Long-term durable efficacy of lifileucel one-time treatment: Post-hoc landmark analysis of overall survival by response in advanced melanoma patients (C-144-01 study)

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Background

- Advanced melanoma that has progressed on anti–PD-1 and anti–CTLA-4 therapy carries a poor prognosis, with no approved treatment options until recently
- Lifileucel is a one-time, autologous T-cell immunotherapy approved for advanced melanoma that has demonstrated a 5-year long-term benefit, meaningful overall survival (OS) and 36-month duration of response (DOR) in the refractory setting[1,2]
- Recent real-world data show that patient selection can result in higher ORR than observed in our registrational trial[3]
- Until now, the magnitude of impact from achieving a response on OS had not been analyzed
- **Here, we focus on the long-term follow-up survival data of responders among population previously reported from the registrational study**

Methods

- A phase 2, multicenter, multicohort, open-label study (C-144-01, NCT02360579) has supported approvals of lifileucel to date in the U.S., Canada and Australia[1]
- A retrospective OS landmark analysis was performed by response at 4.5 Months (M) post-lifileucel
- Responders at landmark were defined as patients with partial response (PR) or complete response (CR) onset before 4.5 M; all other patients who were alive in study at 4.5 M were defined as non-responders
- Median and 95% CI for OS after the landmark were based on Kaplan-Meier method

Conclusions

- Response in TIL-treated patients was prognostic of longer OS after the landmark
- The 37.4 M mOS in responders substantially exceeds the expected OS in this refractory population
- 21/28 (75%) of five-year completers are alive and treatment-free
- This landmark analysis quantifies a magnitude of survival benefit in responders

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Results

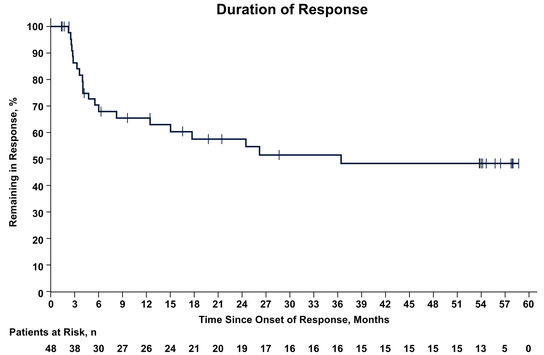
Table 1. Patient Disposition and Baseline Characteristics

Characteristics		Pooled cohorts 2 & 4 (N=153)
Median age, years (range)		56 (20–79)
Male, n (%)		83 (54.2)
ECOG performance status, n (%)	0, 1	104 (68.0), 49 (32.0)
Stage IV melanoma at study entry, n (%)		143 (93.5)
BRAF V600 E/K mutation, n (%)		41 (26.8)
PD-L1 Tumor Proportion Score,[a] n (%)	≥1%, <1%	76 (49.7), 32 (20.9)
LDH level (× ULN), n (%)	<1, 1–2, ≥2	70 (45.8), 54 (35.3), 29 (19.0)
≥3 baseline target and nontarget lesions, n (%)		116 (75.8)
Baseline target lesions in ≥3 anatomic sites, n (%)		109 (71.2)
Liver and/or brain lesions by IRC, n (%)		72 (47.1)
Median target lesion SOD, mm (range)		101.1 (13.5–552.9)
Median number of prior systemic therapies (range)		**3 (1–9)**
Prior BRAF/MEK inhibitor therapy, n (%)		39 (25.5)
Prior anti–CTLA-4 therapy, n (%)		125 (81.7)
Prior anti–CTLA-4 plus anti–PD-1-combination therapy, n (%)		82 (53.6)
Resistance to anti–PD-1/PD-L1 by SITC criteria, n (%)	primary, secondary	109 (71.2), 41 (26.8)
Median cumulative duration of anti–PD-1/PD-L1 therapy (range), months[4]		7.0 (0.7–75.8)

[a]PD-L1 Tumor Proportion Score was missing for 45 patients.

