LONDON CANCER ALLIANCE West and South

Breast Pathway Group – Subcutaneous Trastuzumab in Early Stage Breast Cancer

Indication:

As adjuvant or neoadjuvant therapy for early stage (I-III) confirmed HER2 positive (3+ by IHC or FISH/CISH+) breast cancer

- There should be a gap of 3 weeks from finishing the last cycle of anthracycline chemotherapy before starting trastuzumab.
- If given sequentially adjuvant trastuzumab should be initiated within 3 months of chemotherapy.

Patients receiving intravenous trastuzumab may be offered a switch to the subcutaneous injection.

Refer to LCA Breast Cancer Clinical Guidelines.

Regimen details:

Trastuzumab	600mg	subcutaneous	Day 1

Administration:

Trastuzumab subcutaneous injection over 2 – 5 minutes. The injection site should be alternated between the left and right thigh. New injections should be given at least 2.5cm from the old site.

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.

Reason for Update: LCA Protocol Development	Approved by LCA Consultant: Mark Harries
Version: 2.0 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: November 2016

Patients should be observed for at least 6 hours after the first injection, and for up to 2 hours after subsequent injections 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. Local reactions include erythema, pruritis, oedema and rash at the site of the injection.

Availability of resuscitation equipment must be ensured as a standard precaution.

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

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

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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, ECHO or multigated acquisition, MUGA).

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

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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 with the intravenous preparation.

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 600mg/5ml solution for injection. Available at http://www.medicines.org.uk [accessed 4/10/2013]

LCA Breast Cancer Clinical Guidelines October 2013

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