FILSPARI® (sparsentan)

Effect on Estimated Glomerular Filtration Rate (eGFR)

Summary

Prescribing Information

- FILSPARI is and endothelin and angiotensin II receptor antagonist indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk for rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g[1]
- This indication is approved under accelerated approval based on reduction of proteinuria. It has not been established whether FILSPRI slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial[1]

Background

- Sparsentan is an investigational therapeutic candidate for the treatment of FSGS

Study Data

The PROTECT Study

- Treatment with sparsentan resulted in a clinically meaningful difference compared to irbesartan in eGFR total slope (1.0 mL/min/1.73 m^2 per year; P=0.058) and eGFR chronic slope (1.1 mL/min/1.73 m^2 per year; P=0.037)[2]
- Least-squares mean absolute change in eGFR from baseline to Week 110 was lower with sparsentan versus irbesartan (−5.8 mL/min/1.73 m^2 and −9.5 mL/min/1.73 m^2, respectively; difference=3.7)[2]

The DUET Study

- Mean change in eGFR measured by chronic slope estimate through 108 weeks was −3.56 (95% CI, −5.6 to −1.5) mL/min/1.73 m^2 per year. Mean change in eGFR of on-treatment data, defined as within 1 day of last sparsentan dose, showed a chronic slope estimate of −4.16 (95% CI, −5.8 to −2.5) mL/min/1.73 m^2 per year[3]

The DUPLEX Study

- After 108 weeks of treatment, sparsentan showed a favorable (not statistically significant) difference on total eGFR slope of 0.3 mL/min/1.73 m^2 per year (95% CI, −1.7 to 2.4; P=0.75) and on eGFR chronic slope of 0.9 mL/min/1.73 m^2 per year (95% CI, −1.3 to 3.0; P=0.42) compared to irbesartan[4]
- At Week 112, mean change in eGFR from baseline was −10.4 mL/min/1.73 m^2 with sparsentan and −12.1 mL/min/1.73 m^2 with irbesartan[4]

Prescribing Information

FILSPARI is and endothelin and angiotensin II receptor antagonist indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk for rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g[1]

This indication is approved under accelerated approval based on reduction of proteinuria. It has not been established whether FILSPRI slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial[1]

Laboratory Tests

In the PROTECT study, laboratory tests showed that initiation of FILSPARI may cause an initial small decrease in eGFR that occurs within the first 4 weeks of starting therapy and then stabilizes.[1]

For more information, please refer to the attached Prescribing Information.

Background

Sparsentan is a novel, first-in-class, and the only single molecule antagonist of the ET_A and AT_1 receptors.[5-7] Preclinical studies in rodent models of chronic kidney disease have shown that blockade of both ET_A and AT_1 pathways reduces proteinuria, protects podocytes, and prevents glomerulosclerosis and mesangial cell proliferation.[8-10]

The PROTECT Study

The PROTECT study (NCT03762850) is a phase 3, global, randomized, multicenter, double-blind, parallel-arm, active-controlled clinical trial evaluating long-term antiproteinuric and nephroprotective efficacy and safety of 400 mg of sparsentan compared to 300 mg of irbesartan.[11] The study includes 404 patients ages 18 years and older with biopsy proven IgA nephropathy who experience persistent proteinuria despite available ACEi or ARB therapy. Patients with urine protein ≥1 g/day at screening, eGFR ≥30 mL/min/1.73 m^2, SBP ≤150 mm Hg, and DBP ≤100 mm Hg were eligible.[12] The PROTECT study protocol provides for an unblinded interim analysis of at least 280 patients to be performed after 36 weeks of treatment to evaluate the primary efficacy endpoint, defined as change in proteinuria (UPCR) at Week 36 from baseline. Secondary efficacy endpoints include the rate of change in eGFR following the initiation of randomized treatment over 58-week and 110-week periods, as well as rate of change in eGFR over 52-week and 104-week periods following the first 6 weeks of randomized treatment.[12,13] The PROTECT study also examines change from baseline in UACR based on a 24-hour urine sample at Week 36, and prespecified exploratory endpoints of complete (urinary protein excretion <0.3 g/day) and partial (urinary protein excretion <1.0 g/day) proteinuria remission at least once at any time during the double-blind period. In addition, this study evaluates the proportion of patients in each group reaching a confirmed 40% reduction in eGFR from baseline, KF, or all-cause mortality. KF is defined as initiation of KRT or sustained eGFR value of <15 mL/min/1.73 m^2.[14] Reduction in proteinuria and decline in rate of eGFR are largely accepted as surrogate markers of treatment effect in studies of KF.[14,15]

