Trial in Progress: A Phase 1b study evaluating the safety, tolerability and preliminary anti-tumor activity of NT-I7 (efineptakin alfa), a long-acting human IL-7, post-tisagenlecleucel in subjects with relapsed/refractory large B-cell lymphoma

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BACKGROUND

CD19-directed chimeric antigen receptor T-cell (CAR-T) therapy with tisagenlecleucel is standard of care (SOC) for patients with relapsed/refractory large B-cell lymphoma (r/r LBCL). CAR-T expansion is a strong predictor of response to this therapy. NT-I7 (efineptakin alfa) is a first-in-class, long-acting human IL-7 previously shown to clinically increase the number and functionality of T-cells in peripheral blood and within tumors. In a CD19$^+$ lymphoma xenograft mouse model receiving anti-CD19 universal CAR-T infusion, NT-I7 treatment prolonged survival and enhanced CAR-T gene expression of functional markers, proliferation, persistence, and tumor killing. We hypothesize that NT-I7 administration after tisagenlecleucel SOC for subjects with r/r LBCL may increase expansion and persistence of CAR-T, leading to increased tumor response rate and improved clinical outcomes without safety concerns.

PRIMARY AND SECONDARY OBJECTIVES

For Dose Escalation Phase:

- To evaluate the safety and tolerability of NT-I7 when administered after tisagenlecleucel infusion for r/r LBCL
- To determine the Maximum Tolerated Dose (MTD) and/or the Recommended Phase 2 Dose (RP2D) of NT-I7 when administered after tisagenlecleucel infusion for r/r LBCL

For Dose Expansion phase:

- To explore the Overall Response Rate (ORR) of NT-I7 when administered after tisagenlecleucel infusion for r/r LBCL
- To explore the preliminary anti-tumor activity of NT-I7 when administered after tisagenlecleucel infusion for r/r LBCL based on:
  - Duration of Response (DOR)
  - Progression-Free Survival (PFS)
  - Overall Survival (OS)
- To assess the effect of NT-I7 on CAR-T cell expansion

STUDY DESIGN

This is a multicenter Phase 1b study evaluating the safety, tolerability and preliminary anti-tumor activity of NT-I7 administration following SOC tisagenlecleucel CAR-T therapy for eligible subjects with r/r LBCL. The study consists of a Dose Escalation phase followed by a Dose Expansion phase.

Dose Escalation phase

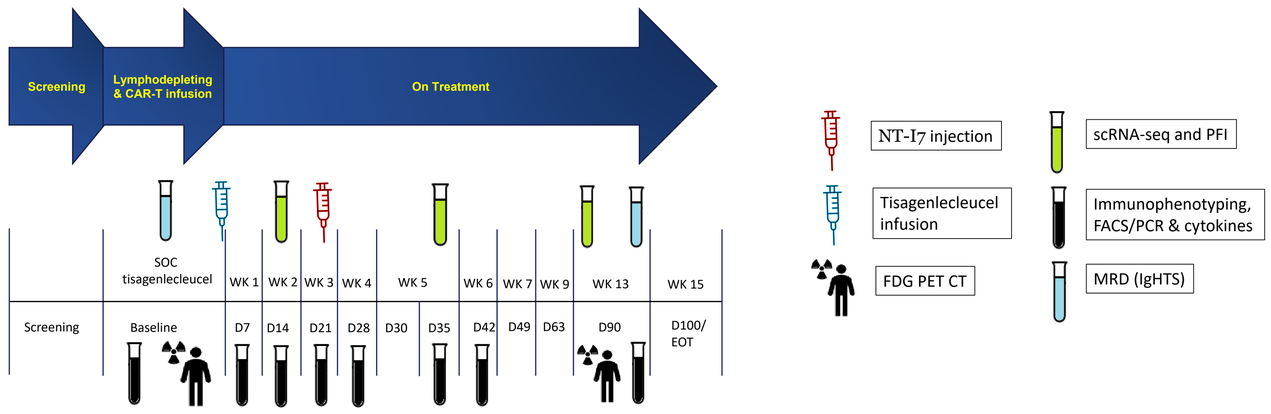
The Dose Escalation phase is designed to assess the safety and tolerability, including determination of the MTD and/or the RP2D of NT-I7 when administered as an intramuscular injection after tisagenlecleucel infusion for r/r LBCL. Seven dose levels (DLs) are planned: the starting DL (DL1) will be 60 µg/kg, and the highest DL to be tested (DL7) will be 720 µg/kg. Other intermediate DLs between 60 µg/kg and 720 µg/kg may be explored based on emerging data. The dose escalation phase will consist of 17 – 42 subjects.

Dose Expansion phase

Once RP2D has been determined from the Dose Escalation phase, up to 15 subjects will be enrolled in the Dose Expansion phase and treated at the RP2D to further evaluate the safety and preliminary anti-tumor activity of NT-I7 administration following SOC tisagenlecleucel CAR-T therapy for eligible subjects with r/r LBCL.

Post-Treatment Follow-up

All subjects will have a safety follow-up visit 100 days after tisagenlecleucel infusion and 90 days post-NT-I7 injection. Subjects will continue to be followed for survival every 90 days after the NT-I7 dosing until the final subject enrolled in the study has completed the safety follow-up visit.



KEY ELIGIBILITY CRITERIA

- Subjects with histologically confirmed relapsed or refractory LBCL after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma; must be eligible for tisagenlecleucel therapy as standard of care
- Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0-1
- Adequate organ function at the start of lymphodepleting chemotherapy as pre-conditioning for tisagenlecleucel infusion
- In Dose Escalation phase: Grade ≥2 cytokine release syndrome (CRS) or Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) post-tisagenlecleucel infusion is exclusionary
- In Dose Expansion phase: Grade ≥3 CRS or ICANS post-tisagenlecleucel infusion is exclusionary
- Has not previously received CD19-directed therapy
- Has not previously received an allogeneic tissue/solid organ transplant or bone marrow transplant
- Has no active central nervous involvement of LBCL
- Has no active autoimmune diseases
- Has no active and clinically relevant bacterial, fungal, viral, or TB infection, including known Hepatitis A, B, or C or HIV (testing not required)

PRIMARY ENDPOINTS AND ASSESSMENTS

Assessments: Safety and Tolerability

- Incidence and nature of DLTs
- Incidence, nature, and severity of adverse events graded according to NCI CTCAE v5.0, except grading of CRS and ICANS which will be based on ASTCT guidelines
- Toxicity assessments graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0
- Safety analysis on all subjects who receive NT-I7 injection, including the frequency of all AEs and laboratory abnormalities
- Grading of CRS and ICANS based on the American Society for Transplantation and Cellular Therapy guidelines

Assessments: Anti-Tumor Activity and Efficacy

- Disease assessment based on IWG response criteria for lymphoma (Lugano classification) based on standard FDG-PET/CT and CT scans
- Monitoring of early disease response performed following tisagenlecleucel and NT-I7 treatment with minimal residual disease (MRD) surveillance compared to SOC FDG-PET/CT scans at Baseline, 1 month, and 3 months
- Overall Response Rate (ORR) at 3 months assessed by Investigators using FDG PET-CT and the Lugano classification (1)

Study Information

Protocol Number: NIT-112 **Status:** Recruiting
Lead Investigator: John F DiPersio, M.D., Ph.D.
Lead Coordinating Center: Washington University School of Medicine—Siteman Cancer Center
ClinicalTrials.gov Identifier: NCT05075603

References: (1) Cheson BD, et al. J Clin Oncol. 2014;32(27):3059-68.