Review

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Current status and challenges of biologic targeted therapy for myasthenia gravis in China

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SUMMARY: Myasthenia gravis (MG) is an autoimmune neuromuscular disorder posing substantial disease burden in China, with significant impacts on patient quality of life. While conventional immunosuppressants remain fundamental therapy, biologic targeted agents—including B-cell targeting drugs, complement C5 inhibitors, FcRn antagonists, and IL-6R inhibitors—have brought major advances, especially for refractory and MuSK-antibody–positive MG. Increasing availability in China has demonstrated promising clinical outcomes, yet substantial barriers remain. Challenges include high drug costs, limited insurance access, insufficient multicenter clinical evidence, and disparities in physician adoption. China's research is improving, exemplified by local innovation with telitacicept and active participation in global trials, though most biologics remain imported. To maximize benefits, clinical application should be guided by antibody subtype and immunopathology, with individualized, dynamic regimens balancing efficacy, safety, and affordability. High-quality randomized trials, updated guidelines, broader insurance coverage, and R&D investment are urgently needed to promote individualized and accessible MG care in China.

Keywords: myasthenia gravis, biological targeted therapy, FcRn antagonist, C5 inhibitor, chimeric antigen receptor T-cell therapy

1. Introduction

Myasthenia gravis (MG) is an acquired autoimmune disease affecting the neuromuscular junction, characterized by fluctuating muscle weakness and fatigability (*1*). It is caused by autoantibodies that attack components of the neuromuscular junction (NMJ). About 85% of patients have antibodies against the nicotinic acetylcholine receptor (AChR), while the rest mainly have antibodies to muscle-specific kinase (MuSK) or lipoprotein receptor-related protein 4 (LRP4). A small proportion lacks detectable antibodies and is classified as seronegative MG (SNMG) (*2*).

Conventional immunosuppressive treatments, such as glucocorticoids, azathioprine, tacrolimus, and mycophenolate mofetil, can achieve good symptom control in most patients (*3,4*). However, about 20% of patients fail to respond to or cannot tolerate conventional treatments, thus becoming refractory MG (*5*). And 10–20% of patients may have acute onset with rapidly worsening symptoms like dysphagia and weakness in swallowing, chewing, limbs, or neck, which may lead to myasthenic crisis (MC) (*5,6*). These patients often experience significantly impaired quality of life and functional prognosis due to recurrent relapses, drug side effects, and long-term immunosuppressive status.

In recent years, the clinical application of biological targeted therapy has brought new breakthroughs in the treatment landscape of MG. Targeted drugs represented by B cell depleting agents (Rituximab and Inebilizumab) (*7,8*), complement C5 inhibitors (eculizumab, ravulizumab and zilucoplan) (*9-11*), and FcRn inhibitors (efgartigimod, rozanolixizumab, batoclimab and nipocalimab) (*12-15*) have shown favorable efficacy and safety in studies.

In China, some biological agents have been gradually applied in clinical practice, and preliminary results indicate that they have good effects in patients with refractory MG and MuSK antibody-positive MG, providing a new option for patients who do not respond significantly to conventional treatments. However, China still faces many challenges in the promotion of biological targeted therapy for MG, including insufficient independent research and development, high treatment costs, limited medical insurance coverage, and lack of multi-center clinical research data. Therefore, this article aims to review the current status and challenges of biological targeted therapy for MG in China, which is of great significance for promoting standardized and precise treatment.

2. Disease burden of MG in China

The annual incidence of MG in China is about 0.68 per 100,000 population, with a prevalence of 7.3 per 100,000. Nationwide, the total number of patients is estimated at approximately 650,000 (*16,17*). The median length of hospital stay was 8 days with median hospitalization cost US$1,037 (*16*). A recent Chinese nationwide registry-based study indicated the median annual direct medical cost was US$2,219.0, with a median of US$1,860.2 contributed by medical costs and a median of US$248.2 for non-medical costs (*18*).

