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

Theresa Medina, MD[1]; Jason A. Chesney, MD, PhD[2]; Harriet M. Kluger, MD[3]; Omid Hamid, MD[4]; Eric D. Whitman, MD[5]; Mike Cusnir, MD[6]; Sajeve S. Thomas, MD[7]; Martin Wermke, MD[8]; Evidio Domingo-Musibay, MD[9]; Giao Q. Phan, MD[10]; John M. Kirkwood, MD[11]; James Larkin, MD, PhD[12]; Jeffrey Weber, MD, PhD[13]; Friedrich Graf Finckenstein, MD[14]; Jeffrey Chou, MD, PhD[14]; Brian Gastman, MD[14]; Xiao Wu, PhD[14]; Rana Fiaz, MD[14]; and Amod A. Sarnaik, MD[15]; for the C-144-01 Investigators

DOI https://doi.org/10.1200/JCO-25-00765

ABSTRACT

Patients with advanced melanoma resistant to immune checkpoint or BRAF/MEK inhibitors have treatment options with relatively low efficacy. Lifileucel, a one-time autologous tumor-infiltrating lymphocyte cell therapy, was approved in the United States on the basis of the pivotal C-144-01 study. A 5-year follow-up of the C-144-01 trial assessed the long-term efficacy and safety of lifileucel. At the cutoff date (November 20, 2024), the objective response rate was 31.4% (complete response [CR], 5.9%; partial response [PR], 25.5%). Overall, 79.3% of patients had tumor burden reduction; 16 had deepened responses with four converting from PR to CR > 1 year after lifileucel infusion; 31.3% of responders completed the 5-year assessment with ongoing responses. The median duration of response was 36.5 months. Responders (n = 48) had lower tumor burden and fewer liver or brain metastases than the overall population. The median overall survival (OS) was 13.9 months, with a 5-year OS of 19.7%. Adverse events were consistent with nonmyeloablative lymphodepletion and interleukin-2 safety profiles and declined rapidly within 2 weeks after lifileucel infusion. Most grade 3/4 cytopenias resolved to grade ≤2 by day 30. This 5-year analysis demonstrated long-term benefit and meaningful OS with one-time lifileucel therapy, with no additional long-term safety concerns.

ACCOMPANYING CONTENT

Appendix
Data Sharing Statement
Data Supplement
Protocol

Accepted May 27, 2025
Published June 2, 2025

J Clin Oncol 00:1-8

INTRODUCTION

Although immune checkpoint inhibitor (ICI) therapy has improved outcomes in patients with metastatic melanoma, many experience disease progression because of primary resistance (36%-72%)[1-3] and acquired resistance (25%-40%).[2,4] Resistance to BRAF/MEK inhibitors is observed in approximately 24%-48% of patients[5-7] and responders may experience disease progression within a year after therapy.[5-7]

Lifileucel is a tumor-derived autologous T-cell immunotherapy approved in the United States for the treatment of adults with advanced (unresectable or metastatic) melanoma after anti–PD-1/PD-L1 therapy and BRAF ± MEK inhibitor, if *BRAF* V600 mutation–positive.[8] In the registrational C-144-01 study, patients who received lifileucel had an objective response rate (ORR) of 31.4%.[9] We report 5-year outcomes from the C-144-01 study demonstrating long-term benefit and meaningful overall survival (OS) in patients with ICI-resistant melanoma.

METHODS

Study Design and Patient Population

C-144-01 (ClinicalTrials.gov identifier: NCT02360579) is a phase II study of lifileucel in patients with advanced melanoma who progressed on or after anti–PD-1/PD-L1 therapy.[10] Study design, methods, and primary results have been reported.[9,10] The study enrolled adults with advanced melanoma and disease progression after ≥1 prior systemic therapy including an anti–PD-1 antibody and, if *BRAF* V600 mutation–positive, BRAF ± MEK inhibitors.[10] Efficacy and safety were assessed for patients enrolled in cohorts 2 and 4.

The study was approved by site-specific institutional review boards and conducted according to the Declaration of Helsinki and Good Clinical Practice guidelines. All patients provided written informed consent.

Treatment

Patients received cryopreserved lifileucel generated from resected tumor tissue.[10] After nonmyeloablative lymphodepletion (NMA-LD), patients received a single infusion of thawed cryopreserved lifileucel (1×10^9 -150×10^9 cells) followed by high-dose interleukin-2 (IL-2; ≤6 doses).[10]

End Points and Assessments

The primary end point was ORR assessed and confirmed by an independent review committee (IRC) using RECIST v1.1.[10] Key secondary end points were duration of response (DOR), disease control rate (DCR), OS, and safety.[10] After the end-of-treatment visit, efficacy assessments occurred every 6 weeks (±3 days) until month 6 (week 24) and then every 3 months (12 weeks) for up to 5 years or until disease progression or start of new anticancer therapy. Survival status was assessed every 3 months for up to 5 years or death, whichever occurred earlier. Adverse events (AEs) were graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (v4.03).

The IRC-assessed ORR and DCR were expressed as binomial proportions with 2-sided confidence intervals on the basis of the Clopper-Pearson exact method. DOR was determined from the time point at which initial response criteria (RECIST v1.1) were met for a complete response (CR) or partial response (PR; whichever occurred first) until the first date that progressive disease or death was objectively documented. OS was determined from the date of lifileucel infusion to the date of death due to any cause. DOR and OS were right-censored; probabilities were determined using Kaplan-Meier estimates. AEs were summarized using descriptive statistics.

RESULTS

Patient Disposition and Baseline Characteristics

Of 189 patients enrolled across cohorts 2 and 4, 153 received lifileucel. At the final 5-year cutoff date (November 20, 2024), 28 patients completed 5 years of follow-up (Fig 1); the median OS follow-up was 57.8 months (cohort 2, 59.3 months; cohort 4, 57.6 months). Patients received a median of three lines of prior systemic therapy (Table 1). Compared with the overall study population (N = 153), responders (n = 48) trended toward lower tumor burden, lower lactate dehydrogenase levels, and fewer liver or brain metastases (Table 1). Similar trends appeared in responders with OS ≥36 months versus OS <36 months (Data Supplement, Table S1, online only).

