Systemic Anti Cancer Treatment Protocol

Cisplatin and Gemcitabine Non-Small Cell Lung Cancer

PROTOCOL REF: MPHACGNSC
(Version No: 1.0)

Approved for use in:

Advanced non-small cell lung cancer

Performance status: 0 to 1

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

Dosage:

Drug	Dose	Route	Frequency
Cisplatin	**80mg/m^2**	IV infusion	Day 1 only of a 21 day cycle
Gemcitabine	**1250mg/m^2**	IV infusion	Days 1 and 8 of a 21 cycle

Maximum of 4 cycles

Supportive treatments:

Anti-emetic risk- High

Aprepitant 125mg one hour before chemotherapy then 80mg once daily on days two and three (for full dose regimen only)

Dexamethasone 4mg oral tablets twice daily for 3 days from day two following cisplatin

Ondansetron 8mg oral tablets twice daily for 3 days from day two following cisplatin

Domperidone 10mg three times a day or as required

Extravasation risk:

Cisplatin: Injection site reactions may occur during the administration of cisplatin. Given the possibility of extravasation, it is recommended to closely monitor the infusion site for possible infiltration during drug administration.

Gemcitabine: neutral

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.

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:

Day	Drug	Dose	Route	Diluent and rate
1	**Aprepitant**	**125mg**	**PO**	60 mins before chemotherapy
	Dexamethasone	**12mg**	**PO**	30 mins before chemotherapy
	Ondansetron	**24mg**	**PO**	30 mins before chemotherapy
	Sodium Chloride 0.9% 1000mL With 20mmol Potassium Chloride		**IV over 90 minutes**	
	Measure urine output volume and record **If urine output averages 100mL/hour over previous 3 hours then proceed with cisplatin infusion** **If urine output is less than 100mL/hour the patient should be assessed and further 500mL sodium chloride 0.9% given IV over 30 minutes** **If urine output still not adequate contact the urology team**			
	Cisplatin	**80mg/m^2**	**IV**	Sodium Chloride 0.9% 1000mL over 90 minutes
	Sodium Chloride 0.9% 1000mL With 20mmol Potassium Chloride		**IV over 90 minutes**	
	Gemcitabine	**1250mg/m^2**	**IV**	Sodium Chloride 0.9% 250mL over 30 minutes
8	**Dexamethasone** 30mins before chemotherapy	**8mg**	**PO**	30 mins before chemotherapy
	Gemcitabine	**1250mg/m^2**	**IV**	Sodium Chloride 0.9% 250mL over 30 minutes

- Vein discomfort throughout infusion of gemcitabine may be eased using heat pack.
- Gemcitabine is a radiation sensitizer: be aware if patients are also receiving radiotherapy**.**

Main toxicities

Thrombocytopenia, neutropenia, anaemia, nausea, vomiting, diarrhoea

Cisplatin	
Cardiac disorders	Arrhythmia, bradycardia, tachycardia
Nephrotoxicity	Urine output of 100 mL/hour or greater will help minimise cisplatin nephrotoxicity
Neuropathies	May be irreversible and may manifest by paresthesia, loss of muscle reflex and a sensation of vibrations. A neurologic examination must be carried out at regular intervals.
Ototoxicity	Observed in up to 31% of patients can be unilateral or bilateral and tends to become more frequent and severe with repeated doses; consider audiometry and referral to ENT specialist
Additional side effects	Loss of fertility Anaphylactic reactions
Gemcitabine	
Hepatobiliary	Elevation of liver transaminases (AST and ALT) and alkaline phosphatase, Increased bilirubin, uncommon reports (≥ l/1000 to <1/100), hepatotoxicity, including liver failure.
Urinary symptoms	Haematuria, Mild proteinuria
Gastrointestinal	stomatitis and ulceration of the mouth, constipation
Additional side effects	alopecia, peripheral oedema, rash, influenza-like symptoms, dizziness during infusion, peripheral neuropathy,

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 1 D8	Cycle 2	Cycle 2 D8	Prior to cycle 3	Cycle 3	Cycle 3 D8	Cycle 4	Cycle 4 D8	Ongoing
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					
FBC	X	X	x	X	x		X	x	X	x	Every cycle
U&E & LFTs & Magnesium	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										
ECG											If clinically indicated
Blood pressure measurement	X										Repeat if clinically indicated
Respiratory Rate											If clinically indicated
PS recorded	X	X		X			X		X		Every Cycle
Toxicities documented	X	X		X			X		X		Every Cycle
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:

If patient develops Grade 2 neuropathy or ototoxicity, consider changing cisplatin to carboplatin. Discuss with Consultant. Consider dose modifications for intolerable grade 2 or any grade 3 toxicities.

Recommended dose reduction for toxicity management, full dose regimen only	Cisplatin	Gemcitabine
First dose reduction	70mg/m^2	1000mg/m^2
Second dose reduction	60mg/m^2	800mg/m^2

Haematological toxicity

Proceed on day 1 if-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 100 x 10^9/L

Delay 1 week on day 1 if-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 99 x 10^9/L

Proceed on day 8 if-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 75 x 10^9/L

Omit on day 8 if-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 74 x 10^9/L

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:

Cisplatin
No dose reduction necessary.

Gemcitabine
AST elevations do not seem to cause dose limiting toxicities. If bilirubin > 27 µmol/L, initiate treatment with dose of 800mg/m2.

Renal Impairment:

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

Gemcitabine: CrCl (mL/min)	**Dose**
>31	1250mg/m^2 (100% dose)
<30	Consider dose reduction – clinical decision.

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 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
- 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