

# Sparsentan As First-Line Treatment of Incident Patients With IgA Nephropathy (IgAN): Interim Analysis of the SPARTAN Trial

**Chee Kay Cheung,<sup>1</sup> Stephanie Moody,<sup>2</sup> Neeraj Dhaun,<sup>3</sup> Siân Griffin,<sup>4</sup> Alexandra Howson,<sup>1</sup> Radko Komers,<sup>2</sup> Alex Mercer,<sup>5</sup> Matthew Sayer,<sup>3</sup> Smeeta Sinha,<sup>6</sup> Lisa Willcocks,<sup>7</sup> Jonathan Barratt<sup>1</sup>**

<sup>1</sup>University of Leicester & Leicester General Hospital, Leicester, UK; <sup>2</sup>Travere Therapeutics, Inc., San Diego, CA, USA; <sup>3</sup>Royal Infirmary of Edinburgh, Edinburgh, UK; <sup>4</sup>University Hospital of Wales, Cardiff, UK; <sup>5</sup>JAMCO Pharma Consulting, Stockholm, Sweden; <sup>6</sup>Salford Royal Hospital Northern Care Alliance NHS Foundation Trust, Salford, UK; <sup>7</sup>Addenbrooke's Hospital, Cambridge University Hospitals, Cambridge, UK

Contact information:  
Chee Kay Cheung, [ckc15@le.ac.uk](mailto:ckc15@le.ac.uk)

Presented at the American Society of Nephrology (ASN) Kidney Week 2024;  
October 23-27, 2024; San Diego, CA, USA

To obtain a PDF of this oral, please scan the Quick Response (QR) code. No personal information is stored.



A visual summary of this presentation is accessible via the QR code.



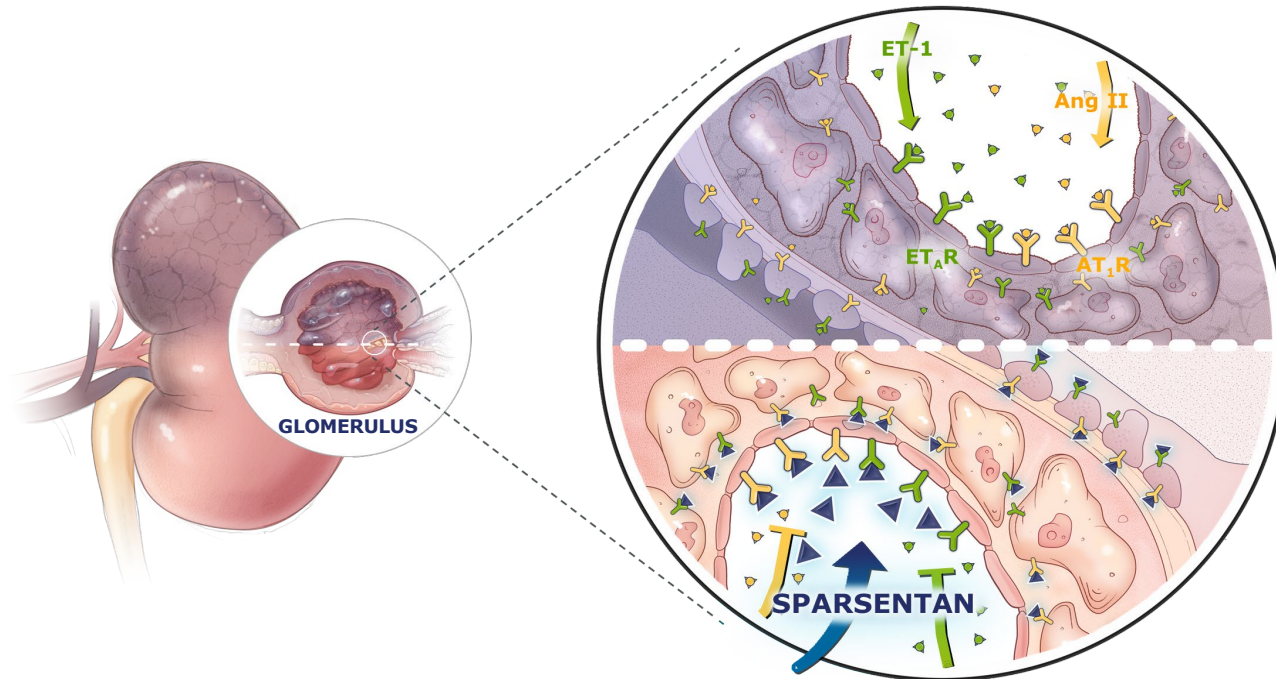
Leicester  
**IgA**  
Nephropathy  
Research Group



