## 783 TRIAL IN PROGRESS: A PHASE 1/2 OPEN-LABEL STUDY (IOV-GM1–201) OF TALEN-MEDIATED PD-1–INACTIVATED AUTOLOGOUS TUMOR-INFILTRATING LYMPHOCYTES (TIL; IOV-4001) IN PATIENTS WITH ADVANCED MELANOMA AND NSCLC

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**Background** Adoptive cell therapy with TIL has demonstrated efficacy in patients with advanced solid tumors, both as monotherapy in melanoma,[1] NSCLC,[2] and cervical cancer,[3] and in combination with anti–PD-1 therapy in melanoma, head and neck cancer, and cervical cancer.[4] IOV-4001 is a TALEN®-mediated *PDCD-1* knockout autologous TIL cell therapy product. Preclinical studies suggest that PD-1 inactivation by *PDCD-1* gene knockout may enhance TIL cell therapy efficacy, with similar quality attributes and phenotypes to those of non-edited TIL.[5]

**Methods** This first-in-human phase 1/2, open-label, nonrandomized, multicenter study (NCT05361174; open to enrollment) will enroll ~53 adult patients. During the phase 1 portion, enrollment and dose level decisions will be based on emerging safety and tolerability data in a 28-day dose-limiting toxicity (DLT) observation period.

Cohort 1 will include patients with unresectable/metastatic melanoma that has progressed during/within 12 weeks of last anti–PD-1/PD-L1 dose (patients must have also received a BRAF ± MEK inhibitor if *BRAF V600* mutation-positive). Cohort 2 will include patients with advanced NSCLC who have received ≤3 prior therapies and whose disease progressed either: (1) during/within 12 weeks after last anti–PD-1/PD-L1 dose (patients without oncogene driver mutations) or (2) during/after ≥1 targeted therapy and either platinum doublet chemotherapy or during/within 12 weeks after last anti–PD-1/PD-L1 dose (patients with oncogene-driven tumors). Patients must have ECOG performance status ≤1, ≥1 resectable lesion(s) (≥1.5 cm), ≥1 remaining RECIST-measurable lesion(s) and recovered from prior surgery/anticancer treatment-related adverse events (AEs; grade ≤1). IOV-4001 is generated from resected tumor in a centralized GMP process. The regimen includes nonmyeloablative lymphodepletion, IOV-4001 infusion, and a short course of high-dose IL–2.

The primary endpoints of phases 1 and 2 are safety (DLTs and AEs) and objective response rate per RECIST v1.1, respectively. Secondary endpoints include complete response rate, duration of response, disease control rate, progression-free survival, overall survival, feasibility, and additional safety.

**Trial Registration** NCT05361174

### REFERENCES

1. Sarnaik AA, *et al*. Lifileucel, a Tumor-Infiltrating Lymphocyte Therapy, in Metastatic Melanoma. *J Clin Oncol*. 2021;**39**(24):2656–2666.
2. Schoenfeld AJ, *et al*. 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). SITC 2021.
3. Jazaeri AA, *et al*. Safety and efficacy of adoptive cell transfer using tumor infiltrating lymphocytes (LN-145) for treatment of recurrent, metastatic, or persistent cervical carcinoma. ASCO 2019.
4. O'Malley D, *et al*. 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. SITC 2021.
5. Natarajan A, *et al*. Preclinical activity and manufacturing feasibility of genetically modified PDCD-1 knockout (KO) tumor infiltrating lymphocyte (TIL) cell therapy. AACR 2022.

**Ethics Approval** The study was approved by the institutional review board at each site and was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines of the International Conference on Harmonization.
**Consent** All patients provided written informed consent.

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