Real-World, Evidence-Based, Retrospective Study of Patients Infused with Commercially Released Lifileucel for Advanced Melanoma

Lilit Karapetyan, MD, MS, FACP,[1] Justin Moser, MD,[2] Barbara Ting-Wen Ma, MD, MS,[3] Christopher Otteni, MD, MBA,[1] Elizabeth Cathcart, BS,[4] Kimberly Loo, MD,[3] Jay Jacoby, BA,[2] Jamie K. Chau,[1] James W. Smithy, MD, MHS,[4] Nikhil Nayee,[2] Anna C. Pavlick, DO,[3] Ahmed Tawashi,[5] Amritha Seshaadri, [5] Min Yi, PhD,[5] Friedrich Graf Finckenstein, MD, PhD,[5] Brian Gastman, MD,[5] and Alexander N. Shoushtari, MD[4]

[1]H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; [2]HonorHealth Research Institute and Arizona State University John Shufeldt School of Medicine and Medical Engineering, Scottsdale, AZ; [3]Weill Cornell Medicine, New York, NY; [4]Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY; and [5]Iovance Biotherapeutics, San Carlos, CA

Disclosures

Lilit Karapetyan: Institutional Research support from Iovance Biotherapeutics and Valar labs; travel, accommodations, and expenses from Immatics.

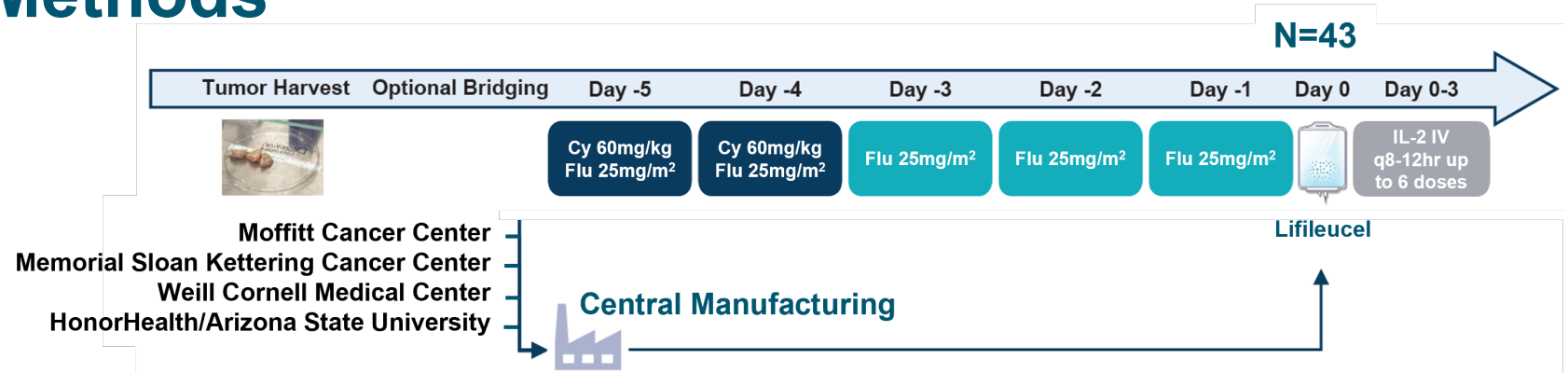
Background

- Lifileucel, a one-time tumor-derived autologous T cell therapy, for advanced melanoma
- 31% ORR and ~20% 5-year OS in C-144-01 study that supported FDA accelerated approval (Feb 2024)[1]
- Limited real-world data published to date
- **First multicenter retrospective analysis** in metastatic melanoma

FDA, Food and Drug Administration; ORR, objective response rate; OS, overall survival.

1. Medina T, et al. *J Clin Oncol.* 2025; 00:1-8.

Methods



Eligibility Criteria

- Age ≥18 years
- Advanced melanoma
- PD-1-resistant after lifileucel approval[a]
- Prior ICI therapy
- ± BRAF/MEK inhibitors *(BRAF* V600–mutant*)*
- Cell product manufactured per QC standards
- ≥2 clinical and/or radiographic assessments

Primary endpoint: Physician-assessed **ORR** across centers

Secondary endpoints: **PFS** and **OS**

Safety: Preliminary evaluation via voluntary adverse event reporting

Study period: *May 16, 2024 – May 13, 2025*

Dose and schedule modifications of lymphodepletion were allowed according to institutional practices. [a] Varies by institution.
Cy, cyclophosphamide; BRAF (or *BRAF*), B-Raf proto-oncogene, serine/threonine kinase; Flu, fludarabine; IL-2, interleukin-2; MEK, Mitogen-activated protein kinase; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q8-12hr, every 8 to 12 hours; QC, quality control.

