70

Presented at the MGFA International Conference on Myasthenia and Related Disorders
May 13–15, 2025
The Hague, NL

RESET-MG: A Phase 1/2, Open-Label Study to Evaluate the Safety and Efficacy of Autologous CD19-Specific Chimeric Antigen Receptor T Cells (CABA-201) in Participants with Generalized Myasthenia Gravis

A. Habib[1] J. Hogan[2] Y. White[2] J. Gresh[2] W. Hull[2] S. Wilkinson[2] C. DiCasoli[2] R. Tummala[2] D. J. Chang[2]
1: UC Irvine, CA, USA; 2: Cabaletta Bio, PA, USA

Cabaletta Bio®

www.cabalettabio.com/technology/posters-publications

Background: CAR T Therapy in Myasthenia Gravis

- Myasthenia gravis (MG) is primarily driven by pathogenic autoantibodies produced by autoreactive B cells[1]
- Current therapies focus on specific symptoms and do not adequately control the underlying autoimmune process; drug-free remission is infrequent; up to 15% of patients are considered to have disease refractory to treatment[2–6]
- 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]

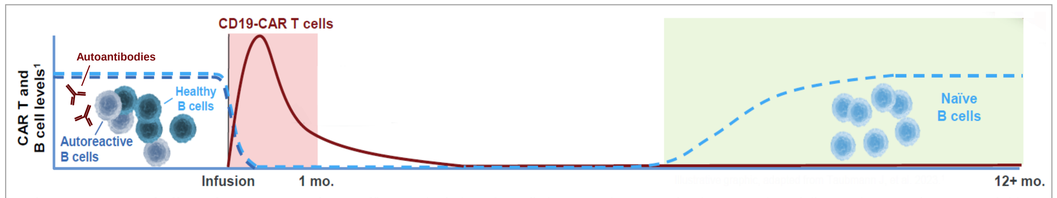

Figure 1. Proposed effect of CD19-CAR T therapy.[10] Deep depletion of B cells in MG patients may lead to cessation of disease by removing a central driver of inflammation (autoreactive B cells) and allowing the immune system to return to a tolerant state, resulting in deep and durable remissions off therapy.[9]

Resecabtagene Autoleucel (rese-cel, also referred to as CABA-201)

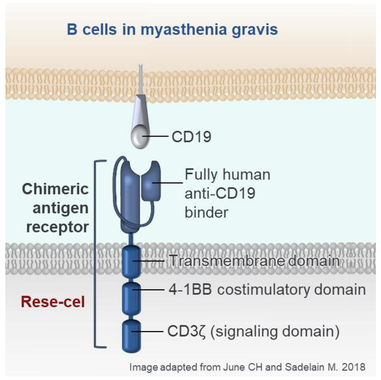

Figure 2. Rese-cel (CABA-201) is an autologous T cell product that is genetically engineered to target B cells via the expression of a CD19-specific CAR containing 4-1BB-CD3ζ intracellular costimulatory and T-cell activation domains.[7,8]

- Rese-cel is an investigational, fully human, autologous 4-1BB CD19-CAR T therapy (Figure 2); it is being studied in the RESET clinical trial program across several B cell-mediated autoimmune conditions, including systemic lupus erythematosus (SLE), idiopathic inflammatory myopathy (myositis), and systemic sclerosis (SSc)[11–13]
- Translational data of the first 10 patients infused with rese-cel showed **rapid B cell depletion in blood followed by re-emergence as early as week 8** following infusion[13]
- Rese-cel demonstrated clinical responses off immunomodulators and steroids in all 10 patients. Responses included:[13*]
  - Remission in three SLE patients;† complete renal response in 1st lupus nephritis patient; major response in 1st dermatomyositis patient‡
- Safety profile continues to suggest favorable risk-benefit in the first 10 patients dosed; 90% of patients experienced either no cytokine release syndrome (CRS) or Grade 1 CRS (fever) and 90% of patients experienced no immune effector cell–associated neurotoxicity syndrome (ICANS)[13*]

*As of January 8, 2025. †Definition of Remission in SLE (DORIS) criteria. ‡Total improvement score (TIS).

