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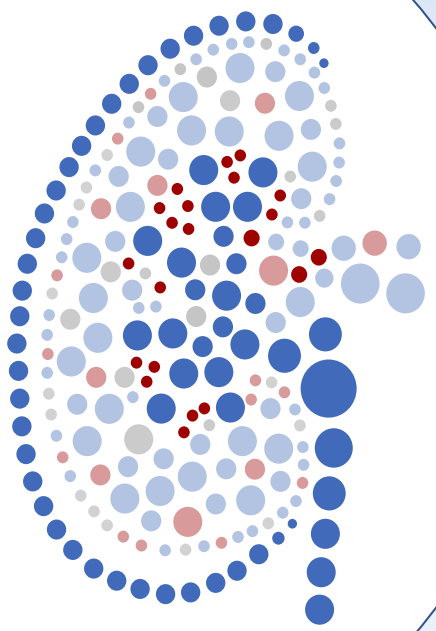
Enclosure:

- PRESENTATION: Perkovic V. Presented at: The American Society of Nephrology (ASN) Kidney Week 2025; November 5-9, 2025, Houston, TX



Sibeprenlimab for the Treatment of IgA Nephropathy: VISIONARY Phase 3 Interim and Prespecified Subgroup Analyses

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On behalf of the VISIONARY trial investigator group

Disclosures

Funding

This study is funded by Otsuka Pharmaceutical Development & Commercialization, Inc. (Princeton, NJ, USA)

Dr Perkovic reports the following disclosures:

Honoraria: AbbVie, Amgen, AstraZeneca, Baxter, Bayer, Biogen, Boehringer Ingelheim, Chinook Therapeutics, DURECT, Eli Lilly & Company, Gilead Sciences, GlaxoSmithKline, Janssen, Merck, Mitsubishi Tanabe Pharma, Mundipharma, Novartis, Novo Nordisk, Otsuka, PharmaLink, Pfizer, Reata Pharmaceuticals, Relypsa, Roche, Sanofi, Servier, Travere Therapeutics, Tricida

Focus of today's presentation

Section	Topic from the VISIONARY Phase 3 Interim Analysis
Efficacy	Recap of 9-month uPCR-24h
	12-month uPCR-24h NEW
	uPCR-24h subgroup analysis NEW
	Hematuria resolution and proteinuric remission NEW
Pharmacodynamics	Change in serum APRIL and Gd-IgA1 levels over time NEW
	Change from baseline in serum IgA, IgG, and IgM NEW
Safety	Incidence of TEAEs from full safety set (N=510) NEW

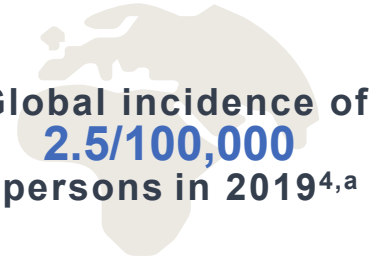
APRIL, a proliferation-inducing ligand; Gd-IgA1, galactose-deficient IgA1; IgA, immunoglobulin A; IgG, immunoglobulin G, IgM, immunoglobulin M; TEAE, treatment-emergent adverse event; uPCR-24h, urine protein creatinine ratio based on 24-hour urine collections.

IgA nephropathy is a progressive, immune-mediated kidney disease

Prevalence

IgA nephropathy is the **most common glomerulonephritis worldwide**[1]

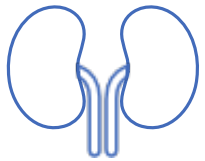
Typically diagnosed in patients **20-40 years old**[2,3]



Global incidence of 2.5/100,000 persons in 2019[4,a]

Disease Burden

- Supportive CKD therapy consists of RASi and/or SGLT2is, as well as BP control and lifestyle factors



- Despite supportive therapy, many patients remain at risk of progressing to kidney failure **within 10 to 15 years of diagnosis**[5,6]

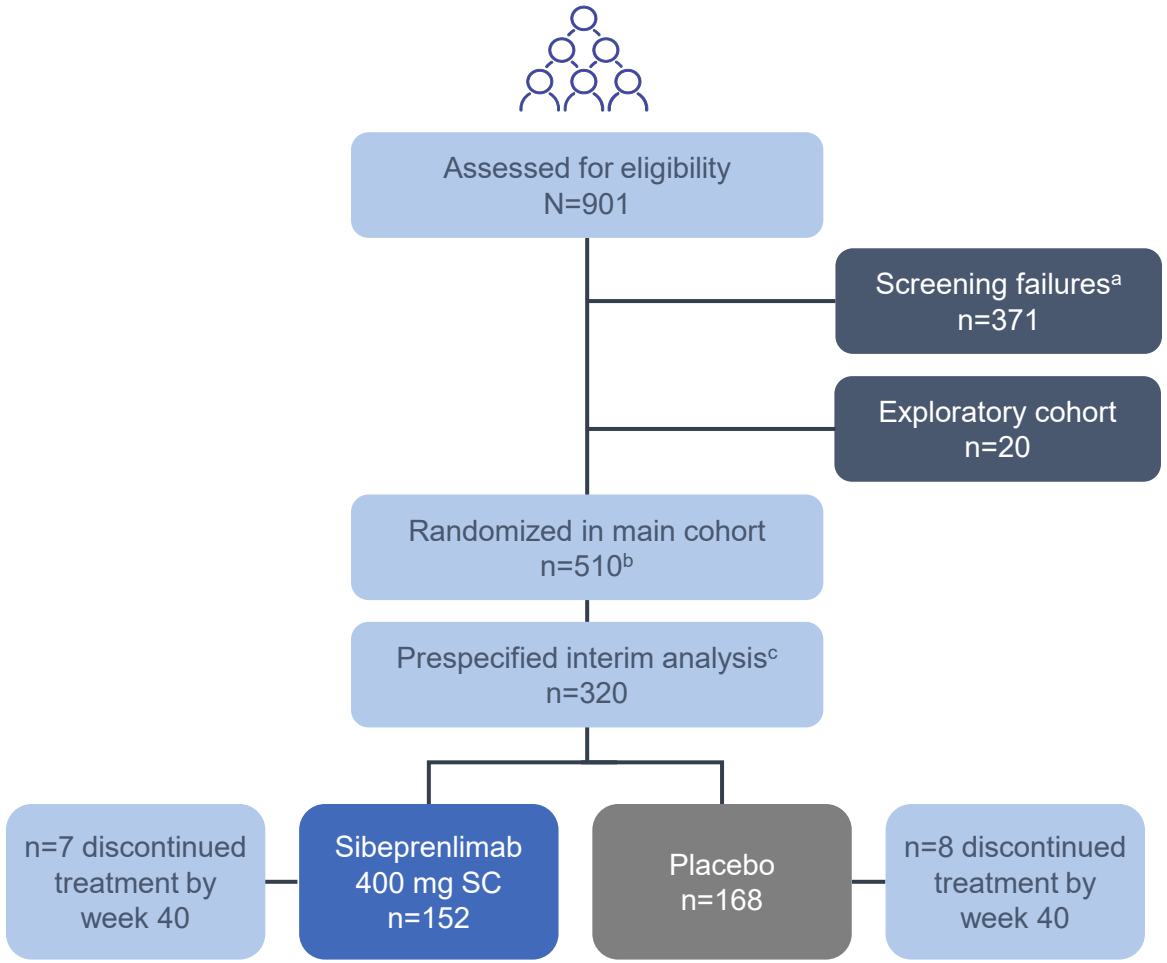
This highlights a need for disease-modifying therapies that address the immune-mediated drivers of IgA nephropathy

