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AUGUST 3-7, 2026

MAUI, HAWAII





Effect of Sibeprenlimab on Circulating Immune Complexes in Adults With IgA Nephropathy in the Phase 3 VISIONARY Trial

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IgA Nephropathy Is an Immune Complex–Mediated Autoimmune Disease

APRIL

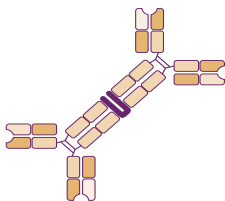
APRIL is a cytokine that acts as a driver of pathogenic Gd-IgA1 production and synthesis of autoantibodies¹



APRIL

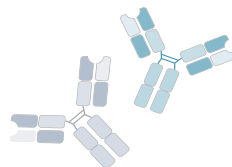
Hit 1

Production of pathogenic Gd-IgA1²



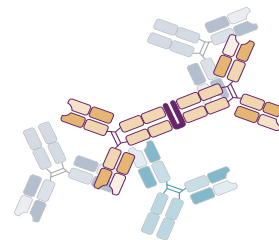
Hit 2

Synthesis of autoantibodies against Gd-IgA1²



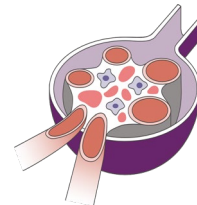
Hit 3

Immune complex formation²



Hit 4

Immune complex deposition in mesangium²



The deposition of Gd-IgA1–containing immune complexes in the glomerular mesangium of the kidneys triggers local inflammation, cellular proliferation, and kidney damage

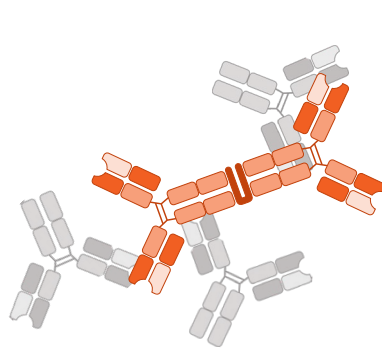
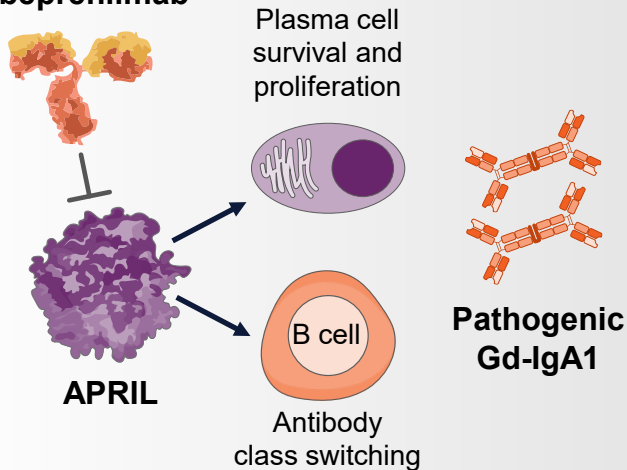
Sibeprenlimab Selectively Blocks APRIL, a Key Driver of IgA Nephropathy Pathogenesis

Sibeprenlimab is a humanized IgG2 mAb that selectively blocks APRIL, reducing pathogenic Gd-IgA1

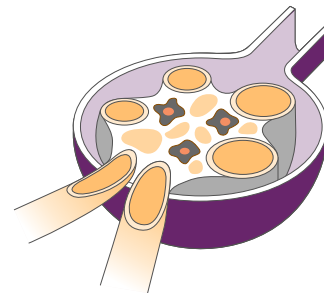
Gd-IgA1–autoantibody immune complex formation

Immune complex deposition in glomeruli

Sibeprenlimab



IgM/IgA- and IgG/IgA-immune complexes form in circulation



Leading to kidney damage and loss of function

Previously Published Results

VISIONARY Phase 3: Interim Analysis¹

- Sibeprenlimab resulted in a placebo-adjusted relative reduction in uPCR-24h of **51.2% (96.5% CI, 42.9%-58.2%; $P<0.001$)** at 9 months (week 40) and **54.3% (95% CI, 46.4%-60.9%)** at 12 months (week 52)^{a,b}
- Treatment with sibeprenlimab decreased levels of serum Gd-IgA1 by **67.1%**, and IgA by **68.8%**, IgG by **35.0%**, and IgM by **74.5%** at week 48^{c,d}
- The safety profile was comparable between sibeprenlimab and placebo. **No deaths** were reported

ENVISION Phase 2: CIC Correlation Analysis²

- Sibeprenlimab resulted in **robust reduction of IgM/IgA-CIC and IgG/IgA-CIC** at month 12
- Reductions in IgM/IgA-CICs and IgG/IgA-CICs were correlated with **reductions in Gd-IgA1 and uPCR** at month 12

^aInterim analysis set comprises the first 62.5% of randomized participants who had the opportunity to complete the 9-month uPCR-24h evaluation (cutoff date: September 4, 2024). ^bThe percentage reduction of uPCR-24h at month 9 is compared with baseline using ANCOVA, calculated as $(-1) \times (1 - \text{GM of uPCR-24h ratio estimated from ANCOVA model}) \times 100\%$. ^cGd-IgA1 was measured in ng/mL. ^dThis 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.

