Supplementary Materials

Supplementary Tables

Supplementary Table S1. Percentage change in UP/C from baseline by CR vs non-CR groups

Weeks	**CR (any UP/C ≤ 0.3 g/g) (*n* = 46) % (95% CI)**	**Non-CR (no UP/C ≤ 0.3 g/g) (*n* = 62) % (95% CI)**	***P* value**
1	-63.1 (-74.2, -47.1)	-12.6 (-35.7, 18.8)	<0.001
4	-57.1 (-69.1, -40.5)	-11.3 (-33.0, 17.4)	0.001
8	-58.1 (-69.2, -43.0)	-13.7 (-34.1, 13.0)	<0.001
16	-68.4 (-76.4, -57.5)	-8.4 (-29.5, 19.0)	<0.001
24	-75.5 (-81.8, -67.0)	-22.0 (-40.3, 1.8)	<0.001
36	-76.6 (-82.6, -68.6)	-16.3 (-36.2, 9.9)	<0.001
48	-76.5 (-82.5, -68.4)	-22.5 (-41.4, 2.5)	<0.001
60	-78.7 (-84.2, -71.4)	-12.0 (-34.2, 17.8)	<0.001
72	-80.1 (-85.2, -73.1)	-20.2 (-41.4, 8.7)	<0.001
84	-81.6 (-86.4, -75.2)	-18.4 (-41.1, 13.2)	<0.001
96	-80.4 (-85.5, -73.5)	-21.5 (-44.0, 10.0)	<0.001
108	-81.1 (-86.0, -74.3)	-21.6 (-44.5, 10.6)	<0.001
120	-79.0 (-84.6, -71.3)	-13.8 (-39.4, 22.6)	<0.001
132	-81.0 (-86.1, -74.1)	-10.1 (-37.3, 28.9)	<0.001
144	-82.7 (-87.4, -76.2)	-13.8 (-40.6, 25.0)	<0.001
156	-82.1 (-87.0, -75.4)	-13.5 (-42.2, 29.4)	<0.001
168	-84.8 (-89.1, -79.0)	-4.0 (-35.8, 43.4)	<0.001
180	-82.3 (-87.3, -75.3)	-11.8 (-42.5, 35.2)	<0.001
192	-83.1 (-87.9, -76.4)	-19.8 (-48.0, 23.9)	<0.001
204	-87.6 (-91.2, -82.6)	-18.0 (-47.6, 28.2)	<0.001

216	-84.2 (-88.8, -77.6)	-12.0 (-45.0, 40.7)	<0.001
228	-83.5 (-88.4, -76.6)	-25.2 (-53.0, 19.1)	<0.001
240	-82.8 (-88.0, -75.4)	-5.9 (-42.0, 52.7)	<0.001
252	-85.1 (-89.7, -78.5)	-28.8 (-58.8, 22.8)	<0.001
264	-87.7 (-91.9, -81.4)	-28.5 (-62.2, 35.1)	<0.001
276	-84.1 (-90.0, -74.8)	-18.8 (-61.5, 71.5)	<0.001
288	-87.0 (-92.1, -78.4)	-50.3 (-75.5, 0.8)	0.003
300	-90.1 (-95.9, -76.1)	-34.5 (-70.1, 43.6)	0.002
312	-94.5 (-97.5, -87.9)	25.3 (-59.0, 282.6)	<0.001

Percent change (95% CI) of UP/C from baseline by CR vs non-CR groups was analyzed using MMRM.

Supplementary Table S2. KRT, ESKD, and reduction in eGFR in CR and non-CR patients

Endpoint, n (%)	**CR** **(any UP/C ≤ 0.3 g/g)** **(*n* = 46)**	**Non-CR** **(no UP/C ≤ 0.3 g/g)** **(*n* = 62)**
KRT	1 (2.2)	3 (4.8)
ESKD	2 (4.3)	8 (12.9)
KRT or ESKD	3 (6.5)	9 (14.5)
Confirmed 40% reduction in eGFR	10 (21.7)	22 (35.5)
KRT, ESKD, or confirmed 40% reduction in eGFR	10 (21.7)	23 (37.1)

eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; KRT, kidney replacement therapy.

