Sparsentan as First-Line Treatment of Incident Patients With IgA Nephropathy: Preliminary Findings From the SPARTAN Trial

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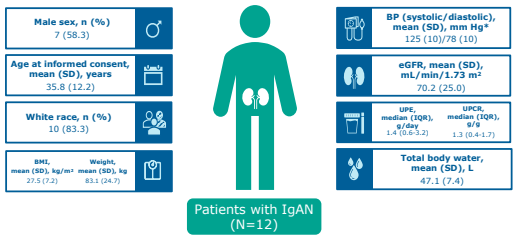
RESULTS

Patient Population

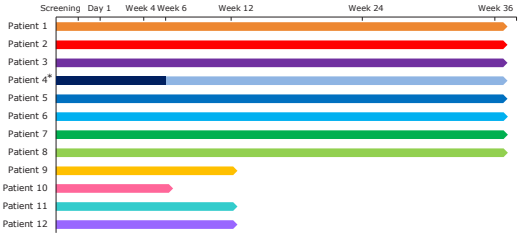
- As of the data cutoff (September 26, 2023), 12 patients received sparsentan and participated in the study for ≥6 weeks (**Figures 2** and **3**)

Figure 2. Patient Demographics and Baseline Characteristics



BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; IgAN, immunoglobulin A nephropathy; UPCR, urine protein-to-creatinine ratio; UPE, urine protein excretion. *Office BP.

Figure 3. Patient Progress in the Study Up to Week 36

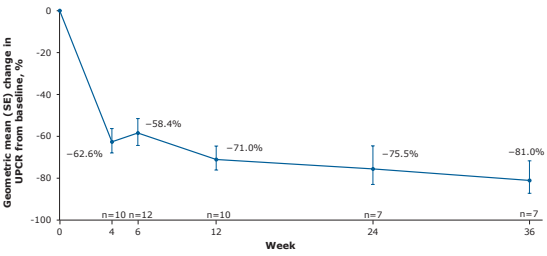


*Patient 4 stopped treatment after the week 6 visit but continued in the study off-treatment to the week 24 visit. All analyses in this study are calculated for patients receiving treatment, and data from patient 4 are excluded after week 6.

Proteinuria

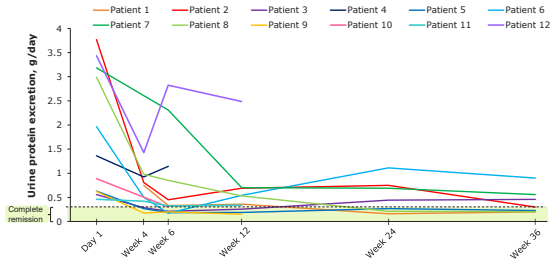
- Reduction in proteinuria at week 4 was ≈60% from baseline, which was sustained over 36 weeks of sparsentan treatment (**Figure 4**)
- Among the 4 patients with protein excretion of >2 g/day at baseline, 3 had proteinuria reductions of ≥75% at any time during the first 36 weeks of treatment (**Figure 5**)
- 67% (8/12) of patients achieved complete remission (<0.3 g/day) at any time during the 36-week treatment period

Figure 4. Proteinuria Change (UPCR) From Baseline



UPCR, urine protein-to-creatinine ratio.

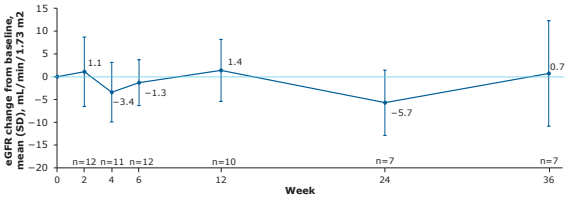
Figure 5. Proteinuria Per Individual Patient



Estimated Glomerular Filtration Rate

- Estimated glomerular filtration rate changes were relatively stable over 36 weeks of treatment with sparsentan (**Figure 6**)

Figure 6. Mean eGFR Change From Baseline

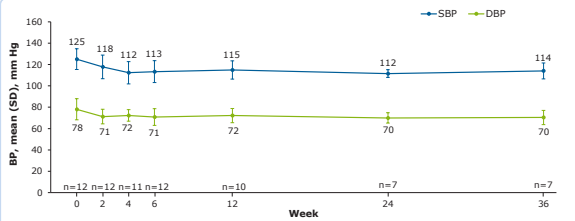


eGFR, estimated glomerular filtration rate.

Blood Pressure

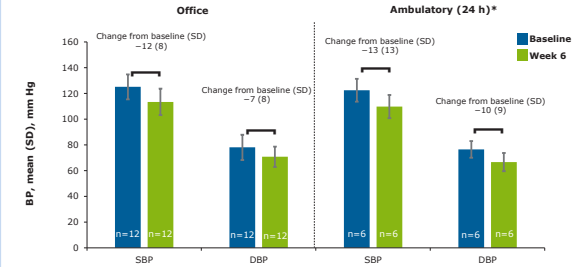
- After an initial decrease, blood pressure (BP) remained stable during the rest of the follow-up (**Figure 7**)
- Office and ambulatory BP showed similar measurements of systolic BP and diastolic BP at baseline and week 6, and ambulatory BP showed a slightly greater change from baseline than office BP (**Figure 8**)

Figure 7. Mean Office BP



BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

Figure 8. Mean Office and Ambulatory BP at Baseline and Week 6



BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure. *Patients who had ambulatory BP data available at baseline and week 6.

