Trial in Progress: A Phase 2, multicenter study of autologous tumor infiltrating lymphocytes (TIL, LN-145) cell therapy in patients with metastatic non-small cell lung cancer (IOV-LUN-202)

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Background

- **Adoptive cell transfer (ACT) using autologous tumor-infiltrating lymphocytes (TIL)** has been shown to be efficient for the treatment of advanced metastatic melanoma, and other solid tumors with high tumor mutational burden.[1,2]
- **Iovance TIL** cell therapy (LN-144 [lifileucel] and LN-145), has demonstrated efficacy and safety in clinical trials for several high unmet medical need patient populations, specifically unresectable and metastatic melanoma, in relapsed, refractory or persistent cervical cancer, and in head and neck squamous cell carcinoma (HNSCC).[3-5]
- Further, TIL cell therapy has shown evidence of efficacy in metastatic non-small cell lung cancer (mNSCLC) in a Phase 1 study in combination with nivolumab.[6]

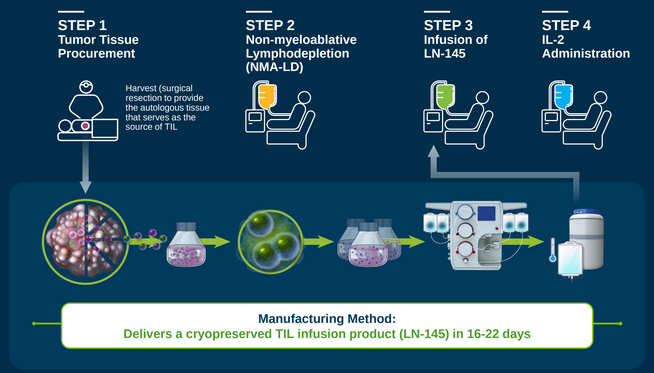
IOV-LUN-202

- The **IOV-LUN-202 (NCT04614103)** clinical trial is evaluating Iovance TIL cell therapy with LN-145 in patients with mNSCLC without actionable driver mutation(s), who have progressed on or following a single line of approved systemic therapy consisting of combined immune checkpoint inhibitors (ICIs) + chemotherapy ± bevacizumab.

Iovance TIL Manufacturing

- **The one-time Iovance TIL cell therapy** requires procurement of a small 1.5 cm sample of tumor tissue, which is shipped to a central manufacturing facility, where outside of the suppressive tumor microenvironment the TIL are reinvigorated and expanded to approximately 10^9–10^{11} cells.
- LN-145 manufacturing is a 16-22 day process.

Figure 1. Patient Journey and Central GMP Manufacturing

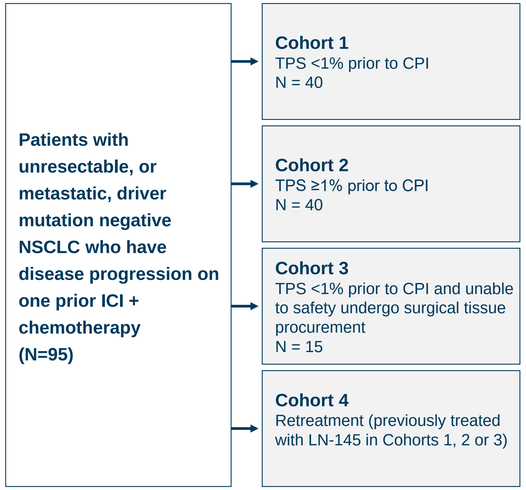


Study Overview & Endpoints

- A total number of approximately 95 patients are planned to be infused with LN-145 in Cohorts 1, 2, and 3.
- Primary endpoint:
  - Efficacy: Objective response rate (ORR) per RECIST 1.1 as assessed by IRC (Cohort 1 and Cohort 2) or by investigator (Cohort 3 and Cohort 4).
- Secondary endpoints:
  - Safety and additional efficacy parameters.
  - Efficiency of generating LN-145 from tumor core biopsies (Cohort 3).
- Exploratory endpoints:
  - Analyses of predictive and pharmacodynamic biomarkers of clinical activity of LN-145.

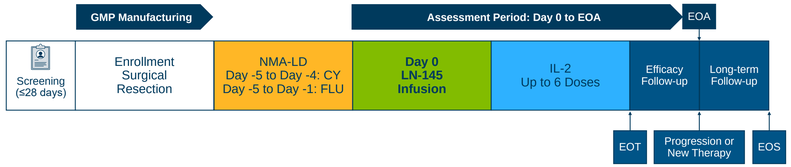
Study Cohorts

Figure 2. Study Design



IOV-LUN-202 TIL Regimen

Figure 3. Patient Treatment Schema



Key Inclusion & Exclusion Criteria

Inclusion Criteria – All Patients

- Confirmed histologic diagnosis of NSCLC and documented PD-L1 expression status as measured by Tumor Proportion Score (TPS) prior to the ICI treatment.
- Prior single line of systemic therapy that included ICI + chemotherapy with documented radiographic disease progression on or following this single line of prior systemic therapy.
- Cohort 1 and Cohort 2: at least 1 resectable lesion; Cohort 3: single measurable lesion; or unable to safely undergo a surgical resection; and able to have tumor harvest via radiology guided core biopsy sufficient for TIL generation.
- Remaining measurable disease as defined by RECIST 1.1.
- ECOG performance status of 0 or 1, and an estimated life expectancy of ≥6 months.
- LVEF >45%, New York Heart Association Class 1; cardiac stress test required.
- FEV_1 >50% or FEV1/FVC >0.7.

Exclusion Criteria – All Patients

- Known oncogene driver mutations (eg, *EGFR*, *ALK*, *ROS*), which are sensitive to targeted therapies.
- Symptomatic and/or untreated brain metastases.
- Organ allograft or prior cell transfer within the past 20 years.
- Receiving systemic steroid therapy ≥10 mg/day of prednisone or other steroid equivalent.
- Any form of primary immunodeficiency.
- Received a live or attenuated vaccination within 28 days prior to the start of treatment.
- Active medical illness(es) that pose increase risk.
- Participated in another interventional clinical study within 21 days of the initiation of treatment.

References:
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[3]Sarnaik A, et al. *JCO.* 2020;38 (suppl; abstr 10006).
[4]Jazaeri A, et al. *JCO.* 2019;37 (suppl; abstract 2538).
[5]Jimeno A, et al. *JITC.* 2020;8 (suppl; abstract A378).
[6]Creelan, B et al. *Can Res.* 2020;80:16 (suppl; abstract CT056).

Abbreviations: ACT, adoptive cell therapy; CY, cyclophosphamide; ICI, immune checkpoint inhibitor; ECOG, Eastern Cooperative Oncology Group; EOA, end of assessment; EOT, end of treatment; EOS, end of study; FLU, fludarabine; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GMP, good manufacturing practice; HNSCC, head and neck squamous cell carcinoma; IL-2, interleukin-2; IRC; independent review committee; LVEF, left ventricular ejection fraction; mNSCLC, metastatic non-small cell lung cancer; NMA-LD, nonmyeloablative lymphodepletion; ORR, objective response rate; PD-L1, programmed death-ligand 1; RECIST, Response Evaluation Criteria in Solid Tumors; TIL, tumor infiltrating lymphocytes; TPS, tumor proportion score (measure of tumor PD-L1 expression).

Disclosures:
• This study and poster are sponsored by Iovance Biotherapeutics, Inc., San Carlos, CA, USA.
• ZG, AC, BY, GC, FGF, MJ, and MF are employees or consultants of Iovance Biotherapeutics, Inc. and have stock options.