Efficacy and Safety of Telitacicept in Patients with Generalized Myasthenia Gravis: Results from a Phase 3 Study

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Financial Disclosure

Dr. George Li serves as a scientific consultant for RemeGen Biosciences.

Dr. Jian Yin is a consultant in a global scientific advisor committee for Alexion.

Dr. Wenxiang Wang is an employee of RemeGen Co., Ltd, and owns company stock.

Dr. Lin Li is an employee of RemeGen Co., Ltd, and owns company stock.

Ms.Yan Sun is an employee of RemeGen Co., Ltd, and receives company stock.

Dr. Qing Zuraw is an employee of Vor Biopharma Inc, formal employee of RemeGen Bioscience and owns RemeGen and Vor Biopharma stocks.

Dr. Jianmin Fang is an employee of RemeGen Co., Ltd, and owns company stock.

Introduction of Generalized Myasthenia Gravis (g)MG

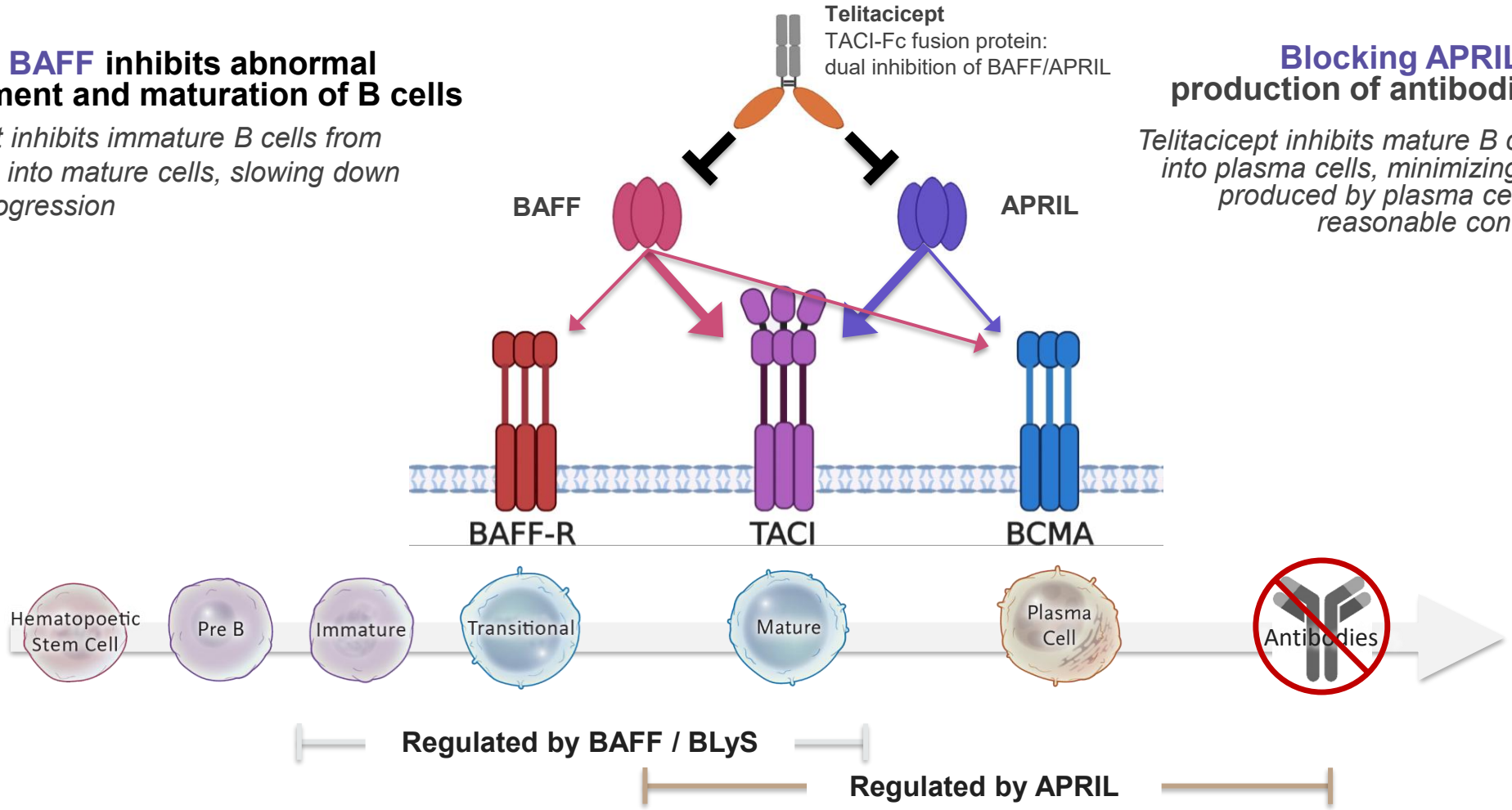
- MG is a rare autoimmune disease affecting about 700,000 people worldwide. In an autoimmune disease, the body's immune system mistakenly attacks its own healthy tissues. The current therapy for MG focuses on treating symptoms caused by the disease, like muscle weakness. However, these treatments do not always help relieve symptoms and can have side effects.
- The focus of MG treatment is shifting from symptom relief to targeting the immune system, where the root cause lies.
- Telitacicept (RC18), a novel TACI-Fc fusion protein, demonstrated consistent sustained and significant clinical meaningful efficacy in a phase 2 and a phase 3 study with a favorable long term safety profile.