The DUET Study

The DUET study (NCT01613118) is a phase 2, randomized, multicenter, double-blind, active-control trial in patients with biopsy-proven FSGS. Patients were randomized to 1 of 3 doses (200, 400, or 800 mg/day) of sparsentan or irbesartan (300 mg/day) and maintained through an 8-week double-blind phase. The primary endpoint was defined as reduction in UPCR after 8 weeks of treatment. The proportion of patients who achieved partial FSGS remission was evaluated as a secondary endpoint. Following the double-blind phase, patients had the option to continue into a 144-week OLE of treatment with sparsentan.[3]

The DUPLEX Study

The DUPLEX study (NCT03493685) is a global, randomized, multicenter, double-blind, active-controlled, phase 3 trial examining the safety and efficacy of sparsentan as compared to irbesartan in patients aged 8 to 75 years with biopsy-proven FSGS. Patients with UPCR ≥1.5 g/g at screening, eGFR ≥30 mL/min/1.73 m^2, and mean seated BP ≥100/60 mm Hg (patients ≥18 years) or above the 5th percentile for sex and height (<18 years) were eligible. After a 2-week washout period, 371 patients were randomized to receive either sparsentan or irbesartan, and subsequently dose titrated over 2 weeks to the maximum dose of either 800 mg/day sparsentan or 300 mg/day irbesartan, as tolerated.[4,16] Patients remained on maintenance doses of sparsentan or irbesartan during a 108-week double blind phase. Standard-of-care treatment, including RAASi, was resumed in Weeks 108-112. The primary efficacy endpoint was eGFR slope over 108 weeks of treatment, defined as eGFR total slope from Day 1 to Week 108 of treatment and eGFR chronic slope from Week 6 to Week 108 (following the initial acute effect of randomized treatment). The key secondary endpoint was percent change in eGFR from baseline to 4 weeks post-cessation of randomized treatment at Week 112.[4] An additional interim endpoint was the proportion of patients achieving partial remission of proteinuria, defined as UPCR ≤1.5 g/g and a >40% reduction (FPRE) at Week 36. Proportion of patients achieving complete remission of proteinuria (UPCR <0.3 g/g) at any time in the double-blind period was also examined. Safety was assessed by double-blind monitoring of adverse events and safety endpoints.[4,16]

Study Data

The PROTECT Study

Key Secondary Efficacy Endpoint

The PROTECT study included a confirmatory endpoint analysis following 2 years of sparsentan treatment. The confirmatory endpoint was the eGFR slope of progression to KF, measured by total slope in the US and by chronic slope in the EU.[19]

- The slope of eGFR following initiation of randomized treatment, from Day 1 to Week 110, defined the eGFR total slope
- The slope of eGFR following the initial acute effect of randomized treatment, from Week 6 to Week 110, defined the eGFR chronic slope

Efficacy endpoints assessing preservation of kidney function favored sparsentan over irbesartan following 2 years of treatment (**Table 1**). Patients taking sparsentan experienced an eGFR total slope 1.0 mL/min/1.73 m^2 per year favorable and clinically meaningful difference as compared to irbesartan. The observed difference in eGFR total slope missed statistical significance (*P*=0.058).

For patients taking sparsentan, eGFR chronic slope showed a clinically meaningful and statistically significant difference of 1.1 mL/min/1.73 m^2 per year as compared to irbesartan (*P*=0.037).[2]

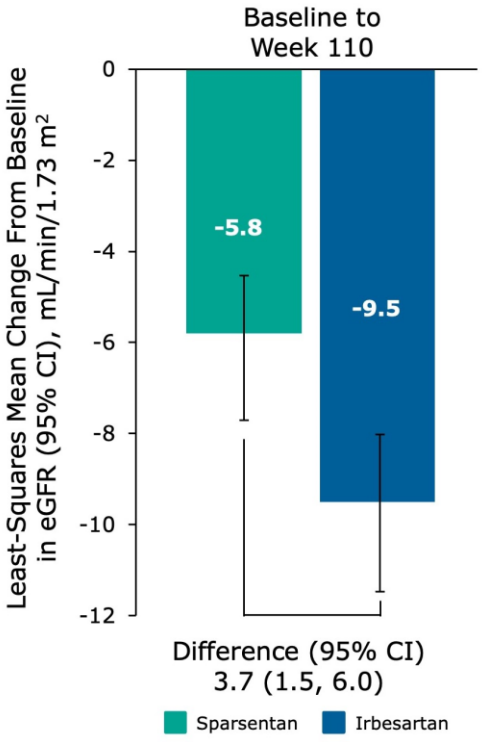
Table 1. Treatment With Sparsentan Demonstrated Long-Term Kidney Function Preservation

Key Secondary Efficacy Endpoints*	Sparsentan Group (n=202)	Irbesartan Group (n=202)	Between-Group Difference (95% CI)	p-value
Chronic slope from Week 6 to Week 110, mL/min/1.73 m^2 per year	-2.7 (-3.4, -2.1)	-3.8 (-4.6, -3.1)	1.1 (0.1, 2.1)	0.037
Total slope from Day 1 to Week 110, mL/min/1.73 m^2 per year	-2.9 (-3.6, -2.2)	-3.9 (-4.6, -3.1)	1.0 (-0.03, 1.94)	0.058

Data are geometric least-squares mean (95% CI) change in proteinuria from baseline to Week 110 unless otherwise stated.
*Assessed in the full analysis set.

