Long-Term Safety, Tolerability, and Efficacy of Efgartigimod in Patients With Generalized Myasthenia Gravis: Interim Results of the ADAPT+ Study

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Efgartigimod Mechanism of Action: Blocking FcRn

- FcRn recycles IgG, extending its half-life and serum concentration\(^1\)

- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity to FcRn\(^2\)

- Efgartigimod was designed to outcompete endogenous IgG, preventing recycling, and promoting lysosomal degradation of IgG, without impacting its production\(^2-5\)
  - Targeted reduction of all IgG subtypes
  - No impact on IgM or IgA
  - No reduction in albumin levels
  - No increase in cholesterol

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**Sources:**

5. argenx Data on File, 2022.

**Abbreviations:**

FC, crystallizable fragment; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M.
ADAPT+ Study Design

**ADAPT+ Study Design**

**ADAPT¹ (Placebo controlled)**
- 26 weeks (max. 3 cycles)
- N=151
- Efgartigimod
- Placebo

**ADAPT+ (Open-label efgartigimod)**
- Up to 3 years
- Part A (1 y)
- Part B (2 y)
- Efgartigimod

**2 weeks screening**
- MGFA Class II, III, IV
- AChR-antibody positive or negative
- MG-ADL score ≥5
- On ≥1 stable gMG treatment
- IgG ≥6 g/L

**Subsequent treatment cycle(s) if required**

Arrows indicate treatment periods of 4 infusions at weekly intervals

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AChR, acetylcholine receptor; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; Wk, week. Note: Patients requiring rescue therapy discontinued from the study treatment.

Efgartigimod Demonstrated Repeatable and Sustained Improvement in Both MG-ADL and QMG Over Multiple Cycles\textsuperscript{a} in ADAPT+

\textit{ACHR-Ab+ Population}

\textbf{MG-ADL Total Score}
Mean Change From Cycle Baseline by Cycle
(Efgartigimod + current TX)

\begin{table}
\begin{tabular}{cccc}
周期 & 患者 & 周期1 & 周期2 & 周期3 & 周期7 & 周期11 \\
1 & 106 & 105 & 102 & 103 & 103 & 57 \\
2 & 99 & 99 & 95 & 95 & 97 & 49 \\
3 & 86 & 85 & 85 & 85 & 81 & 33 \\
4 & 74 & 72 & 73 & 71 & 66 & 22 \\
5 & 61 & 61 & 61 & 61 & 57 & 15 \\
\end{tabular}
\end{table}

\textbf{QMG Total Score}
Mean Change From Cycle Baseline by Cycle
(Efgartigimod + current TX)

\begin{table}
\begin{tabular}{cccc}
周期 & 患者 & 周期1 & 周期2 & 周期3 & 周期7 & 周期11 \\
1 & 106 & 103 & 101 & 100 & 90 & 49 \\
2 & 99 & 93 & 89 & 89 & 73 & 38 \\
3 & 83 & 76 & 73 & 73 & 59 & 25 \\
4 & 65 & 54 & 57 & 55 & 49 & 15 \\
5 & 49 & 47 & 48 & 44 & 40 & 10 \\
\end{tabular}
\end{table}

*Only cycles with data out to week 11 are depicted*
Proportion of Patients With Increasing MG-ADL or QMG Improvement Over Multiple Cycles

**AChR-Ab+ Population**

**Change in MG-ADL Total Score**
- **Efgartigimod (open-label)**
  - Week 3 of cycles 1-5 in ADAPT+
  - Median % (range)
- **Placebo (phase 3)**
  - Week 3 of Cycle 1 in ADAPT

- **≥9**
  - Efgartigimod: 20.0% (0.0%)
  - Placebo: 0.0% (0.0%)
- **≥8**
  - Efgartigimod: 29.4% (0.0%)
  - Placebo: 0.0% (0.0%)
- **≥7**
  - Efgartigimod: 38.9% (1.6%)
  - Placebo: 3.3% (3.3%)
- **≥6**
  - Efgartigimod: 48.2% (3.3%)
  - Placebo: 9.8% (9.8%)
- **≥5**
  - Efgartigimod: 56.5% (9.8%)
  - Placebo: 21.3% (21.3%)
- **≥4**
  - Efgartigimod: 68.4% (21.3%)
  - Placebo: 31.1% (31.1%)
- **≥3**
  - Efgartigimod: 78.4% (31.1%)
  - Placebo: 45.9% (45.9%)
- **≥2**
  - Efgartigimod: 85.9% (45.9%)
  - Placebo: 63.6% (63.6%)
- **1**
  - Efgartigimod: 6.3% (19.7%)
  - Placebo: 5.3% (13.1%)
- **0 (no change)**
  - Efgartigimod: 5.3% (13.1%)
  - Placebo: 5.3% (13.1%)
- **Worsened**
  - Efgartigimod: 3.9% (21.3%)
  - Placebo: 3.9% (21.3%)

