#7562: Updated Clinical Results of First-in-Human Study of CD19/BCMA Dual-Targeting FasT CAR-T GC012F for Patients with Relapsed/Refractory B-cell Non-Hodgkin's Lymphoma

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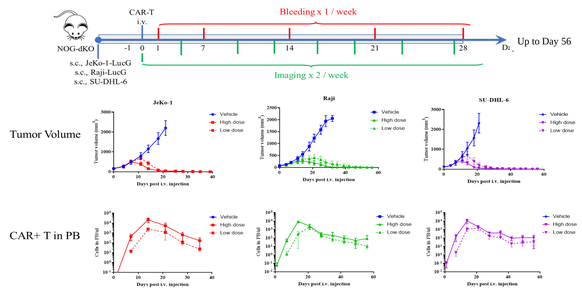
Background:

- CD19-directed CAR-T cell therapy has been demonstrated to be a valuable treatment option for relapsed/refractory B-cell non-Hodgkin's lymphoma (r/r B-NHL)
- It has been shown that 39% to 97% of clinical samples of B-NHL also express BCMA
- To further improve safety and efficacy, we have developed a CD19 and BCMA dual-targeting CAR-T, GC012F, for the treatment of r/r B-NHL



GC012F completely eradicated s.c. inoculated JeKo-1, Raji and SU-DHL-6 in NOG-dKO xenograft model.

Methods:

- Study Design

  Single-center, open label, single-arm investigator-initiated study (N=9-18)

- Key inclusion criteria
  - Male or Female between 18 to 75 years
  - r/r B-NHL with CD19+ and/or BCMA+ expression
  - At least one measurable tumor focus: the longest diameter of nodular lesions ≥ 1.5 cm, and the longest diameter of extra-nodal lesions ≥ 1.0 cm (per 2014 Lugano)
  - Expected survival ≥ 3 months

- Endpoints
  - Primary endpoint:
    - DLTs and AEs
  - Secondary endpoints:
    - ORR (CR+PR), PFS, OS and DOR
    - Pharmacokinetics (PK) of GC012F CAR-T cells

Enrollment → Apheresis → Lympho-depletion (Day -5 to -3) → GC012F infusion (Day 0) → Post-treatment assessment and Long-term follow-up

GC012F Dose Escalation	Dose
Dose Level -1	0.5-1 x 10^5 CAR+ T cells/kg
Dose Level 1 (initial dose)	2-3 x 10^5 CAR+ T cells/kg
Dose Level 2	4-6 x 10^5 CAR+ T cells/kg
Dose Level 3	8-12 x 10^5 CAR+ T cells/kg
Lymphodepletion regimens	**Dose**
Fludarabine	25-30mg/m^2/day x 3 days
Cyclophosphamide	250-300mg/m^2/day x 3 days

Data cut-off April 12th, 2023

*The **CD19 and BCMA** dual-targeting CAR-T, **GC012F**, manufactured on the **novel next-day FasT CAR-T process**, was developed for the treatment of r/r B-NHL.*

- In preclinical studies GC012F demonstrated a younger phenotype of CAR-T cells and highly effective tumor killing activity in animal models.
- This first-in-human trial (ChiCTR2100047061) of GC012F for the treatment of r/r B-NHL showed a manageable safety profile and promising clinical responses.
- GC012F CAR-T cells were detectable in the tumor biopsies, indicating the infiltration of CAR-T cells into the tumor lesions.

We would like to thank the patients, their families, the investigators and all the caregivers involved in this study and Gracell Biotechnologies for providing FasT CAR™ GC012F.
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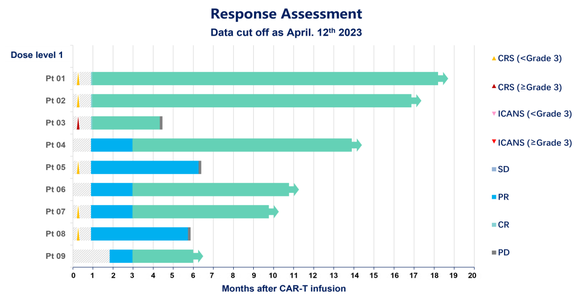
Patient Demographics and Disease Characteristics

Characteristic	n = 9
Median age, years (range)	52 (18-60)
Male, n (%)	5 (56)
Lymphoma subtype, n (%) DLBCL	9 (100)
[1]Disease stage, n (%) III/IV	8 (89)
ECOG 1, n (%)	9 (100)
Median prior lines of therapy, n (range)	2 (2-3)
IPI score ≥ 3, n (%)	4 (44)
SPD, mm^2 (range)	2690.81 (408.3 - 13325.96)

Characteristic	n = 9
Prior auto-SCT, n (%)	2 (22)
Baseline LDH > UNL, n (%)	3 (33)
Immuno-phenotype, n (%)	
CD19	9 (100)
BCMA	7/8 (88)
Prior systemic anti-cancer therapy	
CD20 mAB	9 (100)
BTK inhibitors	4 (44)
Relapse/refractory subgroup, n (%)	
Relapse	8 (89)
Refractory	1 (11)

Results:

-Response Assessment



- High response rate
  - ORR was 100% (9/9) at month 3
  - CR rate was 78% (7/9) at month 3 and 67% (6/9) at month 6

-Safety

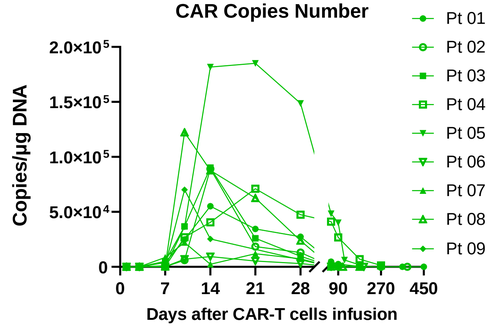
N=9	All Grades n(%)	Grade ≥3 n(%)
Hematologic TEAEs* within 28 days		
Neutropenia	9 (100)	7 (78)
Leukopenia	9 (100)	5 (56)
Thrombocytopenia	6 (67)	3 (33)
lymphocytopenia	3 (33)	1 (11)
Anemia	4 (44)	1 (11)
Non-Hematologic TEAEs* within 28 days		
AST increased	3 (33)	0 (0)
ALT increased	2 (22)	0 (0)
Hypoalbuminemia	2 (22)	0 (0)
Hypocalcemia	2 (33)	0 (0)
Hyponatremia	1 (11)	0 (0)
Hypokalemia	1 (11)	0 (0)
Hypophosphatemia	1 (11)	0 (0)

N=9	CRS[&] n(%)	ICANS[&] n(%)
Grade 1	5 (56)	0 (0)
Grade 2	0 (0)	0 (0)
Grade 3	1 (11)	0 (0)
Grade 4/5	0 (0)	0 (0)

- Favorable safety profile
  - Gr1 CRS: 5/9
  - Gr3 CRS: 1 in dose level 3x10^5/kg over 2 days
  - No grade 4/5 CRS
  - No ICANS in any dose level

*AE were graded according to CTCAE v5.0, TEAE- treatment emergent adverse event, [&]CRS – Cytokine Release Syndrome - ASBMT consensus grading, ICANS – Immune Effector Cell-Associated Neurotoxicity Syndrome

GC012F Expansion in Peripheral Blood



- Good expansion observed in all patients
- Median peak copy numbers: 71,000 copies/μg DNA (range 9263 - 185,039)
- Median peak time: 14 days (range 9 - 21)