Looking beyond the numbers: Interpreting patient experience of rozanolixizumab in generalized myasthenia gravis from the MycarinG clinical trial

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Introduction

- People living with gMG experience fluctuating and variable muscle weakness, muscle weakness fatigability and fatigue; however, each person's experience is different[1,2]
- Improvement in physical fatigue is an important outcome,[2] and is not assessed in the commonly used MG-specific scales that measure symptom severity
- The MG Symptoms PRO scales include five scales, which were developed to understand the important aspects of patients' lived experiences (including physical fatigue) based on findings from qualitative research involving adults with gMG[2]
- In the 15-item MG Symptoms PRO Physical Fatigue scale, responders select how frequently they have experienced each symptom over the past 7 days using a 5-point scale ("none of the time" to "all of the time")
  - Higher scores indicate more frequent experiences of symptoms
- MycarinG (NCT03971422) was a Phase 3 study of rozanolixizumab, a humanized IgG4 monoclonal antibody FcRn inhibitor, in people living with gMG; three MG Symptoms PRO scales were selected as secondary endpoints: Physical Fatigue, Muscle Weakness Fatigability and Bulbar Muscle Weakness[3]
  - At Day 43, MG Symptoms PRO Physical Fatigue scores for patients receiving rozanolixizumab improved (**Figure 1**)
- The objective of this *post-hoc* analysis was to show how the patient-relevant content of the MG Symptoms PRO scale could be used to provide an interpretation of the changes in the MG Symptoms PRO Physical Fatigue score observed in MycarinG that is meaningful to patients

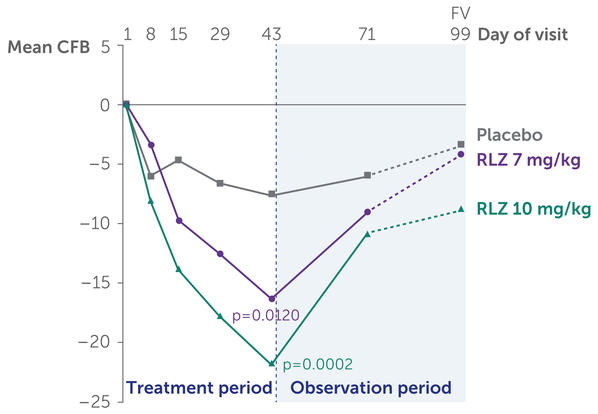
Methods

- MycarinG enrolled patients aged ≥18 years with AChR Ab+ or MuSK Ab+ gMG, MGFA Disease Class II–IVa, MG-ADL score ≥3 (for non-ocular symptoms) and QMG score ≥11[3]
- Patients were randomly assigned to receive one cycle (six weekly infusions) of rozanolixizumab 7 mg/kg, rozanolixizumab 10 mg/kg or placebo
- Secondary endpoints included CFB to Day 43 in MG Symptoms PRO scales
  - MG Symptoms PRO scales were assessed at Days 1, 8, 15, 29, 43, 71 and 99
- The MG Symptoms PRO scales were developed with the Rasch model, a mathematical model that expresses the probability for a respondent to give a response to a specific item as a function of the respondent level of the measured attribute (i.e., the targeted concept) and the level of this attribute that is characterized by the item
  - A probabilistic frame of reference in which the items composing the scales can be ordered in a meaningful hierarchy can be obtained from this model
  - This hierarchy provides the most likely response to each MG Symptoms PRO item for any given level of the concept
  - The Rasch model has been used previously in the context of other commonly used scales in MG: MG-ADL, QMG and MGC[4–7]
- To provide interpretation of the results using the content of the MG Symptoms PRO items, the mean MG Symptoms PRO scales observed in each treatment arm (rozanolixizumab 7 mg/kg, rozanolixizumab 10 mg/kg and placebo) at Day 1 and Day 43 were mapped to this frame of reference to determine the most likely response to the MG Symptoms PRO scales for each group of patients at these timepoints

Results

- 200 patients were enrolled and randomized to receive placebo (n=67), rozanolixizumab 7 mg/kg (n=66) or rozanolixizumab 10 mg/kg (n=67)[3]
- **Figure 2** lists the individual items of the MG Symptoms PRO Physical Fatigue scale in order of severity, and illustrates that patients receiving rozanolixizumab typically:
  - No longer experienced the more severe symptoms and rarely experienced the less severe symptoms (**Figure 2**)
- Patients receiving placebo typically:
  - Experienced more severe symptoms "a little of the time" and experienced the less severe symptoms "some of the time" (**Figure 2**)
- A similar patient experience was obtained across Muscle Weakness Fatigability and Bulbar Muscle Weakness scales