Least-squares mean absolute change in eGFR from baseline to Week 6 was similar between sparsentan and irbesartan (−1.2 mL/min/1.73 m^2 and −1.6 mL/min/1.73 m^2, respectively; difference=0.4). Least-squares mean absolute change in eGFR from baseline to Week 110 was lower with sparsentan versus irbesartan (−5.8 mL/min/1.73 m^2 and −9.5 mL/min/1.73 m^2, respectively; difference=3.7) (**Figure 1**). This effect was maintained 4 weeks after stopping study treatment and resuming SOC; change from baseline to Week 114 was −6.1 mL/min/1.73 m^2 with sparsentan and −9.0 mL/min/1.73 m^2 with irbesartan (difference=2.9).[2]

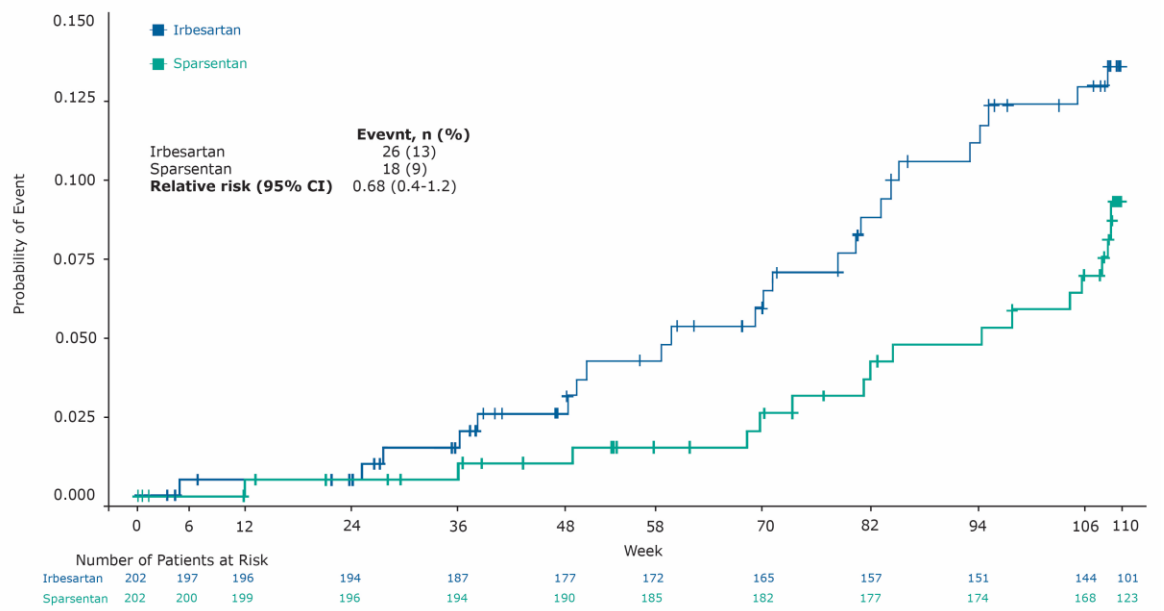
Figure 1. Change in eGFR From Baseline to Week 110



Composite Endpoint

Secondary endpoints included a composite of kidney failure, defined as confirmed 40% eGFR reduction, kidney failure, or all-cause mortality. The composite endpoint was reached by 18 (9%) patients taking sparsentan and 26 (13%) patients taking irbesartan (**Figure 2**). Among these patients, 18 (9%) sparsentan-treated patients and 22 (11%) irbesartan-treated patients had confirmed 40% reduction in eGFR. In the sparsentan group, 9 (4%) patients reached kidney failure and no patient deaths occurred, compared to 11 (5%) patients who reached kidney failure and 1 patient who died in the irbesartan group.[2]

Figure 2. Time to Reach Composite Endpoint



Vertical bars indicate censored patients.

