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Post-hoc analyses from the ADAPT clinical study demonstrate aggregate sustained benefit of Efgartigimod in generalized myasthenia gravis

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ABSTRACT

Objectives: This post-hoc analysis evaluates the long-term efficacy of efgartigimod versus placebo in adult patients with generalized myasthenia gravis (gMG) with acetylcholine-receptor autoantibodies (AChR-Ab+), based on data from the ADAPT RCT and its open-label extension ADAPT+.

Methods: Changes from baseline in Quantitative Myasthenia Gravis (QMG) and Myasthenia Gravis-Activities of Daily Living (MG-ADL) scores were assessed by treatment group over the ADAPT (up to 20 weeks) and ADAPT+ time horizon (extended to 64 weeks for efgartigimod group patients). Response to treatment was defined as 5-point reduction in QMG or 3-point reduction in MG-ADL vs. baseline values.

Results: AChR-Ab+ patients treated with efgartigimod spent a substantially greater percentage of time in response in ADAPT based on at least a 5-point change in QMG compared to the placebo group (44 % versus 13 % respectively, $p = 0.0034$). Analyses based on a 3-point change in MG-ADL in ADAPT showed the percentage of time in response was nearly double for efgartigimod versus placebo (59 % versus 30 % respectively, $p = 0.010$). These trends were also maintained using different response definitions, as well as in patients with and without prior immune therapy exposure and by time from diagnosis (<7 years versus ≥7 years).

Conclusions: The clinical benefit of efgartigimod was sustained over repeat treatment cycles and maintained over the long term. Response to treatment was consistent regardless of response definition and was repeated in different patient subgroups. Overall, the results of this analysis indicate that efgartigimod is an effective therapeutic option, demonstrating a robust benefit among AChR-Ab+ patients with gMG.

1. Introduction

Generalized myasthenia gravis (gMG) is a rare, chronic, autoimmune disorder which causes debilitating muscle weakness. Prevalence estimates indicate gMG affects as many as 60,000 Americans and 103,000 people in the European Union (EU) [1,2]. The majority of gMG patients have antibodies against the acetylcholine receptor, which interfere with neuromuscular transmission. Acetylcholine receptor anti-body positive (AChR-Ab+) gMG accounts for up to 85 % of all patients affected [3]. Disease symptoms associated with gMG include exertional muscle fatigue and weakness, eyelid droop and double vision, difficulties swallowing/chewing, and breathing dysfunction, with up to 20 % of patients experiencing a life-threatening myasthenic crisis over their lifetime [4]. Generalized myasthenia gravis is consequently associated with a high economic burden and important reductions in patient health related quality of life (HRQoL) [5].

Conventional therapies for gMG include acetylcholinesterase inhibitors, as well as other broad acting immunotherapies such as corticosteroids and non-steroidal immunosuppressive therapies (NSISTs) [6]. The therapeutic benefit associated with such conventional therapies may be limited, can have a delay in clinical benefit, and may be associated with side-effects including infections, glucose intolerance, weight gain, arterial hypertension, osteoporosis, gastrointestinal issues, bradycardia and renal dysfunction. There consequently remains a

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significant unmet need for alternative treatments in gMG that are effective, rapidly acting and well tolerated [7]. Emerging, novel, biologic therapies offer a more targeted approach aimed to address the unmet needs of gMG patients [7–9]. Efgartigimod is a novel, first-in-class treatment, designed to target the Fc receptor (FcRn) and is being evaluated for patients with a wide range of autoimmune diseases with confirmed presence of pathogenic immunoglobulin G autoantibodies. Efgartigimod has recently been approved for the treatment of gMG in the US, Japan and Europe following the positive results from the ADAPT clinical trial (clinicaltrials.gov: NCT03669688) [10,11].

ADAPT was a multi-center, double-blind, randomized controlled trial assessing efgartigimod versus placebo in adult patients with gMG. All patients were required to be on a stable dose of at least one conventional therapy (i.e., acetylcholinesterase inhibitors, corticosteroids, or NSISTs). Efgartigimod (10 mg/kg IV) or matching placebo were administered in cycles of 4 weekly infusions, with subsequent cycles initiated according to clinical evaluation or at relapsing of previously improved symptoms. Patients received their randomized treatment in ADAPT for a maximum of 26 weeks and were eligible to continue efgartigimod treatment in ADAPT+ (NCT03770403) [12]. ADAPT+ was a single-arm, open-label follow-up study, designed to assess the long-term safety and tolerability of efgartigimod. The initial results for ADAPT and ADAPT+ are reported elsewhere [11,12].