Response Outcomes

At the data cutoff date, the ORR was 31.4% (CR, 5.9%, 9/153; PR, 25.5%, 39/153), and 79.3% (111/140) of patients had tumor burden reductions (Data Supplement, Fig S1). The median time to response was 1.4 months (range, 1.3-4.2). The median duration of IRC-assessed response was 36.5 months (95% CI, 8.3 to not reached; Fig 2); four patients achieved CR 1 year after lifileucel infusion (Data Supplement, Figs S1B and S1C). The longest response was ongoing at 58.7 months; 31.3% (15/48) of responders completed the 5-year assessment with ongoing responses of CR and PR (Fig 3). The proportion of lifileucel responders who later progressed was 43.8% (21/48; 95% CI, 29.5% to 58.8%; Data Supplement, Table S2).

Overall Survival

The median OS for the overall population was 13.9 months (95% CI, 10.6 to 17.8) with 5-year OS rate of 19.7% (Data Supplement, Fig S2A). There was no meaningful difference in median OS between early and late responders on the basis of the OS landmark analysis at the month 4.5 time point (because all responses started before 4.5 months after lifileucel infusion; Data Supplement, Fig S2B). In a Cox proportional hazards model with deepened response (ie, stable disease converting to PR or PR converting to CR) as a time-varying covariate, no meaningful association between deepened response and OS was observed (hazard ratio, 0.489; $P = .1264$)

Incidence of AEs

AEs were consistent with the known safety profile of NMA-LD and IL-2 and decreased rapidly within 2 weeks after lifileucel infusion (Data Supplement, Fig S3), with no new or late-onset AEs related to lifileucel. In the safety population (n = 156), deaths due to AEs (investigator-reported) of any cause occurred in 12 patients (7.7%); of these patients, four (2.6%) died ≤30 days after lifileucel infusion and eight (5.1%) died after 30 days after lifileucel infusion. There were five deaths (3.2%) that were considered due to treatment-related AEs; four of these (pneumonia, arrhythmia, acute respiratory failure, intra-abdominal hemorrhage) occurred within 30 days after lifileucel while one (bone marrow failure) occurred more than 30 days after lifileucel infusion. Two deaths (1.3%) due to arrythmia and acute respiratory failure were attributed to NMA-LD, 1 death due to pneumonia was attributed to NMA-LD and IL-2, and two deaths (1.3%) due to intra-abdominal hemorrhage and bone marrow failure were attributed to all components of the lifileucel treatment regimen.

All patients experienced grade 3/4 hematologic laboratory abnormalities from initiation of NMA-LD up to 30 days after lifileucel infusion (Data Supplement, Figs S4A-S4E). By day −5, all patients achieved grade 3/4 lymphopenia as intended. In most patients, grade 3/4 cytopenia

