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Lifileucel, a Potential Therapy for Metastatic Melanoma Patients who are Primary Refractory to Prior Anti-PD-1 Therapy

Lifileucel (a cryopreserved autologous tumor infiltrating lymphocyte therapy) produces durable responses at one-year median study follow-up in patients with advanced metastatic melanoma primary refractory to/ previously progressed on multiple prior therapies including anti-PD-1

Amod Sarnaik, MD[1], Nikhil I. Khushalani, MD[1], Jason Alan Chesney, MD, PhD[2], Harriet M. Kluger, MD[3], Karl D. Lewis, MD[4], Theresa Medina, MD[4], Evidio Domingo-Musibay, MD[5], Anna C. Pavlick, MD, MBA[6], Eric D. Whitman, MD[7], Salvador Algarra[8], Pippa Corrie, PhD, BMBCh, FRCP[9], **Omid Hamid, MD[10]**, Jose Lutzky, MD[11], Judit Oláh, MD, DSc[12], Jeffrey S. Weber, MD, PhD[6], James M. G. Larkin, MD, PhD[13], Wen Shi, MD, PhD[14], Kelly DiTrapani, RN, BSN, BA[14], Harry Qin, PhD[14], Renee Wu, PhD[14], Friedrich Graf Finckenstein, MD[14], Maria Fardis, PhD, MBA[14], John M. Kirkwood, MD[15]

[1] H. Lee Moffitt Cancer Center, Tampa, FL, USA
[2] James Graham Brown Cancer Center, University of Louisville, Louisville, KY, USA
[3] Yale University School of Medicine, Smilow Cancer Center, New Haven Hospital, New Haven, CT, USA
[4] University of Colorado Cancer Center - Anschutz Medical Campus, Aurora, CO, USA
[5] University of Minnesota, Masonic Cancer Center, Minneapolis, MN, USA
[6] Laura and Isaac Perlmutter Cancer Center, NYU Langone Medical Center, New York, NY, USA
[7] Atlantic Health System Cancer Care, Morristown, NJ, USA
[8] Clínica Universidad de Navarra, Pamplona, Spain
[9] Cambridge University Hospitals NHS Foundation Trust - Addenbrooke's Hospital, Cambridge, UK
[10] The Angeles Clinic and Research Institute, Los Angeles, CA, USA
[11] Mount Sinai Comprehensive Cancer Center, Miami, FL, USA
[12] University of Szeged - Albert Szent-Györgyi Health Center, Szegedi, Hungary
[13] Royal Marsden NHS Foundation Trust, London, UK
[14] Iovance Biotherapeutics, Inc. San Carlos, CA, USA
[15] Hillman Cancer Center – University of Pittsburgh Medical Center, Pittsburgh, PA, USA

For more information, please contact: publications@Iovance.com

BACKGROUND

- Treatment options are limited for patients with advanced melanoma who have a Best Overall Response (BOR) of progressive disease (PD) to anti-PD-1 checkpoint therapy, known as primary refractory or primary resistance
- 40-65% of all metastatic melanoma patients are primary refractory to initial immune checkpoint inhibitor (ICI) therapy[1]
- Tumor Infiltrating Lymphocytes (TIL) therapy offers a potential therapeutic option in primary refractory metastatic melanoma patients
- C-144-01 (NCT02360579) is an ongoing Phase 2 global multicenter study:
  - Investigational agent: autologous TIL (lifileucel; LN-144)
  - Patient population: unresectable or metastatic melanoma who have progressed on checkpoint inhibitors and BRAF/MEK inhibitors (if BRAF mutated)
  - Manufacturing conditions: central manufacturing of cryopreserved TIL, 22-day duration

METHODS

- Cohort 2 Safety and Efficacy Sets: 42 of 66 patients who had BOR of PD on first anti-PD-1/L1 and underwent resection for the purpose of TIL generation and received lifileucel infusion and Response data shown herein is based on Investigator assessed response by RECIST v1.1