Study Design

- RESET-MG (NCT06359041) is a Phase 1/2 trial evaluating the safety and efficacy of rese-cel in two MG cohorts[13,14]

Key Inclusion Criteria[13,14]

- Age ≥18 and ≤70 diagnosed with MG with generalized muscle weakness, defined as MGFA class II, III, IVa, or IVb
- 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[13,14]

- 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 renal, hepatic, hematological, gastrointestinal, psychiatric, neurological, or cerebral disease

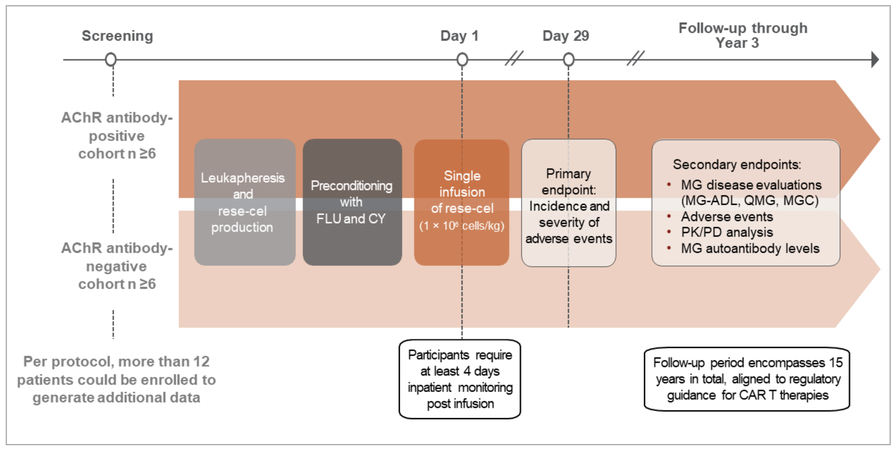

Figure 3. RESET-MG study design.[13,14]
AChR, acetylcholine receptor; CAR, chimeric antigen receptor; CY, cyclophosphamide; FLU, fludarabine; HSCT, haematopoietic stem cell transplantation; LRP4, low-density lipoprotein receptor-related protein 4; MG, myasthenia gravis; MG-ADL, MG – Activities of Daily Living; MGC, Myasthenia Gravis Composite; MGFA, Myasthenia Gravis Foundation of America; MuSK, muscle-specific tyrosine kinase; PD, pharmacodynamic; PK, pharmacokinetic; QMG, Quantitative Myasthenia Gravis Score; RESET, REstoring SElf-Tolerance.

Locations Currently Recruiting

The RESET clinical program has sites across the US and Europe. For a current list of US RESET-MG locations, and further information, visit this trial's ClinicalTrials.gov page at www.clinicaltrials.gov/study/NCT06359041

Information for patients can be found at www.reset-mg-trial.com

Summary

- Rese-cel is an investigational, fully human, autologous 4-1BB CD19-CAR T therapy, designed to potentially reset the immune system via deep B cell depletion followed by **repopulation with naïve B cells to achieve durable clinical responses**[11–13]
- RESET-MG (NCT06359041) is an ongoing Phase 1/2 trial evaluating the safety and efficacy of rese-cel in patients with MG[14]
- The first patient with MG has been infused with rese-cel. No serious adverse events or dose-limiting toxicities were reported during the first 4 weeks post infusion. Additional MG patients are enrolled and will be dosed in the coming months[13§]
- Rese-cel is also being investigated in Phase 1/2 studies in SLE, myositis, pemphigus vulgaris, SSc, and multiple sclerosis[13]

§As of April 29, 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(15 supplement):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.** Taubmann J, et al. OPO141. Abstract presented at: EULAR; May 31, 2023; Milan, Italy. **11.** Dai Z, et al. *J Cell Physiol*. 2021;236(8):5832–5847. **12.** Peng BJ, et al. *Mol Ther Methods Clin Dev*. 2024;32(2):101267. **13.** Cabaletta Bio – Data on File. **14.** NCT06359041. Available online at: www.clinicaltrials.gov/study/NCT06359041 [Accessed May 2025].