ImmunoTargets and Therapy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Effectiveness and Safety of Eculizumab in Highly Active AChR+gMG and Its Therapeutic Response in Different Subtypes of gMG

Tianying Ma[1–3,*], Yanan Liu[4,*], Ying Zhu[1–3], Yan Gao[5], Xue Wang[6], Yong Liang[7], Benqiao Wang[1–3], Ruixia Zhu[1–3]

[1]Department of Neurology, The First Hospital, China Medical University, Shenyang, People's Republic of China; [2]Key Laboratory of Neurological Disease Big Data of Liaoning Province, Shenyang, People's Republic of China; [3]Shenyang Clinical Medical Research Center for Difficult and Serious Diseases of the Nervous System, Shenyang, People's Republic of China; [4]Department of Geriatrics, The second Hospital of Dalian Medical University, Dalian, People's Republic of China; [5]Department of Neurology, Shengjing Hospital of China Medical University, Shenyang, People's Republic of China; [6]Department of Neurology, Anshan Central Hospital, Anshan, People's Republic of China; [7]Department of Neurology, Tieling Central Hospital, Tieling, People's Republic of China

*These authors contributed equally to this work

Correspondence: Ruixia Zhu, Email zrx_200626313@163.com

Background: Eculizumab had been approved for anti-acetylcholine receptor antibody-positive (AChR+) refractory myasthenia gravis (MG), but its effect on the broader group of highly active generalized myasthenia gravis (gMG) in clinical practice has not been fully uncovered.

Methods: We conduct a retrospective multi-center cohort study with prospectively collected data to explore the effectiveness and safety of eculizumab in highly active patients in clinical practice.

Results: Thirty-three patients from 4 research centers were included in our study treated with eculizumab. This study contains 1 early onset MG (EOMG), 13 late-onset MG (LOMG), and 19 thymoma-associated MG (TAMG) patients. At week 12, the mean Myasthenia Gravis Activities of Daily Living (MG-ADL) score decreased by 7.97 ± 3.96 points and Quantitative Myasthenia Gravis (QMG) score decreased by 12.88±5.82 points,13 (40%) patients achieved minimal symptom expression (MSE) and 78.7% patients were ADL responders (the improvement of MG-ADL score ≥3 points and lasted for at least 4weeks). The improvement was sustained for 24 weeks. Overall, four patients had experienced myasthenic crisis (MC), and the time to wean from mechanical ventilation (MV) was 6.33±3.21 days. In muscle subdomains analysis, QMG score decreased more obviously in the ocular group (66%) and bulbar group (49%) than in other muscle groups at week 4. Moreover, subgroup analysis showed that the TAMG and LOMG groups exhibited a similar degree of therapeutic effect in symptom control and ADL response. The mean prednisone dose was reduced by 12.84±20.36 mg/day at week 24. Patients in our study showed well tolerance to eculizumab, and none of them experienced meningococcal infections.

Conclusion: Our study confirmed the safety and effectiveness of eculizumab in highly active gMG patients with reducing steroid dose. TAMG and MC may be suitable indications for treatment with eculizumab. All the muscle groups achieved improvements, especially for the extraocular muscles.

Keywords: eculizumab, highly active generalized myasthenia gravis, thymoma, safety, effectiveness

Introduction

Myasthenia gravis (MG) is an antibody-mediated, complement-involved autoimmune disease characterized by fluctuating muscle weakness, including ocular, bulbar and limb skeletal muscle. Autoantibodies targeting the acetylcholine receptor (AChR) are detected in nearly 85% of MG patients' serum.[1] AChR-Ab+ gMG can be classified into TAMG, EOMG (<50 years), and LOMG (≥50 years) based on thymus pathologies and onset age.[2] Common treatments for MG include acetylcholinesterase inhibitors (ACEIs), corticosteroids, non-steroidal immunosuppressants (NSISTs), as well as rapid-acting therapies. However, some patients still show no improvement despite adequate traditional immunotherapy.

https://doi.org/10.2147/ITT.S559497
Received: 9 September 2025
Accepted: 25 December 2025
Published: 8 January 2026

Currently, novel, specific targeted biologics such as complement inhibitors, human neonatal Fc receptor (FcRn) antagonists and B-cell activating factor inhibitors are emerging.[3] With the advent of novel therapeutics, our aim is to develop tailored treatment strategies for patients across the spectrum of MG and determine the optimal therapy for each individual profile.

Eculizumab, a humanized monoclonal antibody approved for refractory gMG in many countries, inhibits the cleavage of C5, thereby blocking the inflammatory response induced by C5a and preventing the formation of the membrane attack complex (MAC) by C5b.[4] The Phase 3 randomized, double-blind, placebo-controlled, multi-center study (REGAIN study) first demonstrated that higher proportions of eculizumab-treated patients achieved ADL responses compared to placebo.[5] Furthermore, the REGAIN open-label extension (OLE) demonstrated that eculizumab provides rapid, sustained improvements in muscle strength and quality of life for refractory AChR-Ab+ gMG patients, with a manageable safety profile.[5,6] The inclusion criteria for the REGAIN study defined a more restricted MG population compared with the patients who are eligible to receive eculizumab in a real-world study with regard to disease severity, prior treatment, and thymoma history. However, individuals with Myasthenia Gravis Foundation of America (MGFA) class V disease (MC: myasthenia crisis) and TAMG were excluded from REGAIN study. The average age of patients in the REGAIN study was 47.5, while the patients in real world are older. Recently, Lea Gerischer proposed that the assessment of disease severity is based on the MGFA classification, and highly active MG includes a broader group besides refractory MG.[7] MG patients with high disease activity suffer from a huge disease burden and are prone to long-term sequelae and death. Therefore, it is clinically necessary to explore the effectiveness and safety of eculizumab in highly active AChR+gMG patients and its therapeutic responses in different subtypes.

