

Long-Term Safety and Efficacy of Nipocalimab: Approximately 2 Years Follow-Up Results From the Open-Label Extension Phase of Vivacity-MG3 Study

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Key Takeaways

- Nipocalimab demonstrated clinically meaningful and sustained disease control over 120 weeks in a broad population of autoantibody-positive patients with gMG, while maintaining an acceptable safety profile

Conclusions

- In autoantibody-positive patients with gMG, long-term treatment with nipocalimab demonstrated sustained disease control through the 24-week phase 3 Vivacity-MG3 study and the 96-week OLE (120 weeks total)

- Dose reductions in corticosteroid usage were observed through the study with the majority of patients reaching 10 mg or less of prednisone equivalent per day

- There are no new safety concerns and event rates of adverse events were comparable in the DB and OLE phases

Introduction

- Nipocalimab is a fully human monoclonal antibody that binds to the neonatal Fc receptor (FcRn) with high affinity and specificity, reducing circulating levels of immunoglobulin G (IgG), including pathogenic IgG-based autoantibodies
- Nipocalimab is the first approved FcRn blocker for the treatment of generalized myasthenia gravis (gMG) in adult and adolescent (≥12 years of age) patients who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody-positive^{1,2}
- In Vivacity-MG3, a double-blind (DB), placebo-controlled, phase 3 study, nipocalimab treatment demonstrated symptom improvement sustained over 24 weeks³ and up to a further 60 weeks in the open label extension (OLE)⁴
- Results with additional follow-up through Week 96 of OLE of nipocalimab treatment (or Week 120 overall), with a data cut-off at August 24, 2024, are presented

Objective

- To assess the long-term safety and efficacy of nipocalimab in patients with gMG from the ongoing Vivacity-MG3 (NCT04951622) OLE phase through Week 96 (120 weeks overall)

Methods

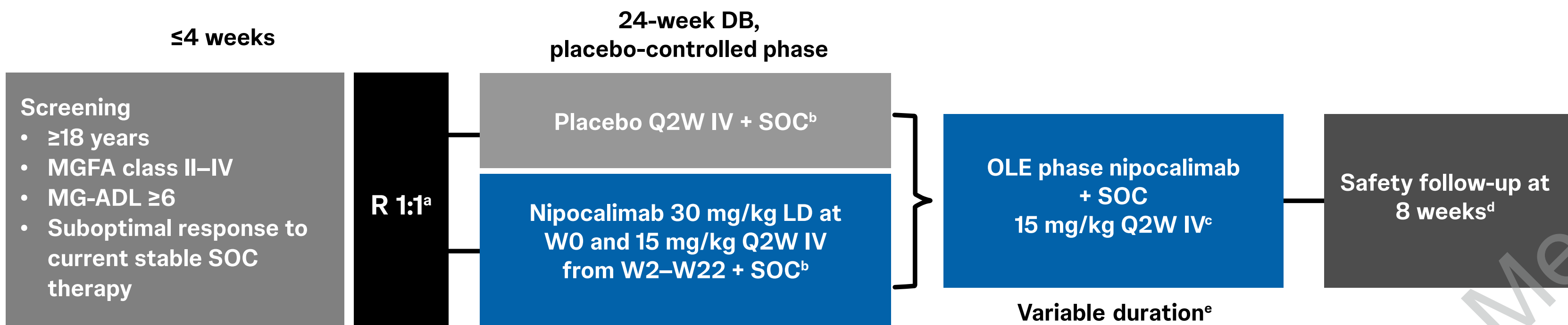
Population

- In Vivacity-MG3, adult patients with gMG (MGFA Class II-IV), inadequately controlled (Myasthenia Gravis-Activities of Daily Living [MG-ADL] ≥6) on standard-of-care (SOC) therapy, were randomized 1:1 to nipocalimab+SOC or placebo+SOC in the 24-week DB phase³
- Participants could continue to receive stable SOC treatment during the study
- Participants who completed the DB phase were eligible to enter the OLE phase with nipocalimab+SOC treatment

Assessments

- Efficacy and safety results are presented for seropositive (anti-AChR positive, anti-MuSK positive, and/or anti-low-density lipoprotein receptor-related protein 4 [anti-LRP4]) patients who received ≥1 dose of study treatment

