

## TRASTUZUMAB (HERCEPTIN) IV for advanced disease

For metastatic breast cancer whose tumour over expresses HER2, according to NICE guidelines, in combination with paclitaxel or vinorelbine

N.B. This protocol should only be used for patients not eligible for pertuzumab plus trastuzumab

Drug/Dosage/Administration:

**Loading dose:** Paracetamol 1000mg pre-med 30 minutes before treatment starts  
Trastuzumab (Herceptin) 8 mg/kg in 250ml sodium chloride 0.9%  
IV infusion over 90 minutes

**Maintenance Doses:** *starting 3 weeks after loading dose*  
Pre-medication not routinely needed.  
Trastuzumab (Herceptin) 6 mg/kg in 250ml sodium chloride 0.9%  
IV inf over 30 minutes, if loading dose tolerated

If the patient misses a dose by more than one week, a re-loading dose of trastuzumab is usually required. However, if the delay was due to cardiac toxicity, the doctor may choose not to re-load the patient.

### In combination with paclitaxel / docetaxel:

For Cycle 1 only, give trastuzumab on Day 1 and give taxane on Day 2.

For future cycles, ideally administer the trastuzumab first, then a short saline flush, followed by the taxane.

(For patients on weekly paclitaxel, administer the pre-medication for the paclitaxel immediately before the trastuzumab infusion)

Patients should be observed for 6 hours after start of first infusion (i.e. 4½ hours post-infusion), and for 30 minutes post-infusion for subsequent doses.

If a decision is made to allow the patient to leave in advance of these times, they must be counselled about the possibility of delayed infusion-related symptoms and instructed to contact the hospital in the event of these occurring.

NB. Infusion-related and pulmonary symptoms may rarely occur more than 6 hours after the start of a trastuzumab infusion. Patients should be warned about this and instructed to contact the hospital if any such symptoms occur.

Frequency: Every 3 weeks - administer until disease progression outside of the CNS

At each clinical review, note that all trastuzumab doses are to be prescribed and confirmed up until the next clinical review is due.

Main Toxicities: cardiotoxicity (see Comments);  
Infusion-related symptoms (mild to moderate in severity): fever; chills; headache; nausea; rash; arthralgia; myalgia (occur mainly with 1<sup>st</sup> dose)  
Infusion-related symptoms (serious but rare): dyspnoea; hypotension; bronchospasm; tachycardia; angioedema; anaphylaxis (occur mainly with 1<sup>st</sup> dose)

Reason for Update: renamed as trastuzumab (Herceptin); review of frequency of cardiac monitoring; advice on cardiac failure updated; b.p. monitoring added	Approved by Consultant: Dr A Neal
Version: 8	Approved by Lead Chemotherapy Nurse: V Mumford
Supersedes: Version 7	Date: 4.3.14
Prepared by: S Taylor	Checked by: C Tucker

Anti-emetics:	mildly emetogenic	
Extravasation:	non-vesicant	
Regular Investigations:	FBC	baseline, at 4 and 8 months, then 6 monthly
	U&Es and LFTs	baseline, at 4 and 8 months, then 6 monthly
	Echo*/MUGA scan	baseline; at 4 and 8 months, then every 6 months thereafter Patients who develop asymptomatic cardiac dysfunction will require more frequent monitoring e.g. every 6–8 weeks.
	Blood pressure**	baseline, at 4 and 8 months, then every 6 months

\* An echocardiogram is the preferred test, but whichever test is used initially for an individual, should ideally be used throughout

\*\* If blood pressure  $\geq$  140/90 mmHg, a diagnosis of hypertension needs to be confirmed by asking patient to visit GP for ambulatory or home blood pressure monitoring. Patients with a confirmed diagnosis of hypertension should be treated with an ACE inhibitor which is also licensed for the treatment of heart failure e.g. ramipril.

Comments: The risk of developing heart failure is greatest when trastuzumab is used in combination with anthracyclines, and so they should not be used concurrently.

Caution should be exercised in treating patients who present with symptomatic heart failure, history of hypertension or documented coronary artery disease.

If LVEF drops  $\geq$  10 ejection fraction points from baseline **and** to below 50%, treatment should be suspended and a repeat LVEF assessment performed within approximately 3 weeks.

If LVEF has not improved, or declined further, after 3 weeks, or symptomatic cardiac failure has developed, discontinuation of trastuzumab should be strongly considered, unless the benefits for the individual patient are deemed to outweigh the risks.

If symptomatic cardiac failure develops during trastuzumab therapy, it should be treated with standard medications for this purpose.

Dose Modifications: No reductions in the dose of trastuzumab were made during clinical trials. Patients may continue trastuzumab therapy during periods of reversible, chemotherapy-induced myelosuppression.

References: Slamon, D J et al; NEJM 2001; Vol 344 (11): 783 - 792  
Verma, S et al; Eur J Cancer; 37 (Suppl 6)  
Castellon, XC et al; Proceedings ASCO 2002; Abstract 73  
Leyland–Jones, B et al; Proceedings ASCO 2002; Abstract 183

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