Chemotherapy Protocol

LUNG CANCER – SMALL CELL (SCLC)

CYCLOPHOSPHAMIDE-DOXORUBICIN-VINCRISTINE

Regimen

- SCLC – Cyclophosphamide-Doxorubicin-Vincristine

Indication

- Second line treatment of SCLC
- WHO Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Cyclophosphamide	Haemorrhagic cystitis, taste disturbances
Doxorubicin	Cardiotoxicity, urinary discolourisation (red)
Vincristine	Peripheral neuropathy, constipation

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

- FBC, LFTs and U&Es prior to each cycle
- A chest x-ray should be performed before each cycle

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.

Haematology

Prior to prescribing on day one of cycle one the following criteria must be met;

Criteria	Eligible Level
Neutrophil	equal to or more than $1x10^9$/L
Platelets	equal to or more than $100x10^9$/L

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

Subsequently if the neutrophils are less than $1x10^9$/L then in the first instance delay treatment for 7 days. If counts recover at this point continue at the initial dose. If counts remain low continue with treatment using a 20% dose reduction. If the myelosuppression recurs despite this dose reduction stop treatment.

If the platelets are less than $100x10^9$/L then in the first instance delay treatment for 7 days. If the counts recover at this point continue at the initial dose. If the counts still fall within this range continue using a 20% dose reduction. If the platelet level falls below $50x10^9$/L reduce the dose by 50%.

For patients experiencing neutropenic sepsis the cyclophosphamide and doxorubicin doses should be reduced by 20% on subsequent courses. Vincristine doses need not be adjusted for haematological toxicity.

Hepatic Impairment

<table>
<tr><th>Drug</th><th colspan="3">Dose</th></tr>
<tr><td>Cyclophosphamide</td><td colspan="3">Dose reduction may not be necessary</td></tr>
<tr><td>Doxorubicin</td><td colspan="3">If the bilirubin is between 20-51umol/L give 50% of the dose
If the bilirubin is between 51-85umol/L give 25% of the dose
If the bilirubin is greater than 85umol/L omit

If the AST is 2-3xULN give 75% of the dose
If the AST is greater than 3xULN give 50% of the dose</td></tr>
<tr><td rowspan="3">Vincristine</td><td>Bilirubin umol/L</td><td>AST / ALT</td><td>Dose</td></tr>
<tr><td>26-51</td><td>60-180</td><td>50%</td></tr>
<tr><td>more than 51</td><td>More than 180</td><td>omit</td></tr>
</table>

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cyclophosphamide (consider mesna)	10-20	75
	Less than 10	50
Doxorubicin	No dose reduction generally required	
Vincristine	No dose reduction necessary	

Regimen

The maximum lifetime cumulative dose of doxorubicin is 450mg/m^2. However, those who have undergone prior radiotherapy to mediastinal/pericardial area should not receive doxorubicin >400mg/m^2.

The maximum single dose of vincristine is 2mg.

21 day cycle for up to 6 cycles

Drug	Dose	Days	Administration
Cyclophosphamide	1000mg/m^2	1	Intravenous bolus
Doxorubicin	50mg/m2	1	Intravenous bolus
Vincristine	1.4mg/m^2 (max 2mg)	1	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

Dose Information

- Cyclophosphamide will be dose banded as per the CSCCN agreed bands
- Doxorubicin will be dose banded as per the CSCCN agreed bands
- Vincristine will not be dose banded

Administration Information

Extravasation

- Cyclophosphamide – neutral
- Doxorubicin – vesicant
- Vincristine - vesicant

Additional Therapy

- SCLC can be very sensitive to chemotherapy. This may lead to the development of tumour lysis syndrome at the start of therapy. For those at risk individuals' allopurinol should be prescribed. This should begin the day

before chemotherapy treatment and continue for as long as a significant chemosensitive tumour bulk remains. Normally one cycle suffices.

- Antiemetics (very high)

  15-30 minutes prior to chemotherapy;

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

  As take home medication;

  - dexamethasone 4mg twice a day for 3 days oral
  - metoclopramide 10mg three times daily when required oral
  - ondansetron 8mg twice a day for 3 days oral

- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed

- Prophylactic antibiotics can be considered if required

Coding (OPCS 4.5 version 2)

- Procurement – X70.2

- Delivery – X72.3

References
1.Nikkanen V, Liippo K, Ojala A et al. Vincristine, doxorubicin and cyclophosphamide with and without etoposide in limited small cell lung cancer. Acta Oncol 1990; 29 (4): 421-4.
2. von Pawel J, Schiller JH, Shepherd FA et al. Topotecan versus cyclophosphamide, doxorubicin and vincristine for the treatment of recurrent small cell lung cancer. J Clin Oncol 1999; 17 (2): 658-667.
3. White S, Lorigan P, Middleton R et al. Randomised phase II study of cyclophosphamide, doxorubicin and vincristine compared with single agent carboplatin in patients with poor prognosis small cell lung cancer. Cancer 2001; 92 (3): 601-608.

REGIMEN SUMMARY

Cyclophosphamide-Doxorubicin-Vincristine

Day One

1. Dexamethasone 8mg oral or intravenous bolus

2. Ondansetron 8mg oral or intravenous bolus

3. Doxorubicin 50mg/m^2 intravenous bolus

4. Vincristine 1.4mg/m^2 (maximum 2mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

5. Cyclophosphamide 1000mg/m2 intravenous bolus

Take Home Medicines

6. Dexamethasone 4mg twice a day oral for 3 days

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

8. Ondansetron 8mg twice a day oral for 3 days starting on the evening of chemotherapy

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	Dec 2013	Header changed Tables used throughout Renal and hepatic dose adjustments updated Name updated and added to summary One and twice daily changed to once a day, twice a day Addition therapy “stat” removed and route written in full Metoclopramide dose changed Vincristine changed to 10 minutes Ondansetron changed to start on the evening of Hospitals and disclaimer added	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1.1	Sept 2010	Font changed to Arial Header altered to include “Strength through Partnership” Drug names given capitals in regimen Extravasation moved to under Administration Information Footer changed to include regimen name and review date removed Standard paragraph added to introduction in dose modifications Dose modifications format (not information) changed Granisetron removed from antiemetic Coding added Summary page added Document control added	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician

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.