Chemotherapy Protocol

GYNAECOLOGICAL CANCER

TOPOTECAN INTRAVENOUS

(1, 8, 15)

Regimen

- Ovary – Topotecan (1, 8, 15)

Indication

- Second-line or subsequent treatment of platinum-refractory or platinum-resistant ovarian cancer, or in women who are allergic to platinum-based compounds, for whom pegylated liposomal doxorubicin and single-agent paclitaxel are considered inappropriate.
- WHO performance status 0,1, 2
- Palliative intent

Toxicity

Drug	Adverse Effect
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 prior to day 1, 8 and 15
- CA125 prior to day 1 of each cycle

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 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

Haemoglobin should reach 9g/dL prior to each cycle. Support with blood transfusions if necessary.

Day 1

Neutrophils ($x10^9$/L)	Dose Modifications (topotecan)
1.5 or greater	100%
Less than 1.5	Day 1 - Delay until recovery to $1.5x10^9$/L or greater then continue with a dose of 3mg/m^2. Day 8 or 15 then omit treatment
Platelets ($x10^9$/L)	**Dose Modifications**
100 or greater	100%
less than 100	Day 1 - Delay until recovery to $100x10^9$/L or greater then continue with a dose 3mg/m^2. Day 8 or 15 then omit treatment

Day 8, 15

Neutrophils ($x10^9$/L)	Dose Modifications (topotecan)
1.5 or greater	100%
less than 1.5	Omit
Platelets ($x10^9$/L)	**Dose Modifications**
100 or greater	100%
less than 100	Omit

Hepatic Impairment

Drug	Bilirubin (µmol/L)	Dose (% of original dose)
Topotecan	less than 170	100%
	170 or greater	Clinical decision

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
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 3mg/m^2 or discontinued as appropriate.

Regimen

28 day cycle for 6 cycles

Drug	Dose	Days	Administration
Topotecan	4mg/m^2	1, 8, 15	Intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes

Dose Information

- Topotecan dose will be rounded to the nearest 0.4mg (up if halfway).

Administration Information

Extravasation

- Topotecan – exfoliant

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 oral
  - metoclopramide 10mg oral three times a day as required

- 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 4.6)

- Procurement – X70.4
- Delivery – X72.3 & X72.4

References

1. Sehouli J, Stengel D, Harter P et al. Topotecan Weekly Versus Conventional 5-Day Schedule in Patients With Platinum-Resistant Ovarian Cancer: A Randomized Multicenter Phase II Trial of the North-Eastern German Society of Gynecological Oncology Ovarian Cancer Study Group. J Clin Oncol 2011; 29 (2): 242-248.
2. Gordon A, Fleagle J, Guthrie D et al. Recurrent epithelial ovarian carcinoma: a randomized phase III study of pegylated liposomal doxorubicin versus topotecan. J Clin Oncol 2001; 19(14): 3312-3322.
3. Ten Bokkel Huinink W, Gore M, Carmichael J et al. Topotecan versus paclitaxel for the treatment of recurrent epithelial ovarian cancer. J Clin Oncol 1997; 15 (6): 2183-2193.
4. NICE Guidance TA91 - Ovarian cancer (advanced) - paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan (review). May 2005

REGIMEN SUMMARY

Topotecan (1, 8, 15)

Day 1, 8, 15

1. Dexamethasone 8mg oral or intravenous

2. Metoclopramide 10mg oral or intravenous

3. Topotecan 4mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes.

Take Home Medicines (day 1)

4. Dexamethasone 4mg once a day for 2 days starting the day after chemotherapy oral
   Administration Instructions
   Please supply sufficient for days 1, 8, 15 of the cycle

5. Metoclopramide 10mg oral three times a day when required for nausea.
   Administration Instructions
   Please supply 60 tablets or nearest appropriate equivalent

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	April 2014	IV removed from name Bolus removed from intravenous bolus throughout text Metoclopramide dose changed to 10mg OPCS codes updated Disclaimer updated	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.