UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K
Current Report

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (date of earliest event reported): November 18, 2022

IOVANCE BIOTHERAPEUTICS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware	
(State of Incorporation)	
001-36860	**75-3254381**
Commission File Number	**(I.R.S. Employer Identification No.)**
825 Industrial Road, 4th Floor **San Carlos, California**	**94070**
(Address of Principal Executive Offices)	**(Zip Code)**

(650) 260-7120
(Registrant's Telephone Number, Including Area Code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425).

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12).

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)).

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c)).

Indicate by check mark whether the registrant is an emerging growth company as defined in as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter). Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $0.000041666 per share	IOVA	The Nasdaq Stock Market, LLC

Item 8.01. Other Events.

On November 18, 2022, Iovance Biotherapeutics, Inc. (the "Company") issued a press release providing an update on the Company's biologics license application submission for lifileucel in advanced melanoma. The full text of the press release is attached hereto as Exhibit 99.1 and incorporated herein by reference.

The Company recently issued a press release announcing updated clinical data for lifileucel in advanced melanoma during a rapid oral presentation at the Society for Immunotherapy of Cancer (SITC) Annual Meeting. The full text of the press release is attached hereto as Exhibit 99.2 and incorporated herein by reference.

A copy of the slide presentation referred to in the press release is attached hereto as Exhibit 99.3 and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release of Iovance Biotherapeutics, Inc., dated November 18, 2022.
99.2	Press Release of Iovance Biotherapeutics, Inc.
99.3	Slide Presentation of Iovance Biotherapeutics, Inc.
104	Cover Page Interactive Data File - the cover page interactive date file does not appear in the Interactive Date File because its XBRL tags are embedded within the Inline XBRL document.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this Report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: November 18, 2022

IOVANCE BIOTHERAPEUTICS, INC.

By: /s/ Frederick G. Vogt
Frederick G. Vogt, Interim CEO & General Counsel

Exhibit 99.1

PRIVILEGED AND CONFIDENTIAL

Iovance Biotherapeutics Provides Update on Biologics License Application Submission for Lifileucel in Advanced Melanoma

BLA Submission Ongoing with U.S. Food and Drug Administration

SAN CARLOS, Calif., November 18, 2022 -- Iovance Biotherapeutics, Inc. (NASDAQ: IOVA) today announced that its ongoing rolling Biologics License Application (BLA) submission to the U.S. Food and Drug Administration (FDA) for lifileucel is expected to be completed in the first quarter of 2023.

As part of an amendment to the ongoing investigational new drug application (IND) submitted during the third quarter of 2022, Iovance received recent FDA feedback regarding supplemental assay validation information and comparability data for lifileucel. Iovance will address these FDA comments promptly and will now complete its rolling BLA submission during the first quarter of 2023.

Lifileucel is an investigational tumor infiltrating lymphocyte (TIL) therapy for patients with advanced (unresectable or metastatic) melanoma who progressed on or after prior anti-PD-1/L1 therapy, and targeted BRAF/MEK inhibitor therapy where appropriate. There are no FDA approved therapies in this treatment setting.

Frederick Vogt, Ph.D., J.D., Iovance's Interim President and Chief Executive Officer stated, "We continue to make substantial progress with our ongoing BLA submission and remain close to the finish line. The FDA has provided recent valuable feedback to the IND application and remains supportive during the rolling BLA submission process. Iovance is fully committed to securing FDA approval as soon as possible to deliver the first individualized, one-time cell therapy for advanced melanoma patients, who have a significant unmet medical need."

As previously announced, Iovance held a successful pre-BLA meeting in July 2022, and the rolling BLA commenced in August 2022. A rolling BLA allows Iovance to submit portions of the BLA to the FDA on an ongoing basis, which enables the FDA to begin review as early as possible as documents are received. The rolling BLA submission and eligibility for priority review are benefits available under the FDA's guidance on expedited programs for serious conditions. The FDA previously granted a regenerative medicine advanced therapy (RMAT) designation for lifileucel in advanced melanoma.

The BLA submission for lifileucel is supported by positive clinical data from the C-144-01 clinical trial in patients with advanced melanoma. The Phase 3 trial of lifileucel in combination with pembrolizumab in frontline advanced melanoma, on track to begin in late 2022, is intended to serve as a confirmatory study and is expected to be well underway at the time of a potential approval.

Investor Webcast on Friday, November 18, 8:00 a.m. ET

Iovance will host a webcast on Friday, November 18 at 8:00 a.m. ET to discuss this corporate update. To participate in the webcast, please register at https://register.vevent.com/register/BI99a18daf00f04087b70d9c6b45008d6f. The live webcast and replay can be accessed in the Investors section of the company's website at IR.Iovance.com.

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About Iovance Biotherapeutics, Inc.

Iovance Biotherapeutics aims to be the global leader in innovating, developing and delivering tumor infiltrating lymphocyte (TIL) therapies for patients with cancer. We are pioneering a transformational approach to cure cancer by harnessing the human immune system's ability to recognize and destroy diverse cancer cells in each patient. Our lead late-stage TIL product candidate, lifileucel for metastatic melanoma, has the potential to become the first approved one-time cell therapy for a solid tumor cancer. The Iovance TIL platform has demonstrated promising clinical data across multiple solid tumors. We are committed to continuous innovation in cell therapy, including gene-edited cell therapy, that may extend and improve life for patients with cancer. For more information, please visit www.iovance.com.

Forward-Looking Statements

Certain matters discussed in this press release are "forward-looking statements" of Iovance Biotherapeutics, Inc. (hereinafter referred to as the "Company," "we," "us," or "our") within the meaning of the Private Securities Litigation Reform Act of 1995 (the "PSLRA"). All such written or oral statements made in this press release, other than statements of historical fact, are forward-looking statements and are intended to be covered by the safe harbor for forward-looking statements provided by the PSLRA. Without limiting the foregoing, we may, in some cases, use terms such as "predicts," "believes," "potential," "continue," "estimates," "anticipates," "expects," "plans," "intends," "forecast," "guidance," "outlook," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes and are intended to identify forward-looking statements. Forward-looking statements are based on assumptions and assessments made in light of management's experience and perception of historical trends, current conditions, expected future developments and other factors believed to be appropriate. Forward-looking statements in this press release are made as of the date of this press release, and we undertake no duty to update or revise any such statements, whether as a result of new information, future events or otherwise. Forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and other factors, many of which are outside of our control, that may cause actual results, levels of activity, performance, achievements and developments to be materially different from those expressed in or implied by these forward-looking statements. Important factors that could cause actual results, developments and business decisions to differ materially from forward-looking statements are described in the sections titled "Risk Factors" in our filings with the Securities and Exchange Commission, including our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, and include, but are not limited to, the following substantial known and unknown risks and uncertainties inherent in our business: the effects of the COVID-19 pandemic; risks related to the timing of and our ability to successfully develop, submit, obtain and maintain U.S. Food and Drug Administration ("FDA") or other regulatory authority approval of, or other action with respect to, our product candidates, and our ability to successfully commercialize any product candidates for which we obtain FDA approval; whether clinical trial results from our pivotal studies and cohorts may support registration and approval by the FDA; preliminary and interim clinical results, which may include efficacy and safety results, from ongoing clinical trials or cohorts may not be reflected in the final analyses of our ongoing clinical trials or subgroups within these trials or in other prior trials or cohorts; the risk that enrollment may need to be adjusted for our trials and cohorts within those trials based on FDA and other regulatory agency input; the changing landscape of care for cervical cancer patients may impact our clinical trials in this indication; the risk that we may be required to conduct additional clinical trials or modify ongoing or future clinical trials based on feedback from the FDA or other regulatory authorities; the risk that our interpretation of the results of our clinical trials or communications with the FDA may differ from the interpretation of such results or communications by the FDA (including from the recent pre-BLA meeting with the FDA); the risk that the rolling BLA submission for lifileucel in metastatic melanoma may take longer than expected; the acceptance by the market of our product candidates and their potential reimbursement by payors, if approved; our ability or inability to manufacture our therapies using third party manufacturers or our own facility may adversely affect our potential commercial launch; the results of clinical trials with collaborators using different manufacturing processes may not be reflected in our sponsored trials; the risk that unanticipated expenses may decrease our estimated cash balances and forecasts and increase our estimated capital requirements; and other factors, including general economic conditions and regulatory developments, not within our control.

