Effects of Sparsentan After Maximized Angiotensin Receptor Blocker (ARB) Treatment in Patients With IgA Nephropathy (IgAN) in the PROTECT Trial

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INTRODUCTION

- SPAR is a non-immunosuppressive, dual endothelin angiotensin receptor antagonist (DEARA)[1] indicated in the US to slow kidney function decline in adults with primary IgAN at risk for disease progression[2] and in the EU to treat adults with primary IgAN[3]
- In the phase 3, randomized, DB PROTECT trial of patients with IgAN, SPAR showed sustained proteinuria reduction and preservation of kidney function over 110 weeks that was superior to active control maximum labeled dose IRB[4]
- Eligible patients who completed the DB period could be enrolled in the open-label extension (OLE) to receive SPAR for up to 156 weeks regardless of randomized treatment

Aim

- To report the safety and efficacy of SPAR (up to 48 weeks) in the PROTECT OLE following 110 weeks of maximum labeled dose IRB in the active control arm

DB, double-blind; DEARA, dual endothelin angiotensin receptor antagonist; IgAN, immunoglobulin A nephropathy; IRB, irbesartan; OLE, open-label extension; SPAR, sparsentan.

METHODS

PROTECT DB period:

- Multicenter, randomized clinical trial (NCT03762850)
- Adults with biopsy-proven IgAN and persistent proteinuria despite RASi treatment
- Received SPAR (400 mg/d) vs maximum labeled dose IRB (300 mg/d) for 110 weeks, then resumed RASi for 4 weeks (study drug washout)

PROTECT OLE period:

- To enroll, patients must have completed 110 weeks of randomized treatment and the DB period and have an eGFR of >20 mL/min/1.73 m^2 at week 110
- Will receive SPAR 400 mg/d for up to 156 weeks regardless of treatment in DB period
- Endpoints: UPCR, eGFR, blood pressure, and safety

- We report the safety and efficacy of up to 48 weeks of SPAR in patients who initiated it for the first time in the OLE after completing 110 weeks of maximum labeled dose IRB during the DB period

DB, double blind; eGFR, estimated glomerular filtration rate; IgAN, immunoglobulin A nephropathy; IRB, irbesartan; OLE, open-label extension; RASi, renin-angiotensin system inhibitor; SPAR, sparsentan; UPCR, urine protein-to-creatinine ratio.

RESULTS

Patient Demographics and Baseline Characteristics at the Start of the OLE Period*

