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Nipocalimab for Warm Autoimmune Hemolytic Anemia: Results From the Phase 2/3 Randomized Double-Blind ENERGY Study

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Conflicts of Interest

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Warm Autoimmune Hemolytic Anemia Is a Life-Threatening, Relapsing-Remitting, Autoantibody-Driven Disease

Life-threatening, relapsing-remitting, autoantibody-driven disease¹

- IgG autoantibodies mediate premature destruction of RBCs
- Most patients have severe anemia at onset and ~half require transfusions and hospital admission²

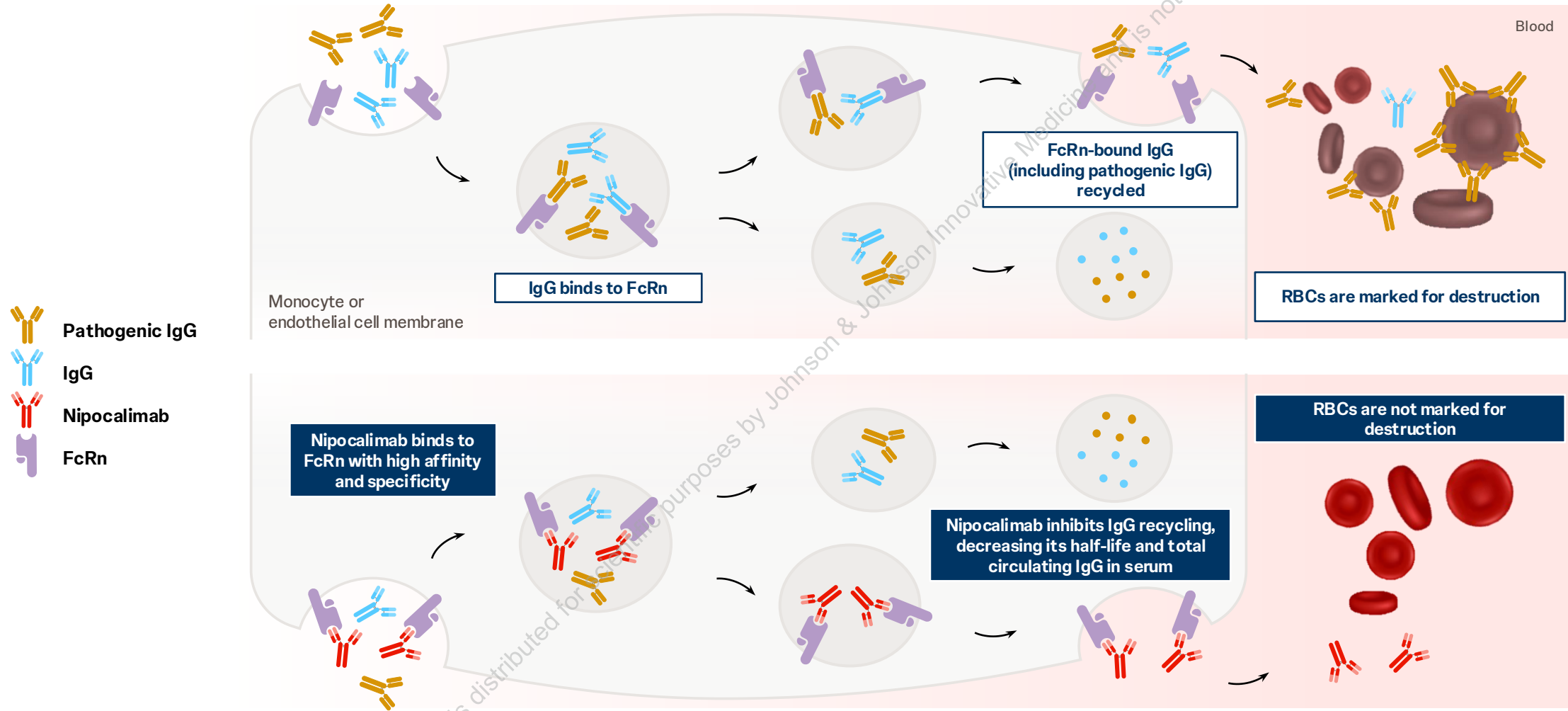
wAIHA results in significant patient burden

- Symptoms include debilitating fatigue
- Main complications include infections and thrombosis³
- 5-year mortality is ~30%⁴

Current management involves off-label broadly immunosuppressive regimens

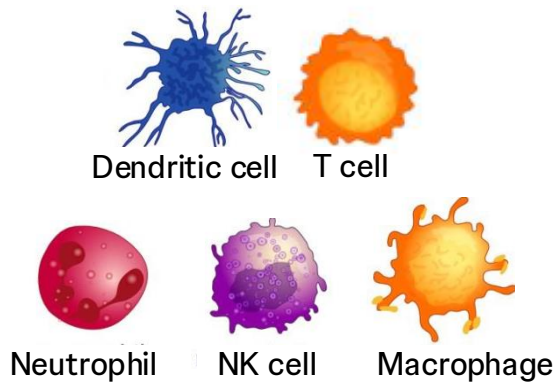
- Current regimens are associated with relapse and AEs
- Corticosteroids: two-thirds of patients relapse or do not respond^{3,5}
- Rituximab: half of patients relapse; 2 to 6 months to induce a response⁶⁻⁷

Nipocalimab Targets FcRn to Reduce Pathogenic Autoantibodies in wAIHA

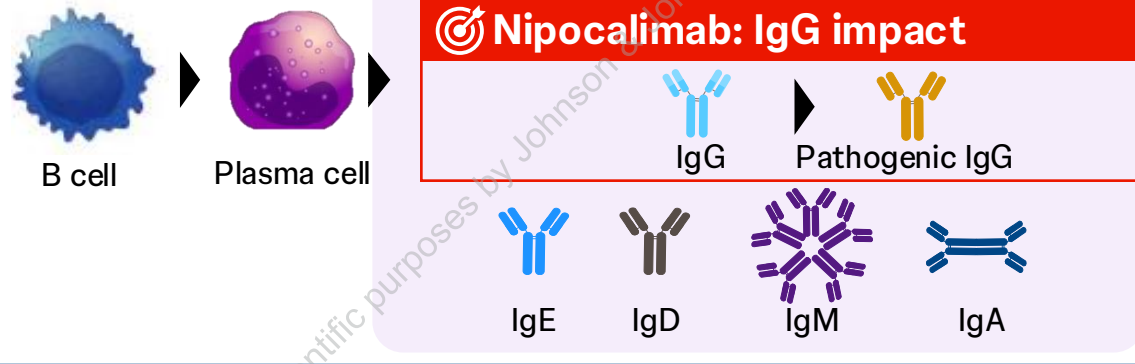


Nipocalimab Lowers IgG, Including Pathogenic Autoantibodies, While Preserving Immune Function¹⁻⁵