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Exhibit 99.2

Iovance Biotherapeutics Announces Updated Clinical Data for Lifileucel in Advanced Melanoma at Society for Immunotherapy of Cancer (SITC) Annual Meeting

31% Objective Response Rate (ORR) and Median Duration of Response (mDOR) Not Reached at 36.5 Months Median Study Follow Up in C-144-01 Trial (Cohorts 2 and 4)

42% of Responses Lasted for 24+ Months

SITC Update and KOL Panel Webcast Thursday, November 10 at 4:30 pm ET

SAN CARLOS, Calif., November 10, 2022 -- Iovance Biotherapeutics, Inc. (NASDAQ: IOVA), a late-stage biotechnology company developing novel T cell-based cancer immunotherapies (tumor infiltrating lymphocyte, TIL, and peripheral-blood lymphocyte, PBL), today announced updated clinical data for lifileucel in advanced melanoma during a rapid oral presentation at the Society for Immunotherapy of Cancer (SITC) Annual Meeting.

Amod Sarnaik, M.D., Professor of Cutaneous Oncology and Immunology at H. Lee Moffitt Cancer Center, presenting author and lead C-144-01 trial investigator, stated, "We are excited to present the comprehensive clinical data on behalf of the C-144-01 investigators. The trial demonstrated a robust and clinically meaningful response rate and long-term durability following one-time treatment. Patients in this study were difficult to treat and lacked approved therapies after current standard of care. We hope to offer lifileucel to many more patients after initial progression on immune checkpoint inhibitors."

The oral presentation for the C-144-01 trial included efficacy data from 153 patients with advanced melanoma enrolled in Cohort 2 (n=66) and Cohort 4 (n=87) with a median study follow up of 36.5 months (data cut off July 15, 2022). All patients had progressed on or after immune checkpoint inhibitor (ICI) therapy and targeted BRAF/MEK inhibitor therapy where appropriate. There are no treatments approved by the U.S. Food and Drug Administration (FDA) for the C-144-01 study population. The current available care is chemotherapy (4-10% ORR; median overall survival [mOS] of 7-8 months).[1-4]

SITC C-144-01 Data Highlights for Pooled Analysis (36.5 Months Median Study Follow Up)

- **Heavily Pretreated Patient Population with Substantial Disease Burden:** Patients had received a median of 3 lines of prior therapy (range 1-9), including anti-PD-1 therapy in 100% of patients (median: 2 lines, range 1-7) and anti-CTLA-4 therapy in 81.7% of patients, with prior combination anti-PD-1 and anti-CTLA-4 therapy received in 53.6% of patients. Baseline disease characteristics were generally similar between Cohorts 2 and 4. However, Cohort 4 patients showed both a higher disease burden (> 3 lesions: 83.9% vs. 65.2%) and a higher proportion of patients with elevated lactate dehydrogenase (LDH; 64.4% vs 40.9%), a well-known negative prognostic factor in melanoma.[5]

- **Clinically Meaningful Response Rate and Durability**
  - **Clinically Meaningful ORR and Deepening of Responses Over Time**: The ORR assessed by an independent review committee (IRC) using RECIST v1.1 was 31.4% (95% CI: 24.1%-39.4%), with 9 complete responses (CRs) and 39 partial responses (PRs). The median time from lifileucel infusion to best response was 1.5 months, and responses deepened over time. Initial PRs converted to CRs in 7 patients, as late as 2+ years post-lifileucel, including 1 conversion to CR in approximately 10 months since the initial data analysis in the abstract.

  - **mDOR (Not Reached) and Durability at 2+ Years:** The mDOR was not reached (estimated by Kaplan-Meier, or KM, method). Responses lasted for 24 months or greater in 41.7% of responders (47.8% of responders in Cohort 2; 36.0% of responders in Cohort 4).

  - **Long-Term Benefit from One-Time Lifileucel Therapy:** The DOR and overall survival (OS) KM plots (see slides) show plateaus characteristic of immunotherapy, supporting the potential for long-term benefit from lifileucel therapy. Median (mOS) had not been reached (95% CI: 30.4-NR) in patients who achieved a response at first assessment (6 weeks). mOS in all patients was 13.9 months (95% CI: 10.6-17.8).

- **Responses Across All Subgroups:** Responders to lifileucel included patients with ICI primary-resistant disease, those who received prior anti–CTLA-4 therapy and/or targeted therapies, and responses were observed regardless of PD-L1 status. LDH and target lesion sum of diameters (SOD; tumor mass across locations) were correlated with ORR (P=0.008). Higher odds of response with lower tumor burden suggest that early intervention with lifileucel after ICI may maximize benefit.

- **Safety**: Treatment-emergent adverse events (TEAEs) were consistent with the underlying disease and known AE profiles of nonmyeloablative lymphodepletion and interleukin-2 (IL-2). Incidence of TEAEs decreased rapidly within the first 2 weeks after lifileucel infusion.

- **94.7% Manufacturing Success Rate:** All patients in both cohorts received the same lifileucel treatment using Iovance's proprietary 22-day manufacturing process (Gen 2). Lifileucel was manufactured within specification in 94.7% of patients across Cohorts 2 and 4.

Friedrich Graf Finckenstein, M.D., Chief Medical Officer of Iovance, stated, "Our C-144-01 trial is the largest clinical trial of a cell therapy in advanced melanoma following anti–PD-1 therapy and the basis for our rolling BLA submission for lifileucel. We observed responses across the spectrum of patients with advanced melanoma, including early responses and deepening responses over time, following anti-PD-1 and anti-CTLA-4 therapy, and regardless of mutation and PD-L1 status. Given the correlation of lower tumor burden and response, we believe there is a strong rationale for treatment with lifileucel as soon as possible after initial progression on anti–PD-1 therapy. The potential for long-term benefit from one-time treatment with lifileucel is promising, as the overall survival data show the desired plateau of maintained benefit with immunotherapy, and include patients who are alive five years after treatment."

The C-144-01 results are available in the oral presentation slide deck on the Iovance corporate website. Data from the pivotal Cohort 4, supportive data from Cohort 2 and the pooled analysis of Cohorts 2 and 4 are part of a rolling Biologics License Application (BLA) submission to the FDA for lifileucel in advanced melanoma, which Iovance initiated in August 2022.

