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Enclosure:

ORAL PRESENTATION: Rizk D, Presented at ASN: October 22-25, 2026: Denver, CO, USA

Sibeprenlimab in IgA Nephropathy: Phase 3 VISIONARY Kidney Outcomes Data

ASN, October 22–25, 2026

Denver, CO

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On behalf of the VISIONARY trial investigator group

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IgA Nephropathy Is a Progressive, Immune-Mediated Kidney Disease

Disease burden

- IgA nephropathy is often diagnosed in adults aged **20-40 years**[1,2]
- Most patients present with **CKD stage 3** at diagnosis[1,3]

Disease progression

- Despite supportive therapy, many patients remain at risk for progressing to kidney failure within **10 to 15 years** of diagnosis[4,5]

KDIGO recommendations

The KDIGO 2025 IgA nephropathy guideline recommends[6]:

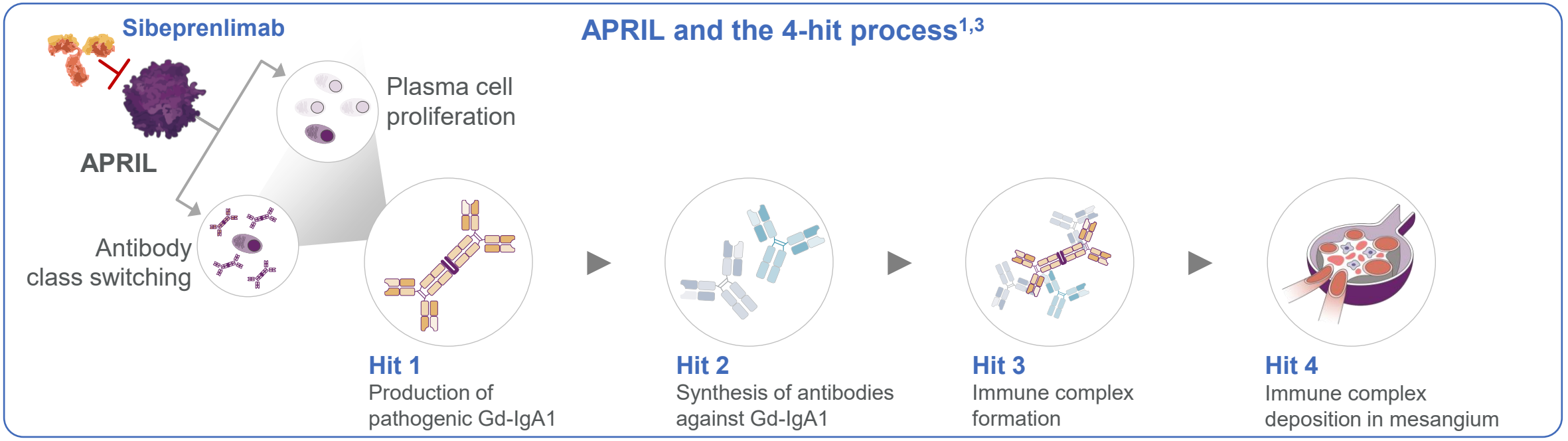
- Simultaneously managing both the **IgA nephropathy–specific immunologic drivers** and generic response to nephron loss
- **Treatment goal:** reduce the rate of loss of kidney function to **<1 mL/min/y** and proteinuria to <0.5 g/d (ideally <0.3 g/d)

CKD, chronic kidney disease; IgA, immunoglobulin A; KDIGO, Kidney Disease: Improving Global Outcomes.

1. Caster DJ, et al. *Kidney Int Rep*. 2023;8(9):1792-1800. **2.** Knoppova B, et al. *J Clin Med*. 2021;10(19):4501. **3.** Kwon CS, et al. *J Health Econ Outcomes Res*. 2021;8(2):36-45. **4.** Pitcher D, et al. *Clin J Am Soc Nephrol*. 2023;18(6):727-738. **5.** Sim JJ, et al. *Nephrol Dial Transplant*. 2025;40(11):2104-2117. **6.** KDIGO. *Kidney Int*. 2025;108(4S):S1-S71.

APRIL Is a Key Driver of the 4-Hit Process of IgA Nephropathy

Sibeprenlimab selectively binds to and blocks APRIL, decreasing Gd-IgA1 production and immune complex formation[1,2]



