TWO-YEAR FOLLOW-UP RESULTS OF C-CAR066, A NOVEL ANTI-CD20 CHIMERIC ANTIGEN RECEPTOR T-CELL (CAR-T) THERAPY IN RELAPSED OR REFRACTORY (R/R) LARGE B-CELL LYMPHOMA (LBCL) PATIENTS AFTER FAILURE OF CD19 CAR-T THERAPY

#2115

P. Li[1], W. Liu[2], L. Zhou[1], S. Ye[1], J. Zhu[3], J. Huang[3], J. Li[3], C Zheng[3], S Zhu[3], X. Yao[3], K. Zhu[4], Y. Yao[3], A. Liang[1], and D. Zou[2]

[1]Tongji Hospital of Tongji University, Shanghai, China
[2]State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China
[3]Cellular Biomedicine Group, Inc., Shanghai, China
[4]University of Maryland School of Medicine, Baltimore, Maryland, USA

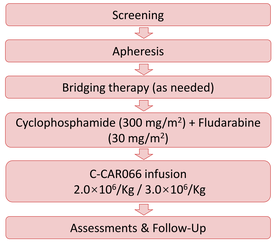
INTRODUCTION

- Clinical outcomes in patients with relapsed/refractory large B-cell lymphoma (r/r LBCL) following CD19 CAR-T therapy are poor.
  - The objective response rate (ORR) and complete response (CR) rate with salvage therapies, including bispecific antibodies and antibody-drug conjugates, were 18-54.1% and 3.8-35%, respectively.[1–9]
  - Median progression-free survival (PFS) was 1.4-3.8 months and overall survival (OS) was 3.8-9.3 months.[1–6]
- C-CAR066, a novel CAR-T therapy targeting the CD20 antigen, had shown a favorable safety profile and promising efficacy in a first-in-human study in patients with r/r LBCL progressed after CD19 CAR-T therapy.[10]
  - At a median follow-up of 4.2 months, the ORR was 100%, with 70.0% (7/10) achieving CR.[10]
- Here we present the updated results to include more patients (N=14) and a longer follow-up of 27.7 months.

METHODS

- This is an open-label, dose-finding, Phase I investigator-initiated trial conducted at two clinical sites in China with a 2-year follow-up. (Figure 1).
- **Primary objective:**
  - Safety: Incidence and severity of treatment-emergent adverse events (AEs).
- **Secondary objectives:**
  - Efficacy: ORR and CR per Lugano 2014 criteria, duration of response (DOR), PFS, OS, and pharmacokinetics
- **Key eligibility criteria:**
  - Aged ≥18 years
  - Historically confirmed diffuse large B-cell lymphoma (DLBCL, including de novo and transformed follicular lymphoma [tFL]), primary mediastinal B-cell lymphoma, follicular lymphoma, and mantle cell lymphoma
  - At least one measurable lesion (longest diameter ≥ 1.5 cm)
  - Prior CD19 CAR-T therapy
  - Positive for CD20

Figure 1. Study design



*As of the cutoff date of Oct 10. 2023, a total of 14 patients received C-CAR066 infusion, 4 had an ongoing CR.

RESULTS

Baseline characteristics

- A total of 14 patients, with a median age of 54.5 years, received C-CAR066, the majority of whom had DLBCL (71.4%) and were Ann Arbor Stage II/IV (85.7%) (Table 1). All patients had received prior CAR-T therapy, and 12 had a response.

