

Safety Profile of Nipocalimab, a New Neonatal Fragment Crystallizable Receptor Blocker in the Phase 3 Vivacity Study

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Background

- Myasthenia gravis (MG) is a rare autoimmune disorder causing muscle weakness and reduced quality of life.
 - Limitations of current therapies highlight the need for safe, more effective treatment options for sustained disease control.^{1,2}
- Nipocalimab, a neonatal fragment crystallizable receptor (FcRn) blocker has demonstrated reduction in levels of circulating immunoglobulin G (IgG) and anti-acetylcholine receptor (anti-AChR) antibodies while preserving immune function.³
- Nipocalimab, added to standard-of-care (SOC), significantly reduced IgG levels from baseline in a phase 1 study³ and demonstrated meaningful clinical improvements with a tolerable safety profile in the phase 2 Vivacity-MG study⁴ in patients with generalized MG.
- The safety profile of nipocalimab + SOC versus placebo + SOC was evaluated in the phase 3 Vivacity-MG3, a randomized, double-blind (DB), placebo-controlled study.⁵

Objective

- To report a comprehensive safety profile of nipocalimab, a novel FcRn blocker, from the phase 3 Vivacity-MG3 study and open-label extension (OLE) phase in adult patients with generalized MG.

Methods

Vivacity-MG3 study

- Vivacity-MG3 (NCT04951622) is a multicenter, randomized, DB, placebo-controlled phase 3 study with an ongoing OLE phase, designed to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of nipocalimab in adults with generalized MG.
- Patients who completed or terminated treatment in the DB phase were eligible to enter the ongoing OLE phase.

Analysis

- Safety (DB) analysis set: participants who received at least 1 dose (partial or complete) of any study intervention in the DB phase.
- Safety (OLE) analysis set: participants who received at least 1 dose (partial or complete) of nipocalimab in the OLE phase.
- For each AE, the number and percentage of patients with ≥1 occurrence of the given event were summarized by intervention group.
- 10-year coronary risk was estimated using the SCORE2 algorithm from the European Society of Cardiology (key inputs were: systolic blood pressure, high-density lipoprotein [HDL], and low-density lipoprotein [LDL]).
- As the duration of DB and OLE phases were different, exposure adjusted incidence rates of AEs are presented.