Corticosteroid and immunosuppressants: broad impact



B-cell depleters: B-cell impact



In wAIHA, nipocalimab lowers anti-RBC pathogenic antibodies and has the potential of decreasing hemolysis and increasing hemoglobin

1. Challa DK, et al. *Curr Top Microbiol Immunol*. 2014;382:249-272. 2. Ling LE, et al. *Clin Pharmacol Ther*. 2019;105(4):1031-1039. 3. Seth NP, et al. *Mabs*. 2025;17(1):2461191. 4. Yu F, et al. *Hum Vaccin Immunother*. 2026;22(1):2664331. 5. Cossu M, et al. *Hum Vaccin Immunother*. 2025;21(1):2491269.

FcRn=neonatal Fc receptor, IgG=immunoglobulin G, NK=natural killer, RBC=red blood cell, wAIHA=warm autoimmune hemolytic anemia.

ENERGY Phase 2/3 Study Design



Objective

- Evaluate the safety and efficacy of nipocalimab versus placebo for the treatment of wAIHA



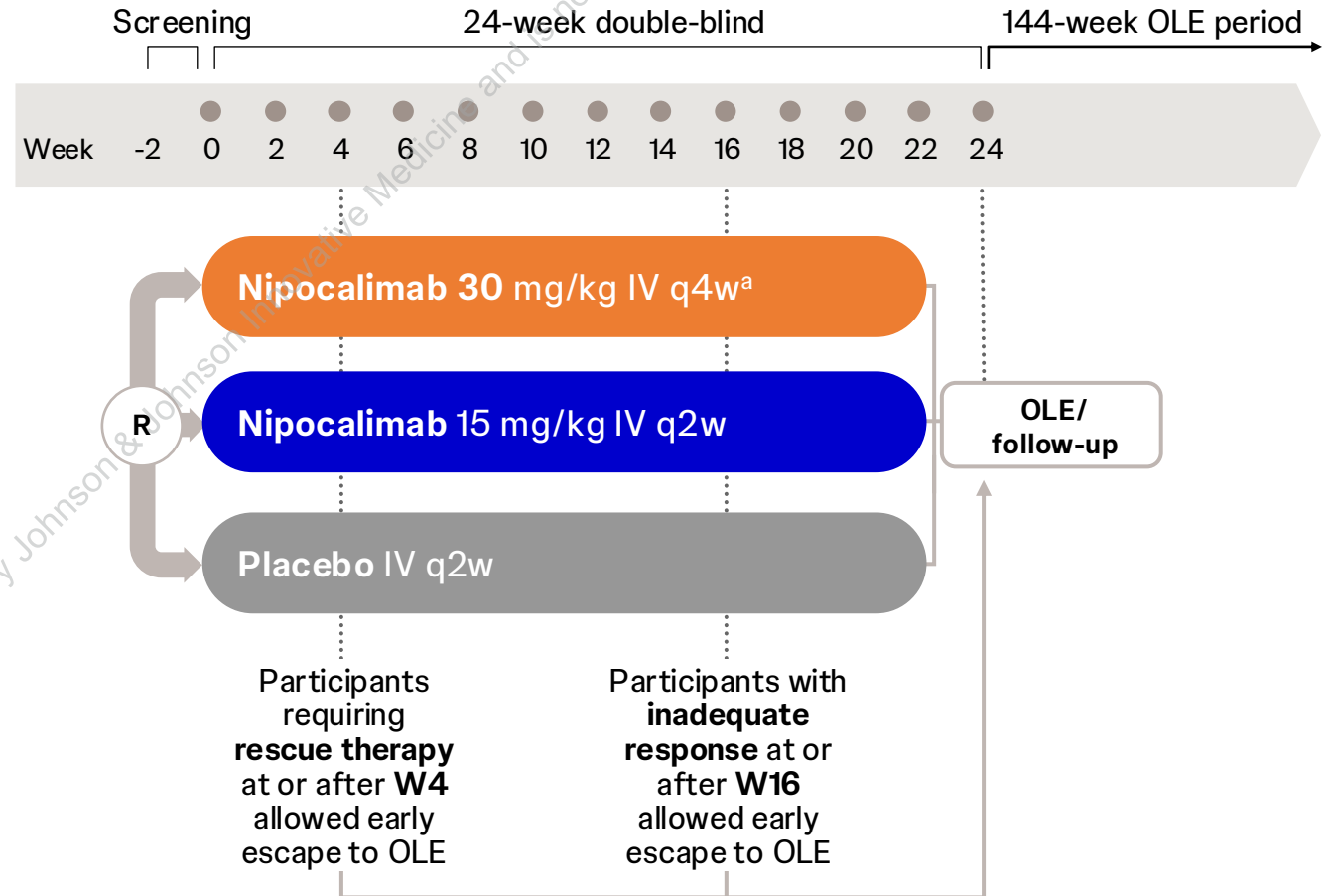
Participants

- ≥18 years of age
- Primary or secondary wAIHA (for ≥3 months)
- Current or previous treatment
- Hgb <10 g/dL
- Positive DAT (IgG or IgG+C3d)
- Evidence of hemolysis



Background treatment

- Stable doses of corticosteroids and/or immunosuppressants allowed
- Those on corticosteroids meeting the primary endpoint are required to taper corticosteroids by 10% q2w



Study Endpoints

Primary Endpoint: Durable Hemoglobin Response

- Hgb ≥ 10 g/dL **AND**
- Hgb increase ≥ 2 g/dL from baseline **AND**
- For 3 consecutive visits (≥ 28 days) **AND**
- Starting by Week 16 **AND**
- Without rescue therapy or dose modification of ongoing stable background treatment for wAIHA, including any increase in oral corticosteroids

Key Secondary Endpoints

- Improvement in FACIT-Fatigue (Week 24)
- Corticosteroid dose reduction (Week 24; % reduction in daily corticosteroid dose^a)

^aPrednisone equivalent.

FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy – Fatigue, Hgb=hemoglobin, wAIHA=warm autoimmune hemolytic anemia.

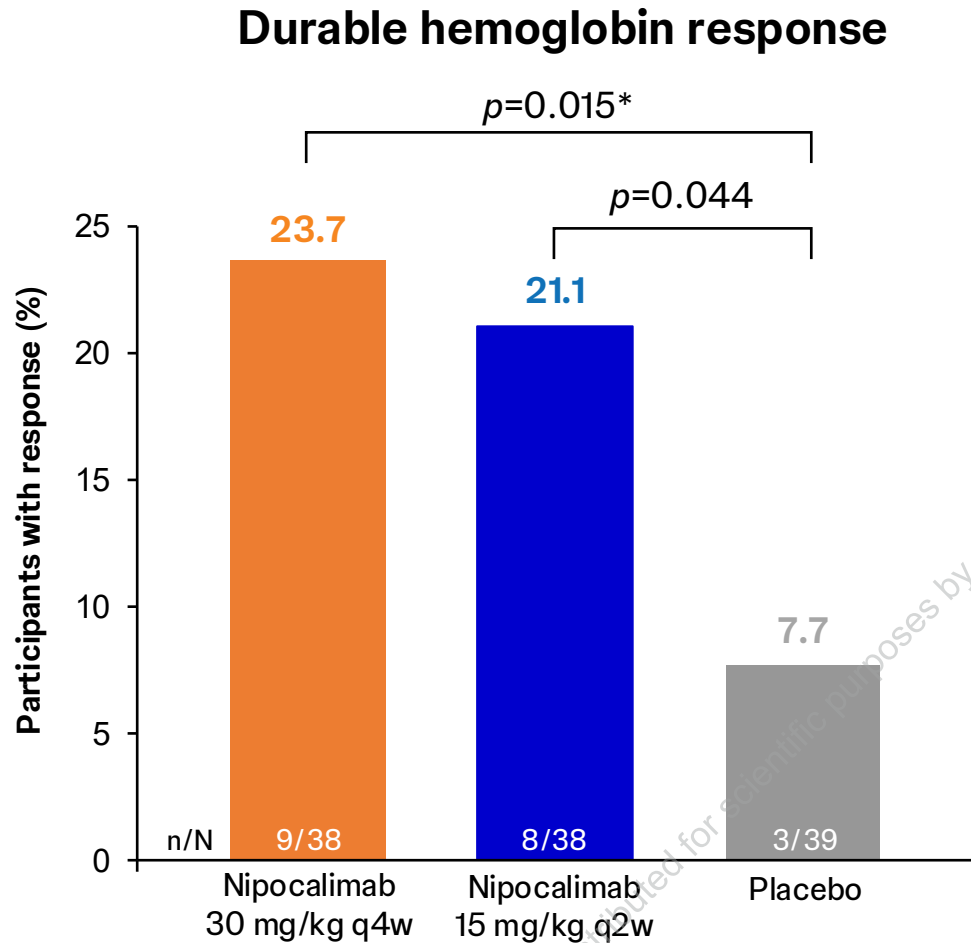
Baseline Characteristics Were Consistent With the wAIHA Patient Population

Baseline characteristics	Nipocalimab 30 mg/kg q4w (n=38)	Nipocalimab 15 mg/kg q2w (n=38)	Placebo (n=39)
Mean age (range), years	56.1 (24-79)	53.1 (18-80)	59.9 (24-86)
Female	55%	58%	51%
Primary wAIHA ^a	92%	87%	82%
Median (IQR) time since diagnosis, months	32 (20-60)	44 (21-81)	23 (17-71)
Mean (SD) baseline hemoglobin, g/dL	9.2 (1.4)	8.6 (1.3)	9.0 (1.4)
Mean (SD) FACIT-Fatigue score	34.5 (10.7)	35.0 (10.5)	31.1 (12.2)
Current treatments for wAIHA (%)			
Any concomitant CS	74%	87%	77%
IST or CS at >20 mg/day of prednisone or equivalent ^a	45%	39%	46%
Prior treatments for wAIHA (%)			
Prior rituximab use	42%	55%	49%
Prior transfusions	58%	58%	59%
Prior splenectomy	3%	16%	10%

^aStratification factors (primary or versus secondary wAIHA; screening hemoglobin \leq 8.5 g/dL or versus $>$ 8.5 g/dL; no treatment or corticosteroids at dose \leq 20 mg/day of prednisone or equivalent with no immunosuppressants versus immunosuppressants or corticosteroids at $>$ 20 mg/day of prednisone or equivalent or no such treatment).

CS=corticosteroids, FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy – Fatigue, IQR=interquartile range, IST=immunosuppressive therapy, q2w=every 2 weeks, q4w=every 4 weeks, SD=standard deviation, wAIHA=warm autoimmune hemolytic anemia.

Nipocalimab 30 mg/kg q4w Significantly Improved Durable Hemoglobin Response Versus Placebo (Primary Endpoint)



