Trial in Progress: A Phase 2, Multicenter Study to Evaluate the Efficacy and Safety Using Autologous Tumor Infiltrating Lymphocytes (LN-145) in Patients with Recurrent, Metastatic, or Persistent Cervical Carcinoma

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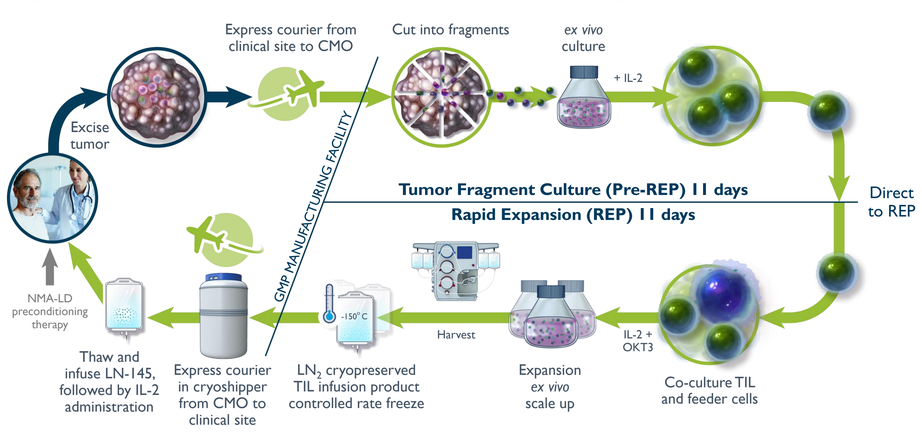
BACKGROUND

- Cervical cancer is a leading cause of cancer-related death in women with over 12,000 new cases and 4,000 deaths in the US alone.[1-2]
- Advanced recurrent/persistent and metastatic forms of cervical cancer have poor outcomes with mean progression free survival (PFS) rates less than 8 months following standard platinum-based chemotherapy with post-progression overall survival of 8.4 mos when bevacizumab is added.[4-6]
- ORR in patients who have failed platinum-containing regimens is 11-24% with short duration of response (≤ 3 mos).[7]
- The presence of tumor-infiltrating lymphocytes (TIL) has been well documented in patients with human papillomavirus (HPV)-associated cancers, including cervical carcinoma, and have been positively correlated with improved patient outcomes.[8-10]
- Several early studies have demonstrated the feasibility of isolation and culture of TIL from cervical tumors.[11,12]
- A pilot study of TIL therapy in 9 patients with previously treated cervical carcinoma demonstrated an ORR of 33% that included 2 durable long-term (46 and 54 mos) complete responses.[13]
- This study was designed to evaluate the efficacy and safety of LN-145, an autologous investigational TIL therapy for the treatment of patients with recurrent, metastatic, or persistent cervical carcinoma.

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



STUDY OVERVIEW

- C-145-04 (NCT03108495) is a Phase 2, multicenter prospective, open label, interventional study was designed to evaluate 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 patients with recurrent, metastatic, or persistent cervical cancer who were unresponsive to or failing prior therapy.
- All squamous cell carcinoma, adenocarcinoma, and adenosquamous pathologies will be enrolled regardless of HPV status
- Up to 40 clinical study sites globally
- The planned sample size, N = 47 treated patients

OUTCOME MEASURES

Primary:

- Objective response rate (ORR)

Secondary:

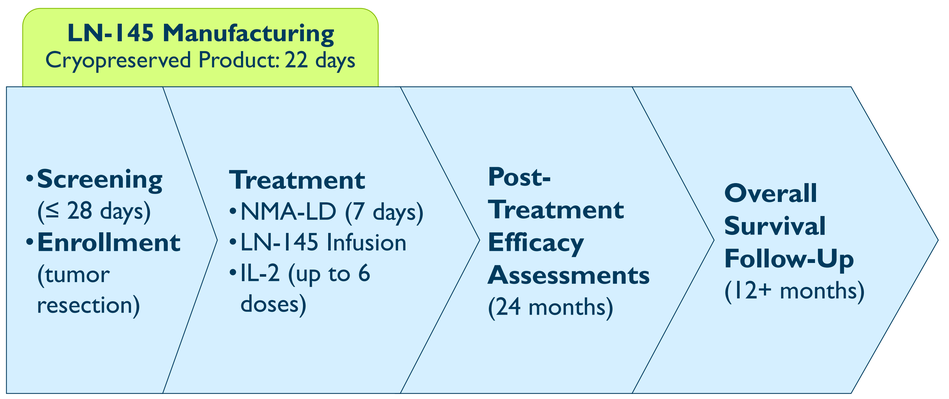
- Safety evaluation
- Duration of response (DOR), disease control rate (DCR), and progression-free survival (PFS)
- Complete response (CR) rate and Overall survival (OS)

Exploratory:

- Persistence of LN-145 and immune correlates of response, survival, toxicity of the treatment
- Efficacy per immune-related RECIST (irRECIST)
- 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

- Metastatic, recurrent, or persistent cervical carcinoma not amenable to curative surgery or radiation and have received at least 1 line of prior systemic therapy for their metastatic, recurrent, or persistent cervical carcinoma;
- 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);
- 18 years of age or older;
- Minimum 28 day washout from last dose of tumor-directed therapy to tumor resection;
- ECOG performance status of 0 or 1;
- Adequate bone marrow, liver, and renal function;
- HIV negative and negative or undetectable for 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 >10 mg/day;
- Greater than grade 1 prior treatment-related toxicities except for peripheral neuropathy, 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% and FEV_1 ≤ 60% at Screening;
- 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.

NCT03108495

Disclosure

This study and poster are sponsored by Iovance Biotherapeutics, Inc.

SUMMARY

- Recurrent, metastatic, or persistent cervical carcinoma presents a high unmet medical need with low survival rates and with limited effective treatment options.
- Presence of TIL have been correlated with improved outcomes in cervical carcinoma.
- TIL have demonstrated efficacy in other solid tumors including responses in heavily pretreated patients irrespective of prior therapy, including checkpoint inhibitors.
- Pilot data using TIL therapy for the treatment of cervical carcinoma has demonstrated the potential for long-term durable complete responses.
- This study aims to assess the potential of TIL therapy for the treatment of cervical cancer patients with recurrent, metastatic, or persistent disease.

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