2025 ASCO® ANNUAL MEETING

Lifileucel in patients with advanced melanoma: 5-year outcomes of the C-144-01 study

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Key Takeaway Points: 5-Year Analysis of the C-144-01 Study

1

One-time lifileucel therapy resulted in durable and deepening responses in patients with advanced melanoma who have limited treatment options after immune checkpoint inhibitor (ICI) therapy.

2

The incidence of adverse events (AEs) declined rapidly within 2 weeks after lifileucel infusion; new or late-onset AEs were not related to lifileucel.

3

Lifileucel demonstrated a long-term treatment benefit in patients with advanced melanoma previously treated with ICIs, with ≈20% of patients remaining alive at 5 years.

Background

- Immune checkpoint inhibitors (ICIs) have improved outcomes in patients with metastatic melanoma but many experience disease progression due to primary[1-3] or acquired resistance[3,4]
- Lifileucel is an autologous T-cell immunotherapy approved for advanced melanoma previously treated with a programmed cell death protein-1 (PD-1)–blocking antibody and, if *BRAF* V600 mutation–positive, BRAF ± MEK targeted therapy[5]
  - The lifileucel regimen consists of nonmyeloablative lymphodepletion (NMA-LD) followed by a single lifileucel infusion and a short course (≤6 doses) of high-dose interleukin-2 (IL-2)[6,7]
- In the registrational C-144-01 study in patients with advanced melanoma after ICI and targeted therapy, lifileucel provided an objective response rate (ORR) of 31.4%[6,7]
- We report final 5-year outcomes from the C-144-01 study, demonstrating a long-term benefit and meaningful overall survival (OS) with lifileucel

1. Long GV, et al. *Clin Cancer Res*. 2021;27:5280-5288. 2. Larkin J, et al. *N Engl J Med*. 2015;373:23-34. 3. Ribas A, et al. *JAMA*. 2016;315:1600-1609. 4. Hamid O, *Ann Oncol*. 2019;30:582588.
5. AMTAGVI [prescribing information]. Iovance Biotherapeutics, Inc.; 2024. 6. Chesney JA, et al. *J Immunother Cancer*. 2022;10:e005755. 7. Sarnaik AA, et al. *J Clin Oncol*. 2021;39:2656-2666.

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[1]		7.0 (0.7–75.8)

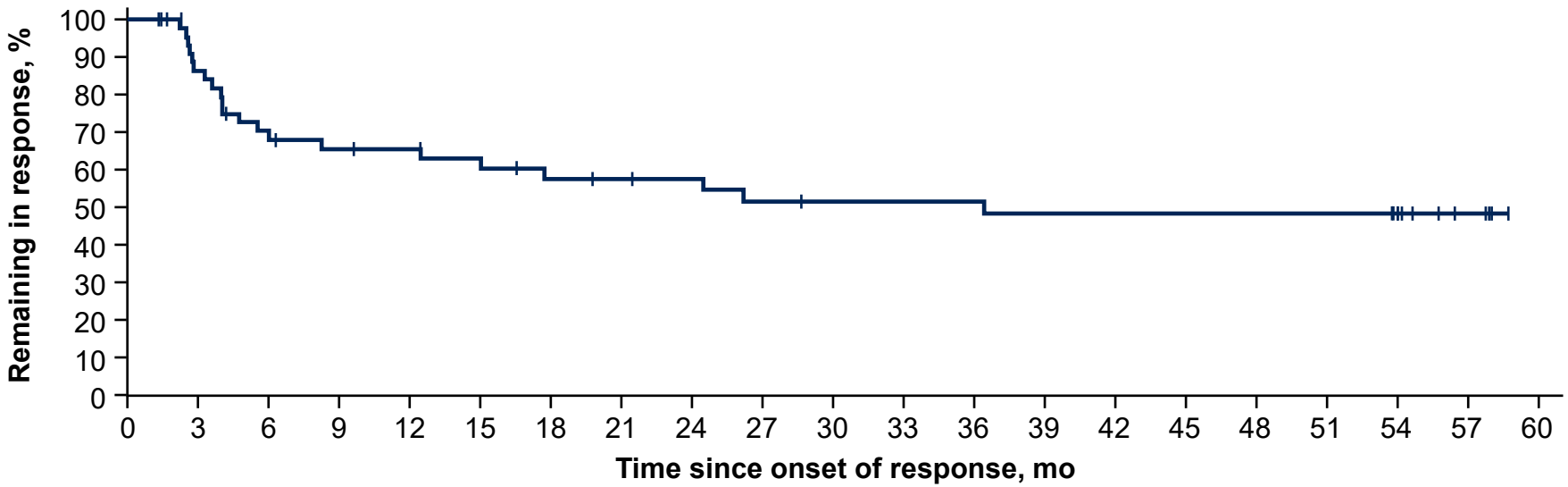
- At the November 20, 2024, data cutoff, the median follow-up was 57.8 months
- All patients had completed or discontinued the study, with 28 (18.3%) patients completing the 5-year study follow-up

