Chemotherapy Protocol

BLADDER

CARBOPLATIN (AUC4.5)-GEMCITABINE

Regimen

- Bladder-Carboplatin-Gemcitabine

Indication

- Locally advanced or metastatic urothelial cancer
- 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>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 1 and 8 of treatment.
- Calculated or measured creatinine clearance prior to each cycle. EDTA may be considered prior to cycle 1 or if there are significant changes in renal function during treatment.

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 the patient is symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

### Day 1

<table>
<thead>
<tr>
<th>Neutrophils ((x10^9/L))</th>
<th>Dose Modifications (carboplatin and gemcitabine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>more than or equal to 1</td>
<td>100%</td>
</tr>
<tr>
<td>less than 1</td>
<td>1st Occurrence Delay until recovery. 2nd Occurrence Delay until recovery then give 75% of the original dose.</td>
</tr>
<tr>
<td>Febrile Neutropenia</td>
<td>1st Occurrence Delay until recovery and then re-start treatment using 75% of the original dose.</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>more than or equal to 100</td>
<td>100%</td>
</tr>
<tr>
<td>Less than100</td>
<td>1st Occurrence Delay until recovery then give 75% of the original dose. 2nd Occurrence Delay until recovery then give 50% of the original dose.</td>
</tr>
</tbody>
</table>

### Day 8

<table>
<thead>
<tr>
<th>Neutrophils ((x10^9/L))</th>
<th>Dose Modifications (gemcitabine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>more than or equal to 1</td>
<td>100%</td>
</tr>
<tr>
<td>0.5 - 1</td>
<td>75%</td>
</tr>
<tr>
<td>less than 0.5</td>
<td>Omit</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Platelets ((x10^9/L))</th>
<th>Dose Modifications (gemcitabine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>more than or equal to 100</td>
<td>100%</td>
</tr>
<tr>
<td>50 - 100</td>
<td>75%</td>
</tr>
<tr>
<td>less than 50</td>
<td>Omit</td>
</tr>
</tbody>
</table>

If dose modifications to gemcitabine dose are required on day 1, continue with reduced dose for day 8.
**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin μmol/L</th>
<th>AST/ALT units/L</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboptin</td>
<td>N/A</td>
<td>N/A</td>
<td>No dose adjustment needed</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>more than 30*</td>
<td>N/A</td>
<td>Initiate treatment with a dose of 800mg/m²</td>
</tr>
</tbody>
</table>

*Limit reflects local practice and may vary from published sources

**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>Carboptin</td>
<td>less than 20</td>
<td>Omit</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>more than or equal to 30</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>less than 30</td>
<td>Consider dose reduction</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 should then be reduced to 75% 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>Carboptin</td>
<td>AUC 4.5</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 and 8</td>
<td>Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes</td>
</tr>
</tbody>
</table>

**Dose Information**

- Carboptin dose will be rounded to the nearest 50mg (up if halfway)
- Gemcitabine will be dose banded as per the CSCCN agreed dose bands
**Administration Information**

**Extravasation**

- Carboplatin – irritant
- Gemcitabine – neutral

**Additional Therapy**

- Antiemetics
  15-30 minutes prior to chemotherapy on **day 1**
  - dexamethasone 8mg oral or intravenous
  - ondansetron 8mg oral or intravenous

  As take home medication on **day 1**
  - dexamethasone 4mg oral twice a day for 3 days
  - metoclopramide 10mg oral three times a day for 3 days then as required
    (supply for day 1 and 8)

  15-30 minutes prior to chemotherapy on **day 8**
  - metoclopramide 10mg oral or intravenous

- Mouthwashes according to local or national policy on the treatment of mucositis
- Gastric protection with a proton pump inhibitor or a \( \text{H}_2 \) 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 & X72.4

**References**

**REGIMEN SUMMARY**

Carboplatin (AUC4.5)-Gemcitabine

**Day 1**

1. Dexamethasone 8mg oral or intravenous
2. Ondansetron 8mg oral or intravenous
3. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes.
4. Carboplatin AUC4.5 intravenous infusion in 500ml glucose 5% over 60 minutes.

**Take Home Medicines**

5. Dexamethasone 4mg oral twice a day for 3 days starting on day two of the cycle
6. Metoclopramide 10mg oral three times a day for 3 days then when required

**Administration Instructions**

Please supply 10 days or an original pack if appropriate to cover day 1 and 8

**Day 8**

7. Metoclopramide 10mg oral or intravenous
8. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
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 Hospitals 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.