

Health-related quality of life in generalised myasthenia gravis: The relationship between Myasthenia Gravis Activities of Daily Living and EQ-5D-5L in the RAISE study

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Objective

- Zilucoplan is a complement component 5 inhibitor in development for the treatment of adults with AChR Ab+ gMG
- Here, we aim to understand the relationship between disease status and HRQoL, as expressed via the EQ-5D-5L instrument using data from RAISE – a Phase 3 study comparing zilucoplan (as an add-on to standard of care) to placebo

Introduction

- gMG is a rare autoimmune disorder that impacts the neuromuscular junction and results in a broad spectrum of symptoms, such as fatigue, limb weakness, difficulty in swallowing and impaired respiration. Symptoms can fluctuate and severity can differ greatly between patients^{1,2}
- Published evidence indicates that gMG patients experience poorer HRQoL than the general population³
- The EQ-5D-5L instrument is a generic preference-based measure where utility weights can be derived using published country value sets. Utility weights are necessary to determine QALYs used in cost-effectiveness analysis
- Limited data are available with respect to the relationship between gMG symptoms (as measured by MG-ADL score) and EQ-5D-5L; therefore, this analysis was conducted using the data collected in RAISE

Methods

- RAISE (NCT04115293) was a randomised, double-blind, placebo-controlled, Phase 3 study that was conducted at 75 sites across Europe, Japan and North America.⁴ Recruitment and randomisation are shown in **Figure 1**
 - The study enrolled patients (aged 18–74 years) with AChR Ab+ gMG (MGFA Disease Class II–IV), an MG-ADL score of at least 6 and a QMG score of at least 12
 - Participants were randomly assigned (1:1) to receive subcutaneous zilucoplan 0.3 mg/kg once daily by self-injection, or matched placebo, for 12 weeks
 - The primary efficacy endpoint was CFB to Week 12 in MG-ADL score in the modified intention-to-treat population (all randomly assigned patients who received at least one dose of the study drug and had at least one post-dosing MG-ADL score)

- The EQ-5D-5L instrument was administered at baseline and at Weeks 1, 2, 4, 8 and 12 to patients in both treatment arms. MG-ADL total scores were available at these timepoints
- Summary descriptive statistics were derived using the van Hout EQ-5D-5L to 3L crosswalk and the UK value set
- An MMRM regression model was fitted to the data to determine the relationship between change in MG-ADL score and utility weights

Results

Patients

- Patient demographics and baseline disease characteristics were generally balanced between treatment arms

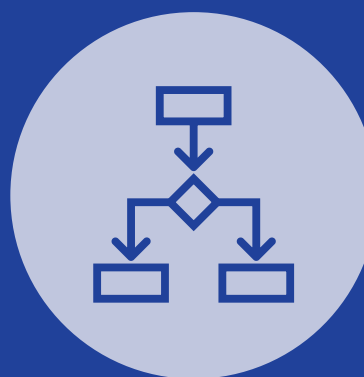
Efficacy

- More patients reported no problems for most dimensions of the EQ-5D-5L in the zilucoplan arm compared to the placebo arm at Week 12 (**Table 1**)
- Patients in the zilucoplan arm achieved a greater mean improvement in utility from baseline than placebo, aligned with greater improvement in disease state severity as measured by MG-ADL and QMG scores (**Table 2**)
- The distribution of MG-ADL score and utility was as expected, with lower MG-ADL scores (lower disease burden) leading to higher utility values (**Figure 2**)
- The MMRM model (**Table 3**) was fitted using MG-ADL total score, baseline utility, and included BMI as an additional statistically significant variable (**Figure 3**). Treatment allocation was found to be not statistically significant
- The model estimated that a 1-point change in baseline MG-ADL score equated to an approximately 0.02 change from baseline in utility score. Similar results were seen when using QMG score as the gMG-related variable
- The HRQoL impact of better MG-ADL score response was confirmed when considering MSE (an MG-ADL score of 0 or 1) with a mean utility score of 0.85 in patients who achieved MSE at Week 12 versus 0.60 in patients who did not achieve MSE at Week 12

Summary and conclusions



The analysis confirmed that improvements in disease status, as measured by MG-ADL score, led to utility improvements and, therefore, QALY gains in patients with gMG



Utility score changes were driven by change in MG-ADL score, not by treatment arm



