

# Efficacy and Safety of Efgartigimod in Participants With Generalized Myasthenia Gravis Who Lack Detectable Anti-Acetylcholine Receptor Antibodies: One-Year Results of ADAPT SERON

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## KEY TAKEAWAYS

The primary endpoint of ADAPT SERON was met, with a statistically significant improvement in MG-ADL total score at Week 4 in the overall participant population treated with efgartigimod IV vs placebo

Clinically meaningful improvements in MG-ADL total scores were observed in the overall population and in anti-MuSK-Ab+, triple-seronegative, and anti-LRP4-Ab+ subgroups in Part B of ADAPT SERON, after up to 1 year of efgartigimod treatment

Results from ADAPT SERON demonstrate that pathogenic IgGs may be an underlying driver of gMG across patient subtypes, regardless of autoantibody status<sup>1-3</sup>

Efgartigimod was well tolerated and demonstrated a safety profile consistent with previous clinical and real-world studies

## BACKGROUND

- Efgartigimod is a human IgG1 antibody Fc fragment that has been engineered for increased affinity to FcRn compared with endogenous IgG and is uniquely composed of only the part of the IgG antibody that normally binds FcRn<sup>4,5</sup>
  - Efgartigimod retains the pH-dependent FcRn binding characteristic of endogenous IgG
- By blocking FcRn, efgartigimod selectively reduces IgG antibodies and pathogenic autoantibodies, and does so without<sup>4,6-8</sup>:
  - Decreasing albumin levels
  - Increasing LDL cholesterol levels
  - Impacting antibody production (including other Ig antibodies) or other parts of the immune system

### Efgartigimod Mechanism of Action<sup>4,9,10</sup>

- Efgartigimod and IgG are internalized into the cell
- Efgartigimod outcompetes endogenous IgG antibodies, including pathogenic IgG autoantibodies, for binding to FcRn, due to increased affinity to FcRn. When bound to FcRn, efgartigimod and IgG escape lysosomal degradation
- Remaining unbound IgG and efgartigimod are degraded in the lysosome
- Efgartigimod and fewer IgG are recycled back into circulation



## RESULTS

**TABLE 1** Baseline Demographics and Clinical Characteristics<sup>a</sup>  
Overall Population, Part A

|                                           | Efgartigimod IV (n=58) | Placebo (n=61) |
|-------------------------------------------|------------------------|----------------|
| Age, years, mean (SD)                     | 50.6 (13.4)            | 51.7 (13.0)    |
| Age category, n (%)                       |                        |                |
| 18<65 years                               | 49 (84.5)              | 50 (82.0)      |
| ≥65 years                                 | 9 (15.5)               | 11 (18.0)      |
| Female sex, n (%)                         | 44 (75.9)              | 46 (75.4)      |
| Race, n (%)                               |                        |                |
| Asian                                     | 8 (13.8)               | 8 (13.3)       |
| Black or African American                 | 1 (1.7)                | 2 (3.3)        |
| White                                     | 48 (82.8)              | 46 (76.7)      |
| Other                                     | 1 (1.7)                | 4 (6.7)        |
| Time since diagnosis, years, mean (SD)    | 5.7 (6.2)              | 6.5 (7.8)      |
| Prior thymectomy <sup>b</sup> n (%)       | 14 (24.1)              | 4 (6.6)        |
| MGFA classification at screening, n (%)   |                        |                |
| Class II                                  | 17 (29.3)              | 23 (37.7)      |
| Class III                                 | 38 (65.5)              | 35 (57.4)      |
| Class IV                                  | 3 (5.2)                | 3 (4.9)        |
| MG-ADL total score at baseline, mean (SD) | 9.9 (3.2)              | 9.4 (3.3)      |
| Antibody serostatus, n (%)                |                        |                |
| Anti-MuSK-Ab+                             | 20 (34.5)              | 20 (32.8)      |
| Anti-LRP4-Ab+                             | 6 (10.3)               | 0              |
| Triple-seronegative                       | 32 (55.2)              | 41 (67.2)      |
| Baseline MG therapy, n (%)                |                        |                |
| Any steroid                               | 39 (67.2)              | 37 (60.7)      |
| Any NSIST                                 | 31 (53.4)              | 22 (36.1)      |
| Any AChEI                                 | 46 (79.3)              | 47 (77.0)      |
| Only AChEI                                | 11 (19.0)              | 13 (21.3)      |

<sup>a</sup>The denominator for the percentage calculation was the number of participants per arm, excluding missing values. Baseline was defined as the last available nonmissing value before the first IMP administration. <sup>b</sup>Participants were excluded if they received a thymectomy <3 months before screening or if thymectomy was planned during the study.

