

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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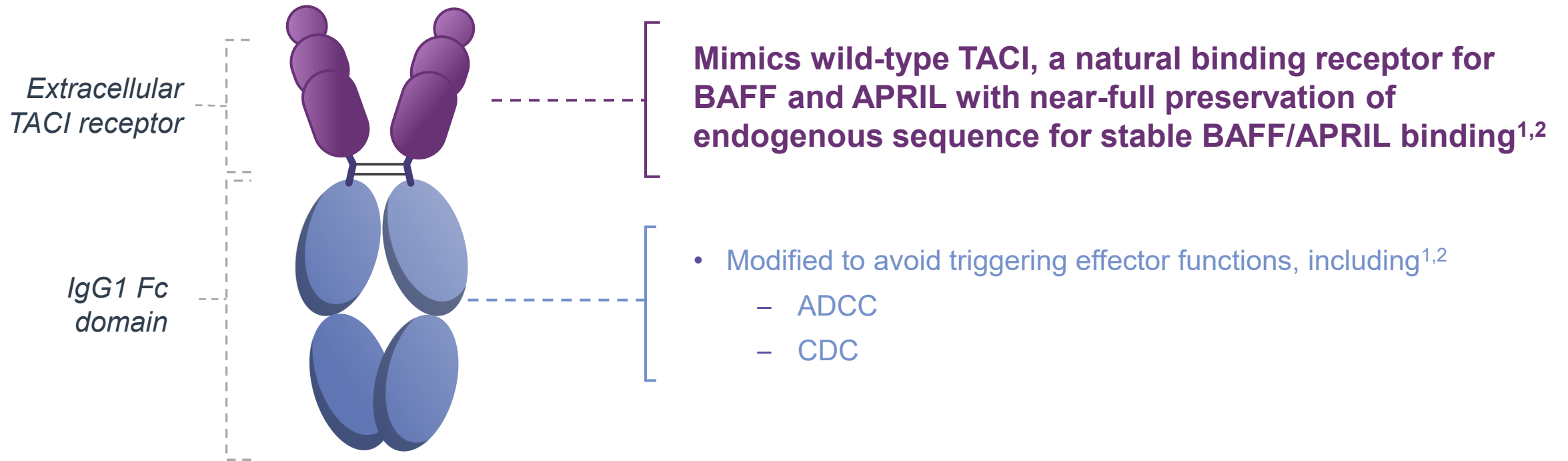
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Disclosures

- 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, MGNet (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.
- 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).
- 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.
- 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.
- 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.
- 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, Amgen, argenx, and AstraZeneca Rare Disease, and participated on advisory boards for Alexion, Amgen, AstraZeneca Rare Disease, and Johnson & Johnson.
- Said Beydoun has received research support from AB Science, Abcuro, 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.
- George G. Li is a consultant for RemeGen Biosciences and is the investigator for this phase 3 study.
- Lawrence Meinert and Jeremy Sokolove are employees of Vor Biopharma, Inc. and own company stock.
- Kristl G. Claeys has received speaker/advisory board honoraria from Alexion, Alnylam, Amicus, argenx, Biogen, CSL Behring, Ipsen, Janssen, Lupin, Pfizer, Roche, Sanofi-Genzyme, UCB, and Vertex.
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- 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.
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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; CDC, complement-dependent cytotoxicity; Fc, fragment crystallizable; IgG1, immunoglobulin G1; TACI, transmembrane activator and calcium-modulating ligand interactor.

