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RESET-MG™: Clinical Trial Evaluating Rese-cel (Resecabtagene Autoleucel), A Fully Human, Autologous 4-1BB CD19-CAR T Cell Therapy in Generalized Myasthenia Gravis

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Background: CAR T Cell Therapy in Myasthenia Gravis

- Myasthenia gravis (MG) is primarily driven by pathogenic autoantibodies originating from autoreactive B cells.[1]
- Current therapies focus on downstream immune effector functions, and do not adequately control the underlying autoimmune process; drug-free remission is infrequent;[2–5] up to 15% of patients are considered to have disease refractory to treatment.[6]
- B cell depletion therapies have shown efficacy in MG, but responses may be incomplete, and relapses remain common, likely due to incomplete depletion and re-emergence of autoreactive B cells.[1,7,8]
- Chimeric antigen receptor (CAR) T cells may have the potential to achieve durable remission through a one-time deep, but transient, depletion of B cells in MG (Figure 1).[9,12]
- Rese-cel (resecabtagene autoleucel) is a fully human, autologous 4-1BB CD19-CAR T cell therapy.[10,11]
- Here, we present data from the RESET-MG (NCT06359041) trial: A Phase 1/2 trial evaluating the safety and efficacy of rese-cel in two MG cohorts (AChR positive and AChR negative). [11,13]

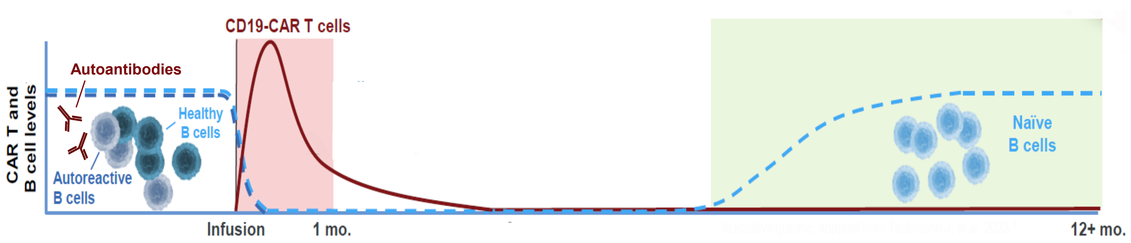

Figure 1. Proposed effect of CD19-CAR T cell therapy.[9,12] Deep depletion of B cells in MG patients may lead to cessation of disease by removing a central driver of inflammation (autoreactive B cells) and allowing the immune system to return to a tolerant state, resulting in deep and durable remissions off therapy.

RESET-MG Study Design

Key Inclusion Criteria[11,13]

- Age ≥18 and ≤70 diagnosed with MG with generalized muscle weakness, defined as MGFA class II, III, and IV
- Active disease despite standard treatment
- Presence of AChR antibodies for the AChR antibody-positive cohort
- AChR antibody-negative cohort: presence of MuSK or LRP4 antibodies OR seronegative

Key Exclusion Criteria[11,13]

- Significant lung or cardiac impairment
- Treatment with B cell-depleting agent within prior ~6 months
- Previous CAR T cell therapy and/or HSCT
- Active infection requiring medication at screening
- Current symptoms of severe, progressive, or uncontrolled organ disease

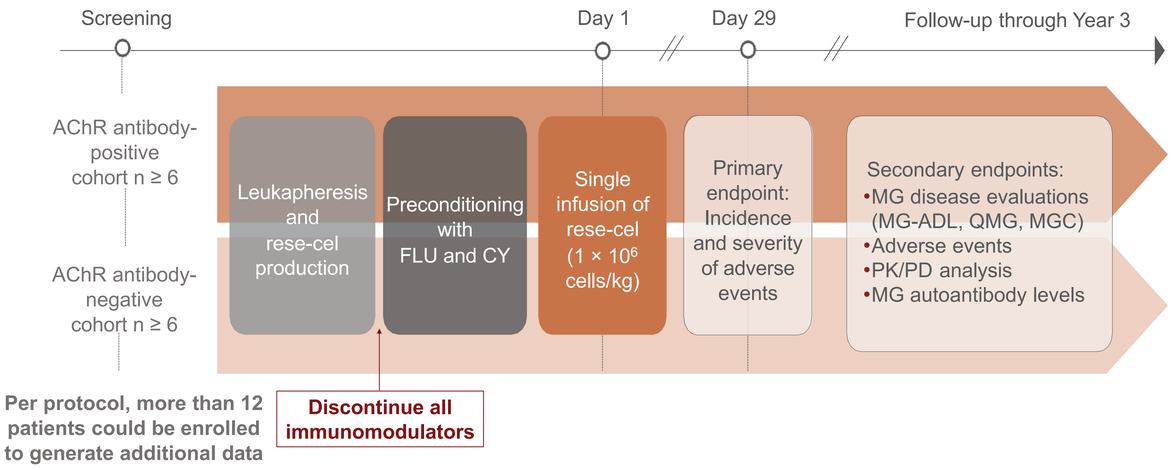

Figure 2. RESET-MG study design[11,13]

