PHASE 2 EFFICACY AND SAFETY OF AUTOLOGOUS TUMOR-INFILTRATING LYMPHOCYTE (TIL) CELL THERAPY IN COMBINATION WITH PEMBROLIZUMAB IN IMMUNE CHECKPOINT INHIBITOR-NAÏVE PATIENTS WITH ADVANCED CANCERS

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Background Immune checkpoint inhibitors (ICI) are standard-of-care in the treatment of several types of cancer; however, an unmet medical need exists for early-line combination therapies that are able to provide higher response rates, more durable responses, and manageable long-term safety. Lifileucel (LN-144) and LN-145, adoptive cell therapies using tumor-infiltrating lymphocytes (TIL), have demonstrated encouraging efficacy with acceptable safety in patients with advanced cancer that has failed ICI.¹⁻² To improve efficacy and safety of early-line treatment options, we explored a combination of TIL and pembrolizumab in patients with ICI-naïve melanoma, head and neck squamous cell carcinoma (HNSCC), and cervical cancer.

Methods IOV-COM-202 (NCT03645928) and C-145-04 (NCT03108495) are ongoing Phase 2 multicenter, multicohort, prospective, open-label studies evaluating TIL cell therapy in ICI-naïve patients with solid tumors. We report efficacy and safety from IOV-COM-202 (Cohort 1A: lifileucel and pembrolizumab in patients with unresectable or metastatic melanoma; Cohort 2A: LN-145 and pembrolizumab in patients with advanced, recurrent, or metastatic HNSCC) and C-145-04 (Cohort 3: LN-145 and pembrolizumab in patients with stage 4b, persistent or recurrent cervical cancer who have not received prior systemic therapy). Eligibility across cohorts included ECOG PS ≤1, ≥1 resectable lesion (diameter ≥1.5 cm post-resection) for TIL manufacturing, and ≥1 measurable lesion for response assessment (by investigator per RECIST v1.1). Lifileucel and LN-145 are cryopreserved TIL infusion products generated at central GMP facilities in a 22-day process. Treatment included tumor resection for TIL manufacturing, followed by 1 dose of pembrolizumab, nonmyeloablative lymphodepletion (cyclophosphamide and fludarabine), TIL infusion, ≤6 interleukin-2 doses (600,000 IU/kg IV), and continued pembrolizumab for ≤24 months.

Results As of 09July2021, 32 patients received TIL and pembrolizumab (full-analysis set [FAS]; table 1). Across all cohorts, the objective response rate (ORR) in the FAS was 56.3% (Cohort 1A [melanoma], 87.5%; Cohort 2A [HNSCC], 42.9%; Cohort 3 [cervical], 50.0%; figure 1). Among confirmed responders (n=17), 10 responses (58.8%) were ongoing at data cutoff, with a median study follow-up of 9.7 months. The treatment-emergent adverse-event (TEAE) profile was consistent with the underlying diseases and known profiles of pembrolizumab, nonmyeloablative lymphodepletion, and interleukin-2. The most common (≥30%) Grade ≥3 TEAEs were thrombocytopenia (53.1%), anemia (50.0%), neutropenia (46.9%), and febrile neutropenia (43.8%).

Abstract 492 Table 1 Baseline demographic and clinical characteristics and efficacy

