

National Horizon Scanning Centre

Pazopanib (GW786034) for advanced and/or metastatic renal cell carcinoma – first/second line

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Pazopanib (GW786034) for advanced and/or metastatic renal cell carcinoma – first/second line

Target group

- Renal cell carcinoma (RCC): advanced and/or metastatic (grade III/IV) – first and second line therapy.

Technology description

Pazopanib hydrochloride (GW786034) is an oral multi-targeted tyrosine kinase receptor inhibitor with anti-tumour activity. Pazopanib inhibits vascular endothelial growth factor receptor (VEGFR) -1, -2 and -3, platelet-derived growth factor receptor (PDGFR), and c-kit, which may result in inhibition of angiogenesis in tumours in which these receptors are upregulated. Pazopanib is administered at 800mg once daily as monotherapy.

Pazopanib hydrochloride is also in phase II/III development for breast cancer, and in phase II trials in patients with gynaecological cancer, non-small cell lung cancer, peritoneal cancer, nasopharyngeal cancer, pancreatic cancer, soft tissue sarcoma, and glioma.

Innovation and/or advantages

Pazopanib may have advantages over oral multi-targeted tyrosine kinase receptor inhibitors currently licensed (sunitinib and sorafenib) in improving efficacy and/or tolerability in patients with metastatic RCC.

Developer

GlaxoSmithKline Ltd.

Availability, launch or marketing dates, and licensing plans:

Pazopanib for RCC is a designated orphan drug in the EU. Pazopanib is in phase III clinical trials.

NHS or Government priority area:

This topic is relevant to the NHS Cancer Plan (2000).

Relevant guidance

- NICE multiple technology appraisal in development. Bevacizumab, sorafenib, sunitinib and temsirolimus for renal cell carcinoma. Expected January 2009¹.
- NICE interventional procedures guidance. Cryotherapy for renal cancers. 2007².
- NICE interventional procedures guidance. Percutaneous radiofrequency ablation of renal cancer. 2004³.
- NICE guidance on cancer services. Improving outcomes in urological cancers – the manual. 2002⁴.
- National Comprehensive Cancer Network. Clinical practice guidelines in oncology: kidney cancer. 2008⁵.
- European Association of Urology. Guidelines on renal cell carcinoma. 2007⁶.
- Cancer Care Ontario - Program in Evidence-Based Care. Clinical practice guideline. Interleukin-2 in the treatment of patients with unresectable or metastatic renal cell cancer. 2006⁷.

Clinical need and burden of disease

Kidney cancers account for around 2% of all cancers in the UK. In 2004, there were 6,180 new kidney cancers diagnosed in England and Wales, of which an estimated 85-90% (5,253-5,562 cancers) were renal cell carcinomas^{1,8}. In 2005, there were 3,134 registered deaths from kidney cancer in England and Wales⁹. RCC is nearly twice as common in men as in women, and most commonly affects adults aged 50-80 years.

Approximately 25% of patients present with advanced and/or metastatic disease (stage III or stage IV), representing around 1,300-1,390 new patients per year¹⁰. In addition, an estimated 50% of patients who have curative resection for earlier stages will develop recurrent and/or metastatic disease (up to around 2,000 patients)¹. Without treatment, median survival is only 6-12 months, and the two-year survival rate is 10-20%¹¹.

Existing comparators and treatments

Advanced and/or metastatic RCC is largely resistant to both hormonal and chemotherapy. The standard treatment is immunotherapy with interferon alpha (IFN-alpha), and less commonly interleukin-2 (IL-2). Not all patients are suitable for immunotherapy. These therapies achieve overall response rates of 4-31%¹², and are often associated with severe morbidity (physical and mental side effects). There are currently no standard treatments for patients with metastatic disease who do not respond to immunotherapy.

Other licensed therapeutic options:

- Sunitinib (Sutent): first and second line therapy for advanced and/or metastatic RCC.
- Sorafenib (Nexavar): first-line therapy for RCC patients who are unsuitable for cytokine therapy or second-line therapy following cytokine failure.
- Temsirolimus (Torisel): an IV mTOR inhibitor, indicated as first-line therapy in patients with >3 poor prognostic indicators.
- Bevacizumab (Avastin): first-line therapy in combination with IFN.

