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A Phase 3 Study to Evaluate the Efficacy and Safety of Telitacicept in Patients With Generalized Myasthenia Gravis: Trial Design Update

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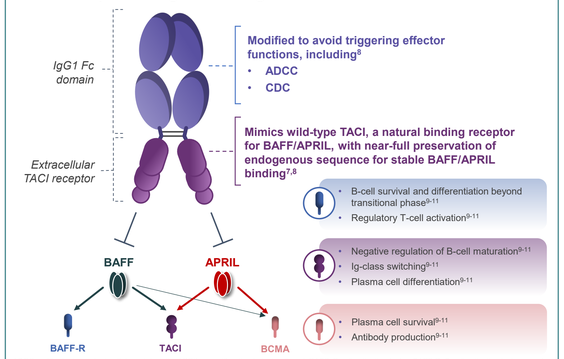
INTRODUCTION

- Myasthenia gravis (MG) is an autoimmune neuromuscular disease in which autoreactive B cells target the postsynaptic membrane of the neuromuscular junction[1]
- The predominant manifestation is fatigable weakness, which affects limb, respiratory, bulbar, and ocular muscle function[2]
- Current therapies for generalized myasthenia gravis (gMG) primarily manage symptoms, induce nonspecific immunosuppression, remove pathogenic antibodies, or block complement-mediated postsynaptic membrane damage but do not address the underlying drivers of disease pathophysiology[1,3,4]
- Telitacicept is a novel, fully human transmembrane activator and calcium-modulator and cyclophilin ligand interactor (TACI)-Fc fusion protein that targets B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL), two cytokines that play critical roles in B-cell development, maturation, and survival[5-8]
- Through this novel dual inhibition mechanism, telitacicept modulates upstream B-cell development and survival, which ultimately may reduce pathogenic autoantibodies implicated in autoimmune disease, including gMG (**Figure 1**)[6-8]

Figure 1. Telitacicept Is a Fusion Protein Based on the Human TACI Receptor Designed to Target BAFF and APRIL



ADCC, antibody-dependent cellular cytotoxicity; APRIL, a proliferation-inducing ligand; BAFF, B-cell activating factor; BAFF-R, B-cell activating factor receptor; BCMA, B-cell maturation antigen; CDC, complement-dependent cytotoxicity; Fc, fragment crystallizable; IgG, immunoglobulin G; TACI, transmembrane activator and calcium-modulator and cyclophilin ligand (CAML) interactor.

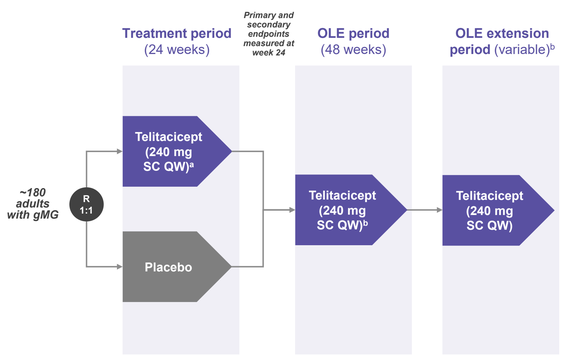
- Data from phase 2 (NCT04302103) and phase 3 (NCT05737160) studies of telitacicept conducted in China showed efficacy and safety in adults with acetylcholine receptor (AChR) autoantibody-positive gMG[12-16]
- In a phase 3 trial conducted in China, telitacicept demonstrated sustained efficacy and was well tolerated in patients with gMG, meeting its primary endpoint of change from baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL) score at week 24, with a change of -5.74 in the telitacicept 240 mg group and -0.91 in the placebo group (P<0.001)[15,16]
- Here, we present the study design of an ongoing, global, phase 3, double-blind, placebo-controlled study (NCT06456580) in adults with gMG to understand the effect of BAFF/APRIL inhibition by telitacicept in a heterogeneous population[17]

METHODS

Study Design

- UPSTREAM MG will randomize ~180 patients with gMG 1:1 to receive either placebo or telitacicept subcutaneously weekly (**Figure 2**)
- UPSTREAM MG will consist of a screening period of ≤4 weeks; a 24-week, double-blind, placebo-controlled phase; and a 48-week open-label extension (OLE)
  - This will be followed by an extended OLE period, which will have a variable duration, defined as after the OLE period until telitacicept is available or the further development in the indication is concluded (**Figure 2**)

Figure 2. Study Design



EOS, end of study; EOT, end of treatment; gMG, generalized myasthenia gravis; OLE, open-label extension; QW, once weekly; R, randomized; SC, subcutaneous. [a]For patients who discontinue treatment before the OLE period, EOT and EOS timepoints are at 24 and 32 weeks, respectively. For those not continuing with the OLE, EOT and EOS timepoints are at 72 and 80 weeks, respectively. [b]Patients who complete week 72 of the ongoing OLE and who, in the opinion of the investigator, continue to benefit from treatment and meet all eligibility criteria may enter the extended OLE and continue receiving open-label telitacicept. The duration of the extended OLE is variable, defined as after the OLE period until telitacicept is approved for myasthenia gravis in the country or the further development in the indication is concluded. This will allow ongoing dosing of patients upon completion of the OLE.