Method

Study and Patients

This is a retrospective multi-center cohort study with prospectively collected data recruited 33 patients with highly active gMG at four hospitals (The First Affiliated Hospital of China Medical University, Shengjing Hospital of China Medical University, Anshan Central Hospital, and Tieling Central Hospital) from April 1, 2024, to March 1, 2025. Inclusion criteria were as follows: 1) aged ≥18 years; 2) generalized myasthenia gravis with high disease activity; 3) seropositivity for AChR-Ab; 4) patients treated with eculizumab and regularly followed-up over 24 weeks (900 mg weekly for the first four infusions, followed by 1200 mg every 2 weeks till week 12, and the subsequent treatment strategy was adjusted based on the symptom). The definition of highly active MG, which also includes refractory MG was as follows:[1] Persistent symptoms relevant to daily living (⇒MGFA IIb) and/or at least two recurrent severe exacerbations/MC requiring therapeutic intervention (IVIg, PE, and Immunoadsorption) within 1 year of diagnosis despite adequate disease-modifying and symptomatic therapy.[2] Persistent symptoms relevant to daily living (⇒MGFA IIa) and severe exacerbation/MC during the past year despite adequate disease-modifying and symptomatic therapy.[3] Persistent mild/moderate symptoms relevant to daily living (⇒MGFA IIa) for more than 2 years in spite of adequate disease-modifying and symptomatic therapy.[8] The diagnosis criteria for refractory MG vary around the world, and our study followed the American consensus in 2016.[9] All the patients were vaccinated against neisseria meningitidis at least 2 weeks before infusion, or regularly antibiotics used until 2 weeks after vaccination. The study was approved by the Ethics Committee of our hospital, and all the participants signed written informed consent.

We separated the participants into TAMG and non-TAMG groups according to thymus pathologies. Additionally, the non-TAMG patients were further divided into EOMG and LOMG according to the onset age. MC and impending MC were classified according to the severity of the symptoms. MC is an emergency state for MG patients when the patients immediately need to be intubated to keep breathing because the respiratory muscle was severely affected. Impending MC is defined as MGFA class IVb, or a QMG score of 2 or 3 for either respiratory or bulbar muscles, or a combined QMG score of ≥4 for these two muscle groups.[9]

Clinical Outcomes

All participants were followed up at baseline and weeks 1, 2, 3, 4, 6, 8, 12, and 24. Myasthenia Gravis Activities of Daily Living (MG-ADL) score and Quantitative Myasthenia Gravis (QMG) score were assessed at baseline, weeks 1, 2, 3, 4, 6, 8, 12, 24 and the last follow-up. Changes in prednisone dose and MG-post-intervention status (PIS) were documented every 4 weeks. Effectiveness was evaluated according to changes from baseline in QMG and ADL scores and based on the ratio of MSE and MG-ADL responders at weeks 8, 12, and 24.

According to the MG-PIS, the patients were divided into 4 types: Minimal Symptom Expression (MSE), improved, unchanged, and exacerbation. In our study, the status of the ADL score ≤1 was defined as MSE, and clinically meaningful improvement (CMI) was referred to as the MG-ADL score improvement ≥2 for at least 2 weeks. The unchanged status was defined as an MG-ADL score improvement of <2 points or a duration of improvement lasting ≤2 weeks. An exacerbation was considered as an increase in the MG-ADL score of more than 2 points for at least 2 weeks. ADL responders were defined as those with an improvement of ≥3 points lasting for at least 4weeks.[9]

Laboratory Investigations and Safety Evaluation

Adverse events associated with eculizumab were closely monitored, including headache, allergy, infection, fever, dizziness, rash, diarrhea, and myalgia. Furthermore, injection site reactions (ISRs), such as erythema, swelling, itching, and pain within a week after injection, were also under surveillance. The levels of serum CH50 and C5b-9 were detected at baseline and the end of week 12, and CD4+T subsets were also monitored. The CD4+ T-cell subset analysis was performed commercially (SHENYANG KINGMED FOR CLINICAL LABORATORY, a certified and internationally recognized clinical laboratory, for professional testing) during the treatment process, consistent with other clinical tests (detection of AChR antibodies, CH50, and sC5b-9) included in this study.

Statistical Analysis

Descriptive statistics were employed to summarize the demographic and clinical characteristics of the study population. Continuous variables were presented as the mean±SD or median (Q1–Q3), whereas categorical variables were expressed as percentages and analyzed by χ^2-tests. Moreover, in the case of a normal distribution, we performed repeated measures analysis of variance (ANOVA) test to compare the ADL score and QMG score at different time points (week 0, 4, 8, 12, and 24). In cases of non-normal distribution, Friedman test was performed. For pairwise comparisons, continuous variables were analyzed using the *t*-test or Mann–Whitney test, depending on the data distribution. A p-value < 0.05 was considered statistically significant. Data analysis was conducted by IBM SPSS Statistic 27 software, and charts were plotted using Prism 10.1.2.

