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Long-Term Efficacy and Safety of Sparsentan in FSGS: 240-Week Analysis of the DUET Open-Label Extension

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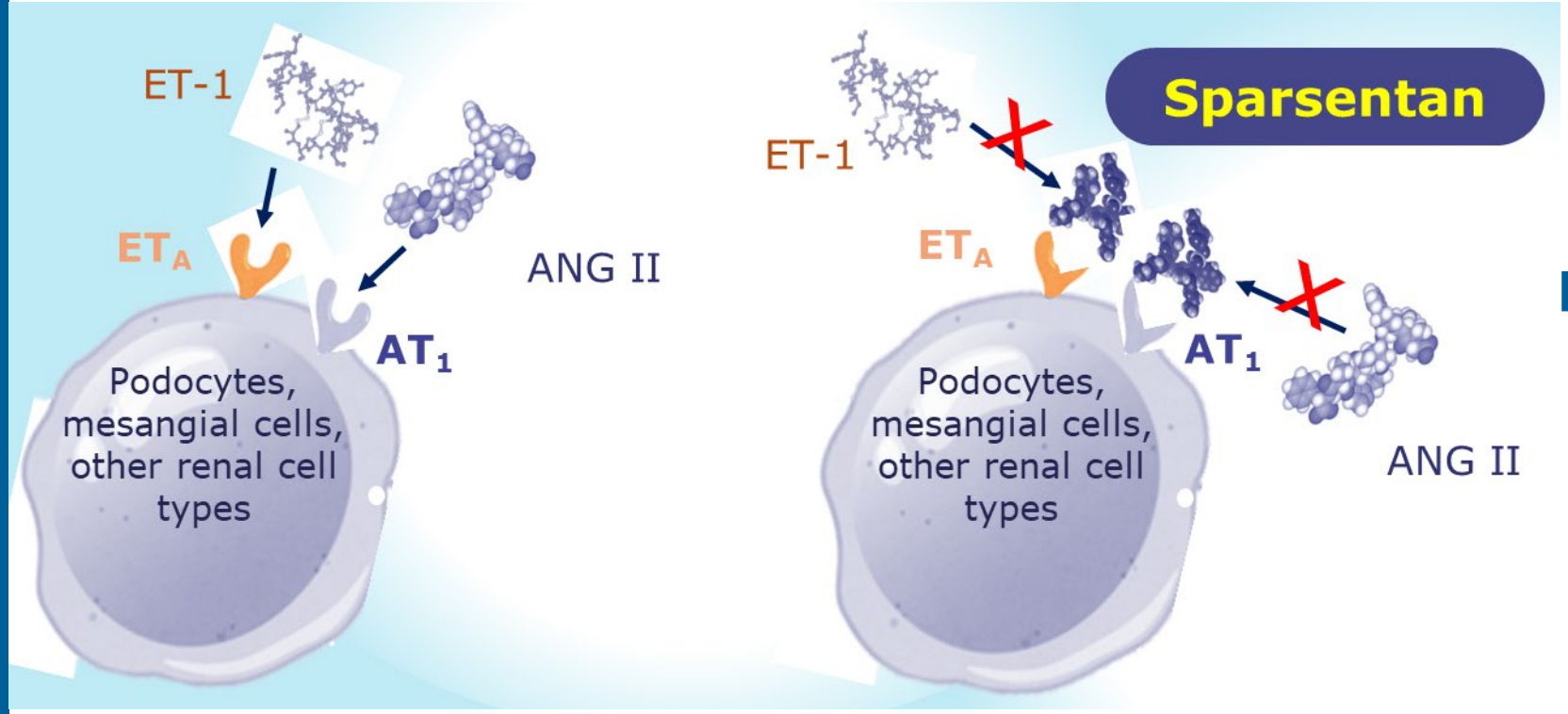
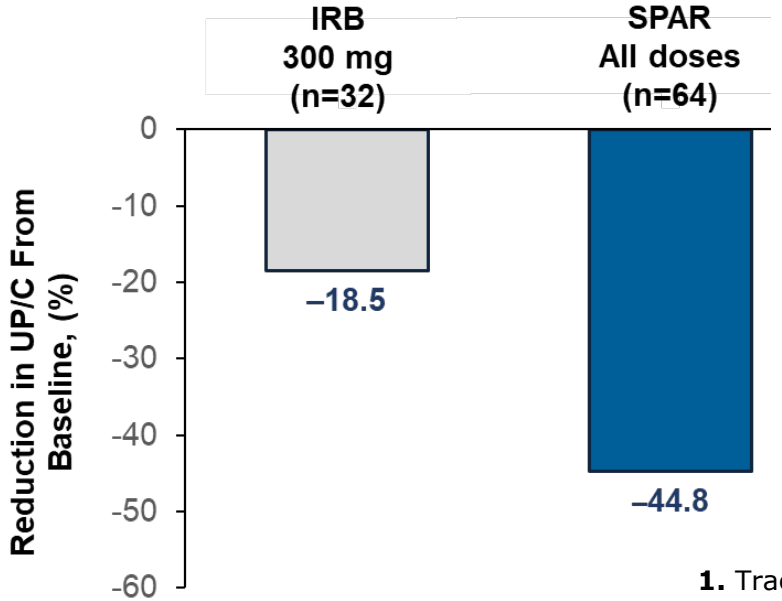
DISCLOSURES

