Systemic Anti Cancer Treatment Protocol

Cisplatin and Vinorelbine Non-Small Cell Lung Cancer

PROTOCOL REF: MPHACIVILU
(Version No: 1.0)

Approved for use in:

Non-small cell lung cancer

PS 0 or 1

Adjuvant and palliative setting

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

Dosage:

Drug	Dose	Route	Frequency
Cisplatin	80mg/m^2	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

Supportive treatments:

Anti-emetic risk (high):

Aprepitant 125mg on day 1.80mg oral tablets once daily for two days (day 2 and 3)

Dexamethasone 4mg oral tablets twice daily for 3 days

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

Extravasation risk:

Cisplatin- 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.

Aprepitant/ Fosaprepitant:

Aprepitant and fosapreptant are theoretically predicted to increase the exposure of vinorelbine. Caution is advised, particularly when given with oral vinorelbine. Consider alternative antiemetic if vinorelbine toxicity occurs.

Carbamazepine

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

Phenytoin:

Vinorelbine, cisplatin 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:

- **Review patient's fluid intake over the previous 24 hours**
- **Review common toxicity criteria and performance status**
- **Calculate creatinine clearance using Cockcroft and Gault equation:**

Male patients $\frac{1.23 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

Female patients $\frac{1.04 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

Treatment schedule:

IV vinorelbine instructions:

Day	Drug	Dose	Route and rate
1	Aprepitant	125mg	PO 1 hour prior to commencing cisplatin
1	Dexamethasone	As prescribed	PO/IV pre-treatment
1	Ondansetron	As prescribed	PO/IV pre-treatment
1	Furosemide	20mg	PO
1 Pre-hydration	Sodium Chloride 0.9% 1000mL (+ 20mmol Potassium Chloride)		IV over 90 mins
1	Monitor urine Output > 200mls/hr proceed		
1	Cisplatin in **1000mL** Sodium Chloride 0.9%	80mg/m^2	IV over 90 mins
1 Post-hydration	Sodium Chloride 0.9% 1000mL (+ 20mmol Potassium Chloride)		IV over 90 mins
1	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	Aprepitant	125mg	PO 1 hour prior to commencing cisplatin
1	Dexamethasone	12mg	PO pre-treatment
1	Ondansetron	24mg	PO pre-treatment
1 Pre-hydration	Sodium Chloride 0.9% **500mL**		IV over 1.5 hour
1	Monitor urine Output > 200mls/hr proceed		
1	Cisplatin in **1000mL** Sodium Chloride 0.9%	80mg/m^2	IV over **1.5 hour**
1 Post-hydration	Sodium Chloride 0.9% **500mL**		IV over 1.5 hour
1	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.

If cisplatin cannot be administered due to tinnitus or renal impairment (creatinine clearance <45ml/min) then carboplatin may be considered as an alternative: please see separate protocol

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
Mg2+ and Ca2+	X	X		X			X		X		Every cycle
CrCl (Cockcroft and Gault)	X	X		X			X		X		Every cycle
CT scan**	X										At the end of treatment and if clinically indicated
Informed Consent	X										
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 upper limit of normal (ULN) or bilirubin >2 x ULN: reduce dose by a third.

Cisplatin
No dose reduction necessary.

Renal Impairment:

Vinorelbine
No dose reduction necessary

Cisplatin	
GFR (mL/min)	**Dose**
> 60	100%
45 to 59	75%
< 45	Consider carboplatin

Inadequate urine output (< 200mls/hr):

- Administering 500ml Sodium Chloride +/- furosemide 20 - 40mg - furosemide 20 – 40mg po may also be given if there is a positive fluid balance of 1.5 litres, a weight gain of 1.5kg or symptoms of fluid overload.
- The patient should be asked to drink 2 litres of fluid in the 24hrs following treatment, and to contact the hospital if this is impossible because of problems e.g. nausea and vomiting.

Neurotoxicity:

If patient develops Grade 2 neuropathy or ototoxicity, discuss with Consultant.

Cumulative: Dose related peripheral sensory neuropathy: Usually occurs after a cumulative dose. It can occur after treatment with cisplatin is completed, and is usually reversible, taking approx 3 – 5 months to recovery.

Hypersensitivity:

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

- Dexamethasone 20 mg IV in 50 mL NS over 15 minutes (or Hydrocortisone 100mg) 30 minutes prior to cisplatin
- 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
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- Stockley's drug interactions: available via www.medicinescomplete.com