Biomarker-Driven Insights to Clinical Response in DAHLIAS: A Nipocalimab Trial for Sjögren's Disease

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Conflicts of Interest

- **HS** received grant funding from the National Institutes of Health (NIH) and the US Department of Veterans Affairs; consulted and participated in advisory boards for IQVIA, Johnson & Johnson, Veloxis Pharmaceuticals, and Vor Bio; and served as a local site investigator for Johnson & Johnson
- **J-EG** consulted for AbbVie, Bristol Myers Squibb, Galapagos, Gilead, Johnson & Johnson, Lilly, MSD, Novartis, Pfizer, Sanofi, and UCB
- **HL**, **DG**, **KM**, **LT**, **CS**, **MJL**, **JJH**, **KC**, **DW**, **SG**, **CC**, **SL**, and **KS** are employees of Johnson & Johnson and own stocks or stock options in Johnson & Johnson

Sjögren's Disease

Autoantibody (aAb)-driven pathology[1]

Characterized by:

- Presence of aAbs
- Lymphocytic infiltration of exocrine glandular tissues
- Immune complex formation, IFN production

Systemic immune dysregulation[1]

- Involves aberrant B-lymphocyte activity
- Abnormally elevated IgG and IgG aAb levels (eg, anti-Ro, anti-La)

Relentless multi-organ burden[2,3]

- ~1.5-fold higher all-cause mortality[4]
- Common symptoms: mucosal dryness, fatigue, and pain
  - ≥1 organ involvement in ~40% to 75% of patients[2-7]

aAb=autoantibody, **IFN**=interferon, **IgG**=immunoglobulin G.

1. Nocturne G, Mariette X. *Nat Rev Rheumatol*. 2013;9(9):544-556. 2. Mariette X, Criswell LA. *N Engl J Med*. 2018;378(10):931-939. 3. Beydon M, et al. *Nat Rev Rheumatol*. 2024;20(3):158-169. 4. Huang H, et al. *Rheumatology (Oxford)*. 2021;60(9):4029-4038. 5. Parisis D, et al. *J Clin Med*. 2020;9(7):2299. 6. Zhang Y, et al. *J Clin Rheumatol*. 2024;30(4):151-158. 7. Retamozo S, et al. *Clin Exp Rheumatol*. 2021;39(suppl 133):S166-S174.

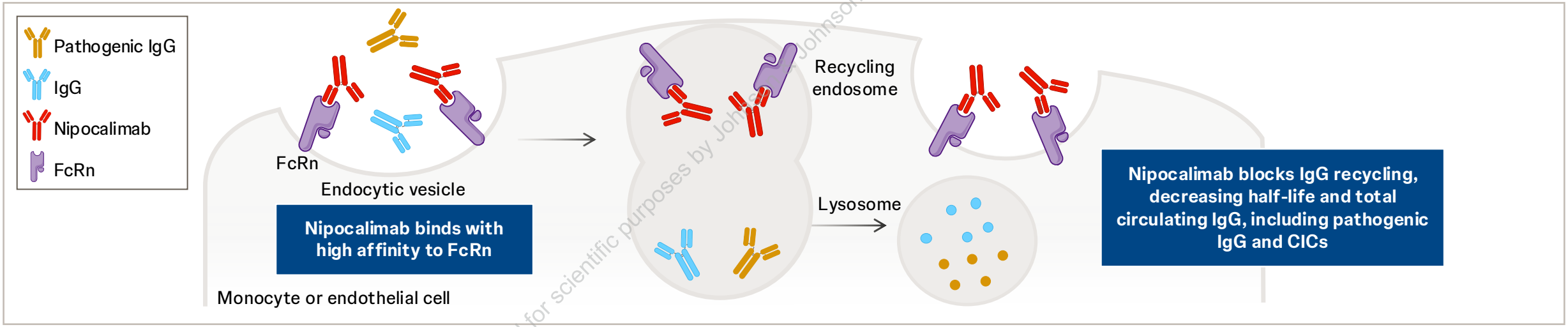
Nipocalimab: FcRn Blocker Decreases Serum IgG, Including Pathogenic IgG, and CICs

FcRn:

- A recycling or transcytosis receptor → maintains IgG levels in circulation[1-3]
- Expressed in multiple cell types, including monocytes and endothelial cells[1-3]

Nipocalimab:

- A high-affinity, fully human, IgG1 FcRn blocker → selectively blocks IgG recycling[4]
- Decreases serum IgG, including pathogenic IgG, and CICs while preserving immune cell functions[4-6]
- Approved for gMG in the US, Brazil, Japan, Europe, and China[7]



Objective: To evaluate whether nipocalimab's MOA and SjD pathology impact response to nipocalimab in participants with SjD in the phase 2 DAHLIAS study, using biomarker stratification approaches

CIC=circulating immune complex, **FcRn**=neonatal crystallizable fragment receptor, **gMG**=generalized myasthenia gravis, **IgG**=immunoglobulin G.

