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RESET-SSc™: Clinical Trial Evaluating Rese-cel (Resecabtagene Autoleucel), A Fully Human, Autologous 4-1BB CD19-CAR T Cell Therapy in Systemic Sclerosis

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Background: CAR T Therapy in Systemic Sclerosis

- The treatment goals for systemic sclerosis (SSc) are to control disease activity, limit progression of organ damage, and decrease long-term morbidity and mortality.[1]
- Therapies providing durable clinical responses without requiring chronic administration are lacking; a recent US cohort demonstrated progression of skin and lung involvement despite immunosuppressive therapy and high mortality (6.0% at 3 years).[2]
- Chimeric antigen receptor (CAR) T cells may have the potential to achieve an “immune system reset” in a majority of patients with durable remission through a one-time deep, but transient, depletion of B cells (Figure 1).[3,4]
- CD19-CAR T cells have demonstrated durable, drug-free responses in SSc patients in an academic program.[3,4]
- Rese-cel (resecabtagene autoleucel, formerly CABA-201) is a fully human, autologous 4-1BB CD19-CAR T cell therapy, designed to deeply and transiently deplete CD19 positive B cells following a one-time weight-based infusion of 1x10^6 CAR T cells/kg.[5,6]
- Here, we report clinical data from RESET-SSc (NCT06328777), an ongoing Phase 1/2 trial evaluating rese-cel in two independent cohorts of adults with SSc and either severe skin or organ involvement.[6,7]

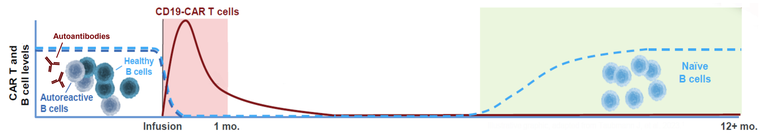


Figure 1. Proposed effect of CD19-CAR T cell therapy.[3,4] Deep depletion of B cells in SSc patients may lead to cessation of disease by removing a central driver of inflammation (autoreactive B cells) and allowing the immune system to return to a tolerant state, resulting in deep and durable remissions off therapy. Some patients may have autoantibodies derived from CD19 negative plasma cells. These remaining autoantibodies may in some, but not all cases, be pathogenic.

RESET-SSc Study Design

Key Inclusion Criteria[6,7]

- Age ≥18 and ≤75 with a limited or diffuse SSc diagnosis (2013 EULAR/ACR classification criteria)
- Early, active disease
- Evidence of significant skin, pulmonary, renal, or cardiac involvement

Key Exclusion Criteria[6,7]

- Severe pulmonary or cardiac impairment
- Treatment with B cell-depleting agent within prior ~6 months
- Previous CAR T cell therapy and/or HSCT

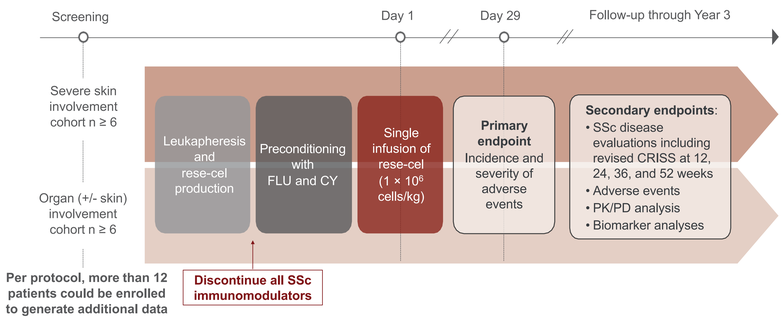


Figure 2. RESET-SSc study design[6,7]

ACR, American College of Rheumatology; ASTCT, American Society for Transplantation and Cellular Therapy; CAR, chimeric antigen receptor; CRISS, Composite Response Index in Systemic Sclerosis; CRS, cytokine release syndrome; CY, cyclophosphamide; DLCO, % predicted diffusing capacity for carbon monoxide; dPCR, digital polymerase chain reaction; EULAR, European Alliance of Associations for Rheumatology; FLU, fludarabine; FVC, forced vital capacity; GC, glucocorticoid; HAQ-DI, Health Assessment Questionnaire Disability Index; HCQ, hydroxychloroquine; HSCT, haematopoietic stem cell transplantation; ICANS, immune effector cell-associated neurotoxicity syndrome; IHC, immunohistochemistry; ILD, interstitial lung disease; IM, immunomodulatory medication; IV, intravenous; IVIg, intravenous immunoglobulin; mAb, monoclonal antibody; MMF, mycophenolate mofetil; MPA, mycophenolic acid; mRNA, messenger ribonucleic acid; mRSS, modified Rodnan Skin Score (measure of skin thickness in SSc across 17 body areas, with a maximum score of 51); NIN, nintedanib; N/A, not applicable; PD, pharmacodynamic; PFT, pulmonary function test; PK, pharmacokinetic; RESET, REstoring SElf-Tolerance; rese-cel, resecabtagene autoleucel; RNA Pol III/RP11, ribonucleic acid polymerase III; SAE, serious adverse event; Scl-70, anti–topoisomerase I antibody; SSc, systemic sclerosis; TOC, tocilizumab; USG, ultrasonography.

