LIFILEUCEL TIL CELL MONOTHERAPY IN PATIENTS WITH ADVANCED MELANOMA AFTER PROGRESSION ON IMMUNE CHECKPOINT INHIBITORS (ICI) AND TARGETED THERAPY: POOLED ANALYSIS OF CONSECUTIVE COHORTS (C-144–01 STUDY)

1Amid Samaik, 2Carl Lewis, 3Harriet Kluger, 4Qumal Hamid, 5Eric Whitman, 6Sajane Thomas, 7Martin Wermink, 8Mike Conn, 9Enid Domingo-Mudby, 10Giao Phan, 11John Kirkwood, 12Jessica Hassel, 13Marlana Orloff, 14James Larkin, 15Jeffrey Weber, 16Andrew Fumess, 17Nikhil Khushhalani, 18Theresa Medina, 19Friedrich Flindtkeinstein, 20Mudan Jagsaia, 21Parameswaran Hari, 22Giri Sullur, 23Wen Shi, 24Kiao Wu, 25Jason Chesney, 26H. Lee Moffitt Cancer Center, Tampa, FL, USA; 27University of Colorado Cancer Center-Anschutz Medical Campus, Aurora, CO, USA; 28Yale School of Medicine and Smilow Cancer Center, Yale New Haven Hospital, New Haven, CT, USA; 29The Angeles Clinic and Research Institute, a Cedars Sinai Affiliate, Los Angeles, CA, USA; 30Atlantic Health System Cancer Care, Morristown, NJ, USA; 31Olando Health Cancer Institute, Orlando, FL, USA; 32Technical University Dresden, NCT/UCC Early Clinical Trial Unit, Dresden, Germany; 33Mount Sinai Medical Center, Miami Beach, FL, USA; 34University of Minnesota, Masonic Cancer Center, Minneapolis, MN, USA; 35Virginia Commonwealth University, Massey Cancer Center, Richmond, VA, USA; 36UMC Hillman Cancer Center, Pittsburgh, PA, USA; 37Ski Cancer Center, University Hospital Heidelberg Heidelberg, Germany; 38Thomas Jefferson University, Sidney Kimmel Cancer Center, Philadelphia, PA, USA; 39The Royal Marsden NHS Foundation Trust, London, UK; 40Laura and Isaac Perlmutter Cancer Center, NYU Langone Medical Center, New York, NY, USA; 41Iovance Biotherapeutics, Inc., San Carlos, CA, USA; 42UofL Health – Brown Cancer Center, University of Louisville, Louisville, KY, USA

Background Despite improved outcomes in advanced (unresectable or metastatic) melanoma, many patients progress after ICI and have low response rates to subsequent therapy.4,5 Lifileucel, a one-time autologous TIL cell therapy, demonstrated an investigator-assessed ORR of 36% in Cohort 2 (C2), which enrolled 66 patients who progressed post-ICI and appropriate targeted therapy.8,9 We now report outcomes of 153 patients enrolled across C2 and C4 (NCT02360579), representing the largest phase 2 study of cell therapy in melanoma.

Methods Eligibility criteria were identical for C2 and C4. Patients had ≥1 lesion(s) (≥1.5 cm in diameter post-resection) and shipped to a central GMP facility for 22-day lifileucel manufacturing. All patients received a nonmyeloablative lymphodepletion (NMA-LD) regimen, a single lifileucel infusion, and up to 6 doses of high-dose IL-2. Primary endpoint was IRC-assessed ORR (RECIST v1.1).

Results The full analysis set included 153 patients (C2: n=66; C4: n=87) treated with lifileucel, with a median of 3 prior treatments (range: 1-7) and substantial baseline disease burden (≥3 target and non-target lesions: 76%; median target lesion SOD: 97.8 mm; LDH >ULN: 54%). ORR was 31% (95% CI: 24.1%-39.4%) (C2: 35%; C4: 29%), with 8 CRs and 40 PRs (figure 1). At median study follow-up of 27.6 months, median DOR was not reached (NR). Forty-two percent of responses extended ≥18 months, and 40% (19/48) of responses were ongoing at time of data cut (figure 2). In multivariable analyses adjusted for ECOG PS, elevated LDH and target lesion SOD >median were independently correlated with ORR (p=0.008); normal LDH and SOD < median were associated with higher odds of response than either (OR=2.08) or both (OR=4.42) risk factors. The median OS was 13.9 months (95% CI: 10.6-17.8). In an analysis of survival by response at first assessment (1.5 months post-lifileucel infusion), median OS in responders was NR (95% CI: 22.5 months-NR). The most common (≥30%) G3/4 TEAEs were thrombocytopenia (77%), anemia (50%), and febrile neutropenia (42%). TEAEs were consistent with known safety profiles of NMA-LD and IL-2, and their incidence decreased within the first 2 weeks post-lifileucel infusion, characteristic of one-time treatment.

Conclusions Lifileucel demonstrated clinically meaningful and durable activity (ORR: 31%; mDOR: NR) in heavily pretreated patients with advanced melanoma and high tumor burden after ICI (and targeted therapy, where appropriate). Favorable safety profile and sustained responses support the potential benefit of one-time lifileucel TIL cell therapy as a novel treatment option for patients without approved therapies post-ICI.

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Trial Registration NCT02360579

References

Ethics Approval: The study was approved by the institutional review board at each site and was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines of the International Conference on Harmonisation. All patients provided written informed consent.
Abstract 789 Figure 2  Time to first response, duration of response, and time on efficacy assessment for confirmed responders (PR or better)