1. Blumberg LJ, et al. *Sci Adv*. 2019;5(12):eaax9586. 2. Roopenian DC, Akilesh S. *Nat Rev Immunol*. 2007;7(9):715-725. 3. Peter HH, et al. *J Allergy Clin Immunol*. 2020;146(3):479-491.e5. 4. Seth NP, et al. *MAbs*. 2025;17(1):2461191. 5. Ling LE, et al. *Clin Pharmacol Ther*. 2019;105(4):1031-1039. 6. Noaiseh G, et al. *Lancet*. 2025;406(10518):2435-2448. 7. IMAAVY™ (nipocalimab-aahu) injection, for intravenous use [prescribing information]. Janssen Biotech, Inc.; 2025.

DAHLIAS Study Design

Study population

- Adults aged 18-75 years
- Moderately to severely active primary SjD (total ClinESSDAI score ≥6)
- Seropositive for anti-Ro60 and/or anti-Ro52 IgG antibodies

Primary endpoint[a]

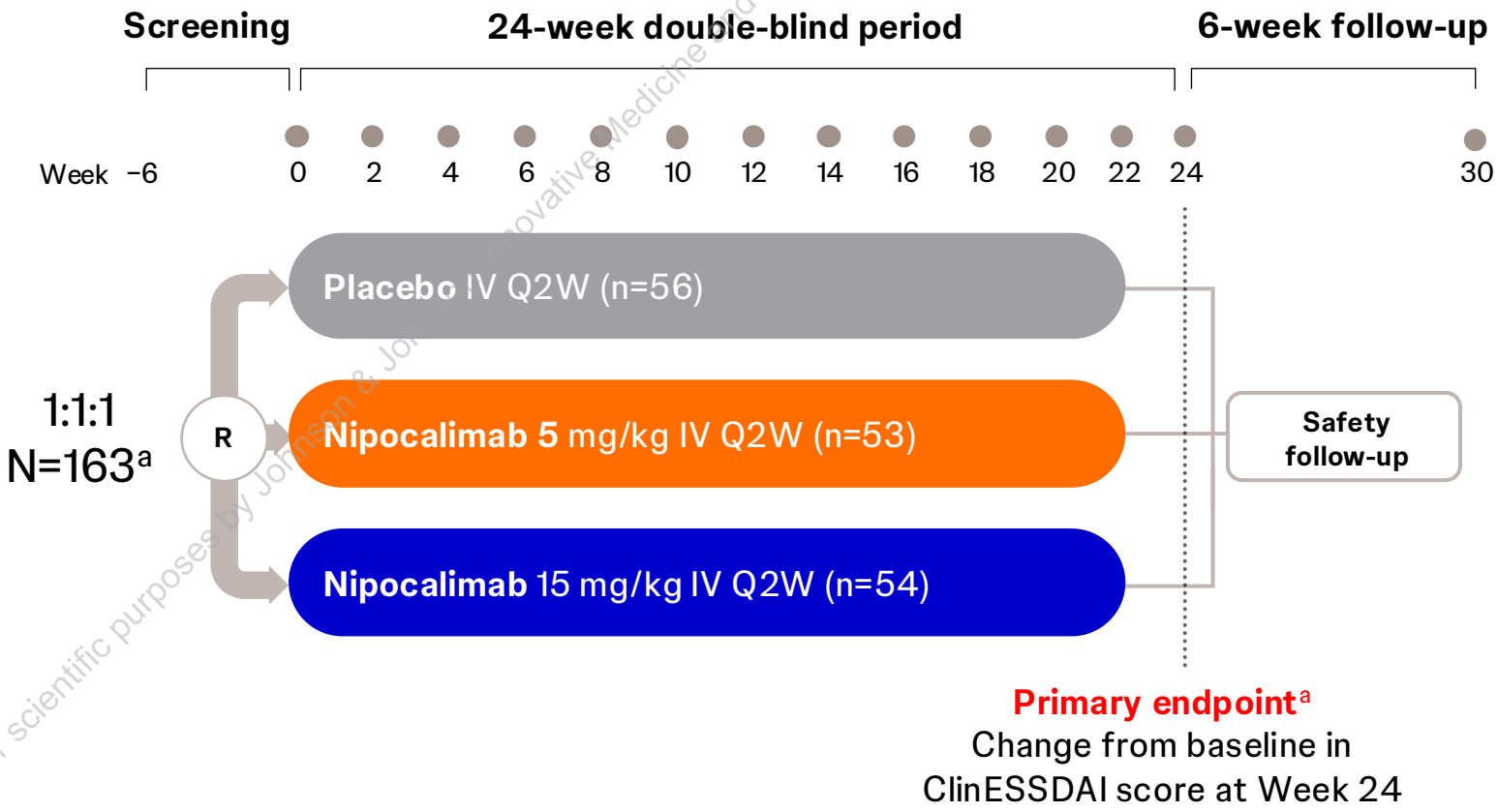
- Change from baseline in ClinESSDAI score at Week 24

