Improving Proteinuria With Sparsentan (SPAR) in Patients With IgA Nephropathy (IgAN): A Case Series

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FINDINGS

- This case series supports the safety and effectiveness of SPAR achieving or maintaining low proteinuria in patients with IgAN, with 5 of 6 reaching or maintaining UPCR ≤0.5 g/g, regardless of UPCR or eGFR prior to SPAR initiation, treatment history, and time since diagnosis
- Two patients received SPAR at the reduced dose of 200 mg/d with effective proteinuria control, with 1 achieving a UPCR of 0.3 g/g and the other maintaining UPCR of ≤0.5 g/g
- One patient who started SPAR at diagnosis showed a marked improvement in proteinuria and achieved complete remission, supporting the benefit of early SPAR initiation

KEY TAKEAWAY

Patients with IgAN receiving SPAR in a real-world setting achieved or maintained low proteinuria (UPCR of <0.3 or <0.5 g/g), the target goal per KDIGO,[6] during follow-up

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INTRODUCTION

- SPAR is a non-immunosuppressive, dual endothelin angiotensin receptor antagonist (DEARA)[1,2] approved in the US, EU, and UK for the treatment of adults with IgAN who are at risk for disease progression[3-5]
- In the PROTECT study, SPAR reduced proteinuria in patients with IgAN, leading to complete remission of proteinuria more often vs maximum labeled dose irbesartan.[2]
  SPAR was well tolerated, with 95% of patients titrated to the target dose (400 mg/d)[2]
- However, evidence on the antiproteinuric effect of SPAR in the real-world setting is limited

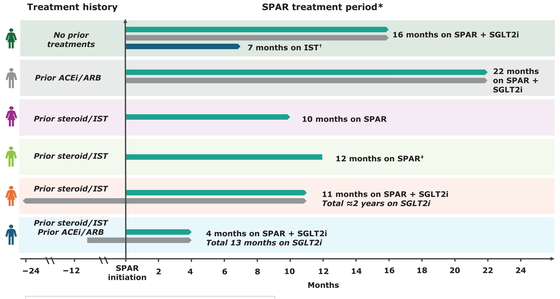
OBJECTIVE

- This case series reports the clinical features and treatment responses of 6 patients with IgAN receiving SPAR in the real-world setting

CASE SERIES METHODOLOGY

- Patients with biopsy-proven IgAN who received SPAR for 4 to 22 months in routine clinical practice at a tertiary care center were elected by their treating healthcare professional (HCP) for inclusion in this case series (**Figure 1**)
  - SPAR was dosed at 200 mg/d for 2 weeks before uptitration to 400 mg/d, according to the prescribing information.[2] In 2 patients with intolerance of the 400-mg/d dose, the 200-mg/d dose was resumed
- Patients provided consent to their HCP for inclusion
- Deidentified patient data, including patient characteristics, treatment history, and clinical assessments, were provided by the patient's HCP

Figure 1. Patient Treatment Summary



Eligibility criteria

- Biopsy-proven IgAN
- ≥3 months on SPAR
- Patient provided consent to HCP

*SGLT2i was initiated prior to SPAR (n=2) or simultaneously with SPAR (n=2). †Tapered and discontinued during the first 7 months. ‡Patient discontinued treatment to start dialysis.

CASE SERIES DESCRIPTIONS

Patients

- Six patients with biopsy-proven IgAN (aged ≈35-65 years) were included in this case series (**Table 1**)
- Prior to SPAR, 5 patients received a RASi, 4 patients received steroid/immunosuppressive treatment (IST), and 2 received an SGLT2i
- One patient concurrently initiated SPAR, an SGLT2i, and a steroid/IST at diagnosis (without receiving a prior RASi). The steroid/IST was tapered and discontinued after 7 months
- The duration of follow-up for patients on SPAR ranged from 4 to 22 months
- Five patients were receiving ongoing SPAR treatment (with or without other treatments) at the last follow-up
  - In 1 patient who initiated SPAR ≈12 years after diagnosis with an eGFR of 21 mL/min/1.73 m², SPAR was discontinued after 12 months to start dialysis when eGFR reached 10 mL/min/1.73 m²

