Mr Tim Irish  
Vice Chair  
National Institute for Health and Care Excellence  
10 Spring Gardens  
London  
SW1A 2BU

10/07/2020

Dear Mr Irish,

**Re: Final Appraisal Determination - Abiraterone for newly diagnosed high-risk hormone-sensitive metastatic prostate cancer**

Prostate Cancer UK and Tackle Prostate Cancer are appealing against the recent Final Appraisal Determination that declined to recommend abiraterone in the above-mentioned indication. There are several points on which we base this appeal, covering the following grounds:

* Ground 1a – NICE has failed to act fairly
* Ground 2 – The recommendation is unreasonable in light of the evidence submitted.

Examining these in greater detail:

**Ground 1a: In making the assessment that preceded the recommendation, NICE has failed to act fairly by neglecting to consider inequalities of healthcare provision caused by its decision.**

Paragraph 2.4.4 of the ***Guide to the processes of technology appraisal*** shows that the process should consider “issues that are likely to affect the potential appraisal, including equality and diversity issues”. Section 3.15 of the Final Appraisal Determination (FAD) explains that its recommendations should apply to all with prostate cancer, including transgender women, then states that “No other equality issues were raised.” This is despite data shared with NICE by Prostate Cancer UK in May 2020 that demonstrated older age as a key factor in chemotherapy ineligibility for men diagnosed with stage IV prostate cancer. With docetaxel chemotherapy being inappropriately viewed as the current standard of care for all men with this stage of disease, our data provided a patient cohort with an unmet need that abiraterone could address. These men are aged between 70 and 80 and are missing out on the additional months of life made possible by chemotherapy. These men, where they have a diagnosis of high-risk metastatic prostate cancer, could be treated with abiraterone and not lose out on this life extension.

Publicly available data from Public Health England released in 2019 links age, stage of disease and treatment received across cohorts of prostate cancer patients from 2013-2017. Prostate Cancer UK analysed these data to understand docetaxel chemotherapy uptake in patient cohorts with stage IV disease by age, focusing specifically on the latest available treatments data from 2016.1 The results showed significant disparity in access to chemotherapy by age. 63.6% of men with a new diagnosis of metastatic prostate cancer aged under 70 receive chemotherapy. This starkly decreases to 21.9% for men aged over 70 and drops further to 5.7% for men aged 80 and above. These data reveal a cohort of men who are not receiving chemotherapy, strongly correlated with their increasing age. This effect parallels that of the uptake of radical prostatectomy by older men with localised disease, where Prostate Cancer UK’s analysis of other data in the Public Health England dataset shows a drop from 27% to 3% in the same age range. In both cases it is very unlikely that the sharp decrease in uptake by age is explained purely by patient choice, but by clinical decision over the physical burden on the patient from the treatment.

Prostate Cancer UK and Tackle Prostate Cancer therefore believe that the recommendation to not approve abiraterone facilitates age discrimination and therefore causes inequality of health provision based on a protected characteristic.

We are concerned that alternative, unreferenced data were used instead in the appraisal process. This outlined that ‘two-thirds of people presenting with metastatic hormone sensitive prostate cancer in England’ have ADT alone. We believe that this cannot be considered a robust evidence base on which to base a decision, especially as it represents a misleading over-simplification that cannot account for the high-risk metastatic population and is neither corroborated by a source nor indicative of the clinical practice that our more detailed data analysis has provided.

Sub-group analysis in LATITUDE suggests a benefit in overall survival for men aged 75 and older, with a hazard ratio of 0.86 (0.62-1.21) in favour of abiraterone.2 Although not statistically significant, which may be due to the small sample size, it shows a consistent treatment effect across the trial sub-groups and suggests that abiraterone can be tolerated in an older prostate cancer patient population and provide them with the potential for additional months of life that they will otherwise be denied. The NICE approvals for abiraterone in relapsed disease in contrast are “age blind” in its effect as abiraterone can be used in men pre-chemotherapy, many of whom never receive docetaxel.

This is supported by further evidence also not considered by NICE that shows abiraterone can provide a suitable alternative for older men ineligible for docetaxel chemotherapy. Presented in a poster at the genitourinary cancers symposium, ASCO in February 2020 and pending publication, *Comparative quality of life in patients randomised contemporaneously to docetaxel or abiraterone* shows average global quality of life (QoL) scores were statistically and clinically significantly higher for patients treated with abiraterone compared to docetaxel at 12, 24 and 104 weeks. Despite not meeting the pre-defined threshold to be clinically meaningful of >4 points improvement in global QoL, the results show that QoL scores were +3.9 points (95% CI 0.6 to 7.2, p=0.02) higher over 2 years in patients treated with abiraterone compared to patients treated with docetaxel. This research demonstrates a considerable difference in quality of life that could enable those who are unable to tolerate docetaxel to be able to receive abiraterone.3

Both sets of evidence illustrate a potential for older men newly diagnosed with high-risk metastatic prostate cancer to benefit from abiraterone. The failure of NICE to consider them during the appraisal period has resulted in a final decision that creates a health inequality. An appeal hearing is needed to ensure that age discrimination is avoided.

