UNIVERSITY OF BIRMINGHAM

NHS National Institute for Health Research

NHSC National Horizon Scanning Centre

Cabazitaxel (XRP-6258) for hormone refractory, metastatic prostate cancer – second line after docetaxel

April 2009

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

Cabazitaxel (XRP-6258) for hormone refractory, metastatic prostate cancer – second line after docetaxel

Target group

- Hormone refractory prostate cancer (HRPC): metastatic – second line; after docetaxel-based treatment.

Technology description

Cabazitaxel (XRP-6258) is a taxane anti-neoplastic agent. It works by disrupting the microtubular network that is essential for mitotic and interphase cellular functions and causes inhibition of cell division and cell death. Cabazitaxel in combination with prednisone is intended to provide a further treatment option for patients with progressive disease following or during docetaxel-based treatment. Cabazitaxel is administered by intravenous (IV) infusion at 25mg/m^2 every 3 weeks.

Innovation and/or advantages

There is no approved agent for men with metastatic HRPC who have progressed during or after a first-line chemotherapy treatment. Cabazitaxel has shown a promising safety profile and activity in patients progressing after docetaxel therapy.

Developer

Sanofi-aventis.

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 appraisal. Docetaxel for the treatment of hormone refractory metastatic prostate cancer. 2006[1].
- NICE clinical guideline. Prostate cancer: diagnosis and treatment. 2008[2].
- NICE cancer service guidance. Improving outcomes in urological cancers - Manual. 2002[3].
- NICE interventional procedure guidance. High dose rate brachytherapy for prostate cancer. 2006[4].
- NICE interventional procedure guidance. Cryotherapy as a primary treatment for prostate cancer. 2005[5].
- NICE interventional procedure guidance. Low dose rate brachytherapy for localised prostate cancer. 2005[6].
- NICE interventional procedure guidance. Cryotherapy for recurrent prostate cancer. 2005[7].
- NICE interventional procedure guidance. High-intensity focused ultrasound for prostate cancer. 2005[8].

- Department of Health Service guideline. Advice on the development of low dose rate (permanent seed implant) brachytherapy services for localised prostate cancer in England. 2006[9].
- The Royal College of Pathologists. Service guidance. Dataset for tumours of the urinary collecting system (Renal pelvis, ureter, bladder and urethra). 2007[10].

- European Association on Prostate Cancer. Guidelines on prostate cancer. 2007[11].

Clinical need and burden of disease

Prostate cancer is the most common cancer diagnosed in men in the UK, with 31,135 new cases registered in 2005 in England and Wales[12]. More than 60% of cases are diagnosed in men over the age of 70. There were 9,052 registered deaths from prostate cancer in England and Wales in 2006[13], accounting for approximately 13% of male cancer deaths. It is estimated that most of these deaths occur in patients with HRPC[1], although epidemiological data for HRPC is limited. Metastatic disease occurs in 55-60% of prostate cancer patients, for whom androgen deprivation is the main treatment. However, this is essentially palliative and all patients will eventually become resistant to hormone therapy at which point the prognosis becomes extremely poor (median survival 7-15 months[14]).

Existing comparators and treatments

The aim of treatment for men with metastatic HRPC that has progressed during or after a docetaxel-based treatment, is to improve symptoms, slow progression of the disease and prolong life. Clinical management is acknowledged to be multimodal rather than sequential, and patients may receive a combination of palliative treatments[1].

Management options include:

- Additional hormonal therapy (e.g. diethylstilbestrol).
- Mitoxantrone with or without steroids - widely used for patients who are fit for chemotherapy (not licensed for this indication).
- Docetaxel (Taxotere) re-challenge in patients initially responsive to docetaxel.

Efficacy and safety

Trial	TROPIC, NCT00417079[15]: XRP-6258 with prednisone vs. mitoxantrone with prednisone; phase III.
Sponsor	Sanofi-aventis.
Status	Ongoing.
Location	EU (inc UK), USA, Canada and other countries.
Design	Randomised, open-label.
Participants and schedule	n=720; prostate cancer previously treated with docetaxel; documented progression of disease; surgical or hormone-induced castration; life expectancy > 2 months ECOG PS[a] 0-2. Randomised to mitoxantrone (IV) and prednisone (oral) or XRP-6258 (IV) and prednisone (oral), every 3 weeks until disease progression, death, unacceptable toxicity, or for a maximum of 10 cycles.
Follow-up	Maximum 2 years.
Primary outcome	Overall survival.
Secondary outcomes	Progression free survival, overall response rate, prostate-specific antigen (PSA) response/ progression, pain response/ progression, overall safety, and pharmacokinetics.
Expected reporting date	May 2010.

