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Lifileucel tumor-infiltrating lymphocyte (TIL) cell therapy in patients (pts) with advanced mucosal melanoma after progression on immune checkpoint inhibitors (ICI): Results from the phase 2 C-144-01 study

Götz Ulrich Grigoleit,[1] Harriet Kluger,[2] Sajeve Thomas,[3] Jason A Chesney,[4] **Evidio Domingo-Musibay,[5]** Miguel F Sanmamed,[6] Theresa Medina,[7] Mirjana Ziemer,[8] Eric Whitman,[9] Friedrich Graf Finckenstein,[10] Jeffrey Chou,[10] Xiao Wu,[10] Giri Sulur,[10] Wen Shi,[10] Amod Sarnaik[11]

[1]Helios Klinikum Duisburg, Duisburg, Germany; [2]Yale Cancer Center, New Haven, CT, USA; [3]Orlando Health Cancer Institute, Orlando, FL, USA; [4]Brown Cancer Center, Louisville, KY, USA; **[5]Masonic Cancer Center, Minneapolis, MN, USA;** [6]Clínica Universitaria de Navarra, Pamplona, Navarra, Spain; [7]University of Colorado Cancer Center, Aurora, CO, USA; [8]Universitätsklinikum Leipzig, Leipzig, Germany; [9]Atlantic Health System, Morristown, NJ, USA; [10]Iovance Biotherapeutics, Inc., San Carlos, CA, USA; [11]H Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA

Presented by: Evidio Domingo-Musibay

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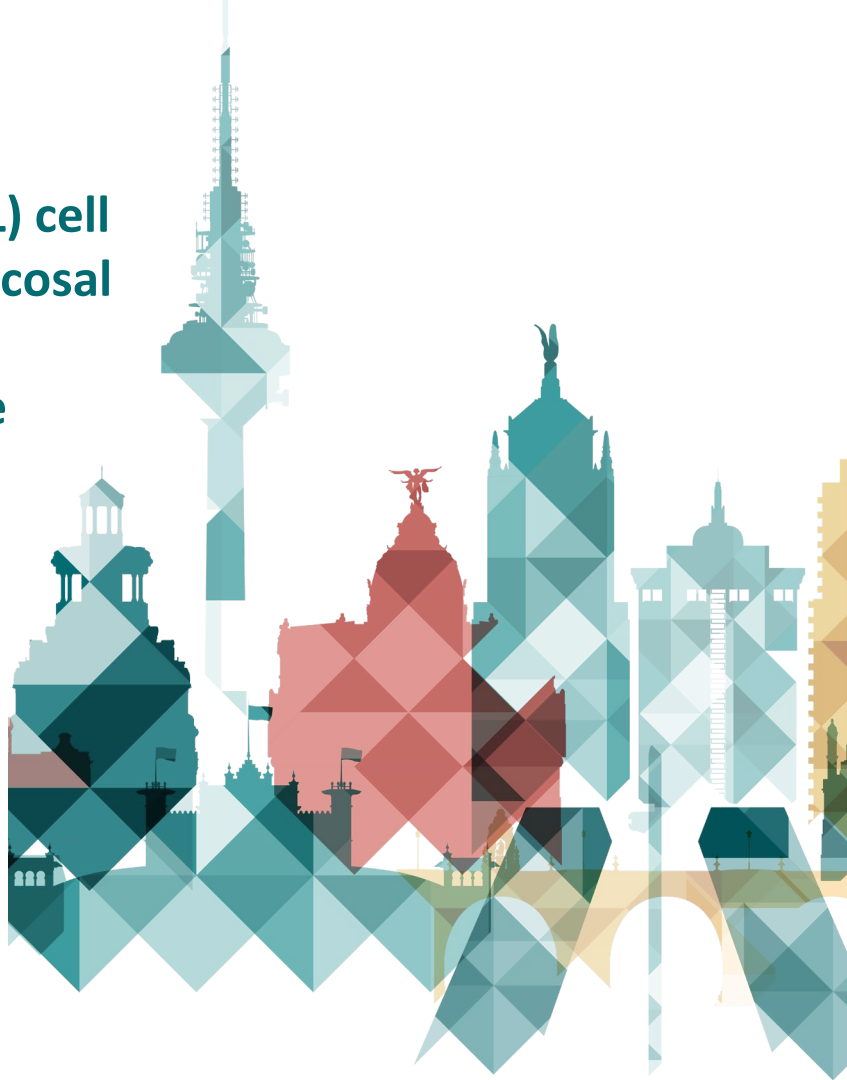


