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Improvement in Patient-Reported Symptoms of Generalised Myasthenia Gravis With Rozanolixizumab in the Randomised Phase 3 MycarinG Study Using the MG Symptoms PRO

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Keywords: clinical trial | myasthenia gravis | patient-reported outcome measure | patient-reported outcomes | phase 3 | rozanolixizumab

ABSTRACT

Background: In the Phase 3 MycarinG study (NCT03971422), rozanolixizumab improved myasthenia gravis (MG)-specific outcomes versus placebo in patients with generalised MG, including those measured by the five independent MG Symptoms patient-reported outcome (PRO) scales: Muscle Weakness Fatigability (MWF), Physical Fatigue (PF) and Bulbar Muscle Weakness (BMW) as secondary endpoints and Ocular Muscle Weakness and Respiratory Muscle Weakness (exploratory endpoints). This research aimed to provide further insights into these improvements.

Methods: *Post hoc* analyses evaluated correlation (Pearson coefficient) between MG Symptoms PRO and subdomain scores of MG Activities of Daily Living (MG-ADL) and Quantitative MG (QMG) at baseline. Proportions of responders reaching clinically meaningful thresholds and analyses at the item level (observed mean change and Rasch modelling of predicted change from baseline) are reported for MWF, PF, and BMW with rozanolixizumab versus placebo at Day 43.

Results: Correlation coefficients between MG Symptoms PRO and MG-ADL were strong (≥ 0.7) for ocular and bulbar scores and moderate (0.5 to <0.7) for other scores. Correlations with clinician-assessed QMG scores were generally weak (<0.5). For MWF, PF, and BMW, greater proportions of responders were observed with rozanolixizumab 7 mg/kg (46.9%, 31.3% and 26.6%, respectively) or 10 mg/kg (56.5%, 48.4% and 32.3%) versus placebo (28.1%, 26.6% and 10.9%). Item-level analyses demonstrated rozanolixizumab benefit at a symptom-specific level.

Discussion: MG Symptoms PRO scales correlate well with concepts in MG-ADL while assessing additional concepts, such as PF and MWF. Results from the MG Symptoms PRO in MycarinG reflected improvements from baseline in patient-relevant symptoms, including fatigue, with rozanolixizumab.

1 | Introduction

Myasthenia gravis (MG) is an autoimmune disorder affecting the neuromuscular junction, caused by autoantibodies that bind to functional proteins at the postsynaptic membrane [1, 2]. The disease is characterised clinically by muscle weakness and fatigability, which fluctuate in frequency, severity, and location, and may vary with continued activity and worsen towards the end of the day [1, 3].

Fatigue has been identified by adults with generalised MG (gMG) as an important symptom which negatively impacts quality of life [4–12]. The prevalence of fatigue has been reported as 44%–82% in patients with gMG compared with 18%–40% in control groups [5]. Muscle fatigability (also known as peripheral fatigue) results from compromised neuromuscular transmission, whereas physical or general fatigue is a lack of physical or cognitive energy unrelated to muscle weakness that may have multiple aetiologies [2, 5].

Established outcome measures in gMG include the MG Activities of Daily Living (MG-ADL) and the Quantitative MG (QMG) scales, which evaluate the severity of signs and symptoms of muscle weakness [13–15]. The two measures were key primary and secondary outcomes in all recent clinical trials in gMG. The eight items comprising the MG-ADL scale include patient assessment of ocular, bulbar, and respiratory muscle weakness symptoms and limb weakness (Table S1) [14], with concordance demonstrated between patient and physician assessment [16]. The QMG scale evaluates muscle weakness and fatigability in ocular/facial, bulbar, respiratory, and gross motor/axial muscles [15], based on clinician assessment of clinical signs and performance of specific tasks requiring these muscles. Neither QMG nor MG-ADL measure physical/general fatigue.

The new MG Symptoms patient-reported outcome (PRO) scales were designed to assess patients' experiences of gMG symptoms that were most relevant to them and to complement existing measures used in gMG [7, 17, 18]. The MG Symptoms PRO comprises five scales that can be used independently to evaluate patients' experiences of symptoms over the past 7 days, measuring severity of muscle weakness (ocular, bulbar and respiratory) and frequency of physical fatigue and muscle weakness fatigability. The MG Symptoms PRO was developed using qualitative and quantitative methods and best practices [19–21], and items (including terminology) were determined to capture the granularity and variability of symptoms of gMG [7]. The scales have demonstrated strong psychometric properties [7, 18], and thresholds to guide the interpretation of meaningful within-patient change (MWPC) in the Muscle Weakness Fatigability, Physical Fatigue, and Bulbar Muscle Weakness scales have been determined [18]. These three scales were secondary endpoints in the Phase 3 MycarinG study that investigated the efficacy and safety of rozanolixizumab, a humanised immunoglobulin G (IgG) 4 monoclonal antibody targeting the neonatal Fc receptor to reduce levels of pathogenic IgG autoantibodies in patients with gMG [22].

Rozanolixizumab showed statistically significant and clinically meaningful improvements from baseline compared with placebo in MG-ADL score, the primary efficacy endpoint, as well as in secondary endpoints based on change from baseline in QMG score and three MG Symptoms PRO scales [22]. There were also improvements in scores on the Ocular Muscle Weakness and Respiratory Muscle Weakness MG Symptoms PRO scales (exploratory endpoints; Table S2). Both rozanolixizumab doses were generally well tolerated.

The current *post hoc* analyses of MycarinG study data aimed to (i) illustrate how the scores from the MG Symptoms PRO scales complement existing measures to provide a comprehensive understanding of patients' lived experiences of gMG symptoms, and (ii) help interpret the meaningfulness of the effect of rozanolixizumab on symptoms from the patients' perspective.

2 | Methods

2.1 | MycarinG Study Design

MycarinG (NCT03971422) was a randomised, double-blind, placebo-controlled, parallel-group, multicentre Phase 3 study; full details of the study design have been published previously [22]. In brief, eligible patients were aged ≥18 years with anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody-positive (Ab+) gMG, Myasthenia Gravis Foundation of America (MGFA) Disease Class II–IVa, MG-ADL score ≥3 (for non-ocular symptoms) and QMG score ≥11, and had been considered for additional therapy such as intravenous immunoglobulin or plasma exchange. Patients were randomly assigned 1:1:1 to receive once-weekly subcutaneous rozanolixizumab 7 mg/kg, rozanolixizumab 10 mg/kg, or placebo for 6 weeks. All patients provided written informed consent. The study was conducted in accordance with the Declaration of Helsinki. A national, regional, or independent ethics committee or institutional review board (depending on site) approved the protocol [22].

