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Updated Results of a Phase I, Open-Label Study of BCMA/CD19 Dual-Targeting FasTCAR-T GC012F for Patients with Relapsed/Refractory Multiple Myeloma (RRMM)

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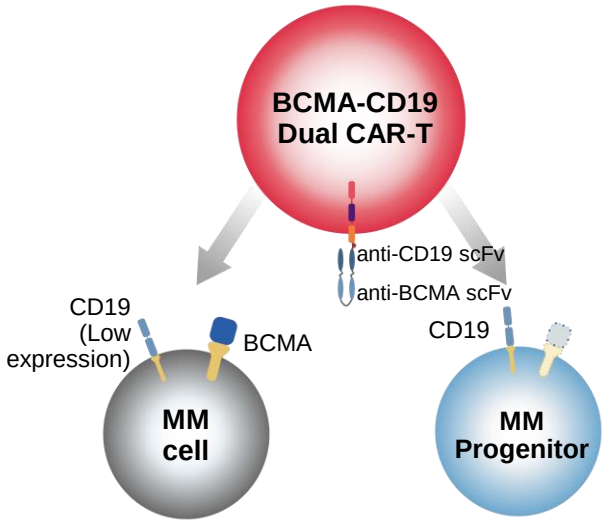
FasTCAR GC012F: BCMA/CD19 Dual-Targeting for Multiple Myeloma

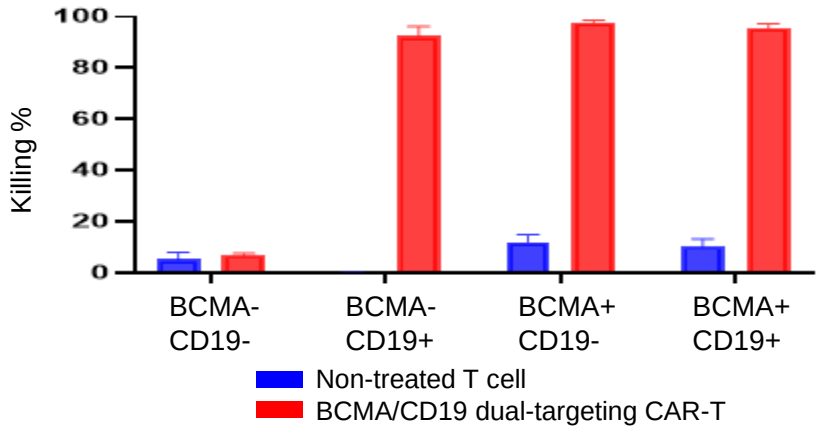


BCMA: a proven target for MM

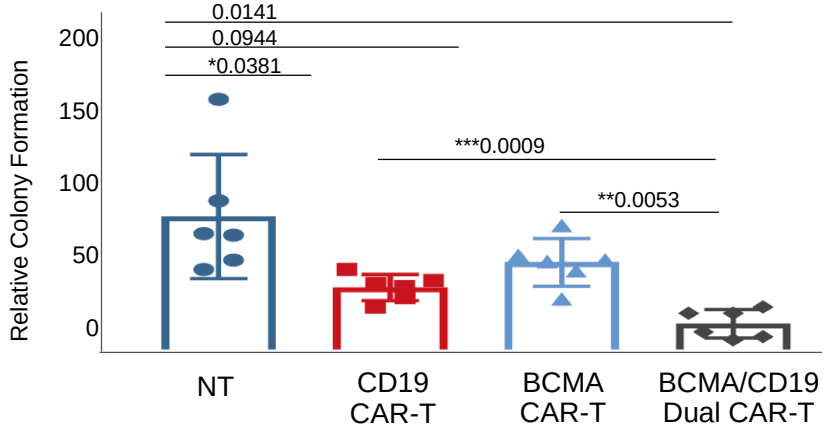
CD19: expressed on majority of MM cells and subsets of **progenitor cells** [1-3]

- CD19+ progenitor cells make up a drug-resistant, colony-forming cell reservoir, which can be eliminated by CD19 targeting of GC012F
- Clinical study in r/r MM patients showed CD19 CAR-T provided PFS benefits in some patients [2]
- Targeting both antigens to maximize the elimination of MM plasma cells and CD19+ progenitor subsets and to drive DEEP and DURABLE response

