Chemotherapy Protocol

GYNAECOLOGICAL CANCER

CISPLATIN-TOPOTECAN

(intravenous)

Regimen

- Cervix-Cisplatin-Topotecan IV

Indication

- Recurrent stage IVB cervical cancer in patients who have not previously received cisplatin
- Palliative intent
- WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity, highly emetogenic
Topotecan	Diarrhoea, anorexia, abdominal pain, pruritis, myelosuppressive

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 prior to day one of treatment
- EDTA or calculated creatinine clearance 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 re-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

Prior to each cycle the following criteria must be met;

Criteria	Eligible Level
Haemoglobin	equal to or more than 9g/dL (after transfusion if necessary)
Neutrophil	equal to or more than $1x10^9$/L
Platelets	equal to or more than 100 $x10^9$/L

Day 1

Neutrophils ($x10^9$/L)	Dose Modifications
1 or greater	100%
less than 1	Delay treatment for 7 days, if resolved to $1x10^9$/L or greater after 7 days continue at full dose
Febrile neutropenia	1st occurrence Reduce the dose of topotecan to 0.6mg/m^2 for all subsequent cycles 2nd occurrence Reduce dose of topotecan to 0.45mg/m^2 for all subsequent cycles
Platelets ($x10^9$/L)	**Dose Modifications**
100 or greater	100%
less than 100	Delay treatment for 7 days, if resolved to $100x10^9$/L or greater after 7 days then continue at full dose
less than 10 at anytime	1st occurrence Reduce the dose of topotecan to 0.6mg/m^2 for all subsequent cycles. 2nd occurrence Reduce dose of topotecan to 0.45mg/m^2 for all subsequent cycles.

Hepatic Impairment

Drug	Bilirubin µmol/L		AST/ALT units	Dose (%of original dose)
Cisplatin	N/A		N/A	No dose adjustment needed
Topotecan	less than 170			100%
	170 or greater			Clinical decision

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cisplatin	60 or greater	100%
	45-59	75%
	less than 45	Consider alternative
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 of the causative agent 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
Cisplatin	50mg/m^2	1	Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a rate of 1mg/min cisplatin (minimum 120 minutes)
Topotecan	0.75mg/m^2	1, 2, 3	Intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes

Dose Information

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

Administration Information

Extravasation

- Cisplatin – exfoliant
- Topotecan - exfoliant

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy on day 1

  - aprepitant 125mg oral
  - dexamethasone 4mg oral or intravenous
  - ondansetron 8mg oral or intravenous

  15-30 minutes prior to chemotherapy on days 2 and 3

  - aprepitant 80mg oral
  - dexamethasone 4mg oral or intravenous
  - ondanseton 8mg oral or intravenous

  As take home medicines (dispensed on day 1)

  - metoclopramide 10mg oral three times a day for 3 days then 10mg three times a day as required.
  - ondansetron 8mg oral on the evening of chemotherapy

- Cisplatin hydration as follows;

  Cisplatin pre-hydration as follows

  - furosemide 40mg oral or intravenous

  - sodium chloride 0.9% 1000ml with 16mmol magnesium sulphate and 20mmol potassium chloride over 60 minutes

  Cisplatin post-hydration as follows

  - sodium chloride 0.9% 1000ml with 16mmol magnesium sulphate and 20mmol potassium chloride over 60 minutes

- 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 (OPCS 14-15)

- Procurement – X70.4
- Delivery – X72.1 & X72.4

References
1. Long H, Bundy B, Grendys E et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol. 2005;23 (21):462-633.
2. NICE Guidance TA183 – Topotecan for the treatment of recurrent stage IVb cervical cancer. Oct 2009.

REGIMEN SUMMARY

Cisplatin-Topotecan IV

Day 1

1. Aprepitant 125mg oral
2. Dexamethasone 4mg oral or intravenous
3. Ondansetron 8mg oral or intravenous
4. Topotecan 0.75mg/m^2 in 100ml sodium chloride 0.9% over 30 minutes
5. Furosemide 40mg oral or intravenous
6. Sodium chloride 0.9% 1000ml with magnesium sulphate 16mmol and potassium chloride 20mmol intravenous infusion over 60 minutes
7. Cisplatin 50mg/m^2 in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion at a rate of 1mg/min cisplatin (minimum 120 minutes)
8. Sodium chloride 0.9% 1000ml with magnesium sulphate 16mmol and potassium chloride 20mmol intravenous infusion over 60 minutes

Day 2, 3

9. Aprepitant 80mg oral
10. Dexamethasone 4mg oral or intravenous
11. Ondansetron 8mg oral or intravenous
12. Topotecan 0.75mg/m^2 in 100ml sodium chloride 0.9% over 30 minutes

Take Home Medicines

13. Metoclopramide 10mg oral three times a day for 3 days then 10mg three times a day when required for nausea
14. Ondansetron 8mg oral each evening for three days on the days of chemotherapy

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	March 2014	Bolus removed from "intravenous bolus" Antiemetics clarified under additional therapies OPCS updated Metoclopramide dose changed to 10mg from 10-20mg Disclaimer added	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1	May 2013	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Clare Green Consultant Medical Oncologist Dr Cheng Yeoh 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.