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Pembrolizumab monotherapy for microsatellite instability tumors with mismatch repair deficient recurrent glioma: results from the multicohort KEYNOTE-158 study

Received: 2 August 2021 / Accepted: 27 October 2021
Volume 157, article number 89 (2022) | Cite this article

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Abstract

Purpose

Recurrent glioma have limited treatment options and dismal outcomes. We report the efficacy and safety of the anti-programmed cell death protein 1 antibody pembrolizumab in participants with recurrent glioma with microsatellite high (MSI-H)/mismatch repair deficient (dMMR) recurrent glioma in KEYNOTE-158.

Methods

The phase 2, multicohort KEYNOTE-158 study (NCT02628067) is evaluating pembrolizumab monotherapy in participants with advanced solid tumors. This analysis focused on participants with recurrent glioma from cohort F when eligible participants were ≥ 20 years old with MSI-H/dMMR recurrent glioma, Karnofsky performance status ≥ 70, and had received prior standard therapy. Primary endpoints were objective response rate (ORR) and progression-free survival (PFS) by independent central radiology review.

Results

Twenty-two participants with recurrent glioma were enrolled. Median (range) follow-up was 20.9 (1.5–43.8) months. Best overall response were partial response (ORR, n = 3; 14%), stable disease (n = 5; 23%), and disease progression (n = 14; 70%). 1 participant (5%) had no postbaseline response assessment. The ORR was 14% (95% CI: 3.0, 36.3) in participants with GBM or astrocytic cancer (median duration of ongoing response was 23.6 months). The participant with PR had progression-free and overall survival of 23.6 and 43.8 months. Median PFS was 2.1 (95% CI: 1.9, 3.7) months and OS was 10.3 (95% CI: 5.8, 23.1) months. Grade ≥ 3 treatment-related AEs occurred in 3 (14%) participants. No treatment-related AEs led to discontinuation.

Conclusion

Pembrolizumab monotherapy demonstrated anti-tumor activity in a small cohort of participants and manageable safety in MSI-H/dMMR recurrent glioma.

Trial registration

ClinicalTrials.gov, NCT02628067, Registered, December 9, 2015.

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Acknowledgements

We thank the participants and their families and caregivers for participating in this study, along with all investigators, including Dr. Marc Sanson for the collection of the data and provision of study information. Medical writing support was provided by Ashfaq Ali, Ph.D., of Merck Sharp & Dohme Corp., a subsidiary of Merck, NJ, and Michael K. Mekonnen, MS, of ICON plc (New York, NY, USA). This extension was sponsored by Merck Sharp & Dohme Corp., a subsidiary of Merck, NJ, and funded by Merck Sharp & Dohme Corp., a subsidiary of Merck, NJ, and by Merck Sharp & Dohme LLC, a subsidiary of Merck, NJ, and Merck Sharp & Dohme Ltd., a subsidiary of Merck, Kenilworth, NJ, USA, and Merck Sharp & Dohme Corporation, Rahway, NJ, USA, and Merck Sharp & Dohme Corporation, Tokyo, Japan, and Merck Sharp & Dohme Corporation, Tokyo, Japan, and Merck Sharp & Dohme Corporation, Tokyo, Japan

DOI
https://doi.org/10.1007/s11060-026-05461-2

Keywords

Pembrolizumab | Microsatellite instability | DNA mismatch repair | Glioma

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