458 FIRST PHASE 2 RESULTS OF AUTOLOGOUS TUMOR-INFILTRATING LYMPHOCYTE (TIL; LN-145) MONOTHERAPY IN PATIENTS WITH ADVANCED, IMMUNE CHECKPOINT INHIBITOR-TREATED, NON-SMALL CELL LUNG CANCER (NSCLC)

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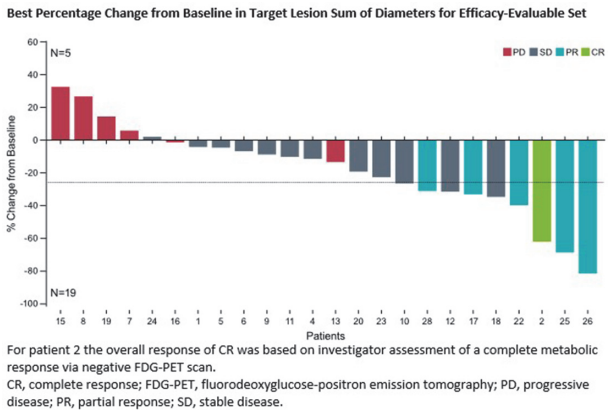
Background A majority of patients with advanced NSCLC develop disease progression with first-line immune-checkpoint inhibitors (ICI) ± chemotherapy. In the setting of ICI resistance, effective strategies to provide deep and durable responses are urgently needed. Lifileucel (LN-144) and LN-145 are centrally manufactured (cryopreserved drug-product, 22-day manufacturing process) autologous TIL products that have demonstrated activity in advanced melanoma, cervical cancer, and head and neck carcinoma.[1–4] Here, we report the first safety and efficacy data for LN-145 as monotherapy in patients with advanced NSCLC.

Methods IOV-COM-202 (NCT03645928) is a phase 2 multicenter, multicohort, open-label study evaluating autologous TIL cell therapy in patients with solid tumors. We report data from Cohort 3B, investigating LN-145 monotherapy in patients with advanced or metastatic NSCLC. Eligibility required 1–3 prior lines of systemic therapy, including either ICI or oncogene-directed therapy. Treatment included nonmyeloablative lymphodepletion, TIL infusion, and ≤6 interleukin-2 doses. Primary endpoints were safety (incidence of Grade ≥3 treatment-emergent adverse events [TEAEs]) and objective response rate (ORR, investigator-assessed using RECIST v1.1). Exploratory biomarker analyses, including T-cell receptor (TCR) repertoire, were performed.

Results As of 24June2021, 28 patients received LN-145 (full-analysis set [FAS]; table 1) and 24 were efficacy-evaluable; all had received prior ICI. TIL were most commonly harvested from lung metastases (57.1%). Safety was consistent with the underlying disease and known TEAE profiles of nonmyeloablative lymphodepletion and interleukin-2. Grade ≥3 TEAEs in ≥30% of patients were thrombocytopenia and anemia. The ORR in the FAS and efficacy-evaluable set was 21.4% (6/28) and 25.0% (6/24; figure 1), respectively. Median duration of response was not reached and 83% (5/6) of responses were ongoing at last follow-up (median study follow-up, 8.2 months). One patient had a complete metabolic response, ongoing at 20.7 months; 2 responses occurred in patients who were PD-L1–negative. All responders received ≥2 prior lines of systemic therapy. Twenty-six patients had TIL available from the final drug-product for TCR repertoire analysis; mean (min-max) number of unique TCR clones was 13,142 (3093–35,734) and Shannon Entropy index was 7.34 (3.7–12). Updated data will be presented.



For patient 2 the overall response of CR was based on investigator assessment of a complete metabolic response via negative FDG-PET scan.
CR, complete response; FDG-PET, fluorodeoxyglucose-positron emission tomography; PD, progressive disease; PR, partial response; SD, stable disease.

Abstract 458 Figure 1 Best percentage change from baseline in target lesion sum of diameters for efficacy-evaluable set

Abstract 458 Table 1 Baseline patient demographic and clinical characteristics; efficacy parameters

Baseline Patient Demographic and Clinical Characteristics; Efficacy Parameters

	COM-202 Cohort 3B (N=28)
Sex, n (%)	
Male	14 (50.0)
Female	14 (50.0)
Median (min, max) age, y	61.0 (40, 74)
Histologic cell type, n (%)	
Nonsquamous cell carcinoma	23 (82.1)
Adenocarcinoma	22 (78.6)
Large-cell carcinoma	1 (3.6)
Squamous cell carcinoma	5 (17.9)
Tumor PD-L1 expression, n (%)*	
TPS <1%	4 (14.3)
TPS ≥1%	18 (64.3)
Median (min, max) number of target and non-target lesions	4.5 (2, 11)
Target lesion sum of diameters, mm	
Median	79.0
Min, max	(22, 179)
Median (min, max) number of prior systemic therapies	2.0 (1, 5)
Prior systemic therapies, n (%)	
Anti–PD-1 and/or anti–PD-L1	28 (100)
Chemotherapy	27 (96.4)
Other monoclonal antibody	9 (32.1)
Anti–CTLA-4	6 (21.4)
EGFR inhibitor	1 (3.6)
Median (min, max) study follow-up, mo	8.2 (0.1+, 22.1)
Efficacy, n/N (%)	
ORR (FAS)	6/28 (21.4)
ORR (efficacy-evaluable set)	6/24 (25.0)
CR	1/28 (3.6)
PR	5/28 (17.9)
SD	12/28 (42.9)
DCR (FAS)	18/28 (64.3)
DCR (efficacy-evaluable set)	18/24 (75.0)
NE†	4/28 (14.3)
Median (min, max) DOR, mo	NR (1.2+, 20.7+)

*Per central laboratory; tumor PD-L1 expression data were missing for 6 patients.
†Excluded from efficacy-evaluable set due to death prior to first assessment.
CR, complete response; CTLA-4, cytotoxic T-lymphocyte–associated protein 4; DCR, disease control rate; DOR, duration of response; EGFR, epidermal growth factor receptor; FAS, full-analysis set; NR, not reached; ORR, objective response rate; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; PR, partial response; SD, stable disease; TPS, tumor proportion score.

Conclusions LN-145 was successfully manufactured and one-time treatment produced an expected safety profile and durable responses in heavily pretreated patients with NSCLC, regardless of PD-L1 expression. The activity of LN-145 monotherapy is encouraging and warrants further investigation of LN-145 as a single-agent and in combination in patients with NSCLC in ongoing studies IOV-LUN-202 (NCT04614103) and IOV-COM-202 Cohorts 3A and 3C (3B closed to enrollment).

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Ethics Approval The study was approved by Advarra Institutional Review Board, approval number Pro00035064 and all study participants provided written consent via signature of the IRB-approved Informed Consent form.

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