Investor Webcast on Thursday, November 10, 4:30 p.m. ET
Iovance will host a webcast on Thursday, November 10 at 4:30 p.m. ET to discuss clinical data updates for lifileucel in advanced melanoma. Iovance senior leadership will be joined by the following key opinion leaders and principal investigators in Iovance clinical studies: Amod Sarnaik; Allison Betof Warner, M.D., Ph.D., Assistant Attending Physician and Melanoma Medical Oncologist, Memorial Sloan Kettering Cancer Center; Miguel Perales, M.D., Chief, Adult Bone Marrow Transplant Service, Memorial Sloan Kettering Cancer Center; and Martin McCarter, M.D., Surgical Director for the Esophageal and Gastric Multidisciplinary Clinic, Vice Chair for Strategy and Program Development Department of Surgery, UCHealth Cancer Care - Anschutz Medical Campus - University of Colorado Cancer Center. The live and archived webcast can be accessed in the Investors section of the company's website here: https://ir.iovance.com/events/event-details/sitc-investor-webcast

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[1]Keytruda USPI accessed Mar 2022
[2]Weber et al., Lancet Oncol 2015
[3]Kirchburger et al., Eur J Cancer 2016
[4]Goldinger et al., J Clin Oncol 2018
[5]Claps et al., Nat Rev Clin Oncol 2022

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IOVANCE
BIOTHERAPEUTICS
Iovance Investor Event & KOL Roundtable
Society for Immunotherapy of Cancer (SITC) Annual Meeting
November 10, 2022
#SITC22
ADVANCING IMMUNO-ONCOLOGY
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Agenda

Introduction	– Friedrich Graf Finckenstein, M.D., Chief Medical Officer, Iovance
Presentation Summary C-144-01 Study in Advanced Melanoma	– Amod Sarnaik, M.D., H. Lee Moffitt Cancer Center
KOL Panel Multi-Disciplinary Perspectives on TIL Therapy	– Madan Jagasia, M.D., M.S., M.M.H.C, EVP, Medical Affairs, Iovanc – Allison Betof Warner, M.D., Ph.D., Memorial Sloan Kettering Canc – Miguel Perales, M.D., Memorial Sloan Kettering Cancer Center – Martin McCarter, M.D., University of Colorado Cancer Center
Q&A	

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Unmet Medical Need for Metastatic Melanoma Therapy

No FDA Approved Treatment Options After Progression on Checkpoint (Anti-PD-1) Therapy and BRAF/MEK

325k Annual new cases worldwide[1]

57k Annual deaths worldwide[1]

100k Annual new cases in U.S.[2]

7.7k Annual deaths in U.S.[2]

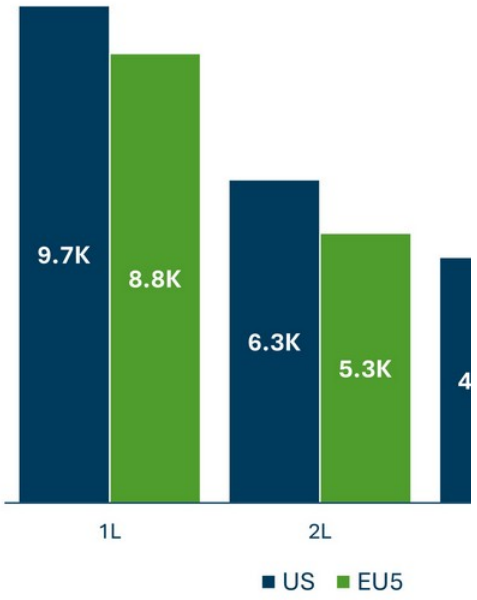
Available Care:

1L Anti-PD-1 Immunotherapy **21%-33% ORR[4]**

2L BRAF/MEK inhibitors if BRAF mutation +

2L+ Chemotherapy **ORR 4-10%[5]** **mOS ~7-8 months[6]**

Melanoma Drug-Treated Popul
Unresectable / Metastatic (U



1. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries, CA Cancer J Clin., May 2021
2. https://seer.cancer.gov accessed May 2022
3. Clarivate DRG Disease Landscape (2021)
4. Keytruda USPI accessed Mar 2022
5. Keytruda USPI accessed Mar 2022 (4%) and Weber et al., Lancet Oncol 2015 (ICC 10%)
6. Kirchburger et al., Eur J Cancer 2016 and Goldinger et al., J Clin Oncol 2018

Abbreviations: EU5=France, Germany, Italy, Spain and United Kingdom, 1L=first line therapy, 2L=second line therapy, 3L=third line therapy, ORR, objective response rate; mOS, median overall survival; PD-1, programmed cell death protein-1

Amod Sarnaik, M.D.

Professor of Cutaneous Oncology and Immunology at H. Lee Moffitt Cancer Center
Presenting Author and Lead C-144-01 Investigator

- Surgical oncologist in Department of Cutaneous Oncology, Immunology Program and Melanom Excellence at Moffitt Cancer Center
- Professor of Oncology and Surgery at University of South Florida
- **Primary research interest**: Novel immunotherapeutic treatments for melanoma
- **Clinical interests**: Surgical treatment of melanoma and other cutaneous-based skin cancers, s node biopsy techniques, and minimizing surgically-related morbidities
- **Education**: Undergraduate degree from Harvard University and medical degree from University School of Medicine
- **Postgraduate training**: University of Cincinnati, OH; Howard Hughes investigational postdoctor in molecular genetics; surgical oncology fellowship at Moffitt Cancer Center
- >90 publications in peer-reviewed literature

KOL Panelists

Multi-Disciplinary Perspectives on TIL Therapy

Medical Oncology

Allison Betof Warner, M.D., Ph.D.

Assistant Attending Physician and Melanoma Medic Oncologist, Memorial Sloan Kettering Cancer Cente

Cell Therapy

Miguel Perales, M.D.

Chief, Adult Bone Marrow Transplant Service, Memo Sloan Kettering Cancer Center

Surgery

Martin McCarter, M.D.

Surgical Director for the Esophageal and Gastric Multidisciplinary Clinic, Vice Chair for Strategy and Program Development Department of Surgery, UCH Cancer Care - Anschutz Medical Campus - Universit Colorado Cancer Center

Lifileucel TIL Cell Monotherapy in Patients With Advanced M After Progression on Immune Checkpoint Inhibitors and Tar Therapy: Pooled Analysis of Consecutive Cohorts (C-144-0

Amod Sarnaik,[1] Karl D. Lewis,[2] Harriet Kluger,[3] Omid Hamid,[4] Eric Whitman,[5] Sajeve Thomas,[6] Martin Wermke,[7] Mike C Domingo-Musibay,[9] Giao Q. Phan,[10] John M. Kirkwood,[11] Jessica C. Hassel,[12] Marlana Orloff,[13] James Larkin,[14] Jeffrey W S. Furness,[14] Nikhil I. Khushalani,[1] Theresa Medina,[2] Friedrich Graf Finckenstein,[16] Madan Jagasia,[16] Parameswaran Har Wen Shi,[16] Xiao Wu,[16] Jason Chesney[17]