Efficacy and safety

Trial code, name, phase	NCT00244764 ¹³ ; pazopanib vs placebo; phase II.	NCT00334282 ¹⁴ with extension trial NCT00387764 ¹⁵ ; pazopanib vs placebo phase III.
Sponsor	GlaxoSmithKline	GlaxoSmithKline
Status	Ongoing	Ongoing
Location	USA, Europe (inc. UK), Asia, Israel, Australia.	Europe (inc. UK), South America, Asia, New Zealand, Tunisia.
Design	Randomised, open label, placebo control.	Randomised, double-blind, placebo control.
Participants in trial	n=230; adults; locally recurrent or metastatic RCC; Eastern Cooperative Oncology Group (ECOG) 0 or 1; no prior treatment or refractory to cytokine or bevacizumab-containing regimen. Randomised to pazopanib 800mg or placebo. At week 12 all patients receive pazopanib in an open-label, single-arm extension study.	n=400; adults; locally advanced or metastatic RCC; measurable disease; no prior systemic therapy or only one prior cytokine based systemic treatment. Randomised to pazopanib 800mg or placebo.
Follow-up	Until disease progression.	Until death.
Primary outcome	Tumour growth and progression.	PFS.
Secondary outcomes	Progression-free survival (PFS), objective response rate, safety.	Overall survival, time to death, overall response rate, adverse events, quality of

		life.
Key results	Pazopanib treated patients at week 12 (n=225): partial and complete response 27%; stable disease 46%.	-
Adverse effects	Severe (grade 3-4) in 26%; grade 5 in <1%; 5% discontinuation due to adverse events.	N/A

Estimated cost and cost impact

The cost of pazopanib is not yet known. The cost of other licensed treatments are^a:

Drug name	Dose range	Annual cost
Interferon alpha	10 MU 3 times per week	£6,734
Sunitinib	50mg daily for first 4 weeks per 6-week cycle	£27,203
Sorafenib	400mg twice daily	£32,649

Potential or intended impact – speculative

Patients

- | | | |
|---|---|---|
| <input type="checkbox"/> Reduced morbidity | <input checked="" type="checkbox"/> Reduced mortality or increased survival | <input checked="" type="checkbox"/> Improved quality of life for patients and/or carers |
| <input type="checkbox"/> Quicker, earlier or more accurate diagnosis or identification of disease | <input type="checkbox"/> Other: | <input type="checkbox"/> None identified |

Services

- | | | |
|--|--|---|
| <input type="checkbox"/> Increased use | <input type="checkbox"/> Service reorganisation required | <input type="checkbox"/> Staff or training required |
| <input checked="" type="checkbox"/> Decreased use: oral administration | <input type="checkbox"/> Other: | <input type="checkbox"/> None identified |

Costs

- | | | |
|--|---|---|
| <input type="checkbox"/> Increased unit cost compared to alternative | <input type="checkbox"/> Increased costs: more patients coming for treatment | <input type="checkbox"/> Increased costs: capital investment needed |
| <input type="checkbox"/> New costs: | <input checked="" type="checkbox"/> Savings: oral monotherapy may enable outpatient use | <input type="checkbox"/> Other: |

References

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^a British National Formulary No. 55, March 2008.

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- ¹⁴ ClinicalTrials. GW786034 (pazopanib) in metastatic renal cell carcinoma. NCT00334282. Available at: <http://www.clinicaltrials.gov/ct2/show/NCT00334282?term=pazopanib&rank=2&flds=Xabej> (Accessed 14/04/2008).
- ¹⁵ ClinicalTrials. Extension study to VEG105192 to assess pazopanib in patients with advanced/metastatic renal cell cancer. NCT00387764. Available at: <http://www.clinicaltrials.gov/ct2/show/NCT00387764?term=pazopanib&rank=20&flds=Xabej> (Accessed 14/04/2008).

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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