Aflibercept for androgen independent metastatic prostate cancer – first line

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This technology summary is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes.
Aflibercept for androgen independent metastatic prostate cancer – first line

Target group
- Androgen independent prostate cancer: metastatic – first line; in combination with docetaxel and prednisolone.

Technology description
Aflibercept (VEGF-Trap, AVE-0005) is a fully human recombinant fusion protein composed of the second Ig domain of vascular endothelial growth factor (VEGF) receptor 1 and the third Ig domain of VEGF receptor 2, fused to the Fc region of human IgG1. Aflibercept binds to all VEGF-A isoforms as well as VEGF-B and placental growth factor (PLGF), thereby preventing these factors from stimulating angiogenesis. Reduced vascularisation of tumours inhibits their growth. Aflibercept is administered by intravenous infusion at 6mg/kg every three weeks in combination with docetaxel and prednisolone.

Aflibercept is in phase III development for:
- Non-small cell lung cancer (second line combination therapy).
- Colorectal cancer (combination therapy), metastatic disease (second line therapy).
- Vascular occlusion and age-related macular degeneration, a purified, iso-osmotic formulation of aflibercept administered by intravitreal injection is under development for retinal.

Innovation and/or advantages
If licensed, aflibercept will offer an additional option for this group of patients who currently have few effective treatments available.

Developer
Sanofi-aventis and Regeneron.

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

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

Relevant guidance
NICE Technology Appraisals
- Docetaxel for the treatment of hormone refractory prostate cancer. 2006¹.

NICE Clinical Guidelines
- Prostate Cancer: diagnosis and treatment. 2008².

Other Guidance

Clinical need and burden of disease
Prostate cancer is the most common cancer in men in the UK, accounting for about 24% of all male cancers⁴. The main risk factor is increasing age, with more than 60% of cases diagnosed over the age of 70⁵. In 2007, there were 36,101 new cases registered in England and 2,552 in Wales, resulting in age standardised rates of 97.2 and 126.1 per
100,000 population respectively\textsuperscript{6,7}. In 2008 there were 10,168 registered deaths from prostate cancer in England and Wales, approximately 12\% of all male cancer deaths\textsuperscript{8}. Metastatic disease occurs in approximately 20-30\% of men with prostate cancer\textsuperscript{9}, the majority of whom eventually become resistant to hormone therapy, at which point survival is not expected to exceed 9 to 18 months\textsuperscript{2,10}.

**Existing comparators and treatments**

There is no curative therapy for metastatic prostate cancer. Treatment is aimed at improving symptoms, slowing disease progression and prolonging life\textsuperscript{2}. Clinical management is multimodal rather than sequential, and patients may receive a combination of palliative treatments which include:

- Docetaxel (Taxotere) in combination with prednisolone. Licensed for up to 10 cycles in hormone refractory disease if Karnofsky performance-status score is $\geq 60\%$.
- Cabazitaxel (Jevtana, Sanofi-aventis), for second line treatment after progression on docetaxel (recently licensed).
- Mitoxantrone with prednisolone (not licensed for this indication).
- Additional hormonal therapy.
- Supportive care given in combination with the above, includes radiotherapy, bisphosphonates, and/or steroids.

### Efficacy and safety

<table>
<thead>
<tr>
<th>Trial</th>
<th>VENICE, NCT00519285; docetaxel and prednisolone with aflibercept or placebo; phase III.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>Sanofi-aventis.</td>
</tr>
<tr>
<td>Status</td>
<td>Ongoing.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Trial registry\textsuperscript{11}.</td>
</tr>
<tr>
<td>Location</td>
<td>EU (inc UK), USA, Canada and other countries.</td>
</tr>
<tr>
<td>Design</td>
<td>Randomised, placebo-controlled.</td>
</tr>
<tr>
<td>Participants and schedule</td>
<td>n=1,200 (planned); adults; metastatic androgen independent prostate cancer; following hormone therapy or surgical castration. Randomised to docetaxel plus prednisolone with either aflibercept 6mg/kg every 3 weeks or placebo.</td>
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<tr>
<td>Follow-up</td>
<td>2 years.</td>
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<tr>
<td>Primary outcome</td>
<td>Overall survival.</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td>Prostate specific antigen (PSA) response; pain measurements; occurrence of skeletal related events.</td>
</tr>
<tr>
<td>Expected reporting date</td>
<td>Interim analysis expected mid-2011, with final results in 2012.</td>
</tr>
</tbody>
</table>

**Estimated cost and cost impact**

The cost of aflibercept is not yet known.

**Claimed or potential impact – speculative**

Patients

- ✓ Reduced mortality or increased length of survival
- □ Reduction in associated morbidity or improved quality of life for patients and/or carers
- □ Quicker, earlier or more accurate diagnosis or identification of disease
- □ Other:
- □ None identified
Services

☐ Increased use  ☐ Service organisation  ☐ Staff requirements

☐ Decreased use  ☐ Other:  ☑ None identified

Costs

☑ Increased unit cost compared to alternative.

☐ Increased costs: more patients coming for treatment

☐ Increased costs: capital investment needed

☐ New costs:

☐ Savings:

☐ Other:

References


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