Carboplatin and Vinorelbine

Indications
Palliative chemotherapy for metastatic or locally advanced non-small cell lung cancer (NSCLC).

Adjuvant treatment of non-small cell lung cancer (NSCLC) when cisplatin is not appropriate.

Induction chemotherapy prior to radical radiotherapy in patients not appropriate for concurrent chemo-radiotherapy.

ICD-10 codes
Codes pre-fixed with C34

Regimen details
Vinorelbine may be given orally or IV as below.

PO Vinorelbine:

Day	Drug	Dose	Route
1 and 8	Vinorelbine	60 mg/m^2 (max 120 mg)	PO
1	Carboplatin	AUC 5	IV infusion

IV Vinorelbine:

Day	Drug	Dose	Route
1 and 8	Vinorelbine	25 mg/m² (max 60mg)	IV infusion
1	Carboplatin*	AUC 5	IV infusion

* Carboplatin dose calculated using the Calvert equation: **Carboplatin dose (mg) = AUC (CrCl +25)**
The creatinine clearance (CrCl) is calculated using the Cockcroft and Gault equation, however for patients where the creatinine level may not truly reflect renal function (e.g. in extremes of BSA or debilitated patients) a formal GFR measurement should be considered.
CrCl should be capped at 125mL/min

Cycle frequency
21 days

Number of cycles
4 cycles

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

Carboplatin is administered in 500mL 5% glucose over 30 minutes.

Oral vinorelbine
Vinorelbine is available as 20mg, 30mg and 80mg capsules. The capsules should be swallowed whole with water and with or after food.

Oral doses should be prescribed as per the table below:

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

Pre-medication

Antiemetics as per local guidelines.

Emetogenicity

This regimen has moderate emetic potential on day 1 and low on day 8.

Additional supportive medication

Antiemetics as per local guidelines.
H_2 antagonist or proton pump inhibitor if required.
Laxatives if required.
Mouthwashes as per local policy.
Consider prophylactic antibiotics day 9 to 15 in patients with recurrent infections.

Extravasation

Carboplatin is irritant (Group 3)
Vinorelbine is 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

Investigations - pre subsequent cycles

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

*In addition FBC is required within 48 hours of day 8 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	≥1.5 x 10^9/L
Platelets	≥100 x 10^9/L
Creatinine Clearance (CrCl)	> 20 mL/min
Bilirubin	<1.5 x ULN
ALT/AST	<1.5 x ULN
Alkaline phosphatase	<2.5 x ULN

Dose modifications

- ### Haematological toxicity

Day 1

If neutrophils < 1.5 x 10^9/L and/or platelets < 100 x 10^9/L delay by 1 week and recheck FBC.
If neutrophils < 0.5 x 10^9/L for more than 5 days or < 0.1 x 10^9/L for more than 3 days
or febrile neutropenia is diagnosed,
or toxicity related delay is > 1 week,
vinorelbine dose should be reduced to 75% (and not escalated for subsequent cycles)

Day 8

If neutrophils < 1.0 x 10^9/L and/or platelets < 100 x 10^9/L omit vinorelbine. Consider reducing subsequent doses to 75% for future cycles.

- ### Renal impairment

Carboplatin is contraindicated if CrCl <20mL/min.
If the calculated creatinine clearance falls by >10% from previous cycle recalculate dose of carboplatin. If the calculated creatinine clearance appears to improve the dose should not be increased unless a clear cause of renal function improvement is documented (e.g. treatment of urinary tract obstruction).

- ### Hepatic impairment

Vinorelbine: If hepatic insufficiency due to liver metastases, liver function may improve with treatment

If bilirubin 1.5-3 x ULN and/or AST/ALT 5-20 x ULN delay vinorelbine for 7 days and recheck LFTs. Once improved consider dose reduction to 50-75% dose.
If toxicity persists beyond 3 weeks or bilirubin > 3 x ULN and/or AST/ALT > 20 x ULN discontinue treatment.

Carboplatin: No dose modification required.

- ### Other toxicities

Neurotoxicity:
If grade 2 neurotoxicity reduce carboplatin dose to 50%.
If ≥ grade 3 discontinue treatment.

If any other grade 3-4 toxicity (except mucositis and alopecia) delay until ≤ grade 1 toxicity and reduce doses of carboplatin and etoposide to 75%.

If grade 3-4 constipation omit vinorelbine. Consider switching to carboplatin and gemcitabine protocol.

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

- **Serious side effects**

Myelosuppression
Neurotoxicity
Peripheral neuropathy
Hypersensitivity
Nephrotoxicity

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Mucositis, stomatitis
Constipation

- **Other side effects**

Alopecia
Fatigue
Myalgia
Electrolyte imbalances
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.
Aprepitant: potential to increase plasma vinorelbine levels.

Carboplatin only:
Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity
Clozapine: increased risk of agranulocytosis, avoid concomitant use
Diuretics: increased risk of nephrotoxicity and ototoxicity
Nephrotoxic drugs: increased nephrotoxicity ; not recommended
Phenytoin: carboplatin reduces absorption and efficacy of phenytoin

Additional comments

References

- National Institute of Health and Clinical Excellence Guideline CG121. Lung Cancer. The diagnosis and treatment of lung cancer Accessed 7 June 2017 via www.nice.org.uk
- Summary of Product Characteristics Carboplatin (Hospira) accessed 1 May 2019 via www.medicines.org.uk
- Summary of Product Characteristics Vinorelbine (Pierre Fabre) accessed 1 May 2019 via www.medicines.org.uk
- O'Brien et al. Ann of Oncol 2004; 15(6): 921-927

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