Figure 1. Study Design³



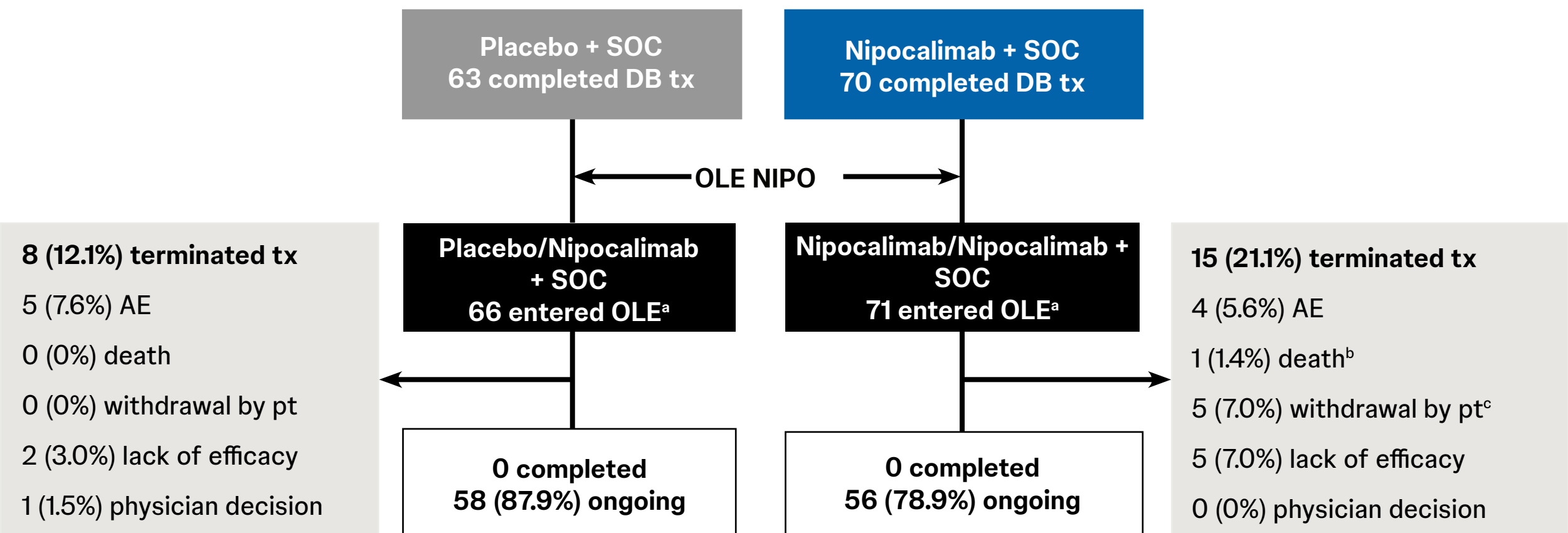
^aRandomization was stratified by autoantibody status (anti-AChR⁺ and/or anti-MuSK⁺, anti-AChR negative and anti-MuSK negative), Day 1 MG-ADL total score (≤9, >9), and region (East Asia, US, rest of world). ^bSOC includes acetylcholinesterase inhibitor, glucocorticosteroid, and/or immunosuppressant. ^cDue to the COVID-19 pandemic, some patients from the phase 2 study (NCT03725987) were unable to enter the phase 2 OLE study (NCT03896295). These patients could directly enter the phase 3 OLE and their data will be disclosed later. ^dPatients who withdraw or discontinue after receiving any amount of study intervention are required to complete a safety follow-up visit 8 weeks after their last dose. ^eIn the EU, the OLE phase will be up to 240 weeks. ^fAChR⁺=acetylcholine receptor positive, COVID-19=coronavirus disease 2019, EU=European Union, IV=intravenous, LD=loading dose, MG-ADL=Myasthenia Gravis-Activities of Daily Living, MGFA=Myasthenia Gravis Foundation of America, MuSK⁺=muscle-specific tyrosine kinase positive, OLE=open-label extension, Q2W=every 2 weeks, R=randomized, SOC=standard-of-care, US=United States, W=week.

