EHA2024
ORAL PRESENTATION

A phase I open-label single-arm study of dual targeting BCMA and CD19 FasTCAR-T AZD0120 (GC012F) as first-line therapy for transplant-eligible newly diagnosed high-risk multiple myeloma

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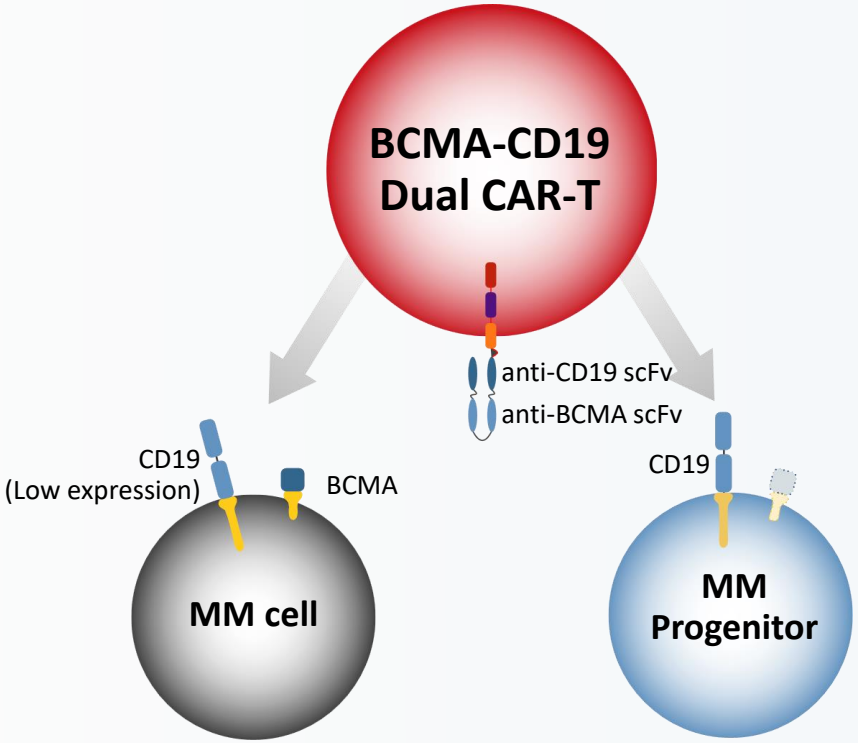
Disclosures

Hereby I confirm that I don't have a conflict of interest.

