**Duration of Trastuzumab with chemotherapy in patients with early stage breast cancer: Six months versus Twelve**

**Full project title**

A phase III, randomised trial comparing six months Trastuzumab treatment with twelve months, in patients with early stage breast cancer, in terms of:

• Efficacy (disease-free and overall survival)
• Cost-effectiveness (Health Resource use and Quality of Life)
• Safety (cardiac and other toxicity)

**Rationale**

The incidence of breast cancer continues to rise in Western Europe and the US and breast cancer remains a major health problem despite considerable improvements in treatment of the disease both in the adjuvant and in the metastatic setting. Trastuzumab (Herceptin®) treatment in patients with early breast cancer and HER2 positive disease has proved a major advance and has demonstrated incontrovertibly the value of targeted therapy in the adjuvant setting for breast cancer in particular and cancer in general. However, the use of 12 months Trastuzumab in the majority of studies is not based on evidence. It is reasonable to consider that since the beneficial effect of adjuvant Trastuzumab is detected early in follow-up (median 1 year), that the majority of the adjuvant benefit results from the first 6 months of therapy. This hypothesis is supported by evidence from the FinHer study which, with only 9 weeks Trastuzumab demonstrates a similar-sized benefit to 12 months treatment, when given concurrently with chemotherapy. The **Persephone** trial will compare 6 months treatment with 12 months, in terms of efficacy and safety.

**Trial design**

- Prospective, phase III two-arm, multi-centre UK randomised clinical trial
- Data on resource use and quality of life will be collected on all patients entered into the study
- Assessment of cardiac function will be made with reference to methods used for assessment, age and other co-morbidities as risk factors. Cardiac function will be routinely assessed prior to commencement of Trastuzumab and minimum 4 monthly for the first year, in both arms of the trial

**Accrual**

- Opened: October 2007
- Target: 4000 eligible patients
- Duration: 8 years
- Approx Sites: 150

- Planned close date: 2015
- Recruited: 3327 patients
- Recruiting period to date: 78 months
- Sites currently open: 154

**Outcome measures**

**Primary:**

- Disease free-survival non-inferiority (equivalence) of 6 months compared with 12 months Trastuzumab

**Secondary:**

- Overall survival
- Expected incremental cost effectiveness
- Safety - cardiotoxicity
Trial Schema

Breast Cancer Diagnosis

Key Eligibility Criteria
• Invasive, HER2 positive breast cancer
• Clear indication for chemotherapy and Trastuzumab
• Written consent and aged over 18
• No metastases and no prior chemotherapy or radiotherapy

RANDOMISATION (anytime prior to patient receiving cycle 10 of Trastuzumab)

Stratification:
• ER status
  - Negative : Positive
• Chemotherapy type
  - Anthracycline based
  - Taxane based
  - Anthracycline + Taxane based
  - No Taxane, No Anthracycline
• Chemotherapy timing
  - Adjuvant : Neo-adjuvant
• Trastuzumab timing
  - Concurrent : Sequential

Arm A
12 months
Trastuzumab IV or Subcut
every 3 weeks
(x 18 in total)

Arm B
6 months
Trastuzumab IV or Subcut
every 3 weeks
(x 9 in total)

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