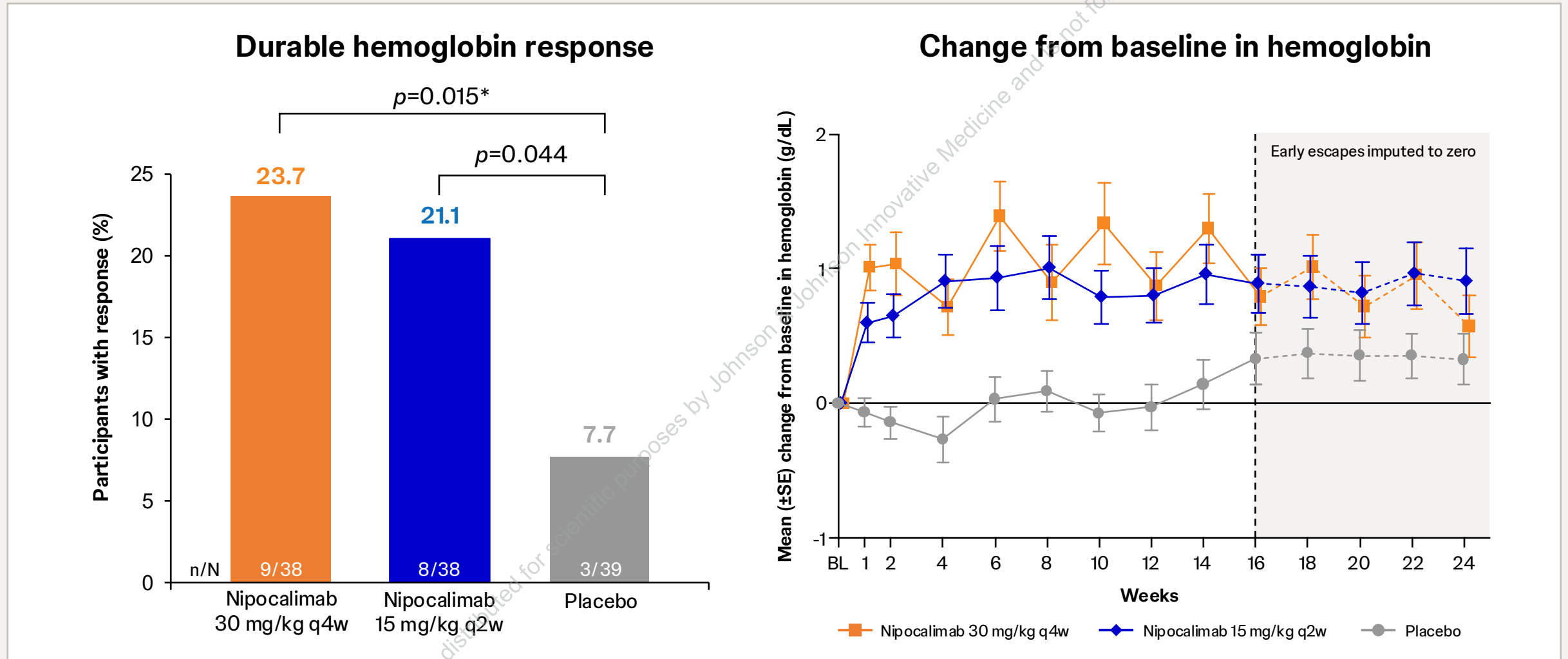
Durable hemoglobin response defined as:

- Hgb ≥ 10 g/dL **AND**
- Hgb increase ≥ 2 g/dL from baseline **AND**
- For 3 consecutive visits (≥ 28 days) **AND**
- Starting by Week 16 **AND**
- Without rescue therapy or dose modification of ongoing stable background treatment for wAIHA, including any increase in oral corticosteroids

Composite analysis strategy (participants with intercurrent events [including any use of rescue therapies or initiation or dose increase of protocol-specified standard-of-care background therapy] were considered to be nonresponders). *P* values based on equal-weight approach to control the family-wise type I error rate.

*One-sided $p < 0.02499$ versus placebo considered significant.

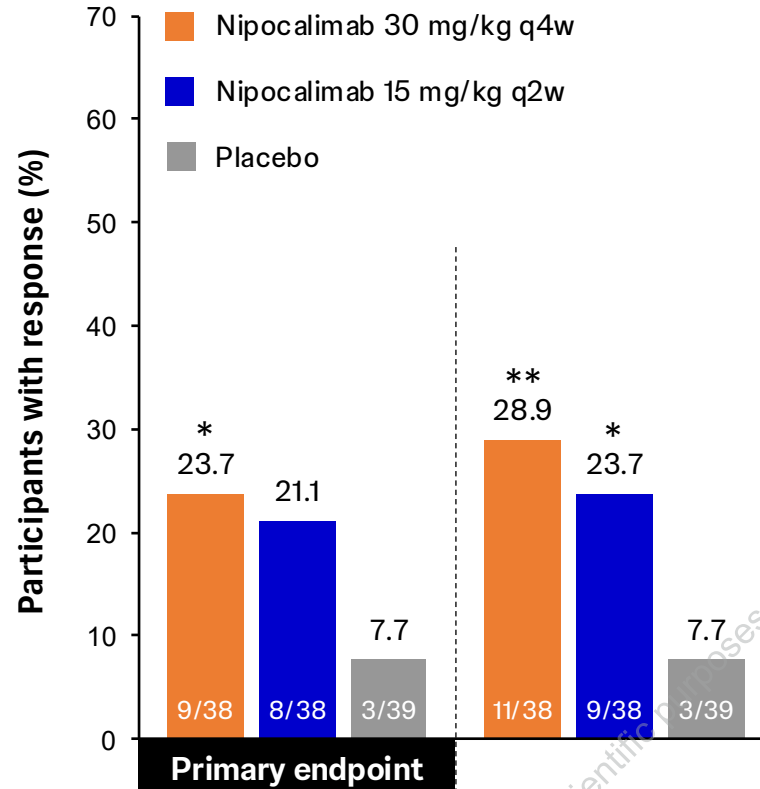
Hemoglobin Improved by Week 1 and Was Maintained Through Week 24 in Nipocalimab Treatment Groups



Composite analysis strategy (participants with intercurrent events [including any use of rescue therapies or initiation or dose increase of protocol-specified standard-of-care background therapy] were considered to be nonresponders). *P* values based on equal-weight approach to control the family-wise type I error rate.

*One-sided *p*<0.02499 versus placebo considered significant.

