Safety and efficacy of cryopreserved autologous tumor infiltrating lymphocyte therapy (LN-144, lifileucel) in advanced metastatic melanoma patients following progression on checkpoint inhibitors

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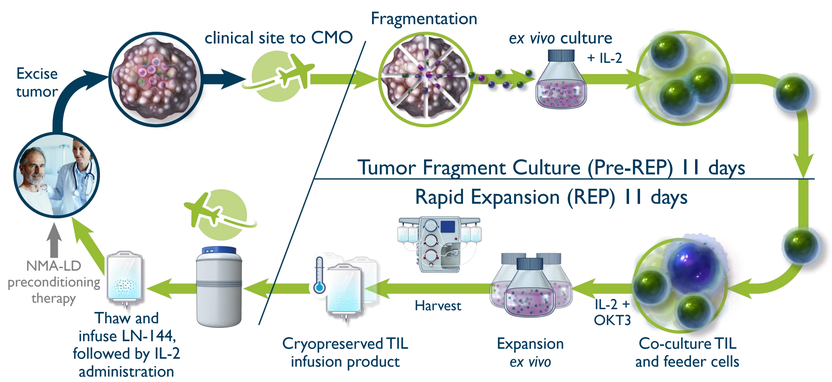
BACKGROUND

- 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]
- C-144-01 (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*, 17(13), 4550-4557.

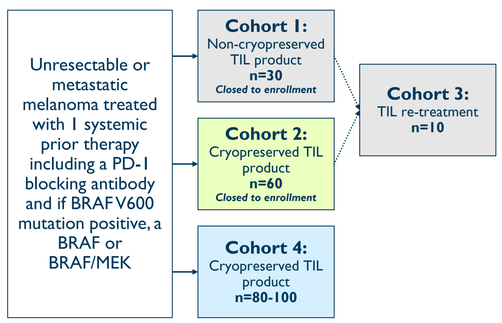
Figure 1. Cryopreserved Autologous TIL (LN-144, lifileucel) Manufacturing Process: 22-days



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)



Endpoints:
- Primary: Efficacy defined as investigator assessed ORR
- Secondary: Safety and efficacy

Study Updates:
- Cohort 2 fully enrolled and closed to new enrollment
- Cohort 2 preliminary efficacy, safety and biomarker data presented here (n=47, Data extract as of 25 Oct 2018)

Cohort 4 will initiate in early 2019:
- 80-100 patients
- BIRC ORR endpoint

METHODS

- Data extract as of 25 October 2018 for Cohort 2
- Cohort 2 Safety & Efficacy Sets: 47 patients who underwent resection for the purpose of TIL generation and received lifileucel infusion
- Biomarker data has been shown for all available data read by the date of the data cut

DISCLOSURE
- This study and poster are sponsored by Iovance Biotherapeutics, Inc
- MF, LK, DB, TT, SS, and NS are employees or consultants of Iovance Biotherapeutics, Inc. and have stock options

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- The authors would like to acknowledge Iovance team for their contributions

RESULTS

Table 1. Patient Characteristics

CHARACTERISTIC	Cohort 2, N=47, (%)
Gender, n (%)	
Male	27 (57)
Female	20 (43)
Age	
Median	56
Min, Max	30, 77
Prior therapies, n (%)	
Mean # prior therapies	3.3
Anti-CTLA-4	37 (79)
Anti-PD-1	47 (100)
BRAF/MEK	12 (26)
Target Lesion Sum of Diameter (mm)	
Mean (SD)	112 (73)
Min, Max	17, 343

CHARACTERISTIC	Cohort 2, N=47, (%)
Baseline ECOG score, n (%)	
0	27 (57)
1	20 (43)
BRAF Status, n (%)	
Mutated V600	14 (30)
Wild Type	32 (68)
Unknown	1 (2)
Baseline LDH (U/L)	
Median	246
1-2 times ULN	12 (26)
> 2 times ULN	7 (15)
Number of Target & Non-Target Lesions (at Base Line)	
>3	37 (79)
Mean	6

