Real-World Reduction in Oral Corticosteroid Utilization Following Efgartigimod Initiation in Patients With Generalized Myasthenia Gravis

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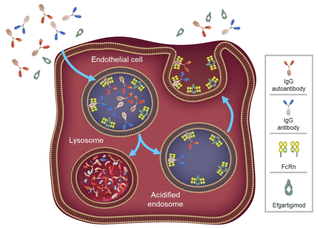
Objective of this study:
To use a real-world dataset to evaluate changes in oral corticosteroids dosing after 6 months of efgartigimod treatment

BACKGROUND

Generalized Myasthenia Gravis (gMG)

- gMG is a rare antibody-mediated, neuromuscular disorder leading to a failure of NMJ transmission[1,2]
- gMG is characterized by fluctuating weakness in ocular, facial, bulbar, axial, and limb muscles[1-3]
- The majority of patients (≈85%) are found to have autoantibodies against the AChR[3]



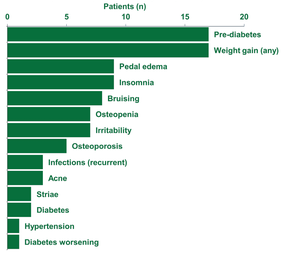
Efgartigimod

- FcRn recycles IgG to extend its half-life and regulate serum concentration[4]
  - FcRn is additionally involved in other cellular processes such as albumin recycling, as well as IgG-dependent phagocytosis and antigen presentation[5]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered to have increased affinity for FcRn and outcompete endogenous IgG[6,7]
- Efgartigimod treatment has been approved for adults with AChR-Ab+ gMG in the United States (2021), the European Union (2022), and Canada (2023) and in Japan (2022) for adults regardless of autoantibody subtype[8-11]
- Efgartigimod binding to FcRn prevents IgG recycling and promotes its lysosomal degradation, reducing IgG levels without impacting IgG production[3-6]
  - Targeted reduction of all IgG subtypes[6,12]
  - No impact on levels of IgM, IgA, IgE, or IgD[6,13]
  - No reduction in albumin or increase in cholesterol levels[12-15]

Oral Corticosteroids (OCS) in gMG

- OCS are the mainstay therapy in the management of many autoimmune conditions, including gMG[16,17]
- OCS are known to be associated with many short- and long-term side effects, especially when used at higher doses (≥10 mg/day)[18,19]
- Recent published case reviews on real-world efficacy for efgartigimod note reduction of OCS with the use of efgartigimod[20]
- There is clinical interest in investigating whether novel gMG treatments can be used as steroid-sparing agents

Corticosteroid-related adverse side effects reported in patients with gMG (N=39)[9]



METHODS

Dataset and study type

Dataset

- US-based insurance open claims-based dataset (IQVIA)* April 2016 to November 2023

Retrospective cohort study

- Inclusion/exclusion criteria:
  - ≥6 months of ongoing efgartigimod usage based on claims captured†
  - First efgartigimod claim between January 1 to December 31, 2022
  - OCS claims present during the 1 year prior to efgartigimod initiation‡
  - Continuous quarterly claims activity to minimize missing data
  - No concomitant usage of eculizumab, rituximab, or ravulizumab with efgartigimod

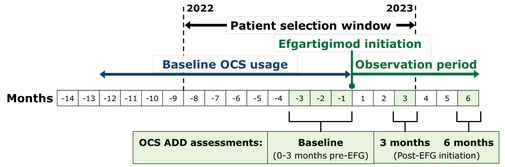
Outcome

- **Average Daily Dose (ADD)** of OCS at baseline (before efgartigimod), 3 months (60-90 days after efgartigimod initiation) and 6 months (150-180 days after efgartigimod initiation)
- **Percentage of OCS tapering** by ≥5, 10, or 20 mg reduction in OCS ADD from baseline (before efgartigimod)

*Based on information licensed from IQVIA: Longitudinal Access and Adjudication Data (LAAD) for the period April 2016 to November 2023, reflecting estimates of real-world activity (all rights reserved). †Patients with a gap of >120 days between consecutive EFG claims were excluded. ‡Baseline OCS usage was defined as any OCS usage present in the 0 to 30 days immediately prior to efgartigimod initiation, and at least ≥90 days of cumulative OCS usage during the 1 year prior to efgartigimod initiation.