ANCOVA, analysis of covariance; CIC, circulating immune complex; Gd-IgA1, galactose-deficient IgA1; GM, geometric mean; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; PD, pharmacodynamics; uPCR-24h, 24-hour urine protein to creatinine ratio.

1. Perkovic V, et al. *N Engl J Med*. 2026;394(7):635-646. 2. Barratt J, et al. Presented at: American Society of Nephrology; October 23-27, 2024; San Diego, CA (abstr FR-OR59).

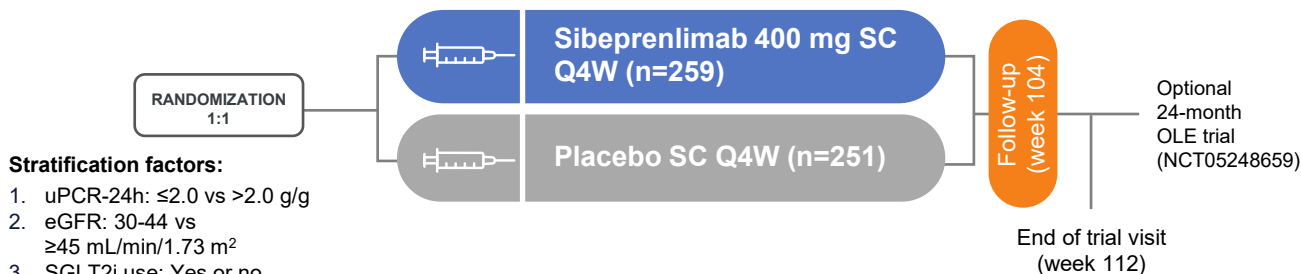
VISIONARY Phase 3: Trial Design



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 m²
- Stable or maximally tolerated dose of ACEi and/or ARB with or without SGLT2i for ≥ 3 months

INTERVENTION PERIOD Day 1 to week 100



Primary endpoint

- 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

- Evaluation of free APRIL and serum Gd-IgA1 concentrations over time
- Change in anti-IgA1 autoantibodies over time
- **Change in CIC from baseline through week 112^a**

Post hoc analysis

- **Correlation of CIC with IgA and Gd-IgA1 at week 36**

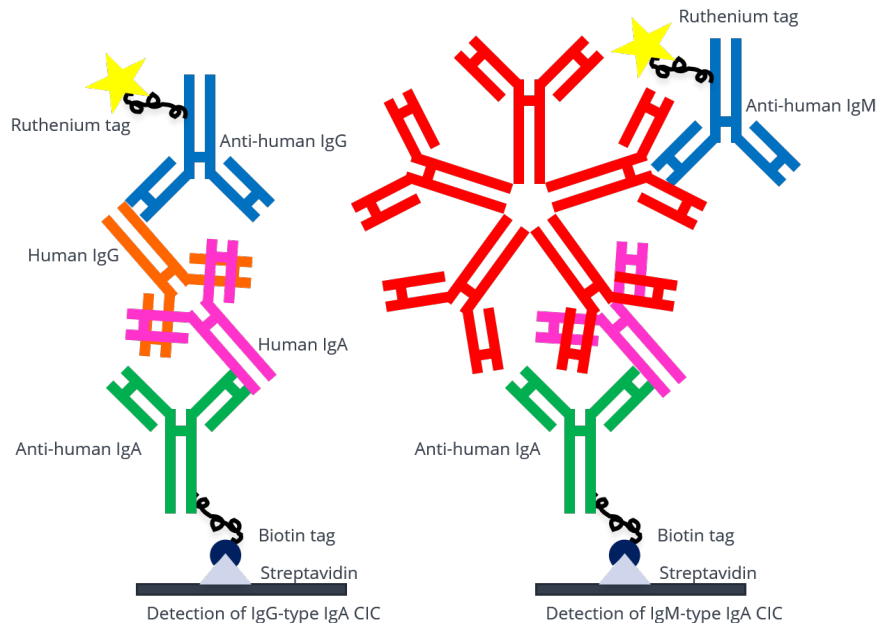
BEING PRESENTED

^aSamples for CIC assessments were collected on day 1 and weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, and 112.

