Pazopanib for the first line treatment of advanced and/or metastatic renal cell carcinoma
Patient/carer Expert Statement.

General information.

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Background:
My late husband was diagnosed with advanced renal cell carcinoma (papillary type stage 4 with additional tumours in lungs, abdomen) in December 2005. He underwent a radical nephrectomy in January 2006 followed by treatment with interferon for 3 months, during which his tumours showed marked progression. In May 2006 he began treatment with sunitinib (Sutent) and was classified as being progression-free for 2 years. In May 2008 Sutent was no longer effective and the disease progressed rapidly. He died in June 2008. I am therefore aware of the benefits, side effects and their management and disadvantages of targeted therapies such as TKIs, which include sunitinib and pazopanib.

I strongly support approval of pazopanib for NHS funding
(a) on the grounds of clinical need
(b) as an end-of-life medicine
(c) because advanced renal cell carcinomas respond to different targeted therapies in a varied way. The nature of the disease means that a "one size fits all" approach is not best serving the needs of patients.

What do patients and/or carers consider to be the advantages and disadvantages of the technology for the condition?

1. Advantages

(a) Please list the specific aspect(s) of the condition that you expect the technology to help with. For each aspect you list please describe, if possible, what difference you expect the technology to make **and**
(b) Please list any short-term and/or long-term benefits that patients expect to gain from using the technology.

(i) Improved progression-free survival

Advanced rcc is largely resistant to radiotherapy, hormone therapy and chemotherapy. The chances of a cure at this stage of the disease are very slight and survival rates beyond 5 years very low. Targeted therapies such as pazopanib aim to slow down, halt or reverse tumour growth thus increasing time patients have with their families. The importance of this cannot be stressed enough and encouraging results from clinical trials show that pazopanib can significantly improve progression-free survival times (median PFS =11.1 months) compared with placebo (median PFS=2.8 months) when patients in both group had received no prior drug treatments.

(ii) Psychological benefits
Although treatments have side-effects (see later) it is possible to maintain a good quality of life and carry out “normal” day-to-day activities, including returning to work. Travel, even long distance, is a possibility and these opportunities give patients, carers and their families a more positive outlook
The potential to plan ahead is also helpful to all concerned.
Conversely, the damaging effects (anger, despair, depression) of knowing there is a possible life-extending treatment which, although licensed for use, is not available to the patient should not be underestimated. These negative aspects can also have an effect on carers and families.

(iii) Slowing of tumour growth
In the aggressive stages of the disease tumour growth (and subsequent decline in the patient’s wellbeing) can be rapid and controlling the effects of this can be difficult. By slowing the growth of tumours it may be possible to assess and control these aspects of advancing disease in a more measured way to the patient’s benefit.

(iv) Side effects
Although the lists of side effects produced by TKIs such as pazopanib are broadly similar, the severity of them differs from therapy to therapy. Pazopanib appears to be well-tolerated, with the symptoms being classified as mild to moderate. Some side effects which patients find very difficult to cope with (eg. blisters on hands and feet, sore mouth) appear to be less pronounced with pazopanib than with other TKIs (eg sunitinib)

(v) Method of action
As each TKI has a different selectivity profile and potency of kinase inhibition, pazopanib may work in some patients where other TKIs would not produce the desired slowing of tumour growth.
Likewise, pazopanib may be more suitable for patients with additional health conditions (not related to rcc) where other TKIs are not.

The comments above are based on my (and my husband’s) experiences with sunitinib, but my researches would indicate that the points are applicable to pazopanib.

2. <u>Disadvantages</u>
Please list any problems with or concerns you have about the technology.

(i) Limitations of technology
Pazopanib is not a cure and can at best delay tumour advance, perhaps for only a short time. Some patients may find the anxiety produced by this knowledge difficult to cope with.

(ii) Suitability
Not all patients will respond to pazopanib (see point v above) and, if approved for NHS use as a first line treatment, its use may exclude the possibility of further treatment with other TKIs (eg sunitinib, sorafanib)

(iii) Side effects
The most common side effects reported are diarrhoea, fatigue, nausea, vomiting and hypertension. Although most can be controlled to a great extent by appropriate medication

and life-style changes, it may take some time before the correct medication and dose is found. This period can be distressing and debilitating for the patient. Some patients will find these side effects unacceptable.

(iv) Potentially serious adverse events
Liver-related and arterial thrombotic events have been noted in clinical trials, as has serious haemorrhaging. Pazopanib would be unsuitable for patients at risk.

3. Are there differences in opinion between patients about the usefulness or otherwise of this technology?
This is a matter of personal choice. Some patients regard the use of this technology as "putting off the inevitable" and manage their disease in other ways. However I think many patients welcome the recent developments in the treatment of advanced renal cell carcinoma. We were astonished and encouraged by the advances made in the treatment of advanced rcc during the course of my husband's illness.

4. Are there any groups of patients who might benefit more from the technology than others? Are there any groups of patients who might benefit less from the technology than others?
As with many conditions, younger, initially fitter, patients may benefit more than substantially older patients with multiple additional health issues, who may find the side effects harder to tolerate.

Comparing the technology with alternative available treatments or technologies

(i) Please list any current standard practice (alternatives if any) used in the UK.

Sunitinib (Sutent) is the only TKI currently approved for NHS use as first line treatment for advanced rcc. However some 25% of patients with the condition do not tolerate sunitinib.
Interferon (immunotherapy) is still used but has a low response rate (less than 10%).
Bevacizumab, sorafenib, and temsirolimus are targeted therapies used to treat advanced rcc, but, although licensed, are not available through the NHS.
Interlukein 2 is effective in a very small number of patients

(ii) Advantages of technology over current standard practice

Better tolerance with potentially fewer, less severe side effects
Particular way in which pazopanib works may mean it is more suitable for some patients (ie better response)

(iii) Disadvantages over current standard practice
The disadvantages of each targeted therapy are broadly similar.

Availability of this technology to patients in the NHS

What key differences, if any, would it make to patients and/or carers if this technology was made available on the NHS?

It would improve the choice of therapies available to clinicians who can then choose the most appropriate treatment with the greatest chance of success. The potential benefit to patients and their families is obvious.

What implications would it have for patients and/or carers if the technology was not made available to patients on the NHS?

Reduced options for clinicians would reduce the chance of a positive treatment outcome.
Anger and frustration amongst patients and their families at the unavailability of a potential life-prolonging treatment.
Financial hardship amongst patients who feel they must pay for the therapy and associated treatments (scans, blood tests, consultations etc) privately
Possible impact on the development of new ways of treating advanced rcc.