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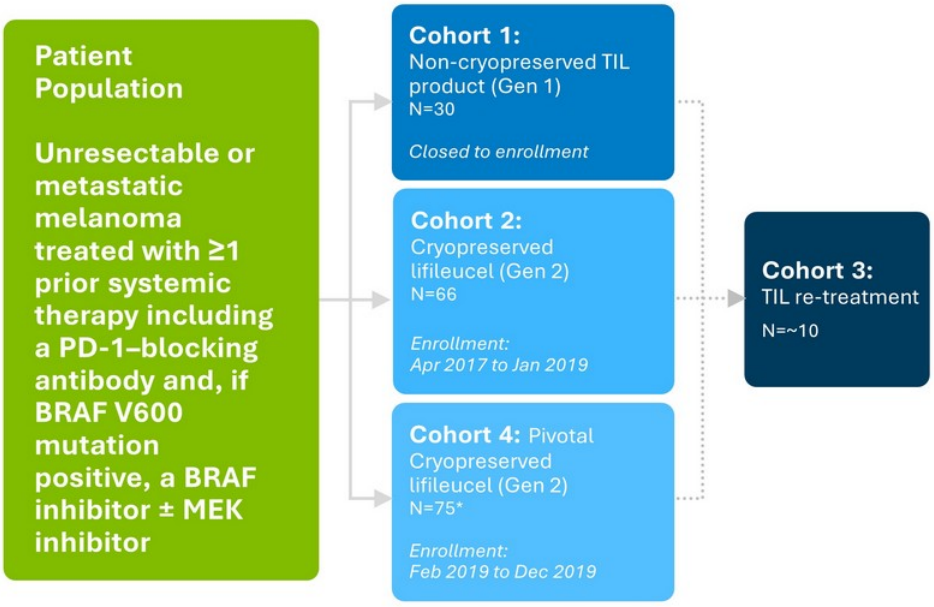
C-144-01 Phase 2 Study Design

Eligibility and treatment were identica Cohorts 2 and 4

Phase 2, multicenter study to assess the efficacy and safety of autologous TIL (lifileucel) for treatment of p metastatic melanoma (NCT02360579



Key Endpoints

- Primary: ORR (IRC-assessed using RECI
- Secondary: DOR, PFS, OS, TEAE inciden

Key Eligibility Criteria

- ≥1 tumor lesion resectable for TIL genera diameter) and ≥1 target tumor lesion for
- Age ≥18 years at time of consent
- ECOG performance status 0–1
- No limit on number of prior therapies

Treatment Regimen

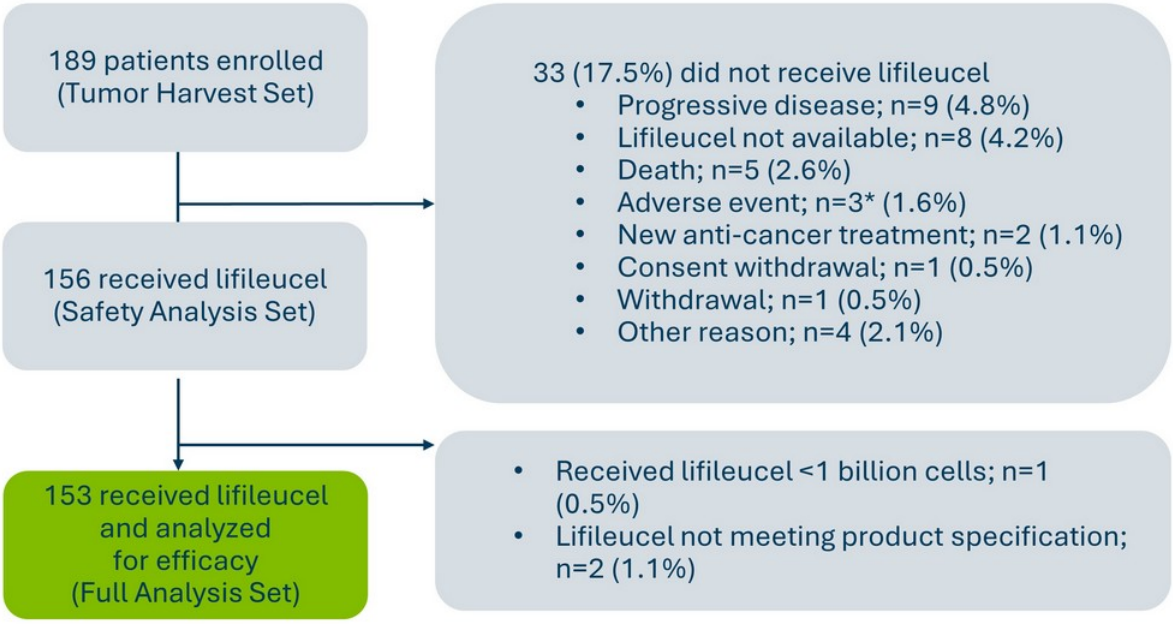
- Lifileucel, a cryopreserved TIL cell therap in Cohorts 2 and 4 and manufactured us Gen 2 process
- All patients received NMA-LD, a single lif up to 6 doses of high-dose IL-2

Data cutoff date: July 15, 2022

Abbreviations: ORR, objective response rate; DOR, duration of response; PD-1, programmed cell death protein-1; IRC, independent review committee

DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; IL-2, interleukin 2; IRC, Independent Review Committee; NMA-LD, nonmyeloablative lymphodepletion; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; RECIST, Response evaluation Criteria in Solid Tumors; TEAE, treatment-emergent adverse events; TIL, tumor-infiltrating lymphocytes.

Patient Disposition



Manufacturi

- Lifileucel n within spec 94.7% of p
- Median nu infused wa (range, 1.2 10^9)

*AEs included: gastrointestinal bleeding, septic shock, and pleural effusion.
IL-2, interleukin 2; TIL, tumor-infiltrating lymphocytes.

SITC 2022 C-144-01 COHORTS 2 + 4 POOLED ANALYSIS ASSESSED BY IRC USING RECIST 1.1

Baseline Patient and Disease Characteristics

Cohorts 2 and 4 Heavily Pre-Treated and Mostly Similar; Cohort 4 had both Higher Disease Burden and Ele

Characteristic	Cohort 2 (n=66)	Cohort 4 (n=87)	Cohort 2+4 (N=153)
Median age (range), years	55.0 (20, 79)	58.0 (25, 74)	**56.0 (20, 79)**
Sex, n (%)			
Male	39 (59.1)	44 (50.6)	**83 (54.2)**
Female	27 (40.9)	43 (49.4)	**70 (45.8)**
Screening ECOG performance status, n (%)			
0	42 (63.6)	62 (71.3)	**104 (68.0)**
1	24 (36.4)	25 (28.7)	**49 (32.0)**
Melanoma subtype,* n (%)			
Cutaneous	39 (59.1)	44 (50.6)	**83 (54.2)**
Mucosal	4 (6.1)	8 (9.2)	**12 (7.8)**
Acral	4 (6.1)	6 (6.9)	**10 (6.5)**
BRAF V600-mutated, n (%)	17 (25.8)	24 (27.6)	**41 (26.8)**
PD-L1 status,† n (%)			
TPS ≥1%	37 (56.1)	39 (44.8)	**76 (49.7)**
TPS <1%	12 (18.2)	20 (23.0)	**32 (20.9)**
Liver and/or brain lesions by IRC, n (%)	28 (42.4)	44 (50.6)	**72 (47.1)**
Median target lesion SOD (range), mm	95.8 (13.5, 271.3)	99.5 (15.7, 552.9)	**97.8 (13.5, 552.9)**

BOR, best overall response; 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; TIL, tumor-infiltrating lymphocytes; TPS, tumor proportion score; ULN, upper limit of normal.

