Safety and efficacy of cryopreserved autologous tumor infiltrating lymphocyte therapy (LN-144, lifileucel) in advanced metastatic melanoma patients who progressed on multiple prior therapies including anti-PD-1

Amod Sarnaik[1], Nikhil I. Khushalani[1], Jason Alan Chesney[2], Harriet M. Kluger[3], Brendan D. Curti[4], Karl D. Lewis[5], Sajeve Samuel Thomas[6], Eric D. Whitman[7], Omid Hamid[8], Jose Lutzky[9], Anna C. Pavlick[10], Jeffrey S. Weber[10], James M.G. Larkin[11], Debora Barton[12], Kelly DiTrapani[12], Renee Wu[12], Maria Fardis[12], John M. Kirkwood[13]

[1]H. Lee Moffitt Cancer Center, Tampa, FL; [2]James Graham Brown Cancer Center, University of Louisville, Louisville, KY; [3]Yale School of Medicine, New Haven, CT; [4]Earle A. Chiles Research Institute at Robert W. Franz Cancer Center, Providence Cancer Institute, Portland, OR; [5]University of Colorado Comprehensive Cancer Center, Aurora, CO; [6]University of Florida Health Cancer Center at Orlando Health, Orlando, FL; [7]Atlantic Health System Cancer Care, Morristown, NJ; [8]The Angeles Clinic and Research Institute, Los Angeles, CA; [9]Mount Sinai Comprehensive Cancer Center, Miami, FL; [10]Laura and Isaac Perlmutter Cancer Center, NYU Langone Medical Center, New York, NY; [11]Royal Marsden NHS Foundation Trust, London, United Kingdom; [12]Iovance Biotherapeutics, Inc., San Carlos, CA; [13]Melanoma Program, UPMC Hillman Cancer Center, University of Pittsburgh, Pittsburgh, PA

NCT02360579

Copies of this poster obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from ASCO® and the author of this poster

For more information, please contact kellyditrapani@iovance.com

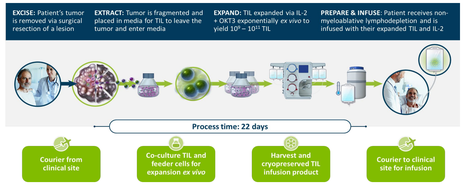
BACKGROUND

- Treatment options are limited for patients with advanced melanoma who have progressed on checkpoint inhibitors and targeted therapies
- Adoptive cell therapy (ACT) utilizing tumor-infiltrating lymphocytes (TIL) leverages and enhances the body's natural defense against cancer
- TIL has demonstrated antitumor efficacy:
  - Durable long-term responses in heavily pretreated patients[1]
- **innovaTIL-01** (NCT02360579) is an ongoing Phase 2 multicenter study:
  - Investigational agent: autologous TIL (lifileucel; LN-144)
  - Patient population: unresectable 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

[1]Rosenberg, S.A., et al. Durable Complete Responses in Heavily Pretreated Patients with Metastatic Melanoma Using T Cell Transfer Immunotherapy. *Clinical Cancer Research*, 2011. 17(13), 4550-4557.

Figure 1. Cryopreserved Autologous TIL (lifileucel)

Manufacturing Process: 22-Days



innovaTIL-01 Study Design

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)

Unresectable or metastatic melanoma treated with ≥1 systemic prior therapy including a PD-1 blocking antibody and if BRAF V600 mutation positive, a BRAF or BRAF/MEK

- **Cohort 1:** Non-cryopreserved TIL product, n=30 — *Closed to enrollment*
- **Cohort 2:** Cryopreserved TIL product, n=60 — *Closed to enrollment*
- **Cohort 4:** Cryopreserved TIL product, n=75 — *Now enrolling*

Cohort 3: TIL re-treatment n=10

Cohort 2 Endpoints:

- Primary: Efficacy defined as investigator assessed Objective Response Rate (ORR)
- Secondary: Safety and efficacy

Study Updates:

- Cohort 2 fully enrolled and closed to new enrollment
- Cohort 2 efficacy, safety data presented here (n=66, Data extract as of 8 May 2019)

Registrational Cohort 4 now enrolling:

- 75 patients
- ORR as assessed by Blinded Independent Review Committee (BIRC)

METHODS

- Data extract as of 8 May 2019 for Cohort 2
- Cohort 2 Safety & Efficacy Sets: 66 patients who underwent resection for the purpose of TIL generation and received lifileucel infusion

DISCLOSURE

- This study and poster are sponsored by Iovance Biotherapeutics, Inc.

ACKNOWLEDGMENT

- The authors would like to thank the patients and their families for participation in the study
- The authors would also like to acknowledge the support and dedication of all site team members from all the clinical trial institutions
- 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. Patient Characteristics

CHARACTERISTIC	Cohort 2, N=66, (%)
Gender, n (%)	
Male	39 (59)
Female	27 (41)
Age	
Median	55
Min, Max	20, 79
Prior therapies, n (%)	
Mean # prior therapies	3.3
Anti-CTLA-4	53 (80)
Anti-PD-1	66 (100)
BRAF/MEK	15 (23)
Baseline ECOG score, n (%)	
0	37 (56)
1	29 (44)

CHARACTERISTIC	Cohort 2, N=66, (%)
BRAF Status, n (%)	
Mutated V600	17 (26)
Wild Type	45 (68)
Unknown	3 (5)
Other	1 (2)
Baseline LDH (U/L)	
Median	244
1-2 times ULN	19 (29)
> 2 times ULN	8 (12)
Target Lesion Sum of Diameter (mm)	
Mean (SD)	106 (71)
Min, Max	11, 343
Number of Target & Non-Target Lesions (at Baseline)	
>3	51 (77)
Mean	6
Patients with Baseline Liver and/or Brain Lesions	29 (44)