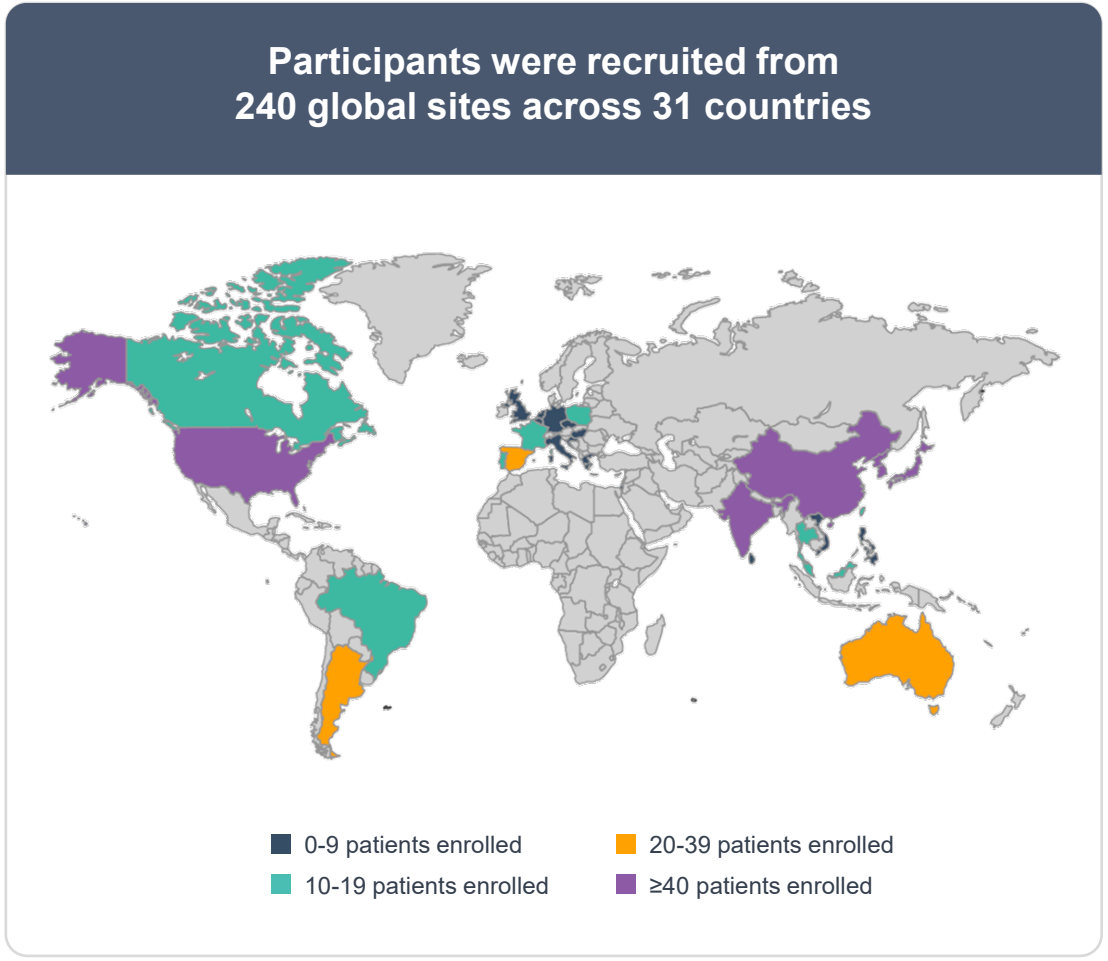
[a] Incidence rate reported in adults.

BP, blood pressure; CKD, chronic kidney disease; IgA, immunoglobulin A; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter 2 inhibitor.

1. Cheung CK, et al. *Front Nephrol*. 2024;3:1346769. **2.** Caster DJ, et al. *Kidney Int Rep*. 2023;8(9):1792-1800. **3.** Knoppova B, et al. *J Clin Med*. 2021;10(19):4501. **4.** McGrogan A, et al. *Nephrol Dial Transplant*. 2011;26(2):414-430. **5.** Pitcher D, et al. *Clin J Am Soc Nephrol*. 2023;18(6):727-738. **6.** Sim JJ, et al. *Nephrol Dial Transplant*. Published online April 30, 2025. doi:10.1093/ndt/gfaf084

Sibeprenlimab Phase 3 VISIONARY trial



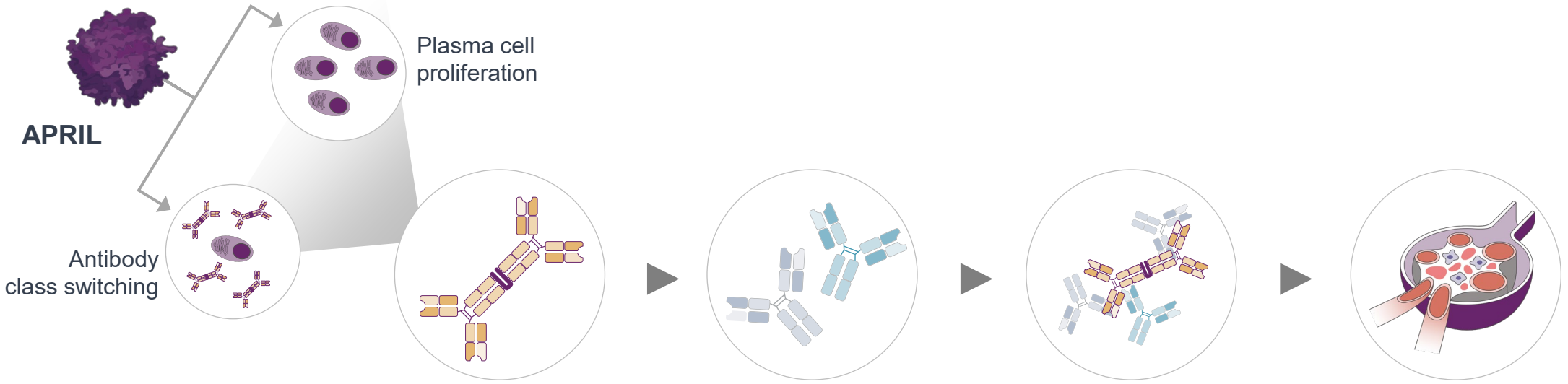


[a] Screening failures included participants who did not meet inclusion criteria or met the exclusion criteria (n=332), who declined to participate (n=7), and who had other reasons (n=39). [b] All enrolled participants who were randomized into the trial. Participants were considered randomized when they were assigned to a treatment group. [c] The interim analysis set comprises the first 62.5% of randomized participants who had the opportunity to complete the 9-month (week 40) 24-hour uPCR evaluation (cutoff date: September 4, 2024).
SC, subcutaneous; uPCR, urine protein creatinine ratio.

APRIL is a key driver of the 4-hit process of IgA nephropathy

- APRIL promotes antibody class switching in activated B cells and survival of plasma cells, leading to the production of IgA and pathogenic Gd-IgA1[1,2]
- The outcome of the 4-hit process is kidney injury, which culminates in kidney damage[3-6]

APRIL and the 4-hit process[7]