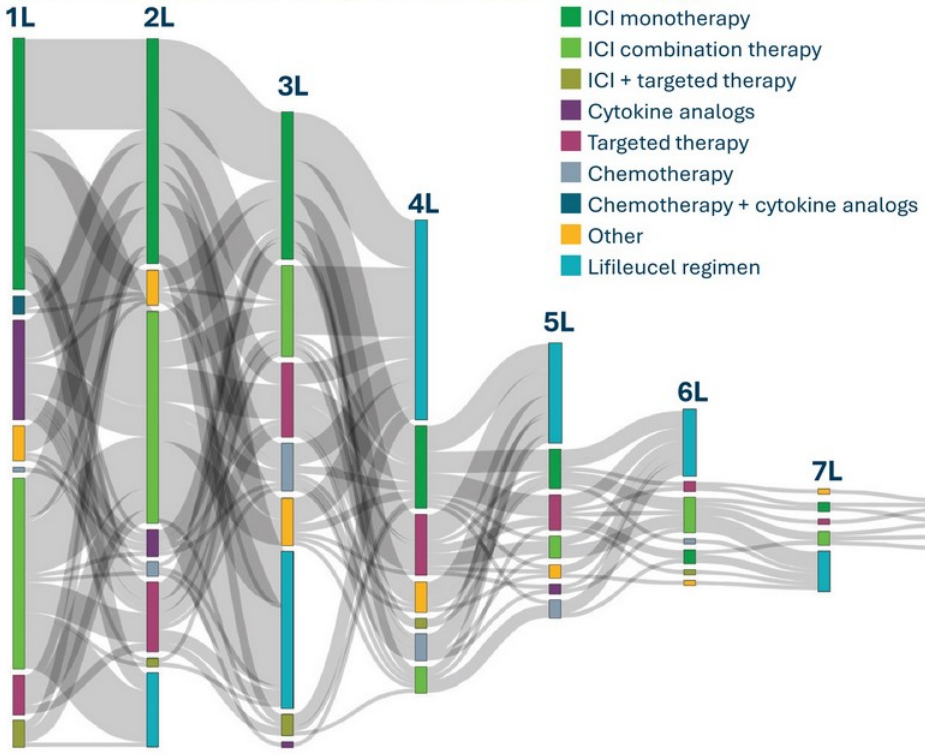
Characteristic	Cohort 2 (n=66)	Cohort 4 (n=87)
Baseline lesions in ≥3 anatomic sites, n (%)	44 (66.7)	65 (74.7)
Baseline target and nontarget lesions,‡ n (%)		
>3	43 (65.2)	73 (83.9)
LDH, n (%)		
≤ULN	39 (59.1)	31 (35.6)
>1–2 × ULN	19 (28.8)	35 (40.2)
>2 × ULN	8 (12.1)	21 (24.1)
Median number of prior therapies (range)	3.0 (1, 9)	3.0 (1, 8)
Prior therapy		
Median number (range)	3.0 (1, 9)	3.0 (1, 8)
Anti–CTLA-4, n (%)	53 (80.3)	72 (82.8)
Anti–PD-1 + anti–CTLA-4 combination, n (%)	34 (51.5)	48 (55.2)
Primary resistance to anti–PD-1/PD-L1 per SITC criteria,[1] n (%)	52 (78.8)	57 (65.5)
Median lines of ICI (range)	2.0 (1, 5)	2.0 (1, 7)
Retreated with ICI, n (%)	48 (72.7)	65 (74.7)

*47 patients (31%) had melanoma of other subtype (including unknown primary subtype or insufficient information).
†45 patients in the Cohorts 2+4 had missing PD-L1 status.
‡One patient in Cohort 2 had missing data on number of baseline target and nontarget lesions.

1. Kluger HM et al. *J Immunother Cancer*. 2020;8:e000398.

Patient Treatment Patterns

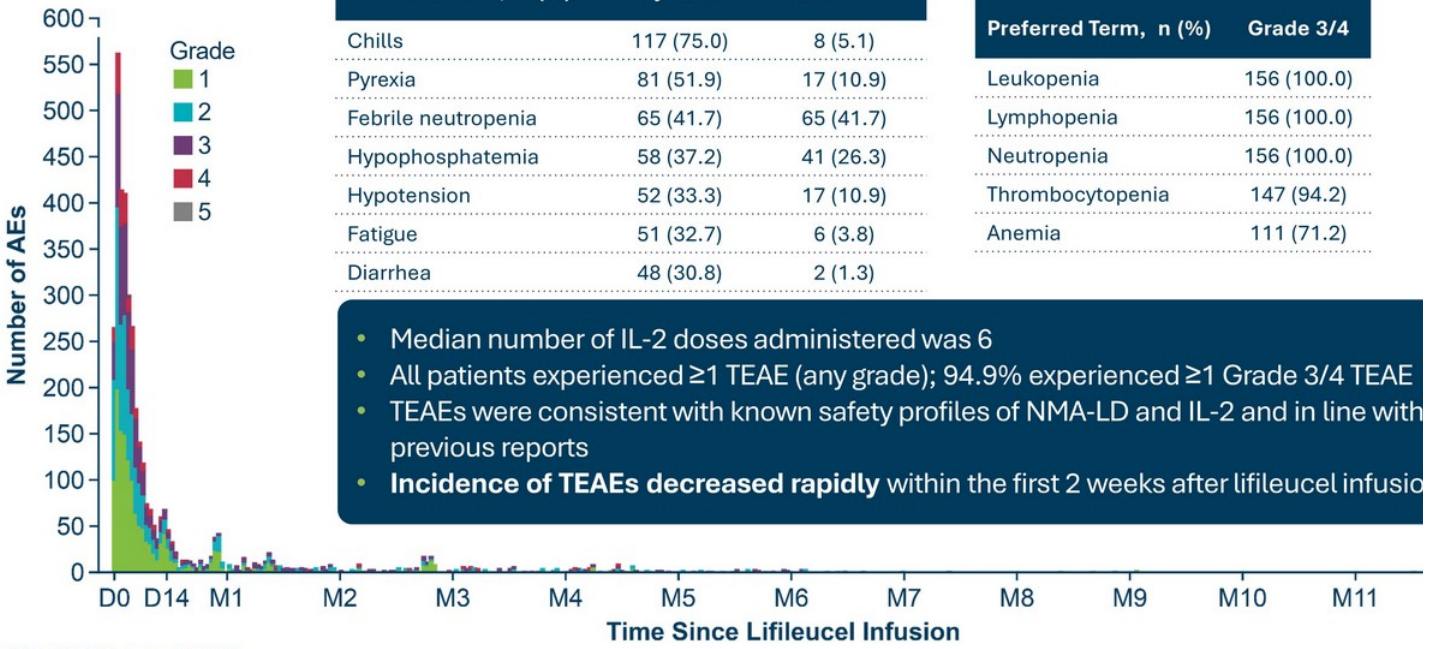
Patients Heavily Pre-Treated (1-9 Prior Lines of Therapy)



- 17 (11.1%) received only therapy
- 125 (81.7%) received anti
- 82 (53.6%) received anti– anti–CTLA-4 combination
- Median of 2 lines (range, ICI-containing therapy
- 113 (73.9%) retreated wi containing therapy prior t

The R package networkD3 was used to generate the Sankey plot.
ICI, immune checkpoint inhibitors; L, line of therapy.

