CT196

Early results of a safety and efficacy study of allogeneic TruUCAR™ GC502 in patients with relapsed/refractory B-cell acute lymphoblastic leukemia (r/r B-ALL)

Shiqi Li[1*], Xinxin Wang[2*], Zhongtao Yuan[1], Lin Liu[1], Yu Li[1], Jia Liu[2], Jiaping He[2], Zhimin Li[2], Wei Zhao[2], Jianning Ge[2], Yajin Ni[2], Lianjun Shen[2], Wei Cao[2], Xi Zhang[3], Martina Sersch[2], Sanbin Wang[1]

[1] 920th Hospital of Joint Logistics Support Force of People's Liberation Army of China, Kunming, China, [2] Gracell Biotechnologies, Shanghai, China. [3] The Second Affiliated Hospital of Army Medical University, Chongqing, China.
*: Co-first author

BACKGROUND

- CD19 targeted autologous CAR-T therapies have been approved for the treatment of r/r B-ALL and greatly improved outcome. However, some patients may not be eligible to receive autologous CAR-T.
- TruUCAR™ GC502 is an allogeneic, universal CAR-T product with CD19/CD7 dual directed CAR. Preclinical data of GC502 were reported at ASH 2021 (Abstract 148500).
- Here, we report early clinical results from a phase I open-label, non-randomized, prospective investigator initiate trial (IIT) of GC502 in r/r B-ALL patients.

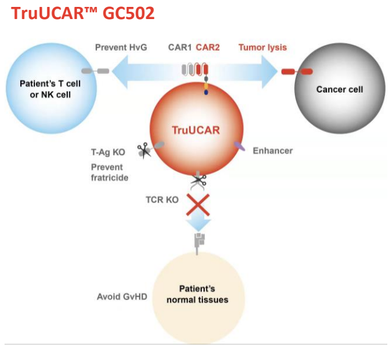
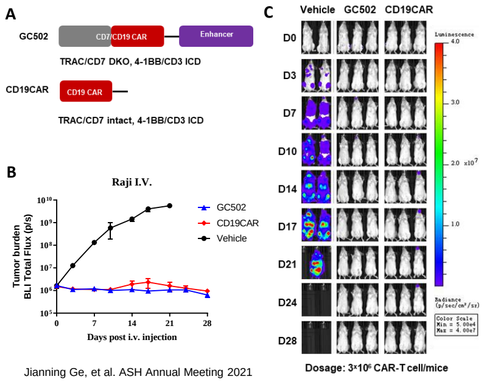


Figure 1. GC502 Demonstrated Robust anti-leukemia Efficacy in B-ALL Xenograft Model



Jianning Ge, et al. ASH Annual Meeting 2021

A. Schematic illustration of GC502 and CD19 CAR.
B-C. GC502 demonstrated potent CD19 CAR efficacy a Raji-based murine xenograft model for B-ALL.

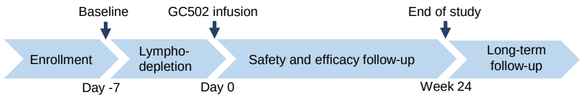
METHODS

Study Design
Single-arm, open-label study to evaluate the safety and anti-leukemia efficacy

Key inclusion criteria
- r/r B-ALL patients with CD19+ expression
- Patient expected survival > 3 months with ECOG score 0-1
- No severe active infection

Endpoints
- Primary endpoints:
  - Dose limiting toxicities (DLTs) in 4 weeks
  - Adverse events within 12 weeks
- Second endpoints:
  - Objective response rate (ORR, measured by CR+CRi) at 4 and 12 weeks
  - Progression free survival (PFS), Objective survival (OS) and duration of response (DOR)
  - Pharmacokinetics (PK) of GC502 UCAR-T cells

Figure 2. Study Design for NCT05105867



GC502 Dose Escalation	Dose
Dose Level -1	0.5 x 10^7 CAR+ T cells/kg
Dose Level 1	1.0 x 10^7 CAR+ T cells/kg
Dose Level 2	1.5 x 10^7 CAR+ T cells/kg
Dose Level 3	2.0 x 10^7 CAR+ T cells/kg
Lymphodepletion regimens	**Dose**
Fludarabine	30mg/m^2/day x 4-5 days
Cyclophosphamide	750 - 2000mg/m^2/day x 4-5 days

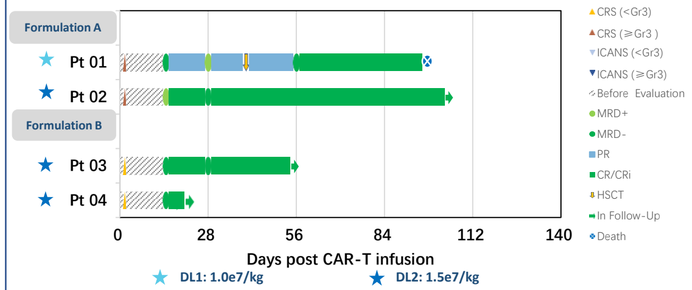
Table 1. Patient Demographics and Disease Characteristics