Introduction

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



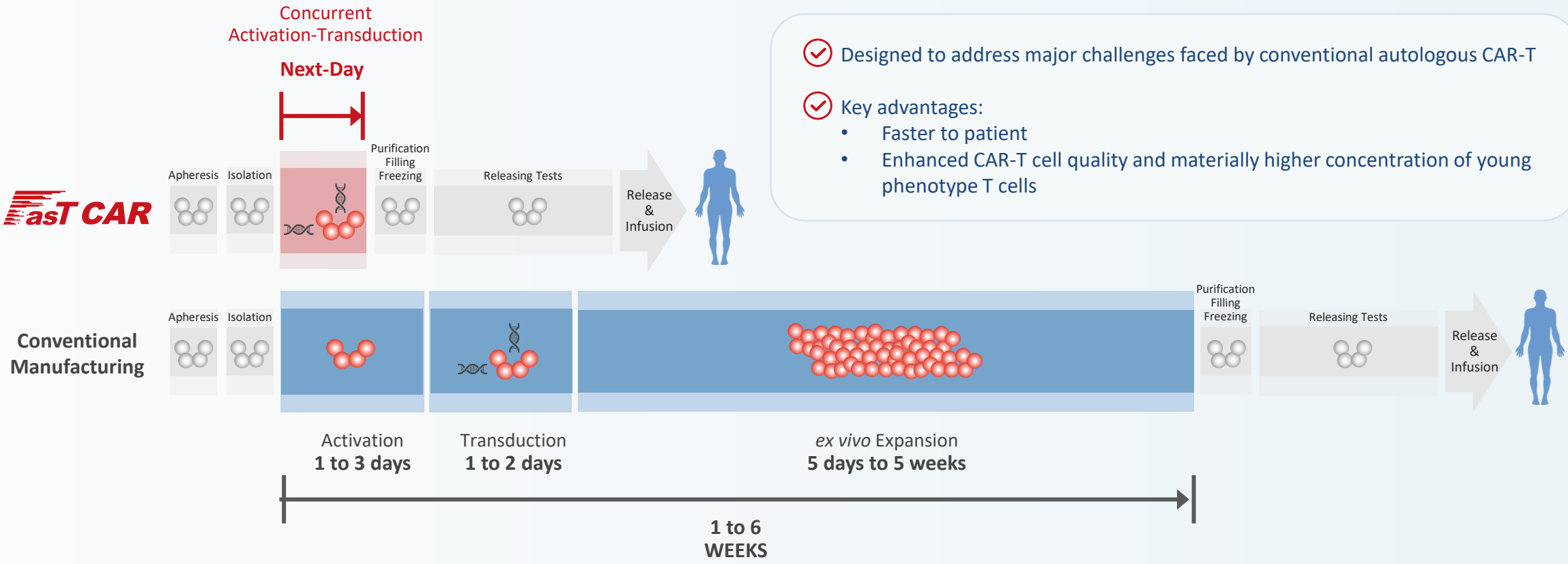
MOA of GC012F for MM

- 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.

GC012F: FasTCAR Process Significantly Shortens Manufacturing Time and Improves T Cell Fitness

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

① Juan Du. et al. 2023 ASH (Oral)
② Juan Du. et al. 2023 ASCO (Oral)