Telitacicept Mechanism of Action

Dual BAFF/APRIL blockade stops B cell survival and plasma cell antibody production

Blocking BAFF inhibits abnormal development and maturation of B cells

Telitacicept inhibits immature B cells from developing into mature cells, slowing down disease progression



Blocking APRIL inhibits abnormal production of antibodies by plasma cells

Telitacicept inhibits mature B cells from differentiating into plasma cells, minimizing antibodies abnormally produced by plasma cells and contributing to a reasonable control of disease activities

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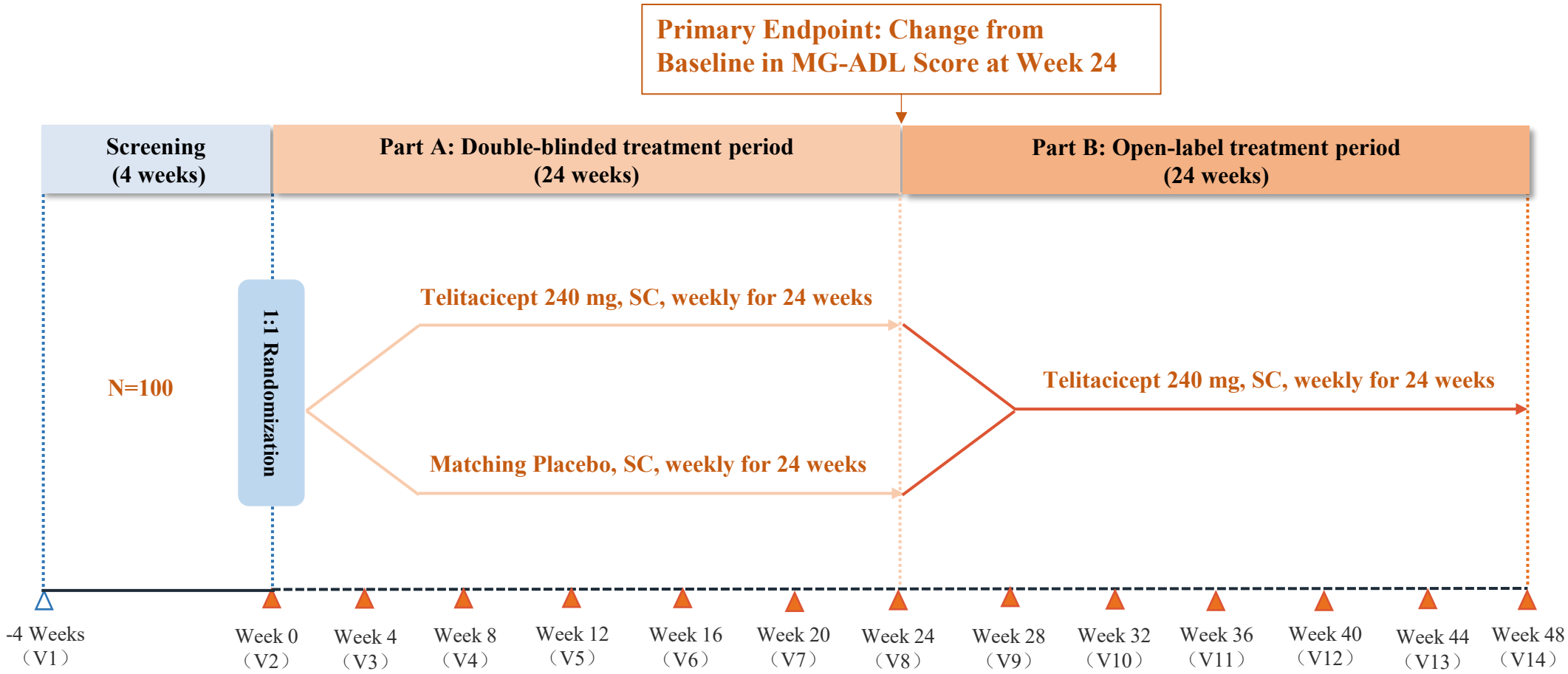
BAFF, B-cell activating factor; BLyS, B Lymphocyte Stimulator; APRIL, a proliferation inducing ligand

Study Design

- A Phase 3, multiple center, randomized, double-blinded, placebo-controlled study
- Patient population: Positive AChR-Ab or MuSK-Ab; MGFA class II, III, or IVa; MG-ADL score ≥ 6; QMG score ≥ 8; and maintenance of a stable standard treatment regimen.



Primary and Secondary Endpoints

Primary Endpoint:

- Change from baseline in MG-ADL score at Week 24

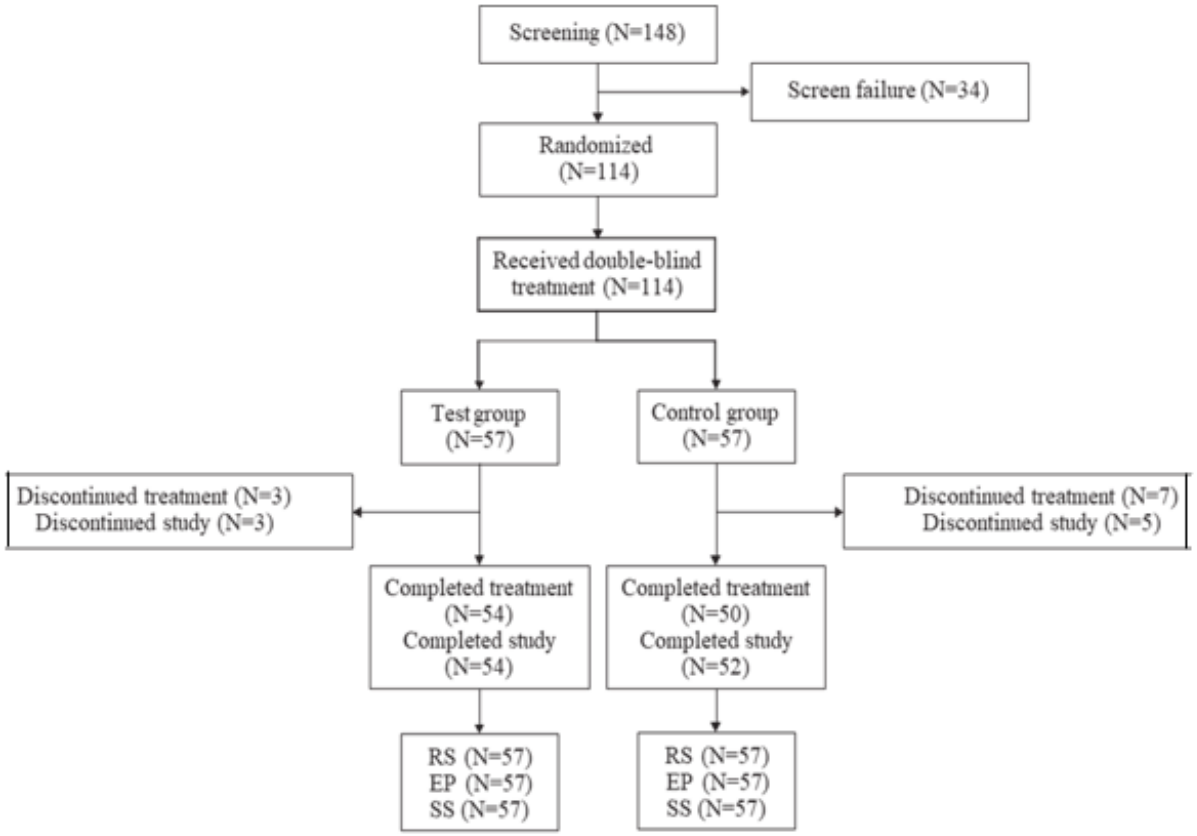
Secondary Endpoints:

- Change from baseline in MG-ADL score at Week 12, 36, and 48
- Change from baseline in QMG score at Week 12, 24, 36, and 48
- Proportion of patients achieved MG-ADL score reduction of ≥3 points at Week 12, 24, 36, and 48
- Proportion of patients achieved QMG score reduction of ≥5 points at Week 12, 24, 36, and 48
- Safety endpoint including Adverse event, abnormal labs, etc.

Other Endpoints:

- Change in MG-ADL score over time from baseline
- Change in QMG score over time from baseline
- Proportion of patients achieved MG-ADL score reduction of ≥3 points over time from baseline
- Proportion of patients achieved QMG score reduction of ≥5 points over time from baseline
- Change in Pharmacokinetic and Pharmacodynamics Markers

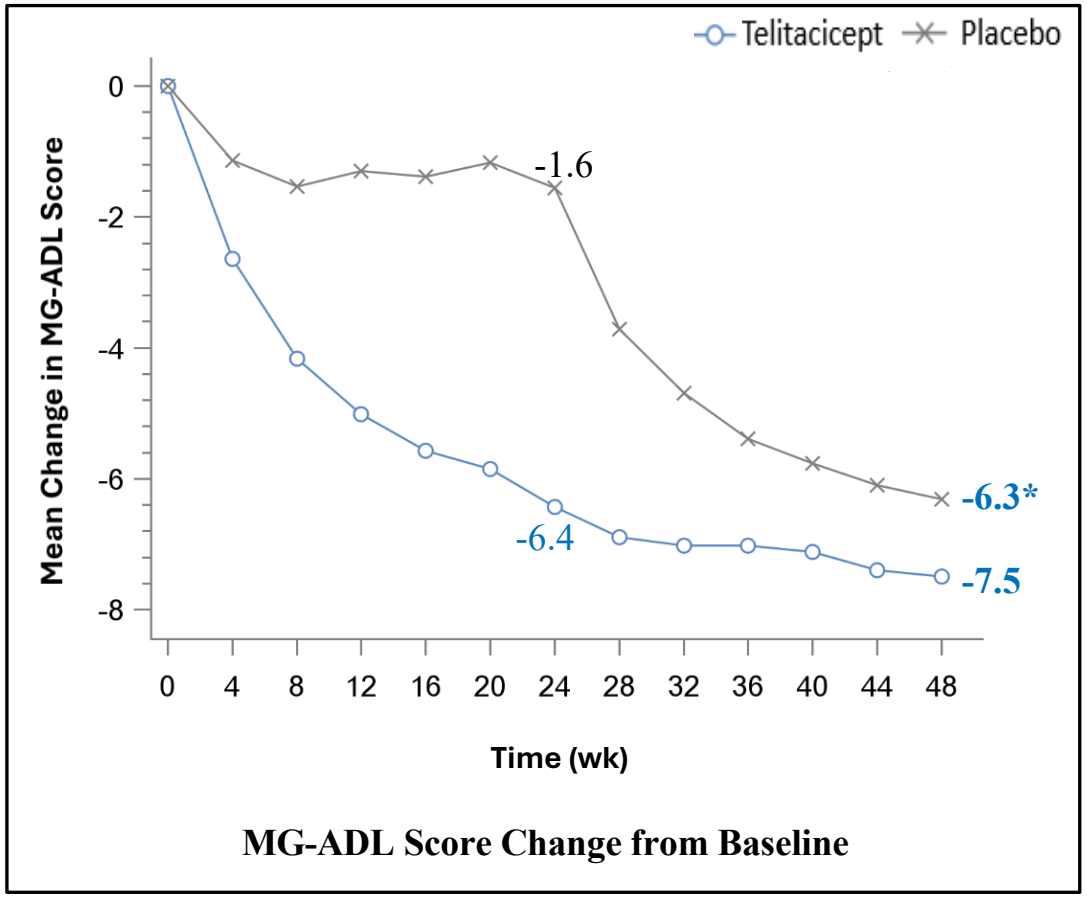
Study Results: Patient Disposition and Baseline Characteristics