C-144-01: Lifileucel in Advanced Melanoma

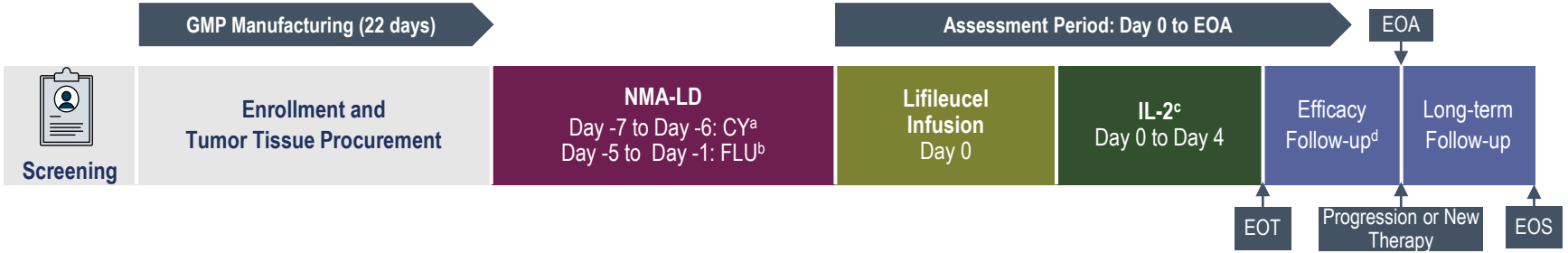
Background

- Advanced mucosal melanoma is rare and difficult to treat with poor outcomes after anti–PD-1 therapy[1-3]
  - ORR: 19%–23%
  - Median OS: 11.3–16 months
- Lifileucel autologous TIL cell therapy demonstrated an ORR of 31.4% in heavily pretreated patients (N=153) with advanced melanoma[4]

Methods and Objectives

- C-144-01 (NCT02360579) is a phase 2, multicenter study of lifileucel in patients with advanced (unresectable or metastatic) melanoma who progressed on or after anti–PD-1/PD-L1 therapy
- We report data in a subgroup of patients with advanced mucosal melanoma treated with lifileucel with a planned follow-up of up to 5 years

Figure 1. Treatment Schema



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[a]60 mg/kg daily x 2 doses. [b]25 mg/m^2 daily x 5 doses.[c]600,000 IU/kg (≤6 doses). [d]Response was assessed by an independent review committee using RECIST v1.1 criteria.

CY, cyclophosphamide; EOA, end of assessment; EOS, end of study; EOT, end of treatment; FLU, fludarabine; GMP, Good Manufacturing Practice; IL-2, interleukin-2; IU, international units; NMA-LD, non-myeloablative lymphodepletion; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein-1; PD-L1, programmed death ligand 1; RECIST, Response Evaluation Criteria in Solid Tumors; TIL, tumor-infiltrating lymphocyte.

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Results: Baseline Patient and Disease Characteristics

Most patients with mucosal melanoma had disease that was primary refractory to prior anti–PD-1/PD-L1 therapy

Table 1. Baseline Patient and Disease Characteristics

Characteristics	Mucosal Melanoma (N=12)
Median age, y (min, max)	61.5 (37–79)
Median number of prior therapies, n (min, max)	2 (1–6)
Primary refractory to anti–PD-1/PD-L1[a], n (%)	**10 (83.3)**
Liver or brain metastasis by IRC, n (%)	5 (41.7)
Tumor tissue procurement site[b], n (%)	
Lymph node	6 (50.0)
Median target lesion SOD, mm (min, max)	**118.9 (20.7–260.9)**
Median target and nontarget lesions, n (min, max)	**6 (3–13)**
BRAF V600 wild-type, n (%)	12 (100)
LDH>ULN	5 (41.7)

- Data cut-off: 15 July 2022
- 12 patients with histologically diagnosed mucosal melanoma received lifileucel
  - The median (range) number of TIL infused was 26.1 × 10^9 cells (3.3–72)
  - The median (range) number of IL-2 doses was 5.5 (3–6)
- Patients had a high disease burden with a median target lesion SOD of 118.9 mm (**Table 1**)

[a]Primary refractory to anti–PD-1/PD-L1 is defined as patients who had best response of progressive disease to prior anti–PD-1/PD-L1; the first anti–PD-1/PD-L1 with documented response is considered if multiple anti–PD-1/PD-L1 therapies are received. [b]6 patients (50%) had other sites, including lung (n=2), liver (n=1), skin/subcutaneous (n=1), groin (n=1), chest wall (n=1).
IL-2, interleukin 2; IRC, independent review committee; LDH, lactate dehydrogenase; PD-1, programmed cell death protein-1; PD-L1, programmed death ligand 1; SOD, sum of diameters; ULN, upper limit of normal; TIL, tumor-infiltrating lymphocyte.