Despite the continuous advancement of treatment methods, the mortality rate associated with MG remains at a relatively high level. Limited evidence showed the crude mortality rate of MG varied from 0.43 to 2.7 per million people over the past three decades. A national population-based study in China indicated that the age-standardized mortality rate of MG was 1.86 per million people and markedly higher in males than in females (2.37 *vs.* 1.31 per million). The median age at death from MG was 59.45 years, significantly lower than that in the general population (75.47 years) (*19*).

MG has a significant impact on the quality of life of both patients and caregivers. The overall quality of life (QoL) scores for patients with MG are lower than those of the general population, with significant impairments particularly evident in physical functioning and daily activities. Greater disease severity, as reflected by higher MG-ADL and QMG scores, is associated with a poorer quality of life. Patients with less social support and greater economic burden experience a more pronounced decline in QoL (*20*). A cross-sectional study conducted in China showed that approximately one-third of patients exhibited clinically significant fear of disease progression (FoP), which is higher than that observed in some other chronic disease populations. Higher FoP was more likely in patients with more severe MG, shorter disease duration, higher levels of anxiety and depression, lower levels of social support, and among female patients (*21*). Additionally, a recent study investigated the family burden experienced by caregivers of patients with MG in Northwest China. The results showed that a significant proportion of caregivers reported notable family burden, with financial strain and daily activity disruption being the most prominent (*22*).

Although most patients with MG can be definitely diagnosed based on clinical symptoms, antibody tests, and repetitive nerve stimulation (RNS), certain atypical presentations are prone to misdiagnosis. These mainly include distal limb weakness, onset confined to bulbar muscles, unilateral or asymmetric manifestations, as well as initial symptoms of non-specific manifestations such as respiratory failure. These features can easily lead to clinical misdiagnosis as stroke, myopathy, peripheral neuropathy, or amyotrophic lateral sclerosis (*23*).

In China, taking a comprehensive approach that includes medical staff education, standardized diagnosis procedure and auxiliary examinations, patient education, and multidisciplinary collaboration can significantly reduce misdiagnosis and missed diagnosis of MG, facilitating early diagnosis and treatment, and thereby improving patient prognosis.

3. Immunopathological mechanisms of MG

The emergence of biologic targeted therapies has been driven by a deeper understanding of the immunopathological mechanisms of MG. According to current immunological perspectives, thymic abnormalities (such as thymic hyperplasia or thymoma) result in aberrant expression of acetylcholine receptor (AChR) or related antigens within the thymus. In this context, self-reactive $CD4^+$ T cells escape central tolerance mechanisms and are activated by AChR antigen-presenting cells (such as dendritic cells and macrophages). These antigen-presenting cells process AChR peptides and present them to naïve $CD4^+$ T cells, thereby initiating T cell activation (*24*).

Activated $CD4^+$ T cells (primarily Th1 and Th17 subsets) facilitate B cell activation by providing secondary signals through cell surface molecule interactions and secretion of various pro-inflammatory cytokines. Additionally, the increased number and enhanced function of Th17 cells, coupled with impaired Treg function, lead to dysregulation of the immune regulatory network, further promoting persistence and progression of autoimmune responses (*25*).

With T cell help, self-reactive B cells recognizing self-antigens such as AChR become activated and subsequently proliferate and differentiate within germinal centers into memory B cells and long-lived plasma cells. Interleukin-6 (IL-6) serves as a key cytokine, promoting B cell differentiation into antibody-secreting cells while simultaneously inhibiting Treg cell generation and function (*26*). The differentiated plasma cells migrate to the bone marrow or inflamed tissues, where they continually produce high-affinity anti-AChR and other autoantibodies (anti-MuSK antibodies).

After AChR antibodies enter the circulation and reach the neuromuscular junction, they disrupt synaptic transmission *via* multiple mechanisms: *i*) upon binding to AChR, they activate the complement cascade (especially the C5b-9 membrane attack complex), directly damaging the postsynaptic membrane; *ii*) they induce cross-linking and accelerated internalization and degradation of AChR, reducing the number of functional receptors; *iii*) they directly block acetylcholine binding sites, thereby interfering with neurotransmitter-receptor interactions (*27*).

