Abiraterone acetate for metastatic, castration-resistant prostate cancer

May 2010

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.

The National Horizon Scanning Centre Research Programme is part of the National Institute for Health Research
Abiraterone for metastatic, castration-resistant prostate cancer

Target group
- Castration-resistant prostate cancer (CRPC): advanced, metastatic - second line in patients who have received chemotherapy containing a taxane; in combination with prednisone.

Technology description
Abiraterone (CB-7598, CB-7630, abiraterone acetate) is a potent selective irreversible inhibitor of 17-alpha-hydroxylase (CYP17), a cytochrome p450 complex involved in testosterone production and a key catalyst in androgen biosynthesis. CYP17 is postulated to drive the androgen receptor (AR) signalling implicated in CRPC. Abiraterone is administered orally at 1,000mg once daily in combination with prednisone 5mg twice daily. The median duration of treatment is currently unknown as studies are ongoing.

Abiraterone is in phase III clinical trials for CRPC in chemotherapy-naive patients and in phase I/II clinical trials for advanced breast cancer.

Innovation and/or advantages
Abiraterone is an androgen biosynthesis inhibitor that may be associated with fewer adverse effects than existing second-line hormonal therapies and may offer the potential for longer progression free survival and overall survival.

Developer
Janssen-Cilag Ltd.

Availability, launch or marketing dates, and licensing plans
In phase III clinical 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 and Clinical Guidelines
- Docetaxel for the treatment of hormone refractory prostate cancer. 2006¹.
- Prostate Cancer: diagnosis and treatment. 2008².

NICE Interventional Procedure Guidance
- High dose rate brachytherapy in combination with external-beam radiotherapy for localised prostate cancer. 2006³.
- Cryotherapy as a primary treatment for prostate cancer. 2005⁴.
- Low dose rate brachytherapy for localised prostate cancer. 2005⁵.
- Cryotherapy for recurrent prostate cancer. 2005⁶.
- High-intensity focused ultrasound for prostate cancer. 2005⁷.

Other Guidance
- Department of Health. Advice on the development of low dose rate (permanent seed implant) brachytherapy services for localised prostate cancer in England. 2006⁹.
Clinical need and burden of disease

Prostate cancer is the most common cancer in men in the UK, accounting for about 24% of male cancers\(^5\). The main risk factor is increasing age with more than 60% of cases diagnosed over the age of 70\(^1\). In 2007 there were 30,201 new cases registered in England and 2,552 in Wales, resulting in the age-standardised rates of 97.2 and 126.1 per 100,000 populations respectively\(^12,13\). There were 9,222 deaths from prostate cancer in England and Wales in 2007, approximately 13% of all male cancer deaths\(^14\). Although epidemiological data on metastatic CRPC is limited, it is estimated that most deaths occur in patients with metastatic CRPC\(^6\). Metastatic disease occurs in 55-60% of men with prostate cancer, the majority of whom eventually become resistant to hormone therapy, at which point survival is not expected to exceed 9 to 12 months\(^1\).

Existing comparators and treatments

There is no curative therapy for CRPC\(^5\). Treatment is aimed to improve symptoms, slow progression of the disease and prolong life\(^4\). Docetaxel with prednisone is the standard first line chemotherapy agent for metastatic CRPC. There is no standard care for patients who fail first line chemotherapy. Clinical management is multimodal rather than sequential, and patients may receive a combination of palliative treatments which include:

- Docetaxel (Taxotere) retreatment in combination with prednisolone.
- Mitoxantrone with or without steroids (not licensed for this indication).
- Steroids alone.
- Additional hormonal therapy.
- Supportive care with radiotherapy, bisphosphonates, and/or steroids.

Efficacy and safety

<table>
<thead>
<tr>
<th>Trial</th>
<th>NCT00485303; post-docetaxel; abiraterone with prednisone; phase II.</th>
<th>NCT00474383; post-paclitaxel or docetaxel; phase II.</th>
<th>NCT00638690; COU-AA-301; metastatic CRPC; post-docetaxel; prednisone with abiraterone or placebo; phase III.</th>
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<tbody>
<tr>
<td>Status</td>
<td>Published.</td>
<td>Published.</td>
<td>Ongoing.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Publication(^15).</td>
<td>Publication(^16).</td>
<td>Trial registry(^17).</td>
</tr>
<tr>
<td>Location</td>
<td>EU (inc UK), USA.</td>
<td>EU (inc UK), USA.</td>
<td>EU (inc UK), USA, Canada and Australia.</td>
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<tr>
<td>Participants and schedule</td>
<td>n=58; adults; metastatic CRPC with serum testosterone &lt;50ng/dl; disease progression after androgen deprivation therapy and docetaxel-based chemotherapy; prostate specific antigen (PSA) progression with a PSA &gt;5ng/ml. Received abiraterone 1,000mg daily with prednisone 5mg twice daily for up to 12 cycles each of 28 days.</td>
<td>n=47; adults; metastatic CRPC with serum testosterone &lt;50ng/dl; prior treatment with regimen(s) containing paclitaxel or docetaxel; PSA progression with a PSA &gt;5ng/ml. Received abiraterone 1,000mg daily in 28-day cycles.</td>
<td>n=1,158 (planned); adults; metastatic CRPC; disease progression after ≤2 prior cytotoxic chemotherapy (including docetaxel); medical or surgical castration with testosterone &lt;50ng/dl. Randomised to abiraterone 1,000mg once daily or placebo. All patients receive prednisone 5mg twice daily.</td>
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</table>
Follow-up | Until death. | Until death. | Until death or study completion.
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Primary outcome | Decline in PSA ≥50%. | Decline in PSA ≥50%. | Overall survival.
Secondary outcomes | Time to PSA progression; disease progression; cancer tumour cell counts. | Time to PSA progression; disease progression. | Proportion of patients achieving a PSA decline ≥50%; time to PSA progression; progression free survival (radiographic).
Key results | PSA declines of ≥50% in 36%. Median time to PSA progression – 169 days (95% CI, 82 – 200 days). | PSA declines of ≥50% and ≥90% in 51% and 15% respectively. Median time to progression – 169 days (95% CI, 113 – 281 days). | -
Adverse effects (AEs) | Majority (nausea, vomiting, fatigue, diarrhoea) were grade 1 to 2. No grade 4 events seen. AEs included: hypokalemia, hypertension and fluid retention. | - | -
Expected reporting date | Reported. | Reported. | 2011.

**Estimated cost and cost impact**

The cost of Abiraterone 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
- None identified

**Services**
- Increased use
- Service organisation
- Staff requirements
- Decreased use; reduction in hospital stay and use of healthcare resources.
- Other: may reduce adverse effects experienced with current therapy.
- None identified

**Costs**
- Increased unit cost compared to alternative
- New costs: new therapeutic option.
- Increased costs: more patients coming for treatment
- Savings: if disease progression is delayed.
- Increased costs: capital investment needed
- Other:

**References**