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Updated Results of a Multicenter First-in-Human Study of BCMA/CD19 Dual-Targeting FasT CAR-T GC012F for Patients with Relapsed/Refractory Multiple Myeloma (RRMM)

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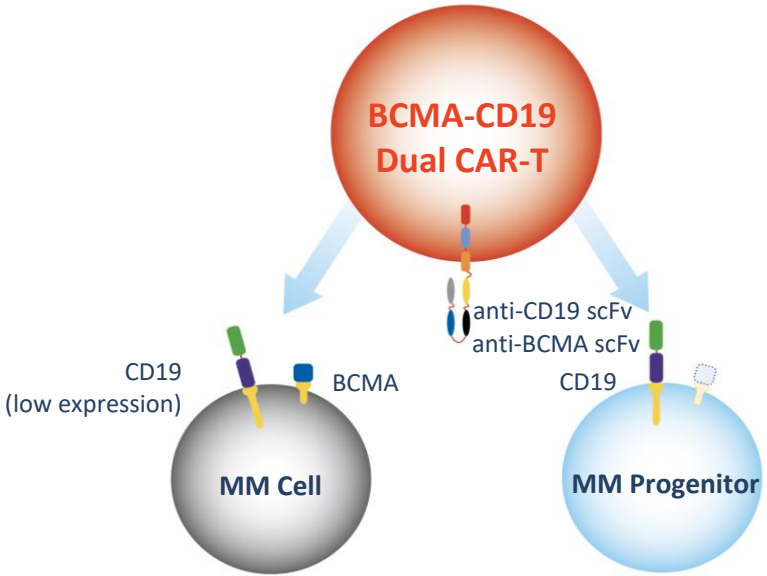
Disclosures

- I have nothing to disclose

Dual targeting BCMA/CD19 for MM

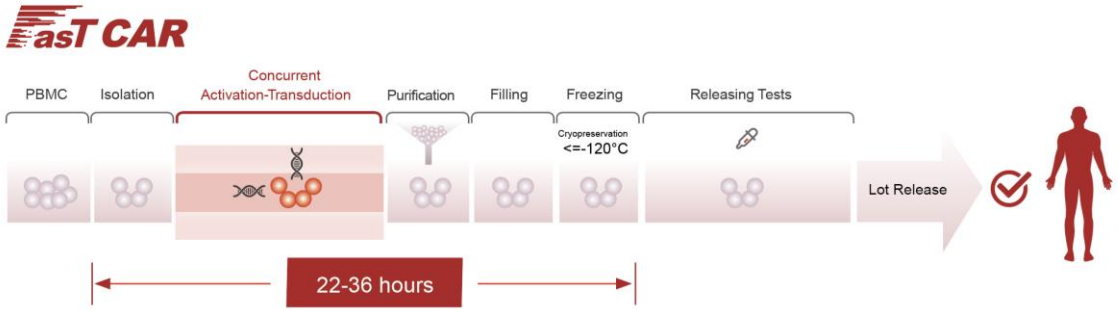


Targeting both Antigens in MM is designed to drive fast, deep and durable Responses in MM Patients

- BCMA is universally expressed on malignant plasma cells[1]
- CD19 is expressed on both multiple myeloma (MM) cells and their progenitors[2]
- Targeting CD19 can trigger elimination of malignant cells by CAR-T[3]

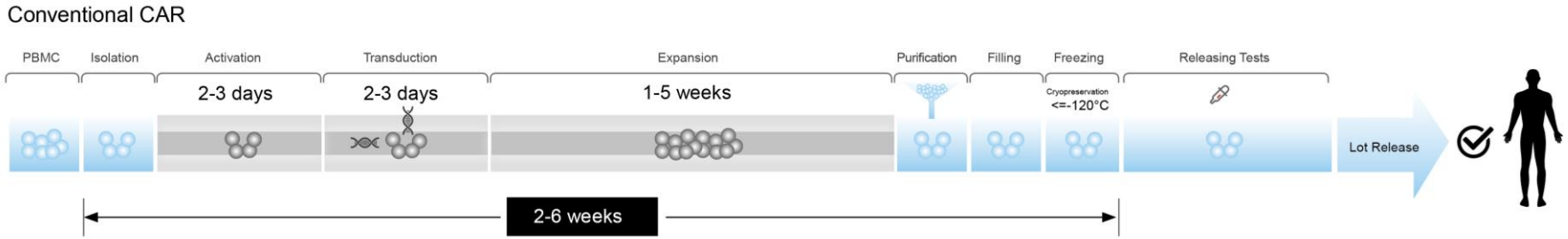
1. Tai YT, Anderson KC. Immunotherapy. 2015;7(11):1187-1199.
2. Boucher K, Parquet N, Widen R, et al. Clin Cancer Res. 2012;18(22):6155-6168.
3. Nerreter T, Letschert S, Götz R, et al. Nat Commun. 2019;10(1):3137.

