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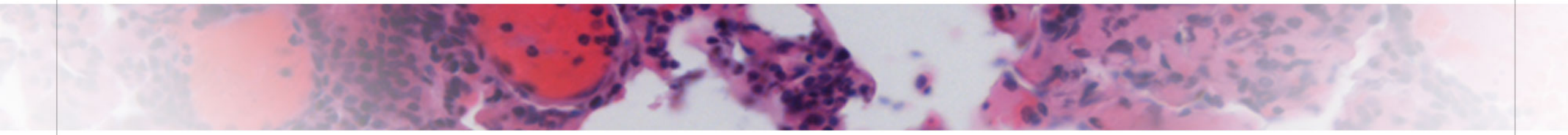

Phase I Open-Label Single-Arm Study of BCMA/CD19 Dual-Targeting Fast CAR-T Cells (GC012F) as First-Line Therapy for Transplant-Eligible Newly Diagnosed High-Risk Multiple Myeloma

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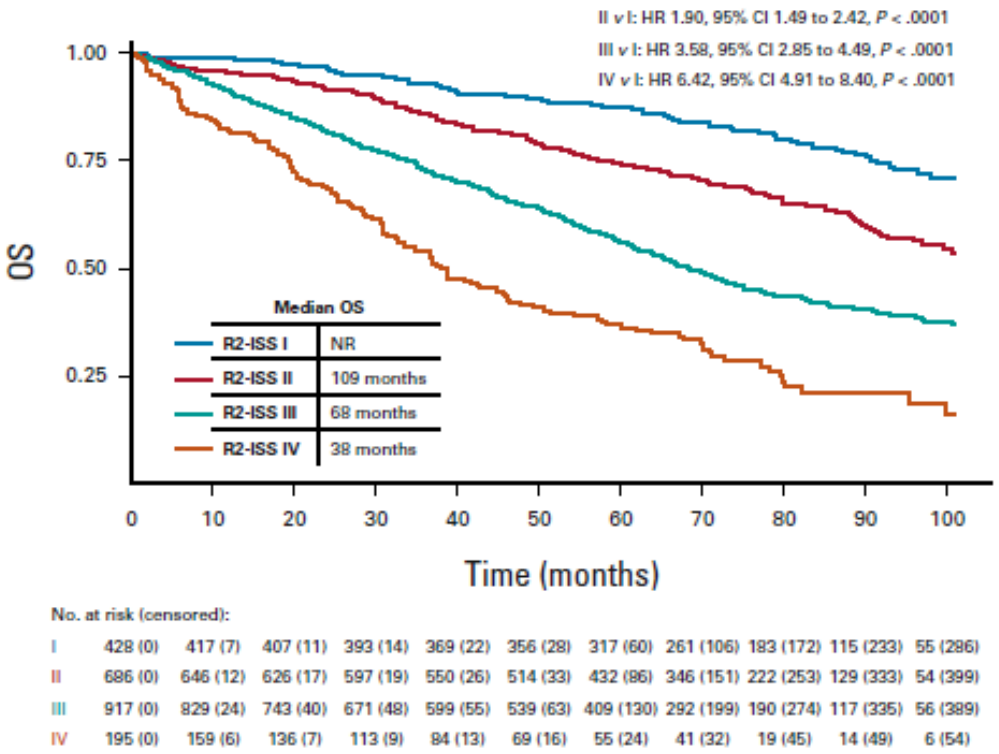
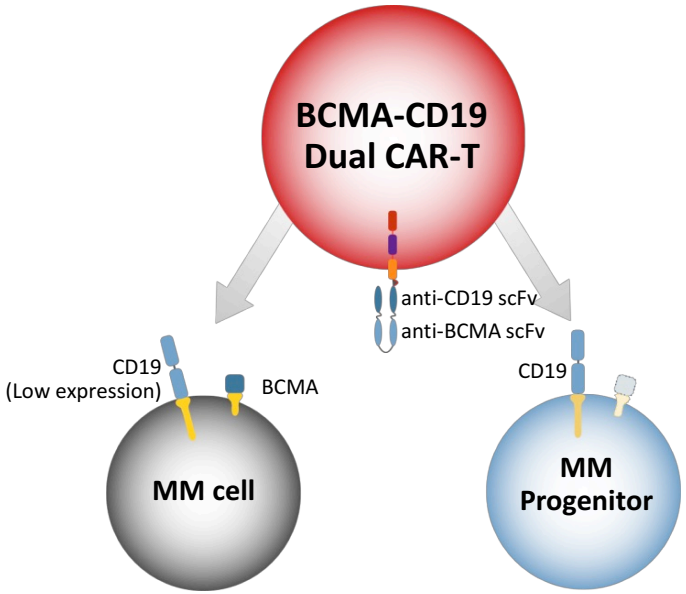
High-risk disease in NDMM and GC012F