Baseline Patient Disease Characteristics

Characteristic	N=43
Median age, years (range)	59 (28–79)
Sex, n (%)	
Male	23 (54)
Female	20 (46)
Melanoma subtypes, n (%)	
Non-acral cutaneous	30 (70)
Acral	4 (9)
Mucosal	8 (19)
Unknown, Primary	1 (2)
Distant metastasis (M stage), n (%)	
M1a	9 (21)
M1b	5 (12)
M1c	17 (40)
M1d	12 (28)

Characteristic	N=43
Liver metastases, n (%)	13 (30)
Brain metastases, n (%)	12 (28)
LDH prior to lymphodepletion, n (%)	
≤ULN	17 (40)
1–2× ULN	21 (49)
>2× ULN	5 (12)
BRAF V600 mutation, n (%)	19 (44)
Median number of prior systemic therapies (range)	3 (1–7)

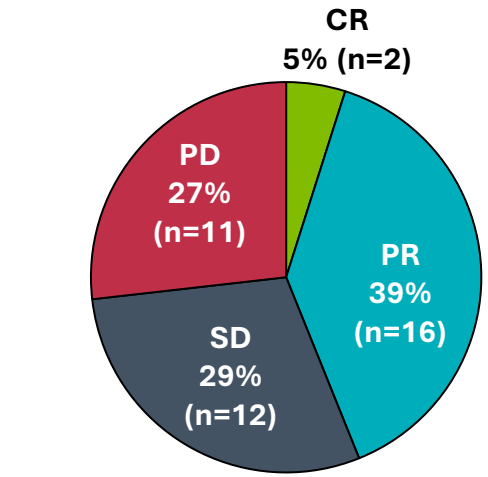
Percentages may not total 100% due to rounding.
BRAF, B-Raf proto-oncogene, serine/threonine kinase; LDH, lactate dehydrogenase; ULN, upper limit of normal.

Tumor Harvest and Treatment Administration (Lifileucel)

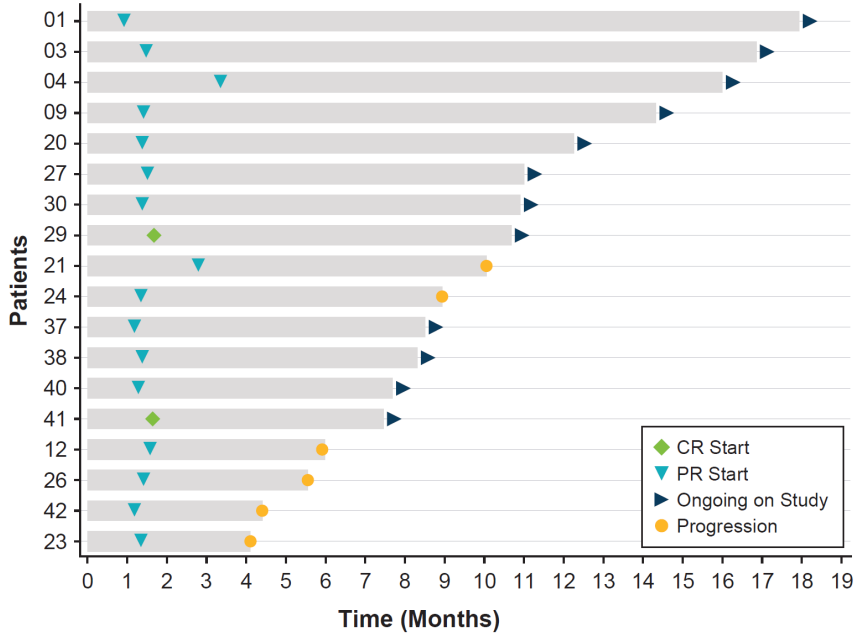
Characteristic	N=43
Tumor harvest site, n (%)[a]	
Lymph node	17 (40)
Subcutaneous	11 (26)
Soft tissue	9 (21)
Lung	5 (12)
Liver	4 (9)
Spleen	1 (2)
Median time from harvest to lymphodepletion, days (range)	44 (35–93)
Bridging therapy, n (%)	19 (44)
Median number of infused TILs (range)	26×10^9 (11–53)
Median number of IL-2 doses (range)	5 (1–6)