Clinical evidence from ADAPT and ADAPT+ have demonstrated that efgartigimod provides rapid, consistent, and repeatable improvements for gMG patients during each treatment cycle (up to 17 cycles). This post-hoc analysis differs from the main ADAPT+ publication [11], in which the treatment cycle results were superimposed, whereas this work explores the efficacy of efgartigimod longitudinally, across repeated treatment cycles and cumulating ADAPT and ADAPT+ follow-up time up to 64 weeks. Furthermore, whilst the ADAPT+ publication [11] mainly focused on safety and tolerability, this analysis evaluates whether a sustained, clinically meaningful, and long-term response can be observed in efgartigimod-treated patients. It is anticipated that the results from this study will enhance the evidence base available for health care decision makers in gMG.

2. Methods

2.1. Standard Protocol Approvals, Registrations, and Patient Consents

This retrospective analysis uses pooled data from the randomized controlled trial ADAPT (clinicaltrials.gov: NCT03669688) and its open-label extension study ADAPT+ (clinicaltrials.gov: NCT03770403) [11,12]. Before enrolling patients, independent international review boards and ethics committees provided written approval for the study protocol, protocol amendments, final approved informed consent documentation, relevant supporting information, and patient recruitment information. All patients provided written informed consent before starting the study. The trial was conducted according to the principles outlined in the Declaration of Helsinki.

2.2. Population and setting

The population evaluated in this study represents AChR-Ab+ population consistent with the ADAPT primary endpoint population. Additional analyses have been conducted in subgroups characterized by prior immune therapy exposure and by time from diagnosis. Prior immune therapy exposure has been defined as patients who have been previously treated with two or more immunosuppressive therapies, or at least one immunosuppressive therapy with IV immunoglobulins (IVIg) or plasma exchange given at least four times per year for 12 months without symptom control. This definition is similar to the definition used to describe a refractory population in a previous Phase III study in gMG[12]. Subgroup populations by time from diagnosis have been presented for patients diagnosed with gMG for less than 7 years versus 7 years or greater, with 7 years being the median time since diagnosis in this sample.

2.3. Response Definition

In ADAPT, the key primary and secondary measures used to evaluate clinical efficacy were based on the Myasthenia Gravis-Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) instruments respectively [13,14]. The MG-ADL is a patient-reported outcome scale designed to assess MG symptoms based on eight items (rated between 0 and 3, total maximum score: 24). The QMG is a physician captured strength scale, which consists of 13 bodily functions (rated between 0 and 3, total maximum score: 39).

In ADAPT, a response to treatment was defined as a $\geq$ 2-point reduction in the total MG-ADL score compared to the baseline for at least four consecutive weeks during the first treatment cycle (i.e., by Week 8). The improvement was additionally required to begin within one week of their last infusion [7]. For this analysis, the primary trial response definition could not be incorporated because the response was evaluated across treatment cycles without consecutive measures at all time points. In contrast, a response to treatment has been defined as an improvement in QMG total score by at least 5 points, or MG-ADL total score by at least 3 points at any time point, compared to the baseline value. This alternative definition generated similar response rates in cycle 1 for both the efgartigimod and placebo arms as the primary trial response definition (Table 1). Sensitivity analysis have also been presented to explore the impact of using the published and validated minimal clinically important difference (MCID) for MG-ADL (2-point change) and QMG (3-point change) [13,15,16].

2.4. Timing of assessments, data availability and treatment group definition

In ADAPT, patients were allowed to roll over to ADAPT+ from week 18 onwards and the remaining patient numbers in ADAPT reduced rapidly after that. In ADAPT+ each cycle of efgartigimod administration started with 4 weekly assessments, which were followed by monthly assessments until the next treatment cycle began. The timing of the

Table 1
Response to MG-ADL and QMG in the ADAPT Phase 3 trial.

Proportion of patients responding to treatment based on the following response definitions:	Efgartigimod group $n = 65$	Placebo group $n = 64$
MG-ADL $\geq$2 point reduction from baseline at week 4	77.8 %	48.3 %
MG-ADL $\geq$3 point reduction from baseline at week 4	73.0 %	36.7 %
MG-ADL responder definition in cycle 1 from ADAPT	67.7 %	29.7 %
QMG $\geq$3 point reduction from baseline at week 4	74.2 %	25.9 %
QMG $\geq$5 point reduction from baseline at week 4	59.7 %	12.1 %
QMG responder definition in cycle 1 from ADAPT	63.1 %	14.1 %

Footnotes: n number of participants for whom the observation was reported, MG-ADL Myasthenia Gravis Activities of Daily Living, QMG Quantitative Myasthenia Gravis. Ranges for the clinical outcome assessments are as follows: MG-ADL total score 0 to 24, QMG score 0 to 39.

treatment administration in ADAPT+ was individualized based on clinical evaluation, hence, patients' QMG and MG-ADL assessments were not synchronized across the trial period.