[a] The ECOG PS (Eastern Cooperative Oncology Group Performance Status) scale assesses a patient's disease progression, living abilities, and determines appropriate treatment and prognosis. The scale runs from 0-5 with: 0=asymptomatic; 1=symptomatic but completely ambulatory; 2=symptomatic, <50% in bed during the day;

Estimated cost and cost impact[b]

The cost of cabazitaxel is not yet known. The cost of 6 cycles (18 weeks) of docetaxel at a dose of 75mg/m^2 IV every 21 days for metastatic HRPC is £5,262[16].

Potential or intended impact – speculative

Patients

☑ Reduced morbidity	☑ Increased length of survival	☐ 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: e.g. length of stay, out-patient visits	☐ Service reorganisation required	☐ Staff or training required
☐ 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: Additional therapeutic option	☐ Savings:	☐ Other:

References

[1] National Institute for Health and Clinical Excellence. Docetaxel for the treatment of hormone-refractory metastatic prostate cancer. Technology Appraisal TA101. London: NICE; June 2006.

[2] National Institute for Health and Clinical Excellence. Prostate cancer: diagnosis and treatment. Clinical guideline CG58. London: NICE; February 2008.

[3] National Institute for Health and Clinical Excellence. Improving outcomes in urological cancers - Manual. Cancer service guidance. London: NICE; September 2002.

[4] National Institute for Health and Clinical Excellence. High dose rate brachytherapy for prostate cancer. Interventional procedure guidance IPG174. London: NICE; May 2006.

[5] National Institute for Health and Clinical Excellence. Cryotherapy as a primary treatment for prostate cancer. Interventional procedure guidance IPG145. London: NICE; November 2005.

[6] National Institute for Health and Clinical Excellence. Low dose rate brachytherapy for localised prostate Cancer. Interventional procedure guidance IPG145. London: NICE; November 2005.

[7] National Institute for Health and Clinical Excellence. Cryotherapy for recurrent prostate cancer. Interventional procedure guidance IPG119. London: NICE; May 2005.

[8] National Institute for Health and Clinical Excellence. High-intensity focused ultrasound for prostate cancer. Interventional Procedure Guidance IPG118. London: NICE; May 2005.

[9] Department of Health Service guideline. Advice on the development of low dose rate (permanent seed implant) brachytherapy services for localised prostate cancer in England. November 2006.

[10] The Royal College of Pathologists. Service guidance. Dataset for tumours of the urinary collecting system (Renal pelvis, ureter, bladder and urethra). January 2007.

[11] European Association on Prostate Cancer. Guidelines on prostate cancer. March 2007

[12] Cancer Research UK. UK prostate cancer incidence statistics 2009. http://info.cancerresearchuk.org/cancerstats/types/prostate/incidence/ Accessed 17 March 2009.

[13] Cancer Research UK. UK prostate cancer mortality statistics 2009. http://info.cancerresearchuk.org/cancerstats/types/prostate/mortality/ Accessed 17 March 2009.

[14] Dowling AJ, Tannock IF. Systemic treatment for prostate cancer. Cancer Treat Rev. 1998; 24:283-301.

[15] ClinicalTrials.gov. XRP6258 plus prednisone compared to mitoxantrone plus prednisone in hormone refractory metastatic prostate cancer (TROPIC). http://www.clinicaltrials.gov/ct2/show/NCT00417079?term=XRP-6258&rank=1#locn Accessed 08 April

2009.
16 National Institute for Health and Clinical Excellence. Prostate cancer (hormone-refractory) - docetaxel: analysis of cost impact London: NICE; September 2006. http://www.nice.org.uk/guidance/index.jsp?action=download&o=33354 Accessed 08April 2009.

The National Institute for Health Research National Horizon Scanning Centre Research Programme is funded by the Department of Health.
The views expressed in this publication are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health

The National Horizon Scanning Centre,
Department of Public Health and Epidemiology
University of Birmingham, Edgbaston, Birmingham, B15 2TT, England
Tel: +44 (0)121 414 7831 Fax +44 (0)121 414 2269
www.pcpoh.bham.ac.uk/publichealth/horizon