[a] Multiple tumor harvest anatomic sites may be present in a patient.
IL-2, interleukin-2; TIL, tumor-infiltrating lymphocyte.

Clinical Activity of Lifileucel in Advanced Melanoma



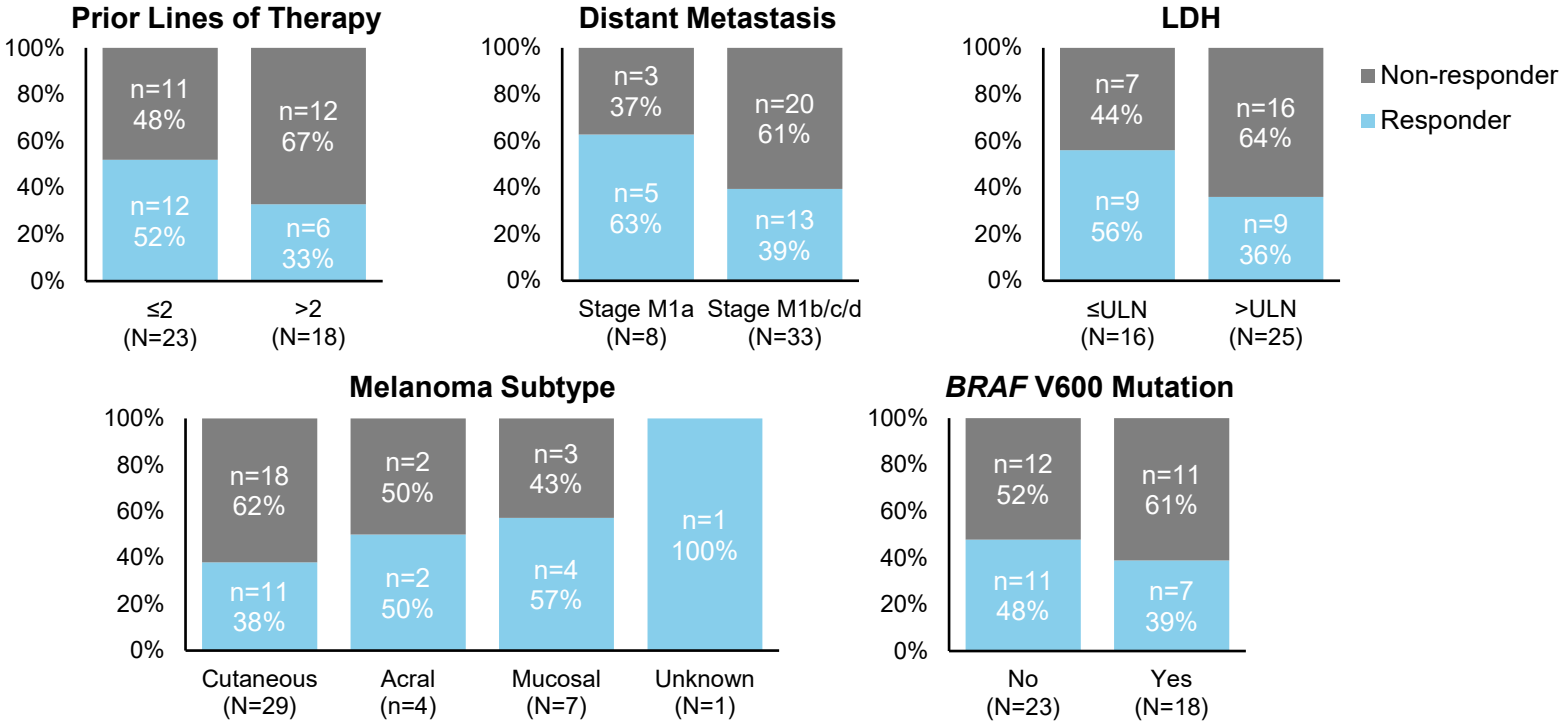
ORR: 44% (n=18) | DCR: 73% (n=30)