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

Methodology: CIC Assay

- CICs were evaluated in 338 patients enrolled in the VISIONARY trial at the time of the interim analysis
- Serum CICs were measured using a semiquantitative, plate-based, sequential electrochemiluminescence immunoassay (ECLIA)
- IgG/IgA-CICs and IgM/IgA-CICs were captured by biotin-tagged anti-human IgA and detected by ruthenylated anti-human IgG or anti-human IgM, respectively



Demographics and Clinical Characteristics

For participants with available CIC data (N=338)^a

Demographic characteristics	Sibeprenlimab 400 mg SC (n=167)	Placebo (n=171)
Median age (range), years	45 (18-75)	45 (18-74)
Sex, n (%)		
Male	96 (57.5)	94 (55.0)
Female	71 (42.5)	77 (45.0)
Race, n (%)		
Asian	86 (51.5)	83 (48.5)
White	74 (44.3)	78 (45.6)
Other	7 (4.2)	10 (5.8)
Geographic region, n (%)		
East Asia	51 (30.5)	52 (30.4)
Europe	46 (27.5)	48 (28.1)
South/Southeast Asia	31 (18.6)	30 (17.5)
North America	23 (13.8)	20 (11.7)
South America	16 (9.6)	21 (12.3)

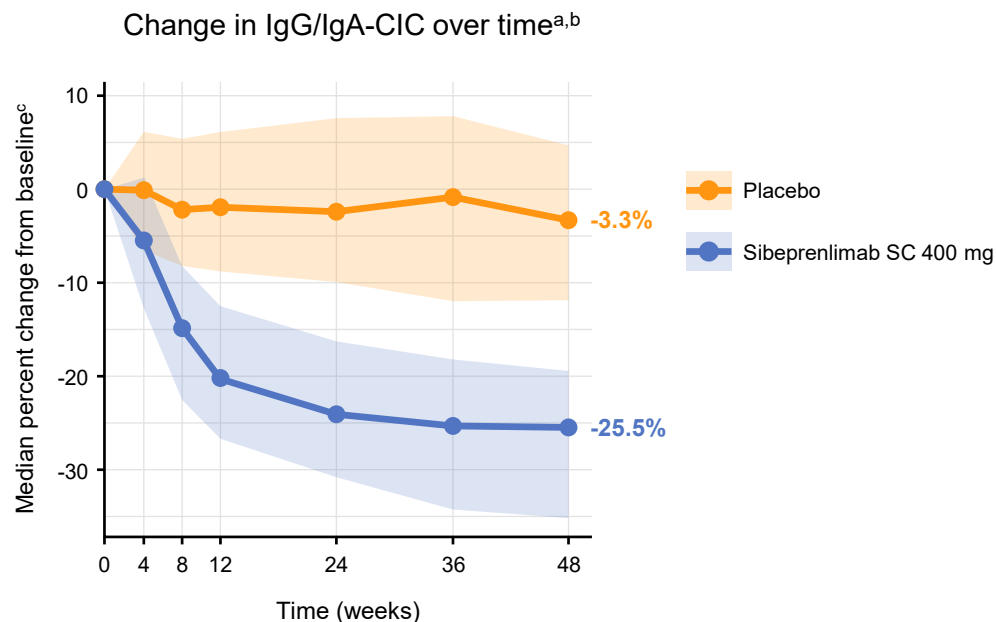
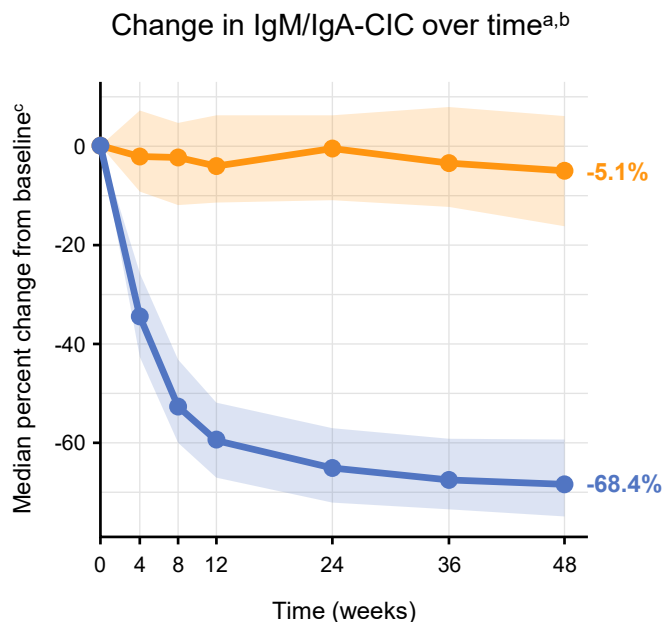
Clinical characteristics	Sibeprenlimab 400 mg SC (n=167)	Placebo (n=171)
Median time from initial biopsy to randomization (range), years	1.5 (0.0-23.7)	1.7 (0.0-34.0)
Baseline uPCR-24h, ^b g/g		
Geometric mean (GSD)	1.3 (1.6)	1.3 (1.6)
Median (range)	1.3 (0.6-5.4)	1.2 (0.5-4.9)
Baseline eGFR, ^b mL/min/1.73 m ²		
Mean (SD)	63.9 (24.4)	64.5 (25.6)
Median (range)	59.0 (26.0-134.0)	60.0 (27.0-130.0)
Prior use of immunosuppressive drugs, ^c n (%)	9 (5.4)	3 (1.8)
Background regimen, n (%)		
ACEi and/or ARB	163 (97.6)	166 (97.1)
SGLT2i ^d	72 (43.1)	92 (53.8)
Baseline dipstick hematuria, ^b n (%)		
Positive ^e	131 (78.4)	123 (71.9)
Negative	36 (21.6)	48 (28.1)