③ Juan Du. et al. 2023 IMS (Poster)
④ Juan Du. et al. 2022 EHA (Poster)
⑤ Juan Du. et al. 2022 ASH (Oral)
⑥ Juan Du. et al. 2022 EHA (Oral)
⑦ Juan Du. et al. 2022 ASCO (Oral)
⑧ Juan Du. et al. 2019 ASH (Oral)

GC012F: Study Design

Single-center, open label, single-arm IIT[1] study (N=22)

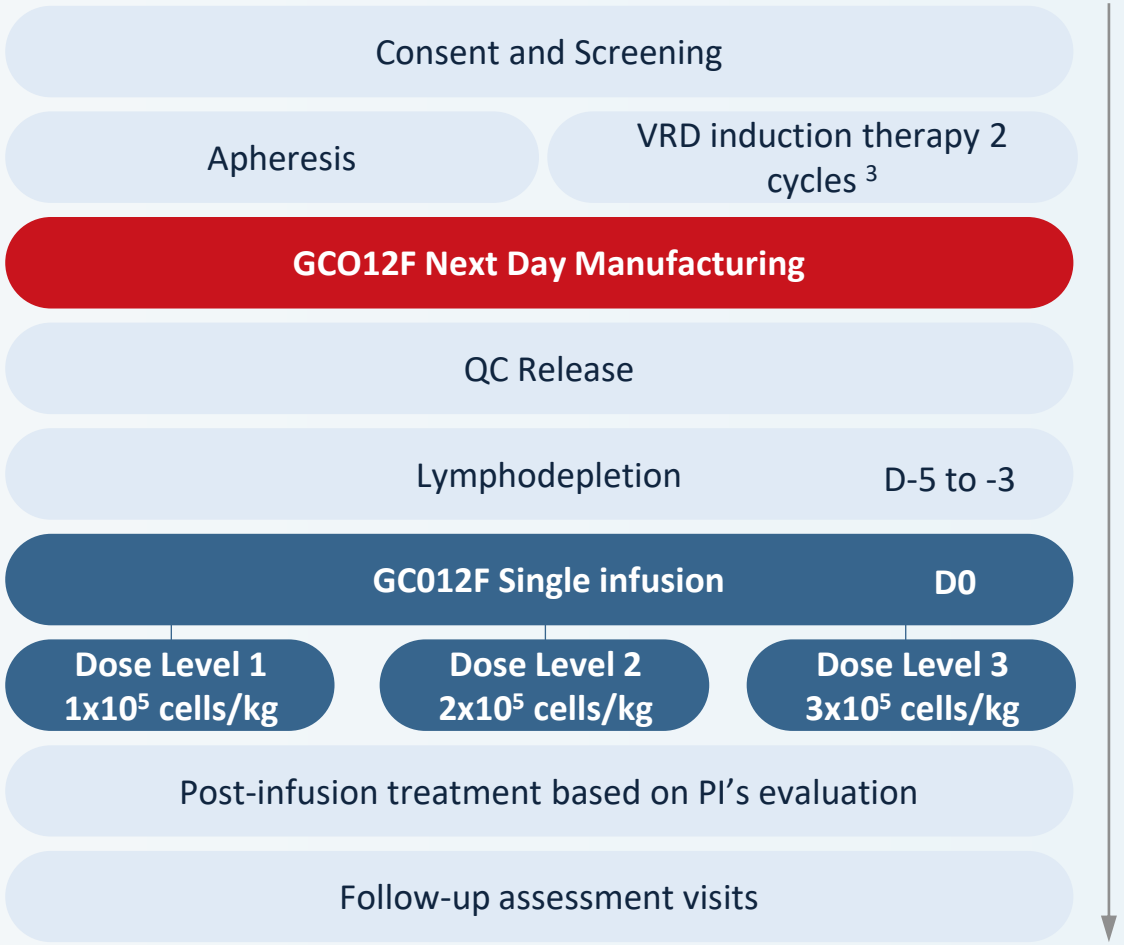
- FPI August 2021
- Patients continue to be assessed for response
- Data cut-off **Apr 23rd 2024**