Prespecified Primary Endpoint Analyses Support Durable Hemoglobin Response

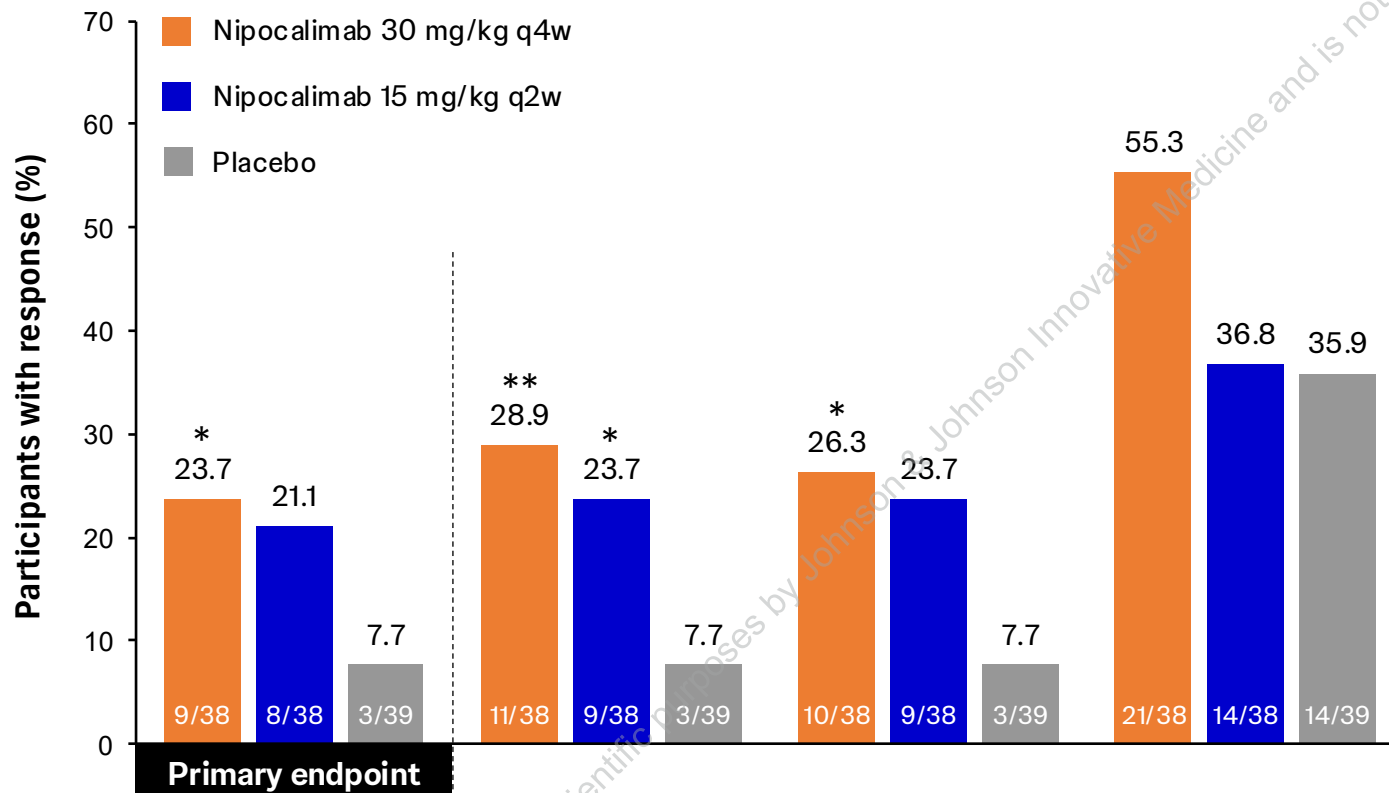


Hgb ≥ 10 g/dL	✓	✓
Hgb increase ≥ 2 g/dL	✓	✓
Consecutive visits	≥ 3	≥ 3
Achieved by	Week 16	Week 24

Except for the primary endpoint, all p values are nominal. Composite analysis strategy (participants with intercurrent events [including any use of rescue therapies or initiation or dose increase of protocol-specified standard-of-care background therapy] were considered to be nonresponders).

* $p < 0.02499$, ** $p < 0.01$, *** $p < 0.001$ versus placebo.

Prespecified Primary Endpoint Analyses Support Durable Hemoglobin Response

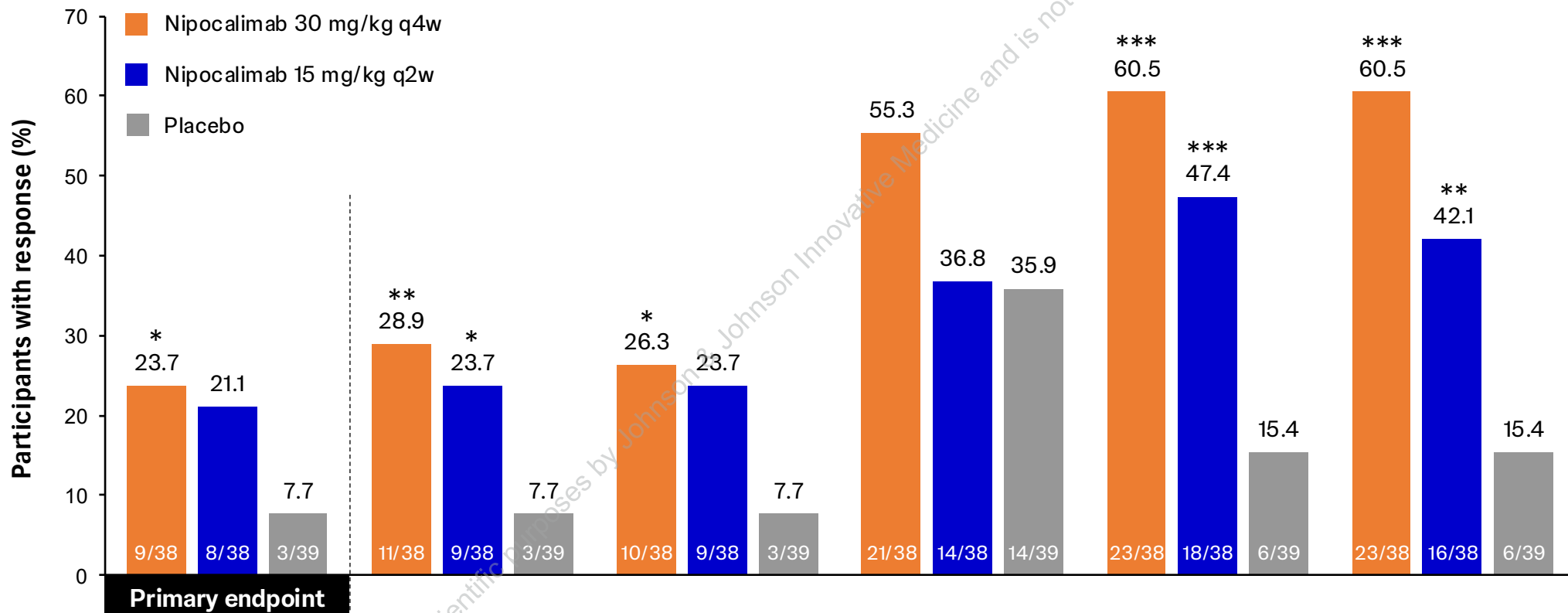


Hgb ≥ 10 g/dL	✓	✓	-	✓
Hgb increase ≥ 2 g/dL	✓	✓	✓	-
Consecutive visits	≥ 3	≥ 3	≥ 3	≥ 3
Achieved by	Week 16	Week 24	Week 16	Week 16

