Chemotherapy Protocol

LUNG CANCER – SMALL CELL (SCLC)

CISPLATIN-ETOPOSIDE

(Intravenous)

Regimen

- SCLC – Cisplatin-Etoposide IV

Indication

- Limited stage SCLC
- Usually given concurrently with radical thoracic radiotherapy
- WHO Performance status 0, 1, 2
- Radical intent

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>Etoposide</td>
<td>Hypotension on rapid infusion, hyperbilirubinaemia</td>
</tr>
</tbody>
</table>

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

Monitoring

Disease

- A baseline chest x-ray should be performed before starting treatment and up to date (ideally within 1 month) cross section imaging should also be performed

Regimen

- EDTA or calculated creatinine clearance before the first cycle
- FBC, LFTs and U&Es prior to each cycle
- A chest x-ray should be performed before each cycle
- Consider formal audiology test if relevant
**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 or 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.

**Haematology**

Prior to prescribing on day one of the 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 1.5x10⁹/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>equal to or more than 100x10⁹/L</td>
</tr>
</tbody>
</table>

If radiotherapy is being given as part of the treatment pathway the haemoglobin should be kept above 12g/dL during the radiotherapy.

Thereafter the following modifications are appropriate based on day one blood counts.

<table>
<thead>
<tr>
<th>Neutrophils (x10⁹/L)</th>
<th>Platelets (x10⁹/L)</th>
<th>Dose Modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than or equal to 1.5</td>
<td>or Less than or equal to 100</td>
<td>Delay both cisplatin and etoposide until the counts have recovered to the eligible levels</td>
</tr>
<tr>
<td>Febrile neutropenia or treatment delay for a grade 4 neutropenia of more than seven days duration</td>
<td>or Grade 4 thrombocytopenia requiring medical intervention or grade 2 and above bleeding in association with thrombocytopenia</td>
<td>In the first instance reduce the dose to 80% of the original dose. For a second episode following dose reduction reduce the dose to 50% of the original dose. Stop treatment if a third event occurs following a 50% dose modification.</td>
</tr>
</tbody>
</table>
**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin</th>
<th>AST</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>No adjustment necessary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etoposide</td>
<td>26-51 or 60-180</td>
<td>more than 51 or more than 180</td>
<td>50 or clinical decision</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>Do not use</td>
</tr>
<tr>
<td>Etoposide</td>
<td>more than 50</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>15-50</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>less than 15</td>
<td>50</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 both agents should then be reduced to 75% of the original dose.

**Cisplatin**

Peripheral neuropathy is a common complication of cisplatin therapy. Where this occurs at NCI-CTC grade 2 or above delay treatment until resolution to NCI-CTC grade 1 or below and then restart treatment after reducing the cisplatin to 50% of the original dose (the etoposide remains at the previous level). Alternatively substitute the cisplatin with carboplatin AUC 6 for a calculated creatinine clearance or AUC 5 for an EDTA clearance.
**Regimen**

21 day cycle for 4 cycles

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>25mg/m²</td>
<td>1, 2, 3</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/minute (minimum time 60 minutes)</td>
</tr>
<tr>
<td>Etoposide</td>
<td>100mg/m²</td>
<td>1, 2, 3</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes</td>
</tr>
</tbody>
</table>

**Dose Information**

- Cisplatin will be dose banded as per the CSCCN agreed bands
- Etoposide (intravenous) will be dose banded as per the CSCCN agreed bands

**Administration Information**

- The etoposide is administered in 1000ml sodium chloride. This will form the post-hydration for cisplatin. No other fluid is required as post-hydration

**Extravasation**

- Cisplatin – exfoliant
- Etoposide – irritant

**Additional Therapy**

- Antiemetics
  
  15-30 minutes prior to chemotherapy;

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

  As take home medication;

  - dexamethasone 4mg once a day oral for 2 days starting the day after chemotherapy finishes
  - metoclopramide 10mg three times a day when required oral
  - ondansetron 8mg on the evening of each day of chemotherapy and then 8mg twice a day for two days starting the day after chemotherapy
- Cisplatin pre and post hydration as follows;
  
  **Pre**
  
  Furosemide 40mg when required oral or intravenous bolus
  
  500ml sodium chloride 0.9% with 8mmol magnesium sulphate over 30 minutes
  
  The etoposide is administered in 1000ml sodium chloride 0.9%. This forms the post hydration.
  
  Patients should be advised to drink at least 2 litres of fluid in the 24 hours after administration of cisplatin.

- 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

- Prophylactic antibiotics can be considered if required

- Growth factors as per local policy

**Coding (OPCS 4.6)**

- Procurement – X70.1
- Delivery – X72.1, X72.4

**References**

REGIMEN SUMMARY

Cisplatin-Etoposide IV

Days One, Two, Three

1. Dexamethasone 8mg oral or intravenous bolus

2. Ondansetron 8mg oral or intravenous bolus

3. Furosemide 40mg when required oral or intravenous bolus

4. Sodium chloride 0.9% 500ml with 8mmol magnesium sulphate over 30 minutes

5. Cisplatin 25mg/m² intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/minute (minimum time 60 minutes)

6. Etoposide 100mg/m² in 1000ml sodium chloride 0.9% over 60 minutes

Take Home Medicines

7. Dexamethasone 4mg once a day for two days oral starting the day after chemotherapy finishes

8. Metoclopramide 10mg three times a day when required oral

9. Ondansetron 8mg on the evening of the days of chemotherapy and then 8mg twice a day for two days starting the day after chemotherapy finishes oral
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 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.