- **TS** has received research funding from National Institutes of Health, Travere Therapeutics, Inc., Alexion, Mallinckrodt Pharmaceuticals, and Bristol Meyers Squibb.
- **VT** is a consultant to Travere Therapeutics, Inc., AbbVie, Amgen, Bayer, Boehringer-Ingelheim, ChemoCentryx, and Fresenius Medical Care.
- **KNC** is a consultant to Travere Therapeutics, Inc., Goldfinch, Calliditas, and has received grants and personal fees from Mallinckrodt.
- **MNR** is a site primary investigator for Travere Therapeutics, Inc., Advicenne, Reata, and Genentech and has received research funding from Goldfinch Bio, Novartis, NIDDK, and Department of Defense.
- **RK, EM** are employees of Travere Therapeutics, Inc. and may have an equity or other financial interest in Travere Therapeutics, Inc.
- **HT** is a consultant to and/or member of a data monitoring committee for Akebia, Chemocentryx, Goldfinch Bio, Inc., Natera, Otsuka, Travere Therapeutics, Inc., and Walden.
- **LG** is a consultant to Travere Therapeutics, Inc., AstraZeneca, GSK, Novartis, Estor, CSL Vifor, previously a consultant to Pharmadoc, Sandoz, Sanofi, Baxter, Mundipharma, Chinook, and has received grants from Abionyx and Sanofi.



Sparsentan Mechanism of Action[1,2]

