

Efficacy of rozanolixizumab in muscle-specific kinase antibody-positive generalized myasthenia gravis: Outcomes from the randomized, Phase 3 MycarinG study

AANEM 2022, Nashville, TN, USA; MGFA Scientific Session; 21 September 2022

Summary

What we did



- MycarinG assessed the efficacy and safety of the FcRn inhibitor rozanolixizumab in patients with AChR Ab+ and MuSK Ab+ gMG

What we found



- Rozanolixizumab improved MG-specific outcomes in MuSK Ab+ gMG, consistent with the AChR Ab+ and overall populations

Why it matters



- MuSK Ab+ gMG is often more severe and harder to treat than AChR Ab+ gMG and these results suggest that rozanolixizumab could be a potential treatment option for these patients

Objective

- To assess the efficacy and safety of rozanolixizumab in patients with AChR Ab+ and MuSK Ab+ gMG

Introduction

- gMG is a rare, chronic, heterogeneous and unpredictable autoimmune disease caused by pathogenic IgG autoantibodies against NMJ components such as AChR and MuSK^{1,2}
- In MuSK Ab+ gMG, IgG4 autoantibodies bind MuSK, interfering with normal MuSK function to reduce post-synaptic AChR clustering, disrupting neuromuscular transmission²
- MuSK Ab+ gMG is often more severe and harder to treat than AChR Ab+ gMG.³ There is an unmet need for efficacious, well-tolerated treatment options⁴
- Rozanolixizumab is a humanized IgG4 mAb that targets the IgG-binding region of FcRn, accelerating lysosomal degradation of IgG, including pathogenic autoantibodies⁵
- MycarinG (MG0003/NCT03971422) was a Phase 3, double-blind, randomized, placebo-controlled study of rozanolixizumab in patients with AChR Ab+ or MuSK Ab+ gMG⁶

Methods

- The study included patients with gMG aged ≥ 18 years who were AChR Ab+ or MuSK Ab+, had MGFA Class II–IVa disease with an MG-ADL score of ≥ 3 and a QMG score of ≥ 11 , were considered for additional therapy such asIVIg or PLEX and had a body weight of ≥ 35 kg
 - Antibody status for MuSK Ab+ and AChR Ab+ patients was determined using confirmed positive medical records of antibodies against MuSK
- Patients were randomized 1:1:1 to receive weekly rozanolixizumab 7 mg/kg, 10 mg/kg or placebo for 6 weeks, followed by an 8-week observation period (**Figure 1**)
- The primary endpoint was CFB to Day 43 in MG-ADL score in the overall population
- Secondary endpoints included CFB to Day 43 in MG-ADL, QMG and MGC analyzed by autoantibody subgroup (AChR Ab+ and MuSK Ab+ gMG)
- The MG-ADL (≥ 2.0 -point improvement), QMG and MGC (both ≥ 3.0 -point improvement) response were also assessed in a descriptive post-hoc analysis of MuSK Ab+ patients

Results

Patients

- A total of 200 patients (21 MuSK Ab+) were randomized to rozanolixizumab 7 mg/kg (66 patients [five MuSK Ab+]), rozanolixizumab 10 mg/kg (67 patients [eight MuSK Ab+]) or placebo (67 patients [eight MuSK Ab+])
- Baseline characteristics were generally balanced between groups (**Table 1**)

Efficacy

- MG-ADL CFB to Day 43 (primary endpoint) in both rozanolixizumab 7 mg/kg and 10 mg/kg groups was clinically meaningfully and highly statistically significantly improved compared with placebo in the overall population ($p < 0.001$ for both doses; **Figure 2**)
- In patients with MuSK Ab+ gMG, CFB to Day 43 in MG-ADL, MGC and QMG was higher in both rozanolixizumab groups than in the placebo group (**Figure 2**)
- In patients with AChR Ab+ gMG, CFB to Day 43 in MG-ADL (rozanolixizumab 7 mg/kg -3.03 , rozanolixizumab 10 mg/kg -3.36 , placebo -1.10), MGC (-4.45 , -6.70 , -1.83) and QMG (-6.14 , -7.77 , -3.09) was also higher in the rozanolixizumab groups than in the placebo group
- All 12 patients with MuSK Ab+ gMG with data available at Day 43 were MG-ADL, MGC and QMG responders except for one patient who was not a QMG responder (**Figure 3**)