UNIVERSITY OF  
**LEICESTER**

- **CKC** has received consulting fees and research funding from Traverre Therapeutics, Inc.
- **SM** is an employee and stockholder of Traverre Therapeutics, Inc.
- **ND** and **JB** have received consulting fees and research funding from Traverre Therapeutics, Inc.
- **SG** has received consulting fees from CSL Vifor and Alexion; honoraria from Bayer and Traverre Therapeutics, Inc.; travel support from Alexion; and has been part of advisory boards for Emmes and ICON plc.
- **RK** is an employee and shareholder of Traverre Therapeutics, Inc.
- **AM** has received consulting fees from Traverre Therapeutics, Inc., Vera Therapeutics, and HI-Bio.
- **SS** has received research funding from Johnson and Johnson, AstraZeneca, CSL Vifor, and Sanofi Genzyme; consulting fees from Novartis, Bayer, Sanofi-Genzyme, Vifor Pharma, Boehringer Ingelheim, AstraZeneca, GSK, Sanifit, and Inozyme Pharma Inc.; honoraria from AstraZeneca, Menarini, Napp, CSL Vifor, GSK, Novartis, Bayer, Sanofi Genzyme, Chiesi, and Medscape; travel support from AstraZeneca, Novartis, and CSL Vifor; and is the National Clinical Director of Renal Medicine for NHS England.
- **LW** has received consulting fees from Traverre Therapeutics, Inc., Novartis, Chinook, and Goldfinch Bio; honoraria from Traverre Therapeutics, Inc., Novartis, and Otsuka; and has been part of advisory boards for Eledon Pharmaceuticals.
- **AH** and **MS** have no conflicts of interest.

- Sparsentan, a non-immunosuppressive novel dual endothelin and angiotensin receptor antagonist (DEARA), is approved in the US and the EU to treat adults with IgAN based on data from the Phase 3 PROTECT trial<sup>1-4</sup>



**Sparsentan targets glomerular injury and slows kidney function decline<sup>1,5</sup>**

**EFFECTS:**

Anti-inflammatory<sup>6-9\*</sup>

Anti-proliferative<sup>6,7,9\*</sup>

Anti-fibrotic<sup>8,9\*</sup>

Anti-proteinuric<sup>4</sup>

\*These effects are based on pre-clinical animal modeling data.

Ang II, angiotensin II; AT<sub>1</sub>R, angiotensin II type 1 receptor; ET-1, endothelin 1; ET<sub>A</sub>R, endothelin-1 type A receptor.

1. FILSPARI (sparsentan). Prescribing Information. September 2024. Travere Therapeutics, Inc. San Diego, CA, USA; 2. FILSPARI (sparsentan). European Medicines Agency (EMA). <https://www.ema.europa.eu/en/medicines/human/EPAR/filspari> (Accessed October 2, 2024); 3. Heerspink HJL, et al. *Lancet*. 2023;401(10388):1584-1594; 4. Rovin BH, et al. *Lancet*. 2023;402(10417):2077-2090; 5. Kohan DE, et al. *Clin Sci*. 2024;138:645-6625; 6. Jenkinson C, et al. Poster presented at: ISN World Congress of Nephrology; April 12-15, 2019; Melbourne, Australia. SAT-010; 7. Reily C, et al. *Am J Physiol Renal Physiol*. 2024;326:F862-F875; 8. Nagasawa H, et al. *Nephrol Dial Transplant*. 2024;39:1494-1503; 9. Jenkinson C, et al. Presentation at: International Symposium on IgANephropathy; September 27-29, 2018; Buenos Aires, Argentina.

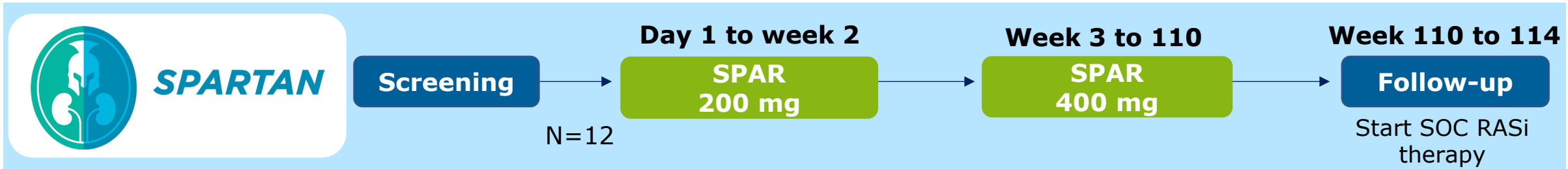
- In the PROTECT trial, sparsentan showed reduced proteinuria and long-term kidney function preservation in prevalent IgAN patients vs maximally titrated irbesartan<sup>1,2</sup>
- The effect in newly diagnosed, RASi-naive patients remains unknown
- SPARTAN (NCT04663204) is a Phase 2, open-label, single-arm, multicenter trial investigating the safety, efficacy, and mechanistic actions of sparsentan as first-line therapy in patients newly diagnosed with IgAN<sup>3</sup>

## Objective

- Here we report interim clinical findings over the first 24 weeks of treatment with sparsentan from SPARTAN