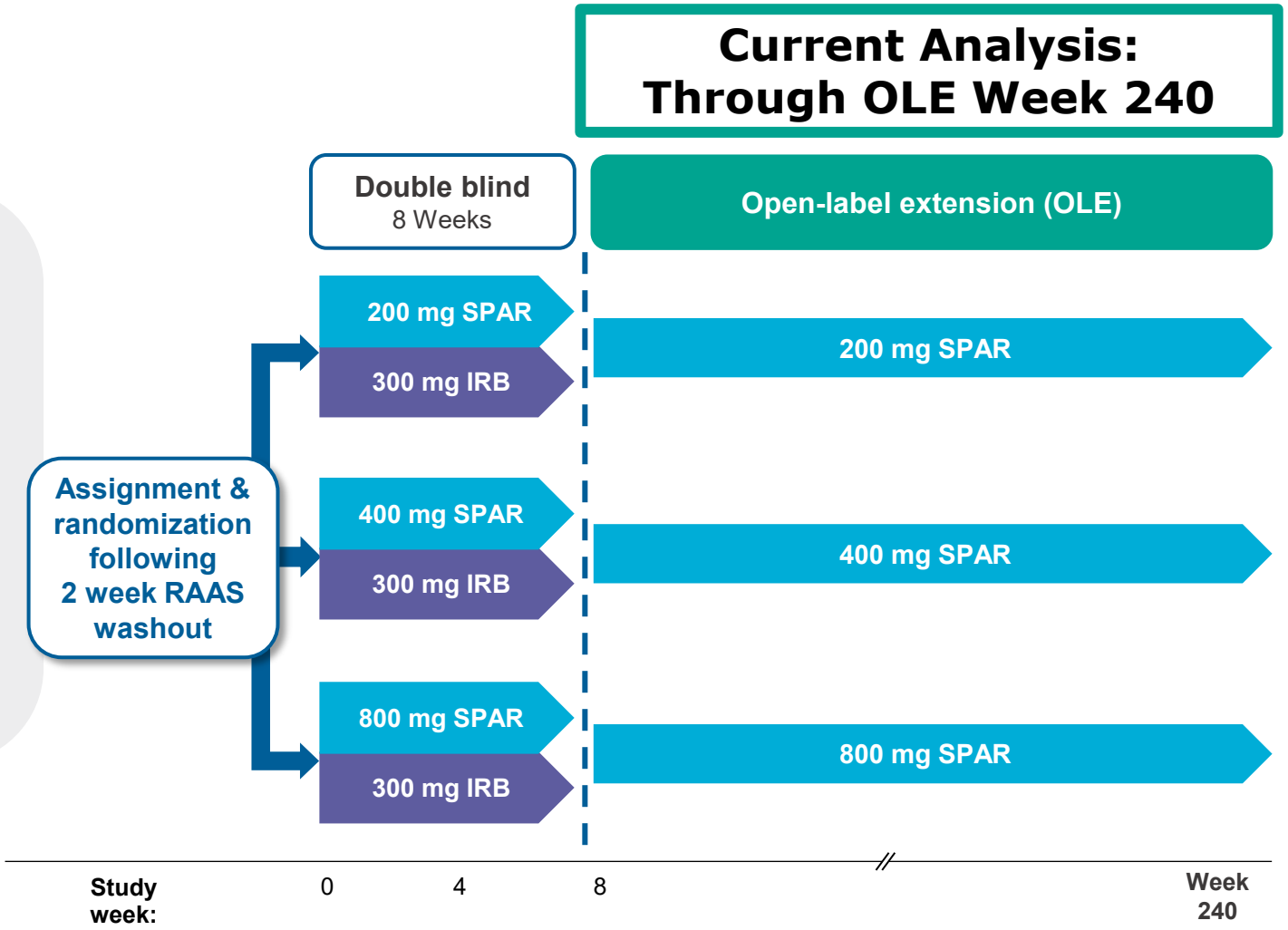


Phase 2 DUET Double-Blind Period Change in Proteinuria From Baseline[3]

1. Trachtman H, et al. *Drugs Future*. 2020;45:79; **2.** Kowala MC, et al. *J Pharmacol Exp Ther*. 2004;309:275-284; **3.** Trachtman H, et al. *J Am Soc Nephrol*. 2018;29:2745-54. IRB, irbesartan; SPAR, sparsentan.

Selection criteria

- Patients aged 8–75 (US) or 18–75 (EU) years
- Biopsy-proven FSGS or documented genetic mutation associated with FSGS; patients with secondary FSGS were excluded
- UP/C ≥1.0 g/g
- eGFR >30 mL/min/1.73 m^2



- All patients included from the first dose of sparsentan (N=108)
  - Baseline for SPAR:SPAR patients was Day 1
  - Baseline for IRB:SPAR patients was the first day of Week 8

