SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Carboplatin

Small Cell Cancer Any Solid Tumour Site

PROTOCOL REF: MPHACARLU

Version No: 1.1

Approved for use in:

- First line treatment of small cell lung cancer (SCLC) ECOG Performance Status (PS) 2 patients.
- Second line treatment of SCLC if combination treatment with platinum-etoposide not appropriate.
- Small cell cancer of any site.

Dosage:

Drug	Dose (mg)	Route	Frequency	Duration
Carboplatin	***AUC 5**	IV infusion	Every 21-28 days	6 cycles

*Use area under the curve (AUC) 5 for GFR calculations utilising Wright formula. This formula will then need to be used throughout the course of carboplatin treatment. **As this is an estimate dose, it should be reviewed with the patient's clinical condition taken into account. The dose of carboplatin needs to be checked ahead of each cycle of treatment** using the Wright formula application available on the Remote Citrix Web Portal, please refer to 'Carboplatin dosing calculator' SOP for full details.

Calvert formula for Carboplatin dosage

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

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

NOTE: Avoid the use of Cockcroft and Gault formula as it is less accurate.

Counselling Points

Confirm patient understanding of the need to **ensure good oral fluid intake** while on SACT to aid the clearance of carboplatin and therefore minimise toxicities.

Please contact the triage line if any of the following symptoms occur:

- Easy bruising or bleeding.
- Uncontrolled nausea, vomiting, constipation or diarrhoea.
- New or worsening cough, chest pain or shortness of breath
- Severe jaw pain or headache.
- Redness, swelling, pain or sores where the needle was place or along the arm.
- Redness, swelling, pain or sores on your lips, tongue, mouth or throat.
- Skin rash or itching.
- Ringing in your ears or hearing problems.
- Numbness or tingling in feet or hands or painful leg cramps.
- Signs of anaemia such as unusual tiredness, dizziness, shortness of breath or weakness.

Emetogenic risk:

Moderately emetogenic.

Supportive treatments:

- Dexamethasone tablets 4mg orally twice daily for three days
- Metoclopramide 10mg tablets, 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. **Carboplatin is contraindicated if glomerular filtration rate is ≤ 20mL/min. Do not give carboplatin and discuss with clinical team.** 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. **The dose of carboplatin needs to be checked ahead of each cycle of treatment** using the Wright formula application available on the Remote Citrix Web Portal, please refer to 'Carboplatin dosing calculator' SOP for full details.

Hepatic	No dose adjustment is necessary

Interactions:

Refer to SmPC for full list of interactions.

Concomitant use contraindicated

- **Yellow fever vaccine**: risk of fatal disease.

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	30minutes before chemotherapy
	Dexamethasone	8mg	PO	30 minutes before chemotherapy
	Sodium Chloride 0.9%	50ml	IV	Flush
	Carboplatin	**AUC 5**	**IV**	500ml glucose 5% over 30-60 minutes
	Sodium Chloride 0.9%	100ml	IV	Flush

Every 21 to 28 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	Cycle 5	Cycle 6	Ongoing
Informed Consent	x							
Clinical Assessment	x		x		x		x	Alternate cycles or as clinically indicated
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 and check carboplatin dose using the carboplatin calculator*	x	x	x	x	x		x	Every cycle
CT scan	x				x			After cycles 3 and 6
Full observations *(Temp, HR, BP, RR and O_2 sats)*	x	x	x	x	x	x	x	Every cycle
Height recorded	x							
Weight recorded	x	x	x	x	x	x	x	Every cycle

*Please refer to:

- The dosage section for full details on carboplatin dosing.
- 'Carboplatin dosing calculator' SOP outlines the process for checking carboplatin doses ahead of each cycle of treatment.

Dose Modifications and Toxicity Management:

- Please refer to the dosage section for full details on carboplatin dosing.
- 'Carboplatin dosing calculator' SOP outlines the process for checking carboplatin doses ahead of each cycle of treatment.

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 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% 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. 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.
2. Carboplatin 10 mg/ml Intravenous Infusion SmPC, Hospira UK ltd. Available from www.medicines.org.uk/emc/medicine. Last updated 30th September 2022.
3. NICE Guideline (NG122). Lung cancer: diagnosis and management. Last updated: 14 March 2023.

Circulation/Dissemination

Date added into Q-Pulse	7th September 2023
Date document posted on the Intranet	N/A

Version History

Date	Version	Author name and designation	Summary of main changes
June 2023	1.1	**Hala Ghoz** **Lung SRG Pharmacist**	V1.1 Routine protocol update