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ORIGINAL RESEARCH

Efgartigimod Followed by Telitacicept in Adult Generalized Myasthenia Gravis: A Retrospective Case Series

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Video abstract

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Background: The emergence of biologics for the treatment of generalized myasthenia gravis (gMG) has increased therapeutic options, but evidence on their flexible use remains limited.

Purpose: This study retrospectively analyzed gMG patients treated with efgartigimod followed by telitacicept.

Methods: A retrospective analysis was conducted on gMG patients treated with efgartigimod followed by telitacicept. Outcomes included changes in Quantitative Myasthenia Gravis (QMG) and Myasthenia Gravis-Activities of Daily Living (MG-ADL) scores from baseline to weeks 13 and 28, Minimal Manifestation Status (MMS), corticosteroid-sparing potential, safety, and serological markers.

Results: Among seven patients included for efficacy evaluation, the baseline QMG and MG-ADL scores were 12.4±4.3 and 7.1±3.6, respectively. These scores decreased by 8.4±3.9 and 5.7±4.2 at week 13 and further decreased by 8.7±3.2 and 6.8±3.4 by week 28 (both $P < 0.001$). Six patients (86%) achieved Minimal Manifestation Status (MMS), with a median time to achieve MMS being 9 weeks. The average prednisone dosage was significantly reduced from 51.43±14.64 mg at baseline to 5.71±1.89 mg by week 28 ($P < 0.05$). Common adverse events included mild injection site reactions (n=2) and upper respiratory infections (n=2), with no serious events reported. IgM and IgA levels significantly declined by week 17 ($P < 0.05$), while BAFF levels increased significantly following telitacicept treatment by week 21 ($P < 0.05$).

Conclusion: This regimen demonstrated favorable efficacy and safety, suggesting its potential as an effective option for gMG management.

Keywords: generalized myasthenia gravis, efgartigimod, telitacicept, sequential therapy, targeted therapy

Introduction

Myasthenia gravis (MG) is a chronic autoimmune disorder marked by antibody-mediated attacks on the neuromuscular junction, leading to direct or indirect impairment of acetylcholine receptor (AChR) function impairment and resulting in fluctuating skeletal muscle weakness and fatigue, particularly in extraocular, bulbar, and limb muscles.[1,2] Treatment traditionally involves acetylcholinesterase inhibitors, thymectomy, and immunosuppressive therapies. However, symptomatic therapy alone is often inadequate, necessitating corticosteroids and additional non-steroidal immunosuppressants (NSISTs) to achieve disease control.[3] Despite their utility, these treatments can lead to severe long-term side effects, and symptom recurrence upon dosage tapering is common, presenting significant clinical and psychological burdens.[4,5] In recent years, advances in the molecular understanding of MG pathogenesis have fostered the development of targeted biologics that directly inhibit pathogenic pathways, such as immunoglobulin recycling and specific immune cells involved in MG. Biologics like efgartigimod, eculizumab, and ravulizumab have shown promise for refractory generalized MG (gMG).[6] However, targeted therapies have thus far been largely adjunctive rather than primary alternatives to NSISTs.[7–11] While these new targeted

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therapies offer promise, their role remains largely supportive rather than as standalone alternatives to NSISTs, with limited data on their use as primary treatments in gMG. Consequently, there is a significant need to investigate innovative, effective sequential regimens that could provide robust disease control with reduced side effects compared to traditional therapies.

Efgartigimod, an FcRn antagonist, has demonstrated efficacy in improving muscle strength in gMG with a favorable safety profile. By binding to FcRn receptors, efgartigimod disrupts IgG recycling, leading to a rapid reduction in pathogenic antibody levels associated with disease activity.[12–15] However, this effect is transient, typically lasting 4 to 12 weeks, necessitating repeat injections or concurrent NSISTs to prevent antibody rebound.[8,13] Real-world studies have compared FcRn inhibitors (efgartigimod) and complement inhibitors (eculizumab) in gMG management. While eculizumab demonstrates greater Quantitative Myasthenia Gravis (QMG) score improvement and a stronger steroid-sparing effect, both therapies achieve comparable reductions in Myasthenia Gravis-Activities of Daily Living (MG-ADL) scores.[16] Unlike eculizumab, efgartigimod does not require pre-treatment vaccination or prophylactic antibiotics, offers a more flexible treatment schedule, and has demonstrated efficacy across various antibody subtypes, making it a clinically accessible alternative. While no biomarkers currently guide optimal re-dosing, efgartigimod's fast-acting profile may provide an essential therapeutic window for subsequent immunosuppressive treatment.

