# HOSPITALIZATION AND EXACERBATION ESTIMATES OF EFGARTIGIMOD VS. CONVENTIONAL THERAPY IN GENERALIZED MYASTHENIA GRAVIS PATIENTS: A POST-HOC ANALYSIS OF THE PHASE 3 ADAPT STUDY

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## Background

- Myasthenia gravis (MG) is a rare, chronic, autoimmune neuromuscular disease which can affect functional and mental aspects of health and health-related quality of life (HRQoL).
- The two most common forms of MG are ocular (affecting the muscles of the eyes and eyelids) and generalized MG. Generalized MG (gMG) affects muscles all throughout the body, causing difficulties with vision, swallowing, speech, mobility, limb strength and respiratory function. Patients suffer from fatigue and frequently experience anxiety and depression.
- Although 85% of MG patients progress to gMG, approximately 37% of MG patients are intolerant for or have an inadequate response to conventional therapy (CT).[1]
- Efgartigimod (Efg) has demonstrated its efficacy over CT in the ADAPT phase 3 trial (NCT: NCT03669588), in terms of improvements in the Quantitative MG (QMG) total score and Myasthenia Gravis Activities of Daily Living (MG-ADL) total score.
- Recently, Efg got approved by the US FDA for treatment of gMG patients with anti-acetylcholine receptor antibody-positive (AChR+) disease(2021)

## Objectives

- The objective of this study is to examine whether efgartigimod reduces the rate of hospitalization (all-cause and MG-related) and the risk of exacerbation rates among adults with gMG using data from the ADAPT clinical study.
- Results are evaluated among the ADAPT intent-to-treat (ITT) and AChR+ population.

## Methods

ADAPT is a 26-week, global phase 3, randomized, double-blind, placebo-controlled trial of 167 gMG patients (77% AChR+), of whom 84 received receive CT+Efg and 83 received CT alone.

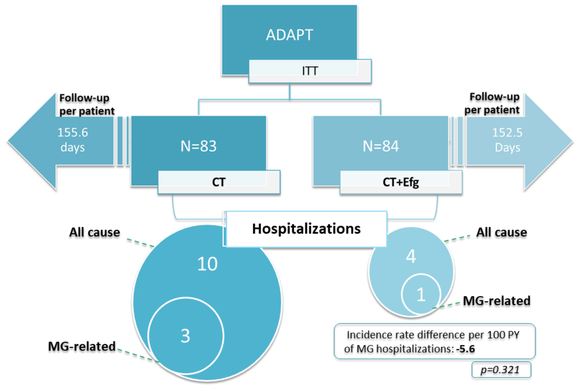
- The outcomes used were obtained through the following validated PRO instruments: QMG, MG-ADL, MGC, MG-QoL, EQ-5D.
- Mean changes from baseline were calculated for all patient-reported outcomes, and all exacerbations, hospitalizations and discontinuations were recorded.
- The primary clinical analysis was performed among AChR+ patients. A detailed description of the study design can be found in the original publication by Howard et al. (2019).[2]
- In this post-hoc analysis, the observed number of all-cause and MG-related hospitalizations during the trial were combined with the patient follow-up time in the study to calculate an incidence rate of hospitalizations per treatment arm.
  - Poisson confidence interval around the incidence rate were computed. The difference in incidence rate between treatment arms and its confidence interval was calculated using a "Test Based method", and its p-value was based on a Chi-Square test.[3]
- The proportion of patients with exacerbations in each treatment arm was also compared using a Chi-Square test.
  - An exacerbation event is defined as a 3-point worsening in QMG score compared to baseline.
- The QMG scale assesses ocular (two items), facial (one item), bulbar (two items), gross motor (six items), axial (one item) and respiratory (one item) symptoms by giving scores of 0-3 to 13 different items, resulting in an unweighted total score of 0-39. A QMG score of ≥ 16 is the cut-off point for severe disease and a 3-point change is identified as the MID.[4]

## Results

### 1. Hospitalizations

- A total of 14 hospitalization events were observed during the study (4 CT+Efg; 10 CT).
- Among these, 4 hospitalizations were related to MG (1 CT+Efg ; 3 CT) (Figure 1).
- CT+Efg patients had a 60% lower rate of all-cause hospitalization (11.4 vs. 28.3 per 100 patient-year [PY]) and 67% lower rate of MG-related hospitalization (2.8 vs. 8.5 per 100 PY) than CT patients (p-value not significant).

**Figure 1. Hospitalization estimates: ITT population**




*Abbreviations: QMG = Quantitative MG score; CT = conventional therapy; Efg = efgartigimod*

### 1.2 MG-related Hospitalizations

- MG-related hospital admissions lasted an average of 47 days.
- The mean QMG score at baseline from those patients was high (19) and did not reduce significantly over time.
- The risk of MG hospitalizations are significantly higher among patients with a high QMG score: 12.5 MG-related hospitalizations per 100 PY of FU among patients with a QMG higher than 16, versus 0 among patients with a QMG lower than 16 (p=0.03).