FasTCAR Platform: Next-Day Manufacturing



Designed to address major hurdles of conventional autologous CAR-T

-Faster vein-to-vein time
-Potential of no need for bridging therapy prior to CAR-T infusion
-T-cell quality



GC012F DUAL CAR-T for MM : Study Design

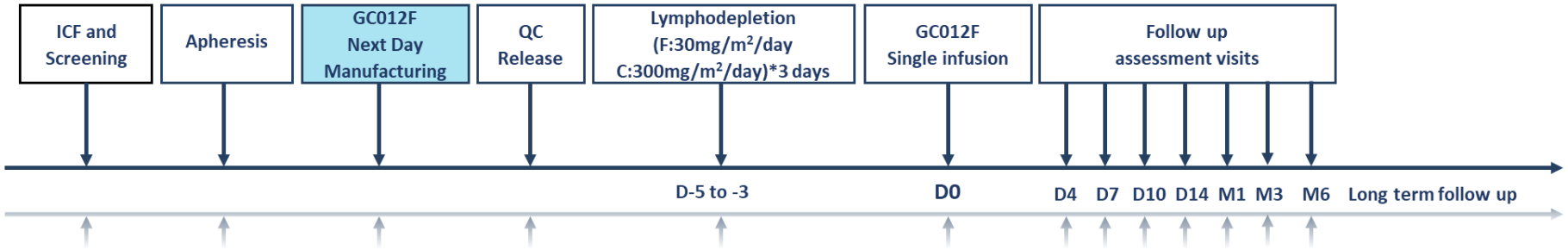
Multicenter, open label, single-arm IIT[1] study (N=29)
FPI October 2019, LPI January 2022
Pts continued to be assessed for response
Data cut-off June 8th, 2022

- **Primary endpoint:**
  - Adverse Events
- **Secondary endpoints:**
  - ORR, BOR
  - MRD assessment at pre-specified timepoints post CAR-T infusion
  - PK/PD

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

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 MM : Baseline Characteristics

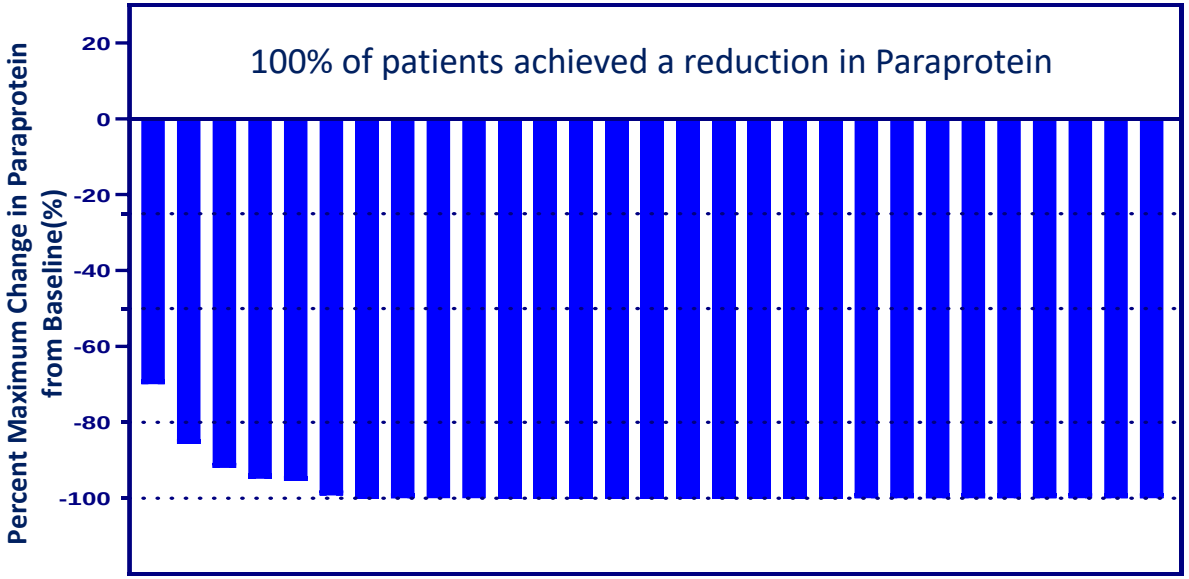
Baseline Characteristics	Total (N=29)
Median age, years (range)	57 (27-76)
Male, n(%)	17 (59)
Type of myeloma, n(%)	
IgG	13 (45)
IgA	6 (21)
IgD	5 (18)
Light chain	5 (18)
Median years since diagnosis (range)	4 (1-10)
High-risk profile[a], n(%)	26 (90)
Double-hit[b], n(%)	3 (10)
Extramedullary plasmacytoma ≥ 1, n(%)	8 (28)

