Subcutaneous rozanolixizumab in pediatric patients with generalized myasthenia gravis: Clinical study design

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Introduction

- Pediatric myasthenia gravis is a rare disorder that displays predominantly similar clinical phenotypes to adult MG. Due to a lack of clinical trial data, management of pediatric MG is guided by treatment recommendations for adult MG or individual practitioner experience, with significant variability[1]
- As such, many of the current treatments are off-label and not always efficacious
  - No formal guidelines exist for the use of immunosuppressive therapy in pediatric gMG[1–3]
  - Corticosteroids are recommended as first-line immunosuppressive therapies in pediatric gMG despite known adverse effects[3]
- Recently, several targeted therapies have been approved in adults with refractory gMG, and one targeted therapy for children with AChR autoantibody positive gMG[4]
- Rozanolixizumab, a fully humanized IgG4 monoclonal antibody that inhibits FcRn (**Figure 1**), has demonstrated statistically significant and clinically meaningful improvements in key MG clinical outcome measures in adults with gMG in the Phase 3 MycarinG (MG0003) study.[5] US FDA approval of rozanolixizumab for adults with gMG was granted in 2023[6]
- The Phase 2/3 roMyG (MG0006) study is a multicenter, international, open-label, single-arm study that aims to assess the safety, tolerability and activity of SC rozanolixizumab over one 6-week treatment cycle in patients with gMG aged ≥2 to <18 years (**Figures 2, 3, 4**)
- roMyG+ (MG0008) is the Phase 3 open-label extension study (**Figure 2**) and will assess the long-term safety and tolerability of additional symptom-driven cycles (**Figure 5**) of rozanolixizumab in children transitioning from roMyG; it will also assesses the activity of rozanolixizumab during additional symptom-driven 6-week treatment cycles

Abbreviations: AChR, acetylcholine receptor; ADA, antidrug antibody; AESM, adverse events of special monitoring; CGI-S, Clinical Global Impressions scale - Severity; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; Ig, immunoglobulin; IMP, investigational medicinal product; IVIg, intravenous immunoglobulin; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MuSK, muscle-specific tyrosine kinase; Neuro-QoL, Quality of Life in Neurological Disorders; OP, observation period; OPtex, extension of the observation period 1; PD, pharmacodynamic; PedsQL, Pediatric Quality of Life; PGI-S, Patient Global Impressions scale - Severity; PK, pharmacokinetic; PLEX, plasma exchange; QMG, Quantitative Myasthenia Gravis; SC, subcutaneous; TEAE, treatment-emergent adverse event; TP, treatment period; US FDA, United States Food and Drug Administration.

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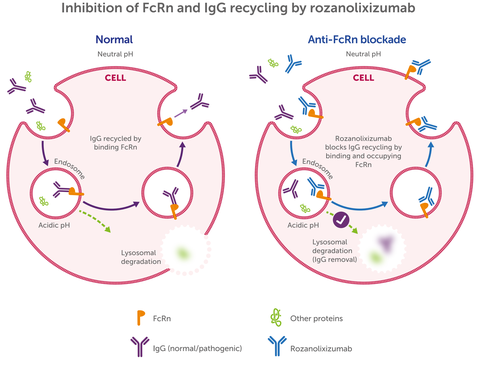
Figure 1 Mechanism of action of rozanolixizumab[7–10]



Rozanolixizumab is an FcRn inhibitor which prevents recycling of IgG by binding IgG FcRn receptors. Rozanolixizumab binding results in degradation and thus reduction of pathogenic IgG autoantibodies in patients with MG

Figure 3 roMyG and roMyG+ inclusion and exclusion criteria

Key inclusion criteria

- Aged ≥2 to <18 years
- Anti-AChR or anti-MuSK antibody-positive MG with MGFA Disease Class II to IVa
- Has previously received existing conventional treatment(s) for gMG (e.g. pyridostigmine, corticosteroids and/or immunosuppressants)
- Has had unsatisfactory clinical response to prior treatment or worsening of gMG symptoms
- **roMyG+ patients must meet one of the following:**
  - Patients who completed roMyG according to protocol and will benefit from further treatment with rozanolixizumab
  - Patients who completed TP1 in roMyG according to protocol and have a worsening of symptoms in OP1 of roMyG

