Safety and Effectiveness of Nipocalimab in Adolescent Participants in the Open Label Phase 2/3 vibrance-mg Clinical Study

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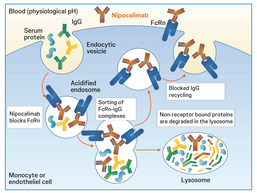
Background

Nipocalimab is an investigational monoclonal antibody, designed to bind with high affinity and selectively block FcRn to reduce levels of circulating immunoglobulin G (IgG) antibodies, while preserving immune function without causing broad immunosuppression[1,2]

Nipocalimab may ameliorate generalized myasthenia gravis (gMG) disease manifestations by selectively targeting FcRn IgG recycling and lowering IgG, including pathogenic autoantibodies in gMG[3]



FcRn=Anti-neonatal Fc receptor; gMG=Generalized myasthenia gravis; IgG=Immunoglobulin.

Objectives

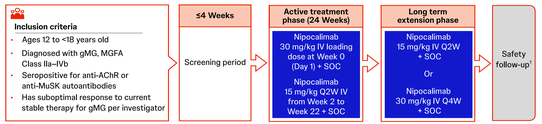
The objectives of the vibrance-mg study are to evaluate the pharmacodynamics (IgG), pharmacokinetics, efficacy, and safety of nipocalimab in pediatric patients with gMG who have an insufficient clinical response to ongoing, stable standard-of-care therapy

- Here, we have summarized the study results in adolescents (aged 12 to <18 years) through a clinical cutoff of December 15, 2023

Methods

- The **vibrance mg** (NCT05265273): A global, multi-center, open label phase 2/3 study of Nipocalimab + SOC in children and adolescents with gMG (**Figure 1**)

Figure 1. Study Design



[1]Participants who withdraw or discontinue after receiving any amount of study intervention will be required to complete a safety follow-up visit 8 weeks after their last dose. AChR=Acetylcholine receptor; gMG=Generalized myasthenia gravis; IV=Intravenous; MGFA=Myasthenia Gravis Foundation of America; MuSK=Muscle-Specific Kinase; Q2W=Every 2 weeks; Q4W=Every 4 weeks, SOC=Standard-of-care

- The vibrance-mg study is on-going, with enrollment open to patients from 2 to <18 years of age
- Results are presented through the active treatment phase (study Day 1 through Week 24)

Study Endpoints

Primary Endpoint

- The effect of nipocalimab on total serum Immunoglobulin G
- Safety and tolerability

Secondary Endpoints

- The effect of nipocalimab on:
  - Myasthenia Gravis Activities of Daily Living (MG-ADL) Score
  - Quantitative Myasthenia Gravis (QMG) Score

Results are presented from an analysis of adolescent participants in the ongoing study

Results

Table 1. Demographics and baseline characteristics

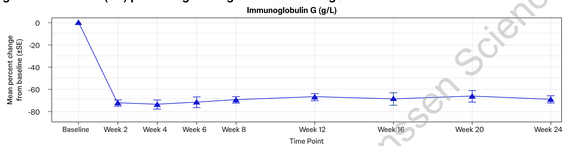
Adolescent participants N=7	
Age, years	
Mean (SD)	14.1 (1.86)
Range	(12; 16)
Sex, n (%)	
Female	6 (85.7)
Male	1 (14.3)
Race, n (%)	
American Indian/Alaska Native	0
Asian	4 (57.1)
Black or African American	1 (14.3)
White	0
Unknown	2 (28.6)
Ethnicity, n (%)	
Hispanic or Latino	1 (14.3)
Not Hispanic or Latino	5 (71.4)
Unknown	1 (14.3)
Weight, kg	
Mean (SD)	58.19 (26.741)
Range	(30.9; 95.5)
Autoantibody type, n (%)	
AChR	7 (100)
Baseline MG-ADL total score	
Mean (SD)	4.29 (2.430)
Range	(2.5; 9.5)
Baseline QMG total score	
Mean (SD)	12.50 (3.708)
Range	(6.5; 17.0)
Duration of MG, years	
Mean (SD)	4.44 (3.645)
Range	(0.8; 11.5)
Age at onset of MG, years	
Mean (SD)	9.70 (4.306)
Range	(0.5; 13.4)
Baseline MGFA Clinical Classification, n (%)	
IIa	4 (57.1)
IIb	0
IIIa	2 (28.6)
IIIb	1 (14.3)
IVa	0
IVb	0
Participants with ≥1 concomitant MG medications	7 (100.0)
Immunosuppressants	6 (85.7)
Corticosteroids for systemic use	5 (71.4)
Other nervous system drugs[1]	3 (42.9)

[1]Includes AChEIs of pyridostigmine and pyridostigmine bromide. MG-ADL=Myasthenia Gravis Activities of Daily Living; QMG=Quantitative Myasthenia Gravis; MGFA=Myasthenia Gravis Foundation of America; SD=Standard deviation.

