Efficacy of Nipocalimab, a Novel Neonatal Fragment Crystallizable Receptor Blocker, as Measured using Quantitative Myasthenia Gravis Assessment: Findings from the Phase 3 Vivacity-MG3 Study

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Introduction

- Generalized myasthenia gravis (gMG) is a rare chronic condition characterized by muscle weakness caused by autoantibody-mediated disruption of neurotransmission that severely affects the daily functioning and health-related quality of life of patients[1,2]
- Nipocalimab, a monoclonal antibody that blocks neonatal fragment crystallizable receptor (FcRn) to reduce levels of circulating Immunoglobulin G (IgG) antibodies, has demonstrated sustained efficacy based on Myasthenia Gravis-Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) scores in the Vivacity-MG3 study in seropositive patients with gMG[3,4]
- **Vivacity-MG3 study:** A 24-week, phase 3, randomized, double-blind study evaluated efficacy and safety of nipocalimab+standard-of-care (SOC) vs placebo+SOC
  - Quantitative Myasthenia Gravis (QMG) total score over weeks 22 and 24; Least-square (LS)-mean change (standard error [SE]): −4.9 (0.50) vs −2.1 (0.50); difference: −2.8 (0.71); p<0.001

Objective

- To assess the efficacy of nipocalimab+SOC using QMG in patients with gMG

Methods

Efficacy analysis population

- All patients who received ≥1 dose of nipocalimab+SOC or placebo+SOC in the double-blind phase and were antibody positive for a gMG-related pathogenic antibody (anti-acetylcholine receptor [anti-AChR], anti-muscle-specific tyrosine kinase [anti-MuSK], or anti-low-density lipoprotein receptor 4 [anti-LRP4])

Assessments

Improvement in QMG total score from baseline

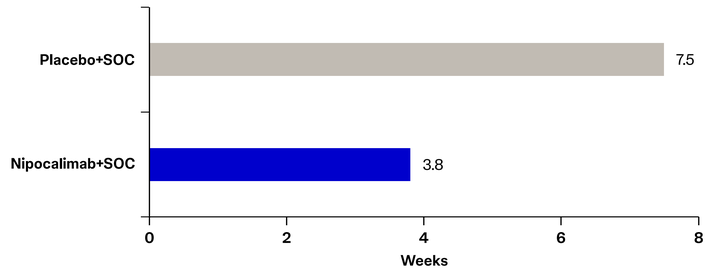
- Proportion of patients with ≥3-point improvement[5,6] in QMG total score (QMG-3)
- Proportion of patients with sustained QMG-3 improvements over time

Results

Proportion of patients achieving QMG-3

- Proportion of patients with QMG-3 improvement at week 24: 48.1% (37/77) in nipocalimab+SOC vs 28.9% (22/76) in placebo+SOC group
- Earliest week improvements (mean [standard deviation (SD)]) QMG-3 were 3.8 (3.88) weeks for nipocalimab+SOC vs 7.5 (6.33) weeks for placebo+SOC (**Figure 1**)

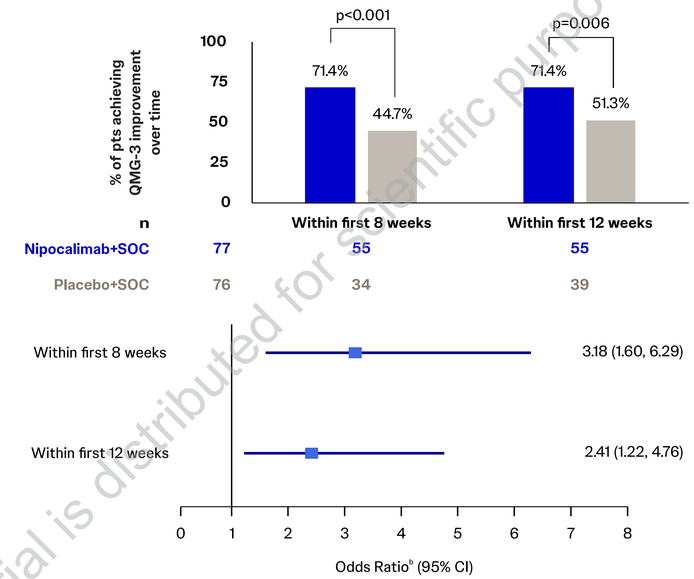
FIGURE 1: Earliest week QMG-3 improvement



QMG=Quantitative myasthenia gravis; SOC=Standard of care.

