B E P

Non-seminomatous germ cell tumours

Drug/Dosage:	Etoposide	165mg/m^2	IV	D1, D2 and D3
	Cisplatin	50mg/m^2	IV	D1 and D2
	Bleomycin	30,000iu*	IV	D2, D9 & D16

Administration: Etoposide in 1 litre 0.9% Sodium Chloride over 1 hour
Bleomycin in 100ml 0.9% Sodium Chloride over 15 minutes

Cisplatin: 1 litre 0.9% Sodium Chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 4 hours
Mannitol 20% 100ml IV over 15 minutes
Cisplatin in 1 litre 0.9% Sodium Chloride IV over 4 hours
1 litre 0.9% Sodium Chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 6 hours
1 litre 0.9% Sodium Chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 6 hours

Frequency: 3 weekly cycle: Primary treatment 3 cycles
Adjuvant use 2 cycles
In the rare case where a 4th cycle may be given, bleomycin must only be included on Day 2 of the 4th cycle (i.e. max 10 doses)

Main Toxicities: myelosuppression; nephrotoxicity; ototoxicity; mucositis; neurotoxicity; alopecia; skin changes; infertility; pulmonary toxicity; rigors during bleomycin infusion (see Comments)

Anti emetics: highly emetogenic

Extravasation: non-vesicants

Regular Investigations:	FBC	D1, D9 and D16
	U&Es and LFTs	D1
	Mg^{2+} and Ca^{2+}	D1
	AFP, βHCG, LDH	D1, D9 and D16
	EDTA	Prior to 1st cycle
	Chest X-ray	D1

Comments: *After 3 cycles, cumulative dose of bleomycin = 270,000iu. Due to increasing risk of bleomycin toxicity with increasing age for this total dose, consider reducing dose or omitting bleomycin in **patients aged ≥ 60 years**. If in doubt, seek advice.

Hydrocortisone 100mg should be given with bleomycin on D9 and D16 to prevent rigors.

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 30% change in serum creatinine.

Ensure careful review so that side effects such as peripheral neuropathy, hearing loss and pulmonary toxicity are detected early.

Check electrolytes – additional potassium, calcium or magnesium may be required.

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

Reason for Update: Markers checked weekly, 4th cycle removed, bleo info amended	Approved by Lead Chemotherapy Nurse: C Palles-Clark
Version: 2	Approved by Consultant: Dr J Money-Kyrle
Supersedes: Version 1	Date: 1.12.07
Prepared by: S Taylor	Checked by: S Seymour

litres, a weight gain of 1.5kg or symptoms of fluid overload. The patient should be asked to drink 2 litres of fluid in the 24hrs following treatment, and to contact the hospital if this is impossible because of problems e.g. nausea and vomiting.

Dose Modifications

Haematological Toxicity:

Dose modification and delays can compromise outcome and should be avoided. G-CSF should be prescribed as needed (but not on Days 1 – 3 of treatment) to maintain treatment schedule. If a patient needs treatment at any point with G-CSF, prophylactic G-CSF should be routinely prescribed with all future cycles.

Day 1: 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.

Day 9 and Day 16: Bleomycin is not significantly myelosuppressive and may be given in the presence of neutropenia or thrombocytopenia. However, FBC should be noted and managed accordingly.

Renal Impairment:

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

GFR (ml/min)	Cisplatin Dose
> 60	Give 100%
50 – 60	Give 75%
40 – 50	Give 50%
< 40	CI (consider carboplatin)

GFR (ml/min)	Bleomycin Dose
> 50	Give 100%
10 – 50	Give 75%

CrCl (ml/min)	Etoposide Dose
60	Give 85%
45	Give 80%
30	Give 75%

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

Pulmonary Toxicity:

Bleomycin must be discontinued permanently if symptoms of pulmonary toxicity occur, e.g. dyspnoea, abnormal CXR or decreased pulmonary function. **This is a Consultant decision only.** If bleomycin is discontinued, a 4th cycle of treatment may be required. Again, discuss with Consultant.

Skin Toxicity:

Severe skin lesions may require bleomycin to be discontinued – **Consultant decision only**

Mucosal Toxicity:

Severe mucositis will require delay of chemotherapy cycle to allow healing

Neurotoxicity:

Seek further advice if patient reports symptoms indicative of oto- or neurotoxicity

References:

MRC Trial TE20, Testicular Tumour Working Party, May 1995
Dearnley, DP et al (1991); Eur J of Cancer, Vol 27: (6): 684 – 691

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