**TABLE 3** Primary Endpoint: LS Mean MG-ADL Total Score Change From Baseline to Week 4,<sup>a</sup>  
Overall Population Part A

| Population                                | Efgartigimod IV               | Placebo                       | Efgartigimod IV vs placebo    | P value <sup>b</sup> |  |
|-------------------------------------------|-------------------------------|-------------------------------|-------------------------------|----------------------|--|
|                                           | LS mean (90% CI) <sup>a</sup> | LS mean (90% CI) <sup>a</sup> | LS mean (90% CI) <sup>b</sup> |                      |  |
| Overall (N=118)                           | -3.35 (-3.98 to -2.72)        | -1.90 (-2.51 to -1.28)        | -1.46 (-2.33 to -0.58)        | 0.007                |  |
| Anti-MuSK-Ab positive <sup>c</sup> (n=40) | -4.24 (-5.31 to -3.17)        | -1.89 (-2.96 to -0.82)        | -2.35 (-3.86 to -0.85)        | 0.01                 |  |
| Triple-seronegative <sup>c</sup> (n=73)   | -2.80 (-3.65 to -1.94)        | -1.82 (-2.56 to -1.08)        | -0.98 (-2.10 to -0.15)        | 0.15                 |  |

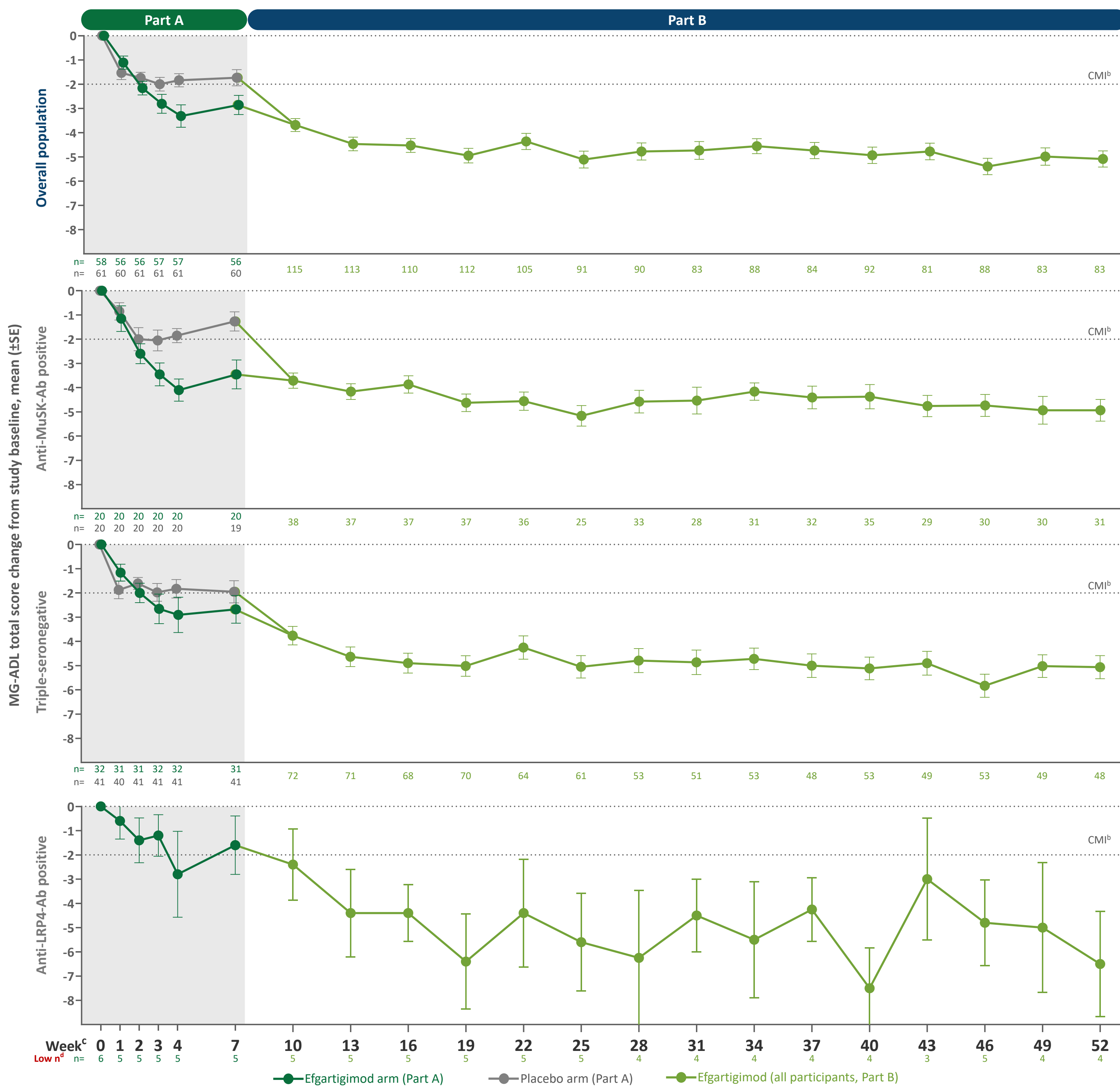
<sup>a</sup>O Mean (SE) MG-ADL total score change from baseline to Week 4 in the anti-LRP4-Ab positive population (n=5) was -2.8 (1.8)<sup>d</sup>  
<sup>b</sup>For the overall population, an MMRM was used with treatment, analysis visit, treatment-by-analysis visit interaction, and anti-MuSK-Ab serostatus as fixed effects, with baseline MG-ADL total score value as covariate. For the anti-MuSK-Ab positive and triple-seronegative subpopulations, an MMRM was used with treatment, analysis visit, antibody serostatus-by-treatment interaction, and antibody-serostatus-by-treatment-by-analysis visit interaction as fixed effects, with baseline MG-ADL total score value as covariate. An unstructured covariance matrix for the error terms was assumed for modeling within-participant correlation. <sup>c</sup>2-sided CI and 2-sided P value are presented. <sup>d</sup>Comparisons in the anti-MuSK-Ab positive and triple-seronegative subgroups were not tested formally, as a prespecified endpoint in the study's hierarchical testing strategy was not statistically significant. <sup>e</sup>Due to the small sample size within the anti-LRP4-Ab subgroup, it was not possible to generate reliable estimates from the model. <sup>f</sup>\*\*2-sided P<0.01.