Key exclusion criteria

- Any medical or psychiatric condition that would compromise ability to participate in the study
- Previous treatment with rozanolixizumab or anti-FcRn drugs
- Any clinically relevant active infection or serious infection within 6 weeks prior to the first dose of IMP
- A history of thymectomy in the last 6 months
- Known hypersensitivity to any components of the study medication
- A current or medical history of primary immunodeficiency or IgA deficiency
- A current or medical history of hyperprolinemia

Figure 4 roMyG and roMyG+ endpoints

Primary endpoints

- Occurrence of serious TEAEs
- Occurrence of TEAEs leading to permanent withdrawal of the IMP
- Occurrence of AESM

Secondary endpoints

- Percent and absolute change in total IgG from baseline to the end of each TP
- Percent and absolute change from baseline in MG-specific autoantibody (anti-AChR or anti-MuSK) levels at each scheduled assessment during each TP and OP
- Change from baseline in MG-ADL and QMG total scores at the end of each TP

Other endpoints

- Change from baseline in MG-ADL, QMG, Neuro-QoL, PedsQL, CGI-S and PGI-S during TP1 and OP1 and subsequent symptom-driven TPs and OPs.
- Plasma concentration of rozanolixizumab at each scheduled assessment during each TP
- Development of ADAs at each scheduled assessment during each TP

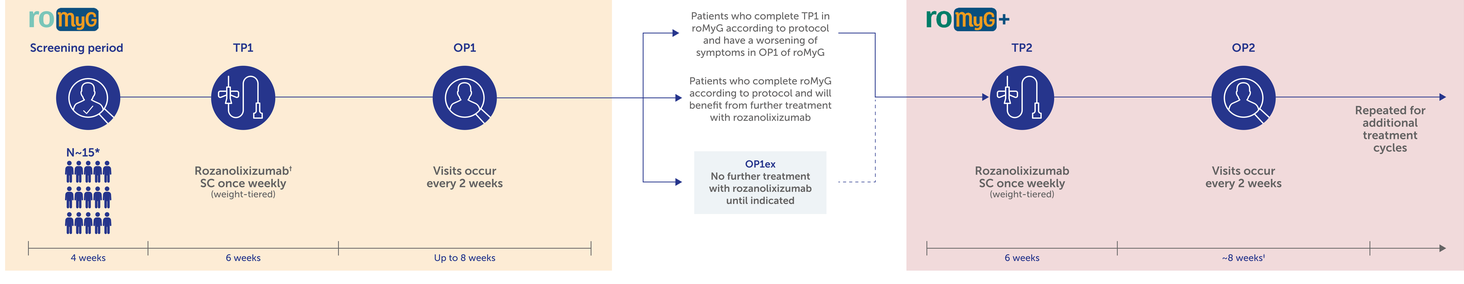
Summary

There is a need for safe and effective treatments for the pediatric gMG population as current treatments are not always effective and are associated with side effects that can lead to long-term complications

Rozanolixizumab has been demonstrated to markedly lower serum IgG and IgG autoantibody levels and improve key MG clinical outcome measures in adults with gMG[5]

roMyG will evaluate one symptom-driven treatment cycle of rozanolixizumab; roMyG+ will evaluate repeated symptom-driven treatment cycles of rozanolixizumab, providing long-term data to determine the safety and efficacy in pediatric patients aged ≥2 to <18 years

Figure 2 roMyG and roMyG+ study designs

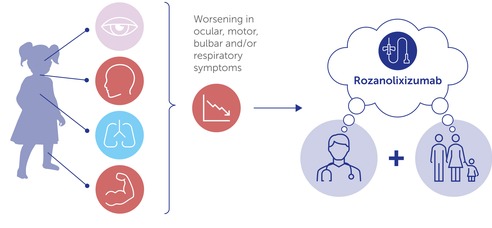


OP, observational period; TP, treatment period

*The number of patients enrolled will be determined based on response to treatment. †For roMyG, an interim PK/PD evaluation will confirm the treatment dose and inform the number of enrolled patients. ‡The observation period in roMyG+ may be expanded for the individual patient as needed until a new symptom-driven treatment cycle is indicated.

Figure 5 Protocol-defined criteria for initiating a symptom-driven cycle of rozanolixizumab

Between two consecutive visits at any time during OPs



Comprehensive individualized assessment best reflects the disease dynamics and variability of symptoms in children with gMG from day to day

A new treatment cycle of rozanolixizumab in roMyG+ may be initiated at the discretion of the investigator and in agreement with the study participant and/or caregivers