^aPreviously reported IA cohort was used for the correlation analysis. ¹ Change over time analysis cohort (as shown here) included participants from the exploratory cohort. ^bBaseline measurements were defined as the last available assessment at or prior to the first dose of sibeprenlimab, unless stated otherwise. ^cIncludes systemic corticosteroids and other immunosuppressive therapies. ^dIncludes patients on ACEi and/or ARB and SGLT2i and those on SGLT2i only. ^ePositive hematuria is defined as trace, 1+, 2+, 3+.

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CIC, circulating immune complex; eGFR, estimated glomerular filtration rate; GSD, geometric standard difference; IA, interim analysis; SC, subcutaneous; SGLT2i, sodium-glucose cotransporter 2 inhibitor; uPCR-24h, 24-hour urine protein to creatinine ratio.

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

Effect of Sibeprenlimab on CIC Over Time

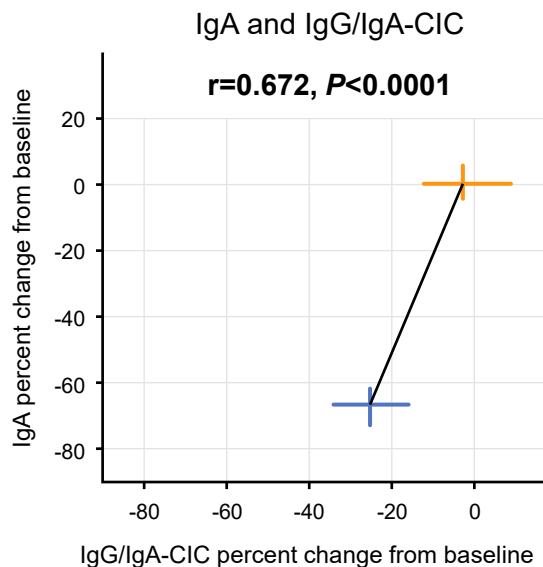
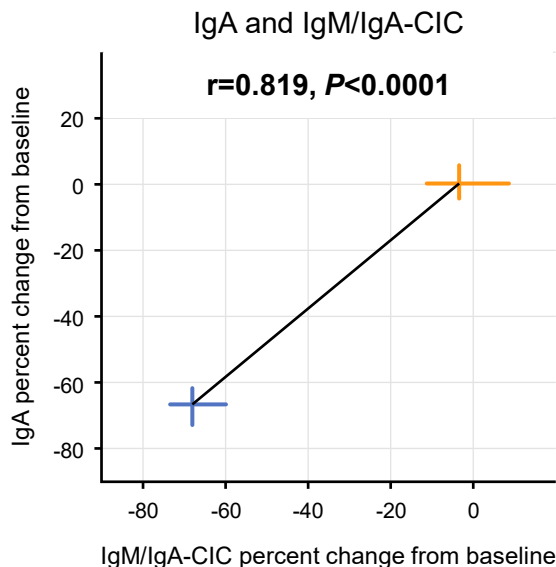


^aMixed immune complexes comprising IgA and IgM (IgM/IgA-CIC) or IgA and IgG (IgG/IgA-CIC) were quantified in serum using plate immunoassay. ^bCIC data were available for 338 participants (sibeprenlimab, n=167; placebo, n=171). ^cLongitudinal median percentage change with IQR by Analyte.

