



REAL-WORLD TREATMENT PATTERNS IN ADULTS WITH GENERALIZED MYASTHENIA GRAVIS INITIATING INTRAVENOUS IMMUNOGLOBULIN 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 United States 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 contributes 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 limited evidence exists around utilization patterns of gMG treatments following IVIg initiation in the real world.
- To evaluate real-world usage patterns of gMG treatments among IVIg initiators, 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.

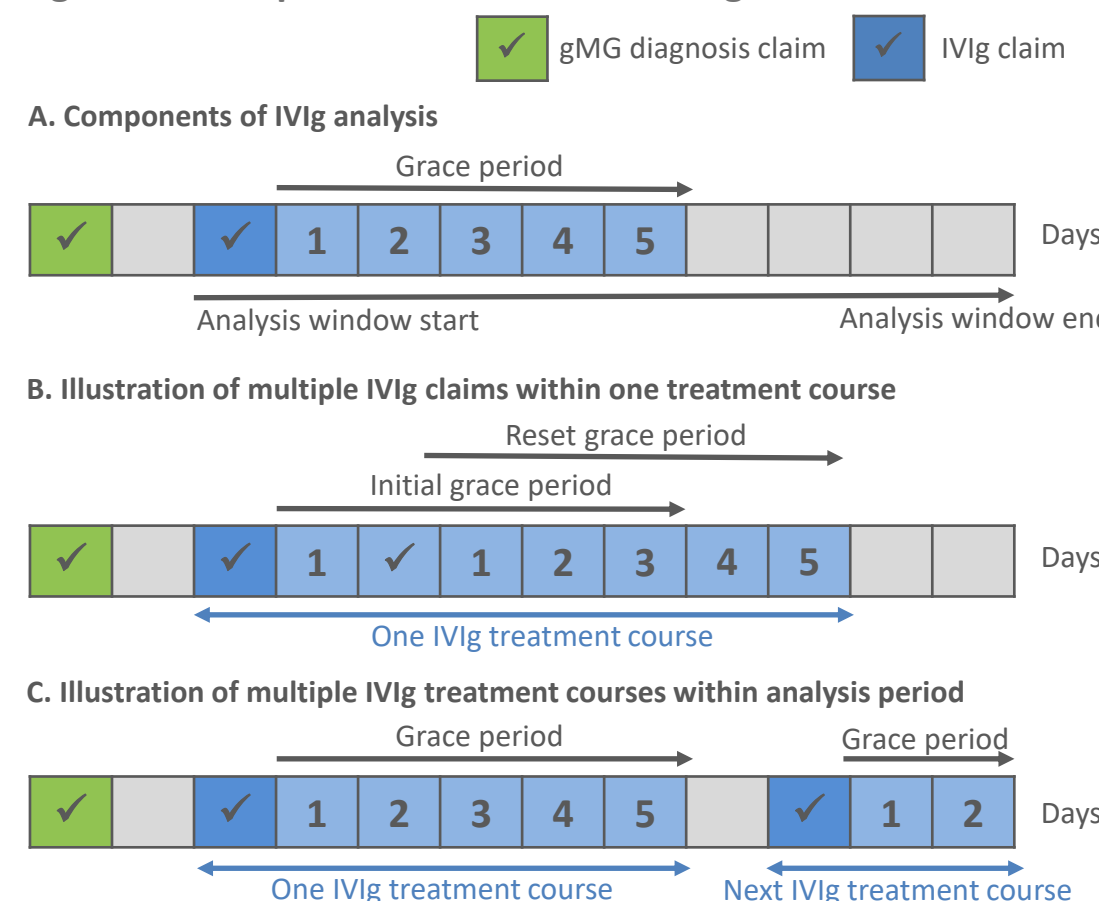
Methods

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 diagnosis 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	Broader gMG cohort
<ul style="list-style-type: none">First IVIg claim in 2015–2016 included an MG diagnostic code or was within 7 days of an outpatient claim with an MG diagnostic code.Continuous quarterly claims activity across the span of 12 months prior to 36 months after the first IVIg claim.	<ul style="list-style-type: none">≥1 MG diagnostic claim in 2015–2016.Continuous quarterly claims activity across 12 months prior to 12 months after their index date.