Key secondary endpoints

- ClinESSDAI-4 response[b] at Week 24

Post hoc analyses in biomarker-based populations

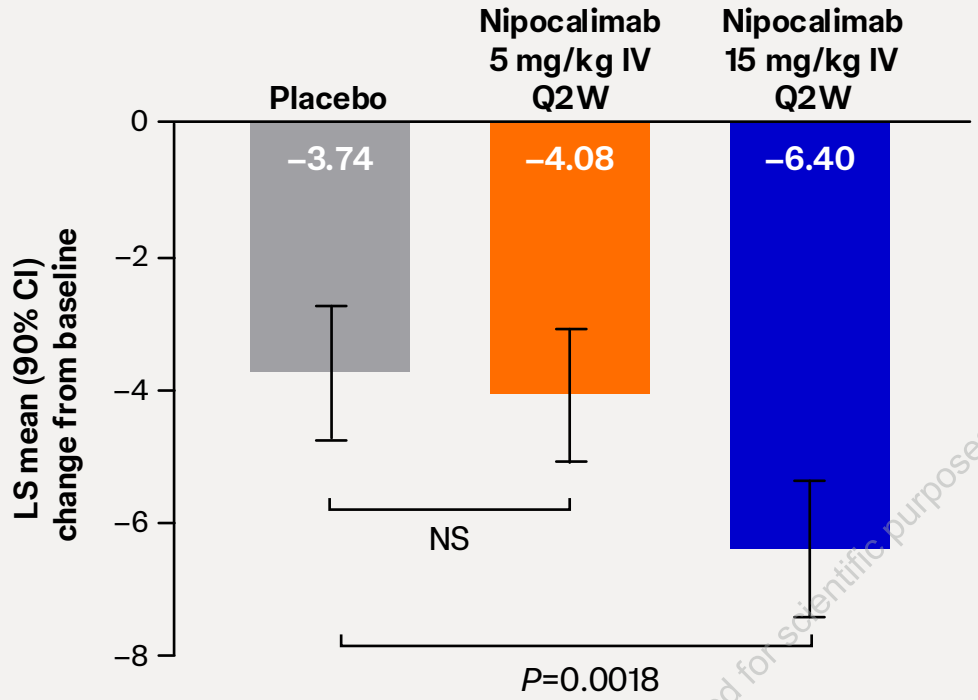
- ClinESSDAI-4 response[b] at Week 24



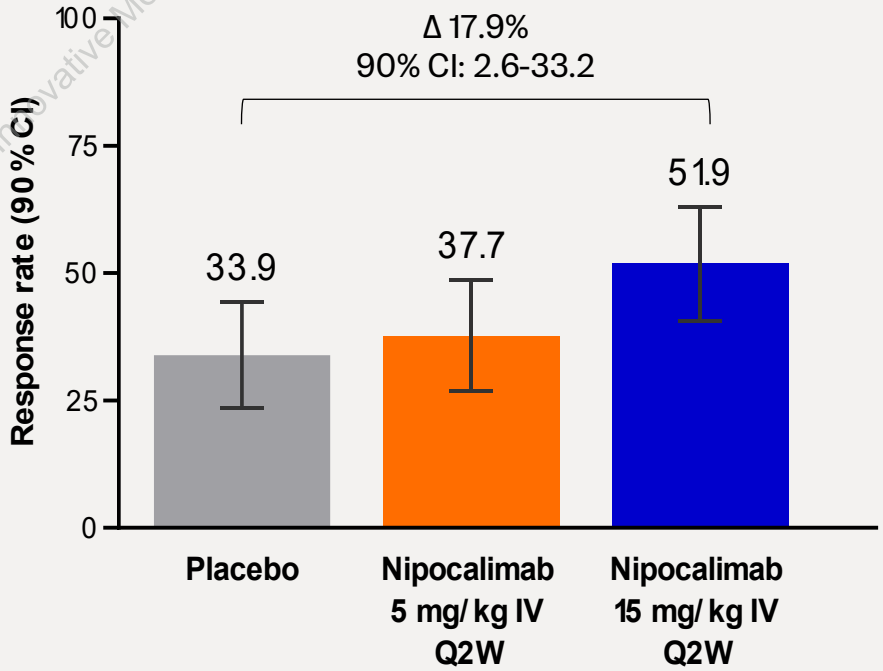
[a]The DAHLIAS study was pre-specified to use a 2-sided alpha level of 0.1 without multiplicity control. [b]Defined as improvement of ≥4 points from baseline in ClinESSDAI score.
ClinESSDAI=clinical European Alliance of Associations for Rheumatology Sjögren's Syndrome Disease Activity Index, **IgG**=immunoglobulin G, **IV**=intravenous, **Q2W**=every 2 weeks, **SjD**=Sjögren's disease.
Noaiseh G, et al. *Lancet*. 2025;406(10518):2435-2448.

DAHLIAS Primary Results: Efficacy and Safety

Primary endpoint:
Change from baseline in ClinESSDAI score at Week 24



Secondary endpoint:
ClinESSDAI-4 response at Week 24



Safety: Nipocalimab was well tolerated in participants with SjD, with no new safety signals observed