1. Zeng L, et al. *J Autoimmun.* 2024;148:103291. 2. European Patent Agency. Patent EP3868403 A1.

Proposed Bifunctional Effect of Telitacicept: Modulates B-Cell Development and Autoantibody Production

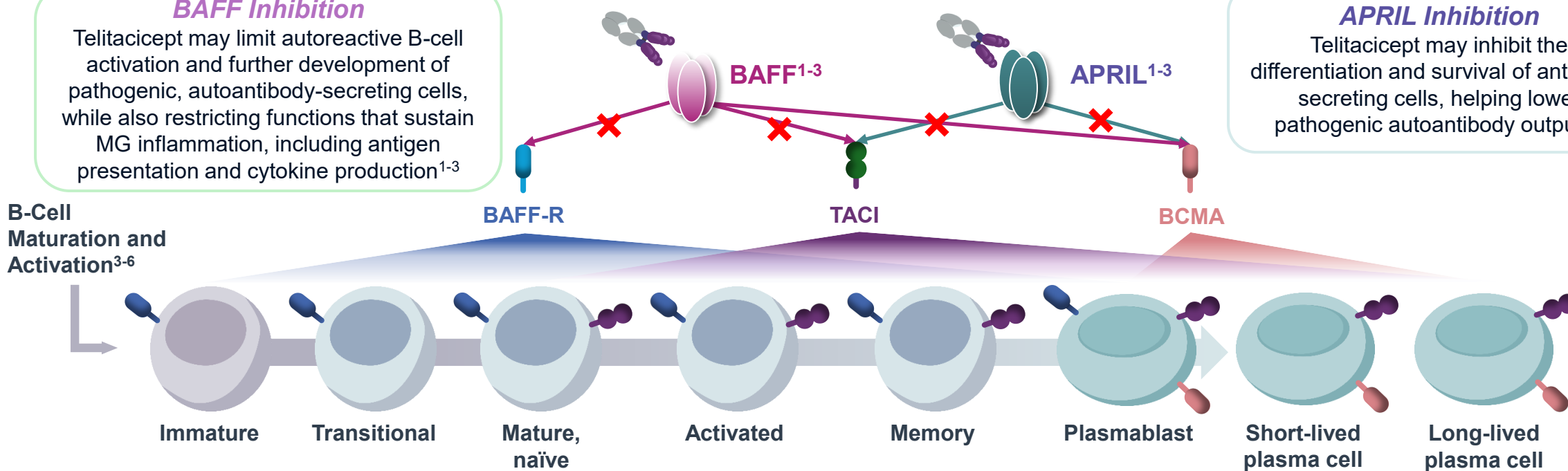
ONE MECHANISM, TWO EFFECTS

BAFF Inhibition

Telitacicept may limit autoreactive B-cell activation and further development of pathogenic, autoantibody-secreting cells, while also restricting functions that sustain MG inflammation, including antigen presentation and cytokine production¹⁻³

APRIL Inhibition

Telitacicept may inhibit the differentiation and survival of antibody-secreting cells, helping lower pathogenic autoantibody output¹⁻³

