Systemic Anti Cancer Treatment Protocol

Carboplatin
Gynaecological Cancer

PROCTOCOL REF: MPHAGYNCAR
(Version No: 1.1)

Approved for use in:

- 1st line epithelial ovarian cancer (every 21 days)
- 2nd line epithelial ovarian cancer (> 6 months post platinum (every 21-28 days))
- 1st line epithelial ovarian cancer with mucinous histology (every 21 days)
- Advanced/metastatic endometrial carcinoma

Dosage

Drug	Dose	Route	Frequency
Carboplatin	**AUC 5 or 6 x (GFR +25)**	IV infusion	Every 21-28 days x 6 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.

Creatinine clearance should be capped at 125mL/min for carboplatin

Avoid the use of Cockcroft and Gault formulae as it is less accurate.

Supportive Treatments:

Dexamethasone tablets 4mg orally twice daily for three days

Domperidone 10mg tablets, three times a day when required

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

Carboplatin 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.

Extravasation risk

Carboplatin: Irritant

Refer to the network guidance for the prevention and management of extravasation

Administration

Day	Drug	Dose	Route	Diluent and rate
1	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Dexamethasone	8mg	PO	30 minutes before chemotherapy
	Sodium Chloride 0.9%	50mL	**IV**	Flush
	Carboplatin	**AUC 5 or 6**	**IV Infusion**	**500mL glucose 5% over 30 to 60 minutes**
	Sodium Chloride 0.9%	100mL	IV	Flush

Facilities to treat anaphylaxis must be present when administering carboplatin. If a patient experiences an **infusion-related reaction**, give future does with pre-medication cover of IV chlorphenamine 10mg and IV hydrocortisone 100mg.

Main Toxicities

Gastrointestinal	Nausea, vomiting, diarrhoea, constipation, mucositis
General disorders	Decreases in serum electrolytes (sodium, magnesium, potassium and calcium) Renal function impairment Hyperuricaemia: Serum levels of uric acid can be decreased by allopurinol. Malaise, urticaria. flu-like syndrome, rash, pruritus, alopecia

Haematological	Neutropenia, anaemia, thrombocytopenia Myelosuppression may be more severe and prolonged in patients with impaired renal function, extensive prior treatment, poor performance status and age above 65.
Hepatobiliary	Abnormalities of liver function tests (usually mild to moderate The alkaline phosphatase level is increased more frequently than transaminases or total bilirubin. The majority of these abnormalities regress spontaneously during the course of treatment.
Hypersensitivity reactions	Skin rash, urticaria, erythematous rash, and fever with no apparent cause or pruritus Risk of hypersensitivity and anaphylaxis may increase with previous exposure to platinum therapy
Nervous system	Paraesthesia and decreased deep tendon reflexes.
Ototoxicity	Hearing loss

Investigations

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Ongoing
Medical Assessment	X				X			After cycles 3 and 6 then as per management plan
SACT Assessment	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	X	X	Every cycle
CrCl (Wright)	X	X	X	X	X	X	X	Every cycle
CA125*	X	X	X	X	X	X	X	Every cycle *ovarian patients only
CT scan	X				X			After cycles 3 and 6
Informed Consent	X							
PS recorded	X	X	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management

Haematological Toxicity

Proceed on day 1 if-

Plt ≥ 100 x 10^9/L	ANC ≥ 1.0 x 10^9/L

Delay 1 week on day 1 if-

Plt ≤ 99 x 10^9/L	ANC ≤ 0.9 x 10^9/L

Non-haematological Toxicity

Grading and Management of Toxicity

Toxicity should be grading according to the CTCAEV4 criteria. Following assessment treatment should be withheld for any toxicity until resolved to grade 0/1. For dose modification, follow the general guidance below and discuss with treating clinician.

	Grade 2	Grade 3	Grade 4
1st appearance	Interrupt treatment until resolved to grade 0/1, then continue at 100% of original dose with prophylaxis where possible	Interrupt treatment until resolved to grade 0/1, then continue at 75-80% or AUC 4 of original dose with prophylaxis where possible	Discontinue treatment
2nd appearance	Interrupt treatment until resolved to grade 0/1, then continue at 75-80% of original dose or AUC 4	Interrupt treatment until resolved to grade0/1, then continue at 50% of original dose or AUC 3.5	
3rd appearance	Interrupt treatment until resolved to grade 0/1, then continue at 50% of original dose or AUC 3.5	Discontinue treatment	
4th appearance	Discontinue treatment		

Hepatic Impairment: No dose adjustment is necessary

Renal Impairment: Patients with creatinine clearance values of less than 60 ml/min are at greater risk to develop myelosuppression. Carboplatin is contraindicated if glomerular filtration rate is ≤ 20 ml/min.

The optimal use of carboplatin in patients presenting with impaired renal function requires adequate dosage adjustments and frequent monitoring of both haematological nadirs and renal function.

References

http://www.medicines.org.uk/

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)

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