Sparsentan in Pediatric Patients With Rare Proteinuric Kidney Disease: Preliminary Findings From the EPPIK Study

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RESULTS

Efficacy

- At data cutoff (February 15, 2024), 34 patients received ≥1 dose of sparsentan **(Table 1)**

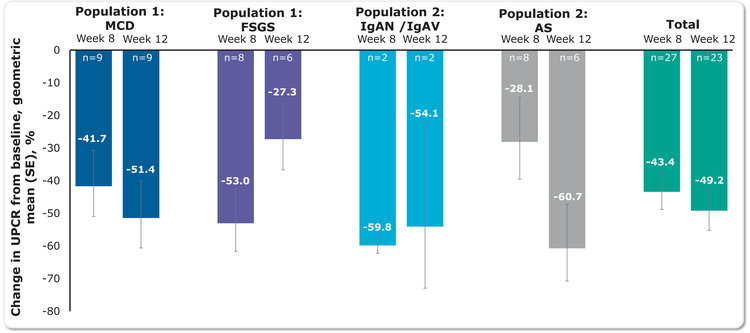
Table 1. Baseline Characteristics

Characteristic	Population 1: MCD (n=10)	Population 1: FSGS (n=11)	Population 2: IgAN/IgAV* (n=4)	Population 2: AS (n=9)	Total (N=34)
Male, n (%)	5 (50.0)	3 (27.3)	2 (50.0)	8 (88.9)	18 (52.9)
Age†, median (IQR), years	7.5 (6.0-11.0)	5.0 (3.0-14.0)	13.0 (9.5-13.5)	12.0 (11.0-14.0)	8.5 (6.0-13.0)
White, n (%)	9 (90.0)	9 (81.8)	3 (75.0)	4 (44.4)	25 (73.5)
UPCR, median (IQR), g/g	2.75 (2.13-3.61)	4.91 (4.33-11.28)	2.27 (0.67-3.18)	2.61 (2.30-3.74)	3.08 (2.36-4.98)
Nephrotic-range proteinuria (UPCR >2 g/g), n (%)	8 (80.0)	10 (90.9)	2 (50.0)	8 (88.9)	28 (82.4)
eGFR, mean (SE), mL/min/1.73 m²	149.2 (14.95)	73.9 (6.14)	127.0 (22.66)	89.3 (10.42)	106.4 (8.04)
Immunosuppressant use at baseline, n (%)	5 (50.0)	6 (54.5)	2 (50.0)	0 (0.0)	13 (38.2)
Blood pressure, systolic/diastolic, mean (SE), mm Hg	110.4 (4.52)/ 66.1 (2.92)	114.3 (4.08)/ 75.0 (9.78)	117.5 (9.90)/ 68.0 (2.55)	110.4 (1.98)/ 67.9 (3.27)	112.5 (2.18)/ 69.7 (1.62)

*One patient with IgAV. †At screening.

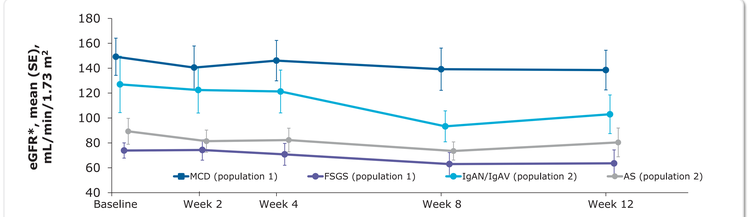
- Proteinuria decreased in all diagnosis subpopulations from baseline over 12 weeks of treatment (**Figure 3**)

Figure 3. UPCR Percentage Change from Baseline



- eGFR was broadly stable over 12 weeks of treatment (**Figure 4**)

Figure 4. eGFR* at Each Visit

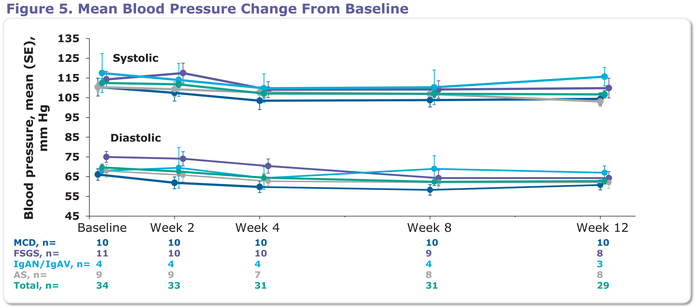


	Baseline	Week 2	Week 4	Week 8	Week 12
MCD, n=	10	10	10	10	10
FSGS, n=	11	9	9	8	7
IgAN/IgAV, n=	4	4	4	3	3
AS, n=	9	8	7	8	8