- Post baseline QMG-3 improvements were nipocalimab+SOC: 75.3% (58/77); placebo+SOC: 63.2% (48/76)
- Within 8 weeks of treatment initiation, 71.4% (55/77) of nipocalimab+SOC vs 44.7% (34/76) of placebo+SOC group patients achieved QMG-3 improvement (p<0.001[a]) (**Figure 2**)

FIGURE 2: Proportion of patients with QMG-3 improvement during the 24-week RCT

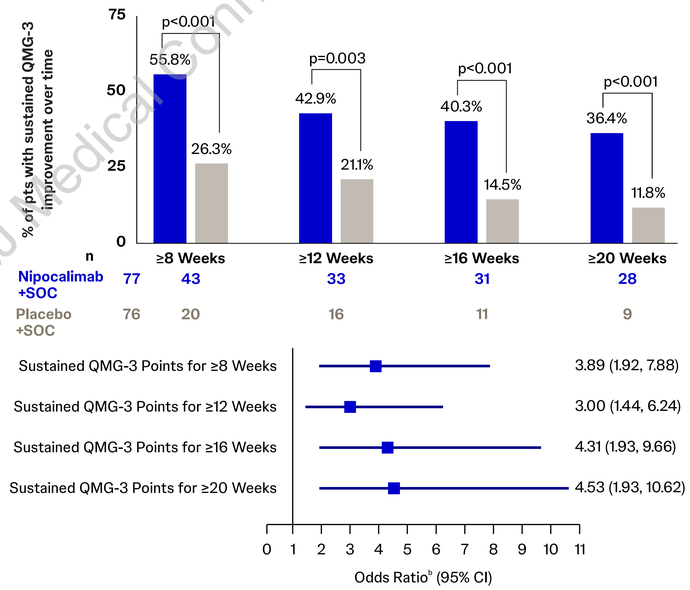


CI=Confidence interval; Pts=patients; QMG=Quantitative myasthenia gravis; RCT=Randomized clinical trials; SOC=Standard of care
[a]Based on Cochran-Mantel-Haenszel tests controlling for the autoantibody status and region.
[b]Based on logistic regression adjusting for autoantibody status and region

Proportion of patients with sustained QMG-3 improvements

- Significantly greater proportion of patients from the nipocalimab+SOC (55.8% [43/77]) vs placebo+SOC (26.3% [20/76]; p<0.001[a]) group sustained QMG-3 improvement for ≥8 weeks (**Figure 3**)
- Patients receiving nipocalimab+SOC vs placebo+SOC were >4-times more likely to sustain QMG-3 improvement for ≥16 weeks (odds ratio [OR] 95% confidence interval [CI]: 4.31 [1.93, 9.66]) and for ≥20 weeks (OR [95% CI]: 4.53 [1.93, 10.62])

FIGURE 3: Proportion of patients with sustained QMG-3 improvement during the 24-week RCT



CI=Confidence interval; Pts=patients; QMG=Quantitative myasthenia gravis; RCT=Randomized clinical trials; SOC=Standard of care.
[a]Based on Cochran-Mantel-Haenszel tests controlling for the autoantibody status and region.
[b]Based on logistic regression adjusting for autoantibody status and region.

Proportion of time spent in QMG-3 improvement

- Significantly more patients from nipocalimab+SOC vs placebo+SOC (36.4% vs 10.5%; p<0.001) group spent ≥75% of study duration with QMG-3 improvement (**Table 1**)

TABLE 1: Time spent in QMG-3 improvement during the 24-week RCT

	Nipocalimab + SOC (n=77)	Placebo + SOC (n=76)	p-value	OR (95% CI)
Time with QMG-3 improvements in QMG up to week 24, mean (SD) in days	74.8 (65.26)	32.8 (49.70)		
Percentage of time with QMG-3 improvement up to week 24, mean (SD)	44.5 (38.84)	19.5 (29.59)	p<0.001[a]	
≥50% of time with QMG-3 improvement up to week 24, mean (SD)	34 (44.2%)	13 (17.1%)	p<0.001[b]	4.17 (1.93, 9.00)
≥75% of time with QMG-3 improvement up to week 24, mean (SD)	28 (36.4%)	8 (10.5%)	p<0.001[b]	5.15 (2.13, 12.44)

CI=Confidence interval; QMG=Quantitative myasthenia gravis; RCT=Randomized clinical trials; OR: Odds ratio; SD: Standard deviation; SOC=Standard of care.
[a]p-value from 2-sample t-test.
[b]Based on Cochran-Mantel-Haenszel test adjusting for autoantibody status ("anti-AChR positive or anti-MuSK positive" or "anti-AChR negative and anti-MuSK negative") and region (East Asia, United States or Rest of World).

Conclusions

- This post hoc analysis demonstrated that nipocalimab+SOC provides sustained disease control which was achieved in most patients within first 8 weeks as assessed by QMG.
- Nipocalimab+SOC demonstrated statistically significant and clinically meaningful improvement in QMG total score from baseline in patients with gMG.

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