Figure 1. Lifileucel Manufacturing Process: 22-Days

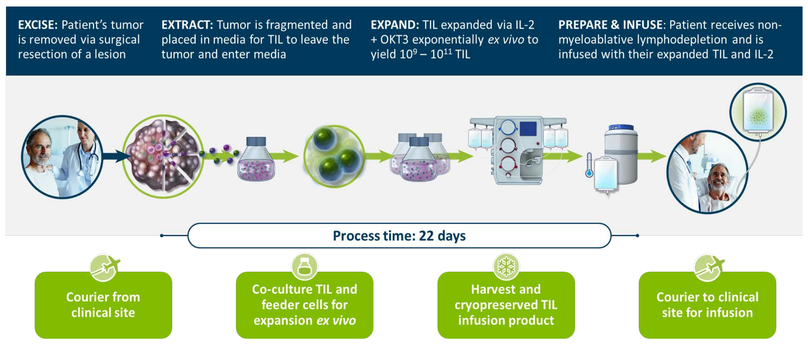
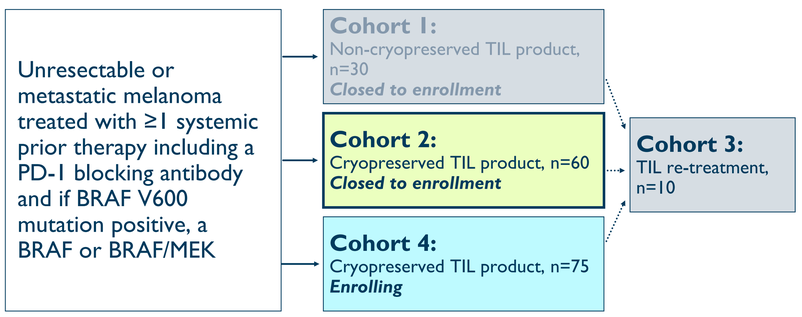


Figure 2. C-144-01 Study Design: Iovance C-144-01 Phase 2 Trial in Metastatic Melanoma

Phase 2, multicenter study to assess the efficacy and safety of autologous Tumor Infiltrating Lymphocytes (LN-144) for treatment of patients with metastatic melanoma (**NCT02360579**)



Cohort 2 Endpoints:

- Primary: Efficacy defined as investigator assessed Objective Response Rate (ORR)
- Secondary: Safety, efficacy, ORR by independent review committee (IRC)

Study Updates:

- Cohort 2 safety and Investigator assessed efficacy for the subpopulation with BOR of PD to first Anti-PD-1/L1 presented here (n=42, Data extract as of 24 Sept 2019)
- Cohort 4 in C-144-01 is ongoing in support of lifileucel registration with the primary endpoint of ORR by IRC

References

[1] Gide T.N., et al. Primary and Acquired Resistance to Immune Checkpoint Inhibitors in Metastatic Melanoma. *Clin. Cancer Res.* 2018;24:1260–1270.

Disclosure

- This study and poster are sponsored by Iovance Biotherapeutics, Inc
- WS, KDT, HQ, RW, FGF, and MF are employees of Iovance Biotherapeutics, Inc and have stock options

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- The authors would like to acknowledge Iovance team for their contributions
- All listed authors meet the criteria for authorship set forth by the International Committee for Medical Journal Editors

RESULTS

Table 1. Cohort 2 Patient Characteristics

- In n=42 patients primary refractory to Anti-PD-1/L1, defined as BOR of PD to the earliest anti-PD-1/L1 treatment:
  - Mean duration on first anti-PD-1/L1 was 3.1 months
  - 57% PD-L1 High/Positive (TPS ≥ 1%)

CHARACTERISTIC	n=42 (%)
Gender	
Male	26 (62)
Female	16 (38)
Age	
Median	56
Min, Max	20, 77
Prior therapies, n (%)	
Mean # prior therapies	3.3
Anti-CTLA-4	33 (79)
Anti-PD-1	42 (100)
BRAF/MEK	9 (21)
Progressive Disease (PD) for at least 1 prior therapy	
Anti-CTLA-4	29 (88)*
Anti-PD-1	42 (100)
Baseline ECOG score, n (%)	
0	25 (60)
1	17 (40)