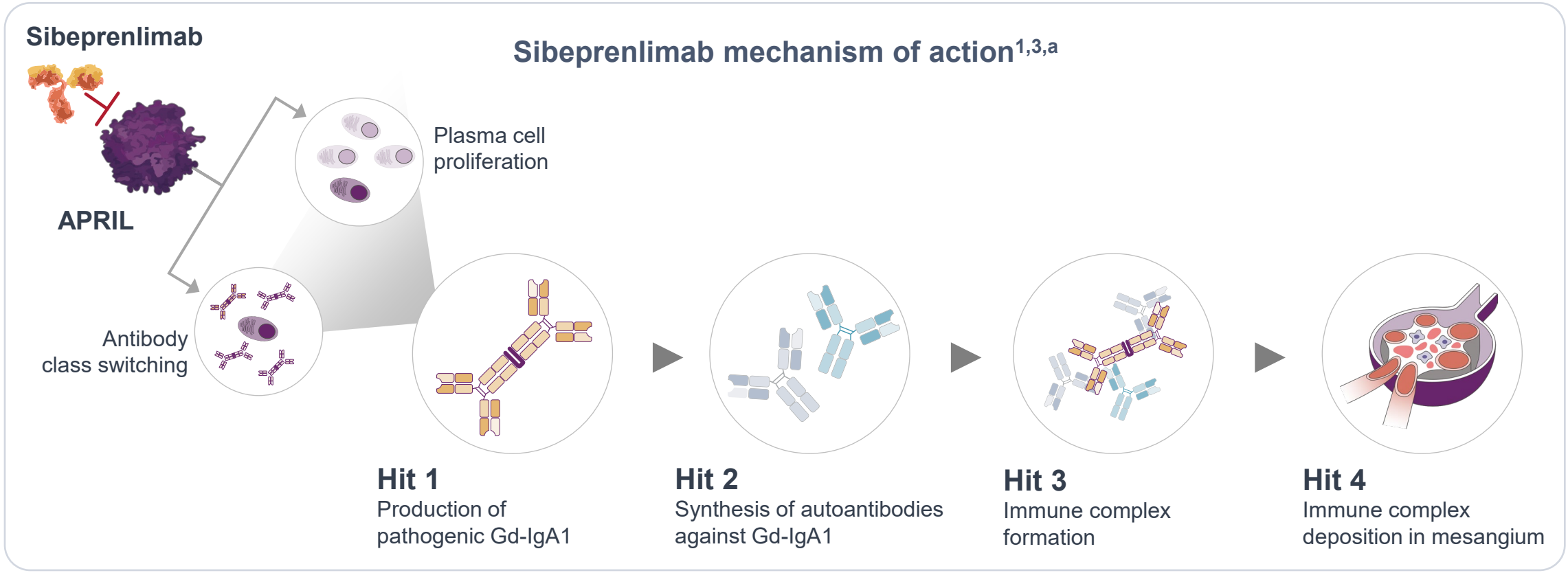


APRIL, a proliferation-inducing ligand; Gd-IgA1, galactose-deficient immunoglobulin A1; IgA, immunoglobulin A.

1. Chacko B, et al. *ASN Kidney News.* 2024;16(1):11-12. **2.** Cheung CK, et al. *Front Nephrol.* 2024;3:1346769. **3.** Suzuki H, et al. *J Am Soc Nephrol.* 2011;22(10):1795-1803. **4.** Mathur M, et al. *J Clin Med.* 2023;12(21):6927. **5.** Perše M, Večerić-Haler Ž. *Int J Mol Sci.* 2019;20(24):6199. **6.** Lai KN, et al. *Nat Rev Dis Primers.* 2016;2:16001. **7.** Cattran DC, et al. *Kidney Int Rep.* 2023;8(12):2515-2528.

Sibeprenlimab selectively binds to and inhibits the biological activity of APRIL

- Sibeprenlimab is a humanized IgG2 mAb that selectively inhibits APRIL[1]
- Sibeprenlimab decreases Gd-IgA1 production and immune complex formation[1,2]



[a] Sibeprenlimab binds to APRIL in a 3:3 ratio.[4]

APRIL, a proliferation-inducing ligand; Gd-IgA1, galactose-deficient immunoglobulin A1; IgG2, immunoglobulin G2; mAb, monoclonal antibody.

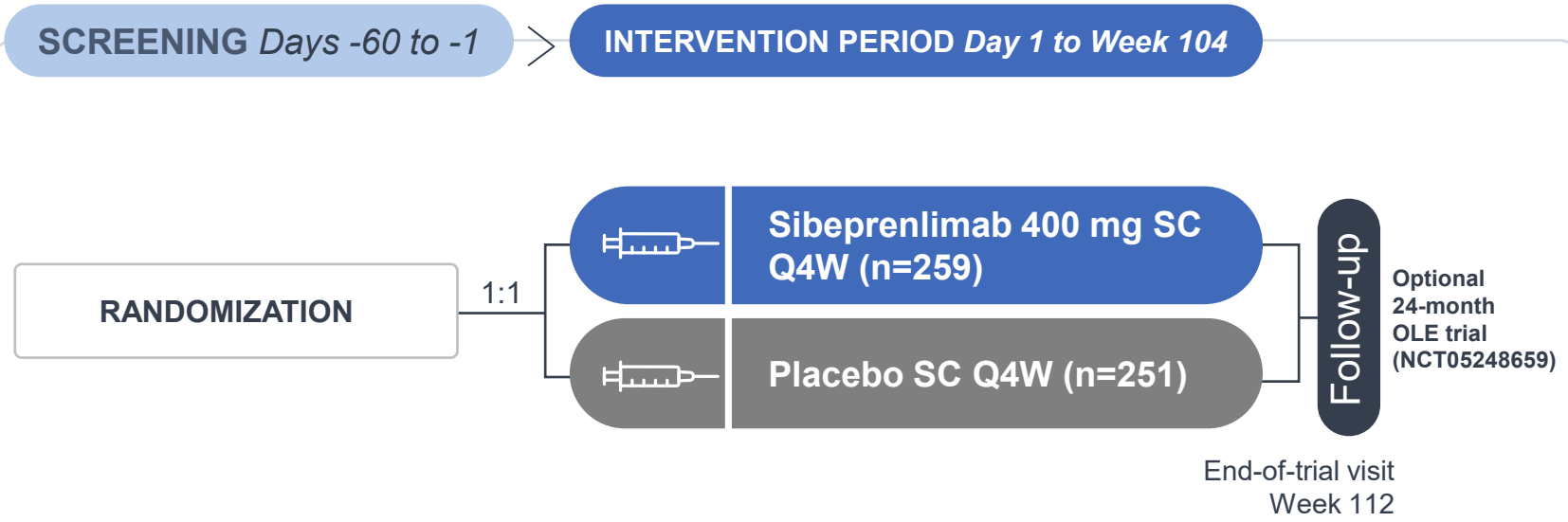
1. Mathur M, et al. *N Engl J Med*. 2024;390(1):20-31. **2.** Barratt J, et al. Presented at: American Society of Nephrology: October 23-27, 2024; San Diego, CA (abstr FR-OR59). **3.** Mathur M, et al. *J Clin Med.* 2023;12(21):6927. **4.** Myette JR, et al. *Kidney Int.* 2019;96(1):104-116.

VISIONARY Phase 3: Trial design

Interim efficacy analysis comprises the first 62.5% of randomized patients who completed the 9-month uPCR-24h evaluation **(N=320)**
Safety analysis includes all randomized patients who received at least 1 dose of sibeprenlimab **(N=510)**

Key inclusion criteria

- Biopsy-confirmed IgAN
- Age ≥18 years
- uPCR ≥0.75 g/g or urine protein ≥1.0 g/d
- eGFR ≥30 mL/min/1.73 m^2
- Stable or maximally tolerated dose of ACEi and/or ARB with or without SGLT2i for ≥3 months



Primary endpoint

- Ratio of uPCR at 9 months vs baseline based on 24-hour urine collection

Secondary endpoints

- Key: Annualized slope of eGFR estimated over ~24 months
- Other: Safety; change from baseline in total serum IgA, IgG, and IgM

Exploratory endpoints

- Change from baseline in uPCR-24h at 12 months
- Change in spot uPCR, hematuria, serum Gd-IgA1, and APRIL concentrations and proteinuric remission (urine total protein <0.5 g/d at 12 months)

ACEi, angiotensin-converting enzyme inhibitor; APRIL, a proliferation-inducing ligand; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; Gd-IgA1, galactose-deficient IgA1; Ig, immunoglobulin; IgAN, immunoglobulin A nephropathy; OLE, open-label extension; Q4W, every 4 weeks; SC, subcutaneous; SGLT2i, sodium-glucose cotransporter 2 inhibitor; uPCR, urine protein creatinine ratio; uPCR-24h, urine protein creatinine ratio based on 24-hour urine collections.

