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)

Background Despite improved outcomes in advanced (unresectable or metastatic) melanoma, many patients progress after ICI.1–3 and have low response rates to subsequent therapy.4–7 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) resected (~1.5 cm in diameter post-resection) and shipped to a central GMP facility for 22-day 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 lines of therapy (range: 1–9) 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.
Abstract 789 Figure 2  Time to first response, duration of response, and time on efficacy assessment for confirmed responders (PR or better)