E P

a) Stage IIC – IV seminoma

b) Alternative therapy to 5-day BEP in germ cell tumours where Consultant chooses to avoid using bleomycin, **only** for patients not suitable for the IPE regimen

Drug/Dosage:	Etoposide	100 mg/m^2	IV	once daily for 5 days on Days 1 - 5
	Cisplatin	20 mg/m^2	IV	once daily for 5 days on Days 1 – 5

G-CSF primary prophylaxis for 5 days, starting on Day 6 (no earlier than 24 hours after chemotherapy completed)

Administration: 1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 2 hours (only required on Day 1 of each cycle)
Etoposide in 1 litre 0.9% sodium chloride over 1 hour
Mannitol 20% 100ml IV over 15 minutes
Cisplatin in 500ml 0.9% sodium chloride IV over 1 hour (max rate 1mg/min)
1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 2 hrs

The patient should be encouraged to drink well (absolute minimum of 1 litre of fluid per day) at home between each day of cisplatin-based chemotherapy. They should also be asked to drink 2 litres of fluid in the 24 hours following Day 5 of treatment. They should be told to contact the hospital if this is impossible because of problems e.g. nausea and vomiting.

Frequency: 3 weekly cycle for 4 cycles

Main Toxicities: myelosuppression; nephrotoxicity; neurotoxicity / ototoxicity; alopecia; mucositis; electrolyte imbalance; infertility

Anti emetics: highly emetogenic, including aprepitant - pre-chemo anti-emetics on proforma
TTO anti-emetics include:
aprepitant 80mg po Days 2 & 3
ondansetron 8mg po every evening on Days 1-5
Dexamethasone 4mg po bd x 3 days, to start on day 6
Domperidone 10mg po tds x 8 days, then prn

Extravasation: non - vesicants

Regular Investigations:	FBC	Day 1
	U&Es & LFTs	Day 1
	Mg^{2+} and Ca^{2+}	Day 1
	AFP, βHCG, LDH	Day 1
	EDTA	Prior to 1st cycle

Comments: For patients receiving this in the Day Case setting (Mon-Fri), please ensure that the Consultant / registrar in clinic reviews the patient the week before the next cycle is due (about Day 16) with regard to fitness to continue with the next cycle **and** pre-prescribes Days 1 -5 of the next cycle – ready to be confirmed by a competent nurse on Chilworth ward on Day 1, once Day 1 blood results are available.

For patients on Cycle 1 whose EDTA is not yet available, Cockcroft and Gault may be used to predict GFR. Cisplatin dose should be adjusted if necessary once EDTA available. EDTA should only be repeated if the result is border-line at the start of treatment or if there is a 30% change in serum creatinine.

Reason for Update: changed to 5-day regimen, in line with RMH practice and updated reference; primary G-CSF included; added E-Carbo info	Approved by Consultant: Dr J Money-Kyrle
Version: 5	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 4	Date: 17.6.14
Prepared by: S Taylor	Checked by: C Tucker

Check electrolytes - additional supplementation of potassium, magnesium or calcium may be required.
Consider the use of allopurinol if patient has significantly bulky disease.

Careful review is required to ensure that side effects such as peripheral neuropathy or hearing loss are detected early.

Weight should be recorded prior to and at the end of cisplatin treatment, and a strict fluid balance chart should be maintained. An average urine output of at least 100ml/hr must be maintained throughout treatment, and cisplatin infusion should not be commenced unless this urine output is achieved. If the urine output is inadequate, the patient should be assessed and urine output increased by administering 500ml sodium chloride 0.9% IV +/- furosemide 20 – 40mg. Furosemide 20 – 40mg po may also be given if there is a positive fluid balance of 1.5 litres, a weight gain of 1.5kg or symptoms of fluid overload.

Dose Modifications

Haematological Toxicity:

Dose modification and delays can compromise outcome and should be avoided.
G-CSF should be prescribed as above, plus as needed, to maintain treatment schedule.
N.B. Patient must not be delayed without Consultant approval

Neutrophils < 1.0 x 10^9/l or Platelets < 100 x 10^9/l	Delay for 3 days, and initiate G-CSF if appropriate. Repeat FBC and, if recovered, continue with full dose treatment. If FBC still low after 3 days, seek advice from Consultant.

Renal Impairment

N.B. Cisplatin is both eliminated primarily (> 90%) in the urine and is itself nephrotoxic.

CrCl (ml/min)	Cisplatin Dose
≥ 60	Give 100%
45 – 59	Give 75%
44 - 20	Cisplatin C/I Consider substituting with Carboplatin AUC 5 on Day 1 only, administered in 250ml 5% glucose over 30 - 60 minutes **EP is the treatment of choice and E-Carbo should only be used in exceptional circumstances**
< 20	Carboplatin C/I

CrCl (ml/min)	Etoposide Dose
> 50	Give 100%
15 – 50	Give 75%
< 15	Give 50%

Hepatic Impairment:

Creatinine clearance is the strongest predictor of etoposide clearance. There is conflicting information about dose reduction with hepatic impairment. Use the table below but, if in doubt, discuss with Consultant.

Bilirubin (μmol/l)		AST (units/l)	Etoposide Dose
26 – 51	**or**	60 - 180	Give 50% dose
> 51	**or**	> 180	Clinical decision

Neurotoxicity:

Seek further advice if the patient reports symptoms indicative of ototoxicity (tinnitus, deafness) or neurotoxicity (paraesthesias, difficulty with motor control).

Reference:

Kondagunta, GV et al; JCO (2005); 23: 9290-9294

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