Real-World Analysis of Treatment Patterns and Disease Exacerbations Among Patients Initiating Therapy for Myasthenia Gravis

HSD92

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BACKGROUND

- Myasthenia gravis (MG) is a rare autoimmune condition that impairs neuromuscular transmission, resulting in weakness[1]
- Symptoms of MG can become life-threatening when muscle weakness involves the diaphragm or intercostal muscles responsible for breathing; the most dangerous complication of MG, known as myasthenic crisis, requires hospitalization and may necessitate mechanical ventilation[2,3]
- Traditional pharmacological treatment for MG includes acetylcholinesterase inhibitors (ACH) with or without immunosuppression with oral glucocorticoids (OG) and/or systemic non-steroidal immunosuppressants (SYS), and/or intravenous immunoglobins (IVIG); IVIG or plasmapheresis are utilized during acute exacerbations[4]
- Development of targeted biologic therapies has rapidly changed the treatment landscape, with the approval of biologics vastly expanding treatment options from 2017 to 2023

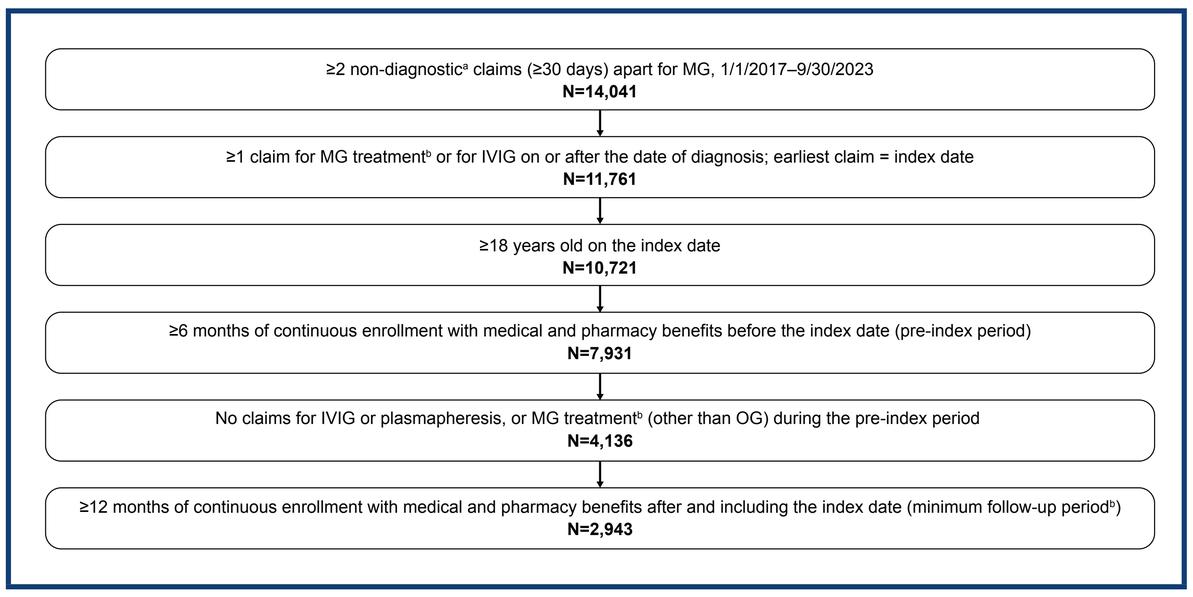
OBJECTIVE

- To describe treatment patterns and disease outcomes (exacerbations and crises) among patients initiating treatment for MG

