ASSOCIATION BETWEEN MYASTHENIA GRAVIS-ACTIVITIES OF DAILY LIVING (MG-ADL) AND EQ-5D-5L UTILITY VALUES: THE ADDITIONAL EFFECT OF EFGARTIGIMOD ON UTILITIES

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Introduction and Objectives

Introduction

- Generalized Myasthenia gravis (gMG) is a neurological condition affecting muscle strength and often results in problems with energy, vision, swallowing, chewing, limb weakness, and breathing.[1,2]
- Prevalence estimates indicate gMG affects as many as 700,000 people worldwide and 103,000 people in the European Union (EU).[3,4]
- Patients with gMG experience impacts to social function, psychological health, and physical heath and report lower health-related quality of life (HRQoL) compared to the general population.[5-7]

Myasthenia Gravis Activities of Daily Living (MG-ADL) Scale and EuroQol-5-Dimension 5-Level (EQ-5D-5L) HRQoL Instrument

- The MG-ADL is a valid and reliable disease-specific clinician-reported outcome measure assessing gMG symptoms and functional status.[2,8] Eight items (talking, chewing, swallowing, breathing, brushing teeth/combing hair, rising from a chair, double vision, and eyelid droop) are assessed across 4 domains (bulbar, respiratory, limb weakness, and ocular).[1] It is increasingly used in observational studies, as a primary endpoint in trials, and in clinical practice.[2]
- The EQ-5D-5L is an HRQoL instrument used in a variety of indications, including gMG, that can summarize responses to 5 questions as a utility value using a country-specific value set.[9,10] Utility values range from 1 = full health to 0 = death, but negative values are also possible to indicate health states worse than death.[9]
- Little is known about the association between functional status (as measured by the MG-ADL) and utility values in patients with gMG. The ADAPT phase 3 study is one of the few clinical trials that assessed both MG-ADL and EQ-5D-5L in patients with gMG.[11]

Study Objectives

- To determine the association between MG-ADL and EQ-5D-5L utility values using data from the ADAPT study.
- To assess if the improvement in utility as captured by the EQ-5D-5L is entirely attributable to an improvement in MG-ADL scores, or if there may be additional drivers.

Methods

Data Source

- MG-ADL was measured simultaneously with the EQ-5D-5L on a bi-weekly basis for up to 26 weeks in ADAPT, a Phase-3, multicenter, randomized, placebo-controlled clinical trial among adult patients with gMG who were randomized to efgartigimod in combination with conventional therapy (EFG+CT) or matching placebo plus CT (PBO+CT).[11]

Statistical analysis

- Descriptive statistics were reported for MG-ADL items and total score and for the EQ-5D-5L dimensions and utility values at baseline and at follow-up (all available time points pooled together, from week 1 to week 26).
- A first normal ID regression estimated the association between utility and the eight domains of the MG-ADL.
- A Generalized Estimating Equations (GEE) model was then estimated to predict utility based on the patient's total MG-ADL score and treatment received. This regression also had the utility complement (=1 - utility value) as the dependent variable, and time (in days), time squared, the MG-ADL score, MG-ADL score squared, treatment, and interaction terms between treatment and time, and treatment and MG-ADL score as independent variables.

Results

- 167 patients (84 EFG+CT, 83 PBO+CT) contributed 3064 simultaneous measurements of MG-ADL and EQ-5D-5L scores, of which 167 were at baseline and 2897 at follow-up (all time points combined, from week 1 to week 26).
- Mean MG-ADL and EQ-5D-5L scores were relatively similar between groups at baseline (Table 1) and improved more in the EFG+CT group than the PBO+CT group at follow-up.

