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Improvement in Executive Function Following Nipocalimab Treatment in Patients with Sjögren's Disease: A Randomized Clinical Trial

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Disclosures

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Cognitive Symptoms in Sjögren's Disease (SjD) are a Poorly Understood High Unmet Need

Cognitive Symptoms in SjD[1-4]

- SjD patients often report difficulties with cognition, such as memory, concentration, or "brain fog" in addition to physical symptoms like dryness, pain, and fatigue
- However, the pathophysiology in SjD is poorly understood, as formal cognitive assessment studies (eg, attention, memory, and problem solving), are rare

Pathophysiology of Cognitive Difficulties

- Exploration of treatment effects using objective neuropsychological tests may help better understand the pathophysiology of cognitive difficulties associated with SjD

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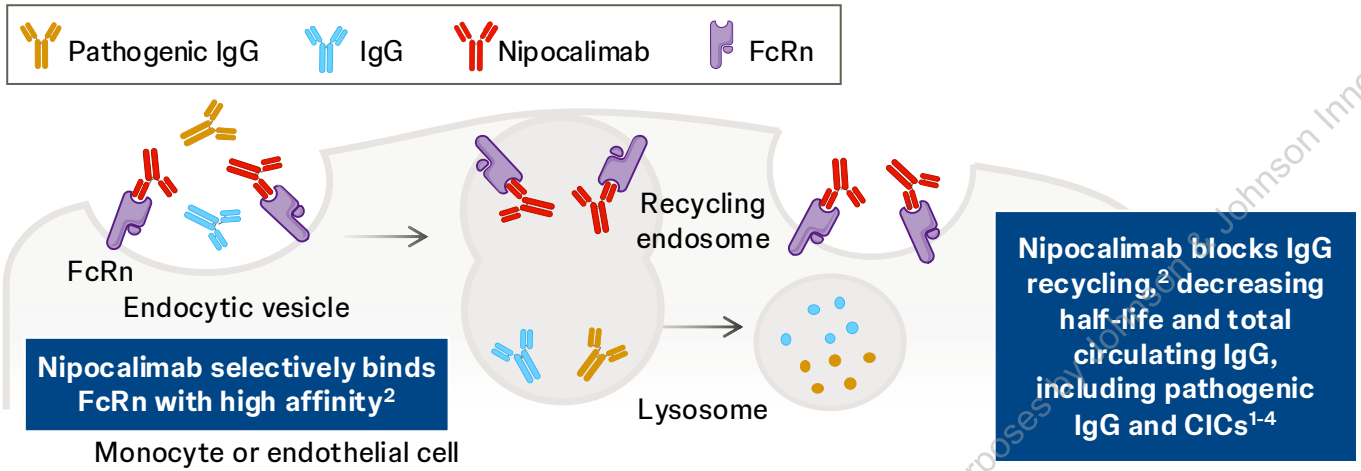
1. Neagu AE, et al. *J Clin Med*. 2026;15(8):2857. **2.** Kolanko M, et al. *J Clin Med*. 2026;15(10):3954. **3.** Jaskólska M, et al. *Rheumatol Int*. 2025;45(2):35. **4.** Mariette X, Criswell LA. *N Engl J Med*. 2018;378(10):931–939.

IgG=immunoglobulin G.

Nipocalimab Lowers IgG Levels and Improves Disease Activity

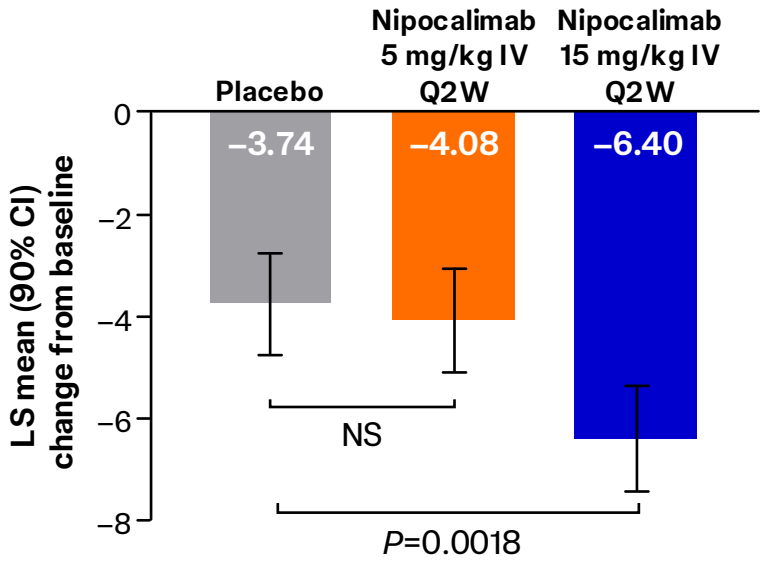
- In the randomized, placebo-controlled, multicenter, double-blind, phase 2 DAHLIAS study of adults with active, autoantibody-positive SjD, nipocalimab significantly improved clinical disease activity, reduced IgG levels, and was generally safe and well tolerated[1]

