

Background

- gMG is a rare, chronic, neuromuscular autoimmune disease, mediated by pathogenic IgG autoantibodies.¹
- Efgartigimod and ravulizumab have both recently been approved for the treatment of gMG in patients who are AChR-Ab+. Both products were studied in gMG patients in separate placebo-controlled randomized controlled trials (see summary in Table 1).

Table 1 – Description of RCTs included in the analysis

	Efgartigimod	Ravulizumab
Drug type and mechanism of action	Humanized IgG1 antibody Fc fragment vs IgG autoantibody	Humanized monoclonal antibody vs complement factor 5
RCT	ADAPT ¹	CHAMPION ²
AChR-Ab+ gMG patients, n	129	175
MG-ADL at baseline	MG-ADL>5	MG-ADL>6

- An understanding of the comparative efficacy of these two therapies would support the decision-making process in gMG treatment, however no direct comparative evidence exists.
- Our objective was to estimate the relative efficacy of efgartigimod versus ravulizumab by means of a Matching-Adjusted Indirect Comparison (MAIC) anchored to the placebo arm.
- The analysis included only AChR-Ab+ patients.

Methods

Matching-Adjusted Indirect Comparison

- Published aggregate data from CHAMPION and individual patient data (IPD) from ADAPT were used.
- The ADAPT population was restricted to align with the eligibility criteria for CHAMPION, therefore 110 ADAPT participants were included in the analysis.
- ADAPT IPD were then weighted to match the baseline characteristics (only treatment effect modifiers) of the CHAMPION population (Table 2).
- This allows estimation of the relative effect of efgartigimod vs placebo if efgartigimod was administered to the CHAMPION population.

Table 2 – Variables used for weighting

Study	ADAPT ¹		CHAMPION ²	
	Efgartigimod	Placebo	Ravulizumab	Placebo
Number of patients at baseline	65	64	86	89
Years since diagnosis, mean (SE)	9.7 (8.3)	8.9 (8.2)	9.8 (9.7)	10.0 (8.9)
Glucocorticoids at baseline, n (%)	46 (71)	51 (79)	56 (65)	65 (73)
Other NSID at baseline, n (%)	40 (62)	37 (58)	56 (65)	65 (73)
MG-ADL score at baseline, mean (SE)	9.0 (2.5)	8.6 (2.1)	9.1 (2.6)	8.9 (2.3)

Main endpoints

- MG-ADL change from baseline to the time of best response (week 4 for efgartigimod and week 26 for ravulizumab) compared with placebo
- MG-ADL change from baseline to week 4 compared with placebo (sensitivity analysis)
- The Number Needed to Treat (NNT) at the time of best response. NNT represents the number of patients who need to be treated to observe an additional patient achieving an MG-ADL reduction of at least 2 points. NNT was defined as the reciprocal of the proportion of participants with a MG-ADL reduction of at least 2 points.

Statistical model

- To align with the data reported in the CHAMPION publication, the MG-ADL change from baseline in ADAPT was calculated using the least squares mean obtained from a mixed model for repeated measurements fitted on the IPD, with weighting to account for the MAIC adjustment.
- The model included treatment, visit and treatment by visit interaction terms as fixed effects, with baseline value and stratification factors (ethnicity, use of corticosteroids at baseline) as covariates. Within-subject correlation was modelled assuming an unstructured covariance matrix for the error terms.
- In ADAPT, the proportion of the cohort that achieved a MG-ADL reduction of at least 2 points was calculated using a weighted generalized linear model with identity link, with treatment arm and baseline MG-ADL as covariates. The model was weighted to adjust for the MAIC analysis.

ABBREVIATIONS:

AChR-Ab+ = Acetylcholine Receptor Autoantibodies Positive
gMG = Generalized myasthenia gravis (gMG)
IPD = Individual Patient Data
MAIC = Matching-Adjusted Indirect Comparison
MGFA = Myasthenia Gravis Foundation of America

MG-ADL = Myasthenia Gravis Activities of Daily Living
NNT = Number Needed To Treat
NSID = Non-Steroidal Immunosuppressive Drug
RCT = Randomized controlled trial

REFERENCES: 1. Howard J. F., et al. (2021); *The Lancet Neurology*, 20(7), 526–536; 2. Vu T., et al. (2022); *NEJM Evidence*, 1(5)

