

## Chemotherapy Protocol

### BREAST CANCER

#### DOCETAXEL-PERTUZUMAB-TRASTUZUMAB

This protocol may require funding

#### Regimen

- Breast Cancer – Docetaxel-Pertuzumab-Trastuzumab

#### Indication

- Locally advanced or metastatic breast cancer that is HER2 or FISH positive provided;
  - prior adjuvant HER<sub>2</sub> therapy has been completed more than 12 months before the diagnosis of metastatic disease
  - there has been no prior treatment with chemotherapy or HER2 therapy in the metastatic setting
- WHO Performance status 0, 1

#### Toxicity

Drug	Adverse Effect
Docetaxel	Hypersensitivity, fluid retention, neuropathy, joint pains, nail changes, fatigue
Pertuzumab	Diarrhoea, hypersensitivity reactions, headache, reduced appetite, dyspnoea, cough, vomiting, nausea, constipation, rash, pain, oedema, fatigue, asthenia, cardiotoxicity
Trastuzumab	Cardio toxicity, acute respiratory distress syndrome, infusion related effects

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

The diarrhoea can be severe in patients treated with pertuzumab. It is important to ensure patients are given appropriate therapy for the treatment of diarrhoea. This is not included in the regimen on Aria and must be added from the support folder.

## Monitoring

### *Regimen*

- HER2 status before initiating therapy
- Cardiac function must be assessed prior to starting treatment Thereafter, cardiac function should be assessed every 9 weeks and as clinically indicated.
- Blood pressure on day 1 of each cycle
- FBC, U&Es and LFTs prior to each cycle with docetaxel

## Dose Modifications

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.

### *Haematology*

The following guidelines apply to docetaxel only. No dose modifications for haematological toxicity are necessary for pertuzumab or trastuzumab. If treatment with pertuzumab or trastuzumab is not tolerated it should be stopped.

Prior to prescribing cycle one the following treatment criteria must be met;

<b>Criteria</b>	<b>Eligible Level</b>
Neutrophil	Greater than or equal to $1.5 \times 10^9/L$ (unless due to bone marrow impairment)
Platelets	Greater than or equal to $100 \times 10^9/L$ (unless due to bone marrow impairment)

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

Toxicity	Grade (NCI-CTC)	75mg/m <sup>2</sup>	60mg/m <sup>2</sup>
Neutropenia	1	75mg/m <sup>2</sup>	60mg/m <sup>2</sup>
	2	Delay until grade 1 then 75mg/m <sup>2</sup>	Delay until grade 1 then 60mg/m <sup>2</sup>
	3	Delay until grade 1 then 75mg/m <sup>2</sup>	Delay until grade 1 then 60mg/m <sup>2</sup>
	4	Delay until grade 1 then 60mg/m <sup>2</sup>	Stop
<b>Febrile Neutropenia</b>			
Febrile Neutropenia	3	Delay until grade 1 then 60mg/m <sup>2</sup>	Stop
	4	Delay until grade 1 then 60mg/m <sup>2</sup>	Stop
<b>Platelets</b>			
Platelets	Greater than or equal to 100x10 <sup>9</sup> /L	75mg/m <sup>2</sup>	60mg/m <sup>2</sup>
	Less than 100x10 <sup>9</sup> /L	Delay until greater than or equal to 100x10 <sup>9</sup> /L the 60mg/m <sup>2</sup>	Stop

#### Hepatic Impairment

Drug	Recommendation					
	Docetaxel	N/A		1.5xULN or greater	and	2.5xULN or greater
Greater than ULN		and/or	3.5xULN or greater	and	6xULN or greater	Not recommended
Pertuzumab	The safety and efficacy of pertuzumab has not been established in hepatic impairment					
Trastuzumab	No dose adjustment necessary					

#### Renal Impairment

Drug	Dose (% of original dose)
Docetaxel	No dose adjustment necessary
Pertuzumab	No dose adjustment necessary in mild to moderate renal impairment. No information in severe renal impairment – clinical decision
Trastuzumab	No dose adjustment necessary

## *Other*

### *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<sup>2</sup> to 60mg/m<sup>2</sup> 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<sup>2</sup> 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<sup>2</sup>. 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 from 75mg/m<sup>2</sup> to 60mg/m<sup>2</sup>. If it occurs with a dose of 60mg/m<sup>2</sup> 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.