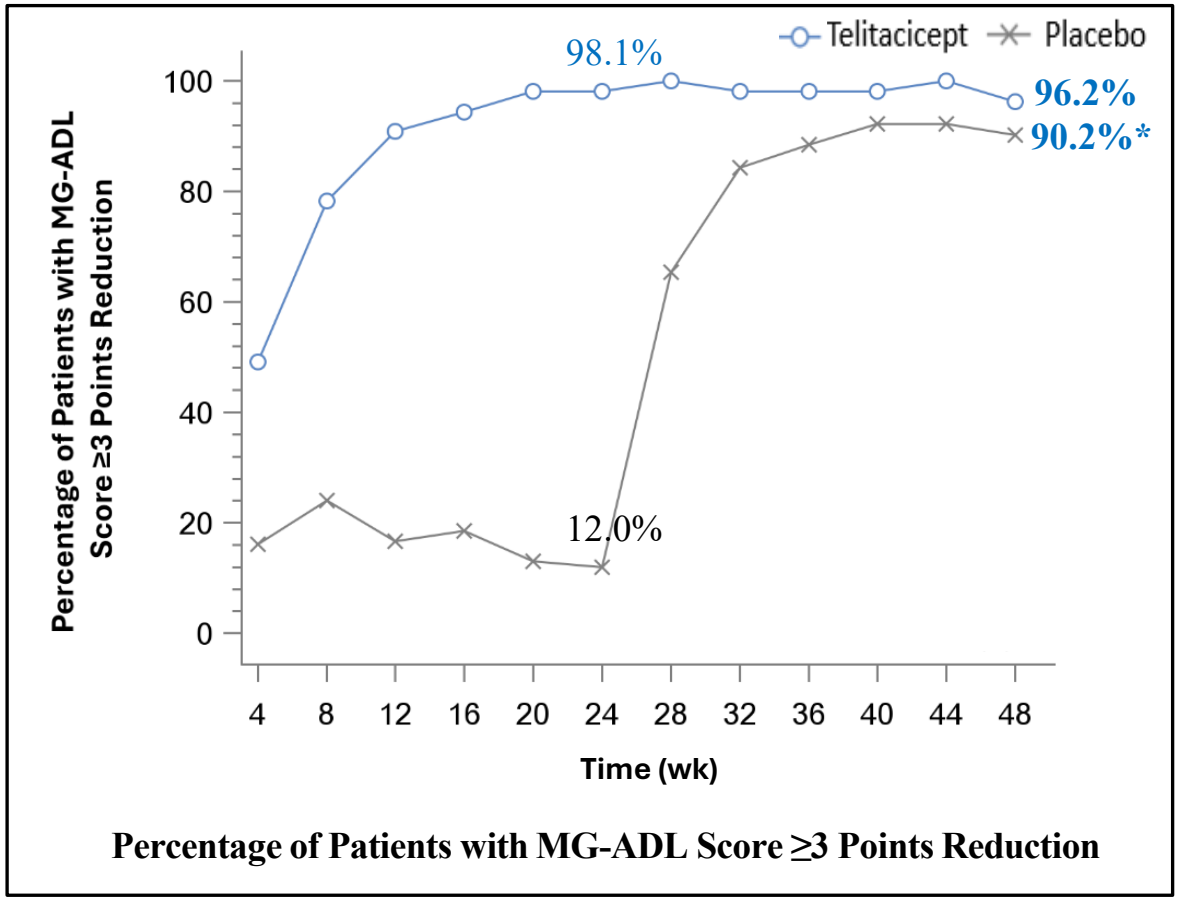
	Telitacicept (N=57)	Placebo (N=57)
Age (yr), mean ± SD	49.1 ± 14.69	49.6 ± 15.03
Sex		
Male, n (%)	30 (52.6)	21 (36.8)
Female, n (%)	27 (47.4)	36 (63.2)
Disease duration (month), mean± SD	83.09 ± 84.507	76.05 ± 87.817
MGFA classification		
Class IIa, n (%)	3 (5.3)	12 (21.1)
Class IIb, n (%)	14 (24.6)	9 (15.8)
Class IIIa, n (%)	25 (43.9)	23 (40.4)
Class IIIb, n (%)	11 (19.3)	12 (21.1)
Class IVa, n (%)	4 (7.0)	1 (1.8)
Baseline MG-ADL score, mean ± SD	10.0 ± 2.60	9.9 ± 2.62
Baseline QMG score, mean ± SD	17.9 ± 3.43	18.8 ± 3.65
Antibody-positive at screening		
AChR, n (%)	55 (96.5)	55 (96.5)
MuSK, n (%)	2 (3.6)	2 (3.5)
Standard-of-care therapy		
Anticholinesterase inhibitors, n (%)	53 (93.0)	52 (91.2)
Steroids, n (%)	36 (63.2)	34 (59.6)
Immunosuppressants, n (%)	34 (59.6)	34 (59.6)

AE, adverse event; AChR, acetylcholine receptor; EP, efficacy population; MG-ADL, Myasthenia Gravis-Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MuSK, muscle-specific tyrosine kinase; QMG, Quantitative Myasthenia Gravis; SD, standard deviation; RS, randomized set; SS, safety set.