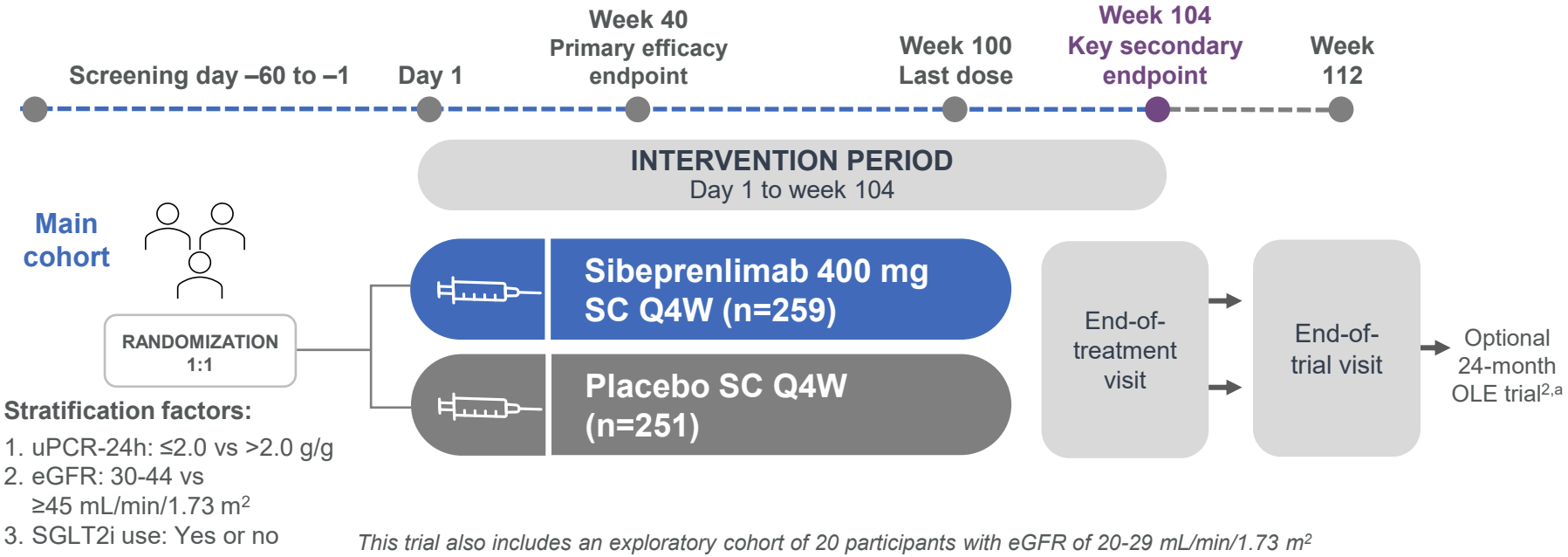
APRIL, a proliferation-inducing ligand; Gd-IgA1, galactose-deficient immunoglobulin A1; IgG2, immunoglobulin G2; mAb, monoclonal antibody.

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 annual meeting; October 23-27, 2024; San Diego, CA (abstr FR-OR59). **3.** Mathur M, et al. *J Clin Med.* 2023;12(21):6927.

VISIONARY Phase 3: Trial Design[1]

Key inclusion criteria

- Biopsy-confirmed IgA nephropathy
- Age ≥18 years
- uPCR-24h ≥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



510 patients were randomized 1:1 to sibeprenlimab 400 mg or placebo every 4 weeks for a 104-week treatment period, with final safety follow-up at week 112

From *New England Journal of Medicine*, Rizk DV, Barratt J, Suzuki Y, et al, Sibeprenlimab in IgA Nephropathy – Final Phase 3 Trial Analysis, Volume No. 396; page oa2609127. Copyright © 2026 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

[a]Patients who completed ≥20 doses and the end-of-trial visit at week 112 were eligible to enter an open-label extension trial (NCT05248659).

ACEi, angiotensin-converting enzyme inhibitor; APRIL, a proliferation-inducing ligand; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; Gd-IgA1, galactose-deficient immunoglobulin A1; IgA, immunoglobulin A; OLE, open-label extension; Q4W, every 4 weeks; SC, subcutaneous; SGLT2i, sodium-glucose cotransporter 2 inhibitor; uPCR-24h, 24-hour urine protein to creatinine ratio.

1. Perkovic V, et al. *Kidney Int Rep*. 2025;10(12):4207-4218. **2.** Phase 2/3 open-label trial of sibeprenlimab in the treatment of immunoglobulin A nephropathy. ClinicalTrials.gov. Updated May 5, 2026. Accessed September 29, 2026. https://clinicaltrials.gov/study/NCT05248659.

VISIONARY Phase 3: Endpoints and Assessments

Efficacy

Proteinuria *(primary)*

Ratio of uPCR at 9 months vs baseline based on 24-hour urine collection[1]

eGFR

- Annualized slope of eGFR over 24 months from week 4 *(key secondary)*
- Mean change of eGFR from baseline at 24 months *(secondary)*

Composite outcome of kidney function decline or kidney failure *(secondary)*

- Time to the first occurrence of a composite kidney outcome:
  - Sustained doubling of serum creatinine, sustained 40% reduction in eGFR, sustained eGFR <15 mL/min/1.73 m^2, or the requirement of kidney replacement therapy
- Incidence of patients experiencing at least one composite kidney outcome event through 24 months