**Change in QMG Total Score**
- **Efgartigimod (open-label)**
  - Week 3 of cycles 1-5 in ADAPT+
  - Median % (range)
- **Placebo (phase 3)**
  - Week 3 of Cycle 1 in ADAPT

- **≥10**
  - Efgartigimod: 12.3% (0.0%)
  - Placebo: 0.0% (0.0%)
- **≥9**
  - Efgartigimod: 16.0% (0.0%)
  - Placebo: 0.0% (0.0%)
- **≥8**
  - Efgartigimod: 23.3% (0.0%)
  - Placebo: 0.0% (0.0%)
- **≥7**
  - Efgartigimod: 28.0% (1.7%)
  - Placebo: 1.7% (1.7%)
- **≥6**
  - Efgartigimod: 36.0% (1.7%)
  - Placebo: 1.7% (1.7%)
- **≥5**
  - Efgartigimod: 41.8% (5.2%)
  - Placebo: 5.2% (5.2%)
- **≥4**
  - Efgartigimod: 53.0% (15.5%)
  - Placebo: 15.5% (15.5%)
- **≥3**
  - Efgartigimod: 63.6% (27.6%)
  - Placebo: 27.6% (27.6%)
- **2**
  - Efgartigimod: 9.1% (12.1%)
  - Placebo: 12.1% (12.1%)
- **1**
  - Efgartigimod: 12.3% (15.5%)
  - Placebo: 15.5% (15.5%)
- **0 (no change)**
  - Efgartigimod: 6.8% (15.5%)
  - Placebo: 6.8% (15.5%)
- **Worsened**
  - Efgartigimod: 7.0% (29.3%)
  - Placebo: 29.3% (29.3%)

AChR-Ab, acetylcholine receptor autoantibody; CMI, clinically meaningful improvement; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis.

*a Only cycles with data out to week 11 are included.*
## Safety: Summary of AEs

**Safety Population**

<table>
<thead>
<tr>
<th></th>
<th>ADAPT (n=83) [34.51 PY]</th>
<th>ADAPT+ (n=84) [34.86 PY]</th>
<th>Efgartigimod (n=139) [138.14 PY]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AEs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IR/PY</td>
<td>7.83</td>
<td>7.23</td>
<td>4.06</td>
</tr>
<tr>
<td>% (n)</td>
<td>84 (70)</td>
<td>77 (65)</td>
<td>81 (112)</td>
</tr>
<tr>
<td><strong>SAEs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IR/PY</td>
<td>0.29</td>
<td>0.11</td>
<td>0.25</td>
</tr>
<tr>
<td>% (n)</td>
<td>8 (7)</td>
<td>5 (4)</td>
<td>15 (21)</td>
</tr>
<tr>
<td><strong>≥1 Infusion-related reaction event</strong></td>
<td>0.26</td>
<td>0.09</td>
<td>0.09</td>
</tr>
<tr>
<td>IR/PY</td>
<td>1.22</td>
<td>1.61</td>
<td>0.84</td>
</tr>
<tr>
<td>% (n)</td>
<td>37 (31)</td>
<td>46 (39)</td>
<td>47 (65)</td>
</tr>
<tr>
<td><strong>Infection AEs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IR/PY</td>
<td>0.09</td>
<td>0.20</td>
<td>0.07</td>
</tr>
<tr>
<td>% (n)</td>
<td>4 (3)</td>
<td>4 (3)</td>
<td>6 (8)</td>
</tr>
<tr>
<td><strong>Discontinued study treatment due to AEs</strong></td>
<td>0.35</td>
<td>0.29</td>
<td>0.41</td>
</tr>
<tr>
<td>IR/PY</td>
<td>0.35</td>
<td>0.29</td>
<td>0.41</td>
</tr>
<tr>
<td>% (n)</td>
<td>10 (8)</td>
<td>11 (9)</td>
<td>19 (26)</td>
</tr>
<tr>
<td><strong>Severe AEs (grade ≥3)</strong></td>
<td>0.35</td>
<td>0.29</td>
<td>0.41</td>
</tr>
<tr>
<td>IR/PY</td>
<td>0.35</td>
<td>0.29</td>
<td>0.41</td>
</tr>
<tr>
<td>% (n)</td>
<td>10 (8)</td>
<td>11 (9)</td>
<td>19 (26)</td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td>0</td>
<td>0</td>
<td>0.04</td>
</tr>
<tr>
<td>IR/PY</td>
<td>0.09</td>
<td>0.20</td>
<td>0.07</td>
</tr>
<tr>
<td>% (n)</td>
<td>0 (0)</td>
<td>4 (3)</td>
<td>7 (10)</td>
</tr>
<tr>
<td><strong>Most frequent AEs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>0.49</td>
<td>0.34</td>
<td>0.14</td>
</tr>
<tr>
<td>IR/PY</td>
<td></td>
<td>12 (10)</td>
<td>11 (15)</td>
</tr>
<tr>
<td>% (n)</td>
<td>18 (15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>0.15</td>
<td>0.32</td>
<td>0.04</td>
</tr>
<tr>
<td>IR/PY</td>
<td></td>
<td>11 (9)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>% (n)</td>
<td>5 (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>0.12</td>
<td>0.26</td>
<td>0.09</td>
</tr>
<tr>
<td>IR/PY</td>
<td></td>
<td>10 (8)</td>
<td>7 (10)</td>
</tr>
<tr>
<td>% (n)</td>
<td>5 (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>1.13</td>
<td>1.15</td>
<td>0.49</td>
</tr>
<tr>
<td>IR/PY</td>
<td></td>
<td>29 (24)</td>
<td>22 (31)</td>
</tr>
<tr>
<td>% (n)</td>
<td>28 (23)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>0.43</td>
<td>0.20</td>
<td>0.07</td>
</tr>
<tr>
<td>IR/PY</td>
<td></td>
<td>8 (7)</td>
<td>5 (7)</td>
</tr>
<tr>
<td>% (n)</td>
<td>11 (9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0.41</td>
<td>0.17</td>
<td>0.11</td>
</tr>
<tr>
<td>IR/PY</td>
<td></td>
<td>7 (6)</td>
<td>9 (12)</td>
</tr>
<tr>
<td>% (n)</td>
<td>11 (9)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AE, adverse event; IR, incidence rate; MG, myasthenia gravis; PY, patient year; SAE, serious adverse event; URTI, upper respiratory tract infection.
# Deaths in ADAPT+: None Related to Efgartigimod per Investigator