Table 1. Key Baseline Characteristics of Patients in the ADAPT Trial

	EFG+CT (n = 84)	PBO+CT (n = 83)
Age, years (SD)	45.9 (14.4)	48.2 (15.0)
Female, n (%)	63 (75%)	55 (66%)
Time since gMG diagnosis, years (SD)	10.1 (9.0)	8.8 (7.6)
Baseline EQ-5D-5L, mean utility score (SD)	0.66 (0.17)	0.62 (0.17)
Baseline MG-ADL, mean score (SD)	9.2 (2.6)	8.8 (2.3)

Adapted from Howard et al. 2021.[11] Baseline EQ-5D-5L data from Argenx Data on File.[12] For a more detailed list of baseline characteristics see Howard et al. 2021.[11]

- Between baseline and follow-up, greater improvements were seen in patients treated with EFG+CT versus PBO+CT in the EQ-5D-5L dimensions of self-care, usual activities, and mobility; changes between the treatment arms were similar for pain/discomfort and anxiety/depression (Table 2).

Table 2. Proportion of Patients Reporting No or Slight Problems on EQ-5D-5L Items at Baseline and Follow-Up

EQ-5D-5L Item	EFG+CT			PBO+CT		
	Baseline	Follow-Up	Change	Baseline	Follow-Up	Change
Mobility	56.1%	75.3%	19.2%	50.6%	58.8%	8.2%
Self-Care	69.6%	87.8%	18.2%	68.6%	63.9%	-4.7%
Usual Activities	40.2%	72.6%	32.4%	37.4%	52.7%	15.3%
Pain/Discomfort	70.7%	80.6%	9.9%	60.2%	70.0%	9.8%
Anxiety/Depression	90.2%	91.4%	1.2%	81.9%	83.3%	1.4%

- Similarly, compared to patients receiving PBO+CT, patients receiving EFG+CT demonstrated greater improvements across most MG-ADL individual items, with an increase in the proportion of patients reporting normal function at follow-up compared with baseline (Table 3).

Table 3. Proportion of Patients Reporting Normal Function on MG-ADL Items at Baseline and Follow-Up

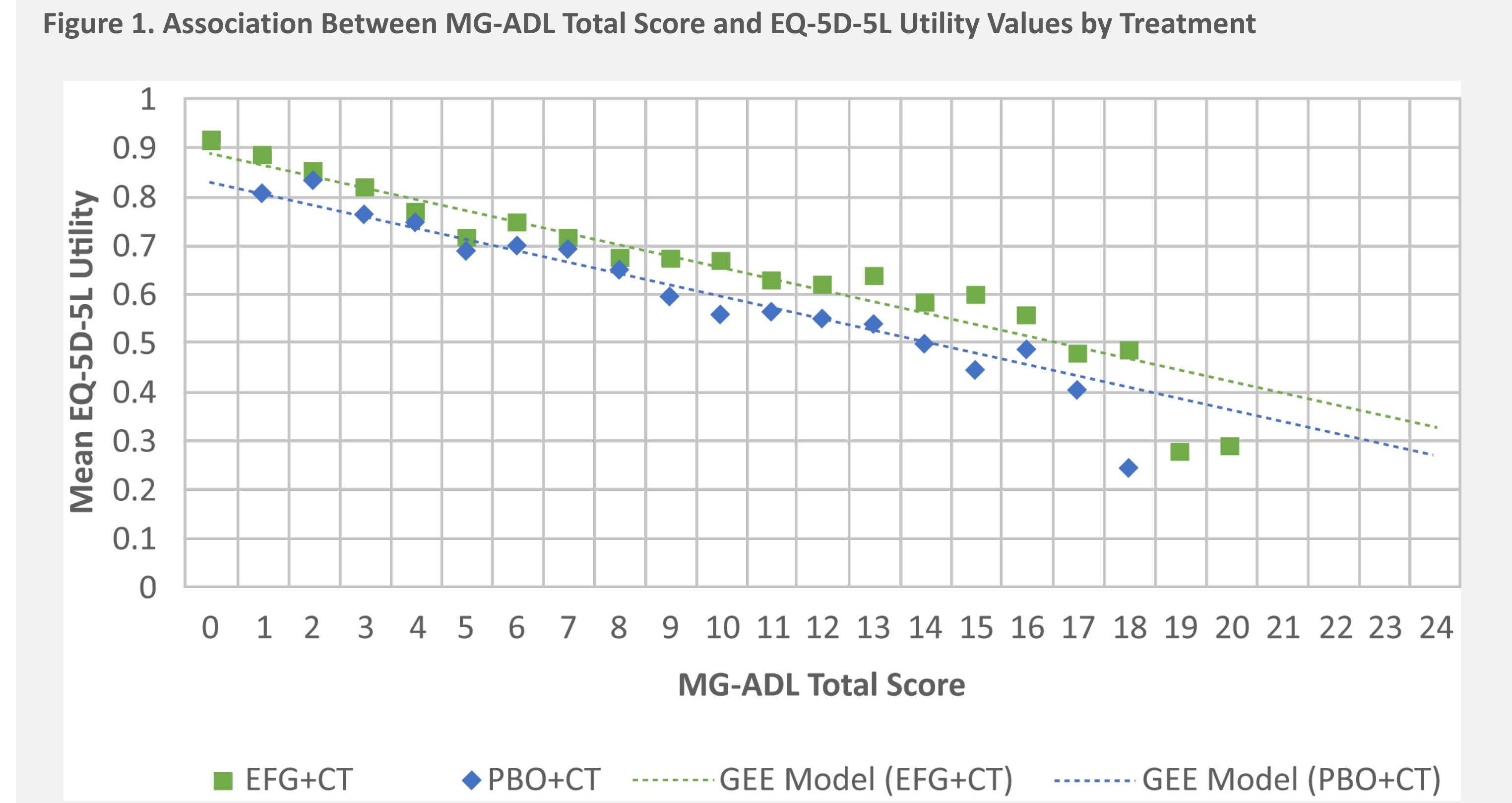| MG-ADL Item	EFG+CT			PBO+CT		
	Baseline	Follow-Up	Change	Baseline	Follow-Up	Change
Talking	24.4%	55.8%	31.4%	22.9%	43.4%	20.5%
Chewing	14.6%	56.5%	41.9%	13.3%	33.7%	20.4%
Swallowing	19.5%	52.1%	32.6%	24.1%	48.7%	24.6%
Breathing	12.2%	33.2%	21.0%	10.8%	23.5%	12.7%
Impairment of Ability to Brush Teeth/Comb Hair	15.9%	49.8%	33.9%	15.7%	29.3%	13.6%
Impairment of Ability to Rise from a Chair	17.1%	42.3%	25.2%	19.3%	32.4%	13.1%
Double Vision	39.0%	46.0%	7.0%	37.4%	47.2%	9.8%
Eyelid Droop	20.7%	41.2%	20.5%	30.1%	35.7%	5.6%