METHODS

- This retrospective cohort study used administrative claims data from the Merative™ MarketScan® Commercial and Medicare Databases between January 1, 2017 and September 30, 2024
- Eligible patients had ≥2 claims (>30 days apart) with an *International Classification of Diseases, 10th Revision* (ICD-10) diagnosis code for MG (G7000, G7001) between January 1, 2017 and September 30, 2024 and ≥1 claim for a MG systemic treatment or for IVIG on or after the earliest diagnosis
  - The date of the earliest MG treatment represents the index date
  - MG treatments included ACH (neostigmine, pyridostigmine), SYS (azathioprine, cyclophosphamide, cyclosporine, methotrexate, mycophenolate mofetil, tacrolimus), biologics (eculizumab, efgartigimod, efgartigimod alfa, efgartigimod hyaluronidate-gvfc, ravulizumab, rituximab, rozanolixizumab-noli, and zilucoplan), and OG
  - Patients were required to be ≥18 years old on the index date, with ≥6 months pre- and ≥12 months post-index enrollment with medical and pharmacy benefits
  - Patients with medical or pharmacy claims for IVIG or plasmapheresis, or a systemic MG treatment (other than OG) in the pre-index period were excluded (**Figure 1**)
- Treatment patterns were assessed during a variable-length follow-up period (≥12 months) from the index date until disenrollment or September 30, 2024 (whichever was earlier) including:
  - Type of index (first-line = first treatment used) regimen (defined by a 30-day window on and after the index date)
  - Index regimen duration and end reason (i.e., switch/add a different MG treatment, discontinuation [gap >90 days), censoring [disenrollment/study end])
  - Proportion of patients moving to a second-line (second treatment used) regimen and type of second-line treatment
- MG exacerbations and crises were assessed during the full follow-up period
  - Exacerbations were defined by a claim for a therapy used to treat myasthenic flares (IVIG, plasmapheresis, or injectable steroids) or an MG-related hospitalization
  - Crises were identified as an MG-related hospitalization, defined by an MG diagnosis in the primary position (with intensive care unit stay or with evidence of respiratory failure or mechanical ventilation during the admission) and with a claim for a treatment used for flares within +/-7 days of the admission date
  - The proportion of patients with at least one exacerbation or crisis and the number of exacerbations and crises were reported separately
- OG use and dose (in prednisone equivalents) were accessed during the follow-up period and reported as a categorical variable with patients grouped as having low (≤5mg), medium (6-15mg), or high (>15mg) initial and average daily doses

Figure 1. Selection of patients with MG newly initiating systemic treatment



[a]Non-diagnostic claims are claims that are not for diagnostic tests and therefore indicate a confirmed diagnosis. [b]MG treatments included ACH, OG, SYS, and biologic therapies. [b]Patients' follow-up periods were variable in length, beginning with the index date and ending with the earliest of either the end of continuous database enrollment or the end of the study period (September 30, 2024).

ACH, acetylcholinesterase inhibitors; ICD-10, international classification of diseases 10th modification, IVIG, intravenous immunoglobin; MG, myasthenia gravis; OG, oral corticosteroids; SYS, systemic non-steroid immunosuppressants.

RESULTS

- The analysis included 2,943 patients initiating MG treatment (**Table 1**)
  - Patients had a mean (SD) age of 58.1 (15.7) years, 52.4% were female, and 67.3% were covered by commercial insurance
  - Systemic therapy was initiated in 76.2% of patients <6 months from the MG diagnosis date
  - Mean (SD) duration of follow-up from the index date was 37.1 (21.4) months
- Overall, 79.0% initiated a monotherapy index regimen (18.4% were on a 2-drug combination and 2.7% were on a combination of ≥3 drugs)
  - ACH were the most commonly used first-line treatment, with approximately 44.9% of the study population receiving first-line ACH with or without IVIG.
  - Additionally, 32.6%, 15.3%, 7.0%, and 0.2% patients with MG initiated treatment with OG, ACH+OG, SYS, or a biologic-based regimen all with or without IVIG, respectively
  - Patients initiating treatment with OG had the shortest duration of index regimen with a mean(SD) of 6.1 (12.8) months, and patients initiating on ACH + OG combination regimens had the longest with a mean(SD) of 11.4 (13.9) months
- During the post-index period, 54.0% of all patients discontinued the index regimen (59.2% of these restarted after discontinuation), 34.7% switched or added a different MG treatment prior to discontinuation, and 11.3% were censored (**Figure 2**)
- Among patients moving to a second-line therapy (n =1,962), OGs were the most commonly used (50.7%) treatment, followed by ACH (26.9%), SYS (15.3%), IVIG (6.5%), and biologic therapies (2.7%) (**Figure 3**)
- During the post-index period, 34.8% of patients had at least one exacerbation and 2.3% had at least one crisis (**Table 2**)
  - Mean (SD) number of exacerbations was 1.5 (1.8) per patient per year
  - Mean (SD) number of crises was 0.5 (0.3) per patient per year
- Overall, OG was the most commonly prescribed treatment, with 79.1% of the study population received a prescription for OG during the post-index period
  - Mean (SD) number of prescriptions was 9.3 (11.3)
  - Among patients with OG and eligible (had claims with non-missing quantity, strength, and days of supply information) for dose quantification (n=2,315), 89.9% initiated on a >5mg daily dose and 65.3% had an average daily dose >15mg in prednisone equivalents (**Table 2**, **Figure 4**)