In MuSK antibody-positive MG, the pathogenic mechanism differs somewhat. Anti-MuSK antibodies are primarily the non–complement-activating IgG4

subclass and mainly disrupt the post-synaptic membrane organization by blocking the agrin–LRP4–MuSK signaling pathway, affecting formation and stability of the neuromuscular junction, with less reliance on complement activation (*28*).

Understanding this complex cascade of immunopathological processes provides a theoretical basis for targeted interventions at various immune stages and explains why targeted therapies against B cells, FcRn, the IL-6 pathway and the complement system have demonstrated clinical efficacy in MG (Figure 1).

4. Progress in biological targeted therapy for MG in China

4.1. B-cell targeted therapies

As an anti-CD20 monoclonal antibody, Rituximab is currently off-label widely used in domestic clinical practice for the treatment of refractory generalized MG (gMG). Several Chinese prospective and retrospective studies have shown that low-dose Rituximab can alleviate patient symptoms, reduce the concurrent use of glucocorticoids, and achieve better treatment outcomes in patients with refractory gMG, especially patients with MuSK antibody appear to have an even better therapeutic response (*29-32*). Additionally, the use of low-dose Rituximab in new-onset gMG patients in China has also achieved favorable efficacy, and real-world research data support the findings of the RINOMAX study that Rituximab demonstrates superior efficacy over placebo in new-onset patients (*7,33,34*). Although there is a lack of support from high-level large, multicenter, prospective randomized controlled trials (RCTs), real-world data have demonstrated the efficacy of rituximab, and European treatment guidelines have recommended it as an alternative first-line option for gMG (*35*). However, a unified standard for individualized medication strategy for Rituximab has not yet been established, and further research is needed to explore an optimal treatment regimen.

Inebilizumab, an innovative anti-CD19 monoclonal antibody targeting B-cells and partial $CD19^{+}$ plasma cells, has completed a pivotal global Phase III clinical trial with positive results (*8*). Through more thorough B-cell depletion, this drug may provide more potent treatment for MG patients with high-titer antibodies. Inebilizumab has been approved in China for treatment of neuromyelitis optica spectrum disorder (NMOSD), but its indication for gMG is still under review by the National Medical Products Administration (NMPA).

Telitacicept is a dual-target recombinant fusion protein that blocks the BAFF (BLyS) and APRIL pathways, broadly suppressing B cells and antibody production. Due to positive results in pivotal phase II and III clinical trials, the drug was approved in China in 2025 for treatment of gMG (Phase III data have not yet been published) (*36*). This is the first biologic targeted therapy for gMG independently developed and approved for marketing in China.

