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**Dyddiad / Date:** **27 August 2008**

Dear Christopher

**Re: NICE's ACD on Bevacizumab, sorafenib, sunitinib and temsirolimus for renal cell carcinoma**

Following the recent publication of the assessment of bevacizumab, sorafenib, sunitinib and temsirolimus for the treatment of advanced and/or metastatic renal cell carcinoma, the Welsh Assembly Government would wish the following views to be taken into account during the consultation process. These views are informed by advice obtained from Wales-based oncologists working specifically in the field of renal cancer.

The response covers a number of issues:

- It is possible that the Health Technology Assessment used by NICE to evaluate sunitinib was done before the survival data from the pivotal study comparing sunitinib (S) with interferon (IFN) was presented at the Annual American Society of Clinical Oncology meeting at the beginning of June. The drug company provided NICE with these data as soon as they were available, however, it is the impression from reading the ACD published by NICE that they have not used the new data in their evaluation.
- If that is the case, we believe that the correct response from NICE should have been to delay their decision and ask the Health Technology Assessment team from the Peninsula Medical School to re-do their cost per QUALY calculations based on the real data rather than the modelled data that they used in the draft ACD.
- The reason that this is important is that many patients in both the S and IFN arms of that study received other treatments after they progressed either on IFN or S. In the group of patients who ONLY received either IFN or S, the average survivals were 14 months for IFN and 28 months for S. A doubling of average survival hardly represents "a few extra months of life" as reported in newspapers at the time of the assessment's publication. Within that study there were some patients who appeared to get long and sustained benefit from sunitinib. This assessment does not seem to take into account this particular group.
- It is likely that, on a population level, more benefit will be obtained from these drugs if patients are crossed over from one treatment to another if treatment fails, as there

is good evidence that second line responses occur. Overall, this is likely to improve the ICER for each drug. However, different approaches are required for patients of differing performance status.

- While the NICE report makes a reasonable estimate of the cost effectiveness as evident from the clinical trials, it does not predict the situation which will arise if the drugs are denied to patients. The quality of life of a patient who knows that he or she is being denied potentially life-prolonging therapy is extremely poor, particularly when the same treatment is available in other countries. It is likely that the most articulate patients would attempt to acquire the drugs through exceptionality claims through the LHB. The cost of the hundreds of appeals cases and possible further legal action which would result has not been calculated, but could run into millions and divert hospitals and commissioners from more important tasks. This is also a huge drain on health resources, with many extra consultations per patient devoted to explaining the situation. It is vitally important that this potentially chaotic situation is not allowed to continue, as virtually every patient with kidney cancer is now aware of the situation.
- It is also clear that the drugs are extremely expensive and that the existing resources cannot cover the cost. However, we believe there is no precedent for turning down drugs which have a survival benefit of around 6 months, whatever the cost.
- With treatment as expensive as this, it is reasonable that it is made available only under strictly regulated conditions. However, as there are many unanswered questions regarding clinical and cost effectiveness, a partnership between Department of Health/WAG research and development, drug company sponsorship and funding from research charities would be a sensible response. Programmes could be developed with NICE to make sure that appropriate clinical and health economic data are collected.
- Appropriate studies of these drugs may also identify whether surgical intervention is also necessary. Considerable cost saving could be incurred if nephrectomy was avoided (£10,000 per patient).
- Temsirolimus is accepted as a suitable treatment for poor performance status patients. It is metabolised to sirolimus. There is an oral formulation of sirolimus (rapamune) already in use as an organ rejection drug, which is a fraction of the cost of temsirolimus, and which gives equivalent or higher plasma levels than temsirolimus. Whilst accepting that the drug does not currently have a license for this indication, it again raises an issue of how situations such as this should be dealt with and what actions can be taken when a potentially much cheaper drug could be made available.
- Finally, this decision has caused dismay amongst oncologists working with renal cancer patients in Wales and is best expressed by a direct quote:

  > ‘All of us who do research into kidney cancer are completely astounded by the decision of NICE. In all the other Western European countries sunitinib is now the standard of care and most patients not only get first line treatment but second and sometimes third line treatment. By not allowing access to any of these new

drugs, the survival of patients with advanced kidney cancer in the UK will be the lowest in Europe.

I'm sorry that I appear passionate about this but those of us who have used these new treatments have patients who are alive with an excellent quality of life more than 3 years after started treatment. These patients would not be alive now if they had only had access to interferon'.

I hope that you will take these points into consideration within this consultation process.

Kind regards

Yours sincerely

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