Chemotherapy Protocol

GYNAECOLOGICAL CANCER

CARBOPLATIN (AUC5) - LIPOSOMAL DOXORUBICIN (Caelyx)

Please note this protocol is based on information for the use of the Caelyx brand of liposomal doxorubicin. Brands may not be interchangeable.

Regimen

- Ovary – Carboplatin (AUC5)- Liposomal Doxorubicin (Caelyx)

Indication

- Second line or subsequent treatment of platinum sensitive or partially platinum-sensitive relapsed ovarian cancer in patients previously treated with a taxane/platinum regimen.
- WHO performance status 0,1, 2
- Palliative intent

Toxicity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>Thrombocytopenia, peripheral neuropathy, nephrotoxicity at high doses, electrolyte disturbances</td>
</tr>
<tr>
<td>Liposomal Doxorubicin</td>
<td>Palmar plantar erythrodysthesia (hand and foot syndrome), rash, GI disturbances, cardiotoxicity, asthenia, paresthesia</td>
</tr>
</tbody>
</table>

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBC, LFT's and U&E’s prior to each cycle
- EDTA or calculated creatinine clearance prior to each cycle
- CA125 prior to each cycle
- Ensure adequate cardiac function before starting therapy. Baseline ECG and LVEF should be measured in patients with a history of cardiac problems or in the elderly. Discontinue liposomal doxorubicin if cardiac failure develops
**Dose Modifications**

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

**Haematological**

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Prior to cycle 1 the following criteria must be met;

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Eligible Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil</td>
<td>equal to or more than 1x10^9/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>equal to or more than 100x10^9/L</td>
</tr>
</tbody>
</table>

**Day 1**

| Neutrophils (x10^9/L) | Dose Modifications  
(carboplatin and liposomal doxorubicin) |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 or greater</td>
<td>100%</td>
</tr>
<tr>
<td>less than 1</td>
<td>Delay one week. If the counts have recovered to 1x10^9/L or greater at this point continue with liposomal doxorubicin 25mg/m^2 and carboplatin AUC 4.</td>
</tr>
<tr>
<td>0.5 or below for at least 7 days or febrile neutropenia</td>
<td>Delay until recovery to 1x10^9/L or greater then continue with liposomal doxorubicin at 25mg/m^2 and carboplatin AUC 4.</td>
</tr>
</tbody>
</table>

| Platelets (x10^9/L) | Dose Modifications  
(carboplatin and liposomal doxorubicin) |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>100 or greater</td>
<td>100%</td>
</tr>
<tr>
<td>less than 100</td>
<td>Delay one week. If recovery to 100x10^9/L or greater at this point continue with liposomal doxorubicin at 25mg/m^2 and carboplatin AUC 4.</td>
</tr>
<tr>
<td>less than 25 or bleeding</td>
<td>Delay until recovery to 100 x10^9/L or greater then continue with liposomal doxorubicin 25mg/m^2 and carboplatin AUC 4.</td>
</tr>
</tbody>
</table>
**Hepatic Impairment**

The doses recommended below are for initial dosing. If the first dose of liposomal doxorubicin is well tolerated with minimal toxicity and no increase in bilirubin or liver enzymes the dose may be increased from *75% to 100% and from **50% to 75% at the next cycle (and from** 75% to 100% on subsequent cycles where appropriate.)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin μmol/L</th>
<th>AST/ALT units</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liposomal Doxorubicin</td>
<td>20 or less</td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>21-51</td>
<td></td>
<td>75%*</td>
</tr>
<tr>
<td></td>
<td>51 or greater</td>
<td></td>
<td>50%**</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>N/A</td>
<td>N/A</td>
<td>No dose adjustment needed</td>
</tr>
</tbody>
</table>

**Renal Impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Creatinine Clearance (ml/min)</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liposomal Doxorubicin</td>
<td>30 or greater</td>
<td>No dose modification needed</td>
</tr>
<tr>
<td></td>
<td>Less than 30</td>
<td>Clinical decision</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>Less than 20</td>
<td>Omit</td>
</tr>
</tbody>
</table>

**Other**

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose of the causative agent(s) should then be reduced to 75% of the original dose or discontinued as appropriate.
**Liposomal Doxorubicin**

### Palmer-Plantar Erythrodesia / Stomatitis

<table>
<thead>
<tr>
<th>NCI-CTC Toxicty Grade</th>
<th>Number of Weeks after the Dose of Liposomal Doxorubicin</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Re-dose unless patient has experienced a previous grade 3 or 4 skin toxicity, in which case wait an additional week</td>
<td>Re-dose unless patient has experienced a previous grade 3 or 4 skin toxicity, in which case wait an additional week</td>
<td>Decrease dose by 25% and return to 4 week interval or stop treatment</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Wait an additional week</td>
<td>Wait an additional week</td>
<td>Decrease dose by 25% and return to 4 week interval or stop treatment</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Wait an additional week</td>
<td>Wait an additional week</td>
<td>Stop treatment</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Wait an additional week</td>
<td>Wait an additional week</td>
<td>Stop treatment</td>
<td></td>
</tr>
</tbody>
</table>