Study design and inclusion criteria

Study design



Inclusion criteria

	N (%)
Adults (≥18 years of age) with first efgartigimod claim January 1 to December 31, 2022	1405 (100)
Continuous quarterly activity*	1233 (88)
Remained on efgartigimod treatment for ≥6 months†	842 (60)
No concomitant usage of eculizumab, rituximab, or ravulizumab with efgartigimod	803 (57)
Evidence of chronic OCS usage prior to efgartigimod initiation‡	**316 (22)**
	Final study cohort

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RESULTS

Baseline patient characteristics

		N=316
Age, years		
	Mean (SD)	61.3 (15.0)
	Median (IQR)	65 (52-73)
Sex, n (%)		
	Male	173 (54.7)
	Female	143 (45.3)
Insurance type for first efgartigimod claim, n (%)*		
	Commercial	168 (53.2)
	Medicare	139 (44.0)
	Medicaid	14 (4.4)
	Other/Unknown	4 (1.3)

Common gMG comorbidities, n (%)	N=316
Hypertension	139 (44.0)
Diabetes	94 (29.7)
Obesity	76 (24.1)
Hyperlipidemia	74 (23.4)
Thyroid-related disorders	45 (14.2)
GERD	37 (11.7)
Coronary artery diseases	29 (9.2)
Myocardial infarction	1 (0.3)
Sleep disorder	90 (28.5)
Depression	35 (11.1)
Osteoporosis	19 (6.0)

NSIST/advanced therapy† usage during 1-year period prior to efgartigimod initiation, n (%)	N=316
NSIST only	95 (30.0)
Advanced therapy† only	58 (18.4)
NSIST + advanced therapy	90 (28.5)
No NSIST or advanced therapy†	73 (23.1)

*Percentages may not add up to 100% as patients may be tagged to multiple payer channels. †Advanced therapy included IVIg/SCIg, PLEX, eculizumab, and rituximab.

- Largely consistent with previous reports of claims-based studies
- High proportion of comorbidities including hypertension
- >75% of patients used NSIST and/or other advanced gMG therapies† concomitantly with OCS prior to efgartigimod initiation

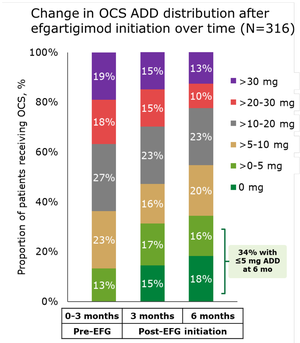
RESULTS (cont'd)

OCS Tapering

Change in OCS daily dose and proportion of patients whose OCS ADD changed or stayed consistent during efgartigimod treatment (N=316)

	Pre-EFG	Post-EFG initiation	
	0-3 months	3 months	6 months
OCS daily dose, mg/day			
Average (SD)	18.6 (15.0)	15.4 (14.9)	13.5 (14.6)
P value*	-	*P*<.001	*P*<.001
Proportion of patients whose OCS ADD tapered, increased, or stayed consistent vs pre-EFG, n (%)			
Tapered ≥5 mg	-	125 (40)	144 (46)
≥10 mg	-	94 (30)	114 (36)
≥20 mg	-	70 (22)	85 (27)
To 0 mg	-	46 (15)	58 (18)
Stable (<±5 mg)	-	127 (40)	119 (38)
Increased ≥5 mg	-	64 (20)	53 (17)

Change in OCS ADD distribution after efgartigimod initiation over time (N=316)



**P* values for ADD were calculated against the ADD at baseline (before efgartigimod) using Wilcoxon signed rank tests. *P*<.05 was considered statistically significant.

SUMMARY

Key conclusions

- **Real-world data based on 316 patients suggested that OCS usage was significantly reduced over 6 months after efgartigimod initiation**
  - **46% and 27% of patients reduced OCS usage by ≥5 mg/day and ≥20 mg/day on average, respectively, by 6 months after efgartigimod initiation**
  - **18% of patients were able to fully taper off OCS usage**
  - **34% of patients with prior steroid usage had OCS ADD of ≤5 mg/day by 6 months after efgartigimod initiation**

Strengths

- **The study enabled inclusion of a large sample size, with results supporting reduction of OCS with the use of efgartigimod observed in a previously published case series[10]**

Limitations

- **Claims-based data analyses are subject to several inherent limitations including assumptions, potential coding errors, and risk of missing data**
- **Insights into how prescribers are approaching OCS tapering on efgartigimod were not assessed and require alternative datasets to explore**