Recent studies highlight B cells as critical modulators in MG, with their regulation affecting both antibody production and immune cell interactions.[17,18] Telitacicept, a novel recombinant fusion protein that combines the ligand-binding domain of the TACI receptor with the Fc portion of human IgG, acts as a competitive inhibitor of the B cell-promoting effects of endogenous BAFF and APRIL.[19] This mechanism effectively reduces the population of long-lived plasma cells responsible for persistent autoantibody production, thus addressing a key aspect of MG pathophysiology.[19] Clinical studies have demonstrated telitacicept's efficacy and safety across various antibody-mediated autoimmune diseases, including such as systemic lupus erythematosus (SLE),[20] rheumatoid arthritis (RA),[21] IgA nephropathy,[22] IgG4-related disease,[23] primary Sjögren's syndrome,[24] neuromyelitis optica spectrum disorders.[25] In recent studies, telitacicept has shown promising results specifically in adult gMG, indicating a stable and favorable efficacy profile.[11] Additionally, a Phase III clinical trial evaluating its use in gMG is currently ongoing. In China, telitacicept has already been approved for treating active SLE and RA, further underscoring its therapeutic potential. Building on the complementary mechanisms of efgartigimod and telitacicept, this study explores the potential of a sequential therapy approach, utilizing efgartigimod's rapid antibody clearance followed by telitacicept's B cell-targeted effects, as a possible alternative to traditional NSISTs in managing adult gMG.

Methods

Study Design and Patients

This retrospective, single-center, real-world study examined the outcomes of sequential treatment with efgartigimod followed by telitacicept as an alternative to NSISTs in patients with gMG. The study received ethical approval from the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University. Clinical data were reviewed for adult patients diagnosed with gMG who underwent efgartigimod therapy followed by telitacicept from December 1, 2023, to November 30, 2024.

Patients included in this analysis were diagnosed with gMG in accordance with the 2020 Chinese guidelines for the diagnosis and treatment of MG. The diagnosis was confirmed based on clinical features, specifically the presence of fluctuating and fatigable muscle weakness, along with at least one positive result from pharmacological testing, serum antibody measurement, or repetitive nerve stimulation (RNS) testing. All patients had a MG-ADL score of at least 5 (≥50% non-ocular) or a QMG score of ≥8 (with four or more items scoring ≥2) prior to treatment. Additionally, patient classification was performed using the Myasthenia Gravis Foundation of America (MGFA) clinical scale. All participants had comprehensive medication histories and follow-up data.

Treatment

Prior to treatment, all patients receiving the combination therapy underwent screening for contraindications, which included severe adverse reactions to immunosuppressive drugs, such as significant diabetes, advanced osteoporosis, avascular necrosis, uncontrolled severe infections, liver or kidney dysfunction, pregnancy or lactation, allergies, and hypogammaglobulinemia.

The treatment regimen was divided into two phases: the first, the rapid induction of remission phase, consisted of efgartigimod injections (10 mg/kg) administered weekly for four doses (weeks 0, 1, 2, and 3). The second phase, for sustaining efficacy, involved continuous telitacicept injections starting at week 4 (240 mg per dose). Injection intervals were gradually extended after achieving clinical stability, occurring at weeks 4, 5, 6, 7, 9, 11, 13, 17, 21 and 25. This flexible schedule was based on telitacicept's half-life, prior studies, patient cost-benefit ratios, and its IgG Fc structure, enabling prolonged circulation. To reduce costs, intervals were extended from weekly to bi-weekly and finally monthly (Figure 1).

Concurrent therapies for MG included only corticosteroids and acetylcholinesterase inhibitors. A high-dose (30–60 mg/d) rapid induction of corticosteroids was initiated at the start of sequential therapy. Treatment decisions were made collaboratively with patients, emphasizing informed consent, with the first week of treatment conducted in a hospital setting and subsequent follow-ups managed on an outpatient basis.

Follow-up and Data Collection

Baseline clinical information was documented prior to therapy initiation, encompassing sex, age, body mass index (BMI), duration of illness, clinical symptoms, thymic status, surgical history, antibody type and titer, comorbidities, and baseline QMG and MG-ADL scores.

The observation period for this study was 28 weeks, with follow-up data collected at baseline and at weeks 1, 4, 5, 6, 9, 13, 17, 21, 24, 28. The primary outcomes included changes in QMG and MG-ADL scores from baseline to weeks 13 and 28, measured as both absolute change values and percentage improvements. Secondary outcomes included the proportion of patients achieving minimal symptom expression (MMS) by week 28, defined as an MG-ADL score of 0 or 1. MMS also reflected a significant reduction in clinical manifestations prior to treatment or a sustained decrease in the use of MG medications.[26,27] Additional secondary outcomes included the duration of continuous MMS within the observation period, the time taken for withdrawal of symptomatic medications, the steroid-sparing effect, and the safety profile of the treatment protocol.

Blood samples were collected prior to treatment initiation and at each follow-up visit to monitor dynamic changes in serological markers. These markers included serum levels of IgG, IgM, and IgA, as well as the percentage of CD19+ B cells among lymphocytes. Following informed consent, serum samples were preserved to assess changes in BAFF and APRIL levels throughout the treatment period. Clinical efficacy scores were evaluated by qualified neurologists, ensuring assessments were conducted at least 3–4 hours after the last dose of acetylcholinesterase inhibitor to mitigate its pharmacological influence. Serum immunoglobulin levels were quantified using immunoturbidimetry, while BAFF and APRIL levels were determined via the Quantikine ELISA Kit (R&D Systems, DBLYS0B). The percentage of CD19+ B cell counts was analyzed using flow cytometry, facilitating a robust evaluation of treatment effects.

