2023 ESMO IMMUNO-ONCOLOGY
Annual Congress

LONG-TERM EFFICACY AND PATTERNS OF RESPONSE OF LIFILEUCEL TUMOR-INFILTRATING LYMPHOCYTE (TIL) CELL THERAPY IN PATIENTS WITH ADVANCED MELANOMA: A 4-YEAR ANALYSIS OF THE C-144-01 STUDY

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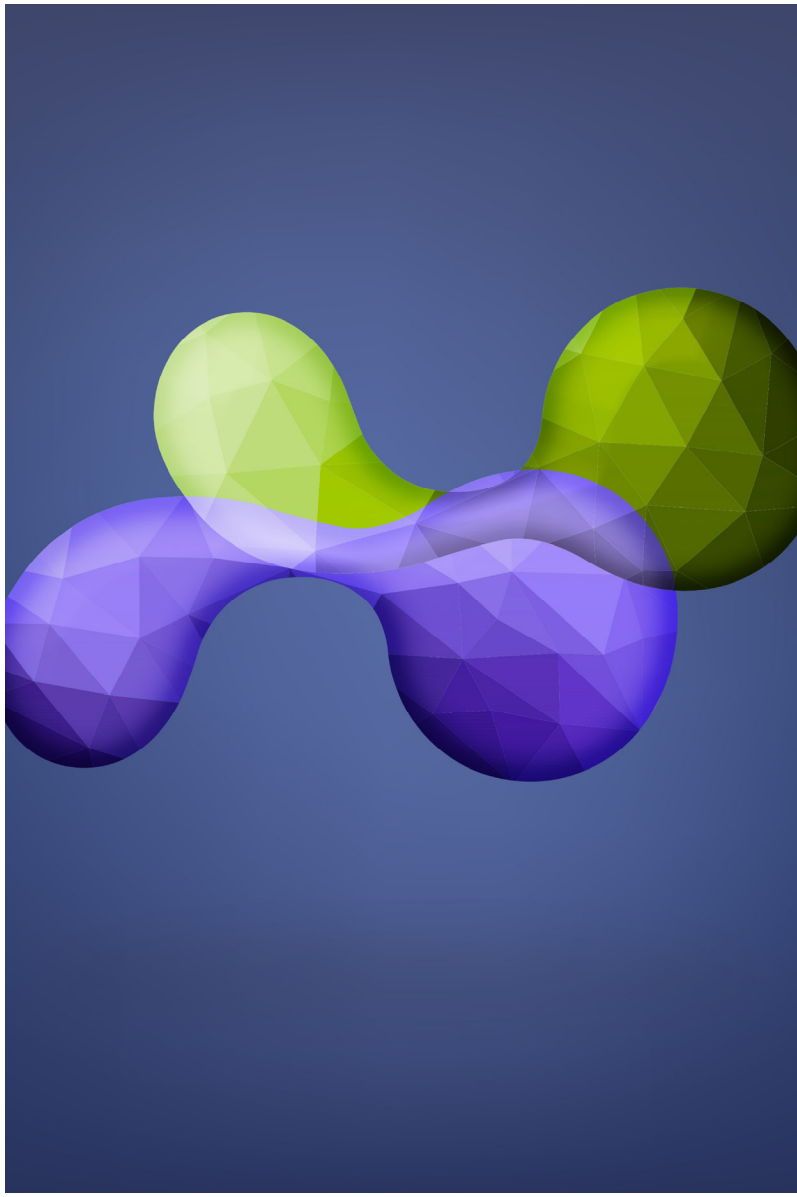
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE



ADVANCED MELANOMA: UNMET NEED AFTER IMMUNE CHECKPOINT INHIBITOR THERAPY

- The large proportion of patients with advanced (unresectable or metastatic) melanoma resistant to immune checkpoint inhibitors define a significant unmet need[1–3]
  - There is a great need for long-term follow-up data in this setting
- Autologous tumor-infiltrating lymphocyte (TIL) cell therapy recognizes and targets a multitude of patient-specific neoantigens to mediate tumor cell death[4,5]
- C-144-01 (NCT02360579) is a prospective phase 2, open-label, multicohort, multicenter study of lifileucel, a one-time autologous TIL cell therapy, in patients with advanced melanoma who progressed on or after anti–PD-1/PD-L1 therapy
  - Lifileucel has demonstrated durable clinical benefit in this setting with an IRC-assessed ORR of 31.4% in a heavily pre-treated population[6,7]

1. Cybulska-Stopa B, et al. Adv Med Sci. 2020;65:316–23. 2. Olson DJ, et al. J Clin Oncol. 2021;39:2647–55. 3. VanderWalde AM, et al. Cancer Res. 2022;82 (12 Suppl):CT013. 4. Schumacher TN, Schreiber RD. Science. 2015;348:69–74. 5. Sarnaik AA, et al. J Clin Oncol. 2021;39:2656–66. 6. Chesney J, et al. J Immunother Cancer. 2022;10:e005755. 7. Sarnaik A et al. Presented at: 2022 SITC Annual Meeting. November 8–12, 2022: Boston, MA. Poster 789.