Nipocalimab Activity:



- Approved for wAIHA in the US, Brazil, and Panama[5]
- Approved for gMG in the US, Brazil, Panama, Japan, Europe, and China[5]

Primary endpoint[1]:
Change from baseline in ClinESSDAI score at Week 24



Objective

To evaluate the efficacy of nipocalimab on cognitive processing speed, psychomotor function, and visual attention in patients with SjD from the DAHLIAS study

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1. Noaiseh G, et al. *Lancet*. 2025;406(10518):2435–2448. **2.** Seth NP, et al. *MAbs*. 2025;17(1):2461191. **3.** Ling LE, et al. *Clin Pharmacol Ther*. 2019;105(4):1031–1039. **4.** Antozzi C, et al. *Neurology*. 2024;102(2):e207937. 5. IMAAVY™ (nipocalimab-aahu) injection, for intravenous use [prescribing information]. Janssen Biotech, Inc.; 2025.

CIC=circulating immune complex, **FcRn**=neonatal crystallizable fragment receptor, **gMg**=generalized myasthenia gravis, **IgG**=immunoglobulin G, **IV**=intravenous, **LS**=least squares, **Q2W**=every 2 weeks, **SjD**=Sjögren's disease, **wAIHA**=warm autoimmune hemolytic anemia.

