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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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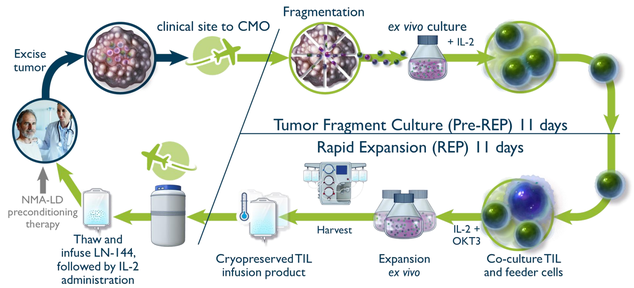
BACKGROUND

- 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.

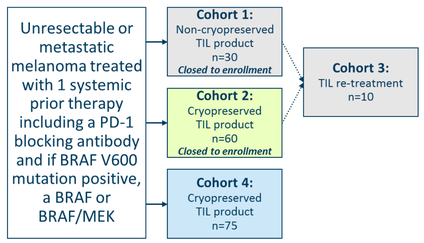
Figure 1. Cryopreserved Autologous TIL (LN-144, lifileucel) Manufacturing Process: 22-days



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)

Registrational Cohort 4 now enrolling:
- 75 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

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

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.[11]

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

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

Table 3. Efficacy

RESPONSE	PATIENTS, N=47 n (%)
Objective Response Rate	**18 (38%)**
Complete Response	1 (2 %)
Partial Response (PR+ uPR†)	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
† uPRs (4) were all due to timing not having reached the second assessment

Figure 2. Efficacy: Best Overall Response

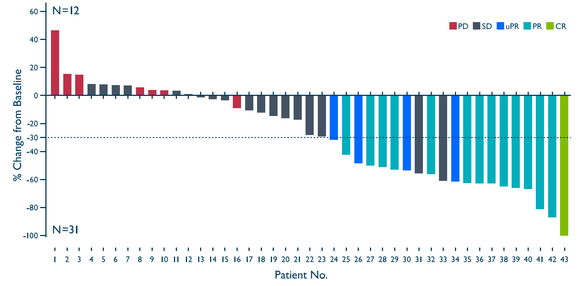


Figure 3. Time to Response for Evaluable Patients (PR or Better)

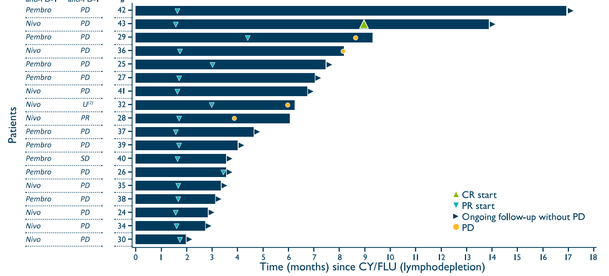
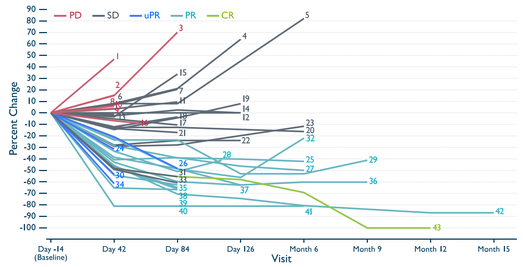


Figure 4. Percent Change from Baseline in Sum of Target Lesion Diameters over Time



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

Lifileucel autologous TIL has potential efficacy for patients with metastatic melanoma

Now enrolling for melanoma registrational Cohort 4

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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