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

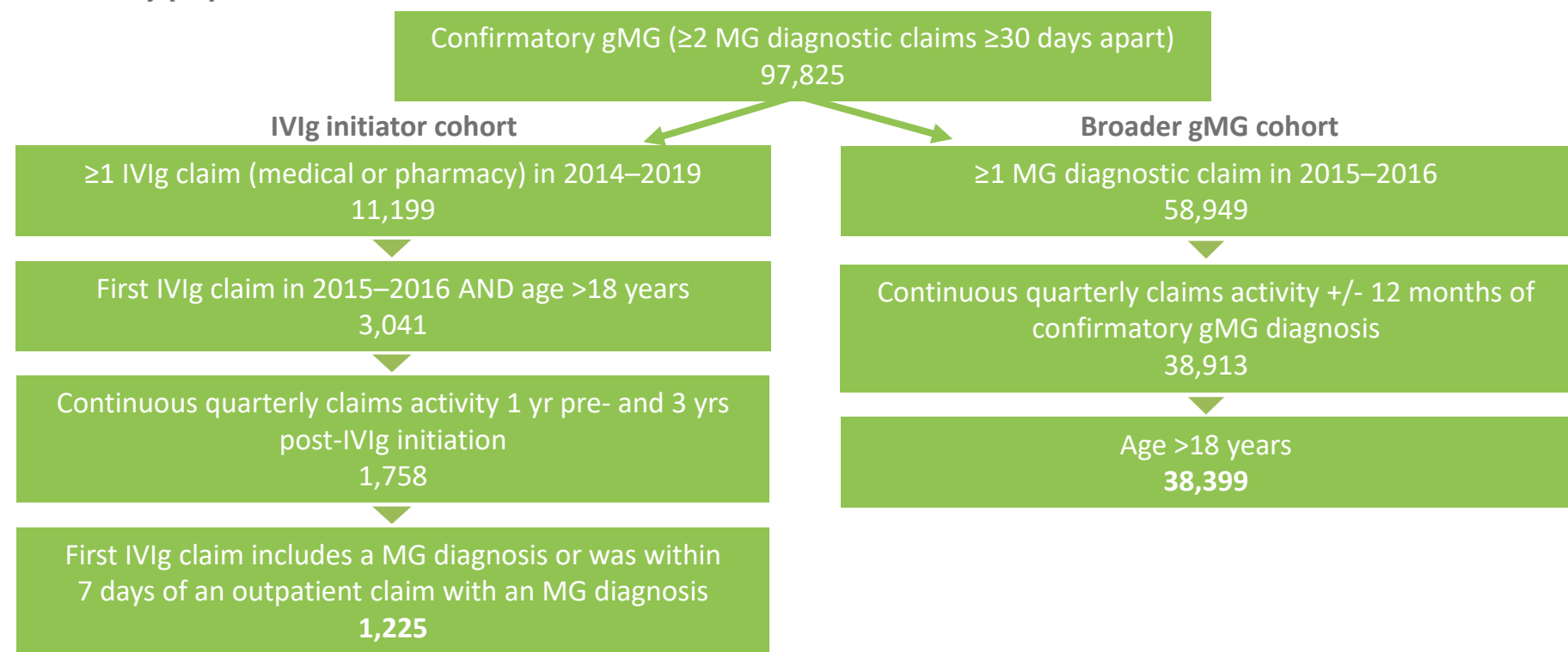
- The number of patients with any claim including the following treatments were investigated within each 12-month period:
- Standard of care (SoC):** Acetylcholinesterase (AChE) inhibitors, corticosteroids, and nonsteroidal immunosuppressive treatments (NSISTs).
 - Add-on treatment:** Plasma exchange (PLEX), rituximab, and eculizumab.

Results

1. Identification of study population

- Of 97,825 total patients with gMG identified in the dataset within the study period, 11,199 patients (11.45%) had at least one claim for IVIg treatment.
- A total of 1,225 patients (1.25%) 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 38,399 patients were identified for the broader gMG comparator cohort.

