A Randomized, Open-label Study on the Effect of Nipocalimab on Vaccine Responses in Healthy Participants

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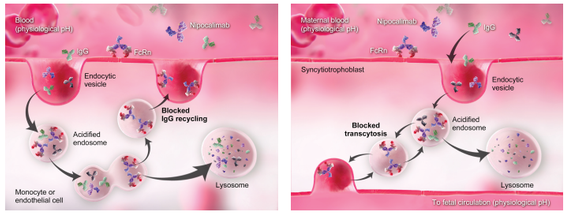
Background

- Nipocalimab, a fully human, high-affinity, effectorless, aglycosylated immunoglobulin (Ig) G1 monoclonal antibody, selectively binds and blocks the IgG binding site on the endogenous neonatal Fc receptor (FcRn; **Figure 1**)[1-3]
- Nipocalimab has demonstrated lowering of IgG levels with an up to 85% maximum reduction from baseline, a favorable safety profile, and an absence of broad immunosuppression[3-5]
  - Nipocalimab does not affect IgG synthesis, antigen recognition, leukocyte proliferation, IgM or IgA response[6]

FIGURE 1: Nipocalimab mechanism of action



FcRn, neonatal Fc receptor; IgG, immunoglobulin G.

Objective

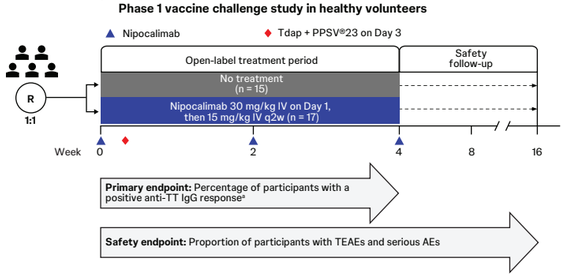
- To investigate the effect of nipocalimab on IgG response to T-cell–dependent/independent vaccines (tetanus, diphtheria, pertussis vaccine [Tdap]; pneumococcal polysaccharide vaccine [PPSV®23], respectively) in healthy participants

Methods

Study design

- This open-label, parallel, single-site, interventional study randomized participants 1:1 to receive either nipocalimab (active arm) or no drug (control arm; **Figure 2**)

FIGURE 2: Study design



AE, adverse event; anti-TT, anti-tetanus; IgG, immunoglobulin G; IV, intravenous; PPSV®23, 23-polysaccharide pneumococcal vaccine; q2w, every 2 weeks; R, randomization; Tdap, tetanus toxoid, diphtheria, and acellular pertussis vaccine; TEAE, treatment-emergent adverse event.
[a]Positive anti-TT response was defined as a participant with a pre-vaccination anti-TT IgG <0.16 IU/mL and a post-vaccination anti-TT IgG ≥0.16 IU/mL or a pre-vaccination anti-TT IgG ≥0.16 IU/mL and a ≥2-fold increase from baseline in post-vaccination anti-TT IgG titers at Week 4.

Assessments

- Assessments included total IgG median percent change from baseline, proportion of participants with a positive IgG response to the tetanus vaccine, change in anti-tetanus (anti-TT) and anti-pneumococcal (anti-PCP) IgG levels over time, and serotype-specific anti-PCP IgG response

Results

Study participants

- The target population consisted of healthy male and female participants, 18 to 65 years of age (inclusive), who had not received a tetanus (eg, Tdap, Td) vaccine in the past ≤5 years and had not received a pneumococcal vaccine (eg, Prevnar 7, 13, and 20 or PPSV®23) in the past ≤10 years
- Overall, 32 healthy participants were randomized into the study:
  - 1 participant in the active arm withdrew prior to the intervention
  - 31 participants were included in the safety analysis (15 in the control arm and 16 in the active arm)
  - 29 participants were included in the vaccine response completers analysis (14 in the control arm and 15 in the active arm)
  - 1 participant in the control arm was excluded due to a delayed end-of-study visit; 2 participants in the active arm were excluded due to withdrawal of consent and discontinuation of study intervention due to an adverse event
- The demographic and baseline characteristics were comparable across treatment groups (**Table 1**)

TABLE 1: Summary of demographic and baseline characteristics

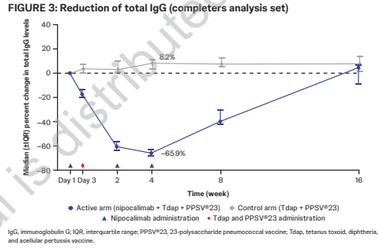
	Control arm (n = 15)	Active arm (n = 17)	Total (N = 32)
Completers, n	14[a]	15[b]	29
Age, years			
Mean (SD)	51.9 (11.5)	46.0 (14.2)	48.8 (13.1)
Median (range)	56.0 (25-61)	52.0 (23-63)	55.0 (23-63)
Sex, n (%)			
Female	7 (46.7)	9 (52.9)	16 (50.0)
Male	8 (53.3)	8 (47.1)	16 (50.0)
Race, n (%)			
White	15 (100)	17 (100)	32 (100)
Ethnicity, n (%)			
Not Hispanic or Latino	15 (100)	17 (100)	32 (100)
Tdap, years from previous booster (range)	8 (5-16)	9 (5-13)	–
Previous PPSV®23, n (%)	0	0	0

