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

Irina Murakhovskaya,[1,*] Bruno Fattizzo,[2,3] Yasutaka Ueda,[4] Kayla Scippa,[5] Michael Zelasky,[6] Cathye Shu[6], Sheryl Pease[5]

[1]Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY, USA; [2]Hematology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [3]Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy; [4]The University of Osaka, Suita, Osaka, Japan; [5]Johnson & Johnson, Raritan, NJ, USA; [6]Johnson & Johnson, Spring House, PA, USA

*Presenting author

This presentation was sponsored by Johnson & Johnson.
Presented at the European Hematology Association (EHA) Congress; June 11–14, 2026; Stockholm, Sweden

Conflicts of Interest

- This study and presentation were sponsored by Johnson & Johnson
- Medical writing support was provided by Chan Yoon, PharmD, of Lumanity Communications Inc., under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med*. 2022;175:1298-1304)
- **IM** received research funding from Alexion, Bioverativ, Sanofi, Annexon, Incyte, Kezar, Principia, Rigel, and Novartis; and served in a consulting role for Alexion, Alpine/Vertex, Apellis, Janssen, Novartis, Sanofi, and Recordati. **BF** received honoraria for service on a consultancy/advisory board from Alexion, Johnson & Johnson, Novartis, Recordati, Roche, and Sobi. **YU** received honoraria from Alexion, Chugai, Incyte, Kaken, Nippon Shinyaku, Novartis, Recordati, Sanofi, and Sobi; received consultancy fees from Alexion, Asahi Kasei, Chugai, Janssen, Johnson & Johnson, Novartis, Ono, Recordati, Sanofi, and Sobi; received research funding from Chugai; and serves as an editor for the *International Journal of Hematology*. **KS, MZ, CS,** and **SP** are employees of and may hold stock in Johnson & Johnson

Warm Autoimmune Hemolytic Anemia Is a Life-Threatening, Relapsing-Remitting, Autoantibody-Driven Disease Associated with Debilitating Fatigue

Life-threatening, relapsing-remitting, autoantibody-driven disease[1-3]

- IgG autoantibodies mediate premature destruction of RBCs
- wAIHA presents significant risk of comorbidities such as VTE, MACE, and serious infections
- Current management involves off-label broadly immunosuppressive regimens that are associated with AEs and relapse

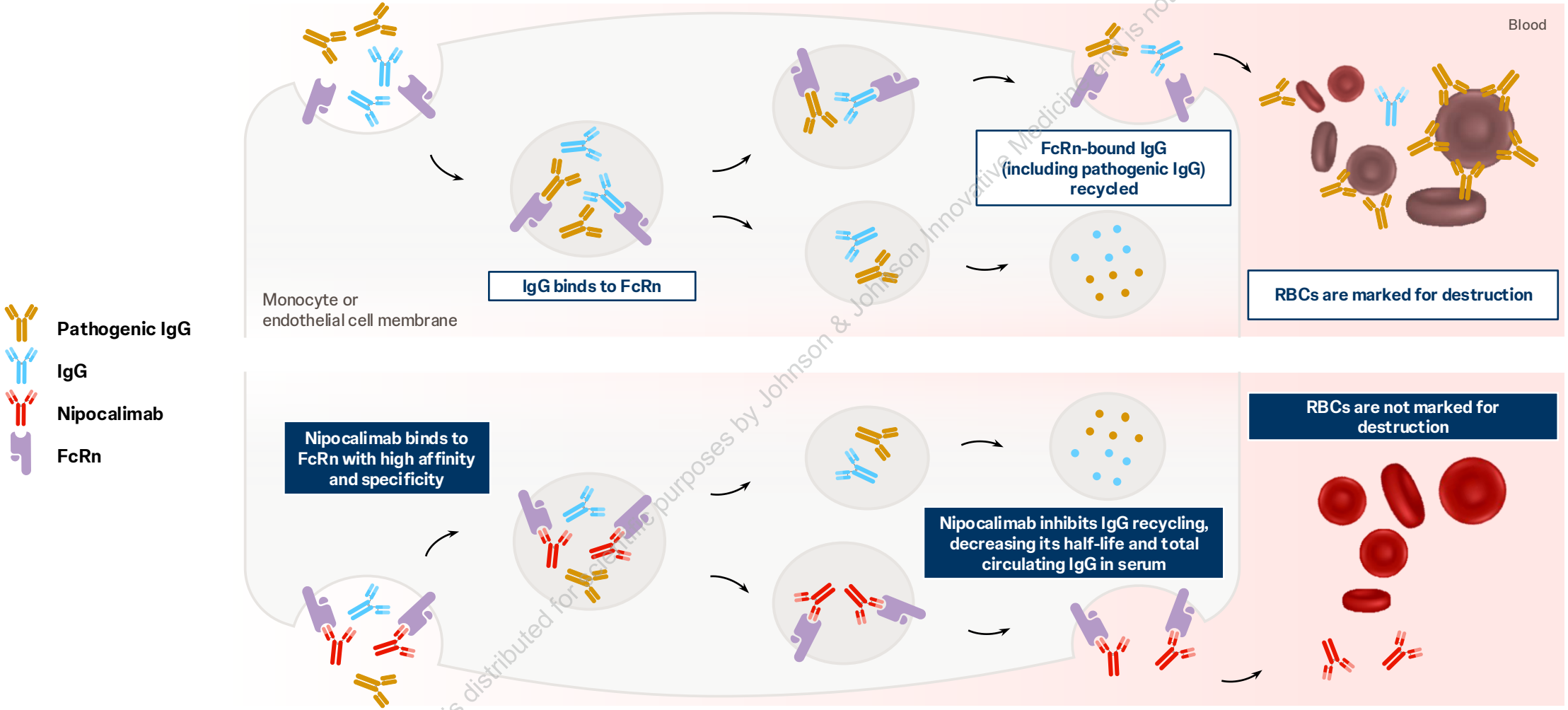
Fatigue is the primary patient-reported symptom of wAIHA[4,5]

- **Fatigue** is identified as the most debilitating symptom by patients with wAIHA, requiring frequent rest during the day and limiting their capacity to function
- Additional symptoms include dizziness, weakness, and shortness of breath
- wAIHA symptoms impact nearly all domains of HRQoL, including daily activities, work, social life, and emotional well-being
- Patients report frustration, anxiety, and fear as consequences of not knowing when they might experience a relapse

1. Barcellini W. *Transfus Med Hemother*. 2015;42(5):287-293. 2. Brodsky RA. *N Engl J Med*. 2019;381(7):647-654. 3. Kuter DJ. *Hematology Am Soc Hematol Educ Program*. 2022;2022(1):105-113. 4. Shukla A, et al. *Orphanet J Rare Dis*. 2025;20(1):403. 5. Pease S, et al. *J Patient Rep Outcomes*. 2025;9(1):97.