Safety assessments

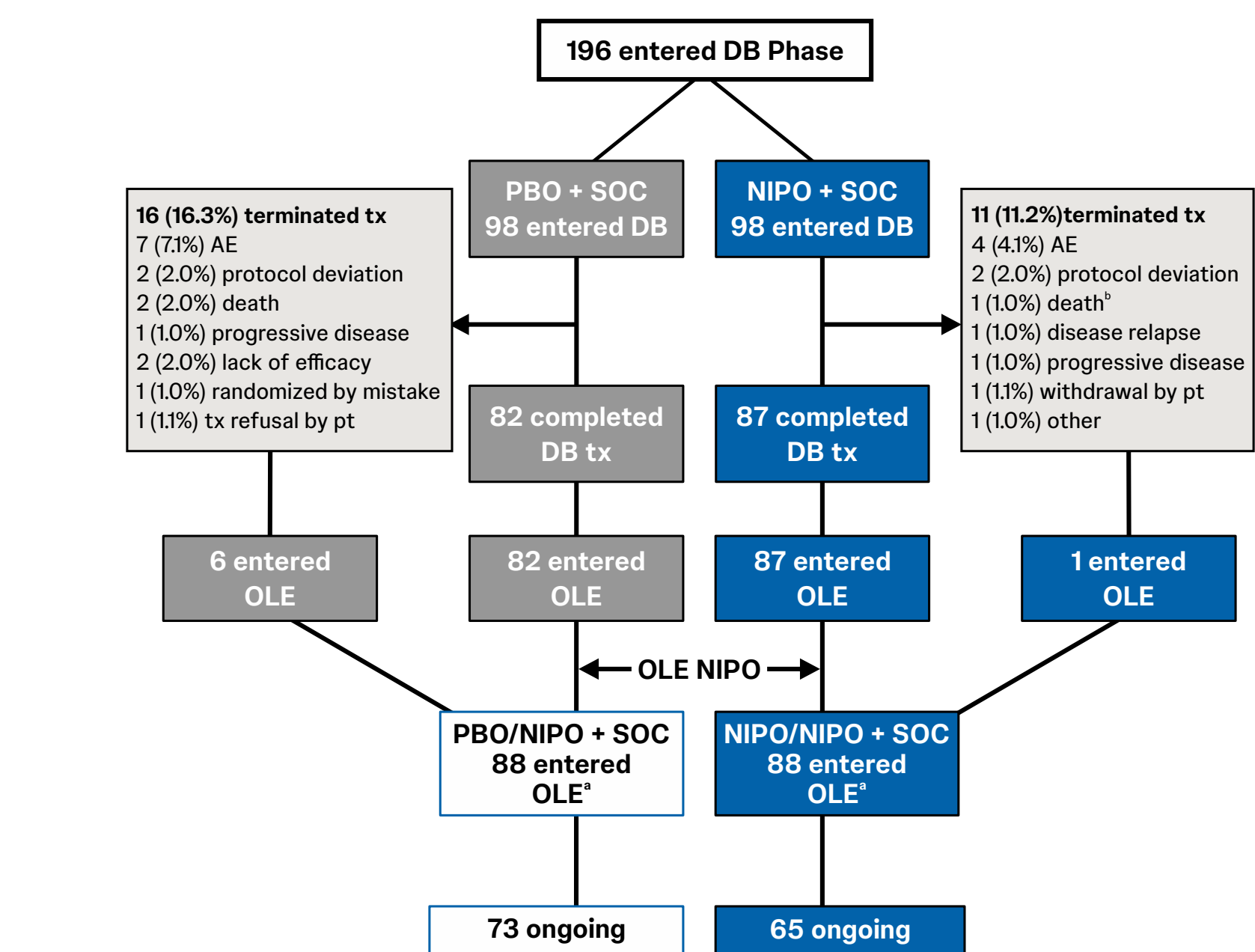
- Treatment-emergent adverse events (TEAEs), TEAEs of interest, serious AEs (SAEs), and AEs leading to treatment discontinuation were summarized for DB phase and OLE phase.
- Additionally, changes and clinically meaningful changes in laboratory values, vital signs, and cardiovascular (CV) risk (Systematic Coronary Risk Evaluation 2 [SCORE2]) were reported.
- TEAEs were coded in accordance with MedDRA, Version 26.1.

Results

DB and OLE phase patient disposition

- Total of 196 (nipocalimab + SOC: 98; placebo + SOC: 98) entered the DB phase of which, 82 in placebo + SOC and 87 in nipocalimab + SOC group completed the DB phase (Figure 1).
- In OLE phase (Figure 1):
 - 88 patients from DB placebo + SOC group (82 completed + 6 from those who discontinued DB) entered OLE phase.
 - 88 patients from DB nipocalimab + SOC group (87 completed + 1 from those who discontinued DB) entered OLE phase.

Figure 1: Patient disposition (DB and OLE safety analysis set)



*Per protocol, participants requiring rescue treatment during the DB phase completed the DB end-of-phase visit and were eligible to enter the OLE per investigator's discretion. Eight patients discontinued the double-blind phase prior to Week 24, but entered the open-label phase: 5 PBO/NIPO and 1 NIPO/NIPO. *Cardiac failure (unrelated to treatment) occurred 2 days after the last dose of study treatment on study day 422. AE=Adverse event, DB=Double-blind, NIPO=Nipocalimab, OLE=Open-label extension, PBO=Placebo, pt=Patient, SOC=Standard-of-care, tx=Treatment

- DB baseline characteristics of patients entering the OLE are similar to the overall DB population (Table 1).