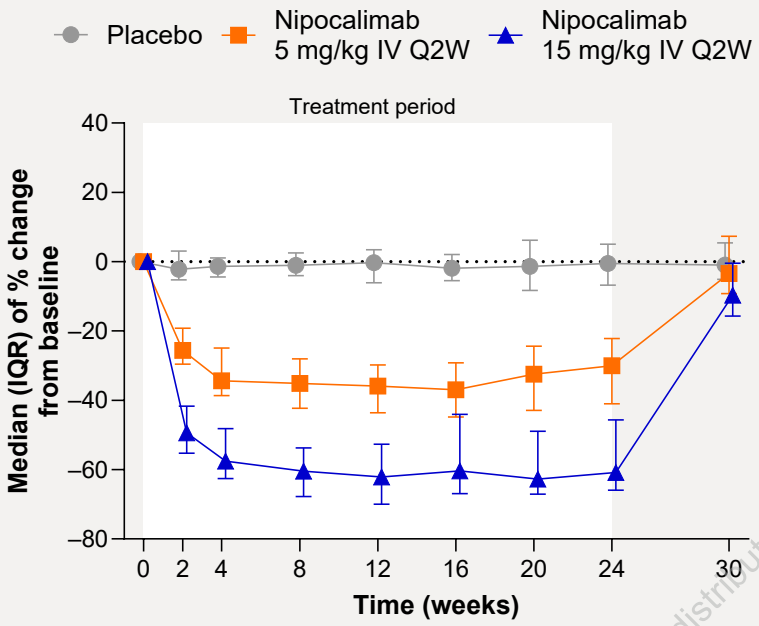
CI=confidence interval, **ClinESSDAI**=clinical European Alliance of Associations for Rheumatology Sjögren's Syndrome Disease Activity Index, **IV**=intravenous, **LS**=least squares, **NS**=nonsignificant, **Q2W**=every 2 weeks, **SjD**=Sjögren's disease.

Noaiseh G, et al. *Lancet*. 2025;406(10518):2435-2448.

DAHLIAS Primary Results: Biomarkers

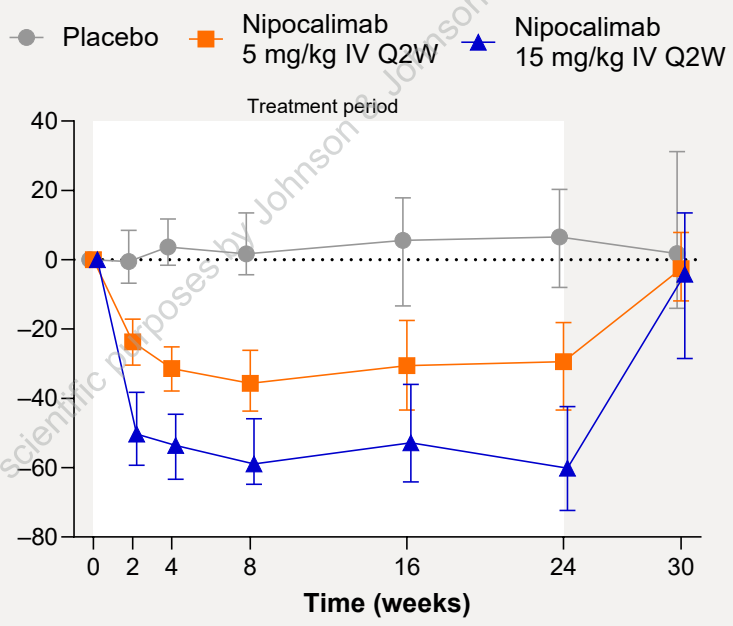
Total IgG reduction

- Observed predose (minimum) median IgG reduction of 61% at Week 24
- 77% maximum reduction in total IgG (PK/PD simulations)



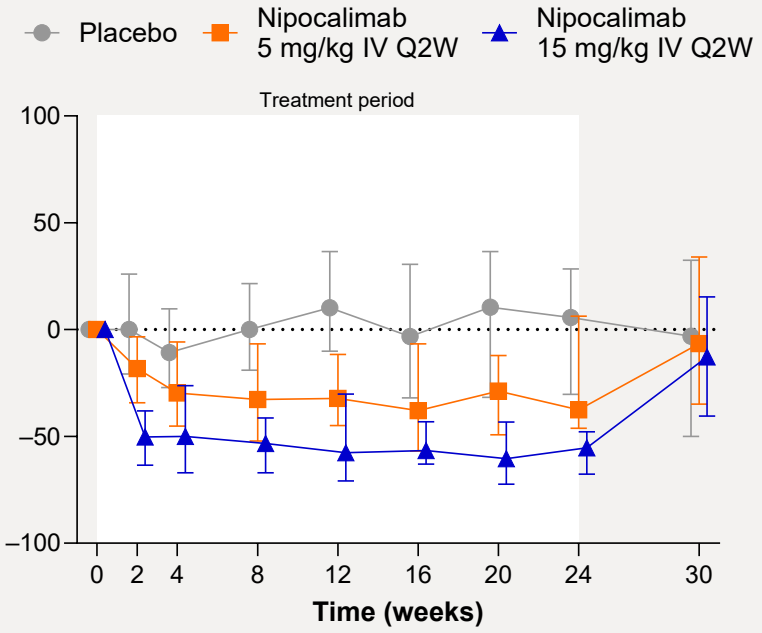
Anti-Ro60 IgG reduction

- Observed consistent reductions in SjD-associated anti-Ro60, anti-Ro52, and anti-La IgG aAbs during treatment



CIC reduction

- Observed reductions in CICs during treatment



aAb=autoantibody, **CIC**=circulating IgG immune complexes, **IgG**=immunoglobulin G, **IQR**=interquartile range, **IV**=intravenous, **PD**=pharmacodynamic, **PK**=pharmacokinetic, **Q2W**, every 2 weeks, **SjD**=Sjögren's disease.

