

Comparing AChR-Ab-positive and AChR-Ab-negative Generalized Myasthenia Gravis: An ADAPT-SERON-Informed Analysis from the German Myasthenia Gravis Registry (MyaReg) Including Antibody-defined Subtypes

Paolo Doksani,¹ Jana B Jarecki,² Cecile Blein,³ Roland Derwand,³ Sihui Zhao,³ Judith ter Horst,³ Yanic Heer,² Frauke Stascheit,¹ Andreas Meisel,¹ Sarah Hoffmann¹

¹Universitätsmedizin Berlin, Berlin, Germany; ²Rewoso AG, Zurich; ³argenx, Ghent, Belgium

KEY TAKEAWAYS



One of the largest real-world characterizations of autoantibody-defined subtypes of generalized myasthenia gravis based on the German Myasthenia Gravis Registry.



Higher disease burden in patients without detectable AChR-Ab than in AChR-Ab positive patients, consistently across disease severity, activities of daily living, quality of life, and fatigue.



Triple-negative patients represent over half of the population without detectable AChR-Ab, likely driving the higher disease burden compared to AChR-Ab positive patients.

BACKGROUND & METHODS

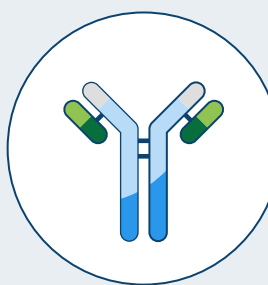
Autoantibody Subtypes are Underrepresented

○ This study presents one of the largest characterization of antibody subtypes in generalized MG.



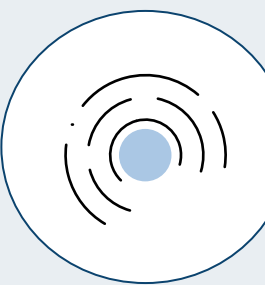
Background

Patients with generalized myasthenia gravis (gMG) without detectable acetylcholine receptor antibodies remain **underrepresented** and heterogeneous due to small sample sizes.



Methods

- Retrospective, cross-sectional (registry entry), real-world study in the German **Myasthenia Gravis Registry**.
- Comparison of **AChR-Ab positive** patients and patients with **AChR-Ab not detectable**, incl. triple-seronegative, MuSK-Ab positive, and LRP4-Ab positive patients.
- Descriptive statistics, group comparisons employing t-tests.



Objectives

- To **characterize** patients with gMG who lack detectable AChR-Ab and their antibody subtypes.
- To **compare** their **clinical characteristics** to AChR-Ab positive patients.



German Myasthenia Gravis Registry

- Large, observational disease registry prospectively collecting clinical routine data of patients with myasthenic syndromes.
- Multi-centric: 21 certified integrated MG centers across Germany.
- Longitudinal: started in 2019.

Study Population

○ Inclusion and exclusion criteria of the real-world study informed by ADAPT-SERON trial assessed at registry entry (**Figure 1**).



Inclusion criteria

- Adults diagnosed with generalized MG
- MGFA class II-IV
- AChR-Ab status documented