Statistical Analysis

Quantitative data were presented as mean ± standard deviation or median with range, while categorical data were expressed as frequencies or percentages. To assess differences in QMG and MG-ADL scores at baseline, week 13, and week 28, paired T-tests were conducted after testing for normality. For prednisone dosage comparisons between baseline and week 28, the Wilcoxon test was employed to address non-parametric distribution. Additionally, Mann-Kendall trend analyses assessed changes in serological markers, including CD19+ B cell counts, IgG, IgM, IgA, BAFF, and APRIL levels. A P-value of less than 0.05 was considered statistically significant. Statistical analyses were performed using SPSS (Version 27.0) or R software (Version 4.3.2), with graphical representations created using Prism (Version 10.2.3).

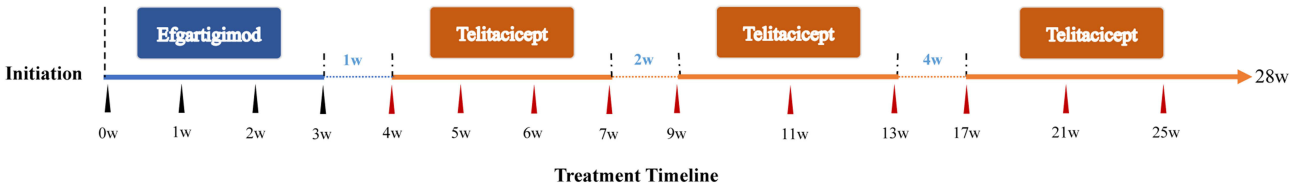

Figure 1 Timeline of medication administration for patients in the 28-week study period. The blue arrows indicate the timing of efgartigimod injections, while the yellow arrows denote telitacicept injections.

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Results

Patients

A total of eleven patients at our center received the sequential treatment of efgartigimod combined with telitacicept. However, four patients were excluded from the final analysis: two discontinued treatments due to financial constraints by week 6, and two others were excluded for irregular injection cycles. These excluded patients were, nonetheless, included in the safety analysis. Ultimately, seven patients were analyzed, with a median age of 62 years (range 46–77) and a median disease duration of 7 months (range 1–108). Notably, one patient had a thymoma and underwent thymectomy four years prior to treatment, while another had thymic hyperplasia without surgical intervention; the remaining patients exhibited normal thymic status. Detailed baseline demographics and clinical characteristics are presented in Table 1.

Primary Outcomes

At baseline, the mean QMG score was 12.4±4.3. By week 13, the QMG score decreased significantly by an average of 8.4±3.9 ($P < 0.001$), reflecting a mean reduction of 67.2%. Notably, 100% of patients achieved a reduction of ≥3 points in QMG scores at this time point. By week 28, the average QMG score ultimately declined by 8.7±3.2 ($P < 0.001$), indicating a sustained mean reduction of 69.1%, with all patients maintaining a decrease of ≥3 points. The duration of continuous QMG reduction of ≥5 points from the initial visit averaged 80.1% of the study period. The baseline MG-ADL score was 7.1±3.6. From baseline to week 13, all patients exhibited an average reduction in MG-ADL scores of 5.7±4.2 ($P < 0.001$), representing a mean decrease of 76.2%. At week 13, every patient achieved MG-ADL scores of ≥2 points. By week 28, the average MG-ADL score decreased further by 6.8±3.4 ($P < 0.001$), demonstrating an overall reduction of 96.2%, with all patients sustaining MG-ADL scores of ≥3 points. Additionally, the duration of MG-ADL reduction of ≥2 points averaged 94.9% of the total study duration (Figure 2A–C and E).

MMS

In our combined treatment regimen, 86% of patients (six out of seven) achieved MMS. The time to reach MMS varied, with Patients 1, 2, and 6 achieving this status by week 4, Patient 4 by week 9, Patient 5 by week 13, and Patient 7 by week 17. During the entire study period, the proportion of time achieving MMS for Patients 1 to 7 was 85.7%, 75.0%, 0%, 67.9%, 53.6%, 75.0%, and 14.3%, respectively (Figure 2B). Patient 3, due to pre-existing spinal infections and severe osteoporosis complications that limited mobility, did not achieve minimal symptom expression (MMS) until week 28. The duration of symptomatic medication withdrawal varied, with most patients discontinuing pyridostigmine bromide within 5 to 52 days (Table 2).

