Abstract 1049

Sparsentan (SPAR) Added to Stable Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2is) in Adults With IgA Nephropathy (IgAN) in the Phase 2 SPARTACUS Trial

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MA-SP-25-0166

Presented at GlomCon Hawaii 2025; September 22-25, 2025; Kahuku, HI, USA

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DISCLOSURES

- **CG, CT, DSL**, **RK**, **BH** and **SM** are employees and may be stockholders of Travere Therapeutics, Inc.
- **IA** reports a contract with George Clinical for being a US national leader on SPARTACUS (payment to their institution for salary support from Travere Therapeutics, Inc.); payment for participation in advisory board activity from Aurinia, Calliditas Therapeutics, GSK, HI-Bio, Otsuka Pharmaceuticals, Sanofi, Travere Therapeutics, Inc., and Vera Therapeutics; and a speaker honorarium from Roche
- **SCWT** reports consulting fees from Boehringer Ingelheim, Novartis, and Travere Therapeutics, Inc.; speakers honoraria from AstraZeneca, Bayer, Boehringer Ingelheim, GSK, and Novartis; their role as president of the Asian Pacific Society of Nephrology (2022-2024); and their role on the executive committee of KDIGO (2020-2023)
- **LAK** is a principal investigator for studies sponsored by Akebia Therapeutics, Alpine Therapeutics, AstraZeneca, Boehringer Ingelheim, Cara Therapeutics, Chinook Therapeutics, CSL Behring, Galderma, Mineralys Therapeutics, Inc., Novartis, Omeros, Otsuka Pharmaceuticals, Reata Pharmaceuticals, Travere Therapeutics, Inc., Vera Therapeutics, Visterra, and Walden Biosciences; and participation on advisory boards for Novartis and Otsuka Pharmaceuticals
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- **BHR** reports consulting fees and clinical trial funding to their institution from Travere Therapeutics, Inc.
- Previously presented at the European Renal Association (ERA) Congress 2025; June 4-7, 2025; Vienna, Austria

- Sparsentan is a non-immunosuppressive, dual endothelin angiotensin receptor antagonist (DEARA)[1,2] approved in the US to slow kidney function decline in adults with primary IgAN at risk for disease progression[3] and in the UK and Europe to treat primary IgAN[4]
- In patients with IgAN, sparsentan showed sustained albuminuria reduction and preservation of kidney function in the phase 3 PROTECT trial[2]
- In an independent subgroup analysis from DAPA-CKD and EMPA-KIDNEY, SGLT2is also reduced albuminuria and kidney disease progression in patients with IgAN[5,6]

Aim

- To report the final analysis of SPARTACUS, which evaluated the efficacy and safety of replacing RASi with sparsentan in adults with IgAN receiving stable SGLT2i therapy

DEARA, dual endothelin angiotensin receptor antagonist; IgAN, immunoglobulin A nephropathy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor.

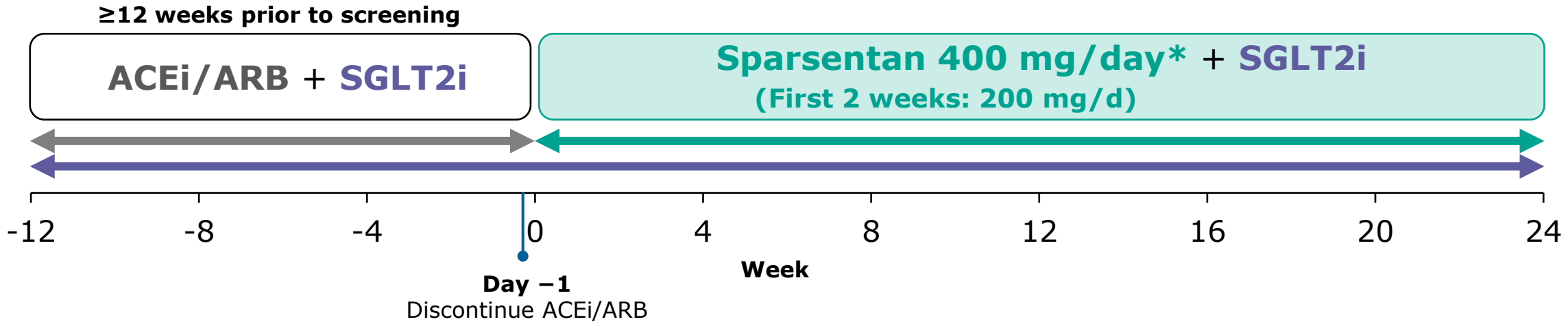
1. Kohan DE, et al. *Clin Sci (Lond)*. 2024;138(11):645-662. **2.** Rovin BH, et al. *Lancet*. 2023;402(10417):2077-2090. **3.** Filspari (sparsentan). Prescribing information. Travere Therapeutics, Inc.; 2025. **4.** Filspari (sparsentan). Summary of product characteristics. CSL Vifor; 2024. **5.** Wheeler DC, et al. *Kidney Int*. 2021;100(1):215-224. **6.** EMPA-KIDNEY Collaborative Group. *Lancet Diabetes Endocrinol*. 2024;12(1):51-60.

