Chemotherapy Protocol

BREAST CANCER

CYCLOPHOSPHAMIDE-DOCETAXEL

Regimen

- Breast Cancer – Cyclophosphamide-Docetaxel

Indication

- Adjuvant therapy for early breast cancer when anthracyclines are contra-indicated
- WHO Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Cyclophosphamide	Dysuria, haemorrhagic cystitis, taste disturbances
Docetaxel	Hypersensitivity, fluid retention, neuropathy, joint pains, nail changes, fatigue

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

Monitoring

Regimen

- FBC, U&E's and LFT's prior to each cycle

Dose Modifications

The dose modifications listed are for haematological, liver and renal function 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. The following is a general guide only.

Haematological

Prior to prescribing the following treatment criteria must be met on day 1 cycle 1 of treatment.

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

If counts on day one are below these criteria for neutrophil and/or platelets then delay treatment for seven days. Only re-start treatment when these levels are reached. If patients experience febrile neutropenia or treatment delay due to neutrophils of less than $0.5x10^9$/L or platelets less than $50x10^9$/L for more than a week, then reduce the dose to 80% of the original dose. If the neutropenia or thrombocytopenia recurs following this dose reduction the dose should be either further reduced to 50% of the original dose or treatment stopped. Growth factors may be considered according to local policy.

Hepatic Impairment

Drug	Bilirubin (µmol/L)		AST/ALT (units)		Alk Phos (units)	Dose (% of original dose)
Cyclophosphamide	Dose reduction may not be necessary					
Docetaxel	N/A		1.5xULN or greater	and	2.5xULN or greater	Consider 75%
	Greater than ULN	and/or	3.5xULN or greater	and	6xULN or greater	Not Recommended

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cyclophosphamide (consider mesna)	More than 20	100
	10-20	75
	Less than 10	50
Docetaxel	No dose reduction necessary	

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.

Docetaxel

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.

Peripheral neuropathy at NCI-CTC grade 3 should result in a dose reduction from 75mg/m^2 to 60mg/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 75mg/m^2 or a NCI-CTC grade 4 toxicity develops consider stopping 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 100mg/m^2 to 75mg/m^2 or from 75mg/m^2 to 60mg/m^2. If it occurs with a dose of 60mg/m2 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

Docetaxel is highly myelosuppressive and in those with poor bone marrow reserves (for example due to extensive prior treatment, bone metastasis or extensive skeletal radiation) consider a starting dose of 55mg/m^2 with a view to increase to 75mg/m^2 if well tolerated.

21 day cycle for 4 cycles

Drug	Dose	Days	Administration
Cyclophosphamide	600mg/m^2	1	Intravenous bolus
Docetaxel	75mg/m^2	1	Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes

Dose Information

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

Administration Information

Hypersensitivity reactions tend to occur with the first or second infusion of docetaxel. Docetaxel infusion should not be interrupted for minor symptoms such as flushing or localised rashes. Immediately discontinue the infusion for severe reactions which include profound hypotension, bronchospasm and generalised erythema.

- Docetaxel doses of more than 200mg should be diluted in 500ml sodium chloride 0.9% (maximum concentration 0.74mg/ml).

Extravasation

- Cyclophosphamide - neutral
- Docetaxel – exfoliant

Additional Therapy

- Antiemetics

  15-30 minutes before chemotherapy;

  - ondansetron 8mg oral or intravenous

  As take home medication

  - metoclopramide 10mg three times a day when required oral

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

- Growth factor according to local formulary choice. For example;

  - filgrastim or bioequivalent 300microgram once a day subcutaneous for seven days starting on day three of the cycle
  - lenograstim or bioequivalent 263microgram once a day subcutaneous for seven days starting on day three of the cycle
  - pegfilgrastim or bioequivalent 6mg once a day subcutaneous on day two

- 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 – X71.2
- Delivery – X72.2

References

1.Jones S, Holmes FA, O'Shaughnessy J et al. Docetaxel with cyclophosphamide is associated with an overall survival benefit compared with doxorubicin and cyclophosphamide: 7 year follow up of US Oncology Research trial 9735. J Clin Oncol (2009); 27:1177-83.

REGIMEN SUMMARY

Cyclophosphamide-Docetaxel

Cycles 1, 2, 3

Day Minus One

1. Dexamethasone 8mg twice a day oral*

Day One

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

3. Ondansetron 8mg oral or intravenous

4. Docetaxel 75mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes

5. Cyclophosphamide 600mg/m² intravenous bolus over 10 minutes

Take Home Medicines

6. Dexamethasone 8mg twice a day oral for 3 days starting the day before the docetaxel infusion

7. Metoclopramide 10mg three times a day when required oral

8. Growth factor according to local formulary choice. For example;

   - filgrastim or bioequivalent 300microgram once a day subcutaneous for seven days starting on day three of the cycle
   - lenograstim or bioequivalent 263microgram once a day subcutaneous for seven days starting on day three of the cycle
   - pegfilgrastim or bioequivalent 6mg once a day subcutaneous on day two of the cycle

Cycles 4

Day Minus One

1. Dexamethasone 8mg twice a day oral*

Day One

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

3.Ondansetron 8mg oral or intravenous

4.Docetaxel 75mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes

5.Cyclophosphamide 600mg/m² intravenous bolus over 10 minutes

Take Home Medicines

6.Dexamethasone 8mg twice a day oral for 1 day*

7.Metoclopramide 10mg three times a day when required oral

8.Growth factor according to local formulary choice. For example;

- filgrastim or bioequivalent 300microgram once a day subcutaneous for seven days starting on day three of the cycle
- lenograstim or bioequivalent 263microgram once a day subcutaneous for seven days starting on day three of the cycle
- pegfilgrastim or bioequivalent 6mg once a day subcutaneous on day two of the cycle

* In Aria Planner the dexamethasone 8mg twice daily will appear on days 1, 2, 3 of treatment. This is the supply for the next cycle. The administration instructions reflect this. On the last cycle no dexamethasone will appear for prescribing in the TTO section.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	August 2014	Header changed Toxicities removed Adverse effects tabulated ≥ removed and written in full Dose modification tabulated Hepatic impairment updated Metoclopramide dose changed to 10mg Bolus removed from intravenous bolus throughout text Mucositis recommendation changed Disclaimer added	Donna Kimber Pharmacy Technician	Dr Debbie Wright Pharmacist
1	Dec 2011	None	Anna Bunch Pharmacist Dr Debbie Wright Pharmacist	Dr Ellen Copson Consultant Medical Oncologist Dr Caroline Archer 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.