DISCLOSURES AND ACKNOWLEDGEMENTS

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ABBREVIATIONS

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REFERENCES

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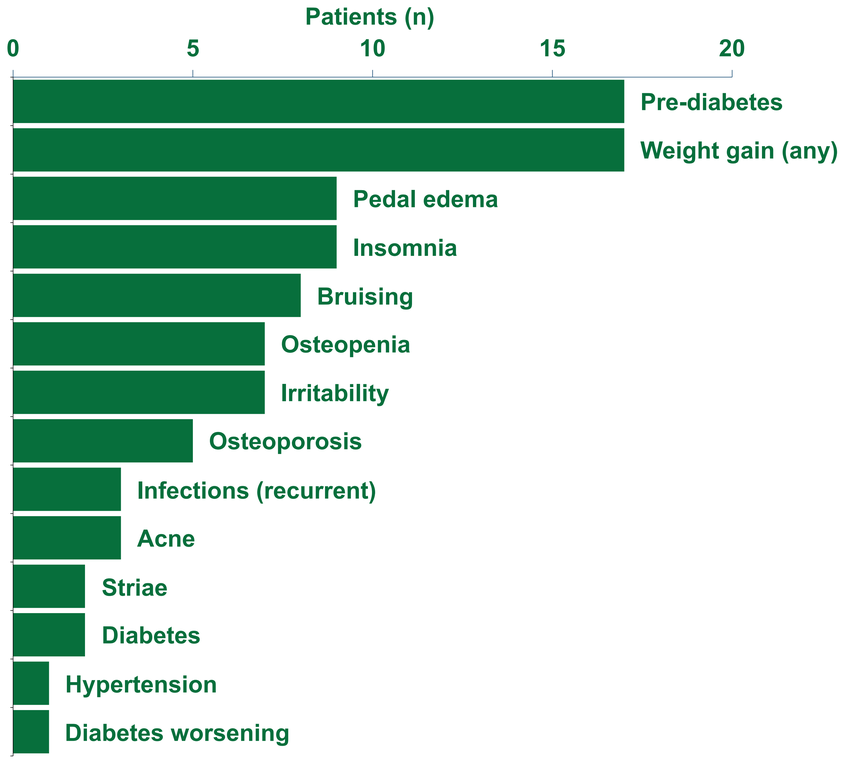

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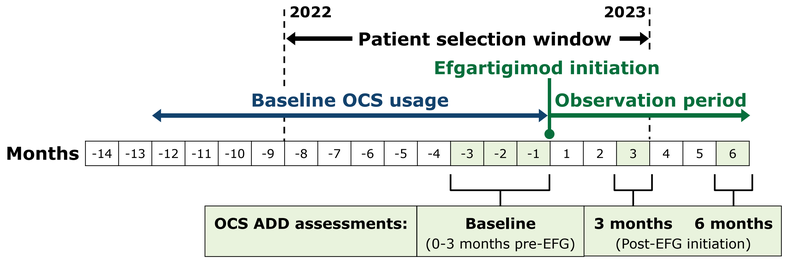

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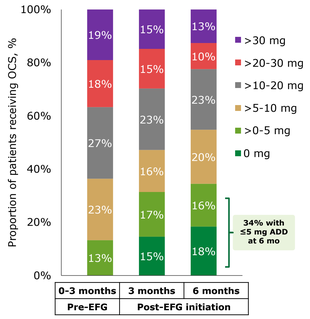

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- CK has participated in advisory boards or served as a speaker for argenx, UCB, Alexion, and Sanofi/Genzyme
- JS has consulted for argenx on glucocorticoid toxicity
- CZQ, DG, MJ, and GP are employees of argenx
- TBS, RRM, and AG are employees of ZS Associates and serve as paid consultants for argenx

ABBREVIATIONS

Ab, antibody; AChR, acetylcholine receptor; ADD, average daily dose; EFG, efgartigimod; Fc, fragment crystallizable; FcRn, neonatal Fc receptor; GERD, gastroesophageal reflux disease; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IQR, interquartile range; IVIg/SCIg, intravenous or subcutaneous immunoglobulin; NMJ, neuromuscular junction; NSIST, nonsteroidal immunosuppressive therapy; OCS, oral corticosteroid; PLEX, plasma exchange; SD, standard deviation.

REFERENCES

1. Gilhus NE, et al. *Nat Rev Dis Primers*. 2019;5(1):30.
2. Howard JF Jr, et al. *Lancet Neurol.* 2021;20(7):526-536.
3. Gilhus NE, Verschuuren JJ. *Lancet Neurol*. 2015;14(10):1023-1036.
4. Sesarman A, et al. *Cell Mol Life Sci.* 2010;67(15):2533-2550.
5. Pyzik M, et al. *Nat Rev Immunol*. 2023;23(7):415-432.
6. Ulrichts P, et al. *J Clin Invest.* 2018;128(10):4372-4386.
7. Vaccaro C, et al. *Nat Biotechnol.* 2005;23(10):1283-1288.
8. Heo YA. *Drugs.* 2022;82(3):341-348.
9. Suzuki S, et al. *Expert Rev Clin Immunol.* 2022;18(12):1207-1215.
10. VYVGART. Product monograph. argenx; 2023. https://pdf.hres.ca/dpd_pm/00073416.PDF
11. VYVGART. Prescribing information. argenx; 2023. https://www.argenx.com/product/vyvgart-prescribing-information.pdf
12. Howard JF Jr, et al. *Lancet Neurol.* 2021;20(7):526-536.
13. Nixon AE, et al. *Front Immunol.* 2015;6:176.
14. Ward ES, et al. *Front Immunol.* 2022;13:892534.
15. Howard JF Jr, et al. *Front Neurol*. 2024;14:1284444.
16. Engel-Nitz NM, et al. *Muscle Nerve*. 2018. doi:10.1002/mus.26114
17. Sanders DB, et al. *Neurology*. 2016;87(4):419-425.
18. Misra UK, et al. *Acta Neurol Belg*. 2020;120(1):59-64.
19. Johnson S, et al. *Med Sci Monit.* 2021;27:e933296.
20. Singer M, et al. *Muscle Nerve.* 2024;69(1):87-92.