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Self-administration of subcutaneous rozanolixizumab in patients with generalized myasthenia gravis: Clinical study design

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Introduction

- gMG is a rare, chronic autoimmune disorder affecting the neuromuscular junction, characterized by fluctuating muscle weakness and fatigue[1]
- Several factors are understood to be drivers of gMG disease pathology, including pathogenic IgG autoantibodies, which can inhibit synaptic transmission at the neuromuscular junction by targeting specific proteins in the post-synaptic motor end plate[1]
- Rozanolixizumab is a humanized IgG4 mAb FcRn inhibitor indicated for the treatment of adults with AChR Ab+ or MuSK Ab+ gMG[2]
- Treatment with rozanolixizumab targets the IgG binding region of the FcRn; binding inhibits IgG salvage and recycling, accelerating IgG catabolism and, ultimately, reduces the concentration of circulating IgG[3]
- In the Phase 3, randomized, placebo-controlled, double-blind MycarinG study (MG0003/NCT03971422), one 6-week cycle of rozanolixizumab was generally well tolerated and provided clinically meaningful improvements in MG-specific outcomes[3]

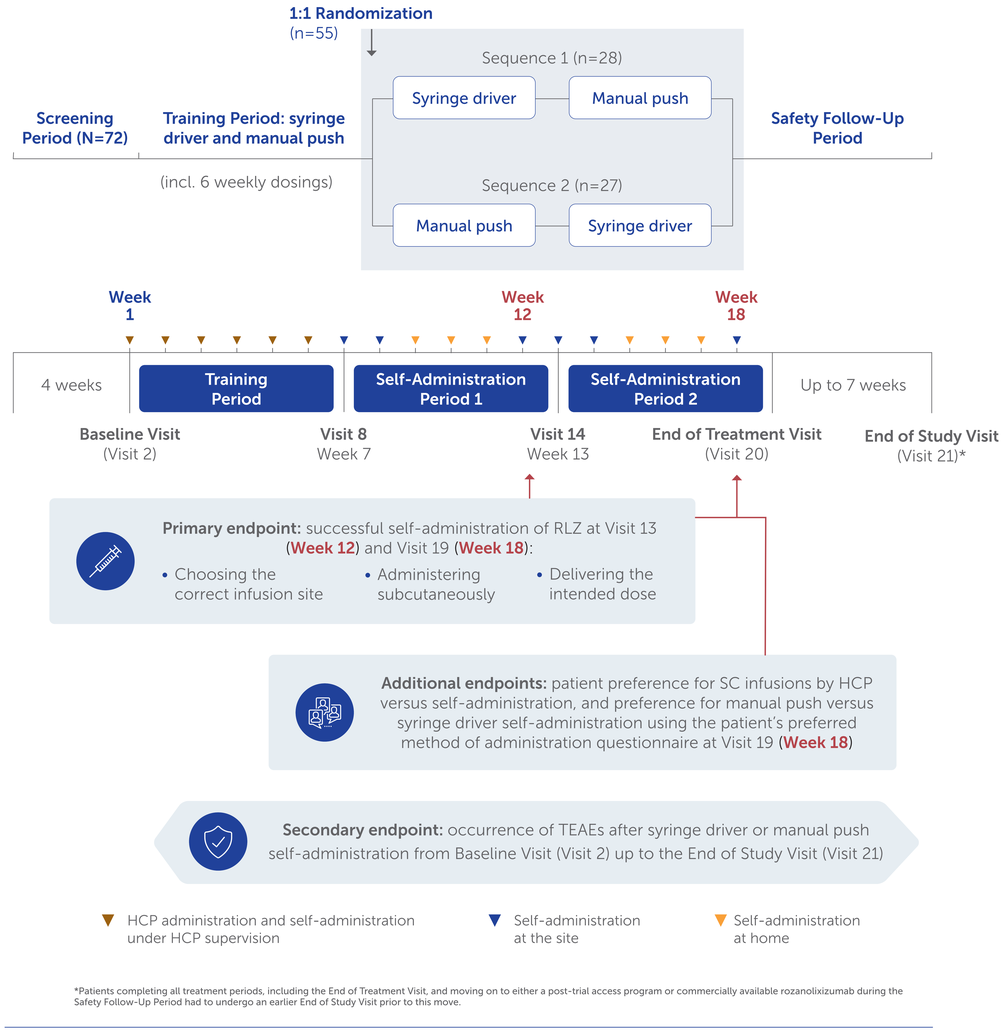
Study rationale

- Self-administered SC treatment offers many advantages such as high patient satisfaction, sense of control, and increased independence owing to the fact that patients do not need to attend regular clinic visits[4]
- Currently, rozanolixizumab is administered by HCPs as an SC infusion once weekly for 6 weeks using programmable syringe drivers[2]
- However, there is interest in providing options for patients to self-administer rozanolixizumab. Programmable syringe drivers and manual push are two potential methods for self-administration of rozanolixizumab[5]
  - Successful self-administration of SC treatment has been demonstrated in patients with gMG using Ig[6]
- While the syringe driver and manual push methods both provide independence from HCP administration, the manual push method is simpler and expected to reduce infusion times. In a study of SCIg self-administration methods, faster infusion rates were seen with manual push compared with syringe driver[5]
- The objective of the MG0020 study was to:
  - Assess the success, safety and tolerability of rozanolixizumab self-administration
  - Evaluate patients' preferred method of rozanolixizumab administration
  - Assess patients' experiences with self-administration of SC infusions at home
- An open-label design was required as the study evaluated self-administration
- A crossover design was used to allow each study participant to evaluate both methods of self-administration

Study design

- In total, 72 patients were screened
- Patients received rozanolixizumab once weekly for 18 consecutive weeks (**Figure 1**) including:
  - A 6-week Training Period in the two self-administration methods
  - Two 6-week Self-Administration Periods, with supervised visits at clinic and unsupervised at home
