Cisplatin and Vinorelbine and radiotherapy (NSCLC)

Indication

First-line chemotherapy for use with concomitant radical radiotherapy for early or locally advanced non-small cell carcinoma (NSCLC)

ICD-10 codes

Codes pre-fixed with C34.

Regimen details

Cycles 1 and 2 – concomitant

Day	Drug	Dose	Route
1	Vinorelbine Or Vinorelbine	40mg/m^2 Or 15 mg/m² (max 30mg)	PO IV infusion
1	Cisplatin	80mg/m^2	IV infusion
8	Vinorelbine Or Vinorelbine	40 mg/m² Or 15mg/m^2 (max 30mg)	PO IV infusion

Cycles 3 and 4 - adjuvant

Day	Drug	Dose	Route
1	Vinorelbine Or Vinorelbine	60-80mg/m^2 (max 160mg) Or 30 mg/m² (max 60mg)	PO IV infusion
1	Cisplatin	80mg/m^2	IV infusion
8	Vinorelbine Or Vinorelbine	60-80mg/m^2 (max 160mg) Or 30mg/m^2 (max 60mg)	PO IV infusion

Cycle frequency

21 days

Number of cycles

4 cycles – as above

Administration

Day 1

IV Vinorelbine is administered in 50 mL sodium chloride 0.9% over 10 minutes, as per national guidance. Nurse to remain with patient throughout infusion.

Cisplatin is administered in 500mL sodium chloride 0.9% over 60 minutes following the pre and post hydration protocol below.

Infusion Fluid & Additives	Volume	Infusion Time
Sodium Chloride 0.9%	1000mL	60 minutes
Mannitol 20% **OR** Mannitol 10%	200mL 400mL	10 minutes 15 minutes
Ensure urine output > 100mL / hour prior to giving cisplatin. Give a single dose of furosemide 20mg iv if necessary.		
Cisplatin	500mL	60 minutes
Sodium Chloride 0.9% + 2g $MgSO_4$ + 20mmol KCl	1000mL	2 hours
TOTAL	**2700 or 2900mL**	**4 hours 10 minutes or 4 hours 15 minutes**

Note: Patients with magnesium or potassium below the normal range should have 2g $MgSO_4$ and 20mmol KCl added to the pre-hydration bag and the duration of the infusion increased to 2 hours

Patients should be advised to drink at least 2 litres of fluid over the 24 hours following cisplatin.

Day 8
Oral vinorelbine is available as 20mg, 30mg and 80mg capsules. The capsules should be swallowed whole with water and with or after food.
IV Vinorelbine is administered in 50 mL sodium chloride 0.9% over 10 minutes, as per national guidance.
Nurse to remain with patient throughout infusion.

Oral doses should be prescribed as per the table below:

BSA (m^2)	**Dose** (40mg/m^2)	**Dose** (60mg/m^2)	**Dose** (80mg/m^2)
0.95-1.04	40mg	60mg	80mg
1.05-1.14	40mg	70mg	90mg
1.15-1.24	50mg	70mg	100mg
1.25-1.34	50mg	80mg	100mg
1.35-1.44	60mg	80mg	110mg
1.45-1.54	60mg	90mg	120mg
1.55-1.64	60mg	100mg	130mg
1.65-1.74	70mg	100mg	140mg
1.75-1.84	70mg	110mg	140mg
1.85-1.94	80mg	110mg	150mg
≥1.95	80mg	120mg	160mg

Pre-medication
Antiemetics as per local guidelines.

Emetogenicity
Day 1 has high emetic potential.
Day 8 has moderate - low emetic potential.

Additional supportive medication
H_2 antagonist or proton pump inhibitor if required.
Laxatives if required.
Mouthwashes as per local policy.
If magnesium levels < normal reference range refer to local magnesium replacement guidelines.

Extravasation

Cisplatin – exfoliant (Group 4)
Vinorelbine – vesicant (Group 5)

Investigations - pre-first cycle

Investigation	**Validity period** (or as per local practice)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
Calcium	14 days
Magnesium	14 days

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local practice)
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days
Magnesium	7 days
Calcium	7 days

In addition FBC is required on day 8 prior to vinorelbine

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥1.0 x 10^9/L
Platelets	≥100 x 10^9/L
Creatinine Clearance (CrCl)	> 60 mL/min
Bilirubin	<1.5 x ULN
ALT/AST	<3 x ULN or < 5 x ULN in presence of liver metastases
Alkaline phosphatase	<2 x ULN

Dose modifications

- **Haematological toxicity**

Day 1

If neutrophils < 1.0 x 10^9/L and/or platelets < 100 x 10^9/L delay by 1 week and recheck FBC.

Day 8

Neutrophils (x 10^9/L)		**Platelets** (x 10^9/L)	**Vinorelbine dose**
≥ 1.0	And	≥ 100	100%
0.5 – < 1.0	Or	50-99	75%
<0.5	Or	< 50	Omit

- **Renal impairment**

CrCl (mL/min)	**Cisplatin dose**	**Vinorelbine dose**
≥ 60	100%	100%
50 - 59	75%	100%
40 – 49	50% (or switch to carboplatin AUC 5)	100%
< 40	Omit	100%*

*If CrCl <30mL/min consider vinorelbine dose reduction.

- **Hepatic impairment**

If bilirubin > 1.5-3 x ULN and/or AST/ALT > 5-20 x ULN delay vinorelbine for 7 days and recheck LFTs.
If toxicity persists beyond 3 weeks or bilirubin > 3 x ULN and/or AST/ALT > 20 x ULN discontinue treatment.

- **Other toxicities**

Toxicity	Definition	Cisplatin dose	Vinorelbine dose
Neurotoxicity	≤Grade 1	100%	100%
	Grade 2	50%	100%
	Grade 3	Omit	100%
	Grade 4	Discontinue	Discontinue
Other toxicities (except alopecia or nausea and vomiting)	≤Grade 2	100% (with or without treatment delay)	100%(with or without treatment delay)
	≤Grade 3	Delay until recovery then consider dose reduction (consultant decision)	Delay until recovery then consider dose reduction (consultant decision)

If grade 3-4 constipation omit vinorelbine and consider switching to gemcitabine.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Neurotoxicity
Infertility
Ototoxicity
Infertility
Cardiotoxicity
Encephalopathy
Peripheral neuropathy
Nephrotoxicity

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Mucositis, stomatitis
Constipation

- **Other side effects**

Alopecia
Fatigue
Taste disturbance

Significant drug interactions – for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.
Phenytoin: cisplatin and vinorelbine reduce absorption and efficacy of phenytoin, monitor levels and adjust dose as necessary.

Vinorelbine only:
Itraconazole: increased risk of neurotoxicity.

Cisplatin only:
Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity when given within 2 weeks of cisplatin.
Diuretics: increased risk of nephrotoxicity and ototoxicity
Nephrotoxic drugs: increased nephrotoxicity ; not recommended
Ototoxic drugs: increased risk of ototoxicity
Anti-gout agents: cisplatin may increase plasma concentration of uric acid therefore dose adjustments may be required to control hyperuricaemia and gout.

Additional comments

References

- National Institute of Health and Clinical Excellence Guideline CG121. Lung Cancer. The diagnosis and treatment of lung cancer Accessed 29 October 2014 via www.nice.org.uk
- Summary of Product Characteristics Cisplatin (Hospira) accessed 29 October 2014 via www.medicines.org.uk
- Summary of Product Characteristics Vinorelbine (Pierre fabre) accessed 29 October 2014 via www.medicines.org.uk

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