SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Carboplatin

Gynaecological Cancer

PROTOCOL REF: MPHAGYNCAR

Version No: 1.2

Approved for use in:

- Epithelial ovarian cancer
- Endometrial cancer
- Cervical cancer

Dosage:

Drug	Dose (mg)	Route	Frequency
Carboplatin	***AUC 5 or AUC 6**	IV infusion	Every 21 days

For 6 cycles

*Use area under the curve (AUC) 5 for GFR calculations utilising Wright formula and AUC 6 when calculating Creatinine Clearance (CrCl) using Cockroft and Gault formula. This formula will then need to be used throughout the course of carboplatin treatment. If estimated GFR is used the **Wright formula and AUC 5** must be used for creatinine clearance.

Note: For carboplatin dosing creatinine clearance should be capped at 125mL/min. Please see renal impairment section for further details

Emetogenic risk:

Highly emetogenic.

Supportive treatments:

Pre-Medication:

Dexamethasone 8mg oral 30 minutes before chemotherapy

Ondansetron 16mg oral 30 minutes before chemotherapy

Aprepitant can be added if additional risk factors

To take home medications

Dexamethasone tablets 4mg oral, twice daily for three days

Metoclopramide tablets 10mg oral, up to 3 times a day as required for a maximum of 5 consecutive days

Ondansetron 8mg tablets oral, twice daily for 3 days

Extravasation risk:

Carboplatin-IRRITANT

Refer to the CCC policy for the 'Prevention and Management of Extravasation Injuries'

Dosing in renal and hepatic impairment:

Renal	Calvert formula is utilised for Carboplatin dose calculation. *Carboplatin dose in mg = AUC x (creatinine clearance + 25)* For carboplatin Meditech calculates creatinine clearance using the Wright formula. **For the AUC 6 dose creatinine clearance will need to be entered manually to use Cockroft and Gault formula**

	The Carboplatin Dose Calculator application for calculating creatinine is available on the Remote Citrix Web Portal - Carboplatin Dose Calculator (clatterbridgecc.nhs.uk) If estimated GFR is used the **Wright formula** must be used for creatinine clearance Any dose adjustments needed from usage of the carboplatin dose calculator see carboplatin SOP for instruction Creatinine clearance should be capped at 125mL/min for carboplatin

Hepatic	No dose adjustment is necessary

Interactions:

Concomitant use contraindicated

- **Yellow fever vaccine**: risk of generalized disease mortality.

Concomitant use not recommended

- **Live attenuated vaccines** (except yellow fever): Risk of systemic, possible fatal disease. This is increased in subjects who are already immunosuppressed by their underlying disease. Use inactivated vaccine where this exist (poliomyelitis).
- **Phenytoin, fosphenytoin**: Risk of exacerbation of convulsions (resulting from the decrease of phenytoin digestive absorption by the cytotoxic drug), risk of toxicity

enhancement or loss of efficacy of the cytotoxic drug (due to increased hepatic metabolism by phenytoin).

Concomitant use to take into consideration

- **Ciclosporin** (and by extrapolation **tacrolimus** and **sirolimus**): Excessive immunosuppression with risk of lymphoproliferation.
- Concurrent therapy with nephrotoxic drugs or ototoxic drugs such as **amino glycosides**, **vancomycin, capreomycin and diuretics**, may increase or exacerbate toxicity, particularly in renal failure patients, due to Carboplatin induced changes in renal clearance.
- **Loop diuretics (furosemide,indapamide,bumetanide):** The concomitant use of carboplatin with loop diuretic should be approached with caution due to the cumulative nephrotoxicity and ototoxicity.

For more detailed interactions please refer to the SmPC.

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1	Dexamethasone	8mg	PO	30 mins before chemotherapy
	Ondansetron	16mg	PO	30 mins before chemotherapy
	Carboplatin	AUC 5 or AUC 6	IV	500mL glucose 5% over 30 to 60 minutes

As with all platinum based chemotherapy, patients may experience allergic reaction during administration. Please refer to the CCC Hypersensitivity; Management Prevention Policy.

For severe reactions, discuss with Consultant before continuing with treatment. It should be strongly noted that patients who have severe reactions should not be re-challenged.

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 (ALP) level is increased more frequently than transaminases or total bilirubin. The majority of these abnormalities regress spontaneously during 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	Tinnitus and hearing loss

Investigations and treatment plan:

	Pre	Cycle 1	Cycle2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Ongoing
Informed Consent	X							
Clinical Assessment	X				X			After cycles 3 and 6 then as per management plan
SACT Assessment (to include PS and toxicities)	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	Every cycle
U&E & LFTs & Magnesium	X	X	X	X	X	X	X	Every Cycle
Calculate GFR or CrCl and check carboplatin dose using the carboplatin calculator*	X	X	X	X	X		X	Every cycle
CA 125	X	X	X	X	X	X	X	Every cycle for ovarian patients only
CT scan**	X				X			After cycles 3 and 6
Full observations (Bp, Resp rate etc)	X	X	X	X	X	X	X	Every cycle
Height recorded	X							
Weight recorded	X	X		X		X		Every cycle

Dose Modifications and Toxicity Management:

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

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:

Grading and Management of Toxicity

Toxicity should be grading according to the CTCAE 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 to 80% or AUC 5 of original dose with prophylaxis where possible	Discontinue treatment
2nd appearance	Interrupt treatment until resolved to grade 0/1, then continue at 75 to 80% of original dose or AUC 5	Interrupt treatment until resolved to grade 0/1, then continue at 50% of original dose or AUC 4	
3rd appearance	Interrupt treatment until resolved to grade 0/1, then continue at 50% of original dose or AUC 4	Discontinue treatment	
4th appearance	Discontinue treatment		

References:

1. Electronic Medicines Compendium (2022, 30 September*), Carboplatin 10mg/ml intravenous infusion* https://www.medicines.org.uk/emc/product/3787/smpc#gref
2. Joint Formulary Committee. *British National Formulary (onlin*e) London: BMJ Group and Pharmaceutical Press
3. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol* 2019; 20: e201–08.
4. Northern Cancer Alliance (2018) *Anti-emetic Guidelines for Chemotherapy Induced Nausea and Vomiting (CINV)* Newcastle Upon Tyne: NHS England
5. Paclitaxel plus carboplatin versus standard chemotherapy with either single agent carboplatin or cyclophosphamide, doxorubicin and cisplatin in women with ovarian cancer: the ICON3 randomised trial Lancet 2002, 360(9332): 505-515

Circulation/Dissemination

Date added into Q-Pulse	9th November 2023
Date document posted on the Intranet	N/A

Version History

Date	Version	Author name and designation	Summary of main changes
	1.1	Anna Burke Advanced Pharmacist NMP	Routine protocol update
	1.2	Sarah Craig Advanced Pharmacist Teacher Practitioner	Slight updates – mainly to supportive meds and renal function to align with other gynae protocols and indications as per consultant comment