Safety and Efficacy of Rese-cel (Resecabtagene Autoleucel) in Severe, Refractory SLE and Lupus Nephritis: Results from the RESET-SLE Clinical Trial Phase 1/2 Cohorts

C. Palma[1] P. Reagan[1] S. Sheikh[2] V. Derebail[2] N. Grover[2] G. Gulati[3] M. Abedi[3] M. Sise[4] M. Frigault[4] C. Edens[5] S. Kosuri[5] C. Elgarten[6] R. Scobell[6] J. Burnham[6] I. Blanco[7] G. Georges[7] J. Hogan[8] Y. White[8] J. Volkov[8] D. Nunez[8] T. Furmanak[8] R. Tummala[8] D. J. Chang[8]

1. University of Rochester, NY, USA; 2. University of North Carolina at Chapel Hill, NC, USA; 3. University of California, Davis, CA, USA; 4. Massachusetts General Hospital, MA, USA; 5. University of Chicago, IL, USA; 6. Children's Hospital of Philadelphia, PA, USA. 7. Northwestern University, Chicago, IL, USA. 8. Cabaletta Bio, PA, USA.

Key Takeaway

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. PC-free rese-cel offers potential to achieve similar outcomes with exploration of higher dose cohort progressing.

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Background:

- 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]
- Chimeric antigen receptor (CAR) T cells may have the potential to achieve an "immune system reset" and durable clinical response off immunomodulatory agents in patients with severe and refractory SLE through a one-time deep, transient depletion of B cells (Figure 1).[4,5]
- 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 (Figure 1).[6,7]
- RESET-SLE™ (NCT06121297) is an ongoing Phase 1/2 trial evaluating the safety and efficacy of rese-cel in 2 cohorts of non-renal SLE and lupus nephritis (LN) patients with preconditioning (PC), as well as a PC-free cohort.[7]
- Emerging data show CAR T expansion, B cell depletion and clinical improvement in patients with pemphigus vulgaris treated with a single dose of PC-free (preconditioning free) rese-cel [8]; avoiding PC in patients with SLE is potentially important to minimize certain adverse events and to reduce the need for hospitalization secondary to fever by eliminating the risk of PC induced neutropenia.
- Here, we report clinical data from 18 patients with non-renal SLE and LN who received rese-cel after PC, as well as initial data from 2 patients in a PC-free cohort treated with 1x10^6 CAR T cells/kg.

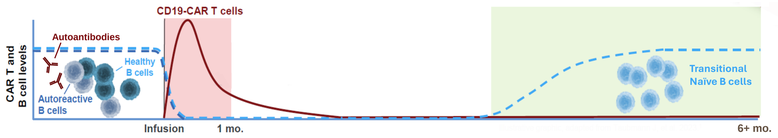

Figure 1. Proposed effect of rese-cel therapy.[4,5] Deep depletion of B cells may lead to cessation of disease by removing autoreactive B cells, although some autoimmune patients may also have antibodies derived from long-lived plasma cells, which are not targeted by CD19-CAR T therapy.

RESET-SLE Study Design

Key Inclusion Criteria[7,9]

- 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[7,9]

- 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

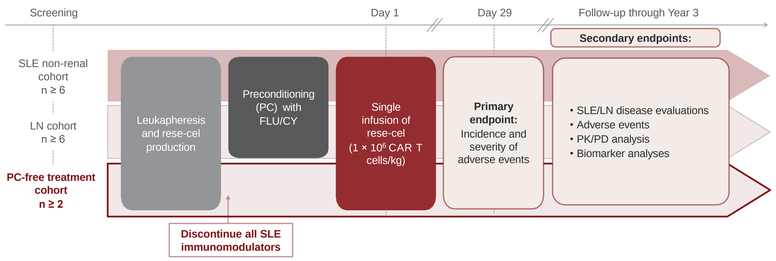

Figure 2. RESET-SLE study design[7,9]

RESET-SLE Results: Baseline Characteristics and Safety*

Table 1. Patient demographics and baseline characteristics of 18 patients in the PC cohorts and 2 patients in the PC-free cohort†

Cohort	Non-renal SLE (n=12)	LN (n=6)	PC-free (n=2)	
			Non-renal SLE	LN
Age, years, median (min, max)	31 (21, 44)	26 (18, 35)	30	44
Female, n (%)	11 (92)	5 (83)	1 (100)	0 (0)
Disease duration,‡ years, median (min, max)	12 (5, 17)	6 (2, 16)	1 (1, 1)	13 (13, 13)
Autoantibodies (%)				
dsDNA	75	67	0	0
Sm	67	83	100	100
Baseline disease activity§	**SLEDAI-2K** (mean)			
	12.75	16	18	10
	UPCR (mg/mg) (mean)			
	1.7**	3.1	3.9**	1.2
Therapies at screening (%):				
Systemic GCs	92	50	100	100
≤2 SLE immunomodulators¶	50	33	100	100
≥3 SLE immunomodulators¶	50	67	0	0
GC dose at screening, mg/day, mean (min, max)	13.25 (0, 30)	5.83 (0, 20)	20	15

†All patients had active, refractory disease and had failed B cell-targeting therapies.
‡Time from diagnosis to screening.
§Baseline disease activity = activity before preconditioning (PC cohorts) or baseline visit (PC-free cohort).
¶SLE medications may include biologics, antimalarials, and immunosuppressants.
**Four patients in the non-renal SLE cohort and the one PC-free non-renal SLE patient had renal involvement that did not meet criteria for the LN cohort.