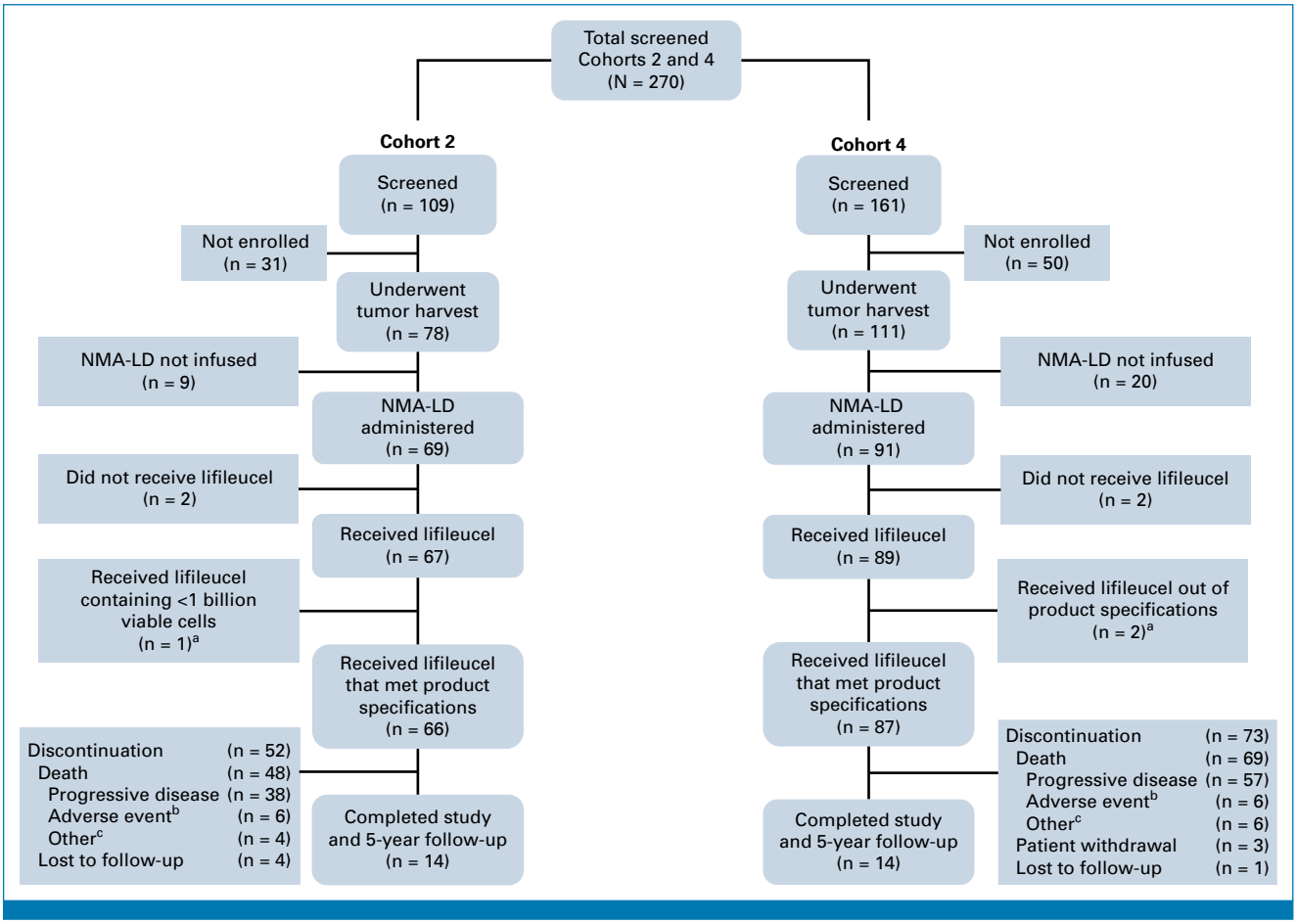

FIG 1. Patient disposition. Four patients underwent tumor harvest but NMA-LD was not administered because of death (cohort 2, n = 1; cohort 4, n = 3). One patient in cohort 2 was administered NMA-LD but lifileucel was not infused because of death. [a]Patients subsequently died due to progressive disease. [b]Deaths due to adverse events unrelated to any component of the lifileucel regimen include septic shock (n = 1), failure to thrive (n = 2), cerebral hemorrhage (n = 1), multiple organ dysfunction syndrome (n = 1), pulmonary embolism (n = 1), and intracranial hemorrhage (n = 1); death due to treatment-related adverse events include pneumonia related to NMA-LD and IL-2 administration (n = 1), arrhythmia related to cyclophosphamide (n = 1), acute respiratory failure related to NMA-LD (n = 1), intra-abdominal hemorrhage related to all components of the lifileucel regimen (n = 1), and bone marrow failure related to all components of the lifileucel treatment regimen (n = 1). [c]Other causes of death were disease progression or metastatic melanoma (n = 5), death during sleep (n = 1), and unknown causes (n = 4). IL-2, interleukin-2; NMA-LD, nonmyeloablative lymphodepletion.

resolved to grade ≤2 by day 30 after lifileucel infusion. Most platelet and RBC transfusions occurred during the first 14 days after NMA-LD initiation (Data Supplement, Figs S5A and S5B).

DISCUSSION

There is a paucity of prospective trial data for treatment-refractory melanoma with multiyear follow-up. This 5-year analysis is the longest follow-up of lifileucel in patients with 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 ongoing IRC-assessed response was 58.7 months with responses deepening over time. No new or late-onset AEs related to lifileucel occurred. The incidence of death due to treatment-related AEs within or after the first 30 days after lifileucel therapy was 3.2% (5/156); most fatal treatment-related AEs were attributed to NMA-LD or IL-2.

In the post-ICI setting of advanced melanoma, retreatment with ICIs[11,12] and post-ICI chemotherapy[13] were shown to induce responses with poor durability, typically lower than what was observed in the C-144-01 trial.[11,13] An ORR of 31.4% and median DOR of 36.5 months with lifileucel in the C-144-01 trial are notable, given that patients had received a median of three prior lines and up to nine prior lines of systemic therapy, and 53.6% had received anti–PD-1/PD-L1/anticytotoxic T-lymphocyte–associated protein-4 combination therapy. Response rates of 45%-66% were observed with other tumor-infiltrating lymphocyte (TIL) therapies administered in earlier treatment settings as first- and second-line

TABLE 1. Demographics and Baseline Disease Characteristics

Characteristic	Pooled Cohorts, 2 + 4 (N = 153)	All Responders (n = 48)	Responders With DOR ≥12 Months (n = 26)
Median age (range), years	56 (20-79)	55 (25-77)	55 (37-77)
Male, No. (%)	83 (54.2)	29 (60.4)	16 (61.5)
ECOG PS at screening, No. (%)			
0	104 (68.0)	32 (66.7)	17 (65.4)
1	49 (32.0)	16 (33.3)	9 (34.6)
Melanoma subtype, No. (%)			
Cutaneous	82 (53.6)	27 (56.3)	16 (61.5)
Mucosal	12 (7.8)	6 (12.5)	5 (19.2)
Acral	10 (6.5)	1 (2.1)	1 (3.8)
Other/unknown[a]	48 (31.4)	14 (29.2)	4 (15.4)
Melanoma stage at study entry, No. (%)			
IIIC	10 (6.5)	5 (10.4)	3 (11.5)
IV	143 (93.5)	43 (89.6)	23 (88.5)
BRAF mutation status, No. (%)			
V600E/K	41 (26.8)	13 (27.1)	9 (34.6)
Wild type	103 (67.3)	32 (66.7)	16 (61.5)
Other	6 (3.9)	2 (4.2)	0
Unknown	3 (2.0)	1 (2.1)	1 (3.8)
PD-L1 status, No. (%)			
TPS ≥1%	76 (49.7)	28 (58.3)	15 (57.7)
TPS <1%	32 (20.9)	11 (22.9)	8 (30.8)
Missing	45 (29.4)	9 (18.8)	3 (11.5)
Liver and/or brain lesions by IRC, No. (%)	72 (47.1)	19 (39.6)	10 (38.5)
Median target lesion SOD (range), mm	101.1 (13.5-552.9)	68.8 (13.5-552.9)	69.1 (17.8-190.1)
Baseline lesions in ≥3 anatomic sites, No. (%)	109 (71.2)	29 (60.4)	15 (57.7)
Baseline target and nontarget lesions, No. (%)			
≤3	36 (23.5)	18 (37.5)	12 (46.2)
>3	116 (75.8)	30 (62.5)	14 (53.8)
Missing	1 (0.7)	0	0
LDH level, No. (%)			
≤ULN	70 (45.8)	27 (56.3)	17 (65.4)
1-2 × ULN	54 (35.3)	18 (37.5)	8 (30.8)
>2 ULN	29 (19.0)	3 (6.3)	1 (3.8)
Median number of prior systemic therapies (range)	3 (1-9)	3 (1-8)	3 (2-8)
Prior systemic therapies, No. (%)			
Anti–PD-1/PD-L1	153 (100)	48 (100)	26 (100)
Anti–CTLA-4	125 (81.7)	41 (85.4)	23 (88.5)
Anti–PD-1 plus anti–CTLA-4	82 (53.6)	22 (45.8)	11 (42.3)
BRAF ± MEK inhibitor	39 (25.5)	12 (25.0)	8 (30.8)
IL-2	13 (8.5)	4 (8.3)	3 (11.5)
Median cumulative duration of prior anti–PD-1/PD-L1 therapy (range), months	7.0 (0.7-75.8)	7.2 (1.4-54.4)	4.5 (1.4-54.4)
Resistance to prior anti–PD-1/PD-L1 therapy as defined by SITC criteria			
Primary resistance[b]	109 (71.2)	36 (75.0)	21 (80.8)
Secondary resistance[c]	41 (26.8)	12 (25.0)	5 (19.2)

(continued on following page)

TABLE 1. Demographics and Baseline Disease Characteristics (continued)

Characteristic	Pooled Cohorts, 2 + 4 (N = 153)	All Responders (n = 48)	Responders With DOR ≥12 Months (n = 26)
Anatomic site of resection, No. (%)			
Lung	12 (7.8)	1 (2.1)	1 (3.8)
Liver	12 (7.8)	6 (12.5)	4 (15.4)
Other[d]	122 (79.7)	41 (85.4)	21 (80.8)
Median total infused TIL viable cells, $\times 10^9$ (range)	21.1 (1.2-99.5)	30.0 (6.2-72.0)	30.9 (7.6-72.0)

NOTE. Disease metastasis data at study entry were collected for cohort 4 but not cohort 2; in cohort 4, 10.3% (9/87) had M1a status, 13.8% (12/87) had M1b status, 63.2% (55/87) had M1c status, and 11.5% (10/87) had M1d status.