Safety

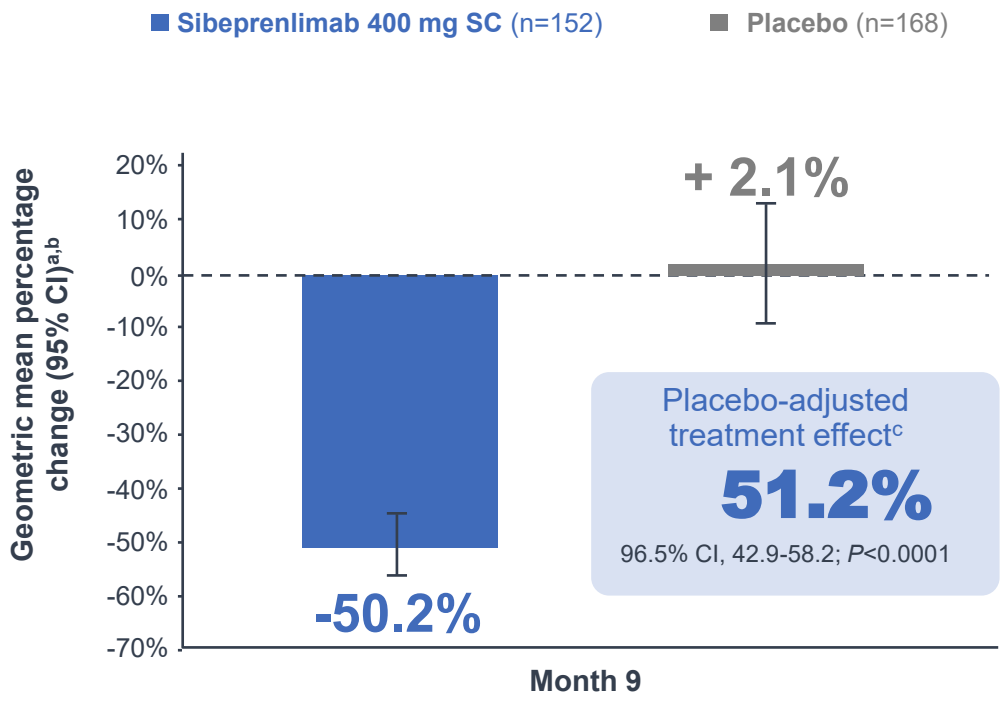
- Safety assessment of treatment-emergent adverse events *(secondary)*

The primary endpoint was assessed in the interim analysis set. eGFR and composite outcome assessments included the full analysis set, comprising all randomized patients with available baseline assessment.
eGFR, estimated glomerular filtration rate; uPCR, urine protein to creatinine ratio.

1. Perkovic V, et al. *N Engl J Med.* 2026;394(7):635-646.

VISIONARY Phase 3: uPCR-24h

Change from baseline in uPCR-24h at month 9 (primary endpoint; ANCOVA)



The primary endpoint (9-month uPCR-24h) was met in the prespecified interim analysis of 320 patients

From *New England Journal of Medicine*, Perkovic V, Trimarchi H, Tesar V, et al, Sibeprenlimab in IgA Nephropathy – Interim Analysis of a Phase 3 Trial, Volume No. 394, pages 635-646. Copyright © 2025 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

[a]The interim analysis set comprised the first 320 randomized participants who had the opportunity to complete the 9-month (week 40) 24-hour uPCR evaluation at the interim data cut. [b]The percentage reduction of uPCR-24h (g/g) at month 9 was compared with baseline using ANCOVA, calculated as (1 – GM of uPCR-24h ratio estimated from ANCOVA model) × 100%. [c]The percentage reduction for treatment effect was calculated as (1 – ratio of GM of uPCR-24h ratio for sibeprenlimab 400 mg SC over placebo estimated from ANCOVA model) × 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 interim analysis.

ANCOVA, analysis of covariance; CI, confidence interval; GM, geometric mean; SC, subcutaneous; uPCR, urine protein to creatinine ratio; uPCR-24h, 24-hour urine protein to creatinine ratio.

Perkovic V, et al. *N Engl J Med*. 2026;394(7):635-646.

24-Month Kidney Outcomes and Safety Results From the Phase 3 VISIONARY Trial

Baseline Demographics and Clinical Characteristics (N=510)

Demographic characteristics	Sibeprenlimab 400 mg SC (n=259)	Placebo (n=251)
Age, years, median (range)	41.0 (18.0-75.0)	43.0 (18.0-83.0)
Sex, n (%)		
Female	103 (39.8)	107 (42.6)
Race, n (%)		
Asian	159 (61.4)	142 (56.6)
White	91 (35.1)	96 (38.2)
Black or African American	1 (0.4)	3 (1.2)
Other	8 (3.1)	10 (4.0)
Geographic region, n (%)		
East Asia	83 (32.0)	76 (30.3)
South/Southeast Asia	69 (26.6)	63 (25.1)
Europe	56 (21.6)	58 (23.1)
North America	35 (13.5)	30 (12.0)
South America	16 (6.2)	24 (9.6)