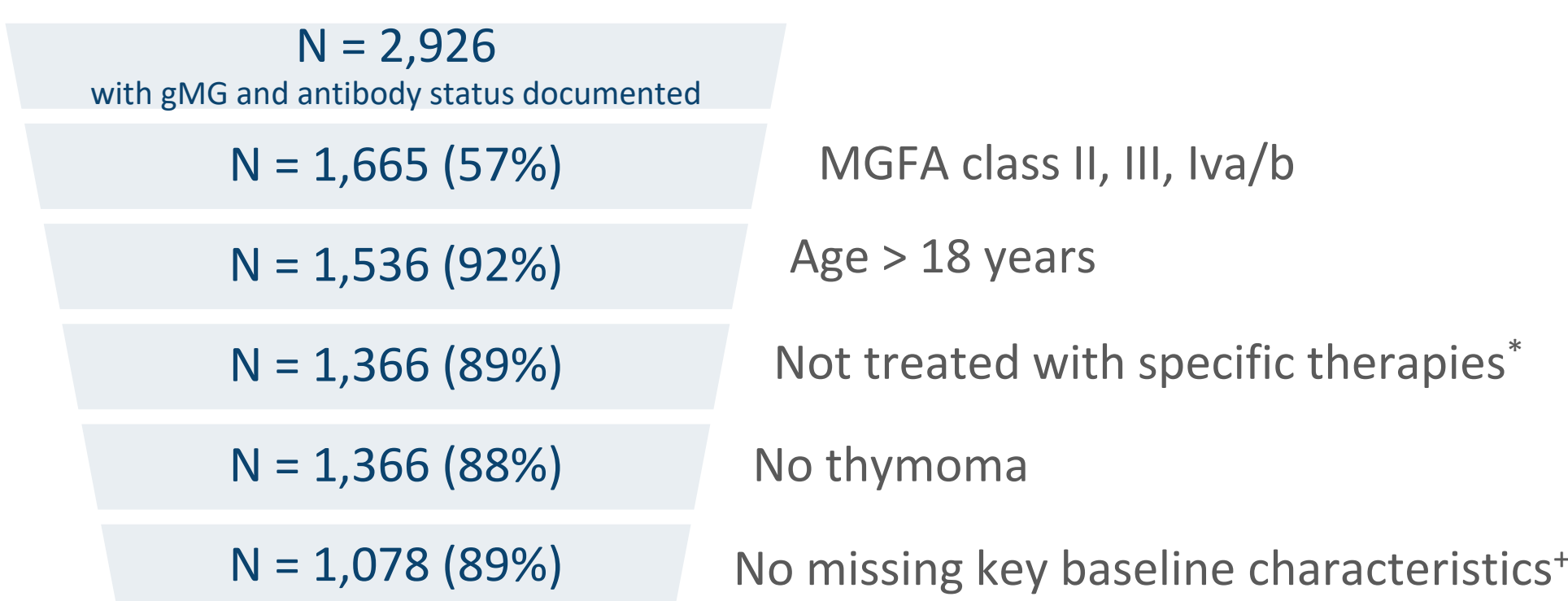


Exclusion criteria

- Treatments* differently prescribed given AChR-Ab status
- Thymoma
- Missing key baseline characteristics

FIGURE 1 Patient Funnel

Assessed at registry entry:



*Excluding patients treated with rituximab, cyclophosphamide, eculizumab, ravulizumab, zilucoplan, rozanolizumab, nipocalimab, inebilizumab, or efgartigimod.
*Excluding patients with missing information on thymectomy before registry entry, time since disease onset, therapy at registry entry.

RESULTS

Patient Characteristics of Autoantibody Subtypes

- Patients without detectable AChR-Ab were more frequently female than AChR-Ab positive patients (72% vs. 55%, $p < 0.001$) and younger at onset (46 vs. 52 years, $p < 0.001$), consistent with previous results [1].
- At least 54% of patients without detectable AChR-Ab were triple-negative (159 of 292) at registry entry (**Table 1**), and 92 patients had an unknown MuSK- or LRP4-Ab status (not shown in Table 1).

