Changes in Nonsteroidal Immunosuppressive Treatment Usage Before and After Efgartigimod Initiation in Patients With Myasthenia Gravis

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INTRODUCTION

Conventional treatments for myasthenia gravis (MG)

- MG is a rare, antibody-mediated neuromuscular disorder leading to a failure of neuromuscular junction (NMJ) transmission, characterized by fluctuating weakness in ocular, facial, bulbar, axial, and limb muscles.[1–3] The majority of patients (~85%) have autoantibodies against the acetylcholine receptor (AChR).[3]
- First-line treatment for MG typically begins with acetylcholinesterase (AChE) inhibitors.[4–6] For patients who may not have symptom control with AChE inhibitors alone, immunosuppressants may be used.[4–6]
- While nonsteroidal immunosuppressive therapies (NSISTs) are commonly used to treat MG,[4,5,7] trials have found limited success demonstrating their efficacy while maintaining disease control,[8] and achieving their full clinical benefit takes time (6 months to 1 year) and is subject to tolerability.[9–11] Patients using NSISTs may have an increased risk of developing hepatotoxicity and gastrointestinal disturbances, which can pose additional clinical burden for patients with MG.[4,9,10]

Efgartigimod

- Efgartigimod is a human immunoglobulin G1 (IgG1) Fc fragment engineered to bind to FcRn on endothelial cells, leading to increased degradation of IgG (including pathological IgG) in the lysosome.[2] Efgartigimod was approved for the treatment of anti-AChR antibody–positive MG in 2021[2,12] and is typically dosed with 4 once-weekly infusions, with subsequent cycles administered according to individualized response.[13]
- While recent evidence suggests reduction of glucocorticoid usage with efgartigimod treatment, evidence of changes in NSIST utilization is limited.[14,15]

Objective

- The objective of this study was to utilize a large dataset based on US claims to evaluate changes in utilization of NSISTs before and after efgartigimod initiation in patients with MG.

METHODS

Study type and dataset

- A retrospective cohort study was conducted using US medical and pharmacy claims (based on information licensed from IQVIA: Longitudinal Access and Adjudication Data for the period April 2016–January 2024, reflecting estimates of real-world activity [all rights reserved]).
- MG-activities of daily living (MG-ADL) scores obtained in My VYVGART Path, a patient support program, were integrated with the primary dataset. No identifiable patient data were obtained by the investigators.

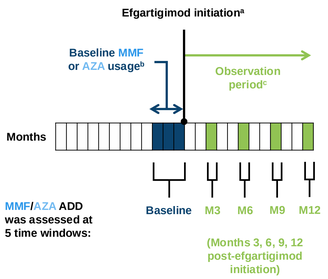
Inclusion/exclusion criteria

- First efgartigimod claim January 1–December 31, 2022 (index), with at least 1 year of ongoing efgartigimod usage based on claims captured[a]; at least 1 mycophenolate mofetil (MMF) or azathioprine (AZA) claim in the 90 days prior to efgartigimod initiation; continuous quarterly claims[c] activity with no claim for eculizumab, rituximab, ravulizumab, rozanolixizumab, or zilucoplan during the observation period.

Outcome

- Mean (SD) average daily dose (ADD) of MMF or AZA was evaluated at baseline (during the 90 days immediately prior to index) and at 3, 6, 9, and 12 months after efgartigimod initiation (Figure 1).
- For the study cohort with both baseline and at least 1 follow-up MG-ADL captured, baseline score (≤90 days before efgartigimod initiation) was compared with follow-up scores captured at consecutive 3-month intervals after efgartigimod initiation.

Figure 1. Study design



[a]Patients with a gap of >120 days between consecutive efgartigimod claims were excluded. [b]At least 1 claim for MMF/AZA in the 3 months prior to efgartigimod initiation was required. [c]Continuous quarterly activity was defined as ≥1 record in the database every quarter from 1 year pre-efgartigimod to 1 year post-efgartigimod initiation.

SUMMARY

Based on data from 161 patients with MG with baseline usage of MMF or AZA who continued efgartigimod treatment for 1 year, MMF/AZA dosing was significantly reduced and patients demonstrated a favorable MG-ADL response.

- At 1 year post-efgartigimod initiation, 35% and 32% of patients with baseline MMF or AZA usage, respectively, were no longer using these treatments.

