Long-term efficacy and safety 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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Background

- Immune checkpoint inhibitors (ICI) have improved outcomes for patients with metastatic melanoma[1–3]
  - Nevertheless, resistance is common, and subsequent treatment options are limited
- 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 phase 2, multicohort, multicenter study of lifileucel autologous TIL cell therapy in patients with advanced (unresectable or metastatic) melanoma who progressed on or after anti–PD-1/PD-L1 therapy (**Figure 1**)[6,7]

Objective

- Here we report a 4-year update on lifileucel treatment outcomes from C-144-01, representing the longest follow-up of the largest population of patients with anti–PD-1–refractory advanced melanoma treated with TIL cell therapy
  - We report independent review committee (IRC)-assessed response data; investigator-assessed data were reported in the abstract

Methods

Key Endpoints

- **Primary:** Objective response rate (ORR) (IRC-assessed using Response Evaluation Criteria in Solid Tumors [RECIST] v1.1)
- **Secondary:** Duration of response (DOR), progression-free survival, overall survival (OS), safety assessments

Key Eligibility Criteria

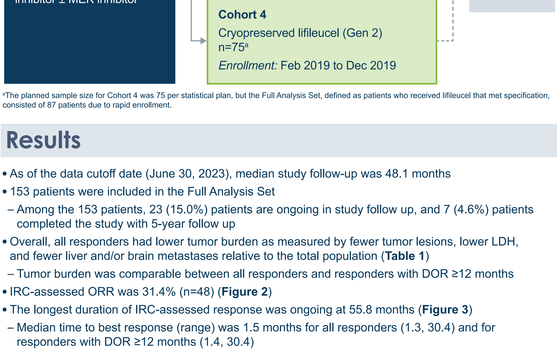
- Documented radiologic disease progression
- ≥1 tumor lesion resectable for TIL generation (≥1.5 cm in diameter) and ≥1 target tumor lesion for RECIST 1.1 response assessment
- Age ≥18 years at time of consent
- Eastern Cooperative Oncology Group performance status of 0–1
- No limit on number of prior therapies

Treatment Regimen

- Lifileucel, a cryopreserved TIL cell therapy product, was used in Cohorts 2 and 4 and was manufactured using the same Gen 2 process
- All patients received nonmyeloablative lymphodepletion, a single lifileucel infusion, and up to 6 doses of high-dose interleukin (IL)-2

Eligibility, lifileucel manufacturing process, and treatment were identical for Cohorts 2 and 4

Figure 1. 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.

Results

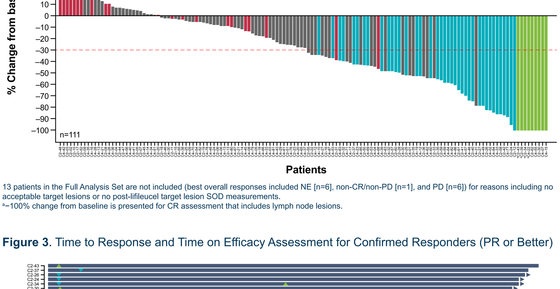
- As of the data cutoff date (June 30, 2023), median study follow-up was 48.1 months
- 153 patients were included in the Full Analysis Set
  - Among the 153 patients, 23 (15.0%) patients are ongoing in study follow up, and 7 (4.6%) patients completed the study with 5-year follow up
- Overall, all responders had lower tumor burden as measured by fewer tumor lesions, lower LDH, and fewer liver and/or brain metastases relative to the total population (**Table 1**)
  - Tumor burden was comparable between all responders and responders with DOR ≥12 months
- IRC-assessed ORR was 31.4% (n=48) (**Figure 2**)
- The longest duration of IRC-assessed response was ongoing at 55.8 months (**Figure 3**)
  - Median time to best response (range) was 1.5 months for all responders (1.3, 30.4) and for responders with DOR ≥12 months (1.4, 30.4)
- Patient responses to lifileucel treatment deepened over time (**Figure 4**)
- The median DOR was not reached (NR) (**Figure 5**)
- Median OS was 13.9 months (**Figure 6**)
  - 1-, 2-, 3-, and 4-year OS rates were 54.0%, 33.9%, 28.4%, and 21.9%, respectively
- 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