Table 1. Baseline patient characteristics

Characteristics	N=14
Median (range) age, years	54.5 (37–67)
≥ 65 years, n (%)	2 (14.3)
Male, n (%)	5 (35.7)
NHL subtype, n (%)	
DLBCL	10 (71.4)
tFL	4 (28.6)
ECOG PS, n (%)	
0	5 (35.7)
1	9 (64.3)
IPI score 3–4, n (%)	8 (57.1)
Ann Arbor Stage III/IV, n (%)	12 (85.7)
Double-expressor lymphoma, n (%)	7 (50.0)
SPD, n (%)	
≥4000 mm²	6 (42.9)
<4000 mm²	8 (57.1)
Median (range) number of prior treatment lines	5 (2–7)
≥4, n (%)	12 (85.7)
Prior ASCT, n (%)	2 (14.3)
Prior CAR-T target, n (%)	
CD19	12 (85.7)
CD19/CD79b or CD19/CD22	2 (14.3)
Best response of prior CAR-T therapy, n (%)	
CR	2 (14.3)
PR	10 (71.4)
SD/PD	2 (14.3)
Median (range) DOR of prior CAR-T therapy, months	1.9 (0.4–6.1)
Median (range) time from prior CAR-T to C-CAR066, months	5.5 (3.4–14.2)
Patients receiving bridging therapy, n (%)	7 (50.0)

ASCT: autologous stem cell transplantation; CAR-T: chimeric antigen receptor T-cell; CR: complete response; DLBCL: diffuse large B-cell lymphoma; ECOG PS: Eastern Cooperative Oncology Group Performance Status; IPI: International Prognostic Index; NHL: non-Hodgkin lymphoma; PD: progressive disease; PR: partial response; SPD: sum of the products of the longest perpendicular diameters; tFL: transformed follicular lymphoma.

Adverse Events of Special Interest (Table 2)

- Only one patient experienced grade 4 CRS on Day 6, which resolved on Day 10 after tocilizumab and steroid treatment.
- No patient experienced ICANS events.
- 8 patients experienced infections, only 2 were grade 3 (1 sepsis, 1 pneumonia). Most common infections were respiratory tract infection.
- No SPM and new safety signals were observed with longer follow-up.

Table 2. Adverse Events of Special Interest

AESI, n (%)	N=14
CRS • Grade≥3 • Median days to onset, d (range) • Median days to resolution, d (range)	12 (85.7) 1 (7.1) 5.5 (2–15) 4.0 (1–15)
ICANS	0
Infections • Grade≥3	8 (57.1) 2 (14.3)
Prolonged Cytopenias* • Neutropenia • Anemia • Thrombocytopenia	4 (28.6) 3 (21.4) 2 (14.3) 2 (14.3)
SPM	0

**Grade 3 or higher cytopenias not resolved by Day 30 following C-CAR066 infusion .*
AE: adverse event; CRS: cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome.

Serious Adverse Event (Table 3)

- 4 patients had 5 SAEs after C-CAR066 infusion.
- Only 2 SAEs in 1 patient were related to C-CAR066, which were CRS and myelosuppression
- All SAEs except pneumonia were observed within 6 months after C-CAR066 infusion.
- As of October 10, 2023, 7 deaths occurred. All were due to disease progression.

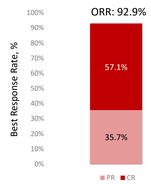
Table 3. Serious Adverse Events

SAEs, n (%)	N=14	Onset Day
SAEs	4 (28.6)	
• C-CAR066-related CRS Myelosuppression	1 (7.1) 1 (7.1) 1 (7.1)	 Day 11 Day 32
• C-CAR066-unrelated Abdominal pain Platelet count decreased Pneumonia	3 (21.4) 1 (7.1) 1 (7.1) 1 (7.1)	 Day 30 Day 112 Day 404

Response (Table 4)

- The ORR was 92.9% with a CR rate of 57.1%.
- Median DOR was 8.3 months (95% CI, 1.7–NA).

Table 4. Response

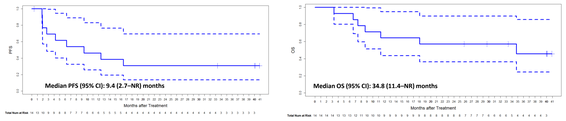


Response	N=14
ORR, n (%)	13 (92.9)
CR	8 (57.1)
PR	5 (35.7)
Median time to response, months (range)	1.0 (0.9–2.8)
Median time to CR, months (range)	2.5 (1.0–2.8)
Median DOR, months (95% CI)	8.3 (1.7-NA)
Median follow-up duration, months (range)	27.7 (3.3–40.9)

PFS and OS (Figure 2)

- With the median follow-up of 27.7 months, median PFS was 9.4 months (2.7 – NA). 4 (28.6%) patients remain in CR for more than 30 months.
- The Kaplan-Meier estimate of median OS was 34.8 months (11.4 – NA).

