Meindert Boyson
Programme Director, Centre for Health Technology Evaluation
National Institute for Health and Clinical Excellence
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03 May 2012

Dear Mr Boysen,

Bevacizumab in combination with capecitabine for the first-line treatment of metastatic breast cancer.

Breakthrough Breast Cancer is dedicated to improving and saving lives through breast cancer prevention, early diagnosis, more targeted treatments and better services for everyone affected by breast cancer.

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. To inform our submission to this consultation, we have consulted with members of our Campaigns & Advocacy Network (Breakthrough CAN) for their views on a range of breast cancer issues. Breakthrough CAN brings together over 1,800 individuals, regional groups and national organisations to take action locally on our national campaigns to secure important improvements to breast cancer research, treatments and services. Through supporting and training members, Breakthrough CAN aims to increase the influence of breast cancer advocates on decisions regarding breast cancer issues.

Breakthrough welcomes the opportunity to comment on the appraisal consultation document regarding the use of bevacizumab in combination with capecitabine for the first-line treatment of metastatic breast cancer. We are disappointed NICE were unable to approve the use of this treatment combination for breast cancer patients. However, we recognise there are significant limitations associated with this treatment and challenges associated with the appraisal.

Bevacizumab is an antibody used to inhibit tumour growth and is administered by intravenous infusion. In accordance with its marketing authorisation bevacizumab can be used in combination with capecitabine as a first line treatment for patients with metastatic breast cancer. These patients may only receive this treatment combination if it is considered inappropriate for them to receive taxanes or anthracyclines or they have not received a taxane or anthracycline-containing regimen in the adjuvant setting within 12 months.

The most relevant evidence that documents the effects of bevacizumab in combination with capecitabine comes from the RIBBON-1 trial which has been considered in this appraisal. The trial included two different cohorts of patients – those who received either a taxane or an anthracycline or those who received capecitabine. Patients were then randomized to receive bevacizumab or a placebo. Only results from the cohort of patients who received capecitabine (and bevacizumab or a placebo) were included in the analysis for this submission.

The data from the RIBBON-1 trial was used to calculate patients' progression free survival and overall survival. No quality of life data was collected in this trial. It was found that bevacizumab plus capecitabine improved progression free survival compared to capecitabine

plus placebo. This is note worthy because there is no cure for metastatic breast cancer so patients highly value treatments that can control their disease and stop it from progressing.

Patients on the RIBBON-1 trial had the option to receive bevacizumab after disease progression as well as their subsequent treatment. However, this presented problems when calculating overall survival gains. Therefore, we recognise that the evidence included in this submission is not robust enough to demonstrate bevacizumab plus capecitabine improved overall survival over capecitabine plus placebo.

Bevacizumab is associated with a number of adverse side effects and it was observed that patients on the bevacizumab plus capecitabine arm of the RIBBON-1 trial experienced more adverse events than those on the control arm. However, the manufacturer stated that when bevacizumab is added to capecitabine the adverse effects were predictable and generally manageable.

Maintaining a high quality of life for as long as possible is currently the best outcome for patients with metastatic breast cancer and attractive treatments options are those which exert as few side effects and adverse reactions as possible. This is highly important as it can allow patients to continue their normal daily lives and maintain the enjoyment they can achieve from spending time with their loved ones.

However, as discussed above no quality of life data was collected as part of this trial. We therefore acknowledge, there is no evidence to demonstrate that patients who received bevacizumab as part of their treatment did not experience a reduction in their quality of life. In the light of potential side effects this is an important consideration.

As well as a lack of quality of life data we recognise why the Committee were unable to approve this treatment regime on the grounds of cost. However, whilst we acknowledge this regimen is expensive it is important to note that patients in the metastatic setting have limited treatment options. The availability of an increased number of safe and effective medicines is therefore highly important.

If you require any further information please contact [redacted], [redacted] on [redacted] or [redacted]@breakthrough.org.uk.

Yours sincerely,

[redacted]