Bevacizumab added to a taxane for the first-line treatment of metastatic breast cancer

NHS organisation statement template

Primary Care Trusts (PCTs) provide a unique perspective on the technology, which is not typically available from the published literature. NICE believes it is important to involve NHS organisations that are responsible for commissioning and delivering care in the NHS in the process of making decisions about how technologies should be used in the NHS.

About you

Your name: Commissioning Support Appraisals Service

Name of your organisation NHS Milton Keynes

Please indicate your position in the organisation:

- Service commissioned by all English PCTs to support PCT participation in NICE appraisals

What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences in opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

Metastatic breast cancer is a life-threatening condition. There are a variety of approaches to treatment, and a number of technologies currently available. A number of treatment guidelines exist, and NICE has issued relevant guidelines and technology appraisal guidance.

It is vital to determine whether any new technology represents a genuine improvement in terms of overall survival (i.e. prolonging patients' lives – not simply changing the mode of death) and/or a genuine improvement in terms of improved quality of life (e.g. reducing suffering or improving ability to perform activities of daily living).

To what extent and in which population(s) is the technology being used in your local health economy?

- is there variation in how it is being used in your local health economy?
- is it always used within its licensed indications? If not, under what circumstances does this occur?
- what is the impact of the current use of the technology on resources?
- what is the outcome of any evaluations or audits of the use of the technology?
- what is your opinion on the appropriate use of the technology?

As this STA is investigating the proposed use of bevacizumab for this indication, it is not possible for this submission to comment on current use outside the published research evidence.

We are aware of two completed randomised controlled trials investigating the use of Bevacizumab added to a taxane for the first-line treatment of metastatic breast cancer: AVADO (not yet fully published in a peer-reviewed publication) and E2100. These suggest improvement in progression-free survival for patients receiving the combination treatment (6 months for E2100 and up to 1.9 months for AVADO higher dose), but not in overall survival (1.5 months for E2100 with P=0.16 and no overall survival results for AVADO). It will therefore be vital to determine the quality of life during the time of delayed disease progression, if this is to be regarded as evidence of clinical effectiveness.

Potential impact on the NHS if NICE recommends the technology

What impact would the guidance have on the delivery of care for patients with this condition?

If this guidance approves this technology, it would make one more treatment available for patients, with a likely impact on mode of death, but not necessarily prolonging life. Delaying disease progression might be regarded by patients as a worthwhile outcome in its own right. It is not clear whether quality of life would be otherwise improved. Patients would require additional visits to hospital and additional procedures to administer and monitor treatment. There would be some additional adverse events, although the frequency of very serious events (e.g. heart failure) appears to be low.

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional resources (for example, staff, support services, facilities or equipment)?

If approved, this technology should be used in secondary care.

Can you estimate the likely budget impact? If this is not possible, please comment on what factors should be considered (for example, costs, and epidemiological and clinical assumptions).

This STA is considering the addition of a new technology to current treatment options. There is no evidence of substitution for other technologies, or of any reduction in health care (or other) costs as a result of using this technology. This technology will therefore represent an increase in total resources. The following represents a crude estimate of the likely number of patients and additional costs for a PCT with 300,000 patients of whom 50% are women, with the same age-distribution as England:

Using incidence figures from Cancer Research UK (2006)
Assume 147 new diagnoses per 100,000 women per year
=> 220 new cases of breast cancer per year
=> approximately 42 cases of advanced disease or disease progression per year

Assume all 42 are eligible for combination therapy with bevacizumab:

Based on the findings from the E2100 trial, the additional annual cost of treating one woman with a combination of paclitaxel and bevacizumab compared with first-line, single-agent paclitaxel (for 5.1 months as per E2100 trial) is £40,468 (£44,910-4,442.46). Therefore, for 42 women, the additional annual drug cost would be £1,699,656 (with no allowance for additional administration, monitoring or adverse-event costs). Median progression-free survival may be prolonged by 6 months. There is insufficient evidence that overall survival would be improved.

The conference reports of the AVADO trial do not state median duration of combination therapy, but if it is assumed that this is the same as progression-free survival, the additional annual treatment costs for one woman is estimated to be £52,659 (60,693.29-8034.24) compared with docetaxel monotherapy. For 42 women,

the additional annual drug cost will be £2,211,678 with no allowance for additional administration, monitoring or adverse-event costs). Median progression-free survival may be prolonged by 1.9 months. There is no evidence that overall survival would be prolonged.

Would implementing this technology have resource implications for other services (for example, the trade-off between using funds to buy more diabetes nurses versus more insulin pumps, or the loss of funds to other programmes)?

If this combination were approved, PCTs would need to divert resources from other treatments to fund it. The quantity of resources to be diverted would be dependent on the drug acquisition cost and the costs of administration, monitoring and managing adverse events. There is no evidence to suggest that this use of bevacizumab would substitute for any other health care costs. It is likely that PCTs would seek to find the additional resources from within cancer or "end of life" budgets, as the limited evidence of improvements in progression-free survival (but not overall survival) would not justify reductions in the budgets for other programmes.

Would there be any need for education and training of NHS staff?

Only with regard to patient selection and administration and monitoring of combination therapy.

Other Issues
Please include here any other issues you would like the Appraisal Committee to consider when appraising this technology.

It is very important to consider the clinical effectiveness of this technology in terms of its absolute benefits compared to other technologies (rather than relative benefits) e.g. absolute improvements in median survival in terms of months – not as a hazard ratio.

Overall survival is the preferred outcome measure. If progression-free survival is considered to be evidence of clinical effectiveness, it will be essential to have robust evidence of the quality of life experienced by patients receiving combination therapy compared to monotherapy.

Cost-effectiveness will be influenced by acquisition cost. We are aware of one cost-effectiveness study, which assessed the cost-effectiveness of bevacizumab in combination with paclitaxel estimating direct costs from the perspective of the Swiss health system based on effectiveness results from the E2100 trial. The study found that adding bevacizumab to weekly paclitaxel cost an additional 40,369€ for a gain of 0.22 QALYs. This gave an incremental cost-effectiveness ratio of 189,427€/QALY. It is not clear how might apply to the NHS.

There are a number of recently completed or ongoing phase III studies that may

contribute to further revisions of the indication for bevacizumab, including:

- BETH study/NCT00625898: investigating the addition of bevacizumab to trastuzumab for HER-2 positive breast cancer (estimated enrolment 3500, estimated completion date June 2021)

- NCT00601900: investigating the addition of bevacizumab to tamoxifen or letrozole in women with stage III or IV breast cancer (estimated enrolment 502, estimated completion date Feb 2009)

- NCT00408408: investigating chemotherapy with or without bevacizumab for women with stage I, II or IIIA breast cancer that can be treated surgically (estimated enrolment 1200, estimated completion date April 2012)

- NCT00520975: investigating the addition of bevacizumab to trastuzumab compared with trastuzumab monotherapy in HER-2 positive breast cancer (estimated enrolment 489, estimated completion date November 2011)

- RIBBON 2/ NCT00281697: investigating the combination of bevacizumab and chemotherapy in previously treatment metastatic breast cancer (estimated enrolment 650, estimated completion date April 2010)

- AVEREL / NCT00391092: investigating the addition of bevacizumab to trastuzumab and docetaxel in patients with HER-2 positive metastatic breast cancer (estimated enrolment 410, estimated completion date December 2011)