Table 1: Double-blind baseline demographic and clinical characteristics

Characteristics	DB phase		OLE phase	
	PBO + SOC	NIPO + SOC	PBO/NIPO + SOC	NIPO/NIPO + SOC
Analysis set: Safety (DB and OLE)*	98	98	88	88
Age, mean (range), years	52.7 (20; 81)	52.9 (20; 81)	52.2 (20; 81)	52.1 (20; 81)
Female, n (%)	56 (57.1%)	66 (67.3%)	52 (59.1%)	59 (67.0%)
Race, n (%)				
American Indian or Alaska native	0	1 (1.0%)	0	1 (1.0%)
Asian	29 (29.6%)	28 (28.6%)	25 (28.4%)	25 (28.4%)
Black/African American	1 (1.0%)	1 (1.0%)	1 (1.0%)	1 (1.0%)
White	65 (66.3%)	66 (67.3%)	59 (67.0%)	59 (67.0%)
Not reported	3 (3.1%)	2 (2.0%)	3 (3.4%)	2 (2.3%)
BMI, mean (SD), kg/m ²	28.8 (6.7)	27.8 (5.9)	28.9 (6.9)	27.7 (5.9)
Baseline MG-ADL total score, mean (SD)	9.3 (2.0)	9.5 (2.7)	9.3 (2.0)	9.5 (2.7)
Baseline QMG total score, mean (SD)	15.6 (4.7)	15.0 (4.8)	15.5 (4.7)*	15.1 (5.0)
Autoantibody status at screening				
Seronegative, n (%)	22 (22.4%)	21 (21.4%)	22 (25.0%)	17 (19.3%)
Seropositive, n (%)	76 (77.6%)	77 (78.6%)	66 (75.0%)	71 (80.7%)
Anti-AChR*	71 (72.4%)	63 (64.3%)	61 (69.3%)	59 (67.0%)
Anti-MuSK*	4 (4.1%)	12 (12.2%)	4 (4.5%)	10 (11.4%)
Anti-LRP4*	1 (1.0%)	2 (2.0%)	1 (1.1%)	2 (2.3%)

*%s for each parameter ref: nt=non-missing values, *n=94. AChR=Acetylcholine receptor antibody-positive, BMI=Body mass index, DB=Double-blind, LRP4=Low density lipoprotein receptor-related protein 4-positive, MG-ADL=Myasthenia Gravis-Activities of Daily Living, MuSK=Muscle-specific, inase antibody-positive, NIPO=Nipocalimab, OLE=Open-label extension, PBO=Placebo, QMG=Quantitative Myasthenia Gravis, SD=Standard deviation, SOC=Standard-of-care.

PRESENTED AT: American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) Annual Meeting, San Francisco, CA, USA, October 29–November 1, 2025. **REFERENCES:** 1. Gilus NE, et al. Myasthenia gravis. *Nat Rev Dis Primers*. 2019;5(30). 2. Dresser L, et al. *J Clin Med*. 2021;10:2235. 3. Ling LE, et al. *Clin Pharmacol Ther*. 2019;105(4):1031–1039. 4. Antozzi C, et al. *Neurology*. 2024;102(2):e207937. 5. Antozzi C, et al. *Lancet Neurol*. 2025;24(2):105–116. **ACKNOWLEDGMENTS:** The authors thank the participants and investigators for their participation in the study. Kelpena Talsky, PhD (SRO Medical Writing Pvt. Ltd.) and Dorey Muz, PhD (Johnson & Johnson) provided editorial assistance. Layout design and reformatting for this abstract presentation was provided by Anna Kevle (SRO Medical Writing Pvt. Ltd., India), with funding from Johnson & Johnson. **DISCLOSURES:** Hans Katzberg: Consultant to Octapharma, UCSF, Allergan, CSL Behring, Alexion, Amgen, X, Bion, Roche, Takeda, Dainippon, Merz. He has been on the DSMB for Alexion, UCSF, Abcurio, Octapharma, and Amgen and has received clinical trial support from Takeda, CSL Behring, Roche and Amgen. Ibrahim Turkoz, Kavita Gandhi, and Sindhu Ramchandren are employees, contractors, or consultants for Johnson & Johnson and may hold stock or stock options in Johnson & Johnson. Maria Ait-Tihyaty: was an employee of Johnson & Johnson at the time of the study and may hold stock or stock options in Johnson & Johnson. Previously presented at the American Academy of Neurology (AAN) Annual Meeting, San Diego, IL, USA, April 5–9, 2025.

Overall safety profile

- For 196 patients in the DB phase (nipocalimab + SOC: 98; placebo + SOC: 98), median follow-up was 24 weeks.
- For 176 patients in the OLE phase (NIPO/NIPO + SOC: 88; PBO/NIPO + SOC: 88), median follow-up was 72 weeks.
- In the DB phase, the proportion of patients experiencing ≥1 AEs was similar between the nipocalimab + SOC (83.7%) and placebo + SOC (83.7 %) groups.
- In the OLE phase, the proportion of patients experiencing ≥1 AEs was similar between (NIPO/NIPO + SOC (89.8%) and PBO/NIPO + SOC (90.9%) groups, Table 2).
- 7 deaths (DB phase: n=3; OLE phase: n=4) were reported:
 - None of the deaths in DB phase were related to study treatment (nipocalimab + SOC: n=1; placebo + SOC: n=2).
 - Of the 4 deaths in the OLE phase:
 - 3 deaths were not considered treatment related and occurred in older patients who had CV comorbidities.
 - 1 death was considered treatment-related (Epstein-Barr virus-associated hemophagocytic lymphohistiocytosis in a patient receiving concomitant tacrolimus; death occurred on study day 224, and 18 days after the last dose of study treatment).