Except for the primary endpoint, all p values are nominal. Composite analysis strategy (participants with intercurrent events [including any use of rescue therapies or initiation or dose increase of protocol-specified standard-of-care background therapy] were considered to be nonresponders).

* $p < 0.02499$, ** $p < 0.01$, *** $p < 0.001$ versus placebo.

Prespecified Primary Endpoint Analyses Support Durable Hemoglobin Response



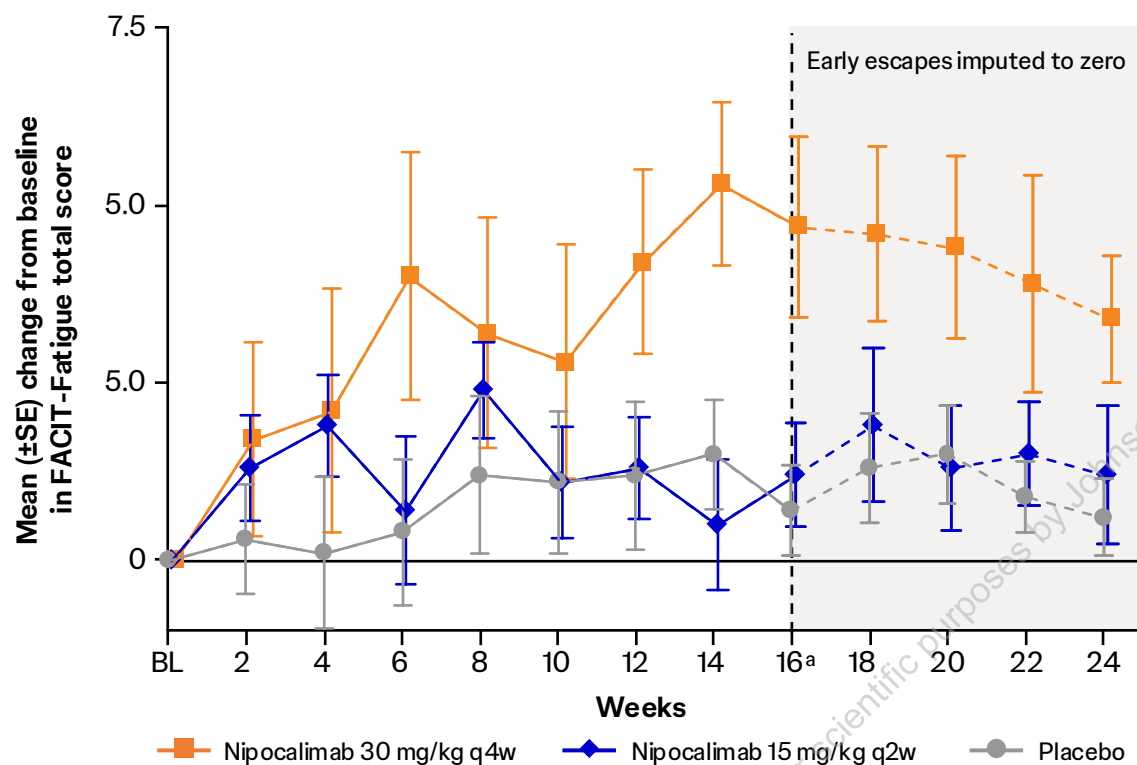
Hgb ≥ 10 g/dL	✓	✓	-	✓	-	✓
Hgb increase ≥ 2 g/dL	✓	✓	✓	-	✓	✓
Consecutive visits	≥ 3	≥ 3	≥ 3	≥ 3	≥ 1	≥ 1
Achieved by	Week 16	Week 24	Week 16	Week 16	Week 24	Week 24

Except for the primary endpoint, all p values are nominal. Composite analysis strategy (participants with intercurrent events [including any use of rescue therapies or initiation or dose increase of protocol-specified standard-of-care background therapy] were considered to be nonresponders).

* $p < 0.02499$, ** $p < 0.01$, *** $p < 0.001$ versus placebo.

Improvements in Secondary Outcomes: FACIT-Fatigue and Steroid Reduction

FACIT-Fatigue total score change from baseline



Fatigue reduction from baseline to Week 24 was nominally significant for nipocalimab 30 mg/kg q4w ($p=0.007$) versus placebo

Reduction in average daily dose of corticosteroids^a at Week 24

	Nipocalimab 30 mg/kg q4w (n=38)	Nipocalimab 15 mg/kg q2w (n=38)	Placebo (n=39)
Patients taking corticosteroids at baseline, n	26	32	28
Mean change from baseline, mg (SD)	-3.7 (8.3)	-2.5 (6.8)	-0.7 (2.7)
Mean change from baseline, % (SD)	-15.1 (28.24)	-14.0 (30.42)	-3.9 (16.33)
One-sided <i>p</i> value (based on LS means on ranks)	0.039	0.055	-

More participants experienced corticosteroid reductions at Week 24 with nipocalimab versus placebo

All *p* values are nominal, based on an equal-weight approach to control the family-wise type I error rate. Composite analysis strategy (participants with intercurrent events [including any use of rescue therapies or initiation or dose increase of protocol-specified standard-of-care background therapy] were considered to be nonresponders).

^aParticipants meeting failure criteria (ie, presence of symptoms and failure to demonstrate ≥ 1 g/dL hemoglobin increase) at or after Week 16 were, at the investigator's discretion, allowed discontinuation of double-blinded treatment and early escape to the OLE.