Results

Characteristics of Subjects

The cohort comprised 33 highly active gMG patients, including 13 (39.39%) with LOMG, 19 (57.58%) with TAMG, and 1 (3.03%) with EOMG. Among the 33 recruited patients (male-to-female ratio 18:15), females constituted 45.45% of the total cohort, 47.37% of the TAMG subgroup, and 46.15% of the LOMG subgroup. The median onset age of the total cohort, TAMG and LOMG subgroups was 58 (26, 83), 54 (26, 70) and 68 (54, 83), respectively. Among the 33 highly active gMG patients, refractory MG accounted for 90.91%. All the patients were classified as III–V according to the MGFA, and III, IV, V subtypes accounted for 42.42%, 45.45% and 12.12%, respectively. Their baseline MG-ADL and QMG scores were 11.94±4.15 and 18.73±6.29 after the administration of corticosteroids (84.85%), NSIST (69.70%), IVIG or PE (45.45%), and other targeted drugs (51.52%). Seventeen patients switched from efgartigimod to eculizumab. Thymectomies were performed in 13 patients (39.39%) among the 19 TAMG patients included in our study, while the remaining 6 patients did not undergo the surgery. The reasons for this were as follows: Firstly, the clinical symptoms of these patients were not under control, and undergoing surgery at this time might worsen the condition or even trigger myasthenia crisis. Secondly, some patients were unwilling to undergo thymectomy because of personal reasons. Specific information is provided in Table 1.

Table 1 Baseline Features of Patients Enrolled, n=33. SD, Standard Deviation

	Total	TAMG	LOMG
Age (years)			
Mean (SD)	57.48(13.10)	51.63(12.57)	66.69(8.29)
Median (range)	58(26–83)	54(26–70)	68(54–83)
≥65, n%	9 (27.27%)	2 (10.53%)	7(53.85%)
Female, n%	15 (45.45%)	9 (47.37%)	6(46.15%)
History of thymoma	19 (57.58%)	19(100%)	0
Thymus surgery	13(39.39%)	13(68.42%)	0
Anti-AChR positive, n%	33(100%)	19(100%)	13(100%)
Severity (MGFA classification) at first dose, n%			
IIIa	5 (15.15%)	2 (10.53%)	3 (23.08%)
IIIb	9 (27.27%)	4 (21.05%)	5 (38.46%)
IVa	6 (18.18%)	3 (15.79%)	2 (15.38%)
IVb	9 (27.27%)	6 (31.58%)	3 (23.08%)
V	4 (12.12%)	4 (21.05%)	0
MG-ADL score, mean (SD)	11.94(4.15)	13.26(4.28)	10.07(3.45)
QMG total score, mean (SD)	18.73(6.29)	20.47(6.30)	15.92(5.65)
Previous treatment			
Corticosterroids	28(84.85%)	17(89.47%)	10(76.92%)
NSIST	23(69.70%)	11(57.89%)	11(84.62%)
Corticosterroids+NSIST	19(57.58%)	10(52.63%)	8(61.54%)
Targeted drugs	17(51.52%)	9(47.37%)	8(61.54%)
IVIG/PE	15(45.45%)	10(52.63%)	4(30.77%)
Switched to eculizumab from efgartigimod, n%	17 (51.52%)	9 (47.37%)	8 (61.54%)
The proportion of refractory MG	30 (90.91%)	19 (100%)	10 (76.92%)

The Effectiveness of Eculizumab in Highly Active gMG

At weeks 4, 8, and 12, the mean changes in total MG-ADL scores were −3.85±2.58, −6.03±3.66, and −7.97±3.96, respectively. There was also an improvement in total QMG from 18.73±6.29 at baseline to 10.06±7.17 at week 4, and to 5.85±5.72 at week 12. MG-ADL and QMG score continued to improve at week 24. Clinical improvement was achieved in 96.9% (32/33) of the patients within 2.34±2.56 weeks. After 12 weeks, 40% of the patients achieved MSE, and 78.7% of the patients were ADL responders. The improvement was sustained for 24 weeks (Figures 1, 2, 3 and 4). However, one of the patients who initially showed improvement experienced a deterioration at the 16th week due to the discontinuation of eculizumab. Another patient showed a poor response to eculizumab and discontinued.

All the muscle groups (ocular, bulbar, respiratory and limb) showed significant improvement from the first administration and sustained until the last follow-up according to QMG subdomains analysis. The percentage decrease from baseline in the ocular, bulbar, respiratory, and limb subdomains were 65.52%, 48.91%, 39.53% and 31.44% at week 4. The QMG of ocular muscle decreased to 1.82±2.13 at week 4 (Figure 5).

For LOMG group, we also observed a meaningful reduction of the mean MG-ADL and QMG score. The MG-ADL and QMG scores were decreased from 10.07±3.45 and 15.92±5.65 to 3.23±2.12 and 4.23±2.27 at week 12, respectively. Additionally, the MG-ADL and QMG scores remained consistently low at week 24. The proportion of ADL responders was the highest in the LOMG group (85%) by the week 12. In addition, 31% of LOMG patients achieved MSE at week 12 (Figure 4).

In the subgroup of TAMG patients, 9 patients (47.37%) were switched from efgartigimod to eculizumab. ADL responder rates were 73.6% and 94.7% at weeks 12 and 24 respectively. Forty-seven percent of TAMG patients achieved

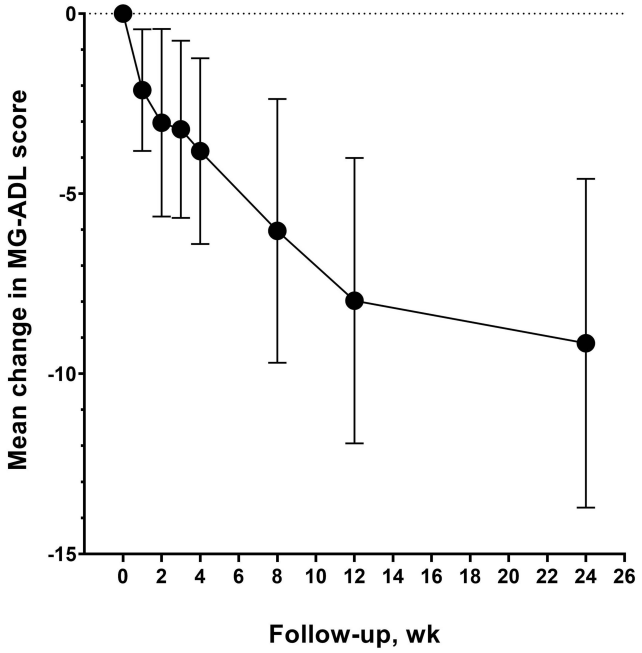

Figure 1 Mean change in MG-ADL score during the follow-up.