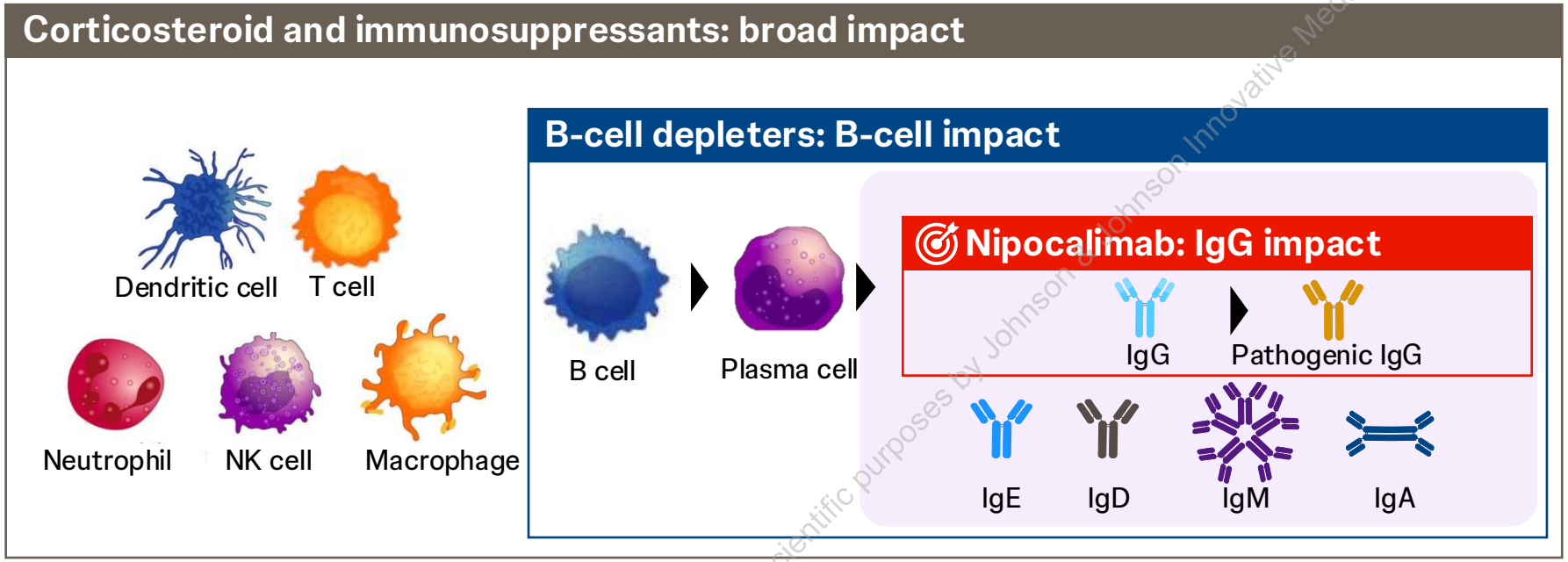
AE=adverse event, **HRQoL**=health-related quality of life, **IgG**=immunoglobulin G, **MACE**=major adverse cardiovascular event, **RBC**=red blood cell, **VTE**=venous thromboembolism, **wAIHA**=warm autoimmune hemolytic anemia.

Nipocalimab Targets FcRn to Reduce Pathogenic Autoantibodies in wAIHA



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

Nipocalimab Lowers IgG, Including Pathogenic Autoantibodies, While Preserving Immune Function[1-5]



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.

