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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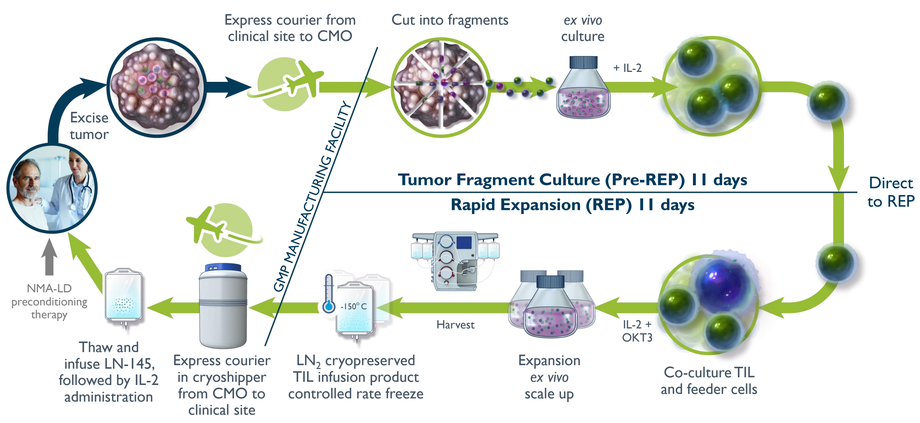
BACKGROUND

- Squamous cell carcinoma of the head and neck (HNSCC) is a major cause of cancer morbidity & mortality with annual reports of over 550,000 cases and 380,000 deaths each year worldwide[1], and 63,000 diagnoses & 13,000 deaths in the United States.[2]
- With 2-year overall survival rates of 57% or less among patients with HNSCC, more effective therapeutic options are needed.[3]
- 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.[4-7]
- While immunotherapeutic approaches (PD-1 inhibitors) are more common, objective response rate (ORR) remains less than 20% in this population.[8, 9]
- Tumor infiltrating lymphocytes (TIL) have demonstrated prognostic value in both HPV-positive and HPV-negative HNSCC tumor specimens[4-7] and these tumors can be used to generate anti-tumor TIL.[4-7, 10-12]
- Given the low response rates to standard therapy and immunogenicity of HNSCC, the use of TIL may lead to 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.

Figure 1. Iovance cryopreserved LN-145 manufacturing process (22 days)



STUDY OVERVIEW

- C-145-03 is a Phase 2, multicenter prospective, open label, interventional study evaluating adoptive cell therapy (ACT) with autologous TIL infusion (LN-145) followed by IL-2 after a non-myeloablative (NMA) lymphodepletion preparative regimen for the treatment of previously treated recurrent and/or metastatic HNSCC
- All squamous cell carcinomas of the head and neck (HPV+/-) will be enrolled including nasopharyngeal SCC (EBV+/-)
- Approximately 15 clinical study sites in the US
- Planned sample size, N = 47 treated patients

OUTCOME MEASURES

Primary:

- Objective response rate (ORR)

Secondary:

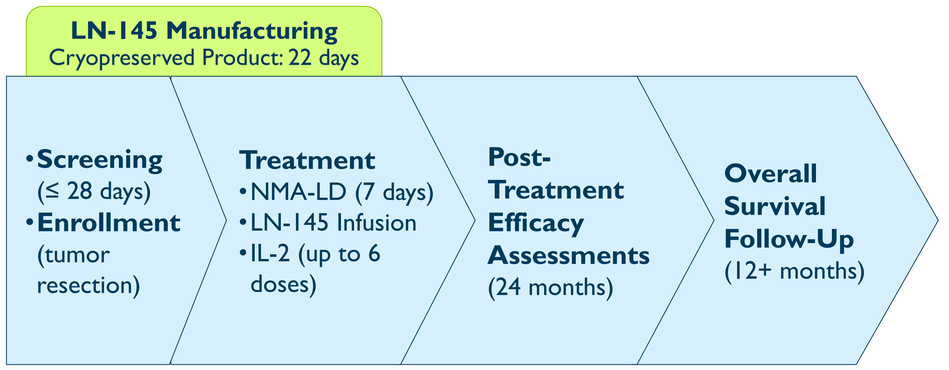
- Safety evaluation
- Duration of response (DOR), disease control rate (DCR), and progression-free survival (PFS)
- Complete response (CR) rate and Overall survival (OS)

Exploratory:

- Persistence of LN-145 and immune correlates of response, survival, and toxicity of the treatment
- Efficacy per immune-related RECIST (irRECIST) criteria
- Health-related quality of life (HRQoL)
- Quality-adjusted time without symptoms or toxicity (Q-TWiST)

STUDY FLOWCHART

Stages of Study: Linear Flow



NMA-LD: nonmyeloablative lymphodepletion; IL-2: Interleukin-2

MAJOR INCLUSION & EXCLUSION CRITERIA

Major Inclusion Criteria

- Recurrent and/or metastatic HNSCC confirmed histologically and have received at least 1 line of prior systemic therapy for their recurrent and/or metastatic HNSCC;
- Must have 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 have 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 (tumor resection);
- Must 18 years of age or older;
- Minimum 28 days washout from last dose of tumor-directed therapy to the start of lymphodepletion;
- ECOG performance status of 0 or 1;
- Adequate bone marrow, liver, and renal function;
- HIV negative;
- Negative or undetectable Hepatitis B and Hepatitis C; and
- Up to 1 year of birth control following completion of study treatment.

Major Exclusion Criteria

- Prior cell transfer therapy except for LN-145;
- Systemic steroid therapy >10 mg/day;
- Greater than grade 1 prior therapy-related toxicities except for alopecia or vitiligo;
- Active immunotherapy-related grade 2 diarrhea or colitis in the previous 6 months; patients may be included if asymptomatic and demonstrated uninflamed colon by colonoscopy;
- Active systemic infections, coagulation disorders, or other active major medical illnesses of the cardiovascular, respiratory, or immune system that, in the opinion of the investigator, would increase the risk of participation;
- Symptomatic and/or untreated brain metastases;
- Primary or acquired immunodeficiency;
- End-stage renal disease requiring dialysis;
- LVEF < 45%;
- FEV_1 ≤ 60% predicted; or walk less than 80% predicted or have hypoxia during a 6-minute walk test;
- Primary malignancy in the previous 3 years requiring treatment in the last year;
- History of hypersensitivity to any component of TIL therapy and other study drugs: cyclophosphamide, fludarabine, antibiotics of the aminoglycoside group (i.e., streptomycin, gentamicin), LN-145 or IL-2.

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Disclosure

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SUMMARY

- Recurrent and metastatic HNSCC remains a high unmet medical need with suboptimal survival rates.
- 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 have been correlated with improved outcomes in both HPV+ and HPV- HNSCC.[13]
- Thus, TIL therapy may have a beneficial role in HNSCC patients with recurrent and/or metastatic disease.

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