Safety and efficacy of tumor infiltrating lymphocytes (TIL; LN-145) in combination with pembrolizumab for advanced, recurrent or metastatic HNSCC

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Introduction

Background

- Single agent immune checkpoint inhibitors (ICIs) are an approved first or second-line therapy in head and neck squamous cell carcinoma (HNSCC), however their efficacy is limited.[1-3]
- Adoptive cell therapy utilizing tumor infiltrating lymphocytes (TIL; LN-145) leverages and enhances the body's natural defense against cancer.
- Iovance autologous TIL immunotherapy cell product (lifileucel/LN-144, LN-145; same manufacturing) has demonstrated efficacy in metastatic melanoma and cervical carcinoma.[4,5]
- To offer TIL in PD-1 blockade naïve patients, a combination of pembrolizumab and LN-145 was explored.
- IOV-COM-202 (NCT03645928) is an ongoing Phase 2 multicenter, multi-cohort, open-label study evaluating LN-145 in multiple settings and indications, and here we report on Cohort 2A:
  - Investigational agent: autologous TIL (LN-145)
  - Patient population: ICI-naïve HNSCC
  - Study regimen: LN-145 and pembrolizumab
  - Manufacturing method: central manufacturing of cryopreserved TIL, 22-day duration

Figure 1: LN-145 Production Method Uses Central GMP Manufacturing in a 22-day Process Yielding a Cryopreserved TIL Product

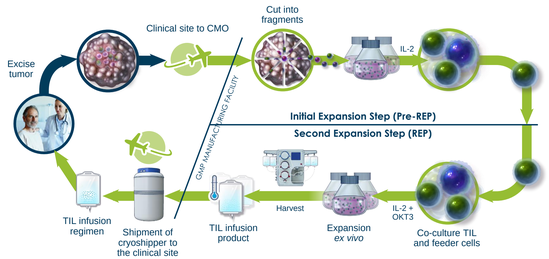
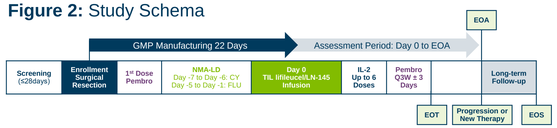


Figure 2: Study Schema



Endpoints

- Objective Response Rate (ORR) per Response Evaluation Criteria In Solid Tumors (RECIST) v1.1 as assessed by Investigator.
- Safety and additional assessments of efficacy.

Methods

- Data extract as of 16 Oct 2020 for Cohort 2A.
- Cohort 2A Safety & Efficacy Sets: 9 patients who underwent resection for the purpose of TIL generation and received LN-145 infusion as well as one dose of pembrolizumab, and could have had at least 1 efficacy evaluation as of the data extraction date.

Results

Table 1. Patient Characteristics

CHARACTERISTIC	Cohort 2A, N=9, (%)
Gender, n (%)	
Male	7 (77.8)
Female	2 (22.2)
Age	
Median	60
Min, Max	24, 62
Prior therapies, n (%)	
Median adjudicated prior therapies (Min, Max)*	1.0 (0, 2)
All Chemotherapy	8 (88.9)
Radiotherapy	5 (55.6)
Baseline ECOG score, n (%)	
0	4 (44.4)
1	5 (55.6)

CHARACTERISTIC	Cohort 2A, N=9, (%)
HPV Status	
HPV positive	4 (44.4)
HPV negative	3 (33.3)
HPV – not done	2 (22.2)
PD-L1 status as CPS#, n (%)	
≥ 20	5 (55.6)
< 20	2 (22.2)
Missing	2 (22.2)
Target Lesion Sum of Diameters (mm)	
Mean (SD)	67.0 (35.0)
Min, Max	21, 134
Number of Target & Non-Target Lesions (at Baseline)	
>3	5 (55.6)
Mean (Min, Max)	4.4 (1, 8)
Baseline LDH (U/L)	
Median	187
Normal	7 (77.8)
1-2 times ULN	2 (22.2)

*A line of therapy is any systemic therapy given for metastatic disease or completed less than 12 months prior to the diagnosis of metastatic disease. Radiotherapy is not considered a line of therapy.
Combined positive score (CPS)