- Most responses were observed at the first radiologic assessment, with 12 ongoing during follow-up[a]

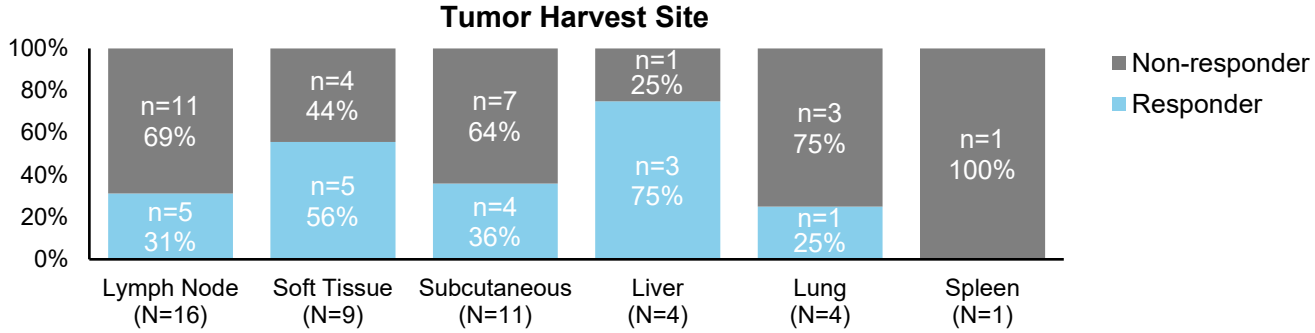
[a] Median follow up time = 6 months. ORR was calculated based on patients with measurable lesions after tumor harvest (n=41). Swimlane plot depicts all patients with confirmed responses.
CR, complete response; DCR, disease control rate; ORR, objective response rate; PD, progressive disease; PR, partial response;
SD, stable disease.

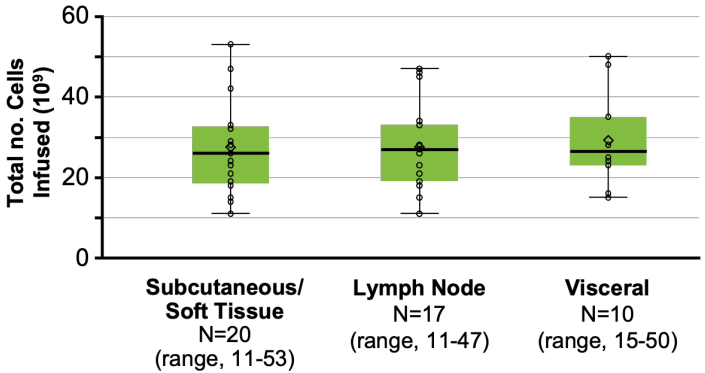
Objective Response to Lifileucel Across Clinical Subgroups

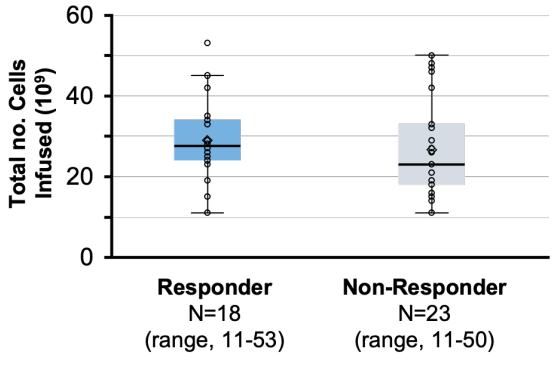


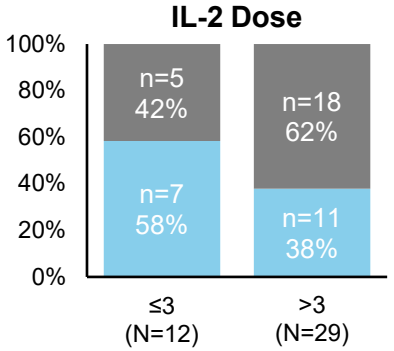
ORR was calculated based on patients with measurable lesions after tumor harvest (n=41).
BRAF, B-Raf proto-oncogene, serine/threonine kinase; LDH, lactate dehydrogenase; ULN, upper limit of normal.