Table 2. Incidence of relevant treatment-emergent adverse events†

Cohort	PC cohorts (n=18)		PC-free (n=2)	
	CRS‡	ICANS‡	CRS‡	ICANS‡
None, n (%)	**12 (67)**	**17 (94)**	**1 (50)**	**2 (100)**
Any Grade, n (%)	**6 (33)**	**1 (6)**	**1 (50)**	**0 (0)**
Grade 1	5 (28)	0 (0)	1 (50)	0 (0)
Grade 2	1 (6)	0 (0)	0 (0)	0 (0)
Grade 3	(0)	0 (0)	0 (0)	0 (0)
Grade 4	(0)	1 (6)‡‡	0 (0)	0 (0)
Time to onset, median (range), days	6 (5–10)	9 (9–9)	12 (12–12)	–
Duration, median (range), days	2.5 (2–5)	3 (3–3)	3 (3–3)	–
Treatments, n (%)				
Tocilizumab	4 (67)	0 (0)	1 (100)	–
Steroids	0 (0)	1 (100)	0 (0)	
Anakinra	0 (0)	1 (100)	0 (0)	

TEAEs of interest	PC cohorts (n=18)	PC-free (n=2)
Prolonged cytopenias (>28 days),§ n (%)	1(6)	0 (0)
Hypogammaglobulinemia,¶ n (%)	0 (0)	0 (0)
Serious infections,** n (%)		
Oophoritis (Gr 3)	1(6)	0 (0)
Related SAEs,†† n (%)	4(22)	0 (0)
Idiopathic intracranial hypertension (Gr 3)	1(6)	0 (0)
Pyrexia (Gr 1)	1(6)	0 (0)
Pyrexia (Gr 1), Febrile neutropenia (Gr 1) and Pancytopenia (Gr 4)	1(6)	0 (0)
Tremor (distal) (Gr 1)	1(6)	0 (0)

†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.
‡Graded per ASTCT Consensus Grading Criteria.
§Grade 3 or higher neutropenia, anemia, thrombocytopenia, or pancytopenia lasting for more 28 days.
¶Grade 3 or higher (IgG level ≤400 mg/dL) and requiring treatment with external immunoglobulin.
**Coded in System Organ Class of Infections and Infestations and meets seriousness criteria.
††Preferred term, as assessed per US Food and Drug Administration guidelines; excludes CRS and ICANS.
‡‡Previously presented.[10]

Rese-cel Expansion & B Cell Kinetics*

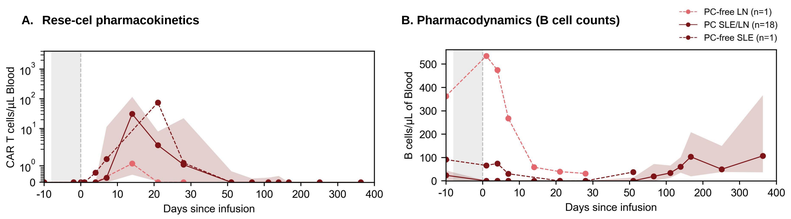

Figure 3[12]. Rese-cel pharmacokinetic (PK) & pharmacodynamic (PD) profiles: (A) Rese-cel PK in SLE and LN patients represented as CAR T cells per µL blood as measured by digital PCR (dPCR) and (B) B cell counts (CD19$^+$CD20$^+$) in peripheral blood at baseline and over time following rese-cel infusion measured by flow cytometry[12]. 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 in applicable patients. Median time of B cell reconstitution was approximately 2.3 months. The two PC-free patients are represented as individual dotted lines. PC-free SLE patient did not have PK/PD samples collected at Day 15.

Clinical Efficacy Data Following Rese-cel Infusion*

Table 3. Clinical efficacy in PC cohorts at 12-month follow-up

	Non-renal SLE (n=4)	LN (n=4)
Immunomodulator-free, n (%)	3 (75)†	4 (100)
GC ≤5 mg/day, n (%)	4 (100)	4 (100)
Mean reduction in PGA§,¶	2.2	2.2
Mean reduction in SLEDAI-2K§	9	15
Achieved DORIS, n (%)	2 (50)	4 (100)
Renal response,** n (%)	0 (0)	4 (100)

†One non-renal SLE patient restarted hydroxychloroquine at Week 48.
§Mean and n numbers are based on SLE/LN patients not receiving prohibited immunomodulatory rescue medications.
¶PGA measured on a 0–3 scale.
**Renal response defined as achieving CRR, PRR, and/or histological response[11] (on repeat biopsy; including one patient at week 54); analyzed for n=1 non-renal SLE and n=4 LN evaluable patients.