D'Agostino M, et al. J Clin Oncol. 2022

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

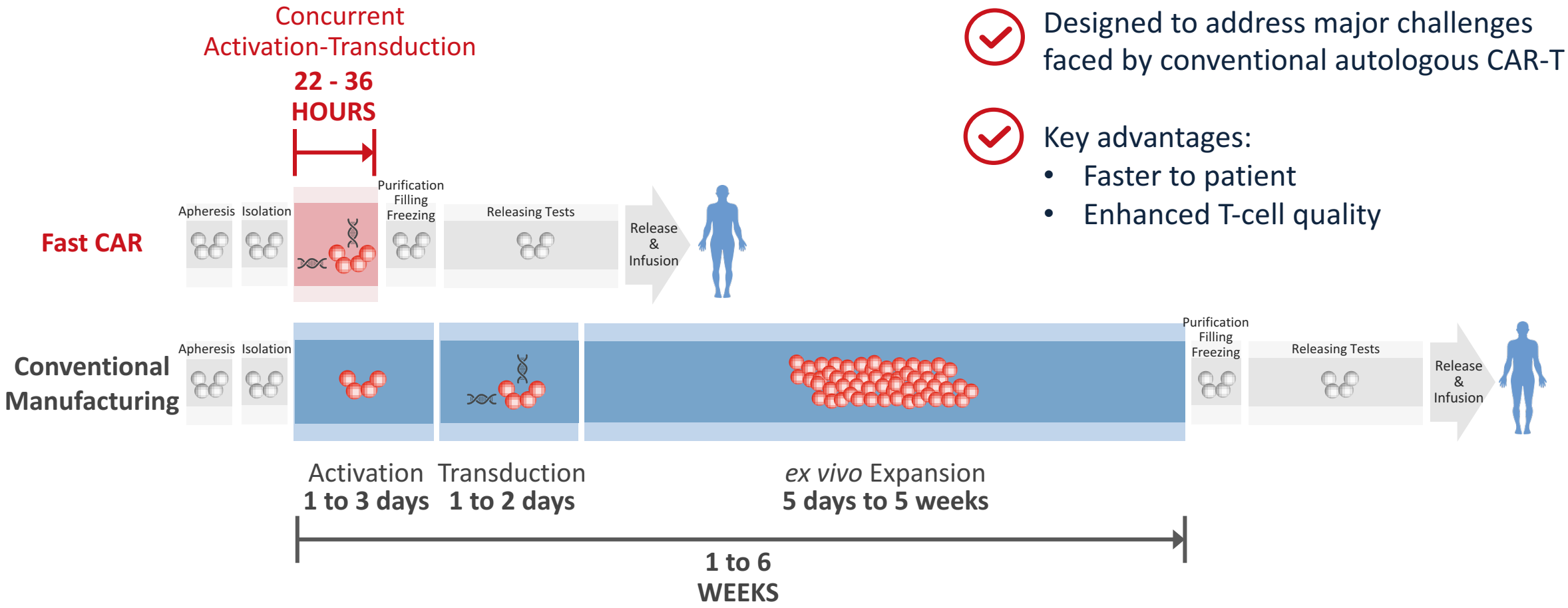


- BCMA is universally expressed on malignant plasma cells[1]
- CD19 is expressed on both multiple myeloma cells and their progenitors[2], making it a valid therapeutic target to treat multiple myeloma

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.