The response data for the randomized placebo arm in ADAPT were calculated based on ADAPT data only, using all available measurements between week 1 and week 20 ("placebo group"). After this timepoint most placebo patients rolled over to ADAPT+ and subsequently received efgartigimod treatment, therefore no data from ADAPT+ was used for the placebo group calculations. The response calculations for the randomized efgartigimod arm in ADAPT were performed combining longitudinal data starting in ADAPT for up to 26 weeks and following these patients in ADAPT+ up to 64 weeks from the ADAPT baseline ("efgartigimod group"). After that time point, whilst more than half of the subjects were still followed-up in the ADAPT+ study, the number of available QMG and MG-ADL assessments per week became too low to draw robust conclusions (<20 patients). This data selection allowed us to maintain the randomized comparison between treatment groups, and to explore the relative efficacy using more mature data for the efgartigimod group, whilst still presenting comparative data at 20 weeks also, based on ADAPT only. See supplemental materials for detailed methodology description.

3. Calculation

3.1. Statistical Analyses

The average **percentage of time** that a patient responded to treatment (according to QMG or the MG-ADL endpoints separately) was calculated as the number of weeks that the patient had a 5-point reduction in QMG or a 3-point reduction in MG-ADL between baseline and each time point, divided by his/her total number of available assessments up to that time point. This was then averaged across all patients in each group. The **percentage of patients** responding to treatment was calculated as the number of responders at each week, divided by the number of patients still in the study at each week. This was then averaged across the applicable time horizons.

Comparative analyses were performed between the efgartigimod and placebo groups using data up to week 20 based on ADAPT trial data only. The difference in the proportion of time in response between baseline and 20 weeks was tested using a regression model, with a beta distribution and a logit link function (using the Glimmix procedure) [17]. Statistical differences in the percentage of patients responding at week 20 between the two treatment groups (the ADAPT trial period) were tested using a generalized estimating equation (GEE), to take the repeated nature of the data into account. The GEE used a binomial distribution, logit link function, an auto-regressive variance-covariance matrix, and included time, treatment and an interaction between time and treatment as independent variables. All analyses were conducted in SAS™ version 9.4.

4. Results

4.1. Study Characteristics

In total, 167 patients were randomized in ADAPT, of these 77 % were AChR-Ab+. The baseline characteristics of AChR-Ab+ patients in the ADAPT study were similar between treatment groups; most patients were female, aged between 44 and 49 years. In total, over 60 % of patients had prior immune therapy exposure at study baseline. The mean time to diagnosis was 9.7 years in the efgartigimod group and 8.9 years in the placebo group, see Table 2 and more details in the original ADAPT publication [11]. Patients followed an individualized dosing schedule; the details on cycle utilization were provided in the ADAPT+ manuscript [12]. The subgroup of patients who rolled over to ADAPT+ had similar characteristics as patients at the start of ADAPT, and patients who stayed in the study for 64 weeks also did not differ on any of the observed baseline characteristics (Table 2). The disposition of AChR-Ab+ patients receiving efgartigimod treatment across the ADAPT and ADAPT+ studies up to week 64 from baseline is displayed in Supplementary Fig. S1.

4.2. Percentage of Time in Response

The evolution of the average percentage of time that patients had a 5-point reduction in QMG for the efgartigimod and placebo groups between baseline and the end of the observation period is shown in Fig. 1. The efgartigimod group spent a substantially greater percentage of time in response across all observed treatment cycles during the ADAPT study (44 % vs. 13 % of the time for efgartigimod vs. placebo groups between 0 and 20 weeks, Table 3). The percentage of time spent in response in the first 20 weeks was 2.37 times greater (95 % CI 1.49, 3.78) for the efgartigimod group ($p = 0.0034$ from beta regression model). Extending the analysis period for efgartigimod to 64 weeks (by incorporating both ADAPT and ADAPT+ data) demonstrated that this effect was sustained in the long-term, with 56 % of the time spent in response (Fig. 1, Table 3).

Analyses based on the MG-ADL response criterion (3-point change in MG-ADL) also showed a substantially greater percentage of time in response for the efgartigimod group compared to the placebo group across all time points within the ADAPT trial period (59 % vs. 30 % of the time for the efgartigimod vs. the placebo group between weeks 0–20, Table 3). Overall, the percentage of time in response during the ADAPT study (first 20 weeks) was 1.68 times greater for the efgartigimod group versus placebo group (95 % CI 1.13, 2.48, $p = 0.010$), based on the beta

Table 2
Baseline characteristics of AChR-Ab+ patients in the ADAPT Phase 3 trial.