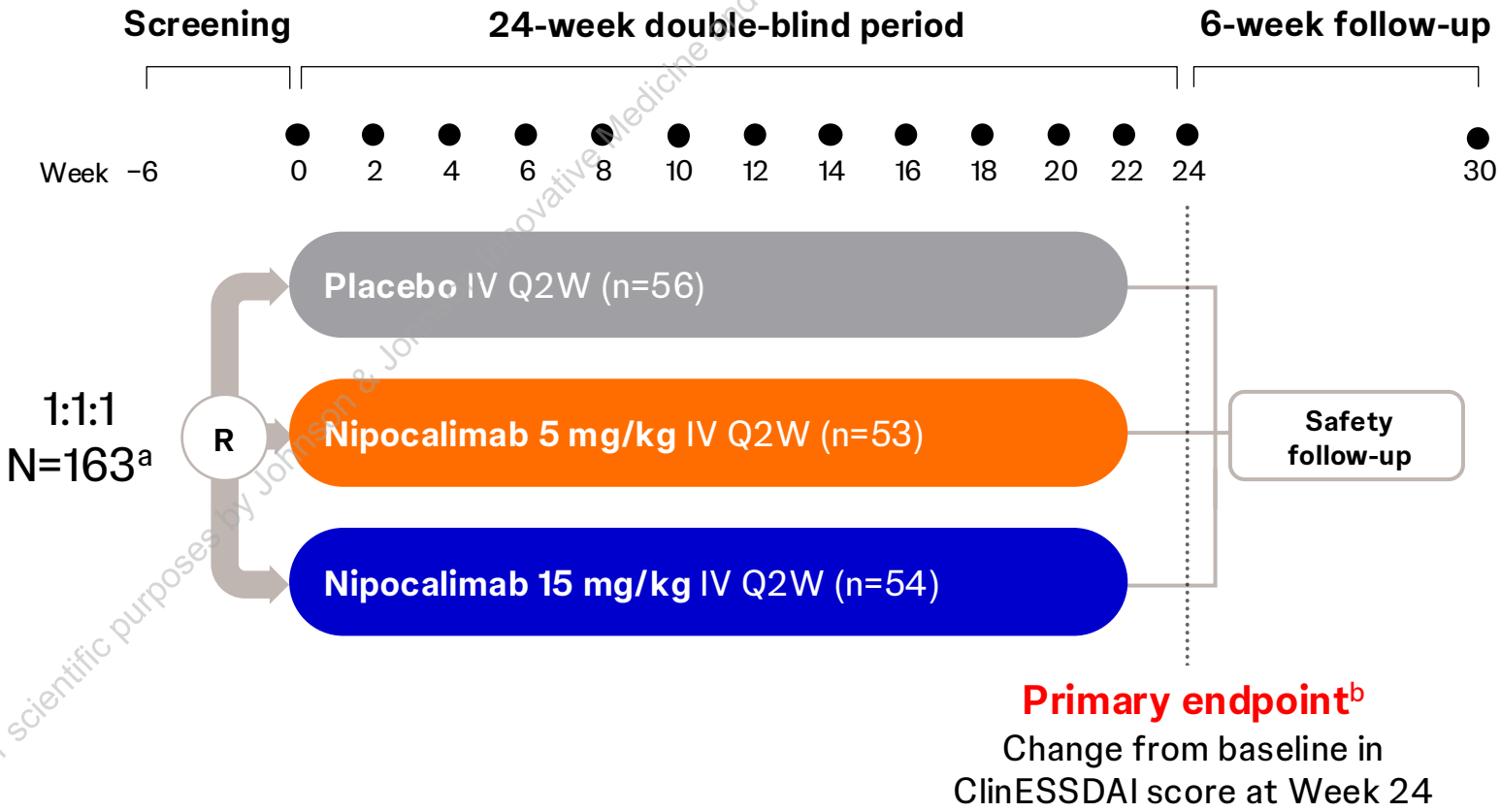
DAHLIAS Study Design

Study population

- Adults aged 18-75 years with moderate-to-severe, active SjD (ClinESSDAI score ≥6) meeting ACR/EULAR 2016 classification criteria
- Seropositive for anti-Ro60 and/or anti-Ro52 IgG autoantibodies

Treatment and evaluation

- Randomized 1:1:1 to placebo, nipocalimab 5 mg/kg or 15 mg/kg administered IV Q2W through Week 22
- Efficacy evaluated through Week 24



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

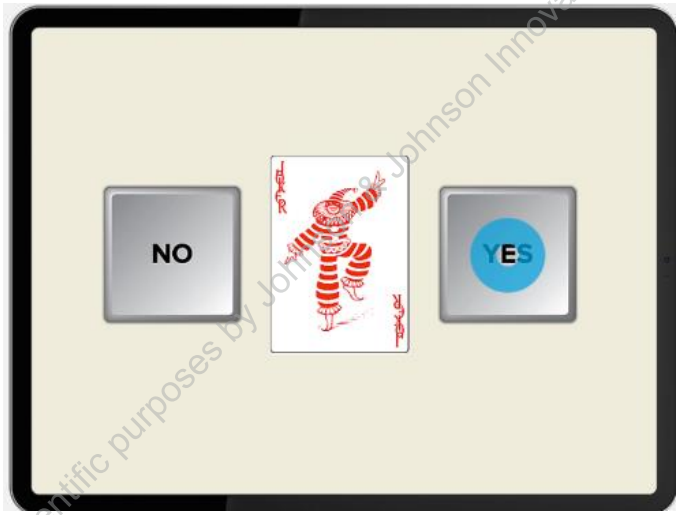
Objective Cognitive Test Examples

Detection Test (psychomotor function)



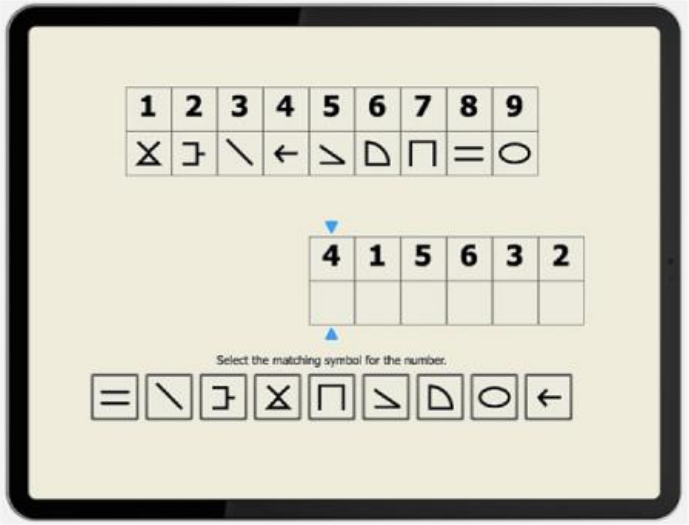
“Has the card turned over?”