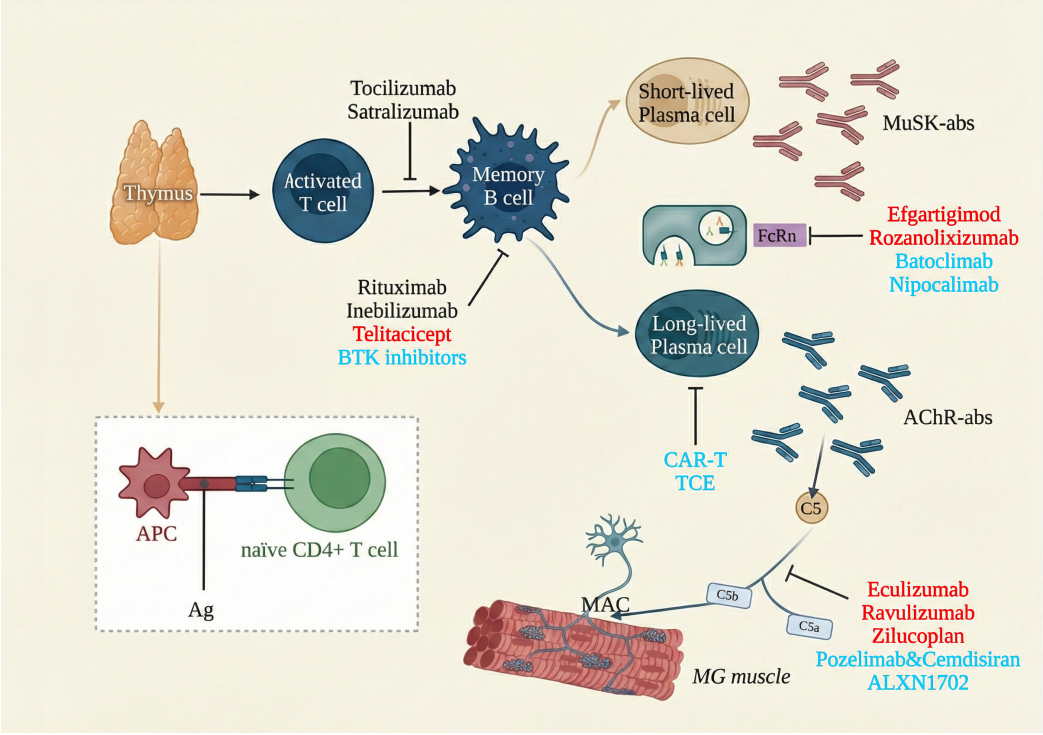

Figure 1. Schematic diagram of the immunopathological mechanisms of myasthenia gravis. APC: antigen presenting cell; Ag: antigen; MAC:membrane attack complex; CAR-T: chimeric antigen receptor T; TCE: T-cell engager. *Red-labeled agents*: biologic targeted drugs approved in China for the treatment of MG. *Black-labeled agents*: biologic targeted drugs approved in China for other indications and used off-label for MG.

4.2. Complement inhibitors

Eculizumab, the first C5 complement inhibitor, blocks terminal complement activation to protect the neuromuscular junction, reduce AChR loss, and improve neuromuscular transmission. It was approved in China in 2023 for the treatment of refractory AChR-positive gMG. Several Chinese prospective observational studies showed favorable efficacy and good tolerability in myasthenic crises, and thymoma-associated MG (TAMG) (*37,38*). Other case reports indicate that eculizumab can be used in special situations such as those involving severe infections and pembrolizumab-induced impending crisis (*39,40*).

Another C5 complement inhibitor, ravulizumab, has been approved in China in 2025 and is soon to be applied in clinical practice. As a long-acting C5 inhibitor, ravulizumab requires maintenance dosing only every 8 weeks after the loading dose (compared to every 2 weeks for eculizumab), which significantly reduces frequency of infusions and associated healthcare burden (*10*). Zilucoplan is a subcutaneously injected macrocyclic peptide targeting C5 with demonstrated efficacy and good safety in global Phase III trials (*11*). As a peptide inhibitor, its binding site differs from that of monoclonal antibodies, offering potential inhibitory advantages against certain C5 variants—such as the p.Arg885His mutation reported in PNH—that limit monoclonal antibody binding (*41*). Zilucoplan has already submitted a marketing application to the NMPA and is expected to receive approval to enter the Chinese market in 2026.

4.3. FcRn antagonists

FcRn binds to IgG within endosomes, mediating recycling and prolongation of IgG half-life. FcRn antagonists bind to FcRn with high affinity, competitively inhibiting the binding and recycling of IgG—including pathogenic autoantibodies such as anti-AChR/MuSK IgG—thereby leading to reduced circulating total IgG levels and decreased titers of pathogenic autoantibodies. FcRn antagonists have become a new milestone in the treatment of gMG. Efgartigimod (Fc fragment) and rozanolixizumab were approved in China in 2023 and 2025, respectively. Multiple real-world studies from China have explored use of efgartigimod in myasthenic crisis, impending crisis, TAMG, new-onset MG, ocular MG, and seronegative MG, providing Chinese evidence for application of efgartigimod in different subtypes of MG patients (*42-47*). However, experience with rozanolixizumab in China is still very limited, and there are currently no relevant data.

