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Consolidation with Loncastuximab Tesirine for Large B-cell Lymphoma Patients in Partial Response After CART: Planned Interim Futility Analysis of a Phase II Trial

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Rationale for Post CAR Consolidation

- **Introduction**. Approximately 30% of patients with large B-cell lymphoma (LBCL) achieve a partial response (PR) after CAR T-cell therapy (CART).
- There is no standard consolidation strategy for these patients, who are typically only observed.
- Loncastuximab tesirine (Lonca) is an antibody-drug conjugate targeting (ADC) CD19.
- We *hypothesized* that Lonca would be a safe and effective consolidation strategy for those who achieve a PR after CART.

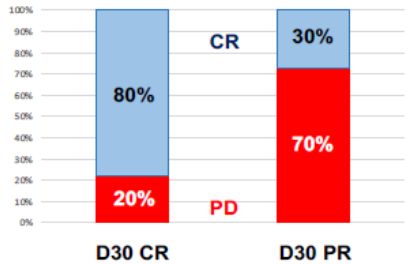

Figure 1: High rates of PD after PR at day 30 post CAR19 infusion.

Trial Overview

- This single arm phase II study (NCT05464719) was conducted between October 2022 and January 2025 (data cut-off 06/2025).
- Adult patients with relapsed or refractory LBCL achieving PR after commercial autologous anti-CD19 CART were included in the study.
- Lonca was administered intravenously, on day 1 of a 21-day cycle, at a dose of 150 mcg/kg for the first 2 cycles, and 75 mcg/kg subsequently, for a total of 6 cycles.
- A first interim futility analysis was planned after the first 10 patients completed treatment, and the study considered futile if less than 4 patients converted to a complete response (CR) or more than 3 experienced an unacceptable toxicity.
- **Inclusion**
  - DLBCL, HGBCL, PMBCL, tFL
  - Treated with SOC CAR T-cell therapy (including upcoming 2nd line)
  - D30 PET-CT evidence of PMR CD19 expression (IHC and/or flow cytometry) not required
- **Exclusion**
  - Treatment with experimental CAR T-cell therapy
  - Previous CNS involvement A
  - NC < 1000/uL, PLT < 50,000/uL

References and Acknowledgements

Scientific references
- Nastoupil J et al, JCO 2020
- Frank MJ et al, Blood 2020
- Al Zaki A et al, Strati P, Blood Adv 2022
- Gouni S et al, Strati P, Blood Adv 2022
- Caimi PF et al, Lancet Onc 2020

Acknowledgements
- Leukemia and Lymphoma Society
- American Society for Transplantation and Cellular Therapy
- **Trial Sponsor ADCT**

Primary and Secondary Objectives

- **Primary Objective Efficacy: conversion to CR**
- **Secondary Objectives Safety and tolerability; efficacy: DOR, PFS, OS**
  EXPLORATORY: pharmacodynamics and biomarkers of response

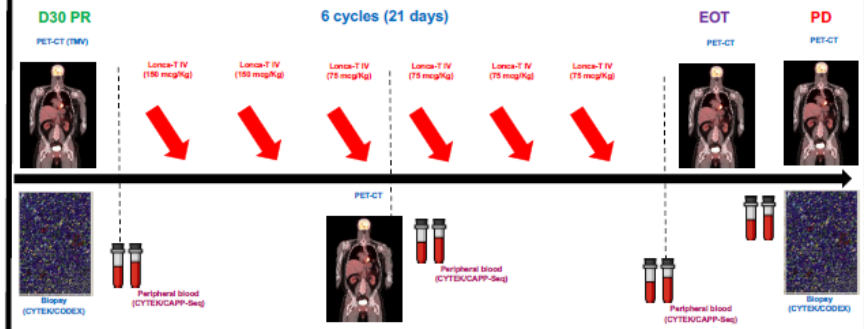

Figure 2: Clinical trial schema with planned correlative endpoints.

