Concomitant Sparsentan and Sodium-Glucose Cotransporter-2 Inhibitors in Adults With IgA Nephropathy in the Ongoing Phase 2 SPARTACUS Trial

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RESULTS

Patient Demographics and Baseline Characteristics

- 20 patients received ≥1 dose of SPAR (**Table 1**)

Table 1. Patient Demographics and Baseline Characteristics

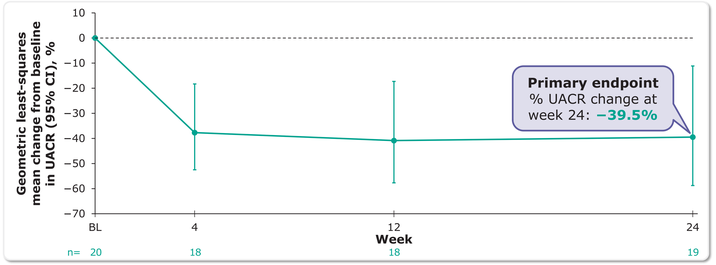
	SPAR + SGLT2i (N=20)
Age at informed consent, mean (SD), y	52.9 (15.0)
Time from initial biopsy to informed consent, median (IQR), y	5.0 (2.5-9.5)
Male sex, n (%)	13 (65)
Race, n (%)	
Asian	9 (45)
White	11 (55)
Weight, mean (SD), kg	90.9 (22.8)
Body mass index, mean (SD), kg/m²	31.4 (5.6)
Blood pressure, mean (SD), mm Hg	
Systolic	129.8 (12.5)
Diastolic	78.8 (10.9)
UACR, median (IQR), g/g	0.84 (0.52-1.26)
UPCR, median (IQR), g/g	1.45 (1.06-2.40)
eGFR, mean (SD), mL/min/1.73 m²	54.8 (20.6)
Hematuria*, n (%)	10 (50)
Glycosuria, n (%)	18† (90)

*Includes categories of trace, 1+, 2+, and 3+. †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.

Efficacy

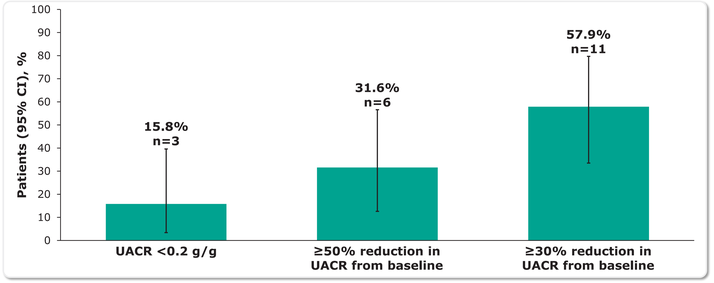
- SPAR added to stable SGLT2i treatment led to rapid and sustained reductions in UACR (**Figure 3**) and UPCR

Figure 3. Change in UACR at Each Visit



- SPAR added to stable SGLT2i treatment allowed patients to reach target response endpoints (**Figure 4**)

Figure 4. Percent of Patients Achieving UACR Reduction Endpoints at Week 24



- eGFR remained relatively stable during the study following the addition of SPAR to stable SGLT2i treatment (**Figure 5**)
- Slight decreases in blood pressure were observed following the addition of SPAR to stable SGLT2i treatment (**Figure 6**)

Figure 5. Change in eGFR at Each Visit

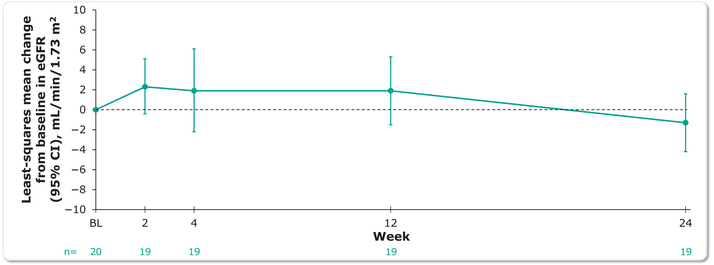
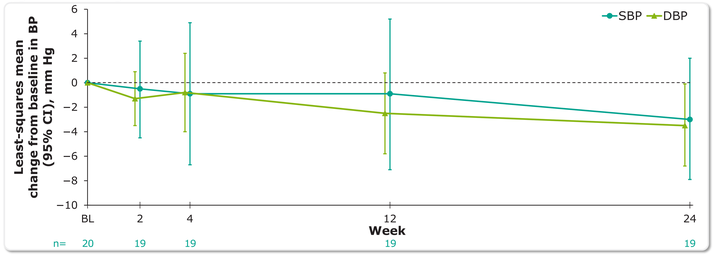


Figure 6. Change in Blood Pressure at Each Visit



Safety

- The addition of SPAR to stable SGLT2i treatment was generally well tolerated, with no unexpected safety signals (**Table 2**)

Table 2. Summary of TEAEs

	SPAR + SGLT2i (N=20)
Any TEAEs, n (%)	12 (60)
SPAR related	5 (25)
SGLT2i related	1 (5)
Any TEAE reported in >1 patient, n (%)	
Dizziness	2 (10)
Headache	2 (10)
Hypertension	2 (10)
Hypotension	2 (10)
Edema	2 (10)
Peripheral edema	2 (10)
Osteoarthritis	2 (10)
Any severe TEAE, n (%)	1 (5)
Gout	1 (5)
Any serious AE, n (%)	2 (10)
Acute kidney injury*,†	1 (5)
Cerebrovascular accident	1 (5)
Osteoarthritis*	1 (5)
Any abnormal liver function test results‡, n (%)	0 (0)
Any TEAE leading to treatment discontinuation, n (%)	1§ (5)

*Reported in the same patient. †The incidence of acute kidney injury was mild, deemed unrelated to SPAR or SGLT2i treatment, and was resolved after interruption of SPAR 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. §Patient discontinued treatment due to a TEAE of vertigo.

