LONDON CANCER ALLIANCE West and South

Breast Pathway Group – Intravenous Trastuzumab in Early Breast Cancer

Indication:

Early stage confirmed HER2 over-expression (3+ by IHC or FISH+) breast cancer after surgery, chemotherapy (neo-adjuvant or adjuvant), and radiotherapy (if applicable).

- There should be a gap of 3 weeks from finishing the last course of anthracycline chemotherapy before starting trastuzumab.
- Adjuvant trastuzumab should be initiated within 3 months of chemotherapy.

NICE TA107

Regimen details:

Trastuzumab	8mg/kg	IV	Day 1, cycle 1
Trastuzumab	6mg/kg	IV	Day 1, cycle 2 onwards

Administration:

In 250ml Sodium Chloride 0.9% IV over 90 minutes
If the initial 90 minute loading dose was well tolerated, the next dose may be administered over 60 minutes; if well tolerated the dose can be administered over 30 minutes for subsequent infusions.

When used in combination with docetaxel / paclitaxel:

In pivotal trials, docetaxel or paclitaxel was administered the day following the first dose of trastuzumab, and immediately after the subsequent doses of trastuzumab if the preceding dose was well tolerated. *However, there is increasing worldwide experience that both trastuzumab and taxanes can be given on the same day: trastuzumab may be administered first, followed by the taxane on Day 1.*
See separate protocol for docetaxel / paclitaxel in early breast cancer for details of doses, monitoring and ongoing treatment.

Patients should be observed for at least 6 hours after the first infusion, and for up to 2 hours after subsequent infusions for signs and symptoms of administration-related reactions.

Version: 1.0 Supersedes: all other versions	Approved by LCA Breast Pathway Chemotherapy Lead: Mark Harries
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Lisa Yuen	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson
Second check by: Laura Cameron	Date prepared: November 2014 Review Date: November2016

	Administration-related reactions/hypersensitivity reactions such as chills and/or fever, dyspnoea, hypotension, wheezing, bronchospasm, tachycardia, reduced oxygen saturation, respiratory distress, rash, nausea, vomiting, headache are known to occur with trastuzumab. Availability of resuscitation equipment must be ensured as a standard precaution.
Missed doses:	If the patient misses a dose by more than one week, a loading dose of trastuzumab should be given. Patients do not need a loading dose when changing from weekly schedule to the 3-weekly schedule.
Frequency:	Day 1, every 21 days, for 18 cycles
Pre-medication:	Paracetamol / Chlorphenamine / Hydrocortisone can be given for administration-related reactions such as chills / fever
Anti- emetics:	Low emetogenicity Follow Local Anti-emetic Policy
Supportive medication:	Not routinely required
Extravasation:	Non-vesicant
Regular investigations:	Prior to cycle 1:

FBC	Baseline, at 4 and 8 months
LFTs	Baseline, at 4 and 8 months
U&Es	Baseline, at 4 and 8 months
LVEF (MUGA/ ECHO)	Baseline, at 4 and 8 months (see cardiac monitoring)
Blood Pressure	Prior to each cycle*

* Treat blood pressure of >140/85mmHg with an ACE inhibitor licensed for the treatment of heart failure.

Toxicities:	Administration-related reactions (see above), cardiotoxicity, pulmonary events, diarrhoea, rash, hepatotoxicity (rare)

DOSE MODIFICATIONS

Haematological Toxicity

Dose reductions are not recommended.
Perform full blood count at the same time as cardiac monitoring.
Patients may continue trastuzumab therapy during periods of reversible, chemotherapy-induced myelosuppression but monitor closely for complications of neutropenia.

Non-haematological Toxicities

Renal Impairment
Dedicated pharmacokinetic studies have not been carried out. Perform renal function tests at the same time as cardiac monitoring.

Hepatic Impairment
Dedicated pharmacokinetic studies have not been carried out. Perform liver function tests at the same time as cardiac monitoring.

Dose modifications for other toxicities as appropriate

Cardiac contra-indications
History of documented congestive heart failure, coronary artery disease with previous Q-wave myocardial infarction or evidence of transmural infarction on ECG, angina pectoris requiring medication, poorly controlled hypertension, clinically significant valvular disease, or high risk of uncontrolled arrhythmias.

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 or multigated acquisition, ECHO or MUGA).
Routine cardiac monitoring is carried out at baseline, at 4 and 8 months. A further end of treatment assessment is recommended in patients requiring cardiovascular intervention during trastuzumab treatment.

Refer to LCA Breast Cancer Clinical Guidelines for cardiac monitoring and discuss with the consultant.

Pulmonary events
Severe pulmonary adverse events have been reported with the use of the intravenous formulation. Fatal events have been reported and may occur as part of an infusion-related reaction or with delayed onset. In addition, cases of interstitial lung disease including lung

infiltrates, acute respiratory distress syndrome, pneumonia, pneumonitis, pleural effusion, respiratory distress, acute pulmonary oedema and respiratory insufficiency have been reported. Patients experiencing dyspnoea at rest due to advanced malignancy or requiring supplementary oxygen therapy may be at increased risk of a fatal administration-related reaction and should not be treated with trastuzumab.

Location of regimen:	Outpatient setting
delivery:	Availability of resuscitation equipment must be ensured as a standard precaution.
Comments:	None
Drug interactions:	No formal drug interaction studies have been performed.

References:

Roche Products Limited, 2013. Summary of product characteristics: Herceptin 150mg powder for concentrate for solution for infusion. Available at http://www.medicines.org.uk [accessed 15/11/2013]

National Institute for Health and Clinical Excellence, 2002. Technology Appraisal Guidance 107: Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer

LCA Breast Cancer Clinical Guidelines 2013