2.2 | Overview of Assessments and Scoring

The scores on all five MG Symptoms PRO scales range from 0 to 100, where a higher score indicates greater symptom severity. Scores were obtained by summing the responses to the items composing each scale and were only calculated when ≥70% of items for that scale were completed.

Estimates for MWPC in MG Symptoms PRO scores (i.e., the change in score that is perceived as meaningful from the patient perspective) were previously obtained through the triangulation

of anchor and distribution methods using blinded data from MycarinG (at baseline and Day 29) [18]. A range of values was proposed to account for expected variability in defining meaningful change in PRO scores, which can depend on context of use, patient population, and study sample. The reference values for meaningful change were −16.67 for Muscle Weakness Fatigability (range: −13.89 to −27.78), −20.00 for Physical Fatigue (range: −16.67 to −26.67) and −20.00 for Bulbar Muscle Weakness (range: −16.67 to −26.67).

MG-ADL has a total score range of 0–24 while QMG has a total score range of 0–39. For both tools, higher scores represent more severe symptoms. In MycarinG, patients were asked about their current situation when completing MG-ADL, while QMG involved clinician assessment on the day of the visit. Items from both scales were categorised by muscle group to provide ocular, bulbar, respiratory, and limb impairment/gross motor subdomain scores (Table S1) [23, 24]. Subdomain scores for MG-ADL and QMG at baseline were assessed *post hoc*.

In MycarinG, MG-ADL and QMG data were collected at screening and every 7 days from Day 1 to Day 43. MG Symptoms PRO data were collected using the same schedule with the exception of no data collection on Days 22 and 36.

2.3 | Statistical Analysis

2.3.1 | Association Between MG Symptoms PRO Scale Scores and MG-ADL and QMG Subdomain Scores

To illustrate how MG Symptoms PRO scale scores complement existing measures, the relationship between each scale and the related symptom subdomain scores of MG-ADL and QMG was assessed using data from baseline, prior to treatment administration, in MycarinG. The correlation between each pair of scores at baseline was estimated using the Pearson correlation test; correlations were considered weak if the coefficient was 0.3 to <0.5, moderate if the coefficient was 0.5 to <0.7, and strong if the coefficient was ≥ 0.7 [17, 25].

2.3.2 | Meaningfulness of Improvements in MG Symptoms PRO With Rozanolixizumab Treatment

To interpret the meaningfulness of the treatment effect of rozanolixizumab on patients' lived experiences, three approaches were utilized. Firstly, the proportion of responders to treatment on the MG Symptoms PRO scales that were secondary endpoints in the MycarinG study were examined. The *preliminary* range of values representing MWPC were used as responder thresholds to interpret the meaningfulness of improvements from baseline [18]. The proportion of responders across the treatment groups was described for the reference value and the higher (most stringent) threshold. Empirical cumulative distribution function (eCDF) plots were used to visualize the effect of treatment across the study population to depict all magnitudes of changes, separation between groups, and the proportion of patients at each point across the scale score continuum who experience change at or below that level. The Ocular Muscle Weakness and Respiratory Muscle Weakness scales were not included in the previous analyses to determine thresholds because they were considered exploratory at that stage [18].

In addition, item-level analyses were conducted for each scale using parametric statistics (mean change from baseline in each item score at Day 43). Parametric statistics are typically not used to analyze ordinal variables (e.g., single-item ordinal responses); however, in conjunction with the Rasch model analysis described below, they provide a more comprehensive picture of patients' experiences of specific symptoms captured by the MG Symptoms PRO.

Finally, we explored how score changes translate into patient experience pre- and post-treatment for Muscle Weakness Fatigability, Physical Fatigue, and Bulbar Muscle Weakness. The pre- and post-treatment patient-relevant experiences corresponding to the severity of symptoms were portrayed for each treatment arm using the underlying psychometric structure of the MG Symptoms PRO. The scales were developed using the Rasch model, a probabilistic model that has been used previously to assess the psychometric properties of commonly used scales in gMG, including MG-ADL and QMG [26–29]. This model defines a probability relationship between the level of the measured concept and the response to each item constituting the scale. The score for each scale was translated into a probability of answering each response option for each item, creating an invariant frame of reference. The mean scores of items in the three scales in each treatment group were mapped to the frame of reference previously established by applying the Rasch model to MG Symptoms PRO data in the MycarinG study [18]. This allowed determination of the most likely response to each item at Day 1 (prior to treatment) and Day 43 (end of treatment), illustrating the experience of those symptoms by a typical patient pre- and post-treatment for each treatment group.

3 | Results

3.1 | MycarinG Study Population

A total of 200 patients were treated in the MycarinG study and received either rozanolixizumab 7 mg/kg ($n=66$), rozanolixizumab 10 mg/kg ($n=67$) or placebo ($n=67$) [22]. Overall, 179 (90%) patients had anti-AChR Ab+ gMG, and 21 (11%) patients had anti-MuSK Ab+ gMG. At baseline, mean (SD) MG-ADL total score and QMG total score in the overall population were 8.3 (3.4) and 15.6 (3.6), respectively. Full baseline characteristics are published elsewhere [22].

3.2 | Association Between MG Symptoms PRO Scale Scores and MG-ADL and QMG Subdomain Scores

Strong correlations were observed between MG Symptoms PRO Ocular Muscle Weakness and Bulbar Muscle Weakness scale scores and related MG-ADL subdomain scores at baseline (Figure 1a). Correlation coefficients among MG Symptoms PRO scales and MG-ADL subdomain scores were lower among concepts that are not explicitly captured by MG-ADL, such as physical fatigue and muscle weakness fatigability. Moderate

