Methods IPI-549-01 (NCT02637531) evaluates eganelisib in advanced solid tumors, as monotherapy and in combination with nivolumab. The combination expansion dose was eganelisib 40 mg QD PO + nivolumab 240 mg Q2W IV. Combination expansion cohorts include SCCHN patients resistant to immediate prior anti-PD(L)1 therapy. Safety, preliminary clinical activity, PK, and correlative study of blood and tumor biopsy samples were mandated.

Results As of June 1, 2020, 180 patients were treated with eganelisib + nivolumab including 21 with SCCHN.The most common (>20% of patients) treatment-emergent adverse events in patients treated with eganelisib + nivolumab (N = 180) were fatigue (34.4%), increased AST (30.0%), increased ALT (26.7%), nausea (25.0%), pyrexia (25.0%), anemia (22.8%), decreased appetite (20.6%), and cough (20.6%). 85 (47.2%) patients experienced at least 1 treatment-emergent serious adverse event (SAE) and 19 (10.6%) had a treatment-related SAE. There were no treatment-related grade 5 adverse events as assessed by investigators. Preliminary data from the SCCHN cohort show that in the efficacy-evaluable population which includes all patients (n=20) who had at least 1 post-baseline response assessment or discontinued treatment due to disease progression, the overall response rate (ORR, ie. CR [complete response] or PR [partial response] per RECIST v1.1) is 10.0%, the disease control rate (DCR, ie. CR, PR, or SD [stable disease]) is 45.0%, and the clinical benefit rate (CBR, ie. CR, PR, or SD of at least 24 weeks from first treatment) is 25.0%, per RECISTv1.1. For patients that received ≤ 2 lines of prior systemic therapy (n=11), the ORR is 20.0%, the DCR is 40.0%, and the CBR is 30.0%. In total, there are 2 patients with PR (duration of response 1.6–9.3 months) and 3 with SD for greater than 6 months' treatment duration. Translational data including T cell proliferation in peripheral blood as well as markers of inflammation in baseline biopsy of PR patient will be presented.

Conclusions Eganelisib + nivolumab demonstrates an acceptable safety profile and preliminary clinical activity in patients with SCCHN who were resistant to immediate prior anti-PD (L)1 therapy. Updated clinical and translational data will be presented.

Ethics Approval The study was approved by WIRB, Study Number 1188591 and IRB Tracking Number: 20180297.

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353 SAFETY AND EFFICACY OF TUMOR INFILTRATING LYMPHOCYTES (TIL, LN-145) IN COMBINATION WITH PEMBROLIZUMAB FOR ADVANCED, RECURRENT OR METASTATIC HNSCC

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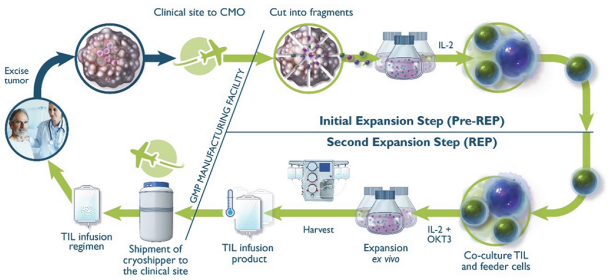
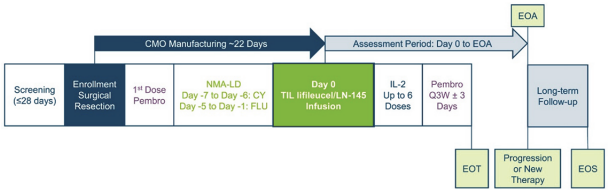
Background Single agent checkpoint inhibitors (CPI) are an approved first or second-line therapy in head and neck squamous cell carcinoma (HNSCC), but their efficacy is limited. Adoptive cell therapy with tumor infiltrating lymphocytes (TIL, LN-145) has demonstrated efficacy in multiple malignancies alone or in combination with CPI. To improve HNSCC therapy, a combination of pembrolizumab and LN-145 was explored.



Abstract 353 Figure 1 Iovance LN-145 (autologous TIL cell therapy product) Manufacturing



Abstract 353 Figure 2 IOV-COM-202 Study Schema

Methods IOV-COM-202 is an ongoing Phase 2 multicenter, multi-cohort, open-label study evaluating LN-145 in multiple settings and indications, and here we report cohort 2A which enrolled CPI naïve HNSCC patients who received the combination of LN-145 and pembrolizumab. Key eligibility criteria include up to 3 lines of prior therapy, ECOG <1, at least one resectable metastasis for LN-145 production, and at least another measurable lesion after tumor resection. Primary endpoints are ORR per RECIST v1.1 by investigator and safety as measured by the incidence of grade ≥ 3 treatment-emergent adverse events (TEAEs). LN-145 production method uses central GMP manufacturing in a 22-day process yielding a cryopreserved TIL product (figure 1). Preconditioning chemotherapy consists of cyclophosphamide/fludarabine, followed by LN-145, and then < 6 doses of IL-2 over <3 days. Pembrolizumab is initiated post-tumor harvest but prior to LN-145 and continues after LN-145 infusion Q3W until toxicity or progression (figure 2).