- Regression analysis (Table 4) demonstrated that all individual MG-ADL items contributed statistically significantly but differently to utility values (except for eyelid droop), with the greatest contributions from brushing teeth/combing hair, rising from a chair, and breathing.

Table 4. Regression of EQ-5D-5L Score by MG-ADL Item

Independent Variables	Parameter Estimate	SE	95% Lower CI	95% Upper CI	Type 3 p-value
Intercept	0.139	0.014	0.113	0.166	< 0.0001
Talking	0.021	0.005	0.011	0.031	< 0.0001
Chewing	0.026	0.005	0.017	0.035	< 0.0001
Swallowing	0.013	0.005	0.003	0.022	0.0098
Breathing	0.026	0.005	0.016	0.036	< 0.0001
Brush Teeth & Hair	0.042	0.004	0.034	0.050	< 0.0001
Rise From a Chair	0.036	0.007	0.023	0.048	< 0.0001
Double Vision	0.015	0.004	0.006	0.023	0.001
Eyelid Droop	0.007	0.004	-0.001	0.016	0.0938

- The GEE model, which included MG-ADL score and treatment as independent variables, showed that each unit improvement in MG-ADL led to a utility increase of 0.0233 (p < 0.001). EFG+CT-treated patients experienced an additional improvement of 0.0598 (p = 0.0079) in utility for the same MG-ADL score (Figure 1 and Table 5).

Figure 1. Association Between MG-ADL Total Score and EQ-5D-5L Utility Values by Treatment

Note: Regression results on utility from the GEE model are represented by the dashed lines.