CHARACTERISTIC	n=42 (%)
BRAF Status	
Mutated V600	11 (26)
Wild Type	29 (69)
Unknown	2(5)
Baseline LDH (U/L)	
Median	259
1-2 times ULN	10 (24)
> 2 times ULN	5 (12)
Target Lesion Sum of Diameter (mm)	
Mean (SD)	114 (78)
Min, Max	17, 343
Number of Target & Non-Target Lesions (at Baseline)	
>3	35 (83)
Mean	6
Patients with Baseline Liver and/or Brain Lesions	21 (50)

*% is calculated based on number of patients received prior anti-CTLA4.

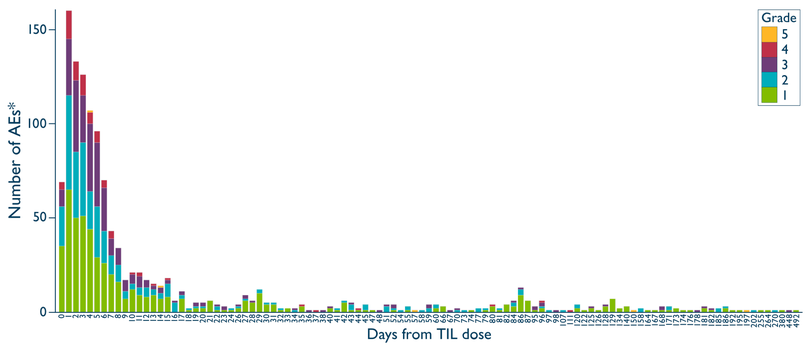
Table 2. Treatment Emergent Adverse Events (≥30%)

PREFERRED TERM	COHORT 2 PATIENTS PRIMARY REFRACTORY TO ANTI-PD-1/PD-L1, (n=42) ANY GRADE n (%)	GRADE ≥3 n (%)	GRADE 5 n (%)
Number of subjects reporting at least one TEAE	42 (100)	41 (97.6)	2 (4.8)
Thrombocytopenia	38 (90.5)	33 (78.6)	0
Chills	32 (76.2)	3 (7.1)	0
Anemia	30 (71.4)	25 (59.5)	0
Pyrexia	25 (59.5)	7 (16.7)	0
Febrile neutropenia	23 (54.8)	23 (54.8)	0
Neutropenia	21 (50.0)	15 (35.7)	0
Hypophosphatemia	19 (45.2)	12 (28.6)	0
Leukopenia	18 (42.9)	15 (35.7)	0
Fatigue	18 (42.9)	1 (2.4)	0
Lymphopenia	15 (35.7)	13 (31.0)	0
Hypotension	14 (33.3)	5 (11.9)	0
Hypocalcemia	14 (33.3)	3 (7.1)	0
Aspartate aminotransferase increased	13 (31.0)	0	0
Diarrhea	13 (31.0)	1 (2.4)	0
Tachycardia	13 (31.0)	1 (2.4)	0

- Patients with multiple events for a given preferred term are counted only once using the maximum grade under each preferred term
- Treatment-Emergent Adverse Events refer to all AEs starting on or after the first dose date of TIL up to 30 days

- AEs are consistent with prior reports on the full Cohort 2 analysis set

Figure 2. Adverse Events Over Time



- Decreasing frequency of AEs over time is reflective of potential benefit of one time treatment with lifileucel
- The adverse event profile was generally consistent with the underlying advanced disease and the profile of the lymphodepletion and IL-2 regimens