Identification Test (attention)



“Is the card red?”

International Digit Symbol Substation Test (executive function)



“Select the symbol that matches the number”

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Assessment of Cognitive Symptoms

Patient-Reported Assessments (screening and Q4W)

- Hospital Anxiety and Depression Scale[1]
- SF-36 (health-related quality-of-life)[2]
- Sjögren's Symptoms questionnaire, fatigue item[3]

Cognitive Performance Assessments (screening and Q2W)

Test	Cognitive domain	Paradigm	Outcome measure	Completion/performance pass criteria	Time for administration
DSST	Cognitive processing speed	Digit-symbol coding	Total number of correct responses	Considered complete if test interval = 2 min; <11 rule-break errors (eg, tapping an invalid area of the screen)	2 min
DET	Psychomotor function	Simple reaction-time	Reaction time (log_{10}-transformed, ms)	Considered complete if ≥27 responses; >75% correct responses	2 min
IDN	Visual attention	Choice reaction-time	Reaction time (log_{10}-transformed, ms)	Considered complete if ≥23 responses; >75% correct responses	2 min

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1. Ravnkilde B, et al. *Scand J Psychol*. 2002;43(3):239–251. **2.** Lee DM, et al. *Pain*. 2010;151(1):30–36. **3.** Noaiseh G, et al. *Lancet*. 2025;406(10518):2435–2448.
DET=detection test, **DSST**=digital symbol substitution test, **IDN**=identification test, **Q2W**=every 2 weeks, **Q4W**=every 4 weeks, **SF-36**=short form-36.

Baseline Characteristics Were Well-Matched Across Treatment Groups

	Placebo (n=56)	Nipocalimab 5 mg/kg Q2W (n=53)	Nipocalimab 15 mg/kg Q2W (n=54)	All randomized patients (N=163)
Age, median (range), y	46.5 (23–73)	49.0 (20–72)	48.5 (24–72)	48.0 (20–73)
Female, %	92.9	92.5	92.6	92.6
White, %	89.3	92.5	90.7	90.8
Time since diagnosis, median (range), y	4.0 (0.6–34.0)	3.7 (0.6–27.9)	4.3 (0.6–18.2)	4.0 (0.6–34.0)
ClinESSDAI score, mean (SD)	10.0 (3.8)	9.4 (3.1)	10.2 (3.6)	9.9 (3.5)
ESSPRI score, mean (SD)	7.0 (1.3)	7.0 (1.3)	7.2 (1.2)	7.1 (1.2)
Total IgG levels,[a] median (range), g/L	14.8 (7.7–40.5)	14.8 (4.6–35.2)	15.5 (7.6–49.6)	14.9 (4.6–49.6)
Autoantibody positivity,[b] %				
Anti-Ro60	98.2	98.1	98.1	98.1
Anti-La	74.5	76.9	64.2	71.9
Anti-Ro52	78.2	86.5	77.4	80.6
RF	78.6	71.7	63.0	71.2

