L.17 DEXAMETHASONE + RITUXIMAB + CYCLOPHOSPHAMIDE (DRC)

INDICATION

Lymphoplasmacytic lymphoma / Waldenstrom's macroglobulinaemia.

NB: For patients with significantly raised viscosity, rituximab may cause a transient rise in the paraprotein (and therefore viscosity) and / or a flare of paraprotein-associated symptoms such as neuropathy. In these patients, consider plasma exchange immediately before giving first cycle; or using Cyclo+Dex only initially and introducing rituximab once the total IgM<40g/dL and / or plasma viscosity < 4.

TREATMENT INTENT

Palliative.

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), presence or absence of B symptoms, clinical extent of disease, bone marrow aspirate and trephine.
3. Blood tests - FBC, DAT, U&Es, LDH, ESR, urate, calcium, magnesium, creatinine, LFTs, glucose, Igs, β₂ microglobulin, hepatitis B core antibody and hepatitis BsAg, hepatitis C antibody, EBV, CMV, VZV, HIV 1+2 after consent, group and save.
4. 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.
5. ECG +/- Echo - if clinically indicated.
6. Record performance status (WHO/ECOG).
7. Record height and weight.
8. 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.
9. Fertility - it is very important the patient understands the potential risk of infertility, all patients should be offered fertility advice (see fertility guidelines).
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).
11. Consider dental assessment / Advise dental check is carried out by patient's own dental practitioner before treatment starts.
12. Treatment should be agreed in the relevant MDT.
DRUG REGIMEN

Day 1  
Pre med - Paracetamol 1 g po, chlorphenamine 10 mg iv, then,  
DEXAMETHASONE 20 mg iv.  
RITUXIMAB 375 mg/m² iv infusion daily in 500 ml sodium chloride 0.9%.  
Omit Rituximab if total IgM > 40g/dL and / or plasma viscosity >4, unless  
plasmapharesis performed immediately prior to first cycle

Days 1 to 5  
CYCLOPHOSPHAMIDE 100 mg/m² po bd (round to the nearest 50mg tablet) (total dose  
per cycle : 1,000 mg/m²)

Note: Dexamethasone is being used as part of the chemotherapy combination regime.

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neuropathy. In these patients, consider plasma exchange immediately before giving first cycle (or  
using DC initially, adding in the rituximab once the paraprotein is reducing/total IgM < 40g/dL and  
plasma viscosity < 4).

CYCLE FREQUENCY

Cycle repeats every 21 days, for a total of 6 cycles.

RESTAGING

Monitor paraprotein and other laboratory parameters prior to every cycle. Repeat CT after 4 cycles,  
and then at end of treatment if measurable disease at baseline. Repeat bone Marrow when  
clinically indicated to confirm disease response or progression.

DOSE MODIFICATIONS

If patient is on clinical trial, modify as per trial protocol.

Hematological toxicity

<table>
<thead>
<tr>
<th>Neutrophils x 10⁹/L</th>
<th>Platelets x 10⁹/L</th>
<th>Cyclophosphamide</th>
<th>Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1.5 and</td>
<td>≥100</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>1.0 - 1.49 and</td>
<td>≥100</td>
<td>75%</td>
<td>100%</td>
</tr>
<tr>
<td>0.5 - 1.0 and/or</td>
<td>50-100</td>
<td>50%</td>
<td>100%</td>
</tr>
<tr>
<td>&lt;0.5 and/or</td>
<td>&lt;50</td>
<td>Omit</td>
<td>100%</td>
</tr>
</tbody>
</table>
Renal/Hepatic impairment

Cyclophosphamide:

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR (ml/min)</td>
<td></td>
</tr>
<tr>
<td>&gt;20</td>
<td>100%</td>
</tr>
<tr>
<td>10-20</td>
<td>75%</td>
</tr>
<tr>
<td>&lt;10</td>
<td>50%</td>
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<td></td>
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<tr>
<td>Clinical decision – consider whether patient is being treated with high dose treatment.</td>
<td>Clinical Decision: SmPC states “not recommended in patients with a bilirubin &gt;17μmol/L or serum transaminases or ALP more than 2-3 x upper limit of normal and doses should be reduced”. However, exposure to active metabolites may not be increased, suggesting dose reduction may not be necessary.</td>
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</tbody>
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INVESTIGATIONS

FBC, renal and liver profiles, only FBC result essential prior to administration of chemotherapy.

CONCURRENT MEDICATION

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose and duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allopurinol</td>
<td>300 mg daily for 7 days starting 24-48 hours prior to chemotherapy cycle 1 only</td>
</tr>
<tr>
<td>Ranitidine (or PPI if specifically indicated - discuss with consultant)</td>
<td>Daily for days 1-5</td>
</tr>
<tr>
<td>Aciclovir</td>
<td>200 mg three times a day for duration of treatment and for 3 months after completion</td>
</tr>
</tbody>
</table>

EMETIC RISK

Moderate emetic risk.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Cyclophosphamide may irritate the bladder mucosa. Patients should be encouraged to drink a minimum of three liters of fluid per 24 hrs.

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REATMENT RELATED MORTALITY

Mortality associated with regimen expected to be approximately 1%.
REFERENCES