Safety



Non-Hematologic TEAEs in ≥30% of Patients*†

Preferred Term, n (%)	Any Grade	Grade 3/4
Chills	117 (75.0)	8 (5.1)
Pyrexia	81 (51.9)	17 (10.9)
Febrile neutropenia	65 (41.7)	65 (41.7)
Hypophosphatemia	58 (37.2)	41 (26.3)
Hypotension	52 (33.3)	17 (10.9)
Fatigue	51 (32.7)	6 (3.8)
Diarrhea	48 (30.8)	2 (1.3)

Grade 3/4 Hematologic Lab Abnormalities*

Preferred Term, n (%)	Grade 3/4
Leukopenia	156 (100.0)
Lymphopenia	156 (100.0)
Neutropenia	156 (100.0)
Thrombocytopenia	147 (94.2)
Anemia	111 (71.2)

- Median number of IL-2 doses administered was 6
- All patients experienced ≥1 TEAE (any grade); 94.9% experienced ≥1 Grade 3/4 TEAE
- TEAEs were consistent with known safety profiles of NMA-LD and IL-2 and in line with previous reports
- **Incidence of TEAEs decreased rapidly** within the first 2 weeks after lifileucel infusio

*Per CTCAE v4.03; Safety Analysis Set (N=156).
†Grade 5 TEAEs included pneumonia (n=1), acute respiratory failure (n=1), arrhythmia (n=1), and intra-abdominal hemorrhage (n=1).
All occurrences of AEs were counted if a patient experienced a new onset of the same AE at different timepoints. If multiple records were reported on the electronic case report form because of toxicity grade decrease of the same AE that had not resolved, then the event was counted once with the highest grade reported.
15 events were reported after Month 12 (Grade 1, n=7; Grade 2, n=6; Grade 3, n=1; Grade 5, n=1).
AE, adverse event; D, day; IL-2, interleukin 2; M, month; NMA-LD, nonmyeloablative lymphodepletion; TEAE, treatment-emergent adverse event.

Objective Response Rate (ORR)

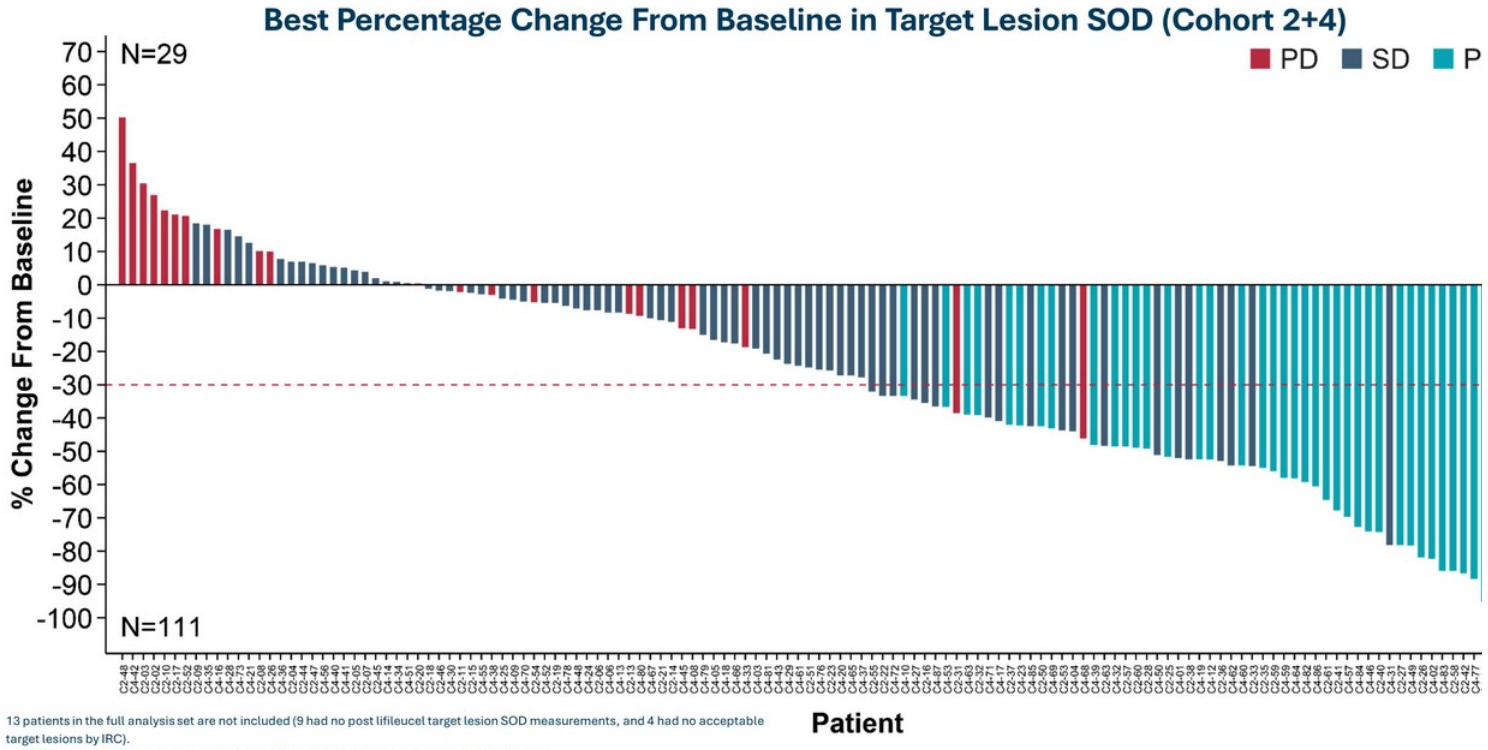
	Cohort 2 (n=66)	Cohort 4 (n=87)	Cohort 2+4 (N=153)
ORR, n (%)	**23 (34.8)**	**25 (28.7)**	**48 (31.4)**
(95% CI)	(23.5, 47.6)	(19.5, 39.4)	(24.1, 39.4)
Best overall response, n (%)			
CR	5 (7.6)	4 (4.6)	9 (5.9)
PR	18 (27.3)	21 (24.1)	39 (25.5)
SD	24 (36.4)	47 (54.0)	71 (46.4)
Non-CR/Non-PD*	1 (1.5)	0	1 (0.7)
PD	15 (22.7)	12 (13.8)	27 (17.6)
Nonevaluable†	3 (4.5)	3 (3.4)	6 (3.9)

- **31.4% IRC-as ORR**
- 91% concorda between IRC- investigator-as ORR
- Median time fr resection to lif infusion was 3

*Patient did not have acceptable target lesions and had best overall response of non-CR/non-PD per IRC assessment.
†Six patients were nonevaluable for response (5 due to early death; 1 due to new anticancer therapy).
CR, complete response; IRC, independent review committee; ORR, objective response rate;
PD, progressive disease; PR, partial response; SD, stable disease.

Tumor Burden Reduction and Best Response to Lifileucel

Reduction of Tumor Burden in 79.3% (111/140) of Patients



13 patients in the full analysis set are not included (9 had no post lifileucel target lesion SOD measurements, and 4 had no acceptable target lesions by IRC).

*-100% change from baseline is presented for CR assessment that includes lymph node lesions.

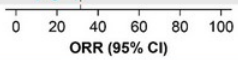
CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; SOD, sum of diameters.