Effective killing of BCMA+ or/and CD19+ tumor cells

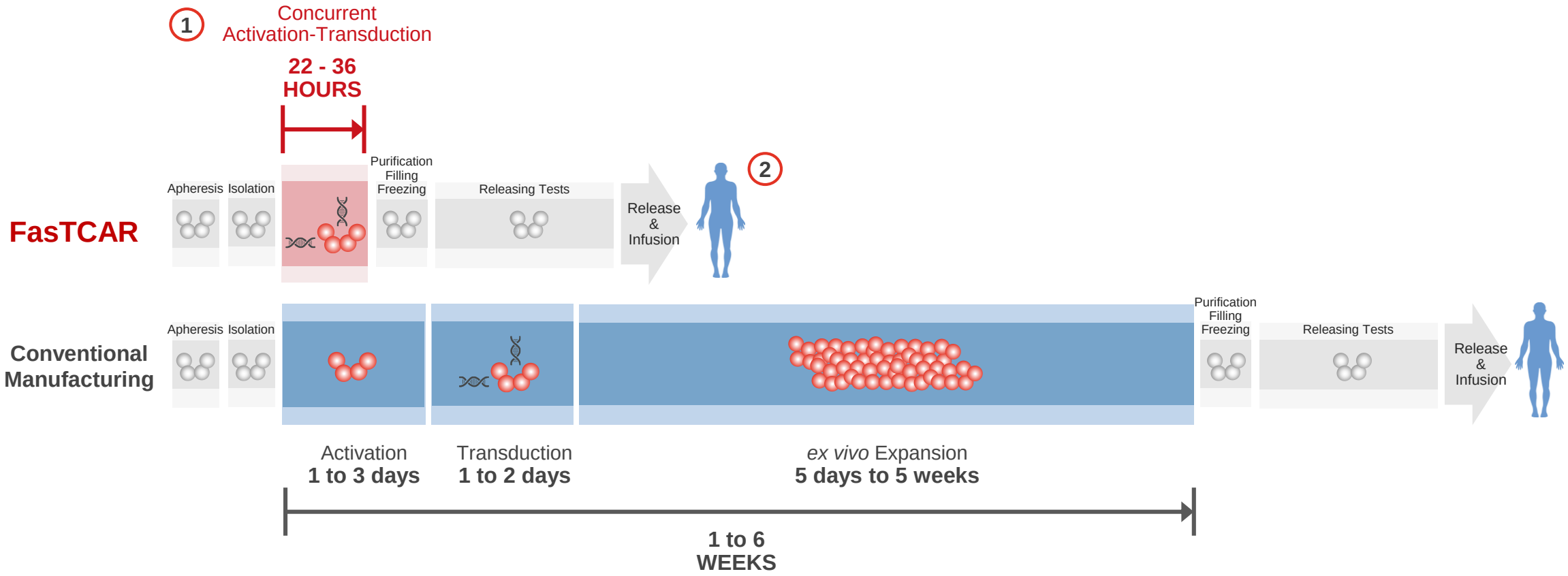


More effective elimination of MM progenitor cells



1. Boucher K, Parquet N, Widen R, et al. Clin Cancer Res. 2012;18(22):6155-6168.
2. Garfall AL, Stadtmauer EA, Hwang WT, et al. Anti-CD19 CAR T cells with high-dose melphalan and autologous stem cell transplantation for refractory multiple myeloma. JCI Insight. 2018;3(8):e120505
3. Hua Jiang, et al. ASH Annual Meeting 2020, 178.

FasTCAR Platform: Next-Day Manufacturing



1 FasTCAR transforms the three primary production steps—activation, transduction and expansion—into a single “concurrent activation-transduction” step.

2 With minimized *ex vivo* culture time, FasTCAR-T cells are younger and shows enhanced proliferation and tumor clearance activities in preclinical studies, making possible the lower cell dosage and eliminating the need for *ex vivo* expansion. Expansion happens in patient body, an optimal condition.