Abbreviations: CTLA-4, cytotoxic T-lymphocyte antigen-4; ECOG, Eastern Cooperative Oncology Group; IL-2, interleukin-2; IRC, independent review committee; LDH, lactate dehydrogenase; PS, performance status; SOD, sum of diameters; SITC, Society for Immunotherapy of Cancer; TPS, tumor proportion score; ULN, upper limit of normal.

[a]Includes diagnoses of melanoma of unknown primary, unknown, or subtype not otherwise specified or classified.

[b]Includes primary resistance to prior anti–PD-1/PD-L1 in the metastatic setting and primary resistance/early relapse to prior anti–PD-1/PD-L1 in the adjuvant setting.[24]

[c]Includes secondary resistance to prior anti–PD1/PD-L1 in metastatic setting and late relapse in adjuvant setting.[24]

[d]Other resection sites included lymph node, skin/subcutaneous, musculoskeletal, breast, peritoneal/retroperitoneal, and others.

melanoma treatment.[14-16] In one retrospective study, lower response rates were observed in patients with metastatic melanoma refractory to anti–PD-1/PD-L1 monotherapy (24%) versus naive patients (56%).[16] In the *BRAF* V600 E/K mutation subgroup, ORRs for patients with and without prior BRAF/MEK inhibitor exposure were 20% and 60%, respectively.[16]

Owing to improved responses with TIL observed in earlier treatment settings, prospective exploration of TIL combined with ICIs first line for advanced melanoma is underway.[17,18] In an ongoing phase II study (IOV-COM-202; NCT03645928), patients with ICI-naive melanoma who received lifileucel plus pembrolizumab had an ORR of 65.2% (CR, 30.4%).[18] This finding supports evaluation of lifileucel in patients with less pretreated melanoma and is the basis for the ongoing phase III TILVANCE 301 trial (ClinicalTrials.gov identifier: NCT05727904) of lifileucel plus pembrolizumab in treatment-naive patients.[19]

A limitation of the C-144-01 study was the absence of a comparator. Subgroup analyses herein should be interpreted

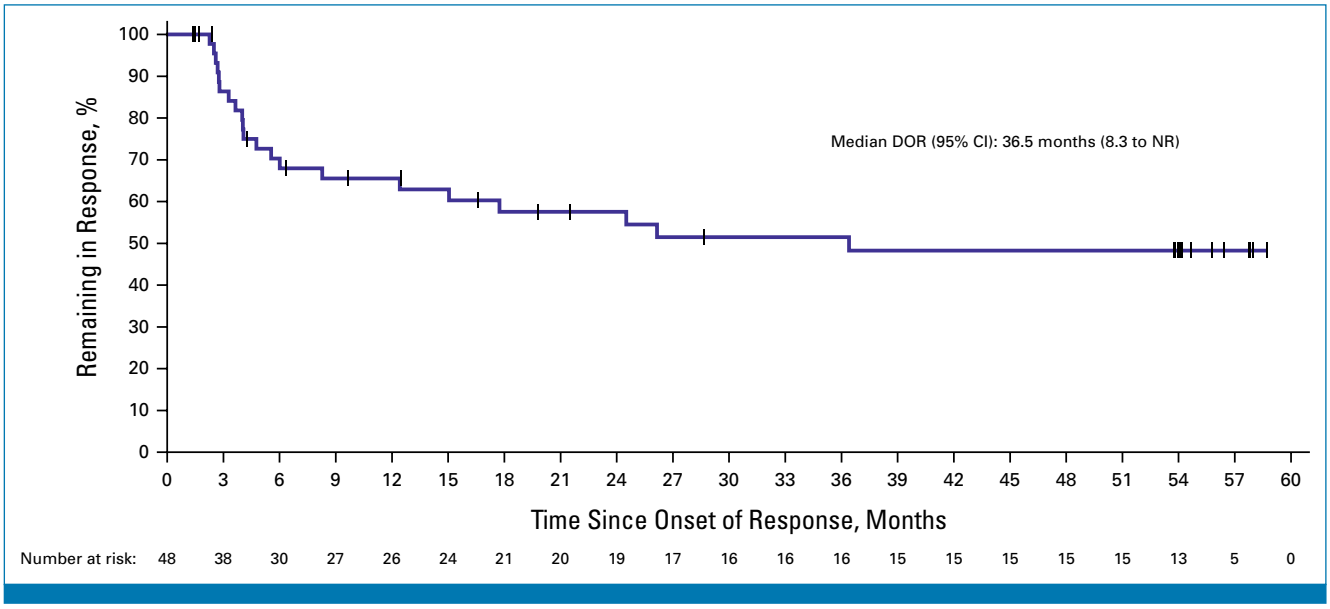

FIG 2. Kaplan-Meier estimated DOR in patients who achieved CR or PR. Tick marks indicate censored patients. CR, complete response; DOR, duration of response; NR, not reached; PR, partial response.

