Systemic Anti Cancer Treatment Protocol

Vincristine, Dactinomycin, Cyclophosphamide Sarcoma (VAC)

PROTOCOL REF: MPHAVINDACY
(Version No: 1.2)

Approved for use in:

Desmoplastic small round cell tumour (maintenance)

Ewing's Sarcoma (consolidation)

Dosage:

Schedule

Desmoplastic small round cell tumour – post surgery maintenance until disease progression or unacceptable toxicity

Ewing's Sarcoma – fixed cycles as per Ewing's protocol after VIDE (if not suitable for VAI due to renal toxicity)

Drug	Dosage	Route	Frequency
Vincristine	1.5mg/m^2 (max 2mg) day 1	IV	Every 21 days
Dactinomycin	0.75mg/m^2 (max 1.5mg) Days 1 and 2	IV	Every 21 days
Cyclophosphamide	1500mg/m^2 day 1	IV	Every 21 days
Mesna	See administration below		

Supportive treatments:

Filgrastim 30MU or 48MU subcutaneous injection daily starting on day 5, for 7 days with repeat FBC and continue for further 7 days if neutrophils not recovered.

Dexamethasone tablets, 4mg twice daily for 3 days

Domperidone 10mg oral tablets, up to 3 times a day or as required

Extravasation risk:

Vincristine – vesicant – follow trust /network policy, specific antidote may apply

Dactinomycin – vesicant – follow trust /network policy, specific antidote may apply

Cyclophosphamide – Non vesicant Administration:

Day	Drug	Dosage	Route	Diluent and Rate
1	Dexamethasone 30 minutes before chemotherapy	8mg	PO	
1	Ondansetron 30 minutes before chemotherapy	16mg	PO	
1	**Vincristine**	1.5 mg/m^2 (max 2mg)	IV	In 50mL sodium chloride 0.9%
1	**Dactinomycin**	0.75mg/m^2 (max 1.5mg)	IV	In 100mL sodium chloride 0.9% over 30 minutes
1	**Mesna**	500mg/m^2	IV	In 500mL sodium chloride 0.9% over 1 hour
1	**Cyclophosphamide + mesna**	1500mg/m^2 + 1500mg/m^2	IV	In 1000mL sodium chloride 0.9% over 3 hours
1	**Mesna**	1500mg/m^2	IV	In 1000mL sodium chloride over 8 hours
2	Dexamethasone	8mg	PO	24 hours after day 1 dose
2	Ondansetron	16mg	PO	24 hours after day 1 dose
2	**Dactinomycin**	0.75mg/m^2 (max 1.5mg)	IV	In 100mL sodium chloride 0.9% over 30 minutes
3	Filgrastim	30MU or 48MU	SC	By subcutaneous injection daily for 7 days and then repeat FBC

Filgrastim dose:

For patients under 70kg: 30MU subcutaneous injection daily

For patients 70kg and above: 48MU subcutaneous injection daily

Notes:

Radiotherapy

This should start concurrent with cycle 7 to the primary site.

Omit dactinomycin for the duration of radiotherapy

Resume dactinomycin after completion of radiotherapy according to symptoms

Omitted doses are not to be given subsequently

Main Toxicities:

Vincristine – neurotoxicity,

Dactinomycin - Myelosuppression, alopecia, mucositis, diarrhoea, liver changes (rare) ovarian failure / infertility

Cyclophosphamide – Myelosuppression, alopecia, mucositis, diarrhoea, haemorrhagic cystitis

Investigations and treatment plan

	Pre	Cycle 7	Cycle 8	Cycle 9	Cycle 10	Cycle 11	Cycle 12	Comments
Medical Assessment	X		X	X	X	X	X	Every cycle
Nursing Assessment	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	Day 1 of each cycle
U&E & LFT	X	X	X	X	X	X	X	Day 1 of each cycle
CrCl (Cockroft and Gault)	X	X	X	X	X	X	X	Day 1 of each cycle
CT scan	X			X				As clinically indicated
Informed Consent	X							
PS recorded	X	X	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	X	X	Every cycle
Urine dipstick for protein / blood	X	X	X	X	X	X	X	Day 1 and 2 of each cycle

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if:-

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 80 x 10^9/L

Parameter	1st Occurrence	2nd Occurrence
Delayed recovery > 6 days OR neutropenic sepsis grade 3 or 4	Reduce cyclophosphamide, dactinomycin and doxorubicin to **80%** of original dose	Reduce cyclophosphamide, dactinomycin and doxorubcin to **60%** of original dose

Non-haematological toxicity

<table>
<tr><td>Renal</td><td>Monitor serum creatinine before each cycle of chemotherapy. Calculate CrCl each time. Routine adjustment of cyclophosphamide is not needed as it is altered hepatically although most sources suggest
<table>
<tr><th>CrCl</th><th>Cyclophosphamide dose</th><th>Etoposide dose</th></tr>
<tr><td>≥10mL/min</td><td>100%</td><td>-</td></tr>
<tr><td><10mL/min</td><td>75%</td><td>-</td></tr>
<tr><td>GFR < 60mL/min/1.73m^2</td><td>-</td><td>70%</td></tr>
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<tr><td>Hepatic</td><td>No specific guidance but consider dose reductions of dactinomycin in severe hepatic dysfunction</td></tr>
<tr><td>Gastric</td><td>Grade 3 or 4 mucositis or GI toxicity – reduce dactinomycin and cyclophosphamide to 80% of original dose for first occurrence and 60% or original dose for second occurrence</td></tr>
<tr><td>Haematuria or haemorrhagic cystitis</td><td>
<table>
<tr><th>Grade</th><th>Action</th></tr>
<tr><td>Microscopic during cyclophosphamide infusion</td><td>Give additional bolus doses of Mesna then a continuous infusion at double dose</td></tr>
<tr><td>Grade 2</td><td>Discontinue cyclophosphamide, continue with double dose continuous Mesna and hydration for 24 hours after cyclophosphamide stopped</td></tr>
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References:

Juergens C, Weston C, Lewis I, Whelan J, Paulussen M, Oberlin O, et al. Safety assessment of intensive induction with vincristine, ifosfamide, doxorubicin, and etoposide (VIDE) in the treatment of Ewing tumors in the EURO-E.W.I.N.G. 99 clinical trial. Pediatric blood & cancer. 2006;47(1):22-9.

Ladenstein R, Potschger U, Le Deley MC, Whelan J, Paulussen M, Oberlin O, et al. Primary disseminated multifocal Ewing sarcoma: results of the Euro-EWING 99 trial. J Clin Oncol. 2010;28(20):3284-91.

Thames Valley Cancer Network http://tvscn.nhs.uk/networks/cancer/cancer-topics/sarcoma/

Wong, H., Hatcher, H., Benson, C., Al-Muderis, O., Horan, G., Fisher, C., Earl, H. and Judson, I. (2013). Desmoplastic small round cell tumour: characteristics and prognostic factors of 41 patients and review of the literature. *Clinical Sarcoma Research*, 3(1), p.14.

Euro Ewing 2012 - International Randomised Controlled Trial for the Treatment of Newly Diagnosed Ewing's Sarcoma Family of Tumours http://www.euroewing.eu/clinical-trials/ee2012-trial