NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Lapatinib and trastuzumab in combination with an aromatase inhibitor for the first-line treatment of metastatic hormone receptor positive breast cancer which over-expresses HER2

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of lapatinib and trastuzumab in combination with an aromatase inhibitor within their licensed indications for the first-line treatment of metastatic hormone receptor positive breast cancer which over-expresses ErbB2 (HER2) receptor.

Background

Breast cancer is the most common cancer affecting women in the UK, accounting for nearly 1 in 3 of all cancers in women. In England and Wales, nearly 40,000 new cases were diagnosed in 2006, and there were nearly 11,000 deaths due to breast cancer in 2007. Many breast cancers are stimulated to grow and change by naturally occurring female sex hormones, oestrogen and progesterone. Tumours that have receptors to these hormones are more likely to respond to hormonal therapies (drugs or treatments that block the effects of hormones, or lower the levels of oestrogen and progesterone), and patients with such tumours tend to have a better prognosis. Approximately 25% to 30% of women with metastatic breast cancer have tumours which over-express ErbB2, a protein commonly referred to as HER2 (human epidermal growth factor), and 50% of these also express hormone receptors. HER2 positive tumours are associated with a worse prognosis and reduced overall survival.

The aim of current treatments for metastatic breast cancer is to palliate symptoms, prolong survival and maintain a good quality of life with minimal adverse events. Choice of treatment depends on previous therapy, oestrogen receptor status, HER2 status and the extent of the disease. The NICE clinical guideline CG81 recommends that if the disease is not imminently life-threatening or does not require early relief of symptoms because of significant visceral organ involvement, pre- or peri-menopausal patients with hormone receptor positive breast cancer should be given tamoxifen and/or ovarian suppression. It is further recommended that patients who are post-menopausal and hormone receptor positive are given an aromatase inhibitor for example anastrozole or letrozole. The NICE clinical guideline CG81 does not make recommendations about combining biological therapies such as

trastuzumab with aromatase inhibitors. For patients with HER2 positive tumours, trastuzumab in combination with either a taxane or an aromatase inhibitor may be used depending on whether a patient is considered to require immediate chemotherapy.

The technology

Lapatinib (Tyverb, GlaxoSmithKline) is an oral therapy which inhibits the tyrosine kinase components of the ErbB2 receptor, and a second receptor, ErbB1 (also commonly known as EGFR), which have been implicated in the growth of various tumour types. Stimulation of ErbB1 and ErbB2 is associated with cell proliferation, and with multiple processes involved in tumour progression, invasion and metastasis.

Lapatinib in combination with an aromatase inhibitor does not have a UK marketing authorisation for the first line treatment of breast cancer. It is being studied in clinical trials in combination with letrozole for the first line treatment of patients with hormone receptor positive metastatic breast cancer who have not previously received treatment for metastatic disease.

Trastuzumab (Herceptin, Roche Products) is a recombinant humanised IgG1 monoclonal antibody directed against the human epidermal growth factor receptor 2 (HER2). Trastuzumab is administered by intravenous infusion.

Trastuzumab has a UK marketing authorisation for use in combination with an aromatase inhibitor for the treatment of postmenopausal patients with hormone-receptor positive metastatic breast cancer, not previously treated with trastuzumab.

Intervention(s)	Lapatinib in combination with an aromatase inhibitor Trastuzumab in combination with an aromatase inhibitor
Population(s)	Post menopausal women with HER2 positive metastatic breast cancer which is oestrogen receptor and/or progesterone receptor positive, who have not previously received treatment for metastatic disease and for whom treatment with an aromatase inhibitor is suitable.
Comparators	• The two interventions should be compared with each other. The interventions should also be compared with • Aromatase inhibitors • Tamoxifen

Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • time to progression • response rate • adverse effects of treatment • clinical benefit rate • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. If evidence allows the appraisal should consider a subgroup of patients based on disease characteristics such as tumour burden, number of metastatic sites and disease free interval.

Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 34, Mar 2002, 'Guidance on the use of trastuzumab for the treatment of advanced breast cancer' Technology Appraisal in Preparation, 'Lapatinib for the treatment of women with previously treated advanced or metastatic breast cancer.' Earliest anticipated date of publication Feb 2010 Related Guidelines: Clinical Guideline No.41, Oct 2006, 'Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care' Clinical Guideline No. 81, Feb 2009, 'Advanced breast cancer: diagnosis and treatment'

Questions for consultation

Have the most appropriate comparators for lapatinib and trastuzumab in combination with an aromatase inhibitor for the first-line treatment of hormone receptor positive metastatic breast cancer which over expresses HER2 been included in the scope?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups that are appropriate?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?