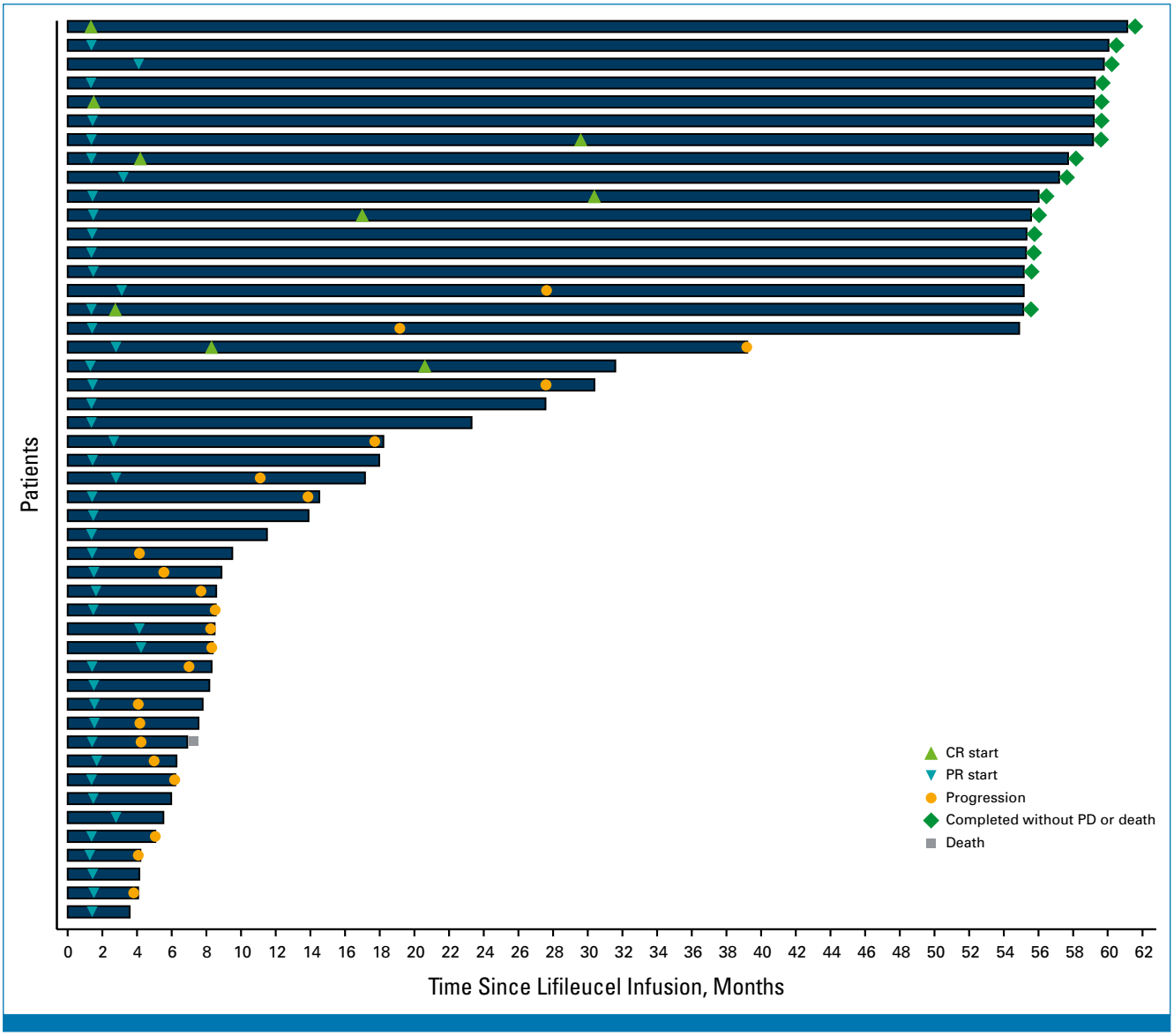

FIG 3. Time to response and time on efficacy assessment for confirmed responders. CR, complete response; PD, progressive disease; PR, partial response.

with caution. The impact of NMA-LD or IL-2 on antitumor response was not assessed. However, no evidence exists that lymphodepleting chemotherapy has activity in melanoma, and IL-2 is administered and present only in the absence[20] of endogenous lymphocytes after lymphodepleting chemotherapy and would therefore not be expected to contribute to the antitumor activity of lifileucel.[21] The observed rate of mortality because of treatment-related toxicity in the phase II C-144-01 study (3.6%) is comparable with that observed in the phase II study of nivolumab and ipilimumab in patients with advanced melanoma, where there was a treatment-related mortality rate of 3.2%.[22] As experience with nivolumab and ipilimumab increased, leading to improvements in patient selection and toxicity management, treatment-related mortality also improved.[3,23]

In conclusion, the 5-year analysis of the C-144-01 study showed long-term benefit and favorable survival with lifileucel and no related long-term safety concerns. Lifileucel provides an optimal response when administered soon after treatment failure with anti–PD-1/PD-L1 or BRAF/MEK inhibitors.

AFFILIATIONS

[1]University of Colorado Cancer Center—Anschutz Medical Campus, Aurora, CO
[2]Brown Cancer Center, Louisville, KY
[3]Yale Cancer Center, New Haven, CT
[4]The Angeles Clinic and Research Institute, a Cedars Sinai Affiliate, Los Angeles, CA
[5]Atlantic Health System, Morristown, NJ

[6]Mount Sinai Medical Center, Miami Beach, FL
[7]AdventHealth Orlando, Orlando, FL
[8]Technical University Dresden—NCT/UCC Early Clinical Trial Unit, Dresden, Germany
[9]Allina Health Cancer Institute, Minneapolis, MN
[10]UConn Health/Neag Cancer Center, Farmington, CT
[11]UPMC Hillman Cancer Center, Pittsburgh, PA
[12]The Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom
[13]Laura and Isaac Perlmutter Cancer Center, NYU Langone Medical Center, New York, NY
[14]Iovance Biotherapeutics, Inc, San Carlos, CA
[15]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL

CORRESPONDING AUTHOR

Theresa Medina, MD; e-mail: theresa.medina@cuanschutz.edu.

PRIOR PRESENTATION

Presented at the 2025 American Society of Clinical Oncology Annual Meeting, May 30-June 3, 2025, Chicago, IL, and at the Society for Melanoma Research Annual Meeting, October, 10-13, 2024, New Orleans, LA.

SUPPORT

Supported by Iovance Biotherapeutics, Inc (San Carlos, CA).

CLINICAL TRIAL INFORMATION

NCT02360579 (C-144-01)

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI https://doi.org/10.1200/JCO-25-00765.

DATA SHARING STATEMENT

A data sharing statement provided by the authors is available with this article at DOI https://doi.org/10.1200/JCO-25-00765.
The data relevant to the study are included within the article and its supplementary data files.

AUTHOR CONTRIBUTIONS

Conception and design: Amod A. Sarnaik
Provision of study materials or patients: John M. Kirkwood, Giao Q. Phan, Amod A. Sarnaik
Collection and assembly of data: John M. Kirkwood
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

ACKNOWLEDGMENT

The authors thank the patients and their families who participated in the study. The authors appreciate the contributions of the late Dr Jeffrey Weber who served as the chair of the steering committee and provided valuable insights to guide this pivotal study, leading to the eventual approval of lifileucel for the treatment of melanoma. Medical writing and editorial support were provided by Kalpana Vijayan, PhD, and Lauren Gallagher, BS Pharm, PhD, of Peloton Advantage, LLC, an OPEN Health company, and funded by Iovance. Coauthor Jeffrey Weber, MD, PhD, died August 18, 2024. C-144-01 Investigators are listed in Appendix Table A1 (online only).

