LONDON CANCER ALLIANCE West and South

Breast Pathway Group – Intravenous Trastuzumab in Advanced Breast Cancer

Indication:

First-line treatment in HER2 positive advanced breast cancer (3+ by IHC or FISH+)

As monotherapy in patients who have received at least two chemotherapy regimens for metastatic disease. Prior chemotherapy will generally have included at least an anthracycline and a taxane unless patients are unsuitable for these treatments.

In combination with docetaxel or paclitaxel in patients who have not received chemotherapy for their metastatic disease and for whom an anthracycline is not suitable.

NICE TA34

Regimen details:

<u>3 weekly regimen</u>	Trastuzumab	8mg/kg	IV	Day 1, cycle 1
	Trastuzumab	6mg/kg	IV	Day 1, cycle 2 onwards
<u>Weekly regimen</u>	Trastuzumab	4mg/kg	IV	Day 1, cycle 1
	Trastuzumab	2mg/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:*

Version: 1.0 Supersedes: all other versions	Approved by LCA Breast Pathway Chemotherapy Lead: Mark Harries November 2014
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: November 2016

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.
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:

3 weekly regimen — 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 regimen.

Weekly regimen — If a dose is missed by more than 2 weeks, a loading dose should be given.

Frequency: Weekly or 3-weekly until disease progression or unacceptable toxicity

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

Version: 1.0 Supersedes: all other versions	Approved by LCA Breast Pathway Chemotherapy Lead: Mark Harries November 2014
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: November 2016

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)
	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 the 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. Beyond this, LVEF should be monitored every 4 to 6 months as clinically indicated. 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 delivery:	Outpatient setting 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 34: Guidance on the use of trastuzumab for the treatment of advanced breast cancer

UCLH- Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009

UCLH- Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009

Version: 1.0 Supersedes: all other versions	Approved by LCA Breast Pathway Chemotherapy Lead: Mark Harries November 2014
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: November 2016