*eGFR determined using the modified Schwartz formula.[12,13]

- Blood pressure remained generally stable during the first 12 weeks of treatment (**Figure 5**)

Figure 5. Mean Blood Pressure Change From Baseline



	Baseline	Week 2	Week 4	Week 8	Week 12
MCD, n=	10	10	10	10	10
FSGS, n=	11	10	10	9	8
IgAN/IgAV, n=	4	4	4	4	3
AS, n=	9	9	7	8	8
Total, n=	34	33	31	31	29

Safety

- Sparsentan was generally well tolerated over the 12-week treatment period (**Table 2**)
  - Peripheral edema as a TEAE was reported in 2 patients, and hyperkalemia in 3 patients; other TEAEs such as edema, aspartate aminotransferase increase, and hypotension each occurred in 1 patient only

Table 2. TEAEs Over 12 Weeks of Sparsentan Treatment

Patients, n (%)	Population 1: MCD (n=10)	Population 1: FSGS (n=11)	Population 2: IgAN/IgAV (n=4)	Population 2: AS (n=9)	Total (N=34)
Any TEAE	**9 (90)**	**7 (64)**	**3 (75)**	**5 (56)**	**24 (71)**
Most common TEAEs (≥15% of the total population)					
Pyrexia	4 (40)	2 (18)	0 (0)	1(11)	7 (21)
Vomiting	2 (20)	2 (18)	1 (25)	0 (0)	5 (15)
Fatigue	4 (40)	0 (0)	1 (25)	0 (0)	5 (15)
Any serious TEAE	**2 (20)**	**2 (18)**	**2 (50)**	**0 (0)**	**6 (18)***

*10 serious TEAEs occurred in 6 patients: acute kidney injury (n=1); nephrotic syndrome (n=1); vomiting (n=1); decreased activity (n=1); fluid retention (n=1); pleural effusion (n=1); hypotension (n=1); COVID-19 (n=1); SARS-CoV-2 positive antibody test (n=1); SARS-CoV-2 positive test (n=1).

CONCLUSIONS

- In pediatric patients with a range of proteinuric glomerular diseases, sparsentan treatment resulted in rapid and robust proteinuria reductions
- Overall, a ~50% proteinuria reduction was observed over 12 weeks of sparsentan treatment
- The oral suspension formulation of sparsentan was well tolerated, with a safety profile consistent with studies of adults with IgAN or FSGS[1-6]
- Enrollment for the EPPIK trial (NCT05003986) is ongoing. Further follow-up will evaluate the long-term efficacy and safety, as well as pharmacokinetics and palatability, in children with rare proteinuric glomerular diseases

ABBREVIATIONS

Ang, angiotensin; **AS**, Alport syndrome; **AT$_1$R**, angiotensin II type 1 receptor; **COVID-19**; coronavirus disease 2019; **eGFR**, estimated glomerular filtration rate; **ET$_A$R**, endothelin A receptor; **ET**, endothelin; **FSGS**, focal segmental glomerulosclerosis; **IgAN**, immunoglobulin A nephropathy; **IgAV**, immunoglobulin A vasculitis; **MCD**, minimal change disease; **RASi**, renin–angiotensin– aldosterone system inhibitor; **SARS-CoV-2**; severe acute respiratory syndrome coronavirus 2; **SOC**, standard of care; **TEAE**, treatment-emergent adverse event; **UPCR**, urine protein-to-creatinine ratio.

