

tumor activity, including durable responses, in patients with mBCC after progression or intolerance on HHI therapy.

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Ethics Approval The study protocols and all amendments were approved by the institutional review board at each participating study site. The study was conducted in accordance with the principles of the Declaration of Helsinki and with Good Clinical Practice guidelines as defined by the International Conference on Harmonization. All patients provided written informed consent before enrollment.

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429 LONG-TERM ANALYSIS OF MASTERKEY-265 PHASE 1B TRIAL OF TALIMOGENE LAHERPAREPVEC (T-VEC) PLUS PEMBROLIZUMAB IN PATIENTS WITH UNRESECTABLE STAGE IIIB-IVM1C MELANOMA

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Background Previous findings from the MASTERKEY-265 phase 1b study showed that the combination of T-VEC and pembrolizumab was well tolerated and produced a high complete response (CR) rate of 43% in patients with advanced melanoma.¹ The 3-year progression-free survival (PFS) and overall survival (OS) rates at that time were 53.6% and 71%, respectively. Here, we report the results of the long-term follow-up efficacy analyses.

Methods The MASTERKEY-265 phase 1b trial (NCT02263508) was an open-label, single-arm study that enrolled patients who had unresectable, stage IIIB-IVM1c melanoma with injectable, measurable lesions and no prior systemic treatment. T-VEC was administered intralesionally at the approved dosing starting day 1 of week 1. Pembrolizumab (200 mg) was administered intravenously Q2W beginning on day 1 of week 6. The maximum treatment period was 2 years. The primary endpoint was dose-limiting toxicities; key secondary endpoints included objective response rate and PFS per modified irRC, OS, and safety.

Results As of the data cutoff (Mar 2, 2020), all 21 patients enrolled were off treatment; 6 died and 15 are in long-term follow-up. The median follow-up time was 58.6 months (range: 1.4–61.6). The CR rate remained 43% (9/21 patients). Twelve of the 13 responders (92.3%) are still in response, including all 9 patients with a CR. Median duration of response was not reached (range: 2.8+–54.3+ months). Median PFS and OS were not reached at the data cutoff. KM estimates of 4-year PFS and OS rates were 55.9% and 71.4%, respectively, which have held stable since the 3-year analysis. Patients who achieved a CR or partial response had better OS ($p=0.0056$) compared to those who did not respond. Median OS for non-responders was 24.4

months and was not reached for responders. No additional safety signals were detected.

Conclusions At almost 5 years of follow-up, median PFS and OS were not reached for patients treated with the combination of T-VEC and pembrolizumab in this phase 1b study of unresectable metastatic melanoma. 92% of responders remained in response with improved OS observed in responders compared with non-responders. The corresponding randomized phase 3 trial has completed enrollment and is currently ongoing.

Trial Registration NCT02263508

Ethics Approval The study was approved by the Ethics Board of each institution involved in this study and can be produced upon request.

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430 A PHASE II STUDY OF NIVOLUMAB + BMS-986016 (RELATLIMAB) IN PATIENTS WITH METASTATIC UVEAL MELANOMA(UM) (CA224–094)

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Background Fifty percent of patients with uveal melanoma (UM) develop metastatic disease, surviving 6–12 months from metastatic diagnosis. Liver-directed therapies, immunotherapy, targeted therapy and chemotherapy have limited activity. Lymphocyte activation gene 3 (LAG-3) is an immune checkpoint receptor associated with decreased T-cell effector function and tumor escape. Preclinical models have shown that dual inhibition of LAG-3 and PD-1 blockade generates synergistic anti-tumor activity.¹ In uveal melanoma, CD8+ T cells express the checkpoint receptor LAG3 to a greater extent than PD1 or CTLA4.^{2 3} This recent discovery nominates LAG3 as a potential candidate for checkpoint inhibitor immunotherapy in UM.

Methods This is an open-label, single arm, single site investigator-initiated phase II study. Based on Simon two-stage minimax design, 13 patients will be enrolled in Stage 1. If at least one response is noted, the study will proceed to Stage 2 and enroll additional 14 patients. The null hypothesis will be rejected if 4 or more responses are observed among 27 patients. This design achieves 5% type I error and 80% power when the true ORR is 20%. Main eligibility criteria includes patients with biopsy proven metastatic uveal melanoma, previously untreated with PD-1, CTLA-4 and/or LAG-3 blocking antibodies and in good performance status. Enrolled patients will be treated in the outpatient setting. Nivolumab 480 mg will be mixed in the same bag with relatlimab 160 mg and administered intravenously over 60 minutes every 4 weeks until disease progression or intolerable toxicity for up to 24 months. The primary endpoint is best objective response rate (ORR). Secondary endpoints include disease control rate (DCR), progression-free survival (PFS), overall survival (OS), median duration of response (mDOR), and adverse events