Pharmacodynamics of Nipocalimab, a Fully Human FcRn-Blocking Monoclonal Antibody, in Adults With Systemic Lupus Erythematosus: Results From a Phase 2, Multicenter, Randomized, Placebo-Controlled, Double-Blind Study (JASMINE-SLE)

Michelle Petri,[1]* Loqmane Seridi,[2] Sheng Gao,[2] Robert Gordon,[2] Federico Zazzetti,[2] Stanley J Marciniak,[2] Steven Leonardo,[2] Kathy Sivils,[2] Leonard Dragone,[3] Linda Okonkwo,[4] Erika Noss,[2] Keying Ma,[2] Ta-Ming Liu,[2] Fang Liu-Walsh,[2] Richard A Furie[5]

[1]Johns Hopkins University School of Medicine, Baltimore, MD, USA; [2]Johnson & Johnson, Spring House, PA, USA; [3]Johnson & Johnson, San Francisco, CA, USA; [4]Johnson & Johnson, Raritan, NJ, USA; [5]Northwell, New Hyde Park, NY, USA, and Division of Rheumatology, Northwell, Great Neck, NY, USA

*Presenting author.

The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

Key Takeaways

- **Nipocalimab led to dose-dependent reductions in total IgG and all IgG subclasses, without notable changes in IgM, IgE, and IgA**
- **Nipocalimab reduced multiple IgG autoantibodies (including anti-dsDNA, anti-Smith, anti-Ro, and anti-La), reduced CICs, and increased C3 levels**
- **Together with the efficacy and safety results of JASMINE-SLE, these pharmacodynamic findings support further evaluation of nipocalimab in SLE and other autoantibody-driven diseases**

Background

- Autoantibodies, predominantly of the immunoglobulin (Ig) G class, cause inflammation and tissue damage in systemic lupus erythematosus (SLE) through various mechanisms, including immune activation by tissue deposition of circulating immune complexes (CICs)[1-3]
- B-cell–targeted therapies have demonstrated variable effects across autoantibody specificities, with effective reductions in some autoantibodies, such as anti–double-stranded DNA (dsDNA), but more limited effects on others, including anti-Ro (Sjögren's-Syndrome-Related Antigen A) and anti-La (Sjögren's-Syndrome-Related Antigen B)[4]
  - Furthermore, currently approved treatments for SLE have not demonstrated reductions in pathogenic CICs
- Nipocalimab is a fully human IgG1 monoclonal antibody that selectively blocks the neonatal Fc receptor (FcRn),[5] thereby preventing IgG recycling and leading to accelerated catabolism of all IgG subclasses, including pathogenic autoantibodies and CICs[6,7]
- In the phase 2 JASMINE-SLE study (ClinicalTrials.gov: NCT04882878), intravenous (IV) 15 mg/kg nipocalimab administered every 2 weeks (Q2W) demonstrated significant improvement in SLE-Responder Index (SRI)-4 composite response rates versus placebo through Week 52, with a safety profile consistent with the known safety profile of nipocalimab

Objective

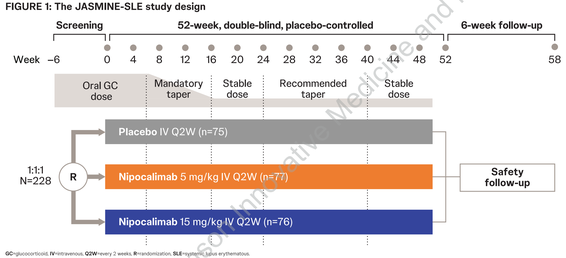
To evaluate the pharmacodynamic effects of nipocalimab in participants with moderate-to-severe SLE enrolled in the JASMINE-SLE study by assessing longitudinal changes in circulating immunoglobulins, SLE-associated autoantibodies, CICs, complement component 3 (C3), and other disease-relevant biomarkers reflecting immune activation, inflammation, and tissue injury

Methods

Study Design

- JASMINE-SLE was a multicenter, randomized, double-blind, placebo-controlled, phase 2 study that enrolled individuals with moderate-to-severe SLE at 86 centers globally
- Eligible participants were adults (18–65 years of age) positive for antinuclear antibodies (ANA) and/or anti-dsDNA and/or anti-Smith, with SLE Disease Activity Index 2000 (SLEDAI-2K) scores ≥6, clinical SLEDAI-2K (excluding headache and serologies) scores ≥4, ≥1 British Isles Lupus Assessment Group (BILAG) A or ≥2 BILAG B domain scores, a Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) activity score ≥6, and/or ≥4 active joints (joints with pain, tenderness, and swelling/effusion), who had not adequately responded to ≥1 standard-of-care treatment
- Participants were randomized (1:1:1) to receive IV nipocalimab 5 mg/kg, nipocalimab 15 mg/kg, or placebo Q2W (**Figure 1**); the study had a total duration of up to 64 weeks and consisted of 3 study periods: a ≤6-week screening period, a 52-week treatment period, and a 6-week follow-up period
- Participants were required to receive ≥1 protocol-permitted standard-of-care treatment during the trial, including oral glucocorticoids (GCs), antimalarials, mycophenolate mofetil/mycophenolic acid, azathioprine/6-mercaptopurine, or methotrexate
  - Participants receiving oral GCs (≥10 mg/day prednisone or equivalent) at baseline were mandated to taper the daily dose between Weeks 6 and 16 to a target ≤7.5 mg/day
  - All participants receiving any dose of oral GCs were eligible to taper at the investigator's discretion from Weeks 24 to 40