Treatment-Related Factors and Response to Lifileucel



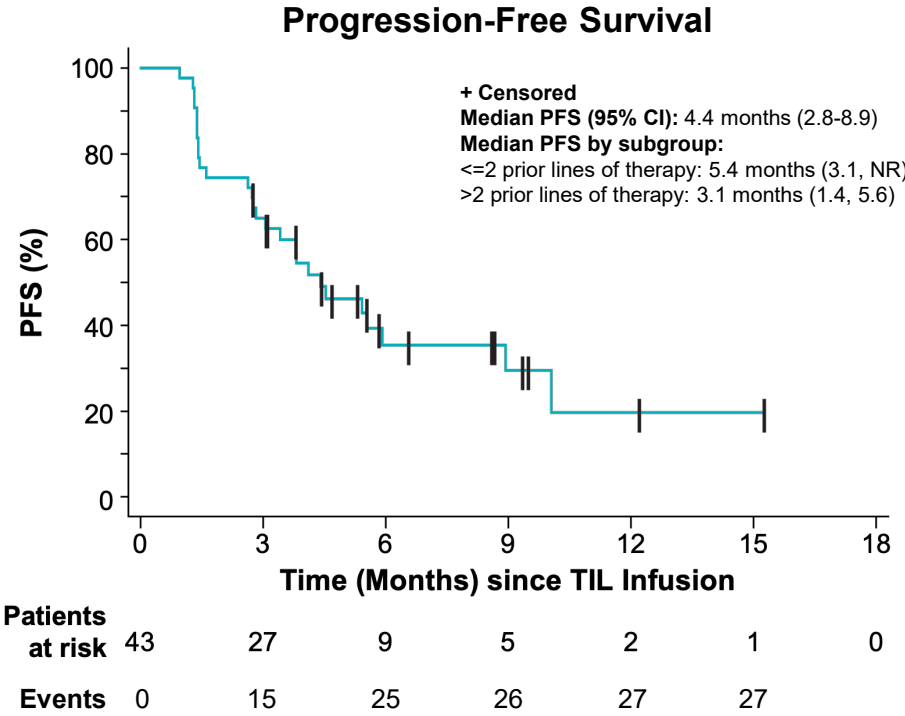


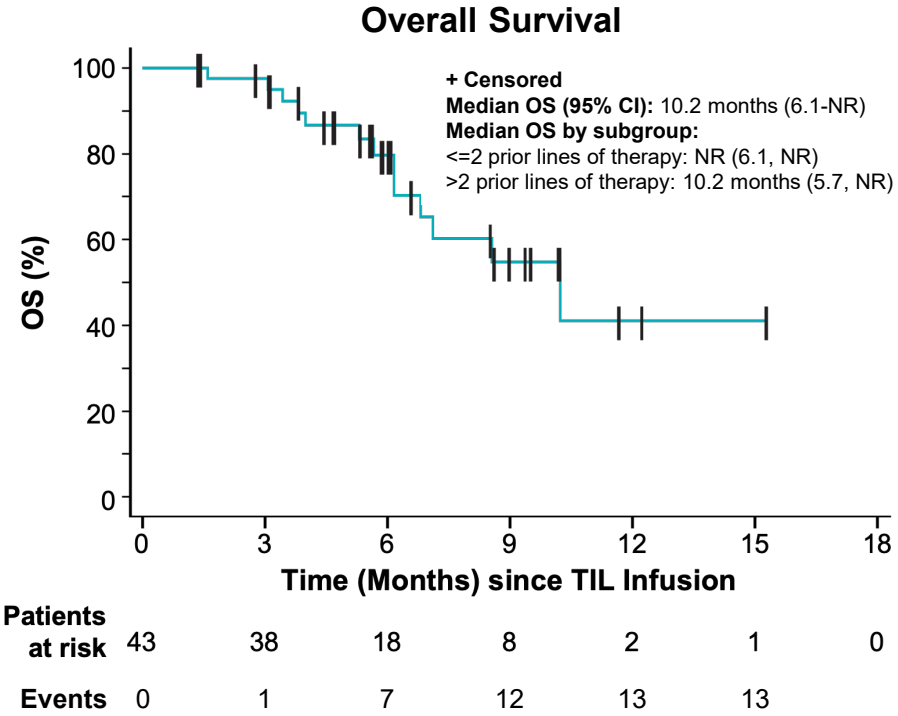




ORR was calculated based on patients with measurable lesions after tumor harvest (n=41).
IL-2, interleukin-2.