Primary Efficacy Endpoint (Total serum IgG)

- The analysis for primary endpoint was conducted in the 5 participants who received ≥1 dose of nipocalimab and had ≥1 post-infusion sample evaluable for serum IgG
- The mean percentage change in total serum IgG from baseline to Week 24 of the active treatment phase was statistically significant at −68.98% (SE, 7.561) (95% CI: −78.4; −59.6)
- The median pre-dose total serum IgG reduction from baseline to Week 2 was −72.00% and to Week 24 was −69.87% (**Figure 2**)

Figure 2. The mean (SE) percentage change in total serum IgG from baseline to Week 24

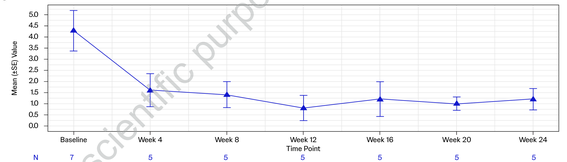


CI=Confidence interval; IgG=Immunoglobulin; SE=Standard error.

Secondary Efficacy Endpoint: Myasthenia Gravis Activities of Daily Living (MG-ADL)

- Clinically meaningful reduction in MG-ADL score was observed at Week 4 and maintained through Week 24 (**Figure 3**)
- The mean (SE) MG-ADL score was 4.29 (0.918) at baseline and improved by –2.40 (0.187) at Week 24
- 4/5[1] (80%) participants showed minimal symptom expression (MG-ADL of 0 or 1) at Week 24

Figure 3. Mean MG-ADL total score over time

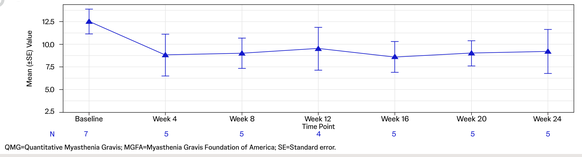


[1]5 of 7 patients completed 24 weeks of active treatment phase at data cutoff. MG-ADL=Myasthenia Gravis Activities of Daily Living; MGFA=Myasthenia Gravis Foundation of America; SE=Standard error.

Secondary Efficacy Endpoints: Quantitative Myasthenia Gravis (QMG)

- Clinically meaningful reduction in QMG score was observed at Week 4 and maintined through Week 24
- The mean (SE) QMG score was 12.50 (3.708) at Baseline and improved by –3.80 (2.683) at Week 24

Figure 4. Mean QMG total score over time



QMG=Quantitative Myasthenia Gravis; MGFA=Myasthenia Gravis Foundation of America; SE=Standard error.

Primary Safety endpoint

- Nipocalimab was generally well-tolerated
- There were no serious adverse events (SAEs) or adverse events (AEs) leading to discontinuation, or AEs of special interest through Week 24 in the adolescent participants in the vibrance-mg study

Table 2. Safety overview

Analysis set: Safety N=7	Adolescent participants (aged 12 to <18 years) n (%)
Average duration of follow-up (Weeks)	18.37
Average exposure (number of administrations)	8.86
Participants with ≥1 AEs	5 (71.4)
Related AEs	2 (28.6)
Participants with ≥1 AE leading to death	0
Participants with ≥1 SAE	0
AEs leading to temporary discontinuation of study treatment	0
AEs leading to permanent discontinuation of study treatment	0
AEs leading to termination of study participation	0
COVID-19 associated AE	1 (14.3)
COVID-19 associated SAE	0
Participants with ≥1 AEs	5 (71.4)
Nasopharyngitis	3 (42.9)
COVID 19	1 (14.3)
Bacterial vaginosis	1 (14.3)
Upper respiratory tract infection	1 (14.3)
Headache	1 (14.3)
Migraine	1 (14.3)
Somnolence	1 (14.3)
Abdominal pain upper	1 (14.3)
Diarrhea	1 (14.3)
Glossitis	1 (14.3)
Anemia	1 (14.3)
Face edema	1 (14.3)
Blood cholesterol increased	1 (14.3)
Hypercholesterolemia	1 (14.3)
Muscle spasms	1 (14.3)
Bacterial vaginosis	1 (14.3)

AE=Adverse event; COVID=Coronavirus disease; SAEs=Serious AEs, gMG=Generalized myasthenia gravis; MG-ADL=Myasthenia Gravis Activities of Daily Living; QMG=Quantitative Myasthenia Gravis; Q2W=Every 2 weeks.

Conclusions

Primary endpoint (efficacy): Nipocalimab (30 mg/kg loading dose followed by 15 mg/kg Q2W) demonstrated a statistically significant reduction in total IgG at Week 24 in adolescents with gMG

Secondary endpoints (efficacy): Clinically meaningful reduction of MG-ADL and QMG scores were observed at Week 4 and maintained through Week 24

Primary endpoint (safety): Nipocalimab was well tolerated in adolescents with gMG in the vibrance-mg study

These are the first clinical trial data reported with an FcRn blocker in adolescents

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Autoantibody: MG