BEP 3 day (adjuvant) (BEP 111)

INDICATION (ICD10) C62

1. Adjuvant treatment for non-metastatic non-seminomatous germ cell tumour (stage 1 only) in patients with vascular or lymphatic invasion (risk of relapse up to 40% without treatment). Consider for patients who are unable to attend for intensive outpatient surveillance. PS 0, 1, 2

REGIMEN

Day 1 Prehydration
CISPLATIN 50mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 2 hours
ETOPOSIDE 167mg/m^2 in 1000ml* sodium chloride 0.9% IV infusion over 60 minutes
Post hydration

Day 2 Prehydration
CISPLATIN 50mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 2 hours
ETOPOSIDE 167mg/m^2 in 1000ml* sodium chloride 0.9% IV infusion over 60 minutes
Hydrocortisone 100mg IM
BLEOMYCIN 30000units in 3ml lidocaine 1% IM
Post hydration

Day 3 ETOPOSIDE 167mg/m^2 in 1000ml* sodium chloride 0.9% IV infusion over 60 minutes

Day 9 Hydrocortisone 100mg IM
BLEOMYCIN 30000units in 3ml lidocaine 1% IM (consider switching to 100ml sodium chloride 0.9% IV infusion over 30 minutes for patients with platelets <50)

Day 16 Hydrocortisone 100mg IM
BLEOMYCIN 30000units in 3ml lidocaine 1% IM (consider switching to 100ml sodium chloride 0.9% IV infusion over 30 minutes for patients with platelets <50)

*etoposide doses 48mg to 88mg in 250ml, doses 96mg to 180mg in 500ml sodium chloride 0.9%

CYCLE FREQUENCY AND NUMBER OF CYCLES

One cycle only

ANTI-EMETICS

High emetic risk days 1 and 2 (Aprepitant may be required)
Low emetic risk day 3
Minimal emetic risk days 9 and 16

CONCURRENT MEDICATION REQUIRED

Bleomycin	Ensure hydrocortisone administered before bleomycin
Cisplatin	Ensure adequate pre and post hydration. If urine output is <100ml/hour or if patient gains >2kg in weight during IV administration post cisplatin give 20-40mg furosemide PO/IV.
GCSF	Consider GCSF

EXTRAVASATION AND TYPE OF LINE / FILTERS

Bleomycin – neutral
Cisplatin – exfoliant
Etoposide - irritant

Peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle, FBC days 9 and 16
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Ideally EDTA GFR should be used
Creatinine clearance (GFR) calculated, at the Consultants discretion
Serum creatinine - each cycle
Pulmonary function tests (including transfer factor) before cycle 1
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Bleomycin	If breathlessness or infiltrates appear not attributable to tumour or co-existence of lung disease bleomycin must be stopped immediately. Consider treatment with corticosteroids and a broad spectrum antibiotic and / referral to chest team. Investigation of choice high resolution CT chest.
Cisplatin	Nephrotoxicity – ensure adequate pre and post hydration is prescribed. Ototoxicity – assess patient for tinnitus or hearing abnormalities.

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Bleomycin	Cisplatin increases the risk of pulmonary toxicity.
Cisplatin	Aminoglycosides increased risk of nephrotoxicity and ototoxicity. Renal function should be well monitored and audiometric tests as required. Cisplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.

DOSE MODIFICATIONS

Bleomycin maximum lifetime dose = 400000units in patients under 60 years

Haematological

Platelets <50x10^9/L consider switching IM bleomycin to 100ml sodium chloride 0.9% IV infusion over 30 minutes

Non-haematological

If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

Hepatic impairment

Etoposide

Bilirubin ≥50micromol/L or decreased albumin	give 50% dose

Renal impairment

Bleomycin

CrCl >50ml/min	give 100% dose
CrCl 10-50ml/min	give 75% dose
CrCl <10ml/min	give 50% dose

Cisplatin

CrCl >60ml/min	give 100% dose
CrCl 45-60ml/min	give 75% dose
CrCl <45ml/min	not recommended

Etoposide

CrCl >50ml/min	give 100% dose
CrCl 15-50ml/min	give 75% dose
CrCl <15ml/min	Further dose reduction

REFERENCES

1. Huddart, RA, . Joffe JK, et al. 111: A single-arm trial evaluating one cycle of BEP as adjuvant chemotherapy in high-risk, stage 1 non-seminomatous or combined germ cell tumors of the testis (NSGCTT). Journal of Clinical Oncology 2017 35:6_suppl, 400-400