[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

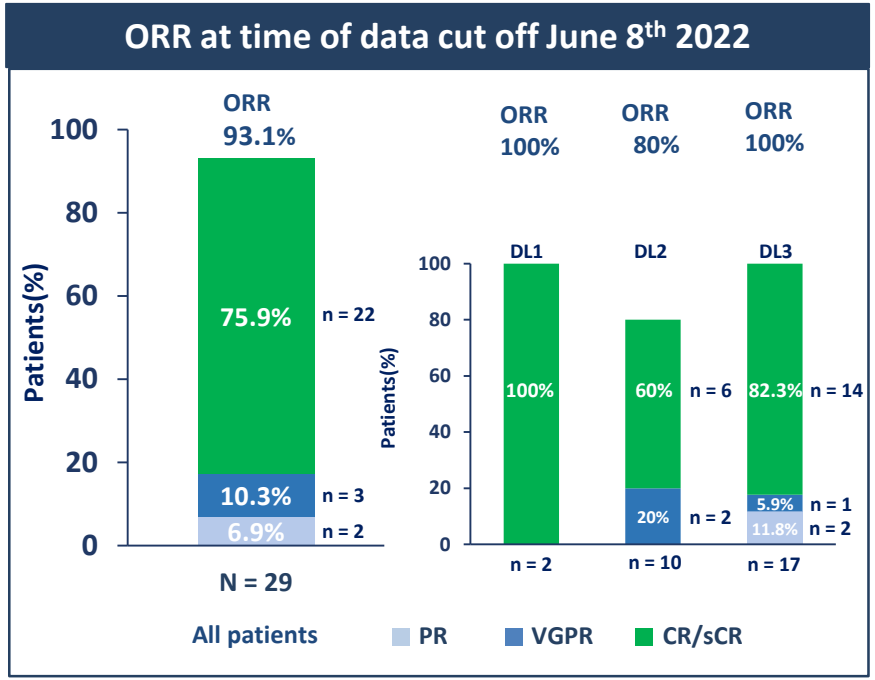
Baseline Characteristics	Total (N=29)
Median prior regimens, n (range)	5 (2-11)
Median prior lines of therapy, n (range)	5 (2-9)
Prior auto-SCT, n(%)	11 (38)
Triple-exposed[c], n(%)	28 (97)
PI refractory	27 (93)
IMiD refractory	27 (93)
anti-CD38 refractory	10 (34)
Penta-exposed[d], n(%)	18 (62)
Primary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

[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 MM : Reduction in Paraprotein



Maximum Reduction in Tumor Burden from Baseline in Response-Evaluable Patients (N=29)