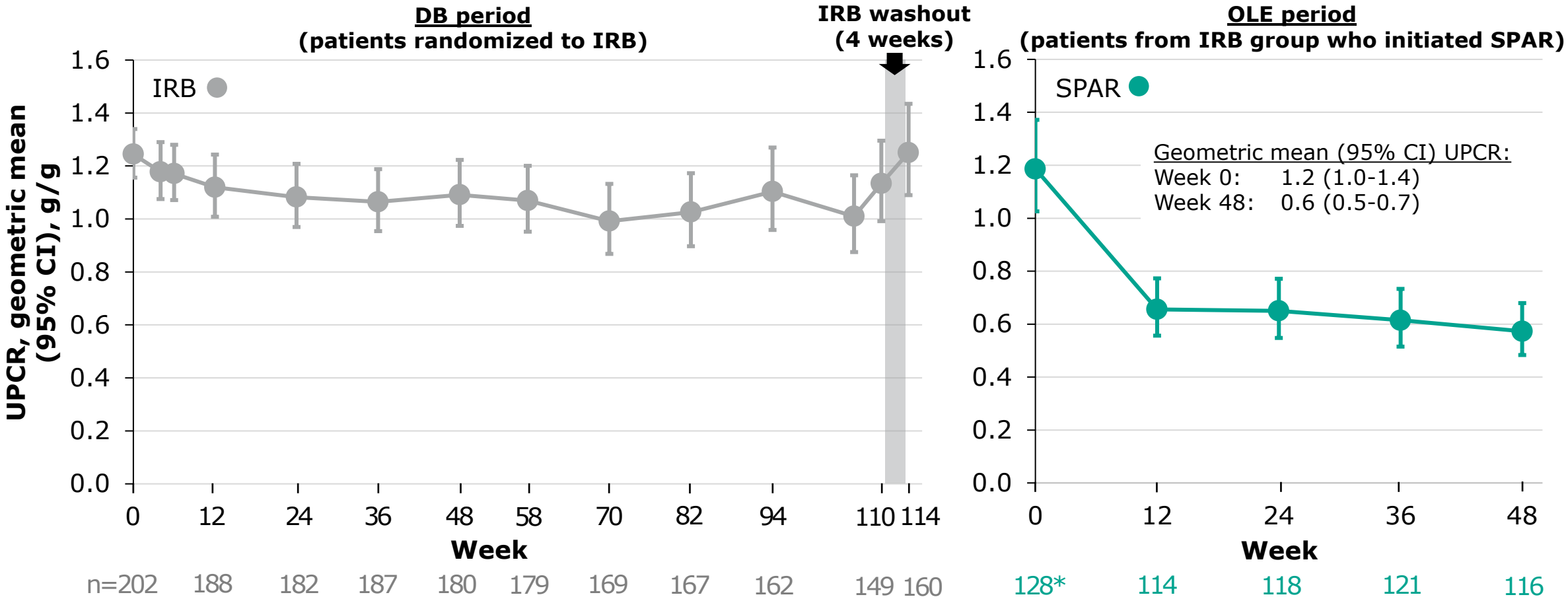
	IRB→SPAR OLE (n=128)
Age at informed consent, mean (SD), y	45.5 (11.99)
Male sex, n (%)	91 (71)
Race, n (%)†	
Asian	27 (21)
Black or African American	1 (1)
Native Hawaiian or Other Pacific Islander	1 (1)
White	94 (73)
Other	6 (5)
Weight, mean (SD), kg	82.89 (17.43)
Body mass index, mean (SD), kg/m²	27.86 (5.16)
Blood pressure, mean (SD), mm Hg	
Systolic	126 (12.57)
Diastolic	82.1 (9.12)
UPCR, median (IQR), g/g	1.30 (0.71-2.13)
UPCR, geometric mean, g/g	1.17
UPE, median (IQR), g/d	1.87 (1.03-2.91)
eGFR, mean (SD), mL/min/1.73 m²‡	52.2 (24.9)

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; DB, double blind; eGFR, estimated glomerular filtration rate; IRB, irbesartan; OLE, open-label extension; SPAR, sparsentan; UPCR, urine protein-to-creatinine ratio; UPE, urine protein excretion. *The start of the OLE period had 128 patients who were treated with IRB in the DB period and then initiated SPAR for the first time in the OLE period. †Patients may have selected >1 race. ‡Calculated using the CKD-EPI equation.

RESULTS

UPCR at Each Study Visit for Patients Randomized to IRB

- SPAR showed a rapid reduction in UPCR that was sustained for up to 48 weeks in the OLE period

