VAC

INDICATION (ICD10) C40, C41, C49

1. Ewing sarcoma consolidation
2. Rhabdomyosarcoma
3. Desmoid fibromatosis

REGIMEN

Day 1 Mesna 500mg/m^2 IV bolus one hour prior to cyclophosphamide
VINCRISTINE 1.5mg/m^2 (maximum 2mg) in 50ml sodium chloride 0.9% IV infusion over 10 minutes
DACTINOMYCIN 0.75mg/m^2 (maximum 1.5mg) IV bolus
CYCLOPHOSPHAMIDE 1500mg/m^2 in 250ml sodium chloride 0.9% IV infusion over 3 hours
Mesna 1500mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 3 hours
Mesna 1000mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 20 hours

Day 2 DACTINOMYCIN 0.75mg/m^2 (maximum 1.5mg) IV bolus

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days for up to 7 cycles
Consolidation post-surgery – 1 cycle of VAI followed by 7 cycles of VAC

ANTI-EMETICS

High emetic risk day 1 (consider aprepitant)
Moderate emetic risk day 2

CONCURRENT MEDICATION REQUIRED

Cyclophosphamide	Ensure mesna administered, using separate lumen from cyclophosphamide. Ensure adequate oral fluid intake. Cotrimoxazole 480mg bd M/W/F for duration of chemotherapy. Difflam
GCSF	Starting at least 24 hours after chemotherapy to maintain dose intensity (until WCC >5x10^9/l)

EXTRAVASATION AND TYPE OF LINE / FILTERS

Cyclophosphamide – neutral
Dactinomycin - vesicant
Vincristine – vesicant

Double lumen central line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every week
Neutrophils x 10^9/L ≥1.0
Platelets x 10^9/L ≥80
DTPA baseline
Creatinine clearance >55ml/min
Serum creatinine every cycle
Vitamin D baseline
Hepatitis B status baseline
ECG (possible ECHO) required if patient has preexisting cardiac disease
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Cyclophosphamide	May irritate bladder, drink copious volumes of water. Microscopic Haemorrhagic cystitis: additional bolus dose 600mg/m^2 then continue infusion at double dose. Grade ≥2 macroscopic haemorrhagic cystitis: discontinue chemotherapy and continue double dose MESNA and hydration x 24 hours post-chemotherapy
Dactinomycin	Myelosuppression, mucositis, liver changes
Vincristine	Neuropathy

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

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

Haematological

Reduce Cyclophosphamide and Dactinomycin dose if:
Delayed recovery >6 days
Neutropenic sepsis grade 3 and 4
Give 80% dose on 1st occurrence and 60% dose on second occurrence.

Non-haematological

Dactinomycin - omit for duration of concurrent radiotherapy (omitted doses are not subsequently given).

Reduce Cyclophosphamide and Dactinomycin dose if:
Delayed recovery >6 days
Mucositis / GI toxicity grade 3 and 4
Give 80% dose on 1st occurrence and 60% dose on second occurrence.

Hepatic impairment

Dactinomycin

Severe hepatic impairment dactinomycin 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	not recommended

Renal impairment

Cyclophosphamide

CrCl 10-29ml/min	give 75% dose

REFERENCES

1. EUROEWING12 2014