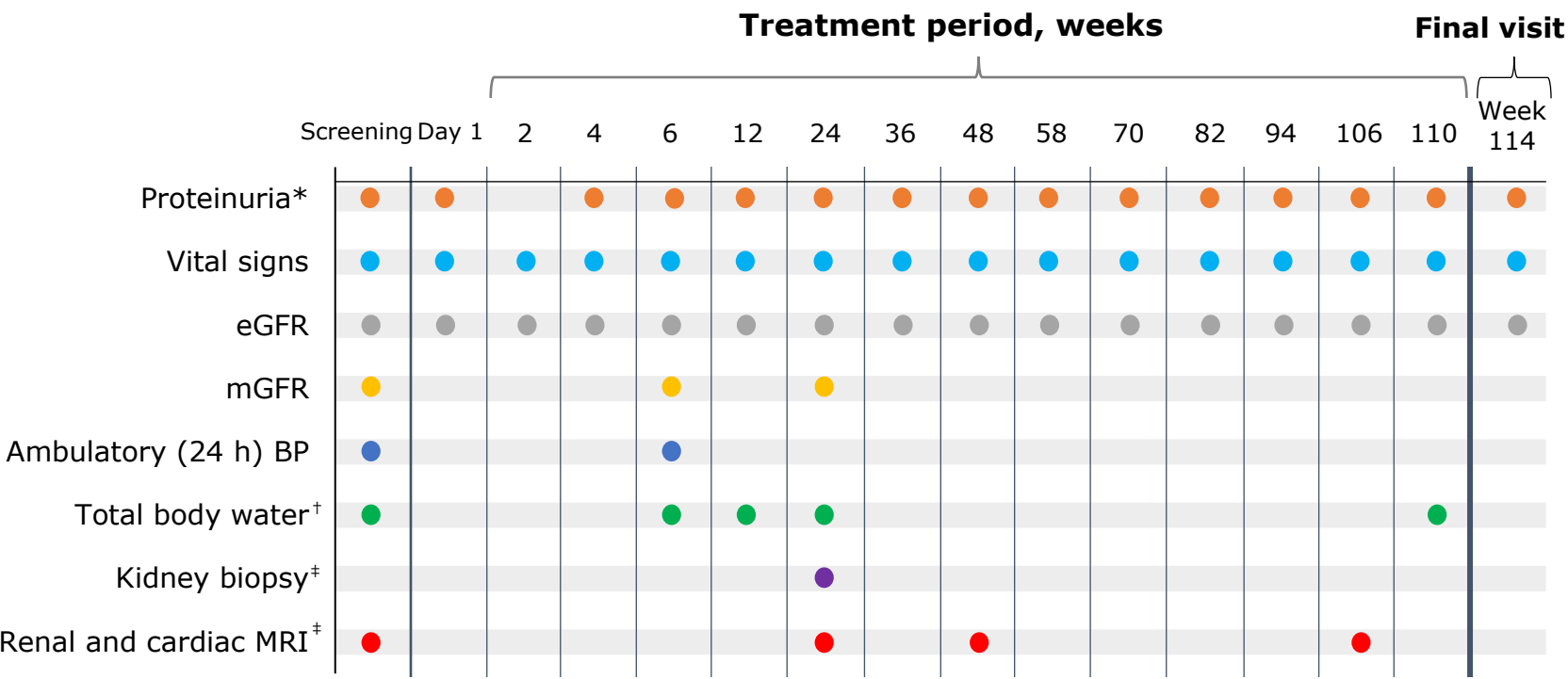
# SPARTAN Study Design (NCT04663204)

- The SPARTAN study is being conducted at 5 participating sites in the UK










- ### Key Eligibility Criteria
- Age  $\geq 18$  years
  - Biopsy-proven IgAN within  $\leq 6$  months
  - Proteinuria  $\geq 0.5$  g/day
  - eGFR  $\geq 30$  mL/min/1.73 m<sup>2</sup>
  - No ACEIs/ARBs within  $\leq 12$  months
  - No systemic IST within  $\leq 6$  months

- ### Key Endpoints
- Safety
  - Change in proteinuria from baseline
  - Complete remission of proteinuria ( $< 0.3$  g/day)
  - Change in GFR and BP from baseline



mGFR, measured glomerular filtration rate; SOC, standard of care; SPAR, sparsentan.  
 \*24-hour collection. <sup>†</sup>Measured by bioimpedance spectroscopy. <sup>‡</sup>For future analyses.

