

Dr Mark Chakravarty

Lead Non-executive Director for Appeals

National Institute for Health and Care Excellence

2nd Floor, 2 Redman Place

London E20 1JQ 28th September 2021

Dear Dr Chakravarty

**Re: Final Appraisal Document – avelumab for maintenance treatment of locally advanced or metastatic urothelial cancer after platinum-based chemotherapy [ID3735]**

Thank you for your letter dated 13 August 2021 addressed to our secretary XXXX XXXXXX XXXXXX in response to XXX original letter of appeal sent on behalf of the British Uro-oncology Group (BUG). I am responding on behalf of our group as XXXX XXXXXX is is currently unavailable.

For avoidance of any confusion, I am also chair of the National Cancer Research Institute Clinical Research Bladder and Renal Studies Group which responds to NICE through the Royal College of Physicians as a stakeholder. To avoid unnecessary duplication (as our oncology membership largely overlaps), no specific appeal was made by the NCRI group via RCP and this response is on behalf of BUG.

I can confirm that our group understands the grounds for which appeal can be made. Thank you for making this clear. However, we wish to clarify some areas prior to your making a final decision about which of our points of appeal may be considered valid for referral to the Appeals Panel.

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

We agree that it is clear that the Committee did, broadly speaking, consider patient and clinician views that an early stopping rule would be accepted in reaching their negative conclusion. However, with regards to our specific point about inconsistency with regards to TA492 (atezolizumab for untreated PDL-1 positive locally advanced or metastatic urothelial cancer when cisplatin is unsuitable), it does not appear that the Committee has acted fairly. Specifically, in section 3.8 of the FAD, the Committee appears to have preferred to consider previous appraisals of avelumab in other diseases (“The Committee noted that other NICE technology appraisals of avelumab have preferred no stopping rules”) over those of other drugs of the same class (anti-PD-L1) in the same disease, albeit in a subtly different setting (ie. after, rather than before failure of first line platinum therapy). We note that the previously completed appraisals for avelumab are for Merkel cell skin cancer (TA691) and renal cancer (TA645). These two tumours are biologically and clinically very different from urothelial cancer to the extent that it would be highly inappropriate to make any form of extrapolation from one disease to the other. In addition, the appraisal in renal cell cancer considered avelumab given in combination with a mechanistically unrelated drug (axitinib). Conversely, TA492, although considering a different drug targeting the same antigen, does address a very similar question in a very similar population of patients as in ID3735. Whilst we acknowledge that some patients who would not be eligible for avelumab (namely those who progressed through platinum chemotherapy) might be considered for second line atezolizumab, and some patients eligible for avelumab might not have been included in the patient population for TA492 (including those who progressed too quickly to access it), we believe the Committee has acted unfairly in preferring to equate this population with Merkel cell and advanced renal cancers.

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

We are delighted that you agree about the validity of this point of appeal. With regards to the comparison with TA692, we fully accept that the populations differ in terms of prognosis (as ID3735 excludes those who primarily fail first line chemotherapy – a poor prognosis group). However, we believe that any difference in biological heterogeneity between these groups is likely to be small and there is no reason why this should result in a difference in relationship between the mean and the median overall survivals considered in the two appraisals. In other words, considering the great difficulties in accurately estimating mean overall survival, we believe that use of the median is just as valid in ID3735 as it was in TA692.

We would also like to remind the Committee that the single most relevant evidence referred to in 3.14 of the FAD (the LAMB trial, Powles et al. 2017. J Clin Oncol. 35(1):48-55) included only UK patients, who were drawn from a broad cross-section of UK NHS clinical practice, and is, therefore, of particular relevance to this appraisal. Furthermore, the LAMB trial had almost identical eligibility criteria as the JAVELIN-100 trial. It is not clear from the FAD whether or not the Committee were aware of this. It is also worthy of note that our broader membership has reacted with significant consternation to the Committee’s conclusion that this group of patients does not meet the End of Life Criteria suggesting that the opinions of the 8 clinicians referred to in the FAD, and those of the patient support group, are widely shared among the UK uro-oncology community.

Finally, I confirm that neither this letter nor the earlier letter written by XXXX XXXXXX contains confidential information.

Please do not hesitate to get in touch if I, or other members of our group, can be of further assistance in this matter.

Yours sincerely,

**XXXXXXXXX XXX X XXXXX**

**Consultant Medical Oncologist**

**On behalf of The British Uro-oncology Group**