Chemotherapy Protocol

SARCOMA

CYCLOPHOSPHAMIDE-TOPOTECAN

Regimen

- Sarcoma – Cyclophosphamide-Topotecan

Indication

- Advanced Ewings sarcoma or rhabdomyosarcoma
- WHO performance status 0,1, 2
- Palliative intent

Toxicity

Drug	Adverse Effect
Cyclophosphamide	Dysuria, haemorrragic cystitis (rare), taste disturbances
Topotecan	Myelosuppression, alopecia, diarrhoea, anorexia, abdominal pain, pruritis

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

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.

In principle all dose reductions due to adverse drug reactions should not be escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.
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

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

Prior to cycle 1 the following criteria must be met;

Criteria	Eligible Level
Neutrophil	equal to or more than $1.5x10^9$/L
Platelets	equal to or more than $100x10^9$/L

Day 1

Neutrophils ($x10^9$/L)	Dose Modifications
1 or greater	100%
0.5 - 1	Delay until recovery to $1x10^9$/L or greater then continue at full dose
less than 0.5	Delay until recovery to $1x10^9$/L or greater then continue at 75% of the original dose
Platelets ($x10^9$/L)	**Dose Modifications**
100 or greater	100%
50 - 99	Delay until recovery to $100x10^9$/L or greater then continue at full dose
less than 50	Delay until recovery to $100x10^9$/L or greater then continue at 75% of the original dose

Hepatic Impairment

Drug	Bilirubin (µmol/L)	Dose (% of original dose)
Cyclophosphamide	Evidence suggests dose reduction not necessary	
Topotecan	less than 170	100%
	170 or greater	Clinical decision

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cyclophosphamide	more than 20	100%
	10-20	75%
	less than10	50%
Topotecan	40 or greater	100%
	20-39	50%
	less than 20	Contra indicated

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose should then be reduced to 75% of the original dose or discontinued as appropriate.

Regimen

21 day cycle for 6 cycles

Drug	Dose	Days	Administration
Cyclophosphamide	250mg/m^2	1, 2, 3, 4, 5,	Intravenous bolus over 10 minutes
Topotecan	0.75mg/m^2	1, 2, 3, 4, 5	Intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes

Dose Information

- Cyclophosphamide will be dose banded according to the agreed bands
- Topotecan dose will be rounded to the nearest 0.1mg (up if halfway).

Administration Information

Extravasation

- Cyclophosphamide - neutral
- Topotecan - exfoliant

Other

Additional Therapy

Antiemetics

15 – 30 minutes prior to chemotherapy

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

As take home medication

- dexamethasone 4mg once a day for 2 days starting on day 6 of the cycle oral
- metoclopramide 10mg oral three times a day as required oral

- Growth factors according to local formulary choice. For example:
  - filgrastim or bioequivalent 30million units once a day for 7 days from day 7 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day for 7 days from day 7 subcutaneous
  - pegfilgrastim or bioequivalent 6mg once only on day 6 subcutaneous
- Ciprofloxacin 500mg twice a day for 7 days starting on day 7 of the cycle
- Mouthwashes according to local or national policy on the treatment of mucositis
- 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.

Coding

- Procurement – X71.1
- Delivery – X72.1, X72.4

References
1. Farah R, Raad R, Khoury NJ et al. Cyclophosphamide and topotecan as first line salvage therapy in patients with relapsed Ewing sarcoma at a single institution. J Pediatr Hematol Oncol 2013: 35 (5): 356-360.

REGIMEN SUMMARY

Cyclophosphamide – Topotecan

Day 1, 2, 3, 4, 5

1. Dexamethasone 8mg oral or intravenous
2. Metoclopramide 10mg oral or intravenous
3. Topotecan 0.75mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 30 mnutes
4. Cyclophosphamide 250mg/m^2 intravenous bolus over 10 minutes

Take Home Medicines (day 1 only)

5. Dexamethasone 4mg once a day in the morning for two days starting on day 6 of the cycle
6. Metoclopramide 10mg three times a day when required for the relief of nausea oral
7. Growth Factors
   Administration Instructions
   Please dispense according to local formulary choices. For example;

   - filgrastim or bioequivalent 30million units once a day for 7 days from day 7 subcutaneous
   - lenograstim or bioequivalent 33.6million units once a day for 7 days from day 7 subcutaneous
   - pegfilgrastim, lipegfilgrastim or bioequivalent 6mg once only on day 6 subcutaneous

8. Ciprofloxacin 500mg twice a day for 7 days starting on day 7 of the cycle

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	April 2016	Dose rounding changed to 0.1mg	Dr Deborah Wright Pharmacist	Dr Nicola Keay Consultant Medical Oncologist
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 Hospital 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.