CONCLUSIONS

- Switching from a RASi to SPAR treatment on a background of an SGLT2i allowed further reduction of proteinuria in adult patients with IgAN, lowering their risk for disease progression
- After the addition of SPAR, UACR was reduced by ≥30% in almost two-thirds of patients and by ≥50% in approximately one-third of patients
- SPAR combined with an SGLT2i was generally well tolerated
- Future analyses of the ongoing SPARTACUS study will report results in a larger number of patients

ABBREVIATIONS

ACEi, angiotensin-converting enzyme inhibitor; **AE**, adverse event; **ALT**, alanine aminotransferase; **ARB**, angiotensin receptor blocker; **AST**, aspartate aminotransferase; **BL**, baseline; **BP**, blood pressure; **DBP**, diastolic blood pressure; **eGFR**, estimated glomerular filtration rate; **IgAN**, immunoglobulin A nephropathy; **MMRM**, mixed model for repeated measures; **SBP**, systolic blood pressure; **SGLT2i**, sodium-glucose cotransporter-2 inhibitor; **SPAR**, sparsentan; **TEAE**, treatment-emergent adverse event; **UACR**, urine albumin-to-creatinine ratio; **ULN**, upper limit of normal; **UPCR**, urine protein-to-creatinine ratio.

DISCLOSURES

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 from Aurinia, Calliditas Therapeutics, HiBio, Otsuka Pharmaceuticals, Sanofi, Travere Therapeutics, Inc., and Vera Therapeutics for participation in advisory board activity; and speaker honorarium from Roche. **ST** reports payment or honoraria from AstraZeneca, Bayer, Boehringer Ingelheim, GSK, and Novartis; role as president of the Asian Pacific Society of Nephrology; and role on the executive committee of KDIGO. **LK** is a principal investigator for studies sponsored by Akebia 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. **PP** is a former employee and stockholder of Travere Therapeutics, Inc. **DSL** and **SM** are employees and stockholders of Travere Therapeutics, Inc. **BHR** reports consulting fees and clinical trial funding to his institution from Travere Therapeutics, Inc.

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REFERENCES

1. Kohan DE, et al. *Clin Sci (Lond).* 2024;138(11):645-662. **2.** FILSPARI (sparsentan). Prescribing information. Travere Therapeutics, Inc.; 2024. **3.** FILSPARI (sparsentan). Summary of product characteristics. CSL Vifor; 2024. **4.** Rovin BH, et al. *Lancet.* 2023;402(10417):2077-2090. **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.

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INTRODUCTION

BACKGROUND

- Sparsentan (SPAR) is a non-immunosuppressive, dual endothelin angiotensin receptor antagonist (DEARA),[1] approved in the US and EU for adults with IgAN[2,3]
- In patients with IgAN, SPAR showed sustained proteinuria reduction and preservation of kidney function in the phase 3 PROTECT trial[4]
- In subgroup analyses from DAPA-CKD and EMPA-KIDNEY, SGLT2is reduced proteinuria and the risk of progression to kidney failure in patients with IgAN[5,6]
- The combination of SPAR and an SGLT2i may therefore provide therapeutic benefits

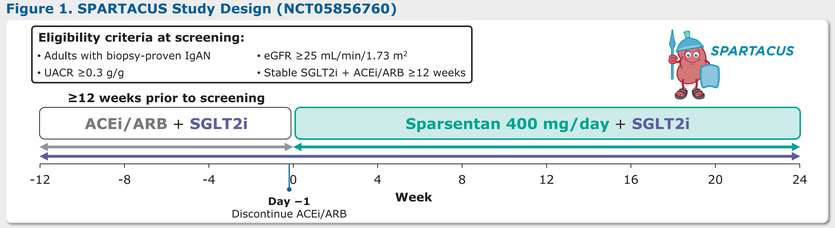
OBJECTIVE

- The ongoing phase 2 SPARTACUS trial is evaluating the efficacy and safety of SPAR added to stable SGLT2i treatment in adults with IgAN. We report results from a prespecified interim analysis

METHODS

- SPARTACUS is a phase 2, exploratory, open-label, single-arm, multicenter study of the efficacy and safety of up to 24 weeks of SPAR added to a stable dose of SGLT2i in patients with IgAN at risk of disease progression (**Figure 1**)
- This was a prespecified interim analysis performed 24 weeks after approximately 20 patients were enrolled

Figure 1. SPARTACUS Study Design (NCT05856760)



- Changes in UACR, UPCR, eGFR, and blood pressure were analyzed with an MMRM approach (**Figure 2**). Other endpoints were summarized using descriptive statistics

Figure 2. SPARTACUS Endpoints

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 in
  - UACR
  - UPCR
  - eGFR
  - Blood pressure

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

*Based on first morning void samples.

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