Chemotherapy Protocol

SARCOMA

DOXORUBICIN-CYCLOPHOSPHAMIDE-ETOPOSIDE-VINCRISTINE (VCDE)

Inpatient Regimen

Regimen

- Sarcoma-InP- Cyclophosphamide-Doxorubicin-Etoposide-Vincristine (VCDE)

Indication

- Rhabdommyosarcoma

Toxicity

Drug	Adverse Effect
Cyclophosphamide	Haemorrragic cystitis, nephrotoxicity
Doxorubicin	Cardiomyopathy, alopecia, urinary discolouration (red)
Etoposide	Hypotension on rapid infusion, hyperbilirubinaemia
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

Drugs

- FBC, LFTs and U&Es (including uric acid, albumin, calcium, magnesium, bicarbonate and phosphate) prior to day one of treatment
- Ensure adequate cardiac function before starting therapy. Baseline LVEF should be measured in patients with a history of cardiac problems, cardiac risk factors or in the elderly. Discontinue doxorubicin if cardiac failure develops
- Lung function tests

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.

Dose/time intensity is regarded as an essential aspect of induction strategy. In case of significant bone marrow toxicity preference should be given to growth factor support rather than dose reduction in to maintain dose intensity. Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Criteria	Eligible Level
Neutrophil	equal to or more than $1x10^9$/L
Platelets	equal to or more than $100x10^9$/L

If haematological recovery has not occurred by day 7 then reduce the etoposide dose by 20%. If the patient develops neutropenic sepsis at NCI-CTC grade 3 or 4 then the etoposide dose should be reduced by 20%. If a further episode of toxicity occurs, the etoposide dose should be reduced by an additional 20%. The etoposide may need to be omitted, rather than reduce the doses of the other three drugs.

Consider blood transfusion 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
Doxorubicin	less than 30	and	2-3xULN	75%
	30-50	and/or	more than 3xULN	50%
	51-85		N/A	25%
	more than 85		N/A	omit
Etoposide	30-51	or	60-180	Consider reducing dose to 50%
	more than 51	or	more than 180	Clinical decision
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
Doxorubicin	Less than 10	Consider dose reduction in severe renal failure
Etoposide	More than 50	100%
	15-50	75%
	Less than 15	50%
Vincristine	N/A	No dose adjustment needed

Other

If a NCI-CTC grade 3 or 4 mucositis devlelops reduce the etoposide dose by 20%. If further episode of toxocity occurs, the etoposide dose should be reduced by an additional 20%. Etoposide may need to be omitted, rather than reduce the doses of the other three drugs.

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.

Doxorubicin

Discontinue doxorubicin if cardiac failure develops. This may be substituted with dactinomycin 1.5mg/m^2 on day two of the cycle.

Etoposide

Where significant reductions in albumin levels occur consider reducing the dose of etoposide.

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 6 cycles

Drug	Dose	Days	Administration
Mesna	300mg/m^2	1	Intravenous infusion in 100ml sodium chloride 0.9%
Cyclophosphamide	1500mg/m^2	1	Intravenous infusion in 1000ml sodium chloride 0.9%over 3 hours
Doxorubicin	20mg/m^2	1,2,3	Intravenous bolus over 10 minutes
Etoposide	150mg/m^2	1,2,3	Intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes
Vincristine	1.5mg/m^2 (max 2mg)	1	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

Dose Information

- Cyclophosphamide will be dose banded according to the agreed bands
- Doxorubicin will be dose banded according to the agreed bands
- The maximum lifetime cumulative dose of doxorubicin is 450mg/m². However prior radiotherapy to the mediastinal / pericardial area should receive a lifetime cumulative doxorubicin dose of no more than 400mg/m².
- Etoposide will be dose banded according to the agreed bands
- Mesna will be dose banded according to the agreed bands
- 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
- Doxorubicin – vesicant
- Etoposide – irritant
- Vincristine - vesicant

Additional Therapy

This is an inpatient regimen please ensure all supportive and take home medicines are prescribed on the inpatient chart or general electronic prescribing system.

