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Phase I open-label single-arm study of dual targeting BCMA and CD19 FasTCAR-T cells (GC012F) as first-line therapy for transplant-eligible newly diagnosed high-risk multiple myeloma

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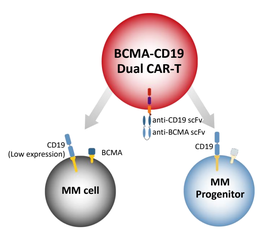
INTRODUCTION

High-risk disease in NDMM and GC012F

GC012F: Targeting BCMA/CD19 is designed to drive fast, deep and durable responses in multiple myeloma (MM) patients

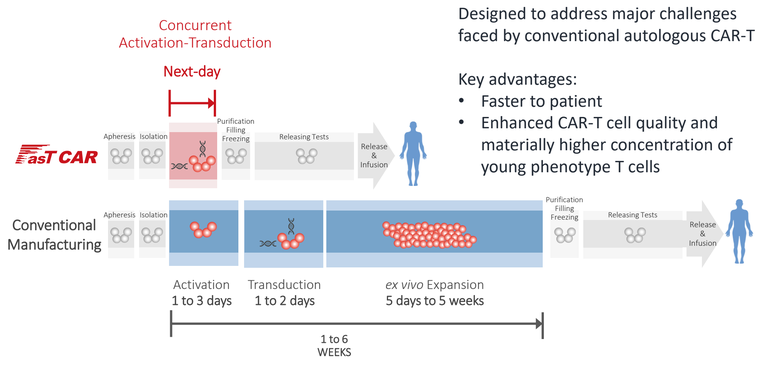


- BCMA is universally expressed on malignant plasma cells[1]
- CD19 is expressed on both multiple myeloma cells and their progenitors[2], making it a valid therapeutic target to treat multiple myeloma

1. Tai YT, Anderson KC. Immunotherapy. 2015;7(11):1187-1199.
2. Boucher K, Parquet N, Widen R, et al. Clin Cancer Res. 2012;18(22):6155-6168.

FasTCAR Cuts Manufacturing Time to Next-Day

Combines Activation & Transduction Steps, and Eliminates Need for *ex vivo* Expansion



Designed to address major challenges faced by conventional autologous CAR-T

Key advantages:
- Faster to patient
- Enhanced CAR-T cell quality and materially higher concentration of young phenotype T cells

METHODS

Single-center, open label, single-arm IIT[1] study (N=19)

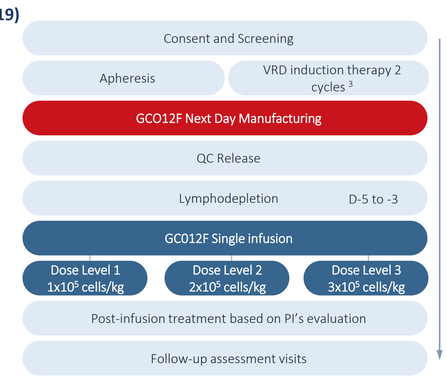
FPI August 2021

Patients continue to be assessed for response

Data cut-off **Aug 1st 2023**

Endpoints
- Primary: Adverse Events
- Secondary: ORR, BOR, DOR, MRD; PK/PD

Key eligibility criteria
- High-risk[2], transplant eligible, newly-diagnosed multiple myeloma (NDMM)
- Measurable disease
- 18-70 years old
- ECOG 0-2
- Expected survival ≥3 months



[1] IIT – Investigator Initiated Study
[2] High-risk is defined as meeting at least one of the following: a) R-ISS stage II or III; b) High-risk cytogenetics: del17p, t(4;14), t(14;16), or 1q21 ≥4 copies; c) Extramedullary disease; d) IgD or IgE subtype; e) High-risk definition according to mSMART3.0; f) LDH > the upper limit of normal.
[3] 2 cycles of induction therapy VRD (PAD cycle in one case) are given before or after apheresis.

RESULTS – BASELINE & SAFETY

Baseline Characteristics

Baseline Characteristics (N=19)	
Median age, years (range)	59 (43-69)
Male, n (%)	12 (63)
Type of myeloma, n (%)	
IgG	8 (42)
IgA	6 (32)
IgD	2 (11)
Light chain	3 (16)
Induction therapy, n (%)	
2 cycles RVd [1]	18 (95)

Baseline Characteristics (N=19)	
High-risk, n (%)	19 (100)
R-ISS stage II/III	17 (89)
High-risk cytogenetics[2]	9 (50)
Extramedullary plasmacytoma ≥1	12 (63)
High-risk as mSMART3.0	18 (95)
LDH > upper limit of normal	3 (16)
ECOG performance status, n (%)	
0	3 (16)
1	10 (53)
2	6 (32)

[1] except one cycle of PAD (bortezomib, doxorubicin, and dexamethasone)
[2] 18 pts evaluable for cytogenetics high risk.