**TABLE 2** Summary of TEAEs  
Overall Population

|                                     | Part A                           |                          | Parts A/B <sup>a</sup>           |                 |
|-------------------------------------|----------------------------------|--------------------------|----------------------------------|-----------------|
|                                     | Efgartigimod IV (n=58; PYFU=9.0) | Placebo (n=61; PYFU=9.5) | Total EFG IV (N=118; PYFU=136.6) |                 |
|                                     | n (%)                            | ER <sup>b</sup>          | n (%)                            | ER <sup>b</sup> |
| ≥1 TEAE                             | 36 (62.1)                        | 10.3                     | 30 (49.2)                        | 10.9            |
| ≥1 Serious TEAE                     | 3 (5.2)                          | 0.7                      | 1 (1.6)                          | 0.1             |
| ≥1 Fatal TEAE <sup>c</sup>          | 1 (1.7)                          | 0.2                      | 1 (1.6)                          | 0.1             |
| ≥1 Grade ≥3 TEAE                    | 3 (5.2)                          | 0.7                      | 1 (1.6)                          | 0.5             |
| ≥1 IRR event <sup>d</sup>           | 1 (1.7)                          | 0.1                      | 3 (4.9)                          | 0.3             |
| Discontinued treatment due to TEAEs | 0                                | 0                        | 0                                | 0               |
| Most frequent TEAEs <sup>e</sup>    |                                  |                          |                                  |                 |
| Upper respiratory tract infection   | 5 (8.6)                          | 0.6                      | 3 (4.9)                          | 0.3             |
| Nausea                              | 4 (6.9)                          | 0.8                      | 3 (4.9)                          | 0.3             |
| Headache                            | 3 (5.2)                          | 0.6                      | 7 (11.5)                         | 1.3             |
| Urinary tract infection             | 3 (5.2)                          | 0.3                      | 3 (4.9)                          | 0.4             |
| Diarrhea                            | 2 (3.4)                          | 0.2                      | 0                                | 0               |
| Fatigue                             | 2 (3.4)                          | 0.6                      | 5 (8.2)                          | 0.7             |
| Arthralgia                          | 2 (3.4)                          | 0.2                      | 2 (3.3)                          | 0.2             |
| Myasthenia gravis                   | 2 (3.4)                          | 0.2                      | 0                                | 0               |
| Nasopharyngitis                     | 1 (1.7)                          | 0.1                      | 2 (3.3)                          | 0.2             |
| Influenza                           | 1 (1.7)                          | 0.1                      | 2 (3.3)                          | 0.2             |
| Dizziness                           | 1 (1.7)                          | 0.4                      | 1 (1.6)                          | 0.1             |
| Oropharyngeal pain                  | 1 (1.7)                          | 0.1                      | 1 (1.6)                          | 0.1             |
| Cough                               | 0                                | 0                        | 3 (4.9)                          | 0.3             |
| Myalgia                             | 0                                | 0                        | 2 (3.3)                          | 0.4             |