### *Pertuzumab*

The diarrhoea can be severe in patients treated with pertuzumab. It is important to ensure patients are given appropriate therapy for the treatment of diarrhoea. This is not included in the regimen on Aria and must be added from the support folder.

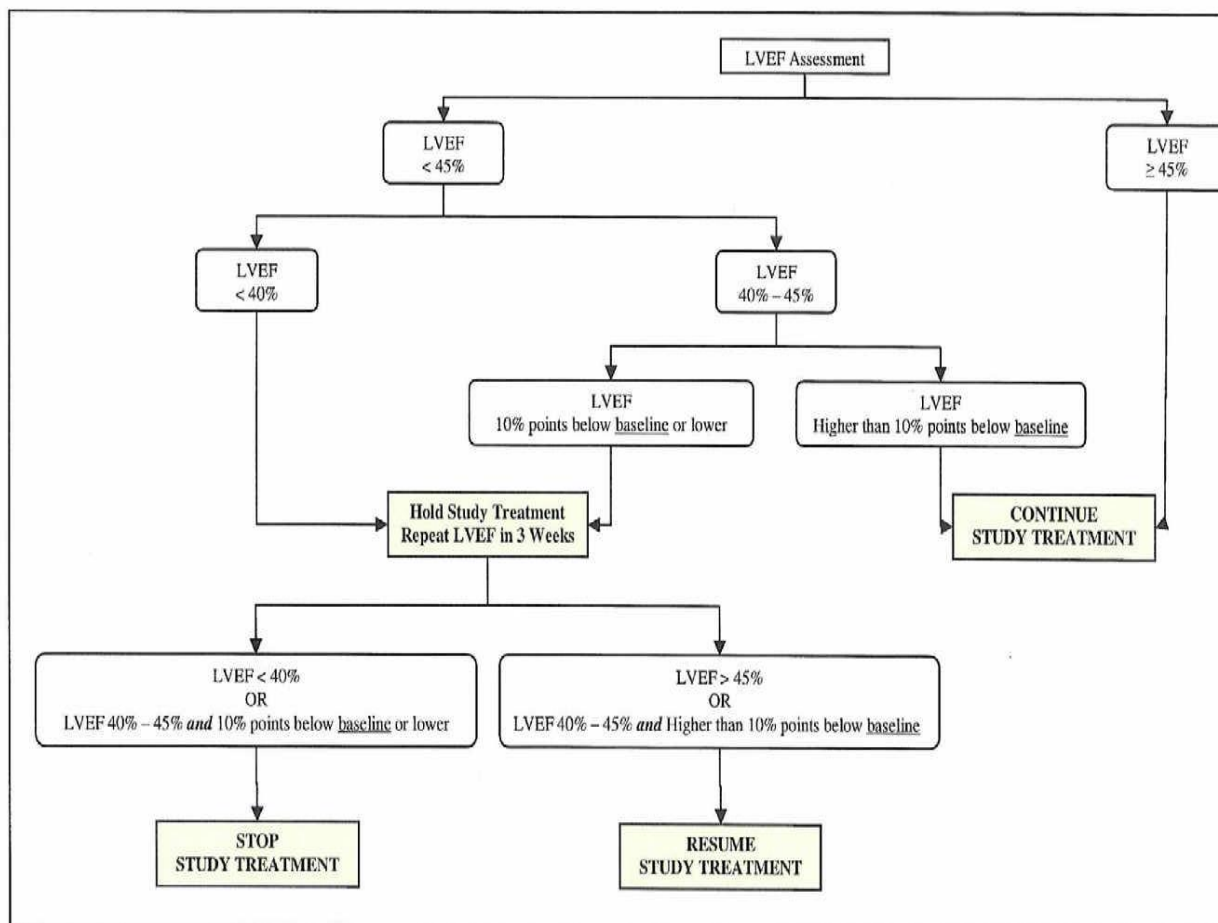
### *Pertuzumab and Trastuzumab*

#### *Cardiac*

The LVEF should be fifty or above before starting cycle one of pertuzumab and trastuzumab.