- Antiemetics

  Starting 15-30 minutes prior to chemotherapy

  -dexamethasone 4mg twice a day for 5 days oral
  -metoclopramide 10mg three times a day when required for nausea oral
  -ondansetron 8mg twice a day for 5 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 5 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day for 10 days starting from day 5 subcutaneous
  - pegfilgrastim or bioequivalent 6mg once only on day 4 subcutaneous

- Anti infective prophylaxis

  -ciprofloxacin 500mg twice a day from day 8 to day 15 inclusive

- 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.

- Oral mesna use a dose of 900mg/m^2 (rounded upwards to the nearest 400mg tablet) at 0, 2, and 6 hours after the end of the cyclophosphamide infusion.

Additional Information

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

Coding

- Procurement – X71.3

- Delivery – not required

References

1. Straus SJ, McTiernan A, Driver D et al. Single center experience of a new intensive induction regimen for Ewings family of tumours: feasibility, toxicity and stem cell mobilisation properties. J Clin Oncol 2003; 21 (15): 2974-2981

REGIMEN SUMMARY

InP-Cyclophosphamide-Doxorubicin-Etoposide-Vincristine (VCDE)

Other than those listed below, supportive medication for this regimen will not appear in Aria as prescribed agents. The administration instructions for each warning describes the agents which must be prescribed on the in-patient chart or general electronic prescribing system

Day 1

1. Warning – Check supportive medication prescribed
   Administration Instructions
   1. Dexamethasone 4mg twice a day, days 1 to 5 oral or intravenous
   2. Metoclopramide 10mg three times a day, days 1 to 5 oral or intravenous
   3. Ondansetron 8mg twice a day, days 1 to 5 oral or intravenous
   4. Mesna 900mg/m^2 at 0, 2 and 6 hours post cyclophosphamide infusion oral
   5. Ciprofloxacin 500mg twice a day days 8-15 oral
   6. 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 or bioequivalent 6mg once only on day 4 subcutaneous
   7. Consider gastric protection
   8. Consider mouthwashes

2. Doxorubicin 20mg/m^2 intravenous bolus over 10 minutes

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

4. Etoposide 150mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes

5. Mesna 300mg/m^2 in 100ml sodium chloride 0.9% over 15 minutes

6. Cyclophosphamide 1500mg/m^2 in 1000ml sodium chloride 0.9% intravenous infusion over 180 minutes

Day 2

7. Warning – Check supportive medication prescribed
   Administration Instructions
   1. Dexamethasone 4mg twice a day, days 1 to 5 oral or intravenous
   2. Metoclopramide 10mg three times a day, days 1 to 5 oral or intravenous
   3. Ondansetron 8mg twice a day, days 1 to 5 oral or intravenous
   4. Mesna 900mg/m^2 at 0, 2 and 6 hours post cyclophosphamide infusion oral
   5. Ciprofloxacin 500mg twice a day days 8-15 oral
   6. 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 or bioequivalent 6mg once only on day 4 subcutaneous
   7. Consider gastric protection
   8. Consider mouthwashes

8. Doxorubicin 20mg/m^2 intravenous bolus over 10 minutes

9. Etoposide 150mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes

Day 3

10. Warning – Check supportive medication prescribed
    Administration Instructions
    1. Dexamethasone 4mg twice a day, days 1 to 5 oral or intravenous

2. Metoclopramide 10mg three times a day, days 1 to 5 oral or intravenous
3. Ondansetron 8mg twice a day, days 1 to 5 oral or intravenous
4. Mesna 900mg/m^2 at 0, 2 and 6 hours post cyclophosphamide infusion oral
5. Ciprofloxacin 500mg twice a day days 8-15 oral
6. 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 or bioequivalent 6mg once only on day 4 subcutaneous
7. Consider gastric protection
8. Consider mouthwashes

11. Doxorubicin 20mg/m^2 intravenous bolus over 10 minutes

12. Etoposide 150mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	February 2016	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.