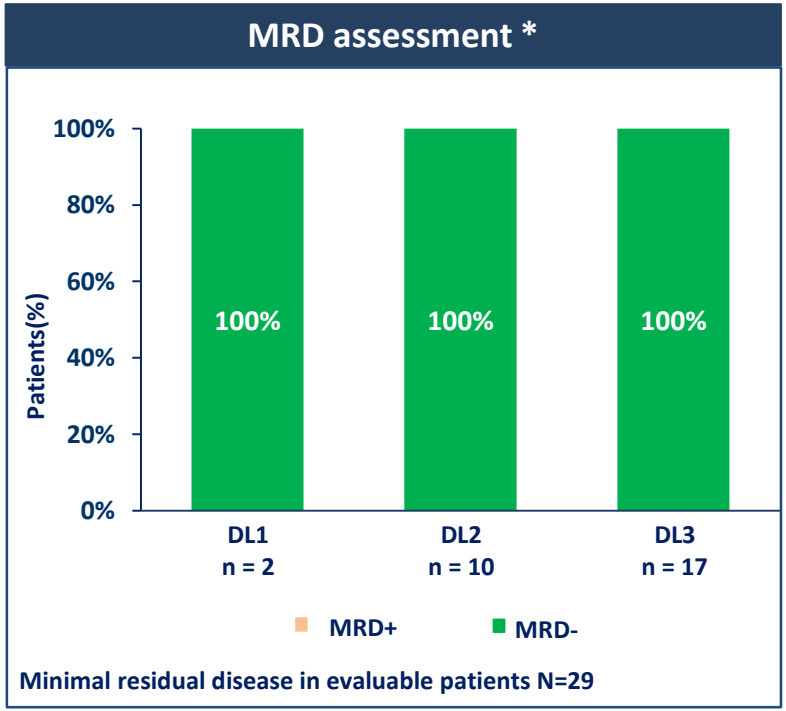


- Time to earliest response: 28 days as first assessment timepoint
- ORR = 93.1% (27/29) patients

  Best response achieved to date

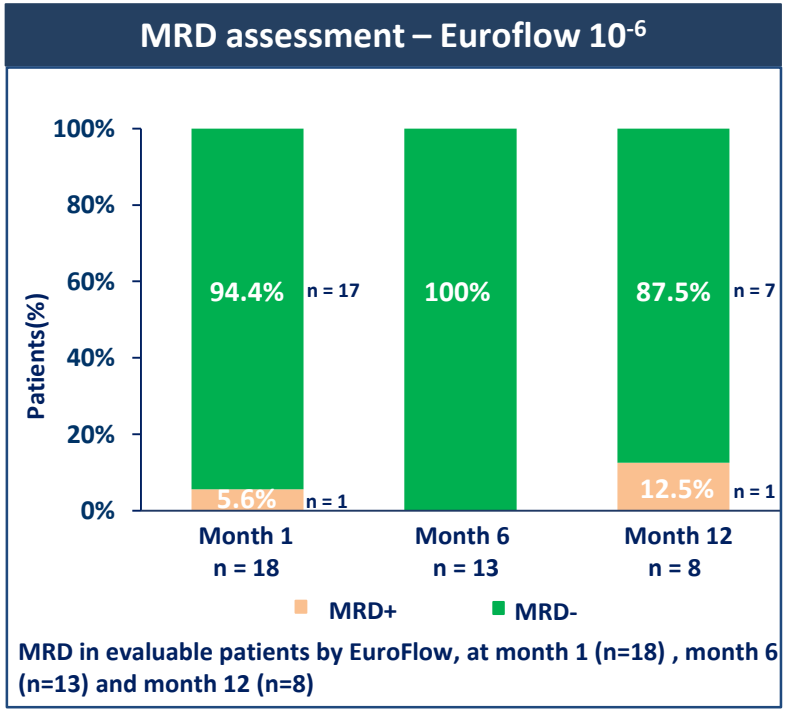
  75.9% (22/29) MRD^{-} sCR

  86.2% (25/29) VGPR or better
- Median duration of response (DOR) at data cut off was 15.7 months (95% CI: 7.6-33.1)
- Median duration of follow up 11.0 months (range 4.9 months to 34.5 months)



- All patients with baseline and at least one post-baseline bone marrow sample N=29
- 100% of evaluable patients achieved MRD negative in DL1 (n=2)
- 100% of evaluable patients achieved MRD negative in DL2 (n=10)
- 100% of evaluable patients achieved MRD negative in DL3 (n=17)

*Sensitivity of MRD- :
- At 10^{-4} in 9 patients tested by flow cytometry
- At 10^{-6} in 20 patients tested by EuroFlow



MRD in evaluable patients by EuroFlow, at month 1 (n=18) , month 6 (n=13) and month 12 (n=8)

- 100% of evaluable pts assessed by Euroflow were MRD negative at Month 6 (n=13)
- Some pts with shorter duration of follow up could not get re-assessed by time of data cut off May 30th 2022
- **87.5% of evaluable patients were MRD negative at Month 12**

GC012F DUAL CAR-T for MM : 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)

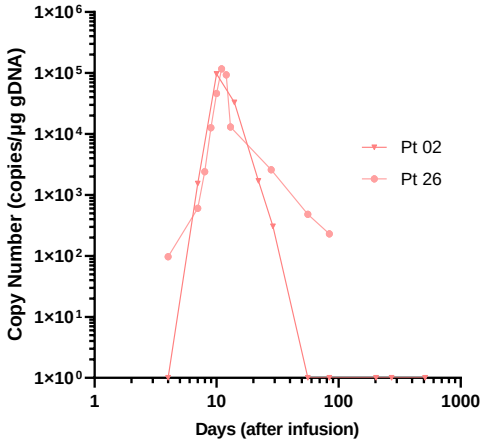
N=29	CRS[1], n (%)	ICANS[2], n (%)
Grade 0	4 (14)	0 (0)
Grade 1	14 (48)	0 (0)
Grade 2	9 (31)	0 (0)
Grade 3	2 (7)	0 (0)
Grade 4-5	0 (0)	0 (0)