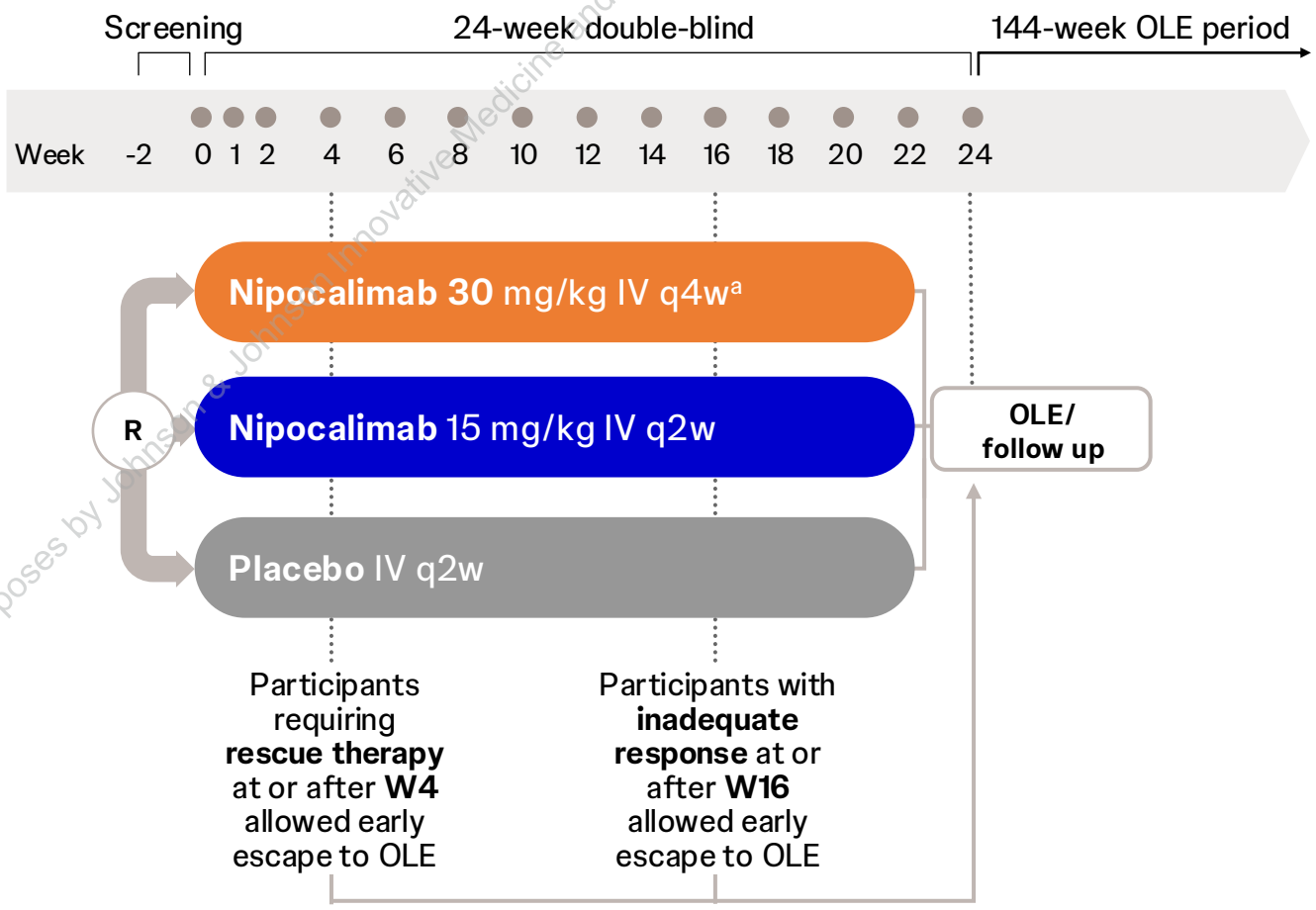
ENERGY Phase 2/3 Study Design

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



ClinicalTrials.gov identifier: NCT04119050. Statistical significance determined based on equal-weight approach to control the family-wise type I error rate.
[a]Nipocalimab 30 mg/kg IV at Week 0 and q4w through Week 20 and placebo IV at Week 2 and q4w through Week 22.
C3d=complement component 3d, **DAT**=direct antigen test, **Hgb**=hemoglobin, **IgG**=immunoglobulin G, **IV**=intravenous, **OLE**=open-label extension, **q2w**=every 2 weeks, **q4w**=every 4 weeks, **R**=randomized, **wAIHA**=warm autoimmune hemolytic anemia.

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

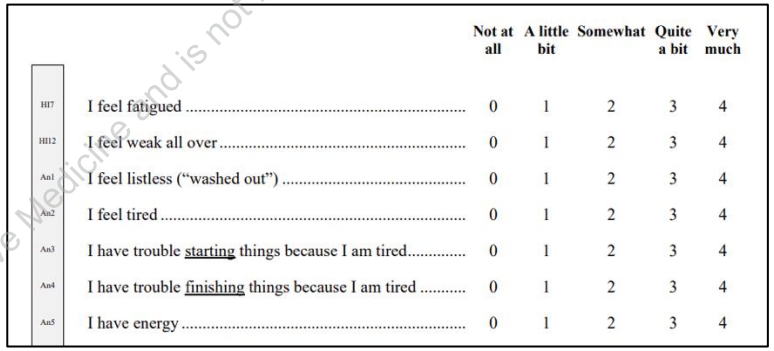
- Improvement in FACIT-Fatigue (Week 24)
- Corticosteroid dose reduction (Week 24; % reduction in daily corticosteroid dose[a])

[a]Prednisone equivalent.
FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy – Fatigue, **Hgb**=hemoglobin, **wAIHA**=warm autoimmune hemolytic anemia.

FACIT-Fatigue Is a Fit-For-Purpose PRO to Evaluate wAIHA-Related Fatigue

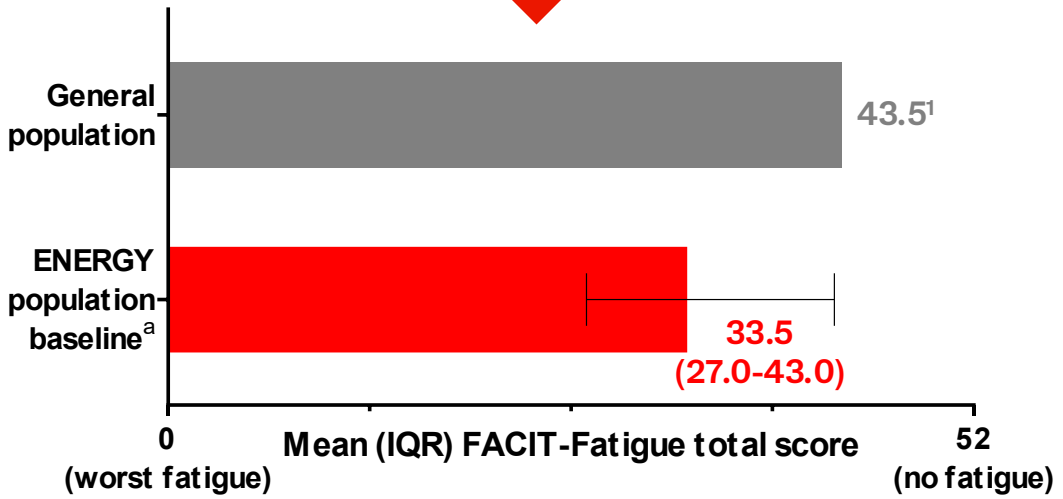
FACIT-Fatigue

- Thirteen items scored on a 5-point Likert scale from 0 to 4
  - Total score range: 0 (worst fatigue) to 52 (no fatigue)
- Contains experience (feeling of fatigue; 5 items) and impact (daily functioning; 8 items) subscales
- 7-day recall period
- Meaningful change threshold (MCT) for an individual patient-level improvement on FACIT-Fatigue total score established as 6 points
  - Previously established using an anchor-based approach with PGIS, supplemented with distribution-based methods



		Not at all	A little bit	Somewhat	Quite a bit	Very much
HI7	I feel fatigued	0	1	2	3	4
HI12	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble starting things because I am tired	0	1	2	3	4
An4	I have trouble finishing things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4

Total score calculated



[a]Efficacy population (n=115) excluding 3 participants randomized to a discontinued 30 mg/kg q2w group.

