

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

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Introduction:

Generalized myasthenia gravis (gMG) is an autoimmune neuromuscular disease driven by autoreactive B cells. B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL) are required for B-cell development, differentiation, and survival. BAFF is a key player in the pathway to overcome negative selection of autoreactive B cells at immune checkpoints, allowing for the development of pathogenic B cells and autoimmunity. Telitacicept is a fully human, novel TACI-Fc fusion protein that binds soluble BAFF and APRIL, preventing binding to their receptors (TACI, BCMA, BAFF-R) on B cells. Phase 2 (NCT04302103) and 3 (NCT05737160) studies demonstrated efficacy/safety of telitacicept in Chinese adults with acetylcholine receptor autoantibody-positive gMG.

Objective:

To provide an update on the enrollment of the ongoing, global, phase 3 study (NCT06456580).

Methods:

The global study will enroll ~180 adults with confirmed gMG, a Myasthenia Gravis Activities of Daily Living (MG-ADL) score ≥ 6 with $< 50\%$ of the total score due to ocular symptoms, and Quantitative MG score ≥ 8 , with ≥ 4 items scoring ≥ 2 at screening and baseline. The study includes a 24-week double-blind treatment period with 1:1 randomization to subcutaneous telitacicept (240 mg) or placebo once weekly, followed by a 48-week open-label extension (OLE) period and a variable OLE extension period. The primary endpoint is change from baseline in MG-ADL score at week 24.

Results:

Study enrollment is ongoing across over 13 countries with top-line results anticipated mid-2027.

Conclusions:

Results from this global population of adults with gMG will augment the established efficacy and safety of BAFF/APRIL inhibition with telitacicept in a broader population.

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Disclosures:

1. Ali A. Habib has received research support/honoraria from Alexion/AstraZeneca, Amgen, Arcellx, argenx, Cabaletta Bio, Cartesian, COUR Pharmaceuticals, GC Biopharma, Grifols, Immunovant, Janssen/Johnson & Johnson, Kyverna, Merck, MGNNet (grant number: U54NS115054), Nkarta, NMD Pharma, Novartis, Regeneron, and UCB; has served on a Data and Safety Monitoring Board for Genentech/Roche, Immunis Biomedical, and the National Institutes of Health/National Institute of Neurological Disorders and Stroke; and has served on a Trial Steering Committee for Dianthus, Janssen, Johnson & Johnson, and Kyverna.
2. Mamatha Pasnoor is a University of Kansas site principal investigator for the RemeGen MG trial; served as medical advisor or consultant for Alexion, Amgen, Annexon, argenx, BVBA, Catalyst, CSL Behring, Grifols, Immunovant Pharmaceuticals, Janssen, Johnson & Johnson, Momenta, Takeda, and Terumo BCT; and serves on the board of directors for the Myasthenia Gravis Association (MGA).
3. 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, Johnson & Johnson, NMD Pharma, Novartis, Regeneron, UCB, and Vor Biopharma Inc. 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 Biopharma Inc.
4. Bhupendra O. Khatri is Medical Director at the Center for Neurological Disorders at Ascension St. Francis Hospital and has received speaker and consulting fees from Alexion, Biogen, Bristol Myers Squibb, EMD Serono, Genentech, Genzyme, Horizon, Novartis, Terumo BCT, TG Therapeutics, and UCB.
5. 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, Novartis, Roche, and Vor Biopharma Inc.
6. Amit Sachdev has served as Michigan State University site principal investigator for MG clinical trials sponsored by Alexion, AstraZeneca Rare Disease, argenx, COUR, Dianthus Therapeutics, EMD Serono, Immunovant, Johnson & Johnson, Novartis, UCB, and Vor Biopharma Inc. He has served as a speaker for Alexion, AstraZeneca Rare Disease, Amgen, and argenx and participated on advisory boards for Alexion, AstraZeneca Rare Disease, Amgen, and Johnson & Johnson.
7. Said Beydoun has received research support from Abcuro, AB Science, ALS Healey Center, Immunovant, Janssen, Novartis, Regeneron, RemeGen, and Sanofi and consulting and/or speaker honoraria from Alexion, Alnylam, Amgen, argenx, AstraZeneca, Catalyst, CSL Behring, Janssen, Pfizer, Takeda, and UCB.

8. George G. Li is a consultant for RemeGen Biosciences and is the investigator for this phase 3 study.
9. Shaída Khan is the site principal investigator for the RemeGen MG trial at UT Southwestern Medical Center. She also serves as a consultant for UCB.
10. Lawrence Meinert is an employee of Vor Biopharma Inc. and owns company stock.
11. Jeremy Sokolove is an employee of Vor Biopharma Inc. and owns company stock.
12. 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.
13. Francesco Saccà has received public speaking honoraria from Alexion, argenx, Biogen, Genpharm, Johnson & Johnson, Medison Pharma, Medpharma, 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, LediAnt, Lexeo, Novartis, Prilenia, Remgen, and Sanofi.
14. 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, Muscular Dystrophy Association, Myasthenia Gravis Foundation of America, National Institutes of Health, NMD Pharma, and UCB Biosciences. 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 Pharma, Regeneron Pharmaceuticals, Seismic Therapeutics, TG Therapeutics, Toleranzia AB, UCB Biosciences, and Vor Biopharma Inc. He has received speaker fees from AcademicCME, CheckRare CME, PeerView CME, Physicians' Education Resource (PER) CME, and PlatformQ CME.