Symptom Severity Assessment Using MG-ADL Items and Domains in a 24-week, Phase 3 Study (Vivacity) of Nipocalimab in Generalized Myasthenia Gravis

Constantine Farmakidis[1*], Kavita Gandhi[2], Maria Ait-Tihyaty[3], Ibrahim Turkoz[4], Sheryl Pease[2], Zia Choudhry[5], Charlotte Gary[6], Antoine C El Khoury[2], Sindhu Ramchandren[4]

[1]University of Kansas Medical Center, Kansas City, KS, USA; [2]Janssen Global Services, LLC, Raritan, NJ, USA; [3]Janssen Global Medical Affairs, Titusville, NJ; [4]Janssen Research & Development, LLC, Titusville, NJ; [5]Janssen Scientific Affairs, LLC, Titusville, NJ, USA; [6]Janssen-Cilag, Issy-les-Moulineaux, France.

Presenting author

Introduction

- Generalized myasthenia gravis (gMG) is a rare, chronic autoimmune disorder characterized by impaired neuromuscular transmission mediated by immunoglobulin-G (IgG) antibodies, leading to fatigable weakness in the bulbar, respiratory, and axial muscles, which adversely impacts daily functioning and health-related quality of life.[1,2]
- Current treatment options include standard-of-care therapies such as acetylcholinesterase inhibitors, corticosteroids, nonsteroidal immunosuppressants, immunomodulators (e.g. intravenous IgG) and advanced immunotherapies (e.g. C5 complement inhibitor, neonatal Fc receptors [FcRn] blockers etc.).[3]
- Nipocalimab is a fully human monoclonal antibody that binds to FcRn receptors with high affinity and specificity resulting in a reduction of IgG levels without affecting other immunoglobulin classes or compromising humoral or cellular immune functions.[4]
- In the double-blind phase 3 Vivacity-MG3 study in gMG, nipocalimab plus standard-of-care (SOC) treatment demonstrated sustained disease control with statistically significant improvement compared with placebo + SOC from baseline over weeks 22, 23, and 24 in the Myasthenia Gravis Activities of Daily Living (MG-ADL), a measure of MG symptom severity.[5]

Objective

- To evaluate if changes in MG-ADL total score with nipocalimab + SOC versus placebo + SOC were driven by individual items, domains, or distinct muscle function groups.

Methods

- The Vivacity-MG3 study enrolled adult patients with gMG who had an insufficient clinical response (MG-ADL score of ≥6 at screening and baseline, and a Myasthenia Gravis Foundation of America [MGFA] Class of IIa/b, IIIa/b, or IV a/b at screening) to ongoing, stable SOC.
- The study consisted of a screening period of up to 4 weeks, a 24-week double-blind placebo-controlled phase and an open label extension phase of variable duration.
  - Participants on stable SOC treatment were randomized (1:1) to either placebo or nipocalimab (30 mg/kg IV loading dose followed by 15 mg/kg every two weeks) intravenously every two weeks.
- The MG-ADL (**Figure 1**) is an 8-item, clinician reported assessment based on patient recall of activities of daily living across four muscle function groups with higher scores indicating greater symptom severity.
- A change of at least 1-point on MG-ADL items may be meaningful from an individual patient's perspective; for example, a 1-point change in the respiratory domain could be the difference between experiencing shortness of breath or requiring a ventilator.

Figure 1 : MG-ADL Items and Domains

Domain function		Score = 0	Score = 1	Score = 2	Score = 3	Your Score
Bulbar	Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal speech, but can be understood	Difficult to understand speech	
	Chewing	Normal	Fatigue with solid food	Fatigue with solid food	Gastric tube	
	Swallowing	Normal	Rare episode of choking	Frequent choking necessitating change in diet	Gastric tube	
Respiratory	Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependence	
Limb Function	Brushing teeth or hair	Normal	Extra effort, but no rest periods needed	Rest periods needed	Cannot do one of these functions	
	Arising from chair	Normal	Mild, something uses arms	Moderate, always uses arms	Severe, required assistance	
Ocular	Double vision	Normal	Occurs, but not daily	Daily, but not constant	Constant	
	Eyelid droop	Normal	Occurs, but not daily	Daily, but not constant	Constant	
					Your Total Score =	

MG-ADL=Myasthenia Gravis Activities of Daily Living.

