Long-term Follow-up Results of a Multicenter First-in-Human Study of the Dual BCMA/CD19 Targeted FasT CAR-T GC012F for Patients with Relapsed/Refractory Multiple Myeloma

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Background and Rationale

➢**GC012F – a DUAL targeting BCMA/CD19 CAR-T for R/R Multiple Myeloma**

- 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]
- Our preclinical work demonstrated effective elimination of MM cells by BCMA/CD19 Dual CAR-T[4]

➢**GC012F is manufactured on the FASTCAR™ – platform enabling overnight manufacturing**

Patient Demography

Table 1. Baseline Characteristics

Baseline Characteristics	Total (N=19)
Median age, years (range)	55 (27-71)
Male, n(%)	12 (63)
Type of myeloma, n(%)	
IgG	8 (42)
IgA	5 (26)
IgD	3 (16)
Light chain	3 (16)
Median years since diagnosis (range)	3 (1-10)
High-risk profile[a], n(%)	18 (95)
Double-hit[b], n(%)	3 (16)

Baseline Characteristics	Total (N=19)
Median prior regimens of therapy, n (range)	5 (2-11)
Median prior lines of therapy, n (range)	5 (2-9)
Prior auto-SCT, n (%)	7 (37)
Triple-exposed[c, d], n(%)	18 (95)
PI refractory	18 (95)
IMiD refractory	17 (89)
anti-CD38 refractory	4 (21)
[d]Penta-exposed, n(%)	12 (63)
Primary refractory, n (%)	3 (16)
Refractory to last therapy, n (%)	15 (79)

[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;

Safety Profile

Table 2. TEAE, CRS and ICANS

N=19	All Grades (n,%)	Grade ≥3 (n,%)
Hematologic TEAE* (≥ 25% All Grades)		
Neutropenia	15 (79)	15 (79)
Lymphopenia	14 (74)	14 (74)
Leukopenia	13 (68)	13 (68)
Thrombocytopenia	13 (68)	13 (68)
Anemia	8 (42)	7 (37)
Non-Hematologic TEAE* (≥ 25% All Grades)		
LDH increased	12 (63)	0 (0)
Hypoalbuminemia	8 (42)	0 (0)
AST increased	7 (37)	5 (26)
Diarrhea	4 (21)	0 (0)
Lower respiratory tract infection	3 (16)	3 (16)

N=19	CRS[1] (n,%)	ICANS[#] (n,%)
Grade 0	1 (5)	0 (0)
Grade 1-2	16 (84)	0 (0)
Grade 3[#]	2 (11)	0 (0)
Grade 4-5	0 (0)	0 (0)

[#]CRS treated with Tocilizumab, vasopressors and dexamethasone

CRS any grade	Median (days)	Min, Max (days)
Time to onset	6	2,10
Duration	4	1,8

No ICANS observed

*AE were graded according to CTCAE v5.0, [1]CRS criteria, ASBMT consensus grading, AST Aspartate Aminotransferase, TEAE- treatment emergent Adverse Event, LDH Lactase dehydrogenase, CRS – Cytokine release syndrome, [#]ICANS – Immune effector cell-associated neurotoxicity syndrome

Study Design

Multicenter, open-label, single-arm IIT[1] study

➢ **Key Eligibility Criteria**

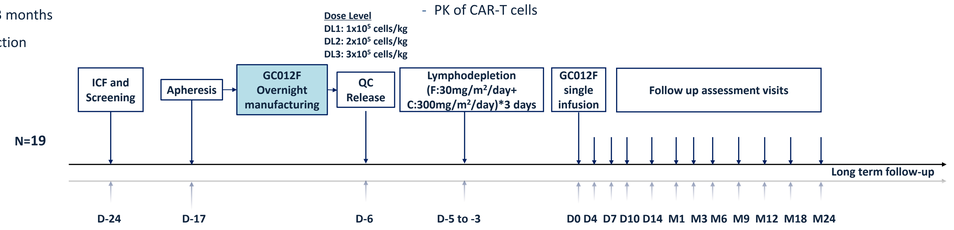
- Relapsed/Refractory Multiple Myeloma (IMWG criteria 2016)
- Expected survival ≥ 3 months
- Adequate organ function

➢**Primary endpoint:**

- Adverse Events

➢**Secondary endpoints:**

- MRD at pre-specified timepoints post CAR-T infusion
- ORR
- PFS, OS and DOR at 3 months and 6 months after CAR-T infusion
- PK of CAR-T cells



[1]IIT – investigator initiated trial

Figure 1. Study Schema

Efficacy: Response (data cut off Jan 12th 2021)

