

Axitinib for the treatment of advanced renal cell carcinoma after failure of prior systematic treatment

Patient/carer Expert Statement.

General information.

Name:

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Organisation:

I am a trustee of Kidney Cancer UK

Background:

My late husband was diagnosed with advanced renal cell carcinoma (papillary type stage 4 with additional tumours in lungs, abdomen) in December 2005. After a radical nephrectomy he eventually began treatment with sunitinib (Sutent) and was classified as “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 using TKIs. I have also talked at length to a patient who has been treated with axitinib for 2 years (as a second-line treatment after the failure of interferon-alpha) as part of a trial.

I strongly support approval of axitinib for NHS funding as a second-line treatment

- (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.
- (d) there is currently no NHS-funded treatment available after a first line treatment has failed

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

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 axitinib aim to slow down, halt or

reverse tumour growth thus increasing the time patients have with their families. The importance of this cannot be stressed enough.

Axitinib treatment led to a significant and clinically meaningful improvement in progression-free survival (median PFS = 6.7 months) compared with sorafenib (median PFS = 4.7 months) in patients with treatment-refractory renal-cell carcinoma (RCC) in a phase 3 study presented at the 27th Annual European Association of Urology (EAU) Congress (Feb. 2012). This study also demonstrated that axitinib is a more potent inhibitor of vascular endothelial growth factor (VEGF) receptors than other VEGF-targeted therapies currently available.

(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. ***My patient contact reported that he could pursue his usual activities (driving long distances, walking the dog, etc) with only minor changes to his routine to allow for the side effects of the treatment.***

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.

"I doubt I would be here now if I wasn't on this treatment" (direct quote from my patient contact).

(iv) Side effects

Although the lists of side effects produced by TKIs such as sunitinib, pazopanib and axitinib are broadly similar, the severity of them differs from therapy to therapy. Axitinib 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 axitinib than with other TKIs (eg sorafenib). The most common side effects reported were diarrhoea, fatigue and hypertension and ***my patient contact said he found the first 2 the most noticeable but they could be managed relatively easily.***

(v) Method of action

As each TKI has a different selectivity profile and potency of kinase inhibition, axitinib may work in some patients where other TKIs would not produce the desired slowing of tumour growth.

Likewise, axitinib may be more suitable for patients with additional health conditions (not related to RCC eg diabetes, high cholesterol) where other TKIs or everolimus are not.

As it is taken orally my patient contact found it much easier to administer than his previous (first-line) treatment, interferon-alpha, which was injected.

2. Disadvantages

Please list any problems with or concerns you have about the technology.

(i) Limitations of technology

Axitinib 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 axitinib (see point v above) and, if approved for NHS use as a second-line treatment, its use may exclude the possibility of further treatment with other TKIs (eg sunitinib, sorafenib)

(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

.Hypothyroidism and hypertension can be potentially dangerous. Axitinib would be unsuitable for patients at high 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. However, ***my patient contact is over 70 and continuing to benefit from treatment with axitinib.***

Comparing the technology with alternative available treatments or technologies

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

There is currently no drug recommended for NHS funding for second-line treatment of renal cell carcinoma. Everolimus is widely used as a second-line treatment but was not recommended by NICE (although acknowledged as being clinically effective) on the grounds that it was not cost-effective. Everolimus is sometimes available via the Cancer Drugs Fund, but this is not always so and any delay in progressing from a first-line to a second-line treatment can lead to a rapid deterioration in the patient's condition.

If recommended for NHS funding, axitinib would fulfil the need for an effective, readily available second-line treatment and it also represents a major step forward in the field of advanced kidney cancer treatment.

(ii) Advantages of technology over current standard practice

Better tolerance with potentially fewer, less severe side effects

The particular way in which axitinib works may mean it is more suitable for some patients (ie it may produce a better response with fewer side effects).

(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.

Jacqueline Lowe (Trustee, Kidney Cancer UK)

30th August, 2012