Results: Clinical Efficacy of Lifileucel in Mucosal Melanoma

Lifileucel demonstrated clinically meaningful antitumor activity with durable responses

- The median follow-up was 35.7 months
- The ORR (confirmed responses) was 50.0% (6/12; 95% CI, 21.1–78.9) (**Table 2; Figure 2**)
- Median DOR was NR (95% CI: 12.5–NR) (**Table 3**)
- 4 of 6 responders had durable and ongoing responses at the time of the datacut (**Figure 3**)

Table 2. IRC-Assessed Response (RECIST v1.1)

	Mucosal Melanoma (N=12)
Best Overall Response	
CR	1 (8.3)
PR	5 (41.7)
SD	4 (33.3)
PD	2 (16.7)

Table 3. Duration of Response

	Mucosal Melanoma (N=12)
DOR[a], n (%)	
≥6 months	6/6 (100)
≥12 months	5/6 (83.3)
≥24 months	4/6 (66.7)

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

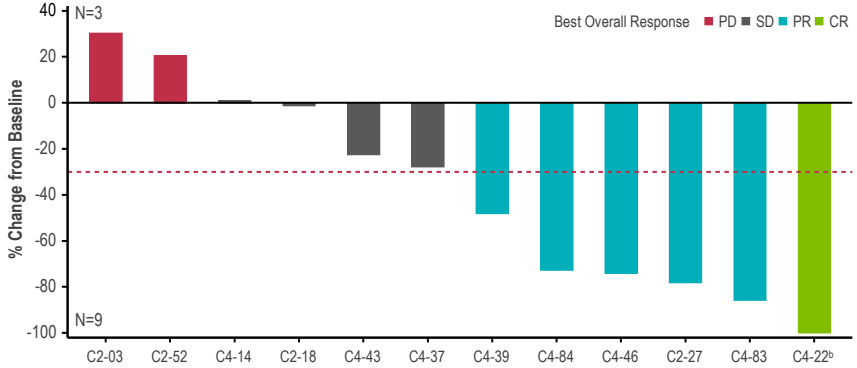
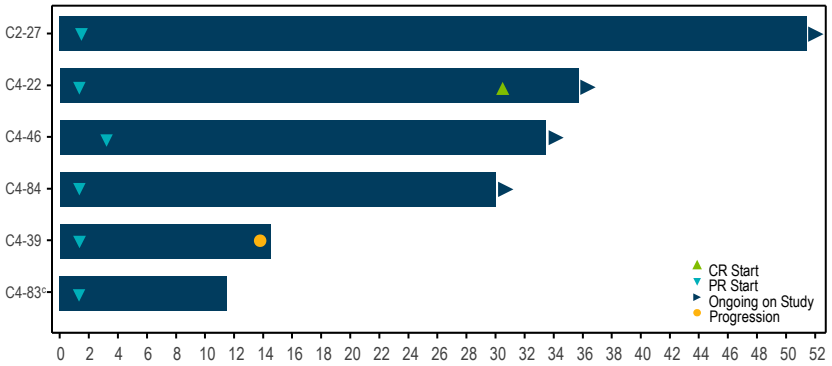


Figure 3. Time to Response and Time on Efficacy Assessment for Confirmed Responders (PR or Better)



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[a]Includes patients who achieved CR or PR. [b]Presented for CR assessment that includes lymph node lesions. [c]Patient C4-83 discontinued the efficacy follow-up at time of data cut.
CI, confidence interval; CR, complete response; DOR, duration of response; IRC, independent review committee; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SOD, sum of diameters; TIL, tumor-infiltrating lymphocyte.

Results: Safety in Mucosal Melanoma

Safety was consistent with known safety profiles of nonmyeloablative lymphodepletion and IL-2

- The most common grade 3/4 nonhematologic TEAEs were febrile neutropenia and hypotension (**Table 4**)
- Grade 3/4 hematologic laboratory abnormalities were consistent with nonmyeloablative lymphodepletion (**Table 5**)

Table 4. Nonhematologic TEAEs in ≥30% of Patients

Preferred Term, n (%)	Mucosal Melanoma (N=12)	
	Any grade	Grade 3/4
Chills	9 (75.0)	0
Febrile neutropenia	7 (58.3)	7 (58.3)
Diarrhea	7 (58.3)	0
Pyrexia	5 (41.7)	0
Pruritus	5 (41.7)	0
Hypotension	5 (41.7)	4 (33.3)
Alopecia	5 (41.7)	0
Hypokalemia	4 (33.3)	0
Hypoxia	4 (33.3)	2 (16.7)

Table 5. Grade 3/4 Hematologic Lab Abnormalities

Preferred Term, n (%)	Mucosal Melanoma (N=12)
Neutropenia	12 (100)
Leukopenia	12 (100)
Lymphopenia	12 (100)
Thrombocytopenia	12 (100)
Anemia	8 (66.7)

IL-2, interleukin-2; TEAE, treatment-emergent adverse event.

