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RESET-SLE™: Clinical Trial Evaluating Rese-cel (Resecabtagene Autoleucel), a Fully Human, Autologous 4-1BB CD19-CAR T Cell Therapy in Non-Renal SLE and Lupus Nephritis

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Background: CAR T Cell Therapy in Systemic Lupus Erythematosus

- Current goals of treatment for systemic lupus erythematosus (SLE) are to achieve low disease state/remission, prevent flares, minimize organ damage, and decrease long-term morbidity and mortality.[1]
- Therapies providing durable clinical responses without requiring chronic administration are lacking.[2,3]
- **<12%** of patients achieved DORIS across all treatment arms in biologic RCTs.[2,3]
- 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, transient depletion of B cells (Figure 1).[4,5]
- CD19-CAR T cells have demonstrated durable, drug-free responses in some SLE patients in an academic program.[5]
- 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.[6,7]
- Here, we report clinical data from RESET-SLE (NCT06121297), an ongoing Phase 1/2 trial evaluating the safety and efficacy of rese-cel in two cohorts of non-renal SLE and lupus nephritis (LN) patients.[7]

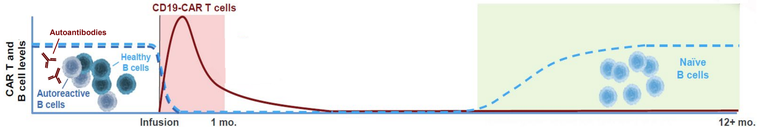

Figure 1. Proposed effect of CD19-CAR T therapy.[4,5] Deep depletion of B cells in SLE patients may lead to cessation of disease by removing a central driver of inflammation (autoreactive B cells) and allowing the immune system to return to a tolerant state, resulting in deep and durable remissions off therapy. Some autoimmune patients may also have antibodies derived from long-lived plasma cells, which are not targeted by CD19-CAR T therapy.

RESET-SLE Study Design

Key Inclusion Criteria[7,8]

- Age ≥18 and ≤65 with an SLE diagnosis
- Positive ANA or anti-dsDNA at screening
- Evidence of active disease despite prior or current treatment with standard of care
- **For SLE (non-renal) cohort**: SLEDAI-2K ≥8; pure Class V LN patients eligible for this cohort
- **LN cohort**: biopsy-proven LN Class III or IV (± Class V)

Key Exclusion Criteria[7,8]

- Presence of kidney disease other than LN
- Previous CAR T cell therapy and/or HSCT
- Treatment with B cell-depleting agent within prior ~6 months

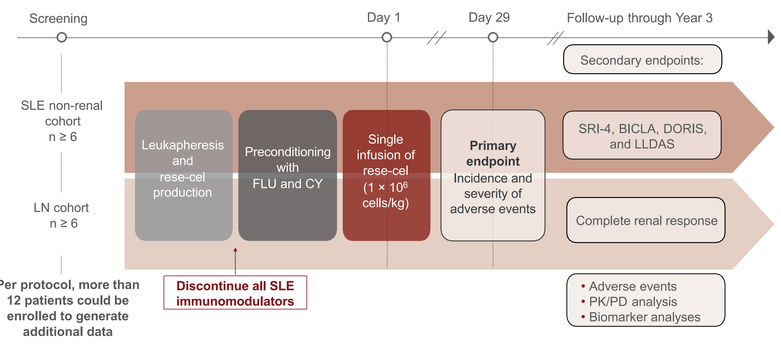

Figure 2. RESET-SLE study design.[7,8]