RESET-MG Results: Baseline Characteristics and Safety*

Table 1. Baseline characteristics of first 4 patients in RESET-MG

	AChR Positive		AChR Negative	
Patient / Cohort	AChR-pos-1	AChR-pos-2	AChR-neg-1	AChR-neg-2
Age, sex	62, M	44, F	54, F	70, F
Disease duration (approx. years)	1	6	4	1
Autoantibodies	AChR	AChR	Seronegative‡	Seronegative‡
QMG†	11	18	22	21
MG-ADL†	15	13	17	14
Therapies at screening	GC, AZA, IVIg, PYR	EFG, PYR	GC, PYR, PLA	PYR, MMF, ROZ
Other prior therapies	–	GC, IVIg, MMF, AZA, ECU, PLA	IVIg, AZA, RTX, ECU, EFG	IVIg
GC dose at screening (mg/day)	25	–	15	–

†Baseline disease activity = activity before preconditioning.
‡Seronegative = no anti-AChR, anti-MuSK and anti-LRP4 antibodies.

AChR, acetylcholine receptor; ASTCT, American Society for Transplantation and Cellular Therapy; AZA, azathioprine; CAR, Chimeric antigen receptor; CRS, Cytokine Release Syndrome; CY, cyclophosphamide; ECU, eculizumab; EFG, efgartigimod; FLU, fludarabine; GC, glucocorticoid; HSCT, hematopoietic stem cell transplantation; ICANS, Immune Effector Cell-Associated Neurotoxicity Syndrome; IVIg, intravenous immunoglobulin; LRP4, low-density lipoprotein receptor-related protein 4; MG, myasthenia gravis; MG-ADL, MG – Activities of Daily Living; MGC, Myasthenia Gravis Composite; MGFA, Myasthenia Gravis Foundation of America; MMF, mycophenolate mofetil; MuSK, muscle-specific tyrosine kinase; PCR, polymerase chain reaction; PD, pharmacodynamic; PK, pharmacokinetic; PLA, plasmapheresis; PYR, pyridostigmine; QMG, Quantitative Myasthenia Gravis Score; RESET, REstoring SElf-Tolerance; rese-cel, resecabtagene autoleucel; ROZ, Rozanolixizumab; RTX, rituximab; SAE, serious adverse event.

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

	AChR Positive		AChR Negative	
Patient / Cohort	AChR-pos-1	AChR-pos-2**	AChR-neg-1	AChR-neg-2
CRS‡	None	Grade 2	None	None
ICANS‡	None	None	None	None
Serious infections§	None	None	None	None
Related SAEs (Grade)¶ (Excluding CRS/ICANS)	None	Anorexia (Grade 3) Physical deconditioning (Grade 3)	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.
§Coded in System Organ Class of Infections and Infestations and meets seriousness criteria.
¶As assessed per US Food and Drug Administration guidelines.
**AChR-pos-2: Week 4 safety data presented; efficacy follow-up ongoing.

Rese-cel expansion & B cell kinetics*

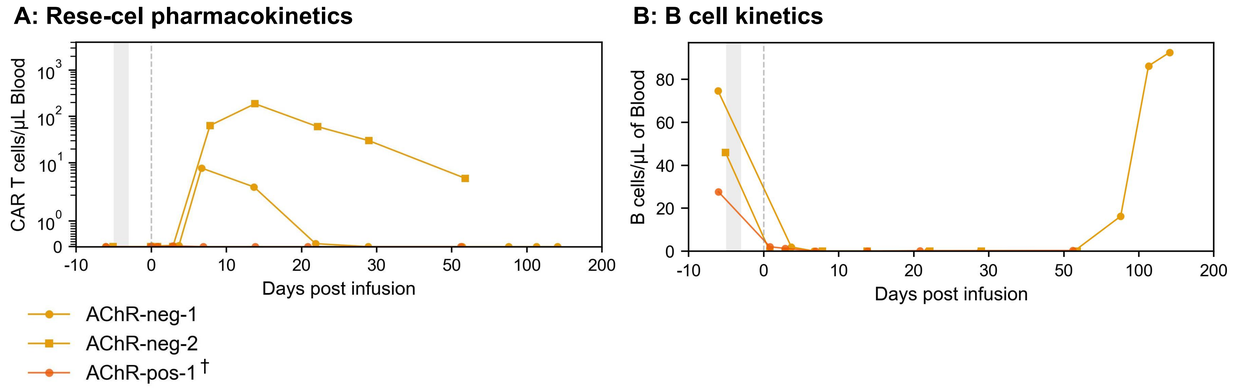

Figure 3. Rese-cel pharmacokinetic (PK) profile and B cell kinetics: (A) Rese-cel PK profile in MG patients in CAR T cells per µL blood measured by digital PCR and (B) B cell counts ($CD19^+CD20^+$) in peripheral blood of MG patients at baseline before preconditioning and over time following rese-cel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

†Reduced rese-cel expansion observed in AChR-pos-1 may be attributed to patient's continued use of AZA, a prohibited medication, until day of infusion (Day 1).