BEING PRESENTED

Baseline demographics

Demographic characteristics	Demographics for main trial cohort[a] (N=510)		Demographics for interim efficacy analysis cohort[b] (N=320)	
	Sibeprenlimab 400 mg SC (n=259)	Placebo (n=251)	Sibeprenlimab 400 mg SC (n=152)	Placebo (n=168)
Age, years, median (range)	41.0 (18-75)	43.0 (18-83)	42 (18-75)	43 (18-83)
Sex, n (%)				
Male	156 (60.2)	144 (57.4)	100 (65.8)	100 (59.5)
Female	103 (39.8)	107 (42.6)	52 (34.2)	68 (40.5)
Race, n (%)				
Asian	159 (61.4)	142 (56.6)	94 (61.8)	95 (56.5)
White	91 (35.1)	96 (38.2)	55 (36.2)	66 (39.3)
Other	8 (3.1)	10 (4.0)	3 (2.0)	7 (4.2)
Geographic region, n (%)				
East Asia	83 (32.0)	77 (30.7)	43 (28.3)	48 (28.6)
South/Southeast Asia	69 (26.6)	63 (25.1)	46 (30.3)	48 (28.6)
Europe	56 (21.6)	57 (22.7)	30 (19.7)	36 (21.4)
North America	35 (13.5)	30 (12.0)	22 (14.5)	21 (12.5)
South America	16 (6.2)	24 (9.6)	11 (7.2)	15 (8.9)

[a]All enrolled participants who were randomized into the trial. Participants were considered randomized when they were assigned to a treatment group. [b] Interim Analysis Set comprises the first 62.5% of randomized participants who had the opportunity to complete the 9-month 24-hour uPCR evaluation (cutoff date: September 4, 2024).
SC, subcutaneous.
Perkovic V, et al. *Kidney Int Rep* [in press]. DOI: 10.1016/u.ekir.2025.09.031.

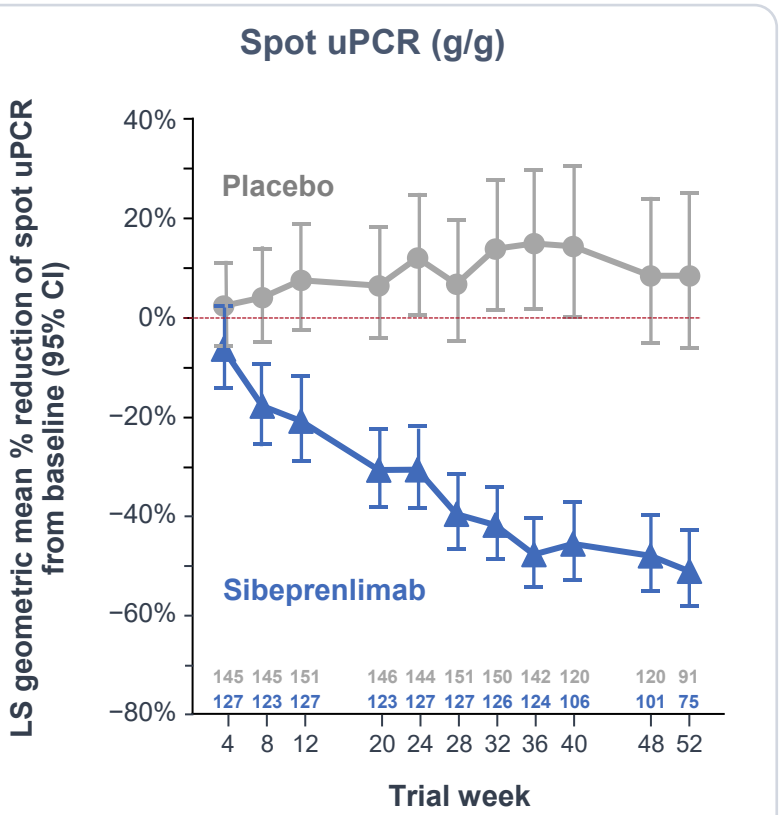
Baseline clinical characteristics

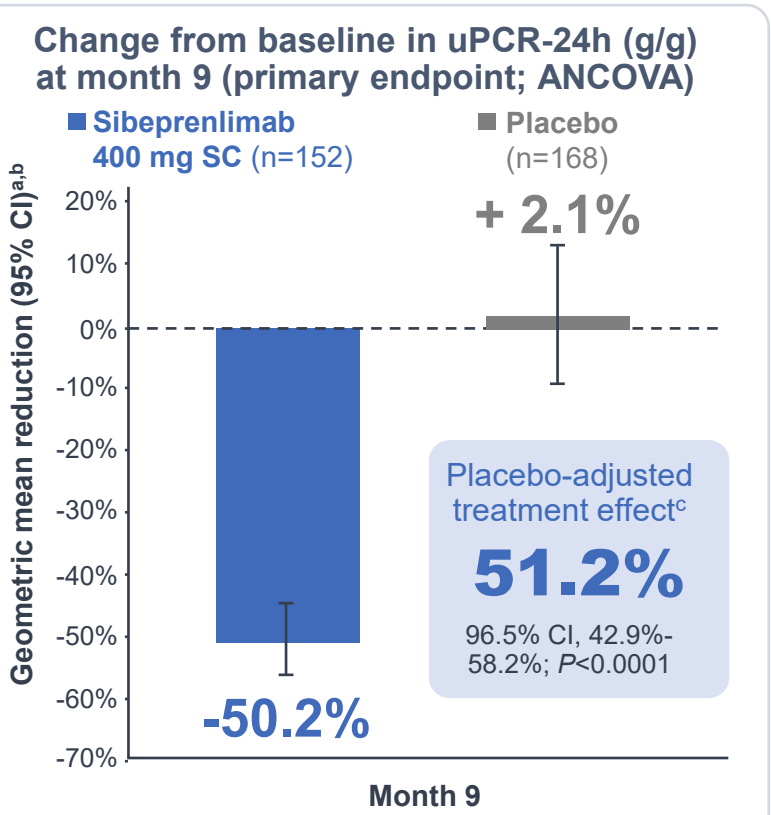
Clinical characteristics	Clinical characteristics for main trial cohort[a] (N=510)		Clinical characteristics for interim efficacy analysis cohort[b] (N=320)	
	Sibeprenlimab 400 mg SC (n=259)	Placebo (n=251)	Sibeprenlimab 400 mg SC (n=152)	Placebo (n=168)
Time from initial biopsy to randomization, years, median (range)	1.30 (0.0-23.7)	1.50 (0.0-34.0)	1.30 (0.10-23.7)	1.85 (0.0-34.0)
Baseline uPCR-24h[c], g/g				
Geometric mean (GSD)	1.36 (1.7)	1.33 (1.6)	1.33 (1.7)	1.32 (1.6)
Median (range)	1.25 (0.5-7.8)	1.27 (0.5-5.5)	1.22 (0.5-6.7)	1.28 (0.5-5.5)
Baseline eGFR[c], mL/min/1.73 m^2				
Mean (SD)	65.0 (25)	63.4 (25.7)	63.5 (24.4)	63.4 (25.3)
Median (range)	61 (25.0-134.0)	59 (27.0-130.0)	57.5 (25.0-131.0)	60.0 (27.0-129.0)
Prior use of immunosuppressive drugs, n (%)[d]	14 (5.4)	8 (3.2)	6 (3.9)	6 (3.6)
Background regimen, n (%)				
ACEI and/or ARB	254 (98.1)	245 (97.6)	149 (98.0)	163 (97.0)
SGLT2i[e]	111 (42.9)	119 (47.4)	56 (36.9)	72 (42.9)
Baseline dipstick hematuria[c], n (%)				
Negative	52 (20.1)	68 (27.1)	33 (21.7)	49 (29.2)
Positive[f]	207 (79.9)	183 (72.9)	119 (78.3)	119 (70.8)