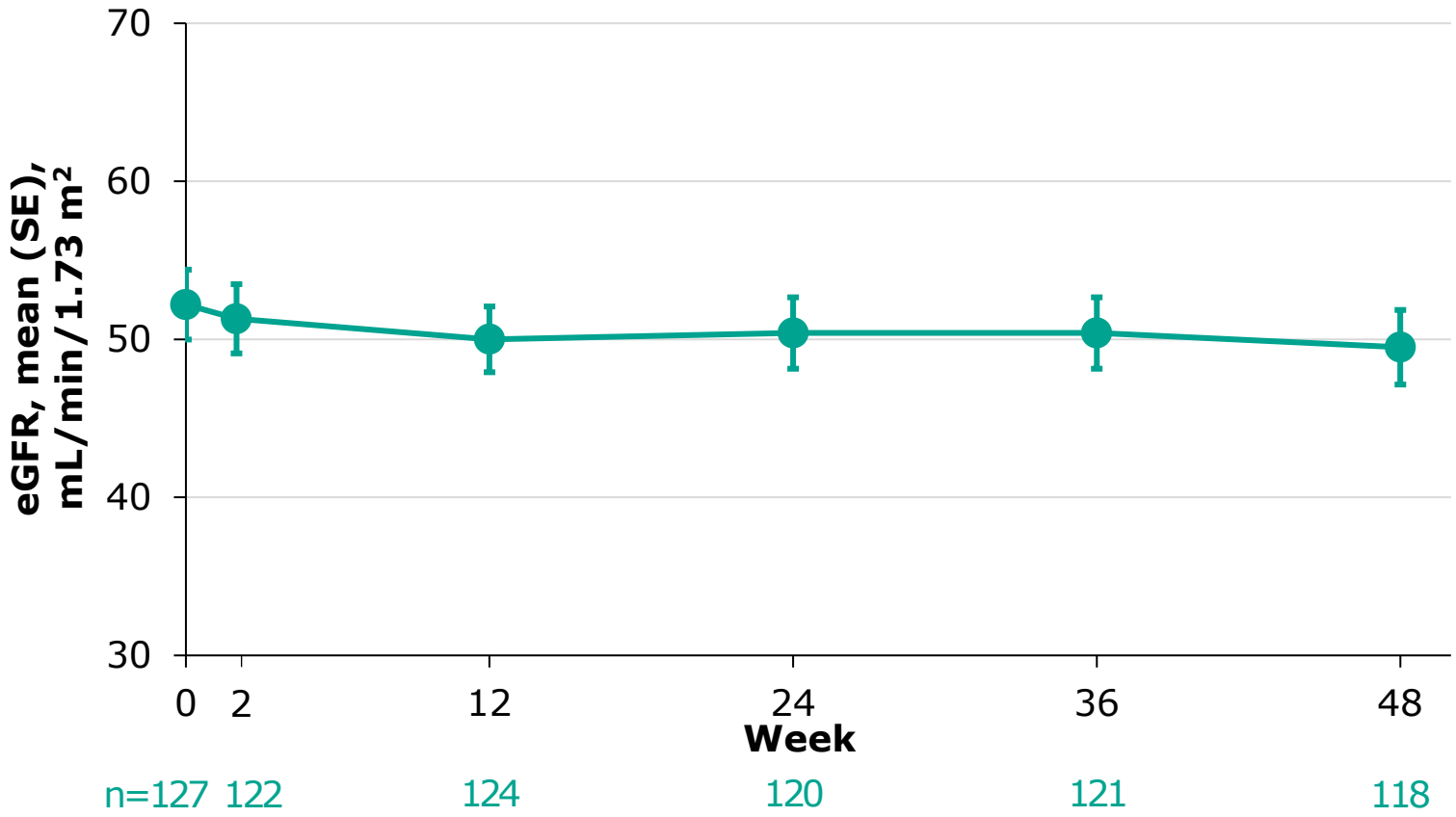


DB, double blind; IRB, irbesartan; OLE, open-label extension; SPAR, sparsentan; UPCR, urine protein-to-creatinine ratio. *Baseline of the OLE period was also week 114 of the DB period. 160 Patients completed the DB period, and 128 of them entered the OLE.