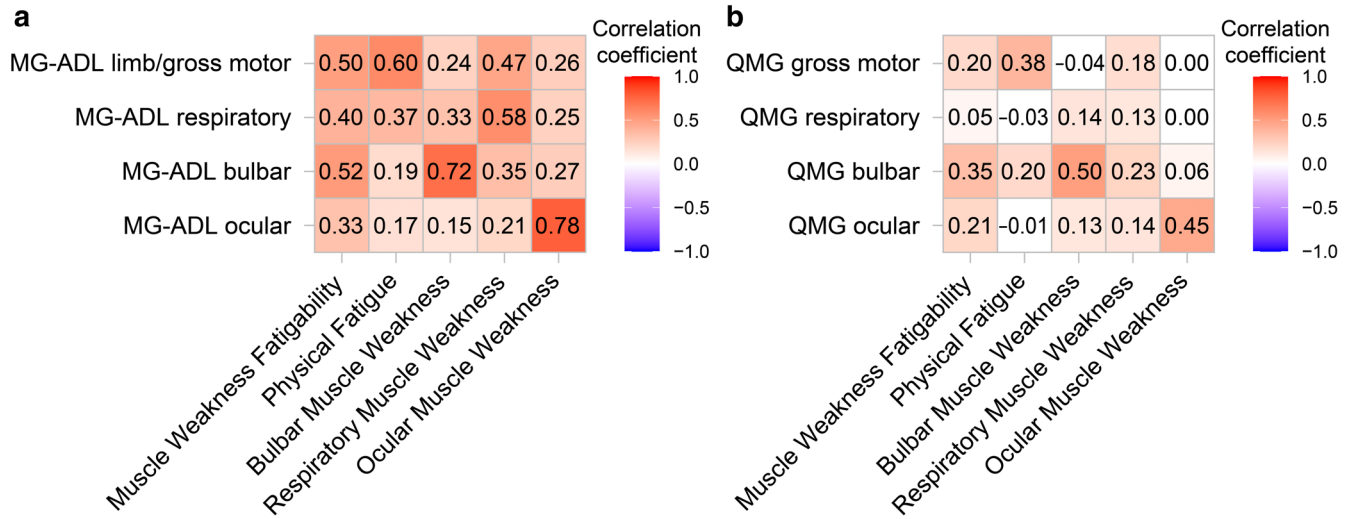


FIGURE 1 | Correlations between MG Symptoms PRO scales and subdomains of (a) MG-ADL and (b) QMG. MG Symptoms PRO data at baseline were recorded for all treated patients. MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; PRO, patient-reported outcome; QMG, Quantitative Myasthenia Gravis.

correlations were observed between the Physical Fatigue scale and the MG-ADL limb/gross motor subdomain scores and between the Muscle Weakness Fatigability scale and MG-ADL bulbar and limb/gross motor subdomain scores. A moderate correlation was also observed for respiratory symptoms, measured by three items in the Respiratory Muscle Weakness scale and a single item in MG-ADL.

Correlation coefficients between the MG Symptoms PRO scale scores and the QMG subdomain scores were generally weak; however, a moderate correlation was observed between the Bulbar Muscle Weakness scale and the QMG bulbar subdomain score (Figure 1b). Scatter plots of patients' scores on the MG Symptoms PRO versus QMG showed substantial variability, particularly for the scores with low correlation coefficients, reflecting high variability in how disease severity was scored across the scales (data not shown).

3.3 | Meaningful Improvements in MG Symptoms PRO With Rozanolixizumab Treatment

3.3.1 | Responder Analysis at Day 43

eCDF curves for change from baseline were generated for the three MG Symptoms PRO scales that were secondary endpoints in MycarinG (Muscle Weakness Fatigability, Physical Fatigue and Bulbar Muscle Weakness; Figure S1), and the proportions of patients achieving a meaningful improvement at Day 43 were derived using the reference values as well as the higher threshold of the range (Figure 2). Across the three scales, higher proportions of patients treated with rozanolixizumab reached both the reference value and the higher threshold compared with placebo, with higher proportions in the rozanolixizumab 10 mg/kg group versus the 7 mg/kg group. Of the rozanolixizumab-treated patients, 69%–73% of responders in the three scales were also responders in MG-ADL (≥ 2-point improvement) and QMG (≥ 3-point improvement). Conversely, 70%, 57%, and 48% of MG-ADL responders were responders in the Muscle Weakness Fatigability, Physical Fatigue, and Bulbar Muscle Weakness scale, respectively, with similar proportions for QMG responders (71%, 64% and 44%, respectively).

3.3.2 | Item-Level Analysis of Change From Baseline at Day 43 in MG Symptoms PRO Scale Scores

For Muscle Weakness Fatigability, Physical Fatigue, and Bulbar Muscle Weakness, mean change from baseline at Day 43 at the item level was consistently greater in both rozanolixizumab groups than in the placebo group (Figure 3). Across most items, the 10 mg/kg group had greater improvements than the 7 mg/kg group except for one item in the Muscle Weakness Fatigability scale and four items in the Bulbar Muscle Weakness scale. These results may be artefacts due to the use of mean change for the ordinal rating, especially as baseline level per group was not controlled. Similar results were observed in the item scores for the Ocular Muscle Weakness and Respiratory Muscle Weakness scales (Figure S2).

3.3.3 | Description of MG Symptoms PRO Responses Before and After Treatment Using the Rasch Model

For Muscle Weakness Fatigability, Physical Fatigue, and Bulbar Muscle Weakness, the most probable response to each item before and after treatment was established (Figure 4). Items are ordered according to severity per the initial Rasch model, with less severe items at the top and more severe items at the bottom.

For Muscle Weakness Fatigability (Figure 4a), the mean score before treatment (dashed lines at Day 1, upper panel) was slightly lower for the placebo group than for the rozanolixizumab groups; based on the Rasch model, this translates into milder symptoms for about half of the items. After treatment (Day 43, bottom panel), the mean item scores suggested that in both rozanolixizumab groups a typical patient would be