GC012F: Fast CAR Cuts Manufacturing Time to 22-36 Hours

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 T-cell quality

GC012F: Study Design

Single-center, open label, single-arm IIT[1] study (N=16)

FPI August 2021

Patients continue to be assessed for response

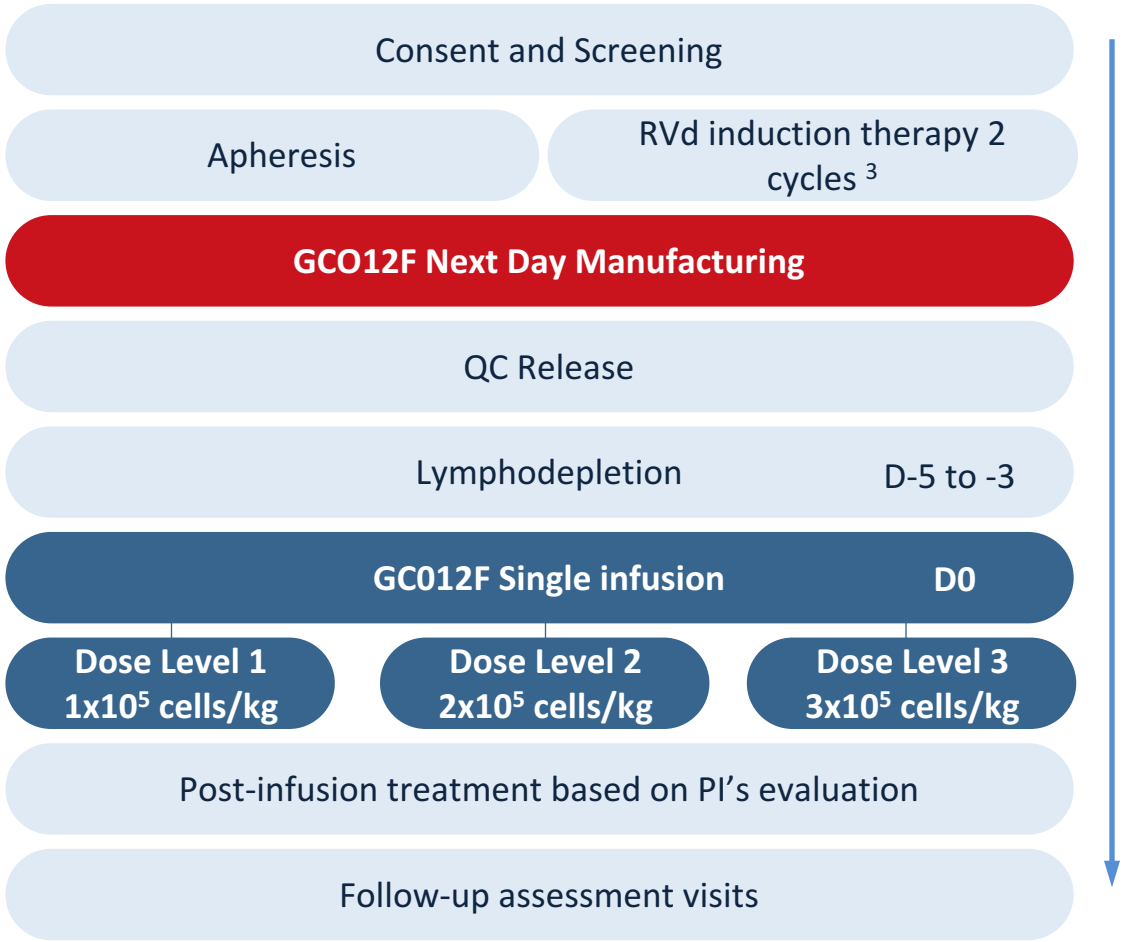
Data cut-off **Oct 14th 2022**

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 RVd (PAD cycle in one case) are given before or after apheresis.

GC012F: Baseline Characteristics

Baseline Characteristics (N=16)	
Median age, years (range)	59 (43-69)
Male, n (%)	11 (69)
Type of myeloma, n (%)	
IgG	7 (44)
IgA	4 (25)
IgD	2 (13)
Light chain	3 (19)
Induction therapy, n (%)	
2 cycles RVd [1]	15 (94)

Baseline Characteristics (N=16)	
High-risk, n (%)	16 (100)
R-ISS stage II/III	15 (94)
High-risk cytogenetics[2]	7 (47)
Extramedullary plasmacytoma ≥1	11(69)
High-risk as mSMART3.0	15 (94)
LDH > upper limit of normal	3 (19)
ECOG performance status, n (%)	
0	3 (19)
1	9 (56)
2	4 (25)