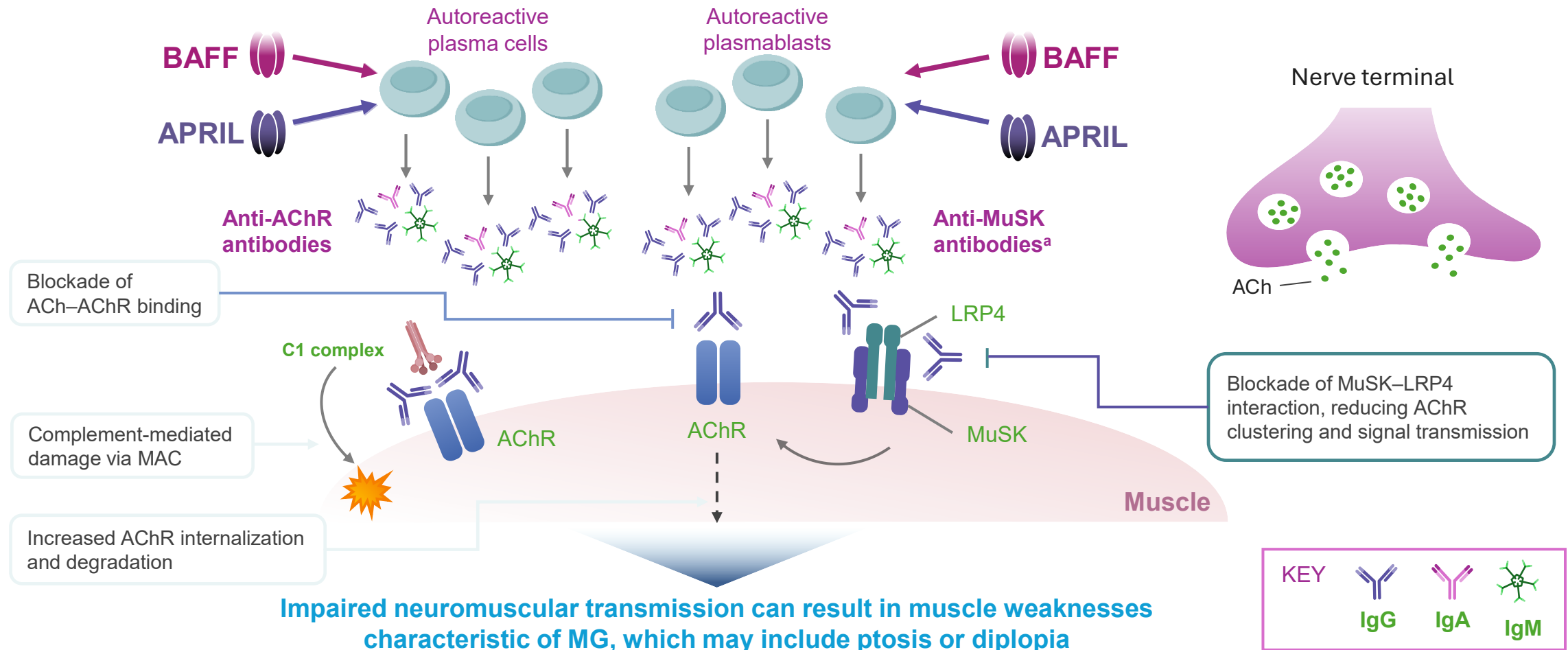


By blocking BAFF and APRIL binding, telitacicept is designed to modulate B-cell maturation and plasma cell survival signals, potentially reducing both autoantibody production and the proinflammatory functions of B cells that drive autoimmune disease^{1,3}

APRIL, a proliferation-inducing ligand; BAFF, B-cell activating factor; BAFF-R, B cell-activating factor receptor; BCMA, B-cell maturation antigen; MG, myasthenia gravis; TACI, transmembrane activator and calcium-modulating ligand interactor.

1. Zeng L, et al. *J Autoimmun.* 2024;148:103291. 2. European Patent Agency. Patent EP3868403 A1. 3. Vincent FB, et al. *Nat Rev Rheumatol.* 2014;10(6):365-373. 4. Abeles I, et al. *Annu Rev Immunol.* 2024;42(1):103-126. 5. Tagami N, et al. *Int J Clin Oncol.* 2024;29(11):1676-1683. 6. Smulski CR, Eibel H. *Front Immunol.* 2018;9:2285.

Telitacicept Helps Disrupt B-Cell–Mediated Autoantibody Production That Attacks the Neuromuscular Junction in Myasthenia Gravis¹⁻¹³