Analysis

- In this post hoc study, all analyses were based on the primary efficacy analysis set (anti-AChR+, anti-MuSK+, anti-LRP4+) which included all randomized anti-AChR+, anti-MuSK+, anti-LRP4+ participants who received ≥1 dose of any study intervention.
- Baseline demographic and disease characteristics were summarized.
- Baseline distribution scores of MG-ADL items and domains were evaluated for potential floor effects (score =0).
- Mean change from baseline in MG-ADL items were reported at Weeks 22, 23, and 24.
- Differences between nipocalimab + SOC and placebo + SOC groups in mean change from baseline in MG-ADL domains at Week 24 were analyzed using analysis of covariance (ANCOVA) models, with fixed effects for treatment group, autoantibody status, and region, and the corresponding baseline value as a covariate.
- The odds of achieving a 1-point improvement in MG-ADL items and a 2-point improvement in MG-ADL domains were analyzed using Generalized Estimating Equations (GEE) with repeated measures.
  - Correlations of the within-subject repeated measures were modeled using an autoregressive covariance structure.
  - Odds ratios and corresponding 95% confidence intervals were reported.

Results

- Median baseline scores on all MG-ADL domains ranged from 1.0 to 3.5 and no domain floor effects were observed for nipocalimab + SOC or placebo + SOC groups (**Table 1**).

Table 1: Demographics and baseline characteristics

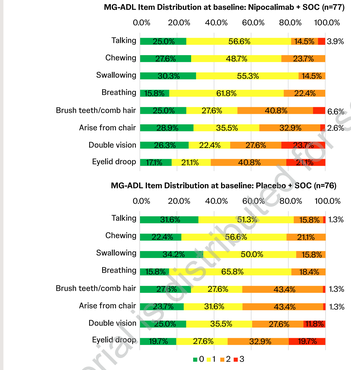
	Nipocalimab + SOC N=77	Placebo + SOC N=76	Total N=153
A. Demographics			
Age, years			
Mean (SD)	52.5 (15.66)	52.3 (16.37)	52.4 (15.97)
Range	20-81	20-81	20-81
≥65 years old, n (%)	18 (23.4)	19 (25.0)	37 (24.2)
Sex, n (%)			
Male	27 (35.1)	34 (44.7)	61 (39.9)
Female	50 (64.9)	42 (55.3)	92 (60.1)
Race, n (%)			
White	49 (63.6)	47 (61.8)	96 (62.7)
Asian	24 (31.2)	25 (32.9)	49 (32.0)
Others[a]	4 (5.2)	4 (5.3)	8 (5.2)
B. Baseline characteristics			
Duration of MG, mean (SD), years	6.9 (7.44)	8.9 (8.13)	7.9 (7.83)
Baseline MG-ADL total sore, mean (SD)	9.4 (2.73)	9.0 (1.97)	9.2 (2.38)
MG-ADL domain scores			
Bulbar, mean (SD)	2.7 (1.52)	2.7(1.51)	-
Median (Range)	2.5 (0-7)	2.5 (0-7)	-
Respiratory, mean (SD)	1.1 (0.54)	1.0 (0.50)	-
Median (Range)	1.0 (0-2)	1.0 (0-2)	-
Limb function, mean (SD)	2.4 (1.27)	2.5 (1.12)	-
Median (Range)	2.0 (0-5)	2.5 (0-5)	-
Ocular, mean (SD)	3.2 (1.71)	2.8 (1.35)	-
Median (Range)	3.5 (0-6)	2.8 (0-6)	-

[a]Includes Black or African American, American Indian or Alaska Native and not reported; MG=Myasthenia Gravis; MG-ADL=Myasthenia Gravis Activities of Daily Living; SD=Standard deviation; SOC=Standard of care.

MG-ADL item analyses (primary efficacy set [AChR+, MuSK+ and LRP4+])

- In 153 participants, median baseline MG-ADL item scores were 1.0-2.0; no item level floor effects were observed (**Figure 2**).

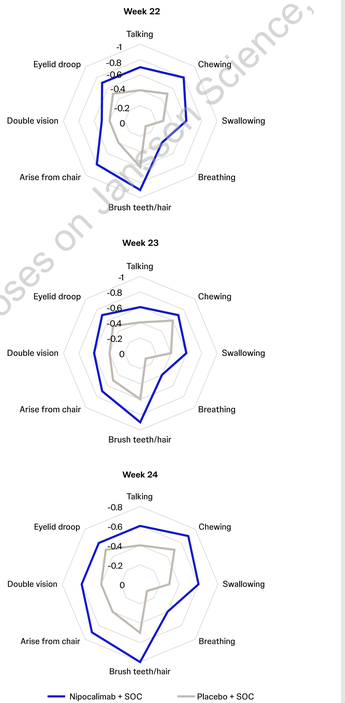
Figure 2: Baseline MG-ADL item score distribution



Note: 0=Normal. MG-ADL=Myasthenia Gravis Activities of Daily Living; SOC=Standard of care.