[a]PD-L1 Tumor Proportion Score was missing for 45 patients. 1. Chesney JA, et al. *J Immunother Cancer.* 2022;10:e005755.
CTLA, cytotoxic T-lymphocyte associated protein-4; ECOG, Eastern Cooperative Oncology Group; IRC, independent review committee; LDH, lactate dehydrogenase; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; SITC, Society for Immunotherapy of Cancer; SOD, sum of diameters; ULN, upper limit of normal

Durable responses were observed with lifileucel

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

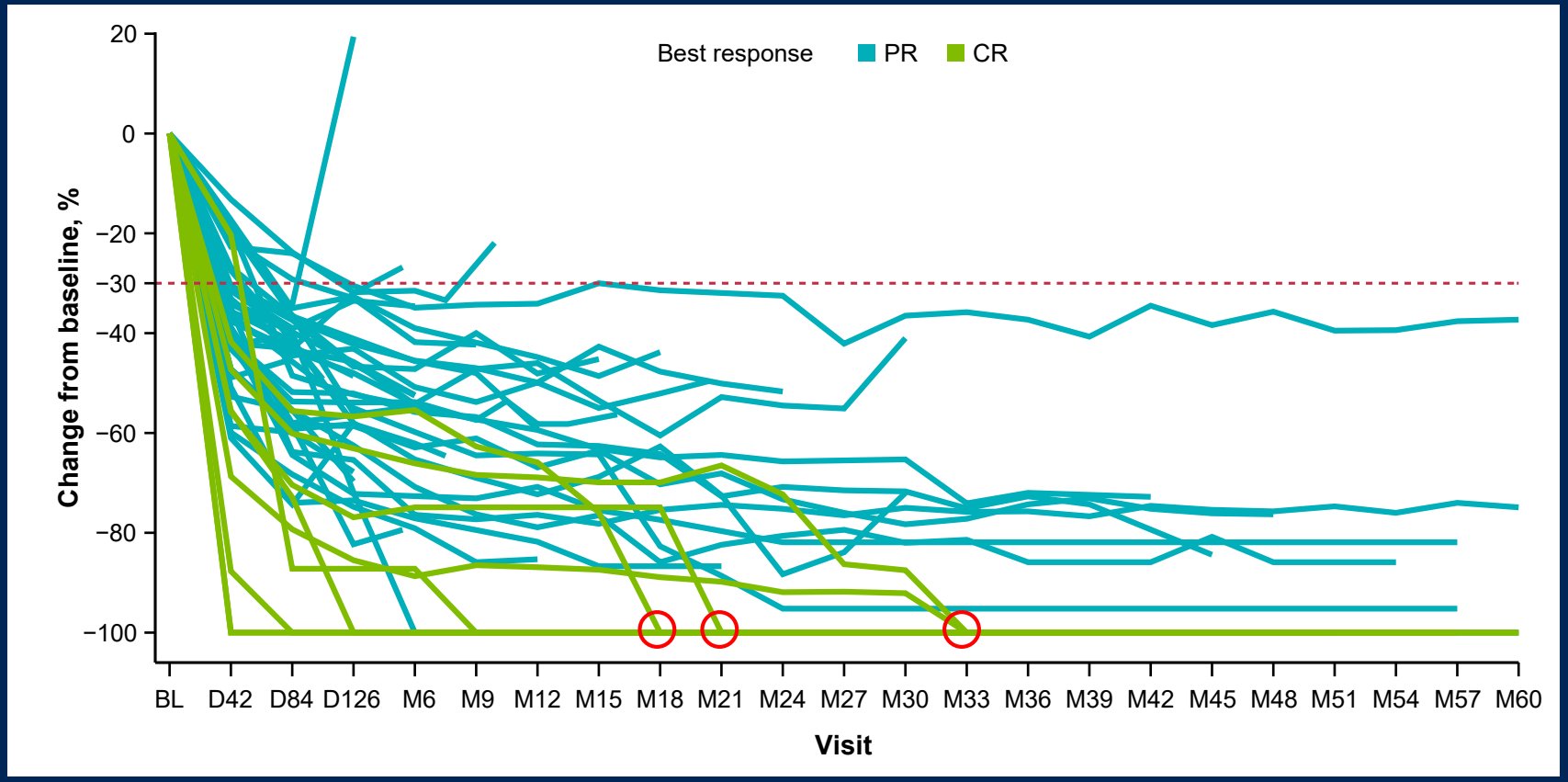
Duration of Response



CI, confidence interval; IRC, independent review committee; mo, months; NR, not reached; ORR, objective response rate.