Study Design

- SPARTACUS (NCT05856760) was an open-label, multicenter study of the efficacy and safety of 24 weeks of sparsentan added to a stable SGLT2i in patients with IgAN at risk of disease progression

Eligibility criteria at screening:

- Adults with biopsy-proven IgAN
- Spot UACR ≥0.3 g/g
- eGFR ≥25 mL/min/1.73 m^2
- Stable SGLT2i + ACEi/ARB ≥12 weeks



ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; IgAN, immunoglobulin A nephropathy; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UACR, urine albumin-to-creatinine ratio.
*Sparsentan was titrated up to the target dose of 400 mg, from the initial 200-mg dose, at the start of week 3.

Endpoints

Primary efficacy

- Change from baseline in UACR* at week 24

Secondary efficacy

- Achievement of:
  - UACR <0.2 g/g at week 24
  - ≥30% reduction from baseline in UACR at week 24
  - ≥50% reduction from baseline in UACR at week 24
- Change from baseline at each visit:
  - UACR
  - UPCR
  - eGFR
  - Blood pressure

Safety

- TEAEs
- Serious AEs
- AEs of interest
- AEs leading to treatment discontinuation

AE, adverse event; eGFR, estimated glomerular filtration rate; TEAE, treatment-emergent adverse event; UACR, urine albumin-to-creatinine ratio; UPCR, urine protein-to-creatinine ratio.
*Based on first morning void samples.

