Low dose induction etoposide and cisplatin (or carboplatin)

Indication

Advanced germ cell cancer where patient is not fit enough to commence standard treatment. As soon as condition is stabilised patient should be considered for appropriate radical schedule.
This schedule should only be prescribed after discussion with germ cell MDT/consultant.

ICD-10 codes

Codes pre-fixed with C38, C48, C56, C62, C63, C75.3.

Regimen details

Etoposide/Cisplatin

Day	Drug	Dose	Route
1	Cisplatin	20 mg/m^2	IV infusion
1 and 2	Etoposide	100 mg/m^2	IV infusion

OR

Etoposide/Carboplatin

Day	Drug	Dose	Route
1	Carboplatin	AUC 3	IV infusion
1 and 2	Etoposide	100 mg/m^2	IV infusion

Cycle frequency

N/A

Number of cycles

One cycle only.

Administration

Cisplatin is administered in 500mL sodium chloride 0.9% over 60 minutes 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. If a patient develops fluid retention i.e. weight gain >2.5kg or urine output < 100ml/ hour during treatment give a single dose of 20mg furosemide or mannitol (200mL mannitol 20% OR 400mL mannitol 10%). Do not give more than a single dose of either furosemide or mannitol without discussing with consultant.		
Cisplatin	500mL	1 hour
Sodium Chloride 0.9% + 2g $MgSO_4$ + 20mmol KCl	1000mL	2 hours
TOTAL	**2700mL or 2900mL**	**4 hours 30 minutes**

Note: Patients with magnesium or potassium below the normal range should have 2g $MgSO_4$ and 20mmol KCl added to the pre-hydration bag and the duration of the infusion increased to 2 hours.
All patients must be advised to drink at least 2 litres of fluid over the following 24 hours.

Carboplatin is administered in 500mL 5% glucose over 60 minutes.

Etoposide is administered in 1000-2000mL sodium chloride 0.9% (concentration dependent) and infused over a minimum of 1 hour.

Pre-medication
Nil

Emetogenicity
This regimen has moderate emetic potential.

Additional supportive medication
Consider allopurinol 300mg OD (100mg OD if CrCl< 20mL/min) for patients with a high tumour burden
H_2 antagonist or proton pump inhibitor if required.
Mouthwashes as per local policy.
Anti-emetics as per local policy.

Extravasation
Cisplatin is an exfoliant (Group 4)
Etoposide and carboplatin are irritant (Group 3)

Investigations – pre first cycle

Investigation	Validity period
FBC	48 hours
U+E (including creatinine)	48 hours
LFTs	48 hours
Magnesium	48 hours
AFP, HCG, LDH	48 hours
LH, FSH and testosterone	28 days
CXR	28 days
Audiology	28 days*

*May be done when commences subsequent radical treatment

Consider formal EDTA measurement of creatinine clearance in patients with a low body surface area or calculated CrCl ≤ 60ml/min renal function.

Where appropriate offer pre-treatment sperm storage.

Standard limits for administration to go ahead
If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
WBC	≥ 1.5 x 10^9/L
Neutrophils	≥ 0.5 x 10^9/L
Platelets	≥ 75 x 10^9/L
Calculated CrCl	> 50 ml/min
Bilirubin	< 3 x ULN
AST/ALT	< 4 x ULN

Dose modifications

- **Renal impairment**

Full dose cisplatin should be administered if calculated CrCl is ≥ 60ml/min. An EDTA creatinine clearance should be arranged if CrCl falls below this value.

CrCl (mL/min)	**Cisplatin dose**
>60	100%
51 – 60	75%
40 – 50	50%
<40	Discuss with consultant

Carboplatin is contraindicated if CrCl is < 20ml/min

- **Hepatic impairment**

If bilirubin > 3.0 x ULN or AST/ALT > 4.0 x ULN discuss etoposide dose with consultant.
No dose modification required for cisplatin or carboplatin.

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

- **Serious side effects**

Myelosuppression
Nephrotoxicity
Ototoxicity
Neurotoxicity
Infertility
Long term risk of cardiovascular disease and metabolic syndrome
Osteonecrosis of the hip

- **Frequently occurring side effects**

Myelosuppression
Constipation, diarrhoea
Stomatitis, mucositis
Alopecia
Nausea and vomiting
Anorexia

- **Other side effects**

Electrolyte disturbances
Fatigue

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

Warfarin/coumarin anticoagulants: Avoid use due to elevations in INR. Switch to low molecular weight heparin during treatment.

Antibiotics: The renal toxicity of cisplatin is potentiated by aminoglycoside antibacterials (e.g. gentamicin) and amphotericin. Aminoglycosides should be avoided. If aminoglycosides are prescribed, close monitoring of renal function and serum antibiotic levels is required.

Avoid all nephrotoxic drugs where possible

Phenylbutazone, sodium salicylate and salicylic acid: can affect protein binding of etoposide.

Additional comments

References

- Summary of Product Characteristics Cisplatin (Hospira) accessed 6 April 2016 via www.medicines.org.uk
- Summary of Product Characteristics Etoposide (Hospira) accessed 6 April 2016 via www.medicines.org.uk
- A randomised phase 2 trial of intensive induction chemotherapy (CBOP/BEP) and standard BEP in poor-prognosis germ cell tumours (MRC TE23, CRUK 05/014, ISRCTN 53643604)

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