Trial In Progress: A Phase 2 Multicenter Study (IOV-LUN-202) of Autologous Tumor-Infiltrating Lymphocyte (TIL) Cell Therapy (LN-145) in Patients With Metastatic Non-Small Cell Lung Cancer (mNSCLC)

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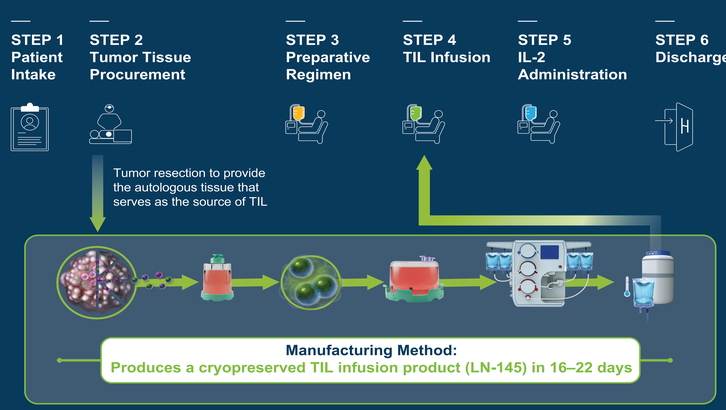
Background

- Patients with metastatic non-small lung cancer (mNSCLC) without actionable driver mutations have limited second-line (2L) treatment options[1] after progression on first-line treatment with concurrent or sequential immune checkpoint inhibitors (ICI) + chemotherapy ± bevacizumab[2]
- Lifileucel and LN-145, investigational autologous tumor-infiltrating lymphocyte (TIL) cell therapies, have demonstrated efficacy and safety in unresectable and metastatic melanoma; relapsed, refractory, or persistent cervical cancer; metastatic head and neck squamous cell carcinoma; and mNSCLC[3-5]
  - Early clinical experience with LN-145 in heavily pretreated patients with mNSCLC has demonstrated feasibility, safety, and a 21.4% objective response rate (ORR)[6]
  - TIL cell therapy has also shown evidence of efficacy in mNSCLC in a Phase 1 study in combination with nivolumab[7]
- To address the urgent need for better 2L therapeutic options, the ongoing IOV-LUN-202 trial has been amended (Protocol Version 2.0) to clarify prior therapies that will be permitted and allow patient enrollment for tumor resection and TIL generation prior to disease progression to minimize the time between confirmed disease progression and initiation of TIL therapy

Figure 1. TIL Manufacturing and Patient Journey

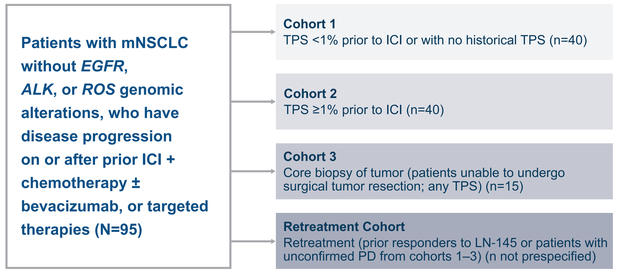


IOV-LUN-202 Study Overview (Protocol Version 2.0)

- **IOV-LUN-202 (NCT04614103)** is a prospective, open-label, multicohort, multicenter Phase 2 study evaluating adoptive cell therapy with autologous TIL (LN-145) in patients with mNSCLC without *EGFR*, *ALK*, or *ROS* genomic alterations, who have progressed on or following prior therapy, including concurrent or sequential ICI + platinum-based chemotherapy ± bevacizumab, or targeted therapies
- Patients may be enrolled for tumor resection and LN-145 generation prior to disease progression, with the intent to proceed with TIL cell therapy upon progression

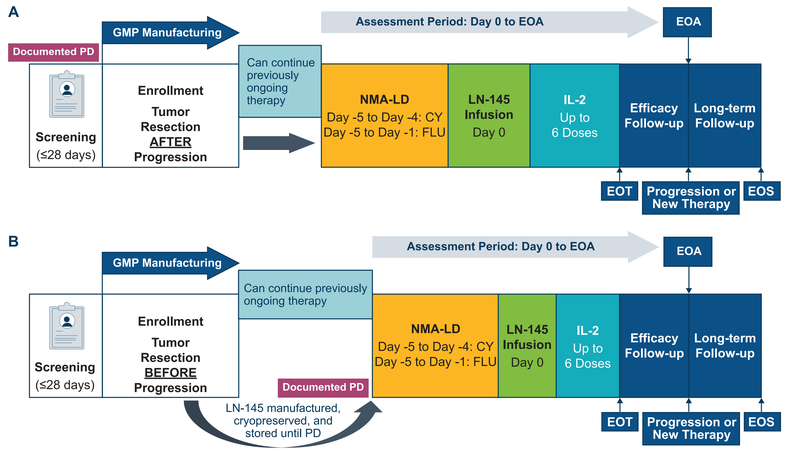
Study Design and Treatment Regimen

Figure 2. IOV-LUN-202 Study Design and Endpoints



- Approximately 95 patients are planned to be infused with LN-145 in Cohorts 1, 2, and 3
  - LN-145 is manufactured using a 22-day centralized Generation 2 (Gen 2) GMP process in Cohorts 1 and 2
  - In Cohort 3, a 16-day centralized Gen 3 GMP process that is optimized for a low volume of starting material is used to manufacture LN-145 from core biopsies of tumors
- Primary endpoint:
  - ORR per RECIST 1.1 as assessed by IRC (Cohorts 1 and 2) or by investigator (Cohort 3 and Retreatment Cohort)
- Secondary endpoints:
  - Safety and additional efficacy parameters
  - Percentage of TIL products successfully generated from core biopsies of tumors (Cohort 3)
- Exploratory endpoints:
  - Analyses of predictive and pharmacodynamic biomarkers of clinical activity of LN-145