ADAPT studies	ADAPT baseline		ADAPT + baseline		ADAPT + at week 64	
	Efgartigimod group n = 65	Placebo group n = 64	Efgartigimod group *n* = 61	Placebo group	Efgartigimod group *n* = 51	Placebo group
Age, years (SD)	44.7 (15.0)	49.2 (15.5)	44.6 (15.3)	n/a	44.5 (15.0)	n/a
Female, n (%)	46 (70.8 %)	40 (62.5 %)	42 (68.9 %)	n/a	34 (66.7 %)	n/a
Time since gMG diagnosis, years (SD)	9.68 (8.3)	8.93 (8.2)	9.59 (8.3)	n/a	9.76 (8.2)	n/a
Prior immune therapy exposure n (%)	40 (62 %)	41 (64 %)	48 (62.3 %)	n/a	31 (60.8 %)	n/a
QMG mean score at baseline (SD)	16.0 (5.1)	15.8 (4.6)	16.0 (5.3)	n/a	15.9 (5.5)	n/a
MG-ADL mean score at baseline (SD)	9.0 (2.5)	8.5 (2.0)	9.0 (2.6)	n/a	8.8 (2.6)	n/a

Footnotes: n number of participants for whom the observation was reported, SD standard deviation, AChR-Ab+ acetylcholine receptor antibody–positive, gMG generalized myasthenia gravis, MG-ADL Myasthenia Gravis Activities of Daily Living, QMG Quantitative Myasthenia Gravis. Ranges for the clinical outcome assessments are as follows: MG-ADL total score 0 to 24, QMG score 0 to 39.
More information can be found in Howard JF, Jr., et al. Safety, efficacy, and tolerability of efgartigimod in patients with generalized myasthenia gravis (ADAPT): a multicenter, randomized, placebo-controlled, phase 3 trial. Lancet Neurol. 2021;20(7):526–536. https://doi.org/10.1016/S1474-4422(21)00159-9. Erratum in: Lancet Neurol. 2021;20(8):e5. PMID: 34146511.

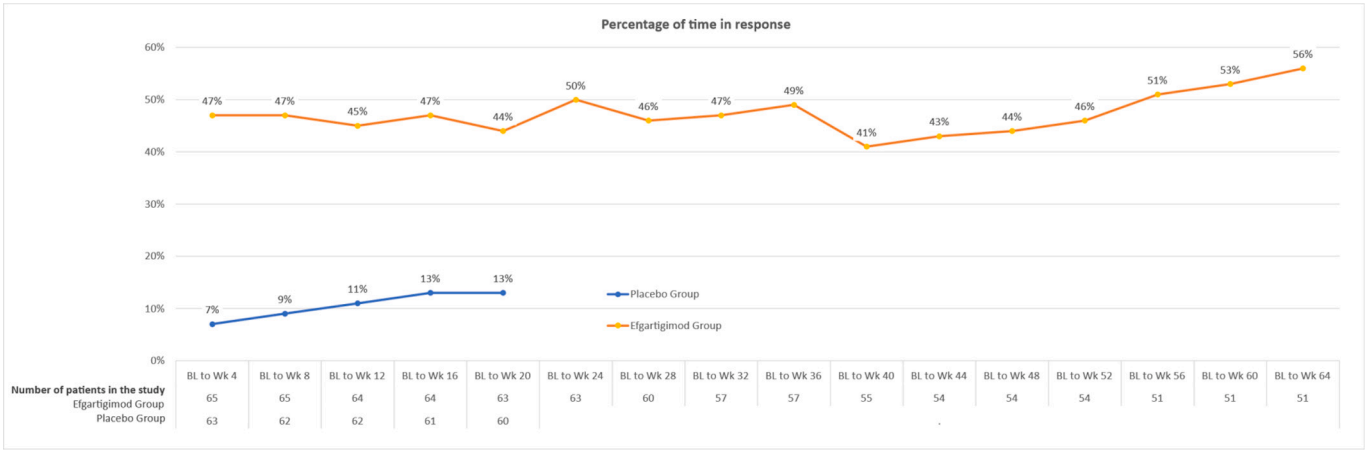

Fig. 1. Cumulative percentage of time in response in the AChR-Ab+ population, with response defined as a 5-point change in QMG.
Footnotes: AChR-Ab+ acetylcholine receptor antibody–positive, QMG Quantitative Myasthenia Gravis.

Table 3
Impact of AChR+ patient subgroups and response definition on results.