Univariable and Multivariable Analyses of ORR

Response to Lifileucel Observed Across All Subgroups Analyzed

ORR by Patient and Disease Characteristics

Subgroup	n/N	ORR	95% CI
Overall	48/153	31.4	(24.1, 39.4)
Age Group, years			
<65	39/117	33.3	(24.9, 42.6)
≥65	9/36	25.0	(12.1, 42.2)
Baseline ECOG Performance Status			
0	32/84	38.1	(27.7, 49.3)
≥1	16/69	23.2	(13.9, 34.9)
BRAF Mutation Status			
V600E or V600K Mutated	13/41	31.7	(18.1, 48.1)
Non-Mutated	35/112	31.3	(22.8, 40.7)
PD-L1 Status			
TPS ≥1%	28/76	36.8	(26.1, 48.7)
TPS <1%	11/32	34.4	(18.6, 53.2)
Patients with Baseline Liver Lesions	17/59	28.8	(17.8, 42.1)
Patients with Baseline Liver and/or Brain Lesions	19/72	26.4	(16.7, 38.1)
Baseline Target Lesion Sum of Diameters			
<Median (98 mm)	34/74	45.9	(34.3, 57.9)
≥Median (98 mm)	14/75	18.7	(10.6, 29.3)



ORR by Disease and Prior Therapy Cha

Subgroup	n/N	ORR	95% CI
Baseline LDH			
≤ULN	27/70	38.6	(27.2, 51.0
>ULN	21/83	25.3	(16.4, 36.0
>2×ULN	3/29	10.3	(2.2, 27.4
Prior Lines of Therapy			
1-3	32/99	32.3	(23.3, 42.5
≥4	16/54	29.6	(18.0, 43.6
Prior Anti–CTLA-4 Use			
Yes	41/125	32.8	(24.7, 41.8
No	7/28	25.0	(10.7, 44.9
Prior Anti–PD-1 + Anti–CTLA-4 Combination Use			
Yes	22/82	26.8	(17.6, 37.8
No	26/71	36.6	(25.5, 48.9
Primary Resistance to Prior Anti–PD-1 or PD-L1 by SITC Definition[1]	36/109	33.0	(24.3, 42.7

1. Kluger HM et al. *J Immunother Cancer*. 2020;8:e000398.

95% CI is calculated using the Clopper-Pearson Exact test.

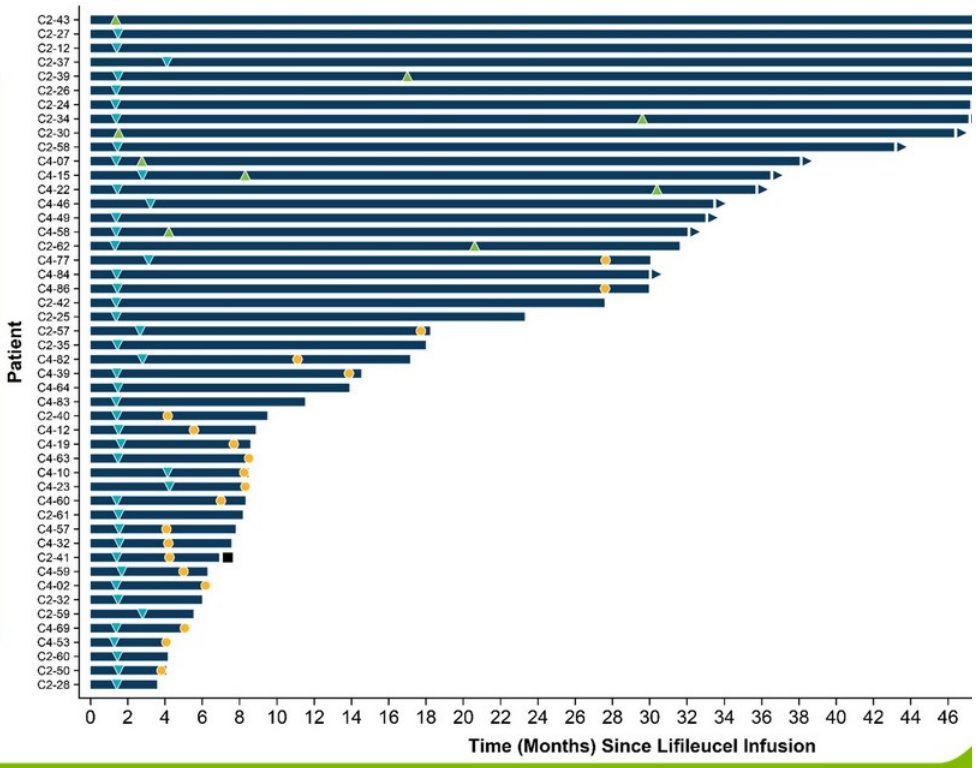
Vertical dotted line represents overall ORR (31.4%).

- In adjusted (ECOG PS) multivariable analyses, **LDH** and **target lesion sum of diameters (SOD; tumor mass across** were correlated with ORR (*P*=0.008)
  - Patients with normal LDH and SOD <median had greater odds of response than patients with either (odds ratio (OR): 2 (OR: 4.42) risk factor(s)
- Higher odds of response with lower tumor burden suggest that early intervention with lifileucel after ICI may maximiz

CTLA-4, cytotoxic T lymphocyte-associated protein 4; ECOG, Eastern Cooperative Oncology Group; LDH, lactate dehydrogenase; OR, odds ratio; ORR, objective response rate; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PS, performance score; SOD, sum of diameters; TPS, tumor proportion score; ULN, upper limit of normal.

Time to Response, Duration of Response, and Time on Effic Assessment for Confirmed Responders (PR or Better)

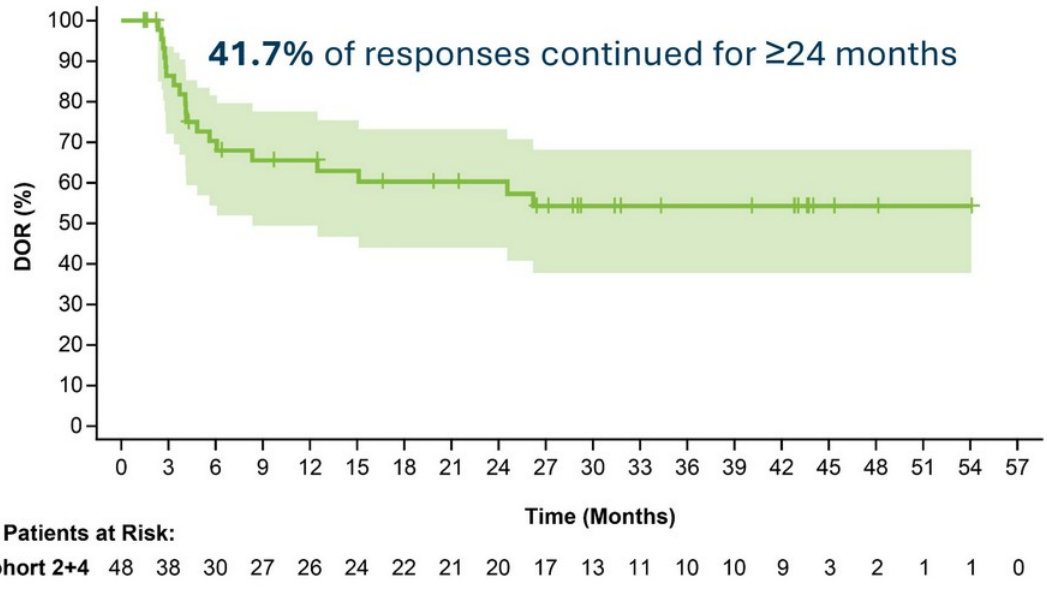
- **Median time from lifileucel infusion to best response was 1.5 months**
- **Responses deepened over time**
  - 7 patients (14.6%) initially assessed as PR were later confirmed CR
  - 4 patients (8.3%) converted to CR >1 year post-lifileucel infusion; 2 (4.2%) of these 4 patients converted after 2 years
  - Best response of 10 patients (20.8%) improved from SD to PR
- **35.4% of responses ongoing as of data cutoff**



CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.