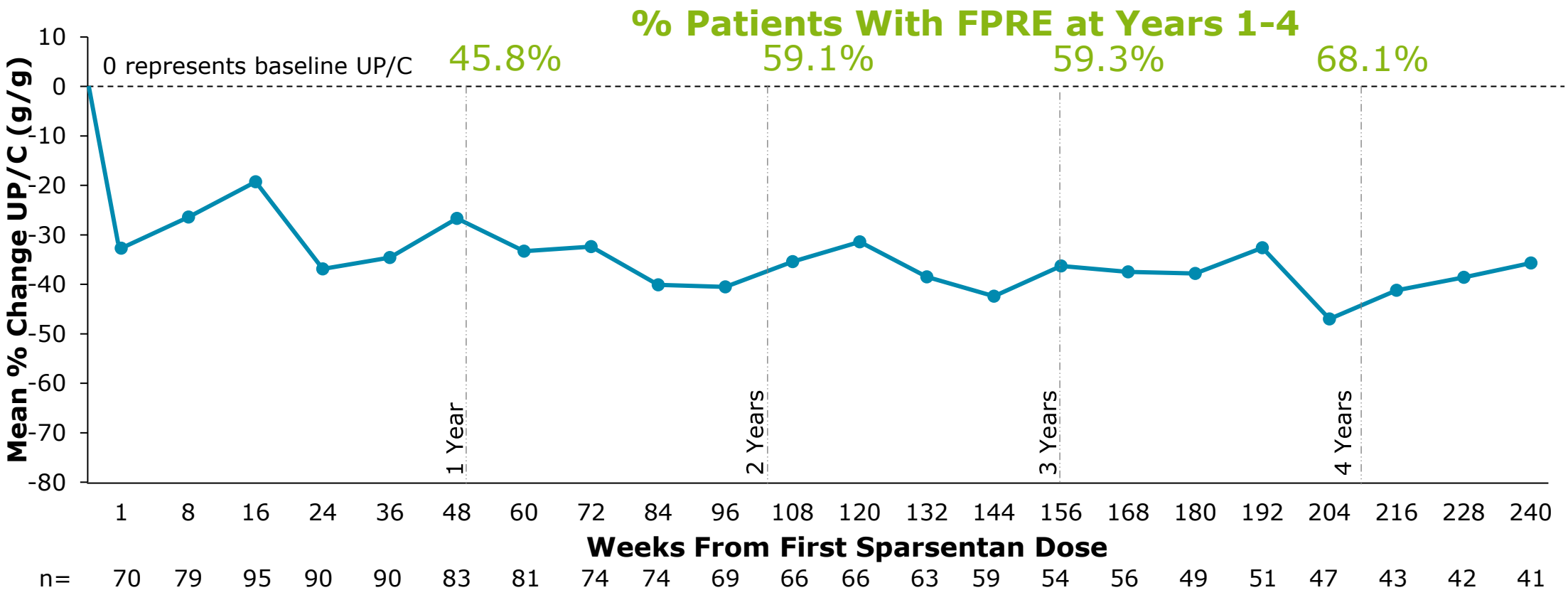
METHODS

Outcomes Examined in the Current 240-Week Analysis of the DUET OLE

- Proteinuria
  - UP/C mean percentage change from baseline at each study visit
  - Percentage of patients achieving FPRE (UP/C ≤1.5 g/g and >40% reduction in UP/C from baseline) at years 1-4
  - Percentage of patients achieving ≥1 complete remission of proteinuria (UP/C ≤0.3 g/g) at any time
- eGFR
- Blood pressure
- Most common TEAEs

FPRE, FSGS partial remission endpoint; UP/C, urine protein/creatinine ratio in a first morning urine sample.

