REAL-WORLD USAGE PATTERNS AND COSTS OF IVIG TREATMENT IN ADULTS WITH GENERALIZED MYASTHENIA GRAVIS IN THE UNITED STATES

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Introduction and objectives

- Myasthenia gravis (MG) is a rare autoimmune disorder impacting neuromuscular junction transmission.[1] Currently, prevalence of MG in the US is estimated to be 60,000 patients.[2] Most MG cases progress to generalized MG (gMG) with bulbar, limb, trunk, and respiratory muscles severely affected,[3] which contribute to significant patient burden.[4] Currently, there is no known cure for gMG,[2] and available treatments aim to minimize symptoms or functional limitations.[5]
- Although not FDA-approved for gMG, intravenous immunoglobulin (IVIg) is included in clinical guidance for gMG—primarily positioned as a short-term treatment to control exacerbations.[5] Though IVIg can also be considered as a maintenance therapy for some patients with gMG,[5] high-quality studies on the efficacy of long-term IVIg in gMG is lacking.
- To evaluate real-world usage patterns of IVIg in gMG, we isolated patients with gMG who initiated IVIg treatment using a US-based claims database. We report our findings over a 3-year period following IVIg initiation.

Methods

Dataset description and inclusion criteria

- From a large US-based de-identified claims dataset (Symphony Health, an ICON plc Company, Integrated Dataverse [IDV]®, January 1, 2014–December 31, 2019), patients with ≥2 diagnostic claims for MG filed at least 1 month apart were considered to have confirmatory gMG diagnoses and selected for the study.
  - Excluded: Patients with MG diagnostic claims filed ONLY by ophthalmologic specialists as they were considered more likely to be diagnosed with ocular MG instead of gMG.
- From this population, two cohorts (aged ≥18 years) were identified:

IVIg initiator cohort

- First IVIg claim in 2015–2016 included an MG diagnostic code or was within 7 days of an outpatient claim with a MG diagnostic code.
- Continuous quarterly claims activity across the span of 12 months prior to 36 months after the first IVIg claim.

Broader gMG cohort

- ≥1 MG diagnostic claim in 2015–2016.
- Continuous quarterly claims activity across 12 months prior to 12 months after their index date.

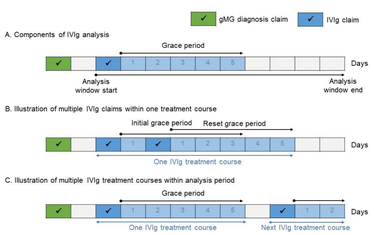
IVIg usage definitions

One IVIg treatment course was defined as ≥1 claim including IVIg treatment filed consecutively with ≤5 days between each claim **(Figure 1).**

IVIg cost analysis

Estimated paid amounts were derived from charged amounts for medical procedures provided in the IDV® dataset. Mean annual costs were evaluated at the patient level from the payer perspective,[4] and standardized to 2018 US dollars.[6]

Figure 1. Examples and definitions of IVIg* treatment courses



*Claims including the following treatments were considered as IVIg therapy: ASCENIV™, BIVIGAM®, CARIMUNE®, CUVITRU®, FLEBOGAMMA®, FLEBOGAMMA® DIF, GAMMAGARD®, GAMMAKED™, GAMMAPLEX®, GAMUNEX®, GAMUNEX®-C, HIZENTRA®, HYQVIA®, OCTAGAM®, PRIVIGEN®, and VIVAGLOBIN®.

gMG treatment usage pattern analysis

The number of patients with any claim including the following treatments were investigated within each 12-month period:

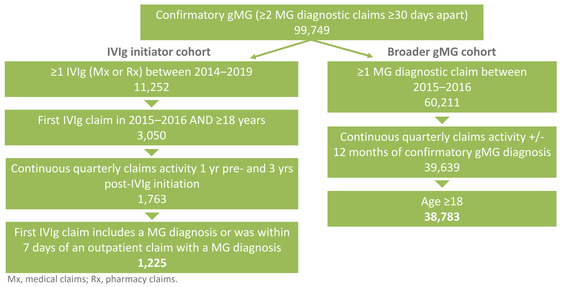
- **Standard of care (SoC):** acetylcholinesterase (AChE) inhibitors, corticosteroids, and nonsteroidal immunosuppressive treatments (NSISTs).
- **Add-on treatment:** plasma exchange (PLEX), rituximab, and eculizumab.