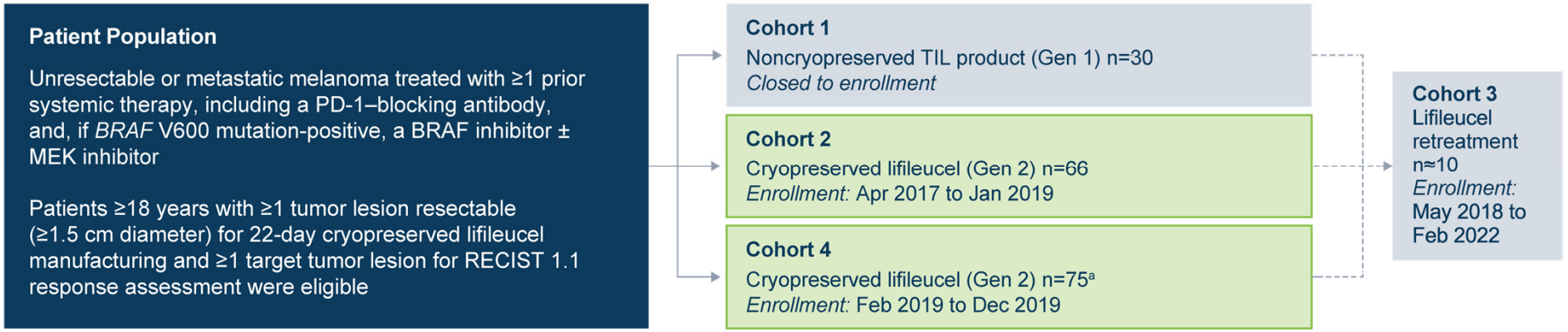
IRC, independent review committee; ORR, objective response rate; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; TIL, tumor-infiltrating lymphocyte.

Presenter: Martin Wermke

C-144-01: LIFILEUCEL IN ADVANCED MELANOMA

- We report 4-year follow-up data from C-144-01 (Cohorts 2 and 4) on lifileucel's treatment outcomes and patterns of response
  - Eligibility, lifileucel manufacturing process, and treatment were identical for Cohorts 2 and 4

C-144-01 Study Design



[a]The planned sample size for Cohort 4 was 75 per statistical plan, but the Full Analysis Set, defined as patients who received lifileucel that met specification, consisted of 87 patients due to rapid enrollment.
PD-1, programmed cell death protein-1; RECIST, Response Evaluation Criteria in Solid Tumors; TIL, tumor-infiltrating lymphocyte.

Presenter: Martin Wermke

BASELINE PATIENT AND DISEASE CHARACTERISTICS

Most patients with advanced melanoma were heavily pretreated

Characteristic	Total (N=153)
Median age, years (range)	56 (20, 79)
PD-L1 Tumor Proportion Score,[a] n (%)	
≥1%	76 (49.7)
<1%	32 (20.9)
Liver and/or brain lesions by IRC, n (%)	72 (47.1)
Median target lesions SOD, mm (range)	101.1 (13.5, 552.9)
Baseline lesions in ≥3 anatomic sites, n (%)	109 (71.2)
>3 baseline target and nontarget lesions, n (%)	116 (75.8)
LDH, n (%)	
≤ULN	70 (45.8)
1−2 × ULN	54 (35.3)
>2 × ULN	29 (19.0)
Median number of prior therapies (range)	3 (1, 9)
Primary resistance to prior anti–PD-1/PD-L1 per SITC criteria,[b] n (%)	109 (71.2)