Table 2: Overall patient proportion summary of AEs (DB and OLE safety analysis set)

Safety analysis set	DB phase		OLE phase	
	PBO + SOC (n=98), n (%)	NIPO + SOC (n=98), n (%)	PBO/NIPO + SOC (n=88), n (%)	NIPO/NIPO + SOC (n=88), n (%)
AEs	82 (83.7)	82 (83.7)	80 (90.9)	79 (89.8)
Related AEs*	27 (27.6)	28 (28.6)	35 (39.8)	37 (42.0)
SAEs*	14 (14.3)	9 (9.2)	21 (23.9)	25 (28.4)
Related SAEs	1 (1.0)	1 (1.0)	4 (4.5)	2 (2.3)
AEs leading to permanent discontinuation of study treatment ^{a,d}	7 (7.1)	5 (5.1)	8 (9.1)	5 (5.7)

*An AE is assessed by the investigator as related to study agent. *Related SAEs in OLE phase were Epstein-Barr virus infection (only in NIPO/NIPO group), Pneumonia (in both PBO/NIPO and NIPO/NIPO group), Cellulitis, Hemophagocytic lymphohistiocytosis, Weight increase were present in PBO/NIPO group only. In DB phase SAEs were Herpes zoster oticus in NIPO/NIPO group, and Appendicitis, was in PBO/NIPO group. *AEs leading to permanent discontinuation of study treatment in OLE phase in PBO/NIPO group were Myasthenia gravis, Intracranial mass, Myasthenia gravis crisis, Oedema peripheral, Hemophagocytic lymphohistiocytosis, Cellulitis, Urinary tract infection, and Acute respiratory failure. AEs leading to permanent discontinuation of study treatment in OLE phase in NIPO/NIPO group were Myasthenia gravis, Granulomatous lymphadenitis, Cardiac failure, and Oedema peripheral. In DB phase in PBO/NIPO group were Myasthenia gravis, Myasthenia gravis crisis, Cerebral haemorrhage, Cardiac arrest, Myocardial infarction, Liver disorder, Appendicitis, COVID-19, Sepsis, and Femur fracture. In DB phase, NIPO/NIPO group AEs leading to permanent discontinuation of study treatment were Myasthenia gravis, Myasthenia gravis crisis, Thrombocytopenia, Respiratory failure, and, Urticaria. *AEs leading to permanent discontinuation of study treatment is based on AE action taken of drug withdrawal. Treatment discontinuation for an AE with onset in DB occurred in DB. AE=Adverse event, DB=Double-blind, MG=Myasthenia Gravis, OLE=Open-label extension, NIPO=Nipocalimab, PBO=Placebo, SAE=Serious adverse events, SOC=Standard-of-care.

AEs in either arm in DB or OLE (events per-patient per-year)

- There were no unexpected AEs during the DB or OLE phase.
- Rates of AEs were generally similar in the DB PBO and OLE nipocalimab combined group.

Table 3: Safety and tolerability (exposure adjusted incidence rate)

Safety analysis set	DB phase			OLE phase		
	PBO + SOC (n=98)	NIPO + SOC (n=98)	NIPO combined (n=176)	PBO + SOC (n=98)	NIPO + SOC (n=98)	NIPO combined (n=176)
Average follow-up duration, wks	23	23	70.53			
P-Y*	43.3	43.2	237.9			
Events/ P-Y*	Events, n	Pts, n*	Events/ P-Y*	Events, n	Pts, n*	Events/ P-Y*
All AEs	7.54	326	82	8.73	377	82
Serious AEs	0.60	26	14	0.42	18	9
Fatal AEs	0.05	2	2	0.02	1	1
Tx discontinuation due to AE*	0.25	11	7	0.16	7	5
Infection and infestations	1.14	61	42	1.64	71	42
Infusion-related reactions*	0.62	27	11	0.37	16	10
Adjudicated MACE, fatal	0.05	2	2	0	0	0
Adjudicated MACE, not fatal	0.02	1	1	0	0	0