REFERENCES

1. Long GV, Robert C, Butler MO, et al: Standard-dose pembrolizumab plus alternate-dose ipilimumab in advanced melanoma: KEYNOTE-029 cohort 1C, a phase 2 randomized study of two dosing schedules. Clin Cancer Res 27:5280-5288, 2021
2. Ribas A, Hamid O, Daud A, et al: Association of pembrolizumab with tumor response and survival among patients with advanced melanoma. JAMA 315:1600-1609, 2016
3. Wolchok JD, Chiarion-Sileni V, Rutkowski P, et al: Final, 10-year outcomes with nivolumab plus ipilimumab in advanced melanoma. N Engl J Med 392:11-22, 2025
4. Hamid O, Robert C, Daud A, et al: Five-year survival outcomes for patients with advanced melanoma treated with pembrolizumab in KEYNOTE-001. Ann Oncol 30:582-588, 2019
5. Robert C, Grob JJ, Stroyakovskiy D, et al: Five-year outcomes with dabrafenib plus trametinib in metastatic melanoma. N Engl J Med 381:626-636, 2019
6. Ascierto PA, Dréno B, Larkin J, et al: 5-year outcomes with cobimetinib plus vemurafenib in BRAFV600 mutation-positive advanced melanoma: Extended follow-up of the coBRIM study. Clin Cancer Res 27:5225-5235, 2021
7. Schadendorf D, Dummer R, Flaherty KT, et al: COLUMBUS 7-year update: A randomized, open-label, phase III trial of encorafenib plus binimetinib versus vemurafenib or encorafenib in patients with BRAF V600E/K-mutant melanoma. Eur J Cancer 204:114073, 2024
8. Amtagvi [package insert]. Philadelphia, PA, Iovance Biotherapeutics, 2024
9. Chesney J, Lewis KD, Kluger H, et al: Efficacy and safety of lifileucel, a one-time autologous tumor-infiltrating lymphocyte (TIL) cell therapy, in patients with advanced melanoma after progression on immune checkpoint inhibitors and targeted therapies: Pooled analysis of consecutive cohorts of the C-144-01 study. J Immunother Cancer 10:e005755, 2022
10. Sarnaik AA, Hamid O, Khushalani NI, et al: Lifileucel, a tumor-infiltrating lymphocyte therapy, in metastatic melanoma. J Clin Oncol 39:2656-2666, 2021
11. Nardin C, Hennemann A, Diallo K, et al: Efficacy of immune checkpoint inhibitor (ICI) rechallenge in advanced melanoma patients' responders to a first course of ICI: A multicenter national retrospective study of the French Group of Skin Cancers (Groupe de Cancérologie Cutanée, GCC). Cancers (Basel) 15:3564, 2023
12. Long GV, Robert C, Blank CU, et al: Outcomes in patients (pts) treated with ipilimumab (ipi) after pembrolizumab (pembro) in KEYNOTE-006 [abstract]. Pigment Cell Melanoma Res 30:118, 2017
13. Goldinger SM, Buder-Bakhaya K, Lo SN, et al: Chemotherapy after immune checkpoint inhibitor failure in metastatic melanoma: A retrospective multicentre analysis. Eur J Cancer 162:22-33, 2022
14. Rohaan MW, Borch TH, van den Berg JH, et al: Tumor-infiltrating lymphocyte therapy or ipilimumab in advanced melanoma. N Engl J Med 387:2113-2125, 2022
15. Goff SL, Dudley ME, Citrin DE, et al: Randomized, prospective evaluation comparing intensity of lymphodepletion before adoptive transfer of tumor-infiltrating lymphocytes for patients with metastatic melanoma. J Clin Oncol 34:2389-2397, 2016
16. Seitter SJ, Sherry RM, Yang JC, et al: Impact of prior treatment on the efficacy of adoptive transfer of tumor-infiltrating lymphocytes in patients with metastatic melanoma. Clin Cancer Res 27: 5289-5298, 2021
17. L'Orphelin JM, Lancien U, Nguyen JM, et al: NIVO-TIL: Combination anti-PD-1 therapy and adoptive T-cell transfer in untreated metastatic melanoma: An exploratory open-label phase I trial. Acta Oncol 63:867-877, 2024
18. Thomas SS, Gogas H, Hong YK, et al: Efficacy and safety of lifileucel, an autologous tumor-infiltrating lymphocyte cell therapy, and pembrolizumab in patients with immune checkpoint inhibitor-naive unresectable or metastatic melanoma: Updated results from IOV-COM-202 cohort 1A. J Clin Oncol 42, 2024 (suppl 16; abstr 9505)
19. Olson D, Hong Y, Thomas SS, et al: A phase 3 study (TILVANCE-301) to assess the efficacy and safety of lifileucel, an autologous tumor-infiltrating lymphocyte cell therapy, in combination with pembrolizumab compared with pembrolizumab alone in patients with untreated unresectable or metastatic melanoma. J Clin Oncol 41, 2023 (suppl 16; abstr TPS9607)
20. Jarkowski A, Wong MKK: A re-assessment of the safety and efficacy of interleukin-2 for the treatment of renal cell carcinoma. Clin Med Ther 1:527-540, 2009
21. Williams KM, Gress RE: Immune reconstitution and implications for immunotherapy following haematopoietic stem cell transplantation. Best Pract Res Clin Haematol 21:579-596, 2008

22. Hodi FS, Chesney J, Pavlick AC, et al: Combined nivolumab and ipilimumab versus ipilimumab alone in patients with advanced melanoma: 2-year overall survival outcomes in a multicentre, randomised, controlled, phase 2 trial. Lancet Oncol 17:1558-1568, 2016
23. Schenker M, Burotto M, Richardet M, et al: Randomized, open-label, phase 2 study of nivolumab plus ipilimumab or nivolumab monotherapy in patients with advanced or metastatic solid tumors of high tumor mutational burden. J Immunother Cancer 12:e008872, 2024
24. Kluger HM, Tawbi HA, Ascierto ML, et al: Defining tumor resistance to PD-1 pathway blockade: Recommendations from the first meeting of the SITC Immunotherapy Resistance Taskforce. J Immunother Cancer 8:e000398, 2020