RESET-SSc Results: Baseline Characteristics and Safety*

Table 1. Patient demographics and baseline characteristics of first 6 patients in RESET-SSc†

	Severe Skin Cohort			Organ Cohort		
Patient / Cohort	**SSc-Skin-1**	**SSc-Skin-2**	**SSc-Skin-3**	**SSc-Organ-1**	**SSc-Organ-2**	**SSc-Organ-3**
Age, sex	66 F	55 F	59 M	70 M	43 F	60 F
Disease duration (y)	~2	~0.5	~2	~5	~2	~1
Autoantibodies	RNA Pol III	Scl-70	RNA Pol III	–	Scl-70	Scl-70
Baseline‡ mRSS	**42**	**38**	**45**	**12**	**9**	**24**
Baseline‡ HAQ-DI	2.25	2.125	2.875	0.75	0.50	2.50
Baseline‡ PFTs (% predicted)	FVC: 91 DLCO: 70	FVC: 93 DLCO: 58	FVC: 50 DLCO: 89	FVC: 69 DLCO: 58	FVC: 76 DLCO: 66	FVC: 83 DLCO: 78
ILD presence§	✓	–	–	✓	✓	✓
Therapies at Screening	MMF	GC, MPA	MMF	MMF, TOC, NIN	GC, TOC	MMF, IVIg, HCQ

†All patients had active, refractory disease
‡Baseline disease activity = activity before preconditioning.
§Per patient history and HRCT.

Table 2. Incidence of CRS, ICANS, serious infections, and related serious adverse events†

	Severe Skin cohort			Organ Cohort		
Patient	**SSc-Skin-1**	**SSc-Skin-2**	**SSc-Skin-3**	**SSc-Organ-1**	**SSc-Organ-2**	**SSc-Organ-3**
CRS‡	Grade 2**	None	Grade 1	None	None	Grade 1
ICANS‡	None	Grade 3††	None	None	None	None
Serious infections§	None	None	None	None	None	None
Related SAEs (Grade)¶ (Excluding CRS/ICANS)	None	Neutropenic fever (1)	Hypercapnic Respiratory Failure (4) Encephalopathy (4)	None	None	None

†Primary endpoint of the Phase 1/2 study is incidence and severity of adverse events through Day 29. No patient experienced clinical sequelae from CRS, ICANS or related SAEs. Serious infections and related SAEs are reported to latest follow-up.
‡Graded per ASTCT Consensus Grading Criteria.
§Coded in System Organ Class of Infections and Infestations and meets seriousness criteria.
¶As assessed per US Food and Drug Administration guidelines.
**Transient hypotension on Day +10 resolved with IV hydration; no tocilizumab administered.
††Productive cough & fever prior to infusion. Low grade fever & rigors on Day +8, treated with IV cefepime, vancomycin, and morphine. ICE 3 score on Day +9, progressed to ICE 1 on Day +10: arousable; able to speak and follow commands but answered all questions to the ICE assessment incorrectly; no evidence of seizure, elevated intracranial pressure or cerebral edema; resolved within 2 days following dexamethasone.

Rese-cel expansion & B cell kinetics*

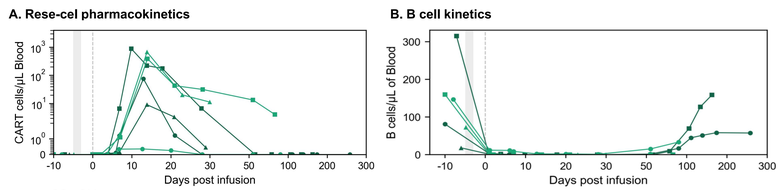


Figure 3. Rese-cel pharmacokinetic (PK) profile & B cell kinetics: (A) Rese-cel PK profile represented as CAR T cells per µL blood and measured by digital PCR (dPCR) and (B) B cell counts (CD19$^+$CD20$^+$) in peripheral blood at baseline before preconditioning and over time following rese-cel infusion measured by flow cytometry. X-axes represent time following rese-cel infusion in days; the vertical gray dotted line indicates the day of rese-cel infusion and the vertical gray shading prior to infusion indicates the window in time for preconditioning across all SSc patients.

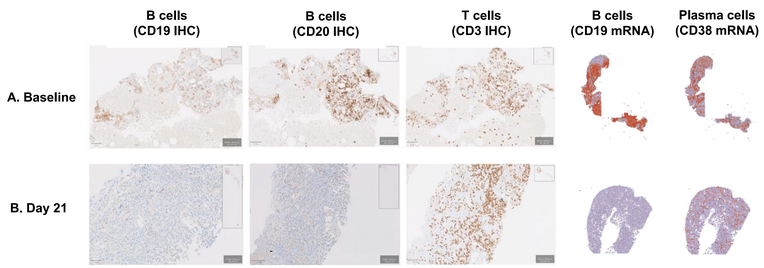
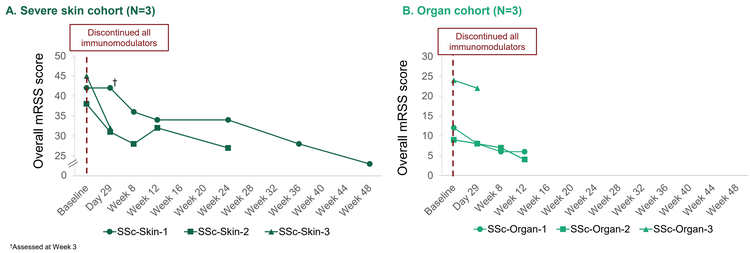


