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ELEVENTH ANNUAL MEETING

# SAFETY AND EFFICACY OF AN ACADEMIC ANTI-CD19 CHIMERIC ANTIGEN RECEPTOR (CAR) T-CELL THERAPY FOR NON-HODGKIN LYMPHOMA AND ACUTE LYMPHOBLASTIC LEUKEMIA DEVELOPED IN BRAZIL: INCREASING ACCESS IN A PUBLIC HEALTH SYSTEM.

B. G. Pires[1], D. V. Clé[1,2], C. D. Donadel[2], F. M. Gava[1], L.C. Palma[1], G. C. De Santis[1,2], V. Rocha[3], R. T. Calado[1,2], D. T. Covas[1,2]
1. Department of Medical Imaging, Hematology, and Oncology, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, Brazil.
2. Regional Blood Center of Ribeirão Preto, Ribeirão Preto Medical School, Ribeirão Preto, Brazil.
3. Service of Hematology, Transfusion and Cell Therapy, LIM31, University of Sao Paulo Medical School, São Paulo, Brazil

## INTRODUCTION

- The approval of commercial CAR-T cell products has revolutionized cancer treatment, however, its high cost imposes limiting access to this therapy, especially in low and middle-income countries.
- It is urgent to implement strategies that provide equitable access to this treatment, for example cost-efficient CAR-T cell production, including academic and local manufacturing.

## AIM

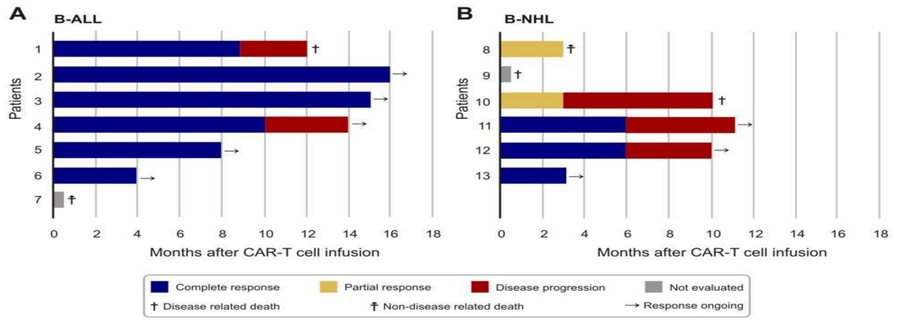
Evaluate the safety and efficacy of administering a locally produced academic anti-CD19 CAR-T cell, in patients diagnosed with relapsed/refractory B-cell non-Hodgkin lymphoma (NHN) or B-cell acute lymphoblastic leukemia (B-ALL).

## METHODS

- This retrospective observational study analyzed safety and efficacy data from 13 patients (6 B-NHL, 7 B-ALL) treated at two centers affiliated to the University of São Paulo in Brazil, between September 2019 and May 2023.
- CAR-T cell manufacturing involved activating mononuclear cells with anti-CD3/anti-CD28 antibodies, followed by transduction using a lentiviral vector encoding second-generation anti-CD19 CAR which signals through a 4-1BB and CD3-ζ endodomain.
- Manufacturing took 10 to 12 days, and the final product was cryopreserved in 5% DMSO, then thawed before infusion at 37°C.

## RESULTS

Median follow-up: 275 days (380 days for ALL, and 185.5 days for NHL).
ALL:
D30 ORR: 86% (CR with negative MRD); One patient died on day 19 due to septic shock.
D90 ORR: 86%. One patient had a positive MRD on day 65. This patient received a HLA-identical sibling hematopoietic stem cell transplantation with a myeloablative TBI-based conditioning regimen 91 days after CAR-T cell infusion.
NHL:
D30 ORR: 83% (50% CR and 33% PR). One patient died on day 16 as a consequence of advanced disease, before response assessment.
D90 ORR: 50%. One patient with a partial response experienced disease progression, and the other one died due to a domestic accident.
After D90, two patients with ALL (D301 and D380) and two patients with lymphoma (D146 and D175. The other patient with CR was still in remission during the last follow up, on D90.




| Patients characteristics *(median/range) | Total (n = 13) | ALL (n = 7) | NHL (n = 6) |
|---|---|---|---|
| Age (yr)* | 34 (7-64) | 24 (7-34) | 40.5 (36-64) |
| Sex (M/F) | 10/3 | 5/2 | 5/1 |
| ECOG 0-1 (%) | 10 (77) | 7 (100) | 3 (50) |
| Prior lines of therapy* | 4 (2-9) | 4 (3-9) | 4 (2-4) |
| Previous HSCT (auto/allo) | 2/6 | 0/6 | 2/0 |
| Days to cell infusion* | 116 (70-645) | 139 (72-405) | 97.5 (70-645) |
| CAR-T cell dose ($x10^6$/kg)* | 2.25 (0.5-9.52) | 2.24 (0.5-5.7) | 3.5 (0.7-9.52) |

| AE of special interest | Any | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|---|---|
| CRS | 11 | 4 | 3 | 4 | 0 | 0 |
| ICANS | 2 | 0 | 1 | 0 | 1 | 0 |
| Hypogammaglobulinemia | 8 | 6 | 2 | 0 | 0 | 0 |
| carHLH | 2 | 0 | 0 | 2 | 0 | 0 |
| Coagulopathy | 4 | 4 | 0 | 0 | 0 | 0 |

## CONCLUSIONS

This study demonstrates the feasibility of an academic CAR-T cell produced in Brazil. While further trials are necessary, our findings indicate that locally manufactured products exhibit a favorable response rate and safety profile, and is a promising option to ensure equitable access to healthcare for patients in LMIC.
We intend to start a phase I/II trial in the fourth quarter of 2023, including 81 patients (48 with ALL-B and 33 with NHL-B).

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Regional Blood Center of Ribeirão Preto Medical School, University of São Paulo, Brazil

## CONTACT INFORMATION

terapia@hemocentro.fmrp.usp.br