- Following the Training Period, 55 patients were randomized 1:1 to the syringe driver or manual push self-administration method, subsequently crossing over to the alternative method
- The study included a Safety Follow-Up Period of up to 7 weeks
- The primary endpoint was successful self-administration of rozanolixizumab by syringe driver and manual push, evaluated by an HCP at the end of each 6-week Self-Administration Period (Weeks 12 and 18), which was defined as:
  - Choosing the correct infusion site
  - Administering subcutaneously
  - Delivering the intended dose
- Secondary endpoints were occurrence of TEAEs, local site reactions and medication errors associated with adverse reactions
- Additional endpoints included patient preference for self-administration versus administration by an HCP, and for manual push versus syringe driver administration methods, pre- and post-SIAQ domain scores, CFB in MG-ADL score and total IgG level during the study

Figure 1 MG0020 study design



*Patients completing all treatment periods, including the End of Treatment Visit, and moving on to either a post-trial access program or commercially available rozanolixizumab during the Safety Follow-Up Period had to undergo an earlier End of Study Visit prior to this move.

Inclusion criteria

- Documented diagnosis of gMG
- ≥18 years of age
- Serum total IgG level ≤16 g/L and ≥5.5 g/L at Screening
- Body weight ≥35 kg at Screening

Additional endpoints

- CFB in MG-ADL score
- Successful self-administration of RLZ via manual push or syringe driver at each of the three home self-administration visits during Self-Administration Period 1 or 2
- PRE-SIAQ domain scores at Baseline Visit (Week 1) and POST-SIAQ domain scores at Visit 12 (Week 11) and Visit 18 (Week 17)
- Total IgG level over time during the Treatment Period
- Anti-RLZ antibodies (status and titer at trough during both Self-Administration Periods)
- Occurrence of TEAEs leading to permanent withdrawal of RLZ

Summary and conclusions

- MG0020 was a Phase 3, open-label, randomized, crossover study in patients aged ≥18 years with gMG
- The study will assess the success, tolerability and safety of rozanolixizumab self-administration via the syringe driver and manual push methods
- This study will also provide data on patient preference for self-administration or administration by an HCP, and for manual push or syringe driver administration methods
- Results are expected in 2025

Abbreviations: AChR Ab+, acetylcholine receptor autoantibody positive; CFB, change from baseline; FcRn, neonatal Fc receptor; gMG,generalized myasthenia gravis; HCP, healthcare professional; Ig, immunoglobulin; IgG, immunoglobulin G; IgG4, immunoglobulin G subclass 4; mAb, monoclonal antibody; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MuSK Ab+, muscle-specific tyrosine kinase autoantibody positive; RLZ, rozanolixizumab; SC, subcutaneous; SCIg, subcutaneous immunoglobulin; SIAQ, Self-Injection Assessment Questionnaire; TEAE, treatment-emergent adverse event.

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