1. Montan I, et al. *Value Health*. 2018;21(11):1313-1321.

FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy – Fatigue, **IQR**=interquartile range, **MCT**=meaningful change threshold, **PGIS**=Patient Global Impressions of Severity, **PRO**=patient-reported outcome, **wAIHA**=warm autoimmune hemolytic anemia.

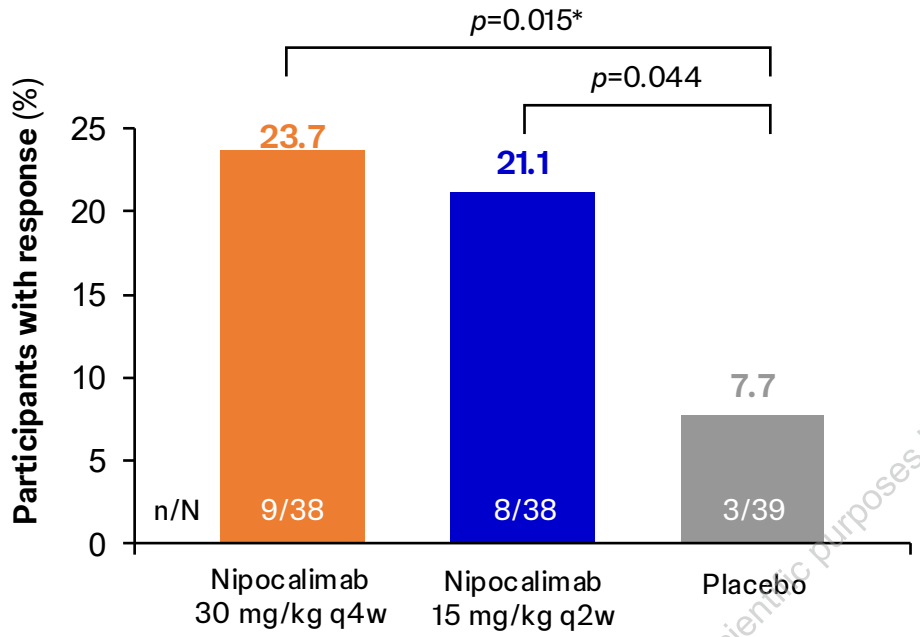
Baseline Characteristics Were Consistent With the wAIHA Patient Population

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%

[a]Stratification factors (primary or versus secondary wAIHA; screening hemoglobin ≤8.5 g/dL or versus >8.5 g/dL; no treatment or corticosteroids at dose ≤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) and was Generally Well Tolerated

Primary endpoint: Durable hemoglobin response



Summary of AEs

AE, n (%)	Nipocalimab 30 mg/kg q4w (n=38)	Nipocalimab 15 mg/kg q2w (n=38)	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 DVT and/or PE	1 (2.6)	0	0
Hypoalbuminemia (albumin <20 g/L)	0	0	0
Death	0	2 (5.4)	0

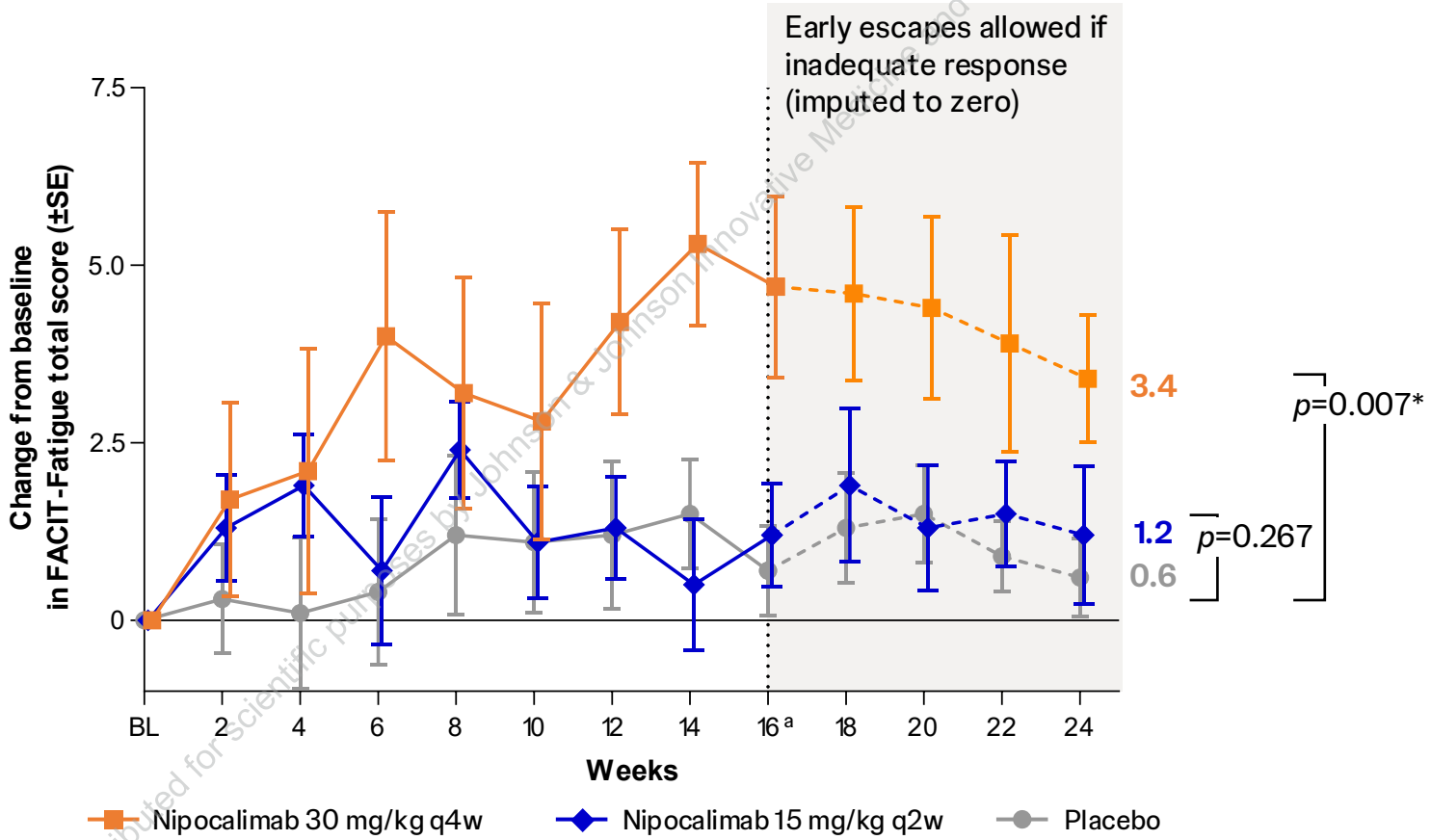
Composite analysis strategy (participants with intercurrent events [including any use of rescue therapies or initiation or dose increase of protocol-specified standard-of-care background therapy] were considered to be nonresponders). *P* values based on equal-weight approach to control the family-wise type I error rate with a 1-sided α=0.02499 using a Cochran-Mantel-Haenszel test. *One-sided p<0.02499 versus placebo considered significant.