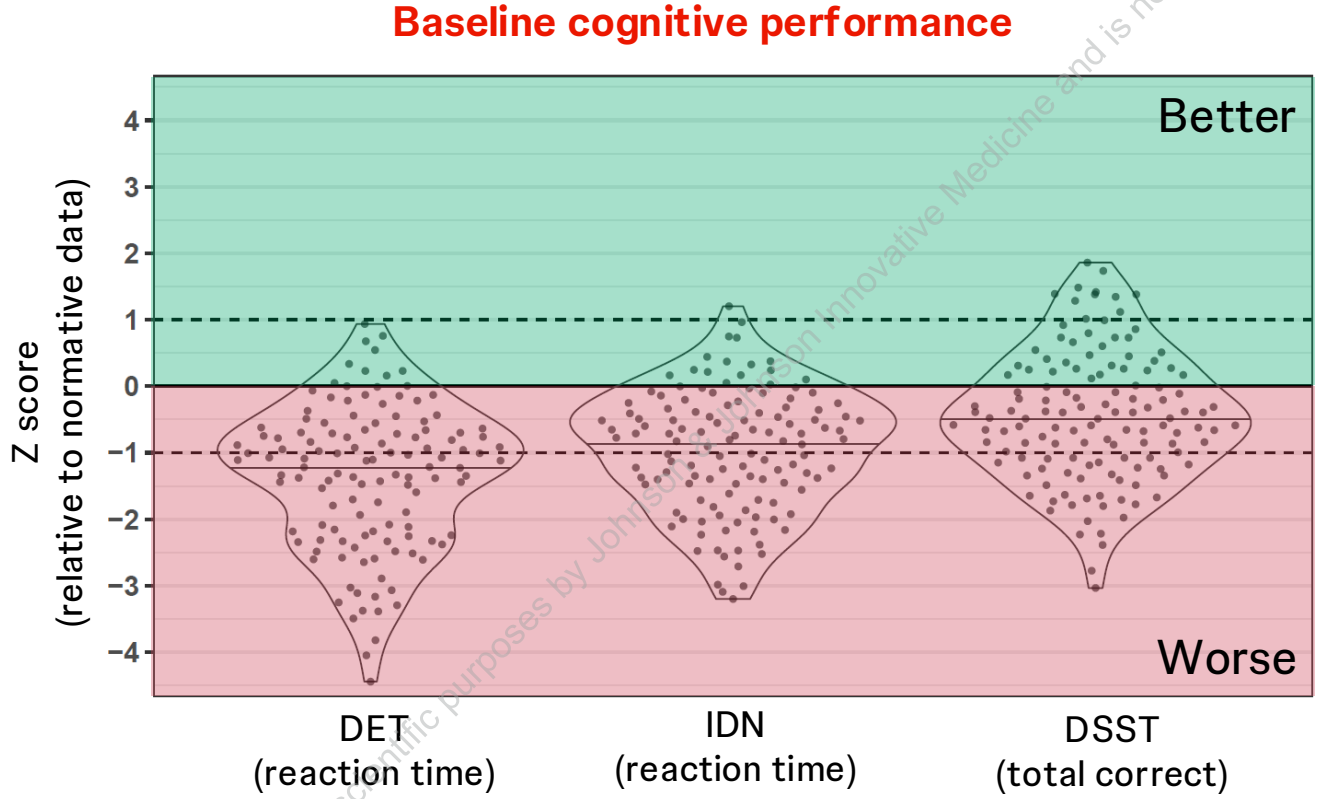
[a]Measured at a central laboratory; reference range: 6.03–16.13 g/L. [b]All patients were seropositive at screening; each treatment group had 1 patient missing baseline values in the anti-Ro autoantibodies dataset.

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

ClinESSDAI=Clinical EULAR Sjögren's Syndrome Disease Activity Index, **EULAR**=European Alliance of Associations for Rheumatology, **ESSPRI**=EULAR Sjögren's Syndrome Patient Reported Index, **IgG**=immunoglobulin G, **Q2W**=every 2 weeks, **RF**=rheumatoid factor, **SD**=standard deviation.

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Subtle Impairment in Attention and Executive Function in SjD at Baseline