Noaiseh G, et al. *Lancet*. 2025;406(10518):2435-2448.

Methods: Participant Stratification

DAHLIAS participants were stratified using 3 approaches based on nipocalimab's MOA and SjD pathology to test their impacts on response to nipocalimab:

Baseline aAbs

Serum baseline levels of anti-Ro60, anti-Ro52, and anti-La aAbs:

- **aAb-high:** all 3 aAb levels in the top tertile

Baseline IFN scores

IFN gene signature scores derived from whole-blood RNA sequencing:

- **IFN-high:** scores >75th percentile + 1.5 × IQR of healthy controls

Baseline IgG

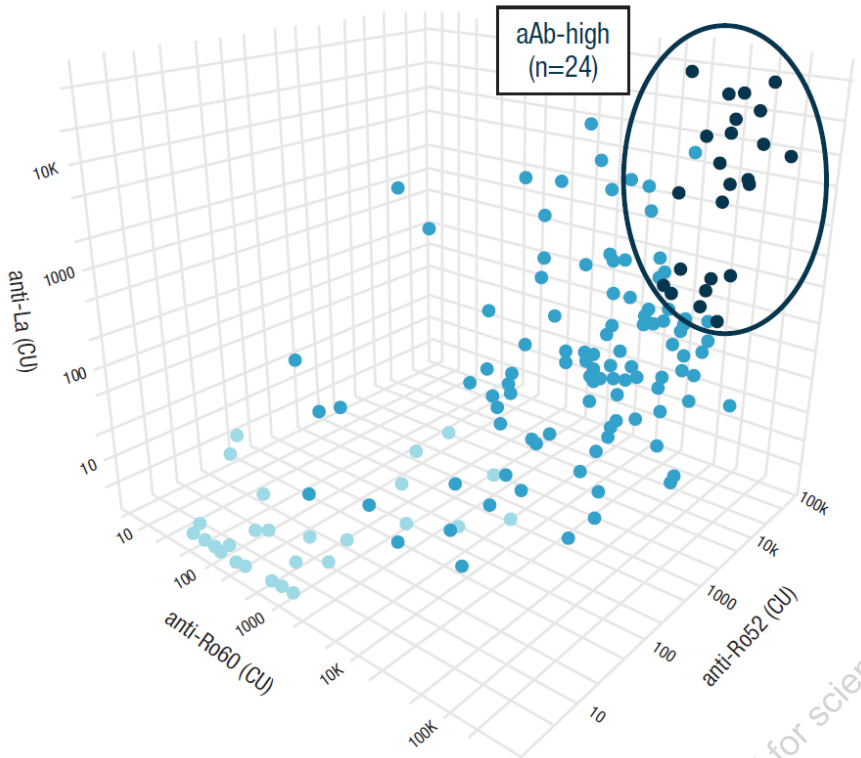
Total serum IgG levels at baseline:

- **IgG-high:** IgG >25% quartile of overall study population

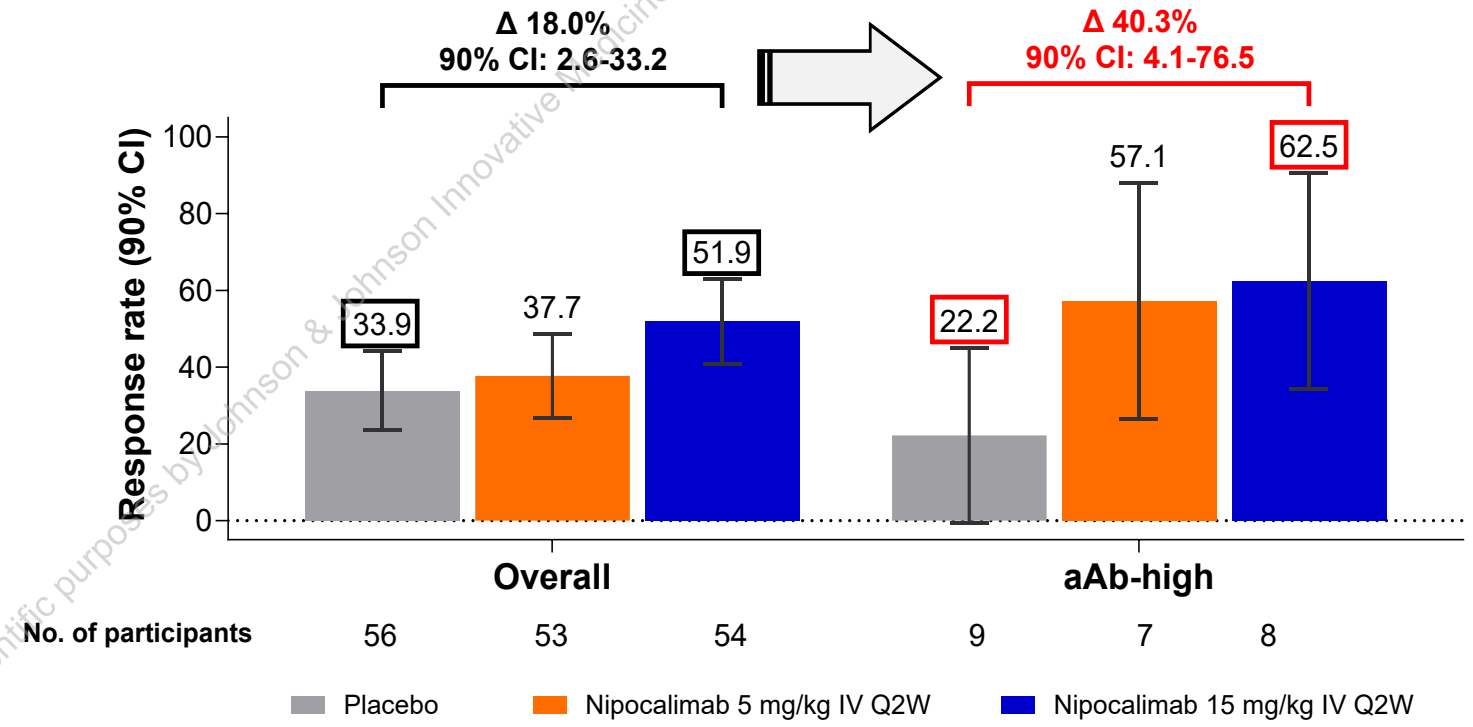
aAb=autoantibody, **IFN**=interferon, **IgG**=immunoglobulin G, **IQR**=interquartile range, **MOA**=mechanism of action, **SjD**=Sjögren's disease.

