Phase 2 Study to Assess the Efficacy and Safety of Autologous Tumor Infiltrating Lymphocytes (LN-145) Alone and In Combination with Anti-PD-L1 Inhibitor Durvalumab (MEDI4736) in Patients with Locally Advanced or Metastatic Small Cell Lung Cancer (NSCLC)

Sylvia Lee1, Liza Villanueva2, Susie Tananay3, Igor Garbuschevsky4, Sam Suzuki4, Maria Faridi5, Misaki Hugetz4
1University of Washington, Seattle, WA; 2University of Pittsburgh Medical Center - Hillman Cancer Center, Pittsburgh, PA; 3Iovance Biotherapeutics, San Carlos, CA; 4Atlantic Health System/Morristown Medical Center, Morristown, NJ

BACKGROUND

- Lung cancer is the leading cause of human cancer deaths worldwide, with approximately 1.7 million deaths reported in 2015, of which 80% to 85% are attributed to nonsmall cell lung cancer (NSCLC).
- For patients with locally advanced or metastatic disease, the standard chemotherapy shows objective response rate (ORR) of 10% to 40%, and a median survival of approximately 1 year.6

STUDY OVERVIEW

- **Phase 2, multicenter, open-label, 2-cohort study** evaluating ACT with autologous TIL therapy (LN-145) alone or in combination with durvalumab in Cohort 1.
- **Approximately 10 investigational centers in the US** for patient accrual.
- **Cohort 2 patients** receive 1500 mg IV durvalumab as a single infusion followed by up to 6 infusions of IV IL-2 (600,000 IU/kg).
- **Primary** and **secondary** endpoints include the evaluation of efficacy and safety parameters performed by treatment cohort.

STUDY DESIGN

- **LN-145** is prepared at a central GMP facility from TIL extracted from surgically resected tumors. LN-145 infusion is preceded by a non-myeloablative lymphodepletion regimen of cyclophosphamide (60 mg/kg, 2 days) and fludarabine (25 mg/m², 2 days), followed by up to 6 infusions of IV IL-2 (600,000 IU/kg).
- **Cohort 1 patients** receive LN-145 therapy alone. Patients in Cohort 1 who do not receive LN-145 or those who progress following LN-145 therapy may go on to receive durvalumab 1500 mg IV Q4W until disease progression or unacceptable toxicity.
- **Cohort 2 patients** receive 1500 mg IV durvalumab as follows: 2 weeks prior to and 2 weeks after tumor harvest; then 2 weeks following LN-145 infusion and continue 1500 mg IV durvalumab Q4W until disease progression or unacceptable toxicity.
- **Patients in either cohort** will be allowed to go on to receive durvalumab alone.

STUDY OUTCOMES

- **Primary:** To evaluate the efficacy of LN-145 therapy alone or in combination with durvalumab in patients with locally advanced or metastatic NSCLC using the objective response rate (ORR).
- **Secondary:** To evaluate the safety of LN-145 therapy alone or in combination with durvalumab in patients with locally advanced or metastatic NSCLC as measured by any Grade 3 adverse event (AE).

MATERIAL INCLUSION & EXCLUSION CRITERIA

**Major Inclusion Criteria**

- **Histologically/cytologically confirmed diagnosis of Stage III or Stage IV NSCLC (squamous, nonsquamous, adenocarcinoma, large cell carcinoma),** and have received ≥ 1 prior systemic therapy in the study population by assessing complete response (CR) rate and disease control rate (DCR).
- To explore the persistence of LN-145 and immune correlates of response, survival, and toxicity of the treatment.
- To explore efficacy based on immune-related Response Evaluation Criteria in Solid Tumors (iRECIST).7
- To assess health-related quality of life (HRQoL) per the EORTC QLQ-C30 and QLQ-LC13.

**Major Exclusion Criteria**

- History of malignancies, except for curatively treated with no evidence of disease for ≥ 3 years.

**Study Design**

- **Flowchart** at the end of the study.

SUMMARY

- This study aims to assess the potential of TIL therapy with LN-145 either alone or in combination with durvalumab for the treatment of patients with locally advanced or metastatic NSCLC.

Disclosure

This study is sponsored by Iovance Biotherapeutics, Inc., in collaboration with Medimmune, the global biologics research and development arm of AstraZeneca.

References

11. The primary statistical analysis is based on the use of descriptive methods and evaluation of efficacy and safety parameters performed by treatment cohort.