DOXORUBICIN CISPLATIN ETOPOSIDE (EDP)

INDICATION (ICD10) C74, D44.1

1. Metastatic adrenal cancer. PS 0, 1, 2

REGIMEN

Day 1 DOXORUBICIN 40mg/m^2 IV bolus
Day 2 ETOPOSIDE 100mg/m^2 in 1000ml* sodium chloride 0.9% IV infusion over 60 minutes
Days 3 and 4 Prehydration
CISPLATIN 40mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 2 hours
ETOPOSIDE 100mg/m^2 in 1000ml* sodium chloride 0.9% IV infusion over 60 minutes
Post hydration
*doses 48mg to 88mg in 250ml, doses 96mg to 180mg in 500ml sodium chloride 0.9%

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days for 6 cycles

ANTI-EMETICS

High emetic risk day 1
Low emetic risk day 2
High emetic risk days 3 and 4

CONCURRENT MEDICATION REQUIRED

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.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Cisplatin – exfoliant
Doxorubicin - vesicant
Etoposide - irritant

Peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
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,
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Cisplatin	Nephrotoxicity – ensure adequate pre and post hydration is prescribed. Ototoxicity – assess patient for tinnitus or hearing abnormalities.
Doxorubicin	Cardiotoxicity – monitor cardiac function. Doxorubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.

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

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
Doxorubicin maximum lifetime dose
= 400mg/m^2 (in patients with cardiac dysfunction or exposed to mediastinal irradiation)
= 450-550mg/m^2 (with normal cardiac function)

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

Hepatic impairment
Doxorubicin

Bilirubin 20-50micromol/L	give 50% dose
Bilirubin 51-86micromol/L	give 25% dose
Bilirubin >86micromol/L or Child-Pugh C	not recommended

Etoposide

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

Renal impairment
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. FIRM-ACT regimen, April 24 2004
2. Bradbury. P., Talbot. D. 2007 Systemic treatment of thymoma in “the thymus Gland”. Ed. Anastasiadis + Ratnatunga Springer-Verlag 91-975) Fassnacht M et al Combination chemotherapy in advanced adrenocortical carcinoma. NEJM 366;23 nejm.2190 org june 7, 2012