RESULTS

eGFR values at Each Visit in the OLE Period

- eGFR values remained consistent for up to 48 weeks in the OLE period

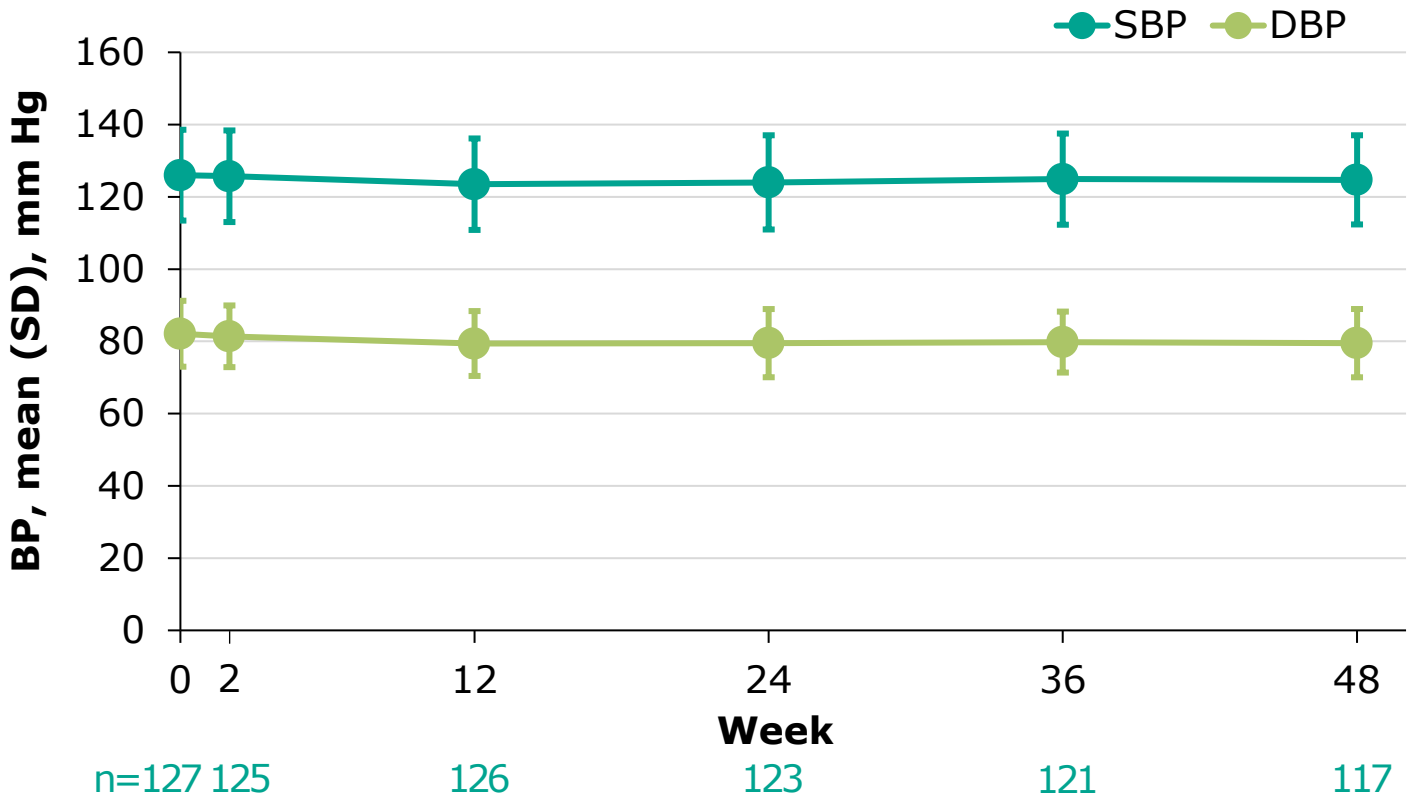


eGFR, estimated glomerular filtration rate; OLE, open-label extension.

RESULTS

BP at Each Visit in the OLE Period

- BP remained well controlled throughout the OLE
- At 48 weeks, mean changes (SD) from OLE baseline in SBP and DBP were −1.0 (11.03) and −2.2 (8.82) mm Hg, respectively



BP, blood pressure; DBP, diastolic blood pressure; OLE, open-label extension; SBP, systolic blood pressure.

RESULTS

Safety in the OLE Period

- Rates of AEs in the OLE were low, with no new safety signals identified

	IRB→SPAR OLE (n=128)
Patients with any TEAE, n (%)	103 (80)
Any TEAEs in ≥5% of patients, n (%)	
COVID-19	23 (18)
Hyperkalemia	15 (12)
Peripheral edema	13 (10)
Upper respiratory tract infection	11 (9)
Dizziness	9 (7)
Hypotension	9 (7)
Hypertension	8 (6)
Nasopharyngitis	8 (6)
Gout	7 (5)
Proteinuria	7 (5)
Headache	7 (5)

OLE, open-label extension; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- Patients previously treated with maximum labeled dose IRB for 2 years experienced rapid and sustained proteinuria reductions with SPAR

- SPAR treatment was generally well tolerated, with stable blood pressure and no new safety signals

IRB, irbesartan; SPAR, sparsentan.

REFERENCES

1. Kohan DE, et al. *Clin Sci (Lond)*. 2024;138(11):645-662.

2. Filspari (sparsentan). Prescribing information. Travere Therapeutics, Inc.; 2024.

3. Filspari (sparsentan). Summary of product characteristics. CSL Vifor; 2024.

4. Rovin BH, et al. *Lancet*. 2023;402(10417):2077-2090.

DISCLOSURES

- **JF** reports consulting fees, honoraria, and speakers bureaus from AstraZeneca, Bayer, Boehringer Ingelheim, Calliditas, CSL Vifor, HI-Bio Novo Nordisk, Novartis, Omeros, Otsuka, Roche, Stada, Travere Therapeutics, Inc., Vera Therapeutics, and Visterra.
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