Duration of Response*

Median DOR Not Reached at Median Study Follow Up of 36.5 Months



Patients at Risk:

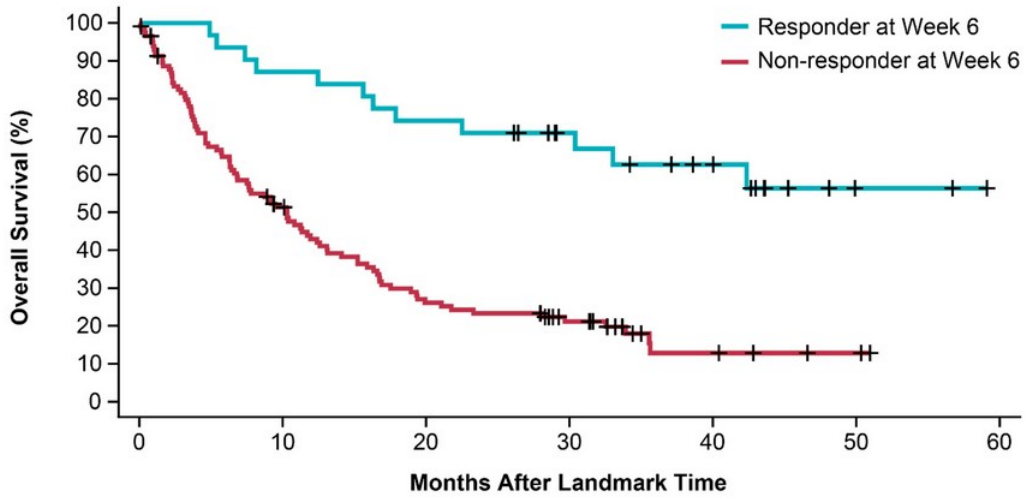
Cohort 2+4	48	38	30	27	26	24	22	21	20	17	13	11	10	10	9	3	2	1	1	0

	Cohort 2 (n=23)	C
Median follow-up, months	45.1	
95% CI	(44.2, 51.4)	(30
Median DOR†, months	NR	
95% CI	(NR, NR)	(4
Min, max (months)	1.4+, 54.1+	1.4
DOR ≥12 months, n (%)	**15 (65.2)**	**11**
DOR ≥24 months, n (%)	**11 (47.8)**	**9**

*Patients not experiencing PD or who did not die prior to the time of data cut had their event times censored at the last adequate tumor assessment. For patients who received new anticancer therapies, DOR was censored at the date of last tumor response assessment prior to the start of new anticancer therapies. For patients with PD or death immediately after ≥2 consecutive missing tumor assessment visits, DOR was censored at the last adequate tumor assessment prior to the missing tumor assessments.
†Based on Kaplan-Meier estimate.
Shaded area indicates 95% CI
DOR, duration of response; NR, not reached; PD, progressive disease.

Overall Survival by Response at 6 Weeks After Lifileucel Inf

mOS Not Reached in Patients Who Achieved Response at First Assessment



Patients at Risk							
Responders	31	27	23	17	11	2	0
Non-responders	116	56	28	18	5	2	0

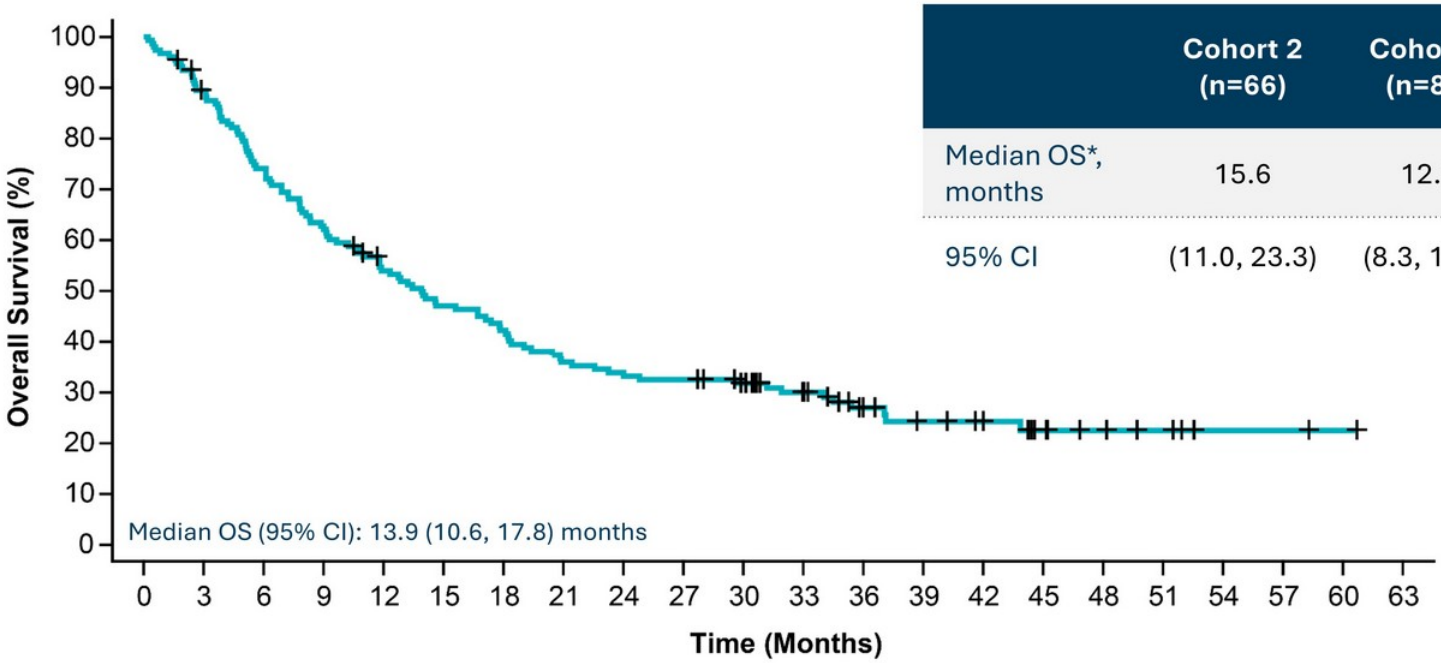
	Median (mont by respo 6 wee
Responders	NR
Non-responders	10.
Log-rank *p*-value	

- mOS not reached analysis in patient response at first a weeks post-lifileuc

1. Buyse M, Piedbois P. On the relationship between response to treatment and survival. *Stat Med*. 1996;15:2797-2812.
*Based on Kaplan-Meier estimate.
NR, not reached; OS, overall survival.

Overall Survival

mOS was 13.9 Months and 12-Month OS Rate was 54.0% (95% CI: 45.6%, 61.6%)



	Cohort 2 (n=66)	Cohort (n=87
Median OS*, months	15.6	12.7
95% CI	(11.0, 23.3)	(8.3, 17

Patients at Risk:

Total	153	134	111	94	78	68	61	52	49	47	42	32	21	17	14	10	7	5	2	2	1	0

*Based on Kaplan-Meier estimate.
OS, overall survival.

Takeaways

Multi-Disciplinary Perspectives on TIL Therapy

- Madan Jagasia, M.D., M.S., M.M.H.C, Executive Vice President, Medical Affairs (Moderator)
- Allison Betof Warner, M.D., Ph.D., Assistant Attending Physician at Memorial Sloan Kettering Cancer Cent
  Medical Oncologist, Memorial Sloan Kettering Cancer Center
- Miguel Perales, M.D., Chief, Adult Bone Marrow Transplant Service, Memorial Sloan Kettering Cancer Cer
- Martin McCarter, M.D., Surgical Director for the Esophageal and Gastric Multidisciplinary Clinic, Vice Cha
  Program Development Department of Surgery, UCHealth Cancer Care - Anschutz Medical Campus - Univ
  Cancer Center

Q&A

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Thank You

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