Treatment Outcomes among Patients with Generalized Myasthenia Gravis in the Czech Republic: Results from MYasthenia gravis REGistry (MyReg)

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Introduction

- Myasthenia gravis (MG) is a rare, chronic autoimmune disease characterized by antibody-mediated interference with neuromuscular (NM) transmission at the NM junction.[1]
- With no curative treatment available, clinical practice aims at symptom management and prevention of symptom worsening.
  - Corticosteroids (CS) or immunosuppressants (IST) are used among patients with generalized MG (gMG) if adequate symptom control is not achieved through symptomatic treatment with anticholinesterase inhibitors (AChEi).[2,3]
- The Myasthenia Gravis Activities of Daily Living (MG-ADL) scale has been used as a primary or secondary endpoint in clinical studies and observational studies to assess symptoms and functional status of patients with gMG. A MG-ADL score ≥5 or ≥6 is used as patient recruitment criteria in many clinical studies.[4]
- To improve disease management and patient care, it is critical to get a better understanding of patient characteristics and the effectiveness of the available treatments among patients with gMG in the real-world setting.

Objective

- To describe patient characteristics and treatment outcomes among patients with gMG in clinical practice

Methods

Data Source

- Data were obtained from 12 clinical centers that participated in the MYasthenia gravis REGistry (MyReg), which was established in 2015 in the Czech Republic.[5]

Study Measures

- Symptom severity: Measured using the MG-ADL scale, which is an 8-item patient-reported instrument that measures the symptoms and functional status of MG; each response is graded on a scale of 0 (normal) to 3 (most severe) and the total score ranges from 0 to 24.[6]
- Clinical improvement: Defined as time to the first observed reduction of MG-ADL score ≥2 points from the index date.[7]

Study Patients

- Adult patients with clinical diagnosis of Myasthenia Gravis Foundation of America (MGFA) class II-IV from January 2015 to September 2023.
- Patients had to have ≥1 valid record of MG-ADL post-baseline, during the study period.
- Patients were classified into two non-mutually exclusive groups based on their MG-ADL score:
  - MG-ADL score ≥6 (main analysis): Date of the first visit with MG-ADL score ≥6 was designed as index date
  - MG-ADL score ≥5 (sensitivity analysis): Date of the first visit with MG-ADL score ≥5 was designed as index date
- Patients had received a treatment for gMG (e.g., AChE inhibitor, CS and/or IST) at the index date.

Statistical Analyses

- Mean, standard deviation (SD), median and interquartile ranges were reported for continuous variables whereas frequency and percentage were reported for categorical variables.
- Changes in mean MG-ADL score from the index date were tested using Bonferroni-corrected paired t-test.
- Kaplan-Meier curves were used to display time-to-clinical improvement.
- All data analyses were conducted using SAS version 9.4 and R version 4.0.5.

Results

- 271 patients with index MG-ADL score ≥6 and 351 patients with index MG-ADL score ≥5 were included in the analysis [**Table 1**].

Table 1: Demographic and clinical characteristics of patients with gMG

	MG-ADL score ≥6 N=271		MG-ADL score ≥5 N=351	
Age at index date [years]				
mean (SD)	62.7	14.9	63.1	15.14
median (IQR)	64	51.0, 75.0	65	51.0, 75.0
Gender (n, %)				
Male	106	39.1%	145	41.3%
Female	165	60.9%	206	58.7%
Length of follow-up from index date [months]				
mean (SD)	8	10.4	8.4	10.7
median (IQR)	2.3	0.0, 15.3	3.1	0.0, 15.9
Time from MG diagnosis to the index date, months				
mean (SD)	107.2	115.2	103.9	109.6
median (IQR)	63.7	17.5, 159.3	64.5	19.2, 157.7
MGFA classification (n, %)				
IIa	59	21.8%	86	24.5%
IIb	105	38.7%	145	41.3%
IIIa	61	22.5%	68	19.4%
IIIb	40	14.8%	46	13.1%
IVa	2	0.7%	2	0.6%
IVb	4	1.5%	4	1.1%
Antibody assays (n, %)				
Untested	28	10.3%	36	10.3%
AChR+	196	72.3%	254	72.4%
AChR–	4	1.5%	5	1.4%
MuSK+	5	1.8%	6	1.7%
AChR–/MuSK–	38	14.0%	50	14.2%
LRP 4+	0	0.0%	0	0.0%

AChR: Acetylcholine receptor; IQR: Interquartile range; gMG: generalized Myasthenia Gravis; LRP-4: Lipoprotein receptor-related protein 4; MG: Myasthenia Gravis; MG-ADL: Myasthenia Gravis-Activities of Daily Living; MGFA: Myasthenia Gravis Foundation of America; MuSK: Muscle-specific kinase; SD: Standard deviation.

- 12.2% and 11.4% of study patients used AChEi monotherapy at index date, while 84.1% and 84.9% used CS/IST either as monotherapy or combination therapy in the MG-ADL score ≥6 and ≥5 cohorts, respectively [**Table 2**].