GC012F DUAL CAR-T for RRMM : **Study Design**

Multicenter, open label, single-arm IIT[1] study (N=29)
FPI October 2019, LPI January 2022; Pts continued to be assessed for response
Data cut-off April 12th, 2023

Key Eligibility Criteria

- Relapsed/Refractory Multiple Myeloma[2]
- 3+prior lines of therapy and/or refractory to PI and IMiDs, primary refractory
- Expected survival ≥ 3 months

Primary endpoint:

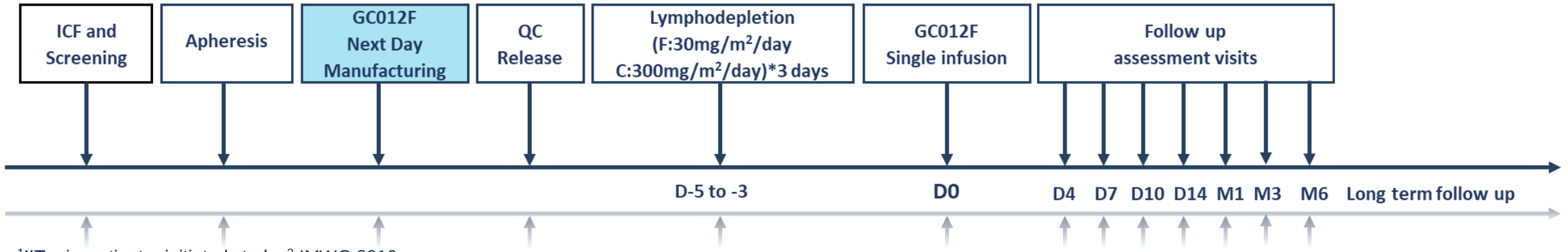
- Adverse Events

Secondary endpoints:

- ORR, BOR
- MRD assessment at pre-specified timepoints post CAR-T infusion
- PK/PD

Dose Levels

- DL1: $1x10^5$ cells/kg
- DL2: $2x10^5$ cells/kg
- DL3: $3x10^5$ cells/kg



[1]IIT – investigator initiated study; [2] IMWG 2016

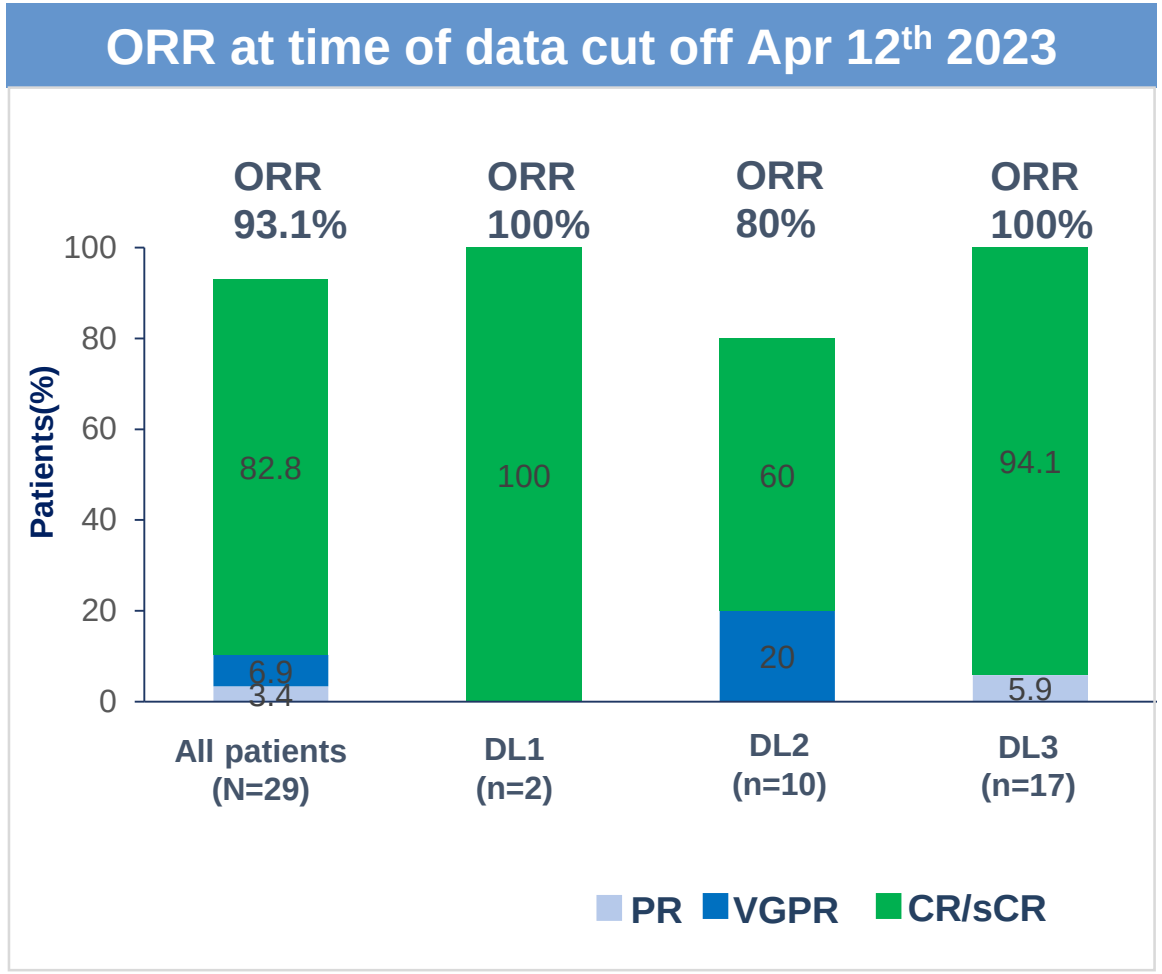
GC012F DUAL CAR-T for RRMM : Baseline Characteristics

