KIDNEY CANCER UK (KCUK)

SUBMISSION TO NICE

SINGLE TECHNOLOGY APPRAISAL (STA) OF AXITINIB FOR THE TREATMENT OF ADVANCED RENAL CELL CARCINOMA AFTER FAILURE OF PRIOR SYSTEMATIC TREATMENT

AUGUST, 2012

KCUK is delighted that there is now a further proven treatment option available to people living in the United Kingdom with advanced kidney cancer. It is pleased that this will provide great help to those whose disease has progressed following failure of prior systematic treatment. The availability of Axitinib is an important step in enabling this population of patients to have their disease further controlled.

KCUK strongly supports approval of Axitinib for NHS funding (1) on the ground of clinical need (2) as an end-of-life medicine and (3) because it breaks new ground with an innovative mode of action in the treatment of the disease.

We now consider these points in turn.

Clinical need

Some very encouraging results from clinical trials and other studies show that Axitinib has much to offer patients.

First of all it has been found that the relative potency of Axitinib is 40-450 times greater than that of the first–generation of VEGFR inhibitors (Sonpavde G et alia. 'Axitinib for renal cell carcinoma'. *Expert Opin Investig Drugs* 2008; 17:741-48.)

In a phase II study of patients with cytokine-refractory renal cell carcinoma, the objective response rate with Axitinib as a single agent was 45%, with a median time to progression of 15.7 months (Rixie O et alia. 'Axitinib treatment in patients with cytokine-refractory metastatic renal cell carcinoma: a phase 2 study'. *Lancet Oncology* 2007; 8:975-84.) In addition, in 2010 a phase III trial for previously treated renal cell carcinoma showed for Axitinib significantly extended progression-free survival when compared to the drug Sorafenib, 6.7 months as against 4.7 months (Rini B I et alia. 'Comparative effectiveness of Axitinib versus Sorafenib in advanced renal cell carcinoma (AXIS): a randomised phase 3 trial' *The Lancet* 2012; 379: 1245-55).

A further advantage with Axitinib is that is it is relatively well tolerated by patients. Its side effects are, for the most part, less troublesome than is the case with many other anti-cancer drugs. This is a very important consideration for patients, many of whom, especially the older ones, often present with other conditions as well as cancer.

With both greater potency and lesser side effects, Axitinib was earlier this year licensed both by the US Food and Drug Administration and by the European Medicines Agency.

End-of-life medicine

The Richards Review on *Improving access to medicines for NHS patients* made certain recommendations about end-of life medicines, recommendations which were taken up by the Government, appraised by NICE and implemented in the multiple technology appraisal of four kidney cancer drugs published in 2008. The recommendation of most crucial significance in the present context is the proposal for NICE to recommend drugs used as end-of-life medicines for rarer cancers, to recommend them even when their incremental cost-effectiveness ratios are above the £30,000 per QALY benchmark.

The criteria to be used in selecting drugs to which this may apply are put as follows.

First the drug must be licensed for the treatment of a patient population not exceeding 7,000 patients each year. Then the drug must be indicated for the treatment of patients with a diagnosis of a terminal illness and who are not, on average, expected to live more than 24 months. Finally, there must be sufficient evidence to indicate that the drug offers a substantial average extension to life compared to the current alternative treatment.

Axitinib meets these criteria very closely. It easily meets the patient population criterion. Annually in the UK there are about 8,000 new registrations of renal cell carcinoma, of which only some 40% present (or go on to present) with metastatic disease. Even amongst those with metastatic disease, only a certain proportion survives long enough to require second-line treatment. Thus Axitinib is to serve the needs of a small number of patients and can in this respect qualify as a ‘rarer’ cancer; and, as we are all only too painfully aware, the average life expectancy of patients receiving second-line treatment is below the 24 months figure.

Innovation

There is currently no drug recommended for NHS funding for second-line treatment of renal cell carcinoma (with Everolimus being previously been turned down as not cost-effective). Axitinib fulfils that need; and it also represents a major step forward in the field of kidney cancer.

It is clear that there are very likely to be a further set of drugs to deal with advanced kidney cancer. Currently there are around 25 to 30 of these drugs at various stages in their development. Innovation is proceeding apace; and a very important secondary benefit to come from the prescription of Axitinib is what can be learnt from applying the drug in practice. It is unfortunate but the UK has not been exactly the best country in the world in which to combat metastatic renal cell carcinoma. Patients have had more chances of gaining free access to new drugs if they were resident in North America or in many countries in Western Europe. The UK has often compared unfavourably against other countries in this respect. Even in countries such as Romania, Slovakia and the Czech Republic, as well as in Argentina and South Korea, patients often have greater chances of access to newly developed drugs. So in this respect the UK compares unfavourably, not just against countries at similar stages in development, but also against some less advanced countries. It is possible that these unfavourable comparisons are also reflected in international cancer survival rates. Some statistics recently released appear to indicate that, whilst survival rates are improving everywhere, other countries are tending to improve at a faster speed than is being achieved here in the UK. Of course there could be a whole host of reasons explaining why survival rates vary over time and from country to country. But it has more than just crossed our minds that variation in the speed at which new innovative anti-cancer drugs are taken up has got something to do with variation in survival rates. This is a general point affecting all forms of cancer, but it seems especially germane to kidney cancer where the improvement in survival rates has been so disappointingly slow.

Everything should be done to encourage innovation here.

* * * * *