Supplementary Table S3. TEAEs in ≥10% of patients in either the CR or non-CR groups

TEAEs, n (%)	**CR (any UP/C ≤ 0.3 g/g) (*n* = 46)**	**Non-CR (no UP/C ≤ 0.3 g/g) (*n* = 62)**
Any TEAE	43 (93)	59 (95)
Headache	15 (33)	17 (27)
Edema peripheral	13 (28)	14 (23)
Hyperkalemia	13 (28)	8 (13)
Hypotension	12 (26)	10 (16)
Nausea	10 (22)	11 (18)
Diarrhea	9 (20)	12 (19)
Proteinuria	9 (20)	4 (6)
Blood creatinine increased	8 (17)	7 (11)
Upper respiratory tract infection	8 (17)	7 (11)
Metabolic acidosis	8 (17)	1 (2)
Pyrexia	7 (15)	9 (15)
Blood creatinine phosphokinase increased	7 (15)	7 (11)
Back pain	7 (15)	5 (8)
Anemia	6 (13)	9 (15)
Oropharyngeal pain	6 (13)	5 (8)
Gout	6 (13)	4 (6)

Pain in extremity	6 (13)	4 (6)
Chest pain	6 (13)	3 (5)
Hypertension	5 (11)	13 (21)
Vomiting	5 (11)	12 (19)
Dizziness	5 (11)	11 (18)
Cough	5 (11)	7 (11)
Nasopharyngitis	5 (11)	6 (10)
Nasal congestion	5 (11)	5 (8)
Influenza	5 (11)	3 (5)
Hemoglobin decreased	5 (11)	1 (2)
Pneumonia	5 (11)	0
Arthralgia	4 (9)	7 (11)
Muscle spasms	4 (9)	6 (10)
Acute kidney injury	3 (7)	8 (13)
Fatigue	3 (7)	7 (11)
Urinary tract infection	3 (7)	7 (11)
Glomerular filtration rate decreased	1 (2)	10 (16)

TEAEs indicating acute kidney injury include the preferred terms blood creatinine increases, acute kidney injury, and glomerular filtration rate decreased. TEAEs indicating fluid retention include the preferred terms oedema peripheral, oedema fluid overload, joint effusion, joint swelling, and pleural effusion. TEAE, treatment-emergent adverse event.

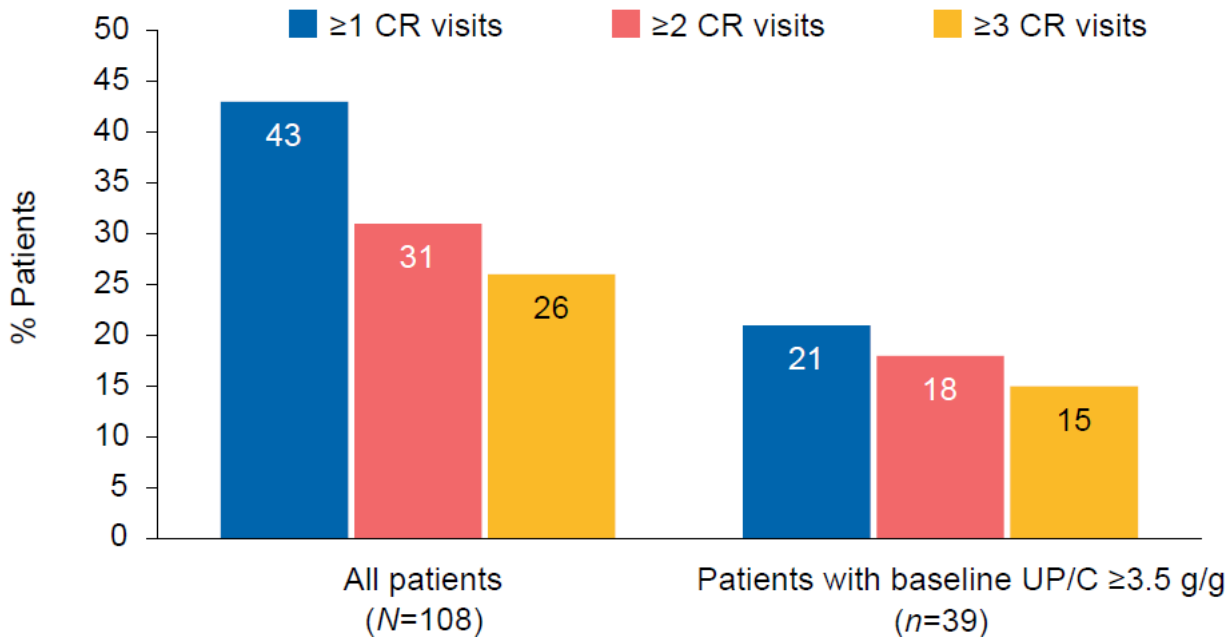
Supplementary Table S4. SAEs by CR and non-CR patients

SAE, n (%)	**CR (any UP/C ≤ 0.3 g/g) (*n* = 46)**	**Non-CR (no UP/C ≤ 0.3 g/g) (*n* = 62)**
Any SAE	18 (39)	16 (26)
Chest pain	4 (9)	0
Acute kidney injury	3 (7)	4 (6)
Pneumonia	3 (7)	0
Atrial fibrillation	2 (4)	0
Coronavirus test positive	2 (4)	0
Syncope	1 (2)	2 (3)
Fluid overload	1 (2)	1 (2)
Hyperkalemia	1 (2)	1 (2)

SAE, serious adverse event.