Results

Patient disposition

- The OLE phase is ongoing
- ~83% of patients entering the OLE phase were still receiving treatment at data cut-off (August 2024)

Figure 2. Disposition (Seropositive population)



^aPer 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. Four patients discontinued the DB phase prior to Week 24, but entered the open-label phase: 3 PBO/NIPO and 1 NIP/OLE. ^bCardiac failure (unrelated to treatment) occurred 2 days after the last dose of study treatment on study day 422. Reasons for withdrawal: lack of improvement; participant was unsatisfied; travel to site was too tiring after surgery; personal reasons; and participant concern about poor vascular access. ^cAE=adverse event, DB=double-blind, LRP4=low-density lipoprotein receptor-related protein 4, NIP=nicotinic, OLE=open-label extension, PBO=placebo, pt=participant, SOC=standard-of-care, tx=treatment.

Baseline characteristics

- Baseline characteristics of patients entering the OLE are similar to that of the overall population at DB baseline

Table 1. Baseline demographics and characteristics (Seropositive population)

	DB ^a		Open-label	
	Placebo+SOC	Nipocalimab+SOC	Placebo/Nipocalimab+SOC	Nipocalimab/Nipocalimab+SOC
Analysis Set: Seropositive efficacy (DB and OLE) ^a	76	77	66	71
Age, mean (range), years	52.3 (20, 81)	52.5 (20, 81)	51.6 (20, 81)	51.1 (20, 81)
Female, n (%)	42 (55.3)	50 (64.9)	38 (57.6)	46 (64.8)
Race, n (%)				
American Indian or Alaska native	0	1 (1.3)	0	1 (1.4)
Asian	25 (32.9)	24 (31.2)	21 (31.8)	22 (31.0)
Black/African American	1 (1.3)	1 (1.3)	1 (1.5)	1 (1.4)
White	47 (61.8)	49 (63.6)	41 (62.1)	45 (63.4)
Not reported	3 (3.9)	2 (2.6)	3 (4.5)	2 (2.8)
BMI, mean (SD), kg/m ²	28.5 (5.73)	27.6 (5.39)	28.6 (5.99)	27.5 (5.30)
Baseline MG-ADL total score, mean (SD)	9.0 (1.97)	9.4 (2.73)	9.0 (1.98)	9.3 (2.75)
Baseline QMG total score, mean (SD)	15.7 (4.92)	15.1 (4.78) ^b	15.6 (4.90)	15.2 (4.85) ^c
Anti-AChR ⁺ /Anti-MuSK ⁺ /Anti-LRP4 ⁺ , n	71/4/1	63/12/2	61/4/1	59/10/2

^aAll randomized seropositive patients who received ≥1 dose of study intervention in the DB phase or all seropositive patients who received ≥1 dose of nipocalimab in the OLE phase. ^bn=73, ^cn=67. ^dAChR⁺=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 tyrosine kinase antibody-positive, OLE=open-label extension, QMG=Quantitative Myasthenia Gravis, SD=standard deviation, SOC=standard-of-care.