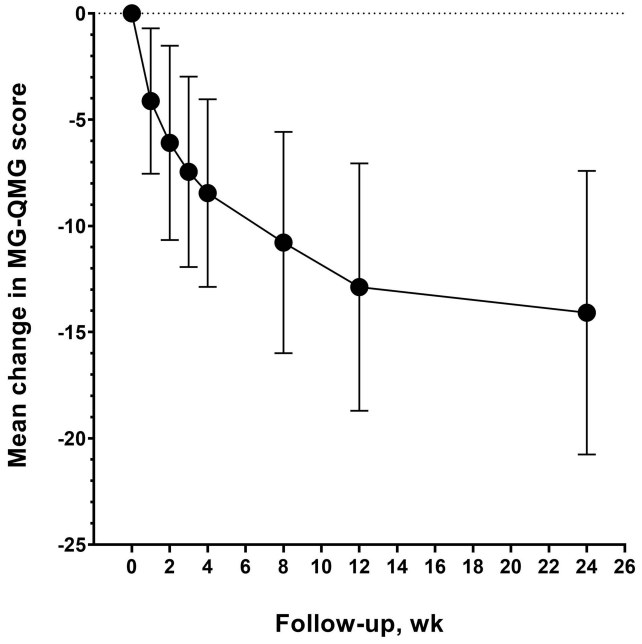

Figure 2 Mean change in QMG score during the follow-up.

MSE at week 12. At week 12, the mean changes from baseline were −9.0±4.12 for MG-ADL and −13.68±6.33 for QMG. At week 24, the changes were −10.1±4.97 and −14.84±7.74, respectively.

All the four MC patients were successfully weaned from mechanical ventilation. The time to wean off the ventilator was 6.33±3.21 days. After the initiation of eculizumab, the QMG score was decreased from 24±5.60 to 6.25±5.80 and MG-ADL was decreased from 16.75±3.10 to 2.50±2.65 at week 12. All the four patients achieved MSE at week 24. They remained in remission at week 24 with a mean QMG score of 2.75±2.50 and ADL score of 0.50±0.58.

https://doi.org/10.2147/ITT.S559497

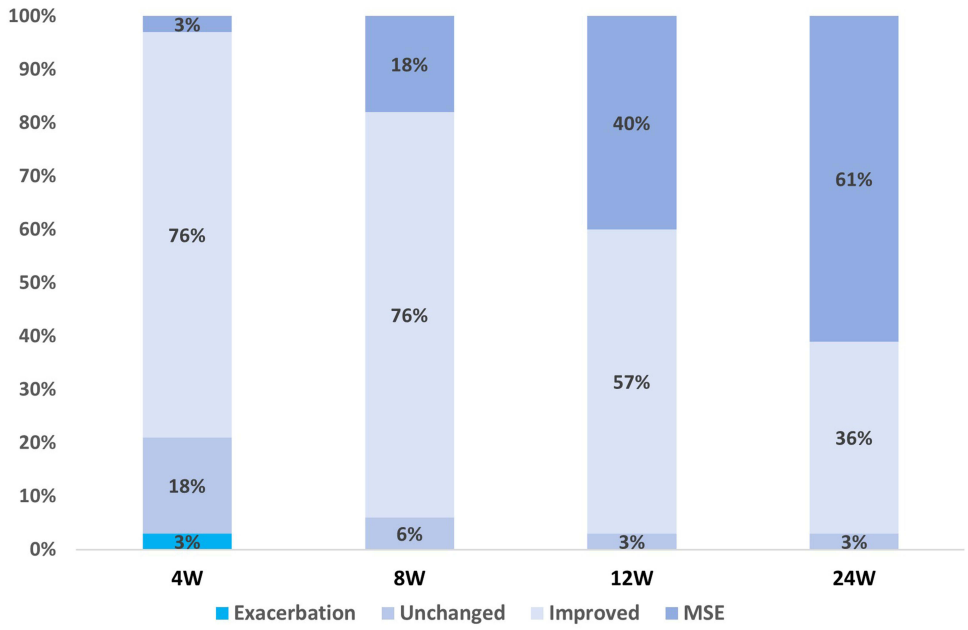

Figure 3 The proportion of patients who have reached MSE, improved, unchanged and exacerbation.