Safety

- Safety assessments were performed for patients who had received at least one dose of rozanolixizumab
- A higher proportion of TEAEs occurred in the rozanolixizumab 7 mg/kg (81.3%) and 10 mg/kg (82.6%) groups than in the placebo group (67.2%)
 - The majority of TEAEs were mild or moderate across all groups
 - The most frequent TEAEs were headache, diarrhea, pyrexia and nausea

Figure 2 CFB to Day 43 in MG-ADL (a), MGC (b) and QMG (c)

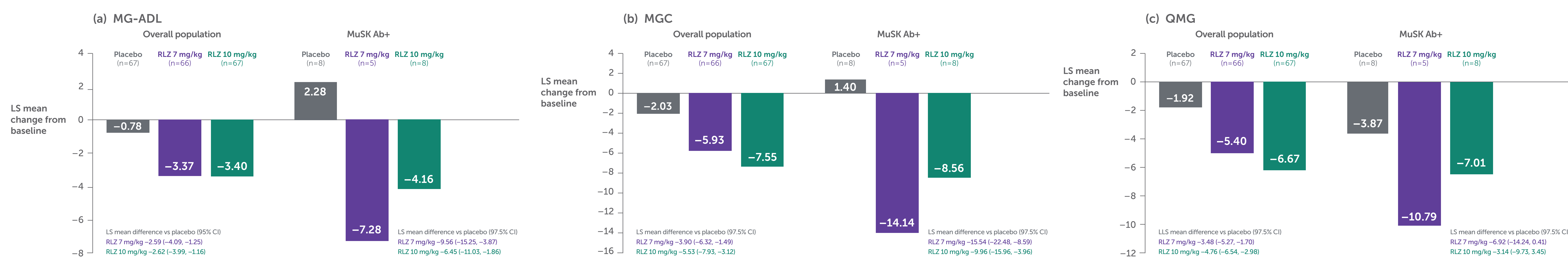
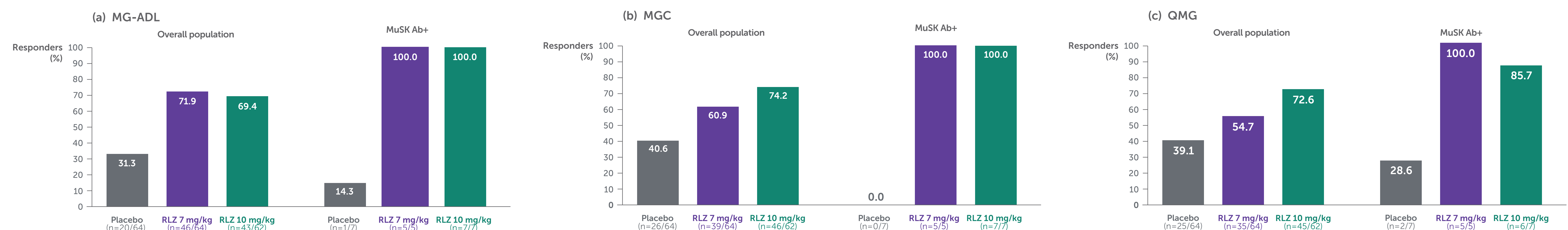


Figure 3 MG-ADL (a), MGC (b) and QMG (c) responders at Day 43



Abbreviations: Ab+, autoantibody positive; AChR, acetylcholine receptor; AChR Ab+, positive for autoantibodies against acetylcholine receptors; CFB, change from baseline; CI, confidence interval; d, day; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IVIg, intravenous immunoglobulin; LS, least squares; mAb, monoclonal antibody; MGC, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Composite; MGFA, Myasthenia Gravis Foundation of America; MuSK, muscle-specific kinase; MuSK Ab+, positive for autoantibodies against muscle-specific kinase; NMJ, neuromuscular junction; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation; TEAE, treatment-emergent adverse event; WK, week.