Results

1. Identification of study population

- Of 99,749 total patients with gMG identified in the dataset within the study period, 11,252 patients (11.28%) had at least one claim for IVIg treatment.
- A total of 1,225 patients (1.23%) who initiated IVIg treatment during the study period and met the full inclusion criteria were included in the IVIg cohort **(Figure 2).**
- A total of 38,783 patients were identified for the broader gMG comparator cohort.

Figure 2. Study population



Mx, medical claims; Rx, pharmacy claims.

2. Baseline patient demographics and characteristics

IVIg initiator cohort vs. broader gMG cohort (Table 1):

- IVIg initiators were significantly younger and more likely female compared with the broader gMG cohort (p<0.05).
- More IVIg initiators had commercial insurance compared with the broader gMG cohort. A lower proportion of IVIg initiators had Medicare coverage compared with the broader gMG cohort (p<0.05), consistent with patients being younger.

Table 1. Baseline demographics and patient characteristics

	gMG (n=38,783)	All IVIg initiators (n=1,225)	Intermittent IVIg (n=706)	Chronic IVIg (n=519)
Gender, n (%)				
Female	20,384 (52.6)	697 (56.9)[a]	405 (57.4)	292 (56.3)
Male	18,399 (47.4)	528 (43.1)[a]	301 (42.6)	227 (43.7)
Mean age (SD)				
All	63.47 (13.34)	58.89 (14.77)[a]	59.73 (14.36)	57.74 (15.22)
Female	60.39 (14.72)	55.12 (15.66)[a]	56.25 (15.12)	53.56 (16.25)
Male	66.88 (10.64)	63.86 (11.78)[a]	64.42 (11.76)	63.11 (11.77)
Median age (IQR)				
All	68 (57–75)	62 (49–72)	63 (50–73)	61 (47–71)
Female	64 (51–75)	58 (43–69)	59 (45–69)	56 (39–67)
Male	71 (62–75)	67 (58–75)	67 (58–75)	65 (58–73)
Mx payer type[b], n (%)				
Commercial	31,068 (80.1)	1085 (88.6)[a]	632 (89.5)	453 (87.3)
Medicare	21,571 (55.6)	571 (46.6)[a]	325 (46.0)	246 (47.4)
Medicaid	4160 (10.7)	142 (11.6)	70 (9.9)	72 (13.9)
Other	3305 (8.5)	121 (9.9)	67 (9.5)	54 (10.4)
Rx payer type[b], n (%)				
Commercial	25,312 (65.3)	833 (68.0)[a]	481 (68.1)	352 (67.8)
Medicare	21,216 (54.7)	525 (42.9)[a]	313 (44.3)	212 (40.8)
Medicaid	6282 (16.2)	184 (15.0)	104 (14.7)	80 (15.4)
Other[c]	20,834 (53.7)	545 (44.5)[a]	321 (45.5)	224 (43.2)

IQR, interquartile range; IVIg, Intravenous immunoglobulin; Mx, medical claims; Rx, pharmacy claims; SD, standard deviation. [a]Chi-squared or two-sample t-tests: p<0.05 as compared with the broader gMG cohort. [b]Percentages may not add up to 100% as patients may have had multiple plan subscriptions during the analysis duration. [c]Other includes assistance programs and cash.

3. IVIg usage patterns and associated costs

IVIg usage patterns (Table 2):

- **Intermittent:** 57.6% (706/1,225) of patients received 1 to 5 IVIg treatment courses in the first year and were followed as intermittent IVIg users.
- **Chronic:** 42.4% (519/1,225) of patients received ≥6 IVIg treatment courses in the first year and were followed as chronic IVIg users.
- Baseline demographics and characteristics were similar for intermittent vs. chronic IVIg users **(Table 1)**.

Costs (Table 2):

- Mean annual medical cost per patient was $64,888 for intermittent IVIg users, who on average received 2.12 treatment courses; IVIg costs accounted for 54.2% of medical costs. Mean annual medical cost per patient for chronic IVIg users was almost 2.5-fold higher ($161,478), with IVIg costs accounting for 82.5% of medical costs.

Table 2. IVIg usage pattern and costs 0–12 months post-initiation

	Intermittent IVIg	Chronic IVIg
Patients, n (%)	706 (57.6)	519 (42.4)
Costs[a]		
Annual medical cost per patient (mean)	$ 64,888	$ 161,478[b]
Total medical cost per treatment course (mean)	$ 17,699	$ 11,005[b]
IVIg cost per patient (mean)	$ 35,202	$ 133,155[b]
IVIg cost per treatment course (mean)	$ 16,580	$ 10,704[b]
Treatment courses per patient (mean)	2.12	12.44[b]
Duration per treatment course (mean in days)	1.81	1.37[b]

[a]Five patients were removed from the chronic IVIg cohort for the cost analysis as outliers due to extreme treatment dosages that inflated costs. [b]Wilcoxon rank sum test: p<0.001 as compared to the intermittent IVIg cohort.

