LONG-TERM EFFICACY AND SAFETY OF LIFILEUCEL TUMOR-INFILTRATING LYMPHOCYTE (TIL) CELL THERAPY IN PATIENTS WITH ADVANCED MELANOMA: A 4-YEAR ANALYSIS OF THE C-144–01 STUDY

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Background Immune checkpoint inhibitors (ICI) have improved outcomes for patients with metastatic melanoma; nevertheless, resistance is common and subsequent treatment options are limited. Lifileucel, a one-time autologous TIL cell therapy, achieved a 31.4% objective response rate (ORR) with a median duration of response (DOR) not reached at a median of 36.5 months of follow-up, in patients with advanced (unresectable or metastatic) melanoma who progressed after ICI and targeted therapy (if appropriate; Sarnaik SITC 2022). We report updated, long-term follow-up data on lifileucel treatment outcomes from C-144–01, representing the largest population of patients with anti-PD-1-refractory advanced melanoma treated with TIL cell therapy.

Methods C-144–01 (NCT02360579) is a prospective, open-label, multicohort, multicenter, nonrandomized phase 2 study; this 4-year update includes investigator-assessed efficacy data from patients in Cohorts 2 and 4 (combined due to identical eligibility, lifileucel manufacturing process, and treatment regimen). Patients had ≥1 lesion(s) resected (~1.5 cm diameter) for 22-day cryopreserved lifileucel manufacturing. The treatment regimen included preparative lymphodepletion (cyclophosphamide 60 mg/kg × 2d, fludarabine 25 mg/m² × 5d), a single lifileucel infusion, and up to 6 doses of high-dose IL-2 (600,000 IU/kg). Investigators assessed response per RECIST v1.1.

Results As of the data cutoff (16 June 2023), median study follow-up was 48.1 months. Median overall survival (OS) was 13.9 months (95% CI: 10.6 to 17.8). One-, 2-, 3-, and 4-year OS rates were 54.0%, 33.9%, 28.3%, and 22.2%, respectively. Forty-eight of 153 (31.4%) lifileucel-treated patients achieved an investigator-assessed objective response; 54.2%, 39.6%, 33.3%, and 20.8% of responses lasted ≥12, ≥24, ≥36, and ≥48 months, respectively (figure 1). Twelve responses (25.0%) were ongoing at time of analysis and longest response was ongoing at 59.9 months. Treatment-emergent adverse events (AEs) were consistent with known safety profiles of lymphodepletion and IL-2, and their incidence decreased over time. No new serious treatment-related AEs were reported after 6 months post-lifileucel infusion. Characteristics of long-term responders and patterns of response will be presented.

Conclusions This 4-year analysis represents the longest follow-up to date of patients treated with lifileucel TIL cell therapy in the post-ICI setting. In heavily pretreated patients with advanced melanoma, one-time lifileucel TIL cell therapy demonstrated a 4-year OS rate of 22.2%, and 20.8% of responses were ongoing ≥4 years. These promising results continue to show favorable survival outcomes, durable responses, and no long-term safety concerns, supporting the use of lifileucel as a potential treatment option in these patients.

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Trial Registration NCT02360579

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 Harmonization. All patients provided written informed consent.