Table 1. Case Summaries

	Patient characteristics				Treatment				UPCR, g/g		eGFR, mL/min/1.73 m²		Blood pressure, mm Hg	
	Age range, years	Sex	Race	Time from biopsy to SPAR initiation	Other treatment history*	Concurrent treatments	Duration of follow-up on SPAR	SPAR dose, mg/d	SPAR initiation†	Follow-up	SPAR initiation†	Follow-up	SPAR initiation†	Follow-up
	50-55	Female	Asian	0 months	• None	• Prednisone‡ • Dapagliflozin	16 months	400§	10.2 →	0.1	61 →	68	139/85	117/69
	50-55	Male	White	3 years	• Ramipril • Fish oil	• Dapagliflozin	22 months	400§	0.3‖ →	0.2	59 →	63	118/81	106/67¶
	35-40	Female	Asian	10 years	• Steroids • Losartan • Piperazine • Ramipril	• None	10 months	400§	5.8 →	0.4	88 →	74	127/83	115/83#
	60-65	Male	Asian	12 years	• Valsartan • Prednisone	• Fish oil	12 months**	400§	1.5 →	1.4	21 →	10	112/68	134/80
	45-50	Female	Hispanic	8 years	• Prednisone • Lisinopril	• Empagliflozin	11 months	200††	0.3‡‡ →	0.5	37 →	38	122/78	122/82
	35-40	Male	Hispanic	5 years	• TRF-budesonide • Losartan • Prednisone	• Dapagliflozin	4 months	200††	0.7 →	0.3	25 →	24	150/68	105/72

UPCR: ≥0.5 <0.5 <0.3 eGFR: ≤45 >45 to ≤90 >90

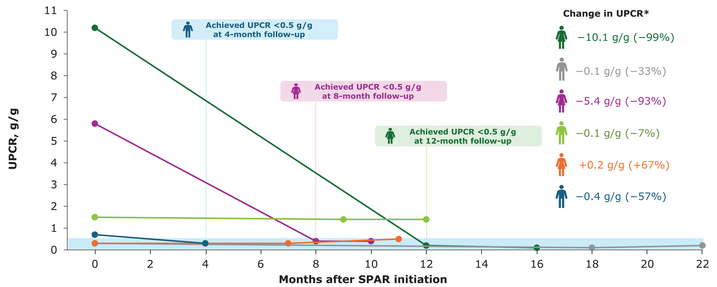
*Treatment(s) discontinued before SPAR initiation. †Values at initiation derived from visit at which SPAR was initiated or most recent visit prior to initiation. ‡Tapered and discontinued after 7 months. §After 2 weeks at 200 mg/d. ‖Patient initiated SPAR at UPCR of 0.3 g/g based on prior history of elevated proteinuria; proteinuria decreased at visit in which SPAR was initiated. ¶Follow-up duration of 14 months. #Follow-up duration of 8 months. **Patient developed ESKD and started dialysis after 12 months on SPAR. ††Dose reduced due to intolerance of 400-mg/d dose. ‡‡Patient initiated SPAR at UPCR of 0.3 g/g due to continued drop in eGFR while on prior treatments (despite low proteinuria).