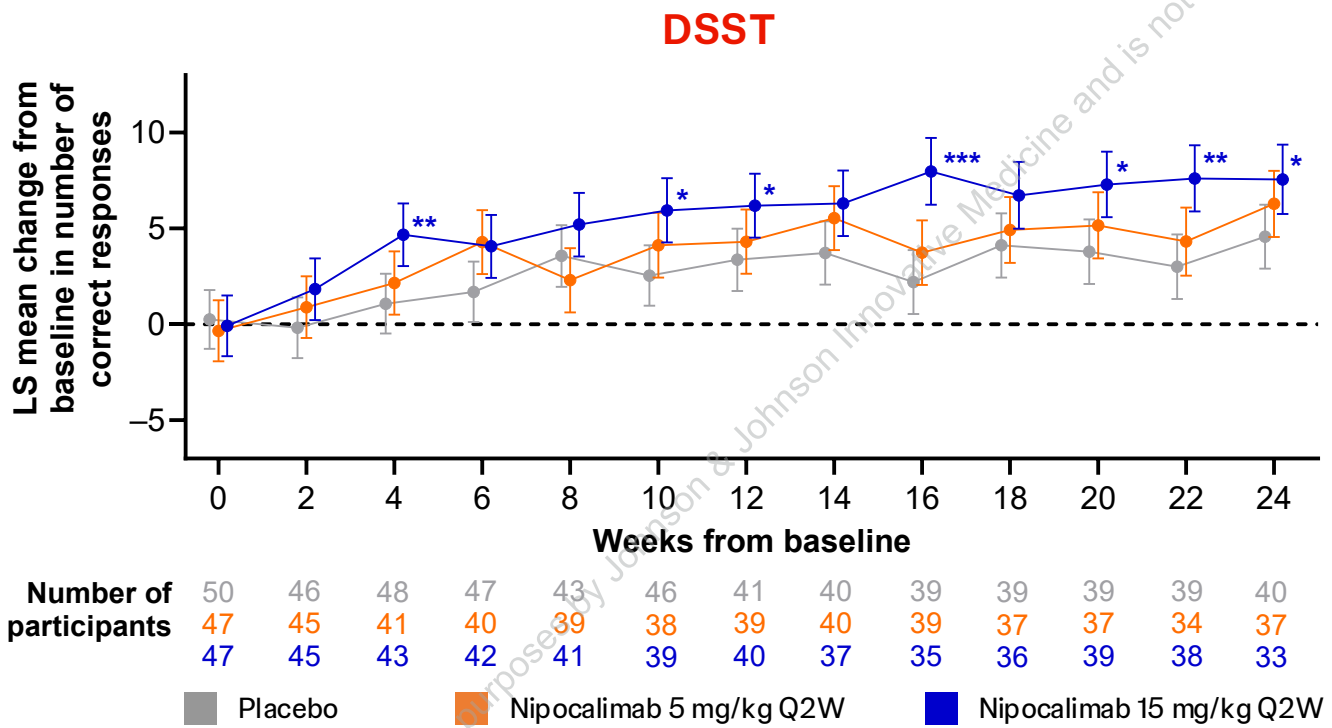


- Participants with SjD tended to have slower reaction times (median, ~1 SD slower) for the DET and IDN tests and fewer correct responses (median, ~0.5 SD fewer) on the DSST than the age and sex-matched normative population

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At baseline, cognitive performance was compared with a cognitively unimpaired age- and sex-matched reference population. 17 patients not shown; normative data unavailable for their age range.
Estimates of minimum meaningful change thresholds (0.5 SD) for DET, IDN, and DSST are 0.03 $\log_{10}$ ms, 0.025 $\log_{10}$ ms, and 5 total correct scores, respectively.
DET=Detection Test, **DSST**=International Digital Symbol Substitution Test – Symbols, **IDN**=Identification Test, **SD**=standard deviation, **SjD**=Sjögren's disease.

Nipocalimab Significantly Improved DSST Performance vs Placebo



Week 24

+7.56 (90% CI: 5.76–9.37)

+4.57 (90% CI: 2.90–6.24)