Legend: ■ EFG+CT   ◆ PBO+CT   ···· GEE Model (EFG+CT)   ···· GEE Model (PBO+CT)

Table 5. GEE Model: Association Between MG-ADL Total Score and EQ-5D-5L Utility Values

Independent Variables	GEE model, with MG-ADL and treatment	
	Parameter	p-value SCORE test
Intercept	0.1696	-
MG-ADL Score	0.0233	< 0.0001
Efgartigimod	-0.0598	0.0079

Limitations

- Length of follow-up time was limited to up to 26 weeks.
- The first regression assumed that each additional change from one level to the next within each MG-ADL item has the same impact on utility, but a different impact between items; this is unlikely to be the case.
- The GEE model predicting EQ-5D-5L utility from MG-ADL total score assumed that any unit of improvement in an item has the same utility impact.
- The EQ-5D-5L may capture dimensions not included in the primary clinical outcome, MG-ADL, which are commonly associated with gMG, such as usual activities and anxiety.
- Results may not be generalizable outside of a clinical trial setting.

Conclusions

- Improvements in gMG symptoms were significantly associated with higher utility values. MG-ADL scores alone were not sufficient to capture the utility gained from efgartigimod therapy.
- Models in this study provide a method for predicting EQ-5D-5L utility values based on MG-ADL total score (GEE model) or based on individual MG-ADL items (normal ID regression), which can be used to convert MG-ADL data from existing trials to EQ-5D-5L utilities for use in economic models.
- The EQ-5D-5L allows for comparisons across disease states and informs QALY calculations needed for treatment assessments.

References

1. Boscoe AN, Xin H, L'Italien GJ, Harris LA, Cutter GR. Impact of Refractory Myasthenia Gravis on Health-Related Quality of Life. J Clin Neuromuscul Dis. 2019;20(4):173-81.
2. Muppidi S, Silvestri NJ, Tan R, Riggs K, Leighton T, Phillips GA. Utilization of MG-ADL in myasthenia gravis clinical research and care. Muscle Nerve. 2022;65(6):630-9.
3. European Medicines Agency. EU/3/18/1992: Orphan Designation for the Treatment of Myasthenia Gravis. Available from: https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu3181992.
4. Sanders DB, Wolfe GI, Benatar M, Evoli A, Gilhus NE, Illa I, et al. International consensus guidance for management of myasthenia gravis: Executive summary. Neurology. 2016;87(4):419-25.
5. Paul RH, Nash JM, Cohen RA, Gilchrist JM, Goldstein JM. Quality of life and well-being of patients with myasthenia gravis. Muscle Nerve. 2001;24(4):512-6.
6. Szczudlik P, Sobieszczuk E, Szyluk B, Lipowska M, Kubiszewska J, Kostera-Pruszczyk A. Determinants of Quality of Life in Myasthenia Gravis Patients. Front Neurol. 2020;11:553626.
7. Gelinas D, Parvin-Nejad S, Phillips G, Cole C, Hughes T, Silvestri N, et al. The humanistic burden of myasthenia gravis: A systematic literature review. J Neurol Sci. 2022;437:120268.
8. Wolfe GI, Herbelin L, Nations SP, Foster B, Bryan WW, Barohn RJ. Myasthenia gravis activities of daily living profile. Neurology. 1999;52(7):1487-9.
9. Barnett C, Bril V, Bayoumi AM. EQ-5D-5L and SF-6D health utility index scores in patients with myasthenia gravis. Eur J Neurol. 2019;26(3):452-9.
10. Barnett C, Bril V, Bayoumi AM. EQ-5D-5L and SF-6D health utility index scores in patients with myasthenia gravis. Eur J Neurol. 2019;26(3):452-9.
11. Howard JF, Jr., Bril V, Vu T, Karam C, Peric S, Margania T, et al. Safety, efficacy, and tolerability of efgartigimod in patients with generalised myasthenia gravis (ADAPT): a multicentre, randomised, placebo-controlled, phase 3 trial. Lancet Neurol. 2021;20(7):526-36.
12. Argenx. Data on file. Summary of analyses conducted on the ADAPT(+) dataset on the association of MG-ADL and EQ-5D utility. June 2022.