Baseline Characteristics	Total (N=29)
Median age, years (range)	57 (27-76)
Male, n(%)	17 (59)
Type of myeloma, n(%)	
IgG	13 (45)
IgA	6 (21)
IgD	5 (18)
Light chain	5 (18)
Median years since diagnosis (range)	4 (1-10)
High-risk profile[a], n(%)	*26 (90)*
Double-hit[b], n(%)	3 (10)
ECOG, n(%)	
0&1	23 (79)
2	4 (14)
3	2 (7)

Baseline Characteristics	Total (N=29)
Extramedullary plasmacytoma ≥ 1, n(%)	8 (28)
Median prior regimens, n (range)	5 (2-11)
Median prior lines of therapy, n (range)	5 (2-9)
Prior auto-SCT, n(%)	11 (38)
Triple-exposed[c], n(%)	28 (97)
PI refractory	27 (93)
IMiD refractory	27 (93)
anti-CD38 refractory	10 (34)
Penta-exposed[d], n(%)	18 (62)
Primary refractory, n (%)	3 (10)
Refractory to last therapy, n (%)	24 (83)

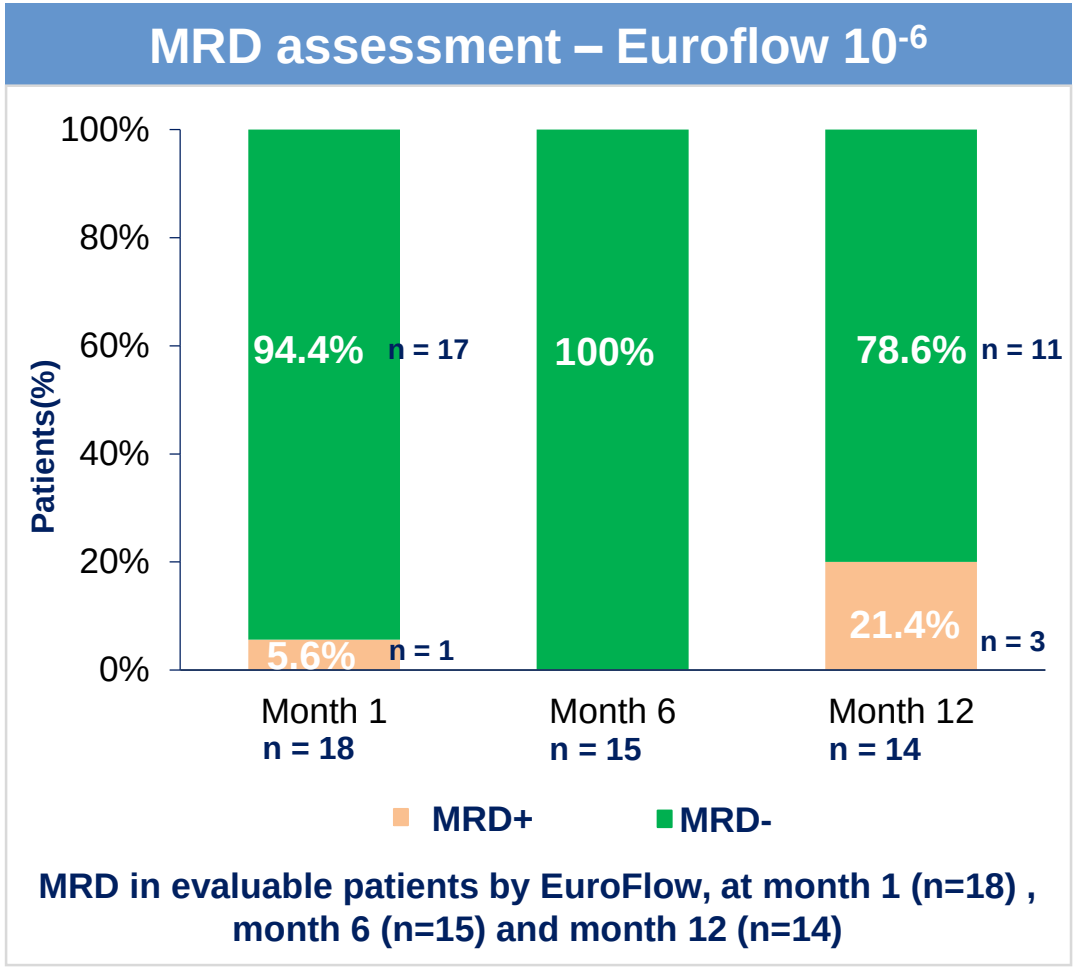
[a] By mSMART 3.0;
[b] By presence two of del(17p), t(4;14), t(14;16), t(14;20), gain 1q, or p53 mutation
[c] PI, IMiD and any other therapies including anti-CD38 antibody;
[d] ≥1 PI (Ixazomib and Bortezomib were approved in China), ≥1 IMiDs (only-Lenalidomide is approved for MM in China) and ≥ 3 other anti-myeloma drugs of any other class.

GC012F DUAL CAR-T for RRMM : Response Assessment ORR



- ORR = 93.1% (27/29) patients