Additional sensitivity analyses examined long-term preservation of kidney function. ITT analysis including all eGFR measurements through study end regardless of premature treatment discontinuations found an annualized difference (95% CI) between sparsentan and irbesartan in eGFR chronic slope of 1.3 (0.36 to 2.32) mL/min/1.73 m^2 per year. The difference between treatment groups in eGFR total slope was 1.2 (0.23 to 2.16) mL/min/1.73 m^2 per year. Rescue analysis excluded all eGFR measurements taken after initiation of rescue immunosuppression for renal diseases, which was initiated sooner and more frequently in the irbesartan group (n=16; 8%) than with sparsentan treatment (n=6; 3%).[2,20] The difference (95% CI) between treatment groups was 1.2 (0.16 to 2.15) mL/min/1.73 m^2 per year for chronic slope and 1.0 (0.03 to 1.99) mL/min/1.73 m^2 per year for total slope (**Table 2**).[20] Sparsentan patients also consistently maintained greater kidney function over time as compared to irbesartan (**Table 3**).[2]

Table 2. Pre-specified Sensitivity Analyses

All Randomized Patients (Irrespective of Early Treatment Discontinuations – mITT Analysis)	Sparsentan (n=202)	Irbesartan (n=202)	Treatment Difference (Sparsentan – Irbesartan) (95% CI)
eGFR total slope, mL/min/1.73 m^2 per year	**-3.0**	**-4.2**	**1.2** (0.23, 2.16)
eGFR chronic slope, mL/min/1.73 m^2 per year	**-2.9**	**-4.2**	**1.3** (0.36, 2.32)
Exclusion of Assessments After Initiation of Immunosuppression for Renal Disease	**Sparsentan (n=202)**	**Irbesartan (n=202)**	**Treatment Difference (Sparsentan – Irbesartan) (95% CI)**
eGFR total slope, mL/min/1.73 m^2 per year	**-2.9**	**-3.9**	**1.0** (0.03, 1.99)
eGFR chronic slope, mL/min/1.73 m^2 per year	**-2.8**	**-3.9**	**1.2** (0.16, 2.15)

Results obtained using the same models as the main analyses without multiple imputation.

Table 3. Sparsentan Demonstrated Treatment Benefit on Kidney Function Endpoints

Absolute Overall Change in Kidney Function	Sparsentan (n=202)	Irbesartan (n=202)	Difference (Sparsentan – Irbesartan) (N=404)
Absolute change in eGFR Mean change from baseline at week 110[a]	**-5.8**	**-9.5**	**3.7** (1.5, 6.0)
Absolute change in eGFR Mean change from baseline to 4 weeks post-cessation of randomized treatment week 114[b] (Patients who completed the blinded treatment period)	**(n=174)**	**(n=154)**	
	-6.1	**-9.0**	**2.9** (0.5, 5.3)
	Sparsentan (n=202)	**Irbesartan (n=202)**	**Difference (Sparsentan – Irbesartan)**
Confirmed 40% reduction in eGFR, ESRD, or death during the study, n (%)	**18** (9.0)	**26** (13.0)	**RR: 0.68** (0.4, 1.2)[c]

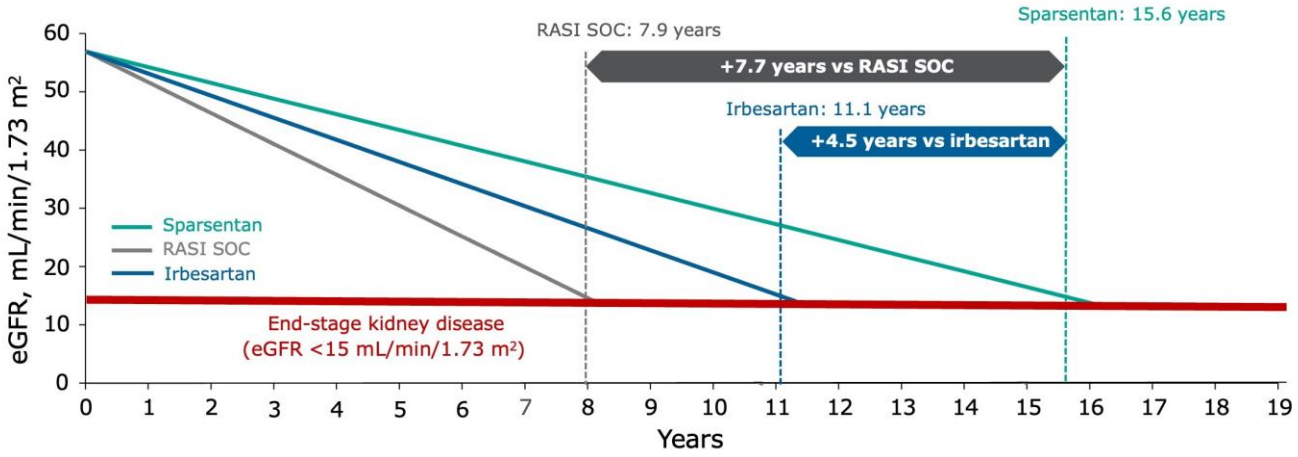
[a]LS mean and 95% CI from MMRM analysis including on-treatment data through Week 110; mL/min/1.73 m^2.
[b]LS mean and 95% CI from ANCOVA adjusted for eGFR at baseline; mL/min/1.73 m^2.
[c]RR of events and 95% CI from Poisson regression model.

