Zilucoplan treatment of severe exacerbations leading to hospitalization in generalized myasthenia gravis: Study design

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Poster 25

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Summary and conclusions

This Phase 3b, open-label, multicenter, interventional study (NCT07215949) will evaluate the efficacy and safety of zilucoplan in adult patients with anti-AChR Ab+ gMG who are experiencing severe gMG exacerbations requiring hospitalization

Zilucoplan has the potential to rapidly alleviate the most severe symptoms of gMG, and could be a treatment option for adult patients with severe exacerbations beyond IVIg and PLEX

Objective

The objective of this Phase 3b, open-label study is to evaluate the efficacy and safety of SC zilucoplan in adult patients with anti-AChR Ab+ gMG who are experiencing severe exacerbations requiring hospitalization

Rationale

Patients with gMG may require hospitalization due to severe exacerbations, with symptoms that can progress to myasthenic crisis, a life-threatening complication often requiring ventilatory support[1]

The treatment goal for severe exacerbations is to rapidly reduce symptoms and avoid progression to myasthenic crisis

IVIg and PLEX are currently the SOC for severe exacerbations; however, while both may be effective, they often require prolonged hospital stays and are associated with other challenges[2]

Challenges with **IVIg**

- Supply relies on blood donors and shortages exist in some countries[2]
- Risk of venous thrombosis and pulmonary embolism[3]

Challenges with **PLEX**

- Requires specialized equipment that may only be available in large metropolitan areas[2]
- Requires the use of a central venous catheter with risk of trauma to the large bore vein, pneumothorax and/or infection[2,4]
- Risk of venous thrombosis and pulmonary embolism[3]

Zilucoplan is a complement C5 inhibitor approved for the treatment of adult patients with anti-AChR Ab+ gMG, and is self-administered once daily as an SC injection

In the Phase 3 RAISE study (NCT04115293), zilucoplan had a rapid onset of action with effects observed within the first week of treatment[5]

Given zilucoplan's rapid onset of action and less invasive SC administration, it may offer a viable alternative to IVIg/PLEX for adult patients with severe exacerbations, and case studies report its potential benefits in myasthenic crisis[6]

Patients

Adult patients who are experiencing severe exacerbations and meet the inclusion criteria will be offered SOC or study enrollment to receive zilucoplan

Inclusion criteria include:

- Anti-AChR Ab+ gMG
- MGFA Disease Class II–IVb
- Experiencing severe gMG exacerbation that requires hospitalization*
- ≥18 years of age
- MG-ADL score ≥6 (non-ocular domains)
- Meningococcal vaccinations complete, or vaccinate and start antibiotic prophylaxis†

Exclusion criteria include:

- Current use or failure of C5 inhibitors in previous 3 months
- IVIg or PLEX in previous 4 weeks
- Required intubation prior to enrollment

*For example, bulbar and/or respiratory symptoms or neck extension weakness, requiring hospitalization. †Patients must have completed meningococcal vaccinations (serogroups A, C, W, Y, and B) ≥2 weeks prior to the first dose of zilucoplan or must have updated boosters per current ACIP recommendations. For patients who have not completed or updated meningococcal vaccinations, vaccinations for serogroups A, C, W, Y, and B will be initiated as soon as possible and antibiotic prophylaxis given prior to the first dose of zilucoplan and continued until ≥2 weeks after vaccinations are completed; recommended antibiotic prophylaxis: penicillin 250 mg twice daily or erythromycin 250 mg twice daily.