  - Best response achieved to date
  - 82.8% (24/29) MRD$^-$ sCR
  - 89.6% (26/29) VGPR or better
- Median time to best response: 3 months (range, 0.9-15.3)
- Median DOR was 37.0 months (95% CI: 11.0 - NR)
- Median duration of follow up was 30.7 months (range: 14.6 – 43.6 months)

GC012F DUAL CAR-T for RRMM : Minimal Residual Disease Landmark Analysis



MRD in evaluable patients by EuroFlow, at month 1 (n=18) , month 6 (n=15) and month 12 (n=14)

- 100% patients achieved MRD negativity
- 100% of evaluable pts assessed by Euroflow at sensitivity of 10^{-6} were MRD negative at Month 6 (n=15)
- 78.6% of evaluable patients were MRD negative at Month 12

GC012F DUAL CAR-T for RRMM : PFS analysis

Subgroup	n	PFS, Median (95% CI, mo)	12-month PFS rate	36-month PFS rate
All patients	29	38.0 (11.8, NE)	69.0%	50.5%
sCR	24	38.0 (13.7, NE)	83.3%	61.0%
12-month sustained MRD negativity	10	NE (38.0, NE)	100%	100%
12-month sustained MRD negative CR	10	NE (38.0, NE)	100%	100%

- mPFS is 38.0 months at data cutoff among a predominantly high risk patient population
- Longer PFS was achieved in patients with 12-month sustained MRD negativity
- 34% (10/29) of all GC012F-treated patients sustained MRD-negative for more than 12 months