Endpoints

- The primary endpoint is the change from baseline in MG-ADL score at week 24
- Secondary efficacy endpoints include
  - Change from baseline in Quantitative Myasthenia Gravis (QMG) score at week 24
  - Change from baseline in MG Quality of Life 15-item Revised scale (MG-QOL15r) at week 24
  - Proportion of patients with a ≥2-point decrease in MG-ADL score at week 24
  - Proportion of patients with a ≥3-point decrease in QMG score at week 24
  - Proportion of patients who achieved minimal symptom expression (defined as having an MG-ADL score of 0 or 1) at week 24
- Incidence of adverse events and evaluation of other vital signs and safety laboratory measurements will also be used to assess the safety and tolerability of telitacicept

Eligibility Criteria

- Inclusion and exclusion criteria are outlined in **Figure 3**
- Eligible patients may also receive up to 2 stable concomitant medications (not counting cholinesterase inhibitors) for the treatment of gMG if they meet the stability criteria prior to baseline
  - Varying standard of care regimens will be allowed, including cholinesterase inhibitors, oral corticosteroids, and nonsteroidal immunosuppressive treatments
- Patients who have recently received prohibited immunosuppressants (pimecrolimus, vincristine, vinblastine, or cyclophosphamide) other than protocol-permitted stable concomitant medications, biologics, or other agents will be excluded
  - Washout periods will be required for prohibited medications including any prior biologic or intravenous immunoglobulin use
- Patients will be excluded if they have a chronic or acute infection

Figure 3. Inclusion and Exclusion Criteria

Key Inclusion Criteria

- 18+ Male or female aged ≥18 years at time of screening
- QMG score ≥8, with ≥4 items having a score ≥2 at screening and baseline
- Positive antibodies against AChR or MuSK at screening
- MG-ADL score ≥6 points at screening and baseline with ocular-related score <50% of the total score
- Prior confirmed diagnosis of gMG with generalized muscle weakness[a]
- Stable concomitant medications[b]
- Prior exposure to biologics (mAbs and fusion proteins) permitted with required washout

Exclusion Criteria

- Diagnosed with any other autoimmune disease, which can pose a safety or efficacy confounding risk
- Acute or chronic infection
- Thymoma within 5 years or received thymectomy ≤6 months prior to screening[c]
- Current or history of primary immunodeficiency
- History of malignancy within the last 5 years[d]
- Prior or continuing diagnosis of serious cardiovascular disease

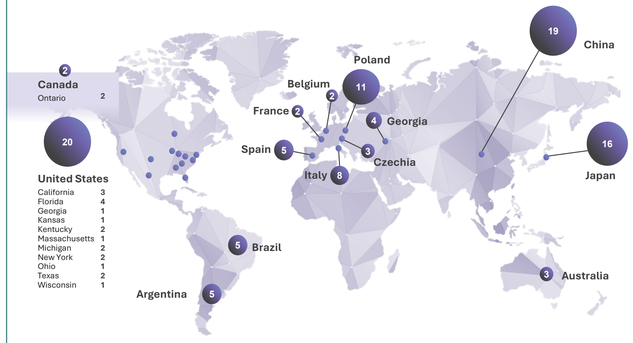
AChR, acetylcholine receptor; gMG, generalized myasthenia gravis; mAb, monoclonal antibody; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MuSK, muscle-specific kinase; QMG, Quantitative Myasthenia Gravis. [a]Typical pattern of weakness meeting the clinical criteria for diagnosis of myasthenia gravis as defined by the MGFA clinical classification II-IV. [b]Stable concomitant medications, with a limit of 2 (not counting cholinesterase inhibitors). Allowed medications include cholinesterase inhibitors, oral corticosteroids, and nonsteroidal immunosuppressive treatments. [c]However, patients with a thymoma diagnosed 3-5 years prior to screening may be eligible if the thymoma was at a localized stage and definitively treated with complete surgical resection. [d]Excludes adequately treated nonmelanoma skin cancer or any early-stage cancer considered cured with resection.

RESULTS

Study Locations

- Study enrollment is ongoing across 14 countries with top-line results anticipated in the first half of 2027
- Study locations are shown in **Figure 4**

Figure 4. Study Locations and Number of Sites



As of May 7, 2026.