High Baseline aAb Level Enriches Responders to Nipocalimab

Baseline aAb levels



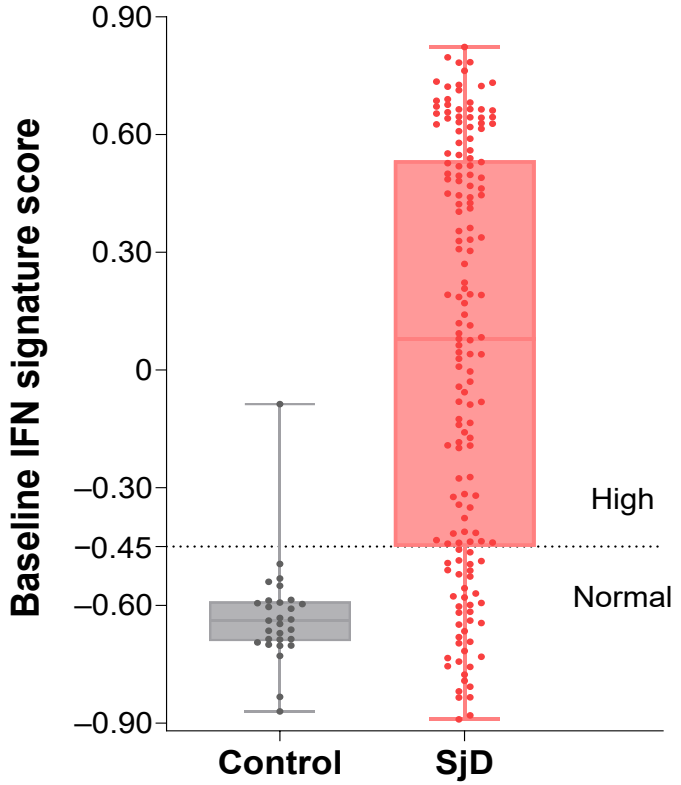
ClinESSDAI-4 responses at Week 24 in aAb-high participants