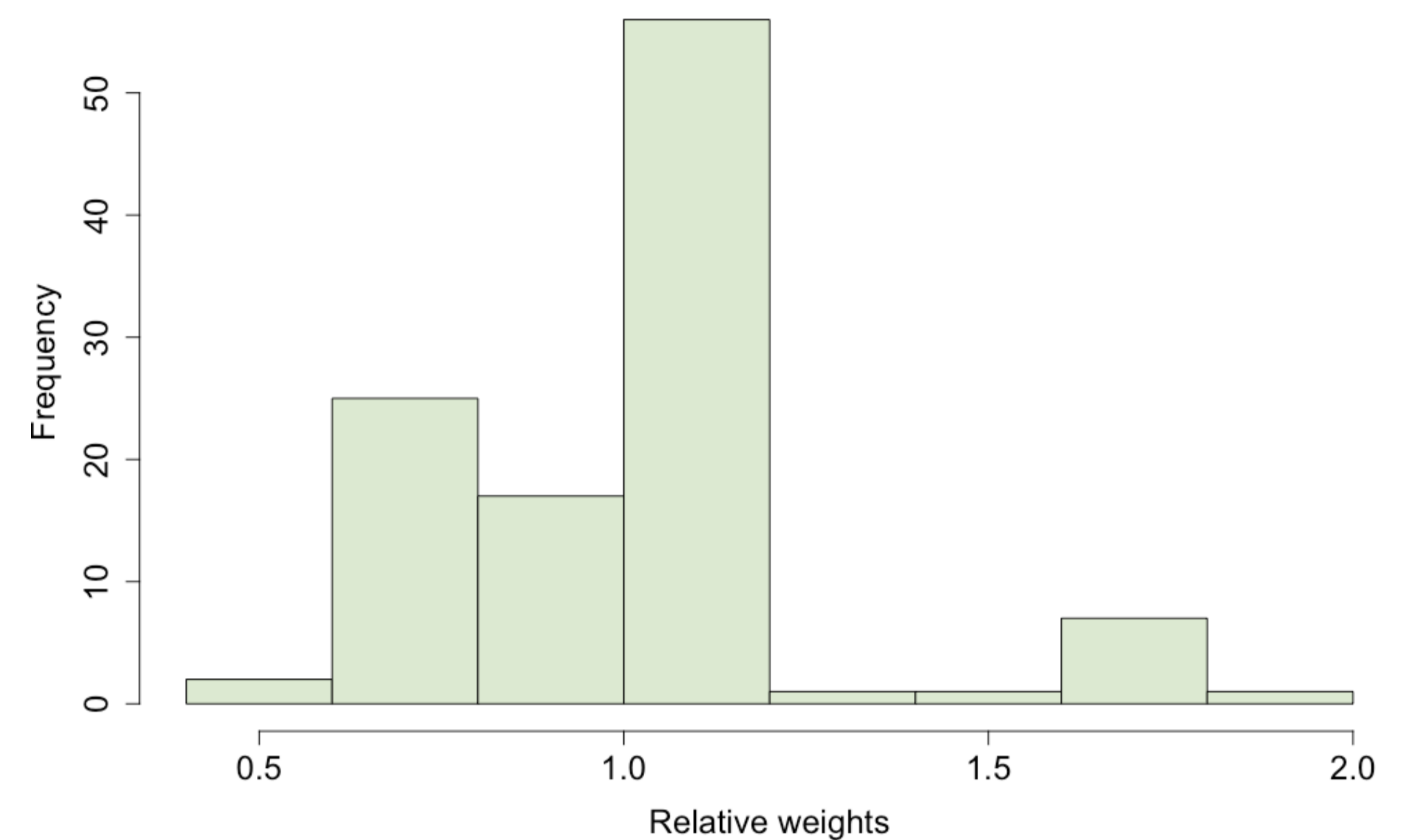
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Results

MAIC reweighting

- A convergence of the baseline characteristics of the ADAPT and the CHAMPION populations was obtained for the variables used in the weighting.
- The effective sample size amounted to 102.4 (93.1% of the included sample size).
- The weights were evenly distributed in the cohort with few outliers (Figure 1).

Figure 1 – Distribution of the relative weights estimated by means of the MAIC analysis



MG-ADL reduction

- At time of best response, the reduction in MG-ADL from baseline was 1.4 points greater (SE= 0.7, 95% CI=[0.0, 2.8], p-value <0.05) for efgartigimod than ravulizumab.
- At week 4, the reduction in MG-ADL from baseline was 1.9 points greater (SE= 0.7, 95% CI =[-0.6, 3.2], p-value <0.001) for efgartigimod than ravulizumab.

Table 2 –MG-ADL change from baseline for efgartigimod vs ravulizumab

	Mean (SD)	95% CI (lower; upper)	P-value
Efgartigimod and ravulizumab separately vs placebo			
Efgartigimod vs placebo at week 4 (time of best response)	-3.0 (0.5)	-4.0; -2.0	<0.001
Ravulizumab vs placebo at week 26 (time of best response)	-1.6 (0.5)	-2.6; -0.6	<0.001
Ravulizumab vs placebo at week 4	-1.1 (0.5)	-2.0; -0.1	<0.05
Efgartigimod vs ravulizumab			
Efgartigimod vs ravulizumab at time of best response	-1.4 (0.7)	-2.8; 0.0	<0.05
Efgartigimod vs ravulizumab at week 4	-1.9 (0.7)	=-3.2; -0.6	<0.05

NNT (MG-ADL reduction of at least 2 points)

- At time of best response, the estimated NNT to observe one patient with MG-ADL reduction of at least 2 points was 3.1 for efgartigimod and 9.2 for ravulizumab.
- The proportion of cohort with at least 2 MG-ADL point reduction was not reported at week 4 in the CHAMPION study and therefore NNT at week 4 for ravulizumab could not be estimated.

Conclusions

- This is the first study indirectly comparing the efficacy of efgartigimod and ravulizumab in the treatment of gMG AChR-Ab+ patients.
- Efgartigimod was associated with greater reduction in MG-ADL from baseline than ravulizumab both at the time of best response and at week 4.
- The estimation of NNT at time of best response suggests that that more patients need to be treated with ravulizumab to observe one patient with at least 2 points MG-ADL reduction than with efgartigimod.
- A limitation of the current study pertains to the covariates adjusted in the MAIC, which were selected in alignment with stratification variables used for the subgroup analyses in ADAPT. No formal analysis was conducted to verify that these are effectively treatment effect modifiers.
- Notwithstanding the limitation outlined above, the MAIC provides initial evidence that efgartigimod may be associated with a greater efficacy compared with ravulizumab in the treatment of patients with gMG and AChR-Ab+.