Sustained MG-ADL Reduction Over 48 weeks



MG-ADL Score Change from Baseline

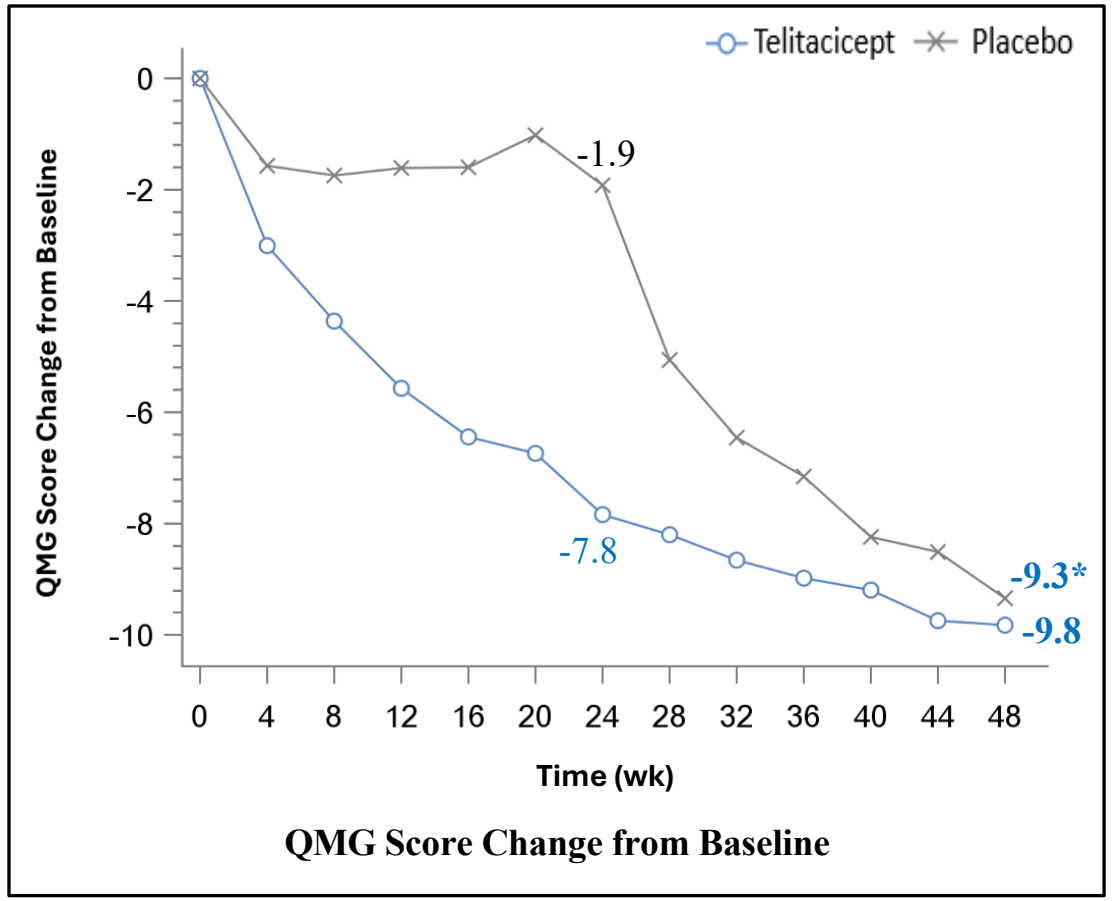


Percentage of Patients with MG-ADL Score ≥3 Points Reduction

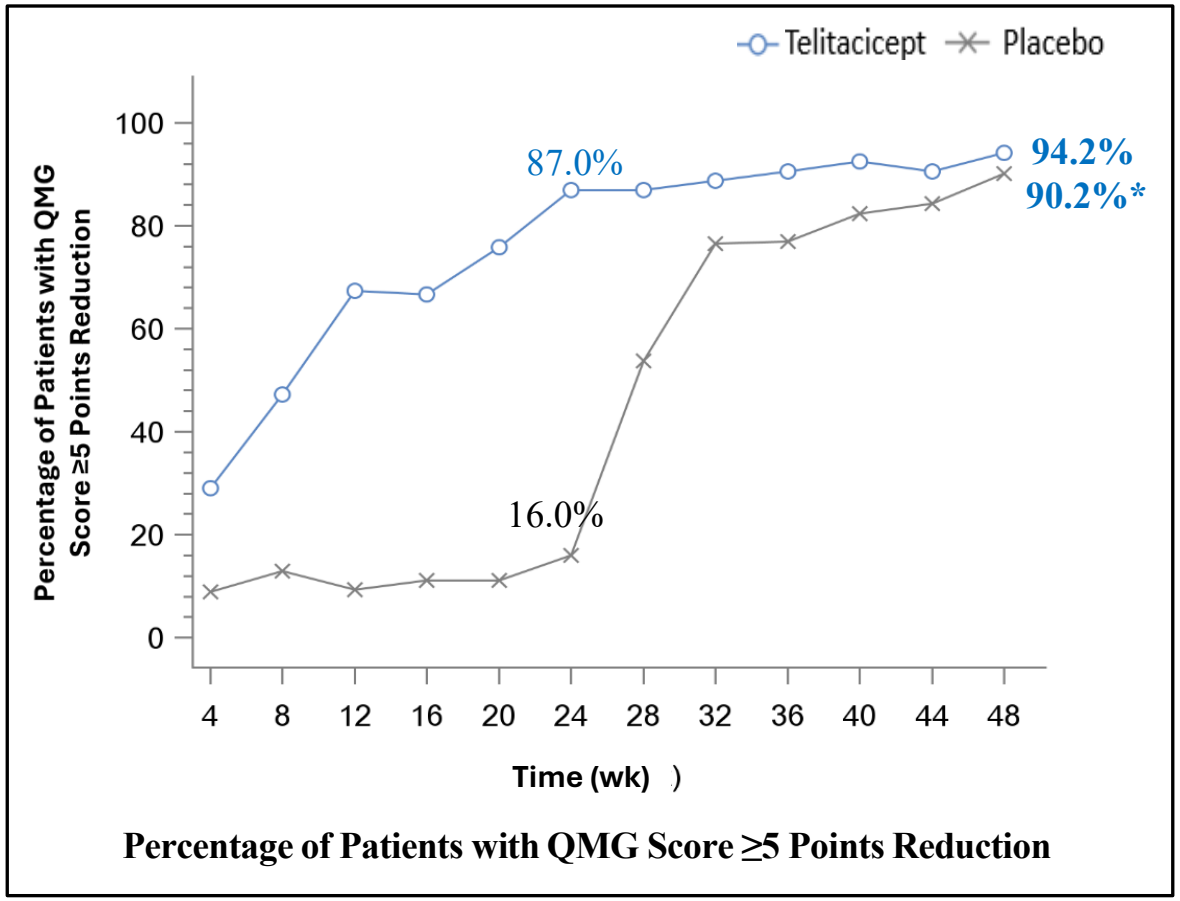
* Telitacicept arm continue with the same treatment, Placebo arm switched to Telitacicept during OLE period.

