Sparsentan (SPAR) as First-Line Treatment of Incident Patients With IgA Nephropathy (IgAN): Findings From the SPARTAN Trial

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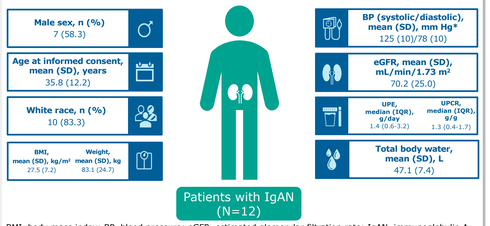
RESULTS

Patient Population

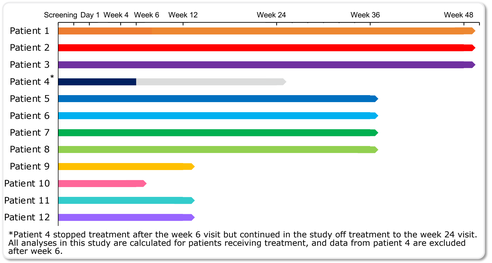
- As of the data cutoff (September 26, 2023), 12 patients received SPAR and participated in the study for ≥6 weeks (**Figures 2** and **3**)

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 48

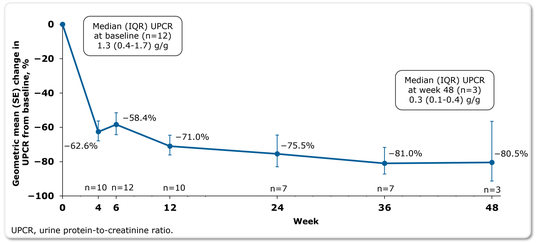


*Patient 4 stopped treatment after the week 6 visit but continued in the study off treatment to the week 24 visit. All analyses in this study are calculated for patients receiving treatment, and data from patient 4 are excluded after week 6.

Proteinuria

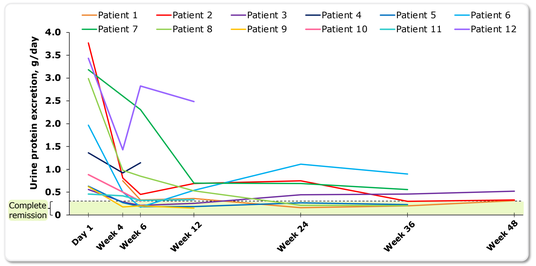
- Proteinuria reductions were rapid (≈60% from baseline at week 4) and sustained over 48 weeks of SPAR treatment (**Figure 4**)
- Among the 4 patients with protein excretion of >2 g/day at baseline, 3 had proteinuria reductions of ≥75% at any time during the first 48 weeks of treatment (**Figure 5**)
- 67% of patients (8/12) achieved complete remission (<0.3 g/day) at any time during the 48-week treatment period

Figure 4. Proteinuria Change (UPCR) From Baseline



UPCR, urine protein-to-creatinine ratio.

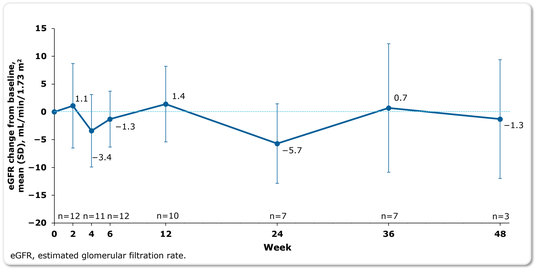
Figure 5. Proteinuria per Individual Patient



Estimated Glomerular Filtration Rate

- Estimated glomerular filtration rate changes were relatively stable over 48 weeks of treatment with SPAR (**Figure 6**)

Figure 6. Mean eGFR Change From Baseline

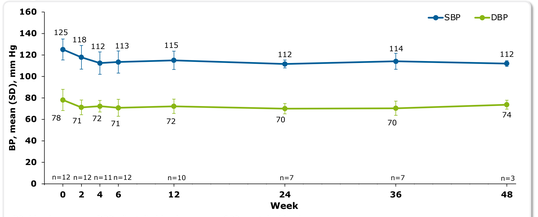


eGFR, estimated glomerular filtration rate.