[a]Prednisone equivalent.

AE=adverse event, **DVT**=deep vein thrombosis, **FACIT-Fatigue**=Functional Assessment of Chronic Illness Therapy – Fatigue, **Hgb**=hemoglobin, **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.

Nipocalimab 30 mg/kg Delivered Rapid Improvements in Fatigue at Week 2, Which Was Maintained Through Week 24

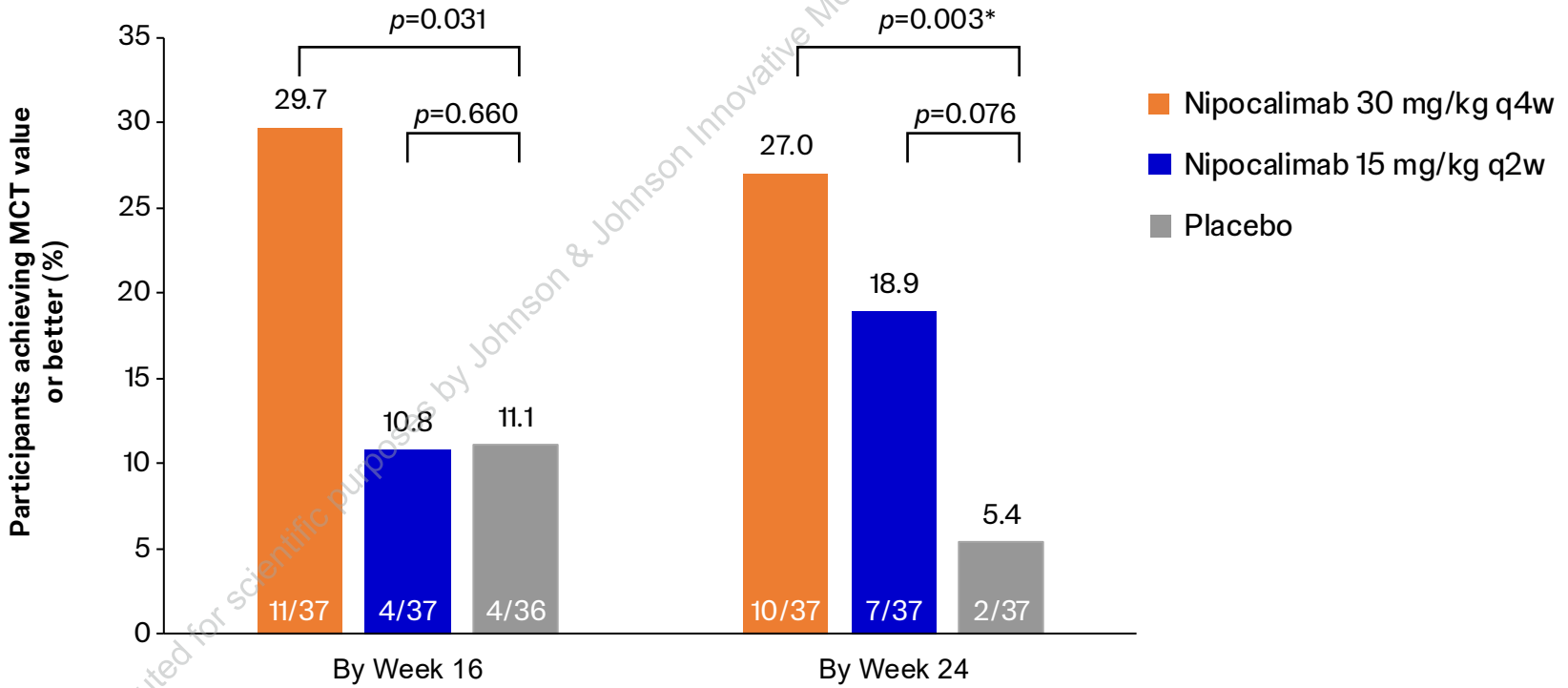
Key secondary endpoint: Change in FACIT-Fatigue total score from baseline



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 nominally significant, based on an equal-weight approach to control the family-wise type I error rate.

[a]Participants 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, **OLE**=open-label extension, **q2w**=every 2 weeks, **q4w**=every 4 weeks, **SE**=standard error.