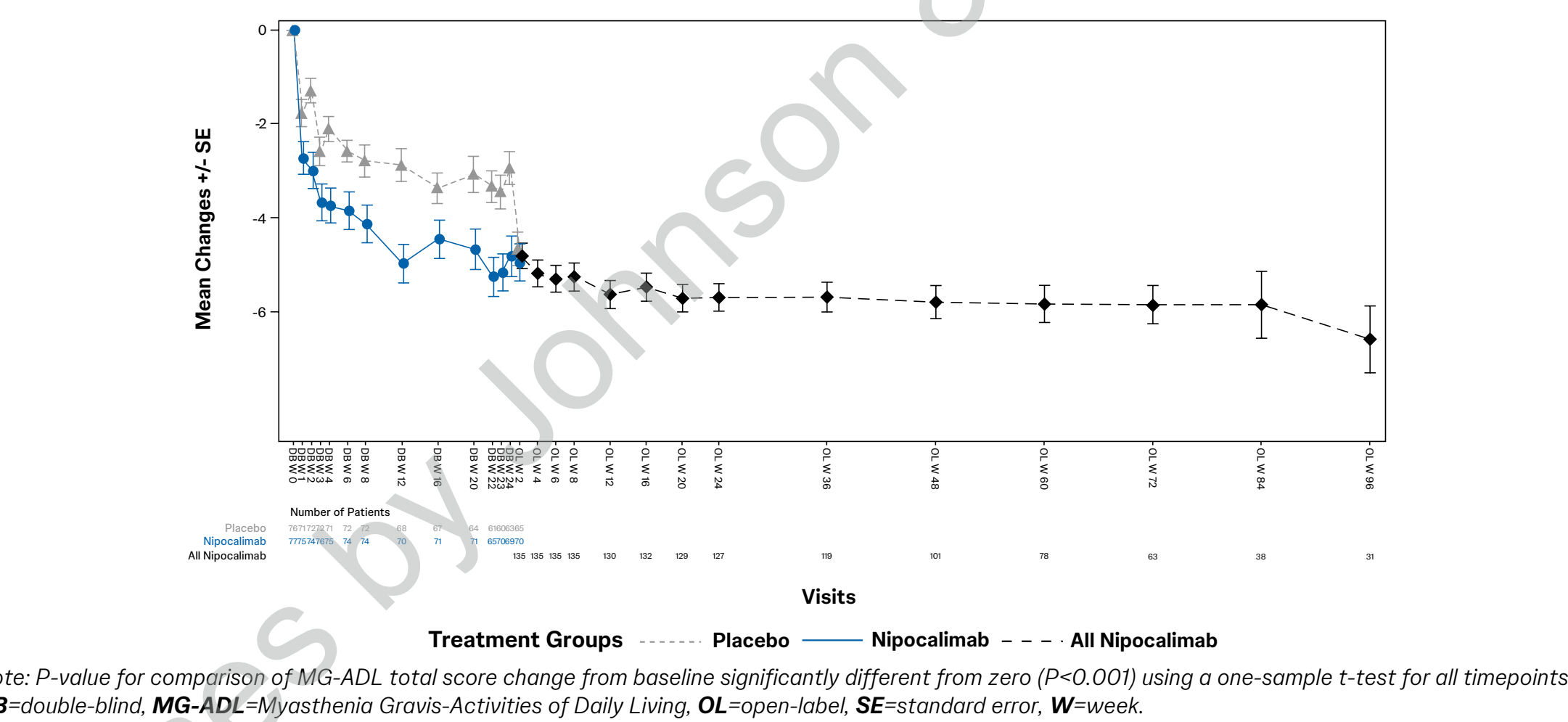
Treatment exposure

- 137 antibody-positive patients were treated with nipocalimab during OLE phase
- Total median (range) duration of treatment for
 - Placebo/Nipocalimab (n=66): 69.1 weeks (8–128)
 - Nipocalimab/Nipocalimab (n=71): 62.1 weeks (8–128)
- Treatment at data cut-off represents ~87–90 patient-years after completion of DB phase in both the Placebo/Nipocalimab and Nipocalimab/Nipocalimab groups
- Among patients in OLE phase, follow-up duration was over 96 weeks

Mean change in MG-ADL

- At OLE week 96, MG-ADL mean (standard error [SE]) change from DB baseline:
 - Placebo/Nipocalimab+SOC: −6.69 (0.85)
 - Nipocalimab/Nipocalimab+SOC: −6.47 (1.20)
 - All Nipocalimab+SOC: −6.58 (0.71)
- 52.6% (72/137) of all patients (Placebo/Nipocalimab and Nipocalimab/Nipocalimab) achieved minimal symptom expression (MSE)⁵ at any time during the OLE phase
- Among the patients who achieved MSE, MSE was sustained for ≥8 weeks in 68.1% (49/72), for ≥12 weeks in 63.9% (46/72), for ≥16 weeks in 51.4% (37/72), and for ≥20 weeks in 48.6% (35/72) during the OLE phase

Figure 3. Change from baseline in MG-ADL over time (Seropositive population)