Steroid-Sparing Effect

Patients received an initial high-dose prednisone regimen ranging from 30 mg to 60 mg/day (Table 1). Specifically, Patient 1, due to low body weight, and Patient 3, with a history of long-term steroid use and multiple steroid-related adverse effects, were initially treated with 30 mg/day. In contrast, Patients 2 and 4–7, who had no prior steroid use or only brief steroid treatment, were started on 60 mg/day. As efgartigimod was administered concurrently, careful monitoring was conducted to mitigate the risk of myasthenic crises associated with high steroid doses. By week 28, the average daily dose of prednisone significantly decreased from 51.43±14.64 mg to 5.71±1.89 mg ($P < 0.05$), marking an 89% reduction. By week 13, all patients had tapered their steroid dosage to ≤15 mg/day, with six patients (86%) reaching 5 mg/day by week 28, without any dosage increases throughout the study (Figure 2D–F).

Safety

The most frequently reported adverse events (AEs) were mild (grade 1) in nature, primarily consisting of localized injection site reactions characterized by redness and pain. Additionally, two patients experienced upper respiratory tract infections, which were self-limiting and required no medical intervention. Importantly, there were no serious AEs reported, and all patients completed the treatment protocol without any treatment interruptions due to AEs. Notably, no instances of mortality were observed. Patient 3, who had a complex medical history including Salmonella bacteremia and spinal infection, demonstrated significant improvement in overall health during the study. Prior to treatment, this

Table 1 Baseline Characteristics of Patients

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Sex	Female	Female	Male	Female	Female	Female	Male
BMI (kg/m^2)	15.8	23.7	21.2	23.4	22.1	27.3	23.7
Age (years)	46	58	62	68	58	77	68
Disease duration from diagnosis to enrollment (months)	45	108	7	1	54	2	5
MGFA clinical classification	IIIb	IIIb	IIIa	IIIa	IIIa	IVa	V
Thymus status	Thymoma	Thymic hyperplasia	Normal	Normal	Normal	Normal	Normal
Thymectomy	Y	N	N	N	N	N	N
Duration of thymectomy (months)	46	N	N	N	N	N	N
Involved muscle groups	Ocular, face, bulbar, neck, limbs, respiratory	Ocular, bulbar, neck, limbs, respiratory	Neck, limbs	Ocular, face, neck, limbs	Neck, limbs	Neck, Ocular, limbs	Ocular, face, bulbar, neck, limbs, respiratory
Ab status	AChR-Ab (+)	AChR-Ab (+)	AChR-Ab (+)	Negative	AchR-Ab (+)	MuSK-Ab (+)	MuSK-Ab (+)
Ab concentration (nmol/L or titre)	15.668	17.13	1:320	N	12.593	1.344	0.779
RNS	N	N	N	Negative	Positive	Negative	Negative
Fatigue test	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Coexisting autoimmune diseases	N	N	N	N	N	N	N
Co-morbid autoimmunity antibody	N	N	Tintin-Ab (+) Ryr-Ab (+)	N	Tintin-Ab (+)	N	N
Concomitant diseases	N	N	Hypertension, osteoporosis, bone fracture, spinal infection, chronic hepatitis B	Chronic hepatitis B, hypertension,	N	Coronary heart disease	Coronary heart disease
Baseline OMG score[a]	15	6	11	13	14	10	20
Baseline MG-ADL score[b]	7	7	5	6	4	6	15
Previous MG medications	Pyridostigmine bromide, Prednisone	Pyridostigmine bromide	Pyridostigmine bromide, Prednisone	Pyridostigmine bromide, Prednisone	None	None	None
Previous GCS treatment duration	8 months	5 days	7 months	3 days	None	None	None
Initial intensified GCS dose at combination regimen start (mg/d)	30mg	60mg	30mg	60mg	60mg	60mg	60mg

Notes: [a]Total QMG scores range from 0 (none) to 39 (severe); [b]Total MG -ADL scores range from 0 (normal) to 24 (severe).

Abbreviations: BMI, body mass index; MG, myasthenia gravis; MGFA, Myasthenia Gravis Foundation of America; AChR-Ab, acetylcholine receptor antibodies; MuSK-Ab, muscle-specific kinase antibody; RNS, repetitive nerve stimulation; QMG, quantitative myasthenia gravis; MG-ADL, Myasthenia Gravis-Activities of Daily Living; GCS, glucocorticoids; Y, yes; N, no.