Table 1. Baseline Patient and Disease Characteristics

Characteristic	Responders with DOR ≥12 months (n=26)	All responders (n=48)	Total (N=153)
Median age (range), years	55 (37, 77)	55 (25, 77)	56 (20, 79)
PD-L1 Tumor Proportion Score,[a] n (%)			
≥1%	15 (57.7)	28 (58.3)	76 (49.7)
<1%	8 (30.8)	11 (22.9)	32 (20.9)
Liver and/or brain lesions by IRC, n (%)	10 (38.5)	19 (39.6)	72 (47.1)
Median target lesion SOD (range), mm	69.1 (17.8, 190.1)	68.8 (13.5, 552.9)	101.1 (13.5, 552.9)
Baseline lesions in ≥3 anatomic sites, n (%)	15 (57.7)	29 (60.4)	109 (71.2)
>3 baseline target and nontarget lesions, n (%)	14 (53.8)	30 (62.5)	116 (75.8)
LDH, n (%)			
≤ULN	17 (65.4)	27 (56.3)	70 (45.8)
1–2 × ULN	8 (30.8)	18 (37.5)	54 (35.3)
>2 × ULN	1 (3.8)	3 (6.3)	29 (19.0)
Median number of prior therapies (range)	3 (2, 8)	3 (1, 8)	3 (1, 9)
Primary resistance to prior anti–PD-1/PD-L1 per SITC criteria,[b] n (%)	21 (80.8)	36 (75.0)	109 (71.2)

[a]3, 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.

Figure 2. Best Percentage Change From Baseline in Target Lesion SOD



13 patients in the Full Analysis Set are not included (best overall responses included NE [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.

Figure 3. Time to Response and Time on Efficacy Assessment for Confirmed Responders (PR or Better)

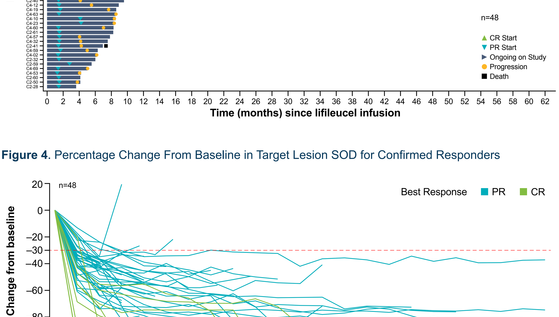
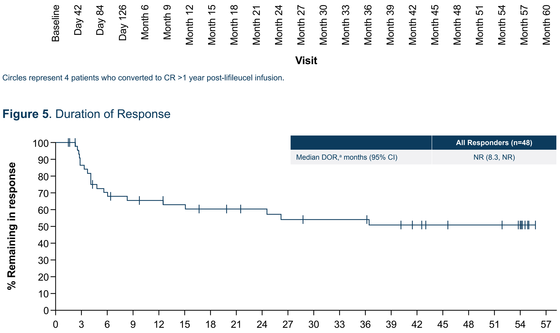
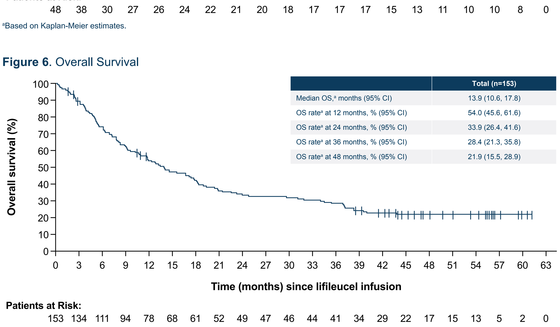


Figure 4. Percentage Change From Baseline in Target Lesion SOD for Confirmed Responders



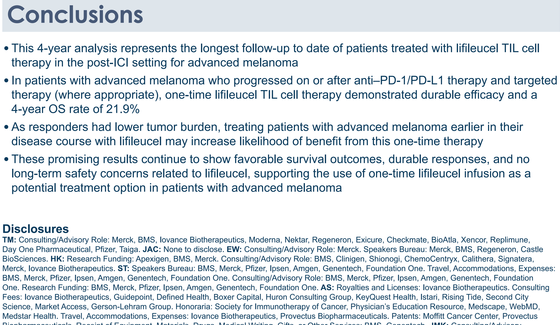
Circles represent 4 patients who converted to CR >1 year post-lifileucel infusion.