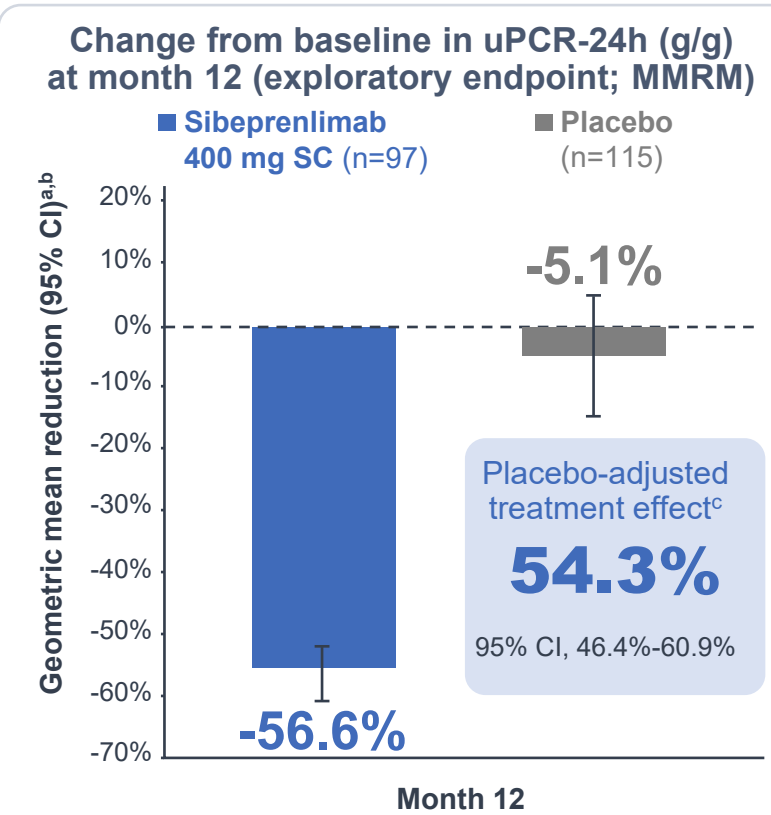
[a]All enrolled participants who were randomized into the trial. Participants were considered randomized when they were assigned to a treatment group. [b]Interim Analysis Set comprises the first 62.5% of randomized participants who had the opportunity to complete the 9-month (week 40) 24-hour uPCR evaluation (cutoff date: September 4, 2024). [c]Baseline measurements were defined as the last available assessment at or prior to the first dose of sibeprenlimab, unless stated otherwise. [d]Included systemic corticosteroids and other immunosuppressive therapies. [e]Includes patients on ACEi and/or ARB and SGLT2i and those on SGLT2i only. [f]Positive hematuria is defined as trace, 1+, 2+, 3+.

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; GSD, geometric standard deviation; SC, subcutaneous; SD, standard deviation; SGLT2i, sodium-glucose cotransporter 2 inhibitor; uPCR-24h, urine protein-to-creatinine ratio based on 24-hour urine collections.

Interim efficacy: uPCR-24h & spot uPCR





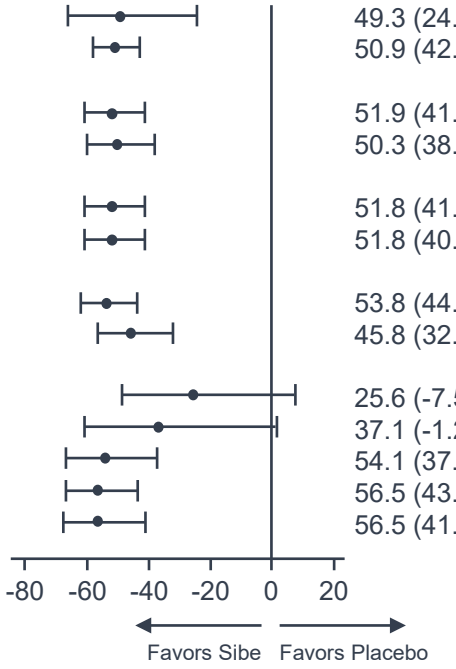


[a] The interim analysis set comprises the first 62.5% of randomized participants who had the opportunity to complete the 9-month (week 40) 24-hour uPCR evaluation. [b] The percentage reduction of uPCR-24h at month 9 is compared to baseline using ANCOVA, calculated as (1 - GM of uPCR-24h ratio estimated from ANCOVA model) x 100%. [c] The percentage reduction for treatment effect was calculated as (1 - ratio of GM of uPCR-24h ratio for sibeprenlimab SC 400 mg over placebo estimated from ANCOVA model) x 100%. The 95% CI corresponds to the treatment-specific reductions, while the 96.5% CI corresponds to the between-treatment difference, aligned with the predefined split alpha of 0.035 used for testing the 24-hour uPCR endpoint in the IA. [d] The line plot is based on the summary statistics of observed 24-hour uPCR. Geometric mean percent change from baseline is calculated as (GM of uPCR-24h compared to baseline - 1) x 100%.
ANCOVA, analysis of covariance; CI, confidence interval; GM, geometric mean; IA, interim analysis; MMRM, mixed model for repeated measures; uPCR-24h, urine protein-to-creatinine ratio based on 24-hour urine collections.

Interim efficacy: uPCR-24h subgroup analysis

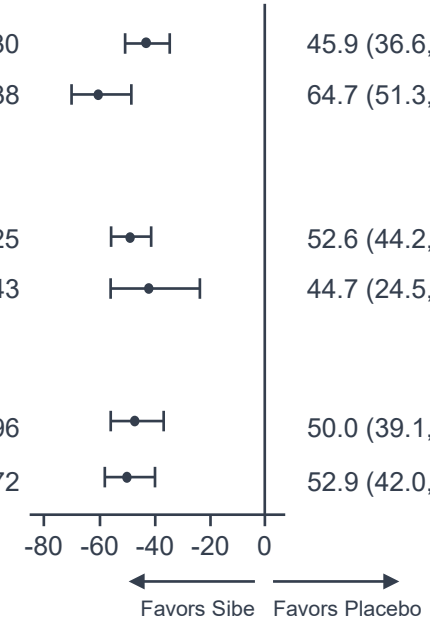
uPCR-24h subgroup analysis by baseline demographics

Subgroup[a]	Sibe (n)	Placebo (n)	Sibe vs Placebo Percentage Reduction (95% CI)
Ethnicity			
Hispanic or Latino	16	22	49.3 (24.4, 65.9)
Not Hispanic or Latino	132	141	50.9 (42.7, 57.9)
Sex at birth			
Male	100	100	51.9 (41.6, 60.4)
Female	52	68	50.3 (38.5, 59.8)
Age group			
≤40 years	69	68	51.8 (41.5, 60.3)
>40 years	83	100	51.8 (40.9, 60.7)
Race			
Asian	94	95	53.8 (44.2, 61.8)
White	55	66	45.8 (32.4, 56.6)
Region			
North America	22	21	25.6 (-7.5, 48.6)
South America	11	15	37.1 (-1.2, 60.8)
Europe	30	36	54.1 (37.7, 66.2)
East Asia	43	48	56.5 (43.3, 66.7)
South/Southeast Asia	46	48	56.5 (41.4, 67.7)



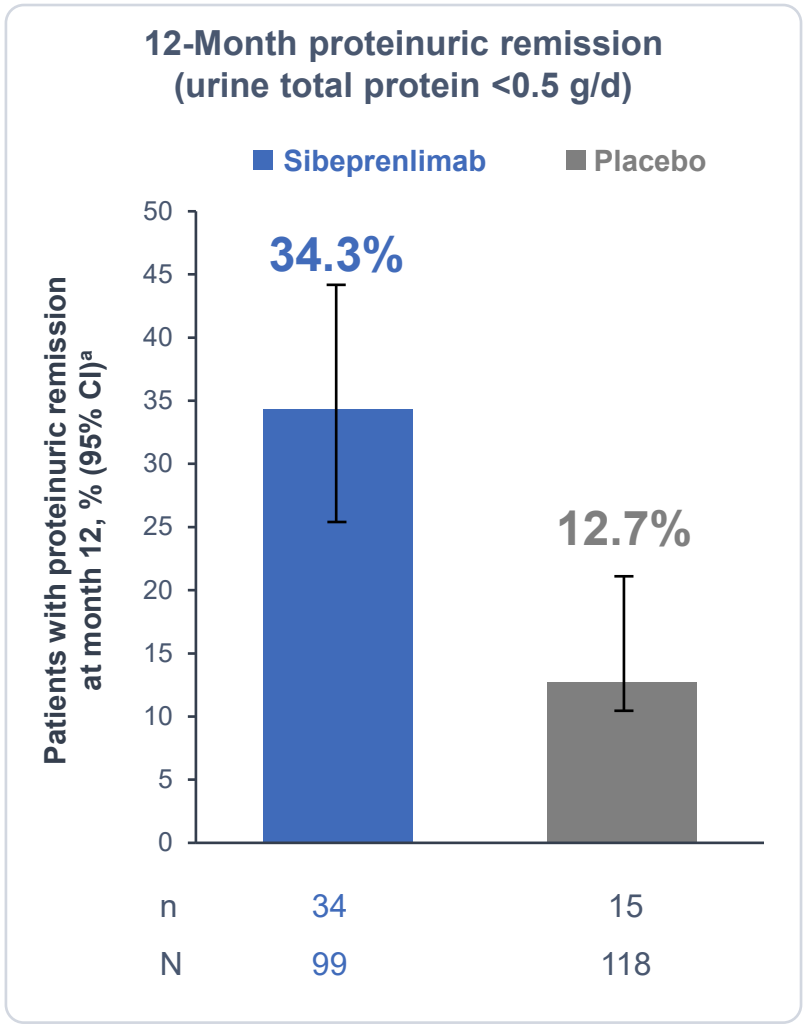
uPCR-24h subgroup analysis by baseline stratification factors