Data cut-off: June 30, 2023; median study follow-up of 48.1 months

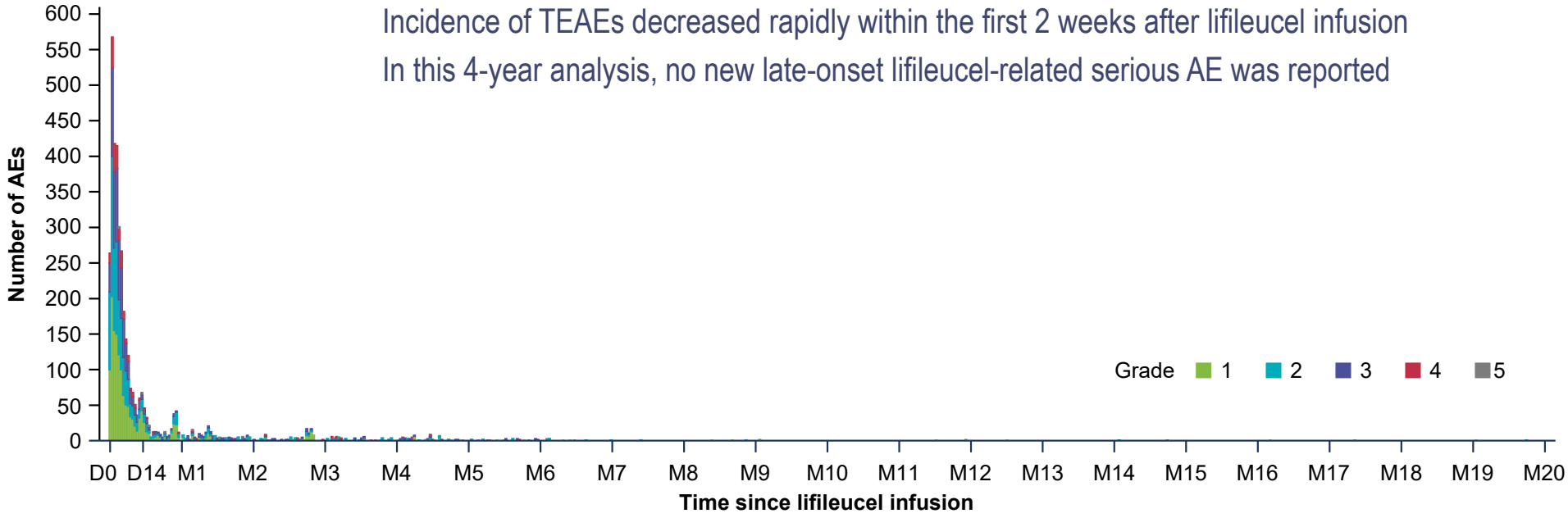
[a]45 patients had missing PD-L1 status. [b]Includes primary resistance to prior anti−PD-1/PD-L1 in metastatic setting and primary resistance/early relapse to prior anti−PD-1/PD-L1 in adjuvant setting.
IRC, independent review committee; LDH, lactate dehydrogenase; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; SITC, Society for Immunotherapy of Cancer; SOD, sum of diameters; ULN, upper limit of normal.

Presenter: Martin Wermke

TEAES WERE CONSISTENT WITH KNOWN SAFETY PROFILES OF NONMYELOABLATIVE LYMPHODEPLETION AND IL-2

Incidence of TEAEs decreased rapidly within the first 2 weeks after lifileucel infusion

In this 4-year analysis, no new late-onset lifileucel-related serious AE was reported

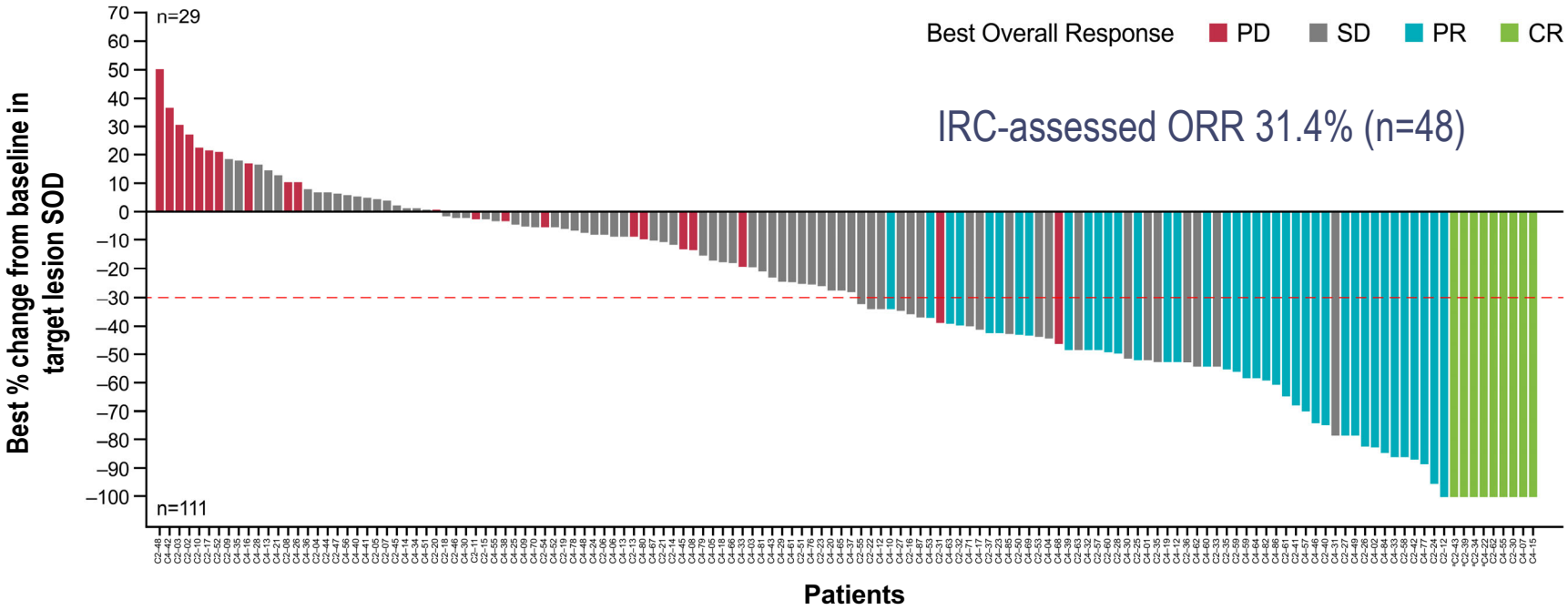


AE, adverse event; D, day; IL-2, interleukin-2; M, month; TEAE, treatment-emergent adverse event.