Enrolled Patient Characteristics

Patients (N=10)	Number (%), Median [range]
Age (years)	74 [45-84]
Males	8 (80)
Caucasians	9 (90)
ECOG PS > 0	8 (80)
DLBCL/HGBCL	10 (100)
Prior lines of systemic therapy	1 [1-3]
Axi-cel	6 (60)
Maximum standardized uptake volume	6.7 [3.6-20.2]
Maximum standardized uptake volume > 10	4 (40)
Deauville Score 5	3 (30)
Lesion diameter (cm)	3.2 [1.1-7.6]
Absolute neutrophil count (K/uL)	1.9 [1-3.8]
Absolute lymphocyte count (K/uL)	0.8 [0.2-2.8]
Hemoglobin (g/dL)	11.4 [9.5-13.6]
Platelet Count (K/uL)	118 [51-240]
Lactate dehydrogenase (U/L)	224 [170-342]
Ferritin (ng/mL)	647 [108-1591]
C-reactive protein (mg/L)	1 [0.2-55]
Biopsy performed	7 (70)
Viable lymphoma in biopsy	3/7 (43)
CD19+ viable lymphoma	0/3 (0)

Table 1: Baseline characteristics of the first 10 enrolled patients.

Interim Futility Analysis

Patients (N=10)	Number (%), Median [range]
PET-3 conversion rate to CMR	3 (30)
PET-6 conversion rate to CMR	4 (40)

Table 2: CMR conversion to CR at 3 and 6 months.

- This trial succeeded in its interim futility analysis and will continue to enroll.
- After a median follow-up of 19 months (95% CI 4-34 months), none of the 4 patients converted to CR have relapsed. Five patients died: 4 due to PD and 1 due to infection while in CR, 16 months later

Tolerability and Toxicity

Patients (N=10)	Grade 1-2	Grade 3-4
Thrombocytopenia	3 (30)	6 (60)
Neutropenia	2 (20)	6 (60)
Anemia	0 (0)	2 (20)
Infections	7 (70)	1 (10)
AST elevation	5 (50)	1 (10)
ALT elevation	4 (40)	1 (10)
GGT elevation	2 (20)	1 (10)
Pericardial effusion	0 (0)	1 (10)
Fatigue	5 (50)	0 (0)
Skin rash	4 (40)	0 (0)
Ascites	3 (30)	0 (0)
Peripheral edema	3 (30)	0 (0)
Anorexia	2 (20)	0 (0)
Myalgia	2 (20)	0 (0)
Pleural effusion	2 (20)	0 (0)
Photosensitivity	2 (20)	0 (0)

Table 3: Adverse events associated with Lonca consolidation.

- Median number of Lonca cycles was 6 (range, 3-6)
- 1 patient required dose reduction due to thrombocytopenia
- 6 (60%) experienced a cycle delay
  - 3 due to thrombocytopenia
  - 2 due to COVID19 infection,
  - 1 due to paresthesia

Interim Efficacy Results: 40% Conversion to CR

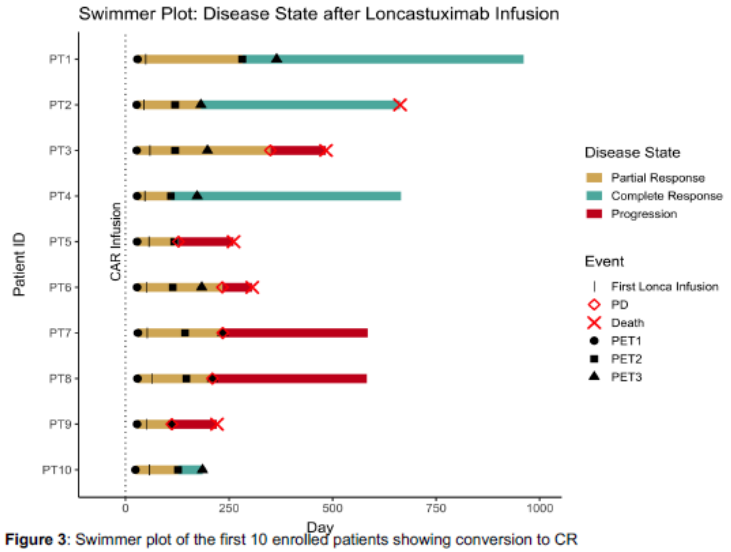

Figure 3: Swimmer plot of the first 10 enrolled patients showing conversion to CR

Conclusions

- Our results indicate that Lonca is a feasible consolidation strategy for LBCL patients who achieve PR after CART.
- This study will continue to enroll another 10 patients to achieve the second interim futility analysis.