Chemotherapy Protocol

LUNG CANCER – SMALL CELL (SCLC)

CISPLATIN-ETOPOSIDE

(Intravenous / Oral)

Regimen

- SCLC – Cisplatin-Etoposide IV/PO

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 cycle one 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 1.5x10^9/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>equal to or more than 100x10^9/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 (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose Modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than or equal to 1.5</td>
<td>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>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</td>
<td>60-180</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>more than 51</td>
<td>more than 180</td>
<td>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 a ETDA 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>80mg/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/minute (minimum time 120 minutes)</td>
</tr>
<tr>
<td>Etoposide</td>
<td>120mg/m²</td>
<td>1</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes</td>
</tr>
<tr>
<td>Etoposide</td>
<td>240mg/m²</td>
<td>2, 3</td>
<td>Oral</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
- Etoposide (oral) will be dose rounded to the nearest 50mg (up if halfway)

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
- Etoposide should be taken an hour before food or on an empty stomach

Extravasation

- Cisplatin – exfoliant
- Etoposide – irritant

Additional Therapy

- Antiemetics
  15-30 minutes prior to chemotherapy on day one only;
    - aprepitant 125mg oral
    - dexamethasone 4mg oral or intravenous bolus
    - ondansetron 8mg oral or intravenous bolus
  As take home medication;
    - aprepitant 80mg once a day oral for 2 days
- dexamethasone 4mg once a day oral for 3 days
- metoclopramide 10mg three times a day when required oral
- ondansetron 8mg twice a day oral for 3 days

- Cisplatin pre and post hydration as follows;
  
  **Pre**
  
  Furosemide 40mg oral or intravenous bolus
  
  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.

- 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

**Additional Information**

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to etoposide (oral)

- It must be made clear to all staff, including those in the community, that this is a short course of oral chemotherapy that must not be continued.

- Patients should be assessed for suitability for oral chemotherapy prior to starting treatment.

**Coding (OPCS 4.6)**

- Procurement – X70.2

- Delivery – X72.1

**References**

REGIMEN SUMMARY
Cisplatin-Etoposide IV/PO

Day One
1. Aprepitant 125mg oral
2. Dexamethasone 4mg oral or intravenous bolus
3. Ondansetron 8mg oral or intravenous bolus
4. Furosemide 40mg oral or intravenous bolus
5. Sodium chloride 0.9% 1000ml with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes
6. Cisplatin 80mg/m$^2$ intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/minute (minimum time 120 minutes)
7. Etoposide 120mg/m$^2$ in 1000ml sodium chloride 0.9% over 60 minutes

Take Home Medicines
8. Etoposide 240mg/m$^2$ once a day oral for two days
9. Aprepitant 80mg once a day oral for two days
10. Dexamethasone 4mg once a day oral for three days
11. Metoclopramide 10mg three times a day when required oral
12. Ondansetron 8mg twice a day oral for three days
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.