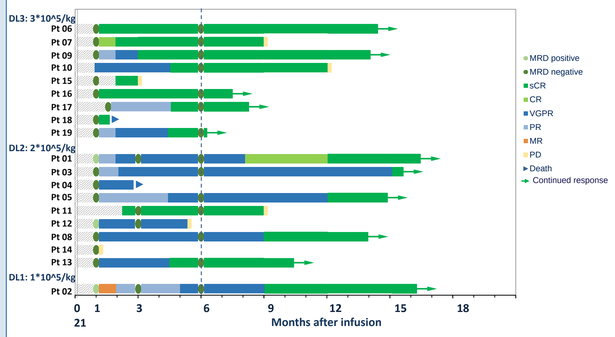


Figure 2. Response assessment. At data cut off, the median time to follow up was 13.8 months (6.1-16.4). 19 patients were evaluable for response. ORR was 94.7%-all response VGPR or better (94.7%-16/18 sCR, 2/18 VGPR) with all patients MRD- by flow cytometry (10^{-4}-10^{-6}) – earliest response d28 post infusion. Best response was MRD-sCR in 16/19 patients (84.2%). Median duration of response (DOR) not yet reached. In DL3 (n=9) 4 additional patients were response evaluable for 6 month follow-up: 100% (9/9) of patients achieved MRD-sCR as best response, 87.5% (7/8) of response evaluable patients maintained MRD-sCR at landmark analysis of 6 months.

CAR-T Expansion and Persistence

Table 2. CAR-T quick expansion with long duration. CAR-T median Tmax was 10 d (range 8-14 d), median peak copy number (Cmax) was 127548 (16,011-374,346) copies/μg DNA with long duration of persistence of up to 60 weeks at time of data cut off.

	Cmax (copies/μg DNA)	
	Median	Min, Max
DL1 (n=1)	96438	96438, 96438
DL2 (n=9)	67970	16011, 272401
DL3 (n=9)	178136	20068, 374346
All patients (N=19)	127548	16011, 374346

Efficacy: ORR

Figure 3. ORR in all patients (N=19) and patients in DL3 (n=9)

*Data cut off as Jan 12th 2021

➢Time to earliest response: 28 days

➢ORR = 94.7% (18/19) patients

➢Best response achieved to date

✓**CR/sCR** – 84.2% (16/19)

✓VGPR or better – 94.7% (18/19)

✓**9 out of 9 (100%) achieved sCR in DL3**

➢Median duration of response (DOR) not yet reached

Efficacy: MRD assessment

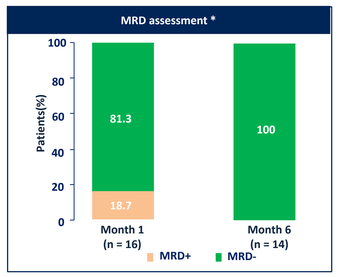


Figure 4. Minimal residual disease in evaluable patients at month 1 (n=16) and month 6 (n=14).

*Sensitivity of MRD- :
- At 10^{-4} in 7 patients tested by Flow cytometry
- At 10^{-6} in 12 patients tested by EuroFlow

➢All patients had at least one post-baseline bone marrow sample available for MRD assessment by NGF (Next Generation Flow)

➢100% of evaluable patients were MRD negative at Month 6 (n=14)

Efficacy: Tumor Burden Reduction

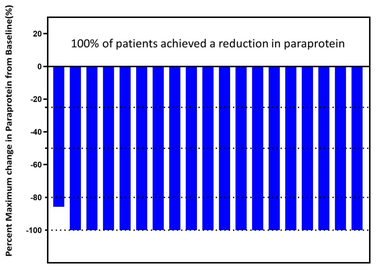


Figure 5. Maximum Reduction in Tumor Burden from Baseline in Response-Evaluable Patients (n=19).

Conclusion

◆**GC012F shows very promising activity in R/R MM patients**

- ✓High Risk patients (18/19, 94.7%) as defined by mSMART 3.0
- ✓Patients heavily pretreated including anti-CD38 mAb, PI, IMiD - median of 5 prior lines of therapy
- ✓**94.7% ORR- all VGPR or better (sCR)**
- ✓100% patients achieving sCR or VGPR as best response were evaluated to be MRD negative
- ✓**100% MRD negative sCR rate in DL3 (n=9)**

◆**Favorable safety profile**

- ✓CRS Grade 1/2 16/19 (84.2%), Grade 3 in 2/19 (10.5%) patients
- ✓ No CRS Grade 4/5 observed
- ✓ **No ICANS observed**

◆**Persistence of CAR-T shows a long duration of up to 60 weeks post CAR-T infusion (at time of data cut off)**

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