<table>
<thead>
<tr>
<th>Age, y/Sex</th>
<th>Cause of Death</th>
<th>Days from last dose</th>
<th>Comorbidities/Medical History</th>
</tr>
</thead>
<tbody>
<tr>
<td>72/F</td>
<td>Unknown; preexisting CV disease, autopsy confirmed coronary artery atherosclerosis and cardiomegaly</td>
<td>4</td>
<td>Pulmonary embolism, chronic obstructive pulmonary disease, hypertension, hypokalemia, and colon bladder fistula</td>
</tr>
<tr>
<td>79/M</td>
<td>MG crisis and progression of underlying disease/	extit{Escherichia coli} pneumonia</td>
<td>79</td>
<td>Chronic rhinitis, anxiety</td>
</tr>
<tr>
<td>66/F</td>
<td>Malignant lung neoplasm (Stage IV)</td>
<td>60</td>
<td>Histoplasmosis, asthma, diabetes mellitus, hypercholesterolemia, macular degeneration, hypertension, squamous cell carcinoma, and bundle branch block</td>
</tr>
<tr>
<td>55/M</td>
<td>Acute MI and generalized unspecified atherosclerosis</td>
<td>24</td>
<td>Anemia, subarachnoid hemorrhage, CTO PCI and angioplasty procedures</td>
</tr>
<tr>
<td>62/M</td>
<td>Septic shock/COVID-19 pneumonia</td>
<td>69</td>
<td>Chronic venous insufficiency, arterial hypertension, deep vein thrombosis, rheumatoid arthritis, and paroxysmal atrial fibrillation</td>
</tr>
</tbody>
</table>

CTO PTI, chronic total occlusion percutaneous coronary intervention; CV, cardiovascular; MI, myocardial infarction; MG, myasthenia gravis; PBO, placebo; PI, principal investigator.
54.6% of patients received ≤5.5 cycles per year
Summary

The safety profile observed during long-term treatment with efgartigimod in ADAPT+ mirrored that seen during ADAPT, even while being conducted during the COVID-19 global pandemic.

This analysis suggests that long-term treatment with efgartigimod is efficacious, providing consistent and repeatable clinically meaningful improvement in function and strength while remaining well tolerated.

ADAPT+ is a planned 3-year study and is currently ongoing.