Outcomes

Proteinuria

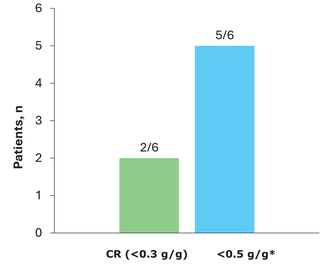
- Proteinuria (UPCR) decreased from SPAR initiation to last follow-up in 5 of 6 patients. In the sixth patient, who initiated SPAR with UPCR of 0.3 g/g, proteinuria was maintained through 7 months, with a slight increase to 0.5 g/g observed at the last follow-up (11 months) (**Figure 2; Table 1**)
- Two patients achieved complete remission of proteinuria (UPCR of <0.3 g/g), and 3 additional patients achieved UPCR of <0.5 g/g at any time during SPAR treatment (**Figure 3**)
  - In 2 patients with intolerance of the 400-mg/d dose, dose reduction to 200 mg/d was well tolerated with effective proteinuria control; in 1 patient, UPCR decreased from 0.7 to 0.3 g/g, and in the other, UPCR was maintained at ≤0.5 g/g
- In 1 patient who initiated SPAR with an SGLT2i and steroid at diagnosis (steroid tapered and discontinued after 7 months), UPCR was substantially lowered (10.2 to 0.1 g/g) and eGFR improved (61 to 68 mL/min/1.73 m²) after 16 months

Figure 2. Change in UPCR



*Values reflect mean change from SPAR initiation (month 0) to last follow-up.

Figure 3. Proportion of Patients Achieving Complete Remission (UPCR <0.3 g/g) and UPCR <0.5 g/g at Any Time During Follow-up

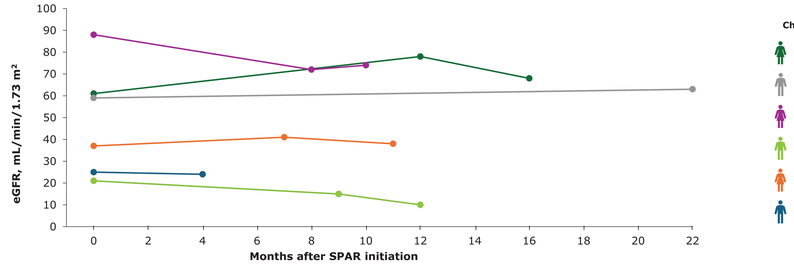


*Patients achieving CR (UPCR <0.3 g/g) have also been counted as achieving UPCR <0.5 g/g.

eGFR

- eGFR remained relatively stable overall, with a slight increase observed in 3 of 6 patients and a slight decrease in 3 of 6 patients (**Figure 4**)
  - In 1 patient who initiated SPAR with an eGFR of 21 mL/min/1.73 m², a decline to 10 mL/min/1.73 m² prompted initiation of dialysis (at which time SPAR was discontinued)

Figure 4. Change in eGFR



*Values reflect mean change from SPAR initiation (month 0) to last follow-up.

Blood pressure

- Blood pressure was generally stable on SPAR
  - In 2 patients with intolerance of the 400-mg/d dose due to patient-reported systolic blood pressure of <100 mm Hg, the 200-mg/d dose was well tolerated, with blood pressure within the expected range (**Table 1**)

Safety

- SPAR treatment (400 mg/d) was generally well tolerated by these patients, with no discontinuations due to safety concerns

ABBREVIATIONS

ACEi, angiotensin-converting enzyme inhibitor; **ARB**, angiotensin receptor blocker; **CR**, complete remission; **DBP**, diastolic blood pressure; **DEARA**, dual endothelin angiotensin receptor antagonist; **eGFR**, estimated glomerular filtration rate; **ESKD**, end-stage kidney disease; **HCP**, healthcare professional; **IgA**, immunoglobulin A; **IgAN**, immunoglobulin A nephropathy; **IST**, immunosuppressive therapy; **KDIGO**, Kidney Disease: Improving Global Outcomes; **RASi**, renin-angiotensin system inhibitor; **SBP**, systolic blood pressure; **SGLT2i**, sodium-glucose cotransporter-2 inhibitor; **SPAR**, sparsentan; **TRF**, targeted-release formulation; **UPCR**, urine protein-to-creatinine ratio.

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DISCLOSURES

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