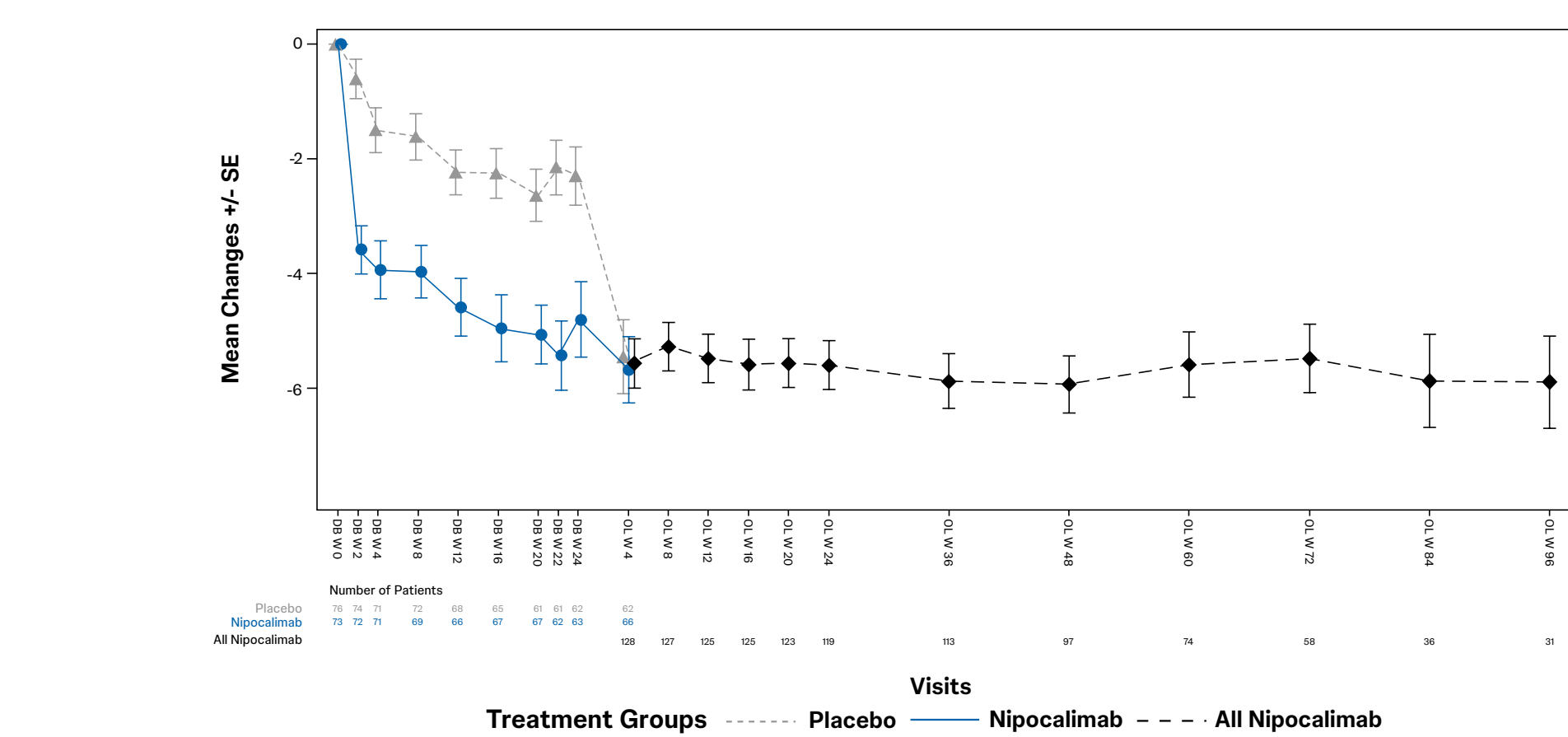


Note: P-value for comparison of MG-ADL total score change from baseline significantly different from zero (P<0.001) using a one-sample t-test for all timepoints. DB=double-blind, MG-ADL=Myasthenia Gravis-Activities of Daily Living, OLE=open-label, SE=standard error, W=week.

Mean change in QMG

- At OLE week 96, QMG mean (SE) change from DB baseline:
 - Placebo/Nipocalimab+SOC: −5.81 (1.03)
 - Nipocalimab/Nipocalimab+SOC: −5.97 (1.29)
 - All Nipocalimab+SOC: −5.89 (0.80)

Figure 4. Change from baseline in QMG over time (Seropositive population)

