A Phase 2, Multicenter Study to Evaluate the Efficacy and Safety of Autologous Tumor Infiltrating Lymphocytes (LN-145) for the Treatment of Patients with Recurrent and/or Metastatic Squamous Cell Carcinoma of the Head and Neck

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Background:
- Squamous cell carcinoma of the head and neck (HNSCC) is a major cause of cancer morbidity & mortality with annual reports of 535,000 cases and 380,000 deaths worldwide, and 63,0005 cases & 13,000 deaths in the United States.1
- With a 2-year overall survival rates of 57% or less among patients with HNSCC, more effective therapeutic options are needed.2
- The inherent immunogenicity of HNSCC and, in particular human papillomavirus (HPV)-associated oropharyngeal cancer, suggests that these tumors may be particularly well suited for immunotherapeutic intervention.3
- While immunotherapeutic approaches (PD-1 inhibitors) are more common, objective response rate (ORR) remains less than 20% in this population.4
- Tumor infiltrating lymphocytes (TILs) have demonstrated prognostic value in both HPV-negative and HPV-positive HNSCC tumor specimens,4,5 and these tumors can be used to generate anti-tumor TIL.6,7
- Given the low response rates to standard therapy and immunogenicity of HNSCC, the use of TIL may provide improved responses, even following checkpoint therapy.
- This study was designed to evaluate the efficacy and safety of LN-145, an autologous investigational TIL therapy (TIL) in patients with previously treated recurrent and/or metastatic HNSCC.

Methods:
- c.16-03 (NCT03308373) is a Phase 2, multicenter prospective, open-label, interventional study evaluating LN-145 infusion (ACT) with autologous TIL infusion (LN-145) following lymphodepletion preparative regimen for the treatment of patients with recurrent and/or metastatic HNSCC.
- All squamous cell carcinoma of the head and neck (HPV+/-) will be enrolled including nasopharyngeal SCC (EBV+/-).
- Approximately 15 clinical sites in the US.

Patients selected are as follows:
- N = 47 treated patients.

Results:
- Major Inclusion Criteria
- 18 years of age or older.
- Recurrent and/or metastatic HNSCC histologically confirmed.
- Must have had at least 1 lesion resectable for TIL generation that yields at least 1.5 cm in diameter of tissue. If previously irradiated, the irradiation must have occurred at least 3 months prior to resection.
- Must remain a remaining lesion measurable as per RECIST 1.1 for response assessment.
- If previously irradiated, the irradiation must have occurred at least 3 months prior to enrollment.
- Must have received at least 1 line of prior systemic therapy for their recurrent and/or metastatic HNSCC.
- Minimum 28 days washout from last dose of tumor-directed therapy to the start of lymphodepletion.
- ECOG performance status of 0-1.
- Adequate bone marrow, liver, and renal function.
- HIV negative.
- Negative or undetectable Hepatitis B and Hepatitis C.

Efficacy:
- 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 RECIST (irRECIST) criteria as assessed by independent review.
- To assess health-related quality of life (HRQoL).
- To assess quality-adjusted time without symptoms of disease or toxicity of treatment (Q-TWST).

Summary:
- Recurrent and metastatic HNSCC remains a high unmet medical need with substantial survival benefits.
- While the addition of checkpoint inhibitors for the treatment of HNSCC is more widely used, response rates remain below 20%.
- TIL have demonstrated efficacy in other solid tumors with potential for durable long-term responses even after progression on checkpoint inhibitors.
- Presence of TIL may have correlated with improved outcomes in both HPV+ and HPV- HNSCC.
- Thus, TIL therapy may have a beneficial role in HNSCC patients with recurrent and/or metastatic disease.

Disclosure:
This study and poster are supported by Iovance Biotherapeutics, Inc.

References: