VAC

INDICATION (ICD10) C40, C41, C49
1. Ewing sarcoma consolidation
2. Rhabdomyosarcoma
3. Desmoid fibromatosis

REGIMEN
Day 1 Mesna 500mg/m² IV bolus one hour prior to cyclophosphamide
   VINCRISTINE 1.5mg/m² (maximum 2mg) in 50ml sodium chloride 0.9%
   IV infusion over 10 minutes
   DACTINOMYCIN 0.75mg/m² (maximum 1.5mg) IV bolus
   CYCLOPHOSPHAMIDE 1500mg/m² in 250ml sodium chloride 0.9% IV infusion over 3 hours
   Mesna 1500mg/m² in 1000ml sodium chloride 0.9% IV infusion over 3 hours
   Mesna 1000mg/m² in 1000ml sodium chloride 0.9% IV infusion over 20 hours

Day 2 DACTINOMYCIN 0.75mg/m² (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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Ensure mesna administered, using separate lumen from cyclophosphamide.</td>
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<tr>
<td></td>
<td>Ensure adequate oral fluid intake.</td>
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<tr>
<td></td>
<td>Cotrimoxazole 480mg bd M/W/F for duration of chemotherapy.</td>
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<tr>
<td></td>
<td>Difflam</td>
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<tr>
<td>GCSF</td>
<td>Starting at least 24 hours after chemotherapy to maintain dose intensity</td>
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<tr>
<td></td>
<td>(until WCC &gt;5x10⁹/l)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>May irritate bladder, drink copious volumes of water. Microscopic Haemorrhagic cystitis: additional bolus dose 600mg/m² 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.</td>
</tr>
<tr>
<td>Dactinomycin</td>
<td>Myelosuppression, mucositis, liver changes</td>
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<tr>
<td>Vincristine</td>
<td>Neuropathy</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Interaction</th>
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<tr>
<td>Cyclophosphamide</td>
<td>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.</td>
</tr>
</tbody>
</table>

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

<table>
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<tr>
<th>Condition</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin 25-51 or AST 60-180u/L</td>
<td>give 50%</td>
</tr>
<tr>
<td>Bilirubin &gt;51micromol/L and normal AST</td>
<td>give 50%</td>
</tr>
<tr>
<td>Bilirubin &gt;51micromol/L and AST &gt;180u/L</td>
<td>not recommended</td>
</tr>
</tbody>
</table>

Renal impairment

Cyclophosphamide

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<th>Condition</th>
<th>Dosage</th>
</tr>
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<tbody>
<tr>
<td>CrCl 10-29ml/min</td>
<td>give 75% dose</td>
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</table>

REFERENCES

1. EUROEWING12 2014