Figure 2. Study population



2. Baseline patient demographics and characteristics

IVIg initiator cohort versus broader gMG cohort (Table 1)

- IVIg initiators were significantly younger and more likely to be 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 patient demographics and characteristics

	gMG (n=38,399)	All IVIg initiators (n=1,225)	Intermittent IVIg (n=706)	Chronic IVIg (n=519)
Gender, n (%)				
Female	20,159 (52.5)	697 (56.9) ^a	405 (57.4)	292 (56.3)
Male	18,240 (47.5)	528 (43.1) ^a	301 (42.6)	227 (43.7)
Mean age (SD)				
All	63.51 (13.32)	58.89 (14.77) ^a	59.73 (14.36)	57.74 (15.22)
Female	60.42 (14.70)	55.12 (15.66) ^a	56.25 (15.12)	53.56 (16.25)
Male	66.93 (10.59)	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	30,757 (80.1)	1085 (88.6) ^a	632 (89.5)	453 (87.3)
Medicare	21,408 (55.8)	571 (46.6) ^a	325 (46.0)	246 (47.4)
Medicaid	4084 (10.6)	142 (11.6)	70 (9.9)	72 (13.9)
Other	3239 (8.4)	121 (9.9)	67 (9.5)	54 (10.4)
Rx payer type^b, n (%)				
Commercial	25,074 (65.3)	833 (68.0) ^a	481 (68.1)	352 (67.8)
Medicare	21,056 (54.8)	525 (42.9) ^a	313 (44.3)	212 (40.8)
Medicaid	6197 (16.1)	184 (15.0)	104 (14.7)	80 (15.4)
Other ^c	20,667 (53.8)	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.
^aChi-squared or two-sample t-tests: p<0.05 as compared with the broader gMG cohort. ^bPercentages may not add up to 100% as patients may have had multiple plan subscriptions during the analysis duration. ^cOther 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 versus 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

^aFive patients were removed from the chronic IVIg cohort for the cost analysis as outliers due to extreme treatment dosages that inflated costs. ^bWilcoxon 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 versus 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

