Chemotherapy Protocol

BREAST CANCER

Pertuzumab / Trastuzumab SC

Regimen

- Breast Cancer – Trastuzumab / Pertuzumab SC

Indication

- Treatment of early breast cancer (EBC) in combination with chemotherapy in:
    - the neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence. Pertuzumab/trastuzumab SC should be administered for 3 to 6 cycles in combination with chemotherapy, as part of a complete treatment regimen for early breast cancer
    - the adjuvant treatment of adult patients with HER2-positive early breast cancer at high risk of recurrence. Pertuzumab/trastuzumab SC should be administered for a total of one year (up to 18 cycles or until disease recurrence, or unmanageable toxicity, whichever occurs first), as part of a complete regimen for early breast cancer and regardless of the timing of surgery. Treatment should include standard anthracycline- and/or taxane-based chemotherapy. Pertuzumab/trastuzumab SC should start on Day 1 of the first taxane-containing cycle and should continue even if chemotherapy is discontinued.
- Treatment of metastatic breast cancer (MBC) in combination with docetaxel in adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer, who have not received previous anti-HER2 therapy or chemotherapy for their metastatic disease.
- WHO Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Pertuzumab/Trastuzumab SC	Injection related reactions, diarrhoea and other GI disturbances, left ventricular dysfunction, rash

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

Diarrhoea can be severe in patients treated with this combination. 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
- LVEF to be assessed at baseline, prior to cycle four and 4 monthly thereafter or as clinically indicated
- Blood pressure on day 1 of each cycle
- FBC, U&Es and LFTs prior to each cycle or as indicated by the chemotherapy regimen then every 3 cycles during maintenance treatment with pertuzumab / trastuzumab SC alone.

Dose Modifications

Dose reductions are not recommended for pertuzumab / trastuzumab SC. If treatment with is not tolerated it 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.

Haematology

Patients may continue pertuzumab / trastuzumab SC treatment during periods of reversible chemotherapy-induced myelosuppression but they should be monitored carefully for complications of neutropenia during this time.

Hepatic Impairment

Drug	Recommendation
Pertuzumab/Trastuzumab SC	No specific dose adjustments are recommended in hepatic impairment

Renal Impairment

Drug	Recommendation
Pertuzumab/Trastuzumab SC	No dose adjustment necessary for mild or moderate renal impairment. No dose recommendations are available for severe renal impairment due to lack of data.

Left Ventricular Dysfunction

Pertuzumab/trastuzumab SC should be withheld for at least 3 weeks for any signs and symptoms suggestive of congestive heart failure. Pertuzumab/trastuzumab should be discontinued if symptomatic heart failure is confirmed, the patient commenced on ACE inhibitor therapy and referred to a cardiologist. Further treatment should be discussed with the relevant oncology consultant.

Patients with early breast cancer

Patients should have a pre-treatment LVEF of greater than or equal to 55% (greater than or equal to 50% after completion of the anthracycline component of chemotherapy, if given).

Pertuzumab/trastuzumab SC should be withheld for at least 3 weeks for a drop in LVEF to less than 50% associated with a fall of greater than or equal to 10% points below pre-treatment values.

Pertuzumab/trastuzumab may be resumed if the LVEF has recovered to greater than or equal to 50% or to a difference of less than 10 % points below pre-treatment values.

Patients with metastatic breast cancer

Patients should have a pre-treatment left ventricular ejection fraction (LVEF) of greater than or equal to 50%.

Pertuzumab/trastuzumab should be withheld for at least 3 weeks for:

- a drop in LVEF to less than 40%
- a LVEF of 40%-45% associated with a fall of greater than or equal to 10% points below pre-treatment value.

Pertuzumab/trastuzumab may be resumed if the LVEF has recovered to greater than 45%, or to 40-45% associated with a difference of less than 10% points below pre-treatment values.

Injection-related reactions

Pertuzumab/trastuzumab SC has been associated with injection-related reactions The injection may be slowed or paused if the patient experiences injection-related symptoms Treatment including oxygen, beta agonists, antihistamines, rapid intravenous fluids and antipyretics may also help alleviate systemic symptoms. The injection should be discontinued immediately and permanently if the patient experiences a NCI-CTCAE Grade 4 reaction (anaphylaxis), bronchospasm or acute respiratory distress syndrome.

Diarrhoea

Pertuzumab/trastuzumab SC may elicit severe diarrhoea. Diarrhoea is most frequent during concurrent administration with taxane therapy. Elderly patients (greater than or equal to 65 years) have a higher risk of diarrhoea compared with younger patients (less than 65 years). Early intervention with loperamide, fluids and electrolyte replacement should be considered, particularly in elderly patients, and in case of severe or prolonged diarrhoea. Interruption of treatment with

pertuzumab/trastuzumab SC should be considered if no improvement in the patient's condition is achieved. When the diarrhoea is under control treatment may be reinstated.