Clinical characteristics[a]	Sibeprenlimab 400 mg SC (n=259)	Placebo (n=251)
Time from qualifying biopsy to randomization, median (range), years	1.4 (0.0-23.7)	1.5 (0.0-34.0)
Baseline uPCR-24h, g/g		
Mean (SD)	1.6 (1.0)	1.5 (0.8)
Median (range)	1.3 (0.5-7.8)	1.3 (0.5-5.5)
Baseline eGFR, mL/min/1.73 m^2		
Mean (SD)	65.0 (25.0)	63.4 (25.7)
Median (range)	61.0 (25.0-134.0)	59.0 (27.0-130.0)
Prior use of immunosuppressive drugs,[b] n (%)	14 (5.4)	8 (3.2)
Background regimen, n (%)		
RASi[c]	254 (98.1)	245 (97.6)
SGLT2i use[d]	112 (43.2)	119 (47.4)
Baseline dipstick hematuria, n (%)		
Positive[e]	206 (79.5)	183 (72.9)
Negative	53 (20.5)	68 (27.1)

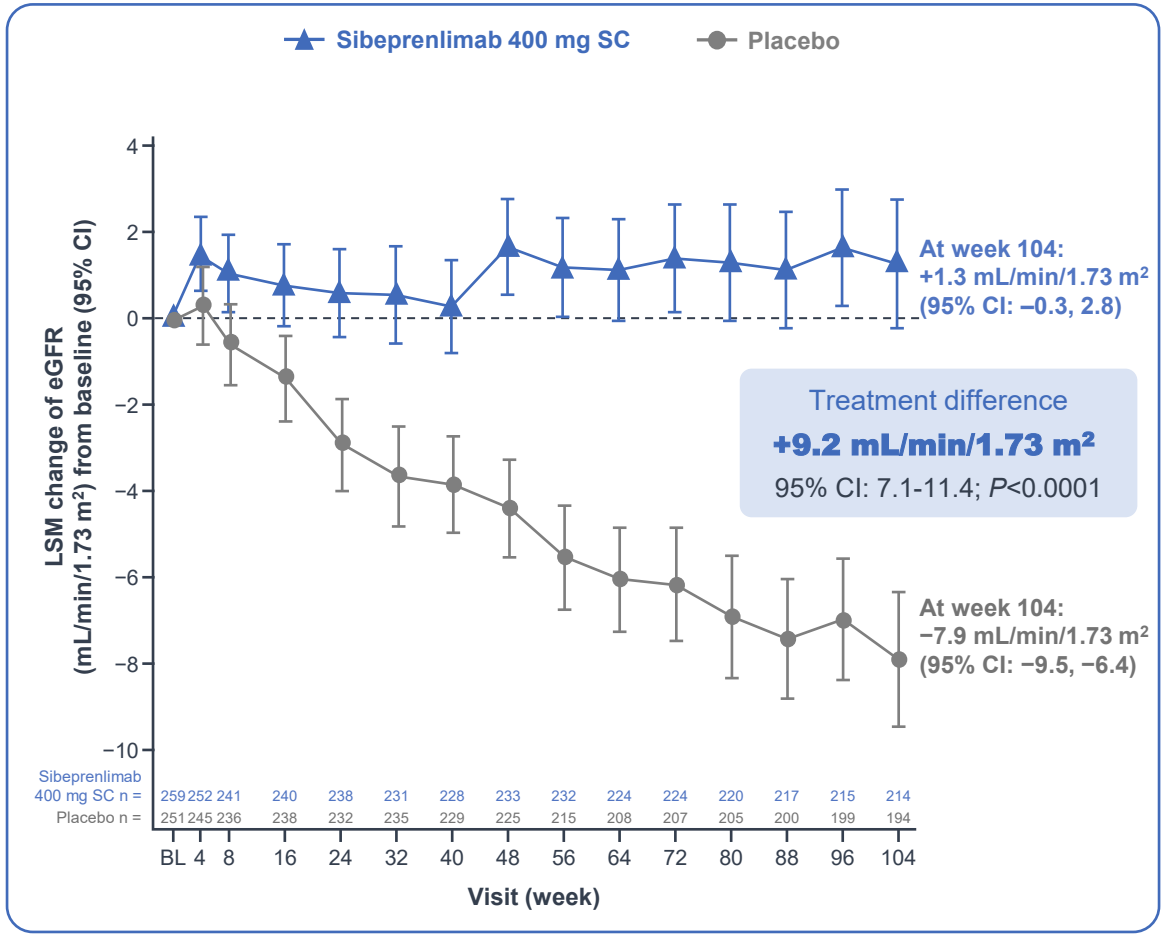
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[a]Baseline measurements were defined as the last available assessment at or before the first dose of study treatment. [b]Previous use included systemic corticosteroids and other immunosuppressive drugs or therapies. [c]Includes patients on an ACEi and/or ARB. [d]Includes patients on ACEi and/or ARB and SGLT2i and those on SGLT2i only. [e]Positive dipstick hematuria is defined as trace, 1+, 2+, or 3+.