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

	Cohort 2A (N=9)		
PREFERRED TERM	Any Grade, n (%)	Grade 3/4, n (%)	Grade 5, n (%)
Number of patients reporting at least one TEAE	9 (100)	9 (100)	2 (22.2)*
Chills	7 (77.8)	0 (0)	0 (0)
Anemia	6 (66.7)	5 (55.6)	0 (0)
Hypotension	6 (66.7)	2 (22.2)	0 (0)
Nausea	6 (66.7)	1 (11.1)	0 (0)
Pyrexia	6 (66.7)	2 (22.2)	0 (0)
Thrombocytopenia	5 (55.6)	3 (33.3)	0 (0)
Diarrhea	4 (44.4)	0 (0)	0 (0)
Fatigue	4 (44.4)	0 (0)	0 (0)
Febrile neutropenia	4 (44.4)	4 (44.4)	0 (0)
Lymphopenia	4 (44.4)	3 (33.3)	0 (0)
Neutropenia	4 (44.4)	4 (44.4)	0 (0)
Tachycardia	4 (44.4)	0 (0)	0 (0)
Anxiety	3 (33.3)	0 (0)	0 (0)
Cough	3 (33.3)	0 (0)	0 (0)
Hypertension	3 (33.3)	3 (33.3)	0 (0)
Hypophosphataemia	3 (33.3)	1 (11.1)	0 (0)
Insomnia	3 (33.3)	0 (0)	0 (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
* Grade 5 events (septic shock, day 5, and respiratory failure, day 212) were not related to TIL therapy

Figure 3. Adverse Events Over Time

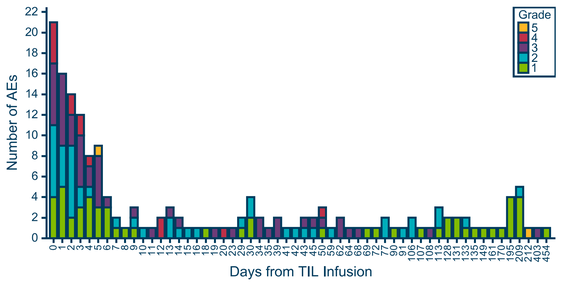


Table 3. Efficacy

RESPONSE (RECIST v1.1)	PATIENTS, N=9 n (%)
Objective Response Rate (ORR)	**4 (44.4)**
Complete Response (CR)	1 (11.1)
Partial Response (PR)	3 (33.3)
Stable Disease (SD)	4 (44.4)
Progressive Disease (PD)	0 (0)
Non-Evaluable	1 (11.1)
Disease Control Rate (DCR)	8 (88.9)
Median Duration of Response (DOR)	**Not Reached**
Min, Max	1.0+, 10.9+

Median study follow up: 8.6 month

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

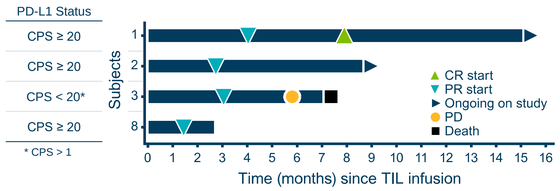
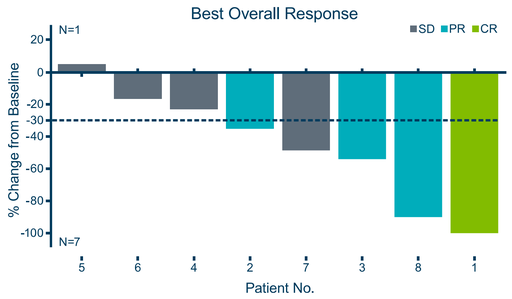
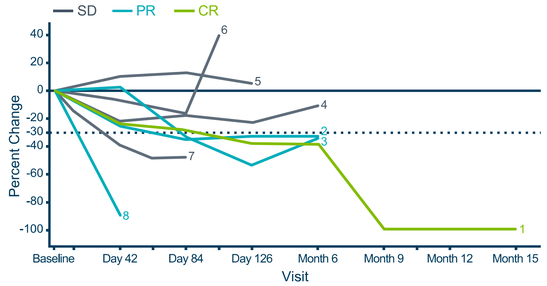


Figure 5. Percent Change from Baseline in Sum of Target Lesion Diameters over Time for all Evaluable Patients



- 87.5% of evaluable patients had a reduction in tumor burden
- Mean number of TIL cells infused: 27.1 x 10^9
- Median number of IL-2 doses administered was 4 (3, 6)
- Median number of pembrolizumab doses was 7 (1, 20)

Figure 6. Percent Change from Baseline in Sum of Target Lesion Diameters over Time



Conclusions

- Metastatic HNSCC presents a high unmet medical need with low survival rates and with limited durable treatment options.
- The Treatment Emergent Adverse Event profile of the combination therapy was consistent with the underlying advanced disease and the known AE profiles of pembrolizumab, lymphodepletion and IL-2 regimens.
- Efficacy for 9 HNSCC patients treated with LN-145 therapy + pembrolizumab:
  - 11.1 % CR
  - 44.4 % ORR
  - 88.9 % DCR
- At median follow up of 8.6 months, the median DOR has not been reached.
- Enrollment in IOV-COM-202 is ongoing (NCT03645928)

LN-145 can be safely combined with pembrolizumab in patients with metastatic HNSCC.

LN-145 plus pembrolizumab shows early signs of efficacy and represents a viable therapeutic option warranting further investigation.

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Disclosure
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