Long-term Follow-up of 3rd Line Tebentafusp Treatment in a 70-year-old Woman with Malignant Uveal Melanoma: A 20-Month Case Follow-up Report

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Introduction

Survival rates are low in patients with metastatic uveal melanoma, and no treatments have been proven to benefit survival. However, in the recent trial by Nathan P et al Tebentafusp has shown overall survival of 73% at 1 year vs 59% by the Investigator's Choice.

Ocular melanoma is the most common ocular, malignancy with five years metastasis incidence rate of 25% with liver being the most common site of metastasis (89%). [1] Metastasis is a poor prognostic factor with a median survival of less than a year. [1,2]

Risk Factors

a) Environmental: [4,5]

UV and Blue Spectrum light, light coloured eyes, fair skin, ocular melanocytosis, xeroderma pigmentosum, dysplastic nevus syndrome.

b) Genetic: [20]

- Chromosomal: (monosomy 3, disomy 3, gain of 8q, gain of 6p)
- Molecular: (**GNAQ**+GNA11, BAP, EIF1AX)
- Epigenetic: (Methylation, micro RNA)

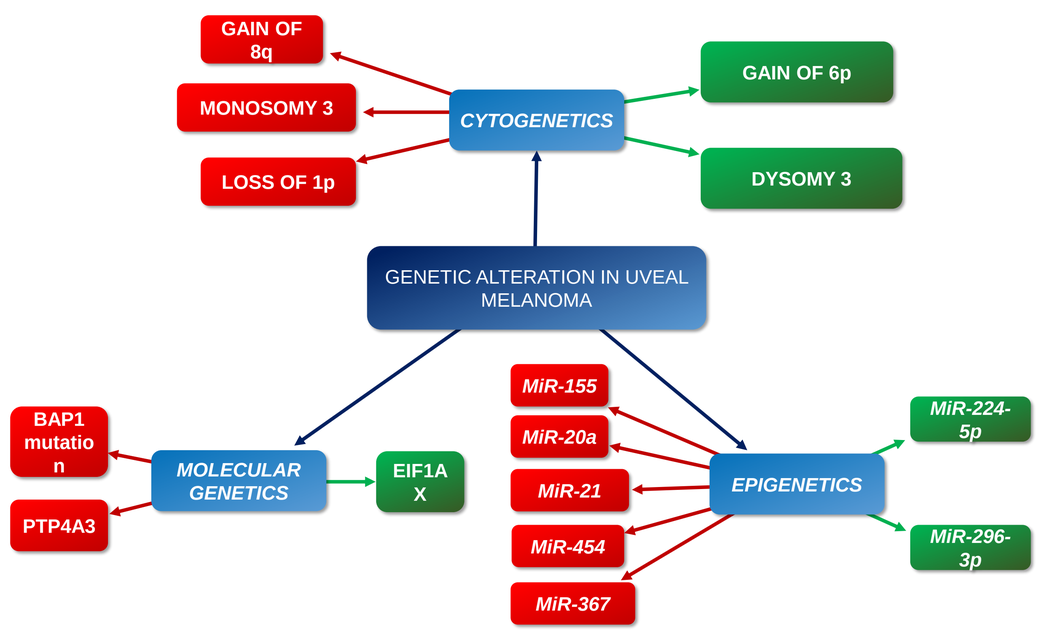


Figure 1: Genetic Variations in Uveal Melanoma(Red= High risk of metastasis, Green= Low risk of metastasis)

Treatment Options

a) Immune checkpoint inhibitor

Immunotherapy, wether used alone or in combination (ipilimumab, pembrolizumab, or nivolumab) has shown limited results. [7]

b) Chemotherapy

Conventional chemotherapy agents as single agent and in combination have been ineffective (6).

c) Tebentafusp

Tebentafusp is a first-in-class bispecific fusion protein (ImmTAC® (Immune mobilizing monoclonal TCRs Against Cancer) designed to target gp100 (a melanoma-associated antigen) bound to HLA A0201 through a high affinity T-cell receptor (TCR) binding domain and an anti-CD3 T-cell engaging domain, which redirects T cells to kill gp100-expressing tumour cells. Data from the largest Phase 3 trial conducted by Nathan Pet al. undertaken in untreated metastatic malignant melanoma showed that Tebentafusp demonstrated unprecedented median OS benefit as a first-line treatment. The estimated overall survival at 1 year was 73% (95% confidence interval [CI], 66 to 79) in the Tebentafusp group and 59% (95% CI, 48 to 67) in the investigator's choice of therapy with single-agent pembrolizumab, ipilimumab, or dacarbazine (control group); the estimated median duration of overall survival was 21.7 months (95% CI, 18.6 to 28.6) and 16.0 months (95% CI, 9.7 to 18.4), respectively. The stratified hazard ratio for death was 0.51 (95% CI, 0.37 to 0.71; P<0.001) in favour of the tebentafusp group. [8]