The efficacy analysis was based on descriptive statistical analysis of the actual data in the full analysis set (FAS), and missing data were not filled.

Sustained QMG Reduction Over 48 weeks



QMG Score Change from Baseline

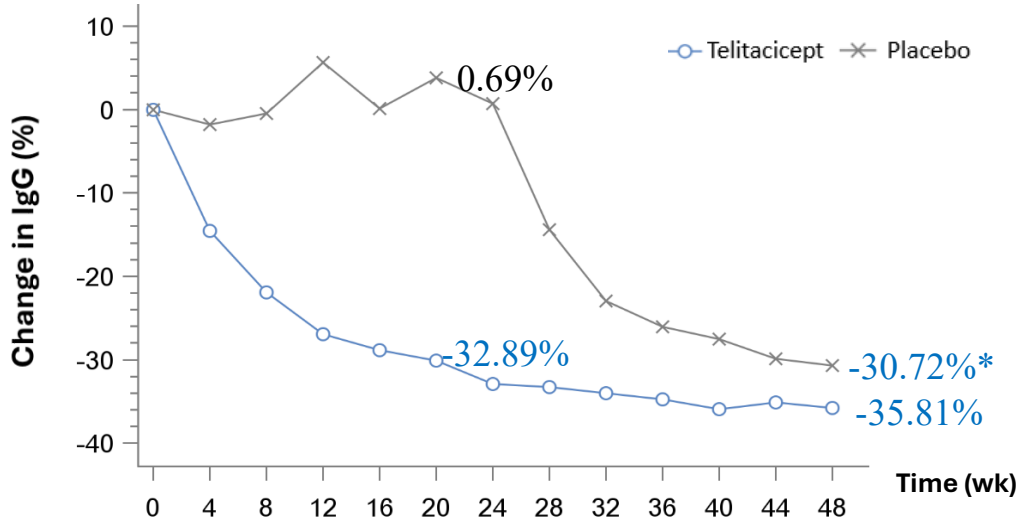


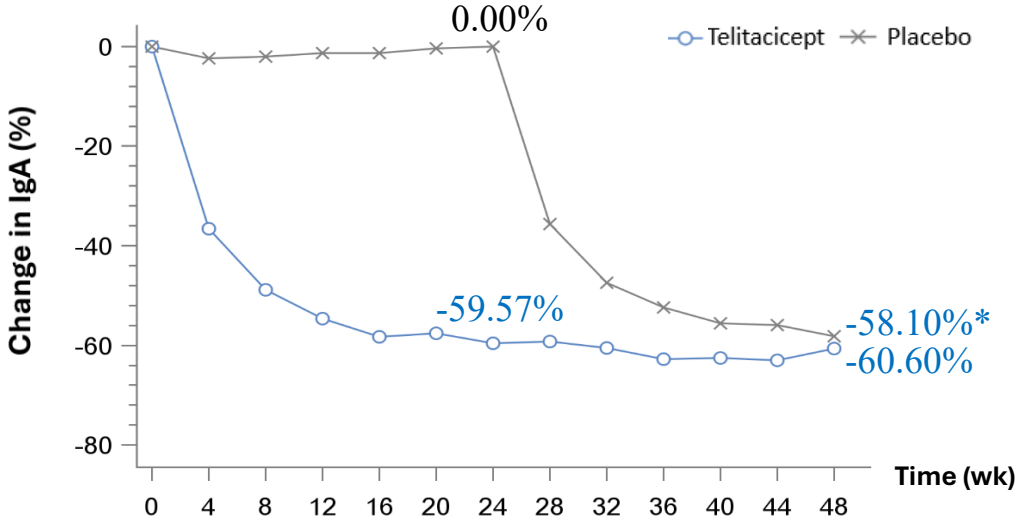
Percentage of Patients with QMG Score ≥5 Points Reduction

