LIPOSOMAL DOXORUBICIN (CAELYX)

A 2nd line or subsequent treatment option for women with ovarian cancer whose disease does not respond to, or whose disease relapses within twelve months from, platinum-based therapy.
NICE approved April 2016

Drug/Dosage: Liposomal doxorubicin (Caelyx) 40mg/m² IV Day 1
The dose may be increased to 50mg/m² on subsequent cycles if well tolerated, and only with Consultant approval

Administration: For doses < 90mg dilute in 250ml 5% glucose
For doses ≥ 90mg dilute in 500ml 5% glucose
Prior to infusion the giving set should be primed with 5% glucose.
Following administration, flush the line with 5% glucose

To minimise the risk of infusion reactions, the initial dose is administered at a rate no greater than 1mg/minute. If no infusion reaction is observed, subsequent Caelyx infusions may be administered over 1 hour.

For infusion-associated reactions to caelyx:
Stop the infusion – usually symptoms resolve without further intervention. However, emergency supportive treatment should be available. In most patients, treatment can be resumed at a slower rate after all symptoms have been resolved, without recurrence.
Infusion reactions rarely recur after the first treatment cycle.

Frequency: 4 weekly cycle for 6 cycles
Clinical review prior to each cycle

Main Toxicities: myelosuppression; palmar/plantar erythema (PPE) (see Comments); stomatitis; infusion associated reactions (see Comments); cardiotoxicity (see Comments); alopecia (uncommon)

Anti-emetics: moderately emetogenic

Extravasation: non-vesicant

Regular Investigations:
FBC Day 1
U&Es Day 1
LFTs Day 1
CA 125 Day 1
MUGA Prior to starting, and during treatment (see Comments)

Comments:
Maximum cumulative dose = 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.

To minimise risk of PPE for the first 4 – 7 days after Caelyx infusion:
Keep hands & 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.

Dose Modifications

Haematological Toxicity:

<table>
<thead>
<tr>
<th>Neutrophil Count</th>
<th>Platelets</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.5 x10^9/l</td>
<td>≥ 75 x10^9/l</td>
<td>Give 100% dose.</td>
</tr>
<tr>
<td>0.5 - 1.4 x10^9/l</td>
<td>25 - 75 x10^9/l</td>
<td>Wait until neutrophil count ≥ 1.5 x10^9/l &amp; platelets ≥ 75 x10^9/l; then continue with 100% dose.</td>
</tr>
<tr>
<td>&lt; 0.5 x 10^9/l</td>
<td>&lt; 25 x10^9/l</td>
<td>Wait until neutrophil count ≥ 1.5 x10^9/l and platelets ≥ 75 x10^9/l; then give 75% dose</td>
</tr>
</tbody>
</table>

Hepatic Impairment:

<table>
<thead>
<tr>
<th>Bilirubin (µmol/l)</th>
<th>Caelyx Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>Give 100%</td>
</tr>
<tr>
<td>20 – 51</td>
<td>Give 75%*</td>
</tr>
<tr>
<td>&gt; 51</td>
<td>Give 50%*</td>
</tr>
</tbody>
</table>

*If the first dose is tolerated without an increase in bilirubin or LFTs, the second dose can be increased to the next dose level (from 50% to 75%; from 75% to 100%) and then titrated to full dose on subsequent cycles if again tolerated.

Cutaneous Toxicity (PPE and Stomatitis): Treat symptoms accordingly, and follow dosing guidelines below for future cycles. Pyridoxine can be used for Grade 1 or above PPE.

<table>
<thead>
<tr>
<th>Toxicity Grade after prior Caelyx dose</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>Grade 1</td>
<td>Give full dose unless patient has experienced a previous Grade 3 or 4 toxicity, in which case wait an additional week</td>
<td>Give full dose unless patient has experienced a previous Grade 3 or 4 toxicity, in which case wait an additional week</td>
<td>Decrease dose by 25% and give 4 weekly or withdraw – clinical decision</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Wait an additional week</td>
<td>Wait an additional week</td>
<td>Decrease dose by 25% and give 4 weekly or withdraw – clinical decision</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Wait an additional week</td>
<td>Wait an additional week</td>
<td>No further treatment</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Wait an additional week</td>
<td>Wait an additional week</td>
<td>No further treatment</td>
</tr>
</tbody>
</table>

Reference: Gordon, AN et al; JCO (2001); 19 (14): 3312-3322