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.

GC012F: Baseline Characteristics

Baseline Characteristics (N=22)	
Median age, years (range)	59 (43-69)
Male, n (%)	14 (64)
Type of myeloma, n (%)	
IgG	9 (41)
IgA	7 (32)
IgD	2 (9)
Light chain	4 (18)
Induction therapy, n (%)	
2 cycles RVd [1]	21 (95)

Baseline Characteristics (N=22)	
High-risk, n (%)	22 (100)
R-ISS stage II/III	20 (91)
High-risk cytogenetics[2]	11 (52)
Extramedullary plasmacytoma	12(55)
High-risk as mSMART3.0	20 (91)
LDH > upper limit of normal	3 (14)
ECOG performance status, n (%)	
0	5 (23)
1	11 (50)
2	6 (27)

[1] One patient received 1 cycle of PAD (bortezomib, doxorubicin, and dexamethasone)
[2] 21 pts evaluable for cytogenetics high risk.

GC012F: Safety Profile

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

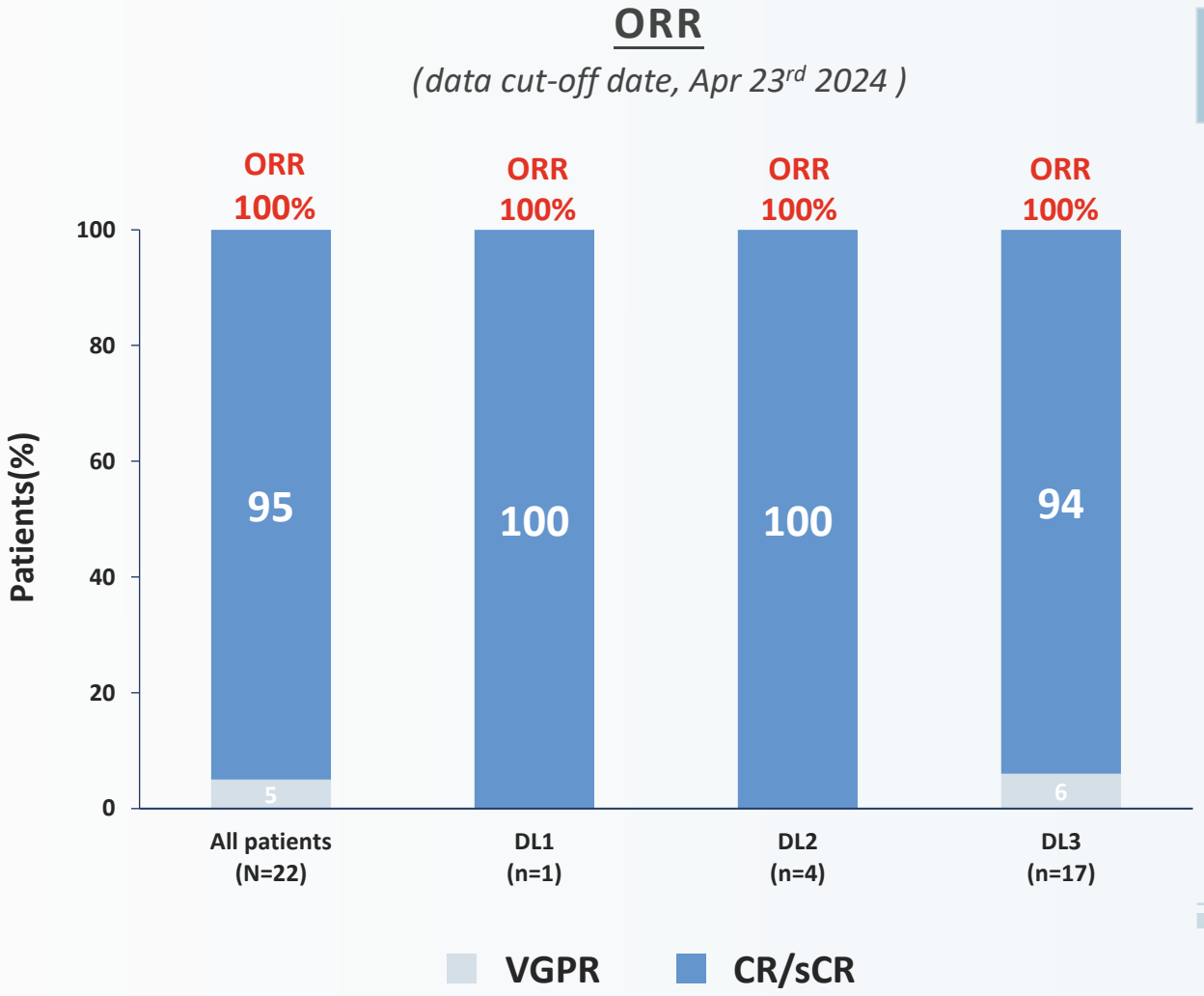
N=22	CRS[1], n (%)	ICANS[2], n (%)
Grade 1	5 (23)	0 (0)
Grade 2	1 (5)	0 (0)
Grade 3	0 (0)	0 (0)
Grade 4-5	0 (0)	0 (0)
All grade	**6 (27)**	**0 (0)**

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

N=22	All Grades, n (%)	Grade ≥3, n (%)
Hematologic TEAEs* (≥20% All Grades)		
Leukopenia	19 (86)	10 (45)
Lymphopenia	17 (77)	14 (64)
Neutropenia	17 (77)	9 (41)
Anemia	8 (36)	1 (5)
Thrombocytopenia	6 (27)	0 (0)
Non-Hematologic TEAEs* (≥20% All Grades)		
LDH increased	9 (41)	0 (0)
Hypoalbuminemia	9 (41)	0 (0)
Hypocalcemia	7 (32)	0 (0)
Infection	6 (27)	4 (18)

*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.

