Chemotherapy Protocol

LUNG CANCER – NON-SMALL CELL (NSCLC)

CISPLATIN-VINORELBINE

(Intravenous)

Regimen

- NSCLC – Cisplatin-Vinorelbine IV

Indication

- First line therapy of stage III or IV NSCLC
- Neoadjuvant therapy stage III
- WHO Performance status 0, 1, 2
- Palliative intent

Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity
Vinorelbine	Neuropathy, stomatitis, transient elevation of LFTs, pain, 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

- 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 / 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 the following criteria must be met;

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

Criteria	Eligible Level
Neutrophil	equal to or more than $1.5x10^9$/L
Platelets	equal to or more than $100x10^9$/L

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

If the neutrophils are less than $1.5x10^9$/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%.

Dose adjustments for day eight should be made according to local practice guidelines or procedures.

Hepatic Impairment

Drug	Bilirubin µmol/L		AST/ALT units	Dose (%of original dose)
Cisplatin	No adjustment necessary			
Vinorelbine	For the intravenous preparation consider a dose reduction to 20mg/m^2 in severe liver impairment For the oral preparation consider a dose of 50mg/m^2/week in moderate liver impairment			

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cisplatin	more than 60	100
	45 - 59	75
	less than 45	Do not use or consider carboplatin
Vinorelbine	No dose adjustment is necessary	

Regimen

The maximum dose of intravenous vinorelbine is 60mg.

21 day cycle for 4 cycles

Drug	Dose	Days	Administration
Cisplatin	80mg/m^2	1	Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/min (minimum time 120 minutes)
Vinorelbine	30mg/m^2 (max dose 60mg)	1, 8	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

Dose Information

- Cisplatin will be dose banded as per the CSCCN agreed bands
- Vinorelbine will be dose banded as per the CSCCN agreed bands

Administration Information

Extravasation

- Cisplatin – exfoliant
- Vinorelbine – vesicant

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy on **day one** only;

  - aprepitant 125mg oral

- dexamethasone 4mg oral or intravenous
- ondansetron 8mg oral or intravenous

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 oral when required
- ondansetron 8mg twice a day oral for 3 days

15 – 30 minutes prior to chemotherapy on **day eight** only;

- metoclopramide 10mg oral or intravenous

- 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.

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

- Prophylactic antibiotics can be considered if required

Additional Information

- There are several protocols that utilise cisplatin and vinorelbine for NSCLC. Some involve radiotherapy, others do not. The dose of vinorelbine must be adjusted where radiotherapy is administered concurrently. Please ensure you have the correct protocol before prescribing.

Coding

- Procurement – X70.3

- Delivery – X72.1 / X72.4

References

1.National Institute of Clinical Excellence (2005). CG24. The Diagnosis and Treatment of Lung Cancer. Methods, Evidence and Guidance. DOH: London.
2.Gebbia V, Galetta D, Lorusso V et al. Cisplatin plus weekly vinorelbine versus cisplatin plus vinorelbine on days 1 and 8 in advanced non-small cell lung cancer: a prospective randomised phase III trial of the G.O.I.M. Lung Cancer 2008; 61 (3): 369-377.

REGIMEN SUMMARY

Cisplatin-Vinorelbine IV

Day One

1. Aprepitant 125mg oral

2. Dexamethasone 4mg oral or intravenous

3. Ondansetron 8mg oral or intravenous

4. Furosemide 40mg oral or intravenous

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

6. Vinorelbine 30mg/m^2 intravenous infusion in 50ml sodium chloride 0.9% over 10 minutes

7. 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)

8. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

Take Home Medicines

9. Aprepitant 80mg once a day for 2 days starting on day 2 of the cycle oral

10. Dexamethasone 4mg once a day for 3 days starting on day 2 of the cycle oral

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

12. Ondansetron 8mg twice a day for 3 days starting on the evening of day 1 of the cycle oral

Day Eight

13. Metoclopramide 10mg oral or intravenous

14. Vinorelbine 30mg/m^2 intravenous infusion in 50ml sodium chloride 0.9% over 10 minutes

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	Jan 2014	Header changed Footer changed Toxicity removed and tabulated Haematological criteria tabulated < and > written in words Renal and hepatic adjustments tabulated and updated Regimen tabulated Vinorelbine changed to 10 minutes Routes written in full Metoclopramide dose changed Regimen name added to summary Bolus removed from ondansetron and dexamethasone Coding updated Antiemetic days added in summary Document control tabulated Hospitals and disclaimer added	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1.1	23rd 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 antiemetics Aprepitant incorporated as per superuser agreement 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.