GC012F DUAL CAR-T for RRMM : **Safety Profile**

N=29	All Grades, n (%)	Grade ≥3, n (%)
Hematologic TEAEs* (≥ 25% All Grades)		
Neutropenia	23 (79)	23 (79)
Lymphopenia	19 (66)	19 (66)
Leukopenia	23 (79)	22 (76)
Thrombocytopenia	22 (76)	16 (55)
Anemia	14 (48)	10 (34)
Non-Hematologic TEAEs* (≥ 25% All Grades)		
LDH increased	18 (62)	0 (0)
Hypoalbuminemia	14 (48)	0 (0)
AST increased	12 (41)	8 (29)
Hypokalemia	19 (66)	4 (14)
Hypophosphatemia	9 (31)	0 (0)
Hypocalcemia	7 (24)	1 (3)

N=29	CRS[1], n (%)	ICANS[2], n (%)
Grade 1	14 (48)	0 (0)
Grade 2	9 (31)	0 (0)
Grade 3	2 (7)	0 (0)
Grade 4-5	0 (0)	0 (0)

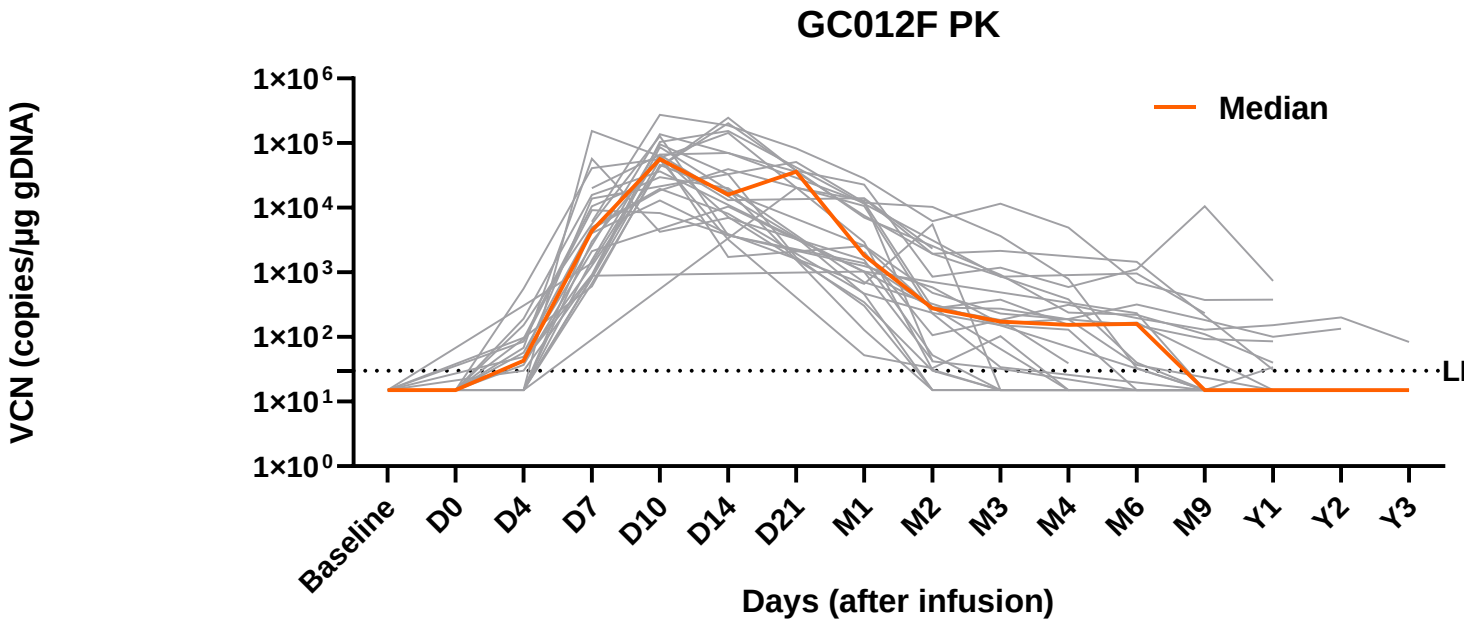
[1]CRS treated with Tocilizumab, vasopressors and dexamethasone

CRS any grade	Median (days)	Range (days)
Time to onset	6	2-10
Duration	3	1-8

- **No new safety findings in the longer term follow-up**
- **No second primary malignancy reported**
- **No any neurotoxicity observed**