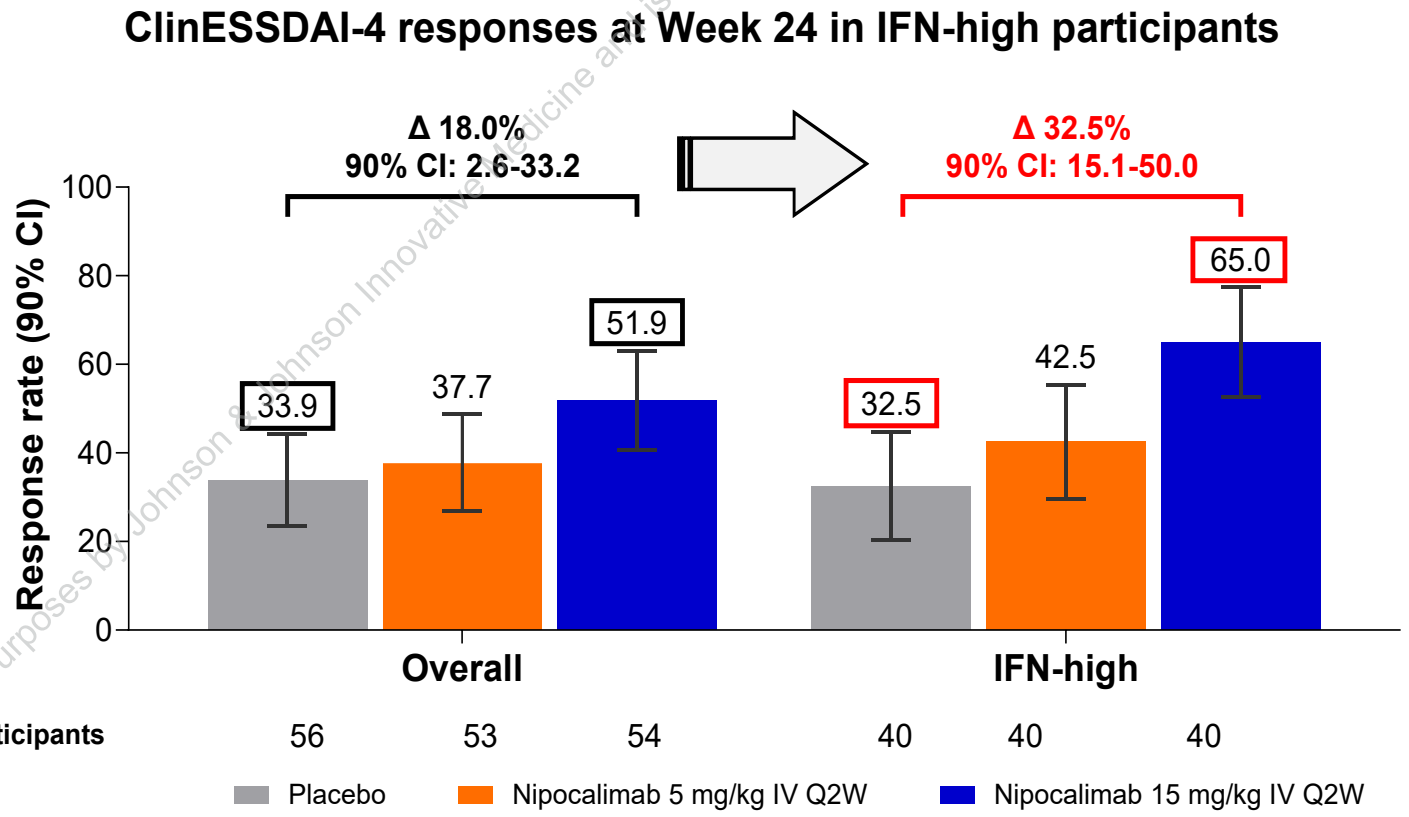


Enriched nipocalimab response in aAb-high population (15% of DAHLIAS participants)

aAb=autoantibody, **CI**=confidence interval, **ClinESSDAI**=clinical European Alliance of Associations for Rheumatology Sjögren's Syndrome Disease Activity Index, **CU**=chemiluminescent unit, **IV**=intravenous, **Q2W**=every 2 weeks.