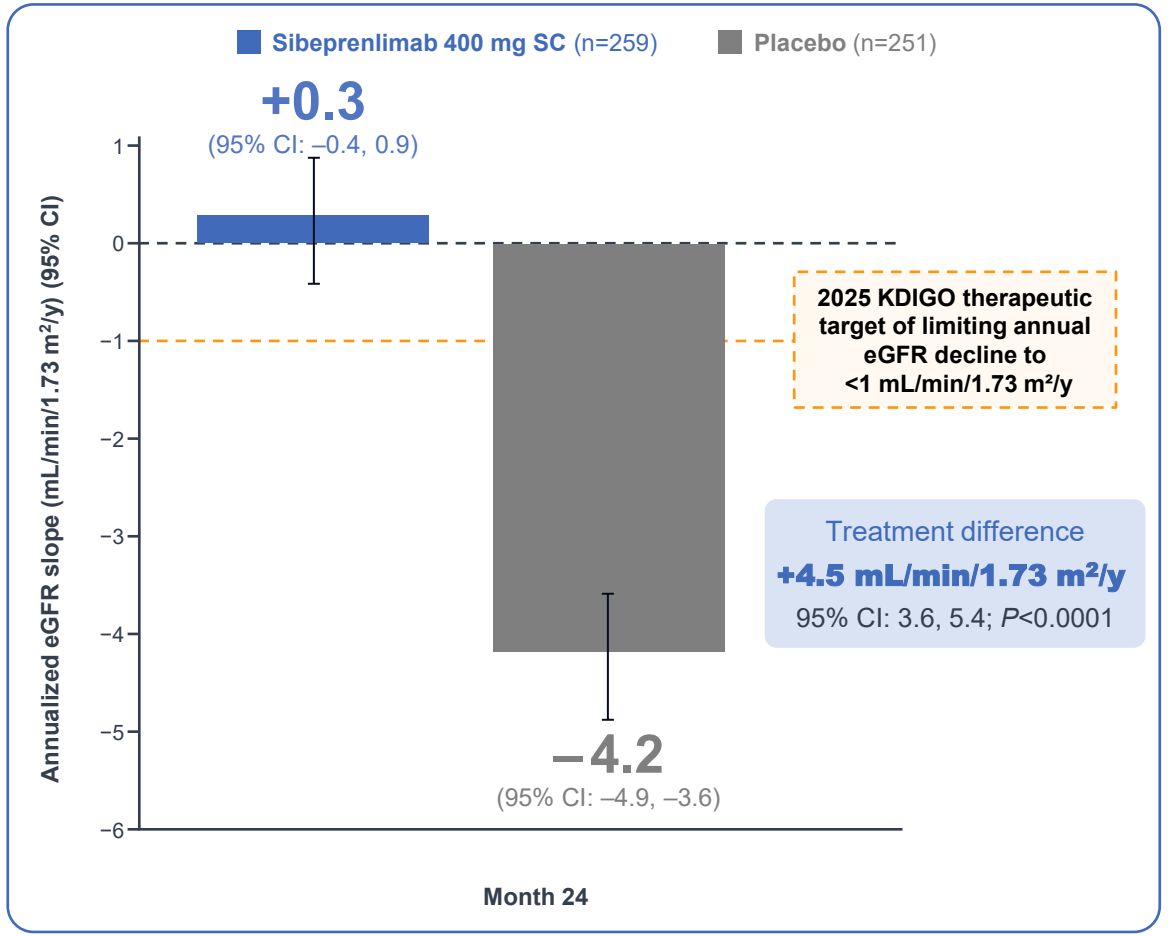
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; RASi, renin-angiotensin system inhibitor; SC, subcutaneous; SD, standard deviation; SGLT2i, sodium-glucose cotransporter 2 inhibitor; uPCR-24h, 24-hour urine protein to creatinine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

Treatment Effect on eGFR[a]

Change from baseline in eGFR over 24 months[b]



Annualized eGFR slope over 24 months[c]