[1] RVd: Lenalidomide(Relimid), bortezomib (velcade) and dexamethasone.
PAD: bortezomib (PS-341), doxorubicin (adriamycin), and dexamethasone; 1 patient received one cycle of PAD and one cycle of RVd.
[2] 15 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

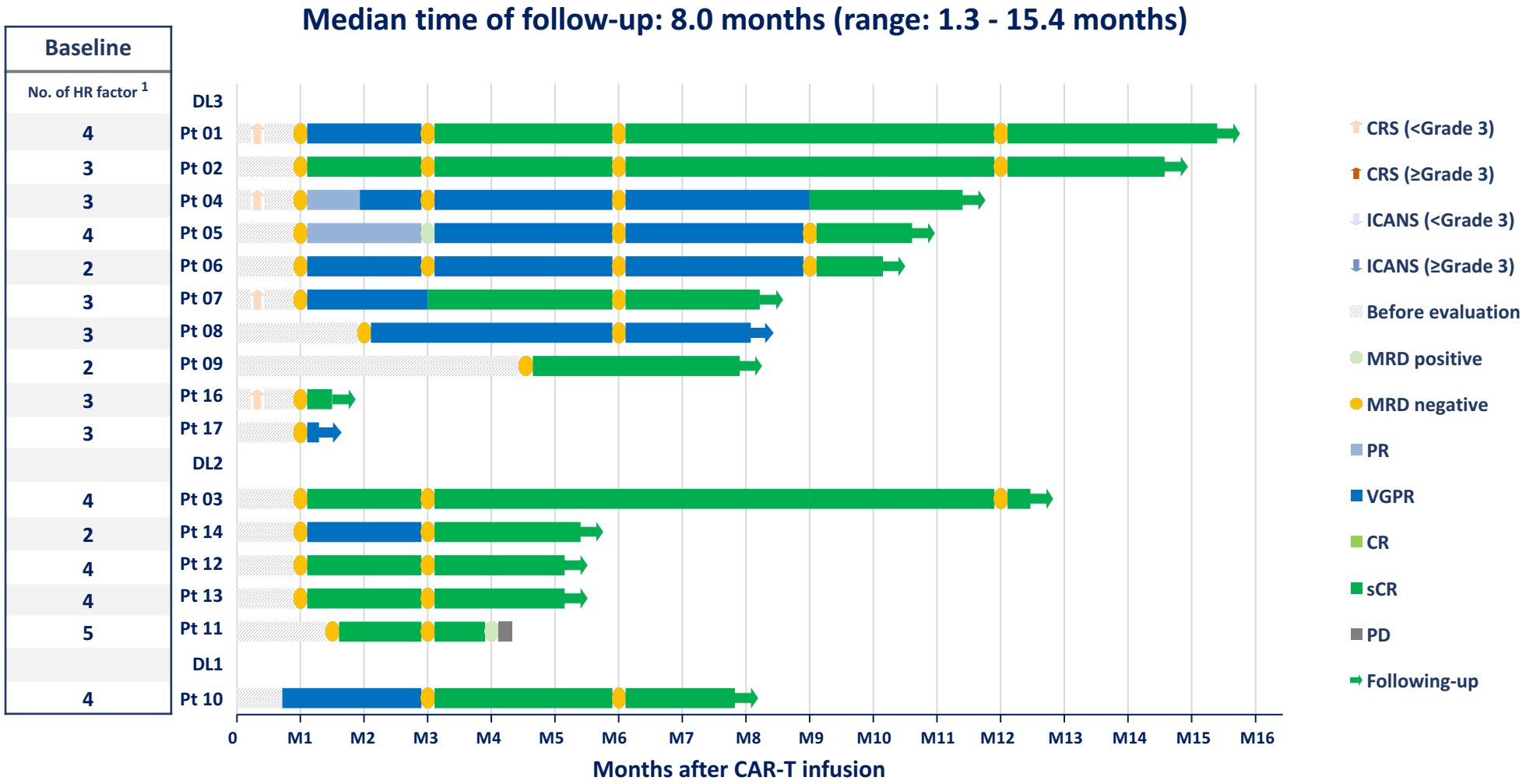
N=16	CRS[1], n (%)	ICANS[2], n (%)
Grade 1	3 (19)	0 (0)
Grade 2	1 (6)	0 (0)
Grade 3	0 (0)	0 (0)
Grade 4-5	0 (0)	0 (0)
All grade	**4 (25)**	**0 (0)**