Patient Demographics and Baseline Characteristics

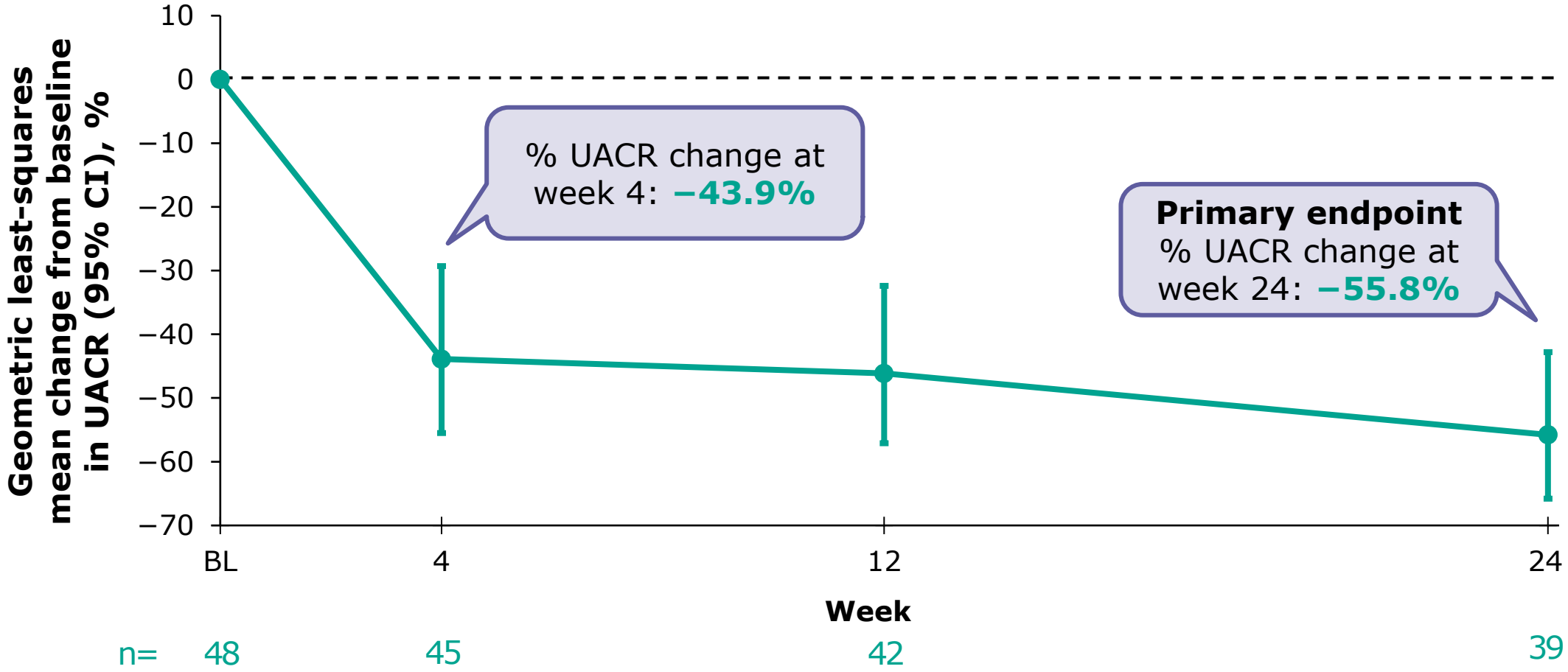
	SGLT2i + Sparsentan (N=48)
Age at informed consent, mean (SD), y	48.9 (13.9)
Time from initial biopsy to informed consent, median (IQR), y	3.0 (1.0-8.0)
Male sex, n (%)	28 (58)
Race, n (%)	
Asian	19 (40)
White	28 (58)
Black or African American	1 (2)
Weight, mean (SD), kg	85.9 (22.3)
Body mass index, mean (SD), kg/m^2	30.0 (5.6)
Blood pressure, mean (SD), mm Hg	
Systolic	128.0 (12.6)
Diastolic	80.0 (10.4)
UACR, median (IQR), g/g	0.70 (0.49-1.01)
UPCR, median (IQR), g/g	1.24 (0.88-1.74)
eGFR, mean (SD), mL/min/1.73 m^2	56.9 (26.0)
Hematuria, n (%)	29 (60)
Glycosuria, n (%)	46 (96)*

eGFR, estimated glomerular filtration rate; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UACR, urine albumin-to-creatinine ratio; UPCR, urine protein-to-creatinine ratio.

*One patient was negative for glycosuria at baseline, despite receiving the maximum labeled dose of an SGLT2i, but was positive for glycosuria at all other assessments including at screening. Another patient who was negative for glycosuria at baseline was not taking an SGLT2i during screening (protocol deviation) and discontinued treatment at approximately week 9.