Acknowledgments: This study was funded by UCB Pharma. The authors acknowledge Bryony McNamara and Luke Worley of Ogilvy Health, London, UK, for editorial assistance, which was funded by UCB Pharma. The authors acknowledge Veronica Forster, PhD, of UCB Pharma, Slough, UK, for publication coordination. The authors thank the patients and their caregivers, in addition to the investigators and their teams who contributed to this study.

Author disclosures: Ali A. Habib has received research support from Argene, Alexion, Cabaletta Bio, Genentech, Regeneron, Sanofi, UCB Pharma, and Vela Bio. He has received consulting fees/honoraria from Argene, Alexion, Immunovant, Regeneron, and UCB Pharma. Henry Kaminski is a Consultant for Roche, Cabaletta Bio, Lincoln Therapeutics, Takeda and UCB Pharma, and is CEO and CMO of ARC Biotechnology, LLC based on US Patent 8,961,98. He is Principal Investigator of the Rare Disease Network for Myasthenia Gravis (McNet), National Institute of Neurological Disorders & Stroke, USA N515054 and Targeted Therapy for Myasthenia Gravis. He has received RLZ NSU0331-01 to ARC Biotechnology. Artur Druzdż and Sabrina Sacconi have nothing to disclose. Julian Grosskreutz has served as a Consultant for Biogen, Alexion and UCB Pharma, and his institution has received research support from the Boris Carassa Foundation. Renato Mantegazza has received funding for travel and meeting attendance or advisory board participation from Alexion, Argene, Biomarin, Cadiak, Sanofi, Regeneron and UCB Pharma. Kimiaki Utsugisawa has served as a paid Consultant for UCB Pharma, Argene, Janssen Pharma, Vela Bio, Chugai Pharma, Hanall BioPharma and Mitsubishi Tanabe Pharma. He has received speaker honoraria from Argene, Alexion Pharmaceuticals and the Japan Blood Products Organization. John Vissing has been a Consultant on advisory boards for Sanofi Genzyme, Sanofi Therapeutics, Vela Bio, Novartis Pharma AG, Fulcrum Therapeutics, Stealth Biotherapeutics, Roche, Biogen, Lupin, Genentech, Amicus Therapeutics, Zogenix, Regeneron, UCB Pharma, Avanos, ML Biopharma, Horizon Therapeutics and Lundbeck Pharma. He has received research, travel support, and/or speaker honoraria from Sanofi Genzyme, Argene, Alexion Pharmaceuticals, Biogen, Lupin, Stealth Biotherapeutics, Edgewise Therapeutics, Fulcrum Therapeutics and UCB Pharma. He is a Principal Investigator in clinical trials for Sanofi Genzyme, Roche, Horizon Therapeutics, Argene.

