Royal College of Physicians
11 St Andrews Place
Regent's Park
London NW1 4LE
Tel: +44 (0)20 3075 1560

www.rcplondon.ac.uk

Professor Carole Longson
Director, Centre for Health Technology Evaluation
NICE

[redacted]

By e-mail
TACommB@nice.org.uk

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Dear Professor Longson

Re: NICE STA: Prostate cancer (metastatic castration resistant) - abiraterone (following cytoxic therapy) - ACD

I write on behalf of the NCRI/RCP/RCR/ACP/JCCO who collaborate to produce joint response to NICE oncological consultations. We are grateful for the opportunity to respond to the above ACD and wish to make the following comments.

Has all of the relevant evidence been taken into account?

Yes

Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

There is agreement that Abiraterone is an effective, safe and well tolerated drug that prolongs life and improves quality of life. We note the difference of opinion between the company and the ERG on the precise details of cost effectiveness modelling and assignation of health Utility Values, but this is beyond the scope of our professional expertise. We have concerns that the ERG assumes that men who may be offered treatment with Abiraterone have a low Utility Value. Our experts would like to point out that these men generally have few co-morbidities otherwise they would not have been fit enough for the previous docetaxel. Any reduced functionality is generally due solely to their cancer. As a group, in our judgement, they are fitter than average for their years. Abiraterone clearly leads to an improvement in quality of life and pain scores in men with symptoms and delays onset of pain in asymptomatic men.

The steep fall off in the trial was a real event and our experts believe that it may represent the ability of the trialists to keep to the protocol and maintain patients on drug/placebo even though they were progressing clinically and biochemically. At 3 months radiological confirmation of disease progression would have resulted in a large number of patients coming off drug (placebo) at the same time point. We believe that this means patients are modelled to stay in the pre-progression state for longer in the prednisolone arm than happened in the trial and thus underestimated the real benefit of Abiraterone. We believe that Abiraterone is an innovative drug as it is the first in class of a biologically targeted agent aimed at inhibiting a key pathway in androgen biosynthesis. Studies with this agent have shown that prostate cancers, far from becoming 'hormone-resistant', remain androgen –driven and indeed are androgen super-sensitive, in that they synthesise and respond to low levels of their own androgen. Abiraterone is the drug that has led to a

redefinition of the disease states in prostate cancer (although our experts are consistently reminded that patients do not like the term 'castrate-resistant').

Another economic consequence of this appraisal would be that UK participation in future international cancer trials is significantly reduced, as NHS standard practice is significantly different from the rest of the international community. The patient representatives on the NCRI Prostate CSG feel particularly strongly about this, as an important issue additional to the concerns about the availability of the drug to suitable patients. For patients whose treatment would have otherwise been funded in a trials setting, the full costs will now fall on the NHS. This deserves to be modelled.

Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

No.

Our experts believe that there is a serious flaw in the reasoning within the ACD. The Committee accepted that Abiraterone met the criteria of an end-of-life medicine, but felt it did not qualify on the basis that it would be given to a lot of patients (para 4.19). This rule clearly discriminates against people suffering from common cancers (eg breast, prostate and lung cancer) and is unfair. We do not accept the conclusion of the Committee that Abiraterone was not 'licensed for a small population', as, under the definitions provided by NICE for end-of-life medications, a population is defined as small if it does not normally exceed 7000. In the ACD, NICE has failed to make any estimates of the numbers of patients who might be treated and exactly how big this population would eventually be. It has accepted, without question, Sanofi's estimates of this number at around 3300. Even if this figure were to rise by 20%, as is forecast (by the manufacturer), it would still be well below the 7000 threshold. If the figure of 3,300 is open to dispute, we suggest that NICE should do its own calculations. If the figure of 3,300 is accepted, then we conclude that the Committee has failed to follow its own guidance on this issue. Previous agreed end of life diseases have included a patient population of over 5000, and our view is that the total population of patients with prostate cancer who are fit enough to receive docetaxel falls well short of the approximately 10-12,000 who die of prostate cancer per year in the UK – in some regions it may be as few as 20% of that figure.

We accept that there may remain some doubt about the ICER. However, we believe that NICE and Janssen should consider innovative approaches to ensuring patient access to Abiraterone while the uncertainties re ICER are addressed.

It is disappointing that the Committee did not include an oncologist. As a consequence, it is not clear that the potential 'cost-benefits' of this novel treatment with a very favourable side-effect profile (as Abiraterone is not a chemotherapeutic agent in the traditional sense) have been appropriately acknowledged and considered. We feel that Abiraterone not only improves survival, but also very effectively controls symptoms and reduces skeletal related events. We believe it will reduce the resources required to look after these patients because of better symptom control.

Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of gender, race, disability, age, sexual orientation, religion or belief?

No.

Are there any equality -related issues that need special consideration and are not covered in the appraisal consultation document?

No.

Yours sincerely

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