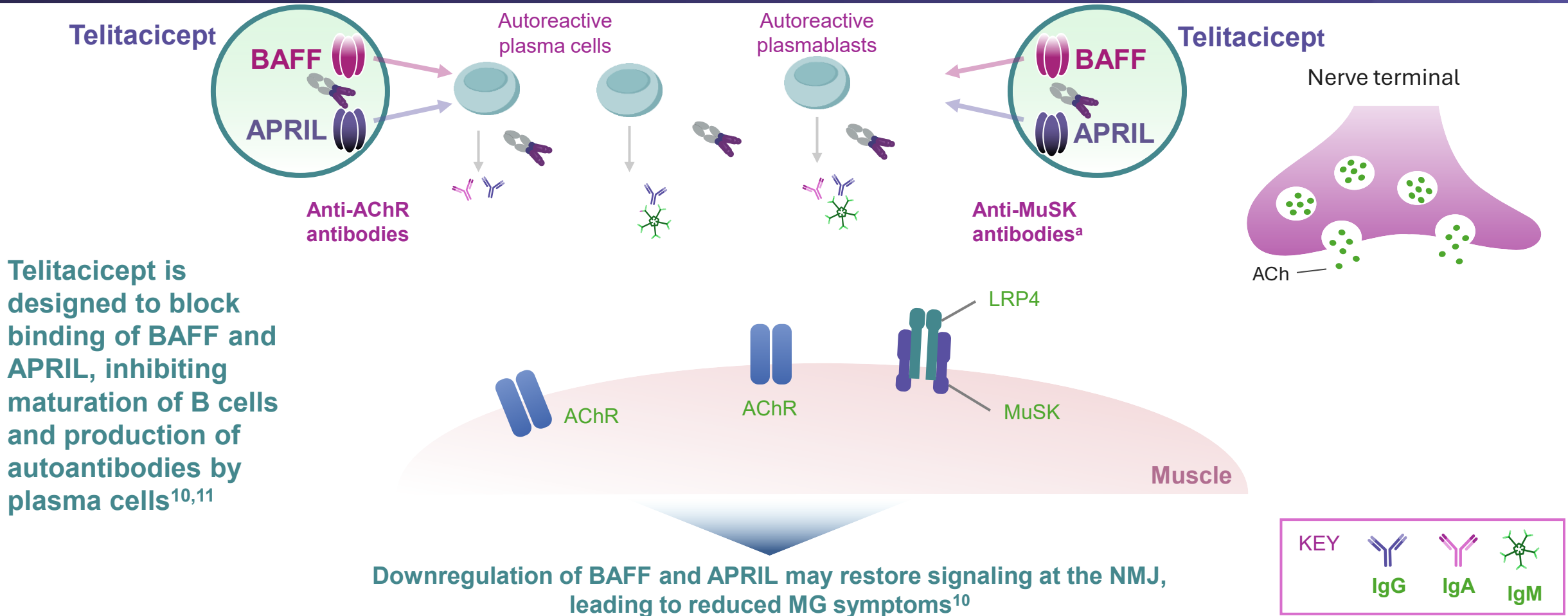


^aSome patients with MG also have anti-LRP4 antibodies, representing a relatively rare subset of patients with MG.¹

ACh, acetylcholine; AChR, acetylcholine receptor; APRIL, a proliferation-inducing ligand; BAFF, B-cell activating factor; Ig, immunoglobulin; LRP4, low-density lipoprotein receptor-related protein 4; MAC, membrane attack complex; MG, myasthenia gravis; MuSK, muscle-specific tyrosine kinase; NMJ, neuromuscular junction.

1. Iorio R. *Nat Rev Neurol*. 2024;20(2):84-98. 2. Gilhus NE, et al. *Nat Rev Dis Primers*. 2019;5(1):30. 3. Menzel SR, et al. *Nat Commun*. 2025;16(1):7106. 4. Davidson A. *Int J Clin Rheumatol*. 2010;5(3):281-285. 5. Yi JS, et al. *Muscle Nerve*. 2018;57(2):172-184. 6. Benson MJ, et al. *J Immunol*. 2008;180(6):3655-3659. 7. Bayer AC, et al. *Int Rev Neurobiol*. 2025;182:43-66. 8. Masi G, et al. *Brain*. 2026;149(6):2091-2106. 9. Lazaridis K, Tzartos SJ. *Front Neurol*. 2020;11:596981. 10. Cai J, et al. *Front Immunol*. 2023;14:1169084. 11. Ji L, et al. *MedComm (2020)*. 2024;5(4):e515. 12. Khani-Habibabadi F, et al. *Neurol Neuroimmunol Neuroinflamm*. 2025;12(5):e200436. 13. Patel P, et al. Immunoglobulin. *StatPearls [Internet]*. StatPearls Publishing. Last updated August 28, 2023. Accessed May 21, 2026. <https://www.ncbi.nlm.nih.gov/books/NBK513460/>.