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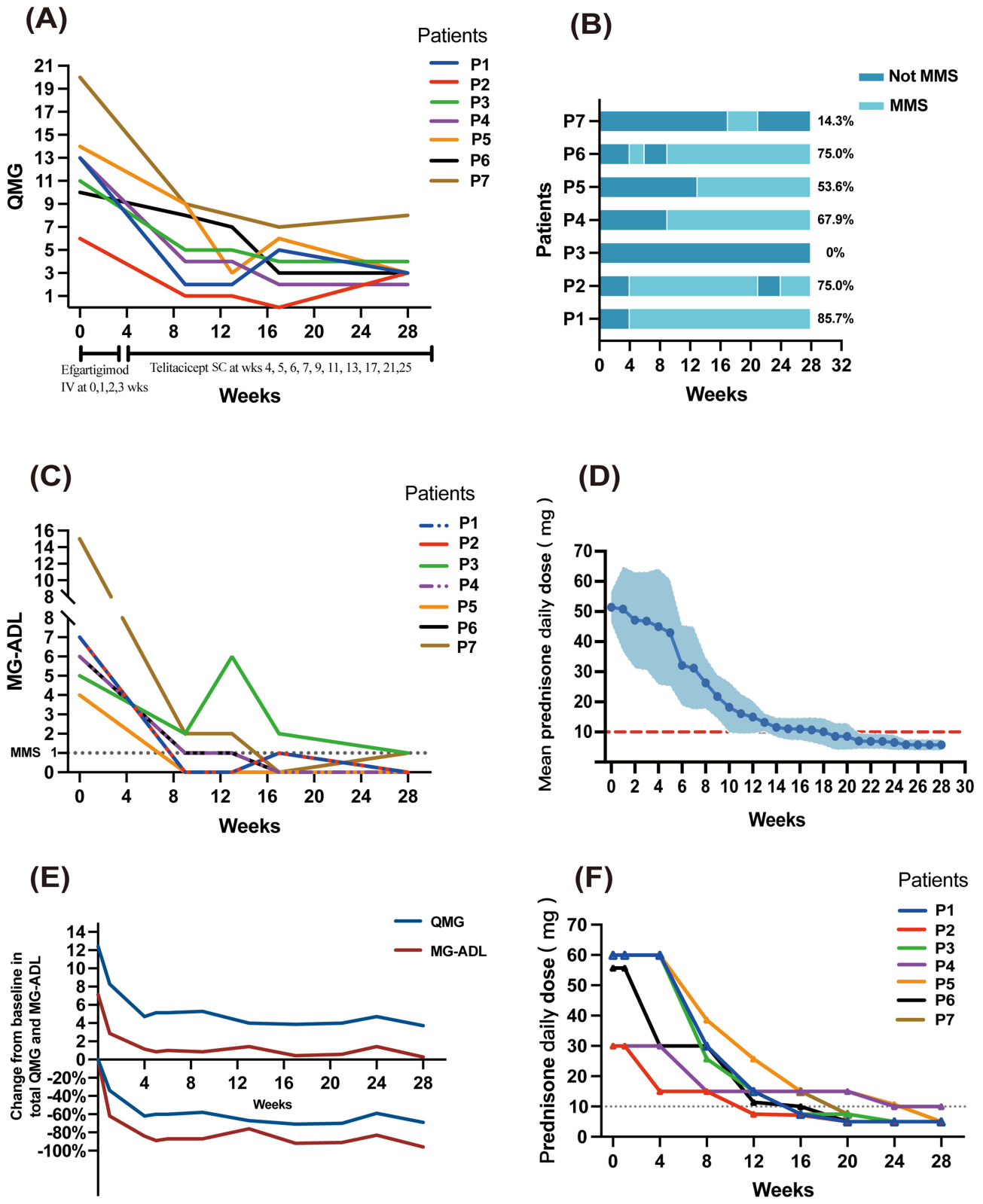

Figure 2 Effectiveness outcomes. (**A**) Individual changes in QMG from baseline to week 28. (**B**) Proportion and time to MMS Achievement in individual patients over a 28-week observation period (**C**) Individual changes in MG-ADL from baseline to weeks 28. (**D**) Mean daily dosage of prednisone from baseline to week 28. (**E**) Mean and percent changes in QMG and MG-ADL from baseline to weeks 28. (**F**) Individual daily prednisone dosage changes from baseline to week 28.

Table 2 Time to Withdraw Symptomatic Medication

Patients	Time to Withdraw Pyridostigmine Bromide (days)
Patient 1	5
Patient 2	7
Patient 3	7
Patient 4	52
Patient 5	N
Patient 6	N
Patient 7	N

Abbreviation: N, no pyridostigmine bromide.

patient was managed with high-level anti-infective therapy, and careful consideration was given to ensure that their infections were controlled before initiation of the new regimen. Throughout the treatment period, no relapses of infection or new AEs were reported (Table 3).

Changes in Serological Markers

Significant reductions in serum IgG, IgM, and IgA levels were observed by week 17, with average decreases of 5.07 ±3.49 g/L, 0.57±0.20 g/L, and 1.36±1.28 g/L, respectively. Mann-Kendall trend analysis indicated significant changes for IgM and IgA ($P < 0.05$), while IgG levels remained stable ($P > 0.05$). The percentage of CD19+ B cells initially increased but subsequently declined, with no significant difference detected over time ($P > 0.05$). Serum BAFF levels initially decreased post-efgartigimod but exhibited a substantial increase following telitacicept administration ($P < 0.05$). Serum APRIL levels showed a slight reduction but were not statistically significant ($P > 0.05$) (Figure 3).

