Clinical trial gives hope of new treatment for aggressive eye cancer

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RESEARCH SUMMARY

Overall Survival Benefit with Tebentafusp in Metastatic Uveal Melanoma

Nathan P et al. DOI: 10.1056/NEJMoa2103485

CLINICAL PROBLEM

Survival rates are low in patients with metastatic uveal melanoma, and no treatments have been proven to benefit survival. Tebentafusp, a bispecific protein, consists of a soluble affinity-enhanced T-cell receptor fused to an anti-CD3 effector that can direct T cells to target glycoprotein 100–positive cells. Tebentafusp showed promise in benefiting overall survival in a phase 2 study.

CLINICAL TRIAL

Design: A randomized, open-label, phase 3 trial assessed the overall survival benefit of tebentafusp in patients with metastatic uveal melanoma.

Intervention: 378 previously untreated HLA-A*02:01–positive patients with metastatic uveal melanoma were assigned to receive either tebentafusp or one of three other agents (pembrolizumab, ipilimumab, or dacarbazine) as the control. The primary end point was overall survival.

RESULTS

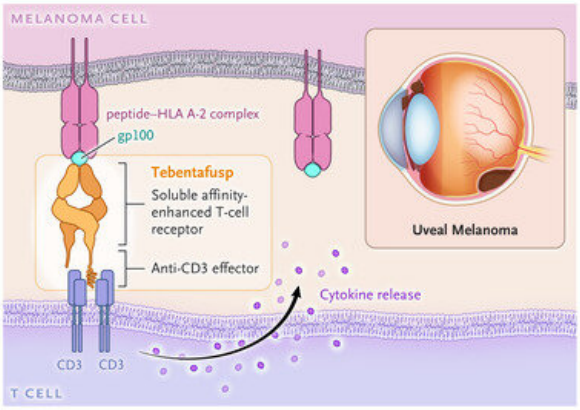
Efficacy: The estimated 1-year overall survival was higher in the tebentafusp group than in the control group. Progression-free survival and objective response were improved with tebentafusp, although not to the same degree as overall survival.

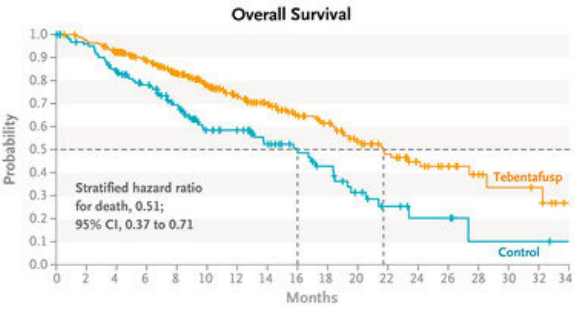
Safety: The most common treatment-related adverse events reported with tebentafusp were cytokine-mediated (including pyrexia and chills) and skin-related (including rash and pruritus). Grade 3 or 4 events occurred in 44% of the patients in the tebentafusp group and in 17% of those in the control group.

LIMITATIONS AND REMAINING QUESTIONS

- The benefits in progression-free survival and objective response were low as compared with the overall survival benefit.
- Anti-tebentafusp antibodies developed in some patients; whether they neutralize the effect of tebentafusp is unclear.

Links: Full Article | NEJM Quick Take





1-Year Survival

Tebentafusp Group	73%	95% CI, 66 to 79
Control Group	59%	95% CI, 48 to 67

Treatment-Related Adverse Events

	Tebentafusp Group (N=245)	Control Group (N=111)
	number of patients (percent)	
Any Event	243 (99)	91 (82)
Grade 3 or 4 Event	109 (44)	19 (17)

CONCLUSIONS

Tebentafusp provided an overall survival benefit in previously untreated patients with metastatic uveal melanoma.

A potentially game-changing trial involving University of Liverpool researchers has shown how an immunotherapy drug can prolong the life of patients with an aggressive form of eye cancer.

The clinical research trial, taking place at The Clatterbridge Cancer Centre, has for the first time shown that a new treatment can improve survival rates in people with secondary uveal melanoma and also can shrink tumors in a small number of patients.

Uveal melanoma is the most common eye cancer in UK adults and many people can be successfully treated for it with the help of Clatterbridge's world-leading proton beam therapy.

However, in about half of patients the cancer spreads to other parts of the body, usually the liver, and once this happens only around 50% of people survive for more than a year.

The 378-patient clinical trial—sponsored by biotechnology company Immunocore and organized with the help of the research team at Clatterbridge—has been using the immunotherapy drug tebentafusp, which helps the body to kill tumor cells. Tebentafusp is a bispecific fusion protein, which helps immune response cells get near enough to cancer cells to destroy them.

The research results have recently been published in US scientific publication the *New England Journal of Medicine* and the paper concludes that tebentafusp should now become the main way to treat this disease.

The results show that patients who used tebentafusp on average survived for 21.7 months, compared with 16 months in those given an alternative

therapy. Also, 9% of patients taking tebentafusp saw their tumors reduce in size, compared with 5% of people being treated differently. Side effects of using the drug were shown to be manageable and severity also reduced as treatment went along.

Dr. Joseph Sacco, from The Clatterbridge Cancer Centre and University of Liverpool, who helped to lead the research, said: "The results of this clinical trial are a first, giving a strong indication that tebentafusp can make a big impact on lengthening the survival time for patients with the metastatic form of this eye cancer, for which there was previously no standard treatment.

"These findings validate the potential of using this drug in patients with uveal melanoma and it can make a very real difference to outcomes.

"I'd like to thank everyone at Clatterbridge and other sites around the world for working so hard on this clinical trial. These results make all that work very worthwhile."

More information: Paul Nathan et al, Overall Survival Benefit with Tebentafusp in Metastatic Uveal Melanoma, *New England Journal of Medicine* (2021). DOI: 10.1056/NEJMoa2103485

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