*Participant-years of observation (P-Y) is calculated as the total duration of follow-up in days/365.25. *Patients with ≥1 AE are shown. *Permanent discontinuation of treatment. Treatment discontinuation for an AE with onset in DB (or OLE) occurred in DB (or OLE). *Indicated as infusion reaction by investigator on eCRF and relationship to study intervention="Related". AE=Adverse event, DB=Double-blind, eCRF=Electronic case report form, MACE=Major adverse cardiovascular event, NIPO=Nipocalimab, OLE=Open-label extension, PBO=Placebo, Pt=Patient, P-Y=Participant-year, SOC=Standard-of-care, Tx=Treatment, Wks=Weeks

AEs with a rate of at least 1 patient in 10 per year (exposure adjusted incidence rate)

- Exposure adjusted incidence rates showed that the overall incidence of AE rates were generally lower in the OLE phase compared to the DB phase.

Table 4: AEs by preferred term in at least 0.1 events per P-Y of pts in either arm in DB or OLE (exposure adjusted incidence rate)

Safety analysis set	DB phase			OLE phase		
	PBO + SOC (n=98)	NIPO + SOC (n=98)	NIPO combined (n=176)	PBO + SOC (n=98)	NIPO + SOC (n=98)	NIPO combined (n=176)
P-Y*	43.3	43.2	237.9			
Events/ P-Y*	Events, n	Pts, n*	Events/ P-Y*	Events, n	Pts, n*	Events/ P-Y*
Upper respiratory tract infection	0.18	8	8	0.14	6	6
Nasopharyngitis	0.25	11	10	0.21	9	9
COVID-19	0.25	11	10	0.3	13	13
Urinary tract infection	0.05	2	2	0.12	5	5
Back pain	0.12	5	5	0.21	9	8
Muscle spasms	0.07	3	3	0.3	13	12
Pain in extremity	0.09	4	3	0.12	5	5
Arthralgia	0.16	7	5	0.05	2	2
Myasthenia gravis	0.37	16	12	0.35	15	12
Headache	0.74	32	17	0.51	22	14
Dizziness	0.02	1	1	0.14	6	5
Peripheral edema	0	0	0	0.3	13	11
Pyrexia	0.02	1	1	0.19	8	7
Diarrhea	0.07	3	3	0.16	7	7
Nausea	0.07	3	2	0.14	6	5
Cough	0.09	4	3	0.19	8	7
Rash	0.12	5	3	0.02	1	1
Anaemia	0.12	5	4	0.09	4	4
Insomnia	0.05	2	2	0.12	5	5

Note: NIPO combined group represent all the patient from PBO/NIPO + SOC (n=88) and NIPO/NIPO + SOC (n=88) who entered OLE phase. *Participant-Years of Observation (P-Y) is calculated as the total duration of follow-up in days/365.25. *Patients with ≥1 AE are shown; Event Rate=Number of Events/P-Y. Adverse Events listed where system organ class event rate is ≥0.1 or preferred term event rate is ≥0.1 in either treatment group. AE=Adverse event, DB=Double-blind, NIPO=Nipocalimab, OLE=Open-label extension, PBO=Placebo, Pt=Participant, P-Y=Participant-year, SOC=Standard-of-care.

Specific AEs: Muscle spasm and peripheral edema

- A total of 12 (12.2%) in the nipocalimab + SOC group in the DB phase and 12 (6.8%) in the nipocalimab combined group had mild to moderate muscle spasm; 11 (11.2%) in the nipocalimab + SOC group in the DB phase and 9 (5.1%) in the nipocalimab combined group had mild to moderate peripheral edema.
- There were no patients who experienced severe muscle spasm or peripheral edema during the DB or OLE phases.

Table 5: Number of patients with treatment-emergent muscle spasms or peripheral edema adverse events

Safety analysis set	DB phase		OLE phase	
	PBO + SOC (n=98)	NIPO + SOC (n=98)	NIPO combined (n=176)	
Preferred Term* Severity*				
Muscle Spasms, n (%)	3 (3.1)	12 (12.2)	12 (6.8)	
Mild	2 (2.0)	9 (9.2)	11 (6.3)	
Moderate	1 (1.0)	3 (3.1)	2 (1.1)	
Peripheral edema, n (%)	0	11 (11.2)	9 (5.1)	
Mild	0	9 (9.2)	8 (4.5)	
Moderate	0	2 (2.0)	2 (1.1)	

Note: NIPO combined group represent all the patient from PBO/NIPO + SOC (n=88) and NIPO/NIPO + SOC (n=88) who entered OLE phase. *Patients are counted only once for any given event, regardless of the number of times they actually experienced the event. *Patients may be counted more than once for any given event. DB=Double-blind, NIPO=Nipocalimab, OLE=Open-label extension, PBO=Placebo, SOC=Standard-of-care.