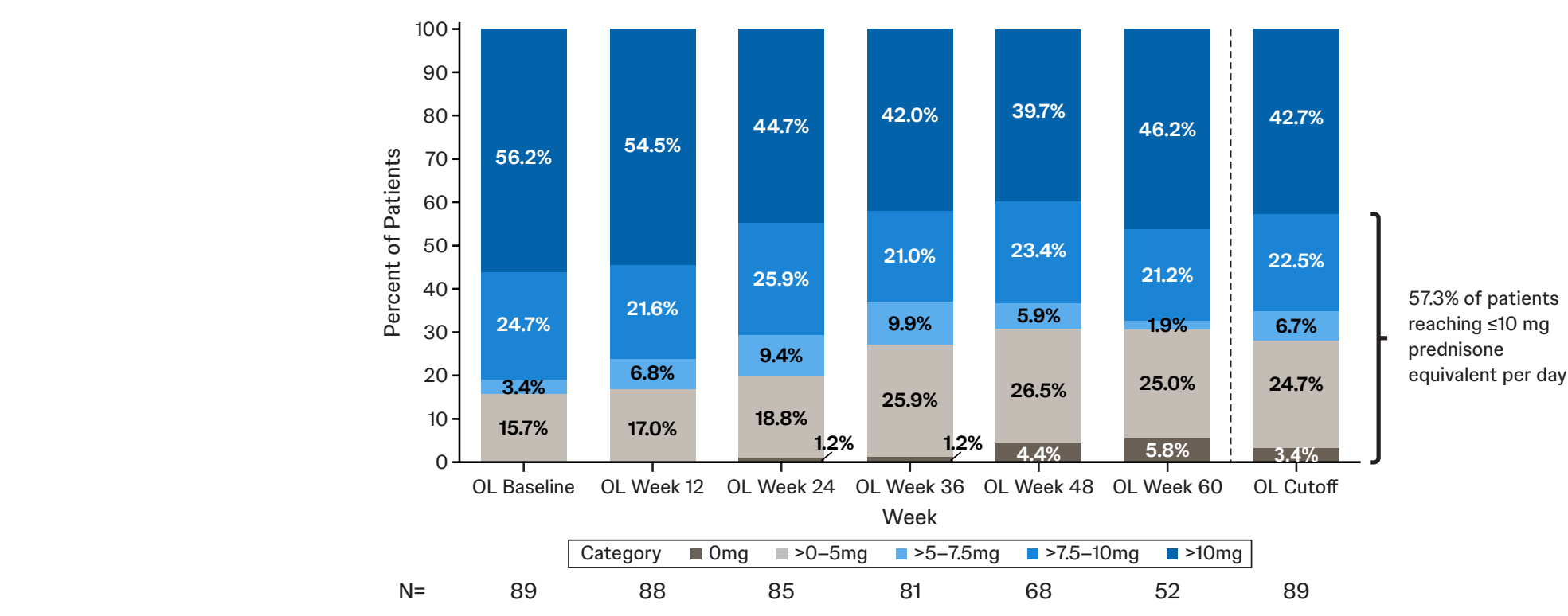


Note: P-value for comparison of QMG total score change from baseline significantly different from zero (P<0.001) using a one-sample t-test, for all timepoints except double-blind week 2 in the placebo group. DB=double-blind, OLE=open-label, QMG=Quantitative Myasthenia Gravis, SE=standard error, W=week.

Corticosteroid-sparing outcomes among treated individuals

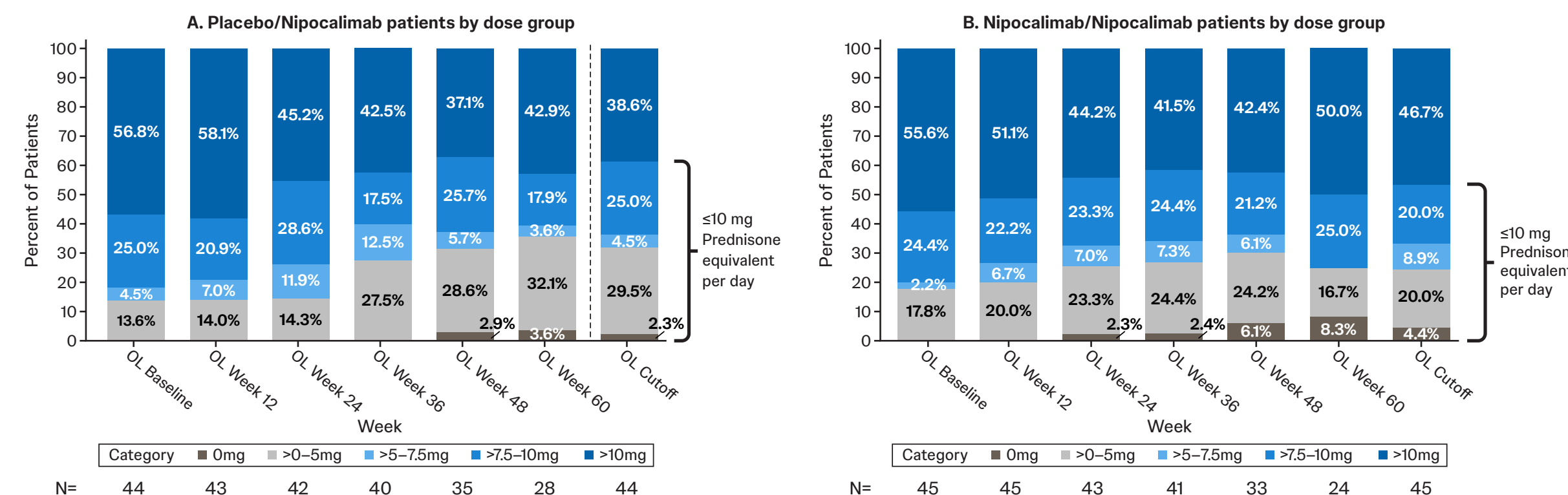
- Corticosteroid use decreased over time in the OLE phase with increasing proportions reaching ≤10 mg prednisone equivalent (eq) per day
- 45% (40/89) of patients receiving corticosteroids at open-label baseline were able to decrease or discontinue corticosteroids at data cut-off
 - Among these patients the mean dose of prednisone decreased from 23 to 10 mg eq per day
- 57% of all patients reached ≤10 mg prednisone eq per day at data cut-off

