Systemic Anti Cancer Treatment Protocol

Cisplatin
Gynaecological Cancer

PROCTOCOL REF: MPHAGYNCIS
(Version No: 1.1)

Approved for use in:

- Advanced stage and refractory ovarian carcinoma, second line.
- Advanced/metastatic endometrial carcinoma
- Neoadjuvant cervical cancer
- Metastatic cervical cancer

Dosage

Dosage	Dose	Route	Frequency
Cisplatin	80mg/m^2	IV Infusion	Repeat at 21 day intervals

Maximum 6 cycles

Supportive treatments:

Dexamethasone 4mg orally, twice daily for 3 days

Domperidone 10mg orally, three times a day when required

Aprepitant 125mg on day 1 and 80mg orally on days 2 and 3

Interactions

Oral anticoagulants - in the event of simultaneous use of oral anticoagulants, it is advisable regularly to check the INR.

Anticonvulsive substances - Serum concentrations of anticonvulsive medicines may remain at sub therapeutic levels during treatment with cisplatin. Cisplatin may reduce

the absorption of phenytoin resulting in reduced epilepsy control when phenytoin is given as current treatment.

Aminoglycosides e.g. gentamicin - Increased risk of nephrotoxicity and ototoxicity

Extravasation risk

Cisplatin- vesicant

Administration

- **Review patient's fluid intake over the previous 24 hours**
- **Review common toxicity criteria and performance status**
- **Calculate creatinine clearance using Cockcroft and Gault equation (see investigation section)**
- **Weigh the patient prior to commencing intravenous fluids**
- **Commence strict fluid balance (input and output)**

Day	Drug	Dose	Route	Diluent and rate
1	**Aprepitant** 1 hour before chemotherapy (80mg to be taken as a single dose on day 2 and day 3)	**125mg**	**PO**	
	Ondansetron tablets 30mins before chemotherapy	**24mg**	**PO**	
	Dexamethasone tablets 30mins before chemotherapy	**12mg**	**PO**	
	Furosemide tablets	**20mg**	**PO**	
	Sodium Chloride 0.9% 1000mL (+ 20mmol Potassium Chloride)		**IV over 90 minutes**	
	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**			
	Cisplatin	**80mg/m^2**	**IV**	Sodium Chloride 0.9% 1000mL over 90 minutes
	Sodium Chloride 0.9% 1000mL (+ 20mmol Potassium Chloride)		**IV over 90 minutes**	

At the end of IV fluids:

- **Weigh the patient and review fluid balance chart**
- **If there is a positive balance of 1.5L or 1.5kg in weight gained then consider furosemide 20mg orally and review output after 30 minutes. Any concerns then discuss with medical team prior to discharging the patient.**

Ensure good oral fluid intake

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

Hypersensitivity

As with all platinum based chemotherapy, patients may experience allergic reaction during administration. The infusion should be stopped and the following should be administered.

- Hydrocortisone 100 to 200mg IV
- Chlorphenamine 10 mg IV

It should be strongly noted that patients who have severe reactions should not be re-challenged.

Cisplatin Dose Guidelines

Cisplatin is nephrotoxic and thus patients must have their renal function measured prior to each cycle.

Creatinine Clearance (mL/min)	Cisplatin dose
> 50mL/min	Give 100%
40 to 50 mL/min	Give 75%
< 40mL/min	No further cisplatin

Main Toxicities

Cardiac disorders	Arrhythmia, bradycardia, tachycardia can occur with cisplatin
Gastrointestinal	Nausea, vomiting, diarrhoea, constipation, mucositis.
General disorders and administration site conditions	Pyrexia (very common), asthenia, malaise, injection site extravasation Dehydration, hypokalaemia, hypophosphataemia, hypocalcaemia, hypomagnesaemia, tetany, muscle spasms
Haematological	Neutropenia, anaemia, thrombocytopenia
Hepatobiliary	Hepatic enzymes and blood bilirubin increased
Musculoskeletal	Muscle spasms
Nervous system	Cisplatin can cause peripheral neuropathy (see below). Neurologic examination must be carried out at regular intervals.
Ototoxicity	Ototoxicity is common with cisplatin and is manifested by tinnitus and/or hearing loss in the high frequency range (4000 to 8000Hz). Decreased ability to hear conversational tones may occur occasionally.
Skin and subcutaneous tissue disorders	Alopecia, rash

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
Mg^{2+}	X	X	X	X	X	X	X	Every cycle
CrCl/Urine output	X	X	X	X	X	X	X	Every cycle
CA125*	X	X	X	X	X	X	X	Every cycle *for 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:-

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

Delay 1 week on day 1 if:-

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

- If platelets or ANC still below required levels for treatment at week 2, delay treatment again and patient will need assessed and chemotherapy dose reduction by Oncologist
- If patient suffers an episode of Grade 3 febrile neutropenia, discuss with Oncologist.

Non-haematological toxicity

Grading and Management of Toxicity

Toxicity should be grading according to the CTCAE v4.0 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% 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	Interrupt treatment until resolved to grade0/1, then continue at 50% of original dose	
3rd appearance	Interrupt treatment until resolved to grade 0/1, then continue at 50% of original dose	Discontinue treatment	
4th appearance	Discontinue treatment		

Peripheral Neuropathy

Severe cases of neuropathies have been reported. These neuropathies may be irreversible and may manifest by paresthesia, areflexia and a proprioceptive loss and a sensation of vibrations. A loss of motor function has also been reported. A neurologic examination must be carried out at regular intervals.

Cumulative:- Dose related peripheral sensory neuropathy: Usually occurs after a cumulative dose. It can occur after treatment with cisplatin is completed, and is usually reversible, taking approx 3 – 5 months to recovery.

Neurotoxicity/Ototoxicity

If patient develops Grade 2 neuropathy or ototoxicity, discuss with Consultant. Patients with functional hearing loss should have cisplatin omitted; carboplatin AUC 3-5 can be substituted.

References

1. https://www.medicines.org.uk/emc/medicine/

2. Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009)

3. Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Renal Impairment (Version 3 - updated January 2009)

4. Stockley's drug interactions. Ninth edition. Edited K. Baxter. Pharmaceutical press. London. 2010