Ongoing and deepening responses were observed

Percent Change From Baseline in Target Lesion SOD for Confirmed Responders

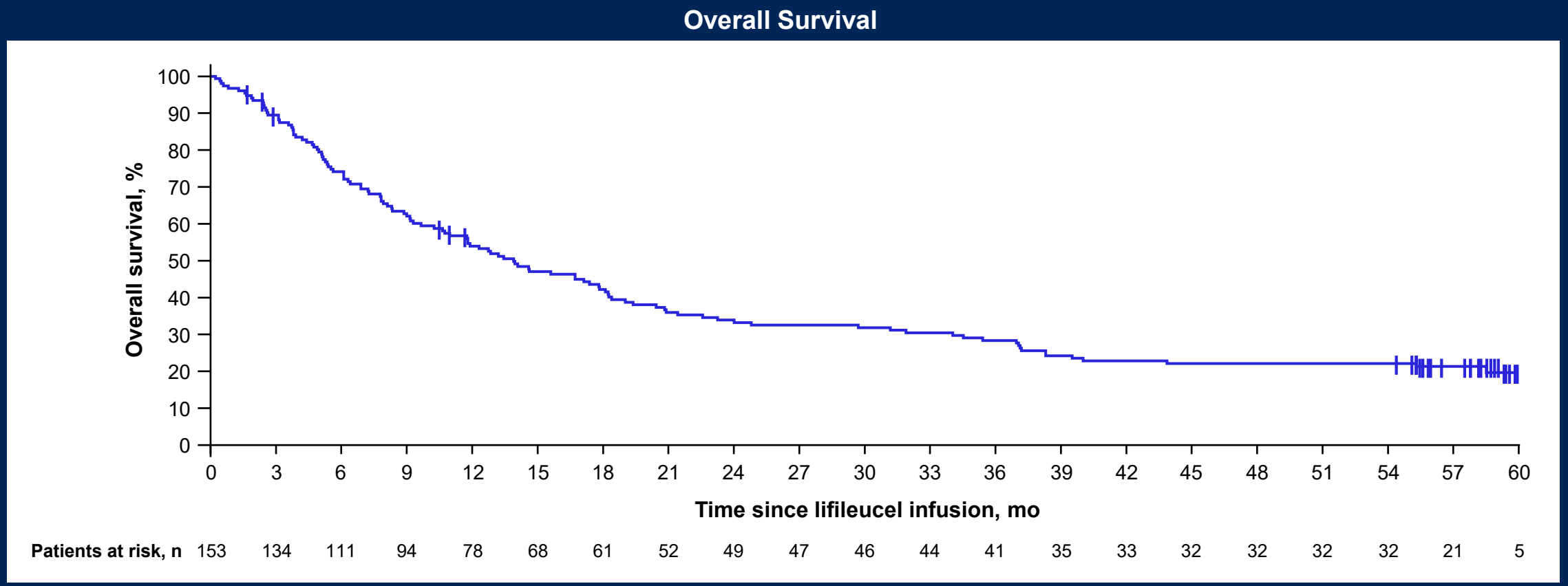


- The longest duration of ongoing response was 58.7 months
- Responses deepened over time
  - 16 patients had stable disease that improved to PR or had achieved PR that improved to CR
  - As depicted by the red circles, 4 patients had a PR 1 year posttreatment that deepened to CR as late as 3 years after lifileucel infusion
- Ongoing responses at year 3 were maintained through year 5

BL, baseline; CR, complete response; D, day; M, month; PR, partial response; SOD, sum of diameters.

Favorable overall survival outcomes were observed

- The median OS for the total population was 13.9 months; the estimated 5-year OS rate was 19.7%