Key Takeaways

- Nipocalimab + SOC was generally well-tolerated during the DB and OLE phases.
 - The proportion of patients with AEs, SAE, discontinuation due to AEs, and fatal AEs was similar in nipocalimab + SOC and placebo + SOC.
 - Muscle spasm and peripheral edema were more common in the nipocalimab + SOC group, and events were mild to moderate in severity.
 - During the long-term OLE phase, there were no evidence of new safety risk with nipocalimab + SOC treatment.
 - Exposure adjusted rates of AEs and SAEs were generally lower in the OLE phase compared with the DB phase.

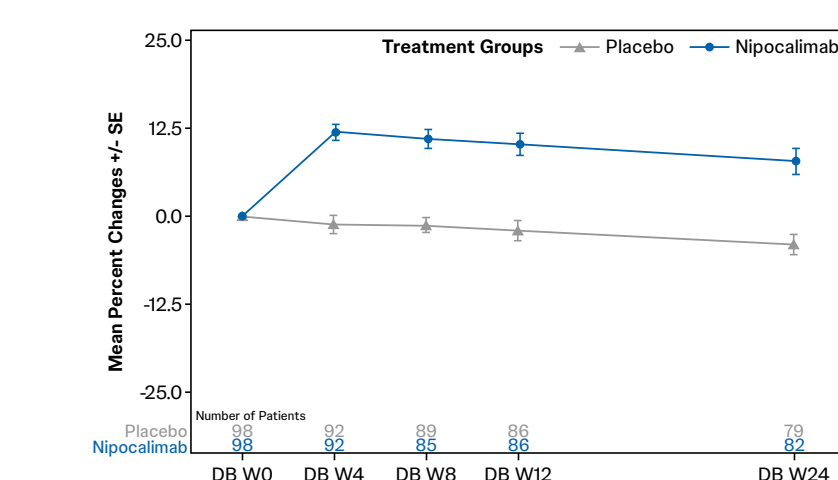
- In the nipocalimab + SOC group, mild increases were observed for total cholesterol, HDL, and LDL which decreased and plateaued by Week 24 of the DB phase.
 - Most patients remained within the same LDL risk category as their initial category.
 - A few patients who initiated lipid-lowering agents demonstrated a rapid reduction of LDL to baseline levels or lower.
 - No difference in rate of MACE or CV risk was observed across patients receiving nipocalimab + SOC and placebo + SOC.

Lipid levels (DB phase)

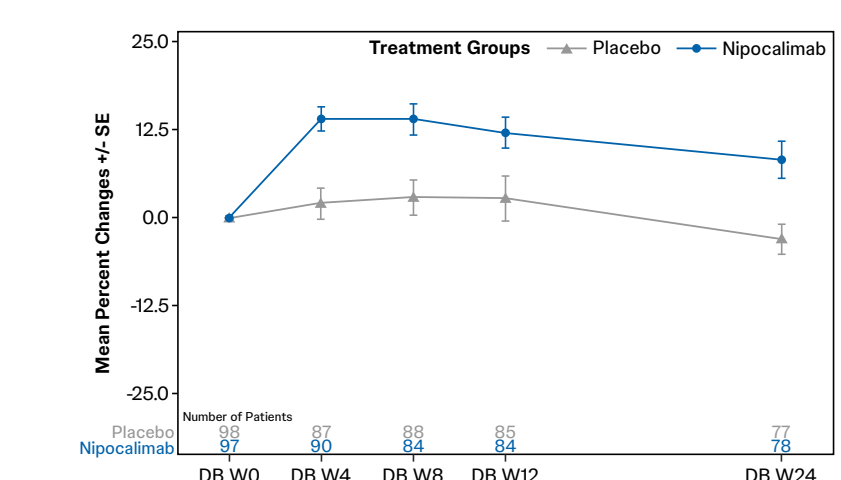
- Mild increases in total cholesterol, HDL, and LDL were observed in patients receiving nipocalimab, by DB Week 24, levels decreased and plateaued (Figure 2A-2C).
- The total Cholesterol/HDL ratio remained under 4 and was similar across treatment groups (Figure 2D).
- A total of 7 patients initiated lipid-lowering agents (usually statins) and a similar rapid reduction of LDL to baseline or lower levels was observed among these patients in both treatment arms (Figure 2E).
- Among placebo + SOC patients, those who had low LDL levels (<4.1 mmol/L) at baseline, 95% maintained low levels at Week 24. Similarly, among the nipocalimab + SOC patients with low LDL levels at baseline, 89% were able to sustain those levels at Week 24.
- Throughout the 24 week DB and OLE phases, there was no difference in rate of major adverse cardiovascular events (MACE) across participants receiving nipocalimab and placebo.