Presenter: Martin Wermke

TUMOR BURDEN REDUCTION AND BEST RESPONSE TO LIFILEUCEL

Most patients had a reduction from baseline in tumor burden



13 patients in the Full Analysis Set are not included (best overall responses included not evaluable [n=6], non-CR/non-PD [n=1], and PD [n=6]) for reasons including no acceptable target lesions or no post-lifileucel target lesion SOD measurements.

[a]–100% change from baseline is presented for CR assessment that includes lymph node lesions.

CR, complete response; IRC, independent review committee; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; SOD, sum of diameters.

Presenter: Martin Wermke

CHARACTERISTICS OF RESPONDERS

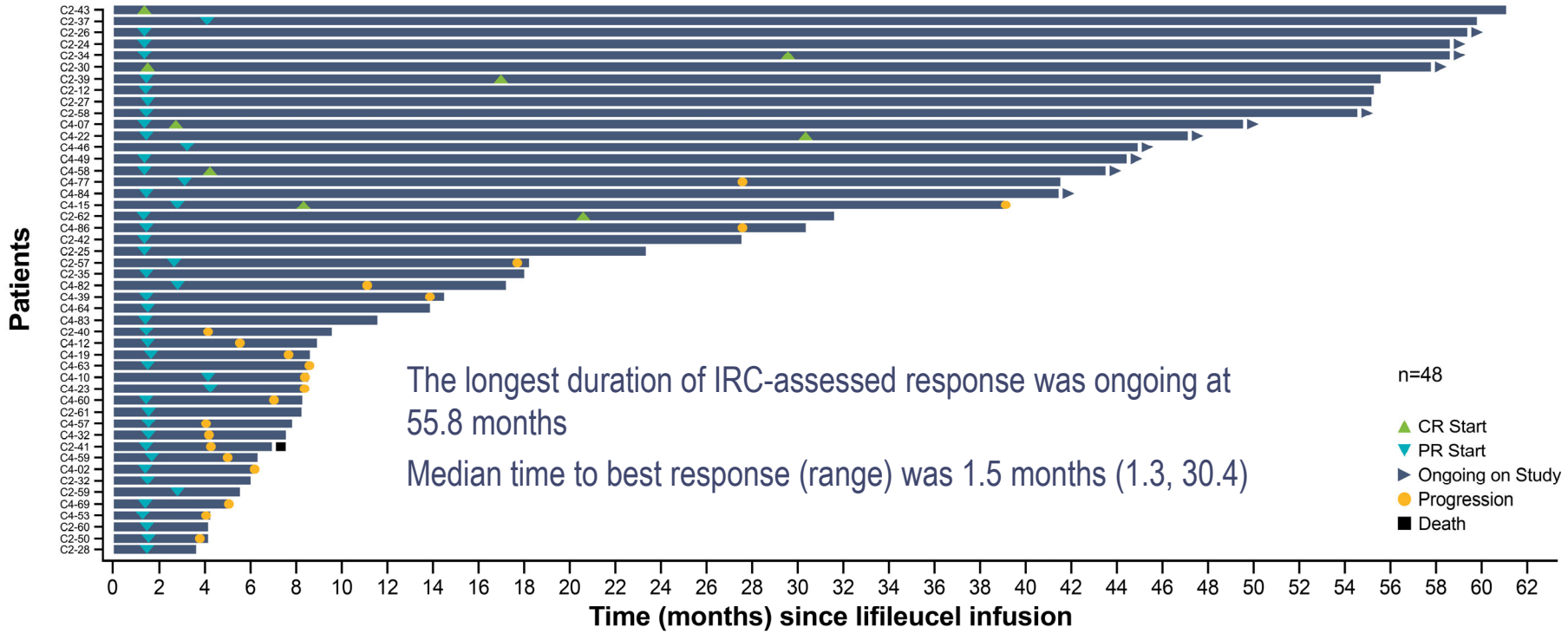
Characteristic	Total (N=153)	All responders (n=48)
Median age (range), years	56 (20, 79)	55 (25, 77)
PD-L1 Tumor Proportion Score,[a] n (%)		
≥1%	76 (49.7)	28 (58.3)
<1%	32 (20.9)	11 (22.9)
Liver and/or brain lesions by IRC, n (%)	72 (47.1)	19 (39.6)
Median target lesions SOD (range), mm	101.1 (13.5, 552.9)	68.8 (13.5, 552.9)
Baseline lesions in ≥3 anatomic sites, n (%)	109 (71.2)	29 (60.4)
>3 baseline target and nontarget lesions, n (%)	116 (75.8)	30 (62.5)
LDH, n (%)		
≤ULN	70 (45.8)	27 (56.3)
1−2 × ULN	54 (35.3)	18 (37.5)
>2 × ULN	29 (19.0)	3 (6.3)
Median number of prior therapies (range)	3 (1, 9)	3 (1, 8)
Primary resistance to prior anti–PD-1/PD-L1 per SITC criteria,[b] n (%)	109 (71.2)	36 (75.0)

[a]9 and 45 patients had missing PD-L1 status, respectively. [b]Includes primary resistance to prior anti−PD-1/PD-L1 in metastatic setting and primary resistance/early relapse to prior anti−PD-1/PD-L1 in adjuvant setting.
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.

