# Sparsentan in Combination With Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2i) in Patients With IgA Nephropathy (IgAN): A Case Series

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## CASE DESCRIPTIONS

### Patients

- Four patients with biopsy-proven IgAN (ages ≈25-65 years) were included in this case series
- Prior to sparsentan initiation, 3 patients received steroid/immunosuppressive treatment (alone or in combination with a RASi); 1 patient received a prior RASi (losartan) alone
- All patients received sparsentan in combination with the SGLT2i dapagliflozin (**Figure 1**)
- Duration of follow-up on sparsentan ranged from 3 to 10 months, with all patients receiving ongoing sparsentan + SGLT2i combination treatment at last follow-up

### Outcomes

- A rapid decrease in proteinuria (UPCR) from sparsentan initiation to follow-up was seen in patients receiving sparsentan + SGLT2i (**Figure 2**)
  - Two patients achieved UPCR <0.5 g/g at any time during sparsentan treatment (**Figure 2**)
- In 1 patient for whom albuminuria (UACR) was evaluated, UACR decreased to <0.3 g/g with sparsentan + SGLT2i (**Figure 3**)
- In all patients, further decreases in proteinuria and albuminuria were observed with sparsentan + SGLT2i compared with the end of previous treatment (**Table 1**)
- eGFR and blood pressure remained relatively stable (**Table 1, Figure 4**)
- Hematuria resolved in 1 of 4 patients (**Table 1**)
- Sparsentan + SGLT2i treatment was generally well tolerated, with no treatment discontinuations due to safety concerns (**Table 1**)

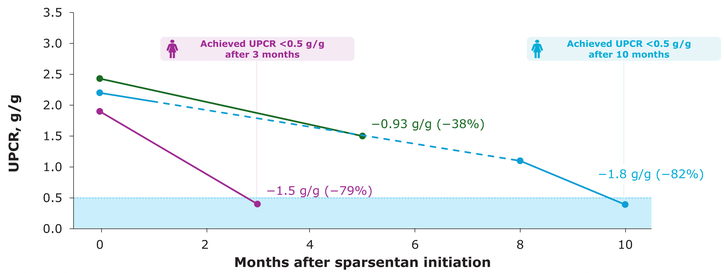
### Table 1. Case Summaries

| | Patient characteristics | | | | Treatment | | | UPCR, g/g | | | eGFR, mL/min/1.73 m² | | Hematuria | | Blood pressure, mm Hg | | Safety |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Age range, years | Sex | Race | Time since IgAN diagnosis | Other treatment history* | SGLT2i duration | Duration of follow-up on SPAR | Diagnosis | SPAR initiation† | Follow-up | SPAR initiation† | Follow-up | SPAR initiation† | Follow-up | SPAR initiation† | Follow-up | |
| 1 | 50-55 | Male | White | 11 years | • Losartan | 2 years | 5 months | 3.6‡ | 2.43 | 1.5 | 20 | 21 | Present | Present | 100/65§ | 115/65‖ | Well tolerated |
| 2 | 40-45 | Female | White | 4 years | • Prednisone<br>• Cyclophosphamide<br>• Mycophenolate mofetil | 12 months¶,** | 10 months | 5.1 | 2.2 | 0.4 | 63 | 51 | Present | Absent | 103/68 | 103/63 | Well tolerated |
| 3 | 60-65 | Female | White | 4 months | • Prednisone<br>• RASi | 3 months | 3 months | 1.8 | 1.9 | 0.4 | 102 | 102 | Present | Present | 144/87 | 139/81 | Well tolerated |
| 4 | 25-30 | Female | White | 5 months | • Prednisone<br>• Rituximab | 3 months** | 4 months** | UACR, g/g††<br>1.1 | 3.48 | 0.16 | 45 | 56 | Present | Present†† | 122/80 | 118/72 | Well tolerated |

**UPCR:** ≥0.5 <0.5 **UACR:** ≥0.3 <0.3 **eGFR:** ≤45 >45 to ≤90 >90 **Hematuria:** Present Absent

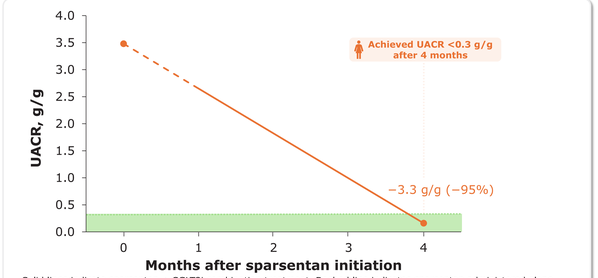
*Treatment(s) discontinued. †Values at initiation derived from visit at which SPAR was initiated or most recent visit prior to initiation. ‡UPE (g/d). §Approximate values (SBP range, 90-110; DBP range 60-70). ‖Approximate values (SBP range, 110-120; DBP range 60-70). ¶Total duration of interrupted treatment. **Approximate duration. ††UPCR data not available for this patient. ‡‡At 3 months after sparsentan initiation.

