

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Trastuzumab for the treatment of HER-2 positive advanced gastric cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of trastuzumab within its licensed indication for the treatment of HER2 positive advanced gastric cancer.

Background

Gastric cancer is a malignant tumour arising from cells in the stomach. Around 95% of gastric cancer cases are adenocarcinomas, which have started in gland cells in the stomach lining. Tumours are staged according to the extent of invasion and spread. Invasive gastric cancer (stages T2–T4) is fatal without surgery. Mean survival without treatment is less than 6 months from diagnosis. Intramucosal or submucosal cancer (stage T1) may progress slowly to invasive cancer over several years.

In 2006, 6,704 people in England and Wales were diagnosed with gastric cancer and in 2007 there were 4,574 deaths from gastric cancer. The 5-year survival rate is approximately 20% which declines to 5% for patients with stage IV disease. A proportion of gastric cancers (7-16%) over-express a growth factor called the human epidermal growth factor receptor 2 (HER2) protein. Over-expression of the HER2 protein is associated with a poor prognosis.

The aim of treatment in advanced gastric cancer is to prevent progression, extend survival and relieve symptoms with minimal adverse effects. Treatment usually consists of surgery which is typically carried out in the earlier stages of gastric cancer, but may also be carried out in advanced stages to relieve pain and discomfort from the disease. In addition chemotherapy and/or radiotherapy is offered and the type of treatment mainly depends on the stage of the disease. Chemotherapy regimens used in gastric cancer include 5-fluorouracil or capecitabine in combination with one or more of the following: cisplatin, oxaliplatin, doxorubicin, epirubicin, docetaxel.

The technology

Trastuzumab (Herceptin, Roche Products) is a recombinant, humanized monoclonal antibody, which specifically targets the HER2 protein expressed on the cell-surface, inhibiting cell proliferation. Immunohistochemistry (IHC) or fluorescence *in situ* hybridization (FISH) are typically used to assess HER2 levels. Trastuzumab does not have a marketing authorisation for the treatment of advanced gastric cancer. It is being studied in clinical trials in

combination with standard treatment (platinum and fluoropyrimidine-based cytotoxic therapy) for patients with HER2 positive advanced gastric cancer. It is also being studied as monotherapy following disease progression after standard treatment.

Intervention(s)	Trastuzumab
Population(s)	Patients with HER2 positive advanced gastric cancer
Comparators	Cytotoxic chemotherapy regimens which may include 5-fluorouracil or capecitabine in combination with one or more of the following: cisplatin, oxaliplatin, doxorubicin, epirubicin, docetaxel
Outcomes	The outcome measures to be considered include: <ul style="list-style-type: none"> • overall survival • progression-free survival • response rate • adverse effects of treatment • 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.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal in preparation, 'Capecitabine for the treatment of advanced gastric cancer'. Earliest anticipated date of publication Aug 2010.