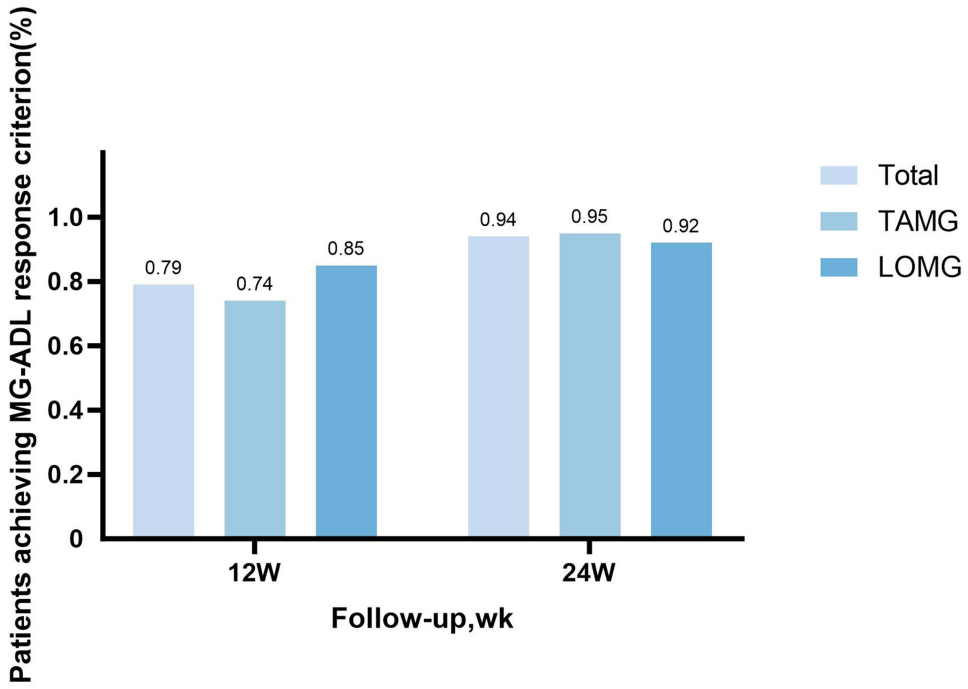

Figure 4 The proportion of patients who achieved MG-ADL response criterion in Total, TAMG and LOMG at 12 and 24 weeks.

Steroid-Sparing Effect Of Eculizumab

The mean(SD) daily prednisone dose decreased from 30.45±21.19 mg at the baseline to 25.75±18.84 mg at week 12, and 17.61±16.84 mg at week 24. The mean prednisone dose was reduced by 12.84±20.36 mg/day at week 24 (Figure 6).

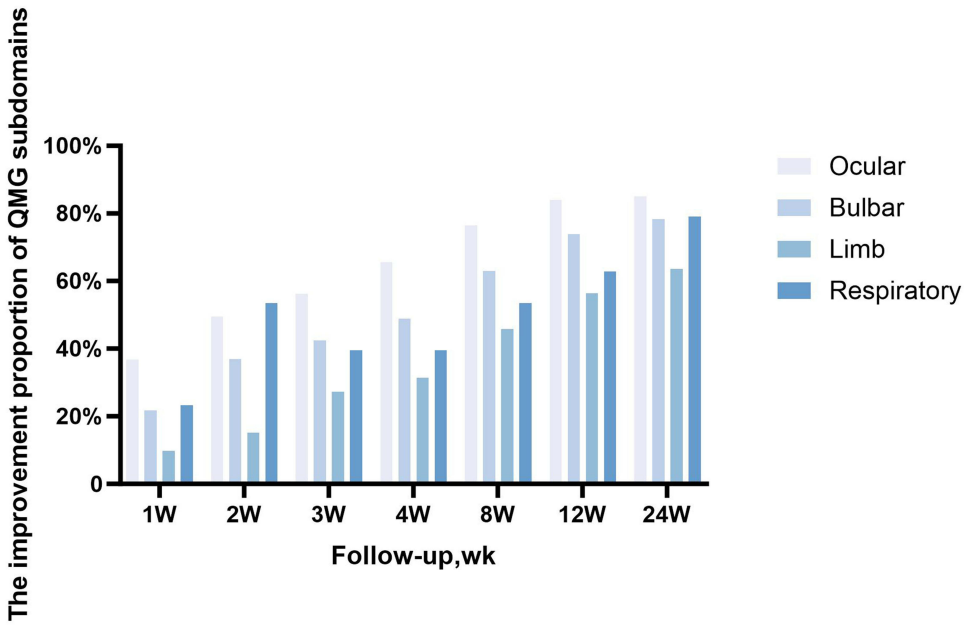

Figure 5 The improvement proportion of QMG subdomains (ocular, bulbar, limb and respiratory muscle groups) compared baseline.

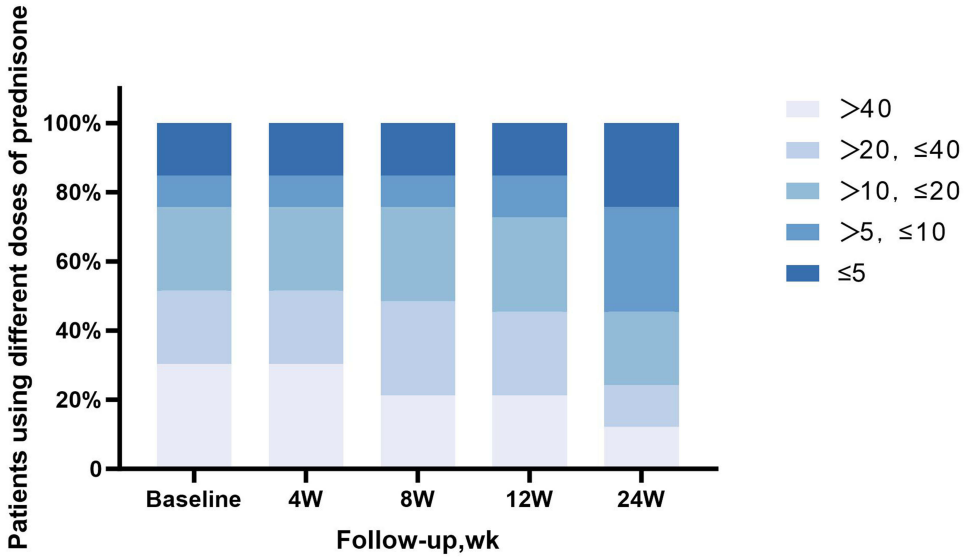

Figure 6 The proportion of patients using prednisone at baseline and 4, 8, 12, 24 weeks.