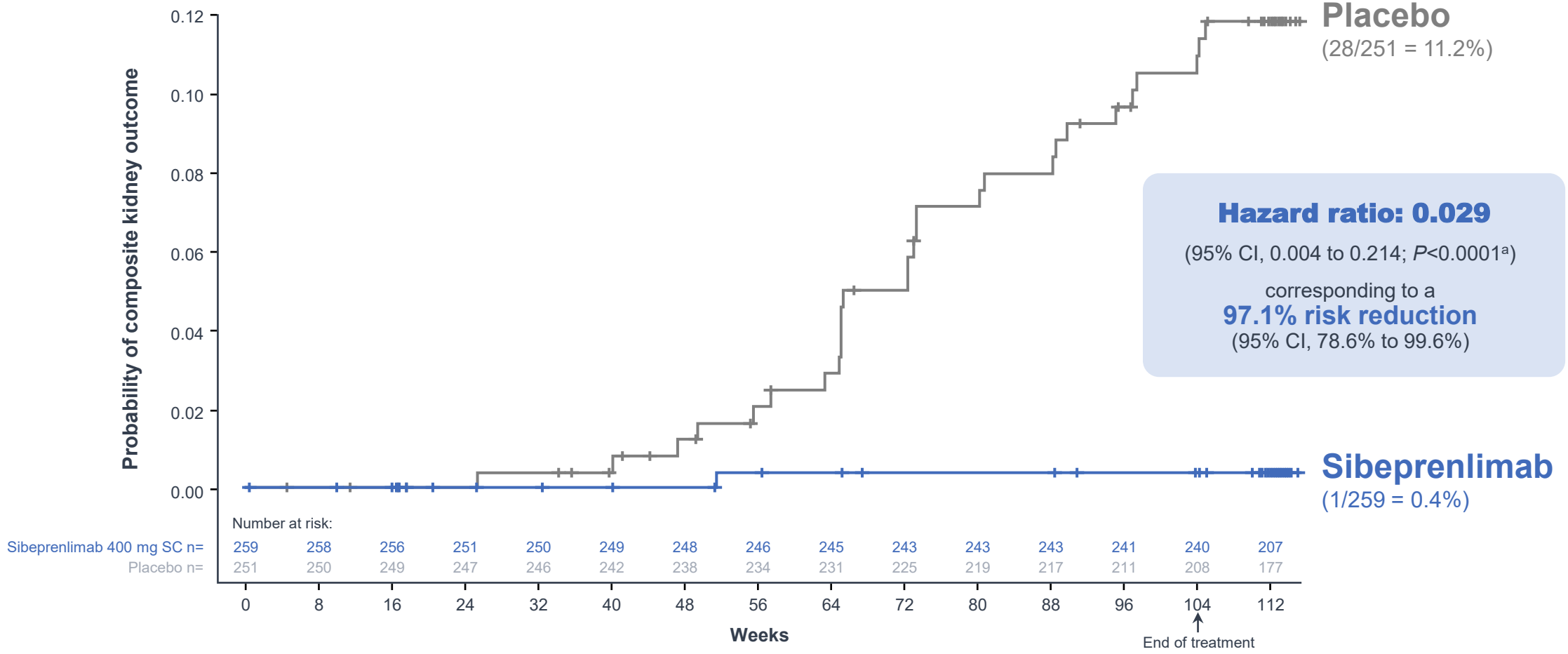


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[a]Analysis included the full analysis population, comprising all randomized patients. The hybrid estimand that includes hypothetical treatment of intercurrent events was applied to the analysis of eGFR. [b]Analyzed by the repeated measures model. The CIs for visits from week 4 through week 96 have not been adjusted for multiplicity and therefore should not be interpreted as providing confirmatory evidence of treatment effects. [c]Annualized slope estimated during planned treatment period with first measurement starting week 4, through week 104, using a linear mixed-effects model.

CI, confidence interval; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes; LSM, least-squares mean; SC, subcutaneous.