Population	% Time in response			% Patients responding		
	Placebo Group	Efgartigimod Group		Placebo Group	Efgartigimod Group	
Average over the time horizon	Week 0 to 20	Week 0 to 20	Week 0 to 64	Week 0 to 20	Week 0 to 20	Week 0 to 64
5-point change in QMG						
AChR+	13%	44%	56%	13%	43%	47%
With prior immune therapy exposure	13%	42%	58%	14%	42%	49%
No prior immune therapy exposure	11%	48%	53%	12%	46%	45%
Disease duration <7 years	14%	51%	60%	10%	51%	51%
Disease duration >=7 years	11%	37%	51%	16%	36%	43%
3-point change in MG-ADL						
AChR+	30%	59%	57%	29%	55%	57%
With prior immune therapy exposure	32%	60%	56%	31%	56%	58%
No prior immune therapy exposure	28%	57%	58%	25%	52%	55%
Disease duration <7 years	33%	63%	61%	33%	62%	65%
Disease duration >=7 years	28%	55%	52%	26%	48%	49%

Footnote: AChR-Ab+ acetylcholine receptor antibody–positive, gMG generalized myasthenia gravis, MG-ADL Myasthenia Gravis Activities of Daily Living, QMG Quantitative Myasthenia Gravis.

regression model. When adding the ADAPT+ period and extending the time horizon to 64 weeks for efgartigimod, results demonstrate that the effect is sustained over time (57 % of the time, Fig. 2).

4.3. Percentage of Patients Responding

The percentage of patients responding to treatment based on a 5-point change in QMG remained consistently higher in the efgartigimod group than in the placebo group over time, see Fig. 3 and Table 3. During the ADAPT period, the average percentage of patients responding to treatment was 43 % for the efgartigimod group versus 13 % for the placebo group. The odds ratio for responding to treatment for the efgartigimod group compared to the placebo group at week 20 was 2.92 (95 % CI: 2.04, 4.18, $p < 0.0001$) based on the GEE model. Long-term evaluation of the change from baseline QMG scores for efgartigimod patients show that QMG response was sustained for the observed 64 weeks (47 %) incorporating data from both ADAPT and ADAPT+.

A consistently greater percentage of AChR-Ab+ patients responded to efgartigimod compared to placebo in the ADAPT period based on a 3-point change in MG-ADL, see Fig. 4. The average percentage of AChR-Ab+ patients responding was significantly higher for the efgartigimod group compared to the placebo group during the first 20 weeks in the ADAPT trial (55 % versus 29 % respectively, Table 3). Based on the GEE model, the odds ratio for responding to treatment at week 20 was estimated to be 2.90 (95 % CI 2.17, 3.87, $p < 0.0001$). Up to week 64, the percentage of patients responding in the efgartigimod group was 57 %, demonstrating sustained benefit (Fig. 4).

4.4. Sensitivity Analysis: Definition of Response

The results for AChR-Ab+ patients were comparable when lower thresholds for response were used. Efgartigimod group patients spent 59 % (week 0–20) and 62 % (week 0–64) of the time in response based on the QMG 3-point change endpoint, compared to 31 % of the time in response for placebo group patients (week 0–20). Additionally, efgartigimod group patients spent 67 % of the time between week 0–20 and 67 % between week 0–64 in response for the 2-point change in MG-ADL, compared to 45 % of time in response for placebo group patients between week 0–20 (Supplemental Material Figs. S2 and S3).

4.5. Other Key Populations

The efgartigimod group showed a consistent and substantial treatment benefit versus the placebo group in the subgroups with versus without prior immune therapy exposure and according to different times from diagnosis (<7 years versus ≥7 years), see Table 3. In all analyses approximately 50 % of patients responded to efgartigimod treatment at any point in time (approximately 45 % with the QMG 5-point change

