Systemic Anti-Cancer Treatment Protocol

Cisplatin 100mg/m^2 Head and Neck Regimen Chemoradiotherapy

PROCEDURE REF: MPHACISHNR
(Version No: 1.4)

Approved for use in:

Locally advanced head and neck cancer **concurrent radiotherapy.**

Metastatic head and neck cancer **(without radiotherapy).**

PS 0 – 1

Dosage:

Drug	Dose	Route	Frequency
Cisplatin	**Curative (with radiotherapy) - 100mg/m^2** **Palliative - 80mg/m^2**	IV infusion	Day 1 only

Carboplatin should be used as an <u>alternative to Cisplatin</u> in patients with a Creatinine Clearance (CrCl) calculated using Cockcroft and Gault (C&G) formula < 40ml/min (curative) or CrCl < 50ml/min (palliative) and/or in case of deafness.

Drug	Dose	Route	Frequency
Carboplatin	**AUC 5**	IV infusion	Day 1 only

Radical concurrent radiotherapy – Nasopharynx and younger (<50yrs), fit oropharynx patients: Cisplatin 100mg/m^2 or Carboplatin AUC5 repeat every 3 weeks for 3 doses (week 1, 4, 7) with concurrent radiotherapy.

All other patients: Cisplatin 100mg/m^2 2 doses (week 1 and 5) or Carboplatin AUC5 with concurrent radiotherapy.

Metastatic head and neck cancer – Cisplatin 80mg/m^2 or Carboplatin AUC5 repeated every 3 weeks for up to 6 cycles.

Supportive Treatments:

Cisplatin

Fosaprepitant 150mg IV pre chemotherapy

Dexamethasone 12mg pre chemotherapy

Dexamethasone 4mg TWICE a day for 3 days

Ondansetron 16mg pre chemotherapy

Cyclizine 50mg THREE times a day when required

Ondansetron 8mg TWICE a day for 3 days

Carboplatin

Dexamethasone 4mg TWICE a day for 3 days

Domperidone 10mg THREE times a day when required

Extravasation risk:

Cisplatin: Irritant

Carboplatin: Irritant

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

Administration:

Cisplatin

- Review patient's fluid intake over the previous 24 hours
- Review common toxicity criteria and performance status
- Calculate creatinine clearance using Cockcroft and Gault (C&G) equation (application for calculating creatinine using C&G formula is available on the Remote Citrix Web Portal) ahead of each cycle of treatment:

Male patients $\frac{1.23 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

Female patients $\frac{1.04 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

- Pre-hydration fluids should be administered immediately before cisplatin infusion is started and post hydration fluids should be administered immediately after cisplatin infusion has finished – There should **NOT** be any gaps in treatment.
- Patients MUST stay on the chemotherapy day ward during administration of the cisplatin infusion. Patients are able to leave the ward during administration of post hydration fluids to attend radiotherapy. AT NO POINT SHOULD THE POST HYDRATION FLUIDS BE STOPPED.

Day	Drug	Dose	Route	Diluent and rate
1	**Fosaprepitant** Immediately prior to hydration	**150mg**	**IV**	100mL Sodium Chloride 0.9% over 30 minutes
	Ondansetron Immediately prior to hydration	**16mg**	**IV**	
	Dexamethasone Immediately prior to hydration	**12mg**	**IV**	
	Sodium Chloride 0.9% 500mL		**IV**	Over 30 minutes
	Sodium Chloride 0.9% 1000mL with 20mmol Potassium Chloride and 10mmol Magnesium Sulphate	**1000mL**	**IV**	Over 2 hours
	Measure urine output volume and record **If urine output averages 100mL/hour over previous 3 hours then proceed with cisplatin infusion** **If urine output is less than 100mL/hour the patient should be assessed and further 500mL sodium chloride 0.9% given IV over 30 minutes** **If urine output still not adequate contact the head and neck team**			
	Cisplatin	**100mg/m^2**	**IV**	Sodium Chloride 0.9% 1000mL over 2 hours

		(80mg/m^2 for palliative)		
	Sodium Chloride 0.9% 1000mL with 20mmol Potassium Chloride and 10mmol Magnesium Sulphate	**1000mL**	**IV**	Over 2 hours

Ensure good oral (or via PEG) fluid intake

- **Confirm patient understanding of the importance of fluid intake**
- **Patient should ensure they have 2 litres of fluid in the 24 hours following chemotherapy**

Fosaprepitant:

Note: incompatible with magnesium containing fluids, therefore IV line must be flushed with sodium chloride prior to starting the pre-hydration.