Mean Percent Change From Baseline in UP/C by Visit

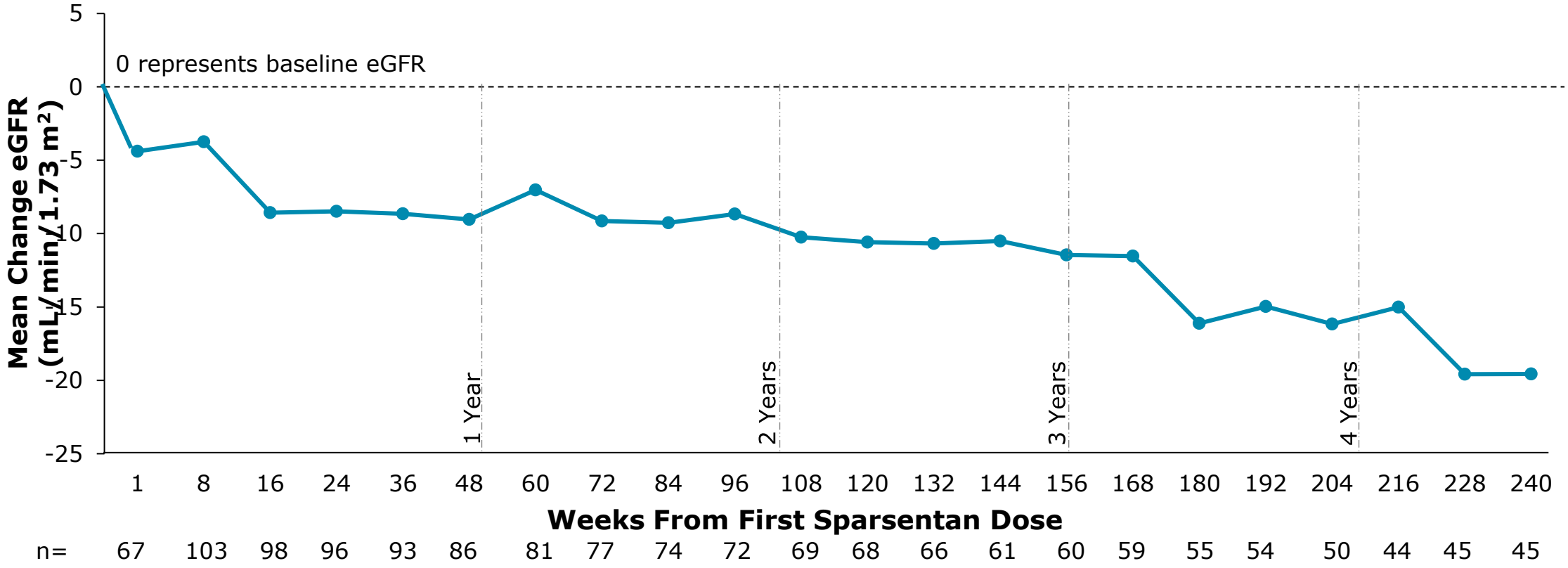


43% of patients experienced ≥1 complete remission of proteinuria at any time

Error bars show SE. Only on-treatment observations (defined as occurring within 1 day of last sparsentan dose) are included. FPRE (UP/C ≤1.5 g/g and >40% reduction in UP/C from baseline). FPRE, FSGS partial remission endpoint.

Mean Change From Baseline in eGFR by Visit

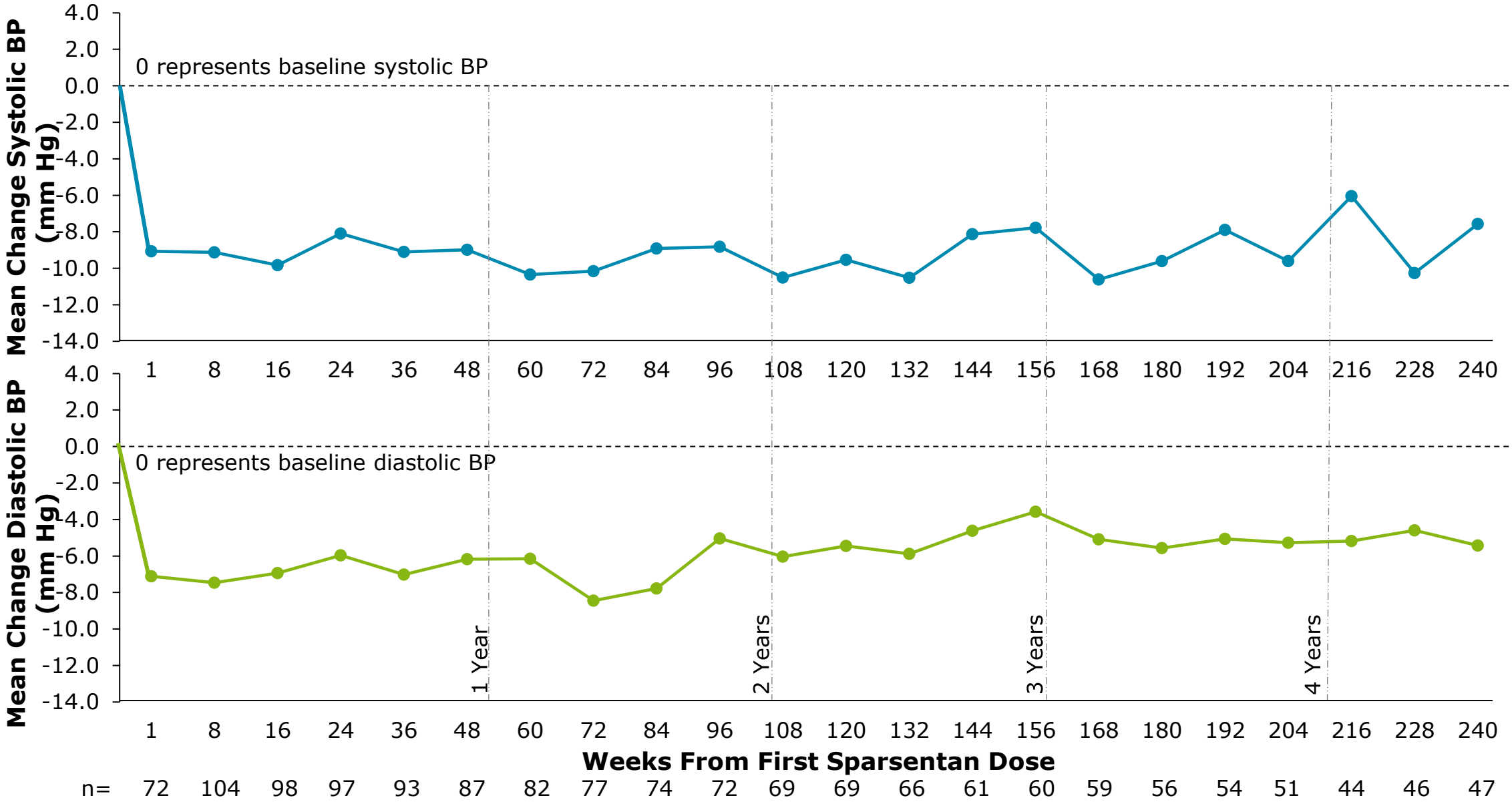
Chronic slope estimate through 108 weeks: -3.56 (95% CI: -5.6, -1.5) mL/min/1.73m^2/year
Chronic slope estimate all on-treatment data: -4.16 (95% CI: -5.8, -2.5) mL/min/1.73m^2/year