Clinical efficacy data following rese-cel infusion*

Table 3. Clinical efficacy measures: As of the latest follow-up 3 of 3 MG patients, with efficacy follow-up, showed improvement in QMG and MG-ADL scores.

	AChR Positive	AChR Negative	
Patient / Cohort	AChR-pos-1†	AChR-neg-1	AChR-neg-2
Latest follow-up	Week 8	Week 20	Week 8
Glucocorticoid-free	*Tapering*	✓	✓
Immunomodulatory medication-free	IVIg	✓	✓
Cholinesterase inhibitor-free	No	✓	✓
QMG (baseline to latest follow-up)	11→7	22→5	21→11
MG-ADL (baseline to latest follow-up)	15→7	17→0	14→7

†AZA, a prohibited medication, was continued until the day of infusion (Day 1). IVIg was stopped prior to rese-cel infusion and restarted 4 weeks after infusion for continued MG symptoms.

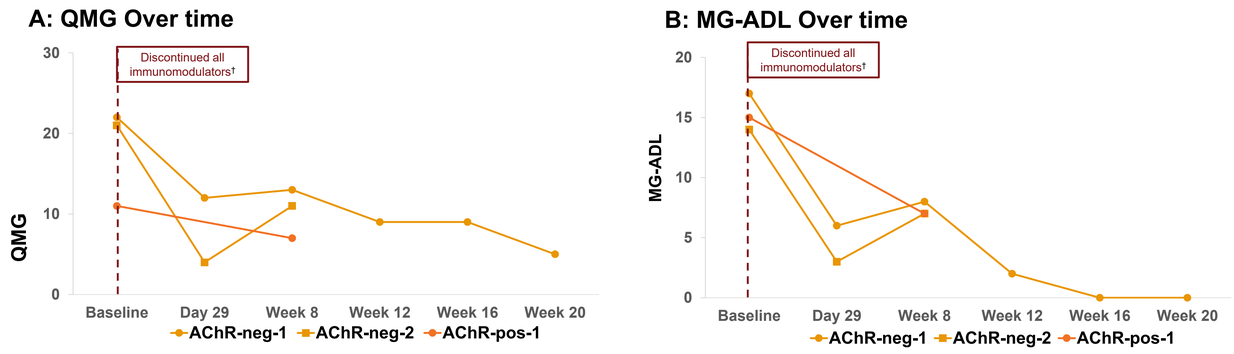

Figure 4. Clinical efficacy: (A) QMG over time (B) MG-ADL over time

†AChR-pos-1: AZA, a prohibited medication, was continued until the day of infusion (Day 1). IVIg was stopped prior to rese-cel infusion and restarted 4 weeks after infusion for continued MG symptoms. AChR-pos-1, Day 29 visit data unavailable.

Summary*

- Rese-cel was generally well tolerated across 2 AChR-positive and 2 AChR-negative patients (both seronegative; no anti-MuSK or anti-LRP4 antibodies).
  - No CRS occurred in 3 of 4 patients.
  - Grade 2 CRS occurred in AChR-pos-2 that resolved with no sequelae.
- At last follow-up, the 2 evaluable patients (AChR-neg-1 and AChR-neg-2) who remain off immunomodulatory medication achieved significant improvements in MG-ADL (with AChR-neg-1 achieving Minimal Symptom Expression).
  - AChR-pos-1 is not evaluable due to use of a prohibited cytotoxic medication that may have inhibited CAR T activity; AChR-pos-2 has insufficient follow-up.
- Rese-cel average peak expansion (T_{max}) occurred on Day 8 post-infusion and B cells were depleted by Day 8 post-infusion in all patients. Transitional naïve B cells began to repopulate by Week 12 in 1 patient with sufficient follow-up.
- Both cohorts have been fully enrolled and patients have been or will be dosed in the coming months.

***As of 11 Sep, 2025**

References: **1.** Yi JS, et al. *Muscle Nerve*. 2018;57(2):172–184. **2.** Bi Z, et al. *Ther Adv Chronic Dis*. 2022;13:20406223221122538. **3.** Suzuki S, et al. *Clin Exp Neuroimmunol*. 2023;14(1):5–12. **4.** Mercelis R, et al. *Acta Neurol Belg*. 2023;123(2):375–384. **5.** Raja S, et al. *Neurology*. 2021;96:2602. **6.** Suh J, et al. *Yale J Biol Med*. 2013;86(2):255–260. **7.** Fichtner ML, et al. *Acta Neuropathol Commun*. 2022;10(1):154. **8.** Huda R. *Front Immunol*. 2020;11:240. **9.** Müller F, et al. *N Engl J Med*. 2024;390(8):687–700. **10.** Peng BJ, et al. *Mol Ther Methods Clin Dev*. 2024;32(2):101267. **11.** NCT06359041. Available online at: www.clinicaltrials.gov/study/NCT06359041 [Accessed Sept 2025]. **12.** Taubmann J, et al. OPO141. Abstract presented at: EULAR; May 31, 2023; Milan, Italy. **13.** Cabaletta Bio – Data on File.