The study will enroll approximately 15 patients and will be conducted at three sites in the US

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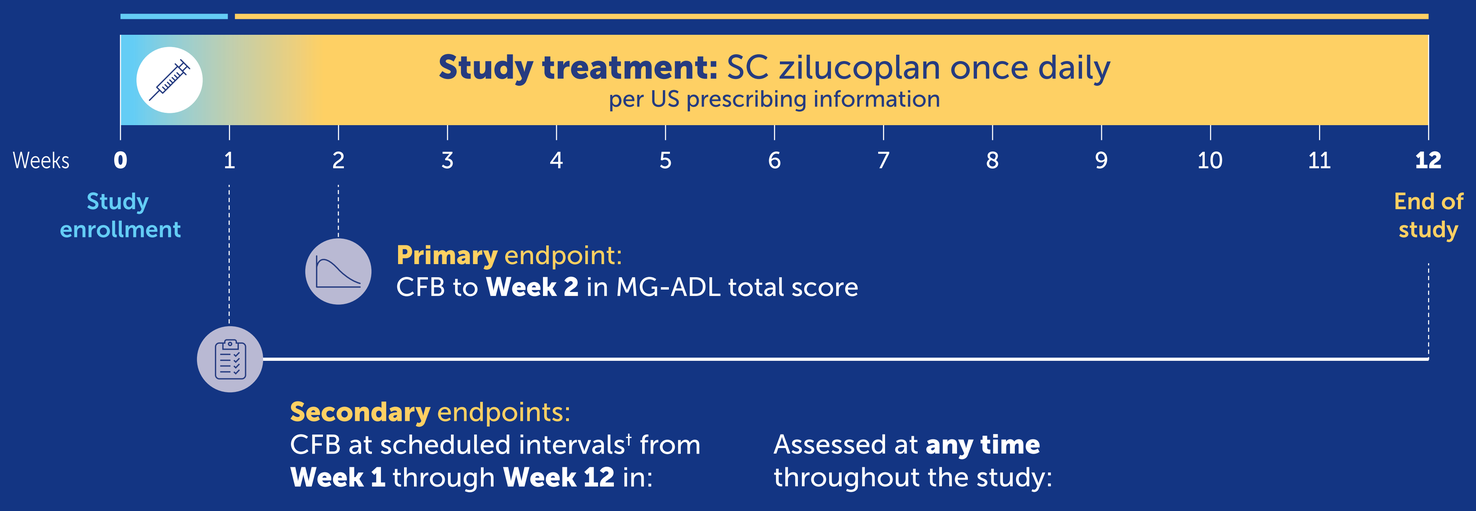
Study design

A Phase 3b, open-label, multicenter, interventional study of zilucoplan in adult patients with anti-AChR Ab+ gMG experiencing severe exacerbations requiring hospitalization

Patients will initially receive SC zilucoplan as an inpatient and, following discharge, will continue to receive SC zilucoplan as an outpatient for a total of 12 weeks

SC zilucoplan **inpatient***

SC zilucoplan **outpatient**



Secondary endpoints:
CFB at scheduled intervals† from **Week 1** through **Week 12** in:

- MG-ADL total score
- QMG total score‡
- MG-QoL15r total score
- Respiratory measures (FVC, NIF)§

Assessed at **any time** throughout the study:

- Need for intensive therapy (ventilation or feeding tube)
- Need for rescue therapy
- Safety and tolerability

Additional endpoints include:
Duration of hospital stay

*The duration of inpatient time will be flexible and depend on individual patient needs. †Weekly for inpatients or at Weeks 1, 2, 4, 8 and 12 during the outpatient period. ‡QMG will also be assessed at Days 1, 3 and 5 to evaluate the onset of response. §Inpatient only. Concomitant medications should not be changed during the study, unless medically necessary. Participants are expected to remain on stable dose regimens of SOC therapy for gMG throughout the study, including corticosteroids and NSISTs.

Abbreviations: Ab+, antibody positive; AChR, acetylcholine receptor; ACIP, Advisory Committee on Immunization Practices; C5, component 5; CFB, change from baseline; FVC, forced vital capacity; gMG, generalized myasthenia gravis; IVIg, intravenous immunoglobulin; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MG-QoL15r, Myasthenia Gravis Quality of Life 15-item revised; NIF, negative inspiratory force; NSIST, non-steroidal immunosuppressant therapy; PLEX, plasma exchange; QMG, Quantitative Myasthenia Gravis; SC, subcutaneous; SOC, standard of care; US, United States.

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