Some limitations should be noted, including that claims-based data analyses are subject to assumptions, potential coding errors, and risk of missing data. MMF/AZA usage was estimated based on claims only. MMF/AZA tapering strategies are not reflected in this dataset, requiring alternative datasets for further exploration. Some potential selection bias for responders should be considered as this analysis was restricted to patients receiving efgartigimod for 1 year.

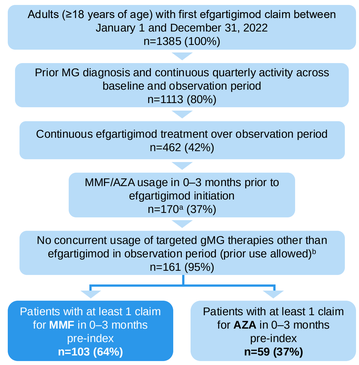
Despite the limitations, this study enabled inclusion of a large sample size, with results supporting reduction of MMF/AZA dosing with efgartigimod usage. Future studies should further evaluate MMF/AZA tapering approaches following efgartigimod initiation in clinical practice using additional datasets.

RESULTS

Patient cohort selection, baseline demographics, and characteristics

- Two cohorts were analyzed: 103 patients with MMF usage and 59 patients with AZA usage before index (Figure 2).
- Overall, the 2 cohorts had similar baseline characteristics, with the AZA cohort trending younger and with lower baseline MG-ADL score compared with the MMF cohort (Table 1 and Figure 5).

Figure 2. Patient selection



[a]1 patient observed to have both MMF and AZA in the 0–3 months before efgartigimod initiation. [b]Targeted gMG therapies include eculizumab, rituximab, ravulizumab, rozanolixizumab, and zilucoplan. Usage of these therapies was allowed before efgartigimod, but patients with usage of these therapies concurrently with efgartigimod during the observation period were excluded.

Table 1. Baseline demographics and characteristics

	MMF cohort (n=103)	AZA cohort (n=59)
Age, years		
Mean (SD)	61.7 (12.9)	56.1 (15.5)
Median (IQR)	63.0 (53.5–72.0)	59.0 (47.5–70.0)
Gender, n (%)		
Female	40 (38.8)	28 (47.5)
Charlson Comorbidity Index (CCI)		
Mean (SD)	1.4 (1.9)	1.0 (1.5)
Common MG comorbidities, n (%)[a]		
Hypertension	46 (44.7)	25 (42.4)
Sleep disorders	34 (33.0)	>0, <20
Diabetes	31 (30.1)	>0, <20
Obesity	26 (25.2)	>0, <20
Hyperlipidemia	25 (24.3)	>0, <20
Insurance type for first efgartigimod claim, n (%)[b]		
Commercial	59 (57.3)	36 (61.0)
Medicare	40 (38.8)	20 (33.9)
Medicaid/other/unknown	>0, <20	>0, <20
MG treatments (1 year pre-index)[c]		
NSIST + GC	46 (44.7)	23 (39.0)
NSIST + GC + adv.	37 (35.9)	25 (42.4)
NSIST only	>0, <20	>0, <20
NSIST + adv.	>0, <20	>0, <20

Note: Patient counts greater than 0 but less than 20 have been masked. [a]Percentages may not add up to 100% since patients can have multiple comorbidities. [b]Percentages may not add up to 100% as patients may be tagged to multiple payer channels. [c]Advanced therapy includes eculizumab, rituximab, ravulizumab, rozanolixizumab, zilucoplan, Ig, and PLEX.

Changes in MMF and AZA ADD after efgartigimod initiation

- Among the MMF cohort, mean ADD (SD) of MMF significantly dropped from 1629.4 (862.7) mg/day at baseline to 1301.6 (1166.6) mg/day by Month 12 after efgartigimod initiation (P<0.05) (Table 2).
- Among the AZA cohort, mean ADD (SD) of AZA significantly dropped from 132.4 (80.3) mg/day at baseline to 90.6 (81.0) mg/day by Month 12 after efgartigimod initiation (P<0.05) (Table 3).
- Approximately one-third of patients in both cohorts had no MMF or AZA usage (35% and 32%, respectively) by Month 12 post-efgartigimod initiation (Figures 3 & 4).