Characteristic	n = 4
Median age (range) – years	26 (15-34)
Disease at screening relapsed/refractory B-ALL	4
Number of prior lines of therapy 1 to 3 ≥4 Median (range)	 0 3 5 (4-7)
Risk Stratification*	2
Extramedullary lesions	1
Prior CART therapy*	4
Prior allo-HSCT	1
Bone marrow tumor burden at baseline(%) < 5 5 to 25 > 25 Median (range)	 0 2 2 48.1 (19.5-92)

Data cut-of as of Jan. 28th
*1 patient was diagnosed with ph+; 1 patient has extramedullary lesions
*Prior CART including CD19 and CD19-CD22 CART

RESULTS

Figure 3. Response Assessment



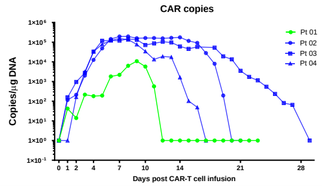
- **4** pts had received a single dose of GC502: 1 at 1x10^7/kg, 3 at 1.5x10^7/kg
- **3/4** pts achieved MRD- complete response (MRD- CR/CRi)
- 1 pt was assessed MRD- in BM but was assessed PR due to EM disease and received allo-HSCT at D39

Table 2. Treatment emergent adverse events within 28 days

N=3	All Grades (n, %)	Grade 1-2 (n, %)	Grade 3 (n, %)	Grade 4 (n, %)	Grade 5 (n, %)
AEs* related to GC502					
Cytokine release syndrome (CRS)	3 (100)	1 (33.3)	2 (66.7)	0 (0)	0 (0)
Acute graft-versus-host disease (aGvHD)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
ICANS	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
AEs* related to lymphodepletion and/or GC502					
Febrile neutropenia	3 (100)	0 (0)	3 (100)	0 (0)	0 (0)
Anemia	3 (100)	0 (0)	3 (100)	0 (0)	0 (0)
Thrombocytopenia	2 (66.7)	0 (0)	1 (33.3)	1 (33.3)	0 (0)
γ glutamine transferase increased	3 (100)	1 (33.3)	2 (66.7)	0 (0)	0 (0)
ALT increased	3 (100)	0 (0)	3 (100)	0 (0)	0 (0)
AST increased	2 (66.7)	0 (0)	2 (66.7)	0 (0)	0 (0)

AE, Adverse event; ICANS, Immune effector cell-associated neurotoxicity syndrome
ICANS & CRS will be graded using the ASTCT Consensus Grading (Lee et al. 2019)
AEs were graded according to CTCAE v5.0

Figure 4. GC502 Expansion in Peripheral Blood



- GC502 expansions measured by qPCR were peaked around day 7-13
- 3/4 pts achieved MRD-CR/CRi. The patient who did achieve a PR at day 28 and received allo-HSCT at day 39, did not show adequate cellular expansion

RESULTS

Table 3. GC502 Expansion in Peripheral Blood was Analyzed by qPCR

Patient #	Tumor Burden	Dose Level	Peak TruUCAR Copies/ug DNA
Pt 01	92%	1	10849（Day9）
Pt 02	61%	2	195400（Day8）
Pt 03	20%	2	146458（Day8）
Pt 04	19.5%	2	153432（Day7）

CONCLUSION

First-in-human data for TruUCAR™ GC502 in patients with r/r B-ALL

- **TruUCAR™ GC502 showed very promising early responses**
  - **Heavily pretreated patients including those who had received prior CART therapy including CD19 and CD19-CD22 CART**
  - **3/4 patients achieved MRD-CR/CRi**
- **TruUCAR™ GC502 showed manageable and reversible adverse events in 2 different dose levels and 2 different formulations**
  - **Formulation A: 2/2 Gr 3 CRS**
  - **Formulation B: 2/2 Gr 2 CRS**
  - **No Gr 4/5 CRS, no ICANs, no GVHD**
- **TruUCAR™ GC502 expansion observed in all patients**
- **Further evaluation in future studies is warranted**

ACKNOWLEDGEMENTS

We would like to thank the patients, their families, the investigators and all the caregivers involved in this study and Gracell Biotechnologies for providing TruUCAR™ GC502.

CONTACT INFORMATION

- **E-mail:**
  Dr. Sanbin Wang: Sanbin1011@163.com
  Dr. Shiqi Li: Lystch@outlook.com