ANA, antinuclear antibody; ASTCT, American Society for Transplantation and Cellular Therapy; BICLA, British Isles Lupus Assessment Group–based Composite Lupus Assessment; CAR, chimeric antigen receptor; C_{max}, maximum concentration of CAR T cells post-infusion; CRR, complete renal response; CRS, cytokine release syndrome; CY, cyclophosphamide; DORIS, definition of remission in SLE; dsDNA, double-stranded DNA; dPCR, digital polymerase chain reaction; eGFR, estimated glomerular filtration rate; FLU, fludarabine; GC, glucocorticoid; HSCT, haematopoietic stem cell transplantation; ICANS, immune effector cell-associated neurotoxicity syndrome; IM, immunomodulatory; LLDAS, lupus low disease activity state; LN, lupus nephritis; N/A, not applicable; PD, pharmacodynamic; PGA, Physician Global Assessment; PK, pharmacokinetic; PRR, partial renal response; RBC, red blood cell; RCT, randomized clinical trial; rese-cel, resecabtagene autoleucel; RESET, REstoring SElf-Tolerance; SAE, serious adverse event; SRI-4, Systemic Lupus Erythematosus Responder Index-4; SLE systemic lupus erythematosus; SLEDAI-2K, SLE Disease Activity Index 2000; Sm, Smith; TCR, T cell receptor; UPCR, urine protein-to-creatinine ratio; WBC, white blood cell.

RESET-SLE Results: Baseline Characteristics and Safety*

Table 1. Patient demographics and baseline characteristics of first 9 patients in RESET-SLE†

Cohort	Non-renal SLE (n=5)	LN (n=4)
Age, years, mean (min, max)	~34 (26, 44)	~26 (18, 35)
Female, n (%)	4 (80)	3 (75)
Time from diagnosis to screening, years, mean (min, max)	11.5 (6.1, 17.3)	7.3 (2.2, 15.7)
Autoantibodies (%)	dsDNA: 100% Sm: 60%	dsDNA: 75% Sm: 75%
Baseline disease activity‡	**SLEDAI-2K** (median)	
	10	16
	UPCR (mg/mg) (median)	
	1.09¶	3.45
Therapies at screening: **Systemic GCs** **≤2 SLE immunomodulators§** **≥3 SLE immunomodulators§**	 80% 60% 40%	 50% 50% 50%
GC dose at screening, mg/day, mean (min, max)	13.4 (0, 30)	6.25 (0, 20)

†All patients had active, refractory disease and had failed B cell-targeting therapies.
‡Baseline disease activity = activity before preconditioning.
§SLE medications may include biologics, anti-malarials, and immunosuppressants.
¶N=2 patients included in UPCR analysis: SLE-1 had pure Class V LN and extra-renal SLE disease activity and SLE-5 had Class II LN with moderate to severe chronicity and extra-renal disease activity that met inclusion criteria for the non-renal cohort.

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

Cohort	Non-renal SLE (n=5)					LN (n=4)			
Patient	**SLE-1**	**SLE-2**	**SLE-3**	**SLE-4**	**SLE-5**	**LN-1**	**LN-2**	**LN-3**	**LN-4**
CRS‡	None	Grade 1	None	None	Grade 1	Grade 1	None	None	None
ICANS‡	None	None	None	None	None	Grade 4	None	None	None
Serious infections§	None	None	None	None	None	None	None	None	None
Related SAEs (Grade)¶ (Excluding CRS/ICANS)	None	None	None	None	None	Fever (1) Neutropenic fever (1) Pancytopenia** (4)	None	None	None

†Primary endpoint of the Phase 1/2 study is incidence and severity of adverse events through Day 29. Serious infections and related SAEs are reported to latest follow-up. No patient experienced clinical sequelae from CRS, ICANS or related SAEs.
‡Graded per ASTCT Consensus Grading Criteria. 7 of 9 patients received anti-seizure prophylaxis. Tocilizumab was administered for CRS in one patient.
§Coded in System Organ Class of Infections and Infestations and meets seriousness criteria.
¶As assessed per US Food and Drug Administration guidelines.
**Consistent with "Prolonged Cytopenias," which is a labeled warning and precaution for approved oncology CAR T products.

