Preliminary Safety, Efficacy, and Cellular Kinetics of CTA313, a CD19/BCMA Dual-Targeted Universal CAR-T Therapy, for Active Systemic Lupus Erythematosus

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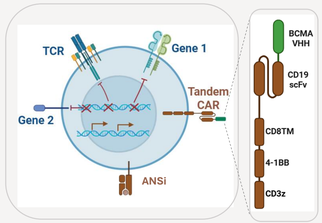
BACKGROUND

- Systemic lupus erythematosus (SLE) is characterized by B cell activation, autoantibody production and autoreactivity.
- Recently, CAR-T therapy has emerged as a promising strategy to deplete autoreactive B cells and induce sustained remission.
- CTA313 is a CD19/BCMA dual-targeted "off-the-shelf" allogeneic CAR-T product developed on the ANSWER platform (ANSi), which enhances persistence and confers resistance to host immune rejection (Fig.1).
- Due to its mechanism of action, CTA313 treatment may provide an alternative means to deplete B cells in blood and tissue of patients with autoimmune diseases, such as SLE and LN.
- The study aims to evaluate the safety, cellular kinetics, and preliminary efficacy and of CTA313 in patients with active SLE.

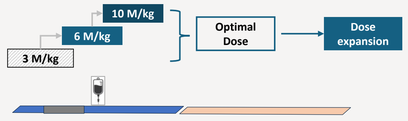
Figure 1. Illustration of CTA313



- TCR knockout prevents GvHD.
- HLA knockout reduces host T-cell rejection and prolongs CAR-T persistence.
- ANSi blocks immune-mediated rejection and supports long-term persistence.
- CNI resistance improves PK, ameliorates CRS, and potentially reduces/eliminates the need for lymphodepletion therapy.

METHODS

- **Design:** Open-label, single arm, dose escalation.
- **Eligibility:** active/refractory SLE/LN aged 18-70 years, SLEDAI-2K score >6 at screening.
- **Primary endpoint**: Safety.
- **Key Secondary endpoints:** Disease specific treatment response, *e.g.,* SLEDAI-2K, PGA; cellular PK, PD (autoantibodies, B-cell aplasia).
- **Study Schema:**



Fludarabine 30mg/m²/day; Cyclophosphamide 300mg/m²/day; D-5 to -3
Tacrolimus is continuous until last detectable CAR-T measurement
Response Assessments and Follow Up through 24 months
CAR-T infusion

SLE, systemic lupus erythematosus; LN, lupus nephritis; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; PGA, physician global assessment; PK: pharmacokinetics; PD: pharmacodynamics

RESULTS

Table 1. By Patient Data – PK/PD findings correspond with efficacy, reflected in sustained dsDNA clearance and patient remission