Progression to Composite Kidney Outcome



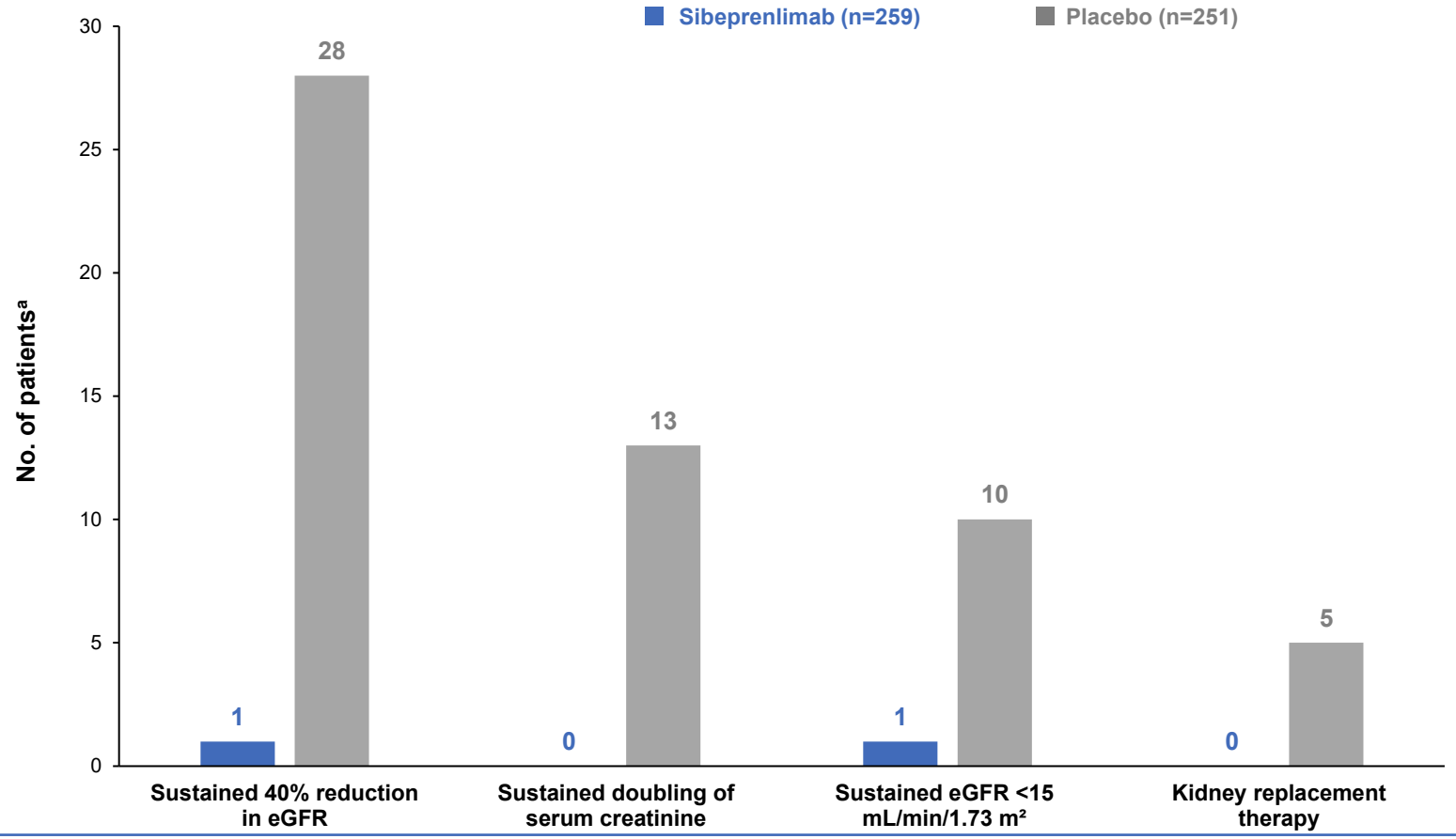
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Analysis included the full analysis population, comprising all randomized patients.

[a]The stratified log-rank test was used to obtain *P* value. Hazard ratio and its CI were obtained using the Cox proportional hazards model with treatment and stratification factors as covariates. Composite kidney outcome was defined as sustained 40% reduction in eGFR, sustained doubling of serum creatinine, sustained eGFR <15 mL/min/1.73 m^2, or requirement for kidney replacement therapy.

CI, confidence interval; eGFR, estimated glomerular filtration rate; SC, subcutaneous.

Components of the Composite Kidney Outcome



Composite kidney outcome event[b]:
Sibeprenlimab, n=1 (0.4%)
Placebo, n=28 (11.2%)

Odds ratio[c]: 0.026 (95% CI, 0.003 to 0.197; *P*<0.001)

Adjusted incidence difference[d]:
-10.8% (95% CI, -14.8 to -6.9)

Analysis included the full analysis population, comprising all randomized patients with available baseline assessment of the primary efficacy endpoint.

[a]Numbers represent patient counts satisfying each condition. Categories are not mutually exclusive; an individual patient may meet multiple conditions and thus appear across several entries. [b]Incidence of patients experiencing at least one composite kidney outcome event through 24 months. [c]Incidence of the composite kidney outcome was compared using a logistic regression model to estimate the odds ratio of the composite kidney outcome. [d]The strata-adjusted Cochran-Mantel-Haenszel method was used to estimate the incidence difference.

eGFR, estimated glomerular filtration rate.

Adverse Events

Adverse events occurring during the treatment period in the main cohort[a]

	Sibeprenlimab 400 mg SC (n=259)	Placebo (n=251)
	number of patients (%)	
Treatment-emergent adverse event (TEAE) occurring during treatment period[b]	235 (90.7)	226 (90.0)
Treatment-related adverse events (TRAEs)	91 (35.1)	82 (32.7)
Serious TEAEs occurring during treatment period[c]	21 (8.1)	32 (12.7)
Infections and infestations	5 (1.9)	10 (4.0)
Serious TRAEs	2 (0.8)	3 (1.2)
Severe TEAEs occurring during treatment period	10 (3.9)	19 (7.6)
TEAEs leading to discontinuation of sibeprenlimab or placebo	3 (1.2)	10 (4.0)
Deaths	0	0

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[a]Patients with multiple adverse events are counted only once per specific MedDRA preferred term. Patients with multiple adverse events in multiple system organ classes are counted only once toward the total. The safety population consisted of all the patients who received at least one dose of sibeprenlimab or placebo. [b]Adverse events are coded according to the Medical Dictionary for Regulatory Activities (MedDRA), version 29.0. [c]Serious adverse events were defined according to the study protocol.