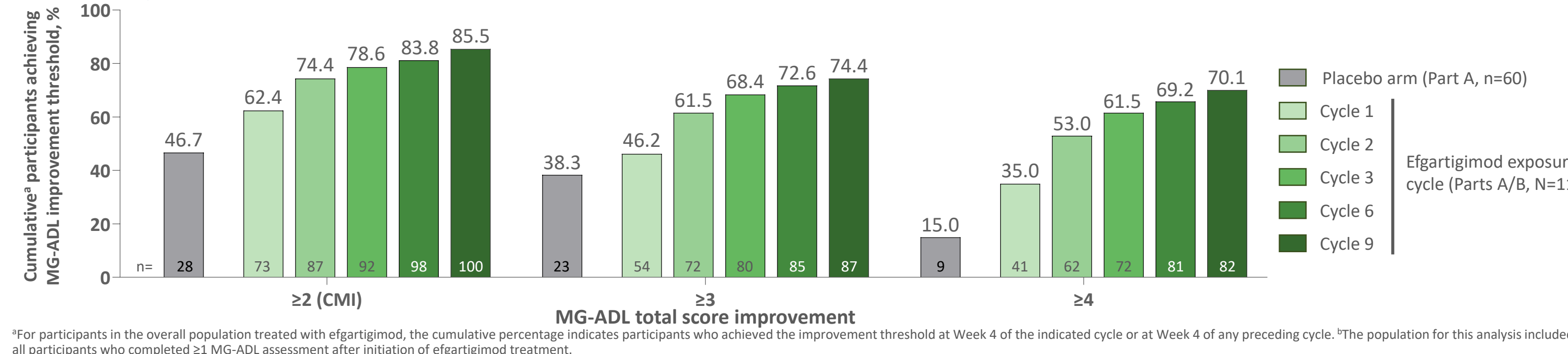
<sup>a</sup>Population of all participants who received ≥1 efgartigimod dose during either part of the study; events with onset after initiation of efgartigimod treatment are reported (events in the placebo arm with onset during Part A are not included). <sup>b</sup>ER was calculated as the number of events/PYFU. <sup>c</sup>Cause of death included large intestine hemorrhage (Part A, efgartigimod IV arm), MG crisis (Part A, placebo arm), sudden unexplained death (Part B, originally efgartigimod IV arm in Part A), and intestinal obstruction (Part B, originally efgartigimod IV arm in Part A). <sup>d</sup>No anaphylactic reactions were observed. <sup>e</sup>≥5% of participants treated with efgartigimod in Part A/B.

**FIGURE 1** Mean MG-ADL Total Score Change From Study Baseline, Overall Population and Serotype Subpopulations<sup>a</sup>