Both batoclimab and nipocalimab are monoclonal antibodies targeting FcRn. Their pivotal phase II and III clinical trials have yielded positive results (*13,15*), and both have already been submitted for pre-market review to the NMPA. Notably, the registration clinical trial for batoclimab was conducted independently in China, and it is the first published drug in China to demonstrate positive results in RCT for the treatment of gMG.

4.4. IL-6R inhibitors

Satralizumab is a humanized monoclonal antibody administered *via* subcutaneous injection that binds to and blocks both membrane-bound and soluble IL-6 receptors (IL-6R), thereby inhibiting both the classical and trans-signaling pathways of IL-6 and reducing downstream inflammatory and immune activation signals such as JAK/STAT. A recent phase III clinical study involving China demonstrated that satralizumab is well tolerated and, compared with placebo, led to modest improvements in both patient-reported and clinician-assessed outcomes at week 24 in patients with AChR antibody positive gMG (*48*). It has been approved for the treatment of NMOSD in China, but Roche terminated the open-label extension study after the phase III trial, possibly due to the perception that its efficacy was not sufficiently remarkable.

Additionally, two prospective cohort studies conducted in China have indicated that another IL-6R inhibitor, Tocilizumab, can improve symptoms of gMG and reduce dosage of glucocorticoids. However, the use of IL-6R inhibitors in treating gMG in China is considered off-label, and further evidence is needed to support their efficacy (*49,50*).

4.5. Frontiers in cell therapy

China has made rapid progress in the field of cellular immunotherapy such as Chimeric Antigen Receptor T (CAR-T) cell therapy, and some projects have taken the lead in clinical exploration for MG. Zhang *et al.* used bispecific BCMA/CD19-targeted CAR-T cell therapy to treat a case of refractory AChR-MG, achieving significant and sustained efficacy with no occurrence of severe cytokine release syndrome or neurotoxicity (*51*). Tian *et al.* used BCMA9-targeted CAR-T cell therapy to treat one case of refractory AChR-MG and one case of refractory MuSK-MG, both of which demonstrated significant and durable efficacy with favorable safety profiles (*52*). These valuable cases suggest that CAR-T therapy holds potential to provide a "functional cure" for MG.

4.6. China's active participation in global R&D of biologically targeted drugs

China's participation in global multi-center clinical trials of biologically targeted drugs has increased significantly. The ongoing phase III trials include Pozelimab/Cemdisiran (C5 inhibitor, Regeneron), ALXN1720 (C5 inhibitor,AstraZeneca), and Remibrutinib (BTK inhibitor, Novartis). A phase Ib clinical trial of a BCMA-

targeting bispecific T cell-engaging antibody (Cizutamig, Candid Therapeutics, Inc.) for the treatment of gMG is also ongoing. This proactive involvement has not only accelerated local adoption of innovative drugs but also enhanced China's international influence in the field of neuroimmunology. In the future, as more domestic enterprises join global research and development networks, China is poised to transform from a "follower" to a "leader", contributing Chinese expertise to treatment of rare diseases worldwide.

At present, targeted therapeutic drugs approved for marketing in China have formed two core therapeutic directions: complement C5 inhibitors and FcRn antagonists. According to the latest data in September 2025, 6 targeted drugs have been approved for the treatment of gMG, and another 3 drugs are under review by the NMPA (Table 1 and Table 2).

5. Challenges and perspectives

5.1. Optimizing the clinical application of conventional and biologic targeted therapies

Conventional agents (including corticosteroid and other immunosuppressants) still remain as fundamental status in MG, but the cumulative risks associated with long-term use—particularly infections—should not be overlooked. The advent of biologic targeted therapies has expanded precision treatment and partially reshaped the treatment landscape; however, stratified, population-specific guidance for Chinese patients is still lacking. Inappropriate combination regimens may increase adverse events and financial burden. One of the main challenges at present is how to optimize conventional therapies and biologic targeted therapies in the context of balancing economic considerations and clinical efficacy.