Change in UACR at Each Visit

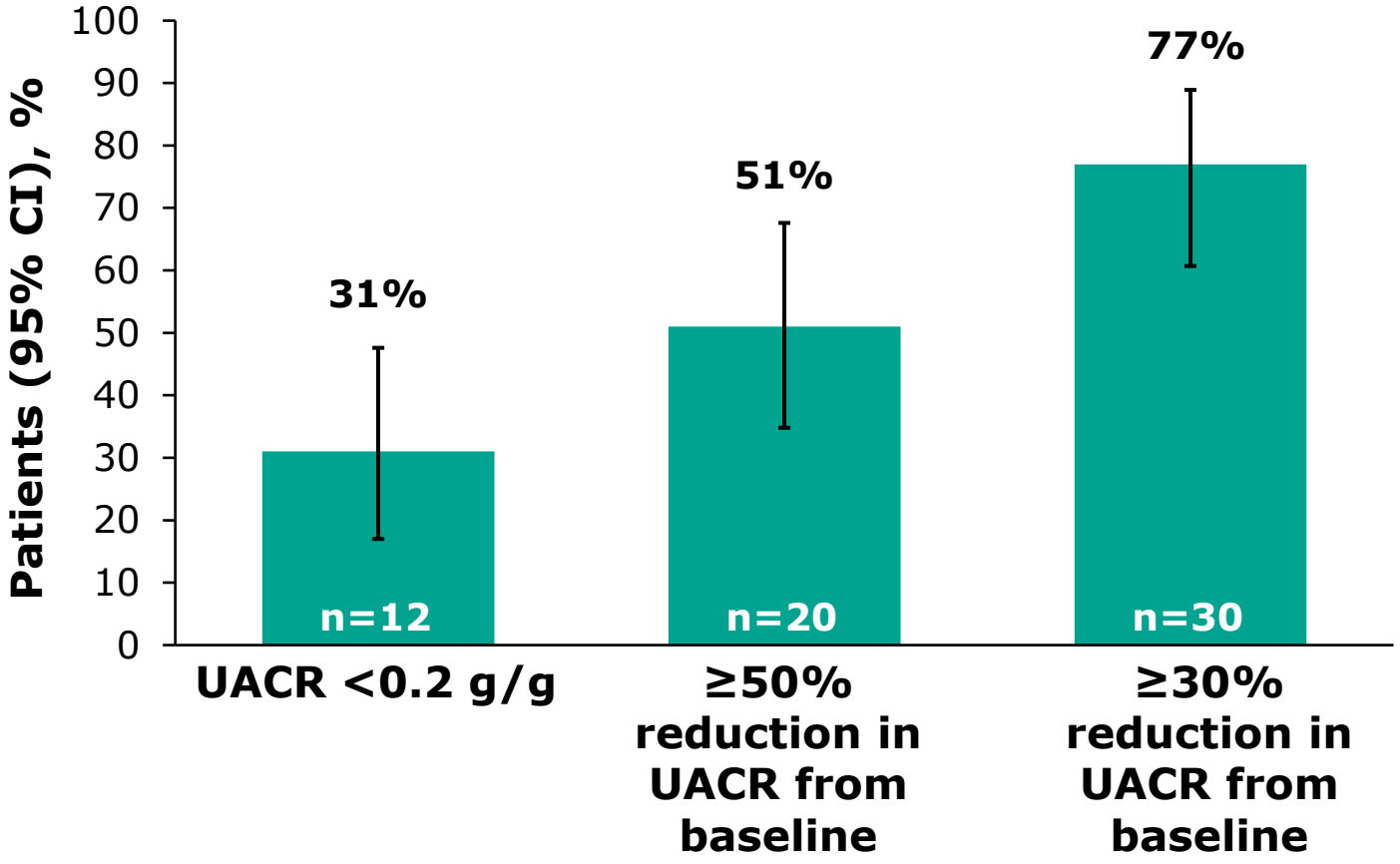
- Replacing RASi with sparsentan in patients receiving stable SGLT2i treatment led to rapid and sustained reductions in UACR



BL, baseline; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UACR, urine albumin-to-creatinine ratio.