Error bars show SE. Only on-treatment observations (defined as occurring within 1 day of last sparsentan dose) are included. Chronic slope was assessed starting at Day 42 of starting sparsentan treatment. CI, confidence interval.

RESULTS

Mean Change From Baseline in Blood Pressure by Visit



Error bars show SE. Only on-treatment observations (defined as occurring within 1 day of last sparsentan dose) are included. BP, blood pressure.

RESULTS

Most Common TEAEs by Year and Cases Per 100 Patient-Years for Total Study Duration

	n (%) Within Each Year					Total Study Duration Cases Per 100 Patient-Years, Cases/100 Patient Years
	Year 0 to <1 n=108	Year 1 to <2 n=87	Year 2 to <3 n=72	Year 3 to <4 n=60	Year 4 to <5 n=54	
Headache	25 (23.1)	5 (5.7)	1 (1.4)	4 (6.7)	2 (3.7)	11.7
Edema peripheral	15 (13.9)	10 (11.5)	3 (4.2)	2 (3.3)	2 (3.7)	11.2
Upper respiratory tract infection	9 (8.3)	5 (5.7)	6 (8.3)	5 (8.3)	2 (3.7)	10.6
Hyperkalemia	7 (6.5)	9 (10.3)	3 (4.2)	6 (10.0)	6 (11.1)	10.4
Hypotension	17 (15.7)	6 (6.9)	3 (4.2)	2 (3.3)	1 (1.9)	9.3
Nausea	17 (15.7)	3 (3.4)	2 (2.8)	4 (6.7)	1 (1.9)	8.5
Hypertension	6 (5.6)	7 (8.0)	2 (2.8)	3 (5.0)	6 (11.1)	7.6
Vomiting	12 (11.1)	2 (2.3)	5 (6.9)	2 (3.3)	1 (1.9)	7.6
Diarrhea	14 (13.0)	3 (3.4)	3 (4.2)	1 (1.7)	4 (7.4)	7.1
Dizziness	14 (13.0)	3 (3.4)	1 (1.4)	2 (3.3)	0	6.3
Blood creatinine increased	11 (10.2)	1 (1.1)	4 (5.6)	0	1 (1.9)	5.5
Blood creatine phosphokinase increased	8 (7.4)	2 (2.3)	0	3 (5.0)	2 (3.7)	4.9
Anemia	11 (10.2)	1 (1.1)	0	2 (3.3)	1 (1.9)	4.1

Reasons for Discontinuation by Year

Reason for Discontinuation	n (%) of 108 Patients Each Year				
	Year 0 to <1 n=108	Year 1 to <2 n=87	Year 2 to <3 n=72	Year 3 to <4 n=60	Year 4 to <5 n=54
Ongoing	85 (78.7)	72 (66.7)	60 (55.6)	54 (50.0)	47 (43.5)
Discontinued	23 (21.3)	13 (12.0)	12 (11.1)	6 (5.6)	7 (6.5)
Adverse event	10 (9.3)	2 (1.9)	2 (1.9)	3 (2.8)	3 (2.8)
Lost to follow-up	3 (2.8)	1 (0.9)	0	0	0
Other	2 (1.9)	2 (1.9)	0	0	0
Physician decision	2 (1.9)	2 (1.9)	5 (4.6)	1 (0.9)	0
Pregnancy	2 (1.9)	1 (0.9)	0	1 (0.9)	0
Protocol deviation	1 (0.9)	0	1 (0.9)	0	0
Withdrawal by subject	3 (2.8)	5 (4.6)	3 (2.8)	1 (0.9)	2 (1.9)
Noncompliance with study drug	0	0	1 (0.9)	0	1 (0.9)
Missing	0	0	0	0	1 (0.9)

