James Whale Fund for Kidney Cancer

Appeal Against the Final Appraisal Determination Document: Bevacizumab, sorafenib, sunitinib (second-line) and temsirolimus for the treatment of advanced and/or metastatic renal cell carcinoma

12th May 2009

The James Whale Fund for Kidney Cancer wishes to appeal against the NICE Final Appraisal Determination Document (FAD) which prevents the use by the NHS of bevacizumab, temsirolimus, sunitinib (second-line) and sorafenib. This appeal is on the basis that NICE has failed to act fairly and has reached illogical and perverse conclusions as set out below. The Fund is appealing on behalf of patients and families who are, or will be, affected by kidney cancer.

1. **Bevacizumab**

   We appeal here on Ground One – procedural unfairness. Bevacizumab in combination with interferon-α (IFN-α) is licensed for the first-line treatment of advanced and/or metastatic renal cell carcinoma.

   The Committee states that the tolerability of IFN-α is poor and therefore that the tolerability of bevacizumab in combination with IFN-α is poor. There is no evidence from patient groups that the combination of bevacizumab and IFN-α is poorly tolerated. The Committee is wrong to assume that the tolerability profile of single agent IFN-α is the same as bevacizumab/IFN-α. The Committee has failed to take into account evidence to indicate that the side effect profile of bevacizumab/IFN-α can be significantly ameliorated by an IFN-α dose reduction without compromising the efficacy of the bevacizumab/IFN-α combination.

   We believe that bevacizumab has been unfairly discriminated against in this instance, both because data relevant to it has not been taken sufficiently into account and because it has been judged on the basis of other data not specific to it.

2. **Sunitinib (second-line)**

   We appeal here on Ground One – procedural unfairness. The Committee has not recommended reimbursement of sunitinib for second-line treatment of advanced renal cell carcinoma, due to the lack of phase III clinical trial data.

   Although there are no randomised, controlled phase III clinical trials to support the use of sunitinib for the second-line treatment of advanced renal cell carcinoma, there are now significant reports and anecdotal evidence to

show activity of sunitinib in the second-line setting, both after cytokine and VEGF-directed therapies. The strength of these reports has led to second-line sunitinib treatment being included in UK, EAU and NCCN guidelines. The There are many cancers where therapies are widely used and the drug reimbursed in the absence of phase III data. Committee has in this instance failed to give significant weight to the body of clinical evidence demonstrating the benefit of sunitinib in this setting and has therefore unfairly discriminated against patients with advanced renal cell carcinoma.

3. Temsirolimus

We appeal here on Ground One – procedural unfairness.

The Committee agrees that temsirolimus has significant clinical activity and has been proven to be an effective treatment for patients with advanced renal cell carcinoma with poor prognosis. Temsirolimus has been shown to extend life expectancy by 50%; invaluable for both patients and their families. The Committee has therefore denied a proven active drug from a small patient group with no other therapeutic options under the NHS, leaving them to die untreated.

We argue that the Committee has acted unfairly by affording insufficient weight to data relating to the extension of life expectancy. Given the small number of patients involved and novelty of the drugs in question, grade one data is hard to come by at this stage. However, we understand that the Committee is bound to give due consideration to the best available evidence and this does demonstrate valuable efficacy for Temsirolimus.

4. Sorafenib

We appeal here on both Ground One – procedural unfairness, and Ground Two – perversity.

Sorafenib is the only drug with phase III comparative data in patients who are unsuitable for INF-α. As a result of the recommendations by NICE, this patient group is unable to receive either INF-α or sunitinib under the NHS, and have been denied a proven active drug where no other therapeutic options are available.

We argue that the failure to take account of the phase III data is procedurally unfair and, as a result, discriminates against Sorafenib in this instance.

The Committee rejected evidence of the clinical effect of sorafenib in patients unsuitable for INF-α from two large prospective, non-comparative studies due to limited, or no, clinical effect. This decision is illogical and perverse given that the evidence provided (subgroups from the phase III trial and the North America and European expanded access programmes) and its acceptance by the clinical community (e.g. EMEA indication and NCCN clinical guidelines). It appears that the Committee has rejected these studies because they are not fully published randomised clinical trials. It is illogical that such evidence is

acceptable to the clinical community and licensing authorities and yet unacceptable to the Committee. The Committee has failed to give significant weight to the body of clinical evidence demonstrating the effectiveness sorafenib in this setting. We argue that the resulting decision by the appriasal committee is i) procedurally unfair and ii) perverse, given its rejection of data regarded as of high quality by all other expert audiences.

Additional Points

We appeal here on Ground One – procedural unfairness.

In this FAD, the Committee has denied clinicians the ability to choose the appropriate therapy for patients with advanced and/or metastatic renal cell carcinoma under the NHS.

The guidance does allow for sunitinib to be prescribed as first-line treatment for patients with advanced and/or metastatic renal cell carcinoma. Patients for whom sunitinib is not a therapeutic option, however, either because of intolerance or co-morbidities (e.g. congestive heart failure, poor nutritional state, impaired mobility, hypertension) or because they are unsuitable for immunotherapy (due to e.g. organ impairment, presence of hepatic metastases, and contraindications such as liver dysfunction or brain metastases), are discriminated against and will not have any therapeutic option under the NHS.

The Appraisal Committee has not considered second-line treatments when first-line treatments fail or the patient is found to be intolerant. The guidance does not in consequence allow for second-line treatments to be reimbursed under the NHS.

The Committee was made aware that a large proportion of renal cell carcinoma patients will not benefit from sunitinib as a first-line treatment option and, therefore, have failed to consider the implications of their earlier guidance when considering the remaining drugs evaluated within the FAD and we believe this to be procedurally unfair.

We ask NICE carefully to weigh the points of appeal that we have raised and to provide us with the opportunity to expand on these points directly to the Appeal Committee in due course.

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Chief Executive
The James Whale Fund for Kidney Cancer