- Change from baseline on MG-ADL total score were driven by all items in nipocalimab + SOC versus placebo + SOC at weeks 22-24 (**Figure 3**).
- Change from baseline on MG-ADL at the item level were numerically higher in nipocalimab + SOC versus in placebo + SOC.

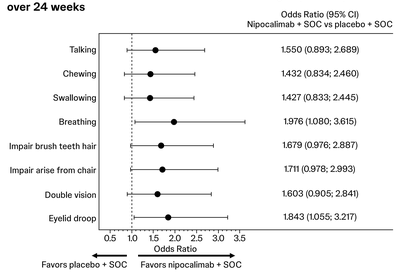
Figure 3: Mean MG-ADL item change from baseline at weeks 22, 23, and 24



Respiratory domain max score was 2 points for the study participants due to study exclusion criteria, forcing the possible score range to be 0-2. MG-ADL=Myasthenia Gravis Activities of Daily Living; SOC=Standard of care.

- At the item level, the proportion of participants achieving the responder threshold (≥1 point improvement) ranged from 42.7% for swallowing to 97.6% for breathing over 24 weeks, with nipocalimab + SOC showing a favorable outcome compared to placebo + SOC for all MG-ADL items (**Figure 4**).

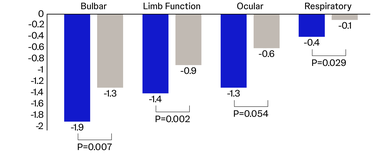
Figure 4: MG-ADL Item- level likelihood of achieving ≥1 point improvement over 24 weeks



MG-ADL=Myasthenia Gravis Activities of Daily Living; SOC=Standard of care.

- At week 24, statistically significant improvements favoring nipocalimab + SOC versus placebo + SOC were observed for mean change from baseline for all MG-ADL domains.

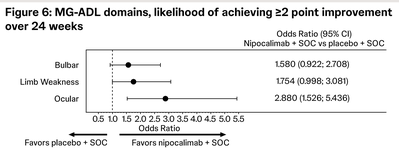
Figure 5: MG-ADL domains mean change from baseline at week 24



Note: Lower scores indicate better status. P-values are from ANCOVA models.
ANCOVA=analysis of covariance; MG-ADL=Myasthenia Gravis Activities of Daily Living; SOC=Standard of care.

- The odds-ratio (95%CI) over 24-weeks were: bulbar 1.6 (0.9-2.7), limb function 1.8 (1.0-3.1) and ocular 2.9 (1.5-5.4), all favoring nipocalimab + SOC versus placebo + SOC (**Figure 6**).

Figure 6: MG-ADL domains, likelihood of achieving ≥2 point improvement over 24 weeks



Note: The respiratory domain has only 1 item (breathing) and is represented in Figure 4.
MG-ADL=Myasthenia Gravis Activities of Daily Living; SOC=Standard of care.

Conclusions

- MG-ADL total score changes were driven by all item and domains of the MG-ADL scale favoring nipocalimab + SOC versus placebo + SOC.
- There was a greater likelihood of achieving at least 1 –point improvement on MG-ADL items and at least 2- point improvement on MG-ADL domains over 24 weeks with nipocalimab + SOC versus placebo + SOC.

Acknowledgements

Editorial support was provided by Sonali Satam, PhD (SIRO Medical Writing Pvt. Ltd.) and Doyel Mitra, PhD (Janssen Global Services, LLC). Layout and designing assistance were provided by Mugdha Rokade (SIRO Medical Writing Pvt. Ltd).

Disclosures

Constantine Farmakidis: Dystrophy Association and medical advisory board participation for Argenx, UCB and Janssen. All other authors are employee, contractor or consultant at Janssen Pharmaceuticals and may hold stock or stock option in Johnson & Johnson.

Funding

This poster was supported by Janssen Scientific Affairs, LLC, Horsham, PA, USA.

For questions related to this presentation, please contact:
Kavita Gandhi, kgandhi9@its.jnj.com

Autoantibody: MG

Presented at the Myasthenia Gravis Foundation of America (MGFA) Scientific Session of the American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) Annual Meeting, Savanah, Georgia, October 15-18, 2024.

References:

1. Gilhus NE, et al. Myasthenia gravis. *Nat Rev Dis Primers*. 2019; 5:30.
2. Dresser L, et al. *J Clin Med*. 2021; 10: 2235.
3. Wiendl H, et al. *Ther Adv Neur Disord* 2023;16:1-31.
4. Ling LE, et al. *Clin Pharmacol Ther* 2019; 105: 1031–9.
5. Antozzi C, et al. *EMJ Neurol*. 2024;12:51-55.