DOXORUBICIN CISPLATIN (AC)

INDICATION (ICD10) C41, C49

1. Neoadjuvant and adjuvant osteosarcoma adjuvant for de-differentiated chondrosarcoma and palliative therapy for selected patients

REGIMEN

Day 1 DOXORUBICIN 25mg/m^2 in 100ml sodium chloride 0.9% IV infusion over 4* hours
Prehydration
CISPLATIN 50mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 2~~8~~ hours
Post hydration

Day 2 DOXORUBICIN 25mg/m^2 in 100ml sodium chloride 0.9% IV infusion over 4* hours
Prehydration
CISPLATIN 50mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over ~~8~~2 hours
Post hydration

Day 3 DOXORUBICIN 25mg/m^2 in 100ml sodium chloride 0.9% IV infusion over 4* hours

*Reduce doxorubicin infusion duration to 1 hour each day for those receiving dexrazoxane (administered 30 minutes before doxorubicin).

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days for 6 cycles

ANTI-EMETICS

High emetic risk days 1 and 2
Moderate risk day 3

CONCURRENT MEDICATION REQUIRED

Cisplatin	Ensure adequate pre and post hydration. If urine output is <100 ml/hour or if patient gains >2kg in weight during IV administration post cisplat.in give 20-40mg furosemide PO/IV.
Doxorubicin – dexrazoxane cardioprotection	Dexrazoxane (Blueteq registration required) for patients under the age of 25 years receiving a cumulative anthracycline dose equivalent to doxorubicin ≥300mg/m^2. See OUH 'Dexrazoxane (Cardioxane®) Guidelines for Preventing Cardiotoxicity with High-dose Anthracyclines in Paediatric Haematology and Oncology' guidelines for dose, number of doses and administration information.
GCSF	GCSF for 7 days starting at least 24 hours after chemotherapy. May be considered until WCC >5.0x10^9/l

EXTRAVASATION AND TYPE OF LINE / FILTERS

Cisplatin – exfoliant
Doxorubicin - vesicant

Central Line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E, Mg^{++} and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥75
GFR ≥70ml/min/1.73m^2
ECHO FS ≥28% or LVEF≥50% at last scheduled assessment
ECG, Echocardiogram (+LVEF), repeat ECHO after every 2 cycles
DTPA baseline
Serum creatinine
Vitamin D baseline
Hepatitis B status baseline
Baseline weight and every cycle
Consider audiometry baseline, repeat before 3rd and 5th 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 to minimise the risk of anthracycline induced cardiac failure. Doxorubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.

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

Cisplatin
If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.
Omit cisplatin if hearing loss extends to 2kHz.

Doxorubicin
Mucositis grade 3 or 4 - reduce doxorubicin to 20mg/m^2/day.
Risk of delayed cardiomyopathy - if 10% reduction in LVEF after 300mg/m^2 - omit doxorubicin.

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

Renal impairment

Cisplatin

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

REFERENCES

1. Souhami et al. Lancet 1997 Sep 27;350:911-7.