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Theresa Medina
Research Funding: Merck (Inst), Replimune (Inst), Bristol Myers Squibb (Inst), Iovance Biotherapeutics (Inst), Immunocore (Inst), Day One Biopharmaceuticals (Inst), Pfizer (Inst), Genentech (Inst), Moderna Therapeutics (Inst), Agenus (Inst), TriSalus Life Sciences (Inst), Ultimovacs (Inst), Regeneron (Inst)

Jason A. Chesney
Consulting or Advisory Role: Iovance Biotherapeutics
Research Funding: Amgen, Replimune, Iovance Biotherapeutics, Bristol Myers Squibb
Patents, Royalties, Other Intellectual Property: University of Louisville US Patents

Harriet M. Kluger
Consulting or Advisory Role: Iovance Biotherapeutics, Signatera, GigaGen, GI Reviewers, Pliant, Invox, Werewolf Pharma, Immunocore, Replimune, Teva, Genmab
Research Funding: Merck (Inst), Bristol Myers Squibb (Inst), Apexigen (Inst)
Travel, Accommodations, Expenses: Apexigen

Omid Hamid
Honoraria: Bristol Myers Squibb, Novartis, Pfizer, Regeneron, Immunocore
Consulting or Advisory Role: Amgen, Novartis, Roche, Bristol Myers Squibb, Merck, BeiGene, Genentech, GlaxoSmithKline, Immunocore, Incyte, Janssen, Regeneron, Tempus, Zelluna, BioAtla, Idera, Pfizer, Iovance Biotherapeutics, Alkermes, Eisai, Bactonix, Georgiamune, GigaGen, Grit Biotechnology, Instil Bio, IO Biotech, KSQ Therapeutics, Moderna Therapeutics, Obsidian Therapeutics, Vial, NGM Biopharmaceuticals
Speakers' Bureau: Bristol Myers Squibb, Novartis, Pfizer, Regeneron, Immunocore
Research Funding: Bristol Myers Squibb (Inst), Genentech (Inst), Immunocore (Inst), Incyte (Inst), Merck (Inst), Merck Serono (Inst), Novartis (Inst), Pfizer (Inst), Roche (Inst), Amgen (Inst), CytomX Therapeutics (Inst), Iovance Biotherapeutics (Inst), NextCure (Inst), GlaxoSmithKline (Inst), Arcus Biosciences (Inst), Aduro Biotech (Inst), Akeso Biopharma (Inst), Exelixis (Inst), Moderna Therapeutics (Inst), Regeneron (Inst), Sanofi (Inst), Seagen (Inst), Torque (Inst), Zelluna (Inst), BioAtla (Inst), Idera (Inst)

Eric D. Whitman
Consulting or Advisory Role: Merck Sharp & Dohme, Castle Biosciences, Sun Pharma, Immuneering, Replimune
Speakers' Bureau: Bristol Myers Squibb, Merck Sharp & Dohme, Castle Biosciences, Regeneron
Research Funding: Bristol Myers Squibb (Inst), Merck Sharp & Dohme (Inst), Castle Biosciences (Inst), Genentech/Roche (Inst), Amgen (Inst), AstraZeneca/MedImmune (Inst), Iovance Biotherapeutics (Inst), Toray Industries (Inst), Seagen (Inst), Astellas Pharma (Inst), BioNTech SE (Inst), Boehringer Ingelheim (Inst), Replimune (Inst), OncoC4 (Inst), Takeda (Inst), Vaxiion Therapeutics (Inst), OncoResponse (Inst), Dragonfly Therapeutics (Inst), BioAtla (Inst), Krystal Biotech (Inst), Ascendis Pharma (Inst)
Patents, Royalties, Other Intellectual Property: Nerve monitoring dissection device, Lighted Polyhedral surgical retractor

Mike Cusnir
Speakers' Bureau: Sirtex Medical, Guardant Health

Sajeve S. Thomas
Speakers' Bureau: BMS, Merck, Pfizer, Natera, SpringWorks Therapeutics

Martin Wermke
Honoraria: Lilly, Boehringer Ingelheim, SYNLAB, Janssen, Merck Serono, GWT, Amgen, Novartis, Pfizer, BMS GmbH & Co. KG, Regeneron, MJH/PER, Takeda
Consulting or Advisory Role: Bristol Myers Squibb, Novartis, Lilly, Boehringer Ingelheim, ISA Pharmaceuticals, Amgen, immatics, Bayer, ImCheck Therapeutics, AstraZeneca, Tacalyx, Regeneron, Daiichi Sankyo Europe GmbH, Zymeworks, PharmaMar, Iovance Biotherapeutics, T-Knife, Genentech
Research Funding: Roche (Inst)
Travel, Accommodations, Expenses: Pfizer, Bristol Myers Squibb, AstraZeneca, Amgen, GEMoaB, Sanofi/Aventis, Immatics, Merck Serono, Janssen Oncology, Iovance Biotherapeutics, Daiichi Sankyo Europe GmbH

Giao Q. Phan
Honoraria: Xeris Pharmaceuticals (I), Alora Pharmaceuticals (I)
Consulting or Advisory Role: Xeris Pharmaceuticals (I), Alora Pharmaceuticals (I)
Expert Testimony: Fenwick & West (I)

John M. Kirkwood
Honoraria: Bristol Myers Squibb
Consulting or Advisory Role: Scopus BioPharma, Pfizer, AXIO Research, Natera, DermTech, Ankyra Therapeutics, IQVIA, Merck, Replimune, Iovance Biotherapeutics, OncoCyte, Takeda, PATHAI, Magnolia Innovation, iOnctura, Jazz Pharmaceuticals, Regeneron, Istari Oncology, CytomX Therapeutics, Lytix Biopharma, PyrOjas Corporation, Bristol Myers Squibb, Valar Labs, Piper Sandler, Novartis, Boxer Capital, Engage Health Media, Lumira Capital Investment Management, Mural Oncology, Zola Therapeutics
Research Funding: Amgen (Inst), Bristol Myers Squibb (Inst), Checkmate Pharmaceuticals (Inst), Immunocore (Inst), Iovance Biotherapeutics (Inst), Novartis (Inst), ImmVira (Inst), Harbor BioMed

