Chemotherapy Protocol

GYNAECOLOGICAL CANCER

CARBOPLATIN (AUC4)-GEMCITABINE (day 1)

Regimen

- Ovary-Carboplatin (AUC4)-Gemcitabine (1)

Indication

- Recurrent platinum sensitive ovarian cancer where re-treatment with paclitaxel is inappropriate
- WHO performance status 0, 1, 2

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>Gemcitabine</td>
<td>Peripheral oedema, diarrhoea, constipation, rash, respiratory problems, influenza like symptoms, radiosensitising</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, LFTs and U&Es prior to day each cycle
- EDTA or calculated creatinine clearance prior to each cycle
- CA125 prior to each cycle

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 each cycle 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 $1 \times 10^9$/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>equal to or more than $100 \times 10^9$/L</td>
</tr>
</tbody>
</table>

### Day 1

<table>
<thead>
<tr>
<th>Neutrophils ($x10^9$/L)</th>
<th>Dose Modifications (carboplatin and gemcitabine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 or greater</td>
<td>Delay one week. If, at this point, the counts are $1 \times 10^9$/L or greater then continue with full dose. If the counts are still less than $1 \times 10^9$/L delay a further week and if the counts recover at this point continue with 80% dose of both agents. Otherwise consider stopping treatment.</td>
</tr>
<tr>
<td>less than 1</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Platelets ($x10^9$/L)</th>
<th>Dose Modifications (carboplatin and gemcitabine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 or greater</td>
<td>Delay one week. If, at this point the platelets are $100 \times 10^9$/L or greater then continue with full dose. If the platelets are still less than $100 \times 10^9$/L then delay a further week. If the counts recover at this point continue with 80% dose of both agents. Otherwise consider stopping treatment.</td>
</tr>
<tr>
<td>50-99</td>
<td>100%</td>
</tr>
<tr>
<td>less than 50</td>
<td>Delay until recovery to $100 \times 10^9$/L or greater then continue with 50% doses.</td>
</tr>
</tbody>
</table>

### Hepatic Impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin $\mu$mol/L</th>
<th>AST/ALT units</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>N/A</td>
<td>N/A</td>
<td>No dose adjustment needed</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>30 or greater</td>
<td>N/A</td>
<td>Initiate treatment at $800mg/m^2$</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>Carboplatin*</td>
<td>less than 20</td>
<td>Omit</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>less than 30</td>
<td>Consider dose reduction</td>
</tr>
</tbody>
</table>
* Significant changes in GFR of more than 10% may require dose adjustment.

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 should then be reduced to 80% of the original dose or discontinued as appropriate.

Regimen

21 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>AUC4</td>
<td>1</td>
<td>Intravenous infusion in 500ml Glucose 5% over 60 minutes</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>1000mg/m²</td>
<td>1</td>
<td>Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes</td>
</tr>
</tbody>
</table>

Dose Information

- For elderly/frail patients or those with poor performance status consider using carboplatin AUC 3 and/or gemcitabine 750mg/m²
- The recommended maximum dose when using a calculated creatinine clearance at AUC4 is 600mg. 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).
- Gemcitabine will be dose banded according to the CSCCN agreed bands.

Administration Information

Extravasation

- Carboplatin – irritant
- Gemcitabine - neutral
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

- 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.

Coding (OPCS 4.6)

- Procurement – X71.1
- Delivery – X72.2

References
REGIMEN SUMMARY

Carboplatin (AUC4)-Gemcitabine (1)

Day 1

1. Dexamethasone 8mg oral or intravenous
2. Ondansetron 8mg oral or intravenous
3. Gemcitabine 1000mg/m² in 250ml sodium chloride 0.9% intravenous infusion over 30 minutes.
4. Carboplatin AUC4 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 and then 10mg three times a day when required for nausea
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.