Figure 3. IOV-LUN-202 Treatment Schema for Patients with Post- **(A)** and Pre-Progression Tumor Resection **(B)**



Key Inclusion and Exclusion Criteria

Inclusion Criteria

- Confirmed histologic or pathologic diagnosis of NSCLC
- mNSCLC without *EGFR*, *ALK*, or *ROS* genomic alterations with documented radiographic disease progression on or following first-line therapy including ICI and platinum-based chemotherapy ± bevacizumab, or targeted therapy
  - **For patients without actionable mutations:** 1 prior line of therapy if concurrent ICI and platinum-based chemotherapy, or ≤2 prior lines if sequential; patients with or without progression between sequential lines of therapy may be enrolled
  - **For patients with actionable mutations** (other than *EGFR*, *ALK*, or *ROS*): 1 additional line of appropriate targeted therapy will be allowed
- **For patients with pre-progression tumor resection and TIL generation:** Presence of residual resectable disease after platinum-based chemotherapy component of either concurrent or sequential ICI and platinum-based chemotherapy
- **Cohorts 1 and 2**: ≥1 resectable lesion and ≥1 measurable lesion; **Cohort 3**: able to undergo tumor resection for TIL generation via core biopsy of the tumor and have sufficient remaining lesion(s) to serve as target lesion(s)
- ECOG performance status of 0 or 1, and an estimated life expectancy of ≥6 months
- LVEF >45%, New York Heart Association Class 1
- FEV_1 >50% or FEV_1/FVC >70%

Exclusion Criteria

- Known actionable *EGFR*, *ALK*, or *ROS* driver mutations
- Symptomatic and/or untreated brain metastases
- Organ allograft or prior cell transfer within the past 20 years
- Systemic steroid therapy ≥10 mg/day of prednisone or another steroid equivalent
- Any form of primary immunodeficiency
- Live or attenuated vaccination within 28 days prior to the start of treatment
- Active medical illness(es) that pose increased risk
- Participation in another interventional clinical study within 21 days of the initiation of treatment

Abbreviations

2L, second line; CY, cyclophosphamide; FLU, fludarabine; ECOG, Eastern Cooperative Oncology Group; EOA, end of assessment; EOS, end of study; EOT, end of treatment; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GMP, good manufacturing practice; ICI, immune checkpoint inhibitor; IL- 2, interleukin-2; IRC, Independent Review Committee; LVEF, left ventricular ejection fraction; NMA-LD, nonmyeloablative lymphodepletion; mNSCLC, metastatic non-small lung cancer; ORR, objective response rate; PD, progressive disease; RECIST, Response Evaluation Criteria in Solid Tumors; TIL, tumor infiltrating lymphocytes; TPS, tumor proportion score (measure of tumor PD-L1 expression).

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Acknowledgments

- The authors would like to thank the participating patients and their families
- This study is sponsored by Iovance Biotherapeutics (San Carlos, CA, USA)
- Editorial support was provided by Second City Science (Chicago, IL, USA) and funded by Iovance Biotherapeutics

Disclosures

- JAC has received research support for trials from Amgen, Iovance Biotherapeutics, Instill Bio, Replimune, and Bristol Myers Squibb (BMS)
- AJS has been a consultant/advisor for Johnson & Johnson, KSQ Therapeutics, Heat Biologics, and Perceptive Advisors and has received research funding from BMS, Merck, GlaxoSmithKline, Iovance Biotherapeutics, Achilles, and PACT Pharma
- TWD is a consultant/advisor for Rakuten, Shattuck Labs, and Caris Life Sciences Molecular Tumor Board; has received clinical research grants (IITs) from Merck & Co., BMS, AstraZeneca, Tesaro/GSK, Janssen, and IsoRay; and has served on the Advisory Board for Head and Neck (Merck & Co.) and the Executive Steering Committee for Cavrotolimod (Exicure)
- AS holds stock options for BMS and Merck & Co.
- KH is a consultant/advisor for Perthera, Mirati Therapeutics, BMS, Iovance Biotherapeutics, and Geneplus and has received research funding from BMS, Mirati Therapeutics, Adaptimmune, Genentech/Roche, GlaxoSmithKline, Amgen, Iovance Biotherapeutics, Abbvie, and OncoC4
- FGF, PH, MJ, SS, ALS, and GC are employees of Iovance Biotherapeutics, and have stock and/or stock options
- YH is a consultant for Iovance Biotherapeutics and advisor for Castle Biosciences