EVIDENCE & VALUE SUMMARY: IMAAVY™ (Nipocalimab-aahu)

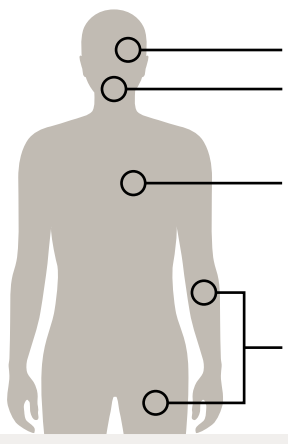
Indication[1]

IMAAVY is indicated for the treatment of **gMG** in **adult and pediatric patients 12 years of age and older** who are **AChR or MuSK antibody positive**.

MG is an antibody-mediated autoimmune disorder[2]

IgG antibodies damage the neuromuscular junction:

- anti-AChR (70-85%)[3]
- anti-MuSK (1-10%)[3]
- anti-Lrp4 (1-5%)[3]



of patients with MG do not achieve an adequate response or are intolerant to conventional treatment[4]

Uncontrolled MG can result in moderate-to-severe exacerbation[4]

15-20% of patients with gMG experience **≥1 myasthenic crisis**[5]:

- **Life-threatening events** characterized by rapidly progressive **muscle weakness and respiratory failure**
- Typically requiring several weeks of **hospitalization, intubation, and mechanical ventilation**

Among refractory MG patients in a 1-year period:

- **>70%** experienced an **exacerbation**[4]
- **50%** required **hospitalization**[4]

Prevalence
~67,300 patients in the US[6]

Pediatric or juvenile MG constitutes
10-15% of US gMG cases[2]

In a 1M member plan:
~155 **AChR+** or **MuSK+ gMG** patients[4]
~23 Patients treated with an **FcRn inhibitor**[4]

IMAAVY is an FcRn blocker designed to reduce serum IgG[7]

IMAAVY is a fully human monocolonal antibody which blocks a fundamental immune pathway by binding to FcRn, which **stops recirculation of IgG**, including pathogenic antibodies **while leaving the rest of the immune system intact**[7-11]

High affinity
Binds at both extracellular (pH 7.6) and endosomal (pH 6.0) pH allowing occupancy of FcRn throughout the recycling pathway[7]

Aglycosylated & effectorless
Inhibits its interaction with Fcγ receptors and complement molecules, reducing activation of immune effector cells[7,8,11]

IMAAVY in adult and pediatric patients with gMG[12,13]

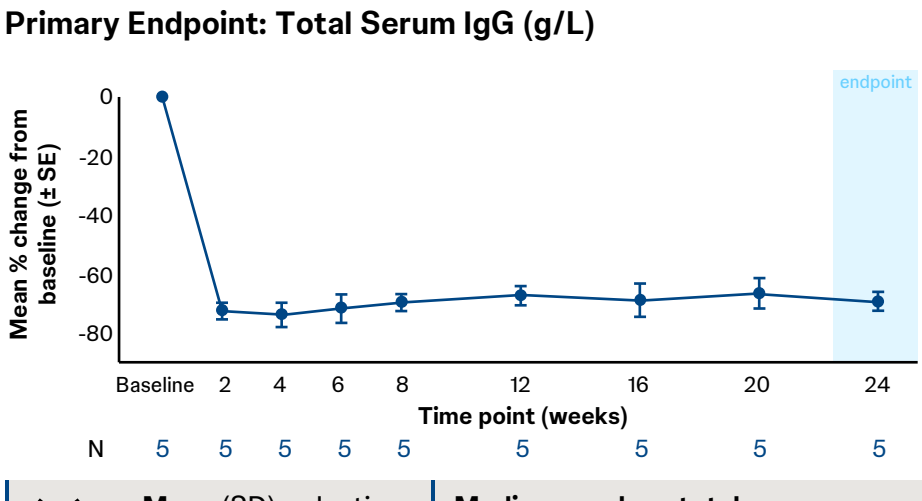
VIVACITY[12]

A **Phase 3, multicenter, randomized, double-blind, placebo-controlled study** of **IMAAVY in gMG** to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of IMAAVY in **adult participants with gMG**

R → **IMAAVY + SOC**: IMAAVY™ 30 mg/kg IV LD at Week 0 and 15 mg/kg IV Q2W Week 2-22
R → **Placebo + SOC**: PBO Q2W via IV infusion

All seropositive (AChR+, MuSK+, or LRP4+) patients were included in efficacy analysis

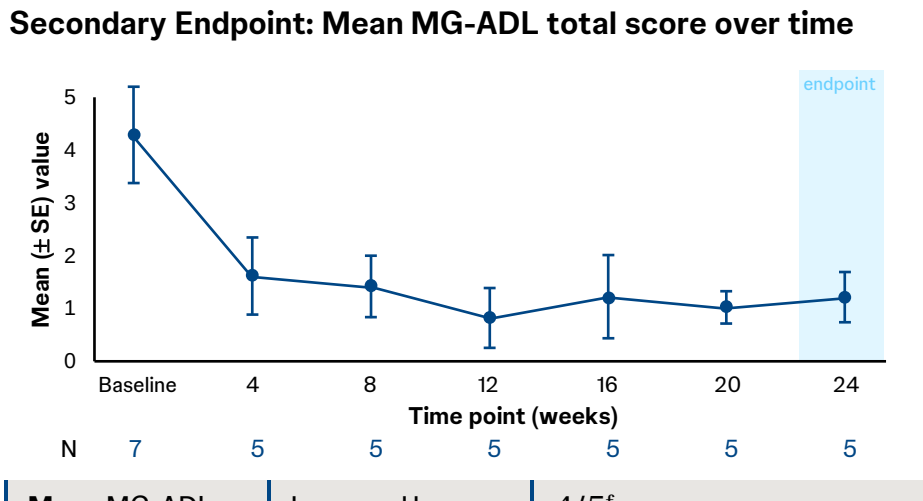
Statistically significant improvement in MG-ADL compared to placebo in antibody positive gMG patients