**Ground 2: The recommendation is unreasonable in the light of the evidence submitted to NICE concerning the effectiveness of abiraterone in patients who cannot receive docetaxel.**

The final appraisal document states “the committee agreed that there are no clear-cut clinical criteria to define who can have abiraterone in combination, but not docetaxel in combination.” There is however no recommendation for how these criteria might be obtained. There was also no attempt made to access evidence that could have defined these criteria, despite previous engagement by NICE with the Chief Investigator of the STAMPEDE trial during the appraisal.

Published STAMPEDE trial data shows that there was an increase in the median age of the patient population accessing the abiraterone trial arm after the docetaxel trial arm closed. This patient population also contained increased frailty characteristics because of chemotherapy ineligibility. The evidence also shows that this patient population had favourable overall survival outcomes to the docetaxel trial arm population (HR 0.59 compared to HR 0.69, respectively).4 This evidence supports our analysis that older men are less likely to receive chemotherapy and could instead benefit from abiraterone.

As mentioned above, there is also evidence from sub-group analysis in the LATITUDE trial that suggests a benefit in favour of abiraterone over Androgen Deprivation Therapy (ADT) alone, with a hazard ratio of 0.86 (0.62-1.21) in men aged 75 and over, which equates to a 14% reduction in risk of death.

The available evidence is drawn from trials that used ADT alone in their control arm. As such this should be the preferred comparator against which abiraterone in this specific older chemotherapy-ineligible population should be assessed for cost-effectiveness. Prostate Cancer UK estimates that there are around 2,200 men each year with high-risk metastatic prostate cancer unable to have chemotherapy and who therefore could benefit from the additional months of life offered by abiraterone,5 making it possible to establish the cost to the NHS. The statement in the FAD that the committee “could not consider … only ADT alone as a comparator” does not make sense considering both the evidence available supporting the use of abiraterone, and the current standards of clinical care in the NHS.

Given this available evidence, Prostate Cancer UK and Tackle Prostate Cancer are concerned by the failure of NICE to identify a chemotherapy ineligible population, especially as this goes against precedent. In 2016, the NICE FAD for radium-223 “accepted the views of the clinical experts that there is a clinically recognised group for whom radium-223 treatment is suitable, because docetaxel is contraindicated or unsuitable.” A definition of this population is given in paragraph 4.31 of the radium-223 FAD. We believe that NICE could have requested a similar clinically-led approach to establish chemotherapy ineligibility in this indication.

These issues with accessing and interpreting evidence during the appraisal mean that the negative decision must be re-visited in light of the full evidence picture we have detailed.

**Conclusion**

We believe the decision not to recommend abiraterone in this indication must be reconsidered, as no reasonable body in light of this evidence could have come to such an unreasonable decision. Prostate Cancer UK and Tackle Prostate Cancer would like this to happen at an oral appeal session. We look forward to receiving your response.

Kind regards,

Xxxxxxx xxxxx  
Director of Support and Influencing, Prostate Cancer UK

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Patient Representative, Tackle Prostate Cancer

References:

1. Get Data Out, PHE. Available at: <https://www.cancerdata.nhs.uk/getdataout/prostate> [Accessed 06/07/20).

*Treatments are grouped by chemotherapy, radiotherapy, surgery and other. We assume that the majority of chemotherapy will represent those having docetaxel, although a minority may have cabazitaxel.*

1. Fizazi, K., et al (2017). Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer. New England Journal of Medicine, 377(4):352–360.
2. Comparative quality of life in patients randomised contemporaneously to docetaxel or abiraterone in the STAMPEDE trial, Rush, H. et. al, DOI: 10.1200/JCO.2020.38.6\_suppl.14 Journal of Clinical Oncology 38, no. 6\_suppl (February 20, 2020) 14-14.
3. James, N.D., et al.,(2017) Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy. New England Journal of Medicine, 377(4):338-351.
4. 2,200 (2202) men each year is based on projections of the number of men with high-risk metastatic prostate cancer in 2019.

*Get Data Out* treatment data for 2016 was projected forwards using ONS population projections from 2016 and using % of high-risk metastatic prostate cancer cases from Hoyle et al 2019.