Systemic Anti Cancer Treatment Protocol

Carboplatin and Gemcitabine

PROTOCOL REF: MPHACAGELU
(Version No: 1.0)

Approved for use in:

Advanced non-small cell lung cancer

Performance status: 0 to 2

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

Dosage:

Drug	Dose	Route	Frequency
Carboplatin	**AUC 5**	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

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:

Anti-emetic risk - Moderate

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

Domperidone 10mg three times a day or as required

Extravasation risk:

Carboplatin- irritant

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:

Day	Drug	Dose	Route	Diluent and rate
1	Sodium Chloride 0.9%	50ml	IV Infusion	Flush
	Dexamethasone	As prescribed	IV/Oral	30mins before chemotherapy
	Ondansetron	As prescribed	IV/Oral	30mins before chemotherapy
	Gemcitabine	**1250mg/m²**	**IV Infusion**	**250mls sodium chloride 0.9% over 30 minutes**
	Carboplatin	**AUC 5**	**IV Infusion**	**500mls glucose over 30-60 minutes**
	Sodium Chloride 0.9%	100ml	IV Infusion	Flush
8	Sodium Chloride 0.9%	50ml	IV Infusion	Flush
	Dexamethasone	As prescribed	IV/Oral	30mins before chemotherapy
	Gemcitabine	**1250mg/m²**	**IV Infusion**	**250mls sodium chloride 0.9% over 30 minutes**
	Sodium Chloride 0.9%	100ml	IV Infusion	Flush

- 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**.**
- Carboplatin risk of hypersensitivity and anaphylaxis may increase with previous exposure to platinum therapy.

Main Toxicities

Anaphylactic reactions, nausea and vomiting, diarrhea, myelosuppression (thrombocytopenia, anaemia and neutropenia), nephrotoxicity, otological impairment, haematuria, oedema/ peripheral odema, mild alopecia, lethargy, mild dyspnoea, flu like symptoms, mucositis.

Investigations and treatment plan

	Pre	Cycle 1 D1	Cycle 1 D8	Cycle 2	Cycle 2 D8	Prior to cycle 3	Cycle 3	Cycle 3 D8	Cycle 4	Cycle 4 D8	Comments
Medical Assessment	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 administration
U&E & LFT	x	x		x			x		x		Every cycle – day 8 only if clinical indication
CrCl **(Wright)**	x	x		x			x		x		Every cycle
CT scan**	x										At the end of treatment
Informed Consent	x										
Blood pressure	x										Repeat if clinically indicated
Respiratory Rate											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

Haematolgical Toxicity:

Proceed on day 1 if-

Plt ≥ 100 x 10^9/L	ANC ≥ 1.0

Delay 1 week on day 1 if-

Plt ≤ 99 x 10^9/L	ANC ≤ 0.9

Proceed on day 8 if-

Plt ≥ 75 x 10^9/L	ANC ≥ 1.0

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:

Carboplatin
Transient increases in liver enzymes have been reported. Probably 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/m^2.

Renal Impairment:

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

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