Response from the British Uro oncology Group (BUG) to the NICE Appraisal Committee's preliminary recommendations on the use of abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen

22 February 2012

This reply is written on behalf of the British Uro oncology Group (BUG) and reflects the responses to the NICE Appraisal recommendations on the use of abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen. The reply summarises the responses of members from BUG who are all clinical or medical oncologists with a specialist interest in the management of urological malignancies.

The overall response from our membership was of great disappointment at this decision and the potential detrimental effects that it will have on our patients. The responses reflected an enthusiasm to prescribe abiraterone in view of the fact that data from COU-AA-301 show a significant survival advantage for men with castration resistant prostate cancer with progression after docetaxel chemotherapy as well as benefits in quality of life during therapy and improved pain control. The experiences of UK oncologists who have treated men with this stage of prostate cancer outside of a clinical trial has been reported as positive and reflect the trial results. There were also comments about how well the drug was tolerated and positive patient feedback.

BUG recently conducted a survey of 80 urological oncologists in the UK (publication in press in *Brit J Urol Int*) to evaluate current management strategies for patients with advanced prostate cancer in order to identify key considerations in the decision making process and to gain insights into the potential role of emerging therapies for future UK practice. The respondents had an average of 189 new referrals for prostate cancer each year, with 24% reporting >200 new referrals annually. There was consensus that there is currently no 'Standard of Care' in the management of patients with castration resistant prostate cancer who relapse after docetaxel chemotherapy. This demonstrates an area of unmet need in prostate cancer management and the requirement for development of new treatments for castration resistant disease after 1st line chemotherapy. Most respondents (78%) felt that their current clinical practice was likely to change over the next five years. The survey findings show an enthusiasm amongst UK oncologists to prescribe abiraterone. When asked about individual agents in late-stage clinical development at that time, **90%** expressed an interest in being able to prescribe abiraterone. 71% of respondents stated that they were very likely to be using abiraterone and a further **19%** stated that they would possibly use this compound in their future practice. Of all the emerging compounds, abiraterone was considered, by the responding urological oncologists to be the drug that they would most like to use in the future. In the survey, abiraterone was described as 'very promising' and likely to 'make a big impact'. Survey respondents indicated that their comments were based on their clinical trial experience of this agent, randomised trial results and reports in the scientific literature.

This enthusiasm for abiraterone in castration resistant prostate cancer has increased with further experience of prescribing from the Cancer Drugs Fund and this has been reflected by the number of positive responses we have received from our membership to support the use of abiraterone in clinical practice. Many members of BUG have also submitted individual responses to NICE.

The recent announcement that the Wales Medicines Strategy Group, has approved the use of abiraterone for men in the end stages of prostate cancer on the NHS in Wales has caused considerable concerns by oncologists with regard to inequity of care and 'postcode prescribing' in the UK. Oncologists have asked that the enormous disappointment expressed by many of their patients in the late stages of prostate cancer be passed on to NICE Committee.

It has been commented that there is a perceived disadvantage for men with prostate cancer and we received the following comment to include in this report:

- 'No other common tumour type is so disadvantaged in terms of lack of access to treatments that improve both quality and quantity of life with manageable (and in the case of abiraterone, minimal) toxicity'
- 'Even lung cancer has at least two lines of chemotherapy plus targeted therapy approved with far less benefit'.

We would be grateful if the NICE Appraisal Committee would consider the following comments.

The criteria used by the NICE Committee to reject abiraterone have been questioned by some BUG members and the recommendations have been criticised on the basis of some of the conclusions drawn.

The Committee agreed that the criteria related to short life expectancy (less than 24 months) without treatment and extension to life (at least 3 months) with treatment were met. However, the Committee concluded that ***abiraterone was not licensed for a small population***, and therefore considered that it does not meet the criteria for an end-of-life treatment.'

We are unable to find a definition of 'small population' and it seems unreasonable that a treatment of comparative cost-effectiveness is approved simply because it is for patients with rarer cancers.' There were several other comments that the population described by NICE who would be eligible for the drug was higher than that anticipated in clinical practice. The view of responding oncologists were that this was more likely to be approximately between 3,000 to 4,000 which could make a difference to the conclusion that abiraterone did not meet end of life criteria.

There were also comments regarding the membership of the NICE Committee: 'It is disappointing that the Appraisal Committee did not involve an oncologist, and consequently, it is not clear that the potential 'cost-benefits' of this novel treatment, with a very favourable side-effect profile, have been appropriately acknowledged and considered. Accordingly, it is worthwhile noting a comment in the submission from NCRI/RCP/RCR/ACP/JCCO: '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'.

The data provided by the commissioning expert state that 20-30% of patients with progressive prostate cancer post docetaxel chemotherapy are treated with mitoxantrone. This is not thought to be a reasonable alternative to abiraterone due to the fact that there is no known data for survival advantage with this chemotherapy regimen and there is considerable toxicity.

The cost of any new drug is of course important and as oncologists we acknowledge that we have a responsibility to prescribe any compound appropriately within its licence and only for the duration of response to therapy. There have been comments that it would be important to have defined end points as to when to withdraw abiraterone therapy. We concur with the opinion of the clinical specialists present at the review that it is very unlikely that abiraterone will be administered to men with an ECOG performance status of 2 and this is verified by the patients entered into the COU-AA-301 study where the minority of patients randomised (10%) were of this performance status. The inclusion and exclusion criteria used in the study are applicable and in keeping with routine clinical practice in the UK and those patients considered for abiraterone would be a similar population to those in the study. This is not consistent with the statement made by the NICE Appraisal Committee that patients treated in routine practice would be fitter than those in the study.

The NICE appraisal committee's rejection on the quality of life data for abiraterone has also been a cause for comment and some variation in opinion. It was accepted that health economic modelling is difficult to unravel and messy. We received the following comments: 'The randomised trial measured quality of life using a different instrument to that required by NICE. It also stopped measuring quality of life on treatment discontinuation so a uniform health utility value (derived from a Swedish study) was applied after that. It might be the case that the abiraterone patients had a different clinical course from the control arm after treatment discontinuation. The conversion of the trial quality of life measurements to the EQ-5D measure required by NICE adds more uncertainty. The quality of life and health utility values have not been adequately measured in the study and consequently the health economic modelling is full of uncertainties.

One BUG member stated that 'NICE has no choice but to make it assessment based on the poor quality cost-effectiveness evidence provided (even though the clinical effectiveness is beyond doubt). In the absence of robust cost-effectiveness data the only conclusion one can draw from this is that abiraterone is too expensive.'

There were other opinions that FACT-P is a reasonable quality of life measurement and accepted by many other authorities including the FDA. It is impossible to satisfy the demands of everyone in an International multi-centre study. The criticism by the NICE Appraisal Committee that quality of life was not recorded in the post progression state seems to be unfair as this is not an unusual situation in many similar studies investigating drugs in the end of life criteria. These statements should not detract from the strong evidence that the quality of life was strongly positive during treatment. Abiraterone has a clinical advantage with a significant overall survival benefit and improvements in pain scores and reduced skeletal events.

There has been considerable strength of opinion from UK oncologists that abiraterone is without doubt a very beneficial end of life drug which has shown good efficacy with minimal toxicity. It is felt that it should be considered by NICE to fulfil the criteria to be considered in this category.

Members of BUG have expressed disappointment and concerns that men with metastatic castration resistant prostate cancer may be denied an effective 2nd line agent that not only significantly improves life expectancy, but also quality of life during treatment if the NICE Committee does not reconsider their ruling for abiraterone.

We thank you for considering this submission and await your final decision.