Presenter: Martin Wermke

TIME TO RESPONSE AND TIME ON EFFICACY ASSESSMENT FOR CONFIRMED RESPONDERS (PR OR BETTER)

Lifileucel demonstrated early and durable responses

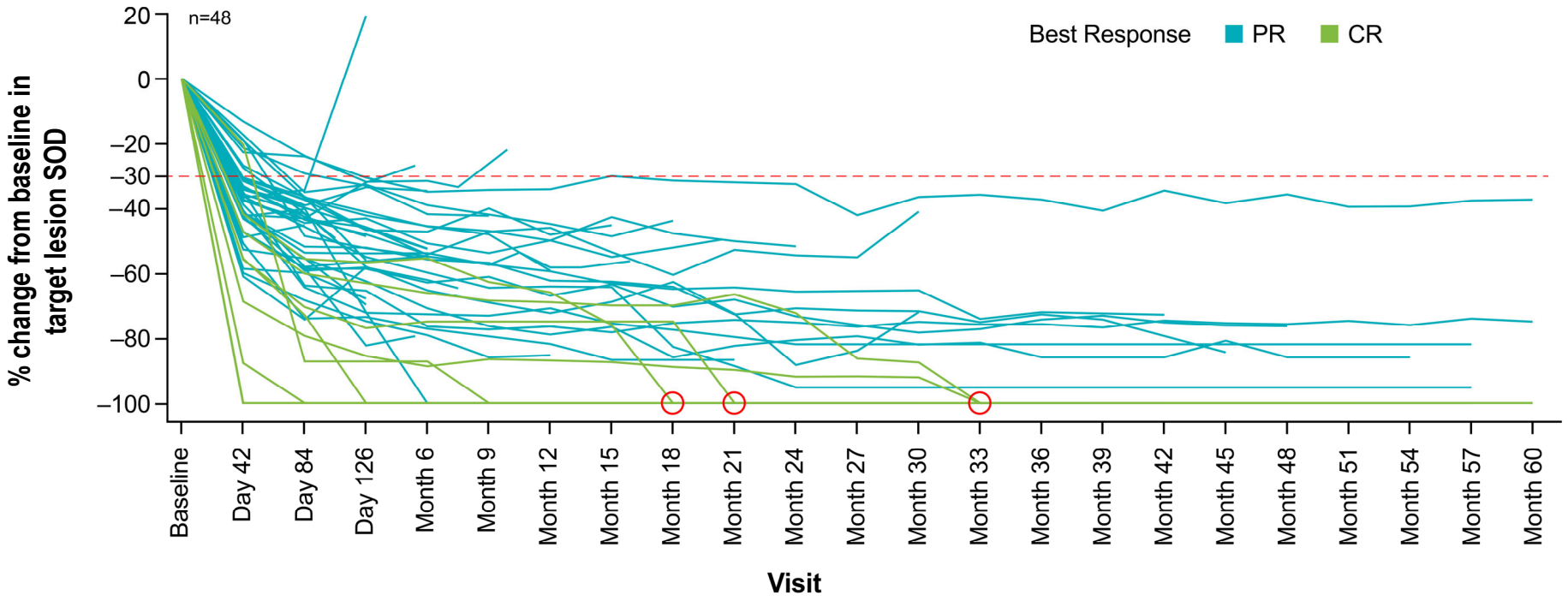


CR, complete response; IRC, independent review committee; PR, partial response.

Presenter: Martin Wermke

PERCENTAGE CHANGE FROM BASELINE IN TARGET LESION SOD FOR CONFIRMED RESPONDERS (PR OR BETTER)