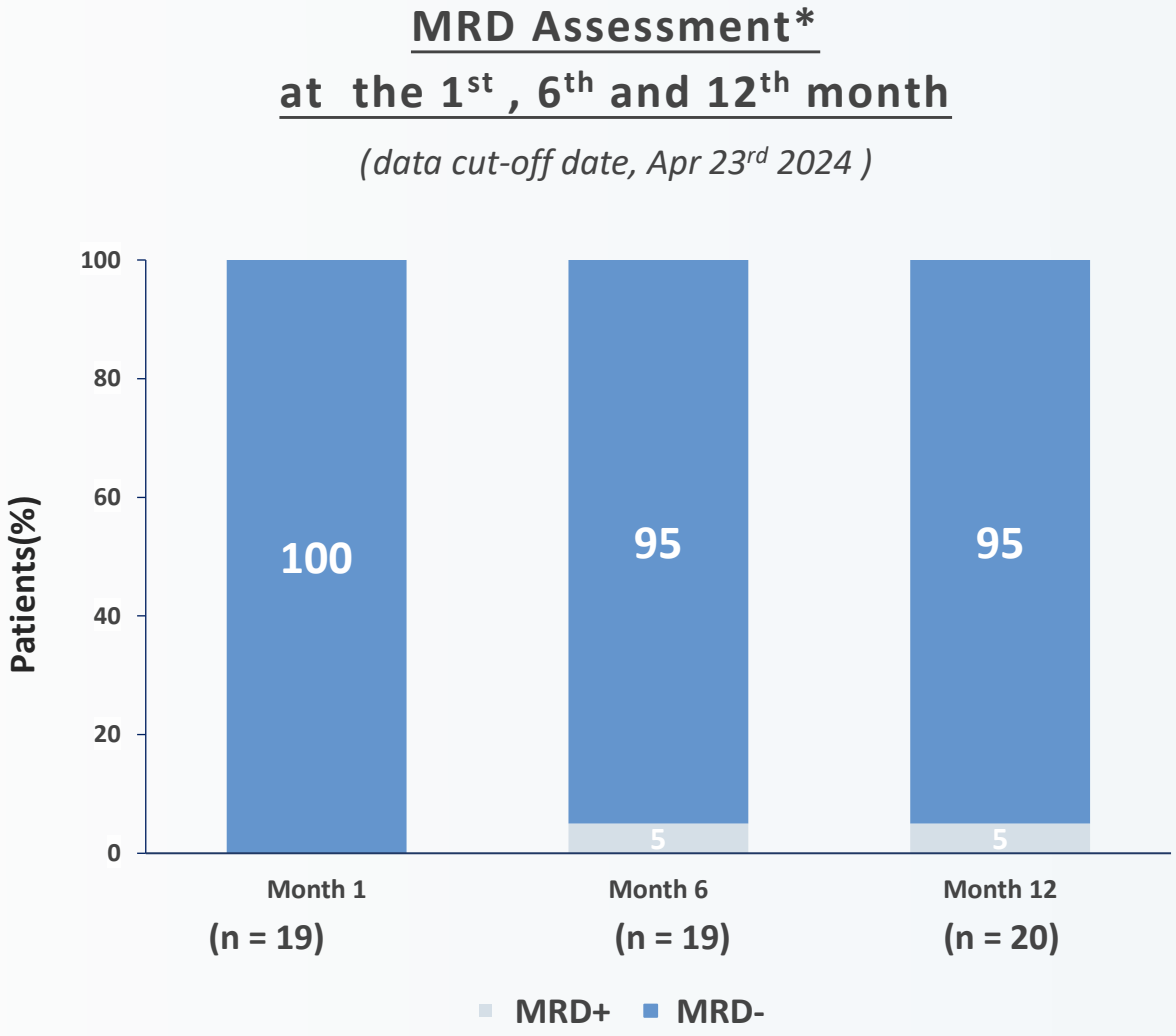
GC012F: Efficacy Assessment - ORR



Efficacy Results

- **ORR = 100% (22/22) patients**
  - ✓ Best response achieved to date
  - ✓ 95% (21/22) MRD- sCR
  - ✓ 100% (22/22) VGPR or better
- Median duration of response (DOR) and median progression free survival (PFS) were not reached at data cut off
- Median duration of follow up 25.2 months (range: 13.5 – 35.3 months)