Δ3.0

d=0.26

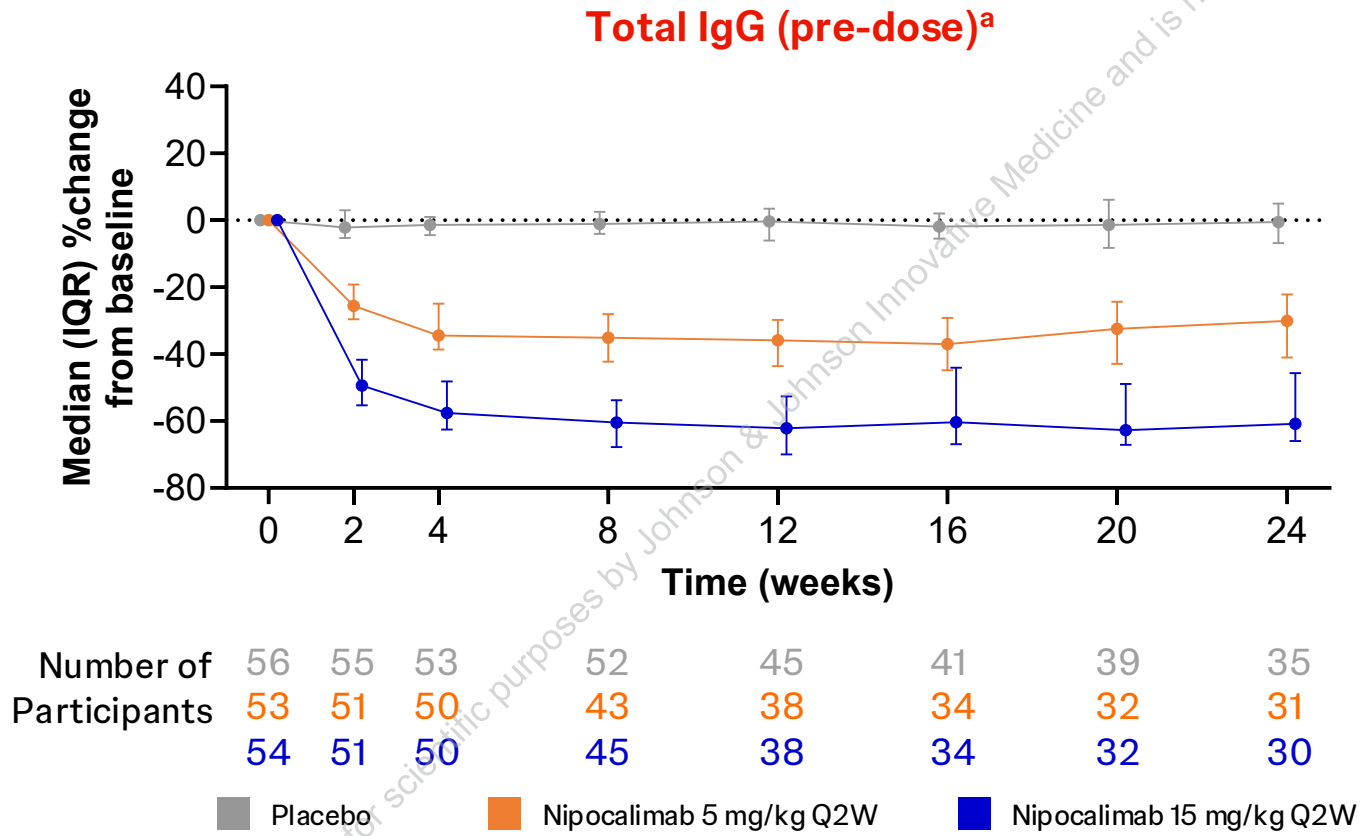
P=0.046

- A statistically significant improvement in the number of correct responses on the DSST was observed in the nipocalimab 15 mg/kg group vs. placebo at Week 24
- This effect remained after adjustment for baseline and change from baseline in depressive symptoms (measured by the HADS-D) and physical health (measured by the SF-36 PCS) (Δ = 3.5, d = 0.31; *P* = 0.018)
- No significant treatment effect was observed for DET (d = –0.15; *P* = 0.34) or IDN (d = –0.11; *P* = 0.49) at Week 24

Points represent LS mean change from baseline in the number of correct responses on the DSST, and error bars represent the 90% CI. Sample size is indicated per treatment group at each time point. Asterisks represent nominally significant P values for the interaction term (Week × Treatment Group) comparing each treatment group to placebo (***P <0.001; **P <0.01; *P <0.05). **CI**=confidence interval, **d**=Cohen's d, **DET**=Detection Test, **DSST**= Digital Symbol Substitution Test, **HADS-D**=Hospital Anxiety and Depression Scale-Depression subscale, **IDN**=identification test, **LS**=least squares, **PCS**=physical component summary, **Q2W**=every 2 weeks.

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Nipocalimab Led to Dose-Dependent Reductions in Total IgG From Weeks 2 to 24