SC, subcutaneous; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Common TEAEs

Adverse events occurring in ≥5% of patients during the treatment period in the main cohort[a]

	Sibeprenlimab 400 mg SC (n=259)	Placebo (n=251)
	number of patients (%)	
TEAEs in ≥5% of patients in either trial group[b]		
Any adverse event	188 (72.6)	204 (81.3)
Infections and infestations	133 (51.4)	128 (51.0)
Upper respiratory tract infection	58 (22.4)	53 (21.1)
Nasopharyngitis	51 (19.7)	48 (19.1)
Influenza	38 (14.7)	29 (11.6)
COVID 19	31 (12.0)	22 (8.8)
Gastroenteritis	14 (5.4)	17 (6.8)
Injection-site erythema	41 (15.8)	36 (14.3)
Injection-site pain	30 (11.6)	27 (10.8)
Injection-site swelling	20 (7.7)	18 (7.2)
Diarrhea	30 (11.6)	24 (9.6)
Pyrexia	25 (9.7)	16 (6.4)
Edema peripheral	9 (3.5)	23 (9.2)

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[a]Patients with multiple adverse events are counted only once per specific Medical Dictionary for Regulatory Activities (MedDRA) preferred term. Patients with multiple adverse events in multiple system organ classes are counted only once toward the total. The safety population consisted of all the patients who received at least one dose of sibeprenlimab or placebo. [b]Adverse events are coded according to MedDRA, version 29.0.

SC, subcutaneous; TEAE, treatment-emergent adverse event.

Conclusions

Sibeprenlimab, a selective APRIL blocker, reduced proteinuria, stabilized eGFR slope, and preserved kidney function over 24 months in patients with IgA nephropathy

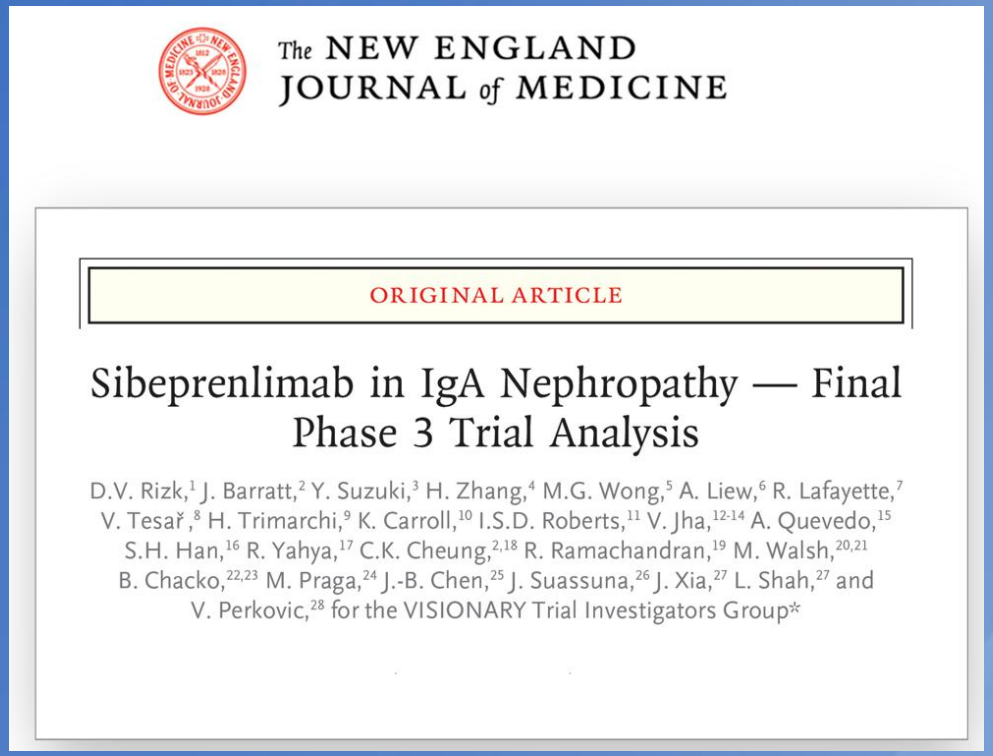
Sibeprenlimab reduced the risk of significant kidney function decline or kidney failure by 97.1%, substantially slowing progression to clinically meaningful kidney outcomes

The safety profile of sibeprenlimab was consistent through 24 months and comparable with placebo, including overall adverse events, infection rates, and injection site reactions

By achieving the 2025 KDIGO eGFR preservation target (<1 mL/min/1.73 m^2/y), reducing the risk of progression to kidney function loss and kidney failure, sibeprenlimab has the potential for disease modification and long-term kidney protection in IgA nephropathy

APRIL, a proliferation-inducing ligand; eGFR, estimated glomerular filtration rate; IgA, immunoglobulin A; KDIGO, Kidney Disease: Improving Global Outcomes.

Additional Resources: Phase 3 Publication



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Sibeprenlimab in IgA Nephropathy — Final Phase 3 Trial Analysis

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SCAN TO VIEW

Thank You!

We sincerely thank the patients and their families, investigators, study site personnel, and all clinical and operational teams whose dedication and collaboration made the Phase 3 VISIONARY trial possible

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