TRASTUZUMAB (HERCEPTIN) IV

For first-line use in HER2 +ve metastatic adenocarcinoma of the stomach or gastro-oesophageal junction, for those tumours expressing high levels of HER2 ***either*** as defined as IHC3 +, ***or*** IHC2+ and +ve FISH result
NICE approved Nov 2010
To be administered in combination with cisplatin and capecitabine (as XP protocol), or Carbo-X
Not to be used in combination with epirubicin

Drug/Dosage/Administration:

Loading dose:	Paracetamol	1000mg pre-med 30 minutes before treatment starts
	Trastuzumab (Herceptin)	8mg/kg in 250ml sodium chloride 0.9% IV over 90 minutes
Maintenance Doses:	*starting 3 weeks after loading dose*	
		Pre-medication not routinely needed.
	Trastuzumab (Herceptin)	6mg/kg in 250ml sodium chloride 0.9% IV 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.

Before initiating the trastuzumab (Herceptin), ensure that the chemotherapy regimen does not include epirubicin.
For Cycle 1 only, give trastuzumab on Day 1 and initiate cisplatin-based chemotherapy on Day 2.
For Cycle 2 onwards, the trastuzumab should be given after the pre-hydration and before the mannitol.
If given in combination with carboplatin-based chemotherapy, both carboplatin and trastuzumab may be administered on Day 1, with the trastuzumab administered first.

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, initially in combination with platinum & capecitabine chemotherapy.
Once chemotherapy course completed, continue with trastuzumab until disease progression.
Clinical review 3 weekly while on chemotherapy **–** this may be extended once chemotherapy is completed. At each clinical review, note that all trastuzumab (herceptin) doses are to be prescribed and confirmed up until the next clinical review is due.

Reason for Update: funded for patients IHC2+ and +ve FISH; Carbo-X added	Approved by Consultant: Dr M Hewish
Version: 5	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 4	Date: 17.11.16
Prepared by: S Taylor	Checked by: C Tucker

Main Toxicities:	Infusion-related symptoms (mild to moderate in severity): fever; chills; headache; nausea; rash; arthralgia; myalgia (occur mainly with 1st dose) Infusion-related symptoms (serious but rare): dyspnoea; hypotension; bronchospasm; tachycardia; angioedema; anaphylaxis (occur mainly with 1st dose) cardiotoxicity (see below)	
Anti-emetics:	mildly emetogenic	
Extravasation:	non-vesicant	
Regular Investigations:	FBC }	every 3 weeks while on chemotherapy, then at the same time as cardiac monitoring
	U&Es and LFTs }	
	Echo*/MUGA scan	baseline (must be ≥ 50%), 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 (see below).
	Blood pressure**	baseline, then 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 ≥ 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

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.

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

Trastuzumab should not be initiated if the baseline LVEF is < 50%. Caution should be exercised in treating patients who present with symptomatic heart failure, history of hypertension or documented coronary artery disease.

If LVEF drops 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, discontinuation of trastuzumab should be strongly considered, unless the benefits for the individual patient are deemed to outweigh the risks. All such patients should be referred for assessment by a cardiologist and followed up.

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

References: Bang, YJ et al; Lancet 2010; 376 (9742): 687 – 697 (ToGA trial)