Four patients converted to CR >1 year post-lifileucel infusion

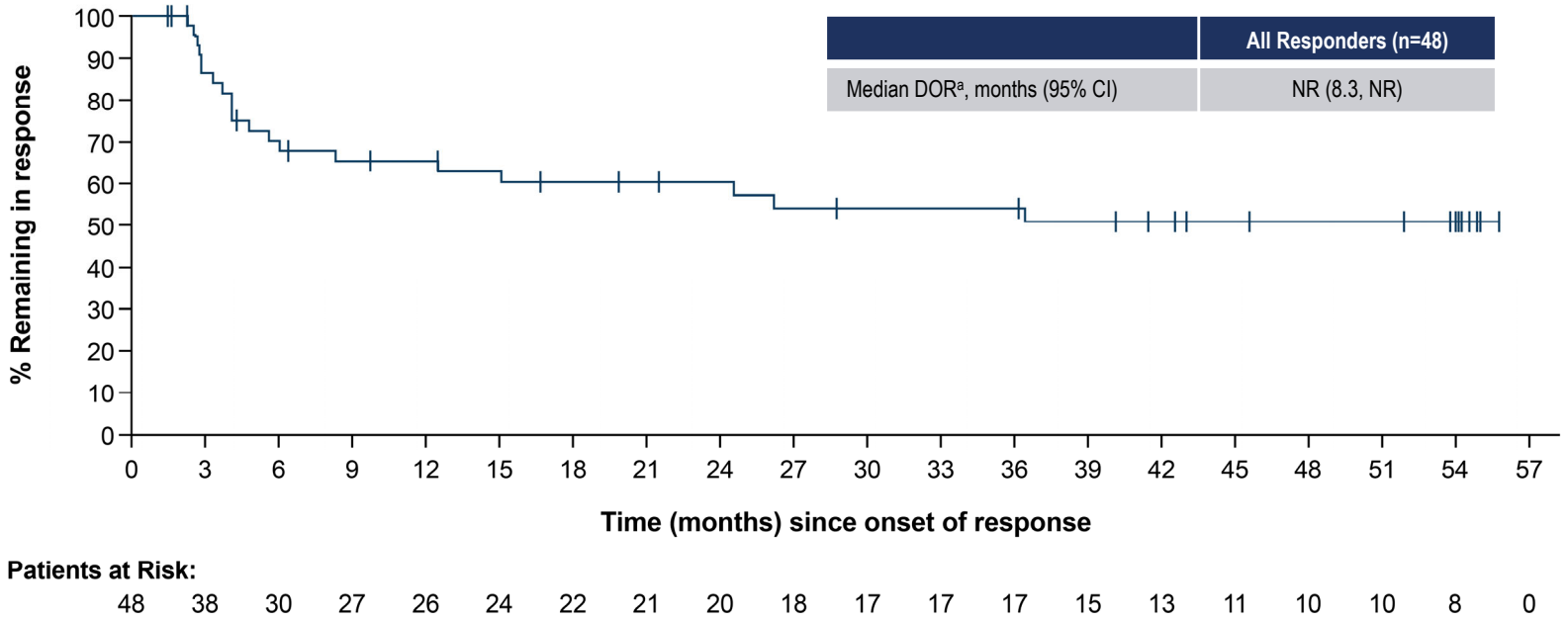


Circles represent 4 patients who converted to CR >1 year post-lifileucel infusion.
CR, complete response; PR, partial response; SOD, sum of diameters.

Presenter: Martin Wermke

DURATION OF RESPONSE

Lifileucel demonstrated clinically meaningful antitumor activity with durable responses



DOR by Patterns of Response

	Early Responder[b] (n=39)	Late Responders[c] (n=9)	Responders With Deepened Response[d] (n=16)	Responders Without Deepened Response (n=32)	All Responders (n=48)
Median DOR, months (95% CI)	NR (6.1, NR)	19.8 (4.1, NR)	NR (8.3, NR)	26.2 (4.1, NR)	NR (8.3, NR)

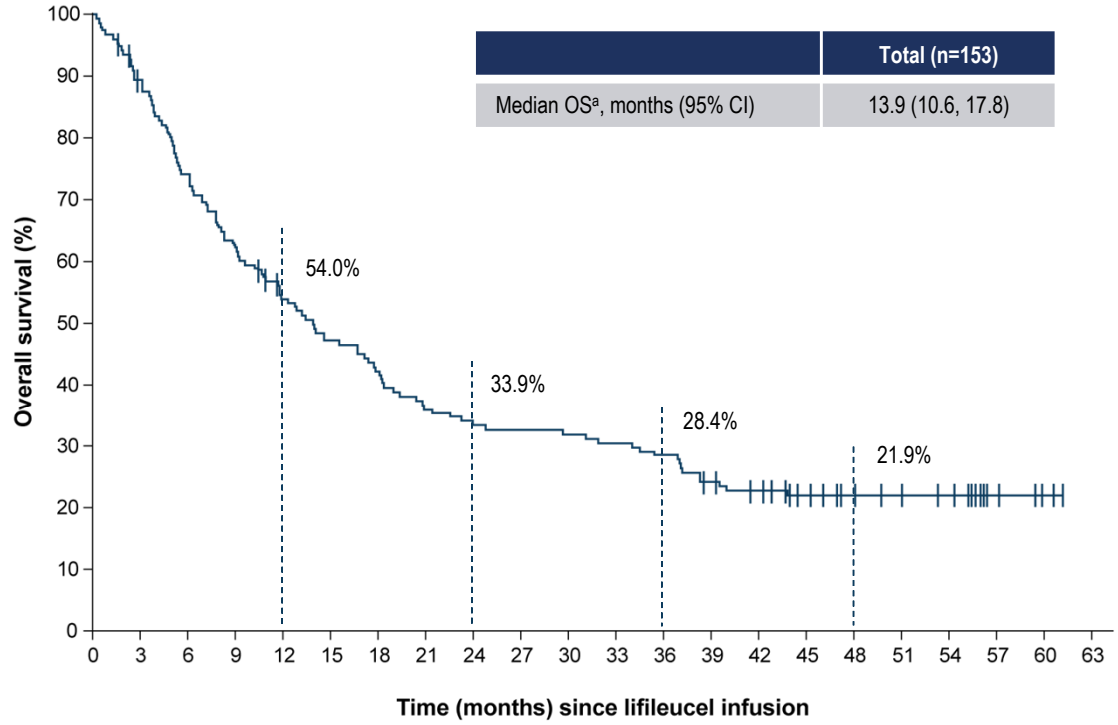
[a]Based on Kaplan-Meier estimates. [b]Patients with CR or PR on Day 42 visit. [c]Patients with CR or PR after Day 42 visit. [d]Patients who had SD and improved to confirmed PR or had PR and improved to confirmed CR.
CI, confidence interval; CR, complete response; DOR, duration of response; NR, not reached; PR, partial response; SD, stable disease.