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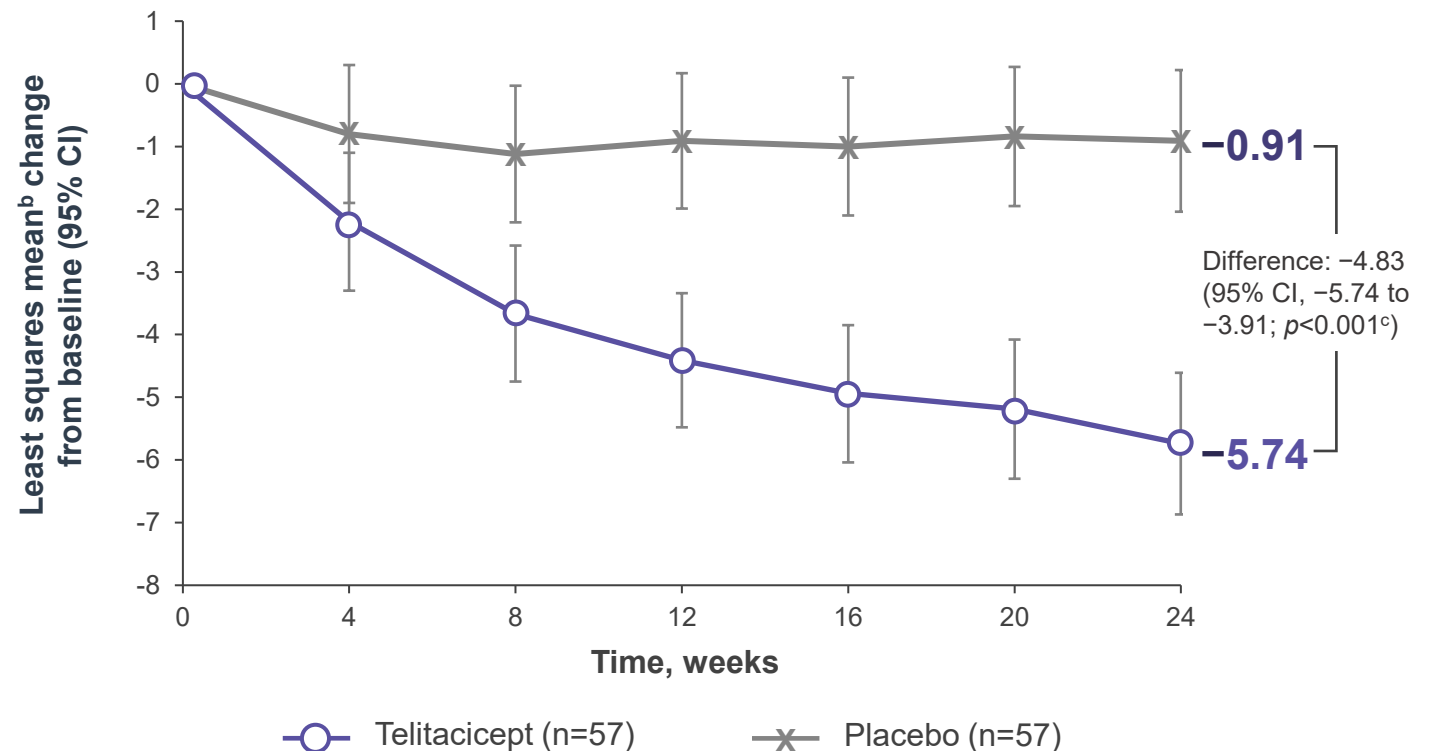
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Telitacept Has Demonstrated Efficacy and Safety in a Phase 3, Randomized, Double-Blind Control Study in China

