Chemotherapy Protocol

BREAST CANCER

CARBOPLATIN (AUC6)-DOCETAXEL

Regimen

- Breast Cancer – Carboplatin (AUC6)-Docetaxel

Indication

- Neo-adjuvant or adjuvant treatment of triple negative breast cancer
- WHO Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Carboplatin	Neuropathy, nephrotoxicity, ototoxicity, thrombocytopenia
Docetaxel	Hypersensitivity, fluid retention, neuropathy, joint pains, nail changes, fatigue, alopecia, neutropenia

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 day one of each cycle
- EDTA or calculated creatinine clearance before the first 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. This is especially true in the adjuvant / neoadjuvant setting where dose delays and reductions may be less appropriate. The following is a general guide only.

Haematological

Prior to prescribing the following treatment criteria must be met;

Criteria	Eligible Level
Neutrophils	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 (80g/L)

If counts on day one are below these criteria for neutrophil and/or platelets then delay carboplatin and docetaxel treatment for seven days. Only re-start treatment when these levels are reached. If patients experience a febrile neutropenia or a treatment delay due to neutrophil count of less than 0.5 $x10^9$/L or platelets less than 50 $x10^9$/L for more than seven days, then reduce the dose of carboplatin and docetaxel to 80% of the original dose. If the neutropenia or thrombocytopenia recurs despite this decrease in dose intensity, the dose should either be further reduced to 50% of the original dose or treatment stopped.

Liver Impairment

Drug	Bilirubin (µmol/L)		AST/ALT (units)		Alk Phos (units)	Dose (% of original dose)
Carboplatin	No dose adjustment needed					
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)
Carboplatin	20ml/min or less	Contra-indicated
Docetaxel	No dose adjustment 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

Peripheral neuropathy at NCI-CTC grade 3 should result in a dose reduction from 75mg/m^2 to 60mg/m^2. If the NCI-CTC grade 3 neuropathy occurred at doses lower than 75mg/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 60mg/m^2 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 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

The starting dose of carboplatin AUC 6 is used with calculated GFR. AUC 5 may be considered with EDTA clearance, seek advice from the appropriate consultant before prescribing. The recommended maximum dose when using a calculated creatinine clearance at AUC 6 is 900mg. This will be set as 890mg in ARIA to comply with national dose bands. If you have an obese patient or an individual with a calculated creatinine clearance above 125ml/min please seek advice from the relevant consultant.

It should be noted that the dose of carboplatin may need to be altered if there is a change (improvement or reduction) in renal function of more than 10% from the previous cycle.

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/m² with a view to increase to 75mg/m² if well tolerated.

21 day cycle for 6 cycles.

Drug	Dose	Days	Administration
Carboplatin	AUC 6 (Maximum dose)	1	Intravenous infusion in 500ml glucose 5% over 60 minutes
Docetaxel	75mg/m^2	1	Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes

Dose Information

- Carboplatin will be dose banded in accordance with national dose bands (10mg/ml)
- The maximum dose of carboplatin for AUC 6 is 900mg. This will be set as 890mg in ARIA to comply with national dose bands
- Docetaxel will be dose banded in accordance with the national dose bands (20mg/ml)
- Docetaxel induced fluid retention can lead to weight gain. This is not a reason to alter the dos

Administration Information

Hypersensitivity reactions tend to occur with the first or second infusion of docetaxel. The docetaxel infusion should not be interrupted for minor symptoms such as flushing or localised rashes. Immediately discontinue the infusion for severe reactions that 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

- Carboplatin - irritant
- Docetaxel – exfoliant

Additional Therapy

- Antiemetics

  This regimen is considered moderately emetogenic. The anti-emetics included in ARIA reflect this. However, it is important to assess, not just the drugs being prescribed, but also the individual patient characteristics. Risk factors for emesis include age (younger patients may be more susceptible), sex (female patients are at higher risk), previous history of nausea and vomiting with chemotherapy, pregnancy, anaesthetics or a history of travel sickness, among others. Consider a combination of an NK1R antagonist, a 5-HT3 receptor antagonist and dexamethasone is high risk patients.

  15-30 minutes before chemotherapy (day 1)

  - 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 oral 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.

- Growth factors according to local formulary choice. For example:

  - filgrastim or bioequivalent 30million units once a day for 7 days starting from day 3 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day for 7 days starting from day 3 subcutaneous

- pegfilgrastim or bioequivalent 6mg once only on day 2 subcutaneous

- Consider oral loperamide 4mg after the first loose stool and then 2mg after each loose motion thereafter. Do not use for longer than 48 hours (maximum daily dose is 16mg) without advice.

