SUBMISSION TO NICE

HEALTH TECHNOLOGY APPRAISAL

BEVACIZUMAB, SORAFENIB, SUNITINIB AND TEMSIROLIMUS

This submission is being made jointly by the organisations Kidney Cancer UK and the James Whale Kidney Cancer Fund. Both of these organisations feel strongly--very strongly--that this new class of targeted drugs should be approved for routine funding on the NHS.

As patient-centred organisations Kidney Cancer UK and the James Whale Fund do not feel medically qualified to offer comment on the available evidence of clinical efficiencies, except to say that we are most impressed by it and to agree with those who interpret the evidence as showing that the new targeted drugs are ushering in a 'revolution' in the treatment of metastatic Renal Cell Carcinoma (mRCC). We understand that other (professional) bodies are making submissions on the clinical aspects. Hence it seems appropriate for us to focus on patients' perspectives on the central issues involved.

Both patient organisations feel that the new drugs should be made available on the basis of their activity. And they are appalled at the inequality of access across the country, when patients' life expectancies can largely be determined by their post-codes.

SURVIVAL RATES

It should surprise nobody that to patients, the most important of all concerns is that of their survival. Until recently patients with mRCC had little or no reason to be hopeful. The disease is highly resistant to chemotherapy and radiation. Treatment with the immunotherapy drug Interferon Alpha does have a modest effect in prolonging survival. Interleukin 2 is not proven to increase survival and has substantially more side effects. The evidence appears to be mounting that the new-targeted drugs do significantly lengthen survival, certainly progression-free survival and probably overall survival too. For example, trial results indicate a median progression-free survival of 11 months for Sunitinib compared with one of 5 months for Interferon, a more-than-doubling effect of the new drug.

Another point is that significantly more patients appear to derive benefit from the new drugs as compared to Interferon. So, in short, the most important facts about the new drugs are that they (a) help more people and (b) help them for longer.

Patients are aware that neither the immunotherapy drugs nor the new-targeted drugs lead to totally curative outcomes. Patients with advanced mRCC realise that one-day they may die from the disease (unless they die from some other cause beforehand). They also realise that, in common with other cancer patients in similar circumstances, the drugs treatment administered to delay the growth/spread of tumours generates some adverse side effects, which they will have to tolerate. Nonetheless they welcome being treated by these drugs because, as the saying goes, 'where there's life, there's hope'. They may hope that provided they can stay alive long enough, some new 'magic bullet' producing curative outcomes may be discovered. Whatever the likelihood of any such discovery, there is absolutely nothing wrong in patients entertaining hopes of it. After all, hope is supposed to be one of the three cardinal virtues.

SIDE EFFECTS

A further advantage with the new-targeted drugs is that they are much more easily tolerated, with the side effects more bearable or more easily managed. From all accounts the toxic effects of high-dose Interleukin are such that, in order to put up with them, a patient could do with the constitution of a highly trained olympic athlete! But the effects of the new-targeted drugs are much less difficult to live with and patients are very conscious of this. It is true that there are still some adverse effects, eg Sunitinib leads to diarrhoea, high blood pressure, hard-foot syndrome and occasional vomiting. But, a very large majority of patients can tolerate these effects well enough to stay on treatment.

Bearing in mind that many mRCC patients, by reason of age, often present with other medical problems, any reduction in adverse side effects is a most valuable benefit. Judging by posts entered on the forums of Kidney Cancer UK and the James Whale Fund websites, where notes are exchanged on various problems associated with treatment, patients do appear to be getting along with the side effects of a drug like Sunitinib quite well.

INTERNATIONAL COMPARISONS

The UK is not exactly the best country in the world in which to combat mRCC. Patients have more chance of gaining free access to the new drugs if they are resident in North America or in other countries of Western Europe like, for example, Sweden which has a very similar health service to that in the UK. (In Sweden there is a body equivalent to NICE; and this Swedish authority has already approved both Sunitinib and Sorafenib as suitable for state funding).

Similar provisions obtain in France, the Netherlands and in countries like Argentina, Mexico and South Korea. So in this respect the UK compares rather unfavourably, not just against countries at a similar stage of development, but also against some less advanced countries. It is clear there are wide inequalities between the UK and other countries. Amongst patients there is obviously a swell of anger and concern that the quality of care is markedly better elsewhere and that life expectancies of kidney cancer patients abroad are longer than those of patients who live in the UK.

It is possible that these unfavourable comparisons are also reflected in international comparisons of 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 over our minds that variation in the speed at which new 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.

'POST-CODE LOTTERIES'

If the UK as a whole is not a particularly good place for mRCC patients, there are some places within it that are worse than others. Some PCT's have shown themselves willing to fund Sunitinib and Sorafenib, the two drugs that already have their marketing authorisations from the European Agency for the Evaluation of Medicinal Products (EMEA). At the same time, other PCT's have steadfastly refused to fund in the absence of a 'cost-effectiveness badge' from NICE or the equivalent bodies in Wales and Scotland. There seems to be, from a patient's point of view, something of a 'hawks and doves' situation here. It can depend crucially upon exactly where you live, ie in which PCT area, whether or not you are going to get NHS funding. In this context the twelve PCT's in the North East of England which have decided, as a group, to fund the drug Sunitinib routinely for all patients appear as doves, whereas just across the border the North Yorkshire PCT might be cast as a hawk. A stark illustration of post-code variation occurred when a patient living in Richmond, seven miles over the border from one of the North East PCT's now funding Sunitinib for all patients, was refused similar funding by North Yorkshire PCT.