Combination therapy should be based on MG immunopathology. FcRn antagonists and complement

Table 1. Biological targeted drugs approved for marketing in China for gMG

Drug Name	Mechanism of Action	Indication	Approval Time	Route of Administration
Efgartigimod	FcRn antagonist	Used in combination with conventional drugs for the treatment of adult patients with AChR antibody positive gMG	July 2023	Subcutaneous / Intravenous
Rozanolixizumab	FcRn antagonist	Used in combination with conventional drugs for the treatment of adult patients with AChR antibody or MuSK antibody positive gMG	May 2025	Subcutaneous
Eculizumab	Complement C5 inhibitor	Used for the treatment of adult patients with refractory AChR antibody positive gMG	June 2023	Intravenous
Ravulizumab	Complement C5 inhibitor	Used in combination with conventional drugs for the treatment of adult patients with AChR antibody positive gMG	April 2025	Intravenous
Zilucoplan	Complement C5 inhibitor	Used in combination with conventional drugs for the treatment of adult patients with AChR antibody positive gMG	Oct 2025	Subcutaneous
Telitacicept	BLyS/APRIL dual-target fusion protein	Used in combination with conventional therapy for the treatment of adult patients with gMG	May 2025	Subcutaneous

Data Source: https://www.nmpa.gov.cn/

Table 2. Biological targeted drugs for gMG under review by NMPA

Name	Mechanism of Action	Indication	Review Stage	Clinical Trial Progress
Batoclimab	FcRn antagonist	Used in combination with conventional drugs for the treatment of gMG	New Drug Application (NDA) submitted	Phase III clinical trial was completed in January 2023, results have been published, showing significant efficacy
Inebilizumab	Anti-CD19 monoclonal antibody	Treatment of adult patients with AChR antibody positive gMG	New Drug Application (NDA) submitted	Results of the global pivotal Phase III MINT trial have been published, showing significant efficacy
Nipocalimab	FcRn antagonist	Used in combination with conventional therapeutic drugs for the treatment of adult patients with gMG	New Drug Application (NDA) submitted	Results of the global pivotal Phase III Vivacity-MG3 trial have been published, showing significant efficacy

Data Source: https://www.nmpa.gov.cn/; data up to Nov 27, 2025.

C5 inhibitors can rapidly and substantially improve symptoms in AChR-positive gMG, yet their targets lie downstream and do not directly deplete upstream memory B cells or plasma cells responsible for autoantibody production. Although efgartigimod may exert an "educational" effect on upstream immune networks (*53,54*), current data suggest this effect is insufficient to reconstitute B-cell compartments or restore immune homeostasis. In clinical practice in China, FcRn antagonists or C5 inhibitors are often used for weeks to months during the acute or induction phase, combined with low-dose glucocorticoids and/or nonsteroidal immunosuppressants. Once stable, biologics are tapered or discontinued while conventional therapies are continued. This approach reflects a concurrent use of upstream conventional agents with downstream biologics. Relevant Investigator-initiated trials (IITs) are ongoing and are expected to refine clinical decision-making. For refractory MG with poor response to conventional therapy, B-cell–targeting agents or C5 inhibitors may be prioritized, though optimal dosing and duration remain to be defined. If response to available biologics is inadequate, participation in CAR T-cell therapy trials may be considered.

Treatment decision making should be guided by antibody subtype (AChR, MuSK, LRP4), clinical classification (ocular *vs.* generalized), and thymoma status. A stratified and rational combination of conventional drugs and biologics, with dynamic assessment of efficacy and safety, is essential to achieve individualized care. In the future, a biomarker-driven, subtype-based therapeutic framework with adaptive strategy adjustment will be vital to realizing precision medicine.