Delay to Kidney Failure

Treatment with sparsentan was associated with projected delay in time to KF, related to change in eGFR slope (**Figure 3**). Baseline eGFR was 57 mL/min/1.73 m^2, based on mean eGFR of the sparsentan group in the PROTECT study interim analysis. eGFR for SOC (maximized ACEi/ARB) equaled the mean of observed slopes reported in previous clinical trials. Observed eGFR chronic slope was −2.7 mL/min/1.73 m^2 per year for sparsentan, −3.8 mL/min/1.73 m^2 per year for irbesartan, and −5.3 mL/min/1.73 m^2 per year for SOC treatment. Corresponding time to KF was reported as 15.6 years, 11.1 years, and 7.9 years for sparsentan, irbesartan, and SOC, respectively.[19]

- Compared to patients utilizing SOC, patients taking sparsentan experienced a mean 7.7 years longer delay to KF
- Compared to patients taking irbesartan, sparsentan-treated patients experienced a mean 4.5 years longer delay to KF

Figure 3. Treatment With Sparsentan Is Associated With Projected Delay in Time to Kidney Failure



Safety

Safety data from the 2-year confirmatory analysis showed sparsentan to be well-tolerated, with a consistent safety profile comparable to irbesartan and no new safety signals. TEAEs were reported in 187 (93%) patients taking sparsentan and 177 (88%) irbesartan-treated patients. SAEs were reported by 75 (37%) patients taking sparsentan and 71 (35%) patients taking irbesartan.[2]

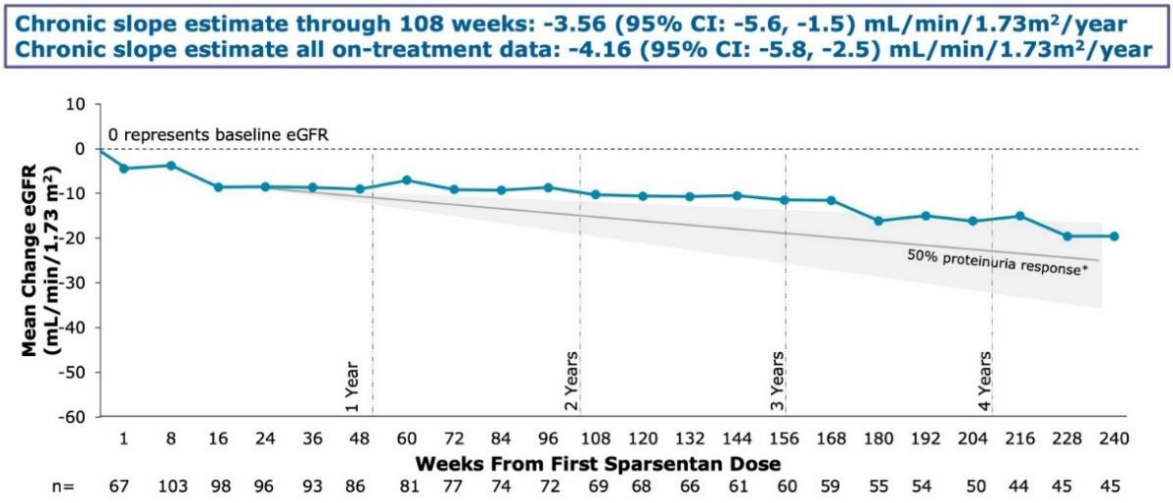
Peripheral edema was similar in both groups, with no increases in body weight. Change from no edema at baseline to severe edema occurred in 0 sparsentan-treated patients and 2 irbesartan-treated patients. Change from no edema to moderate edema occurred in 2 patients taking sparsentan and none taking irbesartan. Diuretic use initiated on or after beginning study drug was reported in 49 (24%) sparsentan patients and 54 (27%) irbesartan patients. The most frequently used class of diuretics was thiazides, utilized by 35 (17%) and 42 (21%) sparsentan and irbesartan patients, respectively. Hepatic TEAEs of interest of ALT or AST increasing >3× the ULN occurred in 5 (2%) patients in the sparsentan group and 7 (3%) patients in the irbesartan group. No cases of drug-induced liver injury occurred in either group.[2]