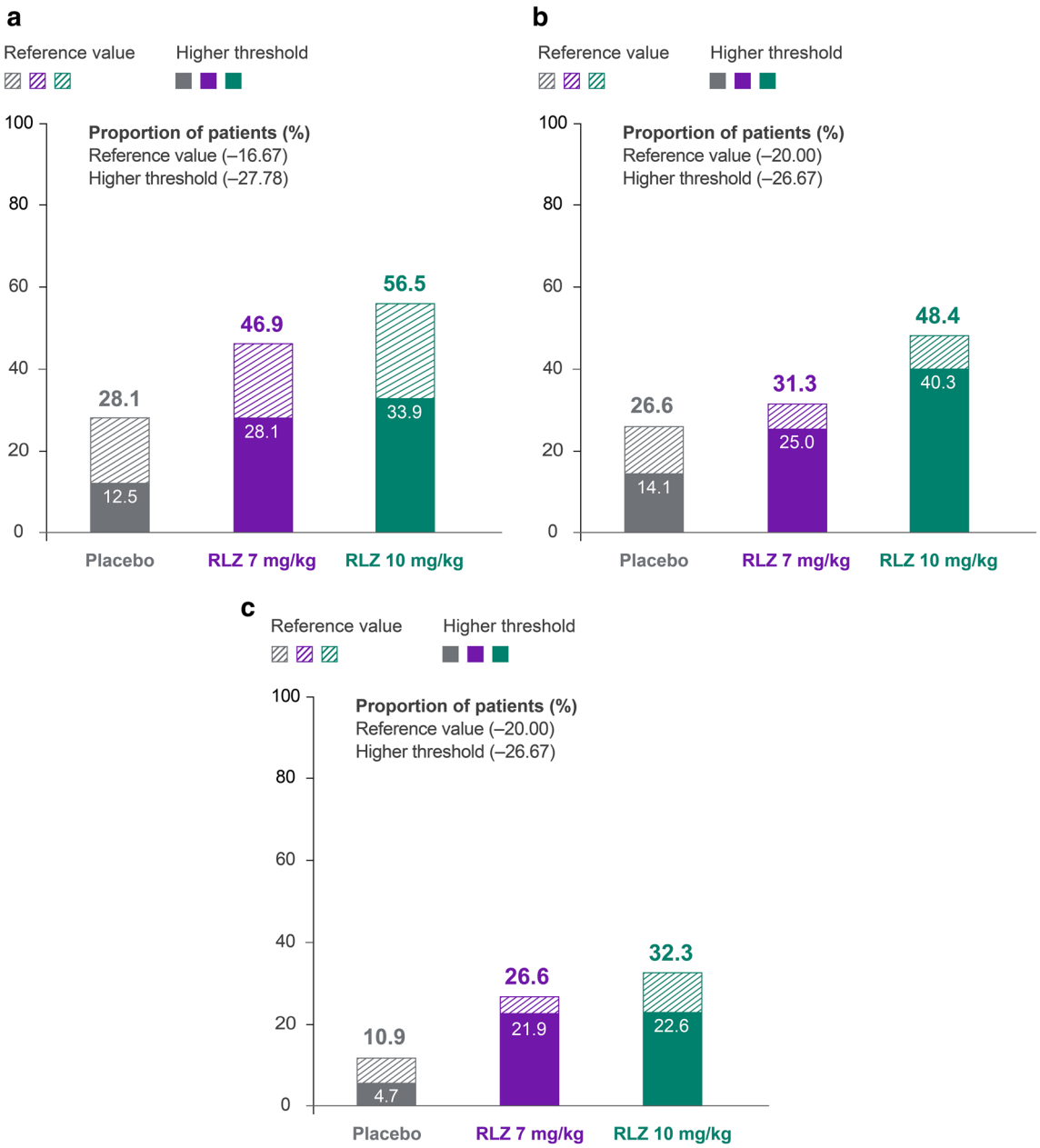
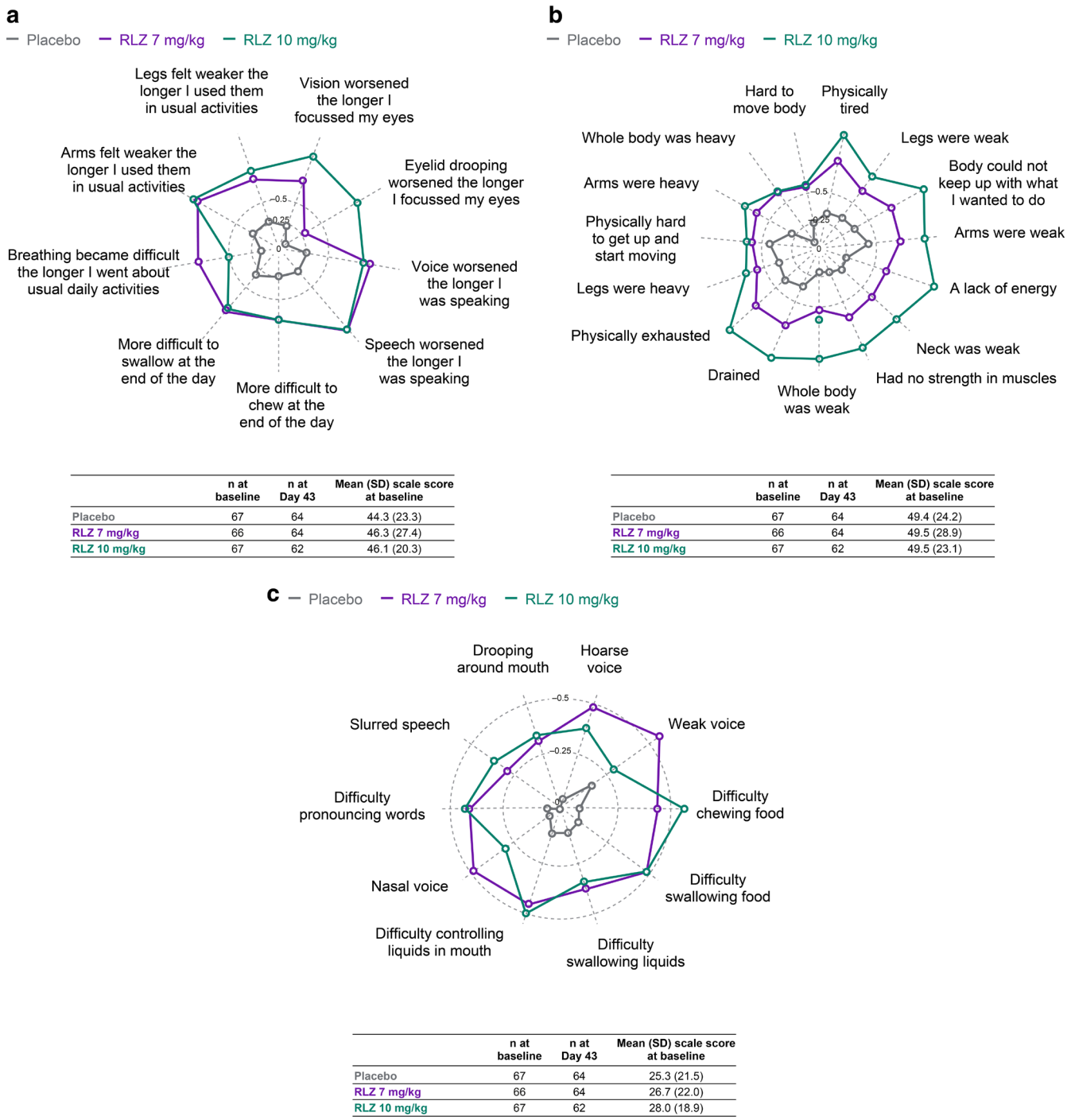


