PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Trastuzumab Subcutaneous Advanced Breast Cancer

PROTOCOL REF: MPHATRASBR
(Version No. 1.1)

Approved for use in:

HER2 positive advanced breast cancer in combination with chemotherapy or endocrine treatment.

OR

As monotherapy in patients with HER2 positive advanced breast cancer expressing **who have received at least two chemotherapy regimens** for metastatic breast cancer. Prior chemotherapy must have included at least an anthracycline and a taxane where these treatments are appropriate. It should also have included hormonal therapy in suitable oestrogen receptor (ER) positive patients.

Dosage:

Drug	Dose	Route	Frequency
Trastuzumab	**600mg**	SC	Every 21 days

Repeated every 21 days until disease progression or unacceptable toxicity

If the only site of disease progression is CNS metastases then trastuzumab may continue

Extravasation risk:

No risk of extravasation

Dosing in renal and hepatic impairment:

Renal	No dose adjustments required

Hepatic	No dose adjustments required

Administration:

Withdraw the contents of the vial into a 10mL syringe using 16g needle and then change the needle to a subcutaneous 24g needle prior to administering the dose

Day	Drug	Dose	Route	Diluent and rate
1	**Trastuzumab**	**600mg**	**SC**	Over 2 to 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 and never into areas where the skin is red, bruised, tender or hard

Following administration of the first dose, monitor for 2 hours after for hypersensitivity reactions.

Main toxicities:

Cardiotoxicity	Congestive heart failure is a common adverse effect associated with trastuzumab. See separate cardiac toxicity below for further details.
Hypersensitivity reactions	Subcutaneous preparation is less likely to cause administration reactions than intravenous. Monitor for dyspnoea, hypotension. See below for further information
Other	Fatigue Injection site reactions Pulmonary events – less common with subcutaneous preparation

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed Consent	x				
Clinical Assessment	x			x	As clinically indicated or at the end of treatment
SACT Assessment (to include PS and toxicities)	x	x	x	x	Every cycle
FBC	x	x	x	x	Every cycle **when administered with chemotherapy**
U&E & LFTs & Magnesium	x	x	x	x	
CT scan	x				As clinically indicated
ECHO	x				Baseline, then at 3 to 4 months for first 12 months, as clinically indicated thereafter
Full observations	x	x	x	x	Every cycle
Weight recorded	x	x	x	x	Every cycle
Height	x				

Dose Modifications and Toxicity Management:

- Refer to relevant chemotherapy protocol, for example weekly paclitaxel.
- No dose adjustments needed for trastuzumab
- **FBC, U&E's (including Mg) and LFTs not required for single agent trastuzumab.**

Pulmonary Impairment:

Trastuzumab:

Pulmonary events have been reported with the use of Trastuzumab. These events have occasionally been fatal.

Caution should be exercised for pneumonitis.

Hypersensitivity

Injection-related symptoms (mild to moderate in severity): fever, chills, headache, nausea, rash, arthralgia/myalgia (occur mainly with 1st intravenous dose) and anaphylaxis. These symptoms should be managed using paracetamol and chlorphenamine or adrenaline if suspected anaphylaxis.

Cardiotoxicity

- Sharp falls in LVEF (10 points or to <50%) during cytotoxic chemotherapy may indicate increased susceptibility to cardiac dysfunction on trastuzumab. Prophylactic ACE inhibitor therapy may be considered for such patients.
- Assessment at the end of treatment is recommended for patients requiring cardiovascular intervention during treatment.

- Additional testing is required in patients who have LV systolic dysfunction.
- Patients developing signs and symptoms of heart failure should have their trastuzumab treatment interrupted, receive an ACE inhibitor and be referred to a cardiologist.
- If the LVEF falls to ≤ 40%, (representing biologically important LV systolic dysfunction) trastuzumab should be interrupted the patient should receive an ACE inhibitor and be referred to a cardiologist for treatment.
- After Trastuzumab interruption and appropriate medical therapy, LVEF should be re-checked after 6–8 weeks. Trastuzumab may be re-initiated if the LVEF is restored to a level above the LLN.
- If the LVEF falls to below the LLN but > 40%, trastuzumab may be continued, but an ACE inhibitor should be initiated.
- If the patient is already on an ACE inhibitor, they should be referred to a cardiologist.
- LVEF assessment should be repeated after 6–8 weeks.
- If the LVEF falls by 10 points or more but remains above the LLN, trastuzumab may be continued. Intervention with an ACE inhibitor is recommended in an attempt to reduce the risk of further LVEF decline of symptomatic CHF.
- LVEF Monitoring should be repeated after 6–8 weeks.
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Cardiac toxicity should be managed used the NCRI recommendations reproduced below:

NCRI recommendations for cardiac monitoring
Ref: British Journal of Cancer 2009 100:684-692

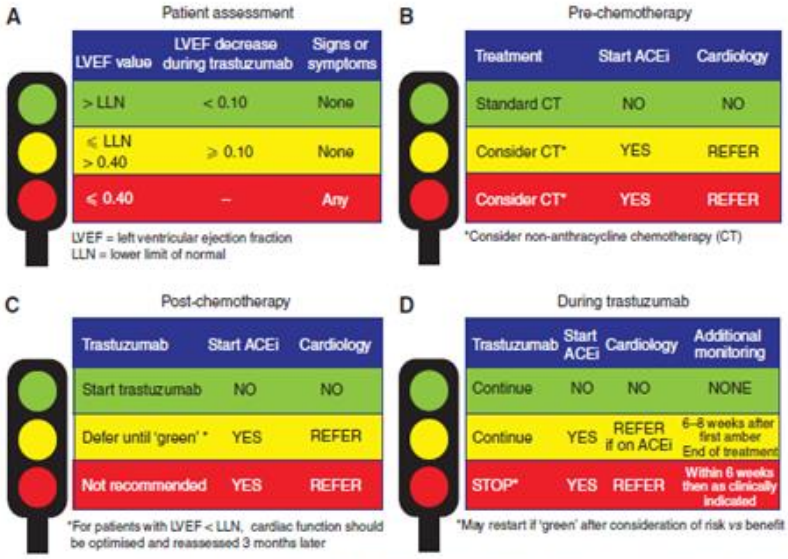

Figure 2 Traffic light system to prevent, monitor, and manage cardiac events in patients undergoing cytotoxic chemotherapy. (**A**) Patient assessment during trastuzumab therapy; (**B**–**D**) indications for ACEi therapy and referral to a cardiologist before (**B**) and after (**C**) chemotherapy, and (**D**) during trastuzumab therapy, when additional cardiac assessments may also be required. ACEi = angiotensin-converting enzyme inhibitor.

References:

1. Herceptin 600 mg solution for injection in vial SmPC, Roche Products Limited accessed via the electronic medicines compendium at https://www.medicines.org.uk/emc (Last updated 28th September 2021)
2. NICE TA34 Guidance on the use of trastuzumab for the treatment of advanced breast cancer. Published: 15 March 2002
3. Supplement to: Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol* 2019; 20: e201–08.

Circulation/Dissemination

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Version History

		Author name and designation	Summary of main changes
		Helen Flint **Consultant Pharmacist**	New regimen protocol V1.0
		Gabriella Langton **Breast SRG pharmacist**	Routine protocol update V1.1