The Serum CH50, sC5b-9 and Immune Cell Subset Level

For complement-related molecules, CH50 levels decreased from 47.19±5.81 U/mL to 13.1±2.5 U/mL, and sC5b-9 levels decreased from 275.73±49.26 ng/mL to 216.54±53.63 ng/mL at week 12. Compared to the baseline, the proportion of CD4+T, including Th1, Th2, Th17, Tfh, and Treg, and B cells showed no significant changes at week 12.

The Safety of Eculizumab in Highly Active gMG

All the patients were vaccinated against Neisseria meningitidis and no patients developed meningococcal infection. The adverse events were mild. Ten patients (30.3%) reported adverse events and none of them discontinued eculizumab. These adverse events included headache (3 patients), rash (1 patient), nausea and diarrhea (4 patients), and myalgia (2 patients) (Table 2).

https://doi.org/10.2147/ITT.S559497

Table 2 Adverse Events Observed in the Study

Adverse events	n (%)
Headache	3(9.09%)
Nasopharyngitis	0
Nausea	1(3.03%)
Diarrhea	3(9.09%)
Infection	0
Muscle pain	2(6.06%)
Allergy	1(3.03%)

Discussion

We explored the effectiveness of eculizumab in the highly active gMG and therapeutic response patterns among different subtypes of MG. We identified that, consistent with the REGAIN study results, eculizumab provided rapid, sustained symptom relief while also reducing steroid doses in all patients. The rapid symptom control implied that eculizumab is a promising rescue therapy for MC. Among the four muscle groups, ocular and bulbar groups exhibited the greatest improvement. Furthermore, we also found eculizumab could be a suitable option for TAMG and LOMG in the subgroup analysis.

In our study, 96.9% patients achieved CMI and the mean duration was 2.34±2.56 weeks. Eculizumab improves muscle strength rapidly, demonstrating its potential as a fast-acting rescue therapy, particularly for severe exacerbations or MC. Four patients had experienced MC and the time to wean from MV was 6.33±3.21 days. Obviously, eculizumab facilitated the weaning process. Additionally, we also paid attention to the impact of eculizumab on different muscle groups (Ocular, bulbar, respiratory, and limb motor muscle groups). A significant improvement in ocular symptoms was observed after one week of eculizumab treatment, followed by the improvement in bulbar groups. However, limb-motor muscle groups may have a delayed response to eculizumab treatment. The REGAIN trial excluded purely ocular MG (OMG), but we can observe the effect of eculizumab on ocular muscle from the setting of generalized disease. Kaminski et al previously demonstrated diminished intrinsic complement regulatory activity in extraocular muscle in the EAMG model, suggesting complement-inhibiting therapies may be effective for OMG.[10]

The mean reduction in MG-ADL score from baseline at week 24 was 9 in the present study; this reduction was 4.2 in the REGAIN study at 26 weeks, 3.6-points in the ELEVATE study at 24 weeks, and 4.3-points in the Japanese post-marketing surveillance at 26 weeks. These findings are consistent with the efficacy and safety results from the REGAIN and other real-world studies. Notably, the reduction magnitude of MG-ADL score in our study was greater than others. We have considered several factors that may contribute to this observation: First, it can be partially explained by differences in the enrolled patient populations, such as inclusion criteria and baseline characteristics. Furthermore, compared to the disease course of 9.9 years in the REGAIN study's eculizumab group, our patients' duration lasted only 2.3 years. It has been found that patients who initiated eculizumab within 2 years of diagnosis achieved significantly greater improvements in MG-ADL score compared to those who started treatment later.[11] Therefore, earlier intervention with a targeted therapy like eculizumab, prior to the establishment of chronic and irreversible damage to the neuromuscular junction, could lead to a more pronounced and rapid recovery in daily living activities. Moreover, although our cohort had a higher average age, older age in AChR+ gMG is not necessarily associated with a diminished treatment response. On the contrary, some real-world evidence suggests that LOMG patients presented better therapeutic effects to biologics and more sustained responses compared with EOMG and TAMG patients.[2] Lastly, it is worth noting that a significant proportion of our patients were treated during MC. Recent studies have shown that eculizumab can promote rapid recovery of bulbar and respiratory muscle strength in refractory MC patients and significant improvements in MG-ADL scores.[12] This specific application in severe, active disease states may further contribute to the pronounced improvement observed in our cohort.

In TAMG, the thymoma destroys normal thymic epithelial micro-environment.[13] Thymic epithelial cells may express AChR-like antigens and further produce autoreactive T cells, leading to aberrant B-cell activation and AChR-Ab

production. These antibodies bind to neuromuscular junction (NMJ) receptors, intensively activating the complement cascade. TAMG patients exhibit greater disease severity and resistance to standard treatments.[14] Jin et al reported that TAMG patients showed clinical fluctuations following efgartigimod administration, with 21.1% requiring transition to other biologic therapies.[15] In another study, 40.9% of TAMG patients exhibited poor response to efgartigimod and transitioned to eculizumab to achieve clinical improvement and reduce the steroid dependence.[2] In our study, 47.37% of TAMG patients transitioned from efgartigimod therapy. After the administration of eculizumab, 73.6% TAMG patients achieved MG-ADL response, and 47% TAMG patients achieved MSE at week 12. Our study suggested eculizumab as an appropriate therapeutic option for TAMG patients. This may be attributable to the activation of complement, which plays an essential role in the process of AChR-Ab receptor blockade and antigenic modulation. It is reported that efgartigimod can rapidly decrease the level of AChR-Ab to 40%–70% of the baseline rather than completely exhaust antibodies. Additionally, Ozawa et al found that TAMG patients exhibited lower serum levels of C5 and higher serum levels of sC5b-9, indicating robust complement activation in the TAMG patients and C5 inhibition was particularly effective.[16] Christopher Nelke categorized patients with heightened disease severity and complement activation as PS3 patients. Through proteomics assessment, it was determined that these patients are likely to benefit from treatment with C5 inhibitors.[17] Based on our research, we speculate that TAMG may belong to the PS3 type, but this still needs further verification. Eculizumab was more potent and could be considered an appropriate treatment option for TAMG.