Table 2. Changes in MMF ADD before and after efgartigimod

MMF (n=103)	Before EFG[a]	After EFG			
		M3[a]	M6[a]	M9[a]	M12[a]
MMF daily dose, mg/day					
Average (SD)[b]	1629.4 (862.7)	1430.9 (1085.2)	1333.0 (1100.6)	1272.5 (1131.4)	1301.6 (1166.6)
P-value[c]	–	0.10	<0.05	<0.05	<0.05

[a]The average dose has been calculated for 60–90 days for M3, 150–180 days for M6, 240–270 days for M9, and 330–365 days for M12. [b]Average daily dose is calculated based on the strength, quantity, and analysis period length over the duration of the observation period (M3, M6, M9, and M12). Patients with no MMF/AZA claims during the period of interest will have 0 mg as ADD. [c]Wilcoxon signed-rank test used to analyze significance.

Figure 3. Proportion of patients at each MMF ADD before and after efgartigimod

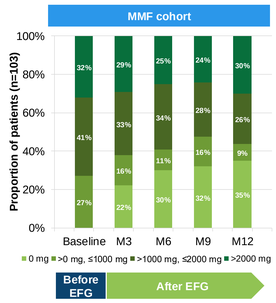
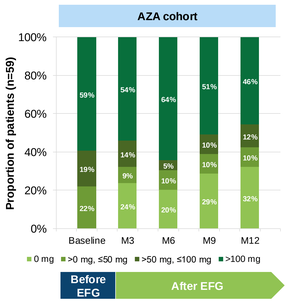


Table 3. Changes in AZA ADD before and after efgartigimod

AZA (n=59)	Before EFG[a]	After efgartigimod			
		M3[a]	M6[a]	M9[a]	M12[a]
AZA daily dose, mg/day					
Average (SD)[b]	132.4 (80.3)	121.3 (95.2)	128.5 (88.8)	102.8 (83.9)	90.6 (81.0)
P-value[c]	–	0.24	0.87	<0.05	<0.05

[a]The average dose has been calculated for 60–90 days for M3, 150–180 days for M6, 240–270 days for M9, and 330–365 days for M12. [b]Average daily dose is calculated based on the strength, quantity, and analysis period length over the duration of the observation period (M3, M6, M9, and M12). Patients with no MMF/AZA claims during the period of interest will have 0 mg as ADD. [c]Wilcoxon signed-rank test used to analyze significance.

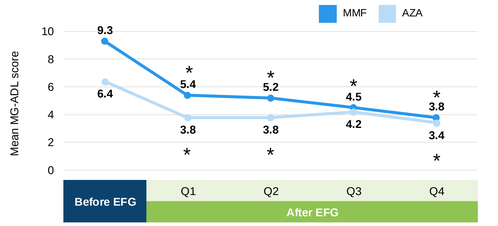
Figure 4. Proportion of patients at each AZA ADD before and after efgartigimod



Changes in MG-ADL after efgartigimod initiation

- 46/103 (45%) and 26/59 (44%) patients had baseline and follow-up MG-ADL scores available. Among both MMF and AZA cohorts, MG-ADL score significantly decreased after efgartigimod initiation (Figure 5).

Figure 5. MG-ADL before and after efgartigimod



Number of patients with MG-ADL scores available						
MMF	46	27	33	37	33	
AZA	26	>0, <20	>0, <20	>0, <20	>0, <20	

Note: A subset of patients with MG-ADL scores available in the integrated dataset were included in the analysis. Any (or best) available MG-ADL score captured during the following quarters post-efgartigimod initiation was used. Patient counts greater than 0 but less than 20 have been masked.
P-values versus baseline were calculated using t-tests. P<0.05 (denoted by) was considered statistically significant.

ABBREVIATIONS: AChE, acetylcholinesterase; AChR, acetylcholine receptor; ADD, average daily dose; ADL, activities of daily living; AZA, azathioprine; CI, confidence interval; EFG, efgartigimod; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; GC, glucocorticoid; gMG, generalized MG; Ig, immunoglobulin; IgG, immunoglobulin G; IQR, interquartile range; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MMF, mycophenolate mofetil; NMJ, neuromuscular junction; NSIST, nonsteroidal immunosuppressive treatment; PLEX, plasma exchange; SD, standard deviation; US, United States.

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