Figure 5. Proportion of patients with corticosteroid reduction over time – All patients by dose group (Seropositive population)



Note: Prednisone (mg) at each week equals the mean daily prednisone dose for the 28 days prior to and including that week. Cut-off is the analysis reference end date for patient. Steroid dose equivalents were calculated as described.^{6,7} OLE=open-label.

Figure 6. Proportion of patients with steroid reduction over time, groupwise (Seropositive population)



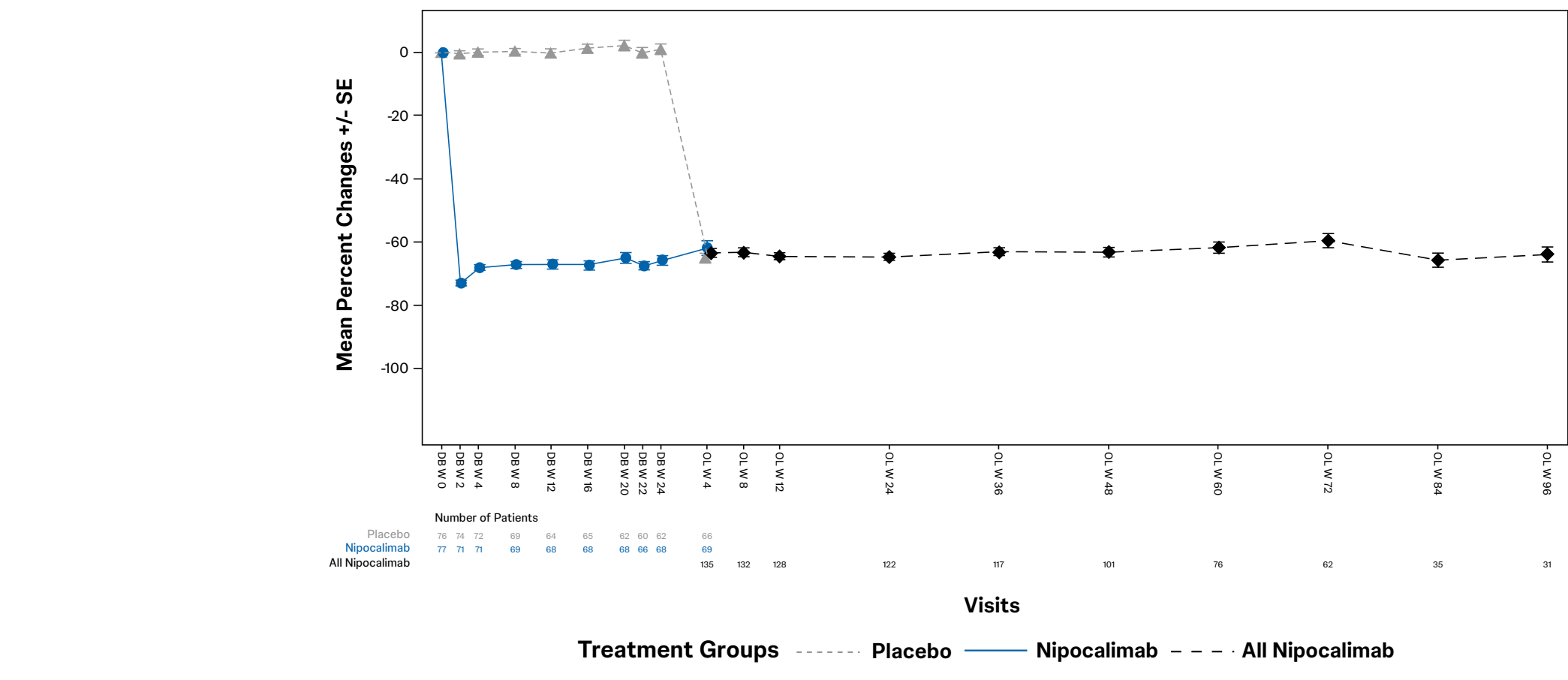
Note: Prednisone (mg) at each week equals the mean daily prednisone dose for the 28 days prior to and including that week. Cut-off is the analysis reference end date for patient. OLE=open-label.