Post-code variation not only appears rather anomalous, it can also seem manifestly unfair.

UNFAIRNESS

The present system governing access to new drugs can appear unfair in other ways as well, maybe not by intent but certainly in effect. And the system can bear spectacularly unfairly upon kidney cancer patients. After all these are patients who may not— for the most regrettable of reasons— constitute much of a charge on NHS funding in other respects. The median age at contracting kidney cancer is 62.4 years. Many people reaching this age will have clocked up 40+ years of National Insurance contributions; and yet they may not be able to look forward to receiving the state pension for the same period of 15 years or more than other people can expect. From a broader perspective the expenditure of large sums of money on new drugs for individual patients does not amount to any great largesse that it may seem at first sight. A further important point here is that because of the very lack of alternative treatment options, the amount of NHS money spent per kidney cancer patient is far less than that spent on the rest of patients with advanced cancer, for many of whom there are multiple lines of treatment.

The new drugs can work out rather expensive on a per-patient basis. Most patients in the UK do not carry private medical insurance; and even if they did it is not always certain that the insurer will cover the (full) cost of drugs not approved as cost-effective. Many patients simply do not have the financial resources to fund treatment for what, it might now fervently be hoped, will be a considerably longer period of time. Some who have been refused funding by their PCT's, like selling (or at least re-mortgaging) their homes, or commuting annual pensions into immediate lump sums. But these courses of action can of course affect other members of the patient's family and consequently cannot be entered into lightly. (In one instance, a patient suffering with mRCC and initially refused funding by his PCT spent up to £27,000 out of savings before the issue became one of selling his house. The patient drew the line at this, because of the impact upon his wife. But happily an appeal to his PCT resulted in the funding decision being reversed).

On top of all this, if a patient chooses to self-fund purchase of a new drug, he/she might then be classed as a private, as opposed to NHS, patient. As a result he/she could be made responsible for the *total* cost of treatment, not just the drug itself. Given that the total costs might include the costs of blood tests, scans, clinician's fees and even the full cost of any further hospitalisation, it is clear that this is rapidly entering the realms of impossibility for many patients.

Another concern lies with the process by which a patient applies to the PCT to be funded as an 'exceptional needs' case. The application process can seem rather formidable. It's like the patient is applying for some kind of job—and a pretty exalted one at that! In addition to a reasoned case set out by the patient's consultant, the application might also contain a supporting statement from somebody like the patient's constituency MP. Then the patient might appear before the relevant panel in the PCT that decides on these things to offer some verbal arguments. And it is not unknown for a patient to arrive for this armed with a PowerPoint presentation. But many patients may feel ill-equipped to do all this and may therefore be deterred from entering an application at all.

THE COST PER QALY BENCHMARK

Many patients question the appropriateness of deciding upon the economic worth of a new drug on the basis of its cost per Quality Adjusted Life Year, QALY, an upper bound, if not limit, for which has been set at £30,000.

The use of a QALY concept in this context raises in our minds a veritable multitude of questions. Here we content ourselves with just a few. To begin with, why £30,000? Why not £60,000? Or why not £90,000? In an article in *The Times* in January last year the Chairman of NICE admitted the £30,000 figure is pretty arbitrary. It seems to be set more in line with what the NHS can currently afford than with any true assessment of the overall *net benefit* of the new treatment. To get that, one really needs a full-blown cost-benefit analysis. In a cost-effectiveness analysis the accent is, naturally enough, very much on costs. In a cost-benefit analysis the evaluation is more even-handed, asking the question whether, *in total*, the benefits of a new drugs treatment are greater than the costs.

Does a QALY represent total benefits? In our view it does not. Consider the case of a patient who on learning that her exceptional-needs case for Sunitinib funding had been accepted and that, as she saw it, she was now going to have an extra year or two to live, spoke very enthusiastically about her plans. One was struck forcibly by the rigour with which she had thought things through. Of course, having cancer often does have the effect of concentrating the mind wonderfully. But in the mind of this patient, the concept of a Quality Adjusted Life Year has only a very limited meaning. The benefits of remaining alive are much, much more than that. The problem is that the 'much, much more' plays no part in the evaluation at all.

If there is a question over what is left out from the benefits side, there is also a question of what is included on the costs side. The query here concerns the treatment of any taxes paid. The costs of acquiring the new drugs should, in an economic analysis of public expenditure, exclude all taxes. For these are not real resource costs, merely transfer payments, from the purchasers of the drugs to the government. Hence the 17.5% VAT an NHS hospital pharmacy has to pay on purchase of Sunitinib and Sorafenib should not, for the purpose of economic evaluation, enter into measurement of the costs of these new drugs. If taxes are not excluded, then real resource costs are being over-estimated.

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16th January 2008