Chemotherapy Protocol

BREAST CANCER

CYCLOPHOSPHAMIDE-DOXORUBICIN

Regimen

- Breast Cancer – Cyclophosphamide-Doxorubicin

Indication

- Primary systemic (neoadjuvant) therapy of breast cancer
- Adjuvant therapy of high risk (greater than 5%) node negative breast cancer
- WHO Performance status 0, 1, 2

Toxicity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Dysuria, haemorrhagic cystitis, taste disturbances</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>Cardiac toxicity, urinary discolourisation (red)</td>
</tr>
</tbody>
</table>

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

Monitoring

Regimen

- FBC, U&E’s and LFT’s prior to each cycle.
- Ensure adequate cardiac function before starting treatment with doxorubicin. Baseline LVEF should be measured, particularly in patients with a history of cardiac problems or in the elderly.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function 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. The following is a general guide only.

**Haematological**

Prior to prescribing the following treatment criteria must be met on day 1 of treatment.

<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>

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

If counts on day one are below these criteria for neutrophil and/or platelets then delay treatment for seven days. Treatment should only be re-started when these levels are reached. Treatment may be resumed at the original dose or reduce the original dose of doxorubicin and cyclophosphamide to 80% of the original dose depending on clinical circumstances. If a second episode of neutropenia and / or thrombocytopenia occurs or the time to reach the eligible level is longer than seven days consider changing or stopping therapy.

**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin (µmol/L)</th>
<th>AST/ALT (units)</th>
<th>Alk Phos (units)</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Dose reduction may not be necessary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>If the bilirubin is between 20-51umol/L give 50% of the dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If the bilirubin is between 51-85umol/L give 25% of the dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If the bilirubin is greater than 85umol/L omit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If the AST is 2-3xULN give 75% of the dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If the AST is greater than 3xULN give 50% of the dose</td>
<td></td>
<td></td>
<td></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>Cyclophosphamide (consider mesna)</td>
<td>More than 20</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>10-20</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>Less than 10</td>
<td>50</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>No dose reduction generally required</td>
<td></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.
Doxorubicin

Discontinue doxorubicin if cardiac failure develops.

Regimen

21 day cycle for 6 cycles

Where the intention is to follow this regimen with another such as paclitaxel only FOUR cycles may be necessary. Always check on prescribing cycle one what is required.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>600mg/m²²</td>
<td>1</td>
<td>Intravenous bolus</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>60mg/m²²</td>
<td>1</td>
<td>Intravenous bolus</td>
</tr>
</tbody>
</table>

Dose Information

- Cyclophosphamide will be dose banded as per the CSCCN agreed bands
- Doxorubicin will be dose banded as per the CSCCN agreed bands
- The maximum lifetime cumulative dose of doxorubicin is 450mg/m²². However prior radiotherapy to mediastinal/pericardial area should not receive a lifetime cumulative doxorubicin dose of more than 400mg/m²².

Administration Information

Extravasation

- Cyclophosphamide - neutral
- Doxorubicin – vesicant

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 twice a day oral for 3 days
- metoclopramide 10mg three times a day when required oral
- ondansetron 8mg twice a day oral for 3 days

- Mouthwashes according to local or national policy on the treatment of mucositis.

- 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**

- Procurement - X70.2
- Delivery - X72.3

**References**


REGIMEN SUMMARY

Cyclophosphamide-Doxorubicin

Day One

1. Dexamethasone 8mg oral or intravenous
2. Ondansetron 8mg oral or intravenous
3. Doxorubicin 60mg/m² intravenous bolus over 10 minutes.
4. Cyclophosphamide 600mg/m² intravenous bolus over 10 minutes.

Take Home Medicines

5. Dexamethasone 4mg twice a day oral for three days starting on day two of the cycle
6. Metoclopramide 10mg three times a day when required oral
7. Ondansetron 8mg twice a day oral for three days starting on the evening of day one of treatment
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.