GC012F: Efficacy Assessment – MRD Negativity

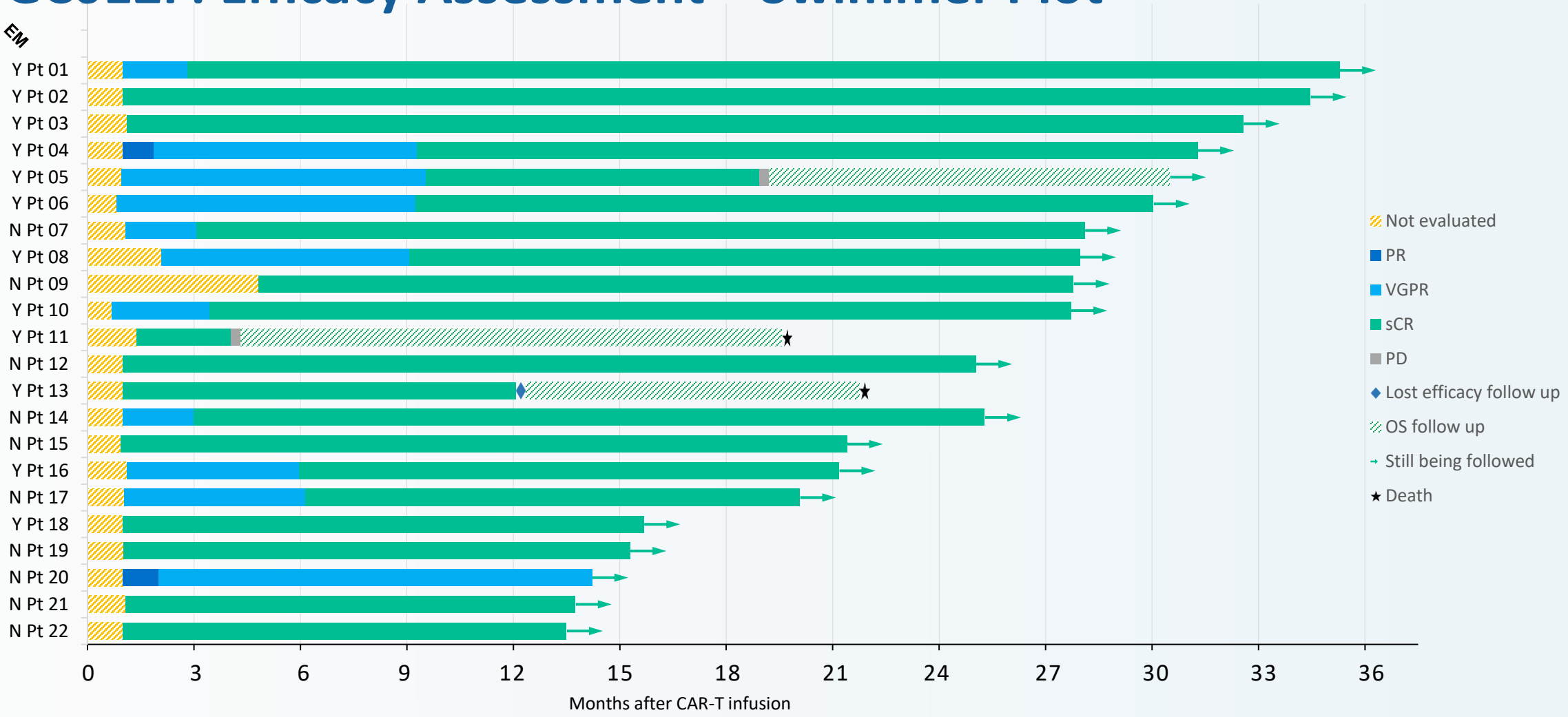


Efficacy Results

- 100% of MRD evaluable patients achieved MRD negativity at Month 1
- 100% of MRD evaluable patients achieved MRD negativity in all dose levels
- All patients achieved MRD negativity before lenalidomide maintenance