Cohort 2 has:
- 3.3 mean prior therapies, ranging from 1-9
- High tumor burden at baseline 112 mm sum of diameters for the target lesions

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

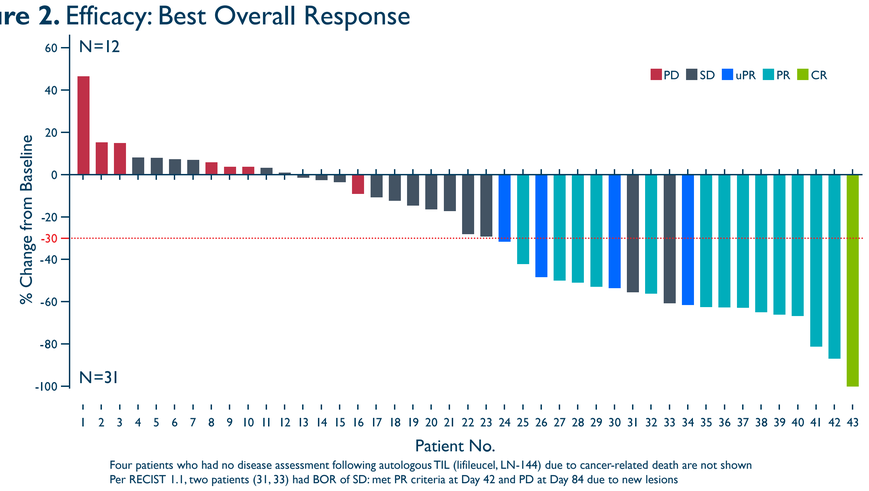
PREFERRED TERM	Cohort 2 (N=47) Any Grade, n (%)	Grade 3/4, n (%)	Grade 5, n (%)
Number of patients reporting at least one Treatment-Emergent AE	47(100)	45 (95.7)	2 (4.3)*
Thrombocytopenia	42 (89.4)	38 (80.9)	0
Chills	36 (76.6)	3 (6.4)	0
Neutropenia	29 (61.7)	25 (53.2)	0
Febrile neutropenia	28 (59.6)	25 (53.2)	0
Anemia	27 (57.4)	22 (46.8)	0
Pyrexia	25 (53.2)	7 (14.9)	0
Hypophosphatemia	23 (48.9)	17 (36.2)	0
Leukopenia	21 (44.7)	20 (42.6)	0
Fatigue	17 (36.2)	0	0
Hypotension	17 (36.2)	4 (8.5)	0
Lymphopenia	17 (36.2)	17 (36.2)	0
Tachycardia	15 (31.9)	1 (2.1)	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.

Cohort 2 (lifileucel): Infusion Product and TIL Therapy Characteristics

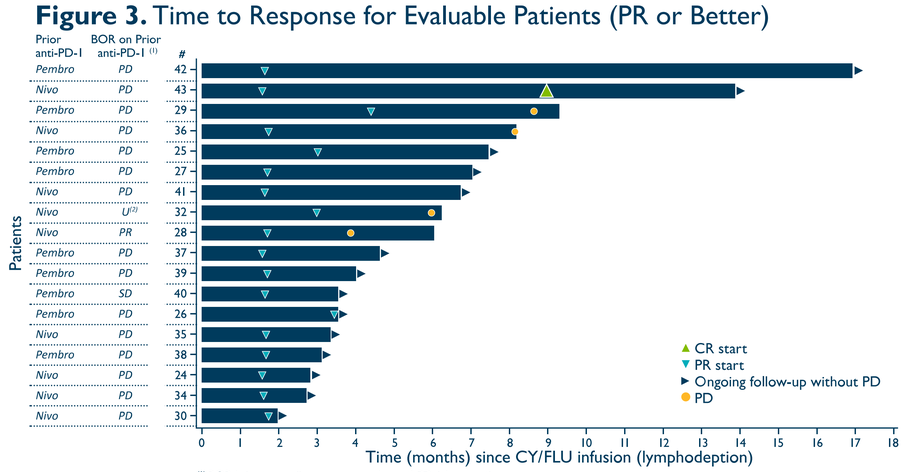
- Mean number of TIL cells infused: 26 x 10^9
- Median number of IL-2 doses administered was 6.0
- 72% of patients had a reduction in tumor burden
- Median follow up is 6.0 months
- Median DOR is 6.4 months
  - Range of DOR was from 1.3+ to 14+ months

