DOXORUBICIN CISPLATIN CYCLOPHOSPHAMIDE VINCRISTINE (ADOC)

INDICATION (ICD10) C37

1. Thymoma

REGIMEN

Day 1 DOXORUBICIN 40mg/m^2 IV bolus
Prehydration
CISPLATIN 50mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 2 hours
Post hydration

Day 4 VINCRISTINE 0.6mg/m^2 (maximum 1.2mg) in 50ml sodium chloride 0.9% IV infusion over 10 minutes
CYCLOPHOSPHAMIDE 700mg/m^2 IV bolus

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days for 6 cycles

ANTI-EMETICS

High emetic risk day 1
Moderate emetic risk day 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
Cyclophosphamide - neutral
Doxorubicin – vesicant
Vincristine - vesicant

Peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every week
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
ECG (possible ECHO) required if patient has preexisting cardiac disease
Creatinine clearance (GFR) calculated, at the Consultants discretion
Serum creatinine
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.
Cyclophosphamide	may irritate bladder, drink copious volumes of water.
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.
Vincristine	Neuropathy

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.
Cyclophosphamide	Cytochrome P450 enzyme inducers (e.g. rifampicin, carbamazepine, phenytoin, St Johns Wort, corticosteroids): may increase active cyclophosphamide metabolites. Allopurinol, Cimetidine and protease inhibitors: may increase active metabolites. Aprepitant, Ciprofloxacin, Fluconazole, Itraconazole: may reduce activation of cyclophosphamide and alter the effectiveness of treatment. Grapefruit juice: decreased or delayed activation of cyclophosphamide. Patients should be advised to avoid grapefruit juice.

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

Vincristine

Bilirubin 25-51 or AST 60-180u/L	give 50%
Bilirubin >51micromol/L and normal AST	give 50%
Bilirubin >51micromol/L and AST >180u/L	omit

Renal impairment

Cisplatin

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

Cyclophosphamide

CrCl 10-29ml/min	Consider giving 75% dose

REFERENCES

1. Meazza et al. Efficacy of topotecan plus vincristine and doxorubicin in children with recurrent/refractory rhabdomyosarcoma. Med Oncol. 2009;26(1):67-72
2. Garaventa A, Luksch R, Biasotti S, Severi G, Pizzitola MR, Viscardi E, et al. A phase II study of topotecan with vincristine and doxorubicin in children with recurrent/refractory neuroblastoma. Cancer. 2003 Dec 1;98(11):2488–94.