Chemotherapy Protocol

SARCOMA

DOXORUBICIN-ETOPOSIDE-IFOSFAMIDE -VINCRISTINE (VIDE)

Inpatient Regimen

Regimen

- Sarcoma-InP- Doxorubicin-Etoposide-Ifosfamide-Vincristine (VIDE)

Indication

- Ewings Sarcoma (induction therapy)

Toxicity

Drug	Adverse Effect
Doxorubicin	Cardiomyopathy, alopecia, urinary discolouration (red)
Etoposide	Hypotension on rapid infusion, hyperbilirubinaemia
Ifosfamide	Haemorrragic cystitis, encephalopathy, nephrotoxicity
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 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)
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
Ifosfamide	more than 20	or	more than 2.5x ULN	Not recommended
	or ALP more than 2.5x ULN			
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)
Doxorubicin	Less than 10	Consider dose reduction in severe renal failure
Etoposide	More than 50	100%
	15-50	75%
	Less than 15	50%
Ifosfamide	More than 60	100%
	40-59	70%
	Less than 40	Clinical decision
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.

Doxorubicin

Discontinue doxorubicin if cardiac failure develops

Etoposide

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

Ifosfamide

In the case of a NCI-CTC grade 1 neurological toxicity to ifosfamide, consider reducing the dose of ifosfamide for the next cycle. If a NCI-CTC grade 2 neurologic toxicity appears or neurologic toxicity worsens despite dose reduction consider stopping the ifosfamide.

Risk factors for CNS toxicity include a low albumin, renal impairment, prior administration of cisplatin, poor performance status, CNS tumour, bulky pelvic disease, concomitant psychotropic drugs and younger age. Methylene blue 50mg four times a day intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes can be used to prevent or treat ifosfamide induced encephalopathy.

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
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
Mesna	600mg/m^2	1,2,3	Intravenous infusion in sodium chloride 0.9% 100ml over 15 minutes
Ifosfamide	3000mg/m^2	1,2,3	Intravenous infusion in 1000ml sodium chloride 0.9% over 3 hours (the ifosfamide and mesna are in the same bag)
Mesna	3000mg/m^2		
Mesna	1800mg/m^2	1,2,3	Intravenous infusion in 1000ml sodium chloride 0.9% over 12 hours (post ifosfamide dose)
Vincristine	1.5mg/m^2 (max 2mg)	1	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

Dose Information

- 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
- Ifosfamide 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

- Doxorubicin – vesicant
- Etoposide – irritant
- Ifosfamide – neutral
- Mesna – neutral
- 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.

- If the last dose of intravenous mesna is to be replaced with oral mesna use a dose of 1200mg/m^2 (rounded upwards to the nearest 400mg tablet) at 0, 2, and 6 hours after the end of the ifosfamide 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-Doxorubicin-Etoposide-Ifosfamide-Vincristine (VIDE)

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. Ciprofloxacin 500mg twice a day days 8-15 oral
   5. 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
   6. Consider gastric protection
   7. 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 600mg/m^2 in 100ml sodium chloride 0.9% intravenous infusion over 15 minutes

6. Ifosfamide 3000mg/m^2 and mesna 3000mg/m^2 in 1000ml sodium chloride 0.9% intravenous infusion over 180 minutes

7. Mesna 1800mg/m^2 in 1000ml sodium chloride 0.9% intravenous infusion over 720 minutes
   Administration Instructions
   On day three of the cycle (after the last dose of the ifosfamide infusions) this may be substituted with oral mesna at a dose of 1200mg/m^2 (rounded upwards to the nearest 400mg tablet) at 0, 2, and 6 hours after the end of the ifosfamide infusion.

Day 2

8. 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 day 1 to 5 oral or intravenous
   3. Ondansetron 8mg twice a day, days 1 to 5 oral or intravenous
   4. Ciprofloxacin 500mg twice a day days 8-15 oral
   5. 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
   6. Consider gastric protection
   7. Consider mouthwashes

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

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

11. Mesna 600mg/m^2 in 100ml sodium chloride 0.9% intravenous infusion over 15 minutes

12. Ifosfamide 3000mg/m^2 and mesna 3000mg/m^2 in 1000ml sodium chloride 0.9% intravenous infusion over 180 minutes

13. Mesna 1800mg/m^2 in 1000ml sodium chloride 0.9% intravenous infusion over 720 minutes
    Administration Instructions
    On day three of the cycle (after the last dose of the ifosfamide infusions) this may be substituted with oral mesna at a dose of 1200mg/m^2 (rounded upwards to the nearest 400mg tablet) at 0, 2, and 6 hours after the end of the ifosfamide infusion.

Day 3

14. 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- 5 oral or intravenous
    3. Ondansetron 8mg twice a day, days 1 to 5 oral or intravenous
    4. Ciprofloxacin 500mg twice a day days 8-15 oral
    5. 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
    6. Consider gastric protection
    7. Consider mouthwashes

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

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

17. Mesna 600mg/m^2 in 100ml sodium chloride 0.9% intravenous infusion over 15 minutes

18. Ifosfamide 3000mg/m^2 and mesna 3000mg/m^2 in 1000ml sodium chloride 0.9% intravenous infusion over 180 minutes

19. Mesna 1800mg/m^2 in 1000ml sodium chloride 0.9% intravenous infusion over 720 minutes
    Administration Instructions
    On day three of the cycle (after the last dose of the ifosfamide infusions) this may be substituted with oral mesna at a dose of 1200mg/m^2 (rounded upwards to the nearest 400mg tablet) at 0, 2, and 6 hours after the end of the ifosfamide infusion.

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 which occur as a result of following these guidelines.