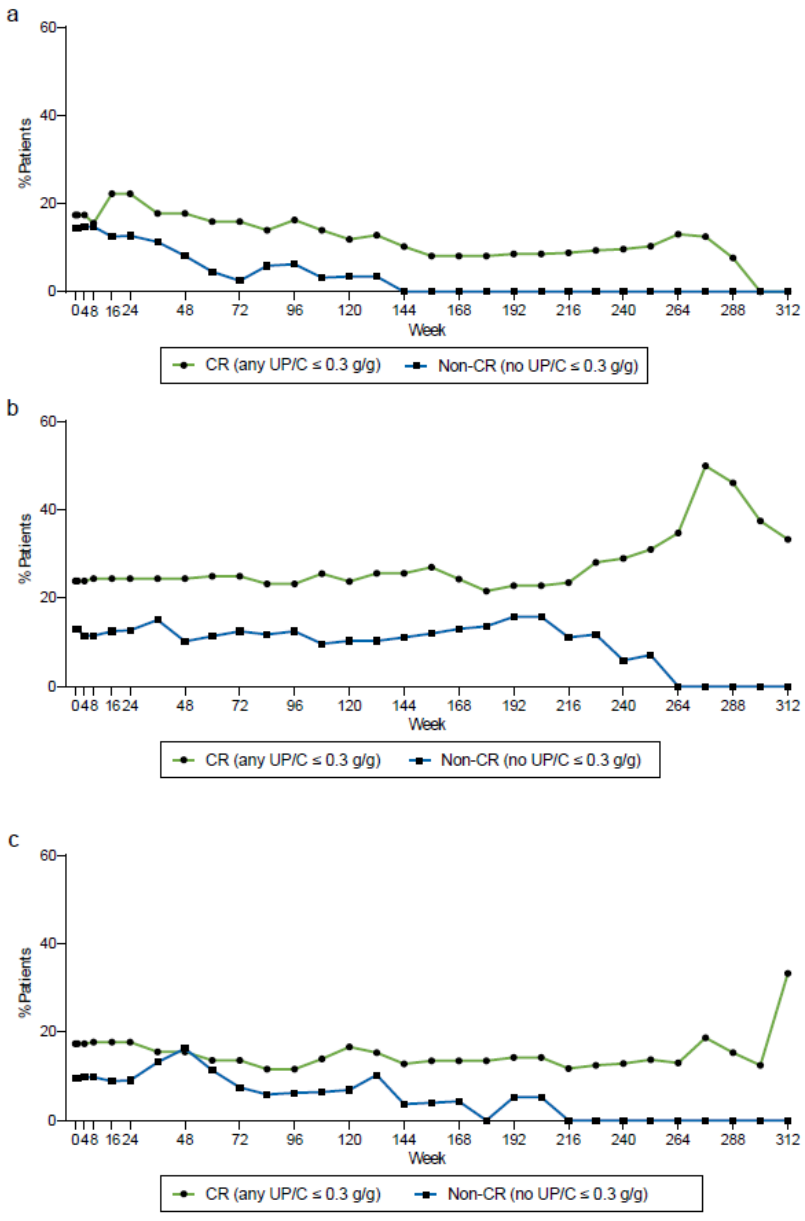
Supplementary Figures

Supplementary Figure S1. Percentage of patients with ≥1, ≥2, or ≥3 CRs in (a) all patients and (b) patients with nephrotic-range proteinuria at baseline.



CR, complete remission.

Supplementary Figure S2. Percentage of patients receiving individual classes of renal-related IST by visit among CR vs non-CR patients for (a) steroids; (b) CNI; and (c) MMF, azathioprine, and other.



CNI, calcineurin inhibitor; CR, complete remission; IST, immunosuppressive treatment; MMF, mycophenolate mofetil; UP/C, urinary protein/creatinine ratio.