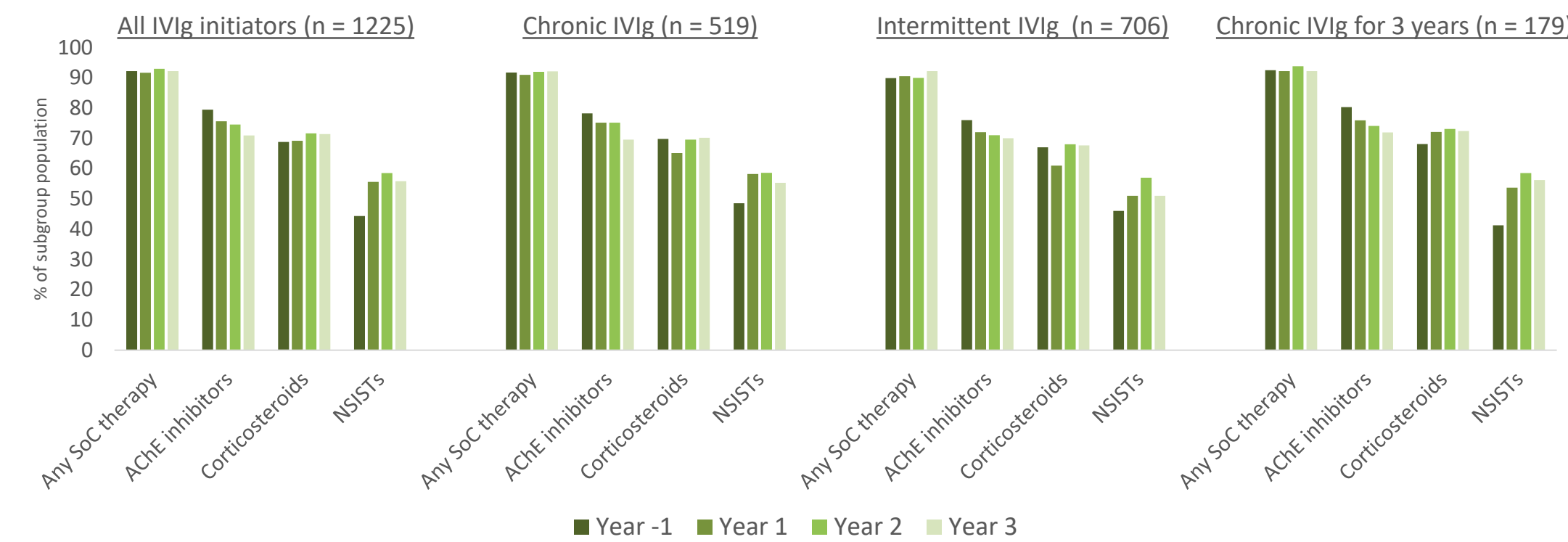
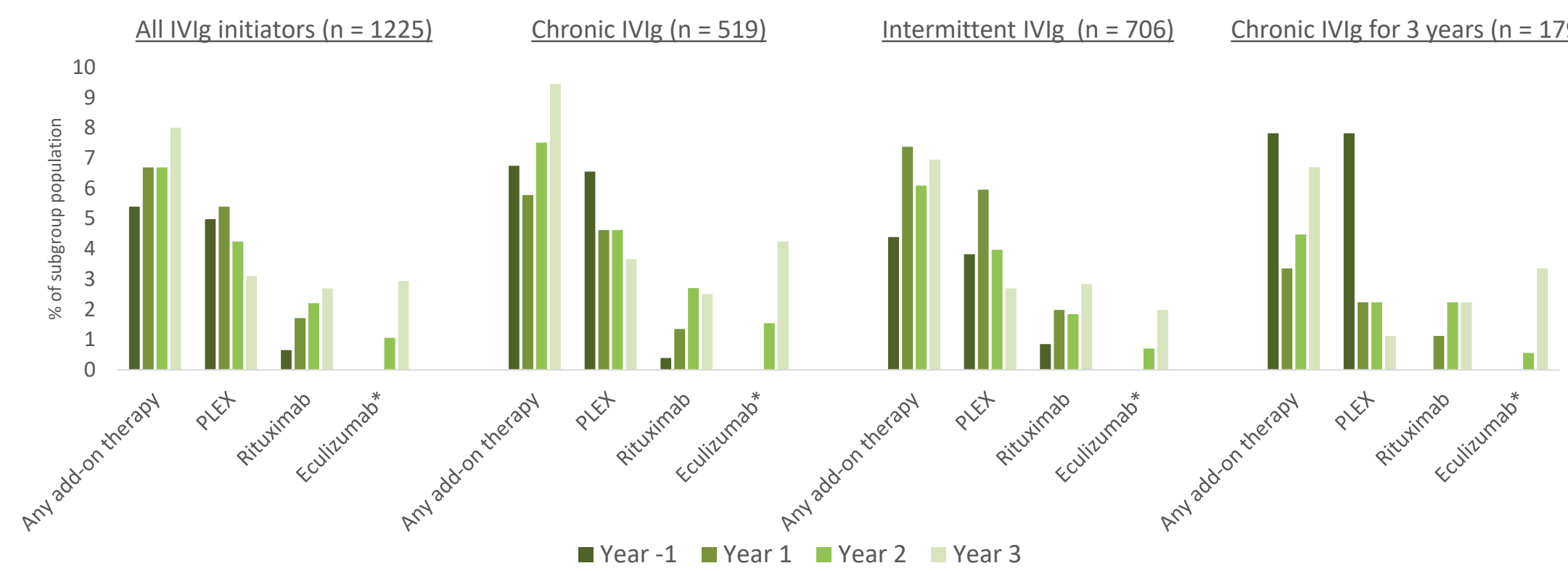


Figure 4. Annual gMG add-on treatment usage patterns 12-months pre-IVIg initiation to 3-years post-IVIg initiation



*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 versus 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.

Financial support This study was funded by argenx US, Inc. (Boston, MA, USA).

Disclosures CQ, TH, DG, EB, and GP are employees of argenx. YL has served as consultant for argenx, Catalist, Immunovant, and UCB, and receives grant support from argenx. AG, AB, MS, and SJ are employees of ZS Associates and serve as paid consultants for argenx. Part of the material in this poster was previously presented at the International Society of Pharmacoeconomics and Outcomes Research (ISPOR) Annual Meeting, May 15–18, 2022, at Washington D.C., USA, and the American Academy of Neurology (AAN) Summer Conference, July 15–16, 2022, at San Francisco, CA, USA.

Acknowledgments The authors thank Sankha Bhattacharya and Chirayu Chhibar (ZS Associates) for conducting the data analysis, Minxuan Huang (ZS Associates) for conducting the statistical analysis, and Aparna Sharma (ZS Associates) for providing editorial support.

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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