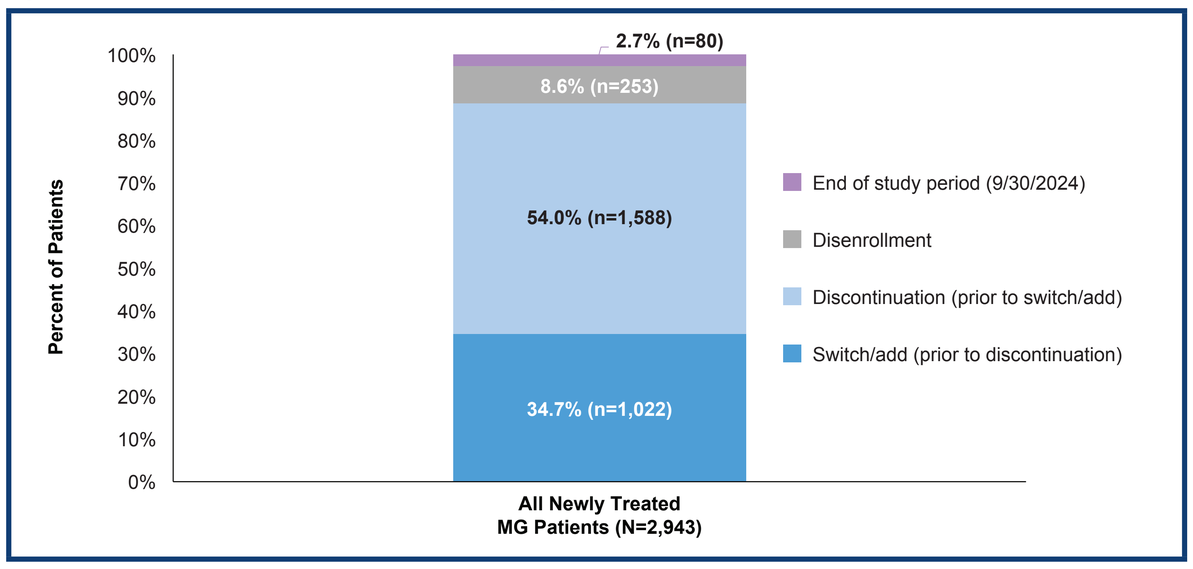
Table 1. Characteristics of patients with MG newly initiating systemic treatment

	All Newly Treated MG Patients N=2,943	Index Regimen Cohorts: ACH inhibitors +/- IVIG N=1,321	OG +/- IVIG N=959	ACH + OG +/- IVIG N=451	Other[c] N=212
Demographic Characteristics on index date					
Age, mean (SD)	58.1 (15.7)	57.9 (16.2)	58.4 (15.2)	58.5 (15.7)	57.4 (14.4)
Female, n (%)	1,543 (52.4%)	670 (50.7%)	568 (59.2%)	195 (43.2%)	110 (51.9%)
Commercial insurance, n (%)	1,982 (67.3%)	890 (67.4%)	642 (66.9%)	298 (66.1%)	152 (71.7%)
Months of follow-up, mean (SD)	37.2 (21.4)	37.2 (21.3)	38.2 (21.9)	35.8 (21.3)	35.2 (20)
Clinical Characteristics during the pre-index period					
Patients with ocular involvement, n (%)[a]	1,660 (56.4%)	779 (59.0%)	488 (50.9%)	278 (61.6%)	115 (54.2%)
Charlson Comorbidity Index, mean (SD)	1.2 (1.8)	1.1 (1.8)	1.2 (1.9)	1.1 (1.8)	1.4 (1.9)
Other diagnoses, n (%)					
Anxiety	423 (14.4%)	186 (14.1%)	157 (16.4%)	74 (16.4%)	20 (9.4%)
Autoimmune condition	288 (9.8%)	116 (8.8%)	110 (11.5%)	38 (8.4%)	33 (15.6%)
Chronic obstructive pulmonary disease	170 (5.8%)	65 (4.9%)	75 (7.8%)	30 (6.7%)	9 (4.2%)
Depression	334 (11.3%)	155 (11.7%)	122 (12.7%)	42 (9.3%)	21 (9.9%)
Dyslipidemia	1,021 (34.7%)	473 (35.8%)	323 (33.7%)	164 (36.4%)	82 (38.7%)
Hypertension	1,261 (42.8%)	554 (41.9%)	406 (42.3%)	231 (51.2%)	96 (45.3%)
Obesity	586 (19.9%)	271 (20.5%)	189 (19.7%)	91 (20.2%)	55 (25.9%)
Osteoporosis	70 (2.4%)	38 (2.9%)	26 (2.7%)	5 (1.1%)	2 (0.9%)
Systemic infection[b]	52 (1.8%)	19 (1.4%)	19 (2.0%)	10 (2.2%)	5 (2.4%)
Type 2 diabetes	578 (19.6%)	290 (22.0%)	159 (16.6%)	89 (19.7%)	48 (22.6%)

