PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Carboplatin

Metastatic Breast Cancer (MBC)

PROTOCOL REF: MPHACMBC
(Version No. 1.0)

Approved for use in:

Triple negative or BRCA mutated metastatic breast cancer.

PS 0-2

Dosage:

Drug	Dosage	Route	Frequency
Carboplatin	**AUC* 5 or 6**	IV	Every 21 days

Repeat 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.

Meditech calculates creatinine clearance using the Wright formula and therefore **creatinine clearance will need to be entered manually to use Cockroft and Gault formula** (applications for calculating creatinine using both formulas are available on the Remote Citrix Web Portal).

NOTE: either calculation is an estimate and the dose should be reviewed with the patients clinical condition taken into account

Calvert formula for Carboplatin dosage-:

Carboplatin dose in mg = AUC x (GFR or CrCl + 25)

Emetogenic risk:

Moderately emetogenic.

Supportive treatments:

Dexamethasone tablets 4mg orally twice daily for three days

Metoclopramide 10mg orally three times a day when required for a maximum 5 consecutive 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	Patients with creatinine clearance values of less than 60 mL/min are at greater risk to develop myelosuppression. 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. Carboplatin is contraindicated if GFR or CrCl ≤ 20 ml/min. Do not give carboplatin and discuss with clinical team.

Hepatic	No need for dose adjustment is required.

Interactions:

Please refer to the SmPC for full list of interactions.

Concomitant use contraindicated

Yellow fever vaccine: risk of generalized disease mortal.

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.

Treatment schedule:

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

Repeated every 21 days for 6 cycles
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	Cycle 2	Cycle 3	Cycle 4	Ongoing
Informed Consent	x					
Clinical Assessment	x		x		x	As clinically indicated or at the end of treatment
SACT Assessment (to include PS and toxicities)	x	x	x	x	x	Every cycle
FBC	x	x	x	x	x	Every cycle
U&E & LFTs & Magnesium	x	x	x	x	x	Every cycle
Calculate GFR or CrCl and check carboplatin dose using the carboplatin calculator*	x	x	x	x	x	Every cycle
CT scan	x				x	Every 3 months or if clinically indicated
ECG						If clinically indicated
Full observations		x	x	x	x	Every cycle
Weight recorded	x	x	x	x	x	Every cycle
Height	x					

* Please refer to:

- 'Dosage' section for full details on carboplatin dosing.
- 'Carboplatin Dosing Calculator' SOP outlining process for checking carboplatin dose ahead of each cycle of treatment.

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

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 CTCAEV5 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. SmPC for Carboplatin 10 mg/ml Intravenous Infusion, Hospira – accessed via electronic medicines compendium at https://www.medicines.org.uk/emc (Last updated June 2020)
2. Tutt A et al. (2018) Carboplatin in BRCA1/2-mutated and triple-negative breast cancer BRCAness subgroups: the TNT Trial. Nat Med. 24(5):628-637.
3. Supplement to: 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.

Circulation/Dissemination

Date added into Q-Pulse	23rd March 2023
Date document posted on the Intranet	N/A

Version History

Date	Version	Author name and designation	Summary of main changes
February 2023	1.0	**Helen Flint** **Consultant Pharmacist**	New Protocol Regimen V1.0