Bevacizumab (Avastin) in combination with docetaxel for metastatic breast cancer – first line

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The National Horizon Scanning Centre Research Programme is part of the National Institute for Health Research
Bevacizumab (Avastin) in combination with docetaxel for metastatic breast cancer – first line

Target group
- Breast cancer: metastatic breast cancer - first line; in combination with docetaxel (or any taxane-based chemotherapy).

Technology description
Bevacizumab (Avastin) is a humanised anti-vascular endothelial growth factor (VEGF) monoclonal antibody that inhibits VEGF-induced signalling and inhibits VEGF-driven angiogenesis. This reduces vascularisation of tumours, thereby inhibiting tumour growth. Bevacizumab is administered as a 10 or 15mg/kg intravenous infusion (IV) with docetaxel every 3 weeks until disease progression (median of around 9 months). Bevacizumab is currently licensed for HER2 metastatic breast cancer: first line treatment in combination with paclitaxel.

Docetaxel (Taxotere) belongs to the taxane class of anticancer drugs and is a semi-synthetic analogue of paclitaxel. Docetaxel halts mitosis and ultimately causes tumour cell death. The use of docetaxel monotherapy in first line treatment of advanced breast cancer is not currently licensed. Docetaxel and paclitaxel are recommended as an option for the treatment of advanced breast cancer where initial cytotoxic chemotherapy (including an anthracycline) has failed or is inappropriate.

Innovation and/or advantages
Bevacizumab in combination with docetaxel may prolong disease-free progression and improve overall survival in this patient group. It would also provide an additional treatment option for this indication, where no standard therapy exists.

Developer
Roche Products Ltd (bevacizumab); Sanofi-Aventis (docetaxel).

Availability, launch or marketing dates, and licensing plans:
In phase III clinical trials.

NHS or Government priority area:
The topic is relevant to the Cancer Reform Strategy (2007) and the NHS Cancer Plan (2000).

Relevant guidance
NICE Technology Appraisals
- NICE technology appraisal in development. Lapatinib for the treatment of advanced or metastatic breast cancer. 13th wave\(^1\).
- NICE technology appraisal. Capecitabine for the treatment of locally advanced or metastatic breast cancer. 2003\(^4\).

NICE Clinical Guidelines
• NICE clinical guideline. Familial breast cancer. 2006 (review planned 2010).

Other Guidelines

Clinical need and burden of disease
Breast cancer is the most common malignancy affecting women in the UK. There were 40,849 women newly diagnosed with breast cancer in England and Wales during 2005 and in 2006 there were 10,984 registered deaths.

Between 16-20% of women (an estimated 6,536 to 8,170 women) presenting with breast cancer have advanced disease with distant metastases and in 2002 NICE estimated that around 50% of those presenting with early or localised breast cancer will eventually develop metastatic breast cancer.

Existing comparators and treatments
The management of HER2 negative metastatic breast cancer is usually problematic, since no standard therapy exists. The role of current treatments for advanced and metastatic breast cancer is to palliate symptoms, prolong survival and maintain a good quality of life.

Current treatment options include:
• First line chemotherapy; usually an anthracycline based regimen or a combination of cyclophosphamide, methotrexate and fluorouracil.
• Following disease progression on an anthracycline, other chemotherapy options such as single-agent taxanes, capecitabine (in combination with docetaxel or as monotherapy), bevacizumab (in combination with paclitaxel), vinorelbine and gemcitabine in combination with paclitaxel are available.

Efficacy and safety

<table>
<thead>
<tr>
<th>Trial</th>
<th>NCT00333775; AVADO (BO17708): previously untreated HER2 negative metastatic breast cancer; bevacizumab with docetaxel vs. docetaxel alone; phase III.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>Hoffman-La Roche.</td>
</tr>
<tr>
<td>Status</td>
<td>Completed, unpublished (interim results published in abstract).</td>
</tr>
<tr>
<td>Location</td>
<td>EU (inc UK), Canada and other countries.</td>
</tr>
<tr>
<td>Design</td>
<td>Randomised, placebo controlled, double blind.</td>
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</tbody>
</table>
| Participants and schedule                                           | n=736; adults (females); HER2 negative inoperable locally recurrent or metastatic breast cancer; no prior chemotherapy.  
Randomised to bevacizumab 7.5mg/kg or 15mg/kg IV with docetaxel 100mg/kg² IV on day 1 of each 3 week cycle, or docetaxel with placebo. |
Follow-up | Up to 9 cycles of treatment (median follow-up of 11 months).
---|---
Primary outcome | Progression-free survival (PFS).
Secondary outcomes | Overall response; response duration, time to treatment failure; quality of life and safety.
Key results | PFS for bevacizumab 15mg/kg and 7.5mg/kg: hazard ratios of 0.61 (p=0.0001) and 0.69 (p=0.0035) respectively, compared to docetaxel alone. Response rates for bevacizumab 15mg/kg and 7.5mg/kg were 63.1% (p=0.0001) and 55.2% (p=0.0295) respectively, compared to 44.4% for docetaxel alone.
Expected reporting date | Study started March 2006. The final analysis for overall survival is expected in 2009.
Adverse effects | Reported adverse effects (grade ≥3) included hypertension and febrile neutropenia.

**Estimated cost and cost impact**

For an average person of 67.5kg, the cost of a dose of bevacizumab will be approximately £2,570 at 15mg/kg (assuming wastage)\(^7\). The estimated minimum 9-month treatment course would cost in the region of £33,000. This will be in addition to the cost of taxane chemotherapy regimen.

Bevacizumab will be administered during the same hospital visit as the other chemotherapy drugs in the combined regimen.

**Potential or intended impact – speculative**

**Patients**
- ☑ Reduced morbidity
- ☐ Quicker, earlier or more accurate diagnosis or identification of disease
- ☑ Reduced mortality or increased survival
- ☐ Other:
- ☑ Improved quality of life for patients and/or carers
- ☐ Non identified

**Services**
- ☑ Increased use
- ☐ Service reorganisation required
- ☐ Staff or training required
- ☐ Decreased use
- ☐ Other:
- ☐ Non identified

**Costs**
- ☑ Increased unit cost compared to alternative
- ☑ New costs: additional therapy
- ☐ Increased costs: more patients coming for treatment
- ☐ Savings:
- ☐ Increased costs: capital investment needed
- ☐ Other:
- ☐ Non identified

**References**