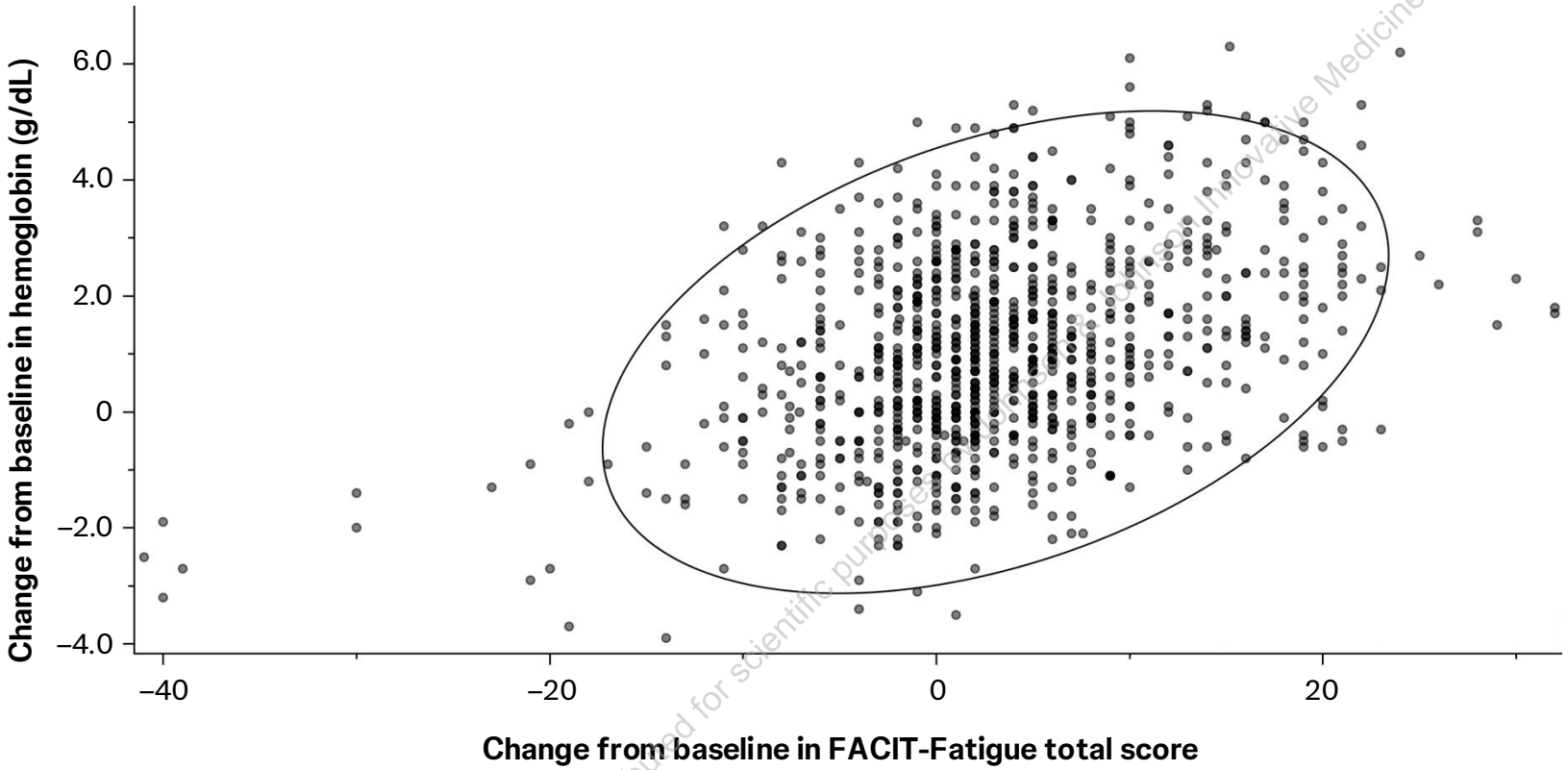
A Greater Proportion of Patients on Nipocalimab 30 mg/kg q4w Met or Exceeded the MCT for FACIT-Fatigue



P value based on a Stratified Cochran-Mantel-Haenszel test with wAIHA disease classification (primary or versus secondary wAIHA), screening hemoglobin value (≤8.5 g/dL versus >8.5 g/dL), and concurrent treatment for wAIHA (no treatment or corticosteroids at dose ≤20 mg/day of prednisone or equivalent with no immunosuppressants versus immunosuppressants or corticosteroids at >20 mg/day of prednisone or equivalent) as stratification factors. If the Mantel Fleiss criterion was not satisfied, then a Fisher's exact test was performed.
*One-sided $p<0.02499$ versus placebo considered nominally significant.

FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy – Fatigue, **MCT**=meaningful change threshold, **q2w**=every 2 weeks, **q4w**=every 4 weeks, **wAIHA**=warm autoimmune hemolytic anemia.

Changes in FACIT-Fatigue Total Score Showed Low to Moderate Correlation With Changes in Hemoglobin



Correlation with all treatment groups combined:

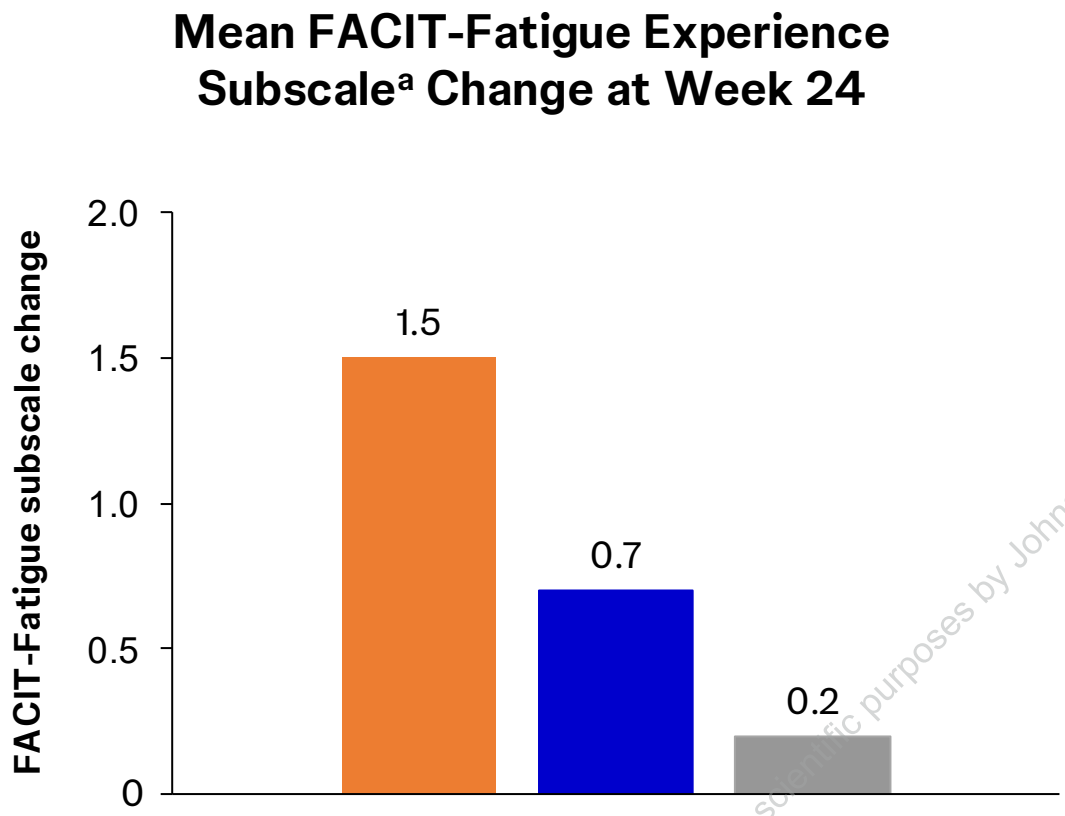
- Across all time points (repeated measures correlation): r=0.4353
- At Week 24: r=0.3331

