutes. Furosemide 40 mg may be added if required.

**Day 1**  
**CISPLATIN** 75mg/m² iv infusion in 1000 ml sodium chloride 0.9% over 2 hours. Cisplatin must be started 4 hours after the gemcitabine infusion.

**Day 1**  
**Post-Hydration**  
1L sodium chloride 0.9% + 20 mmol KCl + 8 mmol MgSO₄ infusion over 2 hours.

**Days 1 to 4**  
**DEXAMETHASONE** 40mg PO once daily

*When used for priming:*

**Days 9 to 15**  
Daily G-CSF as per local policy. Continue until mobilisation completed. *G-CSF should be discontinued after completion of stem cell harvesting. (Pegfilgrastim must NOT be used) Aim to collect days 15/16

*When not used for priming:*

**Days 9 to 15**  
Daily G-CSF as per local policy for cycle 1, rituximab can be administered on the day before the gemcitabine/cisplatin to ensure that enough time is available to use this as a day-unit protocol

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**CYCLE FREQUENCY**

Repeat every 21 days, maximum of three cycles.

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**RESTAGING**

After 2 cycles with either CT or PET/CT

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**DOSE MODIFICATIONS**

Haematological Toxicity
<table>
<thead>
<tr>
<th>Day(s) of cycle</th>
<th>ANC (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>Action this cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 1.0 AND ≥ 75</td>
<td></td>
<td>100% all drugs</td>
</tr>
<tr>
<td></td>
<td>≥ 1.0 AND &lt;75</td>
<td></td>
<td>Delay 1 week⁺</td>
</tr>
<tr>
<td></td>
<td>&lt;1.0 AND ≥ 75</td>
<td></td>
<td>If ANC then ≥ 0.5, proceed with 100% and support with GCSF**</td>
</tr>
<tr>
<td></td>
<td>&lt;1.0 AND &lt;75</td>
<td></td>
<td>Delay 1 week⁺</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>If ANC then ≥ 0.5 and plt ≥ 50, give 100% dosing. Support with GCSF, transfusions as necessary**</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OR</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>If ANC &lt;0.5 and/or plt &lt;50 defer and check counts every 3 days. Resume when ANC ≥0.5 and plt ≥50**</td>
</tr>
<tr>
<td>Day 8</td>
<td>≥1.0 AND ≥75</td>
<td></td>
<td>Give 100% gemcitabine</td>
</tr>
<tr>
<td></td>
<td>0.5 -1.0 AND ≥75</td>
<td></td>
<td>Give 100% gemcitabine and support with GCSF**, or reduce by 25%</td>
</tr>
<tr>
<td></td>
<td>--- 50-75</td>
<td></td>
<td>Reduce gemcitabine by 25%</td>
</tr>
<tr>
<td></td>
<td>&lt;0.5 OR &lt;50</td>
<td></td>
<td>OMIT gemcitabine and start GCSF**</td>
</tr>
</tbody>
</table>

⁺ if counts presumed to be low due to marrow involvement, treat after 1 week delay (i.e. at 28 days) despite counts

** GCSF should be given prophylactically for all future cycles
Renal & Hepatic Dysfunction

Cisplatin:

<table>
<thead>
<tr>
<th>GFR (ml/min)</th>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60</td>
<td>100%</td>
<td>No dose reduction necessary.</td>
</tr>
<tr>
<td>45-59</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>&lt;45</td>
<td>consider carboplatin</td>
<td></td>
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</tbody>
</table>

Consider carboplatin if GFR <45 ml/min. Conflicting information. Where GFR is less than 45 mls/min - clinical decision.

Ototoxicity:
Grade 2 or above, discuss with consultant – dose may need to be reduced.

Gemcitabine:

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl &lt;30 ml/min consider dose reduction - Clinical decision</td>
<td>Gemcitabine: limited information, consider dose reduction if bilirubin elevated. If bilirubin &gt;27 micromol/L, then initiate treatment at 800 mg/m².</td>
</tr>
</tbody>
</table>

Reduce gemcitabine and cisplatin doses by 25% and 50% for all other grade 3 or 4 non-haematological toxicities respectively.

INVESTIGATIONS

- FBC, U&Es, Creatinine, LFTs
- Mg++, Ca++, K⁺.

HARVESTING (if used for priming)

- Stem cell collection performed days 15 & 16
- Aim to collect minimum of 2.0 x 10⁶ with target of 4.0 x 10⁶ CD34-positive cells/kg

CONCURRENT MEDICATION

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose and duration</th>
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<tr>
<td>Allopurinol</td>
<td>300 mg daily for 7 days starting 24-48 hours prior to</td>
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</tbody>
</table>
Ranitidine (or PPI if specifically indicated - discuss with consultant)  
Daily for the duration of treatment

Fluconazole  
50 mg daily for the duration of treatment

Aciclovir  
200 mg three times a day for duration of treatment and for 3 months afterwards

Co-trimoxazole  
480 mg daily on Mon/Wed/Fri for duration of treatment and for 3 months afterwards (Consider reducing the dose to 480 mg twice weekly during neutropenic periods)

G-CSF (priming/standard)  
As per local policy

EMETIC RISK

Day 1 High  
Day 8 low  
Beware of delayed emesis with Cisplatin.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Diarrhoea  
Mucositis  
Cisplatin Nephrotoxicity - ensure adequate pre and post hydration is prescribed.  
Ototoxicity - assess patient for tinnitus or hearing abnormalities.

TREATMENT RELATED MORTALITY

Estimated 1-2%.

REFERENCES


S Daniels, Guy's & St Thomas' NHS Trust April 2001.