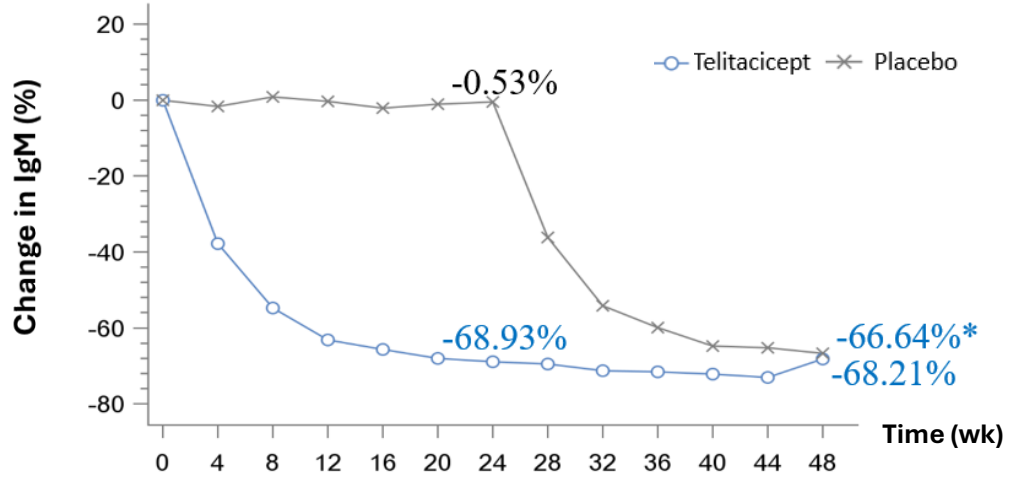
* Telitacicept arm continue with the same treatment, Placebo arm switched to Telitacicept during OLE period.

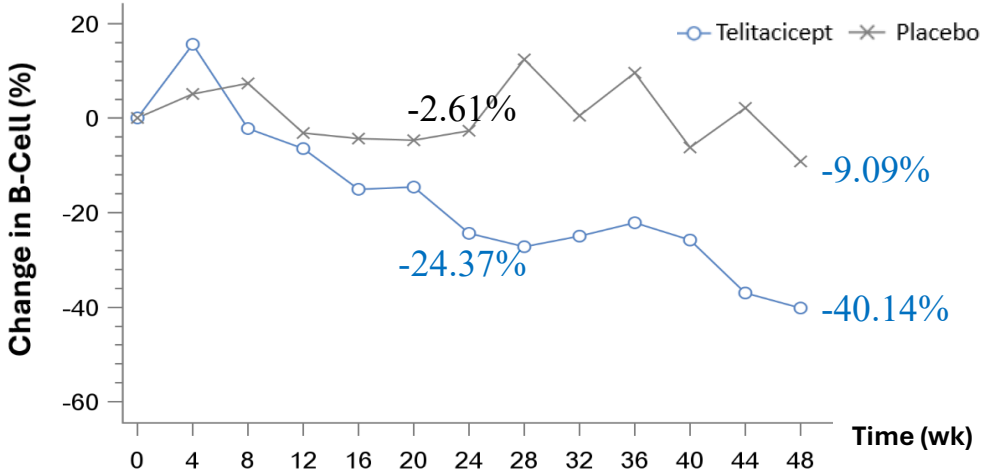
The efficacy analysis was based on descriptive statistical analysis of the actual data in the full analysis set (FAS), and missing data were not filled.

Changes in IgG、IgA、IgM、CD19+ B count









Incidence of Adverse Event (SS)

	Open-label treatment period (Weeks 24-48)		Weeks 0-48	
	Telitacicept 240 mg (N=54)	Placebo → Telitacicept 240 mg (N=53)	Telitacicept 240 mg (N=57)	Telitacicept at least one dose* (N=110)
TEAE n (%)	39 (72.2)	45 (84.9)	51 (89.5)	96 (87.3)
ADR n (%)	25 (46.3)	36 (67.9)	45 (78.9)	81 (73.6)
SAE n (%)	4 (7.4)	3 (5.7)	8 (14.0)	11 (10.0)
SAR n (%)	0 (0)	1 (1.9)	1 (1.8)	2 (1.8)
TEAEs leading to dose reduction n (%)	0 (0)	0 (0)	0 (0)	0 (0)
ADRs leading to dose reduction n (%)	0 (0)	0 (0)	0 (0)	0 (0)
TEAEs leading to dose interruption n (%)	4 (7.4)	7 (13.2)	11 (19.3)	18 (16.4)
ADRs leading to dose interruption n (%)	1 (1.9)	4 (7.5)	6 (10.5)	10 (9.1)
TEAEs leading to treatment discontinuation n (%)	0 (0)	1 (1.9)	2 (3.5)	3 (2.7)
ADRs leading to treatment discontinuation n (%)	0 (0)	0 (0)	1 (1.8)	1 (0.9)
TEAEs leading to actions taken n (%)	24 (44.4)	23 (43.4)	41 (71.9)	64 (58.2)
ADRs leading to actions taken n (%)	8 (14.8)	13 (24.5)	21 (36.8)	34 (30.9)
Severe TEAEs n (%)	0 (0)	2 (3.8)	3 (5.3)	5 (4.5)
Severe ADR n (%)	0 (0)	1 (1.9)	1 (1.8)	2 (1.8)
Significant[#] TEAEs n (%)	24 (44.4)	24 (45.3)	39 (68.4)	63 (57.3)
Significant ADR n (%)	8 (14.8)	12 (22.6)	21 (36.8)	33 (30.0)
TEAEs leading to withdrawal n (%)	0 (0)	0 (0)	3 (5.3)	3 (2.7)
ADRs leading to withdrawal n (%)	0 (0)	0 (0)	1 (1.8)	1 (0.9)

SS: safety set; TEAE: treatment-emergent adverse event; ADR: adverse drug reaction, defined as an AE that was “definitely related, probably related, or possibly related” to the investigational products; SAE: serious adverse event; SADR: serious adverse drug reaction.