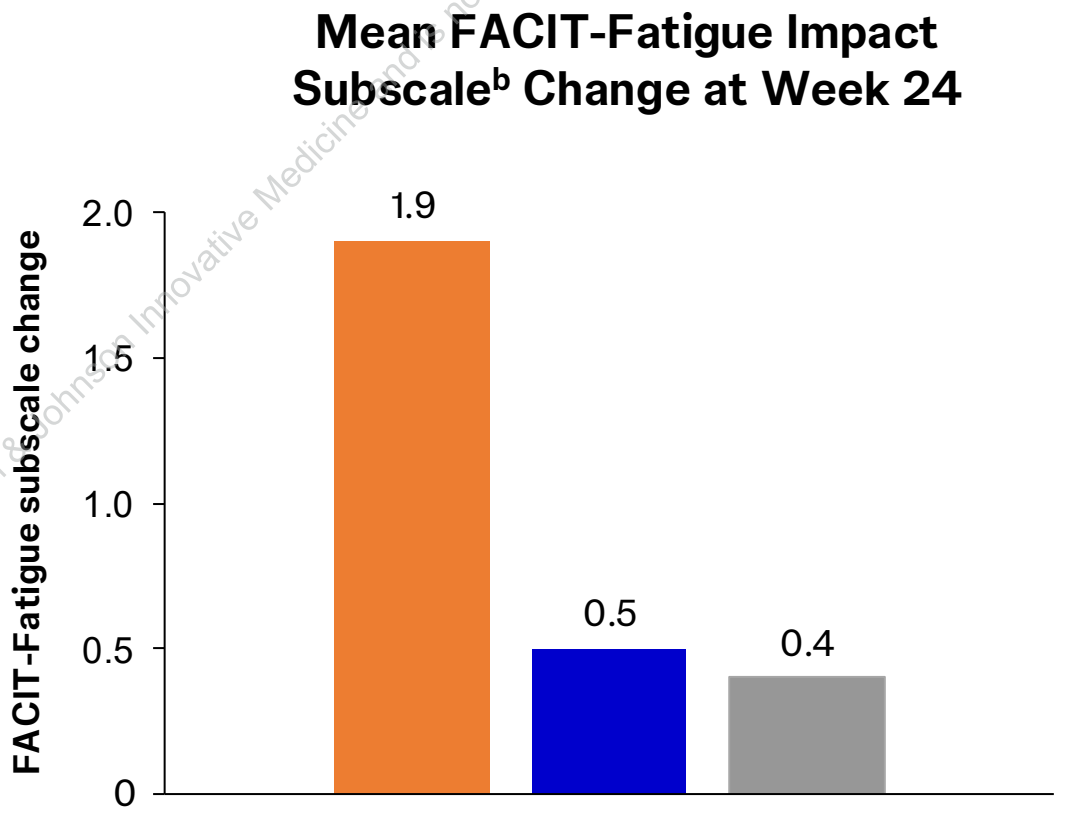
Based on 1020 observations; $p<0.0001$. The correlation coefficient is calculated using all visits and treatments together, therefore one patient contributes multiple pairs of data. A mixed model approach proposed by Hamlett, Ryan, and Wolfinger[1] was used because it fully specifies the correlation structure within a subject's repeated measurements using both the within-subject as well as between subject variation.

1. Hamlett A, Ryan L, Wolfinger R. In: *Proceedings of the 29th Annual SAS Users Group International Conference (SUGI 29)*. 2004:129–198.

FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy – Fatigue.

FACIT-Fatigue Subscales Evaluating Feeling of Fatigue and Impact on Daily Functioning Showed Improvement With Nipocalimab 30 mg/kg q4w





Nipocalimab 30 mg/kg q4w
Nipocalimab 15 mg/kg q2w
Placebo

FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy – Fatigue, **q2w**=every 2 weeks, **q4w**=every 4 weeks.
[a]Experience subscale includes 5 items. [b]Impact subscale includes 8 items.

Conclusions

Nipocalimab demonstrated a benefit in durable hemoglobin response as well as improvements in debilitating fatigue

- ✓ **Rapid and maintained fatigue improvement**
  A greater proportion of patients on nipocalimab 30 mg/kg q4w reported fatigue improvement through Week 24, with improvements observed as early as Week 2

- ✓ **Improvements in feeling of fatigue and daily functioning**
  Participants on nipocalimab reported improvement on FACIT-Fatigue experience and impact subscales

- ✓ **Clinically meaningful change achieved**
  A greater number of nipocalimab-treated participants met or exceeded the FACIT-Fatigue meaningful change threshold (6 points or more) compared with placebo

- ✓ **Positive correlation with hemoglobin**
  FACIT-Fatigue scores showed low to moderate correlation with hemoglobin across the study and at Week 24

FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy – Fatigue, **q4w**=every 4 weeks.

Additional Nipocalimab Presentations at EHA 2026

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

Nipocalimab demonstrated consistent and clinically meaningful benefits across multiple endpoints, including the primary endpoint of durable hemoglobin response

Oral session: Thr 11 June; available online at https://www.congresshub.com/EHA2026/ClassicalHematology/Nipocalimab/Fattizzo
S300 (Fattizzo B, 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.)