Supplementary Methods

Statistical analyses were performed using SAS version 9.4. Differences between CR and non-CR patients in baseline demographic and clinical characteristics were examined using Welch's t-test for continuous variables and Chi-square test or Fisher's exact test (when 25% of the cells have expected counts <5) for categorical variables. The chronic eGFR slope was determined via a mixed model with random coefficients (patient-specific slopes and intercepts) and linear spline (i.e., a two-slope model with knot or change point at Week 6). The change from baseline in urinary protein/creatinine ratio (UP/C) and BP was assessed via a mixed model repeated measures (MMRM) analysis. For eGFR, UP/C, and BP, a patient is included in the CR group if they experienced CR at any time, and all data were included regardless of whether at a visit with CR or without CR.

The chronic estimated glomerular filtration rate (eGFR) slope in defined patient subgroups was determined via a mixed model with random coefficients and linear spline (i.e., a 2-slope model with knot or change point at Week 6). The response variable was on-treatment eGFR from the first dose of sparsentan through data cutoff or treatment discontinuation. Only eGFR values obtained while the patient was on sparsentan were included (i.e., for patients receiving irbesartan in the double-blind period of the study, only eGFR values from the open-label extension period were included). Fixed effects in the model included baseline eGFR (relative to first dose of sparsentan), time (in days) from first dose of sparsentan, time (in days) from change point at 42 days or 0, whichever was greater, and for complete remission of proteinuria (CR) and non-CR group (and difference), numeric indicator of response and interaction terms for time from first dose of sparsentan by indicator and time from change point by indicator. For models assessing

the relationship between chronic slope and use of renal-related immunosuppressive therapies (ISTs), 4 response groups were defined as a cross between CR/non-CR and IST use presence/absence at any time in the treatment period. Random effects for intercept, time from first dose of sparsentan, and time from change point were also included in the model. Unstructured covariance matrix was assumed.

The change from baseline in UP/C in defined patient subgroups was assessed by a MMRM analysis. Because UP/C is a highly right-skewed variable, analyses were performed on log-transformed data. The response variable was change from baseline in on-treatment natural log UP/C from the first dose of sparsentan through data cutoff or treatment discontinuation; only UP/C values obtained while the patient was on sparsentan were included. Fixed effects in the model included baseline UP/C (relative to first dose of sparsentan) in natural log scale, categorical time (in weeks) from first dose of sparsentan, and for CR and non-CR group (and difference), numeric indicator of response and interaction terms for time from first dose of sparsentan by indicator. For models assessing the relationship between change from baseline UP/C and use of renal-related ISTs, an additional fixed effect of numeric indicator of IST use since the last study visit (i.e., time-varying covariate), as well as interaction terms between IST use and time; IST use and response (CR and non-CR); and IST use, response, and time were included. A random effect for a patient was included in the model, and an autoregressive-1 covariance matrix was assumed.

Blood pressure in defined patient subgroups was determined by a MMRM analysis. The response variable was on-treatment blood pressure (systolic or diastolic) from the first dose of sparsentan

through data cutoff or treatment discontinuation; only blood pressure values obtained while the patient was on sparsentan were included. Fixed effects in the model included baseline blood pressure (relative to first dose of sparsentan), categorical time (in weeks) from first dose of sparsentan, and for CR and non-CR group (and difference), numeric indicator of response and interaction terms for time from first dose of sparsentan by indicator. A random effect for subject was included in the model and a compound symmetric covariance matrix was assumed.

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	As a post hoc analysis of the DUET trial OLE, "randomized" is not included in the title.
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2-3
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	4-5
	2b	Specific objectives or hypotheses	5-6
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6-7
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	7
	6b	Any changes to trial outcomes after the trial commenced, with reasons	NA
Sample size	7a	How sample size was determined	6 (primary trial publication referenced)

	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	6 (primary trial publication referenced)
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	6
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	6 (primary trial publication referenced)
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	6 (primary trial publication referenced)
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	6 (primary trial publication referenced)
	11b	If relevant, description of the similarity of interventions	6 (primary trial publication referenced)
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	8, 46-48
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	8, 46-48
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	8-9
	13b	For each group, losses and exclusions after randomisation, together with reasons	8, 30
Recruitment	14a	Dates defining the periods of recruitment and follow-up	8
	14b	Why the trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	23-27
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was	32-37

		by original assigned groups	
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	10-12, 32-37
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	NA
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	10-12, 32-37, 44-45
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	12-13, 28, 41-43
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	16-17
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	15-16
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	13-17
Other information			
Registration	23	Registration number and name of trial registry	18
Protocol	24	Where the full trial protocol can be accessed, if available	NA
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	18

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.