[1]CRS treated with Tocilizumab, vasopressors and dexamethasone

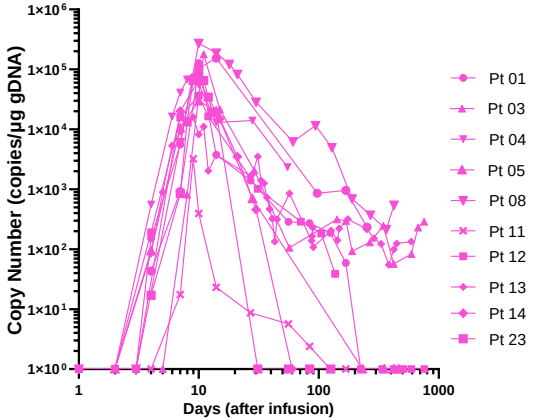
CRS any grade	Median (days)	Range (days)
Time to onset	6	2-10
Duration	3	1-8

*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

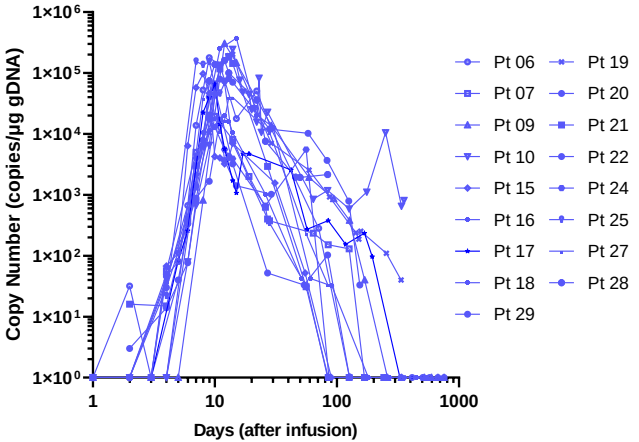
GC012F FasT CAR-T expanded well in all pts with long persistence in all dose levels



DL1 (n=2)



DL2 (n=10)

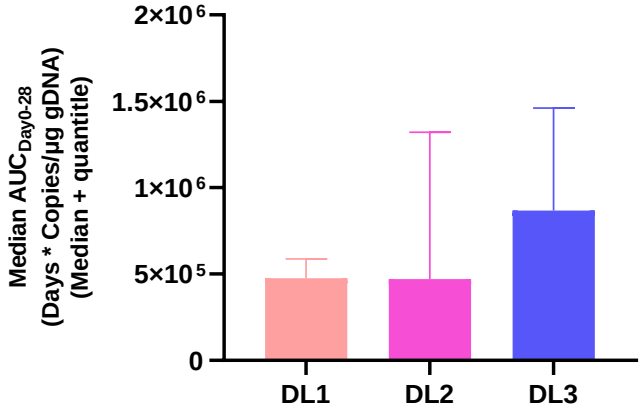


DL3 (n=17)

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

- CAR-T median T_{max} was day 10 (range 7-15)
- Median peak copy number (C_{max}) was 96438 (range 16011-374346 copies/µg genomic DNA)

GC012F DUAL CAR-T for MM : Pharmacokinetics



No 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 MM : Conclusions

- **GC012F continues to show a favorable safety profile with**
  - Mostly low-grade CRS Grade 0-2 93.1% (27/29), no grade 4 or 5 CRS and no ICANs observed
- **High overall responses rate ORR of 93.1% (27/29) in a mostly high risk population**
  - 75.9% MRD - sCR to date – pts still being followed for response assessment for BOR
- **MRD negativity achieved in all treated patients - 100% (29/29), EuroFlow 10^{-6} pts 100% (20/20)**
- **FAST DEEP and durable responses with median DOR of 15.7 months with pts still in follow-up**
- **GC012F dual targeting BCMA/CD19 shows very promising activity in RRMM including High Risk pts and heavily pretreated pts with prior exposure to anti-38 mAb, PI, IMiDs**

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  - Shanghai Changzheng Hospital
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  - Tangdu Hospital/ Xi'an
  - The First Affiliated Hospital of Anhui Medical University
  - The Second Affiliated Hospital of Xi'an Jiaotong University

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