Chemotherapy Protocol

HEAD AND NECK CANCER

CISPLATIN-FLUOROURACIL

In-Patient Regimen

Regimen

- Head and Neck Cancer – InP-Cisplatin-Fluorouracil

Indication

- Neoadjuvant and palliative treatment of squamous cell carcinoma of the head and neck

Toxicity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>Neuropathy, nephrotoxicity, ototoxicity</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>Diarrhoea, stomatitis</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 each cycle

- Patients with complete or partial dihydropyrimidine dehydrogenase (DPD) deficiency are at increased risk of severe and fatal toxicity during treatment with fluorouracil. All patients should be tested for DPD deficiency before initiation (cycle 1) to minimise the risk of these reactions

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.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Eligible Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>1.5x10⁹/L or greater</td>
</tr>
<tr>
<td>Platelets</td>
<td>100x10⁹/L or greater</td>
</tr>
</tbody>
</table>

Defer treatment for 7 days if the neutrophil count is less than 1.5x10⁹/L and/or the platelet count is less than 100x10⁹/L. If the counts have recovered to these levels at 7 days resume treatment. Consider using a 75% dose reduction. If the counts do not recover delay a further seven days. If they are satisfactory at 14 days treatment can be re-started using a 50% dose reduction.

**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin (μmol/L)</th>
<th>AST/ALT units</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>N/A</td>
<td>N/A</td>
<td>No dose reduction necessary</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>less than 85</td>
<td>less than 180</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>more than 85</td>
<td>more than 180</td>
<td>Contra-indicated</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>Cisplatin</td>
<td>more than 60</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>45-59</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>less than 45</td>
<td>consider carboplatin</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>Consider dose reduction in severe renal impairment only</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.

A cycle of chemotherapy should be delayed for up to two weeks to allow for a reduction in the severity of toxic events of NCI-CTC grade 3 or more to a severity of NCI-CTC grade 1 or less (with the exception of alopecia, fatigue, malaise, and nail changes). Delays beyond two weeks required discontinuation of chemotherapy.
Cisplatin

Modifications in the dose of cisplatin are necessary for peripheral sensory and motor neurotoxicity, ototoxicity, or nephrotoxicity. Consider stopping treatment for patients with neurotoxicity or ototoxicity of NCI-CTC grade 3 or more.

Fluorouracil

Modifications in the dose of fluorouracil are necessary for mucositis and diarrhoea.

Regimen

21 day cycle

Neo-adjuvant – 2-3 cycles prior to radiotherapy (3 cycles will be set in Aria)

Palliative – 6 cycles

6 cycles will be set in Aria

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>100mg/m²</td>
<td>1</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/min (minimum time 120 minutes)</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>1000mg/m²</td>
<td>1, 2, 3, 4</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours</td>
</tr>
</tbody>
</table>

Dose Information

• Cisplatin will be dose banded in accordance with the national dose bands (1mg/ml)

• Fluorouracil will be dose banded in accordance with the national dose bands (50mg/ml)

Administration Information

Extravasation

• Cisplatin – exfoliant

• Fluorouracil - inflamitant

Other

• The fluorouracil is given as a continuous infusion over 24 hours. A central or PICC line is recommended for treatment to commence and continue.
Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy
  - aprepitant 125mg oral day 1
  - aprepitant 80mg oral days 2, 3
  - dexamethasone 4mg once a day oral
  - ondansetron 8mg twice a day oral for 5 days
  - metoclopramide 10mg three times a day when required oral

- Cisplatin pre and post hydration as follows;

  Pre

  Furosemide 40mg oral or intravenous

  1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

  Post

  1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

  Patients should be advised to drink at least 3 litres of fluid in the 24 hours after administration of cisplatin.

- Oral loperamide 4mg after the first loose stool then 2-4mg four times a day when required for the relief of diarrhoea (maximum 16mg/24 hours).

- Mouthwashes as per local or national guidelines

- 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

References

REGIMEN SUMMARY

InP-Cisplatin-Fluorouracil

Day 1

1. Warning – Check supportive medication prescribed
   Administration instructions:
   1. Aprepitant 125mg oral day 1
   2. Aprepitant 80mg oral days 2, 3
   3. Dexamethasone 4mg once a day, days 1, 2, 3, 4, 5 oral or intravenous
   4. Metoclopramide 10mg three times a day as required oral or intravenous
   5. Ondansetron 8mg twice a day, days 1, 2, 3, 4, 5 oral or intravenous
   6. Consider gastric protection
   7. Consider mouthwashes

2. Furosemide 40mg oral or intravenous bolus

3. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

4. Cisplatin 100mg/m² intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/minute (minimum time 120 minutes)

5. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

6. Fluorouracil 1000mg/m² intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours

Day 2, 3, 4

Warning – Check supportive medication prescribed
   Administration instructions:
   1. Aprepitant 125mg oral day 1
   2. Aprepitant 80mg oral days 2, 3
   3. Dexamethasone 4mg once a day, days 1, 2, 3, 4, 5 oral or intravenous
   4. Metoclopramide 10mg three times a day as required oral or intravenous
   5. Ondansetron 8mg twice a day, days 1, 2, 3, 4, 5 oral or intravenous
   6. Consider gastric protection
   7. Consider mouthwashes

7. Fluorouracil 1000mg/m² intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours
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 NHS Foundation Trust
- University Hospital Southampton NHS Foundation Trust
- Western Sussex Hospitals NHS Trust

All actions have been taken to ensure these protocols are correct. However, it remains the responsibility of the prescriber to ensure the correct drugs and doses are prescribed for patients.