CIC, circulating immune complex; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; IQR, interquartile range; SC, subcutaneous.

Correlation Between CIC and IgA

Correlation between percentage change from baseline of IgA and IgM/IgA-CIC and IgG/IgA-CIC at week 36^{a-c}



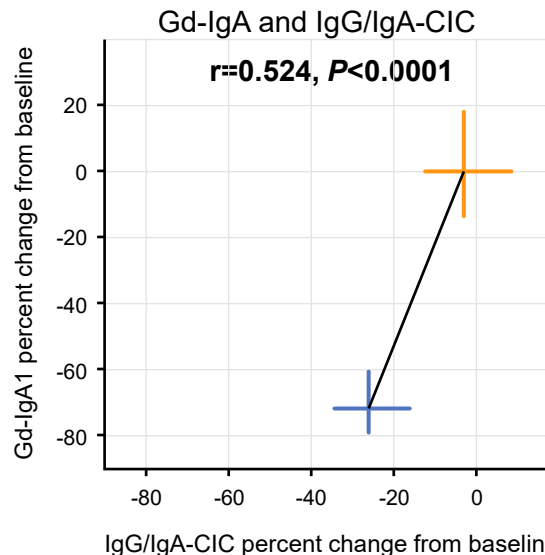
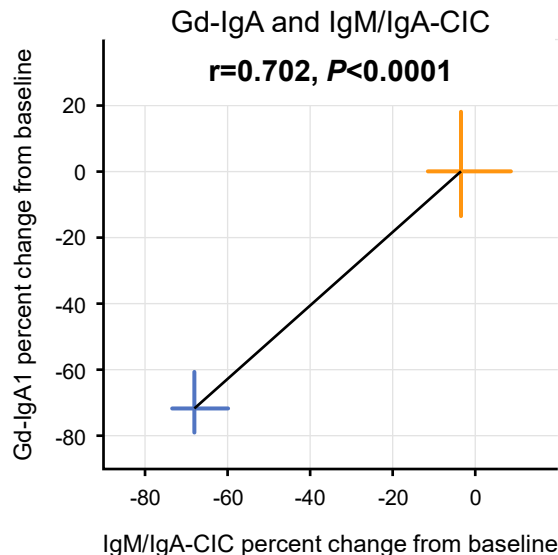
 Placebo
 Sibeprenlimab SC 400 mg

^aMixed immune complexes comprising IgA and IgM (IgM/IgA-CIC) or IgG (IgG/IgA-CIC) were quantified in serum using plate immunoassay. ^bNonparametric Spearman correlation with *P* value for percentage change from baseline to account for outliers and asymmetric distribution where normality does not hold. ^cOnly patients with 9-month Gd-IgA1 and IgA data were included in this analysis.

CIC, circulating immune complex; Gd-IgA1, galactose-deficient IgA1; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; *r*, Spearman correlation coefficient; SC, subcutaneous.

Correlation Between CIC and Gd-IgA1

Correlation between percentage change from baseline of Gd-IgA1 and IgM/IgA-CIC and IgG/IgA-CIC at week 36^{a-c}



 Placebo
 Sibeprenlimab SC 400 mg

^aMixed immune complexes comprising IgA and IgM (IgM/IgA-CIC) or IgG (IgG/IgA-CIC) were quantified in serum using plate immunoassay. ^bNonparametric Spearman correlation with *P* value for percentage change from baseline to account for outliers and asymmetric distribution where normality does not hold. ^cOnly patients with 9-month Gd-IgA1 and IgA data were included in this analysis.

CIC, circulating immune complex; Gd-IgA1, galactose-deficient IgA1; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; *r*, Spearman correlation coefficient; SC, subcutaneous.

Conclusions



- Sibeprenlimab demonstrated robust reduction of IgM/IgA and IgG/IgA-CIC starting as early as 4 weeks in patients with IgA nephropathy



- Correlations between reductions in CICs, reduction in IgA, and reduction in Gd-IgA1 were robust and statistically significant



- Reduction in pathogenic Gd-IgA and CIC provides mechanistic evidence for the effects of APRIL inhibition. These results support IgA, Gd-IgA1, and CICs as closely related biomarkers for treatment response in the context of APRIL inhibition for IgA nephropathy, potentially reflecting the disease-modifying potential of sibeprenlimab in the treatment of IgA nephropathy



- Findings are consistent with Phase 2 results.^{1,2} Future planned analyses include correlation of CIC with clinical outcomes (ie, proteinuria and eGFR)

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