Figure 5. Duration of Response



[a]Based on Kaplan-Meier estimates.

Figure 6. Overall Survival



[a]Based on Kaplan-Meier estimates.

Conclusions

- 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
- 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 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 in patients with advanced melanoma

Disclosures

TM: Consulting/Advisory Role: Merck, BMS, Iovance Biotherapeutics, Moderna, Nektar, Regeneron, Exicure, Checkmate, BioAtla, Xencor, Replimune, Day One Pharmaceutical, Pfizer, Taiga. **JAC:** None to disclose. **EW:** Consulting/Advisory Role: Merck, Speakers Bureau: Merck, BMS, Regeneron, Castle BioSciences. **HK:** Research Funding: Apexigen, BMS, Merck. Consulting/Advisory Role: BMS, Clinigen, Shionogi, ChemoCentryx, Calithera, Signatera, Merck, Iovance Biotherapeutics. **ST:** 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. **AS:** 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. **JMK:** Consulting/Advisory Role: Array BioPharma, 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 Co., Immunocore, Iovance Biotherapeutics, Lion Biotechnologies, Novartis, Takeda, Verastem **JL:** 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, and Agence Unik. **JW:** Consulting: Merck, Genentech, AstraZeneca, GSK, Novartis, Nektar, Celldex, Incyte, Biond, Moderna, ImCheck, Sellas, Evaxion, Pfizer, Regeneron, and EMD Serono. Advisory Role: BMS, CytomX, Incyte, ImCheck, Biond, Sellas, Instil Bio, OncoC4, and NexImmune. Equity: Biond, Evaxion, OncoC4, and Instil Bio. Patents, Royalties: Moffitt Cancer Center and Biodesix. **OH:** Consulting/Advisory Role: Alkermes, Amgen, Bactonix, BeiGene, BioAtla, BMS, Eisai, Roche Genentech, Georgiamune, GigaGen, Grit Bio, GSK, Idera, Immunocore, Incyte, Instil Bio, Iovance, Janssen, KSQ, Merck, Moderna, Novartis, Obsidian, Pfizer, Regeneron, Sanofi, Seattle Genetics, Tempus, Vial Health, and Zelluna. Honoraria: BMS, Immunocore, Novartis, Pfizer, and Regeneron. Research Funding: Arcus, Aduro, Akeso, Amgen, BioAtla, BMS, CytomX Therapeutics, Exelixis, Roche Genentech, GSK, Immunocore, Idera, Incyte, Iovance, Merck, Merck Serono, Moderna, NextCure, Novartis, Pfizer, Regeneron, Seattle Genetics, Torque, and Zelluna. Speakers Bureau: BMS, Immunocore, Novartis, Pfizer, and Regeneron. **MW:** 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. **FGF:** Employment: Iovance Biotherapeutics. Stock or Stock Options: Iovance Biotherapeutics. Patents, Royalties, Other Intellectual Properties: BMS. **JC, BG, GS, XW,** and **WS:** Employment: Iovance Biotherapeutics. Stock or Stock Options: Iovance Biotherapeutics. Travel, Accommodations, Expenses: Iovance Biotherapeutics. **EDM:** Grants or Contracts: Instil Bio.

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Abbreviations

AE, adverse event; CI, confidence interval; CR, complete response; DOR, duration of response; ICI, immune checkpoint inhibitor; IL, interleukin; IRC, independent review committee; LDH, lactate dehydrogenase; NE, not evaluable; NR, not reached; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein-1; PD, progressive disease; PD-L1, programmed death-ligand 1; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SITC, Society for Immunotherapy of Cancer; SOD, sum of diameter; TIL, tumor-infiltrating lymphocyte; ULN, upper limit of normal.

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