Breast Pathway Group – Pertuzumab in Advanced Breast Cancer

Indication: First line treatment of locally advanced or metastatic breast cancer

National Cancer Drug Fund criteria:
- Locally advanced or metastatic breast cancer
- HER2 3+ or FISH positive
- PS 0 or 1
- Prior adjuvant HER2 therapy completed more than 12 months prior to metastatic diagnosis
- No prior treatment with chemotherapy or HER2 therapy for metastatic disease
- To be given as first line treatment in combination with docetaxel and trastuzumab

NOTE: not to be used beyond first disease progression

Ensure funding has been approved prior to starting treatment.

Regimen details:

| Loading dose: | Pertuzumab | 840mg | IV | Day 1 | cycle 1 |
| Loading dose: | Trastuzumab | 8mg/kg | IV | Day 2 | cycle 1 |
| | Docetaxel | 75mg/m² | IV | Day 2 | cycle 1 |

| Maintenance dose: | Pertuzumab | 420mg | IV | Day 1 | cycle 2 onwards |
| Maintenance dose: | Trastuzumab | 6mg/kg | IV | Day 1 | cycle 2 onwards |
| | Docetaxel | 75mg/m² | IV | Day 1 | cycle 2 onwards |

Pertuzumab is given in combination with intravenous trastuzumab and docetaxel; docetaxel should be given for 6 cycles. Due to the potential for hypersensitivity reactions: for cycle 1 only, give pertuzumab on day 1, give trastuzumab followed by docetaxel on day 2.

Disclaimer: The Joint Delivery Chemotherapy Nurse/Oncology Pharmacist Group is a sub-group of the Medicines & Chemotherapy Steering Group (MCSG) working within the London Cancer Alliance Integrated Cancer System (LCA). The output of the LCA MCSG includes documentation that can be adopted by healthcare organisations at their discretion. It is the responsibility of each individual organisation to ensure that appropriate governance and safety clearance procedures within their own clinical service have been followed prior to implementation of any such pieces of work. LCA assume no responsibility for this process within individual organisations, and no responsibility for the clinical management of individual patients or patient groups. Any clinical queries regarding individual patients or documentation should be directed to the relevant clinical team within the most appropriate healthcare organisation.

©LCA Copyright 2014
From cycle 2 onwards, administer pertuzumab and trastuzumab sequentially (in any order) first, followed by docetaxel on day 1. Pertuzumab and trastuzumab may be continued until progressive disease. However if trastuzumab treatment is discontinued for any reason, treatment with pertuzumab should be discontinued.

See separate protocol for trastuzumab in the advanced setting for details of doses, monitoring and ongoing treatment.

See separate protocol for docetaxel in the advanced setting for details of doses, monitoring and ongoing treatment.

**Administration:** Pertuzumab in 250ml sodium chloride 0.9% infuse over 30-60 minutes
Close observation during and for 60 minutes after the first infusion, and during and for 30-60 minutes for subsequent infusions is recommended prior to starting the next agent.

Infusion-related hypersensitivity reactions may occur, such as flushing, rash with or without pruritus, chest tightness, dyspnoea and fever or chills following the start of the infusion; the infusion should be slowed down or interrupted and the necessary supportive medication should be administered. Severe reactions such as hypotension and/or bronchospasm or generalised rash/erythema requires immediate discontinuation. Availability of resuscitation equipment must be ensured as a standard precaution.

**Missed doses:** If the time between two sequential infusions is less than 6 weeks, the 420mg dose should be given as soon as possible. If the time between two sequential infusions is greater than 6 weeks, the patient should receive a re-loading dose of 840mg given over 60 minutes.

**Frequency:** Day 1, every 21 day, until disease progression or unacceptable toxicity

**Pre-medication:** Paracetamol / Chlorphenamine / Hydrocortisone can be given for infusion-related reactions such as chills / fever.