FIGURE 1: The JASMINE-SLE study design



GC=glucocorticoid; IV=intravenous; Q2W=every 2 weeks; R=randomization; SLE=systemic lupus erythematosus.

Outcomes

- Biomarker assessments were performed by Labcorp Central Laboratory Services (Indianapolis, IN, USA) and Plasma Services Group (Moorestown, NJ, USA)
- Blood samples were collected from participants pre-dose to measure changes from baseline through Week 58 in immunoglobulin isotypes (eg, total IgG, IgG subclasses, IgA, IgM, and IgE), IgG autoantibodies (eg, anti-dsDNA, anti-Smith, anti-Ro52, anti-Ro60, and anti-La), and biomarkers (eg, CICs and C3)

Statistical Analysis

- Pharmacodynamic analyses included participants with ≥1 dose (partial or complete) of study intervention and ≥1 valid post-dose blood sample for the pharmacodynamic analysis
- If a participant missed a planned dose of study intervention at any visit, their data were excluded from all subsequent visits after the first occurrence of a missed dose
- Data were summarized using descriptive statistics, without *P* values

Results

Participants

- Of a total of 440 participants screened for eligibility, 228 participants were randomized and received ≥1 IV dose of study intervention (nipocalimab 5 mg/kg, n=77; nipocalimab 15 mg/kg, n=76; placebo, n=75)
  - Participants had a mean age of 43.4 years, 94.7% were female, and 66.2% were White; the average SLE duration was 9.4 years
- The pharmacodynamic analysis set included 223 participants (nipocalimab 5 mg/kg, n=74; 15 mg/kg, n=75; placebo, n=74)
  - Baseline levels of immunoglobulins, autoantibodies, and complement component were similar across groups (**Table 1**)

TABLE 1: Baseline biomarker levels in the pharmacodynamic analysis set

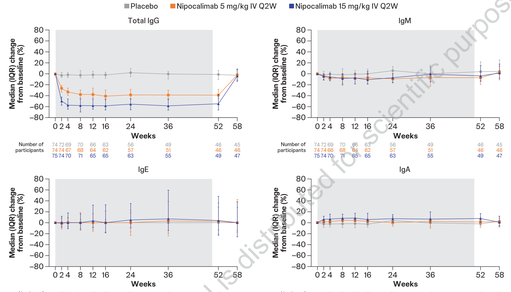
Mean (SD)	Placebo (n=74)	Nipocalimab 5 mg/kg IV Q2W (n=74)	Nipocalimab 15 mg/kg IV Q2W (n=75)
Total IgG, g/L	14.24 (4.81)	15.45 (6.77)	14.59 (5.42)
IgG1	9.99 (3.68)	10.72 (4.85)	10.51 (4.64)
IgG2	3.31 (1.64)	2.99 (1.36)	2.90 (1.13)
IgG3	0.50 (0.35)	0.47 (0.35)	0.44 (0.27)
IgG4	0.60 (0.69)	0.51 (0.54)	0.56 (0.64)
IgA, g/L	2.88 (1.55)	2.68 (1.19)	2.81 (1.60)
IgM, g/L	1.31 (1.21)	1.10 (0.79)	0.98 (0.64)
IgE, mg/L	0.16 (0.36)	0.36 (0.74)	0.30 (0.72)
Anti-dsDNA,[a] IU/mL	(n=22) 528.83 (760.56)	(n=16) 614.85 (561.84)	(n=20) 766.83 (1125.35)
Anti-Smith,[a] CU	(n=18) 422.06 (763.63)	(n=21) 641.04 (1263.08)	(n=17) 852.85 (1379.69)
Anti-Ro52,[a] CU	(n=25) 2569.48 (3867.88)	(n=25) 1763.69 (3383.54)	(n=16) 2066.26 (3271.26)
Anti-Ro60,[a] CU	(n=39) 2906.48 (4233.46)	(n=37) 3791.84 (5481.36)	(n=31) 3839.82 (4759.40)
Anti-La,[a] CU	(n=16) 1767.30 (2768.30)	(n=13) 1801.98 (3744.07)	(n=11) 1284.41 (2107.76)
CIC (C3d),[b] mgEq/L	(n=73) 11.50 (7.83)	(n=71) 12.93 (9.14)	(n=73) 12.01 (8.04)
C3,[c] g/L	(n=20) 0.73 (0.12)	(n=20) 0.74 (0.12)	(n=23) 0.76 (0.09)