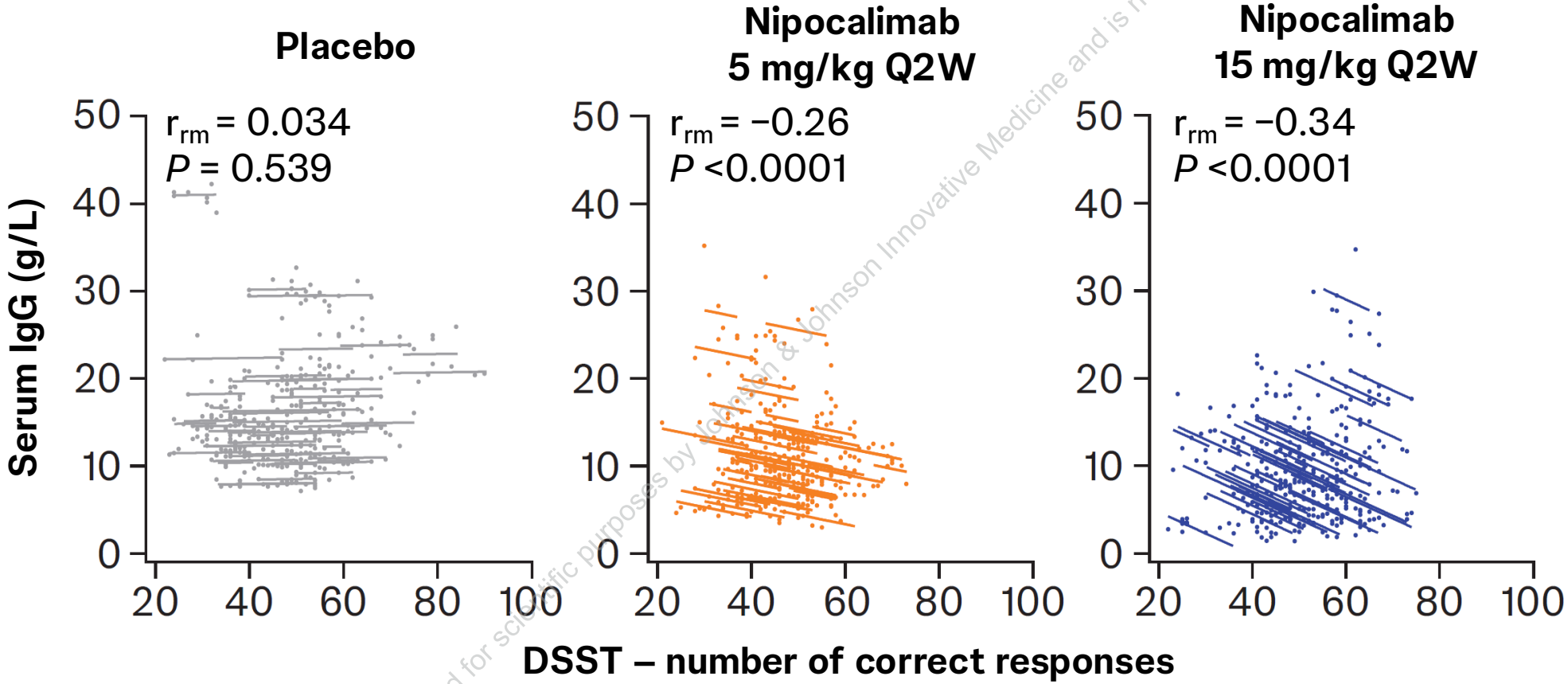


- Nipocalimab treatment also coincided with reductions in baseline anti-Ro60, anti-La, and anti-Ro52 IgG autoantibody levels

[a]IgG was evaluated pre-dose and represents the minimal IgG reduction induced by nipocalimab. PK-PD modeling projects maximal IgG reduction of approximately 77%.
Noaiseh G, et al. *Lancet*. 2025;406(10518):2435-2448.
CI=confidence interval, **IgG**=immunoglobulin G, **IQR**= interquartile range, **PD**=pharmacodynamic, **PK**=pharmacokinetic, **Q2W**=every 2 weeks.

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Improvement in DSST Performance Over 24 Weeks Was Associated with Treatment-Related Reduction in IgG Levels



- Change from baseline DSST score also negatively correlated with patient-reported worst fatigue severity (r_{rm} = –0.26; *P*<0.0001)

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DSST= Digital Symbol Substitution Test, **IgG**=immunoglobulin G, **Q2W**=every 2 weeks.

Key Takeaways

In adults with SjD, 24 weeks of treatment with nipocalimab resulted in objective improvement in DSST performance, a measure of executive function

- ✓ Improvements in executive function were not explained by changes in depressive symptoms, overall physical health, attention, or psychomotor function
- ✓ Improvements in DSST correlated with decreases in IgG levels
- ✓ These findings support further investigation of the potential cognitive benefits of nipocalimab treatment in patients with moderate-to-severely active SjD

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DSST= Digital Symbol Substitution Test, **SjD**=Sjögren's disease.

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