The thymic pathology in LOMG presents involution and atrophy, characterized by the loss of myoid cells, the negative expression of autoimmune regulator (AIRE) and the activation of intolerant T cells. While the REGAIN cohort had a mean age of 47.5 years, ours was significantly older (66.69 years), with 6 patients over 70 years of age. Similarly, the meaningful decline in QMG and MG-ADL was also observed in LOMG patients. The highest proportion of ADL responders was also found among LOMG at the week 12 (85%). Our findings provide evidence that eculizumab is effective in a broad population with MG. Older patients demonstrate higher prevalence of comorbidities, including hypertension, diabetes, hyperlipidemia, and cerebrovascular disease, consequently manifesting increased susceptibility to adverse effects when treated with glucocorticoids and immunosuppressants.[18] Eculizumab was a key strategy to mitigate steroid-related morbidity while maintaining disease control. By week 24, all patients attained a mean steroid reduction of 12.84±20.36 mg/day, corresponding to decreased incidence of glucocorticoid-associated adverse effects, including osteoporosis, diabetes, weight gain, hypertension, and cataracts. The early use of Eculizumab makes steroid dosage taper smoothly. Our research shows that Eculizumab application has a steroid-sparing effect that does not aggravate pre-existing comorbidities for elderly patients.

Complement activation plays a central role in early NMJ damage, therefore eculizumab can preserve NMJ integrity by blocking terminal complement activation. The average reduction in MG-ADL and QMG score from baseline to week 24 was 9.15±4.16 and 14.1±6.67 in our study, which was 4.6 and 6.6 in the REGAIN study. Our study included not only the refractory MG but also the newly diagnosed MG patients. Early initiation of eculizumab in New-onset AChR+ gMG patients with severe disease activity (MGFA III–IV) may delay disease progression and reduce immunosuppressive burden.[11] The RINOMAX study found that new-onset MG with shorter disease duration has favorable response to rituximab.[19] Usually, transition to monoclonal antibody therapy is warranted in MG patients demonstrating intolerance to common therapies, severe side effects, treatment contraindications, or recurrent MC. Our results suggest that early Eculizumab intervention appears beneficial for symptom control and functional improvement in high-activity MG. This preliminary finding requires further exploration.

The effects of eculizumab on peripheral molecules in the complement pathway were also detected. And we observe a significant decrease in serum levels of CH50 and sC5b-9 following 12 weeks of eculizumab treatment. It was confirmed reasonable to evaluate the efficacy of eculizumab by monitoring CH50 and sC5b-9. It was reported that eculizumab could also influence the adaptive immunity and lymphocytes.[20] However, after 12-week eculizumab treatment, there was no significant change in the proportion of CD4+ T subtypes, including Th1, Th2, Th17, Tfh, and Treg.

Patients were well tolerant to eculizumab, and none of them experienced meningococcal infections. All the adverse events were mild and the most common adverse events were headache and muscle pain. Two patients with MC due to infection did not exacerbate after the initiation of eculizumab. By selectively inhibiting terminal C5 primarily, eculizumab preserves proximal complement-mediated opsonophagocytosis and the clearance of immune complexes, thereby avoiding increased infection susceptibility.[21]

In our study, one patient showed no response to eculizumab. Bernhard Bouwman et al reported that a poor response to eculizumab could be attributed to the genetic variations in the C5 polymorphisms.[22] C5 mutations in the non-responder limit eculizumab's ability to bind C5 and inhibit complement activation. Regrettably, the C5 polymorphism was not genotyped in our study. In addition, as an observational study, our research is limited by its small sample size and short time of follow-up, and the number of EOMG was too small to conduct statistical analysis to find which subtypes are preferred to receive eculizumab. Furthermore, our results should be interpreted with caution, given the lack of controls (eg, patients receiving standard or alternative therapies) and treatment selection bias. This limits direct comparative conclusions regarding the effectiveness of eculizumab. We hope that our results will encourage larger, prospective, controlled observational studies to further explore the effectiveness of eculizumab in highly active AChR+gMG patients. Third, LRP4 and triple-seronegative MG patients were not included in our study, which should be taken into account in upcoming research. Ongoing studies are also needed to focus on EOMG, pediatric gMG, and pregnancy gMG groups.

Conclusion

In our cohort study with 33 highly active gMG patients, eculizumab demonstrated safety, effectiveness, and significant steroid-sparing properties. The rapid effect supports the role of eculizumab as a promising rescue therapy for MC. We also identified different responses to various muscle groups, with the ocular and bulbar being the greatest improvement. Our results also have some guidance for clinical treatment. For example, through the analysis of different AChR-Ab+MG subtypes, we found that TAMG may be the suitable indication for eculizumab treatment. LOMG patients also have a good response to eculizumab, and their comorbidities were not aggravated. Circulating complement biomarkers merit further investigation as predictors of eculizumab efficacy to optimize personalized therapeutic strategies. Further larger randomized controlled trial with longer follow-up periods should be conducted to confirm the efficacy of eculizumab in highly active gMG.

Ethical Statement

This study was conducted in accordance with the Declaration of Helsinki. The study was approved by the ethics committee of The First Affiliated Hospital of China Medical University (protocol number 2025-817-2). All the participants provided written informed consent.