Blood Pressure

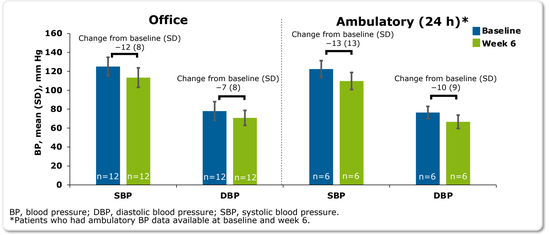
- After an initial decrease, blood pressure (BP) remained stable during the rest of the treatment period (**Figure 7**)
- Office and ambulatory BP showed similar measurements of systolic BP and diastolic BP at baseline and week 6, and ambulatory BP showed a slightly greater change from baseline than 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 48 weeks (**Table 1**)
- Mean total body water change from baseline showed modest reductions during the treatment period

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

Mean (SD) change from baseline	Week 2	4	6	12	24	36	48
n	12	11	12	10	7	7	3
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)	1.7 (4.9)
Total body water, L	–	–	−2.0 (7.2)	−1.9 (7.9)	−3.6 (9.1)	–	–

Safety

- SPAR was generally well tolerated over 48 weeks of treatment
- One patient discontinued treatment due to hypotension after 6 weeks
- There have been 3 serious adverse events, none related to treatment

INTRODUCTION

- Sparsentan (SPAR) is a nonimmunosuppressive, novel dual endothelin and angiotensin receptor antagonist (DEARA) that was granted accelerated approval in the US for the treatment of adults with IgAN at risk of disease progression, based on improvements in proteinuria at 36 weeks (interim analysis) in the ongoing phase 3 PROTECT study[1,2]
- Over 110 weeks in PROTECT, SPAR showed a sustained reduction in proteinuria and a clinically meaningful benefit on long-term kidney preservation vs maximally titrated irbesartan[3]
- Although SPAR has been studied in patients with previous maximized renin-angiotensin system inhibitors,[2,3] 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 SPAR as first-line therapy in patients newly diagnosed with IgAN[4]

Objective

- Here we report preliminary clinical findings over the first 48 weeks of treatment with SPAR from SPARTAN

METHODS

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

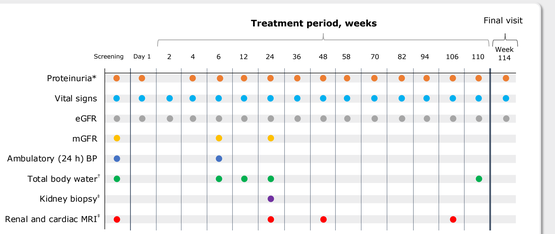
Figure 1. SPARTAN Study Design and Patient Assessment Schedule

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
- No systemic IST within ≤ 6 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; IST, immunosuppressive therapy; mGFR, measured glomerular filtration rate; MRI, magnetic resonance imaging; RAASi, renin-angiotensin-aldosterone system inhibitor; SOC, standard of care; SPAR, sparsentan.
*24-hour collection. †Measured by bioimpedance spectroscopy. ‡For future analyses.

CONCLUSIONS

- These preliminary findings show that SPAR as a first-line treatment in patients newly diagnosed with IgAN was effective in reducing proteinuria and controlling BP
- The rapid and sustained reductions in proteinuria (>80% over 48 weeks), the achievement of complete remission, and the safety profile of SPAR in this study are comparable with those from the phase 3 PROTECT study[2,3]
- eGFR remained stable over 48 weeks of sparsentan treatment
- There was no substantial effect on body weight, which was generally maintained over 48 weeks
- Total body water showed modest reduction over the treatment period with SPAR, with no evidence of fluid retention observed in the study participants
- During the reported study period SPAR 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 SPAR in this patient population and its potential renoprotective effects

DISCLOSURES

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

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