#	Disease	Dose, ×10⁶/kg	CRS	Cmax, Cells / uL	Persistence, days	SLEDAI-2K						C3 (Normal range: 0.9-1.8 g/L)						Anti-dsDNA (Normal range <10 IU/mL)						B cells (Cells/uL)			
						BL	M1	M2	M3	M4	M6	BL	M1	M2	M3	M4	M6	BL	M1	M2	M3	M4	M6	BL	M1	D42	M2
1	SLE/LN	3.0	G1	333.4	D42	12	4	4	8	4	4[P]	0.64	1.42	1.33	1.28	1.66	1.37	151.3	10.7	2.7	1.1	1.2	<1	24.1	0	0	2.3
2	SLE	3.0	G1	572.3	D21	11	4	6	0	0	0	1.19	1.60	1.58	1.13	1.24	1.38	5.4	<1	<1	<1	1.5	3.0	32.2	0	64.6	170.2
3	SLE	3.0	G1	9.5	D10	10	0	0	0	2	0	1.27	1.51	1.45	1.41	1.36	1.26	Neg[a]	Neg	Neg	Neg	Neg	Neg	61.9	2.3	152.2	400.3
4	SLE/LN	3.0	None	11.4	D28	12	6	8	8	6	6[P]	0.49	0.83	0.93	0.86	0.80	0.92	12.6	3.3	<1	<1	n.a.	<1	23.2	0	n.a.	0.3
5	SLE/LN	6.0	None	11.8	D90	12	6	0	8	4[P]	n.d.	0.7	1.38	1.45	1.34	1.13	n.d.	162.9	14.7	3.3	1.3	<1	n.d.	26.2	0	0	0
6	SLE	6.0	None	1.4	D10	18	2	6	10	6	n.d.	1.04	0.99	0.87	0.72	0.83	n.d.	6.1	3.6	10.7	39.5	14.9	n.d.	91.6	4.4	45.1	52.6
7	SLE	6.0	None	303.9	D60	10	4	4	0	0	n.d.	1.2	1.64	1.93	1.5	1.27	n.d.	42.0	3.8	1.1	<1	<1	n.d.	31.8	0	0.3	99.1
8	SLE	6.0	G1	5469.1	D60	8	2	0	0	0	n.d.	1.48	1.4	1.75	1.54	1.54	n.d.	3.4	<1	<1	<1	<1	n.d.	69.2	0	0	0
9	SLE/LN	6.0	None	481.5	D28	12	4	2	2	n.d.	n.d.	1.11	1.49	1.51	1.09	n.d.	n.d.	2.9	<1	<1	<1	n.d.	n.d.	81.1	0	0.8	15.4
10	SLE/LN	6.0	G1	912.1	D42	10	2	0	n.d.	n.d.	n.d.	0.85	1.33	1.33	n.d.	n.d.	n.d.	51.5	3.2	1.3	n.d.	n.d.	n.d.	84.3	0	0	7.07
11	SLE/LN	10.0	None	592.6	D56	12	5	0	n.d.	n.d.	n.d.	1.24	2.06	1.68	n.d.	n.d.	n.d.	1.9	<1	<1	n.d.	n.d.	n.d.	63.2	0	0	1.2
12	SLE/LN	10.0	None	149.5	D21	8	0	0	n.d.	n.d.	n.d.	1.18	1.40	1.09	n.d.	n.d.	n.d.	29.9	1.4	<1	n.d.	n.d.	n.d.	11.5	0	1.2	5.4
13	SLE	10.0	None	1037.7	>D42	11	2	n.d.	n.d.	n.d.	n.d.	0.71	1.15	n.d.	n.d.	n.d.	n.d.	31.2	3.1	n.d.	n.d.	n.d.	n.d.	56.0	0	0	0
14	SLE/LN	10.0	None	92.0	D21	15	3	n.d.	n.d.	n.d.	n.d.	0.54	1.18	n.d.	n.d.	n.d.	n.d.	12.4	2.3	n.d.	n.d.	n.d.	n.d.	52.9	0	n.d.	n.d.

n.d. = no data; n.a. = not available; neg = negative; [P] Proteinuria (SLEDAI-2K score = 4) remains; [a] Pt3 SLEDAI-2K based on local site anti-dsDNA result (central lab positive, local negative).

CONCLUSIONS

- CTA313 exhibits an acceptable safety profile in patients with SLE and LN.
- CTA313 demonstrates robust expansion, and long-term persistence exemplary for an allogeneic cell product.
- CTA313 induced profound yet temporal B-cell depletion associated with ongoing elimination of pathogenic autoantibodies, suggestive of immune-reset; marked clinical improvement, with evolving and durable responses in patients with active SLE and LN
- Ongoing clinical studies are further evaluating CTA313 in patients with other B cell-driven autoimmune diseases.
- CTA313 provides a **"ready-at-point of care"** cell product, which **obviates challenges of autologous** CAR-T (*apheresis, prolonged period off GC/IS Tx risking disease flare*), **maintains safety, efficacy while increasing pt access** to CAR-T therapy in autoimmunity.
- **Global study is planned for early 2026**

RESULTS

Table 2. Baseline Characteristics

- Fifteen patients (9 LN and 6 SLE) received CTA313 at various doses, DL1 (n=4), DL2 (n=6), DL3 (n=5)
- Median age 37 (21-50) years, disease duration median 6.9 (1.2-17.0) years, and 40% patients had previously received biologics including belimumab and telitacicept.