Average change (SE) from baseline at Weeks 22-24:
IMAAVY + SOC: -4.7 (0.329)
Placebo + SOC: -3.25 (0.335)

Difference of LS means:
-1.45 (95% CI -2.38 to -0.52), p=0.0024

Statistically significant improvement in QMG compared to placebo in antibody positive gMG patients



Average change (SE) from baseline at Weeks 22-24:
IMAAVY + SOC: -4.86 (0.504)
Placebo + SOC: -2.05 (0.499)

Difference of LS means:
-2.81 (95% CI -4.22 to -1.41), p<0.0012

Overall adverse events	IMAAVY + SOC (n=98)	Placebo + SOC (n=98)
AE	82 (84%)	82 (84%)
Related AE	28 (29%)	28 (29%)
Serious AE	9 (9%)	14 (14%)
Related serious AE	1 (1%)	1 (1%)
AE leading to discontinuation	5 (5%)	7 (7%)
AE leading to death	1 (1.0%)	2 (2.0%)
AEs of special interest		
Any infection	42 (43%)	42 (43%)
Severe infection[a]	3 (3%)	4 (4%)
Infusion-related reactions	10 (10%)	11 (11%)

	IMAAVY + SOC (n=98)	Placebo + SOC (n=98)
Most common adverse reactions[1b]		
Infection		
Respiratory tract infection[c]	18	15
Urinary tract infection[d]	6	3
Herpes zoster and Herpes simplex	6	2
Oral infection[e]	5	3
Peripheral edema	12	2
Muscle spasm	12	3

VIBRANCE[13]

Phase 3, multicenter, randomized, double-blind, placebo-controlled study of **IMAAVY in gMG** to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of IMAAVY in **adolescent participants with AChR+ or MuSK+ gMG**

All → **IMAAVY + SOC**: IMAAVY 30 mg/kg IV LD at Week 0 and 15 mg/kg IV Q2W Week 2-22

Primary Endpoint: Total Serum IgG (g/L)

Mean (SD) reduction in total serum
Baseline to Week 24:
-68.98% (7.561)
95% CI of (-78.4; -59.6)

Median pre-dose total serum IgG reduction
Baseline to week 2: -72.00%
Baseline to week 24: -69.87%

Secondary Endpoint: Mean MG-ADL total score over time

Mean MG-ADL score was
4.29
(SE, 0.918) at baseline

Improved by ↓
-2.40
(SE, 0.187) at Week 24

4/5[f] (80%) participants showed minimal symptom expression
(MG-ADL=0/1) at Week 24

Overall adverse events (n=7)	IMAAVY + SOC
Participants with ≥1 AEs	71.4% (n=5)
Related AEs	28.6% (n=2)
Participants with AEs leading to death	0.0% (n=0)
Participants with SAEs	0.0% (n=0)
AEs leading to temporary discontinuation of study treatment	0.0% (n=0)
AEs leading to permanent discontinuation of study treatment	0.0% (n=0)
AEs leading to termination of study participation	0.0% (n=0)
COVID-19 associated AEs	14.3% (n=1)
COVID-19 associated SAEs	0.0% (n=0)

[A]or infection requiring invasive treatment [b]≥10% with IMAAVY [c]COVID-19 (and other related terms), pneumonia, bronchitis, pneumonia bacteria [d]other related terms [e]glossitis, oral candidiasis, pericoronitis, pulpitis dental, tooth abscess, tooth infection [f]5 of 7 patients completed 24 weeks of active treatment phase at data cutoff.

AChR, acetylcholine receptors; AE, adverse event; CI, confidence interval; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IV, intravenous; LD, loading dose; Lrp4, lipoprotein receptor-related protein 4; LS, least squares; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MuSK, muscle-specific kinase; Q2W, every 2 weeks; QMG, Quantitative Myasthenia Gravis; R, randomization; SAE, serious adverse event; SD, standard deviation; SE, standard error; SOC, standard of care; Wk, Week.

1. IMAAVY™ (nipocalimab-aahu) [Prescribing Information], Horsham, PA: Janssen Biotech, Inc. 2. Dresser L, et al. J Clin Med. 2021 21;10(11):2235. 3. Li Y, et al. Ann Transl Med. 2023. 11(7):290. 4. Schneider-Gold C, et al. Ther Adv Neurol Disord. 2019 1;12:1756286419832242. 5. Stetefeld, H, et al. Neurol. Res. Pract. 2019;1(19). 6. IPD Analytics. Budget Impact FcRn Antagonists for Generalized Myasthenia Gravis. August 2023. Accessed November 1, 2024. https://www.ipdanalytics.com 7. Ling LE, et al. Clin Pharmacol Ther. 2019;105:1031-1039; 8. Roy S, et al. Am J Obstet Gynecol. 2019;220:498.e1-498.e; 9. Patel D, et al. J Allergy Clin Immunol. 2020;3(146):467-478; 10. Blumberg LJ, et al. Sci Adv. 2019;5:eaax9586.c. 11. Peter HH, et al. J Allergy Clin Immunol. 2020;146(3): 479-491. 12. Antozzi, C. et al. *Lancet Neurol* 2025; 24: 105–16. 13. Strober, J. et al., Poster presented at AANEM Annual Meeting, Savanah, Georgia, October 15-18, 2024.

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