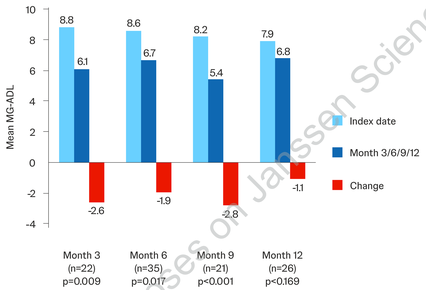
Table 2: Treatment use at index date among patients with gMG

	MG-ADL score ≥6 N=271		MG-ADL score ≥5 N=351	
No treatment (n, %)	**10**	**3.7%**	13	**3.7%**
AChEi only	33	12.2%	40	11.4%
CS only	9	3.3%	10	2.8%
IST only	1	0.4%	1	0.3%
AChEi+CS	96	35.4%	121	34.5%
AChEi+IST	17	6.3%	18	5.1%
CS+IST	6	2.2%	11	3.1%
AChEi+CS+IST	99	36.5%	137	39.0%

AChEi: Acetylcholinesterase inhibitors; CS: Corticosteroid; gMG: generalized Myasthenia Gravis; IST: Immunosuppressants; MG-ADL: Myasthenia Gravis-Activities of Daily Living.

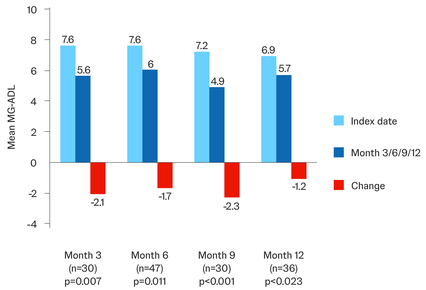
- Among treated patients with index MG-ADL score ≥6 who had a valid MG-ADL score at 6-month post-index (n=35), mean change in MG-ADL was -1.9 at 6 months from the index date (**Figure 1A**).
- Among treated patients with index MG-ADL score ≥5 who had a valid MG-ADL score at 6-month post-index (n=47), mean change in MG-ADL score was -1.7 at 6 months from the index date (**Figure 1B**).

Figure 1A: Mean change in MG-ADL score by 3-month intervals for treated patients with index MG-ADL score ≥6 (N=261)



MG-ADL: Myasthenia Gravis- Activities of Daily Living.
Note: 30-day time window was used to identify valid MG-ADL score observed around each 3-month assessment timepoint after the index date.

Figure 1B: Mean change in MG-ADL score by 3-month interval for treated patients with index MG-ADL score ≥5 (N=338)



MG-ADL: Myasthenia Gravis- Activities of Daily Living.
Note: 30-day time window was used to identify valid MG-ADL score observed around each 3-month assessment timepoint after the index date.

- 22.7% and 46.5% of treated patients with index MG-ADL score ≥6 had ≥2 points reduction after 6 months and 12 months, respectively (**Figure 2A**); among treated patients with index MG-ADL score ≥ 5, 22.2% and 44.0% of patients had ≥2 points reduction in MG-ADL score after 6 months and 12 months, respectively (**Figure 2B**).

Figure 2: Time to improvement for treated patients with index MG-ADL score ≥6 [Figure 2A] or MG-ADL score ≥5 [Figure 2B]

Figure 2A

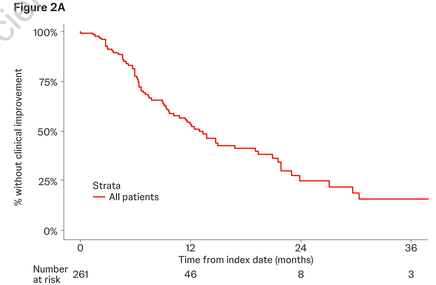
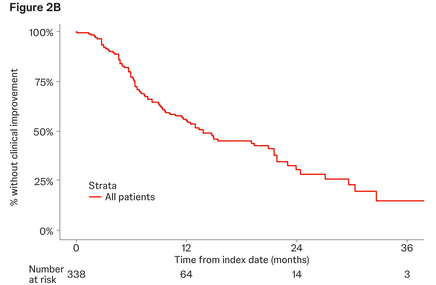


Figure 2B



MG-ADL: Myasthenia Gravis- Activities of Daily Living.

Conclusions

- This real-world study showed that a small percentage of patients with gMG with index MG-ADL score ≥6 or ≥5 receiving conventional therapy (including AChEi) achieved clinical improvement after 6 months and 12 months, respectively.
- Findings underscore the need for more effective treatments to improve patient outcomes, and future research is warranted to assess the impact of MG fluctuation and symptom severity on patients' quality of life.

Strengths and Limitations

- Clinical forms of MG are recorded in the MyReg that helps to differentiate patients with gMG from those with ocular MG; in addition, symptom severity is recorded using instruments such as MG-ADL which is not commonly available in other real-world data sources (e.g., claims, electronic health records [EHR]).
- However, timing for MG-ADL assessment was heterogenous in clinical practice, which may have created biased estimates on time-to-improvement. In addition, treatments such as rituximab and other biologics were rarely utilized in this cohort, and MG-ADL scores were collected 6-7 years after the establishment of MyReg so that index MG-ADL score date might not be the first MG diagnosis date nor treatment initiation date.

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Autoantibody: gMG

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