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A randomized phase II study of autogene cevumeran plus pembrolizumab (pembro) versus pembro in 1L advanced melanoma (IMcode001)

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Background

Many patients with advanced melanoma do not benefit from immune checkpoint inhibitors. Autogene cevumeran is a uridine messenger RNA-lipoplex-based individualized Neoantigen-Specific immunoTherapy (iNeST) aimed at enhancing antitumor immunity.

Methods

Following a safety run-in, this multicenter, open-label study randomized patients with advanced melanoma (2:1) to receive autogene cevumeran plus pembro or pembro for up to 2 years. The primary endpoint was investigator-assessed PFS in the intention-to-treat population. Key secondary endpoints were OS, investigator-assessed ORR per RECIST 1.1, and safety. Assessment of biomarkers associated with clinical responses was an exploratory objective.

Results

At data cutoff (30 May 2024), 125 patients were randomized to combination therapy (n=84) or pembro (n=41), with median follow-up of 30.5 months. Median PFS was 8.3 months in the combination arm and 7.9 months in the pembro arm, with a hazard ratio of 0.78 (p=0.3061). In the combination arm, 12-month OS was 88.71% and 24-month OS was 74.17%, compared to 71.86% and 63.88% in the pembro arm, respectively. Unbalanced early deaths and censoring events were observed across arms. ORR was 41.7% in the combination arm and 48.8% in the pembro arm. The combination was tolerable with no new safety signals. Autogene cevumeran induced ex-vivo detectable, neoantigen-specific T-cell responses in 47/56 (83.9%) patients. Median frequency of neoantigen-specific CD8 T-cell receptors in blood TCRs in 8 assayed patients was 9.4% (range: 2.2% – 29.4%), which were detectable for up to a year. In the combination arm, patients with immune responses against multiple neoantigen targets showed a trend of improved PFS. There was a trend of improved OS in the combination arm versus pembro arm in patients with low tumor mutational burden.

Conclusions

Autogene cevumeran plus pembro did not significantly improve PFS in patients with advanced melanoma. Most evaluable patients showed neoantigen-specific immune responses, with broader responses trending toward improved PFS. Ongoing studies are assessing autogene cevumeran for the adjuvant treatment of resected pancreatic, urothelial, and colorectal cancers.

Clinical trial identification

NCT03815058.

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Legal entity responsible for the study

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Disclosure

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