Acknowledgments

The authors thank all participants of this study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the National Natural Science Foundation of China (81501006) and Natural Science Foundation of Liaoning province(2023-MSLH-406).

Disclosure

The authors declare no conflict of interest.

References

1. Lazaridis K, Tzartos SJ. Autoantibody specificities in myasthenia gravis; implications for improved diagnostics and therapeutics. *Front Immunol*. 2020;11:212. 10.3389/fimmu.2020.00212

2. Jin L, Zou Z, Wang Q, et al. Patterns and predictors of therapeutic response to efgartigimod in acetylcholine receptor-antibody generalized myasthenia gravis subtypes. *Ther Adv Neurol Disord*. 2025;18:17562864251319656. doi:10.1177/17562864251319656
3. Menon D, Barnett C, Bril V. Novel treatments in myasthenia gravis. *Front Neurol*. 2020;11:538. doi:10.3389/fneur.2020.00538
4. Eculizumab DJ. *Am J Health Syst Pharm*. 2008;65(17):1609–1615. doi:10.2146/ajhp080043
5. JF H Jr, Utsugisawa K, Benatar M, et al. Safety and efficacy of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalised myasthenia gravis (REGAIN): a phase 3, randomised, double-blind, placebo-controlled, multicentre study. *Lancet Neurol*. 2017;16(12):976–986. doi:10.1016/S1474-4422(17)30369-1
6. Mantegazza R, Wolfe GI, Muppidi S, et al. Post-intervention status in patients with refractory myasthenia gravis treated with eculizumab during REGAIN and its open-label extension. *Neurology*. 2021;96(4):e610–e618. doi:10.1212/WNL.0000000000011207
7. Gerischer L, Doksani P, Hoffmann S, Meisel A. New and emerging biological therapies for myasthenia gravis: a focussed review for clinical decision-making. *BioDrugs*. 2025;39(2):185–213. doi:10.1007/s40259-024-00701-1
8. Wiendl H, Abicht A, Chan A, et al. Guideline for the management of myasthenic syndromes. *Ther Adv Neurol Disord*. 16(17562864231213240).
9. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: executive summary. *Neurology*. 2016;87(4):419–425. doi:10.1212/WNL.0000000000002790
10. Kaminski HJ, Li Z, Richmonds C, Lin F, Medof ME. Complement regulators in extraocular muscle and experimental autoimmune myasthenia gravis. *Exp Neurol*. 2004;189(2):333–342. doi:10.1016/j.expneurol.2004.06.005
11. Muppidi S, Lee J, Habib A, et al. Effectiveness of eculizumab treatment by time from diagnosis in patients with generalized myasthenia gravis: a retrospective electronic medical record analysis (S15. *Neurology*. 2024;102(7_supplement_1):3457. doi:10.1212/WNL.0000000000205156
12. Song J, Huan X, Chen Y, et al. The safety and efficacy profile of eculizumab in myasthenic crisis: a prospective small case series. *Ther Adv Neurol Disord*. 2024;17:17562864241261602. doi:10.1177/17562864241261602
13. Melzer N, Ruck T, Fuhr P, et al. Clinical features, pathogenesis, and treatment of myasthenia gravis: a supplement to the guidelines of the german neurological society. *J Neurol*. 2016;263(8):1473–1494. doi:10.1007/s00415-016-8045-z
14. Álvarez-Velasco R, Gutiérrez-Gutiérrez G, Trujillo JC, et al. Clinical characteristics and outcomes of thymoma-associated myasthenia gravis. *Eur J Neurol*. 2021;28(6):2083–2091. doi:10.1111/ene.14820
15. Jin L, He D, Zeng Q, et al. Eculizumab in thymoma-associated myasthenia gravis: a real-world cohort study. *Ther Adv Neurol Disord*. 2024;17:17562864241309431. doi:10.1177/17562864241309431
16. Ozawa Y, Uzawa A, Onishi Y, Yasuda M, Kojima Y, Kuwabara S. Activation of the classical complement pathway in myasthenia gravis with acetylcholine receptor antibodies. *Muscle Nerve*. 2023;68(5):798–804. doi:10.1002/mus.27973
17. Nelke C, Schroeter CB, Barman S, et al. Identification of disease phenotypes in acetylcholine receptor-antibody myasthenia gravis using proteomics-based consensus clustering. *EBioMedicine*. 2024;105:105231. doi:10.1016/j.ebiom.2024.105231
18. Saccà F, Salort-Campana E, Jacob S, Cortés-Vicente E, Schneider-Gold C. Refocusing generalized myasthenia gravis: patient burden, disease profiles, and the role of evolving therapy. *Eur J Neurol*. 2024;31(6):e16180. doi:10.1111/ene.16180
19. Piehl F, Eriksson-Dufva A, Budzianowska A, et al. Efficacy and safety of rituximab for new-onset generalized myasthenia gravis: the RINOMAX randomized clinical trial. *JAMA Neurol*. 2022;79(11):1105–1112. doi:10.1001/jamaneurol.2022.2887
20. Li Y, Yi JS, JF H Jr, Chopra M, Russo MA, Guptill JT. Cellular changes in eculizumab early responders with generalized myasthenia gravis. *Clin Immunol*. 2021;231:108830. doi:10.1016/j.clim.2021.108830
21. Keating GM, Lyseng-Williamson KA, McKeage K. Eculizumab: a guide to its use in paroxysmal nocturnal hemoglobinuria. *BioDrugs*. 2012;26(2):125–130. doi:10.2165/11208420-000000000-00000
22. Bouwman HB, Guchelaar HJ. The efficacy and safety of eculizumab in patients and the role of C5 polymorphisms. *Drug Discov Today*. 2024;29(9):104134. doi:10.1016/j.drudis.2024.104134