Figure 2. Efficacy: Best Overall Response



Four patients who had no disease assessment following autologous TIL (lifileucel, LN-144) due to cancer-related death are not shown
Per RECIST 1.1, two patients (31, 33) had BOR of SD: met PR criteria at Day 42 and PD at Day 84 due to new lesions

Figure 3. Time to Response for Evaluable Patients (PR or Better)



(1) BOR is best overall response on prior anti-PD-1 immunotherapy
(2) U: unknown best overall response on prior anti-PD-1 immunotherapy

Figure 4. Percent Change from Baseline in Sum of Target Lesion Diameters over Time

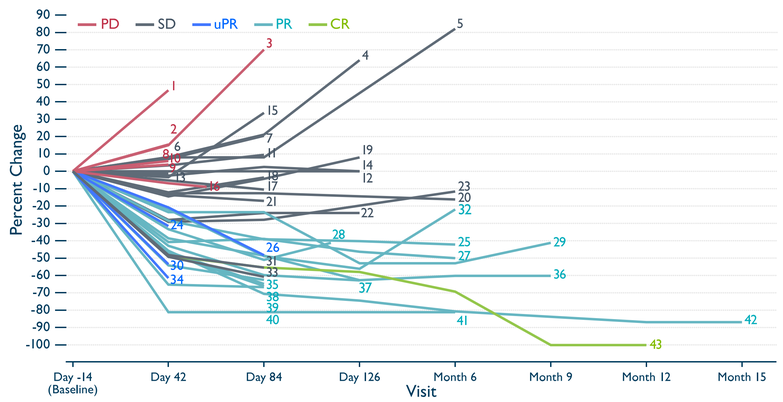
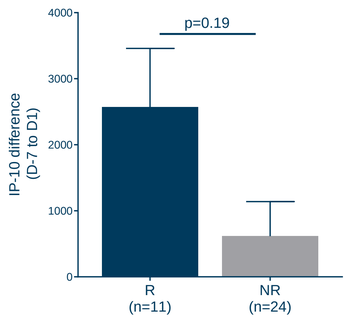


Table 3. Efficacy

RESPONSE	PATIENTS, N=47 n (%)
Objective Response Rate	**18 (38%)**
Complete Response	1 (2 %)
Partial Response (PR+ uPR[1])	17 (36%)
Stable Disease	18 (38%)
Progressive Disease	7 (15%)
Non-Evaluable*	4 (9%)
Disease Control Rate	36 (77%)

* NE due to not reaching first assessment
[1] uPRs (4) were all due to timing not having reached the second assessment

Figure 5. Biomarker of Interest: Change in IP-10 (CXCL10) Level



- Change in IP-10 levels in periphery may have a correlation with response
- Mean change in IP-10 levels from baseline to day 1 post TIL infusion was higher among responders vs nonresponders (p=0.19)

CONCLUSIONS

- In heavily pretreated metastatic melanoma patients, efficacy to date is notable:
  - ORR: 38%
  - Median DOR: 6.4 months, range 1.3+ to 14+
  - DCR: 77%
- 16/17 had no response to prior anti-PD-1
- Biomarker analyses show that an increase in IP-10 levels may correlate with anti-tumor response

Preliminary data supports lifileucel autologous TIL as an efficacious and well-tolerated therapeutic option for patients with metastatic melanoma