[a]Defined by the presence of >1 non-diagnostic inpatient or outpatient claim with an ICD-10 diagnosis code for facial muscle weakness (R29810) or eye muscle weakness (H0582) or a visit to an ophthalmologist. [b]Systemic infections include bacteremia, septicemia, and systemic inflammatory response syndrome. [c]Includes patients with an index regimen on SYS or biologic therapy +/- IVIG

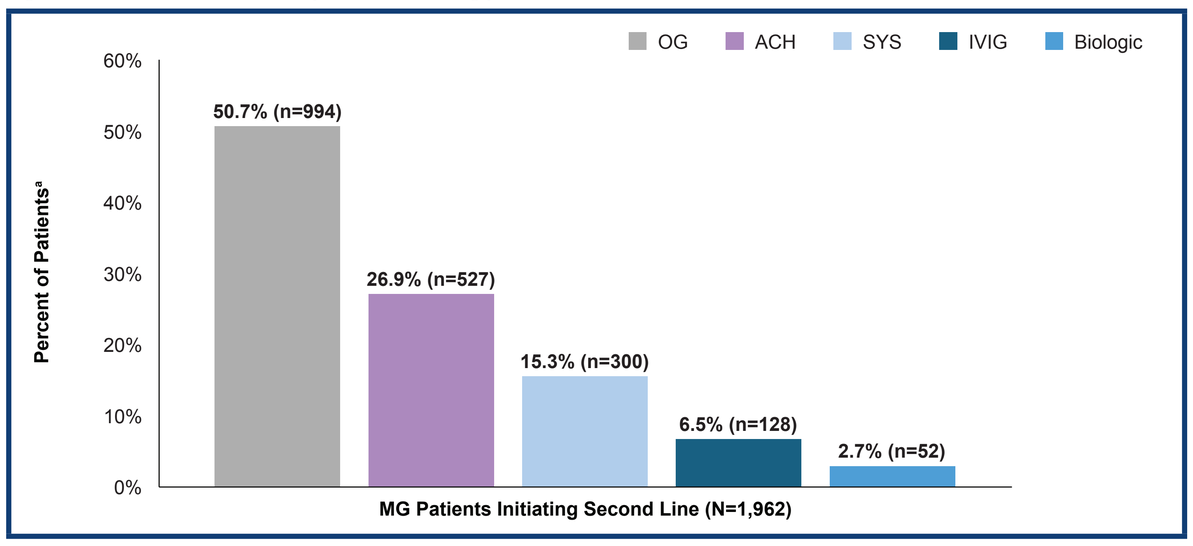
ACH, acetylcholinesterase inhibitors; IVIG, intravenous immunoglobin; MG, Myasthenia Gravis; OG, oral corticosteroids, SD, standard deviation; SYS, systemic non-steroid immunosuppressants

Figure 2. Reason for end of index treatment regimen among patients with MG



MG, Myasthenia Gravis

Figure 3. Second line treatments prescribed among patients with MG



[a]Patients may start second line on more than one drug class, so percents may add to greater 100.

ACH, acetylcholinesterase inhibitors; IVIG, intravenous immunoglobin; MG, Myasthenia Gravis; OG, oral corticosteroids: SYS, systemic non-steroidal immunosuppressants

