1 August 2021

Mr Tim Irish

Vice chair

National Institute for Health and Care Excellence

2nd Floor

2 Redman Place

London E20 1JQ

Dear Mr Irish,

**Re: Final appraisal - Avelumab for maintenance treatment of locally advanced or metastatic urothelial cancer after platinum-based chemotherapy [ID3735]**

Fight Bladder Cancer would like to appeal against the Final Evaluation Determination for the above-mentioned technology appraisal on the following grounds:

Ground one: In making the assessment that preceded the recommendation, NICE has either:

* Failed to act fairly
* Exceeded its powers

Ground two: The recommendation is unreasonable in the light of the evidence submitted to NICE.

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

1a. NICE has failed to act fairly in its decision not to permit the introduction of a stopping rule. This is inconsistent with other technologies in urothelial cancer, such as atezolizumab in second line therapy of urothelial cancer. NICE stated that a stopping line was unethical and unacceptable to patients and clinicians, despite evidence from Patient Experts and Clinical Experts that they would accept the two-year stopping rule if this meant that the treatment would increase the cost-effectiveness to a level that meant that it would be available via the NHS in England.

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

2a. NICE failed to look at the totality of evidence when determining whether this technology falls under “end of life” criteria.

The NICE criteria make no explicit reference to use of either median or mean survival. There is precedent for using median life expectancy (e.g. TA541).

The Javelin Bladder 100 trial demonstrated a median 14.3 months in people who responded to chemotherapy and then had best supportive care alone. An analysis of National Cancer Registration and Analysis Service data looking at patients with locally advanced or metastatic urothelial cancer found a median overall survival of 14.0 months from initiation of first line systemic therapy (https://doi.org/10.1016/j.jval.2020.08.477).

“Most people with locally advanced / metastatic urothelial cancer who respond to platinum-based chemotherapy live for a median of 12-18 months, based on trial data from multiple sources including UK trials. Less than 20% longer than 2 years.” Dr Simon Crabb, Associate Professor in Medical Oncology in Medical Oncology

“Most people with locally advanced / metastatic urothelial cancer who respond to platinum-based chemotherapy live for an average of around 14 months.” Prof Alison Birtle, Consultant Oncologist

In determining whether survival is ‘normally less than 24 months’ for ‘End of life’, we submit that failing to rely on median survival was unreasonable in this context. The patient community has a legitimate expectation that median survival is a more appropriate measure in determining whether or not survival is ‘normally less than 24 months’, rather than mean. This is due to the small number of long-term survivors in this population that unreasonably skew the distribution.

The Appraisal Consultation Document states that “the ERG’s [Evidence Review Group’s] base case predicted a mean overall survival of 27.82 months and a median of 15.6 months”. This fails to account for the fact that patients in clinical trials are often healthier than the population that would be eligible for treatment in general clinical practice, and it is unreasonable of NICE to simply use extrapolation from an economic model to determine overall survival.

**Conclusion**

This negative decision would rob hundreds of terminal bladder cancer patients with valuable good quality time with their loved ones each year.

We know that NICE has a threshold of £50,000 for drugs that fall within the end-of-life category, and a threshold for £30,000 otherwise. We urge NICE to show greater flexibility when looking at these thresholds. Please look at the example of your colleagues within the Scottish Medicines Consortium, who have a more generous definition of end-of-life and more flexible thresholds for funding.

We wish this appeal to proceed at an oral appeal.

Sincerely,

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Chief Executive

Fight Bladder Cancer