Concomitant Sparsentan and Sodium-Glucose Cotransporter-2 Inhibitors in Patients With IgA Nephropathy in the PROTECT Open-Label Extension

Background

- **SPAR**, a **DEARA**, was granted accelerated approval in the US for IgAN based on the **PROTECT** trial of **SPAR** vs irbesartan[1-5]
- Data suggest that **SGLT2is** may reduce the progression of IgAN[6,7]
- Here we report the early experience in the **PROTECT OLE** with **SGLT2is** combined with ongoing **SPAR** to treat IgAN

Study Design

PROTECT double-blind period: SPAR vs irbesartan → **PROTECT OLE period:** SPAR 400 mg per day up to 156 weeks

We assessed pts in the OLE who initiated SGLT2i treatment

Assessments: UPCR, body weight, blood pressure, safety

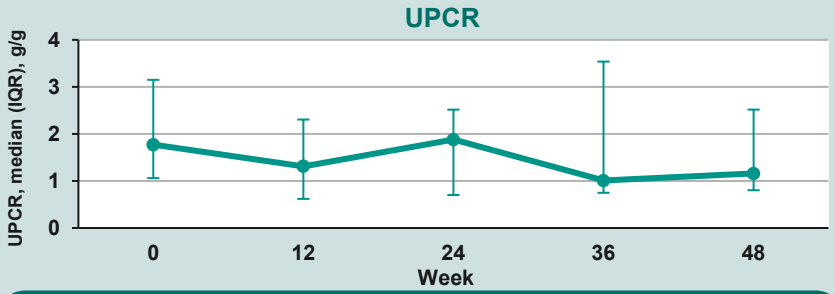
Pts could initiate concomitant SGLT2i treatment during the OLE

Key inclusion criteria
- Enrolled and participating in the PROTECT OLE
- Initiated concomitant SGLT2i treatment during the OLE

Key exclusion criterion
- Enrolled in the randomized PROTECT OLE SGLT2i Substudy

Results

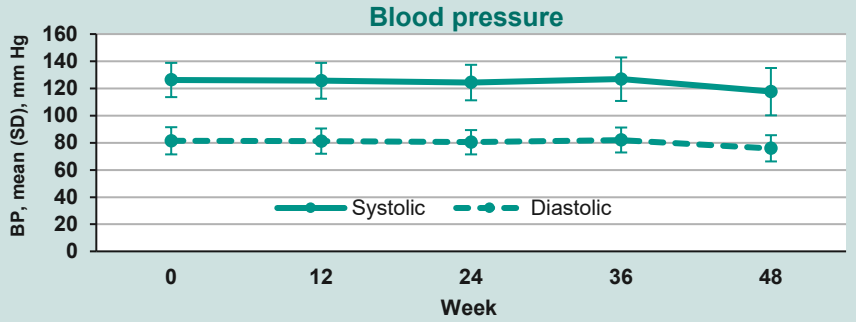
- Reduction in proteinuria was seen for up to **48 weeks** with the addition of an **SGLT2i** to ongoing **SPAR** treatment

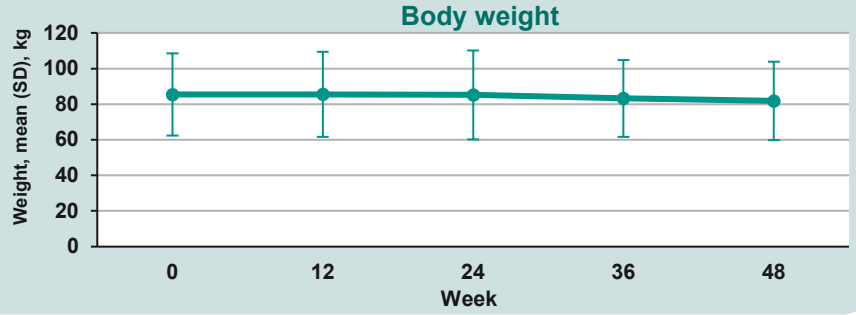


- 39 pts initiated an **SGLT2i***
  - 5 discontinued the **OLE**
  - 2 discontinued the **SGLT2i** but continue to receive **SPAR** in the **OLE**

- 26 pts (67%) had an AE, most commonly hyperkalemia (5 pts [13%]), COVID-19 (4 pts [10%]), and hypertension (3 pts [8%])
- No new safety signals were identified

- Mean **body weight** and **blood pressure** (systolic and diastolic) remained **relatively stable** over time following addition of an SLGT2i to ongoing SPAR treatment





Conclusion

Early experience of pts during the **PROTECT OLE** period shows that an **SGLT2i** added to stable **SPAR** treatment is **generally well tolerated and provides additional benefit on proteinuria reduction** with combination therapy.

PROTECT OLE Substudy (NCT03762850)

A randomized substudy within the PROTECT OLE period is further investigating the safety and efficacy of SPAR with or without concomitant SGLT2i treatment

AE, adverse event; BP, blood pressure; DEARA, dual endothelin angiotensin receptor antagonist; IgAN, immunoglobulin A nephropathy; IQR, interquartile range; OLE, open-label extension; pt, patient; SGLT2i, sodium-glucose cotransporter-2 inhibitor; SPAR, sparsentan; UPCR, urine protein-to-creatine ratio. *Pts in the PROTECT OLE who did not enter the substudy. References: 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. 4. Heerspink HJL, et al. *Lancet*. 2023;401(10388):1584-1594. 5. Filspari (sparsentan). Prescribing information. Travere Therapeutics, Inc.; 2023. 6. Herrington WG, et al. *N Eng J Med*. 2023;388(2):117-127. 7. Wheeler DC, et al. *Kidney Int*. 2021;100(1):215-224.

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