[a]Among participants positive for those specific autoantibodies at baseline (anti-dsDNA, ≥75 IU/mL; anti-Smith/Ro52/Ro60/La, ≥20 CU).
[b]Among participants with available CIC values at baseline.
[c]Among participants with low C3 at baseline (≤59 g/L).
C3=complement component 3; **CIC**=circulating immune complex; **CU**=chemiluminescence unit; **dsDNA**=double-stranded DNA; **Ig**=immunoglobulin; **IU**=International Unit; **IV**=intravenous; **Q2W**=every 2 weeks.

Pharmacodynamic Effects of Nipocalimab on Immunoglobulin Isotypes

- Both nipocalimab doses led to rapid, substantial, and sustained pre-dose percent changes from baseline in total IgG through Week 52 (median [interquartile range (IQR)]: 5 mg/kg, –38.8% [–44.8, –28.4]; 15 mg/kg, –54.6% [–66.0, –37.6]; **Figure 2**)
  - No notable changes from baseline were observed in IgA, IgM, or IgE
- By Week 58 (8 weeks after the last dose), total IgG levels returned to baseline in the majority of participants in both nipocalimab groups (median [IQR] pre-dose change from baseline: 5 mg/kg, –1.9% [–13.0, 7.4]; 15 mg/kg, –4.0% [–13.5, 8.7])

FIGURE 2: Pre-dose percent change from baseline in total IgG, IgM, IgE, and IgA isotypes



Gray shading indicates treatment duration from first to last dose of administration (Weeks 0-50).
Ig=immunoglobulin; **IQR**=interquartile range; **IV**=intravenous; **Q2W**=every 2 weeks.

Pharmacodynamic Effects of Nipocalimab on IgG Subclasses

- Consistent pre-dose percent reductions from baseline were observed among all IgG subclasses at Week 52 (**Table 2**)
- By Week 58, total IgG subclass levels returned to baseline in the majority of participants in both nipocalimab groups (range of median pre-dose reductions from baseline: 5 mg/kg, 0.0%–6.4%; 15 mg/kg, 0.0%–11.1%)

TABLE 2: Pre-dose percent change from baseline in SLE biomarkers at Week 52

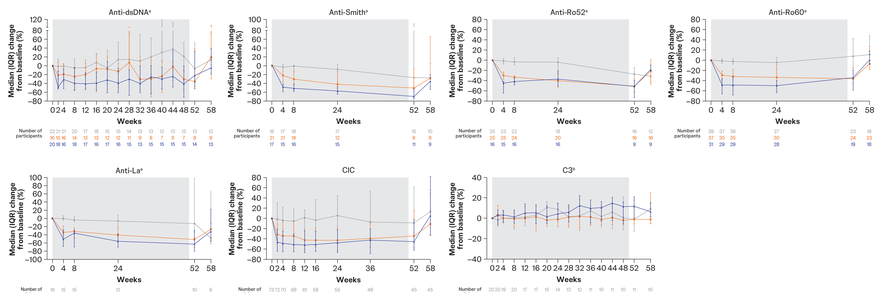
Median % change (IQR) [n]	Placebo	Nipocalimab 5 mg/kg IV Q2W	Nipocalimab 15 mg/kg IV Q2W
Total IgG	**–1.2** (–10.4, 6.3) [46]	**–38.8** (–44.8, –28.4) [46]	**–54.6** (–66.0, –37.6) [49]
IgG1	**–4.5** (–13.3, 4.5) [46]	**–39.2** (–49.9, –26.3) [46]	**–49.9** (–66.5, –38.8) [49]
IgG2	**1.9** (–8.3, 9.7) [46]	**–29.4** (–43.4, –16.5) [46]	**–49.1** (–62.1, –33.8) [49]
IgG3	**–5.3** (–17.7, 12.5) [46]	**–39.2** (–45.5, –23.8) [46]	**–50.0** (–63.2, –34.3) [49]
IgG4	**–2.2** (–24.3, 11.6) [46]	**–31.5** (–45.1, –14.3) [46]	**–48.5** (–59.7, –39.6) [49]
Anti-dsDNA[a]	**–6.7** (–28.2, 52.0) [13]	**–35.8** (–46.7, 39.1) [8]	**–22.0** (–52.1, 32.8) [14]
Anti-Smith[a]	**–27.1** (–50.7, 88.4) [15]	**–50.8** (–59.3, –6.3) [9]	**–69.9** (–76.2, –52.8) [11]
Anti-Ro52[a]	**–27.4** (–44.5, –15.0) [16]	**–50.9** (–62.5, –36.4) [16]	**–51.4** (–73.5, –40.1) [9]
Anti-Ro60[a]	**7.7** (–14.8, 42.6) [23]	**–36.4** (–45.2, –15.9) [24]	**–34.1** (–58.5, –20.1) [19]
Anti-La[a]	**–12.7** (–33.7, 98.0) [10]	**–51.5** (–71.0, –46.6) [10]	**–62.8** (–80.2, –29.5) [8]
CIC (C3d)	**5.4** (–22.0, 44.6) [45]	**–42.9** (–63.0, –18.2) [44]	**–47.8** (–66.9, –22.1) [45]
C3[b]	**–1.1** (–13.1, 17.7) [11]	**–1.2** (–5.4, 12.8) [9]	**11.6** (0.0, 20.8) [17]