Presenter: Martin Wermke

OVERALL SURVIVAL

Lifileucel demonstrated clinically meaningful antitumor activity with long-term survival benefit

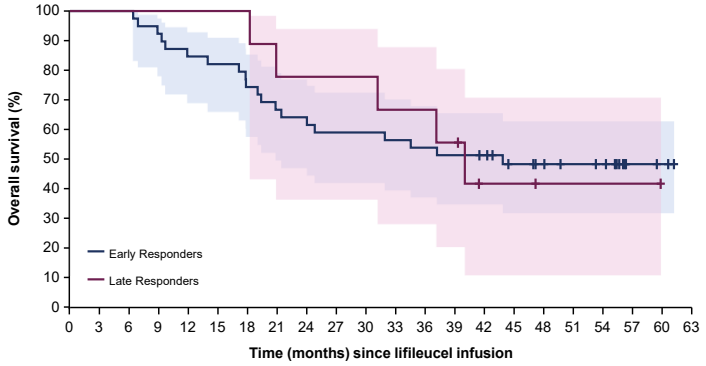
	Total (n=153)
Median OS[a], months (95% CI)	13.9 (10.6, 17.8)



Patients at Risk:

153	134	111	94	78	68	61	52	49	47	46	44	41	34	29	22	17	15	13	5	2	0

OS by Early vs Late Responders[b]



Patients at Risk

Early Responders	39	39	39	36	33	32	29	26	25	23	23	22	21	20	19	15	13	11	10	3	2	0
Late Responders	9	9	9	9	9	9	9	7	7	7	7	6	6	5	2	2	1	1	1	1	0	

OS by Patterns of Response

	Early Responders[c] (n=39)	Late Responders[d] (n=9)	Responders With Deepened Response[e] (n=16)	Responders Without Deepened Response (n=32)	All Responders (n=48)
OS rate at 4 years, % (95% CI)	48.3 (31.9, 62.9)	41.7 (10.9, 70.8)	68.2 (39.5, 85.4)	37.2 (21.0, 53.5)	47.3 (32.5, 60.7)

[a]Based on Kaplan-Meier estimates. [b]Shaded areas represent 95% CIs. [c]Patients with CR or PR on Day 42 visit. [d]Patients with CR or PR after Day 42 visit. [e]Patients who had SD and improved to confirmed PR or had PR and improved to confirmed CR.

CI, confidence interval; CR, complete response; NR, not reached; OS, overall survival; PR, partial response; SD, stable disease.

Presenter: Martin Wermke

CONCLUSIONS

Lifileucel is a potential treatment option for patients with advanced melanoma

- This 4-year analysis represents the longest follow-up to date of patients treated with lifileucel TIL cell therapy in the post-ICI setting for advanced melanoma
  - The longest duration of IRC-assessed response was ongoing at 55.8 months
- In patients with advanced melanoma who progressed on or after anti–PD-1/PD-L1 therapy and targeted therapy (where appropriate), one-time lifileucel TIL cell therapy demonstrated durable efficacy and a 4-year OS rate of 21.9%
- As responders had lower tumor burden, treating patients with advanced melanoma earlier in their disease course with lifileucel may increase likelihood of benefit from this one-time therapy
- These promising results continue to show favorable long-term survival outcomes, durable responses, and no long-term safety concerns related to lifileucel, supporting the use of one-time lifileucel infusion as a potential treatment option for patients with advanced melanoma

ICI, immune checkpoint inhibitor; IRC, independent review committee; OS, overall survival; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; TIL, tumor-infiltrating lymphocyte.

Presenter: Martin Wermke

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DECLARATION OF INTERESTS

Theresa Medina: Consulting/Advisory Role: Merck, BMS, Iovance Biotherapeutics, Moderna, Nektar, Regeneron, Exicure, Checkmate, BioAtla, Xencor, Replimune, Day One Pharmaceutical, Pfizer, Taiga.