IgG=immunoglobulin G, **MOA**=mechanism of action, **RBC**=red blood cell, **wAIHA**=warm autoimmune hemolytic anemia.

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.

ENERGY Investigators: (Brazil) Jacques Kaufman, Andressa Lima Melo, Marcos Laercio Pontes Reis, Renato Tavares; (China) Rong Fu, Guangsheng He, Pengcheng He, Mei Hong, Zenghua Li, Miao Miao, Hongyan Tong, Shunqing Wang, Xiaoqin Wang, Chenlu Yang; (Czechia) Jiri Mayer; (Egypt) Raafat Abdel Fattah, Ashraf El Gandour, Mervat Mattar, Mohamed Moussa, Mohamed Samra; (France) Bernard Bonnotte, Clément Gourguechon; (Germany) Alexander Roth, Ingo Schwaner; (Greece) Argiris Symeonidis; (Hungary) Arpad Illes, Zsolt Lázár, Gabor Mikala, Zsolt Nagy; (Israel) Yariv Carasso, Chezi Ganzel, Ilya Kirgner, Itai Levi, Galia Spectre, Inna Tsoran-Rosenthal; (Italy) Bruno Fattizzo, Luana Fianchi, Andrea Patriarca; (Japan) Shunsuke Hatta, Masaki Iino, Koji Kawamura, Yoshitaka Miyakawa, Takashi Sonoki, Yasutaka Ueda; (Malaysia) Cheng Lay Teh, Sen Mui Tan; (Netherlands) Josephine Vos; (Poland) Jadwiga Dwilewicz-Trojaczek, Sebastian Grosicki, Tadeusz Robak; (South Korea) Jun Ho Jang, Hyunkyung Park; (Spain) Maria Aranzazu Alonso, Maria del Mar Urbano Ramos, Jose Angel Hernandez Rivas, Maria Eva Mingot Castellano, Gemma Moreno Jimenez, Irene Zamanillo; (United Kingdom) Quentin Hill, Sue Pavord, Syed Rashid Saeed Kazmi, David Simcox, Thomas Derrick Wayne; (United States) Gowthami Arepally, Troy Guthrie, Sung Ho Brian Lee, Darla Liles, Allyson Pishko

Backups

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

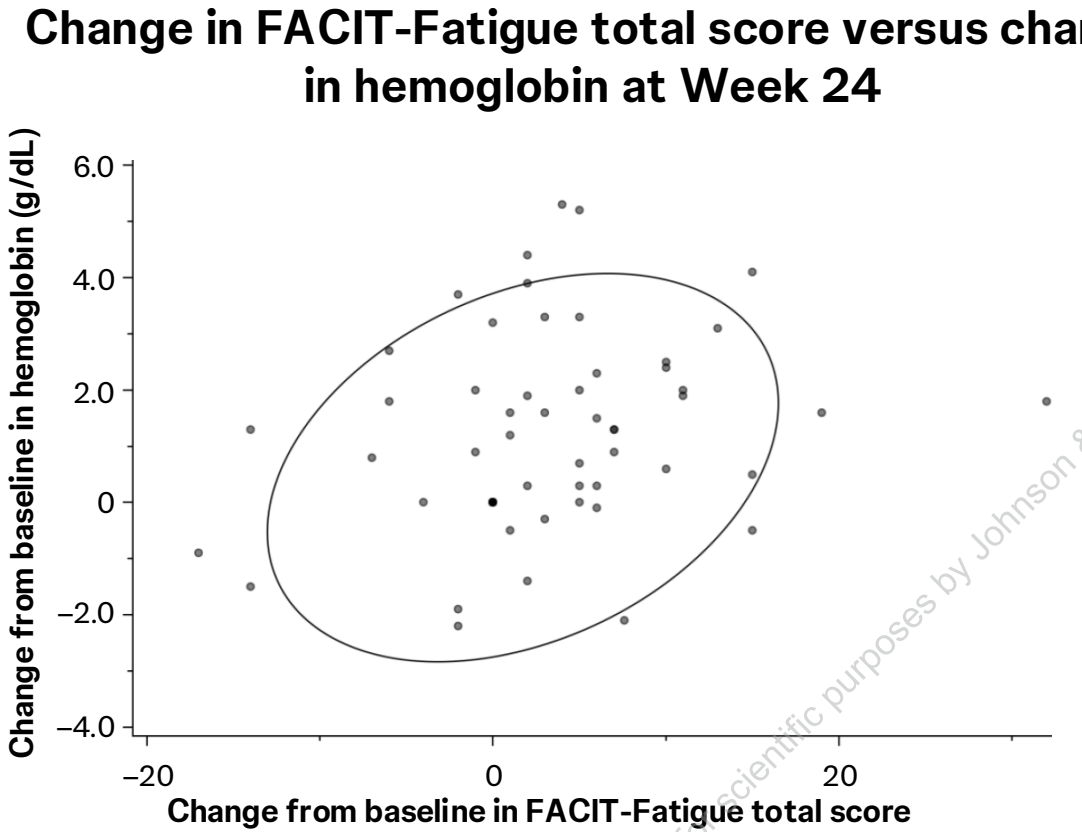
AE, n (%)	Nipocalimab 30 mg/kg q4w (n=38)	Nipocalimab 15 mg/kg q2w (n=37)[a]	Placebo (n=39)
TEAEs	35 (92.1)	30 (81.1)	35 (89.7)
SAEs	8 (21.1)	6 (16.2)	14 (35.9)
AEs leading to discontinuation	2 (5.3)	5 (13.5)	1 (2.6)
AEs of interest			
Grade ≥3 infections	2 (5.3)	3 (8.1)	5 (12.8)
Adjudicated MACE	0	2 (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 receiving nipocalimab 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)

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.

[a]One patient was randomized to nipocalimab 15 mg/kg q2w, but did not receive nipocalimab.

Changes in FACIT-Fatigue Total Score Showed Low to Moderate Correlation With Changes in Hemoglobin



- Correlation (with all treatment groups combined) at Week 24: r=0.3331

Pearson's r, based on 111 observations.

FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy – Fatigue.