

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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### 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.<sup>1</sup> 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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### 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.<sup>1</sup> In uveal melanoma, CD8+ T cells express the checkpoint receptor LAG3 to a greater extent than PD1 or CTLA4.<sup>2 3</sup> 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

(AEs). Correlative studies will evaluate pre- and post-treatment characteristics of T cells in the tumor microenvironment and blood.

Results N/A

Conclusions N/A

Ethics Approval The study was approved by the University of Miami Sylvester Cancer Center PRMC #20200847

Consent N/A

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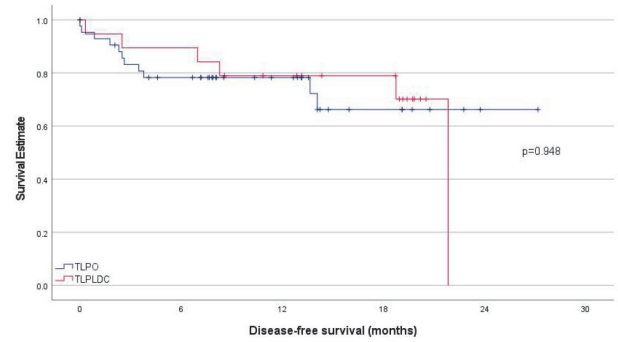
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**PROSPECTIVE, RANDOMIZED TRIAL OF THE TUMOR LYSATE, PARTICLE ONLY VACCINE COMPARED TO THE TUMOR LYSATE, PARTICLE-LOADED, DENDRITIC CELL VACCINE TO PREVENT RECURRENCE FOR RESECTED STAGE III/IV MELANOMA**

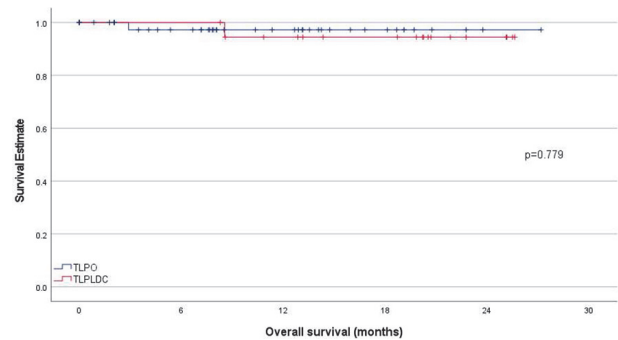
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**Background** The autologous tumor lysate, particle-loaded, dendritic cell (TLPLDC) vaccine is safe and effective in improving 24 and 36-month disease-free survival (DFS) in patients (pts) with resected stage III/IV melanoma who completed the primary vaccine series. The tumor lysate, particle only (TLPO) vaccine has been developed to accelerate production by omitting DC isolation and ex vivo loading in favor of in vivo phagocytosis of the TL-loaded particles. We are currently conducting a randomized and double-blind trial of the TLPO vs TLPLDC to improve DFS and overall survival (OS) in patients with resected late stage melanoma.

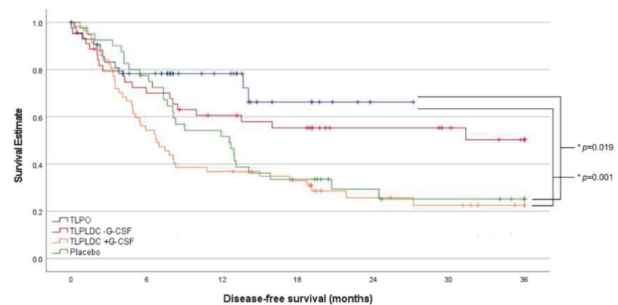
**Methods** Patients with stage III/IV melanoma who were clinically disease-free after standard of care therapies were randomized to receive TLPO vs TLPLDC (2:1) as a continuation of the phase IIb trial comparing TLPLDC vs placebo (2:1). For the TLPLDC vaccine, autologous TL was loaded into yeast cell wall particles (YCWP) which were then phagocytized by isolated autologous DC ex vivo. For the placebo DC were loaded with empty YCWP. For TLPO, the autologous TL-loaded YCWP were coated with a chemoattractant and injected intradermally for in vivo phagocytosis. Some patients in the TLPLDC arm received G-CSF prior to DC harvest to minimize blood draw (60 mL instead of 120 mL without G-CSF). For all arms, six vaccine/placebo doses were administered intradermally at 0, 1, 2, 6, 12, and 18 mos. Data was analyzed by an intention-to-treat (ITT) analysis for DFS and OS by the Kaplan-Meier method and compared by log-rank test.



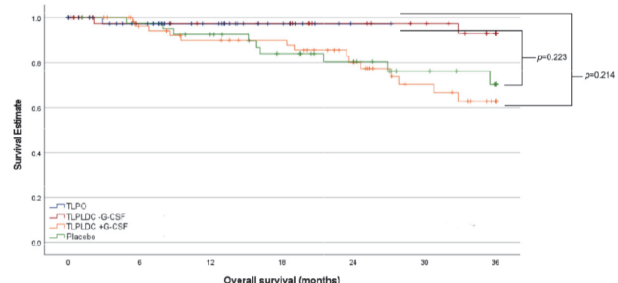
**Abstract 431 Figure 1** TLPO vs TLPLDC (n=20) DFS. Disease-free survival of TLPO patients compared to similar TLPLDC patients (n=20)



**Abstract 431 Figure 2** TLPO vs TLPLDC (n=20) OS. Overall survival of TLPO patients compared to similar TLPLDC patients (n=20)



**Abstract 431 Figure 3** TLPO vs TLPLDC subsets vs Placebo DFS. Disease-free survival of TLPO patients compared to placebo and all TLPLDC patients (n=103) stratified by use of G-CSF



**Abstract 431 Figure 4** TLPO vs TLPLDC subsets vs Placebo OS. Disease-free survival of TLPO patients compared to placebo and all TLPLDC patients (n=103) stratified by use of G-CSF