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Sajeve Thomas: Speakers Bureau: BMS, Merck, Pfizer, Ipsen, Amgen, Genentech, Foundation One. Travel, Accommodations, Expenses: BMS, Merck, Pfizer, Ipsen, Amgen, Genentech, Foundation One. Consulting/Advisory Role: BMS, Merck, Pfizer, Ipsen, Amgen, Genentech, Foundation One. Research Funding: BMS, Merck, Pfizer, Ipsen, Amgen, Genentech, Foundation One.

Amod Sarnaik: Royalties and Licenses: Iovance Biotherapeutics. Consulting Fees: Iovance Biotherapeutics, Guidepoint, Defined Health, Boxer Capital, Huron Consulting Group, KeyQuest Health, Istari, Rising Tide, Second City Science, Market Access, Gerson-Lehram Group. Honoraria: Society for Immunotherapy of Cancer, Physician's Education Resource, Medscape, WebMD, Medstar Health. Travel, Accommodations, Expenses: Iovance Biotherapeutics, Provectus Biopharmaceuticals. Patents: Moffitt Cancer Center, Provectus Biopharmaceuticals. Receipt of Equipment, Materials, Drugs, Medical Writing, Gifts, or Other Services: BMS, Genentech.

John M. Kirkwood: Consulting/Advisory Role: Ankyra Therapeutics, Applied Clinical Intelligence, Axio Research, BMS, Cancer Study Group, Checkmate Pharmaceuticals, CytomX Therapeutics, DermTech, iOnctura, Iovance Biotherapeutics, IQVIA, Istari Oncology, Jazz Pharmaceuticals, Lytix Biopharma, Magnolia Innovation, Merck, Natera, Novartis, OncoCyte Corporation, PathAI, Pfizer, Regeneron Pharmaceuticals, Replimune, Scopus BioPharma, Takeda. Research Funding: Amgen, BMS, Checkmate Pharmaceuticals, Harbour BioMed, ImmVira Pharma, Immunocore, Iovance Biotherapeutics, Lion Biotechnologies, Novartis Pharmaceuticals, Takeda, Verastem.

James Larkin: Consulting/Advisory Role: iOnctura, Apple Tree, Merck, BMS, Eisai, Debiopharm, Incyte, Pfizer, Novartis, and MSD. Grants: Achilles, BMS, MSD, Nektar, Novartis, Pfizer, Roche, Immunocore, Aveo, Pharmacyclics. Honoraria: Eisai, Novartis, Incyte, Merck, touchIME, touchEXPERTS, Pfizer, Royal College of Physicians, Cambridge Healthcare Research, Royal College of General Practitioners, VJOncology, Agence Unik, BMS, Immatics, Insighter, and GCO. Research Funding: BMS, MSD, Novartis, Pfizer, Achilles Therapeutics, Roche, Nektar Therapeutics, Covance, Immunocore, Pharmacyclics, and Aveo. Speakers Bureau: Pierre Fabre, BMS, Ipsen, Roche, EUSA Pharma, Novartis, Aptitude, AstraZeneca, GSK, Eisai, Calithera, Ultimovacs, Seagen, Merck, eCancer, Inselgruppe, Pfizer, Goldman Sachs, MSD, Regional British Society of Gastroenterology, Agence Unik.

Jeffrey Weber: Consulting: Merck, Genentech, AstraZeneca, GSK, Novartis, Nektar, Celldex, Incyte, Biond, Moderna, ImCheck, Sellas, Evaxion, Pfizer, Regeneron, EMD Serono. Advisory Role: BMS, CytomX, Incyte, ImCheck, Biond, Sellas, Instil Bio, OncoC4, NexImmune. Equity: Biond, Evaxion, OncoC4, Instil Bio. Patents, Royalties: Moffitt Cancer Center, Biodesix.

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Martin Wermke: Honoraria: Lilly, Boehringer Ingelheim, SYNLAB, Janssen, Merck Serono, GWT, Amgen, Novartis. Consulting or Advisory Role: BMS, Novartis, Lilly, Boehringer Ingelheim, ISA Pharmaceuticals, Amgen, Immatics, Bayer, ImCheck Therapeutics. Research Funding: Roche. Travel, Accommodations, Expenses: Pfizer, BMS, AstraZeneca, Amgen, GEMoaB, Sanofi/Aventis, Immatics, Merck Serono.

Friedrich Graf Finckenstein: Employment: Iovance Biotherapeutics. Stock or Stock Options: Iovance Biotherapeutics. Patents, Royalties, Other Intellectual Properties: BMS.

Jeffrey Chou, Brian Gastman, Giri Sulur, Xiao Wu, and Wen Shi: Employment: Iovance Biotherapeutics. Stock or Stock Options: Iovance Biotherapeutics. Travel, Accommodations, Expenses: Iovance Biotherapeutics.

Evidio Domingo-Musibay: Grants or Contracts: Instil Bio.

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