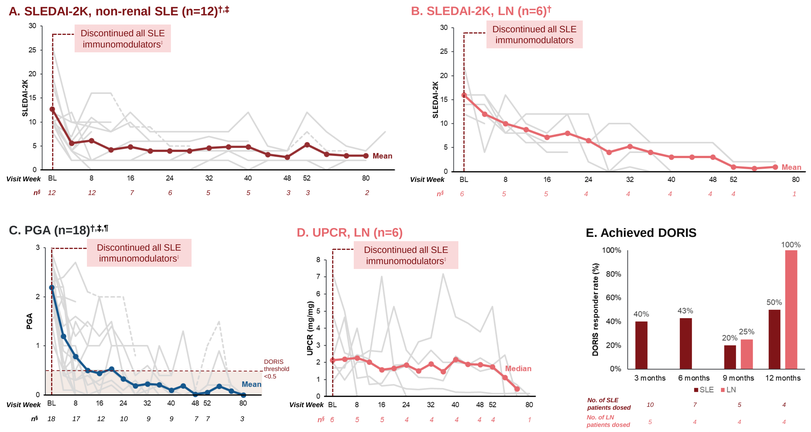

Figure 4. Efficacy data in PC cohorts following rese-cel infusion: (A) SLEDAI-2K over time§ for non-renal SLE cohort; (B) SLEDAI-2K over time§ for LN cohort; (C) PGA over time§ (D) UPCR over time§ for LN cohort; (E) Patients who achieved DORIS.

†Missing data were imputed using last observation carried forward.
‡Dashed single patient trend lines represent patients receiving rescue immunomodulatory medications.
§Mean/median and n numbers are based on SLE/LN patients not receiving prohibited rescue immunomodulators.
¶PGA measured on a 0–3 scale.

Summary*

- Rese-cel following was generally well tolerated in all patients with severe and refractory non-renal SLE and LN treated to date
  - In PC cohorts (n=18):
    - No CRS in 12: Grade 1 CRS in 5 patients; Grade 2 CRS in 1 patient
    - No ICANS in 17: Grade 4 ICANS in 1 patient (previously presented, November 2024[10])
  - In PC-free cohort (n=2): Grade 1 CRS in 1 patient; no ICANS
- Rese-cel peak expansion and deep peripheral B cell depletion occurred by 2 weeks with median repopulation time of ~2.3 months
- After discontinuation of immunomodulators, evaluable patients showed evidence of efficacy after rese-cel infusion with PC at 12 months:
  - **75% (6 of 8) non-renal SLE and LN patients achieved DORIS without the need for immunomodulators**
  - **100% (4 of 4) of LN patients achieved renal response off immunomodulators and GCs (1 CRR; 3 histological remissions on repeat kidney biopsy)**
  - **Mean 13-point reduction in SLEDAI-2K and 2.2 reduction in PGA**
- 83% (15 of 18) of patients in PC cohorts were off immunomodulators and on no or low-dose GCs at latest follow-up
- These data suggest the potential for rese-cel to reset the immune system and achieve meaningful clinical responses off immunomodulators and no or low-dose GCs in non-renal SLE and LN
- If PC-free rese-cel can provide a durable immune reset in the majority of patients treated, it has the potential to reduce adverse events and readmissions. Preliminary PK/PD data from PC-free rese-cel at the lowest dose of 1 x 10^6 CAR T cells/kg is encouraging. Clinical follow up is ongoing while the next higher dose cohort is progressing.

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*PC cohorts: as of 16 April 2026; PC-free cohort: as of May 16, 2026.

Abbreviations: ANA, antinuclear antibody; ASTCT, American Society for Transplantation and Cellular Therapy; CAR, chimeric antigen receptor; CD, cluster of differentiation; 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; FLU, fludarabine; GC, glucocorticoid; HSCT, hematopoietic stem cell transplantation; ICANS, immune effector cell-associated neurotoxicity syndrome; IgG, Immunoglobulin G; IM, immunomodulatory; LN, lupus nephritis; PC, preconditioning; PD, pharmacodynamic; PGA, Physician Global Assessment; PK, pharmacokinetic; PRR, partial renal response; rese-cel, resecabtagene autoleucel; RESET, REstoring SElf-Tolerance; SAE, serious adverse event; SLE systemic lupus erythematosus; SLEDAI-2K, SLE Disease Activity Index 2000; Sm, Smith; TCR, T cell receptor; TEAE, Treatment-Emergent Adverse Event; UPCR, urine protein-to-creatinine ratio.

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