Sparsentan (SPAR) vs Irbesartan (IRB) in Patients With Focal Segmental Glomerulosclerosis (FSGS): Results From the Phase 3 DUPLEX Trial

Background

- SPAR is a dual endothelin angiotensin receptor antagonist (DEARA) that reduced proteinuria in patients with FSGS in a phase 2 trial[1-3]
- The phase 3 DUPLEX trial (NCT03493685) evaluated the efficacy and safety of SPAR vs the active control IRB in patients with FSGS

Methods

Patients with FSGS were randomized 1:1 to receive SPAR (target dose, 800 mg/day) or IRB (target dose, 300 mg/day) for 108 weeks

SPAR, n=184

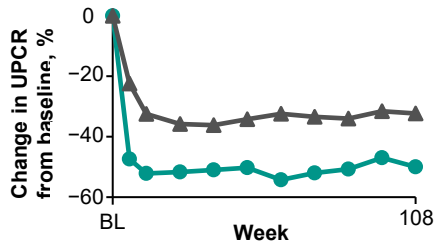
IRB, n=187

Eligibility criteria

- Ages 8-75 years
- No secondary causes of FSGS
- UPCR ≥1.5 g/g
- eGFR ≥30 mL/min/1.73 m^2

Proteinuria

SPAR reduced proteinuria, an effect that was sustained over the 108-week DB period



Change in UPCR at week 108:

- 32% with IRB
- 50% with SPAR

At the 36-wk interim analysis

FPRE* was achieved by:

42% **with SPAR** vs 26% **with IRB**

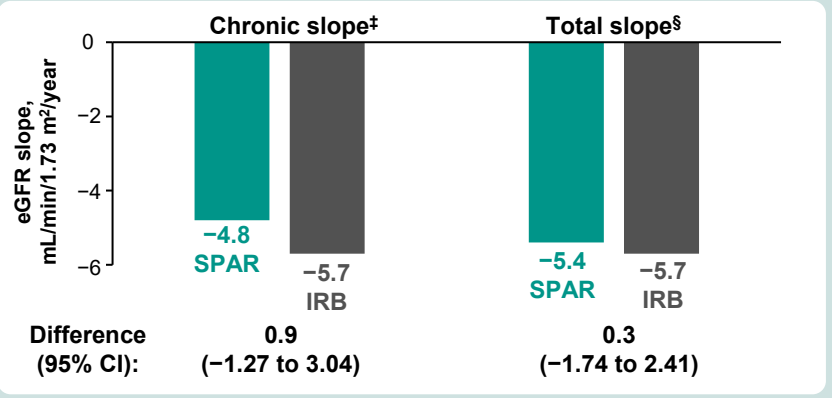
At the final analysis (108-wk DB period)

complete remission† was achieved by:

19% **with SPAR** vs 8% **with IRB**

eGFR Slope

eGFR slopes were lower with SPAR vs IRB, but differences were not statistically significant



Safety

SPAR had a safety profile that was comparable to IRB

Heart failure, drug-induced liver injury, and clinically meaningful fluid retention/edema were not identified as safety concerns

Conclusion

Patients with FSGS who received SPAR achieved a **clinically meaningful reduction in proteinuria** over the 2-year study period, although differences in eGFR slope vs IRB were not statistically significant. The safety profile of SPAR (800 mg/day) was comparable to that of IRB

BL, baseline; DB, double blind; eGFR, estimated glomerular filtration rate; FPRE, FSGS partial remission endpoint; UPCR, urine protein-to-creatinine ratio. * UPCR ≤1.5 g/g and >40% reduction from baseline. † UPCR <0.3 g/g at any time during the study. ‡ Chronic slope was assessed from week 6 to 108. § Total slope was assessed from day 1 to week 108.

1. Trachtman H, et al. *Expert Opin Emerg Drugs*. 2020;25(3):367-375. 2. Kowala MC, et al. *J Pharmacol Exp Ther*. 2004;309(1):275-284. 3. Nagasawa H, et al. *Nephrol Dial Transplant*.2022;37:183.

Rheault MN, et al. ASN Kidney Week 2023 Abstract FR-OR108

©2023 Travere Therapeutics, Inc. All rights reserved