*The safety results of the group receiving Telitacicept at least one dose were the safety data of 57 participants in the Telitacicept 240 mg group at Weeks 0-48 and the safety data of 53 participants in the placebo group who entered stage B at Weeks 24-48.

[#]Significant AEs were defined as any AEs leading to the use of targeted medical measures (such as dose interruption, dose increase/reduction, treatment discontinuation, treatment measures, and withdrawal), with the exception of SAEs.

%: Percentage of participants with AEs among the total number of participants in each group.

Incidence of Infections (SS)

SOC	Open-label Treatment Period				Weeks 0-48			
	Telitacicept 240 mg		Placebo		Telitacicept 240 mg		Telitacicept at Least One Dose	
PT	Number of Participants	Number of Events	Number of Participants	Number of Events	Number of Participants	Number of Events	Number of Participants	Number of Events
N	54		53		57		110	
Infections and infestations n (%)	27 (50.0)	33	21 (39.6)	29	39 (68.4)	81	60 (54.5)	110
Infection upper respiratory n (%)	14 (25.9)	15	11 (20.8)	12	21 (36.8)	33	32 (29.1)	45
Infection urinary tract n (%)	8 (14.8)	10	5 (9.4)	7	13 (22.8)	21	18 (16.4)	28
Nasopharyngitis n (%)	1 (1.9)	1	1 (1.9)	1	3 (5.3)	3	4 (3.6)	4
Gastroenteritis n (%)	1 (1.9)	1	1 (1.9)	1	3 (5.3)	3	4 (3.6)	4
Herpes zoster n (%)	0 (0)	0	3 (5.7)	3	1 (1.8)	1	4 (3.6)	4
Pneumonia n (%)	1 (1.9)	1	0 (0)	0	3 (5.3)	3	3 (2.7)	3
Respiratory tract infection n (%)	1 (1.9)	1	0 (0)	0	2 (3.5)	2	2 (1.8)	2
COVID-19 n (%)	0 (0)	0	2 (3.8)	2	0 (0)	0	2 (1.8)	2
Pharyngitis n (%)	0 (0)	0	0 (0)	0	2 (3.5)	2	2 (1.8)	2
Vaginal infection n (%)	0 (0)	0	2 (3.8)	2	0 (0)	0	2 (1.8)	2
Peritonitis n (%)	1 (1.9)	1	0 (0)	0	1 (1.8)	1	1 (0.9)	1
Conjunctivitis n (%)	1 (1.9)	1	0 (0)	0	1 (1.8)	1	1 (0.9)	1
Oral herpes n (%)	1 (1.9)	1	0 (0)	0	1 (1.8)	2	1 (0.9)	2
Otitis media n (%)	1 (1.9)	1	0 (0)	0	1 (1.8)	1	1 (0.9)	1
COVID-19 pneumonia n (%)	0 (0)	0	0 (0)	0	1 (1.8)	1	1 (0.9)	1
Cytomegalovirus infection n (%)	0 (0)	0	1 (1.9)	1	0 (0)	0	1 (0.9)	1
Tracheitis n (%)	0 (0)	0	0 (0)	0	1 (1.8)	1	1 (0.9)	1
Body tinea n (%)	0 (0)	0	0 (0)	0	1 (1.8)	1	1 (0.9)	1
Bacterial infection n (%)	0 (0)	0	0 (0)	0	1 (1.8)	1	1 (0.9)	1
Pulpitis n (%)	0 (0)	0	0 (0)	0	1 (1.8)	1	1 (0.9)	1
Periodontitis n (%)	0 (0)	0	0 (0)	0	1 (1.8)	1	1 (0.9)	1
Fungal infection n (%)	0 (0)	0	0 (0)	0	1 (1.8)	1	1 (0.9)	1
Bronchitis n (%)	0 (0)	0	0 (0)	0	1 (1.8)	1	1 (0.9)	1

AEs were coded with MedDRA version 27.0. SOCs and PTs were listed in descending order of the total number of participants for each AE.
Number of participants: A participant was counted no more than once under one term (SOC or PT). Number of events: For one term (SOC or PT), a participant was counted according to the number of occurrences.
N: Total number of participants in each group in the safety set. %: The percentage of participants that experienced AEs in each group.
The data of the “Telitacicept at least one dose” group was pooling of data from the Telitacicept 240 mg group for Weeks 0-48 and data from the placebo group for Weeks 24-48.

Conclusion

- Telitacicept showed sustained efficacy for up to 48 weeks and was well tolerated in gMG patients in this phase 3 trial from China.
- A global phase 3 pivotal, multiple center, randomized, double-blind, placebo control trial with long term open label extension study is ongoing to evaluate efficacy and safety of telitacicept in patients worldwide.

Acknowledgement

- Thanks to the patients who participated in the study.
- Thanks to all the investigators and their site staffs for their contribution to the study.