*AE were graded according to CTCAE v5.0, TEAE- treatment emergent adverse event, AST Aspartate Aminotransferase, LDH Lactase dehydrogenase, CRS – [1]Cytokine Release Syndrome - ASBMT consensus grading, [2] ICANS – Immune Effector Cell-Associated Neurotoxicity Syndrome - ASBMT consensus grading

GC012F DUAL CAR-T for RRMM : GC012F persistence

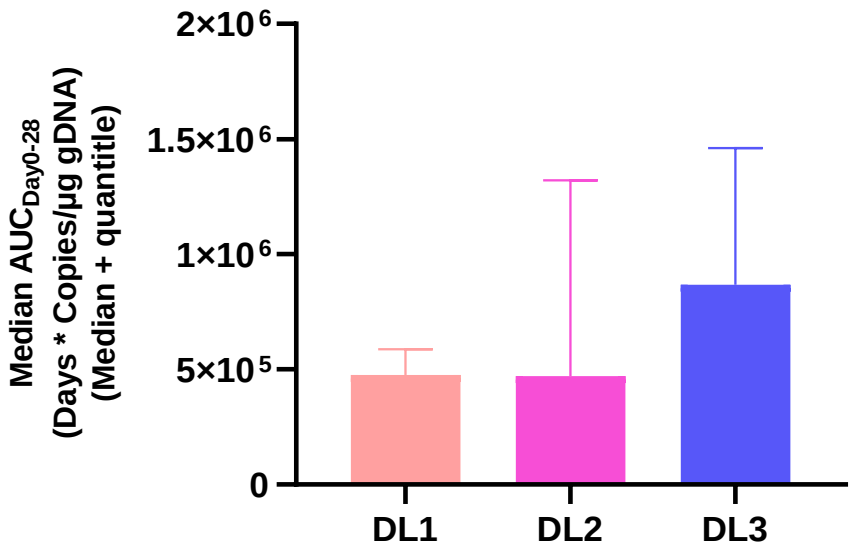


- **Median Cmax = 96,438 copies/μg gDNA**
- **Median Tmax = Day 10**
- **Long-Term Persistence (≥LLOQ):**
- **6 months: 72.2% (13/18)**
- **12 months: 47.1% (8/17)**

The CAR T cells were still detectable at 6 months (median value), indicating the sustained persistence of CAR T cell in RRMM patients

N=29, Cut-off data:2023-04-12; Grey lines: individuals; Red line: median; LLOQ (lower limit of quantification)= 30 copies/μgDNA

GC012F DUAL CAR-T for RRMM : Pharmacokinetics



No significant differences observed for $AUC_{0\text{-}28d}$ between dose levels

$AUC_{0\text{-}28d}$ of CAR-T in each dose level – Median

	$AUC_{0\text{-}28d}$ (copies*day/μg genomic DNA)	
	Median	**Range**
DL 1 (n= 2)	475434	396661- 554207
DL 2 (n=10)	470996	108069-7120348
DL 3 (n=17)	868235	57595-3166990
All patients (N=29)	553679	57595-7120348