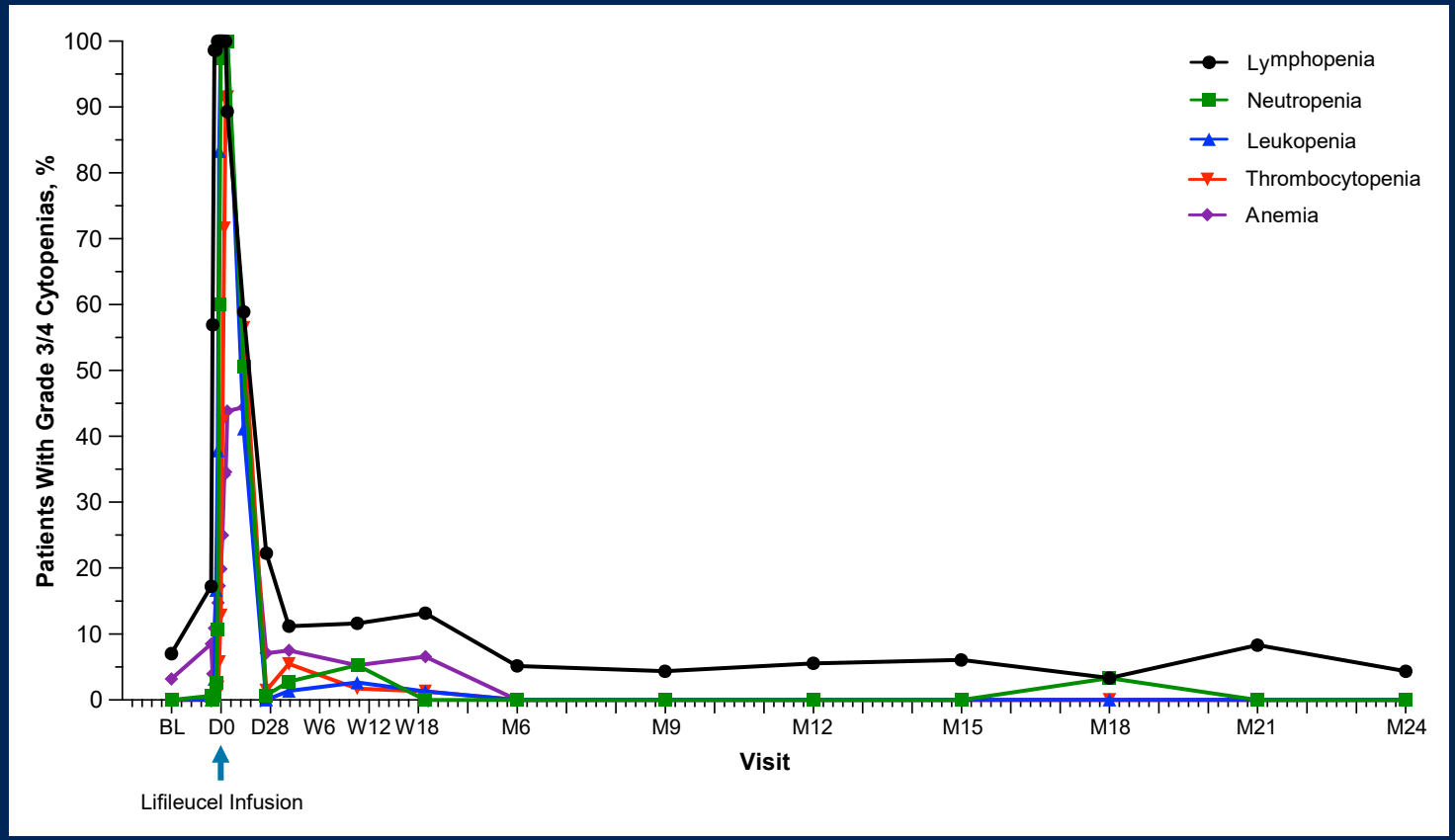


mo, months; OS, overall survival.

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

Prevalence of Laboratory-Assessed Grade 3/4 Cytopenias



AE, adverse event; BL, baseline; D, day; IL-2, interleukin-2; M, month; NMA-LD, nonmyeloablative lymphodepletion; W, week.

Conclusions

- This final 5-year analysis of the C-144-01 trial is the longest prospective follow-up of lifileucel and of any drug in the 2L+ setting for ICI-resistant melanoma
- One-time lifileucel therapy resulted in durable responses and a 5-year OS rate of 19.7%
  - 31.3% of responders completed the 5-year assessment with ongoing responses
  - The longest IRC-assessed duration of ongoing response was 58.7 months
  - Lifileucel resulted in deepening responses that stabilized over time after a single dose, with 4 patients who achieved PR 1 year posttreatment that converted to CR before 3 years after lifileucel infusion
- New or late-onset AEs were not related to lifileucel

The final 5-year analysis of the C-144-01 study showed a long-term benefit and favorable survival with lifileucel, with no new or late-onset AEs related to lifileucel

2L+, second-line or later; AE, adverse event; CR, complete response; ICI, immune checkpoint inhibitor; IRC, independent review committee; OS, overall survival; PR, partial response.

An open-access manuscript on the results of this 5-year follow-up is being simultaneously published in the *Journal of Clinical Oncology* and is available now.

"Long-Term Efficacy and Safety of Lifileucel Tumor-Infiltrating Lymphocyte (TIL) Cell Therapy in Patients With Advanced Melanoma: A 5-Year Analysis of the C-144-01 Study"

- The authors thank the patients and their families, as well as the investigators and study site team members who are participating in the study
- This study was sponsored by Iovance Biotherapeutics, Inc. (San Carlos, CA, USA)