# Demographics and Baseline Characteristics of Patients in the SPARTAN vs PROTECT Trials

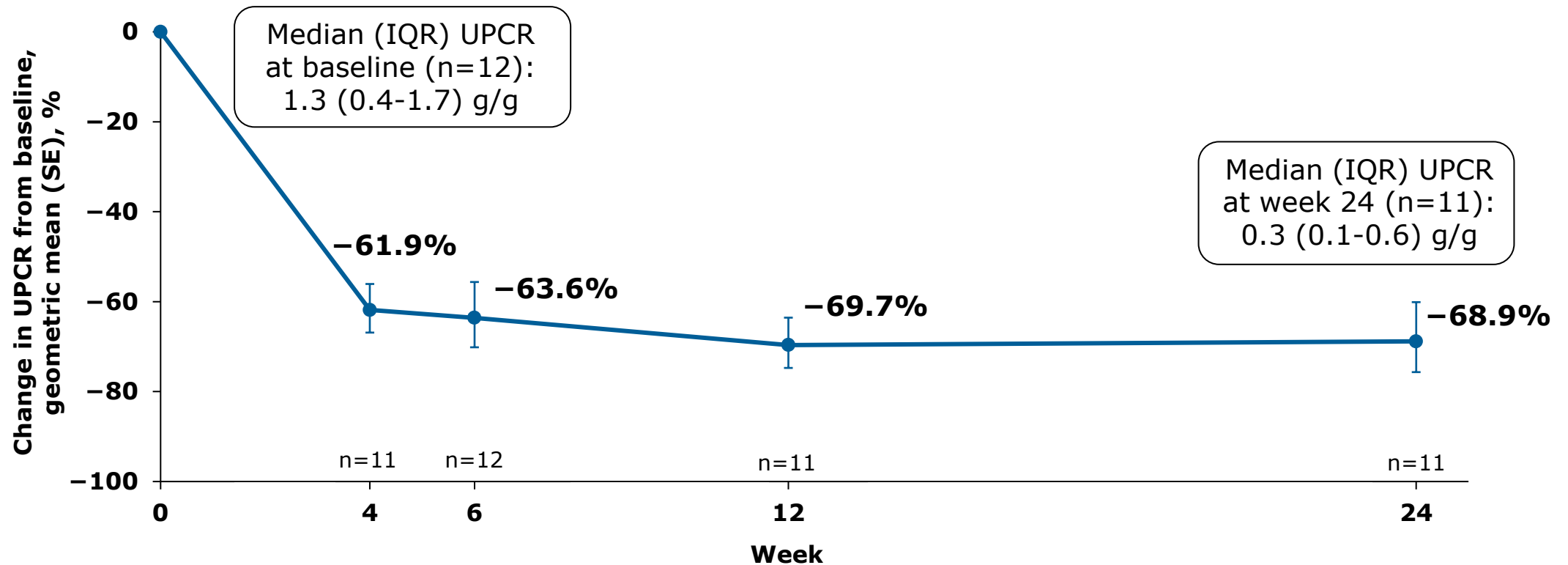
	SPARTAN (N=12)	PROTECT <sup>1,2</sup> (N=402)
 <b>RASi use, %</b>	0*	>99 <sup>†</sup>
<b>IST use, %</b>	0 <sup>‡</sup>	5 <sup>§</sup>
 <b>Time from initial kidney biopsy to informed consent, median (IQR), years</b>	0.25 (0.14-0.39) <sup>  </sup>	4.0 (1.0-10.0)
<b>Age at informed consent, mean (SD), years</b>	35.8 (12.2)	46.0 (12.44)
 <b>Male sex, %</b>	58	70
<b>White race, %</b>	83	67
 <b>UPE, median (IQR), g/day</b>	1.7 (0.6-3.3)	1.8 (1.3-2.8)
<b>UPCR, median (IQR), g/g</b>	1.3 (0.4-1.7)	1.2 (0.8-1.8)
 <b>eGFR, mean (SD), mL/min/1.73 m<sup>2</sup></b>	70.2 (25.0)	56.9 (24.0)
 <b>BP, mean (SD), mm Hg<sup>¶</sup></b>		
<b>Systolic</b>	125 (10)	129 (14)
<b>Diastolic</b>	78 (10)	82 (11)
 <b>Weight, mean (SD), kg</b>	83.1 (24.7)	84.4 (19.8)

\*Eligibility criteria for SPARTAN did not allow ACEIs/ARBs use within ≤12 months. †At screening. ‡Eligibility criteria for SPARTAN did not allow systemic IST within ≤6 months. §For renal indication. ||n=11. ¶Office BP.

1. Rovin BH, et al. *Lancet*. 2023;402(10417):2077-2090. 2. Data on file. Traverre Therapeutics, Inc.

## Proteinuria Change (UPCR) From Baseline\*

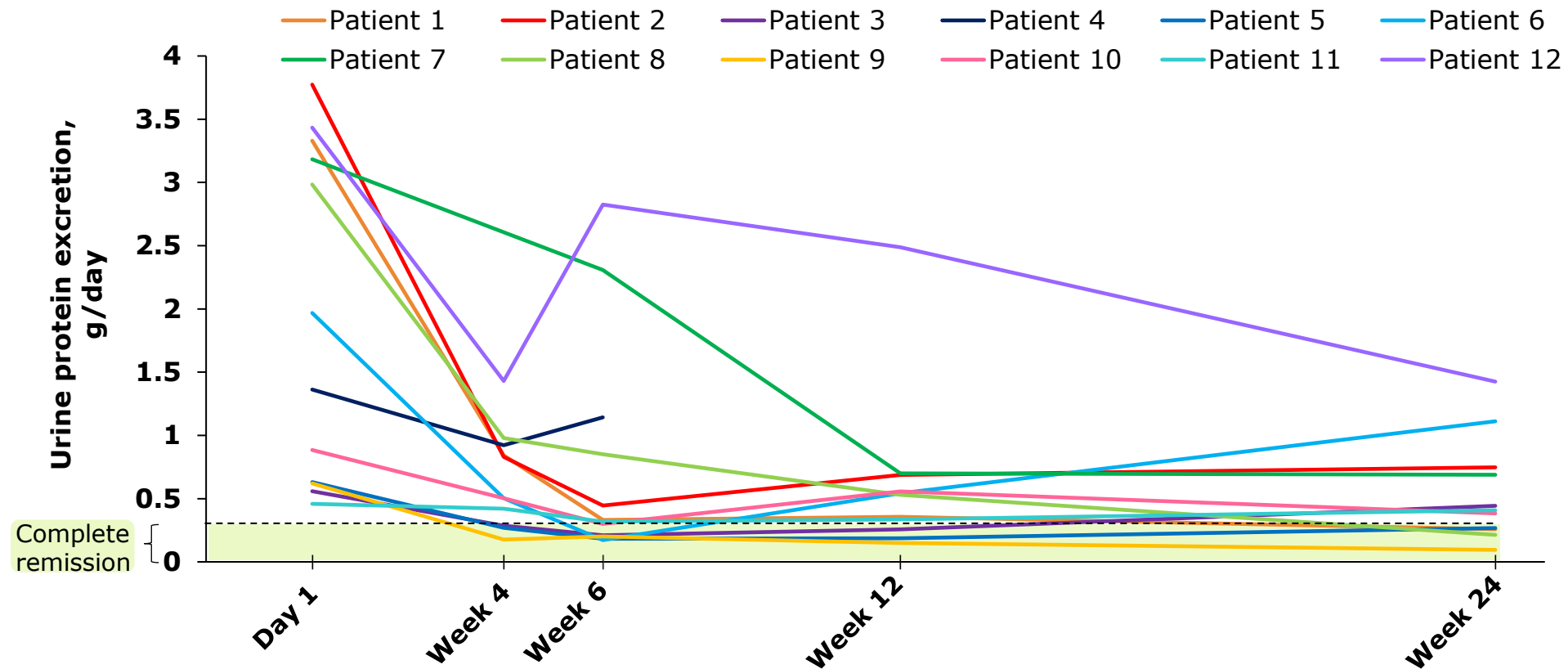
- Proteinuria reductions were rapid ( $\approx 60\%$  from baseline at week 4) and sustained over 24 weeks of sparsentan treatment