TABLE 1 Baseline Characteristics

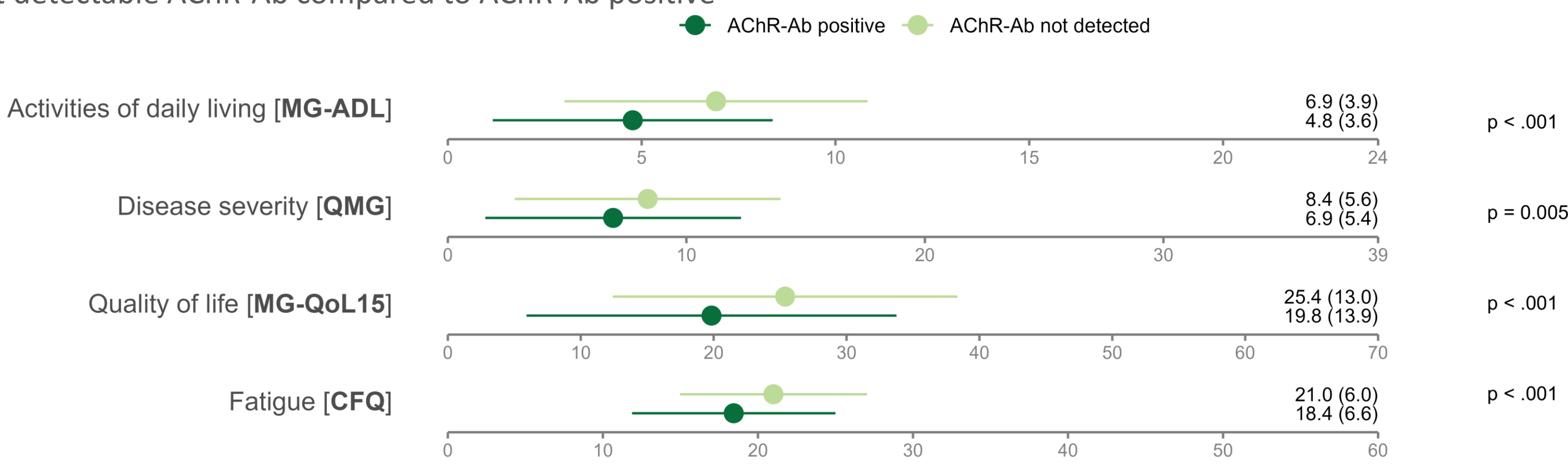
Characteristic*	AChR-Ab positive (N = 768)	AChR-Ab not detected (N = 292)	AChR-Ab not detected		
			Triple-negative (N = 159)	MuSK-Ab positive (N = 20)	LRP4-Ab positive (N = 21)
Female, N (%)	424 (55.2%)	209 (71.6%)	118 (74.2%)	18 (90.0%)	13 (61.9%)
Age at index ¹ , M (SD)	60.2 (18.1)	53.6 (15.1)	54.5 (15.0)	40.8 (13.5)	54.5 (16.7)
Age at onset, M (SD)	52.4 (20.9)	45.6 (16.2)	46.8 (15.7)	35.1 (13.61)	48.7 (15.0)
Age at diagnosis, M (SD)	53.7 (20.0)	48.3 (16.0)	49.5 (15.1)	36.2 (14.3)	51.4 (17.2)
MGFA class at index ¹					
IIa	365 (47.5%)	123 (42.1%)	59 (37.1%)	7 (35.0%)	12 (57.1%)
IIb	251 (32.7%)	93 (31.8%)	54 (34.0%)	9 (45.0%)	4 (19.0%)
IIIa	59 (7.7%)	39 (13.4%)	25 (15.7%)	< 5	0
IIIb	69 (9.0%)	34 (11.6%)	20 (12.6%)	< 5	5 (23.8%)
IVa	5 (0.7%)	< 5	< 5	0	0
IVb	19 (2.5%)	< 5	< 5	0	0
Previous thymectomy, N (%)	250 (32.6%)	60 (20.5%)	31 (19.5%)	< 5	< 5
Previous exacerbation, N (%)	166 (24.3%)	53 (19.2%)	31 (20.3%)	3< 5	6 (30.0%)
Missing information	84	16	6	0	1
RNS decrement, N (%)	249 (61.6%)	79 (38.3%)	42 (38.5%)	8 (61.5%)	< 5
Missing information	364	86	50	7	6
Concomitant autoimmune diseases, N (%)	176 (26.7%)	92 (35.9%)	48 (34.3%)	6 (46.2%)	9 (45.0%)
Missing information	109	36	19	7	1

*Index date for assessment of characteristics defined at registry entry (visit 1) to mitigate prevalent user bias in real-world data