Discussion

Prior research indicates that early intensive induction therapy (EIT) for MG can expedite the attainment of MMS and minimize corticosteroid dependence to ≤5mg/day. However, conventional EIT modalities such as plasmapheresis, IVIG, and high-dose corticosteroids present challenges including high costs, limited availability, and risks of side effects and symptom exacerbation. In this study, we innovatively employed efgartigimod followed by telitacicept as an alternative to IST, aiming for swift symptom alleviation, condition stabilization and a smooth tapering of corticosteroid. Current literature

Table 3 Summary of Adverse Events in All Patients (n=11)

Adverse Event	Number of Patients n (%)
Upper respiratory tract	2 (18.2%)
Infection site reactions	2 (18.2%)
Urinary tract infection	1 (9.1%)
Myalgia	1 (9.1%)
Death	0 (0%)
Serious adverse event	0 (0%)
Adverse event leading to discontinuation	0 (0%)
Headache	0 (0%)
Diarrhea	0 (0%)
Nasopharyngitis	0 (0%)
Nausea	0 (0%)
Anaphylaxis	0 (0%)
Patients with no adverse events	7 (63.6%)

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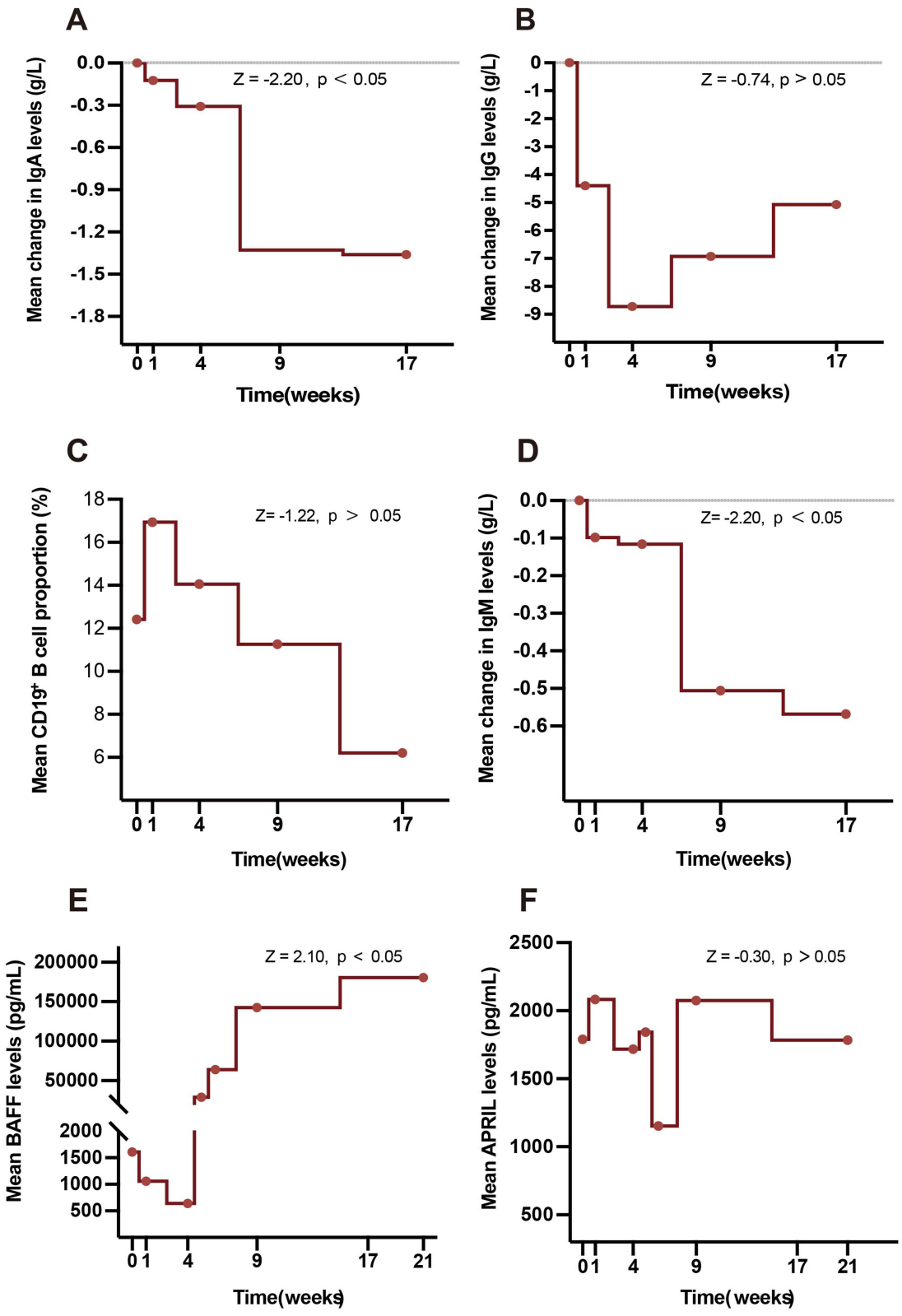

Figure 3 Mean percentage changes in biomarkers. (**A**) Change in IgA over time. (**B**) Change in IgG over time. (**C**) Change in CD19+ B cell counts over time. (**D**) Change in IgM over time. (**E**) Change in BAFF over time. (**F**) Change in April over time. Statistical significance was assessed using Mann-Kendall trend analysis.

