­Sent by email to: [xxxxxxxx@icr.ac.uk](mailto:xxxxxxxx@icr.ac.uk) and [xxxxxxxxxx@rightangleuk.com](mailto:xxxxxxxxxx@rightangleuk.com)

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STAMPEDE Trial Chief Investigator

On behalf of the British Uro-Oncology Group

10 August 2020

Dear xxxxxxxxxxxxxx

**FINAL APPRAISAL DOCUMENT FOR ABIRATERONE FOR HIGH-RISK HORMONE-SENSITIVE METASTATIC PROSTATE CANCER**

Thank you for your letter of 27 July 2020 responding to my initial scrutiny views. This is my final decision on initial scrutiny.

**General comment**

You did not allocate your appeal points to a specific appeal ground in your appeal letter, but I explained in my initial scrutiny letter that I believed they would all fall to be considered under ground 2. I went on to explain why I did not consider points 2, 8, 9 or 10 to be valid appeal points for a number of reasons, including that much of the evidence to which you pointed in your appeal letter appeared wholly or largely to post-date the appraisal.

I remain of the view that the above appeal points are not valid under ground 2, as an appellant may only appeal under ground 2 if they consider that the recommendations in the final draft guidance cannot reasonably be justified from the evidence that was in fact presented to the Committee.

However, having considered your further submissions, I believe that your emphasis is now on whether the Committee unfairly excluded and/or failed to consider certain information. While I would repeat that NICE cannot be expected to receive new information or analysis once an appraisal has completed, I note that this appraisal is somewhat unusual in that the clinical trials were published and your evidence was provided in 2017, you were not asked to provide further input to the Committee before it published the FAD in 2020, and in the intervening period you say “much new information of high relevance to the assessment has become available which BUG strongly believes would and should influence the outcome”. You state that there is “highly relevant information that could have been available to the Committee had they asked for further evidence in the more recent meetings” and that “To have not done this seems to not be due process”.

You appear to suggest that the initial scrutiny response (to “rule out” evidence raised under points 2, 8, 9 and 10) was unfair under ground 1(a). It is not possible to appeal an initial scrutiny letter in this way; the grounds of appeal relate to the FAD. However, I consider your appeal points as expanded upon may now be stronger under ground 1 than ground 2. I set out my final decision in respect of each point below.

If in the light of developments in the appeal hearing a panel is satisfied that an appeal point presented under ground 1 would have been successful under ground 2 (or vice versa), the panel is free to make that finding. However, for the purposes of preparation for and conduct of the hearing it is important that I pass appeal points on only under grounds that I consider to be valid on the basis of the information you have provided.

**Ground 1(a): In making the assessment that preceded the recommendation, nice has failed to act fairly**

*Point 2 The statement “The cost-effectiveness estimates without a commercial arrangement are higher than the range normally considered a cost-effective use of NHS resources.” Is unreasonable*

I remain unpersuaded this is a valid appeal point under ground 2 for the reasons in my previous letter.

That said, I understand your response letter to suggest that the Committee failed to act fairly by not requesting and/or not considering the STAMPEDE group’s recent cost effectiveness analysis referred to in your appeal letter. I conclude this is a valid appeal point under ground 1(a).

*8 The conclusions on Health Economic Modelling and costs are unreasonable*

I remain unpersuaded this is a valid appeal point under ground 2 but I consider there is a limited but valid ground 1(a) point here for the reasons above. For the purpose of preparing for the hearing I decide that the right approach is to refer both your points 2 and 8 onwards as a single appeal point under ground 1(a).

*9 The treatment of QOL is unreasonable*

I remain unpersuaded this is a valid appeal point under ground 2 for the reasons in my previous letter, but I conclude there is a valid appeal point under ground 1(a) that the Committee failed to act fairly by not requesting and/or not considering the STAMPEDE group’s recently presented comparative quality of life data referred to in your appeal letter.

As to your new point that excluding the above data is “particularly harmful to older patients who will be relatively more likely to have severe side effects and quality of life impairment with chemotherapy” and therefore “discriminatory against older patients”, I do not agree that a failure to request and/or consider data is in itself discriminatory, however I accept it is arguable that this could have resulted in a final decision that has a discriminatory effect. I will therefore refer this to the appeal panel as a separate and additional appeal point under ground 1(a). You may also refer here to your argument that failure to account for COVID-19 has resulted in a discriminatory result on “ethnic grounds as well as age grounds”.

*10 COVID-19 should have been taken into account*

Again I am not persuaded that this is a valid appeal point under ground 2 because I understand there was no evidence presented to the Committee on the impact of the pandemic; I can see no arguable point under ground 2 that the recommendations “cannot reasonably be justified from the evidence that was presented to the Committee”.

However, having considered your response carefully, I conclude that there is a valid ground 1(a) point here. While I am mindful that it would be unrealistic to require a Committee to update itself constantly on the detail of a rapidly changing global pandemic, I am also mindful of the high vulnerability of this particular patient group to COVID-19. Given the specific subject matter of this particular appraisal I am prepared to refer your point to the appeal panel for consideration under ground 1(a).

**Ground 2: The recommendation is unreasonable in light of the evidence submitted**

*Point 1 The statement ““There are concerns that the trials may overestimate the effectiveness of abiraterone. This is because the treatments offered in the trials after the disease progresses do not reflect those offered in the NHS, where more people on standard care have effective treatments after their disease progresses than in the trials.” Is unreasonable”*

Already accepted as valid.

*Point 3 The statement “It is not appropriate to consider separately the clinical and cost effectiveness of abiraterone in combination in people who currently have ADT alone” is unreasonable*

Already accepted as valid.

*Point 4 “The statement “The clinical experts explained that people who have previously had docetaxel as first-line treatment in the hormone-sensitive setting can have docetaxel again (for up to an additional 10 cycles)” is unreasonable”*

Already accepted as valid.

*Point 5* “*The statement “The comparison of abiraterone and docetaxel suggest that there may be no difference in overall survival”. is unreasonable”*

Already accepted as valid.

*Point* *6 “The statement “The magnitude of OS benefit for abiraterone may be over-estimated” (section 3.6). is unreasonable”*

Already accepted as valid.

*Point 7 “The statement “Neither STAMPEDE nor LATITUDE likely capture all the benefit on overall survival of follow-on treatments used in NHS clinical practice” is unreasonable”*

Already accepted as valid.

Therefore my final view is that there are the following valid appeal points:

* a ground 1(a) point, related to your points 2 and 8, which is that the Committee failed to act fairly by not requesting and/or not considering the STAMPEDE group’s recent cost effectiveness analysis referred to in your appeal letter;
* a second ground 1(a) point, related to your point 9, which is that that the Committee failed to act fairly by not requesting and/or not considering the STAMPEDE group’s recently presented quality of life data referred to in your appeal letter;
* a third ground 1(a) point that the failure of the Committee to consider the STAMPEDE group’s recently presented quality of life data and/or COVID-19 resulted in a discriminatory decision;
* a fourth ground 1(a) point, related to your point 10, that the Committee failed to act fairly by not taking into account COVID-19; and
* six ground 2 points that are your original points 1, 3, 4, 5, 6 and 7.

Where there are multiple appellants, NICE shares the valid appeal grounds of each appellant with the other appellants to assist with preparation for the hearing.

NICE will be in contact with you regarding the administration of the appeal, which will be held orally.

Many thanks

Yours sincerely

Tim Irish

Vice-Chair

National Institute for Health and Care Excellence