An adjusted indirect comparison of the efficacy of efgartigimod-alfa, ravulizumab, and eculizumab for treating acetylcholine receptor auto-antibody-positive (achr-ab+) generalized myasthenia gravis

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Background and importance

Generalized myasthenia gravis (gMG) is a rare, chronic, neuromuscular autoimmune disease, mediated by pathogenic immunoglobulin auto-antibodies targeting the neuromuscular junction. **Approximately 10-15% of patients have refractory gMG**, meaning they do not respond despite long-term treatment with corticosteroids and at least two different immunosuppressive therapies.

Biologic therapies approved in European Union as a complementary treatment to standard therapy for AChR-Ab+ refractory gMG patients include **eculizumab**, **ravulizumab** and **efgartigimod alfa**. In Spain, only the last two drugs are funded.

Comparisons assessing the **relative effectiveness** of these drugs are **lacking.**

Aim and objectives

To assess the **relative efficacy** of three antibody-based biologic therapies (efgartigimod-alfa, ravulizumab, and eculizumab) in this setting.

Materials and methods

Table 1: An adjusted indirect comparison (AIC) of randomized clinical trials was performed, using Bucher's method

INCLUSION CRITERIA	OUTCOMES
Phase III, double-blind, placebo-controlled including adults with gMG (MGFA class II-IV) and positive anti-AChR autoantibodies, with an MG-ADL score of ≥5.	***MG-ADL score*** reduction of ≥3 points (Δ = 19%) at week 26. ***QMG score*** reduction of ≥5 points (Δ = 24,5%) at week 26.

- Equivalence was assessed using the equivalent therapeutic alternatives (ETA) guidelines (Alegre et al.).
- An adjusted indirect comparison (AIC) of randomized clinical trials was performed, using Bucher's method.

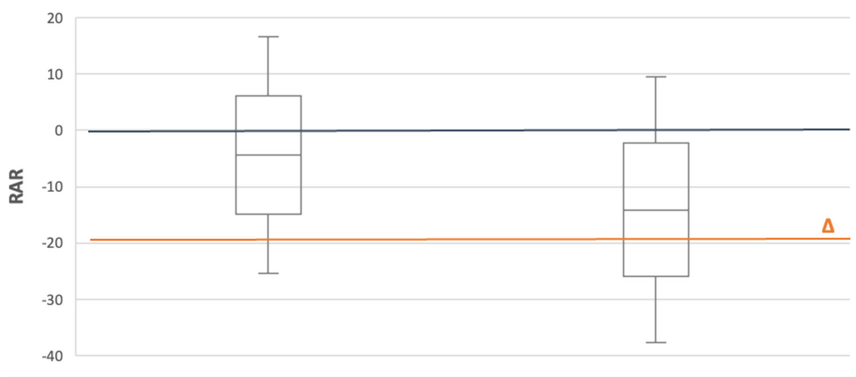
***MG-ADL:** Myasthenia Gravis-Activities of Daily Living.
****QMG:** Quantitative Myasthenia Gravis.

The **main limitation** was the exclusion of other biologic therapies for gMG due to the heterogeneity of outcomes used in clinical trials.

Results

Three trials met the inclusion criteria and shared similar baseline characteristics: **CHAMPION** (efgartigimod-alfa vs. placebo), **ADAPT** (ravulizumab vs. placebo), and **REGAIN** (eculizumab vs. placebo).

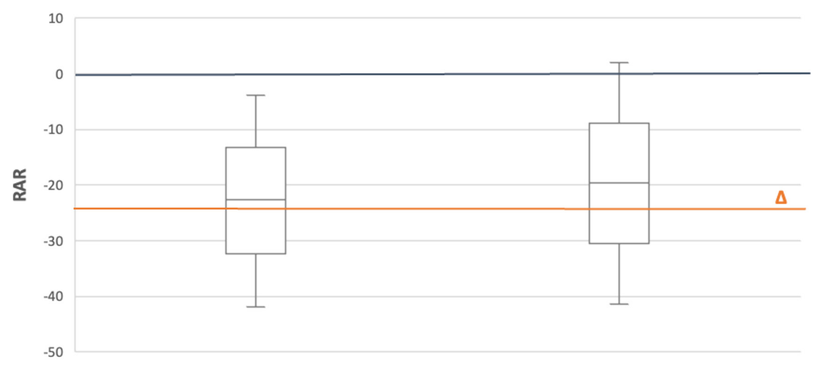
Figure 1. MG-ADL score reduction of ≥3 points vs. Efgartigimod alfa (Δ = 19%).



Ravulizumab
RAR = -4.40
[IC95%: -25.36 – 16.56]
p = 0.681

Eculizumab
RAR = -14.1
[IC95%: -37.78 – 9.58]
p = 0.243

Figure 2. QMG score reduction of ≥5 points vs. Efgartigimod alfa (Δ = 24.5%).



Ravulizumab
RAR = -22.70
[IC95%: -41.98 – -3.92]
p = 0.021

Eculizumab
RAR = -19.7
[IC95%: -41.4 – 2]
p = 0.075

Conclusion and relevance

Our results show that **eculizumab** and **efgartigimod-alfa** present a **probable clinic equivalence** (ETA category: C), but so are **ravulizumab** and **efgartigimod** alfa (ETA category: D) in terms of MG-ADL score reduction. However, there is some inconsistency in case of **ravulizumab** as there could be **statistically relevant differences** versus **efgartigimod alfa** in terms of QMG.

According to ETA guidelines, in cases of inconclusive results such as ours, the absence of equivalence should be assumed. Therefore, more data are needed to position antibody-based biologic therapies.

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