- Patients in the Nipocalimab/Nipocalimab group started to discontinue steroids as early as week 24

Pharmacodynamic (PD) biomarkers

- Nipocalimab demonstrated rapid and sustained lowering of IgG in DB phase
 - The median predose (minimal) total IgG percent change from baseline after the loading dose was −74.6% (interquartile range −79.4 to −68.7) at DB week 2
- At 2-year (OLE week 96, n=31), mean standard deviation (SD) predose (minimal) IgG percentage change from double-blind baseline:
 - Placebo/Nipocalimab+SOC: −63.24% (14.32)
 - Nipocalimab/Nipocalimab+SOC: −64.06% (12.91)

Figure 7. PD biomarker: total IgG reduction from DB baseline (Seropositive population)



IgG=immunoglobulin G, OLE=open-label, PD=pharmacodynamic, SE=standard error, W=week.

Safety

- There were no unexpected adverse events during the OLE
- Adverse event rates including MACE were generally similar in the ‘DB Placebo’ and ‘OLE All Nipocalimab’ groups

Table 2. Safety and tolerability (Seropositive population)

	DB Placebo			DB Nipocalimab			OLE All Nipocalimab		
Analysis Set: Seropositive	76			77			137		
Average follow-up duration, wks	22.92			23.13			68.96		
P-Y ^a	33.4			34.1			181.1		
	Events/P-Y ^a	Events, n	Pts, n ^b	Events/P-Y ^a	Events, n	Pts, n ^b	Events/P-Y ^a	Events, n	Pts, n ^b
All AE	6.98	233	62	8.41	287	64	5.10	924	124
Serious AE	0.57	19	11	0.35	12	5	0.28	51	31
Fatal AE	0.06	2 ^c	2 ^c	0.03	1 ^c	1 ^c	0.02	3 ^{c,d}	3 ^{c,d}
Tx discontinuation due to AE ^e	0.18	6	6	0.18	6	4	0.06	11	11
Infection and infestations	1.32	44	31	1.70	58	33	1.20	217	93
Infection-related reaction ^f	0.51	17	6	0.35	12	9	0.07	12	7
Adjudicated MACE, fatal	0.06	2	2	0	0	0	0.01	2	2
Adjudicated MACE, not fatal	0.03	1	1	0	0	0	0.04	7 ^h	1

^aParticipant-years of observation (P-Y) is calculated as the total duration of follow-up in days/365.25. ^bParticipants with ≥1 AE are shown. ^cInvestigator assessed death(s) as unrelated to treatment. ^dInvestigator assessed 1 death as related to treatment (hemophagocytic lymphohistiocytosis). ^ePermanent discontinuation of treatment. ^fTreatment discontinuation for an AE with onset in DB (or OLE) occurred in DB (or OLE). ^gIndicated as infection reaction by investigator on eCRF and relationship to study intervention. ^hAll 7 adjudicated MACE events occurred in a single patient with a documented history of cardiovascular disease; the last MACE event was fatal. AE=adverse event, DB=double-blind, eCRF=electronic case report form, MACE=major adverse cardiovascular event, OLE=open-label extension, P-Y=participant-year, tx=treatment, wks=weeks.

Lipids over time

- From baseline to DB week 24, cholesterol/high-density lipoprotein (HDL) ratios were stable in both groups and <5
 - The median ratio remained stable to OLE week 96 and <5
- Ratios remained stable because similar percent increases in both HDL and low-density lipoprotein (LDL) were observed with nipocalimab