*MRD was tested by Euroflow at a sensitivity of 10^{-6}

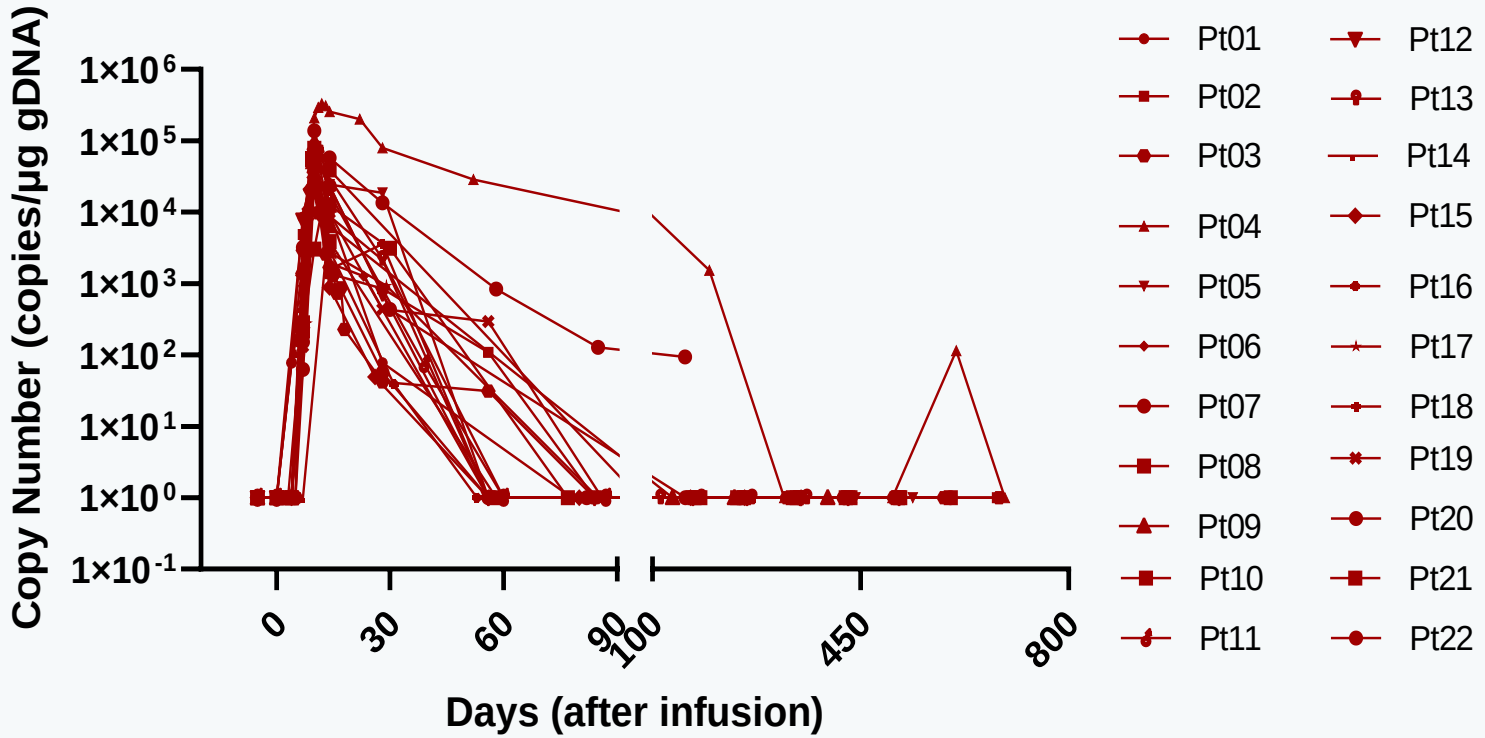
GC012F: Efficacy Assessment – Swimmer Plot



At a median follow up time of 25 months, 2 pts have died.

[1]HR: High-risk factors include: 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.

GC012F: Pharmacokinetics



LLOQ=30 (copies/µg gDNA)

- **Cmax** (copies/µg gDNA)

60652 (8754–331159)

- **AUC_{0-28}** (copies/µg gDNA*Days)

289685 (80181–3985420)

- **Tmax** (Days)

10 (9-14)

GC012F: Conclusion

- **GC012F shows a favorable safety profile in newly diagnosed multiple myeloma patients**
  - Only 27% (6/22) patients experienced Grade 1-2 CRS
  - No Grade ≥3 CRS and no ICANS or any neurotoxicity observed
- **100% (22/22) ORR in high risk population**
  - 95% sCR
  - Patients continue being followed up for durable response
- **100% (22/22) 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**

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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