The DUET Study

Efficacy

Mean change in eGFR measured by chronic slope estimate through 108 weeks was −3.56 (95% CI, −5.6 to −1.5) mL/min/1.73 m^2 per year. Mean change in eGFR of on-treatment data, defined as within 1 day of last sparsentan dose, showed a chronic slope estimate of −4.16 (95% CI, −5.8 to −2.5) mL/min/1.73 m^2 per year (**Figure 4**).[3]

Figure 4. DUET OLE: Mean Change From Baseline in eGFR by Visit



*Research in patients with steroid-resistant FSGS found that changes in proteinuria over 26 weeks were significantly related to eGFR slope. Patients who achieved 50% reduction in proteinuria at 26 weeks of treatment showed eGFR slope decline = 4.0 mL/min/1.73 m^2 per year, whereas patients with persistent proteinuria had significantly more decline, eGFR slope = 6.7 mL/min/1.73 m^2 per year.[21]

Only on-treatment observations (defined as occurring within 1 day of last sparsentan dose) are included.
Chronic slope was assessed starting at Day 42 of starting sparsentan treatment.

Safety

Safety assessments during the double-blind phase showed that compared with patients taking irbesartan, patients treated with sparsentan reported more frequent hypotension (16.4% vs 8.3%), dizziness (13.7% vs 11.1%), edema (12.3% vs 2.8%), and gastrointestinal (nausea, 12.3% vs 8.3%; diarrhea, 8.2% vs 2.8%; vomiting, 8.2% vs 2.8%) TEAEs. Overall, incidence of TEAEs, drug-related TEAEs, serious TEAEs, and the number of study withdrawals were similar between the two groups.[7] Analysis of OLE data found no new or unexpected safety signals.[3]

The DUPLEX Study

Efficacy

Primary Efficacy Endpoint

Sparsentan did not achieve the primary efficacy eGFR slope endpoint over 108 weeks of treatment.[4]

Primary efficacy endpoints were defined as eGFR total slope from Day 1 to Week 108 of treatment (US primary) and eGFR chronic slope from Week 6 to Week 108, following initial acute effect of randomized treatment (EU primary). A decrease from baseline in mean (95% CI) eGFR over the first 6 weeks of treatment was −4.1 (−5.8 to −2.4) mL/min/1.73 m^2 with sparsentan and −0.8 (−2.5 to 0.9) mL/min/1.73 m^2 with irbesartan (difference, −3.3 [−5.7 to −0.9] mL/min/1.73 m^2). After 108 weeks of treatment, sparsentan showed a favorable (not statistically significant) difference on total eGFR slope of 0.3 mL/min/1.73 m^2 per year (95% CI, −1.7 to 2.4; *P*=0.75) and on eGFR chronic slope of 0.9 mL/min/1.73 m^2 per year (95% CI, −1.3 to 3.0; *P*=0.42) compared to irbesartan (**Table 4**).[4]

Table 4. The eGFR Slope and Change in eGFR

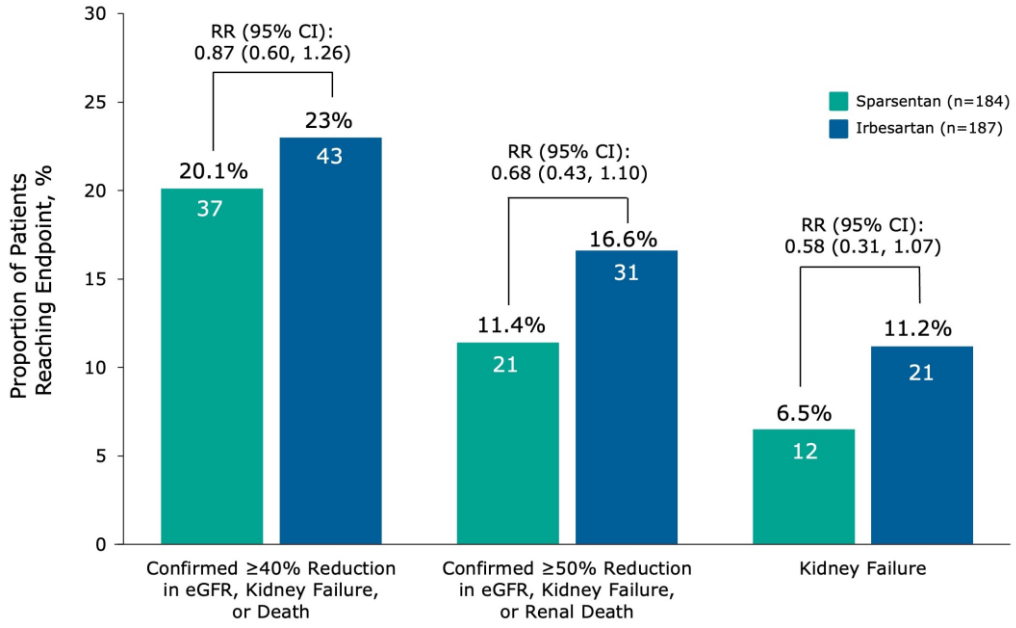
Variable	Sparsentan (n=184)	Irbesartan (n=187)	Difference
Least-squares mean eGFR slope (95% CI), mL/min/1.73 m² per year			
eGFR total slope*	**-5.4** (-6.9, -3.9)	**-5.7** (-7.2, -4.3)	**0.3,** *P*=0.75 (-1.7, 2.4)
eGFR chronic slope†	**-4.8** (-6.3, -3.3)	**-5.7** (-7.2, -4.2)	**0.9,** *P*=0.42 (-1.3, 3)
Least-squares mean change in eGFR from baseline to Week 112 (95% CI), mL/min/1.73 m²‡	**-10.4** (-12.6, 8.1)	**-12.1** (-14.4, -9.9)	**1.8** (-1.4, 4.9)