FIGURE 2 | Proportions of patients achieving a meaningful improvement at Day 43 in (a) Muscle Weakness Fatigability, (b) Physical Fatigue and (c) Bulbar Muscle Weakness. RLZ, rozanolixizumab.

reporting these symptoms "none of the time" (dark green bars) or "a little of the time" (light green bars). In the placebo group, the most likely symptoms at Day 43 were predicted to be only slightly different from at Day 1. The model of mean Physical Fatigue scores (Figure 4b) showed that before treatment, the typical patient was experiencing most symptoms of physical fatigue "some of the time". After treatment, a typical patient in either rozanolixizumab group would be likely to report these symptoms "none of the time" or "a little of the time", whereas a typical patient in the placebo group would likely experience a few symptoms "some of the time" and most symptoms a "little of the time". The model of mean Bulbar Muscle Weakness scores (Figure 4c) indicated that mild symptoms were experienced before treatment. After treatment, in both rozanolixizumab groups a typical patient would be expected to report no symptoms, whereas a typical patient in the placebo group would likely still report the same mild symptoms.

4 | Discussion

These *post hoc* analyses of data collected in the MycarinG study provide further evidence for the added value of the MG Symptoms PRO for evaluating gMG symptoms that are meaningful to patients, including changes following treatment. The MG Symptoms PRO scales provide more granularity than existing tools, and correlations were not expected to be strong for concepts that are not covered by the MG-ADL or QMG, such as physical fatigue. A previous correlation analysis of the five scales with MG-ADL and QMG total scores using data from a Phase 2



	n at baseline	n at Day 43	Mean (SD) scale score at baseline
Placebo	67	64	44.3 (23.3)
RLZ 7 mg/kg	66	64	46.3 (27.4)
RLZ 10 mg/kg	67	62	46.1 (20.3)

	n at baseline	n at Day 43	Mean (SD) scale score at baseline
Placebo	67	64	49.4 (24.2)
RLZ 7 mg/kg	66	64	49.5 (28.9)
RLZ 10 mg/kg	67	62	49.5 (23.1)

	n at baseline	n at Day 43	Mean (SD) scale score at baseline
Placebo	67	64	25.3 (21.5)
RLZ 7 mg/kg	66	64	26.7 (22.0)
RLZ 10 mg/kg	67	62	28.0 (18.9)

FIGURE 3 | Mean change from baseline at Day 43 in item scores for (a) Muscle Weakness Fatigability, (b) Physical Fatigue and (c) Bulbar Muscle Weakness. Mean change from baseline in raw scores for each item. RLZ, rozanolixizumab.

study ($N = 43$) reported moderate-to-strong correlations between MG-ADL and QMG total scores and some MG Symptoms PRO scales [17]. The current analysis used data from a larger Phase 3 study ($N = 200$) to investigate correlations between the MG Symptoms PRO scale scores and subdomain scores of MG-ADL and QMG. Moderate and strong correlations were observed between all five MG Symptoms PRO scale scores and relevant MG-ADL subdomain scores, reflecting similar concepts between the two measures. QMG assesses weakness and fatigability based on clinician evaluation of clinical signs and impairment in the ability to perform standardised tasks during a visit. In contrast, the MG Symptoms PRO asks patients about their experience of symptoms over a 7-day recall period; items also evaluate symptom variability over the course of the day or on sustained use of muscles. The low correlations are not surprising considering that concepts measured by the MG Symptoms PRO are less similar to those in QMG than in MG-ADL, and they suggest that the QMG clinical assessment may not adequately reflect patient experience.

Treatment with rozanolixizumab provided clinically meaningful improvements across a range of symptoms measured by