Figure 4. B cells (CD19, CD20), T cells (CD3), and plasma cells (CD38) in lymph node tissue measured by IHC and spatial sequencing at (A) baseline and (B) Day 21 post-infusion in SSc-Skin-1. Consistent with an academic study in autoimmune disease showing CD19-CAR T cell therapy achieves deep tissue B cell depletion in contrast to mAbs.[8]
Lymph node biopsies were from the left inguinal area using USG at University of Michigan by Dr. Khanna.

Clinical efficacy data following rese-cel infusion*



‡Assessed at Week 3

Figure 5. Clinical efficacy: Overall mRSS over time

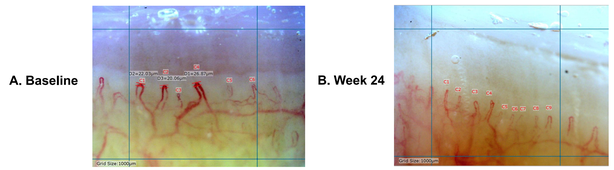


Figure 6. Nailfold Capillaroscopy for SSc-Skin-1 at (A) Baseline and (B) Week 24. Preliminary evidence of vascular recovery or stabilization at Week 24 following rese-cel in the majority of fingers.

Table 3. Clinical efficacy

	Severe Skin Cohort			Organ Cohort		
Patient / Cohort	**SSc-Skin-1**	**SSc-Skin-2**	**SSc-Skin-3**	**SSc-Organ-1**	**SSc-Organ-2**	**SSc-Organ-3**
Latest follow-up	Week 48	Week 24	Day 29	Week 16	Week 12	Day 29
GC-free	✓	✓	✓	✓	✓	–‡‡
IM-free	✓	✓	✓	✓	✓	✓
Antibody and trend†	RNA Pol III ↓	Scl-70 ↓**	RNA Pol III; *too early*	None detected	Scl-70 ↓	Scl-70; *too early*
Revised CRISS-25‡ (time to first response)	✓ Week 12	✓ Week 24	N/A	✓ Week 12	✓ Week 12	N/A
Revised CRISS-50‡ (time to first response)	✓ Week 12§	✓ Week 24	N/A	–	✓ Week 12	N/A
mRSS (baseline to latest follow-up)	42→23	38→27	45→32	12→6	9→4	24→22
FVC¶ [%] (baseline to latest follow-up)	91→105	93→100	N/A	69→72	76→77	N/A
DLCO¶ [%] (baseline to latest follow-up)	70→81	58→75	N/A	58→58	66→75	N/A

†Reflects trend from baseline to latest available timepoint.
‡Revised CRISS is evaluated at Weeks 12, 24, 36, and 52. PFTs from Week 24 are carried forward for Week 36 evaluation.
§Revised CRISS-50 met at Weeks 12 and 36. Not met at Week 24.
¶DLCO and FVC are evaluated at Weeks 12 and 24.
**Based on the research-based, qualified, quantitative Luminex assay.
‡‡Tapering GC.

Summary

- Data from SSc patients infused with rese-cel show an acceptable safety profile following a single weight-based dose of rese-cel.
- Rese-cel peak expansion was observed at approximately 2 weeks after infusion.
- B cells reduced markedly in peripheral blood and lymphoid tissues. Transitional naïve B cells began to repopulate by 2 to 3 months following rese-cel infusion.
- After discontinuation of all immunomodulatory therapies, 100% (4 of 4) of patients with sufficient follow-up to evaluate the revised CRISS achieved CRISS-25, and 75% (3 of 4) achieved CRISS-50. All patients remained off GC and immunomodulatory therapies.
- These initial data suggest the potential for rese-cel to reset the immune system in SSc, allowing patients to achieve meaningful clinical responses off all immunomodulators and GCs.

*As of 11 Sep, 2025.

References: 1. Denton, C, et al. *Rheumatology*. 2024;63(1):2956-2975 **2.** Jaafar S, et al. *Arthritis Res Ther*. 2021;23(1):170. **3.** Müller F, et al. *N Engl J Med*. 2024;390(8):687–700. **4.** Auth J, et al. *Lancet Rheumatol*. 2025;7(2):e83-e93. **5.** Peng BJ, et al. *Mol Ther Methods Clin Dev*. 2024;32(2):101267. **6.** NCT06328777. Available online: www.clinicaltrials.gov/study/NCT06328777. [Accessed Sept 2025] **7.** Cabaletta Bio – Data on File. **8.** Tur C, et al. *Ann Rheum Dis*. 2025;84(1):106–114.