Patients achieving a high-level response, defined as an MG-ADL score of 0 or 1, had a better utility outcome, demonstrating the value of aiming for low disease activity treatment goals for patients with gMG

Figure 1 RAISE study design

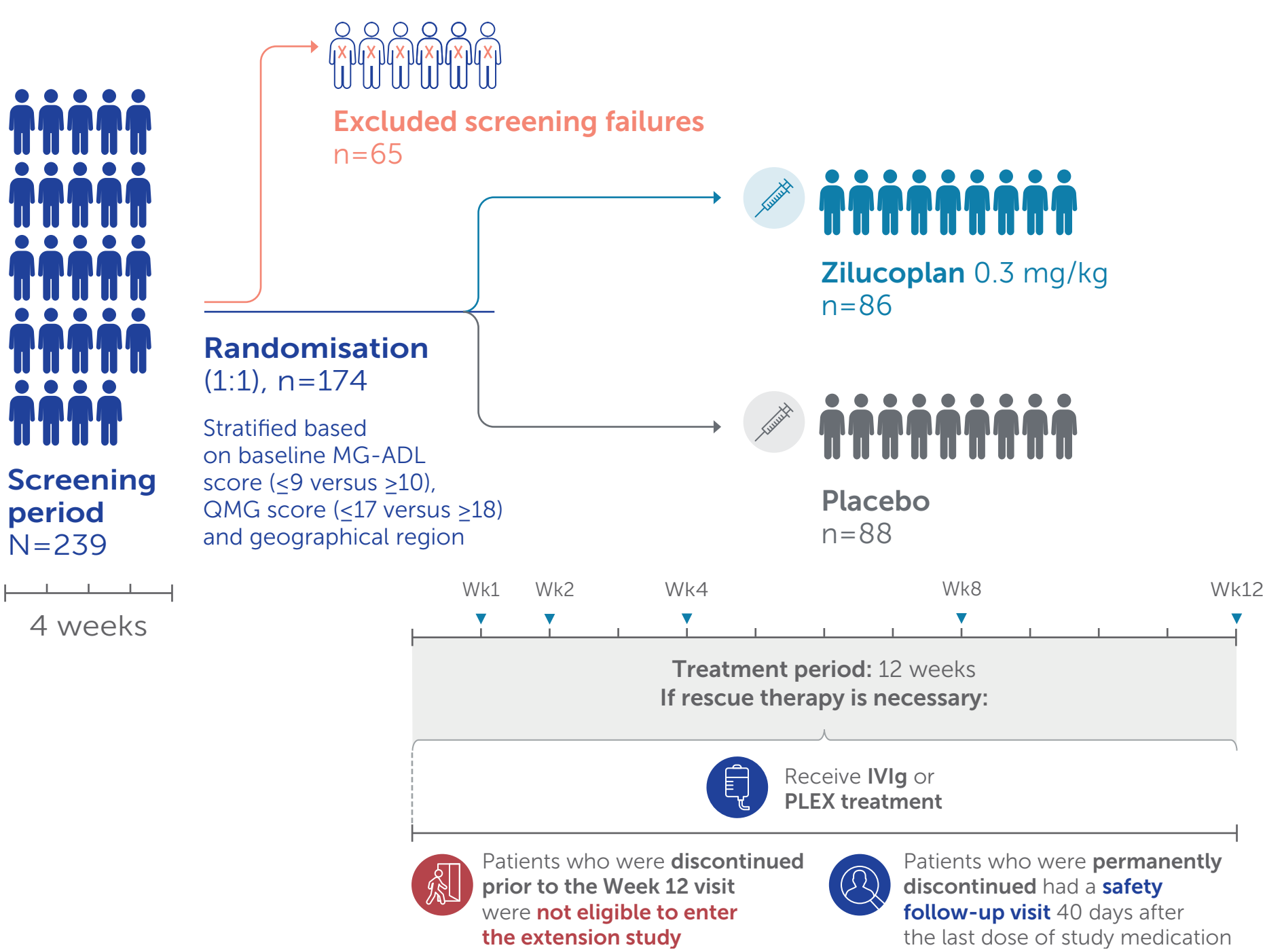


Table 1 Percentage of patients reporting no problems in the EQ-5D-5L at Week 12

	Zilucoplan 0.3 mg/kg (n=86)	Placebo (n=88)
Mobility	36.6	32.5
Self-care	50.0	42.2
Usual activities	30.5	19.3
Pain/discomfort	35.4	36.1
Anxiety/depression	47.6	37.3