4. Usage patterns of other gMG treatments

Baseline:

- **Overall IVIg initiators:** Most patients who initiated IVIg used ≥1 classes of SoC treatments during the year preceding IVIg initiation **(Figure 3)**, with a smaller proportion using add-on therapies **(Figure 4)**.
- **Intermittent vs chronic IVIg users:** No notable differences, though chronic IVIg users trended towards slightly increased usage of NSISTs and PLEX compared with intermittent IVIg users **(Figures 3 & 4)**.

Follow-up of 3 years post-IVIg initiation:

- Both intermittent and chronic IVIg users, as well as a subgroup of 179 patients who received chronic IVIg (≥6 courses annually) for 3 consecutive years post-IVIg initiation, showed similar trends as overall IVIg initiators **(Figures 3 & 4)**.
  - **SoC treatments:** The number of patients using SoC therapies stayed relatively consistent during the 3-year follow-up, though a small proportion of patients decreased use of AChE inhibitors and increased use of NSISTs over time **(Figure 3)**.
  - **Add-on treatments:** A slightly increasing trend was observed in overall add-on therapy usage post-IVIg initiation, driven by increased usage in rituximab and eculizumab **(Figure 4)**.
- Any changes in dosing or frequency of administration were not able to be captured accurately in the dataset.

Figure 3. Annual gMG SoC treatment usage patterns 12-months pre-IVIg initiation to 3-years post-IVIg initiation

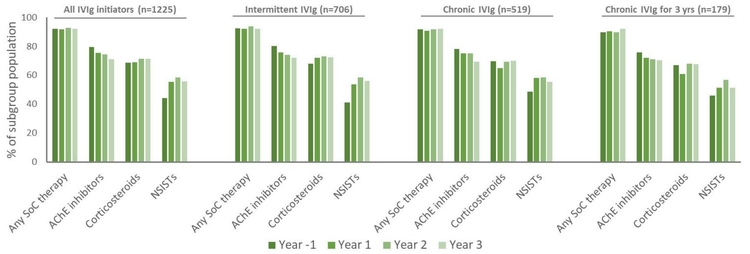
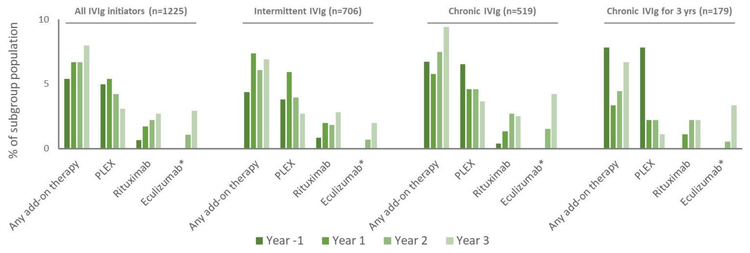


Figure 4. Annual gMG add-on treatment usage patterns 12-months pre-IVIg initiation to 3-years post-IVIg initiation



*Eculizumab was approved for gMG treatment by the FDA in 2017.

Conclusions

- **Nearly half of patients with gMG initiating IVIg received chronic IVIg (≥6 treatment courses) in their first year, incurring >2x annual medical costs compared with intermittent (1–5 IVIg courses) users.**
- **IVIg initiators were younger and more likely to be female compared with a broader gMG population. Further studies are needed to uncover additional key drivers of chronic vs. intermittent use.**
- **For overall IVIg initiators, usage of gMG SoC treatments remained consistent across 1 year pre- and up to 3 years post-IVIg initiation, with a slightly increasing trend in usage of add-on treatments post-IVIg initiation. These trends were also observed in a subgroup of patients who continued chronic IVIg usage over 3 consecutive years, suggesting remaining unmet needs for patients with gMG using IVIg, especially for those using chronic IVIg.**

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Abbreviations AChE, acetylcholinesterase; FDA, Food and Drug Administration; gMG, generalized myasthenia gravis; IQR, interquartile range; IVIg, intravenous immunoglobulin; MG, myasthenia gravis; Mx, medical claims; NSIST, nonsteroidal immunosuppressive treatment; PLEX, plasma exchange; Rx, pharmacy claims; SD, standard deviation; SoC; standard of care; US, United States.

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