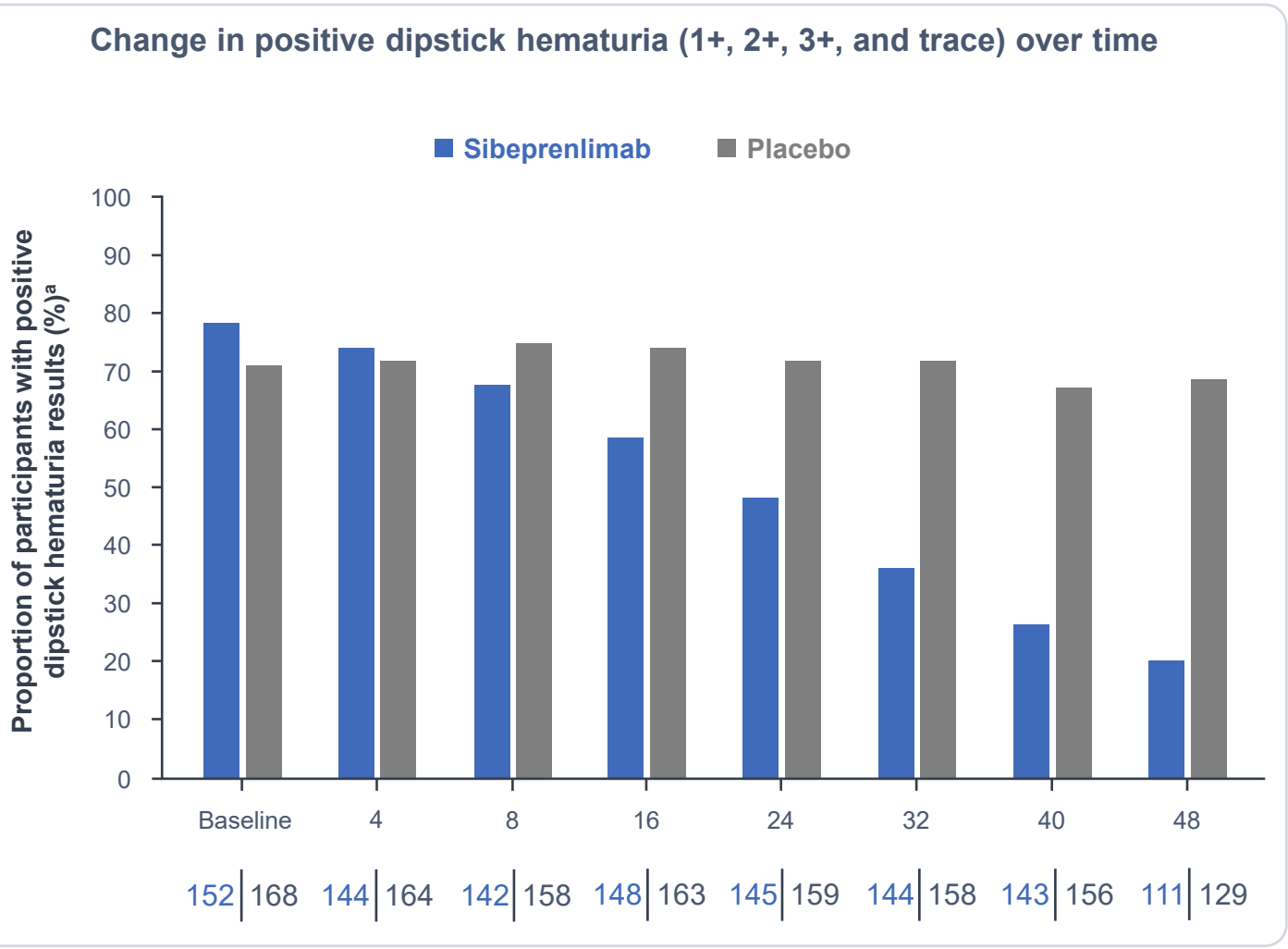
Subgroup[a,b]	Sibe (n)	Placebo (n)	Sibe vs Placebo Percentage Reduction (95% CI)
Screening uPCR-24h			
uPCR ≤2.0 g/g	116	130	45.9 (36.6, 53.9)
uPCR >2.0 g/g	36	38	64.7 (51.3, 74.4)
Screening eGFR			
eGFR ≥45 mL/min	115	125	52.6 (44.2, 59.8)
eGFR 30-44 mL/min	37	43	44.7 (24.5, 59.4)
Screening SGLT2i			
No	98	96	50.0 (39.1, 59.0)
Yes	54	72	52.9 (42.0, 61.8)



[a] This analysis was performed on participants in the Interim Analysis Set who had a baseline uPCR measured from at least one 24-hour urine sample. [b] Based on IRT record.
eGFR, estimated glomerular filtration rate; IRT, interactive response technology; SGLT2i, sodium-glucose cotransporter 2 inhibitor; Sibe, sibeprenlimab; uPCR-24h, urine protein-to-creatinine ratio based on 24-hour urine collections.

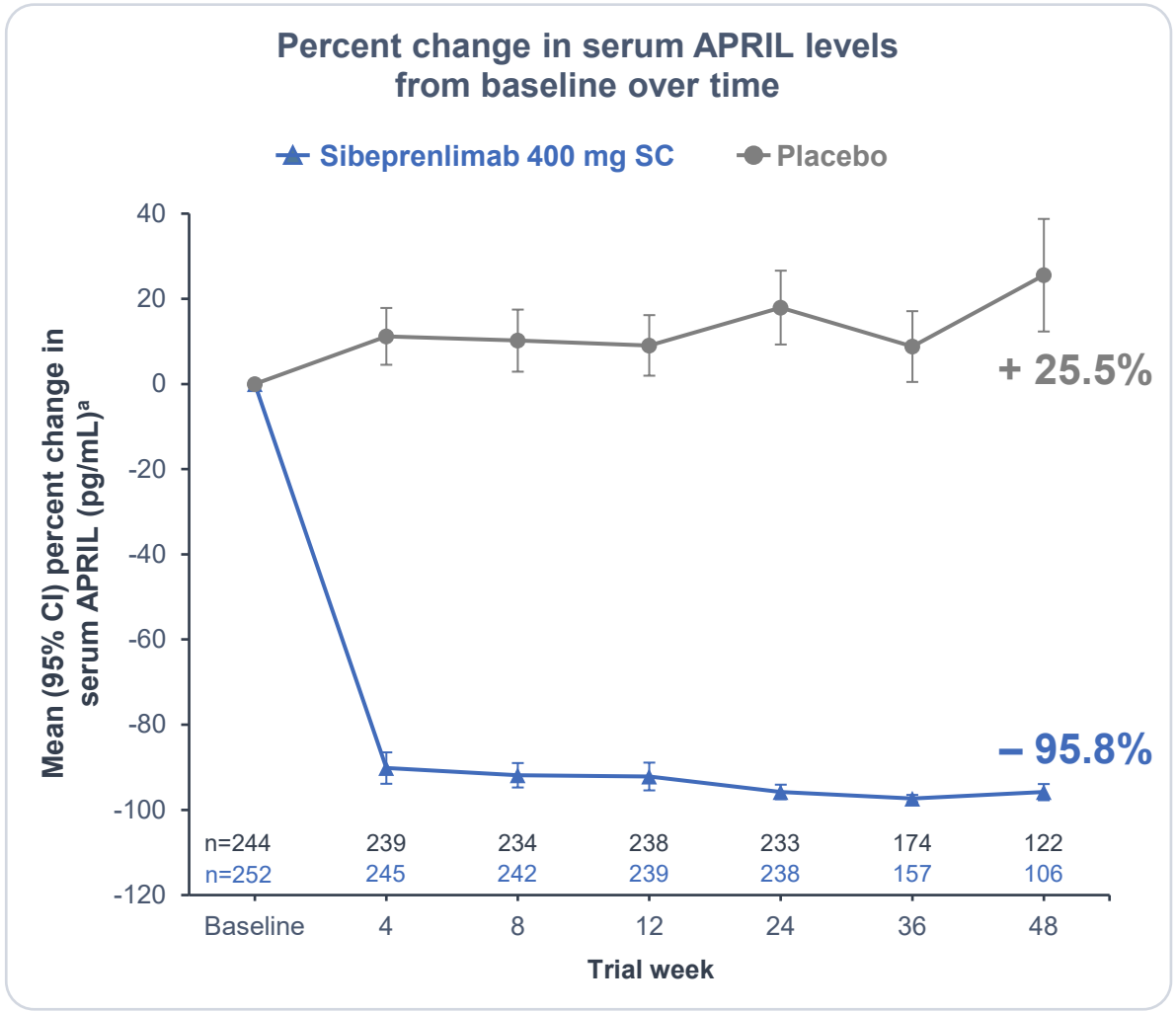
Interim efficacy: proteinuric remission and hematuria resolution

