PIXANTRONE

INDICATION
Monotherapy for relapsed / refractory Diffuse Large B-cell Lymphoma as 3rd or 4th line treatment.

Pixantrone trial only included patients who had responded to an anthracycline-containing regimen for at least 24 weeks.

NOTE: This drug is NICE approved for the above indication.

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) 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.
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. Patients with cardiac disease or risk factors, e.g. baseline LVEF value of < 45%, clinically significant cardiovascular abnormalities (NYHA Grade 3 or 4), myocardial infarction within the last 6 months, severe arrhythmia, uncontrolled hypertension, uncontrolled angina, or prior cumulative doses of doxorubicin (or equivalent) exceeding 450 mg/m² should receive careful risk versus benefit consideration before receiving treatment.
6. Record performance status.
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. 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.
10. Consider dental assessment / Advise dental check is carried out by patient's own dental practitioner before treatment starts.
11. Treatment should be agreed in the relevant MDT.
Lymphoma group

**DRUG REGIMEN**

Days 1, 8, 15  **PIXANTRONE** 50 mg/m² (of base drug which equates to 85 mg/m² of pixantrone dimaleate) daily in 250 ml sodium chloride 0.9% iv infusion over at least 60 minutes.

Final concentration < 0.58 mg/mL.

Infuse via a 0.2 μm pore size in-line filter (polyethersulfone, acrylic, or cellulose acetate).

**CYCLE FREQUENCY**

Repeat every 28 days, normally for up to 6 cycles.

**RESTAGING**

After second course (evidence suggests that most responses after observed by course 2).

**CONTRA-INDICATIONS**

Hypersensitivity to drug or any excipients
Immunisation with live virus vaccines
Profound bone marrow suppression
Severe abnormal hepatic function

**DOSE MODIFICATIONS**

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

**Haematological toxicity**

<table>
<thead>
<tr>
<th>Day</th>
<th>ANC x 10⁹/L</th>
<th>Platelets x 10⁹/L</th>
<th>Dose modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥ 1.0 *</td>
<td>≥ 75 *</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>&lt; 1.0</td>
<td>&lt; 75</td>
<td>delay until recovers to *</td>
</tr>
<tr>
<td>8 &amp; 15</td>
<td>≥ 1.0 **</td>
<td>≥ 50 **</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>0.5 - &lt; 1.0</td>
<td>25 - &lt; 50</td>
<td>delay until recovers to **</td>
</tr>
<tr>
<td></td>
<td>&lt; 0.5</td>
<td>&lt; 25</td>
<td>delay until recovers to ** reduce to 80% dose</td>
</tr>
</tbody>
</table>

**Non-haematological toxicity**

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Grade 3 or 4 drug related non-cardiac toxicity other than nausea and vomiting</td>
<td>Delay until Grade 1. Reduce to 80% dose.</td>
</tr>
<tr>
<td>Any Grade 3 or 4 NYHA cardiovascular toxicity or persistent LVEF decline</td>
<td>Delay treatment and monitor until recovery. Consider discontinuation for persistent decline in LVEF of ≥ 15% of baseline value.</td>
</tr>
</tbody>
</table>
Hepatic and Renal impairment

The safety and efficacy of Pixantrone has not been established in patients with either impaired renal function or impaired hepatic function.

Patients with serum creatinine > 1.5 x ULN were excluded from the randomised study. Thus, Pixantrone should be used with caution in patients with renal impairment.

Pixantrone should be used with caution in patients with mild or moderate liver impairment. Pixantrone is not recommended for use in patients with severe excretory hepatic impairment.

INVESTIGATIONS

FBC, U&Es, Creatinine, LFTs.

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 (first course / cycle only)</td>
</tr>
<tr>
<td>Ranitidine (or PPI if specifically indicated - discuss with consultant)</td>
<td>Daily for the duration of treatment</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>50 mg daily for the duration of treatment</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.

SPECIAL WARNINGS / PRECAUTIONS

- Severe myelosuppression, predominantly neutropenia; G-CSF may be used.
- Changes in cardiac function: decreased LVEF or fatal CHF. Cardiotoxicity may occur whether or not cardiac risk factors are present. Monitor cardiac function before initiation of treatment, during and after. NOTE: patients were included in the pivotal study if they received a cumulative doxorubicin (or equivalent) dose of NO GREATER than 400 mg/m².
- Secondary AML or MDS.
- Infections, e.g. pneumonia, cellulitis, bronchitis, sepsis. Avoid in active, severe infection or with a history of recurring / chronic infections / underlying conditions predisposing to serious infection.
- Tumour lysis syndrome.
- Sun protection strategies (clothing, sunscreen strongly absorbing UV-A).
TREATMENT RELATED MORTALITY

Expected to be 1-2%.

REFERENCES