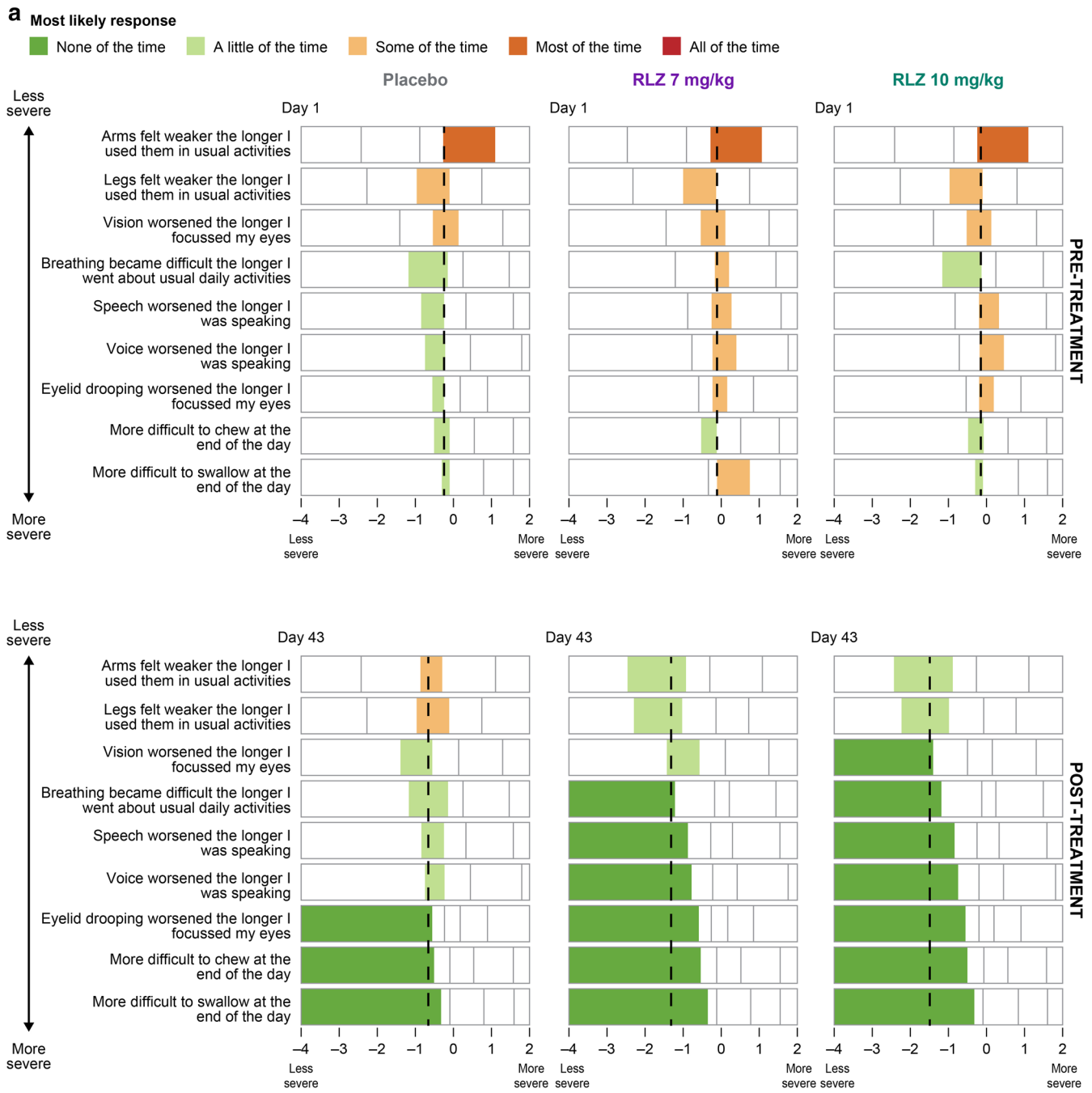


FIGURE 4 | Most probable response to MG Symptoms PRO items pre-treatment (Day 1) and post-treatment (Day 43) based on the Rasch model probability framework by treatment group for (a) Muscle Weakness Fatigability, (b) Physical Fatigue and (c) Bulbar Muscle Weakness. The items are ordered according to their severity (as per the estimation from the initial Rasch model). The dotted lines represent the observed means of overall symptom severity observed in the study for the treatment group at the visit. The coloured bars show the most likely response to the item. RLZ, rozanolixizumab.

the MG Symptoms PRO, supporting the results of change from baseline in MG-ADL, Myasthenia Gravis Composite, and QMG scores [22]. Approximately 70% of MG Symptoms PRO responders were also MG-ADL and QMG responders; however, the reverse analysis was less consistent. The slightly lower MG-ADL/QMG responder rates on Physical Fatigue (57% and 64%, respectively) may reflect the scale's novel concepts of fatigue that are not measured by the MG-ADL or QMG. The lower MG-ADL/QMG responder rates on Bulbar Muscle Weakness (48% and 44%, respectively) may be a result of mild bulbar symptoms at baseline, represented by low baseline mean (SD) scale scores compared with the other scales and infrequent bulbar symptoms experienced pre-treatment (Figure 4c). The Rasch model has been used previously for psychometric evaluation of MG-specific PROs [26–29]; here, we used the model to visualise the experience of symptoms before and after treatment by a typical patient who received rozanolixizumab or placebo in MycarinG. To our knowledge, this type of analysis has not previously been utilized in gMG, with only one example in the literature of a similar graphical representation [30]. The description of

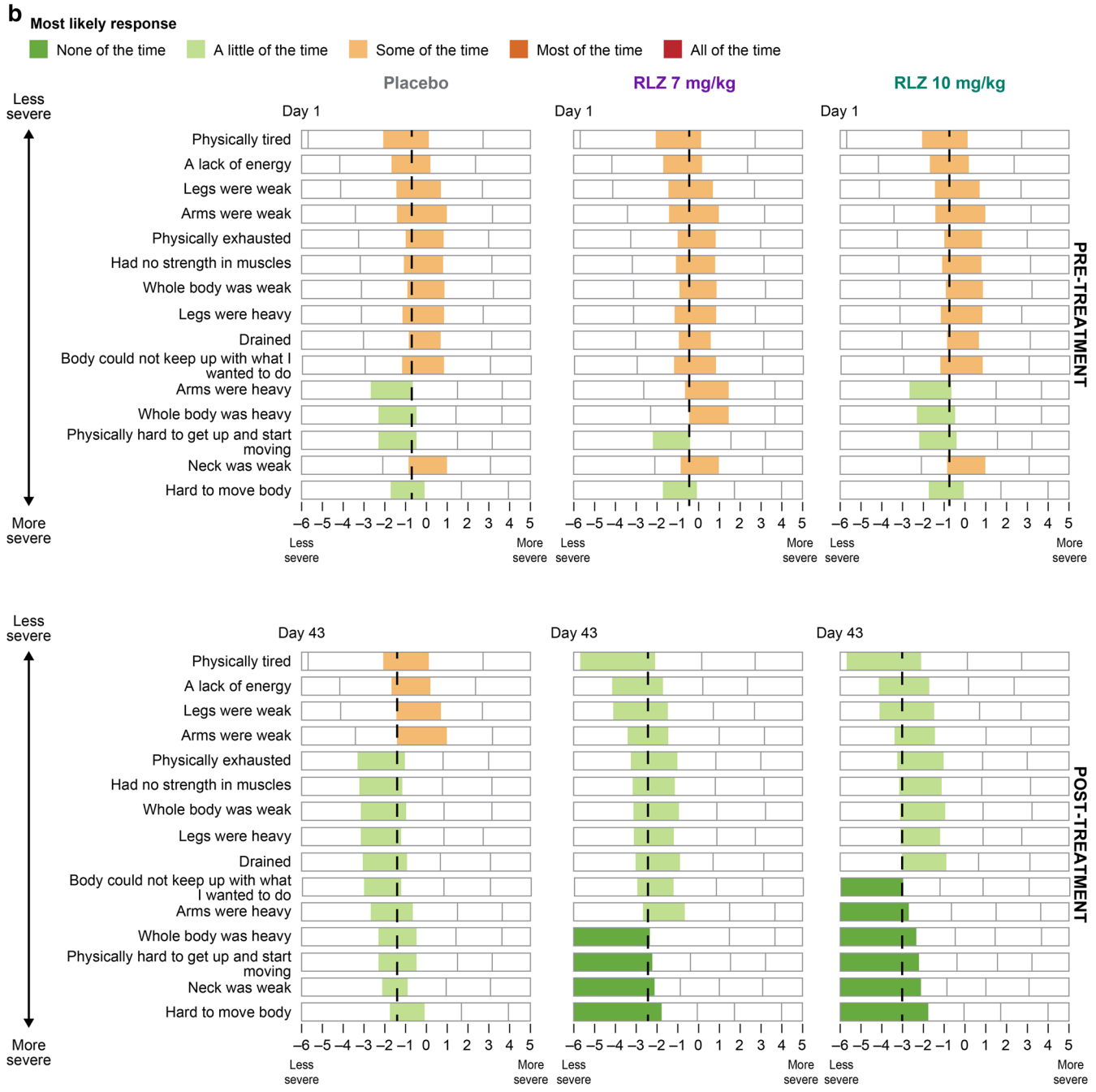


FIGURE 4 | (Continued)

item-level change and the Rasch model analysis for the three MG Symptoms PRO secondary endpoints help to consolidate the demonstration of rozanolixizumab benefit by illustrating improvements in specific symptoms. Patients receiving rozanolixizumab experienced improvements in all individual items, were more likely to no longer experience the more severe symptoms, and would rarely experience the less severe symptoms. Although a typical patient in the placebo group was also likely to experience some symptom improvement, the changes were to a lower extent or in less severe symptoms compared with the rozanolixizumab groups.

