

**Mount Vernon Cancer Centre**

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22/08/2023

Dr Mark Chakravarty

Lead non-executive director for appeals

National Institute for Health and Care Excellence

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Dear Dr Chakravarty,

**Re: Appeal - Final Appraisal Document – Tebentafusp**

Melanoma Focus wishes to appeal against the recent FAD decision on tebentafusp on the following grounds. I am submitting this appeal on behalf of Susanna Daniels, Melanoma Focus CEO, who is currently away on annual leave.

**Ground 2 (a)** The committee’s statement (para 3.11) that “The clinical experts suggested that uveal melanoma is an aggressive disease and that there is no expectation that tebentafusp would be curative. So it is not expected that the overall survival curve would plateau” is flawed, misinterprets expert opinion and makes an inappropriate conclusion to justify use of parametric curves.

There are many examples of aggressive metastatic cancers in which a significant plateau in OS curves is seen with immunotherapy but, because of absence of long term outcome data, oncologists would not claim a patient is cured. For example, the NICE approved combination of ipilimumab and nivolumab for cutaneous melanoma reported 6.5 year overall survival follow up (Wolchok et al J Clin Oncol. 2022 Jan 10; 40(2): 127–137) and shows a robust plateau. There is however a 1% melanoma associated survival drop year on year. 20 year survival follow up would be required to accurately report cure rate.

**Ground 2 (b)** The committee’s statement (para 3.11) that “The committee considered that standard parametric curves should be the starting point for modelling and could be used for this treatment” is illogical and does not adequately reflect that non-parametric modelling has been established by NICE committees as the most appropriate (and now standard) methodology in immunotherapy appraisals. The committee and the ERG have failed to distinguish the most appropriate methodology for an immunotherapeutic despite precedent.

NICE is aware that non-parametric survival curves are commonly seen with immunotherapeutics. The first immune checkpoint immunotherapy for melanoma was ipilimumab. NICE accepted that the best method to model OS data was a 3 part curve. This was published in 2015 (Larkin J, Hatswell AJ, Nathan P, Lebmeier M, Lee D.PLoS One. 2015 Dec 23;10(12)). The committee’s acceptance of the ERG claim that parametric modelling is “standard” is flawed. Parametric modelling is no longer standard with immunotherapy because it is established that immunotherapy survival curves are frequently not parametric. The committee selected to use a modelling methodology that has been shown to be inferior in modelling immunotherapy outcomes despite submitted evidence to the contrary.

**Conclusion**

The impact of a negative decision on our patients unable to access the first agent proven to improve overall survival is profound. A negative decision based upon flawed methodology is devastating.

Uveal melanoma has been classified as a distinct rare disease entity and has been granted orphan disease status by the EU. Tebentafusp is the first treatment to have shown a survival advantage in patients with unresectable or metastatic uveal who test positive for HLA-A\*02:01 (estimated 40 – 50% patients). The availability of tebentafusp is the most critical treatment option for this difficult to manage, rare disease.

We are willing to engage with an oral or written appeals process.

Yours sincerely



Trustee Melanoma Focus