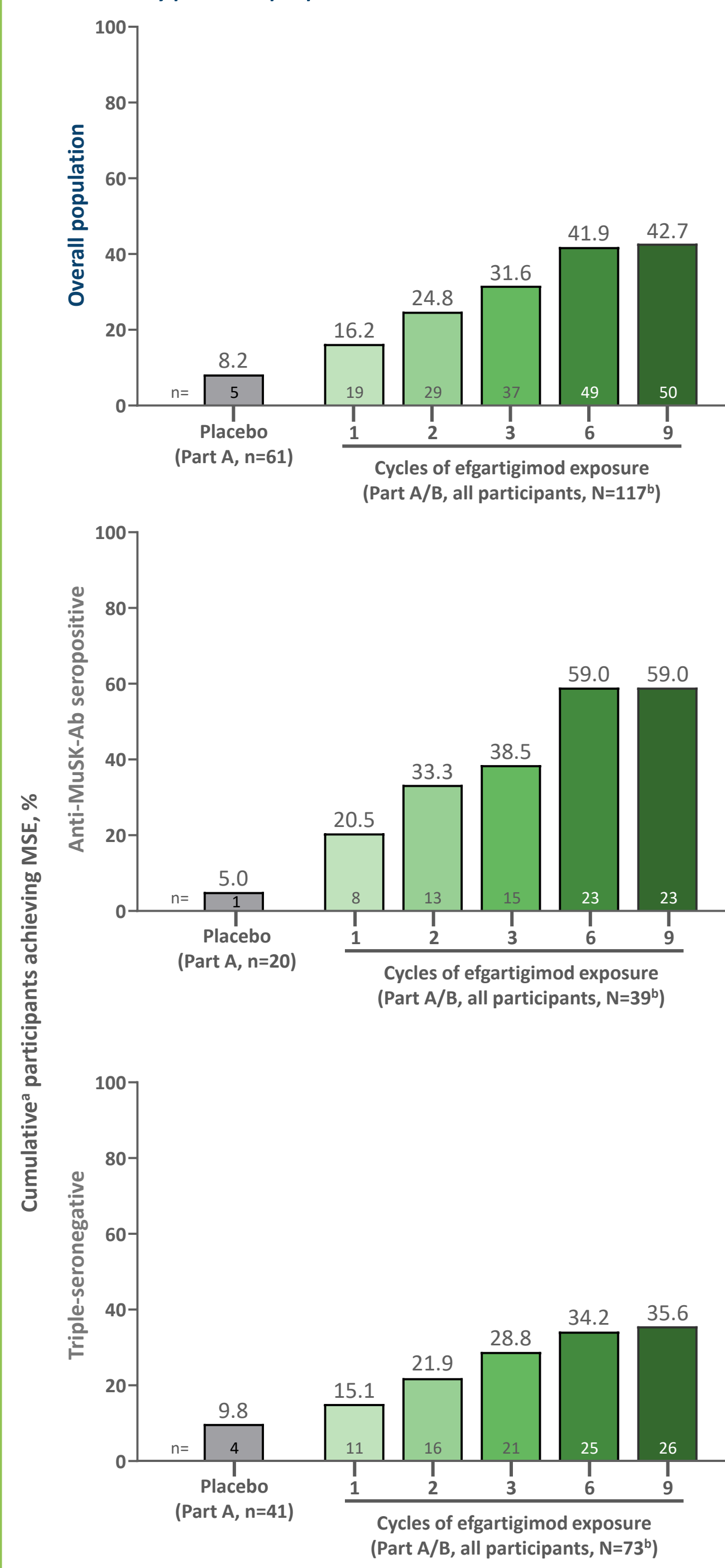
<sup>a</sup>Participant numbers vary over time due to discontinuations, missed clinic visits, or participants not reaching the scheduled timepoint. No participants had missing data (completed clinic visits without a reported MG-ADL assessment). <sup>b</sup>CMI is defined as an improvement of ≥2 points in MG-ADL total score. <sup>c</sup>Time is presented as weeks since the study's start. Analysis windows for each week beginning at Week 7 include assessments completed 110 days from the precise week timepoint. Each time point presents data from a single assessment, and each assessment could be used only one time in the analysis. If ≥1 assessment was available within the analysis window for a given week, only the assessment nearest the week timepoint was used. If 2 assessments were the same duration from the week timepoint, then the later assessment was used. <sup>d</sup>No placebo-treated anti-LRP4-Ab+ patients were enrolled. Analyses are based on a limited number of efgartigimod-treated patients across all visits.

**FIGURE 2** Cumulative Participants Achieving MG-ADL Total Score Improvement Thresholds at Cycle Week 4,  
Overall Population



<sup>a</sup>For participants in the overall population treated with efgartigimod, the cumulative percentage indicates participants who achieved the improvement threshold at Week 4 of the indicated cycle or at Week 4 of any preceding cycle. <sup>b</sup>The population for this analysis included all participants who completed ≥1 MG-ADL assessment after initiation of efgartigimod treatment.

**FIGURE 3** Cumulative Participants Achieving MSE (MG-ADL Total Score 0 or 1), Overall Population and Serotype Subpopulations



<sup>a</sup>For participants in the overall population treated with efgartigimod, the cumulative percentage indicates participants who achieved MSE (MG-ADL total score of 0 or 1) at any time during the indicated cycle or any preceding cycle. <sup>b</sup>The population for this analysis included all participants who completed ≥1 MG-ADL assessment after initiation of efgartigimod treatment.

### ABBREVIATIONS

Ab, antibody; AChEI, acetylcholinesterase inhibitor; AChR, acetylcholine receptor; CMI, clinically meaningful improvement; EFG, efgartigimod; ER, event rate; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IMP, investigational medicinal product; IRR, infusion-related reaction; IV, intravenous; LD, low-density lipoprotein; LRP4, low-density lipoprotein receptor-related protein 4; LS, least squares; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MMRM, mixed model for repeated measures; MuSK, muscle-specific tyrosine kinase; MSE, minimal symptom expression; NSIST, nonsteroidal immunosuppressive therapy; OLP, open-label period; PYFU, participant years of follow-up; TEAE, treatment-emergent adverse event.

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