CRS any grade	Median (days)	Range (days)
Time to onset	6	6-7
Duration	2	1-4

N=16	All Grades, n (%)	Grade ≥3, n (%)
Hematologic TEAEs* (≥20% All Grades)		
Neutropenia	14 (88)	7 (44)
Lymphopenia	14 (88)	13 (81)
Leukopenia	14 (88)	8 (50)
Thrombocytopenia	4 (25)	0 (0)
Anemia	7 (44)	1 (6)
Non-Hematologic TEAEs* (≥20% All Grades)		
LDH increased	7 (44)	0 (0)
Hypoalbuminemia	6 (38)	0 (0)

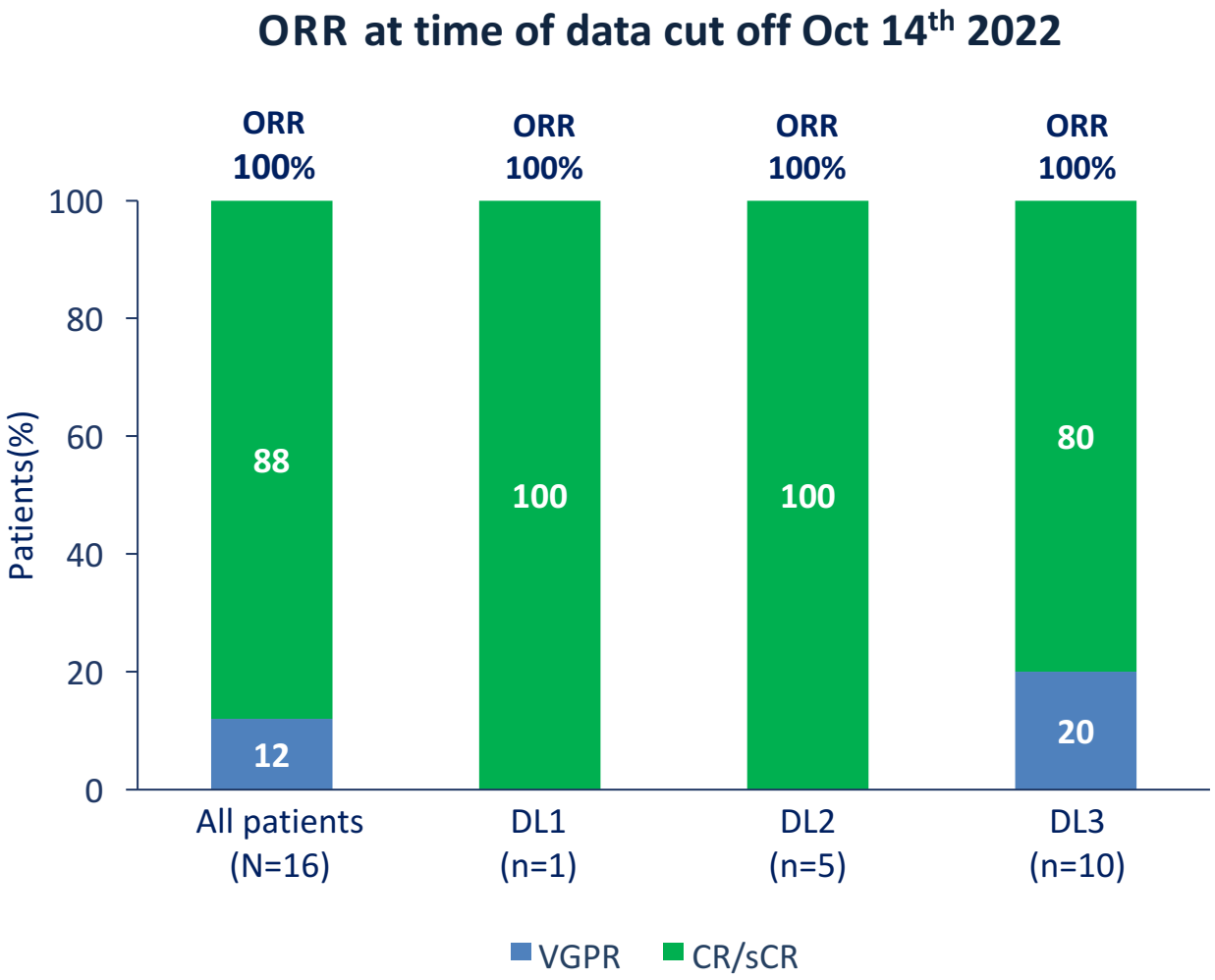
*AEs were graded according to CTCAE v5.0; TEAE-treatment emergent adverse event; LDH-Lactase dehydrogenase.
[1]CRS-Cytokine Release Syndrome, graded by ASTCT Consensus; treated with tocilizumab and/or glucocorticoids.
[2]ICANS-Immune Effector Cell-Associated Neurotoxicity Syndrome, graded by ASTCT Consensus.