- Cohort 2 has:
  - 3.3 mean prior therapies, ranging from 1-9
  - High tumor burden at baseline 106 mm sum of diameters for the target lesions
  - 44% with Liver and/or Brain lesions at baseline

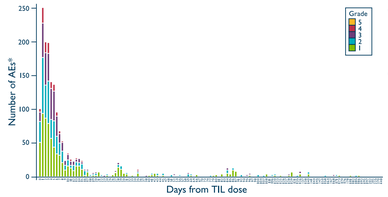
Table 2. Treatment Emergent Adverse Events (≥30%)

PREFERRED TERM	Cohort 2, N=66 Any Grade, n (%)	Grade 3/4, n (%)	Grade 5, n (%)
Number of patients reporting at least one Treatment-Emergent AE	65 (98.5)	63 (95.5)	2 (3.0)*
Thrombocytopenia	59 (89.4)	53 (80.3)	0
Chills	52 (78.8)	4 (6.1)	0
Anemia	44 (66.7)	36 (54.5)	0
Pyrexia	39 (59.1)	11 (16.7)	0
Febrile neutropenia	36 (54.5)	35 (53.0)	0
Neutropenia	36 (54.5)	25 (37.9)	0
Hypophosphatemia	29 (43.9)	22 (33.3)	0
Fatigue	27 (40.9)	1 (1.5)	0
Leukopenia	27 (40.9)	22 (33.3)	0
Hypotension	23 (34.8)	7 (10.6)	0
Tachycardia	22 (33.3)	1 (1.5)	0
Lymphopenia	21 (31.8)	19 (28.8)	0

*One death was due to intra-abdominal hemorrhage considered possibly related to TIL and one was due to acute respiratory failure assessed as not related to TIL per investigator assessment.
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.

Figure 2. Adverse Events Over Time

Distribution of onset dates of AEs starting from TIL Infusion until subsequent anti-cancer treatment or extraction date



- Frequency of AEs over time is reflective of potential benefit of one time treatment with TIL (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 patients dosed

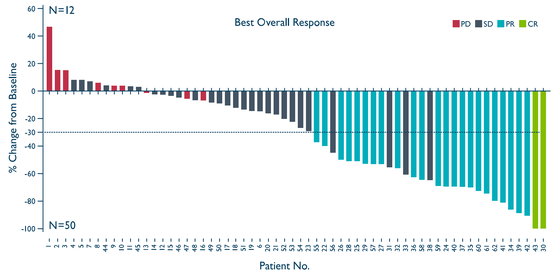
Table 3. Efficacy

RESPONSE (RECIST v1.1)	PATIENTS, N=66 n (%)
Objective Response Rate (ORR)	**25 (38%)**
Complete Response (CR)	2 (3%)
Partial Response (PR)	23 (35%)
Stable Disease (SD)	28 (42%)
Progressive Disease (PD)	9 (14%)
Non-Evaluable	4 (6%)
Disease Control Rate (DCR)	53 (80%)
Median Duration of Response (DOR)	**Not Reached**
Min, Max	1.4+, 19.8 +

ORR BY SUBGROUP	PATIENTS, N=66 n (%)
Prior Anti-CTLA-4	
Yes (n=53)	20 (38)
No (n=13)	5 (39)
BRAF Mutation Status	
Mutated (V600E or V600K), (n=17)	8 (47)
Non-Mutated (n=49)	17 (35)

- Cohort 2: Lifileucel Infusion Product and TIL Therapy Characteristics
  - Mean number of TIL cells infused: 27.3 x 10^9
  - Median number of IL-2 doses administered was 5.5

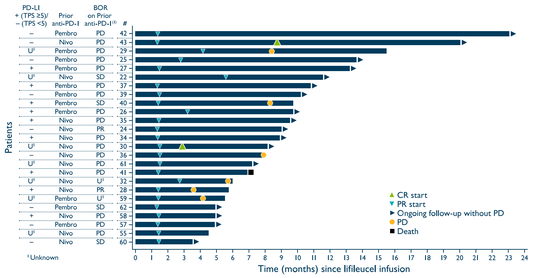
Figure 3. Efficacy: Best Overall Response



Three subjects had no post TIL disease assessment due to early death; one subject had no post-TIL disease assessment due to new cancer therapy.
For subject #30,100% change from baseline is displayed for the CR visit involved lymph nodes.

- 81% of patients had a reduction in tumor burden
- Mean Time to response 1.9 months (range 1.3-5.6)

Figure 4. Time to Response for Evaluable Patients (PR or Better)



[1]Unknown

68% of responders have ongoing response

CONCLUSIONS

- Relapsed and refractory Metastatic Melanoma presents a high unmet medical need with low survival rates and with limited durable treatment options
- In heavily pretreated metastatic melanoma patients, lifileucel TIL therapy results in:
  - 3% CR
  - 38% ORR
  - 80% DCR
- At median follow up of 8.8 months, the median DOR has not been reached
- Patients with PD-L1 negative status (TPS<5%) were among responders

Lifileucel autologous TIL has demonstrated potential efficacy for patients with metastatic melanoma and represents a viable therapeutic option warranting further investigation

Based on these data, a new Cohort 4 in innovaTIL-01 has been initiated to support lifileucel registration

© Iovance Biotherapeutics, Inc. 2019