[a]In participants positive for those specific autoantibodies at baseline (anti-dsDNA, ≥75 IU/mL; anti-Smith/Ro52/Ro60/La, ≥20 CU).
[b]In participants with low C3 at baseline (≤59 g/L).
C3=complement component 3; **CIC**=circulating immune complex; **CU**=chemiluminescence unit; **dsDNA**=double-stranded DNA; **IgG**=immunoglobulin G; **IQR**=interquartile range; **IV**=intravenous; **Q2W**=every 2 weeks; **SLE**=systemic lupus erythematosus.

Pharmacodynamic Effects of Nipocalimab on SLE-Related Autoantibodies and Biomarkers

- Multiple SLE-associated autoantibodies decreased in both nipocalimab groups, including anti-dsDNA, anti-Smith, anti-Ro52, anti-Ro60, and anti-La (**Figure 3** and **Table 2**), among participants positive for those specific autoantibodies at baseline
- CIC levels were also reduced in both nipocalimab groups versus placebo
- Among participants with low C3 at baseline, increases were observed from Week 32 through Week 52 in the 15 mg/kg group, with 8/17 participants returning to normal levels versus 1/11 with placebo

FIGURE 3: Pre-dose percent change from baseline in SLE-related autoantibodies and biomarkers



Gray shading indicates treatment duration from first to last dose of administration (Weeks 0-50).
[a]In participants positive for those specific autoantibodies at baseline (anti-dsDNA, ≥75 IU/mL; anti-Smith/Ro52/Ro60/La, ≥20 CU).
[b]In participants with low C3 at baseline (≤59 g/L).
C3=complement component 3; **CIC**=circulating immune complex; **CU**=chemiluminescence unit; **dsDNA**=double-stranded DNA; **IQR**=interquartile range; **IV**=intravenous; **Q2W**=every 2 weeks; **SLE**=systemic lupus erythematosus.

This material is distributed for scientific purposes by Johnson & Johnson Medical Affairs and is not for promotional use.

PRESENTED AT: The American College of Rheumatology (ACR) Convergence; November 6-11, 2026; Orlando, FL, USA. **REFERENCES: 1.** Jost SA, et al. *Sci World Journal.* 2014;2014:710328. **2.** Yang CW, et al. *Front Immunol.* 2025;16:1656937. **3.** Gómez-Bañuelos E, et al. *Curr Opin Rheumatol.* 2023;35(2):61-67. **4.** Hale M, et al. *Curr Opin Immunol.* 2018;55:81-88. **5.** Seth NP, et al. *Mabs.* 2025;17(1):2461191. **6.** Noaiseh G, et al. *Lancet.* 2025;406(10518):2435-2448. **7.** Antozzi C, et al. *Neurology.* 2024;102(2):e207937. **ACKNOWLEDGMENTS:** The research was sponsored by Johnson & Johnson. Writing and editorial assistance were provided by Sarah M Ferrigno, PhD, of Lumanity Communications Inc., and funded by Johnson & Johnson. **DISCLOSURES: MP** received grant/research support from AstraZeneca, Exagen, and GSK; and received consulting fees from Amgen, Annenberg Center for Health Sciences, AstraZeneca, Blackrock, Eli Lilly, Exagen, Glenmark Pharmaceuticals, GSK, IQVIA, Johnson & Johnson, Merck EMD Serono, Novartis, Quintiles, Sanofi-Japan, Thermo Fisher Scientific, and UCB. **LS**, **SG**, **RG**, **FZ**, **SJM**, **SL**, **KS**, **LD**, **LO**, **EN**, **KM**, **T-ML**, and **FL-W** are employees of and may hold stock or stock options in Johnson & Johnson. **RAF** received personal fees from AstraZeneca, Biogen, Bristol Myers Squibb, Genentech/Roche, GSK, and Johnson & Johnson during the conduct of the study and outside the submitted work; and received grants from Genentech/Roche.