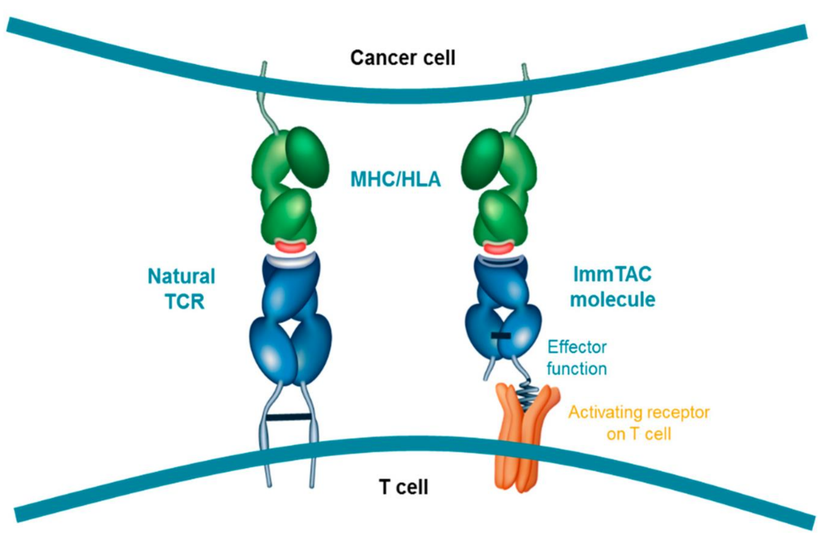
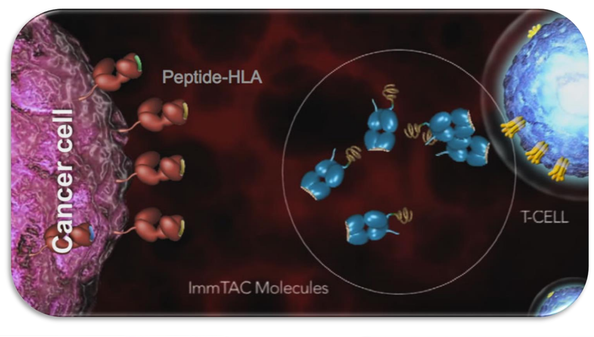


***Figure 2a**: Illustration of Tebentafusp Structure [9]*



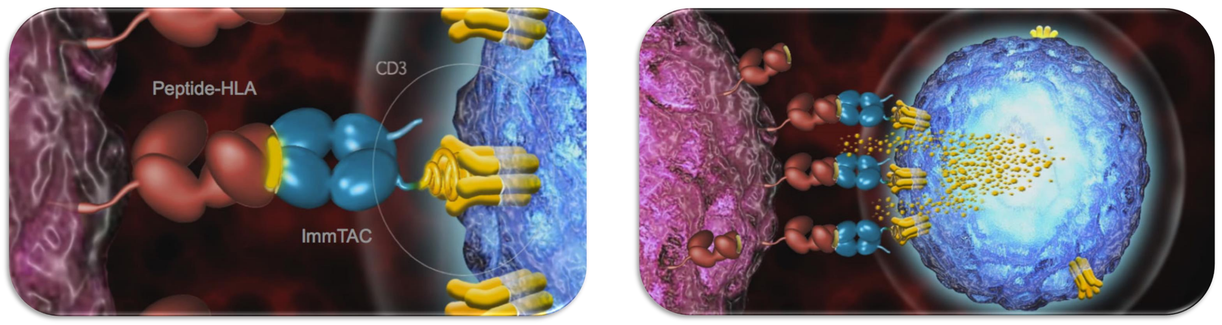


***Figure 2b**: Mechanism of action of tebentafusp. [9]*

Case Presentation

A 72-year-old female with known metastatic Uveal melanoma was initially diagnosed in 2017. She initially received 2 lines of treatment with disease progression.

Tebentafusp was used as 3rd line treatment under early access programme by Immunocore.

Treatment started on 14th Dec 2021; Starting dose of 20mcg on Day 1, 30mcg on Day 8 followed by 68mcg weekly dose. Initially, a partial response to treatment was observed, which has since been followed by the maintenance of stable disease up to the most recent staging scan conducted in September 2023. She has received a total of 97 weeks of treatment till 30th October 2023 with good tolerance apart from mild rash during 2nd cycle and occasional sickness.

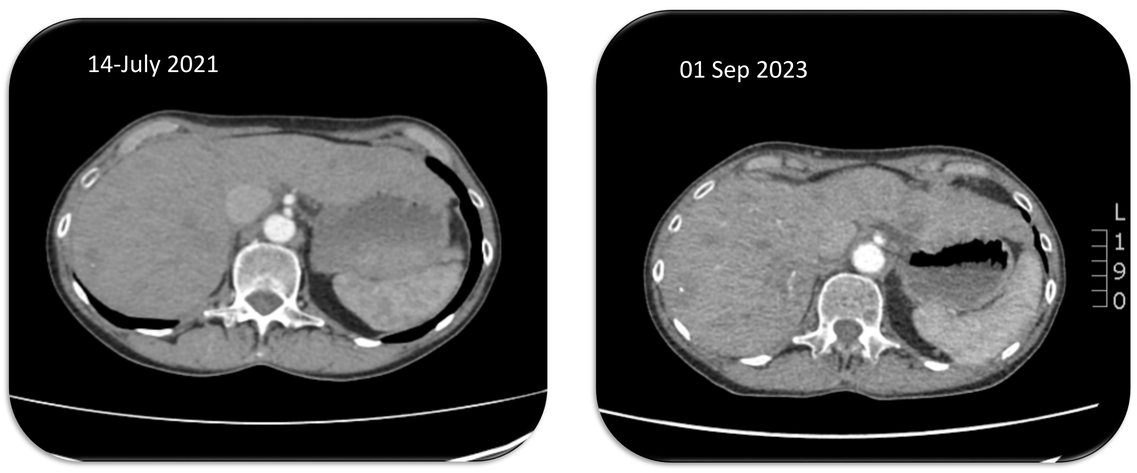


***Figure 3**: Comparison of pre-treatment and 20-month post-treatment liver CT Scan*

Conclusion

Tebentafusp can be considered as a viable treatment option, warranting further research and potential consideration as a 2nd or 3rd line treatment for previously treated metastatic uveal melanoma (mUM). Given the limited options for treatment of metastatic uveal melanoma, Tebentafusp stands as a hopeful addition to the treatment armamentarium, providing insights into its efficacy and paving the way for enhanced understanding of its mechanisms for the broader benefit of patients facing this challenging malignancy.

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