Baseline Demographic and Clinical Characteristics and Efficacy			
	COM-202 Cohort 1A Melanoma (N=8)	COM-202 Cohort 2A HNSCC (N=14)	C-145-04 Cohort 3 Cervical (N=10)
Sex, n (%)			
Male	7 (87.5)	12 (85.7)	0
Female	1 (12.5)	2 (14.3)	10 (100)
Median (min, max) age, y	52.0 (34, 59)	59.5 (24, 66)	52.0 (37, 73)
Tumor PD-L1 expression, n (%)			
TPS <5%	2 (25.0)	CPS <20% 2 (14.3)	CPS <1% 1 (10.0)
TPS ≥5%	4 (50.0)	CPS ≥20% 9 (64.3)	CPS ≥1% 7 (70.0)
Missing	2 (25.0)	Missing 3 (21.4)	Missing 2 (20.0)
Median (min, max) number of target and non-target lesions	4.5 (3, 7)	4.0 (1, 8)	7.0 (2, 10)
Target lesion sum of diameters, mm			
Mean	113.9	64.3	76.9
Min, max	(32, 355)	(21, 134)	(17, 143)
Median (min, max) number of pembrolizumab doses	7.0 (2, 15)	6.5 (1, 26)	5.0 (2, 12)
Median study follow-up, mo*	9.8	9.8	8.7
Efficacy, n/N (%)			
ORR (FAS)	7/8 (87.5)	6/14 (42.9)*	5/10 (50.0)
ORR (efficacy-evaluable set)	7/8 (87.5)	6/13 (46.2)	5/10 (50.0)
CR	3/8 (37.5)	1/14 (7.1)	1/10 (10.0)
uCR†	0	1/14 (7.1)	0
PR	3/8 (37.5)	4/14 (28.6)	4/10 (40.0)
uPR‡	1/8 (12.5)	0	0
SD	1/8 (12.5)	7/14 (50.0)	4/10 (40.0)
DCR	8/8 (100)	13/14 (92.9)	9/10 (90.0)
NE*	0	1/14 (7.1)	0

*Based on overall survival data using the reverse Kaplan-Meier method.

†ORR in SITC 2020 dataset (16October2020 data cutoff; n=9, ORR=44.4%)[3].

‡At the time of the datacut, patient had not yet had confirmatory assessment after initial CR, but was a confirmed PR.

§At the time of the datacut, patient had a first PR assessment, but had not yet reached the confirmatory assessment.

*Excluded from efficacy-evaluable set due to death prior to first assessment.

CPS, combined positive score; CR, complete response; DCR, disease control rate; FAS, full-analysis set; HNSCC, head and neck squamous cell carcinoma; NE, not evaluable; ORR, objective response rate; PD-L1, programmed death-ligand 1; PR, partial response; SD, stable disease; TPS, tumor proportion score; uCR, unconfirmed complete response; uPR, unconfirmed partial response.

Best Percentage Change from Baseline in Target Lesion Sum of Diameters for Efficacy-Evaluable Set*

*One patient in COM-202 Cohort 2A who did not have post-dose tumor response assessment was excluded.

†Patient 1A-08 had a first PR assessment, but had not reached the confirmatory assessment at the time of the datacut.

‡At the time of the datacut, patient 2A-11 had not yet had confirmatory assessment after initial CR.

§For patient C3-04, -100% change from baseline includes lymph node lesions that resolved to <10 mm. CR, complete response; HNSCC, head and neck squamous cell carcinoma; PD, progressive disease; PR, partial response; SD, stable disease; uCR, unconfirmed complete response; uPR, unconfirmed partial response.

Abstract 492 Figure 1 Best percentage change from baseline in target lesion sum of diameters for efficacy-evaluable set*

Conclusions The observed efficacy, including ORR and CR rate, and acceptable safety profile are encouraging and warrant continued investigation of the combination of TIL and pembrolizumab in early-line treatment of patients with advanced cancer. Enrollment is ongoing; updated data will be presented.

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Trial Registration NCT03645928 and NCT03108495

REFERENCES

- Sarnaik AA, et al. *J Clin Oncol* 2021; doi: 10.1200/JCO.21.00612.
- Jazaeri AA, et al. *J Clin Oncol* 2019;37 (suppl; abstract 182).
- Jimeno A, et al. *J Immunother Cancer* 2020;8 (suppl; abstract 353).

Ethics Approval The IOV-COM-202 study was approved by Advarra Institutional Review Board, approval number Pro00035064; the C-145-04 was approved by WIRB Copernicus Group, approval number 7-1425772-1. All study participants provided written consent via signature of the IRB-approved informed consent form.

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