### Figure 2. Change in UPCR



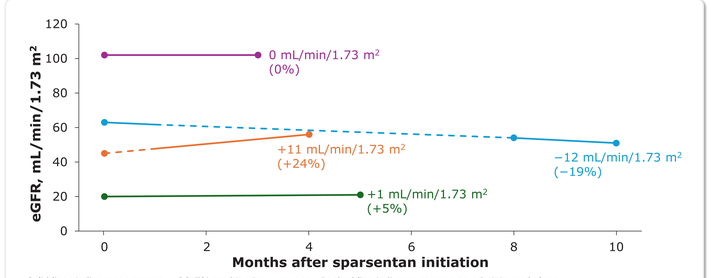

Solid lines indicate sparsentan + SGLT2i combination treatment. Dashed line indicates sparsentan administered alone. Values reflect mean (%) change from sparsentan initiation (Month 0) to last follow-up.

### Figure 3. Change in UACR




Solid lines indicate sparsentan + SGLT2i combination treatment. Dashed line indicates sparsentan administered alone. Values reflect mean (%) change from sparsentan initiation (Month 0) to last follow-up.

### Figure 4. Change in eGFR




Solid lines indicate sparsentan + SGLT2i combination treatment. Dashed line indicates sparsentan administered alone. Values reflect mean (%) change from sparsentan initiation (Month 0) to last follow-up.

## INTRODUCTION

### BACKGROUND

- Sparsentan is a non-immunosuppressive, dual endothelin angiotensin receptor antagonist (DEARA)[1,2] approved in the US and the EU for the treatment of adults with IgAN[3,4]
- Previously reported evidence from patients with IgAN in the PROTECT study open-label extension showed an SGLT2i added to sparsentan had benefit on proteinuria reduction and was well tolerated.[5] However, evidence on the combination treatment in the real-world setting is limited

### OBJECTIVE

- This case series reports the clinical features and treatment responses of 4 patients with IgAN receiving sparsentan in combination with an SGLT2i in the real-world setting

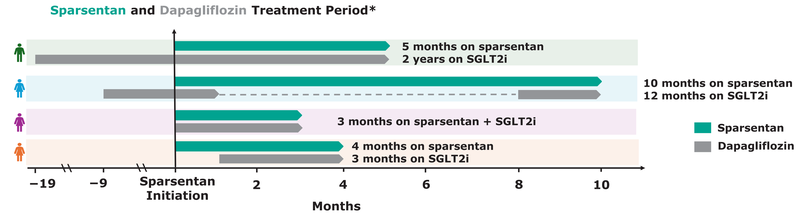
## CASE SERIES METHODOLOGY

- Patients with biopsy-proven IgAN who received sparsentan concurrently with an SGLT2i for ≥3 months in routine clinical practice at a tertiary care center were selected by their treating healthcare provider (HCP) for inclusion in this case series (**Figure 1**)
  - According to the prescribing information,[3] sparsentan was dosed as 200 mg/day for 2 weeks before up titration to 400 mg/day (at closest follow-up visit)
  - Sparsentan and SGLT2i initiation were not required to occur simultaneously
- De-identified 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 sparsentan
- Received an SGLT2i concurrently with sparsentan
- Patient provided consent to HCP




*Dapagliflozin was initiated prior to sparsentan (n=2), simultaneously with sparsentan (n=1), or after sparsentan initiation (n=1).

## FINDINGS

- Improvements in proteinuria were observed in patients receiving sparsentan + SGLT2i, regardless of eGFR or UPCR at sparsentan initiation
- Cases also highlight further proteinuria improvements achieved with sparsentan + SGLT2i compared with previous treatment
- This case series supports the safety and effectiveness of sparsentan in combination with the SGLT2i dapagliflozin in patients with IgAN

### ABBREVIATIONS

**DBP**, diastolic blood pressure; **DEARA**, dual endothelin angiotensin receptor antagonist; **eGFR**, estimated glomerular filtration rate; **HCP,** healthcare provider; **IgA**, immunoglobulin A; **IgAN,** immunoglobulin A nephropathy; **LFT,** liver function test; **RASi,** renin-angiotensin system inhibitor; **SBP**, systolic blood pressure; **SGLT2i,** sodium-glucose cotransporter-2 inhibitors; **UACR**, urine albumin-creatinine ratio; **UPE**, urine protein excretion; **UPCR,** urine protein-to-creatinine ratio.

### DISCLOSURES

**RP, GC,** and **SJE** reports no financial disclosures related to this case series. **APB** and **CG** are employees and stockholders of Travere Therapeutics, Inc. **RS** reports research funding from AstraZeneca; consultancy fees, honoraria, and advisory board participation for Travere Therapeutics, Inc; speakers bureau for Travere Therapeutics, Inc. and Vifor; stock or ownership interest in Akari Therapeutics, Amazon, Aquestive Therapeutics, Bellpointe, Cara Therapeutics, Costco, Cytodyn, Electrocore, Fingermotion, Franco Nevada, Haleon, Intel, Mesoblast, Meta Materials, Nextbridge, Oneok, Seabridge, Terawulf, Tesla, and Travere Therapeutics, Inc.; and employment by Virginia Nephrology Group.

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