Systemic Anti Cancer Treatment Protocol

Carboplatin and Vinorelbine Non-small cell lung cancer

PROTOCOL REF: MPHACAVILU
(Version No: 1.0)

Approved for use in:

Non-small cell lung cancer

PS 0 or 2

Palliative setting. **Only used in the adjuvant setting if Cisplatin is contraindicated.**

Re-challenge is an option if ≥ 6 months progression free survival.

Dosage:

Drug	Dose	Route	Frequency
Carboplatin	AUC 5	IV infusion	Every 21 days
Vinorelbine	25mg/m^2 or 60mg/m^2	IV infusion Or Oral	Days 1 & 8 every 21 days

Up to maximum of 4 cycles

Calvert formula for Carboplatin dosage-

Carboplatin dose in mg = AUC x (creatinine clearance + 25)

If estimated GFR is used the Wright formula must be used for creatinine clearance.

The carboplatin dose should not exceed 750mg (maximum creatinine clearance used to calculate dose=125ml/min).

Supportive treatments:

Dexamethasone 4mg oral tablets twice daily for 3 days

Domperidone 10mg oral tablets 3 times a day or as required

Extravasation risk:

Carboplatin- irritant

Vinorelbine (IV) –vesicant

Refer to the network guidance for the prevention and management of extravasation

Interactions

Aminoglycosides e.g. gentamicin, vancomycin and diuretics

Increased risk of nephrotoxicity and ototoxicity. Renal function should be well monitored and audiometric tests carried out as indicated.

Carbamazepine

Is predicted to decrease the exposure to vinorelbine. Manufacturer advises use with caution or avoid

Phenytoin:

Vinorelbine and phenytoin increase the risk of peripheral neuropathy.

Phenytoin is predicted to decrease the exposure to vinorelbine.

Please consult summary of product characteristics via https://www.medicines.org.uk/emc for full list of interactions.

Administration:

IV vinorelbine instructions:

Day	Drug	Dose	Route
1	**Dexamethasone** 30mins before chemotherapy	**As prescribed**	PO/IV
	Ondansetron 30mins before chemotherapy	**As prescribed**	PO/IV
	Carboplatin	**AUC 5**	IV
	Vinorelbine	25mg/m^2	IV Sodium Chloride 0.9% over 30 minutes

Day	Drug	Dose	Route and rate
8	Vinorelbine	25mg/m^2	IV Sodium Chloride 0.9% over 5 minutes

Oral vinorelbine instructions:

Day	Drug	Dose	Route and rate
1	**Dexamethasone** 30mins before chemotherapy	**8mg**	PO pre-treatment
	Ondansetron 30mins before chemotherapy	**16mg**	PO pre-treatment
1	**Carboplatin**	**AUC 5**	IV
	Vinorelbine	60mg/m^2	**With cold water**

Day	Drug	Dose	Route and rate
8	Dexamethasone	8mg	PO pre-treatment
8	Ondansetron	16mg	PO pre-treatment
8	Vinorelbine	60mg/m^2	**With cold water**

If the patient chews or sucks the vinorelbine capsule by error, the liquid is an irritant. Proceed to mouth rinses with water or preferably a normal saline solution.

- In the event of the capsule being cut or damaged, the liquid content is an irritant, and so may cause damage if in contact with skin, mucosa or eyes. If any contact occurs, immediate thorough washing with water or preferably with normal saline solution should be undertaken.
- In the case of vomiting within a few hours after drug intake, do not re-administer. Supportive treatment such as domperidone or $5HT_3$ antagonists (e.g. ondansetron) may reduce the occurrence of this.
- Vinorelbine soft capsule is associated with a higher incidence of nausea/vomiting than the intravenous formulation. Primary prophylaxis with antiemetics and administration of the capsules with some food is recommended as this has also been shown to reduce the incidence of nausea and vomiting.
- Patients receiving concomitant morphine or opioid analgesics: laxatives and careful monitoring of bowel mobility are recommended. Prescription of laxatives may be appropriate in patients with prior history of constipation.

Main Toxicities:

Highly emetogenic, myelosuppression, mucositis, abdominal pain, alopecia, diarrhoea, fatigue, skin rash, neurotoxicity allergic reactions , cardiotoxicity , ovarian failure/infertility.

Investigations and treatment plan

	Pre	Cycle 1 D1	Cycle 1 D8	Cycle 2 D1	Cycle 2 D8	Prior to Cycle 3	Cycle 3 D1	Cycle 3 D8	Cycle 4 D1	Cycle 4 D8	Comments
Medical Assessment	x						x**		X		As clinically indicated or at the end of treatment
Nursing Assessment	x	x	x	x	x		x	x	X	x	Every cycle
On treatment review*						X					
Radiotherapy (if using)				X	X						
FBC	x	x	X	x	X		x	x	x	X	Every administration
U&E & LFT	x	x		x			x		X		Every cycle – day 8 only if clinical indication
CrCl	x	x		x			x		X		Every cycle
CT scan**	x										At the end of treatment and if clinically indicated.
Informed Consent	x										
ECG											If clinically indicated
Blood pressure measurement	x										Repeat if clinically indicated
PS recorded	x	x		x			x		X		Every cycle – record d8 if deterioration
Toxicities documented	x	x	x	x	x		x	x	x	x	Every administration
Weight recorded	x	x		x			x		X		Every cycle
Blood Glucose	x										Repeat if clinically indicated

*On treatment review: assessment of ongoing benefit including PS, toxicity, patient understanding, symptom control and clinical tumour response (imaging as required based upon assessment)

** For sequential radiotherapy. Organise CT and Clinical Oncology assessment following Cycle 3 (C3 d15)

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if-

Plt ≥ 100 x 10^9/L	ANC ≥ 1.0

Proceed on day 8 if-

Plt ≥ 75 x 10^9/L	ANC ≥ 1.0

Delay 1 week on day 1 if-

Plt ≤ 99 x 10^9/L	ANC ≤ 0.9

Omit on day 8 if-

Plt ≤ 74 x 10^9/L	ANC ≤ 0.9

On day 8 of the cycle if blood results do not meet the above levels the patient will miss that dose and proceed to the next cycle.

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Non-haematological toxicity

Hepatic Impairment:

Vinorelbine
AST/ALT >5 x UNL or bilirubin >2 x UNL: reduce dose by a third.

Carboplatin
Transient increases in liver enzymes have been reported. Probably no dose reduction necessary.

Renal Impairment:

Vinorelbine
No dose reduction necessary

Carboplatin
Dose using Calvert equation: Dose = AUC*(25 + GFR) The carboplatin dose should not exceed 750mg (maximum creatinine clearance used to calculate dose=125ml/min). The initial dose does not need to be recalculated for subsequent cycles unless the patient is experiencing toxicity (including AKI). If CrCl <20ml/min contact consultant oncologist

Hypersensitivity:

Patients who have previously experienced Grade I or II platinum hypersensitivity should be pre-medicated prior to carboplatin with:

- Dexamethasone 20 mg IV in 50 mL NS over 15 minutes (or Hydrocortisone 100mg) 30 minutes prior to carboplatin
- Chlorphenamine 10 mg IV over 20 minutes

It should be strongly noted that patients who have severe reactions should not be re-challenged. For severe reactions, discuss with Consultant before continuing with treatment.

References:

- https://www.medicines.org.uk/emc
- Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009)
- Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Renal Impairment (Version 3 - updated January 2009)
- BNF available via: https://bnf.nice.org.uk/
- NICE: CG121 Lung cancer: diagnosis and management. Published date: April 2011
- Stockley's drug interactions: available via www.medicinescomplete.com