GC012F: Efficacy Assessment



[1]HR 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: Efficacy Assessment - ORR



- **ORR = 100% (16/16) patients**
  - Best response achieved to date
  - 88% (14/16) MRD- sCR
  - 100% (16/16) VGPR or better
- Median duration of response (DOR) was not reached at data cut off
- Median duration of follow up 8.0 months (range: 1.3 - 15.4 months)

GC012F: Efficacy Assessment - MRD Negativity

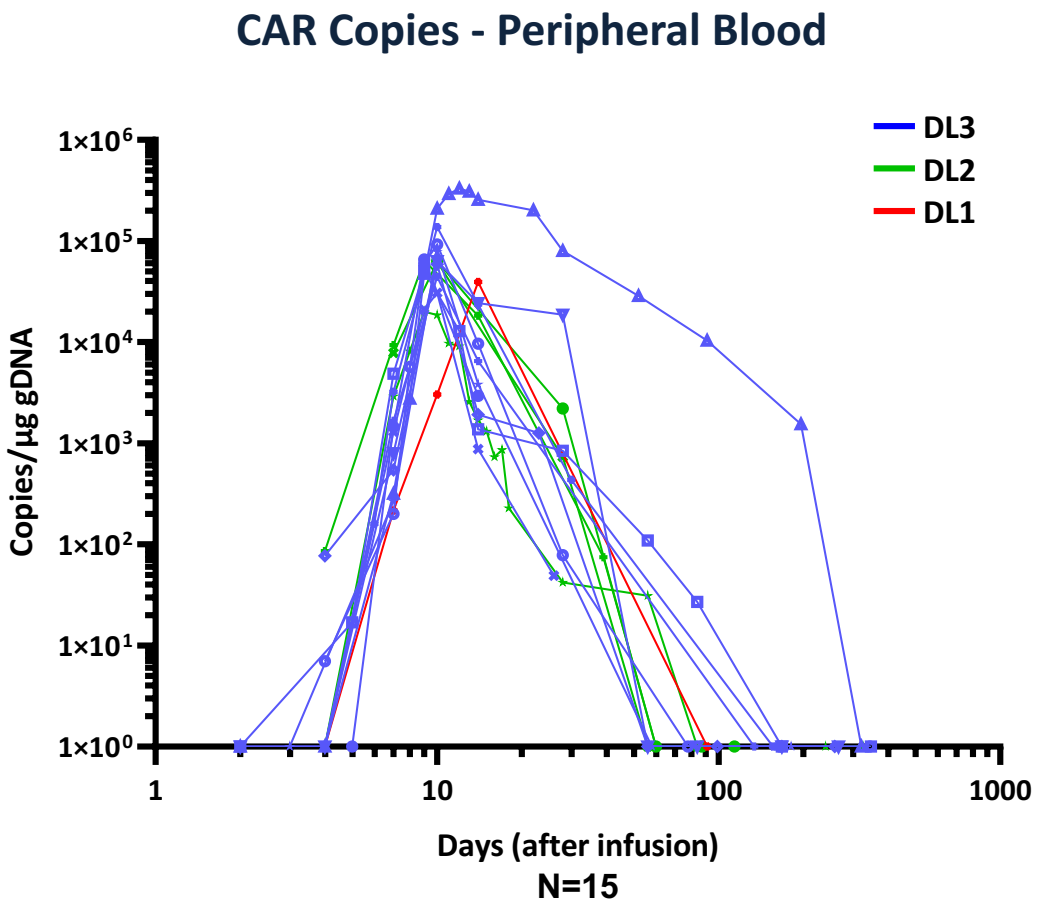
Data cut-off **Oct 14th 2022**

MRD assessment* at the 1st , 6th and 12th month

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

- 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

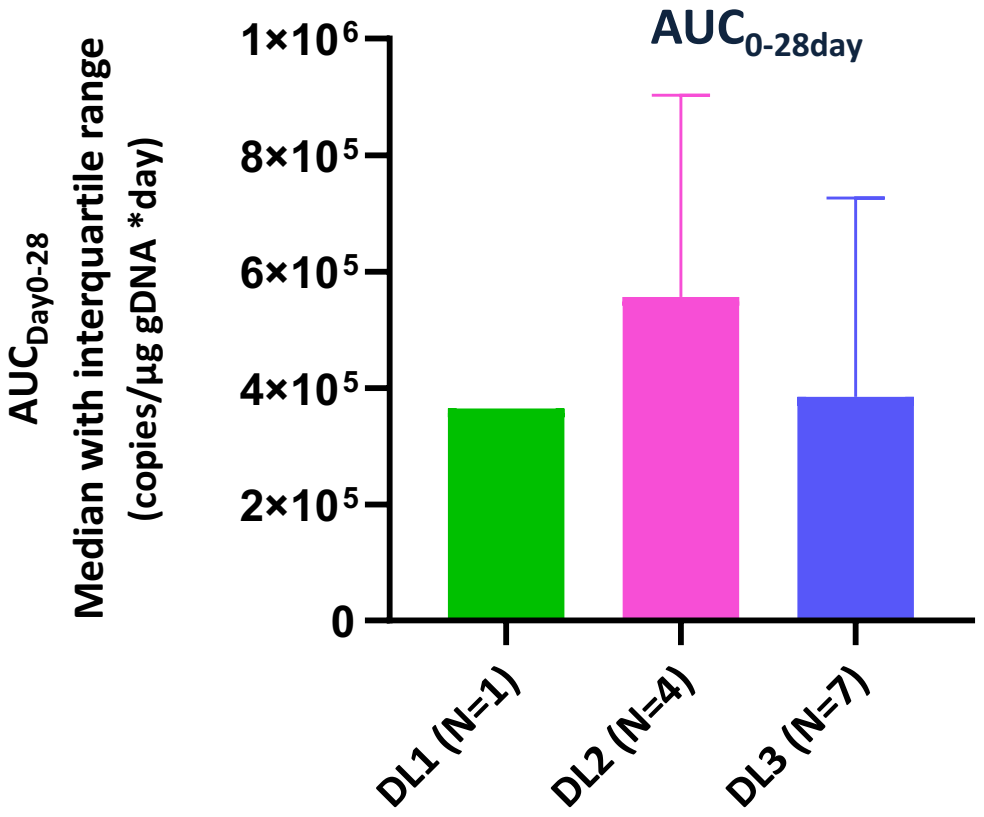
GC012F: Pharmacokinetics



- Fast CAR-T GC012F expanded well in all patients with long persistence in all dose levels
- CAR-T median T_{max} was day 10 (range 9-14)
- Median peak copy number (C_{max}) was 63,086 (range: 20,097-331,159 copies/µg genomic DNA)

Limit of detection (LOD) = 30 copies/µg gDNA
Detection range 30-5x10^6 µg gDNA

GC012F: Pharmacokinetics - AUC



Median $AUC_{0\text{-}28d}$ (copies*day/µg gDNA)

	Median	Range
DL 1 (n=1)	364,687	NA
DL 2 (n=5)	556,061	80,511 – 903,099
DL 3 (n=7)	384,367	118,838 – 3,918,003
Total (N=12)	**398,821**	**80,511 – 3,918,003**

GC012F: Conclusions

- **GC012F shows a favorable safety profile in newly diagnosed multiple myeloma patients**
  - Only 25% (4/16) patients experienced Grade 1-2 CRS
  - No Grade ≥3 CRS and no ICANS or any neurotoxicity observed

- **100% (16/16) ORR in *high risk* population**
  - 88% sCR, 100% ≥VGPR
  - Patients continue being followed up for deepening and durable response

- **100% (16/16) MRD negativity**

- **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**