Interactions with other medicines occurs via the CYP3A4 pathway – discuss with pharmacist if patient taking ciclosporin, tacrolimus, sirolimus, alfentanyl, fentanyl, rifampicin, phenytoin, carbamazepine, fluconazole, clarithromycin.

Cisplatin:

Infusion bag should be protected from light

Store at room temperature

Carboplatin

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**	**IV Infusion**	**500mL glucose 5% over 30 to 60 minutes**
	Sodium Chloride 0.9%	100mL	IV	Flush

Please note: Meditech calculates creatinine clearance/GFR using the Wright formula (application for using Wright formula is available on the Remote Citrix Web Portal). Please refer to 'Carboplatin Dosing Calculator' SOP outlining process for checking carboplatin dose ahead of each cycle of treatment.

Calvert formula for Carboplatin dosage-:
Carboplatin dose in mg = AUC x (GFR or CrCl + 25)

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. Please refer to the CCC Hypersensitivity; Management Prevention Policy.

Carboplatin

Infusion bag should be protected from light
Store at 2 – 8^{o}C

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.

Main Toxicities:

Cisplatin & Carboplatin

Anaphylactic-like reactions: to cisplatin have been reported with both agents.

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

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.

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.

Nephrotoxicity: Urine output of 100 ml/hour or greater will help minimise cisplatin nephrotoxicity.

Nervous system: Paraesthesia- burning or prickling sensation that is usually felt in the hands, arms, legs, or feet. The sensation, which happens spontaneously is usually painless and described as tingling or numbness, skin crawling, or itching. It is mostly described as 'pins and needles".

Decreased deep tendon reflexes.

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.

Ototoxicity: Characterized by **hearing loss and tinnitus** (noise in the ears, such as ringing, buzzing, roaring or clicking). observed in up to 31% of patients receiving cisplatin and about 15% of patients who receive carboplatin, can be unilateral but **tends to be bilateral**. Tends to become more frequent and severe with repeated doses of cisplatin; It is unclear whether ototoxicity is reversible.

Investigations:

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Clinical Assessment	X			X	At end of treatment
SACT Assessment (including PS and toxicity assessment)		X	X	X	Every cycle
FBC	X		X	X	Every cycle, day 1 only
U&E, Mg & LFT	X		X	X	Every cycle, day 1 only
Calculate CrCl	X	X	X	X	Every cycle Refer to 'Administration' section for details
CT scan	X				As clinically indicated
Informed Consent	X				
Weight recorded	X	X	X	X	Every cycle
Height recorded	X				

Dose Modifications and Toxicity Management:

Haematological Toxicity:

Proceed on day 1 if:

Platelet ≥ 100 x 10^9/L	ANC ≥ 1.0 x 10^9/L

For concurrent chemoradiotherapy patients

Discuss with the head and neck team, if

Platelet ≤ 99 x 10^9/L	ANC ≤ 0.9 x 10^9/L

Treatment should ideally be given during the intended week, and the final dose must be administered before radiotherapy course is completed.

For metastatic patients

Delay 1 week if:

Platelet ≤ 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.

Renal impairment:

Review toxicity of previous dose of cisplatin and take account of previous renal impairment when making decision about subsequent doses.

CrCl (mL/min)	Cisplatin Dosing	
	Curative	Palliative
> 60	100mg/m^2 (100% dose)	80mg/m^2 (100% dose)
50-59	75mg/m^2 (75% dose)	60mg/m^2 (75% dose)
40-49	50mg/m^2 (50% dose)	Switch to carboplatin
< 40	switch to carboplatin	

Carboplatin	CrCl > 20ml give at 100% dose **CrCl ≤ 20mls/min- discuss with clinical team prior to administration if creatinine clearance.**

Hepatic impairment:

Both Cisplatin and Carboplatin are renally excreted and therefore no dose reduction necessary for any grade of hepatic impairment.

Non-haematological toxicity management:

Please refer to 'Main toxicities' section for details on the common toxicities that occur and the associated symptoms.

If patient develops Grade ≥ 2 neuropathy or ototoxicity (hearing loss with hearing aid or intervention not indicated, limiting instrumental ADLs and/or moderate symptoms of tinnitus limiting instrumental ADLs) please discuss with consultant.

References:

Cisplatin 1 mg/ml Sterile Concentrate, Summary of Product Characteristics Hospira UK Ltd Warwickshire.06/09/1996. Available from https://www.medicines.org.uk/emc Last updated 30/04/2013.

The Lancet: Dose recommendations for anticancer drugs with renal or hepatic impairment 2019

Carboplatin 10mg/mL concentrate for solution for infusion, Summary of Product Characteristics Hospira UK Ltd Warwickshire. Available from https://www.medicines.org.uk/emc Last updated 16/06/2021