Survival Following Lifileucel Therapy – Preliminary Evaluation

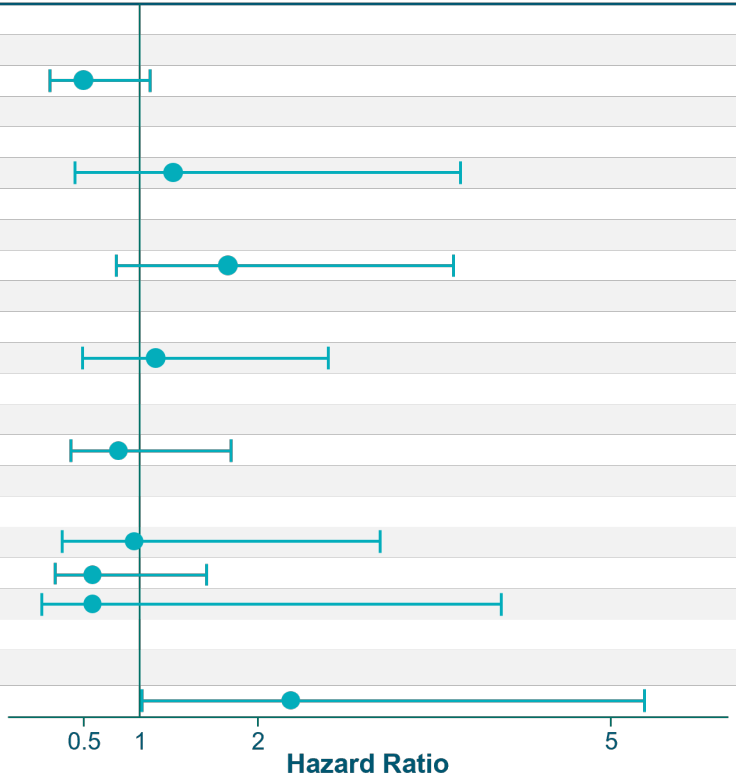




NR, not reached; OS, overall survival; PFS, progression-free survival; TIL, tumor-infiltrating lymphocyte.