\*On-treatment analysis; 1 patient discontinued after week 6.

## Proteinuria Per Individual Patient\*

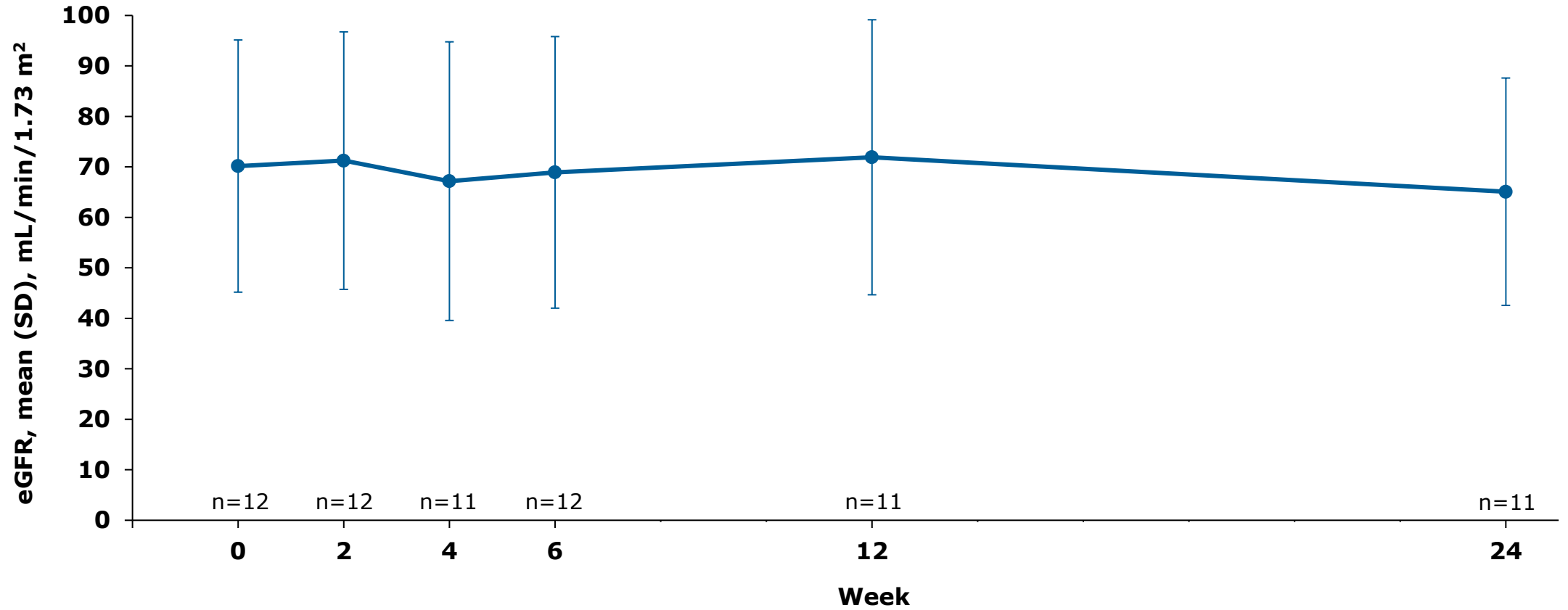
- Among the 5 patients with protein excretion of  $>2$  g/day at baseline, 4 had proteinuria reductions of  $\geq 75\%$  at any time during the first 24 weeks of treatment
- 58% of patients (7/12) achieved complete remission ( $<0.3$  g/day) at any time during the 24-week treatment period



\*On-treatment analysis; 1 patient discontinued after week 6.