BL=baseline, FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy – Fatigue, LS=least squares, OLE=open-label extension, q2w=every 2 weeks, q4w=every 4 weeks, SD=standard deviation, SE=standard error.

Safety Was Consistent With the Known Safety Profile of Nipocalimab and the Known Clinical Risks Associated With wAIHA

AE, n (%)	Nipocalimab 30 mg/kg q4w (n=38)	Nipocalimab 15 mg/kg q2w (n=37) ^a	Placebo (n=39)
TEAEs	35 (92.1)	30 (81.1)	35 (89.7)
SAEs	8 (21.1)	6 (16.2)	14 (35.9)
AEs leading to discontinuation	2 (5.3)	5 (13.5)	1 (2.6)
AEs of interest			
Grade ≥3 infections	2 (5.3)	3 (8.1)	5 (12.8)
Adjudicated MACE	0	2 (5.4)	0
Adjudicated VTE (DVT and/or PE)	1 (2.6)	0	0
Hypoalbuminemia (albumin <20 g/L)	0	0	0
Death	0	2 (5.4)	0

- The majority of TEAEs were grade 2 or 3
- The most common AEs (≥10%) among all participants in the combined nipocalimab group were wAIHA (37.2%), diarrhea (11.5%), and fatigue and pyrexia (both 10.3%); the most common AEs among participants in the placebo group were wAIHA (51.3%) and COVID-19 and nasopharyngitis (both 10.3%)
- No participant experienced hypogammaglobulinemia (total IgG <1 g/L for 2 consecutive visits)
- By preferred term, no TEAE leading to discontinuation was reported in more than 1 participant
- Two cases of MACE occurred in participants with complex medical histories in the nipocalimab 15 mg/kg q2w group, later leading to death (causes of death were not related to study treatment)

^aOne patient was randomized to nipocalimab 15 mg/kg q2w, but did not receive nipocalimab.

AE=adverse event, DVT=deep vein thrombosis, IgG=immunoglobulin G, MACE=major adverse cardiovascular event, PE=pulmonary embolism, q2w=every 2 weeks, q4w=every 4 weeks, SAE=serious adverse event, TEAE=treatment emergent adverse event, wAIHA=warm autoimmune hemolytic anemia, VTE=venous thromboembolism.

Conclusions



Nipocalimab, an FcRn blocker that can selectively lower IgG including pathogenic autoantibodies, demonstrated consistent and clinically meaningful benefits across multiple endpoints

✓ Durable hemoglobin response

Nipocalimab 30 mg/kg q4w showed a significant durable hemoglobin response and favorable responses in prespecified supporting hemoglobin measures

✓ Rapid, maintained improvement in hemoglobin

Hemoglobin increase was rapid, with 1 g/dL improvement observed at Week 1 and maintained over 24 weeks

✓ Fatigue improvement

For nipocalimab 30 mg/kg q4w, improvements in fatigue were evident as early as Week 2 and maintained through Week 24

✓ Consistent, well-tolerated safety

- Nipocalimab was generally well tolerated with no new safety signals identified
- Occurrence of grade ≥ 3 infections were no higher than placebo, and no hypogammaglobulinemia was observed

Additional Nipocalimab Presentations at EHA 2026

Assessment of Nipocalimab Effects on Fatigue in Warm Autoimmune Hemolytic Anemia: Results From the Double-Blind Phase 2/3 ENERGY Trial

Nipocalimab demonstrated a benefit in multiple endpoints measuring debilitating fatigue; improvements in fatigue were not strongly correlated with hemoglobin levels

Oral session: Fri 12 June, 17:15-18:30, A9 Hall S325 (Murakhovskaya I, et al.)



Pharmacodynamic Effect of Nipocalimab in Warm Autoimmune Hemolytic Anemia (wAIHA) and Correlation With Clinical Improvement

Consistent with the expected MOA, a close relationship between IgG and anti-RBC autoantibody lowering and improvement in hemoglobin and decreased hemolysis was observed

Poster session I: Fri 12 June, 18:45-19:45, Hall A PF1297 (Ueda Y, et al.)



Acknowledgments

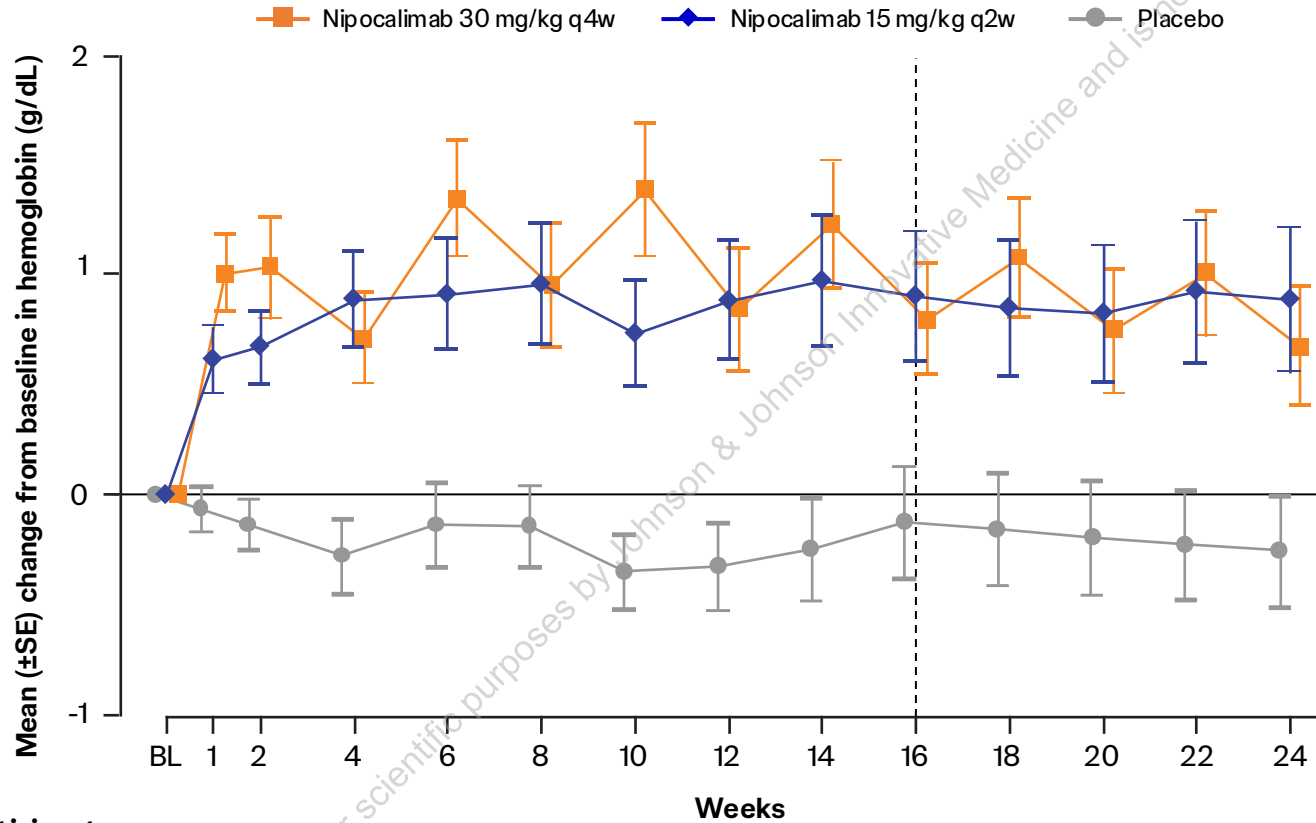
We thank patients who participated in the trial and their families and caregivers, as well as investigators and staff who cared for patients and supported this trial.