- Median years to treatment discontinuation was 3.9
- The most common TEAEs that led to discontinuation (≥2 patients over total study duration) were glomerular filtration rate decreased (5), blood creatinine increased (3), pregnancy (3), acute kidney injury (2), and hepatic enzyme increased (2)

CONCLUSIONS

- This post hoc analysis of the DUET OLE through 240 weeks of treatment supports the long-term nephroprotective potential and safety of sparsentan in FSGS
- Sustained proteinuria reduction was observed over 240 weeks in patients who continued sparsentan treatment
- No new or unexpected TEAEs were observed with long-term sparsentan treatment
- The ongoing phase 3 DUPLEX study is evaluating the long-term antiproteinuric efficacy, nephroprotective potential, and safety of sparsentan versus irbesartan in adult and pediatric patients with FSGS over a double-blind period of 112 weeks followed by an OLE up to 156 weeks

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Questions?

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Demographics and Disease Characteristics at Baseline

	All Sparsentan (N=108)
Age, years, mean±SD/ median (min, max)	36.9±16.5 / 39.0 (8, 71)
Age <18 years, n (%)	18 (16.7)
Female, n (%)	48 (44.4)
Race, n (%)	
White	82 (75.9)
Black or African American	15 (13.9)
Asian	6 (5.6)
Other	5 (4.6)
Systolic / diastolic blood pressure, mmHg, mean±SD	129.0±12.4 / 81.6±8.8
UP/C, g/g, mean±SD / median (min, max)	3.8±3.1 / 2.9 (0.3, 14.0)
Nephrotic range proteinuria, (≥3.5 g/g), n (%)	52 (48.1)
eGFR, mL/min/1.73m^2, mean±SD / median (min, max)	74.4±39.9 / 69.4 (28, 212)
Any immunosuppressive treatment for renal indications at baseline, n (%)	35 (32.4)

eGFR, estimated glomerular filtration rate; UP/C, urine protein/creatinine ratio.

RESULTS

Most Common Treatment Related TEAEs by Year and Cases Per 100 Patient-Years for Total Study Duration

	n (%) Within Each Year					Total Study Duration Cases Per 100 Patient-Years (Cases/100 Patient Years)
	Year 0 to <1 n=108	Year 1 to <2 n=87	Year 2 to <3 n=72	Year 3 to <4 n=60	Year 4 to <5 n=54	
Hyperkalemia	6 (5.6)	8 (9.2)	3 (4.2)	5 (8.3)	5 (9.3)	9.3
Hypotension	14 (13.0)	5 (5.7)	2 (2.8)	2 (3.3)	1 (1.9)	7.9
Dizziness	10 (9.3)	3 (3.4)	0	1 (1.7)	0	4.1
Headache	11 (10.2)	1 (1.1)	0	0	0	3.8
Nausea	8 (7.4)	0	1 (1.4)	1 (1.7)	0	3.5
Blood creatinine increased	6 (5.6)	0	3 (4.2)	0	1 (1.9)	3.0
Edema peripheral	5 (4.6)	2 (2.3)	1 (1.4)	0	0	2.5
Glomerular filtration rate decreased	3 (2.8)	2 (2.3)	0	1 (1.7)	2 (3.7)	2.5
Vomiting	6 (5.6)	0	0	1 (1.7)	0	2.5
Anemia	6 (5.6)	0	0	1 (1.7)	0	1.9
Blood creatine phosphokinase increased	3 (2.8)	0	0	1 (1.7)	2 (3.7)	1.9
Acute kidney injury	2 (1.9)	1 (1.1)	1 (1.4)	0	1 (1.9)	1.6
Orthostatic hypotension	4 (3.7)	0	0	0	0	1.1