Pulmonary events

Severe pulmonary events have been reported with the use of trastuzumab in the post-marketing setting. Patients experiencing dyspnoea at rest due to complications of advanced malignancy and comorbidities may be at increased risk of pulmonary events. Therefore, these patients should not be treated with pertuzumab/trastuzumab SC. Caution should be exercised for pneumonitis, especially in patients being treated concomitantly with taxanes.

Regimen

21 day cycle. The number of cycles will vary depending on the indication at the point at which trastuzumab therapy is initiated. Eighteen cycles will be set in ARIA.

Cycle 1

Drug	Dose	Days	Administration
Pertuzumab / trastuzumab SC	1200mg/600mg (Loading)	1	Subcutaneous injection over 8 minutes

Cycle 2 onwards

Drug	Dose	Days	Administration
Pertuzumab / trastuzumab SC	600mg/600mg (Maintenance)	1	Subcutaneous injection over 5 minutes

Dose Information

- If the time between two sequential injections of pertuzumab/trastuzumab SC is less than 6 weeks, the maintenance dose of 600mg/600mg should be administered as soon as possible. Thereafter continue with the 3-weekly schedule.

- If the time between two sequential injections of pertuzumab/trastuzumab SC is 6 weeks or more, a loading dose of 1200mg/600mg should be re-administered followed by maintenance doses of 600mg/600mg every 3 weeks thereafter.

Administration Information

- Pertuzumab/trastuzumab SC has been associated with hypersensitivity and infusion related reactions. Patients should be observed for 30 minutes after the first injection of the loading dose and for 15 minutes after each subsequent injection.

- Pertuzumab/trastuzumab SC should be administered before any taxane and the observation period must be completed before starting administration of the taxane.

- The pertuzumab/trastuzumab SC injection site should be alternated between the left and right thigh only. New injections should be given at least 2.5 cm from the previous site on healthy skin and never into areas where the skin is red, bruised, tender, or hard. The dose should not be split between two syringes or between two sites of administration. During the treatment course other medicinal products for subcutaneous administration should preferably be injected at different sites.

Additional Therapy

- For treatment of pertuzumab/trastuzumab injection reactions 'once only when required' doses of the following should be prescribed;

  - chlorphenamine 10mg intravenous
  - hydrocortisone 100mg intravenous
  - paracetamol 1000mg once oral

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
2. Gianni L, Pienkowski T, Im YH et al. 5-year analysis of neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early-stage HER2-positive breast cancer (NeoSphere): a multicentre, open-label, phase 2 randomised trial. Lancet Oncol. 2016 Jun;17(6):791-800.
3. Schneeweiss A, Chia S, Hickish T et al. Long-term efficacy analysis of the randomised, phase II TRYPHAENA cardiac safety study: Evaluating pertuzumab and trastuzumab plus standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer. Eur J Cancer. 2018 Jan;89:27-35.
4. von Minckwitz G, Procter M, de Azambuja E et al. Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. N Engl J Med 2017; 377:122-131
5. Phesgo 600 mg/600 mg solution for injection / Phesgo 1200 mg/600 mg solution for injection SmPCs 01 January 2021

REGIMEN SUMMARY

Pertuzumab/Trastuzumab SC

Cycle 1 Day One

1. Pertuzumab/trastuzumab 1200mg/600mg (loading dose) subcutaneous injection over 8 minutes
   Administration Instructions
   Pertuzumab/trastuzumab 1200mg/600mg (pertuzumab 1200mg/trastuzumab 600mg) is a LOADING DOSE
   Administer as a single subcutaneous injection over 8 minutes (the whole dose should be given via a single syringe into a single administration site). The injection site should be alternated between the left and right thigh only. New injections should be given at least 2.5cm from the previous site on healthy skin and never into areas where the skin is red, bruised, tender or hard.
   Patients should be observed for 30 minutes after administration of the loading dose and for 15 minutes after each maintenance dose or according to local policy.
   Administer before any taxane, and the observation period must be completed before starting administration of the taxane.

   Pharmacy please state the brand dispensed by either adding the brand from "favourites" or writing below

   Brand: ……

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

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

4. Paracetamol 1000mg oral when required for infusion related reactions

Cycle 2 onwards

5. Pertuzumab/trastuzumab 600mg/600mg (maintenance) subcutaneous injection over 5 minutes
   Administration Instructions
   Pertuzumab/trastuzumab 600mg/600mg (pertuzumab 600mg/trastuzumab 600mg) is a maintenance dose
   Administer as a single subcutaneous injection over 5 minutes (the whole dose should be given via a single syringe into a single administration site). The injection site should be alternated between the left and right thigh only. New injections should be given at least 2.5cm from the previous site on healthy skin and never into areas where the skin is red, bruised, tender or hard. Patients should be monitored for 15 minutes after each injection or according to local policy

   Administer before any taxane, and the observation period must be completed before starting administration of the taxane.

   Pharmacy please state the brand dispensed by either adding the brand from "favourites" or writing below

   Brand: ……

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

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

8. Paracetamol 1000mg oral when required for infusion related reactions

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	July 2021	None	Rebecca Wills Pharmacist	Dr Sanjay Raj Consultant Clinical 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 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.