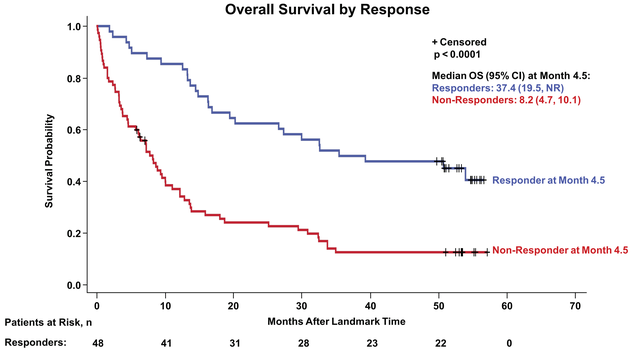
- At the March 05, 2025, data cutoff, the median follow-up was 57.9 M
- All patients had completed or discontinued the study, with 28 (18.3%) patients completing the 5-year study follow-up

Figure 1. Durable Responses were Observed with Lifileucel



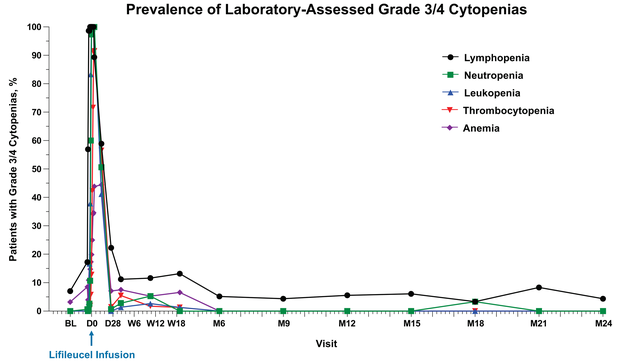
- The ORR was 31.4% (CR, 5.9%; PR, 25.5%), and 79.3% of patients had a reduction in tumor burden
- The median duration of IRC-assessed response was 36.5 M (95% CI: 8.3–NR)
- 31.3% (15/48) of responders completed the 5-year assessment with ongoing responses

Figure 2. Kaplan Meier Curve for Landmark Analysis of Overall Survival by Response



- A significant separation in survival between responders and non-responders reinforces the clinical relevance of a response to lifileucel
- mOS was 37.4 M (95% CI: 19.5–NR) in responders versus 8.2 M (95% CI: 4.7–10.1) in non-responders (**Figure**)
- Notably, 21 of 28 (75%) 5-year completers (7 CR, 11 PR, 3 SD) remained alive and treatment-free (no new anticancer therapy) with OS of 55.0 to 61.7 M after a single lifileucel infusion
- These results build upon a previously published 5-yr study follow-up among all lifileucel treated patients[2] that demonstrated mDOR of 36.5 M (95% CI: 8.3–NR), mOS of 13.9 M (95% CI: 10.6–17.8) and a 5-year OS rate of 19.7% (95% CI: 13.3–27.0)

Figure 3. Adverse Events were Consistent with Known Safety Profiles of NMA-LD and IL-2 Administration



- The incidence of AEs decreased rapidly within the first 2 weeks after lifileucel infusion, and no new or late-onset AEs related to lifileucel occurred
- All patients experienced grade 3/4 cytopenia based on laboratory assessment from the start of NMA-LD up to 30 days after lifileucel infusion (day 0); most cases resolved to grade ≤2 by day 30 after lifileucel infusion
- Most red blood cell and platelet transfusions occurred during the first 14 days after the initiation of NMA-LD

References:
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2. Medina et al., *J Clin Oncol*, 2025; 43 (33):3565-3572.
3. Karapetyan L, et al. *Transplant Cell Ther.* 2026;32:1098-1110.
4. Chesney JA, et al. *J Immunother Cancer.* 2022;10:e005755.

Abbreviations:

AE, adverse event; BL, baseline; CI, confidence interval; CR, complete response; CTLA, cytotoxic T-lymphocyte associated protein-4; ECOG, Eastern Cooperative Oncology Group; IL-2, interleukin-2; IRC, independent review committee; LDH, lactate dehydrogenase; M, month; mDOR, median duration of response; mOS, median overall survival; M, month; NMA-LD, nonmyeloablative lymphodepletion; NR, not reached; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; PR, partial response; SITC, Society for Immunotherapy of Cancer; SD, stable disease; SOD, sum of diameters; TIL, tumor-infiltrating lymphocyte; ULN, upper limit of normal; W, week.

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