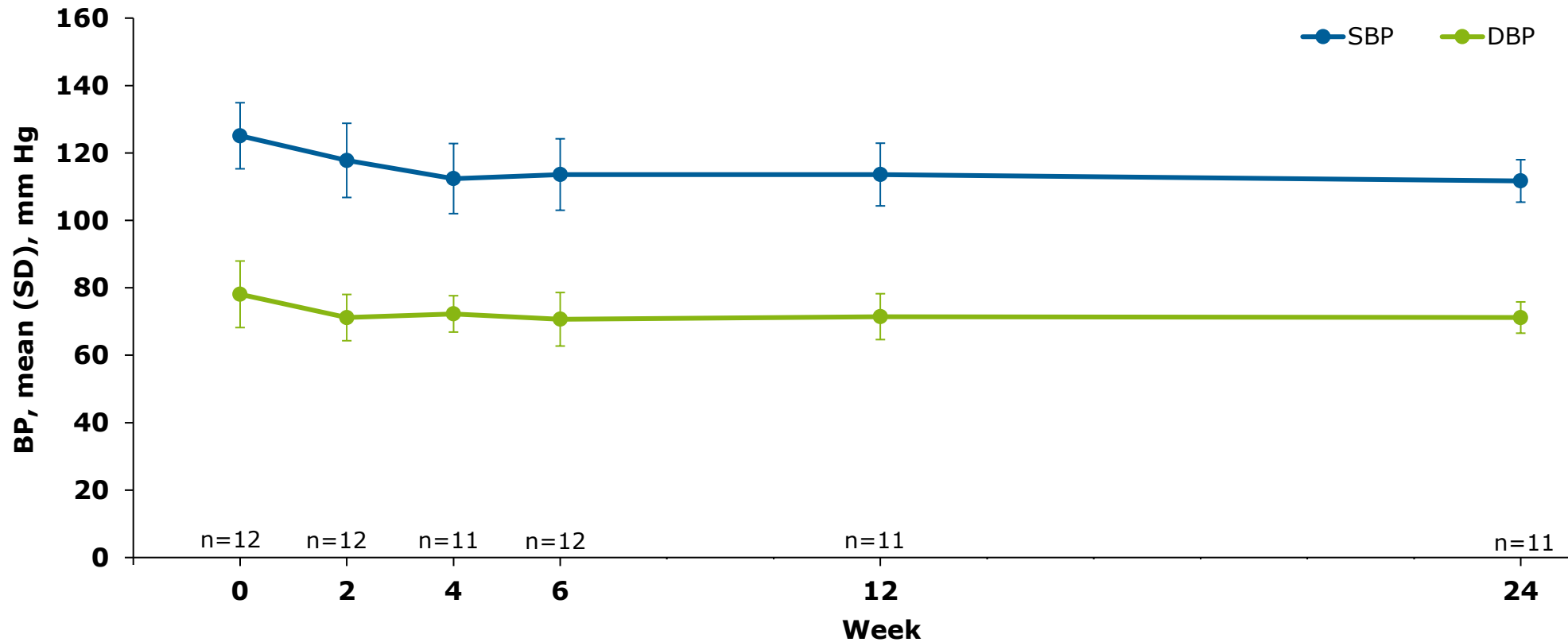
## Mean eGFR at Each Visit Over 24 Weeks\*



\*On-treatment analysis; 1 patient discontinued after week 6.

## Mean Office BP at Each Visit Over 24 Weeks\*

- After an initial slight decrease, BP remained stable during the rest of the treatment period as measured by office and ambulatory BP



DBP, diastolic blood pressure; SBP, systolic blood pressure.  
\*On-treatment analysis; 1 patient discontinued after week 6.

## Mean Weight and Total Body Water Change From Baseline\*

- There were no meaningful changes in body weight over 24 weeks
- Mean total body water change from baseline showed modest reductions during the treatment period

Mean (SD) change from baseline	Week				
	2	4	6	12	24
<b>n</b>	12	11	12	11	11
<b>Weight, kg</b>	-0.3 (0.7)	-0.2 (1.4)	0.3 (1.4)	0.1 (2.7)	-1.0 (3.3)
<b>Total body water, L<sup>†</sup></b>	-	-	-2.0 (7.2)	-2.0 (7.5)	-2.4 (7.4)

\*On-treatment analysis; 1 patient discontinued after week 6. <sup>†</sup>Measured by bioimpedance spectroscopy.

## Safety Over 24 Weeks of Treatment

- Sparsentan was generally well tolerated
- 1 patient permanently discontinued treatment due to hypotension after week 6