### Regimen

28 day cycle for 6 cycles

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>AUC 5</td>
<td>1</td>
<td>Intravenous infusion in 500ml glucose 5% over 60 minutes.</td>
</tr>
<tr>
<td>Liposomal Doxorubicin</td>
<td>30mg/m²</td>
<td>1</td>
<td>Intravenous infusion in 250ml glucose 5%. (The first infusion to be given at a maximum rate of 1mg/minute. If well tolerated subsequent infusions may be given over 60 minutes.)</td>
</tr>
</tbody>
</table>

### Dose Information

- The recommended maximum dose when using a calculated creatinine clearance at AUC5 is 750mg. If you have an obese patient or an individual with a calculated creatinine clearance above 125ml/min please seek advice from the relevant consultant.

- It should be noted that the dose of carboplatin may need to be altered if there is a change (improvement or reduction) in renal function of more than 10% from the previous cycle.

- Carboplatin dose will be rounded to the nearest 50mg (up if halfway).

- Liposomal doxorubicin will be dose banded according to the CSCCN agreed bands
● The maximum lifetime cumulative dose of doxorubicin is 450mg/m². However prior radiotherapy to mediastinal/pericardial area should receive a lifetime cumulative doxorubicin dose of no more than 400mg/m². Also consider previous anthracycline exposure.

**Administration Information**

**Extravasation**

● Carboplatin – irritant

● Liposomal Doxorubicin – exfoliant

**Other**

● The first infusion of liposomal doxorubicin is to be given at a maximum rate of 1mg/minute. If this is well tolerated subsequent infusions may be given over 60 minutes. The default time on Aria is 120 minutes.

● If the patient experiences early symptoms or signs of infusion reaction immediately discontinue the infusion and administer appropriate treatment with chlorpheniramine and hydrocortisone. Once the patient has fully re-covered the infusion may be restarted slowly by infusing 5% of the total dose over the first 15 minutes. If tolerated without reaction, the infusion rate may then be doubled for the next 15 minutes. If tolerated, the infusion may then be completed over the next hour for a total infusion time of 90 minutes.

● Liposomal doxorubicin is incompatible with sodium chloride 0.9%. Always use a glucose 5% flush.

● Do not use in-line filters during the administration of liposomal doxorubicin.

● Doses of liposomal doxorubicin less than 90mg may be diluted in 250ml of glucose 5%. Doses of 90mg and above should be diluted in 500ml of glucose 5%.

**Additional Therapy**

● Antiemetics

15 – 30 minutes prior to chemotherapy

- dexamethasone 8mg oral or intravenous
- ondansetron 8mg oral or intravenous

As take home medication

- dexamethasone 4mg oral twice a day for 3 days
- metoclopramide 10mg oral three times a day as required
- ondansetron 8mg oral twice a day for 3 days
• Mouthwashes for the treatment and prevention of mucositis or stomatitis as per local policy.

• Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

• For patients experiencing infusion reactions with this regimen consider administering premedication with all subsequent cycles:
  - chlorphenamine 10mg intravenous
  - dexamethasone 20mg intravenous (remove anti-emetic dose)
  - ranitidine 50mg intravenous

Coding

• Procurement – X71.3

• Delivery – X72.2

References
REGIMEN SUMMARY
Carboplatin (AUC5)-Liposomal Doxorubicin (Caelyx)

Day 1
1. Dexamethasone 8mg oral or intravenous
2. Ondansetron 8mg oral or intravenous
3. Liposomal doxorubicin 30mg/m² intravenous infusion in 250ml glucose 5% over 120 minutes.
4. Carboplatin AUC5 intravenous infusion in 500ml glucose 5% over 60 minutes.

Take Home Medicines
5. Dexamethasone 4mg oral twice a day for 3 days starting the day after chemotherapy
6. Metoclopramide 10mg oral three times a day for three days then 10mg three times a day when required for nausea
7. Ondansetron 8mg oral twice a day for 3 days starting on the evening of chemotherapy administration
This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts:

- Hampshire Hospitals NHS Foundation Trust
- NHS Isle of Wight
- Portsmouth Hospitals NHS Trust
- Salisbury Hospital NHS Foundation Trust
- University Hospital Southampton NHS Foundation Trust
- Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.