* The eGFR total slope was the slope from day 1 to week 108.
† The eGFR chronic slope was the slope from week 6 to week 108.
‡ Data are for patients who completed the double-blind treatment period (129 patients in the sparsentan group and 136 patients in the irbesartan group).

Composite Endpoints

Composite renal endpoints were also favorable for sparsentan. The number of events for the composite endpoints of a confirmed ≥40% reduction in eGFR, kidney failure, or death and of a confirmed ≥50% reduction in eGFR, kidney failure, or renal death are presented in **Figure 5**.[4]

Figure 5. Composite Renal Endpoints Trended Favorably for Sparsentan



Safety

Over 108 weeks of treatment, TEAEs were reported with similar frequency in the sparsentan (n=172; 93.5%) and irbesartan (n=174; 93%) treatment groups. Serious TEAEs occurred in 68 (37%) sparsentan-treated patients and 82 (43.9%) irbesartan-treated patients. ALT or AST elevations >3× ULN occurred in 5 (2.7%) patients taking sparsentan and 4 (2.2%) taking irbesartan; no cases were concurrent with elevated bilirubin levels ≥1.5× ULN. There were no drug-induced liver injuries with sparsentan; 1 was reported in the irbesartan group.[4]

Abbreviations

ACEi, angiotensin-converting enzyme inhibitor; ALT, alanine aminotransferase; ANCOVA, analysis of covariance; ARB, angiotensin receptor blocker; AST, aspartate aminotransferase; AT_1, angiotensin II type 1; BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; ET_A, endothelin-1 type A; EU, European Union; FPRE, FSGS partial remission of proteinuria endpoint; FSGS, focal segmental glomerulosclerosis; IgA, immunoglobulin A; IgAN, immunoglobulin A nephropathy; ITT, intention-to-treat; KF, kidney failure; KRT, kidney replacement therapy; LS, least squares; mITT, modified intention-to-treat; MMRM, mixed model for repeated measures; OLE, open-label extension; RAASi, renin-angiotensin-aldosterone system inhibitor; RASI, renin-angiotensin system inhibitor; RR, relative risk; SAE, serious adverse event; SBP, systolic blood pressure; SOC, standard of care; TEAE, treatment-emergent adverse event; UACR, urine albumin-to-creatinine ratio; ULN, upper limit of normal; UPCR, urine protein-to-creatinine ratio; US, United States.

References

1. FILSPARI. Prescribing information. Travere Therapeutics Inc; February 2023.
2. Rovin B, Barratt J, Heerspink HJ, et al. Efficacy and safety of sparsentan vs irbesartan in patients with IgA nephropathy: 2-year results from PROTECT, a phase 3 randomized active-controlled clinical trial. *Lancet*. Published online November 3, 2023 doi:/10.1016/S0140-6736(23)02302-4
3. Srivastava T, Tesar V, Campbell KN, et al. Long-term efficacy and safety of sparsentan in FSGS: 240-week analysis of the DUET open-label extension (OLE). Abstract presented at: ASN Kidney Week; November 3-6 2022; Orlando, FL.
4. Rheault MN, Alpers CE, Barratt J, et al. Sparsentan versus irbesartan in focal segmental glomerulosclerosis. *N Engl J Med*. Published online November 3, 2023;doi:10.1056/NEJMoa2308550
5. Komers R, Gipson DS, Nelson P, et al. Efficacy and safety of sparsentan compared with irbesartan in patients with primary focal segmental glomerulosclerosis: Randomized, controlled trial design (DUET). *Kidney Int Rep*. 2017;2(4):654-664. doi:10.1016/j.ekir.2017.02.019
6. Raczynska A, Pawlowicz-Szlarska E, Nowicki M. Sparsentan–a dual antagonist–literature review on endothelin and endothelin antagonists. *Nephrol Dial Pol*. 2021;25:77-82.

