Pivotal Results of the Phase 3 PROTECT Trial of Sparsentan (SPAR) vs Irbesartan (IRB) in Patients (Pts) With Immunoglobulin A Nephropathy (IgAN)

Background

- **SPAR** is a dual endothelin angiotensin receptor antagonist (DEARA)[1-3]

Methods

Patients randomized 1:1 and treated for up to 110 weeks

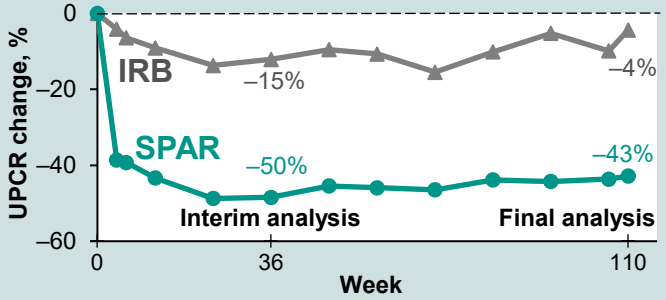
SPAR n=202 400 mg/day **IRB** n=202 300 mg/day

Eligibility criteria

- Adults (age ≥18 years)
- Biopsy-proven IgAN
- Proteinuria ≥1.0 g/day, despite maximum RAS inhibition for ≥12 weeks
- eGFR ≥30 mL/min/1.73 m^2

Proteinuria

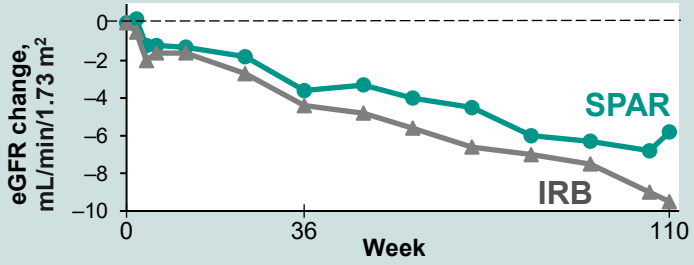
Significant proteinuria reductions with **SPAR** vs **IRB** at 36 weeks (primary endpoint)[4] were maintained throughout the randomized treatment period (110 weeks)

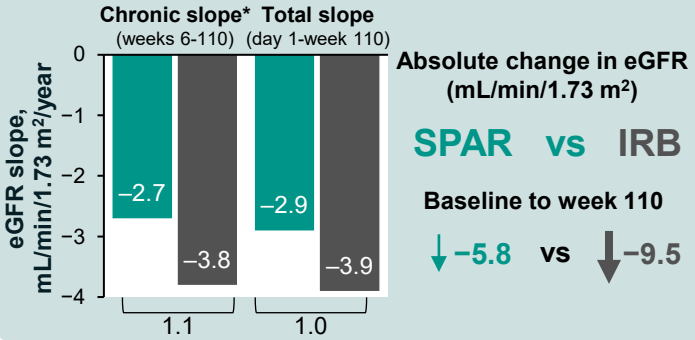


More patients achieved complete proteinuria remission (UPE <0.3 g/day)

eGFR Change (secondary endpoints)

Statistically significant reduction in eGFR chronic slope and clinically meaningful reduction in total slope with **SPAR** vs **IRB** through week 110

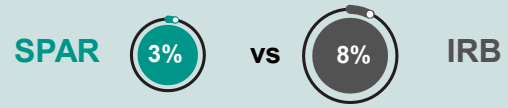




Kidney Survival and IST Use

Composite kidney failure endpoint (40% eGFR reduction, end-stage kidney disease, death):

Initiation of IST with renal indication:



Safety

- ✓**SPAR** had a safety profile that was comparable to **IRB**
- ✓Peripheral edema was similar in both groups, with no increases in body weight
- ✓No drug-induced liver injury occurred

Conclusion

Over 110 weeks of treatment, SPAR vs maximally titrated IRB led to significant reductions in proteinuria and preservation of kidney function

The totality of data from PROTECT suggest that **SPAR is an effective and safe treatment for IgAN** that delivers meaningful clinical benefit beyond RAS inhibition alone

eGFR, estimated glomerular filtration rate; IgAN, immunoglobulin A nephropathy; IST, immunosuppression therapy; RAS, renin-angiotensin system; UPCR, urine protein-to-creatinine ratio; UPE, urine protein excretion. *P=.037.

References: 1. Trachtman H, et al. *Expert Opin Emerg Drugs*. 2020;425(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. 4. Heerspink HJL, et al. *Lancet*. 2023;13;401(10388):1584-1594.

Rovin B, et al. ASN Kidney Week 2023
Abstract FR-OR109