AE, adverse event; PPSV®23, 23-polysaccharide pneumococcal vaccine; SD, standard deviation; Tdap, tetanus toxoid, diphtheria, and acellular pertussis vaccine.
[a]1 participant was excluded from the analysis due to out of window assessments.
[b]1 participant was excluded from the analysis due to withdrawal of consent prior to dosing; 1 participant was excluded from the analysis due to nipocalimab discontinuation (AE).

Pharmacodynamics – total IgG

- The observed median pre-dose (minimal) reduction in total IgG at Week 4 was 65.9% in the active arm compared with an observed median increase of 8.2% in the control arm (**Figure 3**)
  - Total IgG returned to baseline level by Week 16 in the active arm
- IgG subclasses showed a similar profile as total IgG (data not shown)
- The kinetics of IgA and IgM through Week 16 were comparable between the active and control arms, with overall stable levels throughout the study (data not shown)

FIGURE 3: Reduction of total IgG (completers analysis set)

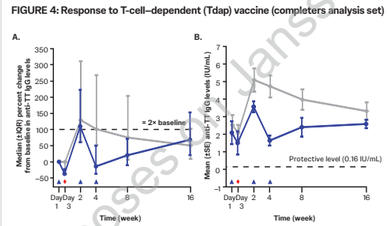


IgG, immunoglobulin G; IQR, interquartile range; PPSV®23, 23-polysaccharide pneumococcal vaccine; Tdap, tetanus toxoid, diphtheria, and acellular pertussis vaccine.

Anti-vaccine antibody responses

- All participants mounted a response to Tdap (**Figure 4**)
- The proportion of participants who met the criteria of a positive anti-TT IgG response at Week 2 was similar in the control arm (71.4%) compared to the active arm (60%)
- After Week 2, the proportion of participants who met the criteria of a positive anti-TT IgG response decreased over time through Week 16, which was more pronounced in the active arm with the largest difference observed at Week 4 (20% in the active arm [3/15] vs 50% in the control arm [7/14])
- The response at Week 16 was comparable between the active and control arms (40% in the active arm [6/15] vs 28.6% in the control arm [4/14])
- All participants in both the active arm and the control arm had anti-TT IgG levels ≥0.16 IU/mL at baseline and maintained protective levels through Week 16

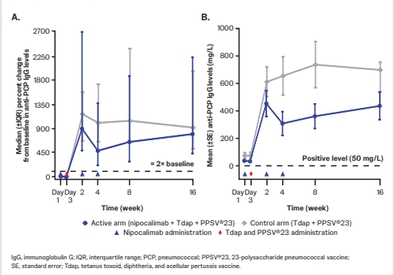
FIGURE 4: Response to T-cell–dependent (Tdap) vaccine (completers analysis set)



IgG, immunoglobulin G; IQR, interquartile range; PPSV®23, 23-polysaccharide pneumococcal vaccine; SE, standard error; Tdap, tetanus toxoid, diphtheria, and acellular pertussis vaccine; TT, tetanus.

- The observed median pre-dose anti-PCP IgG level at Week 4 was numerically lower in the active arm (182.0 mg/L; IQR: 127.5-366.2; median increase from baseline: 475.4%) compared with the observed median in the control arm (495.3 mg/L; IQR: 349.9-812.4; median increase from baseline: 992.7%; **Figure 5**)
- Except for 1 participant in the active arm at Week 4, all participants in both the control arm (100.0%) and the active arm (93.3%) achieved both anti-PCP IgG levels ≥50 mg/L and a ≥2-fold increase in anti-PCP IgG levels at all time points from Week 2 through Week 16

FIGURE 5: Response to T-cell–independent (PPSV®23) vaccine (completers analysis set)

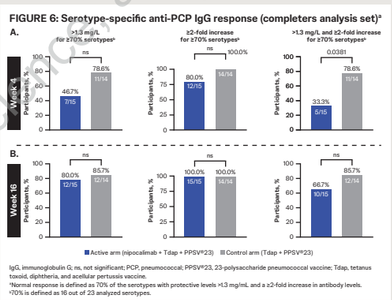


IgG, immunoglobulin G; IQR, interquartile range; PCP, pneumococcal; PPSV®23, 23-polysaccharide pneumococcal vaccine; SE, standard error; Tdap, tetanus toxoid, diphtheria, and acellular pertussis vaccine.