Body Weight and Total Body Water

- Mean body weight changes showed minor fluctuations over 36 weeks (**Table 1**)
- Mean total body water change from baseline showed modest reductions during follow-up

Table 1. Mean Weight and Total Body Water Change From Baseline

Mean (SD) change from baseline	Week					
	2	4	6	12	24	36
n	12	11	12	10	7	7
Weight, kg	−0.3 (0.7)	−0.2 (1.4)	0.3 (1.4)	0.1 (2.8)	−1.2 (3.2)	0.8 (3.0)
Total body water, L	–	–	−2.0 (7.2)	−1.9 (7.9)	−3.6 (9.1)	–

Safety

- Sparsentan was generally well tolerated over 36 weeks of treatment
- One patient discontinued treatment due to hypotension after 6 weeks
- There have been 3 serious adverse events, none related to treatment

CONCLUSIONS

- In these preliminary results, sparsentan as a first-line treatment in patients newly diagnosed with IgAN was effective at reducing proteinuria and controlling BP
- The rapid and sustained reductions in proteinuria, the achievement of complete remission, and the safety profile of sparsentan in this study are comparable with those from the phase 3 PROTECT study[2]
- There was no substantial effect on body weight, which was generally maintained over 36 weeks
- Total body water showed modest reduction over the treatment period with sparsentan, with no evidence of fluid retention observed in the study participants
- During the reported study period sparsentan treatment was generally well tolerated
- Planned analyses of cardiac and renal MRIs, repeat kidney biopsies, and other serum, plasma, and urinary biomarkers will investigate the mechanistic actions of sparsentan in this patient population and its potential renoprotective effects

DISCLOSURES

CKC has received consulting fees from George Clinical and Vera Therapeutics; received honoraria from Stada; received research funding from GSK and Travere Therapeutics, Inc.; served on advisory boards for Alexion, Calliditas, CSL Vifor, and Novartis; steering committees/DSMC for CSL Vifor, Alpine Immune Sciences, and Roche; and received travel support from Otsuka and Chinook Therapeutics. **SM and RK** are employees of Travere Therapeutics, Inc., and may have equity or other financial interest in Travere Therapeutics, Inc. **ND and JB** have received consulting fees and research funding from Travere Therapeutics, Inc. **SG** has received consulting fees from CSL Vifor and Alexion; honoraria from Bayer and Travere Therapeutics, Inc.; served on advisory boards for Emmes and ICON plc; and received travel support from Alexion. **AM** has received consulting fees from Travere Therapeutics, Inc., Vera Therapeutics, and HI-Bio. **SS** has received research funding from Johnson and Johnson (JnJ), AstraZeneca, CSL Vifor, and Sanofi Genzyme; received consulting fees from Novartis, Bayer, Sanofi-Genzyme, Vifor Pharma, Boehringer-Ingelheim, AstraZeneca, GSK, Sanifit, and Inozyme Pharma Inc.; received honoraria from AstraZeneca, Menarini, Napp, CSL Vifor, GSK, Novartis, Bayer, Sanofi Genzyme, and Medscape; served as the National Clinical Director of Renal Medicine for NHS England; and received travel support from AstraZeneca, Novartis, and CSL Vifor. **LW:** honoraria from Travere Therapeutics, Inc., Novartis, and Otsuka; and served on advisory boards for Travere Therapeutics, Inc., CSL Vifor, and Novartis. **AH and MS** have no conflicts of interest.

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1. Filspari (sparsentan). Prescribing information. Travere Therapeutics, Inc.; 2023. **2.** Heerspink HJL, et al. *Lancet*. 2023;401(10388):1584-1594. **3.** ClinicalTrials.gov. Accessed September 11, 2023. https://clinicaltrials.gov/study/NCT04663204.

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INTRODUCTION

- Sparsentan is a novel dual endothelin and angiotensin receptor antagonist (DEARA) that was granted accelerated approval in the US for the treatment of adults with immunoglobulin A nephropathy (IgAN) at risk of disease progression, based on improvements in proteinuria shown in the ongoing phase 3 PROTECT study[1,2]
- Sparsentan has been studied in patients with previous maximized renin-angiotensin system inhibitors,[2] but the effect in newly diagnosed, treatment-naive patients remains unknown
- SPARTAN (NCT04663204) is a phase 2, open-label, single-arm trial investigating the safety, efficacy, and mechanistic actions of sparsentan as first-line therapy in patients newly diagnosed with IgAN[3]

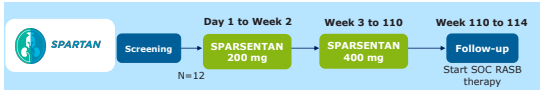
Objective

- Here we report preliminary clinical findings over the first 36 weeks of treatment with sparsentan from SPARTAN

METHODS

- The SPARTAN study is being conducted at 5 participating sites in the UK (**Figure 1**)

Figure 1. SPARTAN Study Design and Patient Assessment Schedule

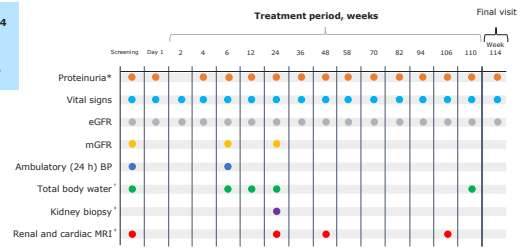


Key Eligibility Criteria

- Age ≥18 years
- Biopsy-proven IgAN within ≤6 months
- Proteinuria ≥0.5 g/day
- eGFR ≥30 mL/min/1.73 m²
- No ACEIs/ARBs within ≤12 months

Key Endpoints

- Safety
- Change in proteinuria from baseline
- Complete remission of proteinuria (<0.3 g/day)
- Change in GFR and BP from baseline



ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; IgAN, immunoglobulin A nephropathy; mGFR, measured glomerular filtration rate; MRI, magnetic resonance imaging; RASB, renin-angiotensin system blocker; SOC, standard of care. *24-hour collection. †Measured by bioimpedance spectroscopy. ‡For future analyses.

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