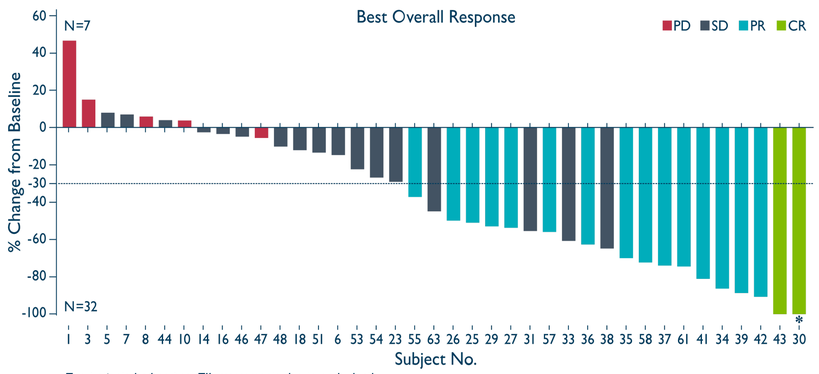
The number of AEs is cumulative and represent the total number of primary refractory patients dosed.

Table 3. Efficacy Assessed by Investigator

- In n=42 patients primary refractory to Anti-PD-1/L1:
  - Median DOR has not been reached at median 12.0 months study follow up
  - ORR was notable in this sub-group at 40.5%

RESPONSE (RECIST v1.1)	COHORT 2 FULL ANALYSIS SET N=66 (%)	COHORT 2 PATIENTS PRIMARY REFRACTORY TO ANTI-PD-1/L1 n=42 (%)
Objective Response Rate (ORR)	**24 (36.4)**	**17 (40.5)**
Complete Response (CR)	2 (3.0)	2 (4.8)
Partial Response (PR)	22 (33.3)	15 (35.7)
Stable Disease (SD)	29 (43.9)	17 (40.5)
Progressive Disease (PD)	9 (13.6)	5 (11.9)
Non-Evaluable	4 (6.1)	3 (7.1)
Disease Control Rate (DCR)	53 (80.3)	34 (81.0)
Median Duration of Response (DOR)	**Not Reached**	**Not Reached**
Min, Max	2.2, 21.2+	2.8+, 21.2+

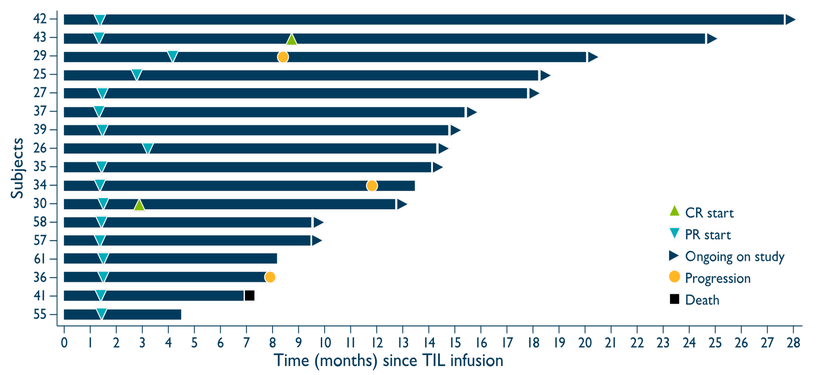
Figure 4. Efficacy: Best Overall Response



Two patients had no post-TIL assessments due to early death.
One patient had no post-TIL assessment due to start of new anti-cancer therapy prior to day 42.
**-100% change from baseline is displayed for the CR visit involved lymph nodes.*

Figure 5. Efficacy: Time to Response (PR or Better)

- 71% of the responders are ongoing on study



CONCLUSIONS

- Relapsed and refractory metastatic melanoma presents a high unmet medical need with low survival rates and with limited treatment options
- Lifileucel treatment resulted in 36.4% investigator assessed ORR in heavily pretreated metastatic melanoma patients with high baseline disease burden
- Lifileucel was equally efficacious in patients who were primary refractory to prior anti PD-1/L1 ICI therapy:
  - 40.5% ORR in patients who were primary refractory to Anti PD-1/L1
  - 71% of responders who were primary refractory to Anti PD-1/L1 remain on study
- At 12 months of study follow up, median DOR has still not been reached for primary refractory or the full population of the cohort

Lifileucel autologous TIL has demonstrated potential efficacy and durability of response for primary refractory patients with metastatic melanoma and represents a viable therapeutic option.

Cohort 4 in C-144-01 is ongoing in support of lifileucel registration