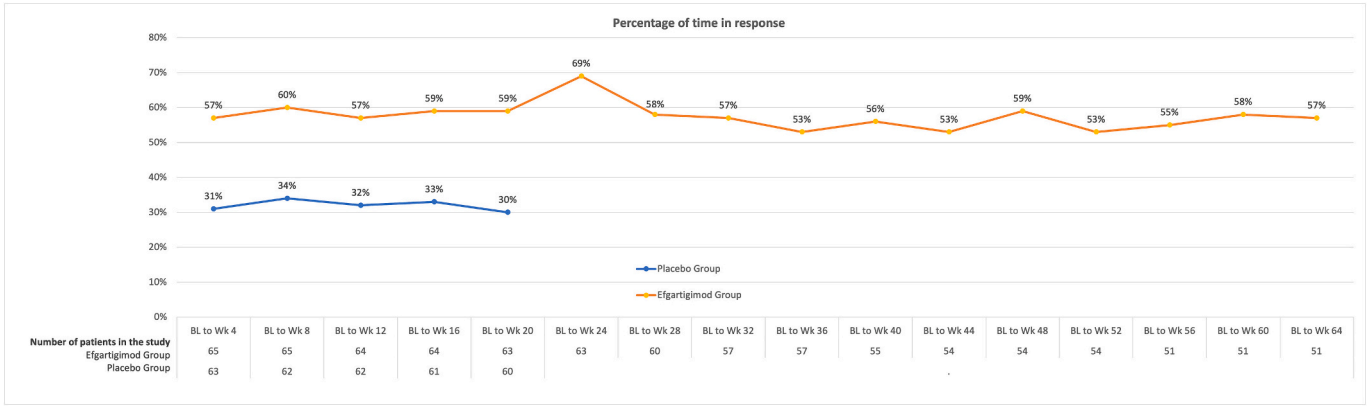

Fig. 2. Cumulative percentage of time in response in the AChR-Ab+ population, with response defined as a 3-point change in MG-ADL.
Footnotes: AChR-Ab+ acetylcholine receptor antibody–positive, MG-ADL Myasthenia Gravis Activities of Daily Living.

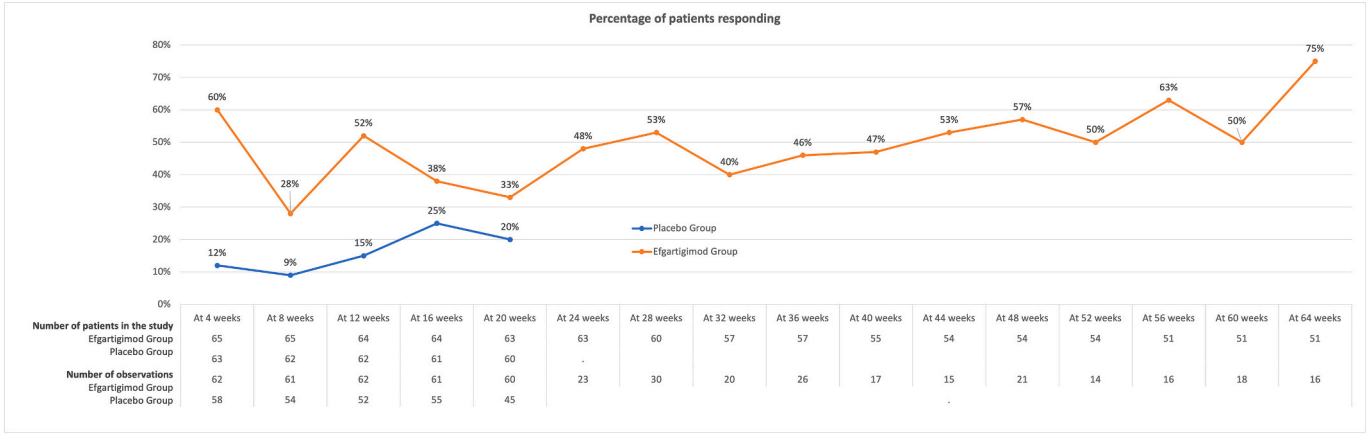

Fig. 3. Percentage of patients responding to treatment in the AChR-Ab+ population, with response defined as a 5-point change in QMG.
Footnotes: AChR-Ab+ acetylcholine receptor antibody–positive, QMG Quantitative Myasthenia Gravis.