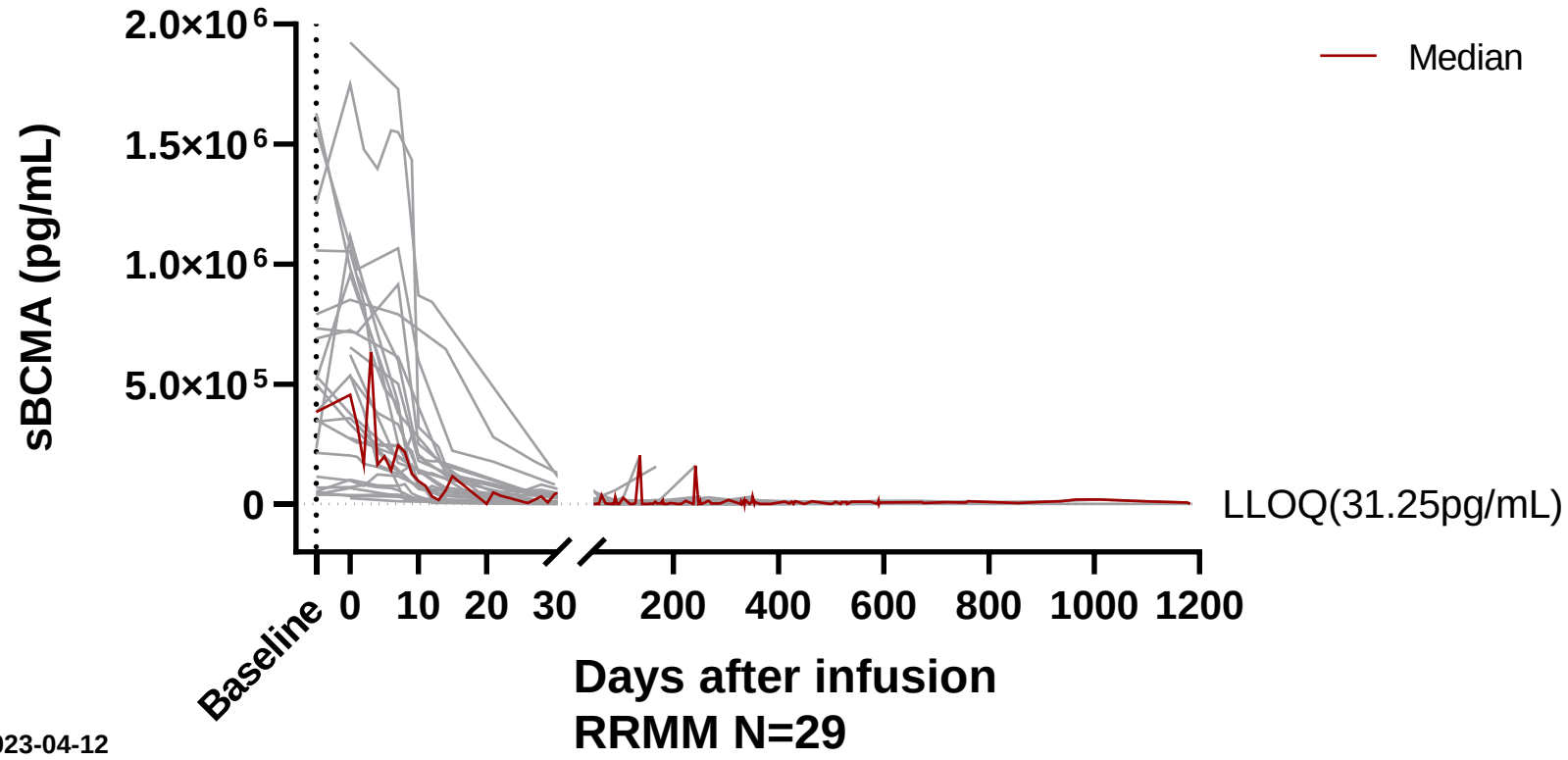
$AUC_{0\text{-}28d}$ of CAR-T in each dose level – Geometric Mean

	$AUC_{0\text{-}28d}$ (copies*day/μg genomic DNA)	
	Geometric Mean	**95% CI**
DL 1 (n= 2)	468863	56007-3925091
DL 2 (n=10)	631540	272026-1466195
DL 3 (n=17)	564843	284221-1039005
All patients (N=29)	579515	331920- 758989

GC012F DUAL CAR-T for RRMM : sBCMA

Serum BCMA (sBCMA) level declined sharply post CAR-T infusion

Median sBCMA level reached minimal at M2



N=29, Cut-off data:2023-04-12
Grey lines: individuals; Red line: median
LLOQ (lower limit of quantification)= 31.25pg/mL

Conclusions

- **GC012F continues to show a favorable safety profile and no new safety findings in the longer term follow-up**
- **High overall responses rate ORR of 93.1% (27/29) and MRD- sCR rate of 82.8% (24/29) in a predominantly high risk population**
- **MRD negativity achieved in all treated patients - 100% (29/29), 100% (22/22) in patients tested by EuroFlow 10^{-6}**
- **FAST, DEEP and DURABLE responses with median PFS 38.0m (95% CI: 11.8 – NE) with patients still in follow-up**
  - Patients with sustained MRD negativity had longer PFS
- **BCMA/CD19 dual-targeting GC012F shows very promising activity in RRMM including High Risk patients and heavily pretreated patients with prior exposure to anti-38 mAb, PI, IMiDs**
- **GC012F IND phase I/II clinical trials in USA and China are starting**