P865 SITC ANNUAL MEETING | NOVEMBER 6-10, 2019 | NATIONAL HARBOR, MD, USA

NCT02360579 ClinicalTrials.gov identifier

Safety and efficacy of lifileucel (LN-144) tumor infiltrating lymphocyte therapy in metastatic melanoma patients after progression on multiple therapies - independent review committee data update

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BACKGROUND & METHODS

- Treatment options are limited for patients with advanced melanoma who have progressed on checkpoint inhibitors and targeted therapies
- Adoptive cell therapy 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
  - Patients receive nonmyeloablative lymphodepletion preparative regimen (cyclophosphamide 60 mg/kg x 2 days, followed by fludarabine 25 mg/m^2 x 5 days), preceding the lifileucel infusion, after which patients receive up to six doses of intravenous IL-2 (600,000 IU/kg)
- Cohort 2 Safety and Efficacy Sets: 66 patients who underwent resection for the purpose of TIL generation and received lifileucel infusion
- Response assessments were conducted by the Investigator and IRC following RECIST v1.1

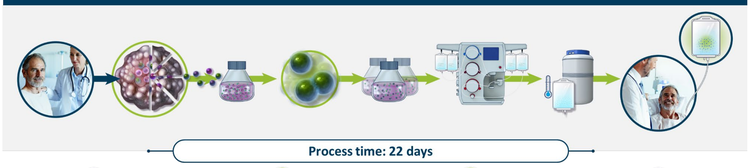
Figure 1. Cryopreserved Autologous TIL (lifileucel) Manufacturing Process: 22-Days

EXCISE: Patient's tumor is removed via surgical resection of a lesion

EXTRACT: Tumor is fragmented and placed in media for TIL to leave the tumor and enter media

EXPAND: TIL expanded via IL-2 + OKT3 exponentially *ex vivo* to yield 10^9 – 10^{11} TIL

PREPARE & INFUSE: Patient receives non-myeloablative lymphodepletion and is infused with their expanded TIL and IL-2



Process time: 22 days

Courier from clinical site

Co-culture TIL and feeder cells for expansion *ex vivo*

Harvest and cryopreserved TIL infusion product

Courier to clinical site for infusion

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)

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 3: TIL re-treatment, n=10

Cohort 4: Cryopreserved TIL product, n=75 *Enrolling*

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 fully enrolled and closed to new enrollment as of 4Q 2018
- Cohort 2 safety and both Investigator and IRC assessed efficacy presented here (n=66, Data extract as of 23 Aug 2019)
- Cohort 4 in C-144-01 is ongoing in support of lifileucel registration with the primary endpoint of ORR by IRC

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)
Progressive Disease (PD) for at least 1 prior therapy	
Anti-CTLA-4	41 (77)
Anti-PD-1	65 (99)
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)	
Mean	464
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)

- 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 3. ORR Concordance Between IRC and Investigator

RESPONSE (RECIST v1.1)	**Cohort 2**, N=66, n (%) ORR BY IRC	ORR BY INVESTIGATOR
Objective Response Rate (ORR)	**23 (34.8%)**	**24 (36.4%)**
Complete Response (CR)	2 (3.0%)	2 (3.0%)
Partial Response (PR)	21 (31.8%)	22 (33.3%)
Stable Disease (SD)	25 (37.9%)	29 (43.9%)
Progressive Disease (PD)	14 (21.2%)	9 (13.6%)
Non-Evaluable	4 (6.1%)	4 (6.1%)
Disease Control Rate (DCR)	48 (72.7%)	53 (80.3%)
Median Duration of Response (DOR)	**Not Reached**	**Not Reached**
Min, Max	1.6+, 21.2 +	2.2, 21.2+

CONCORDANCE RATE	KAPPA COEFFICIENT (95% CI)	P-VALUE
89.4%	0.769 (0.607, 0.930)	<0.0001

- Median DOR as assessed by investigator or IRC has been not reached at the time of this data cut (11.3 months, 23 Aug 2019)

Further, median DOR by investigator has still not been reached as of 24 Oct 2019 at median 12.8 months study follow-up

- Overall concordance rate of investigator and IRC read of response was 89.4%
- The concordance compares favorably with literature reports in a metastatic disease[2]
- High concordance of investigator and IRC assessments is encouraging in this highly metastatic patient population

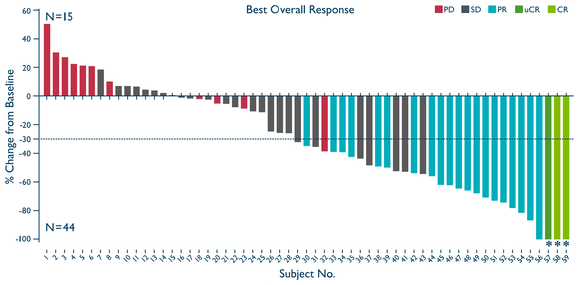
Table 2. Treatment Emergent Adverse Events (≥30%)

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	58 (87.9)	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
Leukopenia	27 (40.9)	22 (33.3)	0
Fatigue	26 (39.4)	1 (1.5)	0
Hypotension	23 (34.8)	7 (10.6)	0
Tachycardia	23 (34.8)	1 (1.5)	0
Lymphopenia	22 (33.3)	20 (30.3)	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.

Figure 4. Efficacy – Best Overall Response

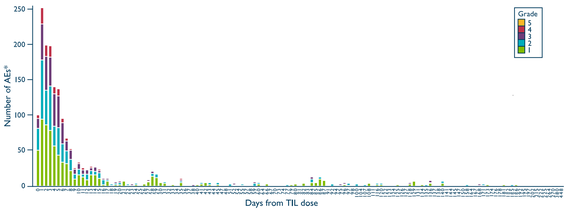


Three patients had no post-TIL assessments due to early death. One patient had no post-TIL assessment due to start of new anti-cancer therapy prior to day 42. Three additional patients did not have acceptable target lesions for IRC measurement.

*-100% change from baseline is displayed for the CR visit involved lymph nodes.

Figure 3. Adverse Events Over Time

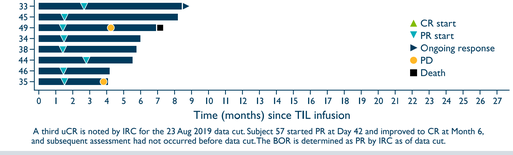
Distribution of onset dates of AEs starting from TIL Infusion until subsequent anti-cancer treatment or extraction date



- 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 patients dosed.

Figure 5. Time to Response for Evaluable Patients with PR or Better



A third uCR is noted by IRC for the 23 Aug 2019 data cut. Subject 57 started PR at Day 42 and improved to CR at Month 6, and subsequent assessment had not occurred before data cut. The BOR is determined as PR by IRC as of data cut.

CONCLUSIONS

- Relapsed and refractory Metastatic Melanoma presents a high unmet medical need with low survival rates and with limited durable treatment options
- Lifileucel treatment resulted in a 36.4% investigator assessed ORR in heavily pretreated metastatic melanoma patients with high baseline disease burden
- At a median study follow up of 11.3 months, median DOR as determined by IRC or investigator has not been reached. 61% of patients remain on study and in response.
- Furthermore, at a median follow up of 12.8 months, median DOR has not been reached as assessed by investigator
- The high concordance of 89.4% between investigator and IRC confirms the assessment of lifileucel efficacy in metastatic melanoma

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

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

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DISCLOSURE

•This study and poster are sponsored by Iovance Biotherapeutics, Inc

•WS, KDT, HQ, MM, RW, TT, MF are employees or consultants of Iovance Biotherapeutics, Inc. and have stock options

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