Percent of Patients Achieving UACR Reduction Endpoints at Week 24

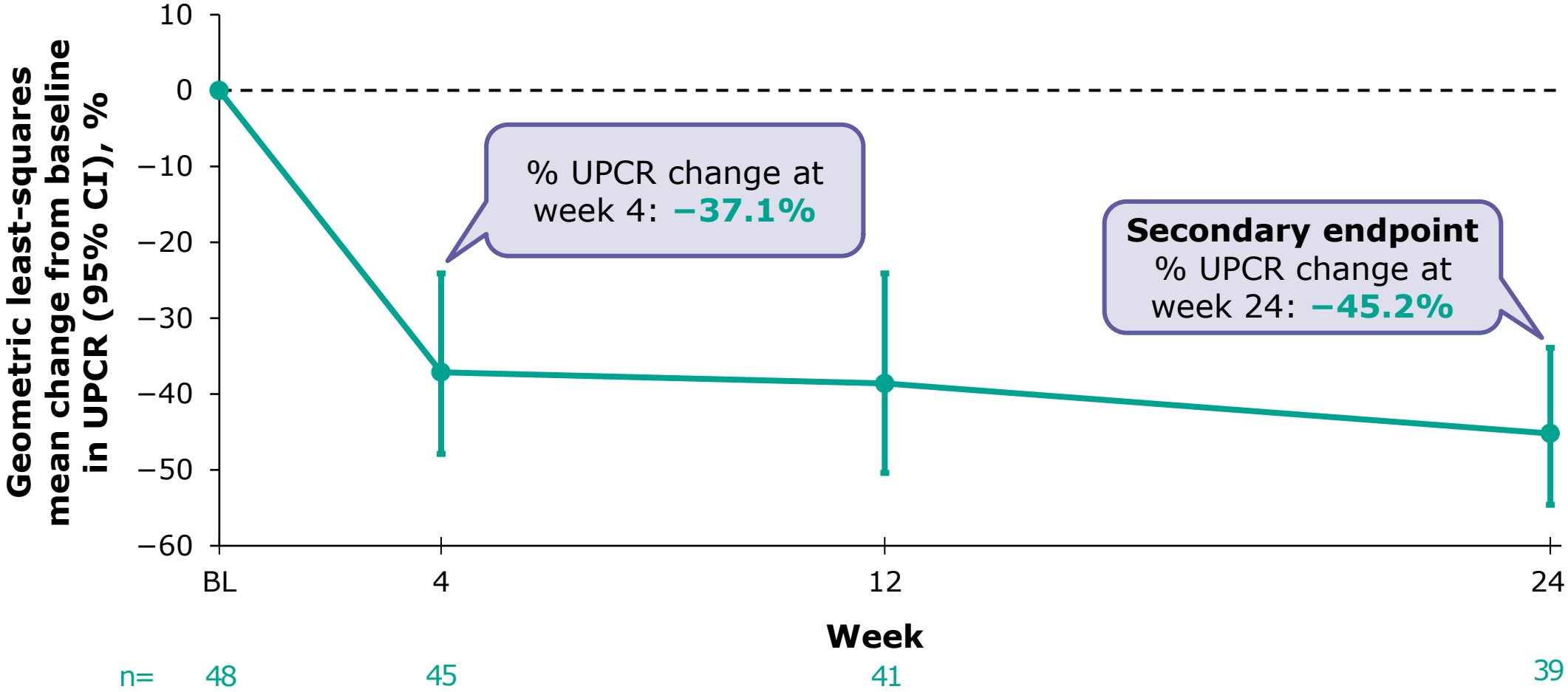
- Replacing RASi with sparsentan in patients receiving stable SGLT2i treatment allowed patients to reach albuminuria target response endpoints



RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UACR, urine albumin-to-creatinine ratio.

Change in UPCR at Each Visit

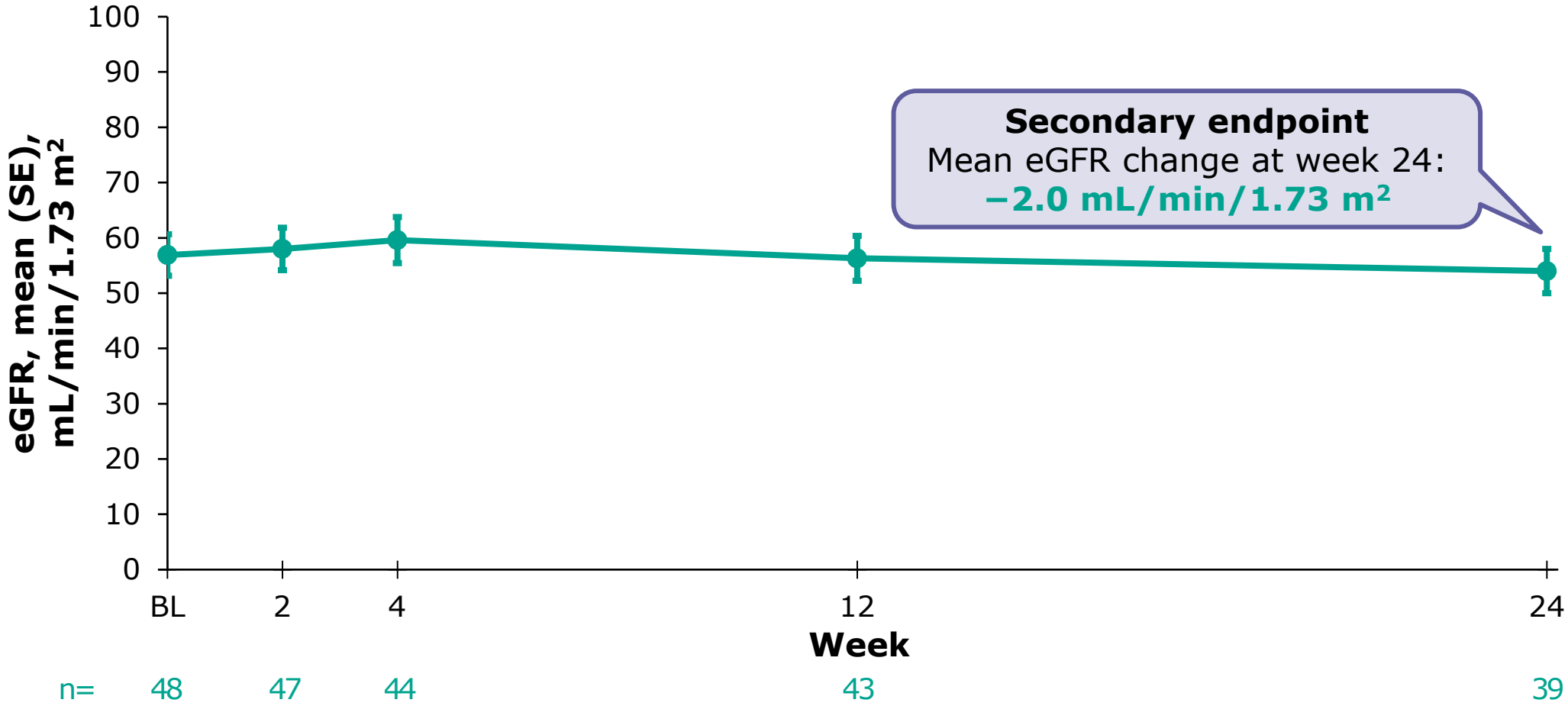
- Replacing RASi with sparsentan in patients receiving stable SGLT2i treatment led to rapid and sustained reductions in UPCR