DISCLOSURES

HT reports receiving consultancy fees from Aclipse, Boehringer Ingelheim, Maze Therapeutics, Natera, PhaseV, Travere Therapeutics, Inc., and Walden; and participated on data safety monitoring or advisory boards for Otsuka. **RC** has participated on data safety monitoring or advisory boards for Amgen, Bayer, Chinook, Menarini, Novartis, Otsuka, Puresprring, STADApharm, and Travere Therapeutics, Inc. **NAMA** has received research funding from Regeneron and is an employee of NJOY LLC and Travere Therapeutics, Inc. **KVL** has received speaker's honoraria from Alexion, Calliditas, and Travere Therapeutics, Inc. **AM** has received consulting fees from Travere Therapeutics, Inc., Vera Therapeutics, Dimerix and HI-Bio. **MNR** has received consultancy fees from Advicenne, ELOXX, ENYO Pharma, and Walden Biosciences; has received research funding from Chinook, Kaneka, Reata, River 3 Renal, Sanofi, Travere Therapeutics Inc.; and participated on data safety monitoring/advisory boards for Neph3C, Alport Syndrome Foundation. **MAS** has received consultancy fees from Travere Therapeutics, Inc., Puresprring Therapeutics and Amphista and Santhera; and owns stock or stock options in Puresprring Therapeutics; and has participated on advisory boards and has received research funding from Travere Therapeutics, Inc. **TS** is an employee of Travere Therapeutics, Inc. **RK** is an employee and shareholder of Travere Therapeutics, Inc.

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For more information about the EPPIK trial, please visit https://www.clinicaltrials.gov/study/NCT05003986

INTRODUCTION

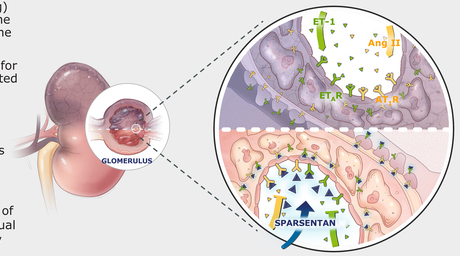
BACKGROUND

- Sparsentan, a novel dual endothelin (ET) angiotensin (Ang) receptor antagonist (DEARA) (**Figure 1**), is approved in the US and EU to treat adults with IgAN based on data from the Phase 3 PROTECT trial[1-4]
  - Sparsentan has also been investigated as a treatment for FSGS in the ongoing DUPLEX Phase 3 trial and completed DUET Phase 2 trial[5,6]
- The ongoing Phase 2 open-label EPPIK (Evaluating Problematic Proteinuria in Kids; NCT05003986) study is examining the safety and long-term antiproteinuric and nephroprotective effects of sparsentan in pediatric patients with various glomerular diseases

OBJECTIVE

- To assess the preliminary efficacy, safety, and tolerability of the oral suspension formulation of sparsentan per individual diagnoses after 12 weeks of treatment in the EPPIK study

Figure 1. Sparsentan Mechanism of Action



Sparsentan targets glomerular injury and slows kidney function decline[1,7]

EFFECTS:

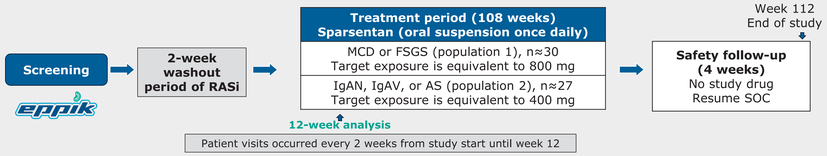
- Anti-inflammatory[8-11]*
- Anti-proliferative[8,9,11]*
- Anti-fibrotic[10,11]*
- Anti-proteinuric[4]

*These effects are based on preclinical animal modeling data.

METHODS

Figure 2. Study Design

- EPPIK is an open-label, single-arm, descriptive, multicenter trial enrolling ≈57 pediatric patients (**Figure 2**)



Key eligibility criteria

- **All patients:** eGFR ≥30 mL/min/1.73 m² at screening
- **Population 1 (FSGS or MCD):** ≥1 to <18 years and UPCR ≥1.5 g/g at screening
- **Population 2 (IgAN, IgAV, or AS):** ≥2 to 18 years and UPCR ≥0.6 g/g at screening
- Patients taking any chronic immunosuppressive medication without a stable dose for ≥1 month were excluded

Endpoints

Primary
- Safety (adverse events)
- UPCR change from baseline through week 108

Other
- eGFR change from baseline through week 112
- Changes in vital signs (eg, blood pressure)

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TRAVERE THERAPEUTICS