#### *Subsequent Echocardiograms*

The flow chart below describes the process to be followed if there is an **asymptomatic** decline in LVEF during pertuzumab and trastuzumab treatment. This is taken from the study protocol as used in the reference section. Study treatment refers to pertuzumab and trastuzumab.



In general patients who develop **symptomatic** cardiac dysfunction should have pertuzumab and trastuzumab discontinued, be commenced on ACE inhibitor therapy and be referred to a cardiologist. Further treatment should be discussed with the relevant oncology consultant.

### [Regimen](#)

**21 day cycle for 6 cycles of docetaxel, pertuzumab and trastuzumab.**

**Pertuzumab and trastuzumab are then continued until disease progression or intolerance. This will be set up in Aria with six cycles.**

#### **Cycle 1**

Drug	Dose	Days	Administration
Docetaxel	75mg/m <sup>2</sup>	2	Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
Pertuzumab	840mg	1	Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
Trastuzumab	8mg/kg	1	Intravenous infusion in 250ml sodium chloride 0.9% over 90 minutes

#### **Cycle 2, 3, 4, 5, 6**

Drug	Dose	Days	Administration
Docetaxel	75mg/m <sup>2</sup>	1	Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
Pertuzumab	420mg	1	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
Trastuzumab	6mg/kg	1	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

#### **Cycle 7, 8, 9, 10, 11, 12 onwards**

Drug	Dose	Days	Administration
Pertuzumab	420mg	1	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
Trastuzumab	6mg/kg	1	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

### [Dose Information](#)

- The dose of docetaxel may be increased to 100mg/m<sup>2</sup> from cycle two onwards if well tolerated.
- Docetaxel induced fluid retention can lead to weight gain. This is not a reason to alter the doses
- Docetaxel will be dose banded as per the CSCCN agreed bands

- If the time between two sequential infusions of pertuzumab is less than six weeks, the 420mg dose should be administered as soon as possible without regard to the next planned dose. If the time between two sequential infusions is 6 weeks or more, the initial loading dose of 840mg should be re-administered as a 60 minute intravenous infusion followed every 3 weeks thereafter by a maintenance dose of 420 mg administered over a period of 30 to 60 minutes.
- Trastuzumab will be dose rounded to the nearest 50mg (up if halfway)
- If the patient misses a dose of trastuzumab by fourteen days or less, then the usual maintenance dose of 6mg/kg should be given as soon as possible. Do not wait until the next planned cycle. Subsequent maintenance doses should be given according to the previous schedule
- If the patient misses a dose of trastuzumab by more than fourteen days, a re-loading dose of 8mg/kg should be given over 90 minutes. Subsequent maintenance doses should then be given every 21 days from that point

#### 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 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)
- Pertuzumab has been associated with hypersensitivity and infusion related reactions. Patients should be observed for 60 minutes after the first infusion and for 30 – 60 minutes after subsequent infusions. If patients have tolerated the first two infusions with no infusion related reactions consideration can be given to reducing this observation period.
- Trastuzumab is associated with hypersensitivity reactions. Patients should be observed for six hours following the start of the first infusion of trastuzumab and for two hours following the start of subsequent infusions. If the patient has tolerated the first two infusions with no infusion related effects consideration can be given to reducing this observation period further

#### Extravasation

- Docetaxel – exfoliant
- Pertuzumab - neutral
- Trastuzumab - neutral

### Additional Therapy

- Antiemetics (docetaxel cycles only)  
15-30 minutes before chemotherapy
  - metoclopramide 10mg oral or intravenousAs 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 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.
- Gastric protection with a proton pump inhibitor or a H<sub>2</sub> antagonist may be considered in patients considered at high risk of GI ulceration or bleed.
- Diarrhoea is a common adverse effect, particularly on cycle one. Consider prescribing loperamide 4mg after the first loose motion then 2mg after each loose motion thereafter. This can be added from the support folder in Aria.
- For treatment of pertuzumab or trastuzumab infusion reactions 'once only when required' doses of the following should be prescribed;
  - chlorphenamine 10mg intravenous
  - hydrocortisone 100mg intravenous
  - paracetamol 1000mg once oral

