Chemotherapy Protocol

GYNAECOLOGICAL CANCER

CISPLATIN-DOCETAXEL

Regimen

- Uterine-Cisplatin-Docetaxel

Indication

- Recurrent/advanced uterine cancer
- Palliative intent
- WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity, highly emetogenic
Docetaxel	Myelosupressive, neuropathy, fluid retention, myalgia, arthralgia, alopecia

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBCs, U&Es, LFTs and EDTA or calculated creatinine clearance prior to 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 each cycle the following criteria must be met;

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

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

Day 1

Neutrophils ($x10^9$/L)	Dose Modifications (cisplatin and docetaxel)
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
Platelets ($x10^9$/L)	**Dose Modifications (cisplatin and docetaxel)**
100 or greater	100%
less than 100	Delay treatment for 7 days, if resolved to $100x10^9$/L or greater after 7 days continue at full dose

Hepatic Impairment

Drug	Bilirubin µmol/L		AST/ALT units		Alk Phos units	Dose (% of original dose)
Cisplatin	N/A		N/A		N/A	No dose adjustment needed
Docetaxel	N/A		1.5xULN or greater	and	2.5xULN or greater	Give 75%
	22 or greater	and/or	3.5xULN or greater	and	6xULN or greater	Not Recommended

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cisplatin	60 or greater	100%
	45-59	75%
	less than 45	Consider alternative
Docetaxel	N/A	No dose adjustment needed

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.

Docetaxel

Peripheral neuropathy at NCI-CTC grade 3 should result in a dose reduction from 70mg/m^2 to 55mg/m^2 once the neuropathy has resolved to NCI-CTC grade 2 or below. If the NCI-CTC grade 3 neuropathy occurred at doses lower than 55mg/m^2 or a NCI-CTC grade 4 toxicity develops stop treatment.

Excessive tearing / lacrimation are related to cumulative docetaxel doses and occur after a median of 400mg/m^2. Symptomatic treatment with hypromellose 0.3% eye drops four times a day may help. However, if the ocular irritation continues reduce the docetaxel dose to 80% of the original dose in the first instance.

Delay the docetaxel where a NCI-CTC grade 3 cutaneous toxicity is present on day one of the cycle until it resolves to NCI-CTC grade 1 or below. The subsequent doses of docetaxel should be reduced to from 70mg/m^2 to 55mg/m^2. If it occurs with a dose of 55mg/m^2 or if there is no recovery after two weeks, docetaxel treatment should be stopped. Where a NCI-CTC grade 3 cutaneous toxicity occurs between cycles with recovery by day one then reduce the docetaxel dose as described. Docetaxel should be stopped in response to a NCI-CTC grade 4 cutaneous toxicity.

Regimen

21 day cycle for 6 cycles

Drug	Dose	Days	Administration
Cisplatin	60mg/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)
Docetaxel	70mg/m^2	1	Intravenous infusion in sodium chloride 0.9% 250ml over 60 minutes

Dose Information

- Cisplatin will be dose banded according to the CSCCN agreed bands.
- Docetaxel will be dose banded according to the CSCCN agreed bands.
- Docetaxel induced fluid retention can lead to weight gain. This is not a reason to alter the doses

Administration Information

Extravasation

- Cisplatin – exfoliant
- Docetaxel - exfoliant

Other

- Hypersensitivity reactions to docetaxel tend to occur with the first or second infusion. For minor symptoms such as flushing or localised rashes the infusion should not be interrupted. For severe reactions including profound hypotension, bronchospasm and generalised erythema discontinue the infusion immediately.
- Docetaxel doses of more than 200mg should be diluted in 500ml sodium chloride 0.9% (maximum concentration 0.74mg/ml)

Additional Therapy

- Antiemetics

  15-30 minutes before chemotherapy

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

  As take home medication

  - metoclopramide 10mg three times a day for three days and then 10mg three times a day when required oral

  - ondansetron 8mg twice a day for 3 days starting on the evening of chemotherapy oral

- To prevent fluid retention and hypersensitivity reactions prescribe dexamethasone 8mg twice a day orally for three days starting 24 hours before the docetaxel administration. On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg once only dose intravenous bolus.

- Cisplatin hydration as follows;

  Cisplatin pre-hydration as follows

  - furosemide 40mg oral

  - 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 – X71.2
- Delivery – X72.1

References

1. Nomura H, Aoki D, Takahashi F et al. Randomized phase II study comparing docetaxel plus cisplatin, docetaxel plus carboplatin and paclitaxel plus carboplatin in patients with advanced or recurrent endometrial carcinoma: a Japanese Gynecologic Oncology Group study (JGOG2041). Annals of Oncology 2011; 22(3): 636-642.

REGIMEN SUMMARY

Cisplatin-Docetaxel

Cycle 1, 2, 3, 4, 5

Day Minus 1

1. Dexamethasone 8mg twice a day oral (from TTO)*

Day 1

2. Aprepitant 125mg oral

3. Dexamethasone 8mg twice a day oral (from TTO)*
   Administration Instructions
   On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone premedication administer dexamethasone 20mg IV stat 15-30 minutes prior to chemotherapy

4. Ondansetron 8mg oral or intravenous

5. Docetaxel 70mg/m^2 in sodium chloride 0.9% 250ml over 60 minutes

6. Furosemide 40mg oral or intravenous

7. Sodium chloride 0.9% 1000ml with magnesium sulphate 16mmol and potassium chloride 20mmol intravenous infusion over 60 minutes

8. Cisplatin 60mg/m^2 in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion at a rate of 1mg/min (minimum 120 minutes)

9. Sodium chloride 0.9% 1000ml with magnesium sulphate 16mmol and potassium chloride 20mmol intravenous infusion over 60 minutes

Take Home Medicines

10. Aprepitant 80mg once a day for 2 days starting the day after chemotherapy administration

11. Dexamethasone 8mg oral twice a day for 3 days. To be taken the before, the day of and the day after docetaxel.

12. Metoclopramide 10mg three times a day when required for nausea

13. Ondansetron 8mg oral twice a day for 3 days starting on the evening of chemotherapy

Cycle 6

Day Minus 1

14. Dexamethasone 8mg twice a day oral (from TTO)*

Day 1

15. Aprepitant 125mg oral

16. Dexamethasone 8mg twice a day oral (from TTO)*
    Administration Instructions
    On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone premedication administer dexamethasone 20mg IV stat 15-30 minutes prior to chemotherapy

17. Ondansetron 8mg oral or intravenous

18. Docetaxel 70mg/m^2 in sodium chloride 0.9% 250ml over 60 minutes

19. Furosemide 40mg oral or intravenous

20. Sodium chloride 0.9% 1000ml with magnesium sulphate 16mmol and potassium chloride 20mmol intravenous infusion over 60 minutes

21. Cisplatin 60mg/m^2 in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion at a rate of 1mg/min (minimum 120 minutes)

22. Sodium chloride 0.9% 1000ml with magnesium sulphate 16mmol and potassium chloride 20mmol intravenous infusion over 60 minutes

Take Home Medicines

23. Aprepitant 80mg once a day for 2 days starting the day after chemotherapy

24. Metoclopramide 10mg three times a day when required for nausea

25. Ondansetron 8mg oral twice a day for 3 days starting on the evening of chemotherapy

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	March 2014	Bolus changed to “intravenous bolus” Metoclopramide dose changed to 10mg from 10-20mg 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.