Figure 2. Kaplan–Meier Estimates of the Progression-free Survival, and Overall Survival

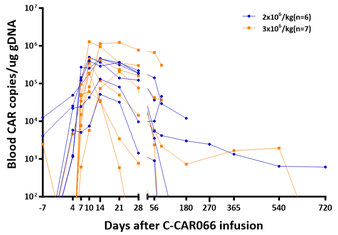


CI: confidence interval; CR: complete response; DOR: duration of response; NR: not reached; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; PR: partial response.

Pharmacokinetic profile of C-CAR066 (Figure 3)

- The pharmacokinetic profile of C-CAR066 showed that C-CAR066 has robust expansion and good persistence

Figure 3. Pharmacokinetic profile of C-CAR066



Pharmacokinetic Parameter	N=13*
Median (range) C_{max}, copies/µg gDNA	398,996 (51,667–1,286,932)
Median (range) $AUC_{0-28days}$, day*copies/µg gDNA	4,437,474 (431,534–17,842,217)
Median (range) T_{max}, days	11 (10–23)
Median (range) T_{last}, days	59 (21–770+)

**13 patients had assessable pharmacokinetic data at day 28.*
AUC: area under the plasma concentration versus time curve; CAR: chimeric antigen receptor; Cmax: maximum plasma concentration; gDNA: genomic DNA; Tlast: time of last measurable concentration; Tmax: time to reach Cmax.

CONCLUSIONS

- **C-CAR066 demonstrated a manageable safety profile.**
  - Most cases of CRS were grade 1/2 with median time to onset of 5 days. No ICANS occurred.
  - No new safety signals were observed in this updated 2-year follow-up.
- **C-CAR066 produced a deep and durable response in patients with r/r LBCL in whom prior CD19 CAR-T therapy has failed.**
  - ORR was 92.9%, with 57.1% CR.
  - With the median follow-up of 27.7 months, median DOR and PFS were 8.3 months (1.7 – NA) and 9.4 months (2.7 – NA) , respectively. 4 (28.6%) patients remain in CR for more than 30 months.
  - The Kaplan-Meier estimate of median OS was 34.8 months (11.4 – NA).
- **C-CAR066 could provide a treatment option for patients progressed after prior CD19 CAR-T therapy.**
- **Further investigation of C-CAR066, including in other population, will be led by Janssen R&D.**
  - An open-label study (NCT05784441) in relapsed or refractory B-cell non-Hodgkin lymphoma is ongoing.

REFERENCES

1. **Spiegel JY, et al**. *Blood*. 2021;137:1832–5.
2. **Alarcon Tomas A, et al.** *Leukemia.* 2023;37:154–63.
3. **Chow VA, et al.** *Am J Hematol.* 2019;94:E209–13.
4. **Di Blasi R, et al**. *Blood.* 2022;140:2584–93.
5. **Caimi PF, et al.** *Clin Lymphoma Myeloma Leuk.* 2022;22:e335–9.
6. **Budde LE, et al.** J Clin Oncol. 2022 Feb 10;40(5):481-491.
7. **Dickinson MJ, et al.** N Engl J Med. 2022 Dec 15;387(24):2220-2231.
8. **Thieblemont C, et al.** J Clin Oncol. 2023 Apr 20;41(12):2238-2247.
9. **Bannerji R, et al.** Lancet Haematol. 2022 May;9(5):e327-e339.
10. **Liang A, et al.** *J Clin Oncol.* 2021;39(Suppl 1):2508.

ACKNOWLEDGEMENTS

This study was sponsored by Cellular Biomedicine Group, Inc.

CONTACT INFORMATION

P. Li: lilyforever76@126.com

D. Zou: zoudehui@ihcams.ac.cn