### Coding (OPCS 4.6)

- Procurement – X70.8 (unspecified)
- Delivery – X72.9

### References

1. Baselga J, Cortes J, Sung-Bae K et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. N Engl J Med 2012; 366 (2): 109-119



## REGIMEN SUMMARY

### Docetaxel-Pertuzumab-Trastuzumab

#### Cycle 1 Day One

1. Pertuzumab 840mg intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
2. Trastuzumab 8mg/kg intravenous infusion in 250ml sodium chloride 0.9% over 90 minutes
3. Chlorphenamine 10mg intravenous when required for infusion related reactions
4. Hydrocortisone 100mg intravenous when required for infusion related reactions
5. Paracetamol 1000mg oral when required for infusion related reactions

#### Take Home Medicines

6. Dexamethasone 8mg twice a day oral for 3 days starting the day before the docetaxel infusion (day two of treatment)

Administration Instructions

Please supply sufficient for cycles one and two.

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

#### Cycle 1 Day Two

8. Dexamethasone 8mg twice a day oral (from TTO)
9. Metoclopramide 10mg oral or intravenous
10. Docetaxel 75mg/m<sup>2</sup> intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes

#### Cycle 2, 3, 4, 5 Day One

11. Dexamethasone 8mg twice a day oral (from TTO)
12. Pertuzumab 420mg intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
13. Trastuzumab 6mg/kg intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
14. Metoclopramide 10mg oral or intravenous
15. Docetaxel 75mg/m<sup>2</sup> intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes

16. Chlorphenamine 10mg intravenous when required for infusion related reactions
17. Hydrocortisone 100mg intravenous when required for infusion related reactions
18. Paracetamol 1000mg once only oral when required for infusion related reactions

#### **Take Home Medicines**

19. Dexamethasone 8mg twice a day oral for 3 days starting the day before the docetaxel infusion
20. Metoclopramide 10mg three times a day when required oral

#### **Cycle Six Day 1**

21. Dexamethasone 8mg twice a day oral (from TTO)
22. Pertuzumab 420mg intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
23. Trastuzumab 6mg/kg intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
24. Metoclopramide 10mg oral or intravenous
25. Docetaxel 75mg/m<sup>2</sup> intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
26. Chlorphenamine 10mg intravenous when required for infusion related reactions
27. Hydrocortisone 100mg intravenous when required for infusion related reactions
28. Paracetamol 1000mg once only oral when required for infusion related reactions

#### **Take Home Medicines**

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

#### **Cycle 7, 8, 9, 10, 11**

30. Pertuzumab 420mg intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
31. Trastuzumab 6mg/kg intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
32. Chlorphenamine 10mg intravenous when required for infusion related reactions
33. Hydrocortisone 100mg intravenous when required for infusion related reactions

34. Paracetamol 1000mg once only oral when required for infusion related reactions

**Cycle 12**

35. Warning – Check further cycles required

36. Pertuzumab 420mg intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

37. Trastuzumab 6mg/kg intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

38. Chlorphenamine 10mg intravenous when required for infusion related reactions

39. Hydrocortisone 100mg intravenous when required for infusion related reactions

40. Paracetamol 1000mg once only oral when required for infusion related reactions

## DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	April 2015	Pertuzumab default administration rate for cycle 2 onwards changed to 30 minutes	Rebecca Wills Pharmacist	Dr Debbie Wright Pharmacist
1.1	Aug 2014	Bolus removed from intravenous bolus throughout text	Donna Kimber Pharmacy Technician	Dr Debbie Wright Pharmacist
1	Dec 2013	None	Dr Deborah 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 Hospitals 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.