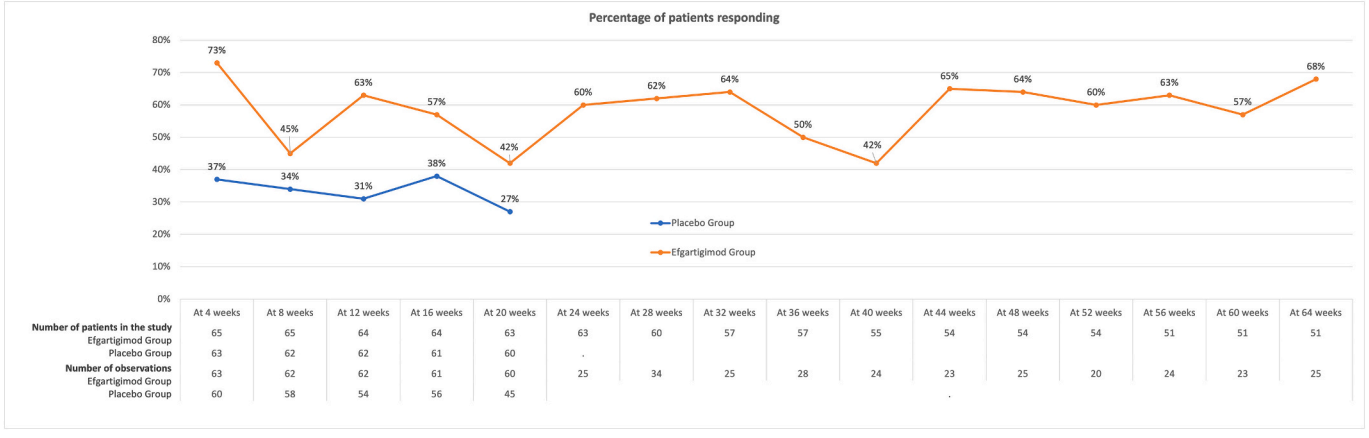

Fig. 4. Percentage of patients responding in the AChR-Ab+ population, with response defined as a 3-point change in MG-ADL.
Footnotes: AChR-Ab+ acetylcholine receptor antibody–positive, MG-ADL Myasthenia Gravis Activities of Daily Living.

endpoint, and approximately 55 % for the MG-ADL 3-point change endpoint).

5. Discussion

In this study we have firstly evaluated whether a significantly greater percentage of efgartigimod treated patients responded to treatment compared to placebo group patients over repeat cycles of therapy, and secondly whether the efgartigimod treatment benefit observed in ADAPT was sustained over the long-term.

The results of our analysis showed that the average percentage of AChR-Ab+ patients that responded to treatment, based on ≥5-point improvement in the QMG score, was three times higher for efgartigimod versus placebo during the first 20 weeks of treatment, and that this result was maintained in the long term over repeat cycles of therapy. Results were similar regardless of the calculation method (proportion of patients responding to treatment or time in response). Trends in results were also similar regardless of the response endpoint used (QMG or MG-ADL). The percentage of patients who responded to treatment and the proportion of time in response were both almost double based on ≥3-point improvement in the MG-ADL score.

In general, higher response rates were observed for the MG-ADL 3-point change endpoint in comparison to the QMG 5-point change endpoint, see Table 3. The high response for the MG-ADL outcome is consistent with trials of other gMG therapies [18–22]. Instruments based on patient reported outcomes, such as the MG-ADL, are often subject to greater variability and data may consequently be noisy in comparison to the QMG endpoint, which is an objective measure based on clinician assessment. The favorable relative results based on clinician assessed QMG score for the efgartigimod group compared to the placebo group is consequently particularly noteworthy.

We have defined response as at least a 5-point reduction in the QMG score or at least a 3-point reduction in the MG-ADL score. The ADAPT trial response definition could not be implemented with this analysis because the response was evaluated across treatment cycles with different measurement schedules. The definitions were consistent with two other key Phase III studies of novel therapies in AChR-Ab+ patients [7,23]. Our sensitivity analyses based on ≥3-point reduction in QMG and ≥ 2-point reduction in MG-ADL show similar trends in results to the base case analysis.

We also examined two calculation methods for the time that patients were responding to treatment: the first calculation method was expressed on a per-patient basis (the percentage of time that a patient was responding to treatment), which is a useful outcome for clinicians making decisions for individual patients. The second calculation method was population-based (the percentage of patients responding), which is more relevant for payers who are assessing treatments for entire patient groups. The strength of the analysis is that consistent results were obtained, regardless of the unit of analysis (individual patient or patient population.

The trend in results was similar for populations with and without prior immune therapy exposure and in patient subgroups with different disease duration, indicating that the efgartigimod treatment effect appears consistent across patient subgroups and that treatment may benefit a broad spectrum of gMG patients with AChR-Ab+. Our study suggests the benefit associated with efgartigimod treatment is maintained across repeat treatment cycles up to 64 weeks, highlighting the durability and sustainability of the efgartigimod response over the long-term.

5.1. Study limitations

It is acknowledged that, as an artifact of the trial design, the proportion of patients responding to treatment fluctuates over time in the ADAPT study. In the ADAPT and ADAPT+ trials, patients were treated with four weekly infusions followed by an observation period during which no investigational or placebo treatment was given. The timing of subsequent cycles was individualized, and each patient received treatment at different time points throughout the study. Patients could only initiate a subsequent treatment cycle if their MG-ADL score, which had previously improved, worsened again to within 2 points of their baseline value. The lack of granular data between cycles means that inter-cycle variations in outcomes could not be analyzed. The strict retreatment criteria in the ADAPT and ADAPT+ studies, as opposed to the more flexible labeled dosing, limit the maximal benefit of administering subsequent cycles of efgartigimod, and was thus likely not captured in this dataset. In a different study, ADAPT-NXT, AChR+ patients received a cyclical treatment regimen like in ADAPT+ but without any retreatment criteria related to worsening of symptoms as in ADAPT, and with only 4 weeks observation in between the 4 efgartigimod infusions. This led to less variation and more stabilized MG-ADL scores over time [24]. In real-world practice, initiation of subsequent cycles is driven by clinical evaluation, allowing for individualized treatment according to patient needs.