Rese-cel expansion & B cell kinetics*

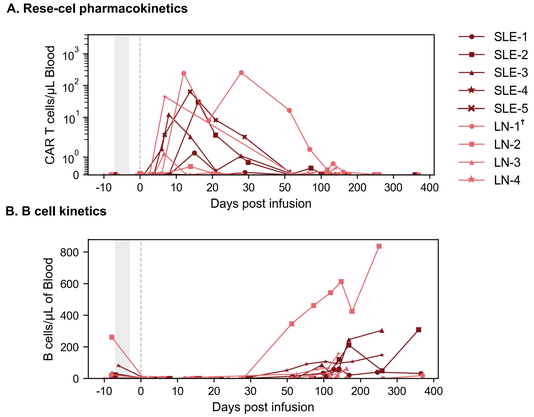

Figure 3. Rese-cel pharmacokinetic (PK) profile & B cell kinetics: (A) Rese-cel PK profile in SLE and LN patients represented as CAR T cells per µL blood and measured by digital PCR (dPCR) and (B) B cell counts (CD19$^+$CD20$^+$) in peripheral blood at baseline before preconditioning and over time following 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 SLE and LN patients.

†LN-1 C_{max} occurred on study Day 29 with T cell receptor sequencing analysis suggesting the second expansion was TCR driven.

Clinical efficacy data following rese-cel infusion*

Table 3. Clinical efficacy†

	Non-renal SLE					LN			
Patient	**SLE-1‡**	**SLE-2**	**SLE-3**	**SLE-4**	**SLE-5‡**	**LN-1**	**LN-2**	**LN-3**	**LN-4**
Latest follow-up	Week 68	Week 52	Week 44	Week 40	Week 8	Week 56	Week 40	Week 28	Week 20
IM-free	✓	✓	✓	✓	✓	✓	✓	✓	✓
GC-free	✓	✓	✓	No	No	✓	✓	✓	✓
DORIS†† (at latest follow-up)	–§	✓	✓	✓	*Too early*	✓	N/A	N/A	N/A
PGA (% improvement from baseline)	93	100	100	64	40	100	100	100	100
SLEDAI-2K improvement (baseline to latest follow-up)	21	8	6	4	7	22	8	12	10**
Anti-dsDNA antibody (change from baseline)	↓	↔ *Transiently negative*	↓	↓	↓	↓ Negative	↓	Negative at baseline	↓
Complement (C3 or C4) (baseline to latest follow-up)	Improving	Normalized	Normal at baseline	*Transiently normalized (up until week 28)*	Normalized	Normalized	Normalized	Normal at baseline	Normal at baseline
CRR†† (at latest follow-up)	✓	N/A	N/A	N/A	–	✓	–	–¶	–
PRR†† (at latest follow-up)	✓	N/A	N/A	N/A	–	✓	✓	–	–
UPCR (mg/mg) (baseline to latest follow-up)	1.08→0.35	N/A	N/A	N/A	1.09→0.81	7.22→0.18	4.85→2	2.04→1.13	1.69→1.83
eGFR (mL/min/1.73m²) (baseline to latest follow-up)	132.7→109.7	N/A	N/A	N/A	108.7→99.2	72.3→123.5	127.2→122.8	133.2→131.8	82.7→60.5

†Lab assessments shown in Table 3 were done at the local sites.
‡SLE-1 had pure Class V LN and extra-renal SLE disease activity and SLE-5 had Class II LN with moderate-severe chronicity and extra-renal disease activity that met inclusion criteria for the non-renal cohort.
§SLE-1 achieved DORIS at Week 48; on cyclosporine therapy between Week 41 and Week 60 for a non-SLE-related, non-rese-cel-related safety event (macrophage activation syndrome with onset at Week 40).
¶LN-3 achieved histologic response (activity index 0/12) on repeat kidney biopsy at 26 weeks post-infusion despite partial reduction in proteinuria.
**Week 20 urinalysis components of the SLEDAI-2K (WBC, RBC and casts) imputed from Week 16 for total SLEDAI-2K score.
††DORIS = Clinical SLEDAI-2K<0 (irrespective of serology); Physician Global Assessment <0.5; antimalarials; low-dose GCs (prednisolone ≤5 mg/day); stable immunosuppressives including biologics. CRR = UPCR ≤0.5 mg/mg; ≥60 mL/min or no confirmed eGFR decrease >20% from baseline; no receipt of rescue therapy. PRR = ≥50% reduction from baseline UPCR.