Results Nine (N=9) HNSCC patients have received LN-145 plus pembrolizumab, with a median duration of follow up of 6.9 months. Nine and 8 patients were evaluable for safety and efficacy, respectively. Mean number of prior therapies was 1.1 with 89% of the patients having received prior chemotherapy. Four were HPV+, 2 HPV-, 3 unknown. The Treatment Emergent Adverse Event (TEAE) profile was consistent with the underlying advanced disease and the known AE profiles of pembrolizumab, the lymphodepletion and IL-2 regimens. The most common TEAE were chills, hypotension, anemia, thrombocytopenia, pyrexia, fatigue and tachycardia. Four patients had a confirmed, objective response with an ORR of 44% (1 CR, 3 PR, 4 SD, 1 NE) per RECIST 1.1. The disease control rate at data cutoff was 89% in 9 patients, and 7 of the 8 evaluable patients (87.5%) had a reduction in target lesions. Median DOR was not reached.

Conclusions LN-145 can be safely combined with pembrolizumab in patients with metastatic HNSCC. LN-145 plus pembrolizumab shows early signs of improved efficacy particularly when compared with literature reports of pembrolizumab alone in a comparable patient population. Enrollment is ongoing and updated data will be presented.

Trial Registration NCT03645928

Ethics Approval The study was approved by Advarra Institutional Review Board, under protocol number: Pro00035064.

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354 A PHASE 1 TRIAL OF CUE-101 A NOVEL HPV16 E7-PHLA-IL2-FC FUSION PROTEIN IN PATIENTS WITH RECURRENT/METASTATIC HPV16+ HEAD AND NECK CANCER

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Background Immuno-STATsTM are novel, modular fusion proteins designed to selectively activate tumor-antigen-specific CD8+ T cells. Human papillomavirus (HPV) associated cancers serve as a model system to assess the safety and efficacy of the Immuno-STAT platform. CUE-101 is comprised of human leukocyte antigen (HLA) complex, HLA A*0201, a peptide epitope derived from the HPV type 16 E7 protein, and 4 molecules of a reduced affinity human interleukin-2 (IL2) designed to bind and activate HPV-specific T cells for eradication of HPV16-driven cancers. In preclinical studies CUE-101 demonstrated selective binding, activation, and expansion of HPV16 E7-specific CD8+ T cells, which translated into anti-tumor activity.[1]

Methods CUE-101-01 is a first-in-human (FIH) phase 1 study in patients diagnosed with HPV16+ recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) refractory to one or more lines of therapy. Trial eligibility includes MHC class I type HLA-A*0201 and a diagnosis of an HPV16 + HNSCC, as assessed by p16 IHC and confirmed by HPV16 mRNA ISH. CUE-101 is administered intravenously over 60 minutes every 21 days. Objectives include determination of safety, pharmacodynamics (PD), pharmacokinetics (PK), recommended phase 2 dose (RP2D), and preliminary anti-tumor activity. The safety results from treated participants will be presented.

Results 19 participants have received CUE-101 monotherapy as of August 7, 2020. Doses ranging from 0.06 to 1 mg/kg were determined to be safe and well-tolerated, enabling dose escalation to 2 mg/kg. Preliminary PK data demonstrate dose-dependent increases in drug exposure which are sustained upon repeat dosing, and low inter-subject variability. Preliminary data from systemic blood analyses show early signals of expansion of HPV-16 E711-20-specific CD8 + T cells. Stable disease (SD), as determined by RECIST 1.1, was observed in several participants in these early dose cohorts, with one subject maintaining SD up to 19 weeks. The maximum tolerated dose (MTD) has not yet been reached. As of May 14, 2020 (the development safety update report (DSUR) data-lock date), no dose limiting toxicities and the following adverse events were observed in the first 12 patients treated with CUE-101: fatigue (n=3), decreased appetite (n=1), arthralgia (n=1), muscular weakness (n=1), parasthesia (n=1), bullous pemphigoid (n=1), and infusion-related reactions (n=1).

Conclusions CUE-101 is a novel agent that is demonstrating acceptable tolerability, favorable PK, and preliminary PD signals that support selective activation of tumor-specific T cells. Neither the MTD nor the monotherapy RP2D have been established. PD and PK analyses are ongoing as dose escalation continues.

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Trial Registration ClinicalTrials. gov NCT03978689

Ethics Approval This study was approved by Ethics and Institutional Review Boards (IRBs) at all study sites; IRB reference numbers: DF/HCC IRB# 19-374 (Massachusetts General Hospital), HRPO# 201905108 (Washington University School of Medicine), IRB 191714 (Vanderbilt University Medical Center Vanderbilt-Ingram Cancer Center), Advarra Pro00037736 (Moffitt Cancer Center), IRB(IRBMED) HUM00165746 (University of Michigan Comprehensive Cancer Center), 2019-087 (Karmanos Cancer Institute), WIRB IRB00112341(Winship Cancer Institute/Emory University), WIRB 2000026098 (Yale Cancer Center), WIRB STUDY00008948 (University of Washington, Seattle), WIRB 1908869642 (University of Arizona Cancer Center, IRB 20-073 (Memorial Sloan Kettering Cancer Center), 2019-0578 (The University of Texas MD Anderson Cancer Center), IRB 52744 (Stanford University School of Medicine).

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355 FIRST-IN-HUMAN PHASE I STUDY OF NKTR-255 IN PATIENTS WITH RELAPSED/REFRACTORY HEMATOLOGIC MALIGNANCIES

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