3-DAY BEP

Non-seminomatous germ cell tumours

Drug/Dosage:	Etoposide	165 mg/m^2	IV	Day 1, Day 2 and Day 3
	Cisplatin	50 mg/m^2	IV	Day 1 and Day 2
	Bleomycin	30,000 iu*	IV	Day 2, Day 9 & Day 16

G-CSF primary prophylaxis for 5 days, starting on Day 4 (no earlier than 24 hours after chemotherapy completed)

*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 Day 9 and Day 16 to prevent rigors.

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
Bleomycin in 100ml 0.9% sodium chloride over 15 minutes
Mannitol 20% 100ml IV over 15 minutes
Cisplatin in 1 litre 0.9% sodium chloride IV over 2 hours (max rate 1mg/min)
1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 2 hrs
500ml 0.9% sodium chloride IV **or** 500ml - 1 litre water orally over 1 hour

The patient should be asked to drink 2 litres of fluid at home between Day 1 and Day 2 cisplatin, and again in the 24hrs following Day 2 of treatment, and to contact the hospital if this is impossible because of problems e.g. nausea and vomiting.

Frequency:

3 weekly cycle
Adjuvant use:
For high risk, stage 1 non seminomatous or combined germ cell tumours 1 cycle only
Primary treatment: 3 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:

Days 1 and 2: highly emetogenic, including aprepitant
Day 3: moderately emetogenic
Pre-chemo anti-emetics are included on the proforma
TTO anti-emetics include: aprepitant 80mg po Days 2 & 3
ondansetron 8mg po in the evening of Days 1 and 2
Dexamethasone 4mg po bd x 2 days, to start on day 4
Domperidone 10mg po tds x 6 days, then prn
Days 9 and 16: no anti-emetics needed

Extravasation:

non-vesicants

Reason for Update: adjuvant use changed to 1 cycle; general review	Approved by Consultant: Dr C Perna
Version: 7	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: Version 6	Date: 2.11.17
Prepared by: S Taylor	Checked by: C Tucker

Regular Investigations:	FBC	Day 1, Day 9 and Day 16
	U&Es and LFTs	Day 1
	Mg^{2+} and Ca^{2+}	Day 1
	AFP, βHCG, LDH	Day 1, Day 9 and Day 16
	EDTA	Prior to 1st cycle
	Chest X-ray	Day 1

Comments: 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 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.

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. G-CSF is indicated if neutrophils < 1.0 x 10^9/l, to ensure that the next cycle can start on time. Assess patient for any signs of sepsis and counsel patient about appropriate self-care. If in doubt, discuss with doctor.

Renal Impairment: NB. 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 carboplatin)
< 20	Carboplatin C/I

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

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

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:

De Wit, R et al; JCO 2001: 19 ; 1629 – 1640
MRC Trial TE20, Testicular Tumour Working Party, May 1995
Dearnaley, DP et al; Eur J of Cancer 1991, Vol 27: (6): 684 – 691
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