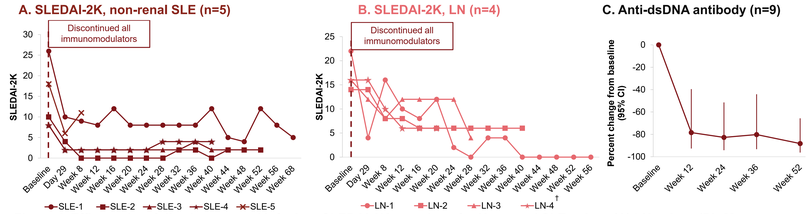

Figure 4. Efficacy data following rese-cel infusion: SLEDAI-2K over time‡ for Non-renal SLE cohort (A) LN cohort (B); Mean percentage (95% CI) change from baseline in anti-dsDNA antibody over time (C)§.

¶Week 20 urinalysis components of the SLEDAI-2K (WBC, RBC and casts) imputed from Week 16 for total SLEDAI-2K score.
‡Lab assessments for SLEDAI-2K were done at the local sites.
§Assessed by ELISA at a central lab at baseline, weeks 12, 24, 36 and 52.

Summary*

- Rese-cel was generally well tolerated across 9 SLE & LN patients treated to date: No CRS in 6 of 9 patients (Grade 1 in 3 patients); no ICANS in 8 of 9 patients (Grade 4 in 1 patient, previously presented).
- After discontinuation of immunomodulatory medications, SLE and LN patients with active and refractory disease showed evidence of efficacy after rese-cel infusion:
  - **75% (3 of 4) SLE patients, with sufficient follow-up achieved DORIS**
    - SLE-1 (pure class V LN) achieved CRR; SLE-5 follow-up ongoing
  - **Median 8-point reduction in SLEDAI-2K and an 89% improvement in PGA** were reported, as of latest follow-up
  - **Significant reduction in anti-dsDNA antibodies has been observed**
  - **Serum complement (C3 or C4) was normalized in 67% (4 of 6) patients** with low complement at baseline, as of latest follow up; 1 additional patient was transiently normalized until week 28 (SLE-4)
  - **75% (3 of 4) LN patients showed renal response**; LN-1 achieved CRR; LN-2 achieved PRR and LN-3 achieved histologic response on repeat biopsy at 26 weeks post-infusion despite a partial reduction in proteinuria
- Peak expansion of rese-cel was observed at approximately 2 weeks after infusion in SLE & LN patients.
- B cells reduced markedly in peripheral blood and in most patients, transitional naïve B cells began to repopulate 1 to 3 months following rese-cel infusion.
- These initial data suggest the potential for rese-cel to reset the immune system in SLE & LN, allowing patients to achieve meaningful clinical responses off all immunomodulators and GCs.

*As of 11 Sep, 2025.

References: 1. Fanouriakis A, et al. *Ann Rheum Dis.* 2024; 83(1):15–29. **2.** Morand EF, et al. *Ann Rheum Dis.* 2023;82(5):639-645. **3.** Parodis I, et al. *Arthritis Rheumatol.* 2023;75 (Suppl 9) Abstr No. 2551. **4.** Taubmann J, et al. OPO141. Abstract presented at: EULAR; May 31, 2023; Milan, Italy. Annals of the Rheumatic Diseases 2023; 82: 93–94. **5.** Müller F, et al. *N Engl J Med.* 2024;390(8):687–700. **6.** Peng BJ, et al. *Mol Ther Methods Clin Dev.* 2024;32(2):101267. **7.** NCT06121297. Available online: www.clinicaltrials.gov/study/NCT06121297 [accessed Sept 2025]. **8.** Cabaletta Bio – Data on File. **9.** Furie RA, et al. *Ann Rheum Dis.* 2022;81(1):100–107.