- In a multicenter, phase 3 trial of telitacept in patients with gMG conducted in China^{1,2}
 - Primary endpoint was met (MG-ADL score at week 24):
 - -5.74 telitacept 240 mg QW vs -0.91 placebo (difference, -4.83; $p<0.001$)
 - ≥ 3 -point reduction in MG-ADL score in 98.1% and 12.0% of patients treated with telitacept and placebo
 - Telitacept was generally well tolerated
 - Most adverse events were mild or moderate

Changes in MG-ADL Score From Baseline to Week 24^a



^aMissing data were not imputed. ^bCalculated by MMRM using treatment group, visit, treatment group*visit, and randomization stratification factor as fixed effects and baseline MG-ADL score as a covariate. ^c $p<0.001$ for all comparisons between treatment groups at all timepoints except mean change in MG-ADL score at 4 weeks ($p=0.001$).

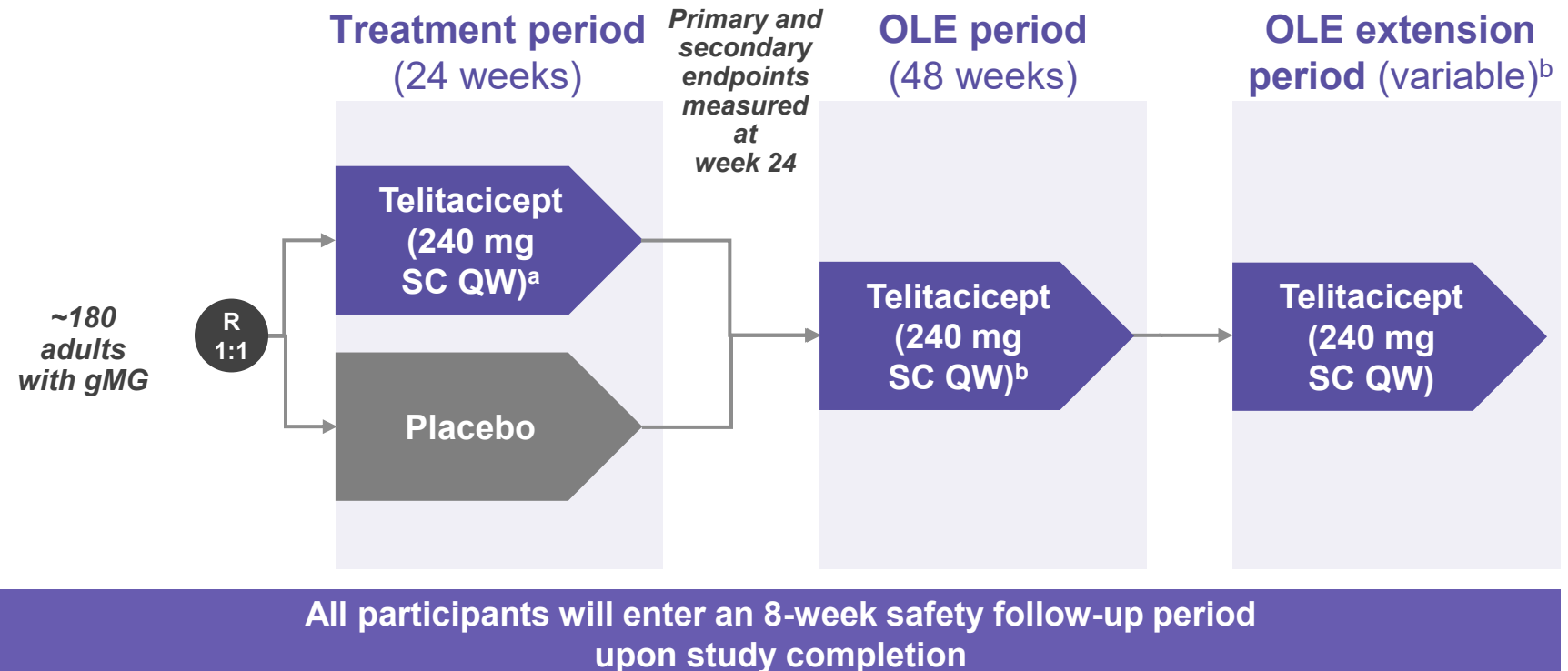
gMG, generalized myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MMRM, mixed models for repeated measures; QW, once weekly.

