Systemic Anti Cancer Treatment Protocol

Trastuzumab Subcutaneous Advanced Breast Cancer

PROTOCOL REF: MPHATRASBR
(Version No: 1.0)

Approved for use in:

HER2 positive breast cancer. In combination with chemotherapy, endocrine treatment or as a single agent in PS3 ER negative

Dosage:

Drug	Dosage	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:

Trastuzumab s/c – no risk of extravasation.

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	Subcutaneous injection	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. Treat with chlorphenamine and hydrocortisone.
Other	Fatigue Injection site reactions Pulmonary events – less common with subcutaneous preparation

Investigations and Treatment Plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Medical Assessment	X				Every 3 months whilst on trastuzumab.
Nursing Assessment		X	X	X	Every cycle
FBC	X				Clinic visits
U&E & LFTs	X				Clinic visits
ECHO	X				Every 4 months whilst on trastuzumab.
CT scan	X				As clinically indicated
Informed Consent	X				
PS recorded	X	X	X	X	
Toxicities documented	X	X	X	X	
Weight recorded	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Refer to relevant chemotherapy protocol, for example weekly paclitaxel.

No dose adjustments for trastuzumab

FBC not required for single agent trastuzumab

Hepatic impairment:

No dose adjustments required for hepatic impairment

Renal impairment:

No dose adjustments required for renal impairment.

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.

Trastuzumab Dose Modifications and Toxicities;

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, with addition of chlorphenamine and hydrocortisone if anaphylaxis suspected.

FBC is not required prior to treatment

- 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.

Cardiac Toxicity- Trastuzumab:

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

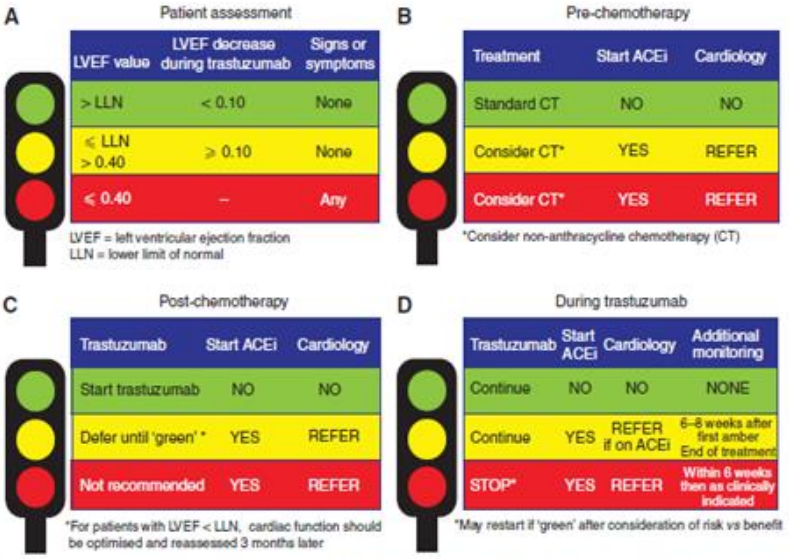

Figure 2 Traffic light system to prevent, monitor, and manage cardiac events in patients undergoing cytotoxic chemotherapy. (**A**) Patient assessment during trastuzumab therapy; (**B**–**D**) indications for ACEi therapy and referral to a cardiologist before (**B**) and after (**C**) chemotherapy, and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

References

NICE Clinical Guideline Advanced Breast Cancer

Updated August 2017

Herceptin SMPC

PrefHer Study

Pivot et al Lancet Oncol 2013 14(10):962-70