Both muscle fatigability (peripheral fatigue) and physical fatigue are experienced by people with gMG, and the two concepts are often confused by patients and treating physicians [31]. The difference between muscle fatigability and physical fatigue in neuromuscular disorders may have a biological basis [2]. Muscle fatigability is defined as a degree of muscle weakness that can fluctuate over time or with activity, with varying severity, and is caused by compromised neuromuscular transmission [2, 5]. Physical fatigue is a persistent feeling of overall exhaustion even after muscle weakness has resolved and may be caused by disordered central nervous system function, concomitant sleep disturbance, psychological factors, or a pathological immune reaction [2, 31, 32]. Confusion in distinguishing between fatigability and fatigue may also account for a relatively high placebo response indicated by the Rasch model analysis in the Muscle Weakness Fatigability and Physical Fatigue scales.

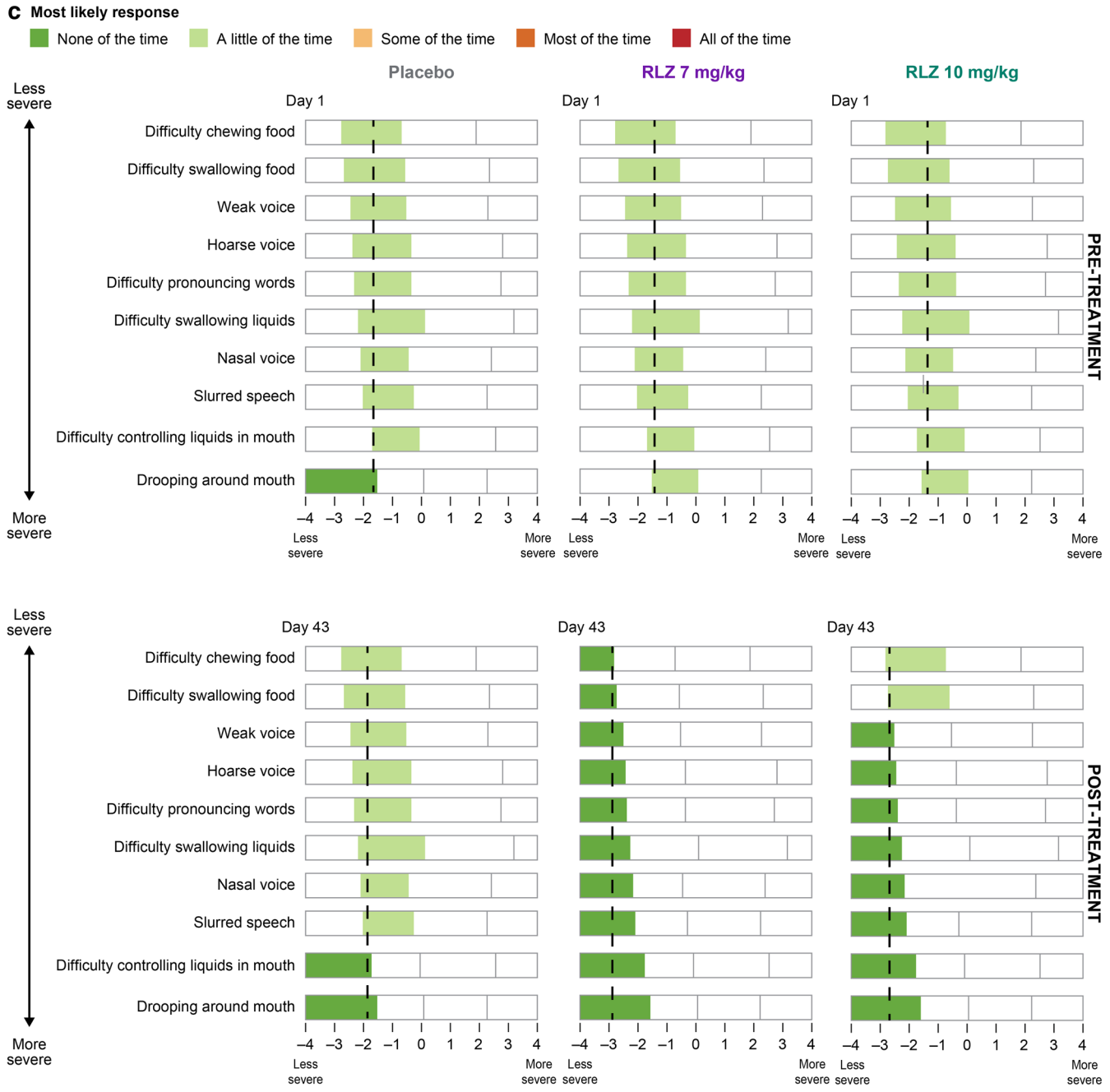


FIGURE 4 | (Continued)

A qualitative study of 28 individuals with gMG reported that the most common goal for symptom management was reduced fatigue or weakness [10], highlighting improvement in fatigue as a treatment goal for patients that may not be adequately considered by physicians. Physical fatigue is not measured by MG-ADL and QMG, and there is a lack of consensus on which scale is most appropriate for evaluating fatigue in gMG [5]. The Quality of Life in Neurological Disorders (Neuro-QoL) Fatigue scale and its short form have been used in some Phase 3 clinical trials in gMG [12, 33]. This scale was developed as a disease-agnostic PRO, and psychometric evidence has supported its use in several disorders including gMG [6]; however, it is not an MG-specific scale. The MG Symptoms PRO Physical Fatigue scale is specific to gMG and enables physicians to assess and monitor fatigue symptoms more systematically to inform disease management.