Safety Profile

All CRS were Grade 1 or 2 and resolved within 4 days · No ICANS or any neurotoxicity was observed

N=19	CRS[1], n (%)	ICANS[2], n (%)
Grade 1	5 (26)	0 (0)
Grade 2	1 (5)	0 (0)
Grade 3	0 (0)	0 (0)
Grade 4-5	0 (0)	0 (0)
All grade	6 (32)	0 (0)

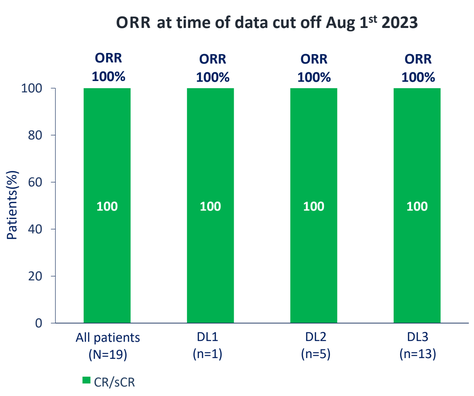
CRS any grade	Median (days)	Range (days)
Time to onset	7	6-9
Duration	1	1-4

N=19	All Grades, n (%)	Grade ≥3, n (%)
Hematologic TEAEs* (≥20% All Grades)		
Neutropenia	16 (84)	8 (42)
Lymphopenia	16 (84)	13 (68)
Leukopenia	17 (89)	10 (53)
Thrombocytopenia	5 (26)	0 (0)
Anemia	8 (42)	1 (5)
Lung infection	2 (11)	2 (11)
Upper respiratory infection	4 (21)	3 (16)
Non-Hematologic TEAEs* (≥20% All Grades)		
LDH increased	8 (42)	0 (0)
Hypoalbuminemia	8 (42)	0 (0)

*AEs were graded according to CTCAE v5.0; TEAE-treatment emergent adverse event; LDH-Lactase dehydrogenase.
[1]CRS-Cytokine Release Syndrome, graded by ASTCT Consensus; treated with tocilizumab and/or glucocorticoids.
[2]ICANS-Immune Effector Cell-Associated Neurotoxicity Syndrome, graded by ASTCT Consensus.

RESULTS – EFFICACY

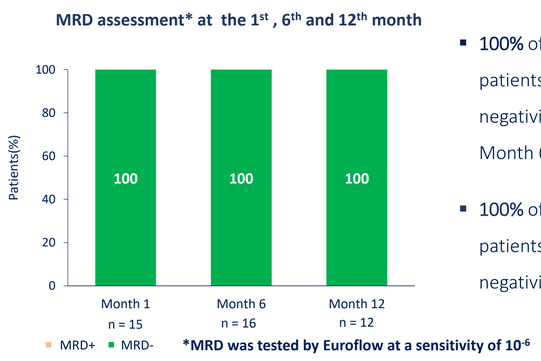
Efficacy Assessment – ORR



- ORR = 100% (19/19) patients
  - Best response achieved to date
  - 100% (19/19) MRD- sCR
  - 100% (19/19) VGPR or better
- Median duration of response (DOR) was not reached at data cut off
- Median duration of follow up 15.3 months (range: 3.1 – 24.5 months)

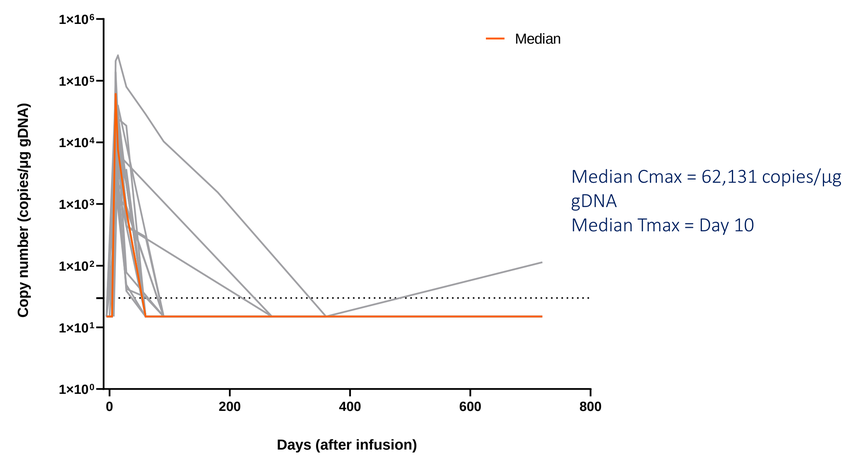
Efficacy Assessment - MRD Negativity

Data cut-off **Aug 1st 2023**



- **100%** of MRD evaluable patients achieved MRD negativity at Month 1, Month 6 and Month 12
- **100%** of MRD evaluable patients achieved MRD negativity in all dose levels

RESULT-PHARMACOKINETICS



Median Cmax = 62,131 copies/µg gDNA
Median Tmax = Day 10

CONCLUSIONS

- **GC012F shows a favorable safety profile in newly diagnosed multiple myeloma patients**
  - Only 32% (6/19) patients experienced Grade 1-2 CRS
  - No Grade ≥3 CRS and no ICANS or any neurotoxicity observed
- **100% (19/19) ORR in *high risk* population**
  - 100% sCR
  - Patients continue being followed up for durable response
- **100% (19/19) MRD negativity at sensitivity of 10^{-6}**
- **FAST and DEEP responses with median DOR not reached**
- **GC012F BCMA/CD19 dual-targeting CAR-T cell therapy shows very encouraging anti-tumor activity in transplant-eligible, high risk, newly diagnosed multiple myeloma patients**

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3.Hua Jiang, et al. ASH Annual Meeting 2020, 178.

CONTACT INFORMATION

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