on telitacicept and efgartigimod has primarily focused on their use in combination with traditional immunosuppressants, complicating the assessment of their specific therapeutic effects in autoimmune diseases.[7–11] In our study, all participants had not received any traditional immunosuppressants prior to treatment, apart from prednisone, facilitating a clearer analysis of the combination regimen's impact on gMG patients. Following one week of efgartigimod treatment, response rates for QMG and MG-ADL scores in our case series were observed at 85.7% and 100%, respectively, indicating significant clinical symptom relief. These results support the prior ADAPT trial.[7] The rapid onset of action associated with efgartigimod was sustained during the subsequent phase of telitacicept administration, with both QMG and MG-ADL response rates reaching 100% by week 28. Achieving MMS is a key treatment goal in gMG management. Prior research has indicated that conventional immunotherapies reach an MMS rate of approximately 50%, with the achievement typically taking around 26 months.[28] In elderly and refractory patients, the rate may be even lower, and the time required may be longer.[29,30] In our study, the median time to first achieve MMS was 9 weeks, with 86% (six out of seven, the majority being elderly) of patients maintaining this status throughout the observation period, demonstrating favorable safety and tolerability. Notably, Patient 3's MMS status was influenced by concurrent spinal infections and osteoporotic fractures. While direct comparisons are challenging, our results suggest that this combination therapy may offer rapid and durable achievement of MMS, presenting encouraging implications for future treatment strategies in gMG.

In treating MG, the use of corticosteroids remains a contentious issue, as clinicians must often balance efficacy against potential side effects. High-dose corticosteroids combined with rapid tapering have been linked to favorable outcomes in previous studies.[31] Previous experience also suggested that for severe patients, early initiation of high-dose corticosteroids together with rescue therapy may be beneficial.[32] In our cohort, considering that the patients were not classified as mild cases, some with acute onset and a tendency toward deterioration, the initial corticosteroid regimen was determined based on clinical experience and aligned with the recommendations in the "2020 Chinese Guidelines for the Diagnosis and Treatment of MG", which suggest a dosing range of 0.5–1.0 mg/kg/day, not exceeding 100 mg/day, allowing for individualized treatment approaches. Therefore, most patients were administered a high initial dose of 30–60 mg/day of corticosteroids at the start of the sequential therapy to rapidly induce symptom control. While some studies indicate an initial exacerbation probability of 19% to 28% with prednisone, particularly at doses exceeding 40 mg per day,[33] our regimen did not result in any exacerbations or the occurrence of myasthenic crises. This may be attributable to the concurrent administration of efgartigimod, which offers a therapeutic effect akin to plasma exchange, potentially reducing exacerbation risk. By week 28, six patients (86%) had reduced their average daily steroid dosage to 5 mg per day. This dosage is generally considered to have minimal side effects on patients, suggesting that this treatment approach may have the potential to facilitate significant steroid reduction. We acknowledge the potential confounding effect of corticosteroids on treatment outcomes, as corticosteroids are the backbone of MG therapy and may contribute to symptom improvement. However, the significant and sustained reduction in QMG and MG-ADL scores, alongside the rapid tapering of prednisone to minimal maintenance doses, suggests that the observed efficacy was primarily driven by the novel sequential therapy with efgartigimod and telitacicept. Additionally, existing trials on efgartigimod and eculizumab have evaluated these biologics as additive treatments to standard therapy, supporting their independent therapeutic effects.[7,9] Future studies should further explore the interaction between steroids and targeted biologic therapy, particularly the optimal timing, dosing strategies, and long-term effects of corticosteroid tapering in sequential treatment regimens.

Starting from week 13 of treatment, slight and temporary fluctuations in QMG and MG-ADL scores were observed in some patients. These changes may be attributed to the prolonged dosing interval of telitacicept and the concurrent tapering of corticosteroids. Statistical analysis revealed no significant differences in QMG and MG-ADL scores between weeks 13 and 28. Thus, while extending the dosing interval may cause short-term variations, it does not appear to significantly impact overall treatment outcomes. Considering the high cost and limited availability of the medications, our case series could serve as a preliminary reference for their clinical application. However, further validation through long-term follow-up and larger controlled trials is essential to substantiate these findings.

Our findings regarding immunoglobulin levels align with previous studies, showing a sustained decline in IgA and IgM levels during telitacicept treatment. While IgG levels generally exhibited a downward trend, they increased as the dosing interval for telitacicept was extended. The rapid IgG clearance effect of efgartigimod, combined with telitacicept's efficacy in reducing IgG levels, suggests that the sequential treatment did not result in a synergistic decrease in IgG, indicating a relatively

safe profile for this regimen. However, due to the limited sample size, further studies with larger cohorts and longer follow-ups are needed to validate this trend. Additionally, the relationship between IgG levels and MG symptoms remains unclear. The proportion of CD19+ B cells initially increased following efgartigimod treatment but showed an overall decline during telitacicept therapy. While this pattern is consistent with prior research, further studies are needed to clarify its underlying mechanisms and potential association with disease progression. Although this study did not establish a direct link between immunological biomarkers and symptom relief in MG, the observed immunological changes may provide mechanistic insights for future research. Despite extensive research on BAFF and APRIL, many questions remain unresolved. Compared to healthy individuals,[20,34] MG patients in our study exhibited elevated levels of both BAFF and APRIL. The effect of the combined therapy on these levels is not yet understood.