Figure 2: Lipids over time during the DB phase (safety analysis set)

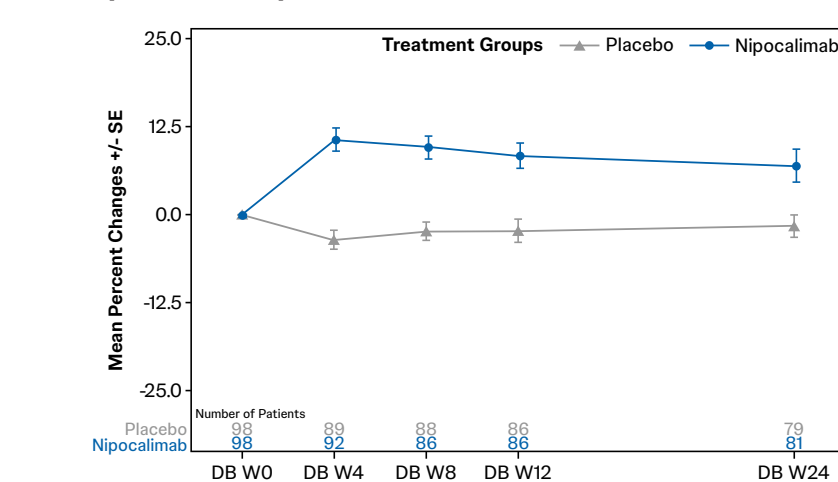
(A) Mean percent changes in CHOL (mmol/L) from DB baseline



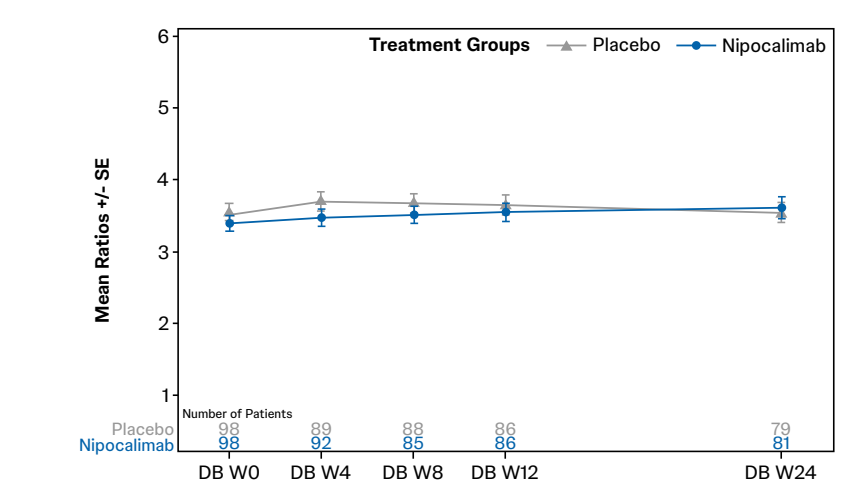
(B) Mean percent changes in LDL CHOL (mmol/L) from DB baseline