Tumor Mutational Burden (TMB) and TIL Persistence

TMB was lower in mucosal melanoma than in cutaneous melanoma

- Mucosal melanoma showed a low TMB compared with cutaneous melanoma (**Figure 4**)
  - Mean TMB of mucosal vs cutaneous melanoma: 2.145 mut/Mb vs 10.47 mut/Mb, respectively
- TIL persistence was similar in patients with mucosal or cutaneous melanoma through month 12 (**Figure 5**)

Figure 4. TMB in Patients with Mucosal or Cutaneous Melanoma

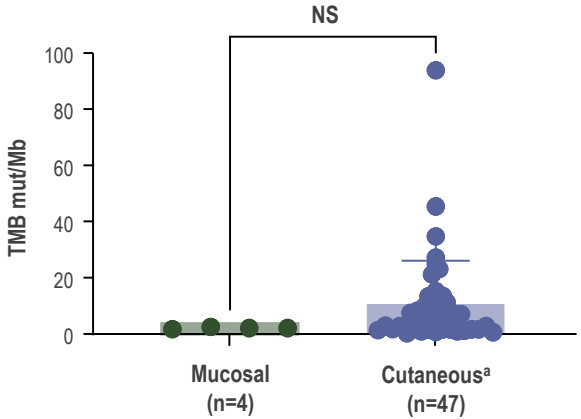
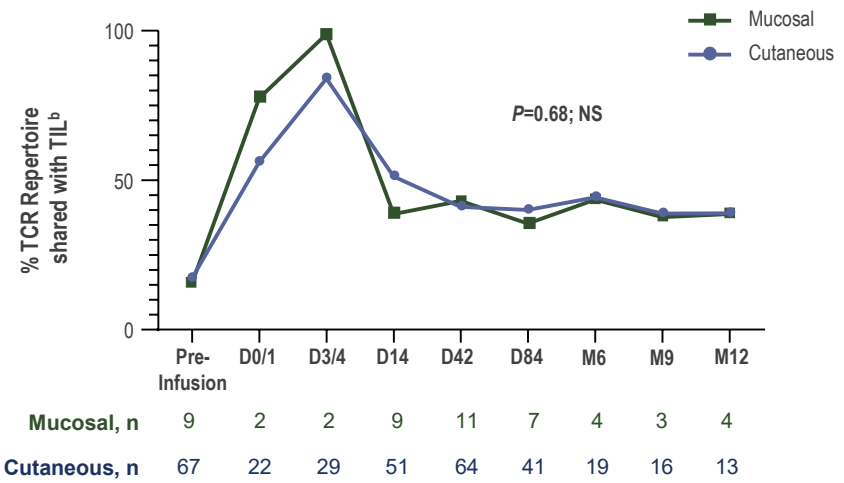


Figure 5. TIL Persistence Over Time in Patients with Mucosal or Cutaneous Melanoma



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[a]The horizontal bar represents the standard deviation. [b]From TIL infusion product.
D, day; M, month; NS, not significant; mut, mutation; TCR, T-cell receptor; TIL, tumor-infiltrating lymphocyte.

Conclusions

Lifileucel demonstrated durable clinical benefit in patients with difficult-to-treat mucosal melanoma

- Lifileucel demonstrated clinically meaningful activity and durable responses in patients with difficult-to-treat, low-TMB mucosal melanoma with progression after anti–PD1/PD-L1 therapy
  - The ORR was 50% (95% CI, 21.1–78.9)
  - At a median follow-up 35.7 months, median DOR was not reached
- The antitumor responses observed in this subgroup of patients with mucosal melanoma were consistent with responses observed in the overall population of patients with advanced melanoma treated with lifileucel
- TEAEs were consistent with the known safety profiles of nonmyeloablative lymphodepletion and IL-2
- These results further support the potential benefit of lifileucel as a one-time treatment that is differentiated from other immunotherapies

DOR, duration of response; IL-2, interleukin-2; NR, not reached; ORR, objective response rate; PD-1, programmed cell death protein-1; PD-L1, programmed death ligand 1; TEAE, treatment-emergent adverse event. TMB, tumor mutation burden.

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DECLARATION OF INTERESTS

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Xiao Wu: Employment: Iovance Biotherapeutics. Stock or Stock Options: Iovance Biotherapeutics. Travel, Accommodations, Expenses: Iovance Biotherapeutics.

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