- 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

References
1. Sharma P, Lopez-Tarruella S, Garcia Saenz JA et al. Pathological response and survival in triple negative breast cancer following neoadjuvant carboplatin plus docetaxel. Clin Cancer Res 2018; 24 (23): 5820-5829.

REGIMEN SUMMARY

Carboplatin (AUC6)-Docetaxel

Cycles 1, 2, 3, 4, 5

Day One

1. Dexamethasone 8mg twice a day oral (from TTO)*
   Administration Instructions
   Ensure the patient has taken the dexamethasone pre-medication the day before and the day of docetaxel administration (and the day after). On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg (or equivalent dose) IV stat 15-30 minutes before chemotherapy. If the patient has already taken a dose of dexamethasone do not administer this dose.

2. Ondansetron 8mg oral or intravenous
   Administration Instructions
   Administer 15-30 minutes prior to SACT. This may be given as 8mg intravenous if required

3. Docetaxel 75mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
   Administration Instructions
   Ensure the patient has taken the dexamethasone pre-medication the day before and the day of docetaxel administration (and the day after). On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg (or equivalent dose) IV stat 15-30 minutes before chemotherapy.

4. Carboplatin AUC6 intravenous infusion in 500ml glucose 5% over 60 minutes
   Administration Instructions
   This recommended maximum dose is 900mg based on a creatinine clearance of 125ml/min. This will be set at 890mg in ARIA to comply with national dose bands

Take Home Medicines

5. Dexamethasone 8mg twice a day oral for 3 days starting the day before the docetaxel infusion.
   Administration Instructions
   This is the supply for the next cycle. Take in the morning and at lunchtime

6. Metoclopramide 10mg three times a day when required oral
   Administration Instructions
   Please 28x10mg tablets or nearest equivalent pack size.

7. Ondansetron 8mg twice a day for three days starting on the evening of day one of the cycle
   Administration Instructions
   Start on the evening of day one of the cycle

8. Growth factor according to local formulary choice
   Administration Instructions
   Growth factors according to local formulary choice. For example;
   - filgrastim or bioequivalent 30million units once a day for 7 days starting from day 3 subcutaneous
   - lenograstim or bioequivalent 33.6million units once a day for 7 days starting from day 3 subcutaneous
   - pegfilgrastim or bioequivalent 6mg once only on day 2 subcutaneous

Cycle 6

Day One

9. Dexamethasone 8mg twice a day oral (from TTO)*
Administration Instructions
Ensure the patient has taken the dexamethasone pre-medication the day before and the day of docetaxel administration (and the day after). On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg (or equivalent dose) IV stat 15-30 minutes before chemotherapy. If the patient has already taken a dose of dexamethasone do not administer this dose.

10. Ondansetron 8mg oral or intravenous
Administration Instructions
Administer 15-30 minutes prior to SACT. This may be given as 8mg intravenous if required

11. Docetaxel 75mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
Administration Instructions
Ensure the patient has taken the dexamethasone pre-medication the day before and the day of docetaxel administration (and the day after). On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg (or equivalent dose) IV stat 15-30 minutes before chemotherapy.

12. Carboplatin AUC6 intravenous infusion in 500ml glucose 5% over 60 minutes
Administration Instructions
This recommended maximum dose is 900mg based on a creatinine clearance of 125ml/min. This will be set at 890mg in ARIA to comply with national dose bands

Take Home Medicines

13. Metoclopramide 10mg three times a day when required oral
Administration Instructions
Please suppy 28x10mg tablets or nearest original pack.

14. Ondansetron 8mg twice a day for three days starting on the evening of day one of the cycle
Administration Instructions
Start on the evening of day one of the cycle

15. Growth factor according to local formulary choice
Administration Instructions
Growth factors according to local formulary choice. For example;
- filgrastim or bioequivalent 30million units once a day for 7 days starting from day 3 subcutaneous
- lenograstim or bioequivalent 33.6million units once a day for 7 days starting from day 3 subcutaneous
- pegfilgrastim or bioequivalent 6mg once only on day 2 subcutaneous

*Cycle one dexamethasone must be prescribed in advance of the chemotherapy. 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.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	Aug 2022	Carboplatin national dose bands Administration Instructions added to summary	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1	March 2019	None	Dr Deborah Wright Pharmacist	Dr Peter Simmonds Consultant Medical Oncologist Dr E Papadimitraki 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 that occur as a result of following these guidelines. These protocols should be used in conjunction with other references such as the Summary of Product Characteristics and relevant published papers.