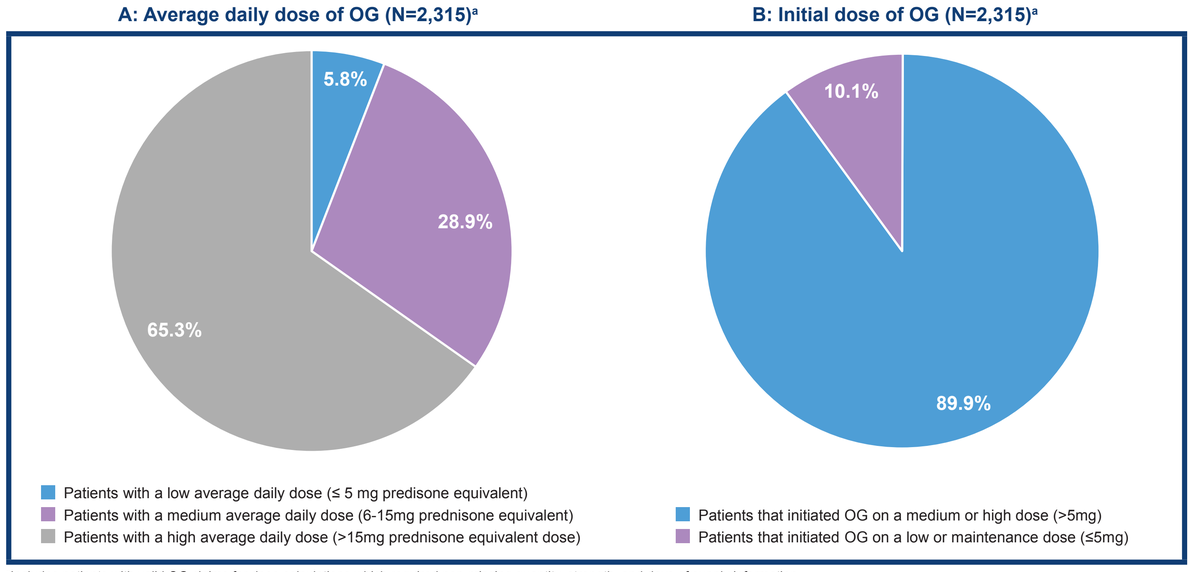
Table 2. MG exacerbations and OG use after initiation of other MG therapies through end of follow-up

	All Newly Treated MG Patients N=2,943
MG exacerbations, n (%)	**1,025 (34.8)**
Number of exacerbations PPPY, mean (SD)	1.5 (1.8)
Median	0.75
MG crises, n (%)	**68 (2.3)**
Number of crises[b] PPPY, mean (SD)	0.5 (0.3)
Median	0.5
OG prescriptions, n (%)	**2,327 (79.1)**
Number of prescriptions, mean (SD)	9.3 (11.3)
Median	5.0
Patients with valid claims for dose calculation, n (%)[a]	**2,315 (78.7)**
Average daily OG dose (prednisone equivalent dose in milligrams), mean (SD)	21.6 (13.7)
Median	18.0

[a]Valid claims required non-missing quantity, strength, and days of supply information. [b]If an event qualified as both an exacerbation and a crisis it was counted as the more severe event (crisis).

MG, Myasthenia Gravis; OG, oral corticosteroids, PPPY; per patient per year, SD; standard deviation

Figure 4. Dosage of OG among MG patients with use after initiation of other MG therapies



[a]Includes patients with valid OG claims for dose calculations which required non-missing quantity, strength, and days of supply information

MG, Myasthenia Gravis; OG, oral corticosteroids

LIMITATIONS

- Results may not be generalizable to patients without employer-sponsored commercial or Medicare Supplemental or Advantage insurance coverage, or those who are uninsured
- Patients with MG who did not meet minimum database enrollment requirements may have different treatment patterns or disease outcomes than those who met all inclusion/exclusion criteria
- Treatment use was largely based on outpatient pharmacy claims for filled prescriptions; patients were assumed to have used treatments as prescribed, though actual usage cannot be confirmed
- As patients and outcomes are identified through administrative claims data, rather than medical records or surveys, there is a potential for coding errors or misclassification of disease exacerbation or other variables

CONCLUSIONS

- **These results suggest that patients with MG initiate treatment on traditional systemic medications, and that even second-line utilization of newer biologic therapies remains low despite evidence of poor disease outcomes**
- **These results suggest that patients with MG initiating treatment on traditional systemic medications have evidence of poor disease outcomes, and utilization of newer second-line biologic therapies remain low, despite these outcomes.**

REFERENCES

1. Dresser L, et al. *J Clin Med*. 2021;10(11). **2.** Rodrigues E, et al. *Muscle Nerve*. 2023;69(2):166–171. **3.** Hehir MK, et al. *Neurol Clin*. 2018;36(2):253–260. **4.** Narayanaswami P, et al. *Neurology*. 2021;96(3):114–122.

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