Pegylated Liposomal Doxorubicin (Caelyx) for Primary Cutaneous T cell Lymphoma

Indication: Advanced Mycosis Fungoides - Stage IIb, IVa and IVb first or subsequent lines
Other tumour stage and Advanced Primary Cutaneous T cell Lymphoma

Regimen details: Pegylated Liposomal Doxorubicin (Caelyx) 20mg/m² IV D1,D15 (q28 days)

(*) For patients with poor performance status (PS):

Pegylated Liposomal Doxorubicin (Caelyx) 20mg/m² IV D1 (q28 days)

Administration: Caelyx, by infusion in 5% Dextrose:

Caelyx dose < 90mg Dilute in 250mls 5% Dextrose

Caelyx is incompatible with Sodium Chloride. The IV line should be flushed before and after the infusion with 5% Dextrose

The initial Caelyx dose should be administered no faster than 1mg/minute, to minimize the risk of infusion reactions. If no infusion reaction occur with the first dose, subsequent Caelyx infusions may be administered over 1 hour

In those patients who experience an infusion reaction, stop temporarily the infusion until symptoms have cleared with or without further therapy (antihistamines, corticosteroids, adrenaline) and resume treatment, at a slower rate, as follows:
5% of the total dose should be infused slowly over the first 15 minutes
If tolerated, without reaction: may double the infusion rate for the next 15 minutes
If tolerated: complete the infusion over the next hour for a total infusion time of 90 minutes

Frequency: Every 28 days, for 6 - 8 cycles

(*) Every 28 days for 6 - 8 cycles (poor PS)

The dose can be increased to 30mg/m² in certain cases to maximise response. Needs discussion with Consultant.

Extravasation: Caelyx: Non-vesicant

Anti-emetics: Caelyx: Low emetogenic
Follow Local Anti-emetic Policy

Supportive medication: Emollients and Pyridoxine 50mg po TDS for Palmar-Plantar Erythrodysesthesia (not scientifically proven)
Regular investigations: FBC D1&D15
LFTs D1&D15
U&Es D1&D15
Clinical Skin scoring and Imaging Every 2 cycles
MUGA scan Prior to 1st cycle in high-risk patients (see Comments)

Comments: Maximum cumulative dose Caelyx = 450 – 550mg/m²
Consider previous anthracycline exposure

A baseline MUGA scan 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 DOSE MODIFICATIONS

Haematological Toxicity

Haematological Toxicity

Neutrophils Platelets Caelyx Dose

1.5 – 1.9 x 10⁹/L or 75 – 150 x 10⁹/L Give 100% dose

0.5 – 1.4 x 10⁹/L or 25 – 74 x 10⁹/L Delay treatment until Neutrophils ≥ 1.5 x 10⁹/L and Platelets ≥ 75 x 10⁹/L; then give 100% dose

< 0.5 x 10⁹/L or < 25 x 10⁹/L Delay treatment until Neutrophils ≥ 1.5 x 10⁹/L and Platelets ≥ 75 x 10⁹/L; then give 75% dose

Renal Impairment: Caelyx: No dose reduction needed

Hepatic Impairment: Caelyx dose should be adjusted as follows:

<table>
<thead>
<tr>
<th>Bilirubin (µmol/L)</th>
<th>Caelyx Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 – 50</td>
<td>Give 50%</td>
</tr>
<tr>
<td>&gt; 51</td>
<td>Give 25%</td>
</tr>
</tbody>
</table>

Reason for Update: Network Protocol Development
Version: 2 Approved by Consultant Clinical Oncologist: Stephen Morris
Supersedes: All other versions Date: 25.03.10
Prepared by: Maria Teresa Pacheca-Palomar Nov’09 Checked by (Network Pharmacist): Jacky Turner
Approved by SELCN DTAC Chair: Janine Mansi Date: 19.05.10
DOSE MODIFICATIONS FOR OTHER TOXICITIES AS APPROPRIATE

<table>
<thead>
<tr>
<th>TOXICITY GRADE After Prior Caelyx Dose</th>
<th>PALMAR-PLANTAR ERYTHRODYSESTHESIA</th>
<th>STOMATITIS</th>
<th>WEEK 4 After Prior Caelyx Dose</th>
<th>WEEK 5 After Prior Caelyx Dose</th>
<th>WEEK 6 After Prior Caelyx Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mild erythema, swelling or Desquamation not interfering with ADL</td>
<td>Painless ulcers, erythema or mild soreness</td>
<td>Redose unless patient experienced a previous Grade 3 or 4 toxicity, in which case wait an additional week</td>
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<td>Give 75% dose and return to 4 week interval or stop treatment-discuss with Consultant</td>
</tr>
<tr>
<td>2</td>
<td>Erythema, desquamation or swelling interfering with but not precluding normal physical activities; small blisters or ulcerations &lt; 2cm in diameter</td>
<td>Painful erythema, oedema or ulcers, but can eat</td>
<td>Wait an additional week</td>
<td>Wait an additional week</td>
<td>Give 75% dose and return to 4 week interval or stop treatment-discuss with Consultant</td>
</tr>
<tr>
<td>3</td>
<td>Blistering, ulceration or swelling interfering with walking or normal daily activities; cannot wear usual clothing</td>
<td>Painful erythema, oedema or ulcers, but cannot eat</td>
<td>Wait an additional week</td>
<td>Wait an additional week</td>
<td>No further treatment</td>
</tr>
<tr>
<td>4</td>
<td>Diffuse or local process causing infectious complications, or a bedridden state or hospitalisation</td>
<td>Requires parenteral or enteral support</td>
<td>Wait an additional week</td>
<td>Wait an additional week</td>
<td>No further treatment</td>
</tr>
</tbody>
</table>

The following measures may help to minimise the risk of PPE for the first 4 – 7 days after Caelyx infusion:

Keep hands and feet as cool as possible
Do not wear tight fitting gloves or socks and avoid wearing tight-fitting footwear and high heeled shoes
Avoid exposing the skin to very hot water, such as the bath or washing up
Do not rub the skin vigorously or use abrasive washcloths. Pat skin dry after washing
Avoid the use of topical anaesthetics as they can worsen skin reactions

Toxicities: Myelosuppresion; infection; mucositis; taste alteration; skin changes; Palmar-Plantar Erythrodysesthesia; hot flashes; backache; photosensitivity; urine discolouration; infusion associated reactions; tiredness; cardiotoxicity

Drug interactions: Caelyx :
- Ciclosporin (high dose) increase Caelyx serum levels and myelotoxicity
- Concomitant use of other cardioactive compounds e.g. calcium channel blockers require monitoring of cardiac function throughout treatment
- Myelotoxic cytotoxic agents : use with caution
- Phenytoin : reduced blood levels of the anticonvulsant and increased seizure activity
- Warfarin : the anticoagulant effect is increased
References:

www.medicines.org.uk
Wollina U et al. Multicentre study of Pegylated Liposomal Doxorubicin in patients with cutaneous T cell Lymphoma. Cancer 2003; Sep 1; Vol 98; n5 9 993 – 1001
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UCLH- Dosage Adjustment for Cytotoxics in Renal Impairment. November 2003
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