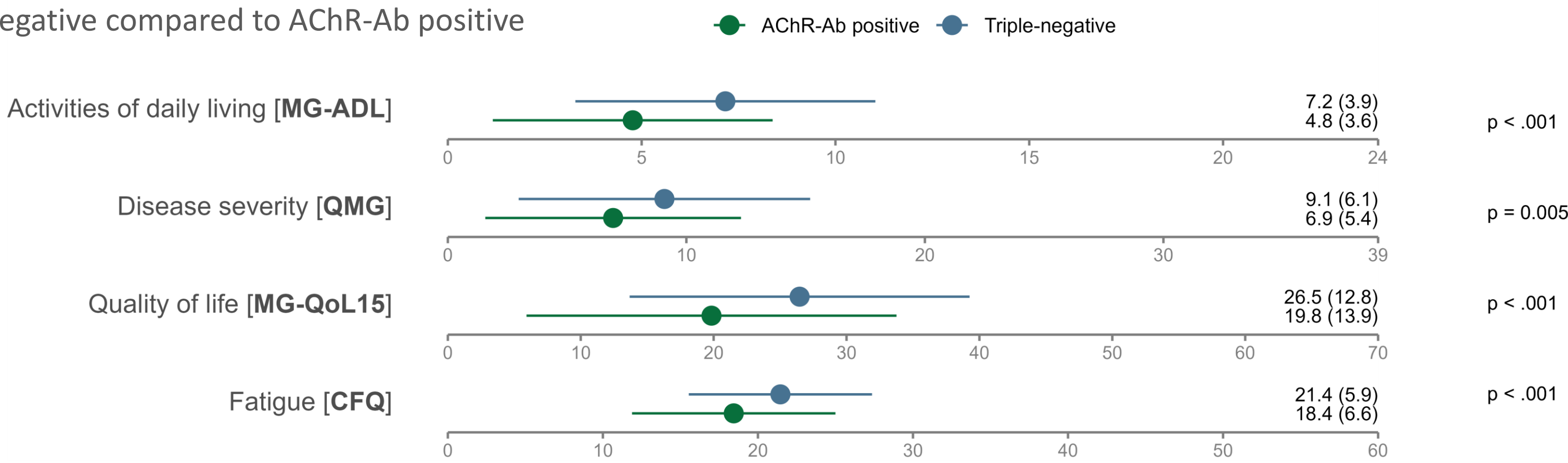
Disease Burden of Autoantibody Subtypes

FIGURE 2 Disease Impairment Comparisons*

a) Without detectable AChR-Ab compared to AChR-Ab positive



b) Triple-negative compared to AChR-Ab positive



Note: CFQ (fatigue) is self-reported fatigue; shown are means (standard deviations).

	AChR-Ab not detected			
	MuSK-Ab positive		LRP4-Ab positive	
	M (SD)	N	M (SD)	N
MG-ADL	5.8 (4.2)	18	8.1 (3.9)	16
QMG	7.6 (5.4)	16	7.5 (4.9)	5
MG-QoL	23.5 (14.5)	17	34.4 (12.3)	16
CFQ	18.9 (7.0)	12	21.1 (6.8)	16

CONCLUSION

Patients without detectable AChR-Ab and patients with triple-negative status exhibited a higher disease burden than AChR-Ab positive, with consistently worse scores for activities of daily living, disease severity, quality of life, and patient-reported fatigue.

LIMITATIONS

The patient cohorts that were compared in this study received conventional MG treatments or no treatment (for details see exclusion criteria).

*Index date for assessment defined at registry entry (visit 1) to mitigate prevalent user bias in real-world data

ABBREVIATIONS

Ab, antibody; AChR-Ab, Acetylcholine receptor antibody; CFQ, Chalder fatigue questionnaire; gMG, generalized myasthenia gravis; MG, myasthenia gravis; MGFA, Myasthenia Gravis Foundation of America; MG-ADL, Myasthenia gravis activities of daily living; M, mean; MyaReg, German Myasthenia Gravis Registry; SD, standard deviation; QMG, Quantitative myasthenia gravis score; MG-QoL15, Myasthenia gravis quality of life 15-item scale; RNS, repetitive nerve stimulation.

DISCLOSURES AND ACKNOWLEDGMENTS

This study was sponsored by argenx US, Inc.; PD has received travel, accommodation and meeting expenses from argenx, and UCB. He has received speaker's honoraria and honoraria for attendance at advisory boards from Alexion Astra Zeneca Rare Disease, argenx and UCB. He received institutional financial research support from argenx. JJ, YH: Employees of Rewoso AG, a real-world data science consultancy. CB, RD, SZ, and JH are employees of argenx. FS has received travel/accommodation/meeting expenses from Alexion and argenx and received speaking honoraria and honoraria for attendance at advisory boards from Alexion, argenx and UCB and received research grants from Alexion Pharmaceuticals, argenx, Cytel and Octapharma. She serves as a member of the German myasthenia gravis society. AM has received speaker or consultancy honoraria or financial research support (paid to his institution) from Alexion Pharmaceuticals, argenx, Amgen, Axunio, Desitin, Grifols, Janssen, Merck, Novartis, Octapharma, Sanofi and UCB. He serves as member of the medical advisory board of the German Myasthenia Gravis Society (DMG e.V.) and chairmen of the Association for Research in Myasthenic Syndromes in Germany (VEMSID e.V.). SH has received speaker's honoraria, consulting fees or institutional financial research support from Alexion, argenx, UCB, Grifols, Kyvernia, Merck, Novartis, Roche, and Johnson&Johnson and is member of the medical advisory board of the German Myasthenia Society.

REFERENCES

- Vincent, A., Bowen, J., Newsom-Davis, J., & McConville, J. (2003). Seronegative generalised myasthenia gravis: clinical features, antibodies, and their targets. The Lancet Neurology, 2(2), 99–106. [https://doi.org/10.1016/S1474-4422\(03\)00306-5](https://doi.org/10.1016/S1474-4422(03)00306-5).



SCAN ME