An additional limitation to this analysis is the frequency of assessments performed after each cycle. In ADAPT, assessments were performed weekly up to week 8, and then bi-weekly thereafter until the initiation of a subsequent cycle. In contrast, ADAPT+ assessments were performed during the 4 weekly infusion visits of a cycle, and then monthly thereafter, resulting in a suboptimal data capture. Nevertheless, despite the individualized administration and outcome schedules, overall, the proportion of patients responding to treatment on efgartigimod stabilized after 20 weeks of observation.

Another limitation is that the ADAPT studies enrolled a broad MG patient population, without the requirement to have failed any specific gMG treatment, or a requirement regarding disease duration or history of prior thymectomy. The main entry criterium was that patients needed a minimum MG-ADL of 5 (with 50 % of the score from non-ocular symptoms) and needed to be on a stable dose of at least one treatment for MG, to enter the study. Most patients were heavily pre-treated (63 % received prior immune therapy), had active disease (baseline QMG of 16 and MG-ADL around 9), and had extended disease duration (mean time since diagnosis was 9 years). As a result, there was a limited patient sample having shorter diagnosis duration <2 years ($N = 6$) and with mild/moderate disease (MG-ADL 5–7, $N = 16$), and therefore any conclusions for these subgroups need to be treated with caution.

ADAPT+ is ongoing, hence, this study has been based on available data up to 64 weeks, beyond which outcome assessments were too infrequent to permit reliable analysis. The reported estimates may still be subject to change over time as further data becomes available. Furthermore, there are some inherent differences between ADAPT and ADAPT+ which effect we have assumed to be negligible, given that the original randomization from ADAPT was maintained. The exploratory analyses presented in this study should thus be interpreted with the context of these limitations.

6. Conclusion

In summary, this secondary analysis of the combined ADAPT studies provided longitudinal data on the efficacy of efgartigimod in a variety of clinically relevant patient subgroups. A significantly greater percentage of efgartigimod patients responded to treatment compared to placebo

patients over repeated cycles of therapy. Results from our analysis indicate that improvements in strength and function are sustained over time in the gMG population and are consistent regardless of the definition of response, and despite the strict re-treatment criteria applied in the ADAPT studies. Notably, the percentage of time in response is maintained across response calculations (time in response, or percentage of patients responding to treatment) and showed equivalent trends across response definitions (QMG or MG-ADL). Treatment response was also maintained across study populations, by prior treatment failure and by time from initial diagnosis. Overall, the results of this analysis indicate that efgartigimod is an effective therapeutic option, demonstrating robust and sustained benefit in a broad patient population with gMG and AChR-Ab+.

Precis

Post-hoc analyses from the ADAPT clinical study demonstrate an aggregate sustained benefit of efgartigimod in generalized myasthenia gravis.

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Role of the funder/sponsor

The funder commissioned and enabled this study, participated in study design, and provided editorial review of the manuscript. Submission of the manuscript for publication was not contingent upon the approval of argenx.

CRediT authorship contribution statement

Sarah Dewilde: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Alison Griffiths:** Writing – review & editing. **Cynthia Z. Qi:** Writing – review & editing. **Glenn Phillips:** Writing – review & editing. **Deborah Gelinas:** Writing – review & editing. **Edward Brauer:** Writing – review & editing. **Renato Mantegazza:** Writing – review & editing. **James F. Howard :** Writing – review & editing.

Declaration of competing interest

CQ, GP, EB and DG are employees of argenx. SD and AG are employed by Services in Health Economics (SHE). SHE received fees from argenx in relation to this study. James F Howard Jr.: Research funding (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, and UCB Pharma; honoraria/consulting fees from AcademicCME, Alexion, AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd., Horizon Therapeutics plc (now Amgen), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB Pharma, and Zai Labs; non-financial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Pharma and Zai Labs.RM received funding for Travel, Meeting attendance or Advisory Board participation from Alexion, argenx, Biomarin, Catalyst, SANOFI, Regeneron and UCB.

Data availability

Anonymized data are available upon reasonable request, and can be provided after review and approval of a research proposal and statistical analysis plan and execution of a data sharing agreement. Requests to access the datasets should be directed to argenx, the owner of the clinical trial data, via ESR@argenx.com.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jns.2024.123264.

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