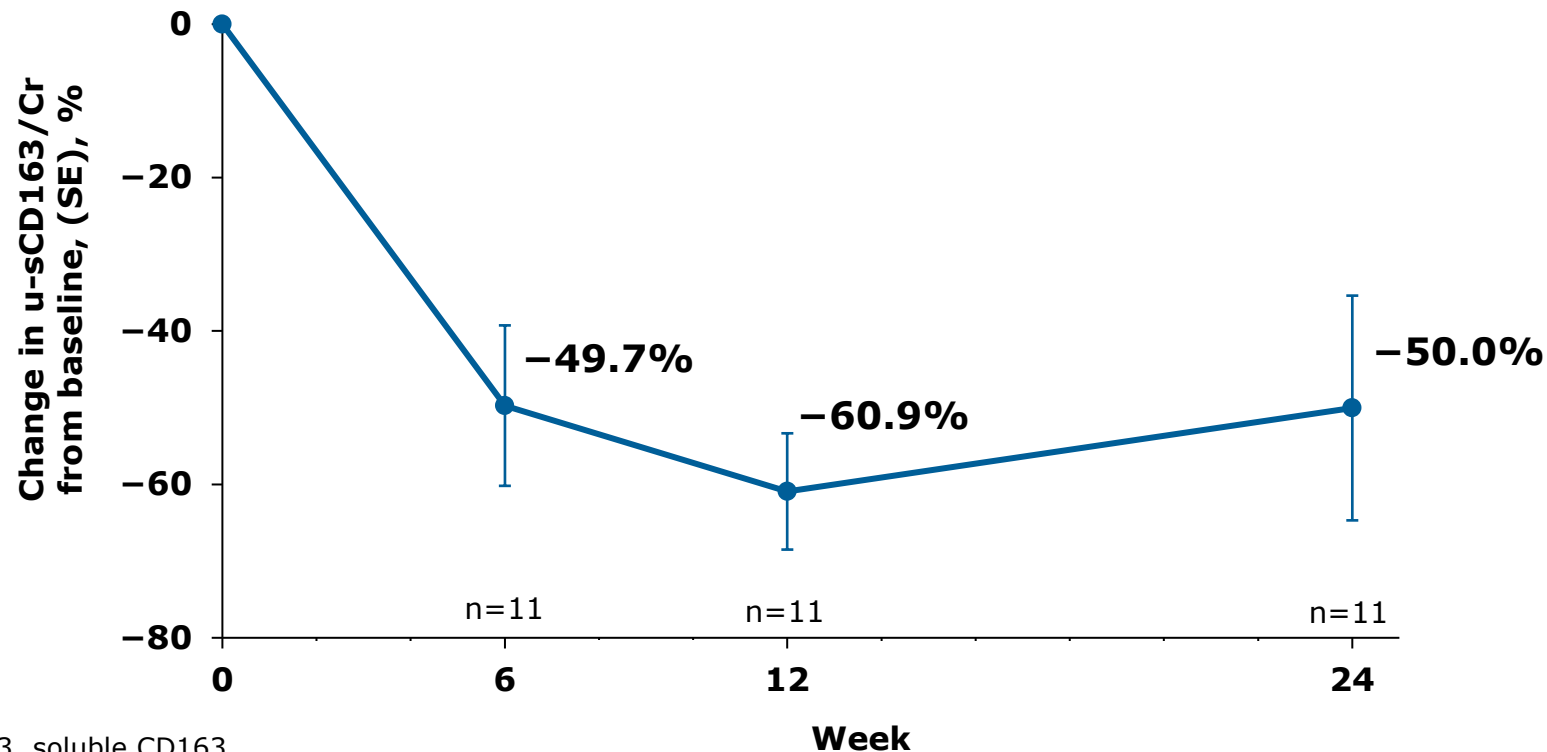
	Sparsentan (N=12)
	n (%)
<b>Any AE</b>	12 (100)
<b>Any serious AE*</b>	1 (8)
<b>Most common AEs (&gt;2 patients)</b>	
Dizziness	6 (50)
Urinary tract infection	3 (25)
Dyspepsia	3 (25)
Vomiting	3 (25)

AE, adverse event.

\*Serious AE was an abscess (limb).

## Urinary sCD163 Levels\*

- Urinary sCD163 (u-sCD163) is a marker for alternatively activated macrophages that has been correlated with kidney macrophage infiltration and active lesions in IgAN. In the TESTING study, a  $\geq 50\%$  reduction of u-sCD163 from baseline was associated with a reduced risk of the composite kidney end points<sup>1</sup>
- Rapid and sustained reduction of u-sCD163 was observed with sparsentan treatment