Figure 2 Distribution of MG-ADL total score and utility value

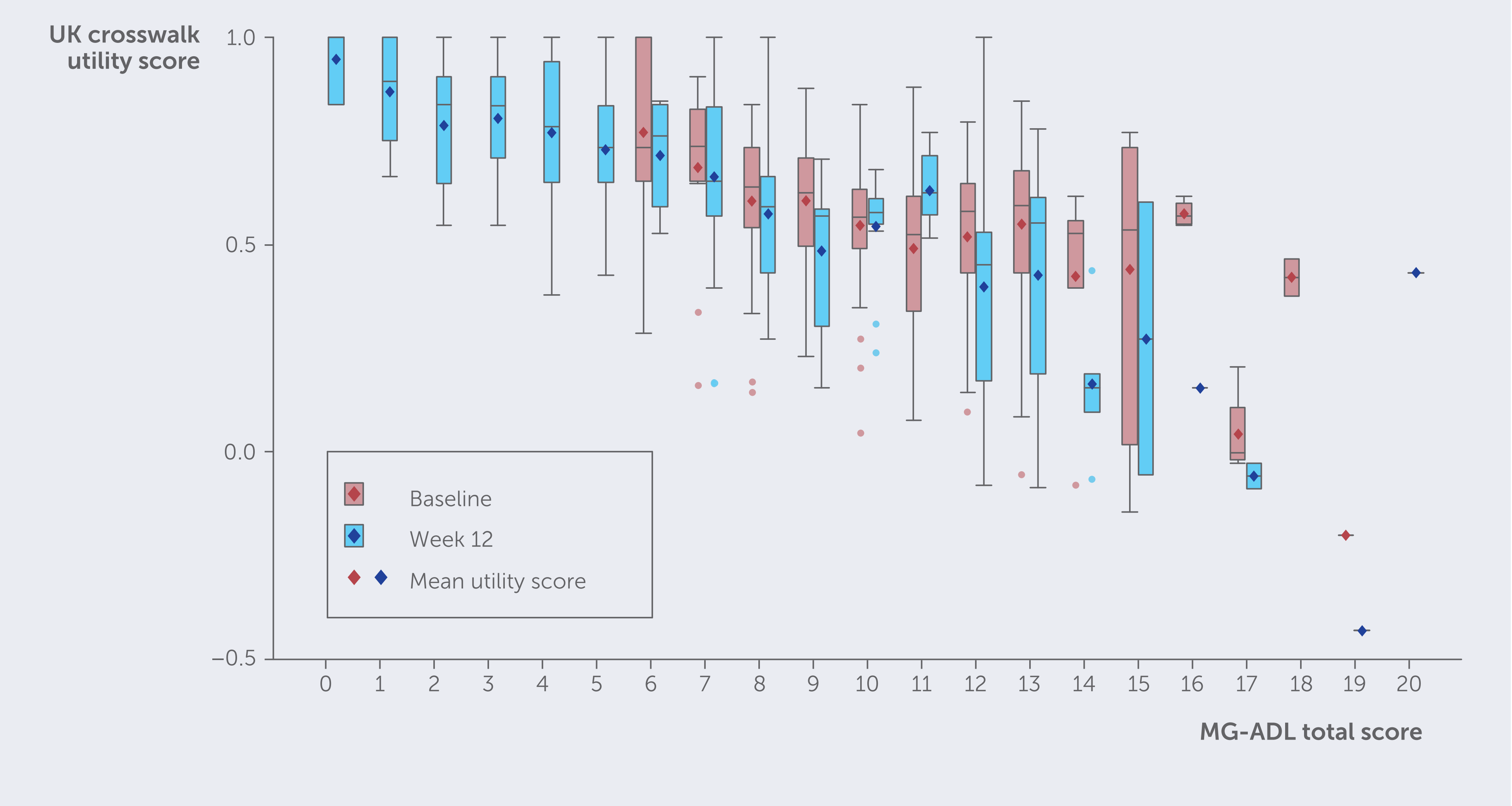
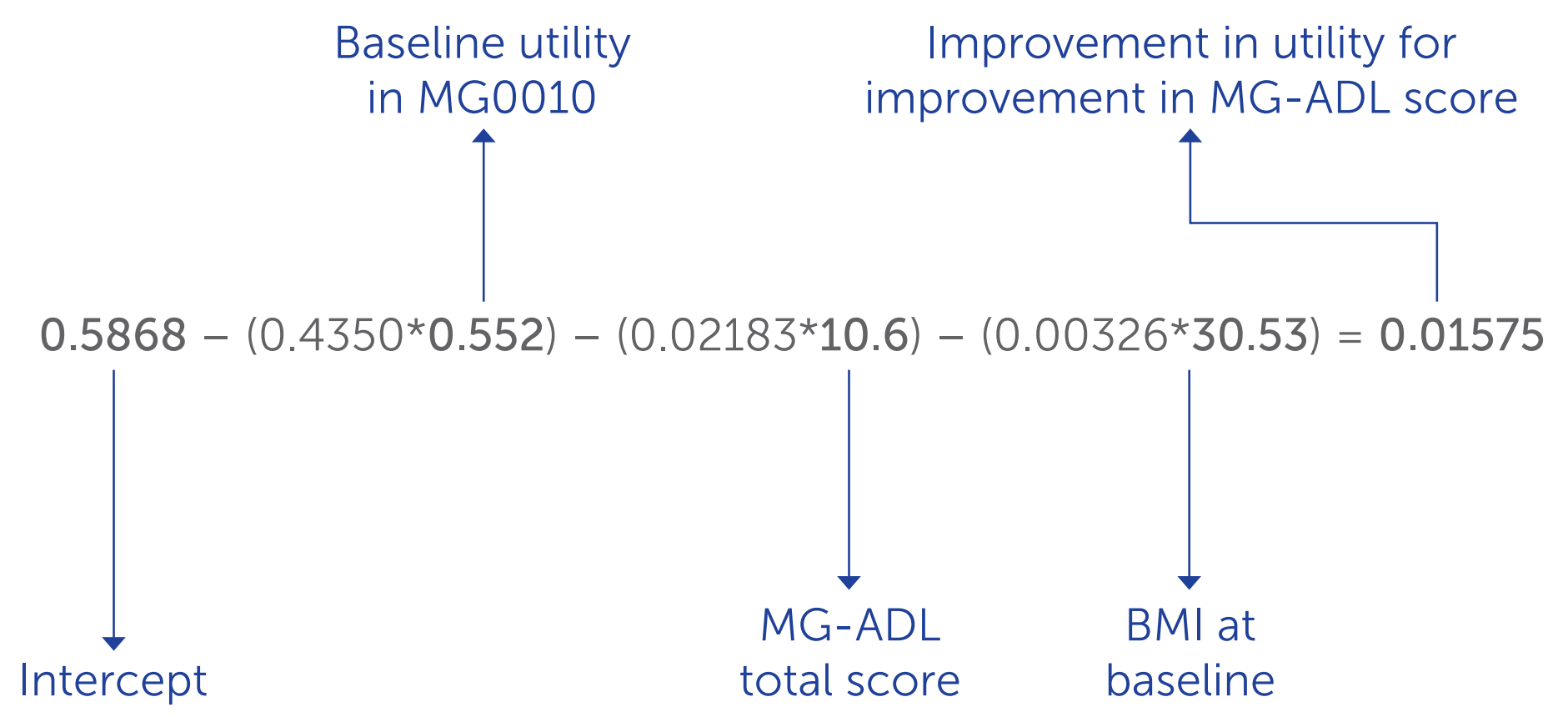


Table 2 Improvement in utility at Week 12

		Mean utility	Mean MG-ADL score	Mean QMG score
Placebo	Baseline	0.536	10.9	19.4
	Week 12	0.609	8.16	16.0
	Mean CFB	0.078	2.74	3.40
Zilucoplan 0.3 mg/kg	Baseline	0.569	10.4	18.8
	Week 12	0.663	5.63	12.2
	Mean CFB	0.104	4.77	6.60

Figure 3 Estimated MMRM model



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Abbreviations: AChR Ab+, positive for autoantibodies against the acetylcholine receptor; BMI, body mass index; CFB, change from baseline; gMG, generalised myasthenia gravis; HRQoL, health-related quality of life; IVg, intravenous immunoglobulin; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MMRM, mixed model for repeated measures; MSE, minimal symptom expression; PLEX, plasma exchange; QALY, quality-adjusted life year; QMG, Quantitative Myasthenia Gravis; SE, standard error; Wk, week.
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