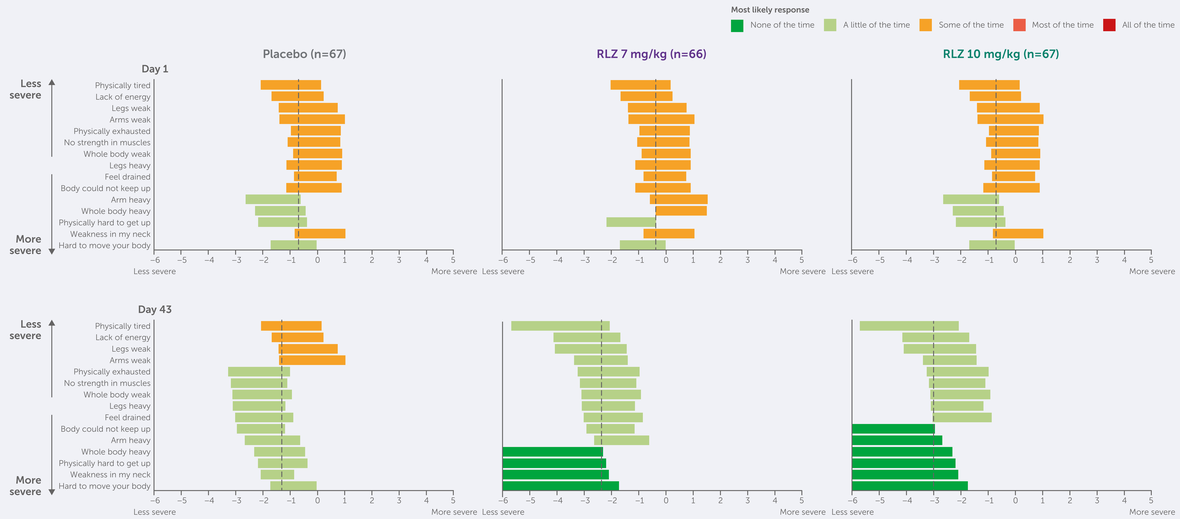
Figure 1 Mean CFB in MG Symptoms PRO Physical Fatigue score in MycarinG



Day	1	8	15	29	43	71	FV 99
Placebo, n	67	67	66	65	64	48	64
RLZ 7 mg/kg, n	66	66	62	63	64	52	64
RLZ 10 mg/kg, n	67	66	64	61	62	59	64

p-values are vs placebo at Day 43.

Figure 2 Most probable response to the items of the MG Symptoms PRO Physical Fatigue scale at Day 1 and Day 43 by treatment arm



Dotted lines represent the observed means in MycarinG.

Summary and conclusions

The 15 items in the MG Symptoms PRO Physical Fatigue scale were developed with input from people living with gMG to evaluate changes that reflect patients' actual experiences

In the Phase 3 MycarinG study of rozanolixizumab, statistically significant improvements vs placebo were observed at Day 43 in the MG Symptoms PRO Physical Fatigue scale scores

These numbers can be translated to fully understand patient-relevant aspects of physical fatigue after treatment

MG Symptoms PRO Physical Fatigue scale	Patients receiving rozanolixizumab typically…	Patients receiving placebo typically…
More severe symptoms		
"Whole body heavy" "Weakness in my neck" "Hard to move body" "Physically hard to get up"	No longer experienced	Continued to experience "a little of the time"
Less severe symptoms		
"Physically tired" "Lack of energy" "Legs weak" "Arms weak"	Rarely experienced	Continued to experience "some of the time"

This *post-hoc* analysis of the MG Symptoms PRO Physical Fatigue scale from MycarinG may help facilitate communication about patients' experiences with rozanolixizumab

For more detailed explanations about the use of Rasch, a modern scientific approach for the evaluation of outcome measures, please see the following references: Browne JP, Cano SJ. *A Rasch measurement theory approach to improve the interpretation of patient-reported outcomes*. Med Care. 2019;57(5 Suppl 1):S18–S23; and data supplement to van Nes SI, et al. *Appendix e-1 supplemental data: Explaining Rasch to neurologists: Rasch-built Overall Disability Scale (R-ODS) for immune-mediated peripheral neuropathies*. Neurology. 2011;76(4):337–345.

Abbreviations: AChR Ab+, positive for autoantibodies against the acetylcholine receptor; CFB, change from baseline; FcRn, neonatal Fc receptor; FV, final visit; (g)MG, (generalized) myasthenia gravis; IgG, immunoglobulin G; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGC, Myasthenia Gravis Composite; MGFA, Myasthenia Gravis Foundation of America; MuSK Ab+, positive for autoantibodies against muscle-specific kinase; PRO, patient-reported outcome; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab.

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For more information on MG Symptoms PRO Scales visit: https://eprovide.mapi-trust.org/instruments/myasthenia-gravis-symptoms-patient-reported-outcome-scales

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