NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Lapatinib for the treatment of previously treated women with advanced, metastatic or recurrent breast cancer

Final scope

Appraisal objective

To appraise the clinical and cost effectiveness of lapatinib plus capecitabine within its licensed indications for advanced, metastatic or recurrent breast cancer[1].

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, over 37,000 new cases were diagnosed in 2002, and there were over 11,000 deaths due to breast cancer in 2004.

There are many risk factors that predispose women to developing breast cancer, the strongest being increasing age. 80% of breast cancer occurs in post menopausal women (assuming average age of menopause is 50). Other risk factors include previous breast cancer, family history, early menarche, late menopause, number of children, genetic mutations and having children late or never having children.

Breast cancer is usually defined using a staging system developed by the American Joint committee on Cancer (AJCC) and the Tumour, Node and Metastasis Staging System (TNM). Advanced (or stage III) breast cancer denotes disease that is locally advanced and/or has spread to regional lymph nodes. Metastatic (or stage IV) breast cancer describes the presence of disease at distant sites such as the bone, liver, or lung (metastases). Between 16% and 20% of women presenting with breast cancer have advanced disease with distant metastases (5,750 to 7,200 women). Approximately 40-50% of women presenting with early or localised breast cancer will eventually develop metastatic breast cancer.

The role of current treatments for advanced and metastatic breast cancer is to palliate symptoms, prolong survival and maintain a good quality of life with minimal adverse events. The key decisions involving choice of treatment are based on previous treatment/therapy, oestrogen receptor status and the extent of the disease. Chemotherapy treatments are increasingly being targeted at subsets of patients with particular molecular characteristics.

[1] The Department of Health and Welsh Assembly government remit to the Institute: "To appraise the clinical and cost effectiveness of lapatinib plus capecitabine within its licensed indications for advanced, metastatic or recurrent breast cancer"

Tumours which over-express a receptor known as human epidermal growth factor receptor 2 (HER2, synonymous with ErbB2) are associated with poor prognosis and reduced overall survival. The average life expectancy after diagnosis of metastatic breast cancer is 18-24 months. This is reduced by up to 50% for patients with tumours over-expressing HER2. Approximately 15% to 20% of women with metastatic breast cancer have tumours which over-express HER2 at the 3+ level measured by an immunohistochemical technique[2].

The technology

Lapatinib (Tyverb, GlaxoSmithKline), is an orally administered dual kinase inhibitor of both EGFR (ErbB1) and HER2 (ErbB2). By targeting a number of signalling pathways simultaneously, dual kinase inhibitors are thought to be more effective at blocking tumour growth than agents that target single receptors. As a small molecule, lapatinib works intracellularly and unlike monoclonal antibodies can block signalling through receptors that have lost or mutated their extracellular domains.

Current information suggests that lapatinib will be used in combination with capecitabine for the treatment of women with advanced or metastatic breast cancer that over-expresses the HER2 receptor who have had prior therapy that includes trastuzumab.

Intervention(s)	Lapatinib in combination with capecitabine
Population(s)	Women with advanced, metastatic or recurrent breast cancer that over-expresses the HER2 receptor who have had prior therapy that includes trastuzumab.
Standard comparators	Capecitabine, vinorelbine, taxane regimens and other appropriate chemotherapy regimens in standard practice in England and Wales.
Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • response rate • adverse effects of treatment • health-related quality of life.

[2] Immunohistochemical techniques can detect the amount of HER2 protein in a tumour sample. The HER2 level is graded from 0 to 3+. A grade 3+ means that there is a higher than normal level of HER2 protein (over-expression) and the result is considered HER2-positive. However, this technique is not as definitive as molecular techniques such as FISH (Fluoroescence in situ hybridisation) which can detect excessive amounts (amplification) in each cell of the HER2/neu gene, which leads to the over-production of the HER2 receptor protein.

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 time horizon of the analysis should attempt to capture the benefits/costs over the period during which the effects of the treatment may be expected to differ from the comparator. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Where evidence permits, the appraisal of lapatinib will identify patient subgroups for whom the technology is particularly appropriate. Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations	Related Technology Appraisals: NICE Appraisal Guidance No.30 – The use of taxanes for the treatment of breast cancer, September 2001. NICE Appraisal Guidance No.34 – The use of trastuzumab for the treatment of advanced breast cancer, March 2002. NICE Appraisal Guidance No.54 – The use of vinorelbine for the treatment of advanced breast cancer, December 2002. NICE Appraisal Guidance No.62 – The use of capecitabine for the treatment of locally advanced or metastatic breast cancer, May 2003. NICE Appraisal Guidance No. 116 – Gemcitabine for the treatment of metastatic breast cancer, January 2007. Related guidelines: National Institute for Clinical Excellence (2002) Guidance on cancer services. Improving outcomes in breast cancer. *Manual update*. London: National Institute for Clinical Excellence. NICE Clinical Guideline No. 41 - Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care, October 2006. Related Guidelines in progress: NICE Clinical Guideline – Advanced breast cancer: diagnosis and treatment. Expected date of issue: September 2008. NICE Clinical Guideline – Early breast cancer: diagnosis and treatment. Expected date of issue: September 2008.