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Backups

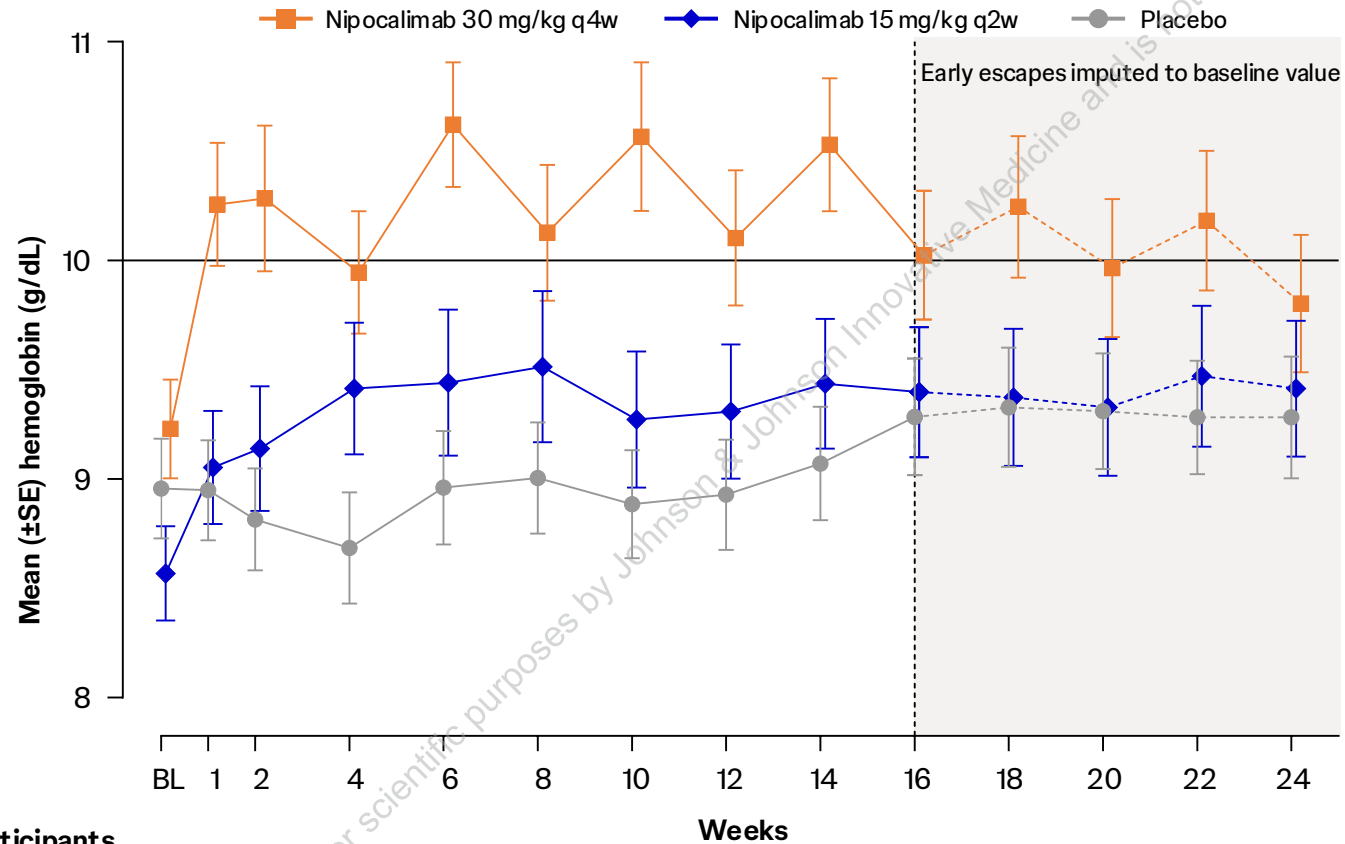
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Mean Hemoglobin Change From Baseline (Last Observation Carried Forward)



Participants	BL	1	2	4	6	8	10	12	14	16	18	20	22	24
Nipocalimab 30 mg/kg IV q4w	38	37	37	38	38	38	38	38	38	38	38	37	38	38
Nipocalimab 15 mg/kg IV q2w	38	33	35	36	36	36	35	36	35	36	36	36	36	36
Placebo	39	35	39	38	38	38	39	39	38	38	39	39	38	39

Absolute Hemoglobin Levels Over Time



Participants	BL	1	2	4	6	8	10	12	14	16	18	20	22	24
Nipocalimab 30 mg/kg IV q4w	38	37	37	38	38	38	38	38	38	38	38	37	38	38
Nipocalimab 15 mg/kg IV q2w	38	34	36	37	37	37	36	37	36	37	37	37	37	37
Placebo	39	35	39	38	38	38	39	39	38	38	39	39	38	39