**Table 1. Details on MG-related hospitalizations**

| Treatment received | QMG at baseline | Duration of hospital stay in days | # of hospital admissions and ER visits in past 12 months | QMG score at time of hospitalization | AChR +/- |
|---|---|---|---|---|---|
| **CT** | 17 | 17 | 5; 5 | 17 | + |
| **CT** | n/a | 87 | 6; 2 | 18 | + |
| **CT** | 21 | 29 | 2; 0 | 19 | + |
| **CT+Efg** | 20 | 55 | 15; 20 | 20 | - |

### 2. Exacerbations

- During the 26-week follow-up, significantly fewer CT+Efg treated patients experienced exacerbations: 21% versus 44% for CT -treated patients (p=0.0016) (Table 2).
- The average worsening in QMG among those 18 CT+Efg and 36 CT patients who are experiencing an exacerbation, is 5.2 (range: 3 to 12) for patients receiving CT+Efg and 5.6 (range: 3 to 15) for patients receiving CT.

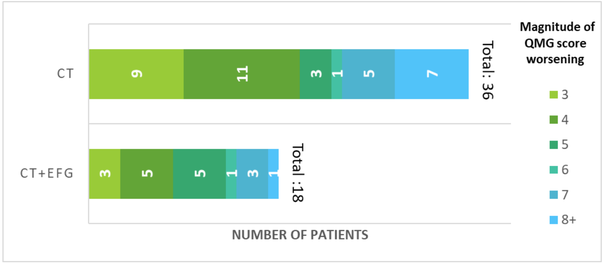
**Table 2. Exacerbations: ITT population**

| | ADAPT – CT | ADAPT – CT+EFG |
|---|---|---|
| **Sample size** | 81* | 84 |
| **Patients with worst QMG of ≥ 3 points higher than baseline, N (%)** | 36 (44%) | 18 (21%) |
| **P-value Chi-Square for proportion** | 0.0016 | |
| **Magnitude of QMG worsening among patients with exacerbation** | 5.6 | 5.2 |

*Abbreviations: QMG = Quantitative MG score; CT = conventional therapy; Efg = efgartigimod*
* 2 with missing baseline QMG data

- Furthermore, significantly fewer patients treated with CT+Efg (1, 1.2%) experienced a QMG worsening of 8 or higher compared to CT patients (7, 8.6%) (Figure 2).

**Figure 2. Magnitude of QMG worsening between CT and CT+Efg**




*Abbreviations: QMG = Quantitative MG score; CT = conventional therapy; Efg = efgartigimod*

### 3. AChR+ Subgroup Results

- Consistent results were seen among patients who are AChR+ (Table 3).
- A total of 12 all-cause hospitalizations were observed in this population (3 CT+Efg; 9 CT), of which 3 related to MG. Those three MG-hospitalizations all occurred in the CT arm (p-value for difference between arms = 0.085)

**Table 3. Hospitalization and exacerbation estimates: AChR+ subgroup**

| | ADAPT – CT | ADAPT – CT+Efg |
|---|---|---|
| **Sample size; follow-up per patient** | 64; 155.6 days | 65; 152.5 days |
| **Hospitalizations** | | |
| **# of hospitalization due to any reason (# of events; rate per 100 PY)** | 9; 25.4 | 3; 8.5 |
| **# of hospitalization related to MG (# of events; rate per 100 PY)** | 3; 8.5 | 0; 0 |
| **Incidence rate difference per 100 PY of MG hospitalizations** | -8.5 | |
| **95% Confidence Interval** | -18.1 to 1.2 | |
| **P-value** | 0.085 | |
| **Exacerbations** | | |
| **# of exacerbations (# of events; N)** | 27; 61 | 17; 65 |
| **P-value** | 0.033 | |

*Abbreviations: CT = conventional therapy; Efg = efgartigimod; PY = person-year*

## Discussion and Conclusions

- Using data from randomized phase 3 trial, we have identified a significant reduction in the risk of exacerbations and numerically lower rates of all-cause and MG-related hospitalization associated with efgartigimod treatment
- These results suggest that efgartigimod may have the benefit to reduce disease burden among patients with gMG, and could potentially result in medical cost offset
- The current analysis is based on limited sample size and follow-up duration, which may have limited the statistical power of its findings
- Future studies with larger sample size and longer follow-up will be important to understand the benefit of efgartigimod in reducing MG disease burden and resource utilization.

**References**

[1] Gilhus, N., Skeie, G., Romi, F. et al. Myasthenia gravis — autoantibody characteristics and their implications for therapy. Nat Rev Neurol 12, 259–268 (2016).[2] Howard JF Jr, Bril V, Vu T, et al. Safety, efficacy, and tolerability of efgartigimod in patients with generalised myasthenia gravis (ADAPT): a multicentre, randomised, placebo-controlled, phase 3 trial [published correction appears in Lancet Neurol. 2021 Aug;20(8):e5]. Lancet Neurol. 2021;20(7):526-536. doi:10.1016/S1474-4422(21)00159-9
[3] Sahai H, Khurshid A (1996) Statistics in epidemiology: methods, techniques, and applications. Boca Raton, FL: CRC Press, Inc.
[4] Thomsen JLS, Andersen H. Outcome Measures in Clinical Trials of Patients With Myasthenia Gravis. Mini Review. Frontiers in Neurology. 2020;11