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A phase 2 study to evaluate the safety and efficacy of using autologous tumor infiltrating lymphocytes (LN-145) in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck

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BACKGROUND

- 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 USA[2]
- With 2-year overall survival rates of 57% or less among patients with recurrent and/or metastatic HNSCC, more effective therapeutic options are needed[3]
- The inherent immunogenicity of HNSCC and, in particular HPV-associated OPC, suggests that these tumors may be particularly well-suited for immunotherapeutic intervention[4-7]
- While immunotherapeutic approaches (PD-1 inhibitors) are more common, 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 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

STUDY OVERVIEW

- 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
- Simon's 2-Stage Design with fifteen patients included in the first stage

OBJECTIVES

Primary objective:

- To evaluate the efficacy of LN-145 in patients with recurrent and/or metastatic HNSCC using the objective response rate (ORR) as assessed by investigators per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1)

Secondary objective:

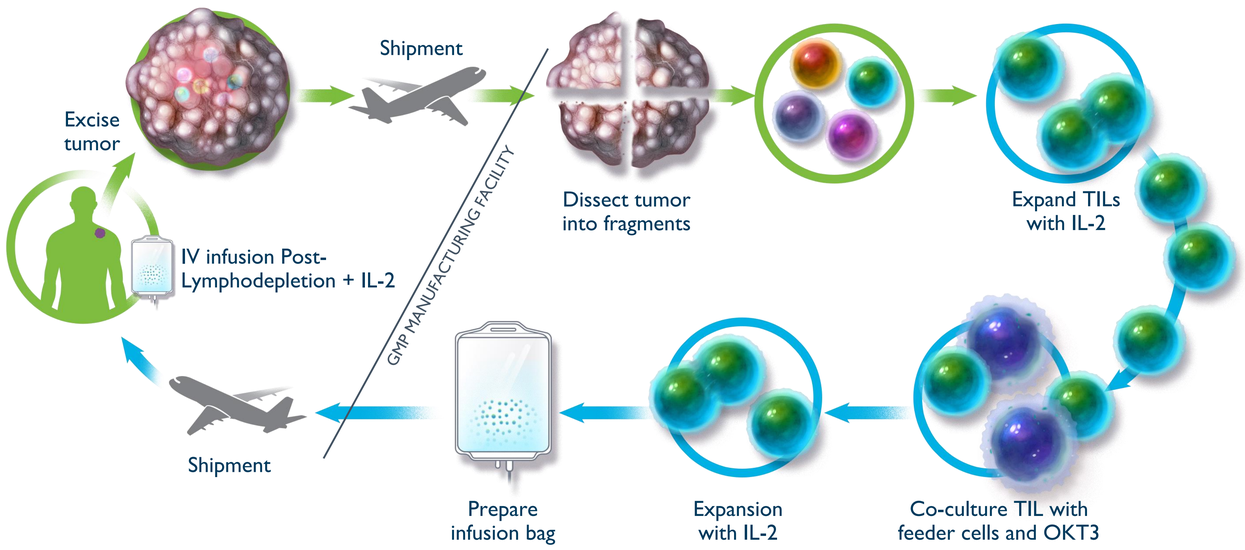
- To characterize the safety profile of LN-145 in patients with metastatic and/or recurrent HNSCC
- To evaluate efficacy of LN-145 in patients with recurrent and/or metastatic HNSCC such as complete response (CR) rate, duration of response (DOR), disease control rate (DCR), and progression-free survival (PFS) by investigators' review per RECIST v1.1, and overall survival (OS)

Exploratory objective:

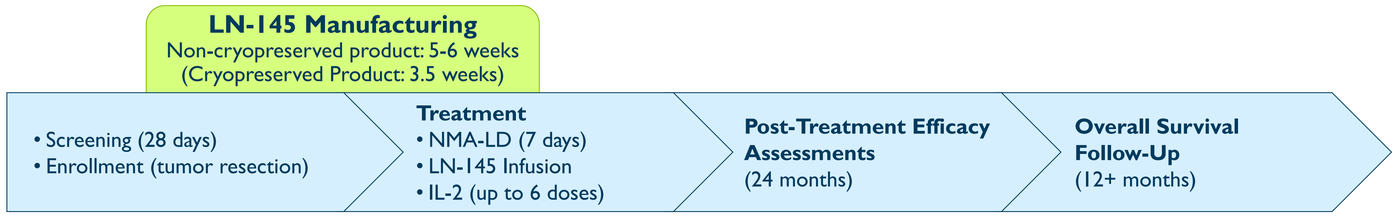
- To explore the persistence of LN-145 and immune correlates of response, survival, and toxicity of the treatment
- To explore efficacy based on immune-related RECIST (irRECIST) criteria as assessed by independent review
- To assess health-related quality of life (HRQoL)
- To assess quality-adjusted time without symptoms of disease or toxicity of treatment (Q-TWiST)

PROCESS, LOGISTICS & STAGES OF STUDY

Manufacturing Process & Logistics



Stages of Study: Linear Flow



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

MAJOR INCLUSION CRITERIA

- 18 years of age or older;
- Recurrent and/or metastatic HNSCC confirmed histologically;
- 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 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 or 1;
- Adequate bone marrow, liver, and renal function;
- HIV negative;
- Negative or undetectable Hepatitis B and Hepatitis C;
- 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 greater than 10 mg daily equivalents of prednisone
- Greater than grade 1 prior therapy-related toxicities except for alopecia or vitiligo prior to enrollment/tumor resection;
- 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;
- Left ventricular ejection fraction < 45%;
- Forced expiratory volume in one second ≤ 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; and
- Pregnant or breastfeeding.

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%
- Presence of TIL have been correlated with improved outcomes in both HPV+ and HPV- HNSCC
- TIL have demonstrated efficacy in other solid tumors including durable long-term responses following progression on checkpoint inhibitors
- This study aims to assess the potential of TIL therapy for the treatment of HNSCC patients with recurrent and/or metastatic disease

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