Chemotherapy Protocol

SARCOMA

CYCLOPHOSPHAMIDE-DACTINOMYCIN-VINCRISTINE (VAC)

Regimen

- Sarcoma-Cyclophosphamide-Dactinomycin-Vincristine (VAC)

Indication

- Ewings Sarcoma

Toxicity

Drug	Adverse Effect
Cyclophosphamide	Dysuria, haemorrhagic cystitis (rare), taste disturbances
Dactinomycin	GI irritation, hepatotoxicity, alopecia
Vincristine	Peripheral neuropathy, constipation, jaw pain

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

- FBC, LFTs and U&Es prior to day one of treatment

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

Haematological

Criteria	Eligible Level
Neutrophil	equal to or more than $1x10^9$/L
Platelets	equal to or more than $80x10^9$/L

Consider blood transfusion or erythropoietin if the patient is symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Hepatic Impairment

Drug	Bilirubin µmol/L		AST/ALT units	Dose (% of original dose)
Cyclophosphamide	more than 30	or	more than 2-3xULN	Clinical decision. Evidence that exposure to active metabolites may not be increased, suggesting dose reduction may not be necessary
Dactinomycin	Consider reduction in severe disease			
Vincristine	30-51	or	60-180	50%
	more than 51	and	normal	50%
	more than 51	and	more than 180	omit

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cyclophosphamide	More than 20	100%
	10-20	75%
	Less than 10	Omit
Dactinomycin	N/A	No dose adjustment necessary
Vincristine	N/A	No dose adjustment necessary

Other

Cyclophosphamide

In the case of NCI-CTC grade 3 or 4 mucositis or GI toxicity consider a dose reduction to 80% on first occurrence and to 60% on second occurrence. Always take consultant advice before reducing the dose. In the case of NCI-CTC grade 3 or 4 neutropenic sepsis reduce dose to 80% on first occurrence and to 60% on second occurrence. In the case of delayed recovery of greater than 6 days, reduce dose to 80% on first occurrence and to 60% on second occurrence.

Dactinomycin

In the case of NCI-CTC grade 3 or 4 mucositis or GI toxicity consider a dose reduction to 80% on first occurrence and to 60% on second occurrence. Always take consultant advice before reducing the dose. In the case of NCI-CTC grade 3 or 4 neutropenic sepsis reduce dose to

80% on first occurrence and to 60% on second occurrence. In the case of delayed recovery of greater than 6 days, reduce the dose to 80% on first occurrence and to 60% on the second occurrence.

The dactinomycin should be omitted if radiotherapy is given concurrently.

Vincristine

Reduce the vincristine dose from 2mg to 1mg if a NCI-CTC grade 2 motor or grade 3 sensory neurological toxicity occurs. For higher toxicity grades or if toxicity increases despite dose reduction stop the vincristine.

Regimen

21 day cycle for 7 cycles

Drug	Dose	Days	Administration
Mesna	500mg/m^2	1	Intravenous infusion in 100ml sodium chloride 0.9% over 15minutes
Cyclophosphamide	1500mg/m^2	1	Intravenous infusion in 1000ml sodium chloride 0.9% over 180minutes
Mesna	1500mg/m^2		
Mesna	600mg/m^2	1	Oral. Take 0, 2 and 6 hours post cyclophosphamide infusion (in take home medicines)
Dactinomycin	750mcg/m^2 (max 1500mcg)	1,2	Intravenous bolus
Vincristine	1.5mg/m^2 (max 2mg)	1	Intravenous bolus in 50ml sodium chloride 0.9% over 10minutes

Dose Information

- Cyclophosphamide will be dose banded according to the agreed bands
- Dactinomycin will be dose banded according to the agreed bands
- The maximum dose of dactinomycin is 1500microgram
- Mesna intravenous will be dose banded according to the agreed bands
- Mesna oral will be dose banded to the nearest 400mg capsule (up if halfway)
- Vincristine will be dose rounded to the nearest 0.1mg (up if halfway)
- The maximum dose of vincristine is 2mg

Administration Information

Extravasation

- Cyclophosphamide – neutral
- Mesna – neutral
- Dactinomycin – vesicant
- Vincristine - vesicant

Additional Therapy

- Antiemetics

  Starting 15-30 minutes prior to chemotherapy

  - dexamethasone 8mg oral or intravenous
  - metoclopramide 10mg oral or intravenous
  - ondansetron 8mg oral or intravenous

  As take home medicines

  -dexamethasone 4mg twice a day for three days oral
  -metoclopramide 10mg three times a day for three days then three times a day as required for nausea oral
  -ondansetron 8mg twice a day for three days oral

- Growth factors according to local formulary choice. For example;

  - filgrastim or bioequivalent 30million units once a day for 10 days starting from day five subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day for 10 days starting from day five subcutaneous
  - pegfilgrastim, lipegfilgrastim or bioequivalent 6mg once only on day four subcutaneous

- Anti infective prophylaxis with ciprofloxacin 250mg twice a day for seven days starting on day ten of the cycle

- Mouthcare for the prophylaxis or treatment of mucositis in accordance with local or national guidelines

- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Additional Information

- The National Patient Safety Agency report NPSA/2008/RRR04 must be followed in relation to intravenous administration of vinca alkaloids.

Coding

- Procurement – X70.8
- Delivery – X72.9

References

1) Euro-EWING 99 protocol

REGIMEN SUMMARY

Cyclophosphamide-Dactinomycin-Vincristine (VAC)

Day 1

1. Dexamethasone 8mg oral or intravenous

2. Metoclopramide 10mg oral or intravenous

3. Ondansetron 8mg oral or intravenous

4. Dactinomycin 750microgram/m^2 (max 1500microgram) intravenous bolus

5. Vincristine 1.5mg/m^2 (max 2mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

6. Mesna 500mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 15minutes

7. Cyclophosphamide 1500mg/m^2 and mesna 1500mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 180minutes
   Administration Instructions
   Please ensure the patient takes oral mesna from the take home medicines as soon as the cyclophosphamide infusion ends.

Take Home Medicines

8. Mesna 600mg/m^2 at 0, 2 and 6 hours post cyclophosphamide oral

9. Dexamethasone 4mg twice a day for three days starting on day two of the cycle

10. Metoclopramide 10mg three times a day for three days then 10mg three times a day when required for the relief of nausea starting on the evening of day one of the cycle

11. Ondansetron 8mg twice a day for three days starting on the evening of day one of the cycle

12. Growth factor according to local formulary choice
    - filgrastim or bioequivalent 30million units once a day for 10 days starting from day 5 subcutaneous
    - lenograstim or bioequivalent 33.6million units once a day for 10 days starting from day 5 subcutaneous
    - pegfilgrastim, lipegfilgrastim or bioequivalent 6mg once only on day 4 subcutaneous

13. Ciprofloxacin 250mg twice a day for seven days starting on day ten of the cycle

Day 2

1. Warning – Check supportive medication has been taken
   Administration Instructions
   Check the patient has taken oral anti-emetics before administration of dactinomycin. If not administer;
   - dexamethasone 4mg oral or intravenous
   - metoclopramide 10mg oral or intravenous
   - ondansetron 8mg oral or intravenous

2. Dactinomycin 750microgram/m^2 (max 1500microgram) intravenous bolus

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	October 2015	None	Dr Deborah Wright Pharmacist	Dr Nicola Keay Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.