1. Yin J, et al. Presented at: American Academy of Neurology Annual Meeting; April 5-9, 2025; San Diego, CA. 2. Li G, et al. Presented at: American Association of Neuromuscular & Electrodiagnostic Medicine Annual Meeting 2025; October 29-November 1, 2025; San Francisco, CA.

UPSTREAM MG: A Phase 3, Randomized, Placebo-Controlled Study With an OLE Period to Evaluate the Efficacy and Safety of Telitacicept in Patients With gMG

- UPSTREAM MG consists of:
 - ≤4 weeks screening period
 - 24-week, double-blind, placebo-controlled phase
 - 48-week OLE
- This is followed by an additional extended OLE period, which has a variable duration until telitacicept is available or further development in the indication is concluded

Study Design: UPSTREAM MG



^aFor 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. ^bPatients 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 MG in the country or the further development in the indication is concluded. This will allow ongoing dosing of patients upon completion of the OLE. EOS, end of study; EOT, end of treatment; gMG, generalized myasthenia gravis; MG, myasthenia gravis; OLE, open-label extension; QW, once weekly; R, randomized; SC, subcutaneous.

Primary and Secondary Endpoints

- **Primary endpoint**
 - Change from baseline in MG-ADL score at week 24
- **Secondary endpoints include:**
 - Change from baseline in QMG score at week 24
 - Change from baseline in 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 (MSE; defined as having an MG-ADL score of ≤ 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

Participation Criteria for the Telitacicept gMG Global Phase 3 Clinical Trial

Key Inclusion Criteria

18+

Male or female aged ≥ 18 years at time of screening



MG-ADL score ≥ 6 points at screening and baseline with ocular-related score $< 50\%$ of the total score



Positive antibodies against AChR or MuSK at screening



QMG score ≥ 8 , with ≥ 4 items having a score ≥ 2 at screening and baseline



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

^aTypical pattern of weakness meeting the clinical criteria for diagnosis of MG as defined by the MGFA clinical classification II-IV. ^bStable concomitant medications, with a limit of 2 (not counting cholinesterase inhibitors). Allowed medications include cholinesterase inhibitors, oral corticosteroids, and nonsteroidal immunosuppressive treatments.

AChR, acetylcholine receptor; gMG, generalized myasthenia gravis; mAb, monoclonal antibody; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MuSK, muscle-specific kinase; QMG, Quantitative Myasthenia Gravis.

Participation Criteria for the Telitacicept gMG Global Phase 3 Clinical Trial (cont'd)

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 ^a
 Current or history of primary immunodeficiency	 History of malignancy within the last 5 years ^b	 Prior or continuing diagnosis of serious cardiovascular disease

^aHowever, 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. ^bExcludes adequately treated nonmelanoma skin cancer or any early-stage cancer considered cured with resection.
gMG, generalized myasthenia gravis.

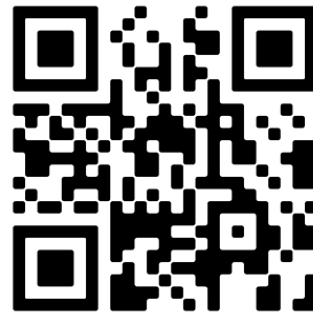
Study Locations and Number of Sites for the Global Phase 3 Study



Study enrollment is completed across 15 countries, with top-line results anticipated in H1 2027

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 population¹
- 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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