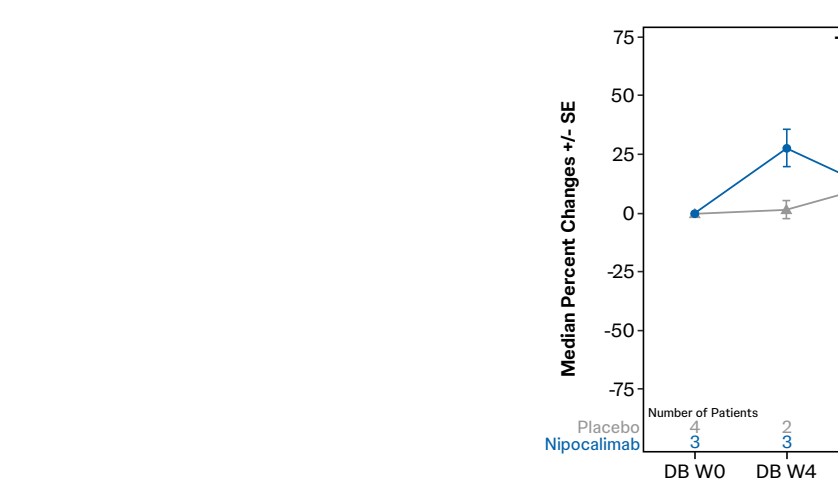
(C) Mean percent changes in HDL CHOL (mmol/L) from DB baseline



(D) Mean CHOL/HDL ratios from DB baseline



(E) Median percent changes in LDL CHOL (mmol/L) from DB baseline with lipid-lowering agents use started in DB phase



CHOL=Cholesterol, DB=Double-blind, HDL=High-density lipoprotein, LDL=Low-density lipoprotein, SE=Standard error, W=Week

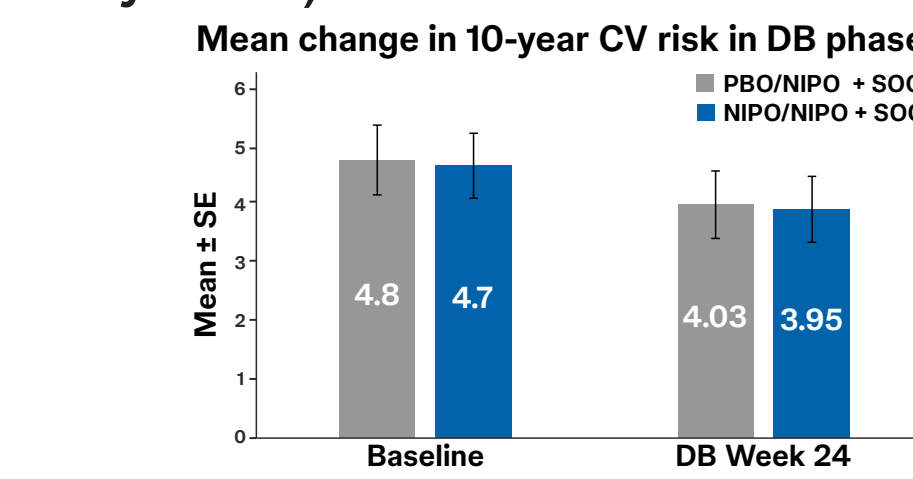
Mean change in systolic blood pressure

- At Week 24 of the DB phase, mean (SD) change from baseline (CFB) in systolic blood pressure was −41 (14.76) mmHg for the nipocalimab + SOC group and −2.2 (12.51) mmHg for the placebo + SOC group.
- At Week 24 of the OLE phase, the mean (SD) CFB in systolic blood pressure was: −3.6 (14.00) mmHg for NIPO/NIPO + SOC and −2.2 (12.86) mmHg for PBO/NIPO + SOC.
- At Week 48 of the OLE phase, the mean (SD) CFB in systolic blood pressure was: −3.5 (16.24) mmHg for NIPO/NIPO + SOC and −5.0 (12.64) mmHg for PBO/NIPO + SOC.

CV risk (SCORE2)

- During the DB phase, the 10-year cumulative CV risk estimate remained similar for nipocalimab + SOC group and for placebo + SOC group after 24 weeks of exposure (Figure 3).
- The trends observed on the calculated 10-year CV risk following 24 weeks of nipocalimab + SOC treatment during the DB phase were preserved for up to 72 weeks of follow-up through OLE phase.
 - mean (SE) 10-year CV risk change after 48 weeks of exposure (i.e., OLE Week 24): −0.21 (0.111).
 - mean (SE) 10-year CV risk change after 72 weeks of exposure (i.e., Week 48 of OLE): −0.28 (0.180).

Figure 3: CV risk* in DB phase (safety analysis set)



*As estimated using SCORE2. DB=Double-blind, CV=Cardiovascular, NIPO=Nipocalimab, PBO=Placebo, SCORE2=Systematic Coronary Risk Evaluation 2, SOC=Standard-of-care, SE=Standard error