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Avelumab in patients with previously treated metastatic Merkel cell carcinoma: long-term data and biomarker analyses from the single-arm phase 2 JAVELIN Merkel 200 trial

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Abstract

Background: Merkel cell carcinoma (MCC) is a rare, aggressive skin cancer associated with a high risk of metastasis. In 2017, avelumab (anti-programmed death-ligand 1 (PD-L1)) became the first approved treatment for patients with metastatic MCC (mMCC), based on the occurrence of durable responses in a subset of patients. Here, we report long-term efficacy and safety data and exploratory biomarker analyses in patients with mMCC treated with avelumab.

Methods: In a cohort of this single-arm, phase 2 trial (JAVELIN Merkel 200), patients with mMCC and disease progression after prior chemotherapy received avelumab 10 mg/kg intravenously every 2 weeks. The primary endpoint was confirmed objective response rate (ORR) by independent review per Response Evaluation Criteria in Solid Tumors V.1.1. Other assessments included duration of response, progression-free survival, overall survival (OS), safety and biomarker analyses.

Results: As of 14 September 2018, 88 patients had been followed up for a median of 40.8 months (range 36.4–49.7 months). The ORR was 33.0% (95% CI 23.3% to 43.8%), including a complete response in 11.4% (10 patients), and the median duration of response was 40.5 months (95% CI 18.0 months to not estimable). As of 2 May 2019 (≥44 months of follow-up), the median OS was 12.6 months (95% CI 7.5 to 17.1 months) and the 42-month OS rate was 31% (95% CI 22% to 41%). Of long-term survivors (OS >36 months) evaluable for PD-L1 expression status (n=22), 81.8% had PD-L1+ tumors. In exploratory biomarker analyses, high tumor mutational burden (≥2 non-synonymous somatic variants per megabase) and high major histocompatibility complex class I expression (30% of tumors with highest expression) were associated with trends for improved ORR and OS. In long-term safety assessments (≥36 months of follow-up), no new or unexpected adverse events were reported, and no treatment-related deaths occurred.

Conclusions: Avelumab showed continued durable responses and meaningful long-term survival outcomes in patients with mMCC, reinforcing avelumab as a standard-of-care treatment option for this disease.

Trial registration number: [NCT02155647](#).

Keywords: biomarkers, tumor; clinical trials, phase II as topic; immunotherapy; skin neoplasms.

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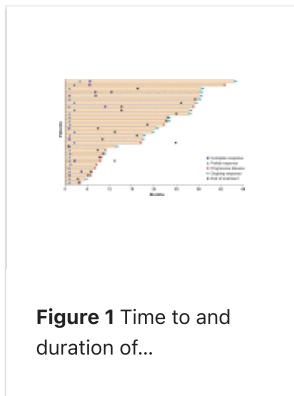


Figure 1 Time to and duration of...

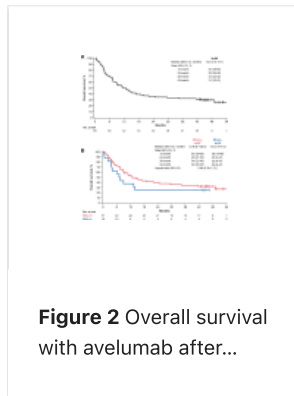


Figure 2 Overall survival with avelumab after...

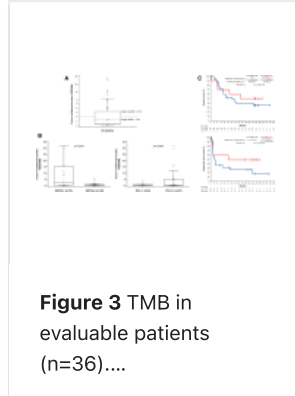


Figure 3 TMB in evaluable patients (n=36)....

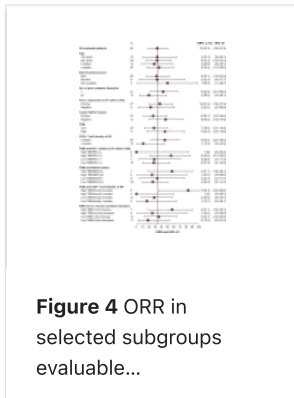


Figure 4 ORR in selected subgroups evaluable...

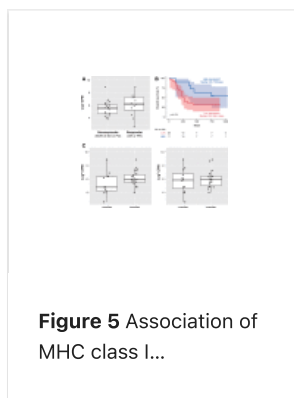


Figure 5 Association of MHC class I...

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