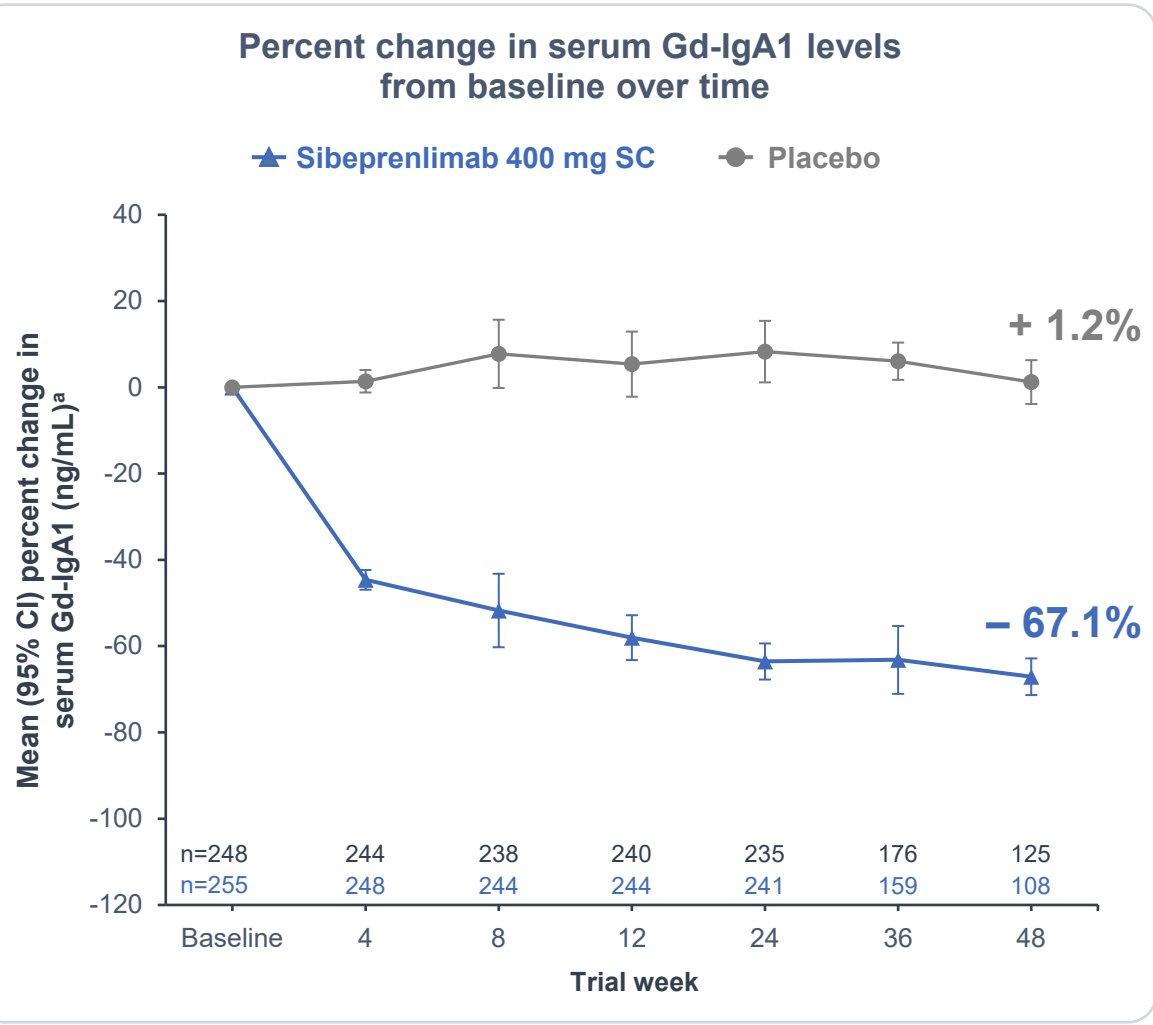




[a] This analysis was performed on participants in the Interim Analysis Set who had a baseline uPCR measured from at least one 24-hour urine sample.
uPCR, urine protein creatinine ratio.

