Systemic Anti-Cancer Treatment Protocol

Carboplatin and Pemetrexed Non-Small Cell Lung Cancer

PROTOCOL REF: MPHACAPELU
(Version No: 1.0)

Approved for use in:

1st line treatment of patients with locally advanced or metastatic non-small-cell lung cancer only if the histology of the tumour has been confirmed as adenocarcinoma or large cell carcinoma. PS 0-1

Mesothelioma patient with PS 0-1 (see separate protocol)

Dosage:

Drug	Dosage	Route	Frequency
Carboplatin	AUC 5	IV infusion	Every 21 days
Pemetrexed	500mg/m²		

Maximum of four cycles.

Supportive Treatments:

Vitamin B12 intra muscular injection should be administered in the week preceding the 1st cycle. Vitamin B12 should be given every 9 weeks thereafter (every 3rd treatment cycle) on the same day as treatment.

Folic acid 400 micrograms once daily during treatment starting least five days before the first dose of pemetrexed, and continuing until 21 days after the last dose of pemetrexed.

Anti-emetic risk

Dexamethasone 4mg twice daily for 5 days, staring day before pemetrexed. If dexamethasone premedication has not been commenced then administer 8mg intravenously 30 minutes prior to pemetrexed, and then continue with the remainder of the oral doses.

Domperidone 10mg tablets, to be taken up to three times a day as required

Extravasation risk:

Carboplatin-irritant

Pemetrexed- 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.

Non-steroidal anti-inflammatory drugs:

These should be avoided from 5 days before each dose of pemetrexed until 2 days after each dose. If concomitant administration of NSAIDs is necessary, patients should be monitored closely for toxicity, especially myelosuppression, renal impairment and gastrointestinal toxicity.

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

Administration:

- **Calculate creatinine clearance using wright formula (calculator available on Citrix)**

• Day	Drug	Dose	Route	Diluent and rate
1	**Ondansetron** 30mins before chemotherapy	**16mg**	PO	
	Pemetrexed*	**500mg/m^2**	IV	In 100mL sodium chloride 0.9% over 10 minutes
	Carboplatin	**AUC 5**	IV	In 500mL glucose 5% over 60 minutes

Main Toxicities:

Carboplatin	
Nephrotoxicity	Impairment of renal function is more likely in patients who have previously experienced nephrotoxicity as a result of cisplatin
Neuropathies	Peripheral neuropathy – more common in elderly patients and those previously treated with cisplatin.
Hepatobiliary toxicity	Raised liver function tests
Ocular	Rare reports of transient visual disturbances, which may include transient sight loss
Ototoxicity	Decreases in hearing acuity, consisting of high-frequency hearing loss In patients who have been previously treated with cisplatin and have developed hearing loss related to treatment, the hearing impairment may persist or worsen.
Additional side effects	Anaphylactic-like reactions to carboplatin have been reported Pulmonary fibrosis manifested by tightness of the chest and dyspnoea. Neutropenia, diarrhoea and vomiting Mucositis (stomatitis, oesophagitis, pharyngitis, proctitis), bitter or metallic taste disturbance, alopecia and loss of fertility. Pulmonary fibrosis manifested by tightness of the chest and dyspnoea.

Pemetrexed	
Skin reactions	Pre-treatment with dexamethasone (or equivalent) can reduce the incidence and severity of skin reactions
Radiation pneumonitis **Radiation recall**	Cases of radiation pneumonitis and radiation recall have been reported in patients treated with radiation either prior, during, or subsequent to their pemetrexed therapy. Particular attention should be paid to these patients and caution exercised with use of other radio sensitising agents.
Cardiovascular events	Myocardial infarction and cerebrovascular events have been reported
Genetically damaging effects.	Sexually mature males are advised not to father a child during the treatment and up to 6 months thereafter. Women of childbearing potential must use effective contraception during treatment with pemetrexed.

Investigations and treatment plan

	Pre	Cycle 1	Cycle 2	Pre Cycle 3	Cycle 3	Cycle 4	Ongoing
Medical Assessment	X			X*		X	At end of treatment
Nursing Assessment	X	X	X		X	X	Every cycle
FBC	X	X	X		X	X	Every cycle
U&E & LFT & Mg	X	X	X		X	X	Every cycle
CrCl (Wright formula)	X	X	X		X	X	Every cycle
Respiratory Rate							If clinically indicated
CT scan	X						End of treatment or as clinically indicated
Informed Consent	X						
Blood glucose	X						Repeat if clinically indicated
Blood pressure measurement	X						Repeat 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

*Medical assessment by clinician with appropriate competencies to capture and communicate ongoing benefit including PS, toxicity, patient understanding, symptom control and clinical tumour response (imaging as required based upon assessment)

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if:-

Platelets ≥ 100	ANC ≥ 1.0

Delay 1 week on day 1 if:-

Platelets ≤ 99	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 toxicities

Hepatic impairment:

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

Pemetrexed
Pemetrexed undergoes limited hepatic metabolism and is primarily eliminated in the urine, with 70% to 90% of the administered dose being recovered unchanged in urine within the first 24 hours following administration. No relationships between AST, ALT or total bilirubin and pemetrexed pharmacokinetics were identified. However patients with hepatic impairment such as bilirubin >1.5 x upper limit of normal (ULN) and/or transaminase > 3.0 x ULN (hepatic metastases absent) or > 5.0 x ULN (hepatic metastases present) have not been specifically studied.

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

Pemetrexed
GFR > 45mL/min 100% dose. If less than 45ml/min the consultant should be contacted as it is a clinical decision if pemetrexed is to continue. May be hazardous in severe renal impairment.

Hypersensitivity:

Patients who have previously experienced Grade I or II Platinum HSR should be pre-medicated with 45 minutes prior to carboplatin:

- Hydrocortisone 100mg IV 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:

- 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 TA 181 Pemetrexed for the first line treatment of non-small-cell lung cancer