**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)**

Chesney JA,1 Schoenfeld AJ,2 Wise-Draper T,3 Sukari A,4 He K5 Graf Finkenstein F,6 Hari P,7 Jazayeri A,3 Samakoglu S,7 Leighton-Swayne A,5 Chen G,6 Hong Y7

1James Graham Brown Cancer Center, University of Louisville, Louisville, KY, USA; 2Memorial Sloan Kettering Cancer Center, New York, NY, USA; 3University of Cincinnati Cancer Center, Cincinnati, OH, USA; 4Karmanos Cancer Hospital, Detroit, MI, USA; 5James Cancer Center, The Ohio State University, Columbus, OH, USA; 6Iovance Biotherapeutics, Inc., San Carlos, CA, USA; 7Cooper University Hospital, MD Anderson Cancer Center at Cooper, Camden, NJ, USA

**Background**

- Patients with metastatic non-small lung cancer (mNSCLC) without actionable driver mutations have limited-line (2L) treatment options after progression on first-line treatment with concurrent or sequential immune checkpoint inhibitors (ICI) + chemotherapy or bevacizumab.
- Early clinical experience with LN-145 in heavily pretreated patients with mNSCLC has demonstrated feasibility, safety, and a 21.4% objective response rate (ORR) with TIL cell therapy.
- The time between confirmed disease progression and initiation of TIL therapy has also shown evidence of efficacy in mNSCLC in a Phase 1 study in combination with nivolumab.
- 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 maximize the time between confirmed disease progression and initiation of TIL therapy.

**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).

**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 pathologic or radiologic diagnosis of NSCLC.
- mNSCLC without EGFR, ALK, or ROS genomic alterations with documented radiographic disease progression or on following first-line therapy including ICI and platinum-based chemotherapy.
- Bevacizumab, or targeted therapy.
- For patients with 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 the 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 2 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).
- EOG progression status of 0 or 1, and an estimated life expectancy of ≥6 months.
- LVFE >45%, New York Heart Association Class 1.
- FEV1, >50% or FEV1/FVC >70%.
- At least 2 lines of prior therapy (other than sequential ICI + platinum-based chemotherapy).
- Anti–PD-L1 antibody or ± bevacizumab, or targeted therapy.
- Any organ atrophy or prior cellular transfer over the past 20 years.
- Systemic steroid therapy ≥10 mg 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 that may increase risk.
- Participation in another interventional clinical study within 21 days of the initiation of treatment.

**Exclusion Criteria**

- Known actionable EGFR, ALK, or ROS driver mutations.
- Symptomatic and/or untreated brain metastases.
- Organ atrophy or prior cellular transfer over the past 20 years.
- Systemic steroid therapy ≥10 mg 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 that may increase risk.
- Participation in another interventional clinical study within 21 days of the initiation of treatment.

**Disclaimer**

- JAC has received research support for trials from Amgen, Bristol-Myers Squibb, Instil Bio, Replication, and Selecta Biosciences.
- AJH has been a consultant/advisor for Johnson & Johnson, Arcturus Therapeutics, Nacor Therapeutics, and responds for a clinical trial.
- JSM has received research funding from Amgen.
- SSW has received research funding from Bristol-Myers Squibb, Genentech, and Amgen.
- CORS has received research funding from Genentech/Roche, GlaxoSmithKline, Amgen, Iovance, Bristol-Myers Squibb, AstraZeneca, and Servier.
- JSM has received speaker fees for Amgen, BMS, OncoCyte, and Takeda.
- LMA has received research funding from Bristol-Myers Squibb, Genentech, and Amgen.
- CORS has received speaker fees for Amgen, BMS, OncoCyte, and Takeda.
- BMS has received honoraria for trials from Merck & Co., Bristol-Myers Squibb, Genentech/Roche, and Amgen.
- CORS has received honoraria from Merck & Co., Bristol-Myers Squibb, Genentech/Roche, and Amgen.
- CORS has served on the steering committee for trials from Merck & Co., Bristol-Myers Squibb, Genentech/Roche, and Amgen.
- JSM has served as a consultant for Genentech/Roche, Genentech, and Amgen.