CONCLUSIONS

- A global, phase 3, pivotal, multicenter, randomized, double-blind, placebo-controlled trial with a long-term OLE period is ongoing to evaluate the efficacy and safety of telitacicept in a global patient population
- Results from this study will augment the established efficacy and safety of BAFF/APRIL inhibition with telitacicept in a broader heterogeneous population

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Conflicts of Interest: **Kristl G. Claeys** has received speaker/advisory board honoraria from Alexion, Alnylam, Amicus, argenx, Biogen, CSL Behring, Ipsen, Janssen Pharmaceuticals, Lupin, Pfizer, Roche, Sanofi-Genzyme, UCB, and Vertex. **Francesco Saccà** has received public speaking honoraria from Alexion, argenx, Biogen, Genpharm, Johnson & Johnson, MedPharma, Medison Pharma, Neopharm Israel, UCB, and Zai Lab. He has also received compensation for advisory boards or consultation fees from Alexion, Amgen, argenx, AstraZeneca, AveXis, Biogen, Dianthus, Johnson & Johnson, Lexeo, Novartis GmbH, Reata, UCB, and Zai Lab. He is principal investigator in clinical trials for Alexion, argenx, Dianthus, Immunovant, Inc., Leadiant, Lexeo, Novartis, Prilenia, RemGen, and Sanofi. **Ali A. Habib** has received research support/honoraria from Alexion/AstraZeneca, Amgen, Arcelix, argenx, Cabaletta Bio, Cartesian, COUR Pharmaceuticals, GC Biopharma, Grifols, Immunovant, Inc., Janssen/Johnson & Johnson, Kyverna, Merck, MGNet (grant number: U54NS115054), Nkarta, NMD Pharma, Novartis, Regeneron, and UCB; has served on a Data and Safety Monitoring Board for Genentech/Roche, Immunis, and the National Institutes of Health (NIH)/National Institute of Neurological Disorders and Stroke; and has served on a Trial Steering Committee for Dianthus, Janssen/Johnson & Johnson, and Kyverna. **Richard J. Nowak** has received research support from Alexion Pharmaceuticals, argenx, Annexon Biosciences, Inc., Genentech Inc., Grifols, S.A., Immunovant, Inc., Momenta Pharmaceuticals, Inc. (now Janssen), Myasthenia Gravis Foundation of America (MGFA), NIH, Ra Pharmaceuticals, Inc. (now UCB S.A.), and Viela Bio, Inc. (Horizon Therapeutics, now Amgen Inc.). He has also served as a consultant and advisor for Alexion Pharmaceuticals, argenx, Cabaletta Bio, Inc., Cour Pharmaceuticals, Immunovant, Inc., Momenta Pharmaceuticals, Inc. (now Janssen), Ra Pharmaceuticals, Inc. (now UCB S.A.), Vor Bio, and Viela Bio, Inc. (Horizon Therapeutics, now Amgen Inc.). **Mamatha Pasnoor** is a University of Kansas site principal investigator for RemeGen MG trial; served as medical advisor or consultant for Alexion, Amgen, Annexon, argenx, BVBA, Catalyst, CSL Behring, Grifols, Immunovant, Inc., Jansen, Johnson & Johnson, Momenta, Takeda, and Terumo BCT; serves on the board of directors for the Myasthenia Gravis Association. **Gil I. Wolfe** serves as an advisor for Alexion, argenx, BPL, Canopy, Cartesian, Dianthus, Grifols, Johnson & Johnson, Takeda, and UCB and receives research support from Immunovant, Inc., Novartis, Roche, and Vor. **Tuan Vu** is a University of South Florida site principal investigator for MG clinical trials sponsored by Alexion/AstraZeneca Rare Disease, Amgen, argenx, Cartesian Therapeutics, COUR, Dianthus Therapeutics, EMD Serono, ImmunAbs, Immunovant, Inc., Johnson & Johnson, NMD Pharma, Novartis, Regeneron, UCB, and Vor. He has served as a speaker for Alexion/AstraZeneca Rare Disease, Amgen, argenx, and CSL Behring and participated on advisory boards for Alexion/AstraZeneca Rare Disease, Amgen, argenx, Dianthus Therapeutics, ImmunAbs, Johnson & Johnson, NMD Pharma, Regeneron, and Vor. **Jeremy Sokolove** is an employee of Vor Bio and owns company stock. **James F. Howard Jr** has received research funding (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, Merck EMD Serono, MGFA, Muscular Dystrophy Association, NIH, NMD Pharma, and UCB Bioscience. He has served as medical advisor or consultant for Alexion AstraZeneca Rare Disease, Amgen, argenx, Biohaven Ltd, Cartesian Therapeutics, CoreEvitas, Curie.bio, H. Lundbeck A/S, Japan Tobacco Company, Kyverna Therapeutics, Merck EMD Serono, NMD Pharma, Novartis Pharmaceuticals, Regeneron Pharmaceuticals, Seismic Therapeutics, TG Therapeutics, Tolerazia AB, and UCB Bioscience. He has received speaker fees from AcademicCME, CheckRare CME, PeerView CME, Physicians' Education Resource (PER) CME, and PlatformQ CME.

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