Safety and efficacy of lifileucel (LN-144), an autologous tumor-infiltrating lymphocyte cell therapy, in combination with pembrolizumab for immune checkpoint inhibitor–naïve patients with advanced melanoma

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Introduction

Background

- Lifileucel (LN-144), a tumor-infiltrating lymphocyte (TIL) cell therapy, has demonstrated efficacy and durability of response in patients with melanoma whose disease has failed anti–PD-1/PD-L1 therapy[1]
- The combination of TIL (LN-145) + pembrolizumab in immune checkpoint inhibitor (ICI)-naïve patients has demonstrated encouraging efficacy with acceptable safety in head and neck squamous cell carcinoma (HNSCC)[2]
- To improve early-line treatment options, we explored a combination of lifileucel + pembrolizumab in patients with ICI-naïve advanced melanoma

Methods

Study Design

- IOV-COM-202 is a prospective, open-label, multicohort, nonrandomized, multicenter Phase 2 study evaluating TIL cell therapy in multiple settings and indications
- We report on Cohort 1A, which is enrolling patients with ICI-naïve advanced melanoma (unresectable or metastatic) for treatment with a combination of lifileucel + pembrolizumab

Cohort 1A Patients

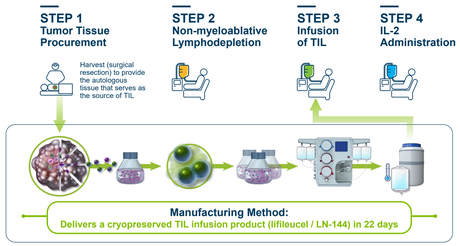
- Key eligibility criteria include age ≥18 years, ICI-naïve, ≤3 lines of prior systemic therapy, ECOG PS 0–1, ≥1 resectable lesion (~1.5 cm in diameter) for lifileucel manufacturing, and ≥1 measurable lesion post-resection for response assessment

Primary Endpoints

- Efficacy, defined as investigator-assessed objective response rate (ORR) per RECIST 1.1
- Safety, as measured by incidence of Grade ≥3 treatment-emergent adverse events (TEAEs)

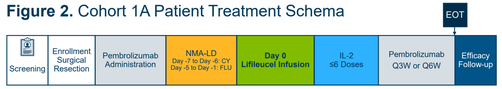
Data cutoff: 29 April 2021

Figure 1. Patient Journey and Central Gen 2 GMP Manufacturing



- Lifileucel is generated at centralized GMP facilities in a 22-day process
- Non-myeloablative lymphodepletion (NMA-LD) using cyclophosphamide and fludarabine is administered preceding a single lifileucel infusion, followed by ≤6 doses of IL-2 (600,000 IU/kg); first dose of pembrolizumab is administered after tumor harvest and continues every 3 or 6 weeks after lifileucel

Figure 2. Cohort 1A Patient Treatment Schema



Results

Table 1. Baseline Patient Characteristics

Characteristic	Cohort 1A (N=7)
Gender, n (%)	
Female	1 (14.3)
Male	6 (85.7)
Age, years	
Median	52.0
Min, max	34, 59
Number of Systemic Prior Therapies, n (%)	
0	5 (71.4)
1	2 (28.6)
Systemic Prior Therapy Type, n (%)	
Chemotherapy	1 (14.3)
Targeted therapy (BRAFi/MEKi)	1 (14.3)
Immunotherapy	0
Other*	1 (14.3)
Baseline ECOG Performance Status, n (%)	
0	5 (71.4)
1	2 (28.6)
Stage, n (%)	
IIIC	1 (14.3)
IV (metastatic)	6 (85.7)

Characteristic	Cohort 1A (N=7)
BRAF Status, n (%)	
Mutated V600E or V600K	1 (14.3)
Wild type	3 (42.9)
Unknown	1 (14.3)
Other†	2 (28.6)
Tumor PD-L1 Expression, n (%)	
PD-L1 positive (TPS ≥5%)	4 (57.1)
PD-L1 negative (TPS <5%)	2 (28.6)
Missing	1 (14.3)
Baseline LDH, n (%)	
<ULN	4 (57.1)
1–2 × ULN	2 (28.6)
>2 × ULN	1 (14.3)
Target Lesions Sum of Diameters (mm)	
Mean	111.4
Min, max	32, 355
Baseline Number of Target and Non-Target Lesions	
>3, n (%)	6 (85.7)
Mean (SD)	4.9 (1.4)
Liver and/or brain lesions, n (%)	5 (71.4)

*1 patient received prednisone as part of chemotherapy regimen.
†2 patients with BRAF mutations other than V600E or V600K: 1 with T599_V600insT mutation and 1 with L584F mutation.

At baseline:
- Patients had high tumor burden: 111.4 mm mean target lesion sum of diameters
- 42.9% of patients had elevated LDH
- 85.7% of patients had >3 lesions

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

	Cohort 1A (N=7)		
Preferred Term, n (%)	Any Grade	Grade 3/4	Grade 5
Number of patients reporting ≥1 TEAE	7 (100)	7 (100)	0
Thrombocytopenia	7 (100)	6 (85.7)	0
Chills	6 (85.7)	0	0
Nausea	6 (85.7)	0	0
Pyrexia	6 (85.7)	2 (28.6)	0
Vomiting	6 (85.7)	0	0
Fatigue	5 (71.4)	1 (14.3)	0
Febrile neutropenia	5 (71.4)	5 (71.4)	0
Hypertension	4 (57.1)	2 (28.6)	0
Neutropenia	4 (57.1)	4 (57.1)	0
Alopecia	3 (42.9)	0	0
Cough	3 (42.9)	0	0
Decreased appetite	3 (42.9)	0	0
Peripheral edema	3 (42.9)	1 (14.3)	0

*TEAEs refer to AEs that occur from the first dose of pembrolizumab or TIL infusion (whichever is earlier) and up to 30 days after last dose of pembrolizumab or TIL infusion (whichever is later) or up to the start of a new anti-cancer therapy. Only clinically significant laboratory abnormalities per investigators were reported as TEAEs. Patients with multiple events for a given preferred term are counted only once using the maximum grade under each preferred term.

