KIDNEY CANCER UK / JAMES WHALE FUND FOR KIDNEY CANCER

SUBMISSION TO NICE

HEALTH TECHNOLOGY APPRAISAL

BEVACIZUMAB, SORAFENIB, SUNITINIB AND TEMSIROLIMUS

Some Comments on the Appraisal Consultation Document (ACD)

August, 2008

Kidney Cancer UK and the James Whale Fund for Kidney Cancer are both most disappointed with the Appraisal Committee's preliminary recommendations that none of the drugs appraised should be NHS treatment options for advanced and/or metastatic renal cell carcinoma. In responding to Dr Longson's letter of 30 July we have arranged our comments under the general headings beneath which the Appraisal Committee is said to be interested.

Do you consider that all the relevant evidence has been taken into account?

No

The ACD contains little or no discussion of the latest empirical evidence on the clinical effectiveness of the new drugs, evidence that was presented at the 2008 Annual Meeting of the American Society of Oncologists. In particular it takes little or no account of the most recent results for sunitinib. These are presented in a paper by Figlin et alia and published in the *Journal of Clinical Oncology,* May 20 supplement, ASCO Abstract 5025. The results demonstrate, very clearly, that median overall survival for patients who received protocol therapy, and no subsequent therapies, was 28.1 months with sunitinib as compared with 14.1 months with interferon-alpha. So, overall survival data representing more than two years has been achieved in the first line setting of advanced and/or metastatic renal cell carcinoma; and this doubling in overall survival is of huge benefit to patients; and so this should be fully reflected in any economic analysis of the new drug.

Evidence on patient benefits has scarcely been considered in the ACD, compared with the enormous amount of space devoted to discussion of the evidence on costs. In our view the central measure of a QALY is a woefully inadequate measure of patient benefit, calibrated as it on the basis on a number of truly heroic assumptions. Patient benefit encompasses far more than a QALY, something that was argued in the submissions from the patient experts. It is disappointing that the views of the patient experts have been almost totally disregarded in the evaluation of the new drugs. (Apart from a single oblique reference in paragraph 4.4.2, the ACD contains nothing at all on the views of the patient experts.)

Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate?

No

The main reason is that the comparisons do not fully reflect vast differences in the ability to control disease as between the new drugs and the present immunotherapy treatment using interferon-alpha. Only 20 per cent of patients have significant tumour

shrinkage on interferon-alpha, whereas modern treatment can reverse this miserable situation with as few as 20 per cent of patients having significant tumour growth on the new drugs.

In short, the new drugs both help more people *and* help them for longer. And this major advantage is not really represented in the ACD.

Do you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS?

No

If adopted, the provisional recommendations would result in large numbers of premature deaths.

They could also have some detrimental effects on incentives to innovate in the treatment of kidney cancer. Calculation of incremental cost effectiveness ratios (ICERs) is in all cases swamped by massive differences in drug acquisition costs. Taking just one example, sunitinib vs interferon-alpha, the £2,952 cost for interferon is playing against a cost of £34,012 for sunitinib (Table 44, page 152 in the Evaluation Report). Why such a large difference? Of course interferon has been in use for a long time and become relatively inexpensive once it was out-of-patent and, after 1980, when some technical advances permitted its mass production from bacterial cultures. By contrast sunitinib is in an entirely new class of drugs, only comparatively recently introduced and still having the burden of recovering substantial R&D expenditures, incurred not just for the drug itself but for all other drugs the company experimented with which did not make the grade. These expenditures have of necessity been large because of the amount of research needed to combat a lethal disease so very difficult to treat with other medications. Huge differences in drug acquisition costs dominate the arithmetic of the incremental analysis, to such a great extent that differences in other factors have only minor effects on calculated ICERs. It might be expected that, in the fullness of time, the costs of the new drugs will fall just as interferon's have. But it is troubling that in the meantime incremental analysis might serve to hold back unduly the march of progress in the area.

When this point is coupled with the point that patient benefits are inadequately represented in the analysis, the basis for the Appraisal Committee's recommendations looks very far from sound. A more academically respectable approach to the evaluation would have involved calculation of net present values (NPVs) in a full-blown cost-benefit analysis. Admittedly, NPV calculations would be much more difficult to make, given that they would require direct valuation of patient benefits. But in this─ as in everything else of course─ there is more to be said for *rough* estimates of the *precise* concept than for *precise* estimates of some *rough* concept. ICER per QALY is a pretty rough concept; and in the ACD, ICERs are solemnly, and most precisely, given down to last £1.

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Kidney Cancer UK and the James Whale Fund urge the Institute to review all the evidence NOW. We are horrified at the proposal for reconsidering the technology in July 2011. This might mean that a reconsidered final report would not be available until December 2013. That would be a unconscionably long time to wait in the circumstance of a very fast rate of development in this field.