Systemic Anti Cancer Treatment Protocol

Cisplatin/Vinorelbine
Chemo-radiation 42 day Regimen

PROTOCOL REF: MPHACPVILU
(Version No: 1.0)

Approved for use in:

Stage II/III Non-small cell lung cancer

Dosage:

Dosage	Dose	Route	Frequency
Cisplatin	75mg/m^2	IV Infusion	Days 1
Vinorelbine	15mg/m^2		Days 1 and 8
Repeated every **4 weeks** for 2 cycles.			

Supportive treatments:

Aprepitant 125mg to be taken on day 1, an hour before chemotherapy and 80mg to be taken as a single dose on day 2 and day 3

Dexamethasone tablets 4mg twice daily for 3 days

Domperidone 10mg tablets, three times a day when required

The 1st cycle of chemotherapy should start along with day 1 or 2 of radiotherapy.

Adjuvant chemotherapy may be considered after this course. This will be decided when the patient attends for medical review at the end of treatment.

Extravasation risk:

Cisplatin- exfoliant

Vinorelbine- 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.

Phenytoin

Cisplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.

Warfarin

The effects of warfarin may be increased. Monitor INR closely.

Please consult summary of product characteristics available via www.medicines.org.uk 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 $\frac{1.04 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

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 1.5 hour
1	Monitor urine Output > 200mls/hr proceed		

1	Cisplatin in 1000mL Sodium Chloride 0.9%	75mg/m^2	IV over 90 minutes
1 Post-hydration	Sodium Chloride 0.9% 1000mL (+ 20mmol Potassium Chloride)		IV over 90 minutes
1	Vinorelbine	15mg/m^2	IV Sodium Chloride 0.9% over 10 minutes
1	Sodium Chloride 0.9%		IV as flush

Day	Drug	Dose	Route and rate
8	Vinorelbine	15mg/m^2	IV Sodium Chloride 0.9% over 10 minutes
8	Sodium Chloride 0.9%		IV as flush

Give 2 cycles at **28 day intervals**

At the end of IV fluids:

- Weigh the patient and review fluid balance chart
- If there is a positive balance of 1.5L or 1.5kg in weight gained then consider furosemide 20mg orally and review output after 30 minutes. Any concerns then discuss with medical team prior to discharging the patient.

Ensure good oral fluid intake

- Confirm patient understanding of the importance of fluid intake
- Patient should ensure they have 2 litres of fluid in the 24 hours following chemotherapy

As with all platinum based chemotherapy, patients may experience allergic reaction during administration.

For severe reactions, discuss with Consultant before continuing with treatment.

Main Toxicities:

Highly emetogenic, myelosuppression, mucositis, diarrhoea, neurotoxicity, allergic reactions, cardiotoxicity, ovarian failure/infertility

Investigations and treatment plan

	Pre	Cycle 1 Day 1	Cycle 1 Day 8	Cycle 2 Day 1	Cycle 2 Day 8	Comments
Medical Assessment	X					Prior to cycle 1 and at the end of treatment
Nursing Assessment	X	X	X	X	X	Every visit
CT Scan	X					Repeated < 3 months after treatment
FBC	X	X	X	X	X	
U&E & LFT	X	X	X	X	X	
Mg2+ and Ca2+	X	X		X		
CrCl (Cockroft and Gault)	X	X		X		
Informed Consent	X					
Blood pressure measurement	X					Repeat if clinically indicated
PS recorded	X	X		X		Every cycle – record d8 if deterioration
Toxicities documented	X	X	X	X	X	Every administration
Weight recorded	X	X		X		Every cycle
Blood Glucose	X					Repeat if clinically indicated

Dose Modifications and Toxicity Management:

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

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

Renal

Cisplatin
Recalculate CrCl using Cockroft and Gault every cycle and consider EDTA if serum creatinine varies by >30% from baseline.

GFR (mL/min)	Cisplatin dose
≥ 60	100% dose
45 to 59	75% dose
< 45	No further cisplatin

If serum creatinine has increased by 50% between cycles then 20% dose reduction is required at next cycle

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.

Vinorelbine
No dose reduction necessary

Hepatic	Cisplatin – no dose modifications needed **Vinorelbine** AST/ALT >5 x upper limit of normal (ULN) or bilirubin >2 x ULN: reduce dose by a third.
Performance status	Defer 1 week and refer to consultant if there is any deterioration in performance status from cycle1 or previous cycles.
Ototoxicity or Neurotoxicity	Ototoxicity observed in up to 31% of patients can be unilateral or bilateral and tends to become more frequent and severe with repeated doses; It is unclear whether ototoxicity is reversible. Neurotoxicity is common. Discuss any reported ototoxicity or neurotoxicity 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 HSR should be pre-medicated with 45 minutes prior to cisplatin:

- 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.

References:

- Cisplatin 1 mg/ml Sterile Concentrate, Summary of Product Characteristics Hospira UK Ltd Warwickshire.06/09/1996. Available from www.medicines.org.uk/emc/medicine. Last updated 30/04/2013.
- BNF available via: https://bnf.nice.org.uk/
- 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)
- Ideal-CRT: A Phase 1/2 Trial of Isotoxic Dose-Escalated Radiation Therapy and Concurrent Chemotherapy in Patients with Stage II/III Non-Small Cell Lung Cancer. Int J Radiation Oncol Biol Phys, Vol. 95, No. 5, pp. 1367e1377, 2016