- The TEAE profile was consistent with the underlying disease and known AE profiles of pembrolizumab, NMA-LD, and IL-2
- No unexpected toxicity was observed with pembrolizumab after TIL
- Median number of IL-2 doses administered was 6

Figure 3. Treatment-Emergent Adverse Events Over Time

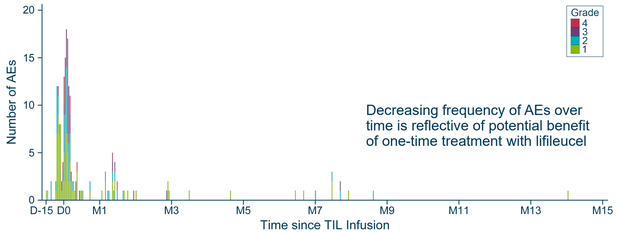


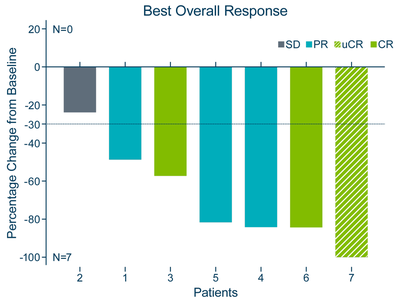
Table 3. Efficacy

Response (RECIST 1.1), n (%)	Cohort 1A (N=7)
Objective Response Rate	**6 (85.7)**
Complete Response*	3 (42.9)
Partial Response	3 (42.9)
Stable Disease	1 (14.3)
Progressive Disease	0
Non-evaluable	0
Disease Control Rate	7 (100)

*Includes 1 unconfirmed CR; patient had not yet reached confirmatory CR assessment at the time of the data-cut, but had previously achieved PR.

- 85.7% of patients responded to combination treatment with lifileucel + pembrolizumab
- Median number of TIL infused was 27.3 × 10^9
- Median follow-up was 8.2 months

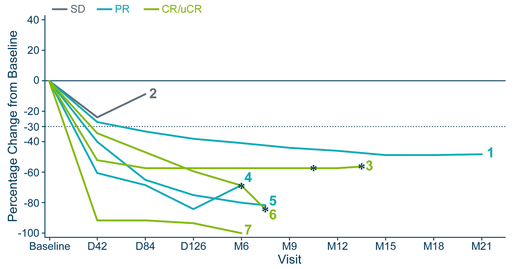
Figure 4. Best Percentage Change from Baseline in Target Lesion Sum of Diameters for All Evaluable Patients



- Median number of pembrolizumab doses was 10

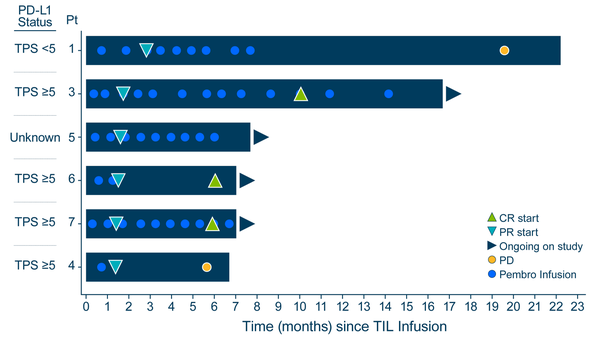
For patients 3 and 6, the overall response of CR was based on investigator assessment of a negative FDG-PET scan.

Figure 5. Percentage Change from Baseline in Target Lesion Sum of Diameters Over Time for All Evaluable Patients



For patients 3 and 6, * is time of negative FDG-PET scan.

Figure 6. Time to First Response, Duration of Response, and Time on Efficacy Assessment for Confirmed Responders Who Achieved PR or Better



Conclusions

- Early data suggest the response rate for lifileucel + pembrolizumab may be additive in patients with ICI-naïve advanced melanoma
  - ORR was 85.7%
  - CR/uCR was 42.9%
  - Responses deepened over time
- Patients, although anti–PD-1 / anti–PD-L1 naïve, had high disease burden at baseline
- In patients with ICI-naïve advanced melanoma, lifileucel can be safely combined with pembrolizumab

These encouraging data confirm the potential feasibility and activity of the combination of lifileucel + pembrolizumab in early-line treatment of patients with advanced melanoma

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Abbreviations
BRAFi/MEKi, BRAF inhibitor ± MEK inhibitor; TPS, tumor proportion score; CR, complete response; CY, cyclophosphamide; ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end of treatment; FDG-PET, fluorodeoxyglucose-positron emission tomography; FLU, fludarabine; GMP, Good Manufacturing Practice; ICI, immune checkpoint inhibitor; IL-2, interleukin-2; LDH, lactate dehydrogenase; NMA-LD, non-myeloablative lymphodepletion; ORR, objective response rate; PD, progressive disease; PD-L1, programmed death ligand 1; pembro, pembrolizumab; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; TEAEs, treatment-emergent adverse events; TIL, tumor-infiltrating lymphocytes; uCR, unconfirmed complete response.

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