BL, baseline; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

eGFR Values at Each Visit

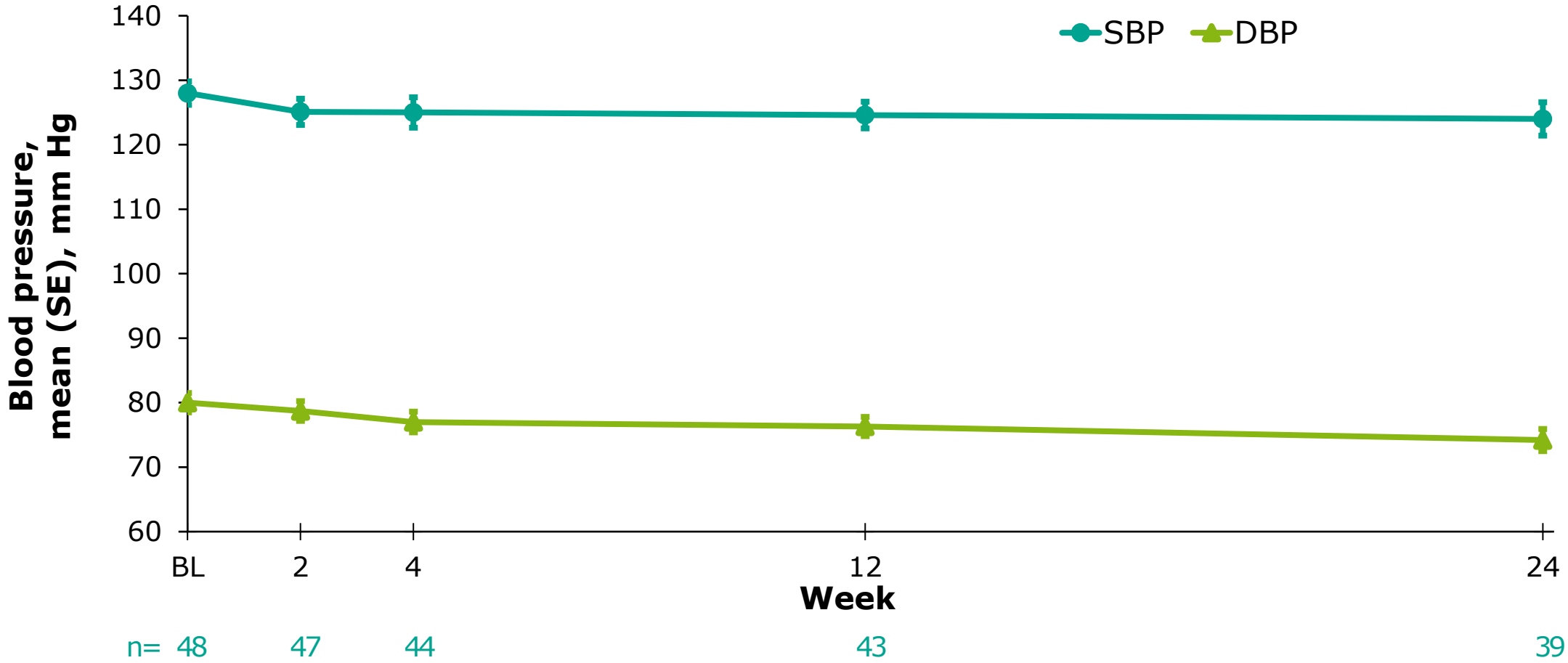
- eGFR remained relatively stable during the study following the replacement of RASi with sparsentan in adults receiving stable SGLT2i treatment