High Baseline IFN Score Enriches Responders to Nipocalimab

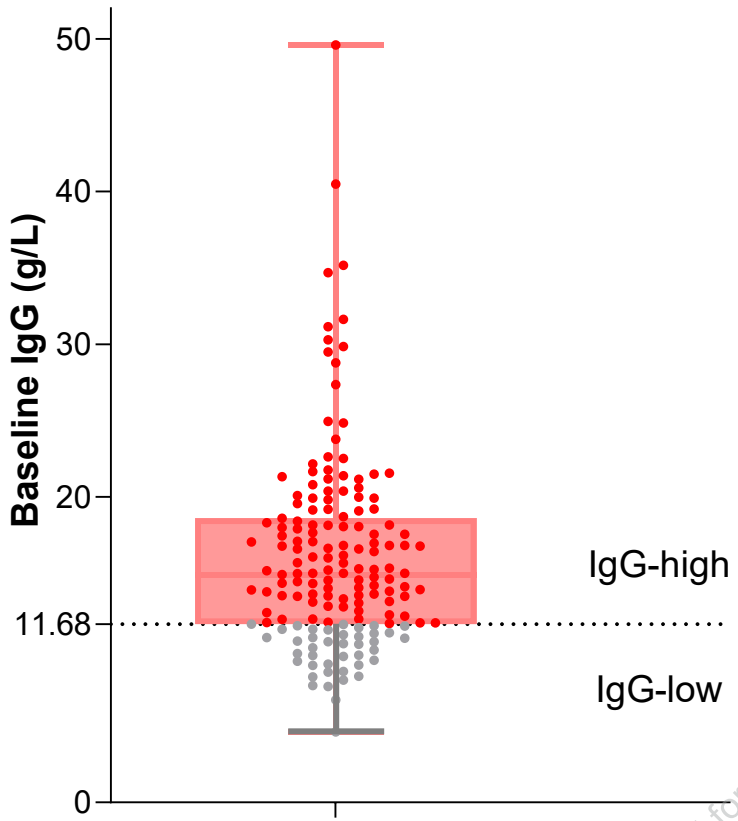


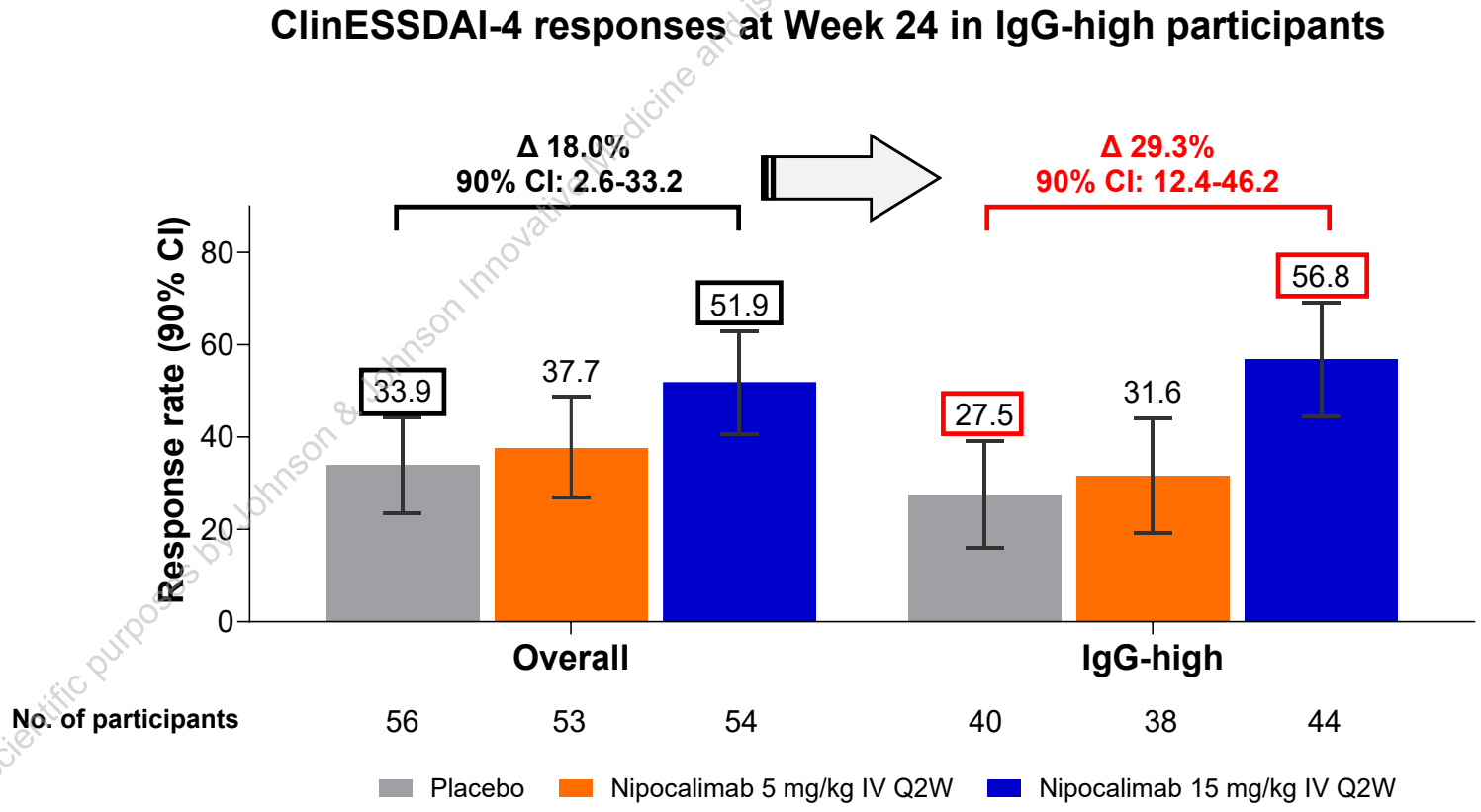


Enriched nipocalimab response in IFN-high population (74% of DAHLIAS participants)

CI=confidence interval, **ClinESSDAI**=clinical European Alliance of Associations for Rheumatology Sjögren's Syndrome Disease Activity Index, **IFN**=interferon, **IV**=intravenous, **Q2W**=every 2 weeks, **SjD**=Sjögren's disease.

High Baseline IgG Level Enriches Responders to Nipocalimab





Enriched nipocalimab response in IgG-high population (75% of DAHLIAS participants)

CI=confidence interval, **ClinESSDAI**=clinical European Alliance of Associations for Rheumatology Sjögren's Syndrome Disease Activity Index, **IgG**=immunoglobulin G, **IV**=intravenous, **Q2W**=every 2 weeks.

Key Takeaways

- In DAHLIAS, nipocalimab 15 mg/kg IV Q2W reduced ClinESSDAI score and total IgG significantly in participants with SjD, with a safety profile consistent with other phase 2 studies[1-3]
- Biomarker analyses reinforce the mechanistic rationale for treatment with nipocalimab in SjD, with enriched response observed among participants with elevated aAbs, IFN, and IgG levels
- This supports the continued development of nipocalimab in SjD in the ongoing phase 3 DAFFODIL study (NCT06741969)

aAb=autoantibody, **ClinESSDAI**=clinical European Alliance of Associations for Rheumatology Sjögren's Syndrome Disease Activity Index, **IFN**=interferon, **IgG**=immunoglobulin G, **IV**=intravenous, **Q2W**=every 2 weeks, **SjD**=Sjögren's disease.

1. Antozzi C, et al. *Neurology*. 2024;102(2):e207937. 2. Moise KJ Jr, et al. *N Engl J Med*. 2024;391(6):526-537. 3. Noaiseh G, et al. *Lancet*. 2025;406(10518):2435-2448.

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