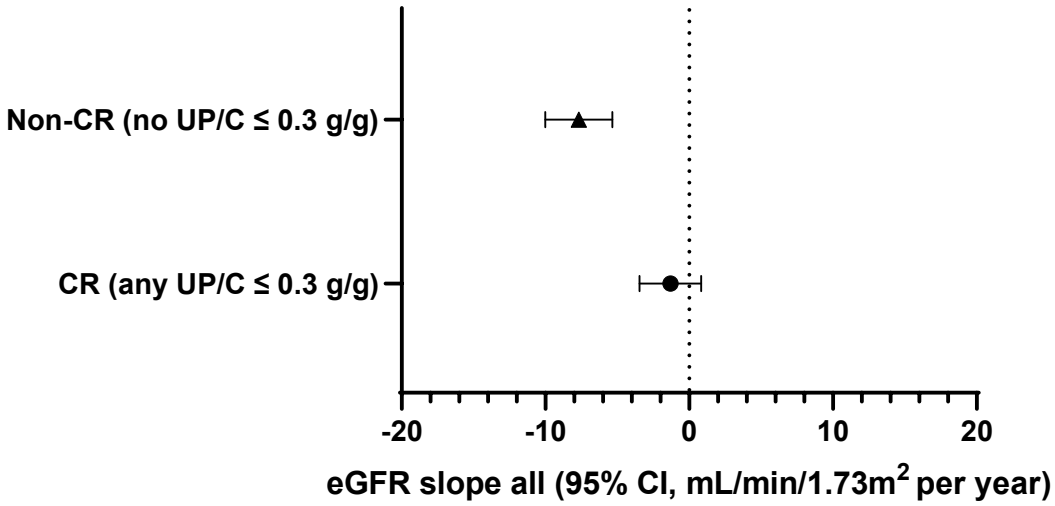
Serious TEAEs in ≥2 Patients by Year and Cases Per 100 Patient-Years for Total Study Duration

	n (%) Within Each Year					Total Study Duration Cases Per 100 Patient-Years (Cases/100 Patient Years)
	Year 0 to <1 n=108	Year 1 to <2 n=87	Year 2 to <3 n=72	Year 3 to <4 n=60	Year 4 to <5 n=54	
Acute kidney injury	2 (1.8)	3 (3.4)	0	0	2 (3.7)	1.9
Chest pain	1 (0.9)	1 (1.1)	1 (1.4)	1 (1.7)	0	1.1
Syncope	2 (1.8)	0	0	1 (1.7)	0	0.8
Atrial fibrillation	0	0	1 (1.4)	1 (1.7)	0	0.5
Coronavirus test positive	0	0	0	0	2 (3.7)	0.5
Fluid overload	1 (0.9)	0	0	0	1 (1.9)	0.5
Hyperkalemia	1 (0.9)	1 (1.1)	0	0	0	0.5
Pneumonia	1 (0.9)	1 (1.1)	0	0	0	0.5

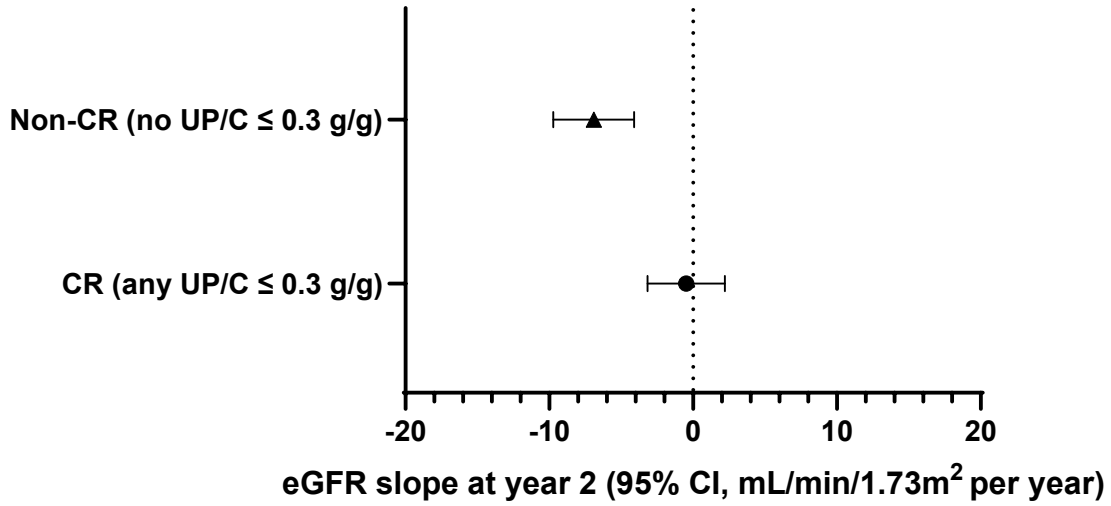
- There were no deaths and no kidney deaths while patients were receiving sparsentan

eGFR Chronic Slope in Patients With ≥1 Complete Remission

All On-Treatment Chronic Slope



2-Year Chronic Slope



Chronic slope estimate all on-treatment data: CR -1.31 vs non-CR -7.68 mL/min/1.73m^2/year
Chronic slope estimate at 2 years: CR -0.47 vs non-CR -6.90 mL/min/1.73m^2/year

CR, complete remission.