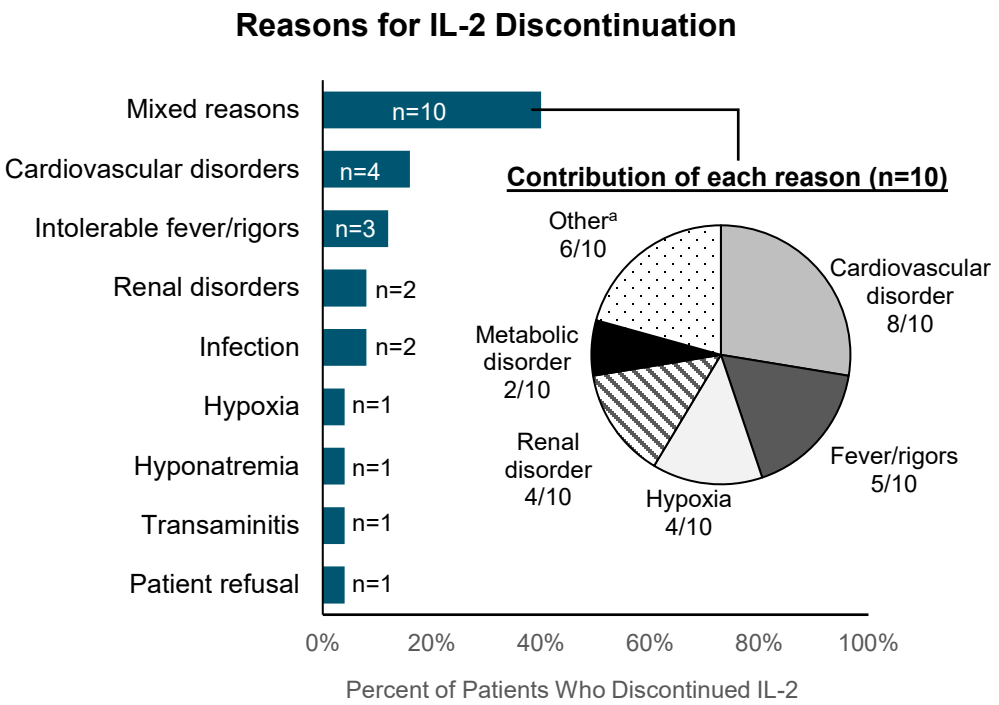
PFS Hazard Ratio by Subgroup

Subgroup	N	Event	HR (95% CI)	*P* Value
***BRAF* V600 mutation**				
Yes	19	14	Ref	
No	24	13	0.508 (0.237-1.085)	0.08
Disease stage				
M1a	9	4	Ref	
M1b/c/d	34	23	1.268 (0.433-3.714)	0.66
Prior lines of therapy (metastatic)				
≤2	25	13	Ref	
>2	18	14	1.725 (0.809-3.675)	0.16
Total viable cell count				
<Median	20	12	Ref	
≥Median	23	15	1.184 (0.553-2.539)	0.66
Dose of IL-2				
≤3	12	8	Ref	
>3	31	19	0.780 (0.332-1.828)	0.57
Melanoma subtype				
Cutaneous	30	19	Ref	
Acral	4	3	0.939 (0.276-3.199)	0.92
Mucosal	8	4	0.539 (0.181-1.599)	0.26
Unknown	1	1	0.537 (0.067-4.309)	0.56
LDH				
≤ULN	17	7	Ref	
>ULN	26	20	2.386 (1.004-5.667)	**0.05**



BRAF, B-Raf proto-oncogene, serine/threonine kinase; HR, hazard ratio;
LDH, lactate dehydrogenase; PFS, progression-free survival; ULN, upper limit of normal.

Safety Summary



- **Hospitalization:** Median **13 days** (range, 4–50)
- **Lymphodepletion interruptions:**
  - Cyclophosphamide: 1 patient (hypotension, fatigue)
  - Fludarabine: 3 patients (tachycardia, surgical decompression, *C. difficile* colitis)
- **Early mortality: No deaths within 45 days** of TIL infusion

[a] Includes 1 each of altered mental state, gastrointestinal bleeding, COVID infection, volume overload, seizure-like activity, and edema.
IL-2, interleukin-2; TIL, tumor-infiltrating lymphocyte.

Conclusions

- **Lifileucel demonstrates meaningful real-world clinical activity** in patients with advanced melanoma
- **Higher response rates** were observed in patients with **lower disease burden** and **fewer prior lines of therapy**, supporting earlier referral for lifileucel
- **Clinical benefit was independent of infused TIL dose**, and responders received fewer IL-2 doses, supporting that efficacy is not driven by IL-2 exposure
- No new safety signals or early mortality were observed

IL-2, interleukin-2; TIL, tumor-infiltrating lymphocyte.

Acknowledgements

- Patients and their families
- Study sponsorship:
  - Moffitt Cancer Center - Cutaneous Oncology Department Immune Cell Therapy Program, Nikhil I. Khushalani, Amod A. Sarnaik, John E. Mullinax, Ricardo J. Gonzalez, Jonathan S. Zager, Matthew C. Perez, Vernon K Sondak, Shari Pilon-Thomas
  - Memorial Sloan Kettering Cancer Center - MSKCC Cellular Therapy Service, Charlotte Ariyan, Ned Bartlett, Carrie Bellerive, Danielle Bello, Erika Castaneda, Jeffrey Kuhn, Alyssa Sebba
  - Weill Cornell Medical Center - NYP Weill Cornell BMT Cell Therapy program, Christopher Hackett, Gaurav Varma, Jessica Palmer
  - Honor Health Research Institute and Arizona State University John Shufedlt School of Medicine and Medical Engineering
  - Iovance Biotherapeutics, Inc. (San Carlos, CA, USA)