Bijal Joshi
Technology Appraisal Project Manager
National Institute for Health and Clinical Excellence
MidCity Place
71 High Holborn
London WC1V 6NA

23rd July 2010

Dear Ms. Joshi,

Bevacizumab in combination with a taxane for the first-line treatment of metastatic breast cancer: Appraisal consultation document response

Breakthrough Breast Cancer is a charity committed to fighting breast cancer through research and education, and has established the UK's first dedicated breast cancer research centre, in order to achieve our vision – a future free from the fear of breast cancer. Breakthrough campaigns for policies that support breast cancer research and better services, as well as promoting breast cancer education and awareness amongst the general public, policy makers, health professionals and the media.

This submission reflects the views of Breakthrough, based on our experience of working with people with personal experience of, or who are concerned about, breast cancer. We regularly consult with members of our Campaigns and Advocacy Network (Breakthrough CAN) for their views on a range of breast cancer issues. Originally founded by women with personal experience of breast cancer, Breakthrough CAN brings together over 1,300 individuals, regional groups and national organisations to campaign for improvements in breast cancer research, treatments and services. Through supporting and training members to become patient advocates in their own right, Breakthrough CAN aims to increase the influence of patients in decisions regarding breast cancer issues.

Breakthrough welcomes the opportunity to comment on the appraisal consultation document regarding the use of bevacizumab in combination with a taxane for the first-line treatment for metastatic breast cancer.

Has all of the relevant evidence been taken into account?
Bevacizumab utilises a novel method of action by targeting the process of angiogenesis so delaying tumour growth. As a result, unlike many other treatments, bevacizumab is not specific to a particular type of tumour (for example, hormone or HER2 receptor positive tumours) and therefore may be effective in cases where the cancer would not respond to other commonly used treatments. This may be of particular benefit in patients with forms of breast cancer that have particularly limited options, such as those with triple negative cancer (i.e. who are negative for the oestrogen, progesterone and HER2 receptors).

As metastatic breast cancer is not curable, it is essential that treatment options which could delay progression or improve survival are made available to this patient group. Patients typically have limited treatment options in the metastatic setting and therefore the need for safe and effective new medicines in this patient group is relatively urgent. If treatments can slow disease progression or cause the tumour to respond, they may also allow the patient to be able to continue to carry out normal daily activities such as caring for their families or continuing to work or just enjoying spending quality time with their loved ones. For patients with metastatic breast cancer this cannot be underestimated. This was echoed by both the clinical and the patient expert who were present at the technology appraisal committee meeting on the 17th June 2010.

We welcome consideration of the patient perspective on acceptance of side effects by people at this stage of disease and would like to see more qualitative evidence regarding the patient perspective taken into account for outcome measures. As noted in the Appraisal Consultation Document, the addition of bevacizumab caused little additional toxicity compared with a paclitaxel alone and these side effects can be relatively easily managed[1].

Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
We are disappointed that the Appraisal Committee is unable to recommend bevacizumab in combination with a taxane as a routine first-line treatment for metastatic breast cancer. However, we acknowledge that there are some concerns regarding the quality of the data including existing limitations and uncertainties in the evidence available. We accept that this is an expensive treatment and currently there is a lack of robust data to confirm a significant clinical benefit.

Breakthrough shares the Appraisal Committee's concerns regarding the limitations of the E2100 study (e.g. open label, no comparison with a placebo and a lack of data collection to explain the overall survival), the use of evidence from primarily one trial and some of the assumptions that were made with the data. However, there is evidence to show that bevacizumab could be an effective treatment option for some patients with metastatic breast cancer as there was a statistically significant

[1] Section 4.5, p. 18, Appraisal Consultation Document

improvement in the progression-free survival when compared with paclitaxel monotherapy[2, 3]. Additionally, if a patient access scheme is approved by the Department of Health, the cost of the treatment will be reduced considerably.

Are the provisional recommendations sound and a suitable basis for guidance to the NHS?
It is disappointing that the committee is unable to recommend bevacizumab in combination with a taxane for the first-line treatment of metastatic breast cancer. As a patient organisation, Breakthrough Breast Cancer would like to emphasise how crucial it is for this patient group to have treatment options.

We do not agree with the Appraisal Committee's assessment of the third criterion for determining if bevacizumab with a taxane meets the criteria for being an end-of-life treatment. Whilst bevacizumab is licensed for a relatively large population across a range of indications such as colorectal cancer and renal cell carcinoma, we feel that the population size should be evaluated in the context of the indication for this appraisal only and therefore should be restricted to the relevant population of breast cancer patients.

Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of gender, race, disability, age, sexual orientation, religion or belief?
None of which we are aware.

If you require any further information please contact Meg McArthur, Senior Policy & Information officer at 020 7280 4264 megm@breakthrough.org.uk

Yours sincerely,

[redacted]

[2] Gray, R., et al. (2009) Independent review of E2100: A phase III trial of bevacizumab plus paclitaxel versus paclitaxel in women with metastatic breast cancer. *Journal of Clinical Oncology*, 27(30): 4966-49972.
[3] Miller, K., et al. (2007) Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer. *The New England Journal of Medicine*, 357(26): 2666-2676.