TRASTUZUMAB (HERCEPTIN) IV
for early stage breast cancer

For use in early-stage HER2-positive breast cancer, following surgery and chemotherapy (neo-adjuvant or adjuvant)
NICE approved August 2006
Initiation with (neo-) adjuvant docetaxel-based chemotherapy has been agreed as standard practice
N.B. The subcutaneous route is now preferred; this protocol should be followed only for patients not tolerating the SC formulation

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

N.B. Patient only routinely needs to be seen in clinic for consent, and then before Doses 7 and 13, when trastuzumab (Herceptin) should be prescribed and confirmed as follows:

- Pre Dose 1: Doses 1 – 6 (and arrange echo / MUGA for after cycle 6)
- Dose 7 visit: Doses 7 - 12 (and arrange echo / MUGA for after cycle 12)
- Dose 13 visit: Doses 13 – 18 (and arrange follow-up)

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.

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 also 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 for 12 months: loading dose, followed by 17 maintenance doses.
To be initiated no earlier than 3 weeks after the last dose of anthracycline-based chemotherapy.
Clinical review pre Doses 7 and 13 (once corresponding LVEF result available)

**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 Comments)
Anti-emetics: mildly emetogenic
Extravasation: non-vesicant

Regular Investigations:
- FBC baseline, then taken with Doses 6 and 12 ready for clinical review
- U&Es and LFTs baseline, then taken with Doses 6 and 12 ready for clinical review
- Echo*/MUGA scan baseline; then after Dose 6 and Dose 12 ready for clinical review pre Dose 7 and Dose 13; then after Dose 18 only if requested by Consultant
- Blood pressure** baseline, then at clinic review pre Dose 7 and Dose 13

* 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.

Comments:
A baseline LVEF > 50% is required for treatment to go ahead.

Prophylactic ACE inhibitor therapy should be initiated for any patient who experiences a significant decrease in LVEF as specified in the table below.

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

Dose Interruptions: In line with national guidance¹, see table below for indications for interruption of trastuzumab treatment, initiation of ACE inhibitor therapy, referral to cardiologist and increased monitoring:

<table>
<thead>
<tr>
<th>LVEF</th>
<th>Signs or symptoms</th>
<th>Trastuzumab</th>
<th>Start ACE inhibitor</th>
<th>Cardiology referral</th>
<th>Additional monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF ≥ 50% and &lt; 10 EF points decrease from baseline</td>
<td>None</td>
<td>Continue</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>LVEF 41 – 49% or ≥ 10 EF points decrease from baseline (even if still &gt; 50%)</td>
<td>None</td>
<td>Continue</td>
<td>Yes*</td>
<td>*Refer if already on ACEI</td>
<td>After 6-8 weeks</td>
</tr>
<tr>
<td>LVEF ≤ 40%</td>
<td>Any</td>
<td>Stop</td>
<td>Yes</td>
<td>Refer</td>
<td>Within 6-8 weeks**</td>
</tr>
<tr>
<td>Any</td>
<td>Yes</td>
<td>Stop</td>
<td>Yes</td>
<td>Refer</td>
<td>Within 6-8 weeks**</td>
</tr>
</tbody>
</table>

**Trastuzumab may be re-initiated if LVEF recovers to > 50%.

References:
Romond, EH et al; NEJM (2005); 353: 1673 – 1684
Piccart-Gebhart, MJ et al; NEJM (2005); 353: 1659 – 1672
¹Jones, AL et al; Br J Cancer 2009; 100: 684 - 692