5.2. Restrictions on accessibility and affordability

Biologic targeted therapies offer meaningful clinical benefit, but high costs and limited medical insurance reimbursement restrict access for some patients. Even after efgartigimod entered the reimbursement list, patients still bear approximately 20–30% out-of-pocket costs, and those in economically disadvantaged rural or remote regions may have no practical access.

Delays in updating the National Reimbursement Drug List (NRDL) have also widened disparities to access. Rozanolixizumab is a humanized monoclonal antibody approved and launched in China for MG. However, although eligible MuSK-MG patients meet the clinical indications, they currently cannot obtain reimbursement because the drug has not yet been listed in the NRDL. There is an urgent need to accelerate the inclusion of novel biologic agents in the NRDL and to explore diversified payment models—such as basic medical insurance combined with commercial insurance—to reduce patients' financial burden and improve equitable access.

5.3. Lack of high-quality evidence

The current evidence base for the treatment of MG in China remains limited. Most available studies are small-sample, retrospective analyses rather than RCTs. For example, domestic investigation of tocilizumab in refractory MG is a single-center cohort study with inadequate sample sizes and insufficient long-term follow-up.

Furthermore, systematic evaluations of how genetic diversity within the Chinese population influences therapeutic efficacy of biological targeted therapy have not been conducted, constraining localization of existing guidelines. Lack of real-world registry studies also impedes development of efficacy prediction models and advancement of individualized treatment strategies. There is an urgent need to establish a national MG database and to initiate high-quality, multidisciplinary RCTs to address evidence gaps and standards of care tailored to Chinese patient characteristics.

5.4. Lag in physicians' practice and academic consensus

There are marked regional disparities in management of MG across China. Tertiary centers in major cities have broadly adopted biologic targeted therapies, whereas primary healthcare institutions largely rely on conventional regimens and demonstrate limited awareness of novel agents such as FcRn antagonists. Although an updated Chinese clinical practice guideline was released in 2025 (*55*), many clinicians have not yet integrated these advances into routine care and remain uncertain about treatment selection.

To address these gaps, it is essential to strengthen academic training and disseminate the latest guidelines through national continuing medical education programs, while establishing regional multidisciplinary platforms to support experience sharing. In parallel, consensus-building among Chinese experts on the use of biologic targeted therapies in MG is needed to clarify treatment prioritization and monitoring indicators across MG subtypes, thereby narrowing disparities in treatment.

5.5. Challenges in innovative Drug R&D for Chinese biotechs

Among drugs approved or under review in China for the treatment of MG, only telitacicept represents a domestically originated innovation. Moreover, of the many RCTs conducted to date, telitacicept and batoclimab remain the sole two studies completed independently in China. Collectively, these observations highlight current limitations in China's research and development capacity for biologic targeted therapies.

This embarrassing situation is due to inadequate accumulation of cutting-edge originality and core technologies. Owing to longstanding dependence on

clinical demand–driven and generic drug pathways, independent innovation capabilities remain relatively limited, with suboptimal investment in basic research and world-leading breakthrough technologies. As a result, "me-too" and "me-better" drugs continue to dominate the market, while truly first-in-class or best-in-class innovative therapies remain uncommon.

Additionally, the evolving policy landscape, difficulties in market access, and complexities of internationalization further challenge Chinese biotechs innovators. Ongoing adjustments in areas such as drug review, pricing, and reimbursement constrain promotion and payment for new therapies and elongate return cycles. At the same time, the overseas regulatory registration, intellectual property barriers, and limited access to global collaborative resources collectively heighten competitive pressures on Chinese biotechs in the global high-end pharmaceutical innovation arena.

6. Conclusion

Biologic targeted therapies have reshaped the MG management landscape in China, offering new hope for refractory patients. However, optimizing clinical use, improving access and affordability, investing in domestic innovation, and generating robust local evidence remain critical for achieving equitable and precise MG treatment nationwide.

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