7. Trachtman H, Nelson P, Adler S, et al. DUET: A phase 2 study evaluating the efficacy and safety of sparsentan in patients with FSGS. *J Am Soc Nephrol*. 2018;29(11):2745-2754. doi:10.1681/ASN.2018010091
8. Nagasawa H, Suzuki H, Jenkinson C, et al. Sparsentan, the dual endothelin angiotensin receptor antagonist (DEARA), attenuates albuminuria and protects from the development of renal injury to a greater extent than losartan in the gddY mouse model of IgA nephropathy: A 16-week study. Abstract presented at: ERA-EDTA Congress; May 19-22, 2022; Paris, France.
9. Nagasawa H, Suzuki H, Jenkinson C, et al. The dual endothelin type A receptor (ET_AR) and angiotensin II type 1 receptor (AT_1R) antagonist, sparsentan, protects against the development of albuminuria and glomerulosclerosis in the gddY mouse model of IgA nephropathy. Poster presented at: ERA-EDTA Virtual Congress; June 6-9, 2020; Virtual Meeting.
10. Bedard P, Jenkinson C, Komers R. Sparsentan protects the glomerular basement membrane and glycocalyx, and attenuates proteinuria in a rat model of focal segmental glomerulosclerosis (FSGS). Abstract presented at: ERA-EDTA Congress; May 19-22, 2022; Paris, France.
11. Barratt J, Rovin B, Wong MG, et al. IgA nephropathy patient baseline characteristics in the sparsentan PROTECT study. *Kidney Int Rep*. 2023:1-14. doi:10.1016/j.ekir.2023.02.1086
12. Barratt J, Rovin B, Diva U, Mercer A, Komers R, PROTECT Study Design Group. Supplementary material: Implementing the kidney health initiative surrogate efficacy endpoint in patients with IgA nephropathy (the PROTECT trial). *Kidney Int Rep*. 2019;4(11):1633-1637. doi:10.1016/j.ekir.2019.08.007
13. Wong M, Barratt J, Komers R, Mercer A, Rosenberg N. Baseline characteristics of adults enrolled in the ongoing phase 3 randomized, double-blind, active-control trial of sparsentan for the treatment of immunoglobulin A nephropathy (PROTECT). Mini Oral presented at: ERA-EDTA Congress; May 19-22, 2022; Paris, France.
14. Heerspink HJ, Radhakrishnan J, Alpers CE, et al. Sparsentan in patients with IgA nephropathy: A prespecified interim analysis from a randomised double-blind active-controlled clinical trial. *Lancet*. 2023;401(10388):1584-1594. doi:10.1016/S0140-6736(23)00569-X
15. Thompson A, Carroll K, Inker LA, et al. Proteinuria reduction as a surrogate end point in trials of IgA nephropathy. *Clin J Am Soc Nephrol*. 2019;14(3):469-481. doi:10.2215/CJN.08600718
16. Komers R, Diva U, Inrig JK, Loewen A, Trachtman H, Rote WE. Study design of the phase 3 sparsentan versus irbesartan (DUPLEX) study in patients with focal segmental glomerulosclerosis. *Kidney Int Rep*. 2020;5(4):494-502. doi:10.1016/j.ekir.2019.12.017
17. Tuttle KR, Kornowske LM, Jones CR, et al. Predictors of major adverse kidney disease events in a real-world population with IgA nephropathy. Poster presented at: ASN Kidney Week; November 2-5, 2023; Philadelphia, PA.
18. Barratt J, Heerspink HJL, Wong MG, et al. Superior proteinuria reduction with sparsentan in immunoglobulin A nephropathy. Mini oral presented at: ERA Congress; June 15-18, 2023; Milan, Italy.
19. Data on file. Travere Therapeutics Inc; 2023.

20. Rovin B, Barratt J, Diva U, Komers R, Perkovic V. Pivotal results of the phase 3 PROTECT trial of sparsentan (SPAR) vs irbesartan (IRB) in patients (pts) with immunoglobulin A nephropathy (IgAN). Oral presentation presented at: ASN Kidney Week; November 2-5, 2023; Philadelphia, PA.

21. Troost JP, Trachtman H, Spino C, et al. Proteinuria reduction and kidney survival in focal segmental glomerulosclerosis. *Am J Kidney Dis*. 2021;77(2):216-225. doi:10.1053/j.ajkd.2020.04.014