**Anti- emetics:** Low emetogenicity
Follow Local Anti-emetic Policy

Supportive medication:
Loperamide can be used to manage diarrhoea

Extravasation:
Non-vesicant

Regular investigations:
FBC Baseline, at 4 and 8 months then 4 to 6 monthly thereafter
LFTs Baseline, at 4 and 8 months then 4 to 6 monthly thereafter
U&Es Baseline, at 4 and 8 months then 4 to 6 monthly thereafter
LVEF (MUGA/ECHO) Baseline, at 4 and 8 months then 4 to 6 monthly thereafter (see cardiac monitoring)

NOTE: see additional investigations required when co-administered with docetaxel and trastuzumab – see separate protocols

Toxicities:
Infusion related symptoms (mild to moderate in severity, occur mainly with first dose): pyrexia, chills, headache, asthenia, hypersensitivity/anaphylaxis and vomiting.
Infusion related symptoms (subsequent cycles): fatigue, dysgeusia, hypersensitivity/anaphylaxis, myalgia.
As pertuzumab is given with trastuzumab and docetaxel, it is difficult to ascertain a causal relationship to a particular medicinal product (see separate protocol for trastuzumab and docetaxel): upper respiratory tract infection, neutropenia including febrile neutropenia, anaemia, insomnia, peripheral neuropathy, increased lacrimation, stomatitis, dyspepsia, alopecia, nail disorder, dry skin and pruritis, arthralgia, pleural effusion, interstitial lung disease (uncommon).
Common events (≥10%) reported in pertuzumab monotherapy patients: headache, decreased appetite, dyspnoea, cough, diarrhoea, vomiting, nausea, constipation, rash, pain, oedema, fatigue, asthenia, cardiotoxicity.

DOSE MODIFICATIONS

Haematological Toxicity
Dose modifications are not recommended.
Patients may continue pertuzumab and trastuzumab therapy during periods of reversible, chemotherapy-induced myelosuppression but should be carefully monitored for complications of...
neutropenia. Patients treated with pertuzumab, trastuzumab and docetaxel are at increased risk of febrile neutropenia compared with patients treated with placebo, trastuzumab and docetaxel, especially during the first 3 cycles of treatment, the higher incidence of febrile neutropenia in pertuzumab treated patients may also be associated with higher incidence of mucositis and diarrhoea.

Non-haematological Toxicities

Renal Impairment
Dose adjustments are not needed in patients with mild or moderate renal impairment. It is recommended to perform renal function tests at the same time as the cardiac monitoring.

Hepatic Impairment
The safety and efficacy of pertuzumab has not been studied in patients with hepatic impairment. It is recommended to perform liver function tests at the same time as the cardiac monitoring.

Dose modifications for other toxicities as appropriate

Cardiac monitoring
A left ventricular ejection fraction (LVEF) above the lower limit of normal (> 50%) is required for the treatment to go ahead (measured on echocardiography, ECHO or multigated acquisition, MUGA).

SmPC suggests cardiac monitoring every 3 cycles, data suggest there is no increased risk of cardiac toxicity therefore cardiac monitoring may be carried out at baseline, at 4 and 8 months then 4 to 6 monthly thereafter as clinically indicated after discussion with the consultant.

Guideline for stopping treatment in the event of reduced cardiac function
If LVEF is <40%, or 40-45% and associated with ≥10% ejection points from baseline, pertuzumab and trastuzumab should be withheld and a repeat LVEF should be performed in 3 weeks. If there is no improvement discuss with consultant and seek cardiology opinion. Discuss with consultant before re-starting.

Location of regimen delivery: Outpatient setting.
Availability of resuscitation equipment must be ensured as a standard precaution.

Comments: None

Drug interactions: No pharmacokinetic interactions were observed between pertuzumab and trastuzumab, docetaxel, gemcitabine, erlotinib and capecitabine.
References:


LCA Breast Cancer Clinical Guidelines October 2013