Fludarabine, Mitoxantrone & Dexamethasone (FMD) ORALLY for Follicular and other indolent lymphomas

Indication: Relapsed Follicular and other indolent lymphomas.

Regimen details:
- Fludarabine 40mg/m² orally Days 1 to 3
- Mitoxantrone 10mg/m² IV Day 1
- Dexamethasone 20mg orally Days 1 to 5

Round the fludarabine dose to the nearest 10mg.

Administration:
- Mitoxantrone: IV infusion in 50-100ml sodium chloride 0.9% over 15 minutes.
- Fludarabine and Dexamethasone: Orally

Premedication: Not applicable

Frequency: Every 28 days

For up to 8 cycles

Extravasation: Mitoxantrone is an irritant

Anti-emetics: Moderate emetogenic potential (< 30%-60% incidence)

Supportive medication:
- Allopurinol 100 - 300 mg od (dependent on renal function) for first cycle only.
- PCP prophylaxis as per local policy until 6 months after the last cycle or CD4 > 200 x 10⁹/L.
- Antifungal and antiviral prophylaxis as per local policy
- PPI or H₂ receptor antagonist as per local policy.

Regular investigations:
- FBC D1
- U&E D1
- LFTs D1
- Baseline DAT

Dose Modifications

Haematological Toxicity due to treatment:

Give full dose for first cycle regardless of counts

<table>
<thead>
<tr>
<th>Neutrophils (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>Fludarabine and mitoxantrone dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.5 x 10⁹/L</td>
<td>&amp;</td>
<td>≥ 100 x 10⁹/L</td>
</tr>
<tr>
<td>&lt; 1.5 x 10⁹/L</td>
<td>&amp; / or</td>
<td>&lt; 100 x 10⁹/L</td>
</tr>
</tbody>
</table>

If after 2 weeks delay the values have not changed, proceed at 50% dose of fludarabine and mitoxantrone.
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Renal Impairment

Creatinine clearance 30 – 60 ml/min give 50% fludarabine dose.

No dose alterations are required for mitoxantrone.

Hepatic Impairment

No dose reductions are required for fludarabine.

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### Hepatic Impairment

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<table>
<thead>
<tr>
<th>Bilirubin (µmol/L)</th>
<th>Mitoxantrone</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1.5 x upper limit normal</td>
<td>100% dose</td>
</tr>
<tr>
<td>1.5- 3.0 x upper limit normal</td>
<td>50% dose</td>
</tr>
<tr>
<td>&gt; 3.0 x upper limit normal</td>
<td>25% dose</td>
</tr>
</tbody>
</table>

Toxicities:

Neutropenia, thrombocytopenia, nausea.

Mitoxantrone: may cause urine, saliva, tears and sweat to turn blue-green for 24 hours post infusion. Whites of eyes may have a blue-green tinge (this is normal). Arrhythmias

Drug interactions:

Not applicable

Comments:

Blood and platelet transfusion according to unit guidelines. Products must be irradiated as patients are at risk of transfusion-associated graft versus host disease - ensure blood transfusion is notified and patient has received a PIL Information for patients needing irradiated blood and Alert Card

Maximum cumulative lifetime dose mitoxantrone = 160mg/m²

A baseline MUGA scan or echocardiogram should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, obese, smoker, elderly, previous exposure to anthracyclines, previous thoracic radiotherapy.

MUGA scan should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative anthracycline dose approaches maximum.

Maximum cumulative lifetime doses of anthracyclines are:

- doxorubicin: 450 – 550 mg/m²
- daunorubicin: 500 - 600mg/m²
- epirubicin: 950mg/m²
- idarubicin: 93mg/m²
- mitoxantrone: 160mg/m²

To calculate total exposure to anthracyclines, calculate for each drug the total dose received as a percentage of the lifetime dose for that drug. Add the percentage for each drug administered in the past. Maximum lifetime cumulative anthracycline dose is 100%.

References: