2025 ACR Convergence

October 24-29 CHICAGO, USA

Autologous CD19-BCMA Dual-Target CAR T Cell Therapy GC012F(AZD0120) for Refractory Systemic Lupus Erythematosus: A Phase I Single-Center, Open-Label Clinical Trial

Chunmei Wu[1,3], Yakai Fu[1], Yan Ye[1], Ran Wang[1], Chunyan Zhang[1], Shaoying Yang[1], Teng Li[3], Zixuan Zhu[3], Xixi Gu[3], Shan Jiang[3], Xintong Feng[2], Peiying Li[4], Ting Li[1], Lianjun Shen[2], Xiaoming Zhang[3], Jia Liu[2], Shuang Ye[1], Qiong Fu[1,3,5]

1 Department of Rheumatology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China
2 Gracell Biotechnologies Ltd & Cell therapy, AstraZeneca, Shanghai, China
3 Key Laboratory of Immune Response and Immunotherapy, Shanghai Institute of Immunity and Infection, Chinese Academy of Sciences, Shanghai, China
4 Clinical Research Center, Renji Hospital, Shanghai Jiao long University School of Medicine, Shanghai, China
5 Shanghai Immune Therapy Institute, Shanghai, China

GRACELL 亘喜生物 — A member of the AstraZeneca Group 阿斯利康集团成员

INTRODUCTION

GC012F (AZD0120) – a DUAL targeting BCMA/CD19 chimeric antigen receptor (CAR)-T cell therapy

- Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by autoantibodies produced by pathogenic plasma cells, long-lived plasma cells, and memory B cells.
- Studies have shown that CD19 CAR-T cell therapy can induce remission in refractory SLE (rSLE).
- Long-lived plasma cells contribute to persistent autoantibody production, particularly in late-stage disease.
- Targeting both B and plasma cells may help reset the autoreactome, eliminating pathogenic autoantibodies and improving clinical outcomes. We are investigating GC012F, a novel CD19/BCMA dual targeting CAR-T, for treating rSLE.

AIM

This trial evaluates the safety and preliminary efficacy of GC012F CAR-T cell therapy in rSLE patients.

METHODS

Consent and Screening

Apheresis

AZD0120 Next Day Manufacturing

QC Release

Lymphodepletion D-5 to -3
(C: 250 mg/m²/day * 3 days, F: 25 mg/m²/day * 3 days)

AZD0120 (GC012F) Single infusion D0

DOSE LEVEL 1	DOSE LEVEL 2	DOSE LEVEL 3
1x10⁵ cells/kg	2x10⁵ cells/kg	3x10⁵ cells/kg

Follow-up assessment visits

Key Eligibility Criteria:

- Male or Female aged from 18 to 70 years
- Diagnosed with SLE meeting the 2019 European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) classification criteria for SLE
- At least two immunosuppressants and at least one approved biologics were used more than 6 months without achieving LLDAS
- SELENA-SLEDAI score ≥ 8

RESULTS

Baseline characteristics

Baseline characteristics		P01	P02	P03	P04	P05	P06	P07	P08	P09	P10
Age, Sex		23 F	27 M	21 F	34 F	42 F	26 F	27 F	19 M	31 F	35 F
SLE duration, years		9	2	13	14	18	3	3	8	6	5
Baseline disease activity	SLEDAI-2K	23	12	12	10	6	16	16	4	10	20
	SELENA-SLEDAI	16	8	8	10	8	12	14	8	10	12
	Lupus Nephritis	Ⅳ	Ⅲ + Ⅴ	Ⅳ	Ⅴ	Ⅳ	Ⅲ	Ⅳ + Ⅴ	Ⅳ + Ⅴ	Ⅳ	Ⅳ
	UPCR	4274.38	6357.33	3737.29	1677.34	356.11	4754.43	906.55	(24hUP 3731.3mg)	5930.98	1031.8
SLE prior treatment *		HCQ, MMF, TAC, BEL, TEL	HCQ, MMF, TAC, BEL	HCQ, MMF, CYC, TAC, BEL, RTX	HCQ, AZA, MMF, CYC, TAC, BEL, TEL	HCQ, MMF, TAC, BEL	HCQ, MTX, MMF, CYC, TAC, BEL	MMF, TAC, CSA, TEL	HCQ, MTX, MMF, CYC, BEL	HCQ, MTX, MMF, CYC, TEL	HCQ, AZA, MMF, CYC, TAC, TEL

*All patients previously received glucocorticoid.
HCQ, Hydroxychloroquine; AZA, azathioprine; BEL, belimumab; CSA, cyclosporin A; CYC, cyclophosphamide; MMF, mycophenolate mofetil; MTX, methotrexate; RTX, rituximab; TAC, tacrolimus; TEL, telitacicept; UPCR, urine protein creatinine ratio.

Safety Profile

Data cut-off on Apr 20, 2025

Safety profile was general manageable at all 3 dose levels.
- The protocol-defined dose limiting toxicity (DLT) criteria were not met.
- CRS events were reported in 70% of patients, with the majority being grade 1.
- No grade ≥ 3 CRS and ICANS of all grades were reported.

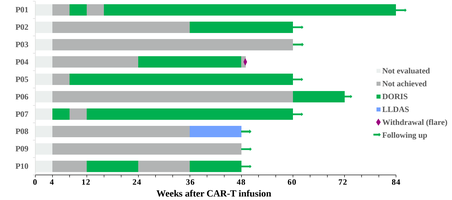
N=10	All Grades, n (%)	Grade ≥3, n (%)
Hematologic TEAEs* (≥ 25% All Grades)		
Neutropenia	8 (80)	6 (60)
Lymphopenia	7 (70)	5 (50)
Leukopenia	9 (90)	3 (30)
Anemia	6 (60)	0 (0)
Non-Hematologic TEAEs* (≥ 25% All Grades)		
Fever	9 (90)	1 (10)
Hypogammaglobulinanemia	10 (100)	0 (0)
Alopecia	6 (60)	0 (0)
Infections	9 (90)	2 (20)
Liver injury	3 (30)	0 (0)
Gastrointestinal disorders	4 (40)	0 (0)

N=10	CRS[1], n (%)	ICANS[2], n (%)
Grade 1	6 (60)	0
Grade 2	1 (10)	0
Grade 3	0	0
Grade 4/5	0	0
All grades	7 (70)	0 (0)

CRS any grade	Median (days)	Range (days)
Time to onset	7	6-14
Duration	1	1-4

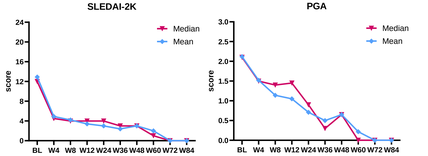
CRS - cytokine release syndrome, ICANS - immune effector cell-associated neurotoxicity syndrome
1 CRS graded by ASTCT Consensus criteria; one patient was treated with tocilizumab.
2 ICANS graded by ASTCT Consensus.
* AEs were graded according to CTCAE v5.0, TEAE - treatment emergent adverse event

Efficacy Profile

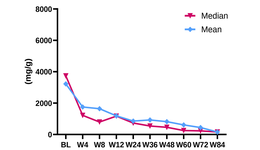


Outcome measures		SRI-4 Total N=10	CRR Total N=10
SLE remission	12W	100%	40%
	24W	100%	40%
	36W	100%	50%
	48W	100%	66.7%
Glucocorticoid Free		60%	
Immuno-suppressant Free		100%	
Biologics Free		100%	

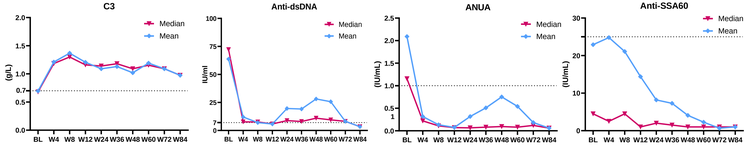
Disease activity assessment



Renal response



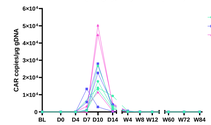
Serological improvement



Pharmacokinetics Profile

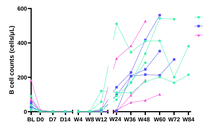
CAR copy number

- Median Cmax, median(range), copies/μg gDNA = 20180 (11482 - 50316)
- Median Tmax, median(range), days= 10 (7-10)

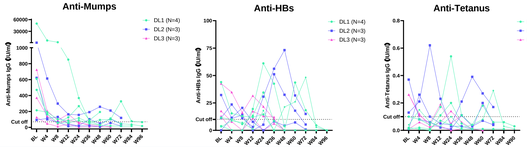


B cell recovery

- B cell recovery, median(range), days = 84 (56-168)
- B cell recovery, median(range), cells/μl = 7.2 (0.4-96.8)



Vaccination Antibody



CONCLUSIONS

- **GC012F has shown a very promising DORIS and SRI-4 remission without the need of treatment with immunosuppressant and other medications, 48-week follow-up shows:**
  - **SRI-4 rate: 100%**
  - **Complete renal response rate: 66.7%**
  - **Glucocorticoid-free rate: 60%**
  - **Immunosuppressant-free rate: 100%**
- **GC012F proliferated in all patients.**
- **B cell depletion occurred post infusion in all patients, followed by the reconstitution of B cells.**
- **Favorable safety profile:**
  - **60% patients experienced CRS grade 1, 10% patients experienced CRS grade 2, no CRS grade ≥3 observed.**
  - **No ICANS observed.**
  - **No DLT observed.**
  - **All AEs were reversible.**

ACKNOWLEDGEMENT

We would like to thank the patients, their families, the investigators and all the caregivers involved in this study and AstraZeneca/Gracell Biotechnologies for providing FasT CAR™ GC012F.

CONTACT INFORMATION

Contact E-mail: fuqiong5@163.com
ye_shuang@163.com
effie.liu@astrazeneca.com