	DL1 (3×10⁶/kg; n=4)	DL2 (6×10⁶/kg; n=6)	DL3 (10×10⁶/kg; n=5)	All (n=15)
Disease				
SLE (n, %)	2 (50)	3 (50)	1 (20)	**6 (40)**
LN (n, %)	2 (50)	3 (50)	4 (80)	**9 (60)**
Age (median, range)	45.5 (39-50)	34 (22-50)	35 (21-37)	**37 (21-50)**
Sex (female/male)	2/2	6/0	5/0	**13/2**
Disease duration (years; median, range)	3.75 (1.3-10)	9.65 (1.2-17)	6.9 (3.4-10.5)	**6.9 (1.2-17)**
Autoantibodies*	ANA (100%) dsDNA (75%) Anti-Sm (50%)	ANA (100%) dsDNA (50%) Anti-Sm (33%)	ANA (100%) dsDNA (80%) Anti-Sm (60%)	**ANA (100%) dsDNA (67%) Anti-Sm (47%)**
Disease activity SLEDAI-2K (median, range)	11.5 (10-12)	11 (8-18)	12 (8-23)	**12 (8-23)**
Median number of prior therapies (range)	4 (4-5)	5.5 (3-7)	7 (5-9)	**5 (3-9)**
Prior biologics use, n(%)	0	2 (33)	4 (80)	**6 (40)**
ISN/RPS classification	IV+V (1)	UNK	IV (1)	**IV+V (1) IV (1) UNK (7)**

SLE, systemic lupus erythematosus; LN, lupus nephritis; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; dsDNA, double-stranded DNA; ANA, antinuclear antibody; ISN/RPS, International Society of Nephrology/Renal Pathology Society; UNK, unknown
**Only autoantibodies with higher specificity to SLE shown;*
Data cut: September 20th, 2025

Figure 2. CTA313 was Well Tolerated with a Favorable Safety Profile

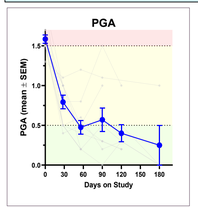
- Only Grade 1 CRS was observed in 6 patients (40%), largely self-limiting
- No ICANS, GvHD were reported
- G3 infections fully resolved with antimicrobial treatment

Adverse Events of Special Interest	3×10⁶ CAR+ cells/kg (n=4)	6×10⁶ CAR+ cells/kg (n=6)	10×10⁶ CAR+ cells/kg (n=5)	All Dose (n=15)
CRS	3 (75%) G1	2 (33%) G1	1 (20%) G1	6 (40%) G1
Tocilizumab use	*None*	*1 (17%)*	*1 (20%)*	*2 (13%)*
ICANS	None	None	None	None
GvHD	None	None	None	None
Infections[a] (Gr ≥2)	None	1 (17%) G3 Herpes zoster 1 (17%) G3 Febrile neutropenia	1 (20%) G3 Pneumonia	1 (7%) G3 Herpes zoster 1 (7%) G3 Pneumonia 1 (7%) G3 Febrile neutropenia

[a]Herpes zoster, Pt07, on D111; Pneumonia, Pt13, on D21; Febrile neutropenia, Pt10, on D21 .