(Inst), Takeda (Inst), Verastem (Inst), Lion Biotechnologies (Inst), Lytix Biopharma (Inst)
Travel, Accommodations, Expenses: Checkmate Pharmaceuticals, Bristol Myers Squibb, Regeneron, Ankyra Therapeutics, Iovance Biotherapeutics

James Larkin
Honoraria: Bristol Myers Squibb, Pfizer, Novartis, Incyte, Merck Serono, Eisai, touchIME, touchEXPERTS, iOnctura, Cancer Research UK, GlaxoSmithKline, Dynavax, Roche
Consulting or Advisory Role: Bristol Myers Squibb, Incyte, iOnctura, Apple Tree Partners, Merck Serono, Eisai, Novartis, Pfizer, Iovance Biotherapeutics, Boston Biomedical, Immunocore, YKT Corporation, MSD Oncology
Research Funding: Pfizer (Inst), Novartis (Inst), MSD (Inst), Bristol Myers Squibb (Inst), Achilles Therapeutics (Inst), Roche (Inst), Nektar (Inst), Covance (Inst), Immunocore (Inst), AVEO (Inst), Pharmacyclics (Inst)
Travel, Accommodations, Expenses: Roche/Genentech, GlaxoSmithKline, ESMO, Bristol Myers Squibb/Roche

Jeffrey Weber
Stock or Other Ownership: Biond, Evaxion, Onco C4, Instill Bio
Consulting or Advisory Role: Merck, Genentech, AstraZeneca, GSK, Novartis, Nektar, Celldex, Incyte, Biond, Moderna, ImCheck, Sellas, Evaxion, Pfizer, Regeneron, EMO Serono, BMS, CytomX, Sellas, Instil Bio, OncoC4, NexImmune
Patents, Royalties, Other Intellectual Property: Moffitt Cancer Center, Biodesix

Friedrich Graf Finckenstein
Employment: Iovance Biotherapeutics, Tenaya Therapeutics (I)
Leadership: Iovance Biotherapeutics
Stock and Other Ownership Interests: Roche/Genentech, Bristol Myers Squibb, Johnson & Johnson (I), Iovance Biotherapeutics, Adverum (I), Tenaya Therapeutics (I)
Travel, Accommodations, Expenses: Iovance Biotherapeutics, Tenaya Therapeutics (I)

Jeffrey Chou
Employment: Iovance Biotherapeutics
Stock and Other Ownership Interests: Iovance Biotherapeutics
Research Funding: Iovance Biotherapeutics
Travel, Accommodations, Expenses: Iovance Biotherapeutics

Brian Gastman
Employment: Iovance Biotherapeutics
Stock and Other Ownership Interests: Iovance Biotherapeutics

Xiao Wu
Employment: Iovance Biotherapeutics
Stock and Other Ownership Interests: Iovance Biotherapeutics
Travel, Accommodations, Expenses: Iovance Biotherapeutics

Rana Fiaz
Employment: Iovance Biotherapeutics, AbbVie

Amod A. Sarnaik
Honoraria: MJH Healthcare Holdings, LLC, Second City LLC, Guidepoint Inc, Iovance Biotherapeutics, Iovance Biotherapeutics (Inst), Society for Immunotherapy of Cancer, Clinical Education Alliance, Gerson Lehrman Group
Research Funding: Provectus (Inst), Genentech (Inst), Iovance Biotherapeutics (Inst), Turnstone Bio (Inst)
Patents, Royalties, Other Intellectual Property: Compositions and methods for improving tumor-infiltrating lymphocytes for adoptive cell therapy, filed March 20, 2014 US Patent Application No. 61/955,970 and second Application No. 61/973,002 (Inst), Rapid method for culture of tumor-infiltrating lymphocytes from core needle biopsies of solid tumors, filed January 2, 2018 US Patent Application No. 62/612,915 (Inst), Method of ex vivo enhancement of immune cell activity for cancer immunotherapy with a small molecule ablative compound, filed August 21, 2018 US Patent Application No. 14/974,357, Tumor-infiltrating lymphocytes and stapled peptoid peptide hybrid peptidomimetics, filed October 11, 2018 US Patent Application No. 16/157,174 (Inst), Culture of Tumor-infiltrating lymphocytes from tumor digest, filed March 24, 2021 US Patent Application No. 17/279,327 (Inst)
Travel, Accommodations, Expenses: Iovance Biotherapeutics, BluPrint Oncology Concepts

No other potential conflicts of interest were reported.

APPENDIX

TABLE A1. C-144-01 Investigators

Study Investigators	Country	Institution
Brendan Curti	The United States	Providence Portland Medical Center
Kevin Kim	The United States	California Pacific Medical Center
Gregory Daniels	The United States	University of California San Diego Moores Cancer Center
Melissa Wilson	The United States	Thomas Jefferson University
Sylvia Lee	The United States	Seattle Cancer Care Alliance
Igor Puzanov	The United States	Roswell Park Cancer Institute
Amy Harker-Murray	The United States	Medical College of Wisconsin
Theodore Logan	The United States	IU Simon Cancer Center
Jan Christoph Simon	Germany	Universitatsklinikum Leipzig
Ioannis Thomas	Germany	Universitatsklinikum Tubingen
Beatrice Schuler-Thurner	Germany	Universitatsklinikum Erlangen
Rose Moritz	Germany	Universitatsklinikum Halle
Jessica Hassel	Germany	Universitatsklinikum Heidelberg
Gotz Ulrich Grigoliet[a]	Germany	Universitatsklinikum Wurzburg
Ana Arance	Spain	Hospital Clinic de Barcelona
Belen Rubio	Spain	Hospital Universitario Quironsalud Madrid
Juan Rodriguez	Spain	Hospital Universitario HM Sanchinarro
Alfonso Berrocal	Spain	Hospital General Universitario de Valencia
Miguel de Sanmamed	Spain	Clinica Universidad de Navarra
Hendrik-Tobias Arkenau	The United Kingdom	Sarah Cannon Research Institute UK
Thomas Evans	The United Kingdom	Beatson West of Scotland Cancer Centre
Pippa Corrie	The United Kingdom	Addenbrooke's Hospital
Stephane Dalle	France	Centre Hospitalier Lyon Sud
Christoph Bedane	France	CHU de Limoges - Hopital Dupuytren
Judit Olah	Hungary	Szegedi Tudomanyegyetem Szent-Gyorgyi Albert
Angela Orcurto	Switzerland	Centre Hospitalier Universitaire Vaudois Lausanne

[a]Deceased.