BL, baseline; eGFR, estimated glomerular filtration rate; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor.

Change in Blood Pressure at Each Visit

- After replacing RASi with sparsentan in adults receiving SGLT2i therapy, a slight decrease in blood pressure was observed through week 24



BL, baseline; DBP, diastolic blood pressure; RASi, renin-angiotensin system inhibitor; SBP, systolic blood pressure; SGLT2i, sodium-glucose cotransporter-2 inhibitor.

Safety

	SGLT2i + sparsentan (N=48)
Any TEAEs, n (%)	30 (63)
Sparsentan related	10 (21)
SGLT2i related	2 (4)
Any TEAE reported in >2 patients, n (%)	
Hypotension	7 (15)
Headache	4 (8)
Edema	4 (8)
Peripheral edema	4 (8)
Upper respiratory tract infection	4 (8)
Dizziness	3 (6)
Any severe TEAE, n (%)	2 (4)
Peripheral edema	1 (2)
Gout	1 (2)
Any serious AE, n (%)	4 (8)
Acute kidney injury*,†	1 (2)
Cerebrovascular accident	1 (2)
Chemical burn	1 (2)
Deep vein thrombosis	1 (2)
Osteoarthritis*	1 (2)
Any abnormal liver function test results >3 × ULN, n (%)‡	0 (0)
Any TEAE leading to sparsentan discontinuation, n (%)	4§ (8)

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SGLT2i, sodium-glucose cotransporter-2 inhibitor; TEAE, treatment-emergent adverse event; ULN, upper limit of normal.
*Reported in the same patient. †The incident of acute kidney injury was mild, deemed unrelated to sparsentan or SGLT2i treatment, and was resolved after interruption of sparsentan and SGLT2i. ‡Abnormal liver function test results met the following criteria: (1) new elevation in ALT or AST >3 × ULN with or without elevation of total serum bilirubin >2 × ULN and (2) 2-fold increase in ALT or AST above the baseline value in patients who had elevated values prior to taking study medication. §One patient each discontinued sparsentan treatment due to a TEAE of vertigo, hypotension, peripheral edema, and Henoch-Schönlein purpura.

CONCLUSIONS

- In patients with IgAN receiving stable SGLT2i therapy, replacing maximally tolerated RASi with sparsentan resulted in rapid and sustained albuminuria and proteinuria reductions, suggesting a potential to further decrease the risk of kidney disease progression
- Nearly one-third of patients achieved UACR <0.2 g/g
- Sparsentan added to SGLT2i therapy is generally well tolerated, with no unexpected safety signals

IgAN, immunoglobulin A nephropathy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UACR, urine albumin-to-creatinine ratio.

ACKNOWLEDGMENTS

- This study was funded by Travere Therapeutics, Inc.
- Medical writing assistance and editorial support were provided under the direction of the authors by CJ Henley-Smith, PhD, and Chris Edwards, PhD, CMPP, of Nucleus Global, an Inizio company, in accordance with Good Publication Practice guidelines, and was funded by Travere Therapeutics, Inc.
- The authors thank all the patients, families, and investigators who made this study possible

Questions?