Figure 3. Marked Improvement in Disease Activity and Remission Achieved

- Evolving responses with dose and time; SRI-4 100%, **LLDAS 79%,** and **43% DORIS remission** at a median follow-up of 4 (1-6) months



M1	M2	M3	M4	M6
LLDAS	LLDAS	LLDAS	LLDAS	LLDAS
LLDAS	SRI-4	DORIS	DORIS	DORIS
LLDAS	DORIS	DORIS	LLDAS	DORIS
SRI-4	SRI-4	SRI-4	SRI-4	SRI-4
SRI-4	LLDAS	SRI-4	LLDAS	
LLDAS	SRI-4	SRI-4	SRI-4	
LLDAS	DORIS	DORIS	DORIS	
LLDAS	DORIS	DORIS	DORIS	
LLDAS	LLDAS	LLDAS		
LLDAS	DORIS			
SRI-4	DORIS			
LLDAS	LLDAS			
SRI-4				
LLDAS				

DL: 3M/kg: 50% (2/4 pts) DORIS Remission

DL: 6M/kg: 50% (3/6 pts) DORIS Remission

DL: 10M/kg: 25% (1/4 pts) DORIS Remission

Figure 4. CTA313 Demonstrates Robust Expansion and Persistence

- D28 days persistence in 67% of patients

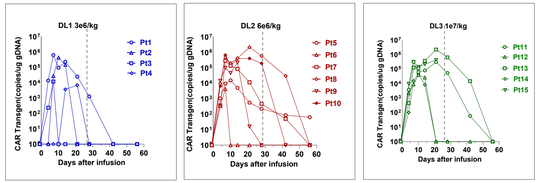
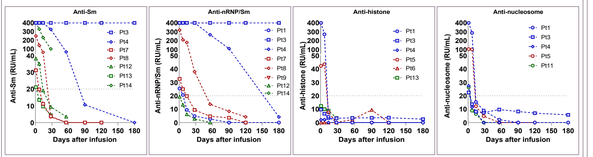


Figure 5. Notable Reduction in all Autoantibodies

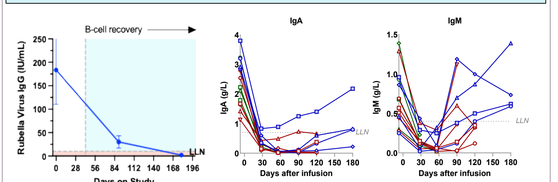
- Reductions were also observed in other autoantibodies, including anti-Sm, anti-histone, anti-nucleosome, anti-nRNP/Sm, and anti-Ro52, anti-SSA/Ro60, anti-SSB (data not shown) antibodies

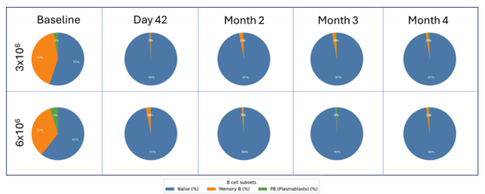


Pts with positive auto-Ab at baseline represented in each graph

Figure 6. B-cell Recovery Following CTA313 Dosing

- Sustained undetectable anti-dsDNA Ab and anti-viral titers from previous vaccination
- B-cell elimination and recovery is commensurate with depletion of circulating Abs; naïve B-cell repopulation leads to sequential resolution of hypoglobulinemia by antibody isotype
- B-cell recovery/repopulation is initially largely naïve B cell phenotype





ABBREVIATIONS

CRS, cytokine release syndrome; GvHD, graft-versus-host disease; G, grade; DLT, dose-limiting toxicity; dsDNA, double-stranded DNA; ICANS, immune effector cell-associated neurotoxicity syndrome; PK, pharmacokinetic; PD, pharmacodynamics; SLE, systemic lupus erythematosus; LN, lupus nephritis; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; PGA, physician global assessment.

DISCLOSURES

None declared: Hanwei Wang, Huan Zhou. Employee of Bioheng Therapeutics Co., Limited: Yue Xie, Guojiao Yang, Lu Han, Jiangtao Ren, Yali Zhou, Wengang Ge, Jan K Davidson-Moncada.

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