Previous studies have shown a decrease in BAFF and APRIL following telitacicept administration. However, in our study, serum BAFF levels increased severalfold from week 4 onward and remained elevated, despite continued clinical improvement. One possible explanation is negative feedback regulation of the immune system, given the initial increase in CD19+ B cells. Another potential factor is sample testing variability, as different forms of BAFF and APRIL exist in circulation, and BAFF-telitacicept complexes may have been detected. These findings suggest that more precise biomarkers are needed to accurately assess telitacicept's therapeutic effects. Additionally, our study highlights the distinct role of FcRn antagonists in MG treatment. Efgartigimod primarily functions by reducing IgG levels, with limited direct effects on B cell populations. The Phase 2 study on pemphigus[35] reported a mild decline in B cells during efgartigimod treatment, while other case reports and case series[36,37] have suggested partial effects on B cells. However, these findings are difficult to compare due to variability in concurrent immunosuppressant use, treatment duration, and dosage differences. Overall, the impact of efgartigimod on B cell function appears to be minimal, reinforcing the need for sequential therapy with telitacicept, which directly targets B cell survival and differentiation pathways. This rationale underscores the therapeutic strategy of combining FcRn antagonists with B cell-targeted agents to achieve more comprehensive and sustained immunomodulation in MG.

In this study, we included both early-onset MG (EOMG) and late-onset MG (LOMG) patients. Although not specifically designed to compare these subtypes, both groups demonstrated favorable clinical improvement with sequential efgartigimod-telitacicept therapy, as reflected by significant reductions in QMG and MG-ADL scores. EOMG is typically associated with thymic hyperplasia and higher anti-AChR antibody prevalence, whereas LOMG is characterized by thymic atrophy and increased antibodies against striated muscle antigens such as titin.[1] Whether these factors influence the response to FcRn and BAFF/APRIL-targeted therapies warrants further investigation.

Our study acknowledges several limitations that warrant consideration. Efgartigimod functions as an IgG-clearing agent, and its co-administration with telitacicept may affect the concentration of telitacicept due to it containing IgG Fc fragment and may be protected by FcRn. Considering the half-life of Efgartigimod and telitacicept, as well as the duration of Efgartigimod's efficacy and the drug onset time of telitacicept, we chose to administer telitacicept at one - week interval subsequent to the administration of Efgartigimod. The optimal dosing interval for bridging efgartigimod and telitacicept necessitates further investigation through rigorous controlled and PK/PD studies. Additionally, as a retrospective study, our research is susceptible to biases and confounding factors. The rarity of MG complicates patient inclusion, and the high costs associated with targeted therapies further restrict sample size, ultimately affecting the robustness of our findings. Furthermore, our study cohort primarily consisted of mild to moderate gMG cases, as these patients were deemed more suitable for evaluating the safety and initial efficacy of this novel regimen. Further studies are needed to explore its efficacy in patients with higher disease burdens. Moreover, while our study demonstrated a favorable safety profile, there is a potential risk of underreporting AEs. Less obvious side effects or recall bias may have led to incomplete AE documentation, which is a common challenge in retrospective studies. Finally, the relatively short follow-up period limits the generalizability of our findings, particularly regarding long-term efficacy and safety. While positive short-term outcomes were observed, further studies with extended follow-up are needed to confirm the durability of treatment effects and assess long-term safety. The low comorbidity burden in our study population also represents a limitation. A recent study found that 86% of MG patients have at least one comorbidity,[38] which may influence treatment efficacy and tolerability.[39] As a result, the applicability of this regimen to patients with a higher comorbidity burden remains unclear. Consequently, larger and more comprehensive prospective controlled trials are essential to replicate and validate our results, ensuring more reliable conclusions about the efficacy and safety of this combination therapy.

Conclusion

In our center's preliminary treatment experience, the sequential administration of efgartigimod and telitacicept supported potential benefits during the observation period, including a reduction in the severity of symptoms of gMG and the maintenance of disease stability. Furthermore, this combined therapeutic approach may help reduce the use of corticosteroids and reliance on traditional immunosuppressive agents. These findings provide preliminary evidence supporting the efficacy and feasibility of this regimen in clinical practice. However, larger-scale studies are required to confirm these results, further assess the long-term safety and effectiveness of this treatment strategy, and explore its impact on improving patients' quality of life.

Ethical Approval

The study protocol was found to comply with the ethical principles outlined by the National Health Commission's "Regulations on Ethical Review of Biomedical Research Involving Humans" (2023), the WMA Declaration of Helsinki, and the CIOMS International Ethical Guidelines for Biomedical Research Involving Humans. The project was approved by the ethics committee with the reference number KY2024-298.

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.

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Disclosure

The authors report no conflicts of interest in this work.

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