Interim efficacy: biomarkers

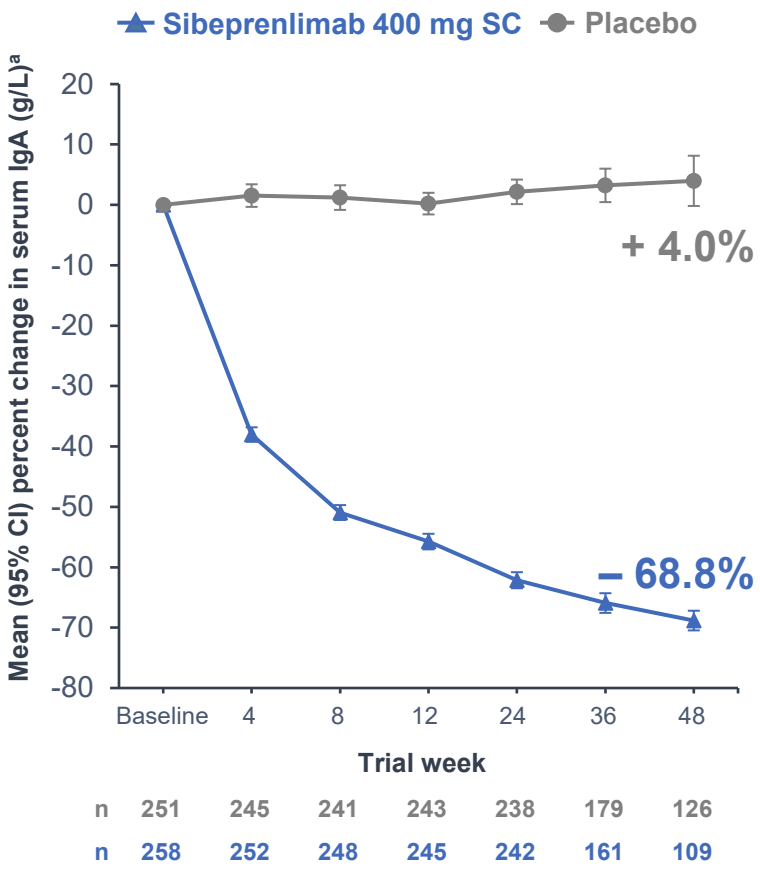




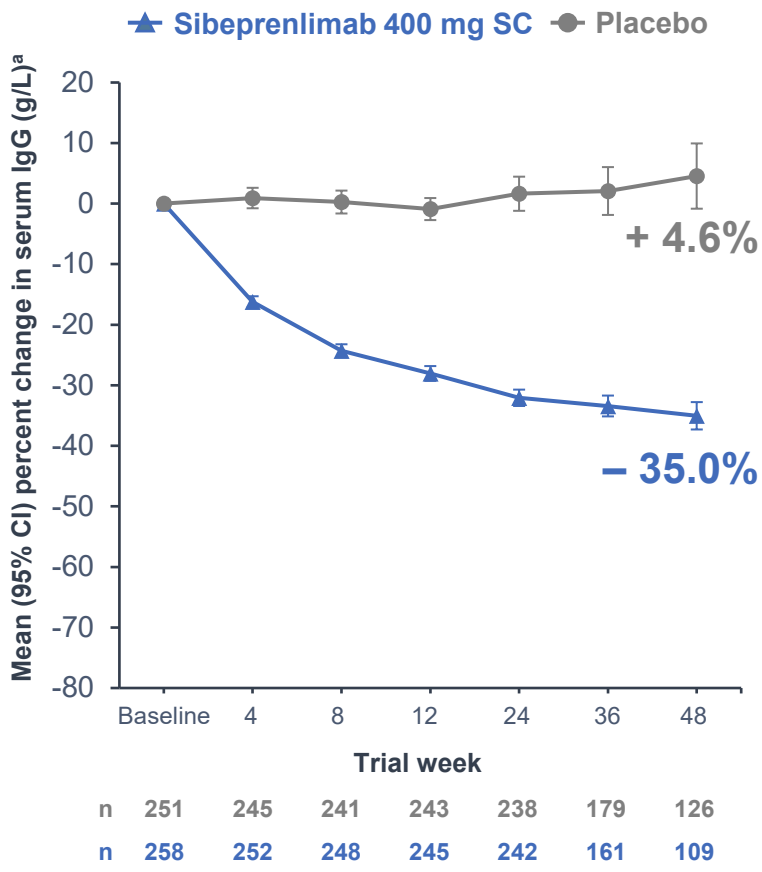
[a] This analysis was performed on all randomized participants who received at least 1 dose of sibeprenlimab and had a baseline and at least 1 postbaseline evaluable PD measurement.
APRIL, a proliferation-inducing ligand; Gd-IgA1, galactose-deficient IgA1; PD, pharmacodynamics; SC, subcutaneous.

Interim efficacy: biomarkers (Cont'd)

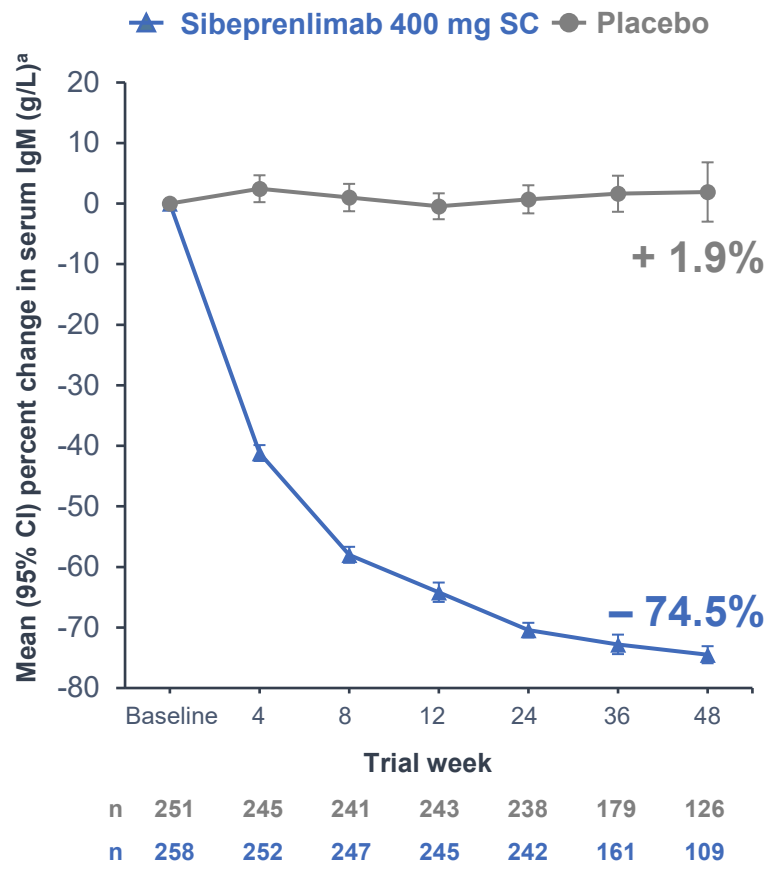
Percent change in serum IgA levels from baseline over time



Percent change in serum IgG levels from baseline over time



Percent change in serum IgM levels from baseline over time



[a] This analysis was performed on all randomized participants who received at least 1 dose of sibeprenlimab and had a baseline and at least 1 postbaseline evaluable PD measurement (data cutoff September 4, 2024).
IgA, immunoglobulin A; IgG, immunoglobulin G, IgM, immunoglobulin M; PD, pharmacodynamic; SC, subcutaneous.

Treatment-emergent adverse events: safety set (N=510)

Treatment-emergent adverse events	Sibeprenlimab, n (%) (n=259)	Placebo, n (%) (n=251)
Any TEAE	192 (74.1)	206 (82.1)
Treatment-related TEAE	75 (29.0)	67 (26.7)
TEAEs occurring in ≥5% of patients in either treatment group		
Upper respiratory tract infection	38 (14.7)	35 (13.9)
Injection site erythema	34 (13.1)	30 (12.0)
Nasopharyngitis	32 (12.4)	25 (10.0)
Injection site pain	26 (10.0)	23 (9.2)
COVID-19	25 (9.7)	17 (6.8)
Influenza	21 (8.1)	16 (6.4)
Back pain	17 (6.6)	14 (5.6)
Injection site swelling	16 (6.2)	13 (5.2)
Pyrexia	14 (5.4)	10 (4.0)
Any serious TEAE	9 (3.5)	11 (4.4)
Any severe TEAE	4 (1.5)	8 (3.2)
Any TEAE leading to treatment discontinuation	1 (0.4)	4 (1.6)
Deaths	0 (0.0)	0 (0.0)

- All randomized patients who received at least 1 dose of sibeprenlimab were included in the safety analysis (N=510)
- At the IA cutoff, among 510 patients, the incidence of TEAEs was similar in the sibeprenlimab (74.1%) and placebo (82.1%) groups

IA, interim analysis; COVID-19, coronavirus disease 2019; IA, interim analysis; TEAE, treatment-emergent adverse event.

Summary

- Sibeprenlimab treatment was associated with a significant placebo-adjusted reduction in uPCR-24h of 51.2% after 9 months and reduction of 54.3% at 12 months

- Treatment effect of sibeprenlimab on uPCR was consistent across sex, ethnicity, region, race, age, screening uPCR-24h, eGFR, and background SGLT2i use

- Sibeprenlimab reduced disease biomarkers (Gd-IgA1 and APRIL) and led to higher rates of hematuria resolution and proteinuric remission up to 12 months

- Safety findings were comparable to placebo
- Safety and efficacy (eGFR) outcomes will be assessed at 24 months in the ongoing VISIONARY trial

- Ongoing studies include a Phase 2/3 OLE (NCT05248659) trial of sibeprenlimab and a Phase 2b open-label biopsy study (VISOR; NCT06740526)

- Anticipated FDA Decision - Prescription Drug User Fee Act (PDUFA) Nov 28, 2025

APRIL, a proliferation-inducing ligand; eGFR, estimated glomerular filtration rate; Gd-IgA1, galactose-deficient IgA1; IgAN, immunoglobulin A nephropathy; OLE, open-label extension; PDUFA, Prescription Drug User Fee Act; SGLT2i, sodium-glucose cotransporter 2 inhibitor; uPCR, urine protein creatinine ratio; uPCR-24h, urine protein-to-creatinine ratio based on 24-hour urine collections.

Acknowledgments

The authors thank the trial participants, their families, and the investigators and research teams for their invaluable contributions to this work

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