The MG Symptoms PRO scales, which can be used individually, provide a more granular assessment of patient-relevant symptoms including physical fatigue and muscle weakness fatigability, to complement existing measures in gMG and help healthcare professionals to monitor outcomes and inform treatment goals regarding fatigue.

Limitations of these analyses include the exclusion of patients with only ocular symptoms (MGFA Disease Class I) or severe weakness affecting oropharyngeal or respiratory muscles (MGFA Disease Class IVb/V) from the MycarinG study, and the absence of responder thresholds for the Respiratory Muscle Weakness and Ocular Muscle Weakness scales. Work is ongoing to explore the adaptation of the MG Symptoms PRO scales for use in clinical practice.

In conclusion, the five independent scales of the MG Symptoms PRO complement existing MG-specific outcome measures by providing a granular and detailed assessment of the breadth of patient-relevant symptoms. The scales encompass the varied symptoms of patients' experiences of gMG and introduce additional concepts that are not considered by existing tools. Data from the MycarinG study showed that patients experienced meaningful improvements following rozanolixizumab treatment in a range of symptoms measured by the MG Symptoms PRO. A description of item-level responses and a novel analysis based on the Rasch model that underpins the scales enrich the interpretation of change in scores observed in the study. Together, these data demonstrate the ability of rozanolixizumab to improve patients' experiences over individual items in the scales. These findings may help facilitate communication about patients' experiences with rozanolixizumab in gMG.

Author Contributions

Henry J. Kaminski: investigation, writing – review and editing. **Carlo Antozzi:** investigation, writing – review and editing. **Ali A. Habib:** investigation, writing – review and editing. **Robert M. Pascuzzi:** investigation, writing – review and editing. **Sabrina Sacconi:** investigation, writing – review and editing. **Kimiaki Utsugisawa:** investigation, writing – review and editing. **John Vissing:** investigation, writing – review and editing. **Antoine Regnault:** methodology, visualisation, writing – review and editing. **Asha Hareendran:** conceptualisation, methodology, supervision, writing – review and editing, writing – original draft. **Fiona Grimson:** formal analysis, data curation, methodology, visualisation, writing – review and editing. **Thaïs Tarancón:** conceptualisation, supervision, methodology, writing – review and editing. **Vera Bril:** conceptualisation, investigation, writing – review and editing.

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Conflicts of Interest

H.J.K. is a Consultant for Cabaletta Bio, Lincoln Therapeutics, Roche, Takeda Pharmaceuticals, and UCB and is CEO and CMO of ARC Biotechnology LLC based on US Patent 8961,98. He is Principal Investigator of the Rare Disease Network for Myasthenia Gravis (MGNet) National Institute of Neurological Disorders & Stroke, U54 NS115054, and Targeted Therapy for Myasthenia Gravis. He has received R41 NS110331-01 to ARC Biotechnology. C.A. has received funding for congress and Institutional Review Board participation from Alexion Pharmaceuticals, argenx, Biogen, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Momenta (now Johnson & Johnson) and UCB. A.A.H. has received research support from Alexion Pharmaceuticals, argenx, Cabaletta Bio, Genentech/Roche, Immunovant, Regeneron Pharmaceuticals, UCB, and Viela Bio (now Amgen). He has received honoraria from Alexion Pharmaceuticals, Alpine Immune Sciences, argenx, Genentech/Roche, Immunovant, Inhibrx, NMD Pharma, Regeneron Pharmaceuticals, and UCB. R.M.P. is Professor Emeritus of Neurology at Indiana University and receives compensation for his professional work from Indiana University Health. He has no financial relationship with any pharmaceutical company and receives no compensation from any pharmaceutical company (present or past). R.M.P. speaks at educational seminars on a broad variety of general neurology topics for primary care physicians through the organisation Medical Education Resources (an educational organisation with no links or ties to any pharmaceutical or healthcare business company). Therefore, R.M.P. has no conflicts of interest related to this research, manuscript, presentation, or publication. S.S. has nothing to disclose. K.U. has served as a paid Consultant for argenx, Chugai Pharmaceutical, HanAll Biopharma, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Merck, Mitsubishi Tanabe Pharma, UCB, and Viela Bio (now Amgen); he has received speaker honoraria from Alexion Pharmaceuticals, argenx, the Japan Blood Products Organisation, and UCB. J.V. has been a Consultant on advisory boards for Amicus Therapeutics, Biogen, Edgewise Therapeutics, Fulcrum Therapeutics, Genethon, Horizon Therapeutics (now Amgen), Lupin, ML Biopharma, Novartis, Regeneron Pharmaceuticals, Roche, Sanofi Genzyme (now Sanofi), Sarepta Therapeutics, and UCB. He has received research, travel support, and/or speaker honoraria from Alexion Pharmaceuticals, argenx, Biogen, Edgewise Therapeutics, Fulcrum Therapeutics, Lupin, Sanofi Genzyme (now Sanofi) and UCB. He is a Principal Investigator in clinical trials for Alexion Pharmaceuticals, argenx, Atamyo Therapeutics, Genethon, Horizon Therapeutics (now Amgen), Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), ML Biopharma, Novartis, Regeneron Pharmaceuticals, Roche, Sanofi Genzyme (now Sanofi) and UCB. A.R. is an employee of Modus Outcomes, a patient-centred outcome research consultancy that received payment from UCB to conduct this research. A.H. is a former employee of UCB. F.G. and T.T. are employees and shareholders of UCB. V.B. is a Consultant for Akcea, Alexion Pharmaceuticals, Alnylam, argenx, CSL, Grifols, Immunovant, Ionis, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Momenta (now Johnson & Johnson), Novo Nordisk, Octapharma, Pfizer, Powell Mansfield, Roche, Sanofi, Takeda Pharmaceuticals, and UCB. She has received research support from Akcea, Alexion Pharmaceuticals, argenx, CSL, Grifols, Immunovant, Ionis, Momenta (now Johnson & Johnson), Octapharma, Takeda Pharmaceuticals, UCB, and Viela Bio (now Amgen).

Data Availability Statement

Underlying data from this manuscript may be requested by qualified researchers 6 months after product approval in the US and/or Europe, or global development is discontinued, and 18 months after trial completion. Investigators may request access to anonymised individual patient-level data and redacted trial documents, which may include analysis-ready datasets, study protocol, annotated case report form, statistical analysis plan, dataset specifications, and clinical study report. Prior to use of the data, proposals need to be approved by an independent review panel at www.vivli.org and a signed data-sharing agreement will need to be executed. All documents are available in English only for a pre-specified time, typically 12 months, on a password-protected portal.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.