3-weekly Cisplatin & Radiotherapy (Endometrial)

Indication

For consideration in patients with stage III endometrial cancer or myoinvasive non-endometrioid endometrial carcinoma of any stage at high risk of recurrence.

4 cycles of neoadjuvant/adjuvant carboplatin and paclitaxel chemotherapy will be added before or after pelvic chemoradiotherapy as per the PORTEC 3 trial.

ICD-10 codes

C54.1

Regimen details

Days	Drug	Dose	Route
1	Cisplatin	50mg/m^2	IV infusion

Cycle frequency

21 days

Number of cycles

2 cycles. Cisplatin should be administered on D1 and D22 alongside radiotherapy.

Administration

Cisplatin is administered in 500mL sodium chloride 0.9% over 1 hour following the pre and post hydration protocol below.

Infusion Fluid & Additives	Volume	Infusion Time
Sodium Chloride 0.9%	1000mL	1 hour
Mannitol 20% **OR** Mannitol 10%	200mL 400mL	30 minutes 30 minutes
Ensure urine output > 100mL / hour prior to giving cisplatin. Give a single dose of furosemide 20mg iv if necessary.		
Cisplatin	500mL	1 hour
Sodium Chloride 0.9% + 2g $MgSO_4$ + 20mmol KCl	1000mL	2 hours
TOTAL	**2700mL or 2900mL**	**4 hours 30 minutes**

Patients with low magnesium levels (<0.7 mmol/L) should have an additional 2g magnesium sulphate added to the pre-hydration bag.

An accurate fluid balance record must be kept. All patients must be advised to drink at least 2 litres of fluid over the following 24 hours.

Pre-medication

Cisplatin: IV hydration as above.

Emetogenicity

This regimen has moderate - high emetic potential.

Additional supportive medication

Proton pump inhibitor if required.
Loperamide if required.
Laxatives if required
Mouthwashes as per local policy

Extravasation

Cisplatin - exfoliant (Group 4)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
Calcium	14 days
Magnesium	14 days

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	72 hours
U+E (including creatinine)	72 hours
LFT	72 hours
Magnesium	72 hours

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥1.5 x 10^9/L
Platelets	≥100 x 10^9/L
Creatinine clearance (CrCl)	≥ 60 mL/min
Magnesium	≥ 0.7 mmol/L

Dose modifications

- **Haematological toxicity**

Defer treatment for 1 week if neutrophils <1.5 x 10^9/L and/or platelets < 100 x 10^9/L. If more than 1 week delay required, then omit.

- **Renal impairment**

CrCl (mL/min)	Cisplatin dose
≥60	100%
50-59	75%
40-49	50%
<40	Cisplatin contraindicated, omit.

- **Hepatic impairment**

No dose reduction necessary.

- **Other toxicities**

Cisplatin

Toxicity	Definition	Dose adjustment
Neurotoxicity	Grade ≥2	Discontinue
Ototoxicity	Grade ≥2	Discontinue

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Nephrotoxicity
Ototoxicity
Hypersensitivity reactions

- **Frequently occurring side effects**

Nausea/vomiting
Myelosuppression
Mucositis, stomatitis
Constipation
Peripheral neuropathy
Alopecia
Fatigue
Electrolyte disturbances
Taste disturbance

Significant drug interactions – for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin or DOAC during treatment or if the patient continues taking an warfarin monitor the INR at least once a week and adjust dose accordingly.

Clozapine: increased risk of agranulocytosis, avoid concomitant use.

Cisplatin:
Allopurinol, colchicine, probenecid, sulfinpyrazone: increase serum uric acid concentration.
Cephalosporins, aminoglycosides, amphotericin B: increase nephrotoxic and ototoxic effects of cisplatin when administered simultaneously or 1-2 weeks after treatment with cisplatin.
Ciclosporin: excessive immunosuppression, with risk of lymphoproliferation.
Cyclizine, phenothiazines: may mask ototoxicity symptoms.

Furosemide, hydralazine, diazoxide, propranolol: intensify nephrotoxicity.
Oral anticoagulants: require an increased frequency of the INR monitoring.
Penicillamine: may diminish the effectiveness of cisplatin.
Phenytoin: reduced serum levels of phenytoin (due to reduced absorption and/or increased metabolism) can reduce epilepsy control. Monitor phenytoin levels.

Additional comments

Nil

References

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- Samant, R. et al. Primary vaginal cancer treated with concurrent chemoradiation using Cis-platinum. Int J Radiat Oncol Biol Phys 2007;69(3):746-750
- Summary of Product Characteristics- Cisplatin. Accessed 14th May 2024. Available at: www.medicines.org.uk
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