Serotype-specific anti-PCP IgG response

- The proportion of participants with both a serotype-specific IgG level >1.3 mg/L and a ≥2-fold increase in anti-PCP IgG response was lower in the active arm at Week 4 (**Figure 6A**; $P = 0.0381$) and was comparable between study arms at Week 16 (**Figure 6B**)

FIGURE 6: Serotype-specific anti-PCP IgG response (completers analysis set)[a]



IgG, immunoglobulin G; ns, not significant; PCP, pneumococcal; PPSV®23, 23-polysaccharide pneumococcal vaccine; Tdap, tetanus toxoid, diphtheria, and acellular pertussis vaccine.
[a]Normal response is defined as 70% of the serotypes with protective levels >1.3 mg/mL and a ≥2-fold increase in antibody levels. 70% is defined as 16 out of 23 analyzed serotypes.

Safety

- Treatment-emergent adverse events reported by study participants are shown in **Table 2**
- Injection-site reactions were consistent with the corresponding vaccine labels and exhibited no disparity across the 2 study arms

TABLE 2: Summary of TEAEs

	Control arm (n = 15)	Active arm (n = 16)
Participants with ≥1 TEAE, n (%)		
TEAEs[a]	5 (33.3)	11 (68.8)
Nasopharyngitis	1 (6.7)	4 (25)
Injection-site pain	2 (13.3)	3 (18.8)
Injection-site swelling	1 (6.7)	2 (12.5)
Dizziness	0	2 (12.5)
Infection[b]	3 (20.0)	6 (37.5)
TEAEs related to nipocalimab	NA	9 (56.3)
TEAEs related to Tdap	1 (6.7)	4 (25.0)
TEAEs related to PPSV®23	2 (13.3)	3 (18.8)
TEAEs by maximum severity		
Mild	3 (20.0)	7 (43.8)
Moderate	2 (13.3)	4 (25.0)
Severe	0	0
Persistent TEAEs[c]	0	1 (6.3)
Serious TEAEs	0	0
TEAEs leading to death	0	0
TEAEs leading to termination of study agent[d]	0	1 (6.3)
TEAEs leading to termination of study	0	0

AE, adverse event; NA, not applicable; PPSV®23, 23-polysaccharide pneumococcal vaccine; Tdap, tetanus toxoid, diphtheria, and acellular pertussis vaccine; TEAE, treatment-emergent adverse event.
[a]TEAEs reported in ≥2 participants are shown.
[b]All infections resolved without complications and did not require treatment.
[c]The TEAE is persistent if its outcome is not resolved/not recovered or resolving/recovering and the AE is ongoing at the end-of-study visit.
[d]Maculopapular rash of mild intensity and related to nipocalimab, Tdap, and PPSV®23.

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

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1. Ling LE, et al. *Clin Pharmacol Ther*. 2019;105(4):1031-1039. 2. Roy S, et al. *Am J Obstet Gynecol*. 2019;220(5):498.e1-498.e9. 3. Moise KJ Jr, et al. *N Engl J Med*. 2024;391(6):526-537. 4. Antozzi C, et al. *Neurology*. 2024;102(2):e207937. 5. Taylor P, et al. *Arthritis Rheumatol*. 2023;75(suppl 9). Abstract 0839. 6. Seth N, et al. Presented at: American Academy of Neurology (AAN) Annual Meeting; April 13-18, 2024; Online & Denver, CO, USA.

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Key takeaways

- Nipocalimab did not impact the development of an adequate response to T-cell–dependent (Tdap) and T-cell–independent (PPSV®23) vaccines
- Nipocalimab coadministration with Tdap and PPSV®23 was safe and well tolerated

Conclusions

- Nipocalimab reduced total serum IgG levels through Week 8, consistent with its mechanism of action
- Nipocalimab-treated participants mounted anti-TT IgG response to Tdap and anti-PCP IgG response to PPSV®23 over time
  - While the anti-TT–specific and anti-PCP–specific IgG levels were numerically lower in the active arm than in the control arm during nipocalimab treatment, they reached comparable levels to those observed in the control arm by Week 16
  - Anti-TT IgG levels remained above the protective level (≥0.16 IU/mL) and disease prevention threshold throughout the study in all participants
  - Anti-PCP IgG levels remained above the 50 mg/L threshold and showed a positive 2-fold increase from baseline throughout the study in both arms
- Overall, the totality of the data suggests that nipocalimab does not impact the development of adequate response to T-cell–dependent and T-cell–independent vaccines
- Results suggest that nipocalimab-treated patients can follow recommended vaccination schedules when receiving nonlive vaccines

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Disclosures

MC, **CBM**, **AJ**, **EM**, **GL**, **EL**, **UHB**, **KW**, **BS**, **JHL**, **SG**, and **DD** are employees of Janssen Research & Development, LLC and may hold stock in Johnson & Johnson.

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