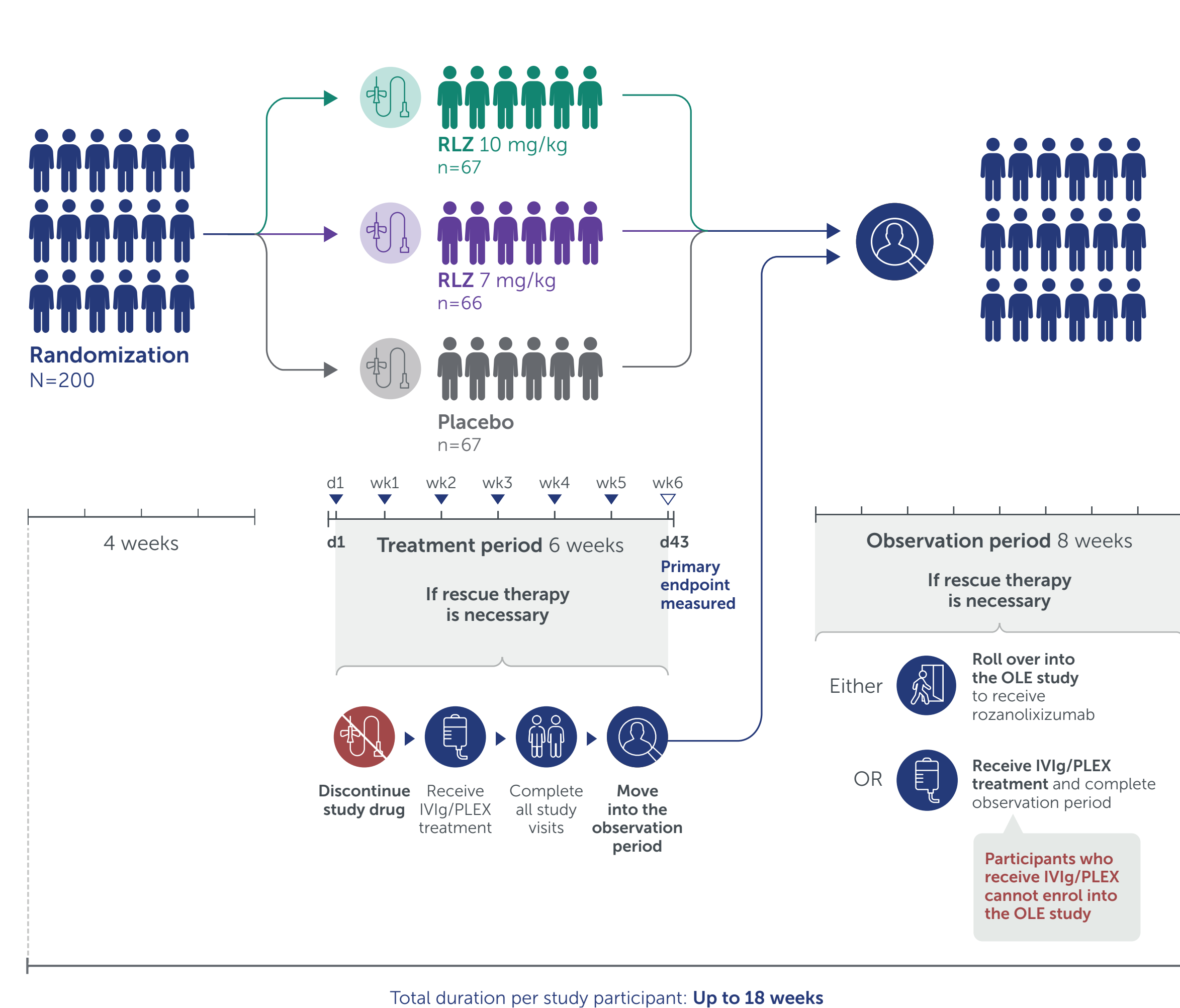
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Conclusions

- Rozanolixizumab improved MG-specific outcomes in MuSK Ab+ gMG, consistent with results in AChR Ab+ gMG and the combined population
- There were 21 MuSK Ab+ patients in the study, and in these patients the efficacy results were numerically better than for the overall population; however, the study was not powered for MuSK Ab+ subgroup statistical analysis
- These results indicate that rozanolixizumab could potentially provide therapeutic benefit in the subset of patients with MuSK Ab+ gMG, who have particularly limited treatment options⁴
- Safety and tolerability outcomes from MycarinG are presented in this session as a data blitz, and responder analyses for the overall population are presented at the AANEM 2022 meeting in Poster 204.

Figure 1 MycarinG study design



Rozanolixizumab is not approved for treatment of myasthenia gravis by any health authority.



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