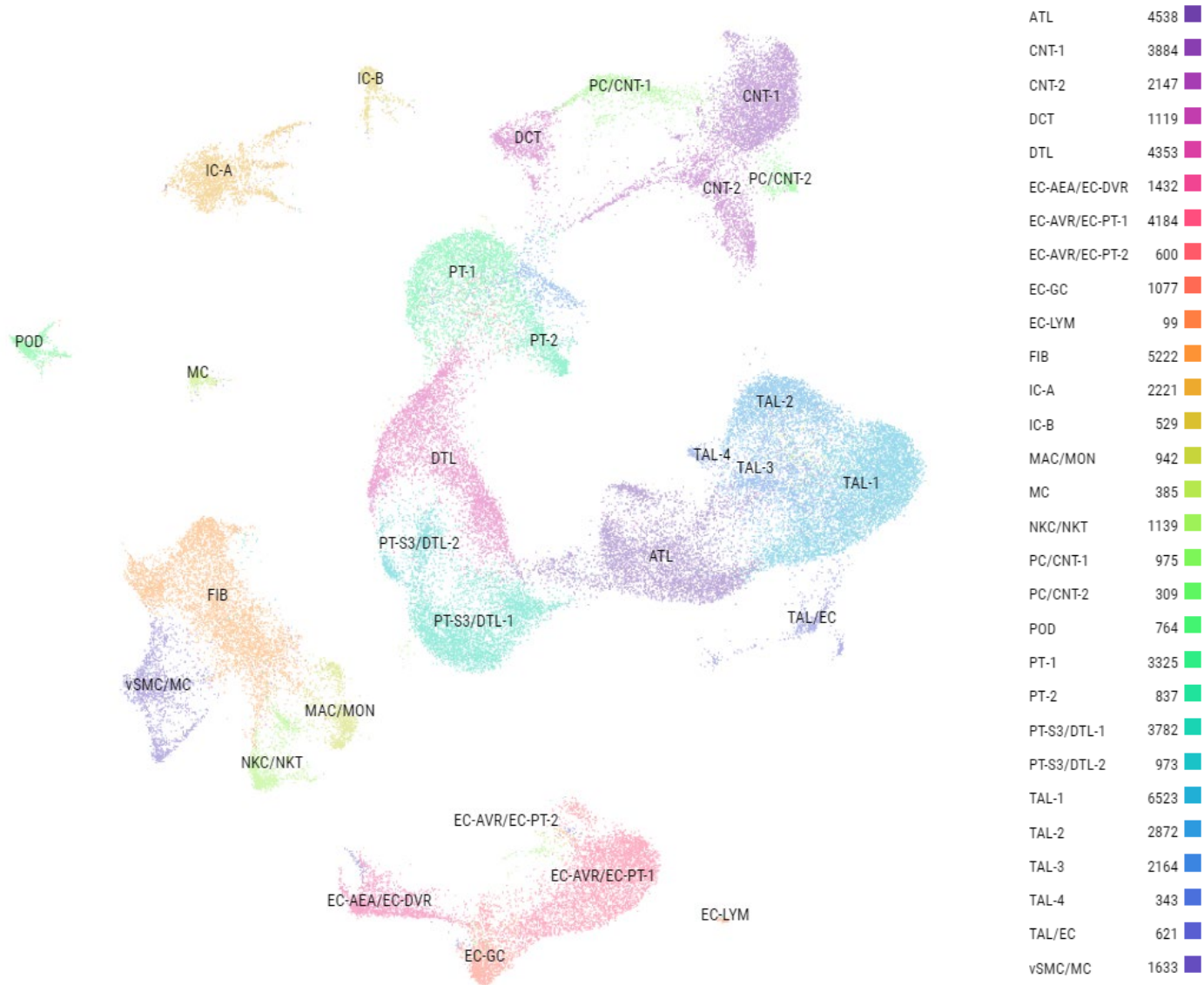


CR, creatinine; sCD163, soluble CD163.

\*1 patient discontinued after week 6 and has been excluded from analysis.

1. Li J, et al., *Kidney Int Rep.* 2024;9:3016-3026.

# Kidney Biopsy Single-Cell Nuclear RNA-seq Gene Expression Profile to Define the Impact of Sparsentan on Kidney Cell Populations



- These interim findings from the SPARTAN trial show that sparsentan, as a first-line treatment in patients with IgAN, led to rapid and sustained reductions in proteinuria (~70% from baseline)
- Within 24 weeks of starting sparsentan, ~60% of patients achieved complete remission of proteinuria, a treatment goal recommended in the draft 2024 KDIGO guidelines<sup>1</sup>
- Sparsentan was generally well tolerated over 24 weeks of treatment, with no evidence of fluid retention. Safety was consistent with the Phase 3 PROTECT study<sup>2,3</sup>
- Rapid reductions in urinary sCD163 were observed. The reduction in this biomarker is the first demonstration of sparsentan's anti-inflammatory effect in humans and supports preclinical data that also showed attenuation of immune and proinflammatory signaling with sparsentan<sup>4,5</sup>
- Further analysis of transcriptomics, kidney biopsies, and additional serum, plasma, and urinary biomarkers is planned to investigate the mechanistic actions of sparsentan and its potential nephroprotective effects

KDIGO, Kidney Disease: Improving Global Outcomes.

1. KDIGO Clinical Practice Guideline for the Management of Immunoglobulin A Nephropathy (IgAN) and Immunoglobulin A Vasculitis (IgAV). <https://kdigo.org/wp-content/uploads/2024/08/KDIGO-2024-IgAN-IgAV-Guideline-Public-Review-Draft.pdf> (accessed September 2024); 2. Heerspink HJL, et al. *Lancet*. 2023;401(10388):1584-1594; 3. Rovin BH, et al. *Lancet*. 2023;402(10417):2077-2090; 4. Nagasawa H, et al. *Nephrol Dial Transplant*. 2024;39:1494-1503; 5. Reily C, et al. *Am J Physiol Renal Physiol*. 2024;326:F862-F875.

- This study was funded by Traverre Therapeutics, Inc.
- Urinary biomarker analysis was provided by:
  - Nadia Nawaz and William Barratt, University of Leicester
- Transcriptomics analysis was provided by:
  - Professor Matthias Kretzler, University of Michigan
    - Francesca Annese, Brad Godfrey, Damian Fermin, Edgar Otto, Felix Eichinger, Phil McCown, Sean Eddy, Viji Nair (University of Michigan)
- Medical writing support was provided by Taryn Ralph, PhD, of Nucleus Global, an Inizio Company, in accordance with Good Publication Practice guidelines and was funded by Traverre Therapeutics, Inc.
- The authors thank all the patients, families, and investigators who made this study possible



# Questions?

