Finerenone in Type 1 Diabetes and Chronic Kidney Disease

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Finerenone in Type 1 Diabetes and Chronic Kidney Disease

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Abstract

Background: The nonsteroidal mineralocorticoid receptor antagonist finerenone has been reported to improve kidney and cardiovascular outcomes in people with type 2 diabetes and chronic kidney disease (CKD). Finerenone efficacy and safety in people with type 1 diabetes and CKD are unknown.

Methods: We randomized 242 adults with type 1 diabetes, CKD (estimated glomerular filtration rate [eGFR], 25 to <90 ml/minute/1.73 m^2 of body-surface area), albuminuria (urinary albumin-to-creatinine ratio [uACR], 200 to <5000 mg/g), and on a renin–angiotensin system inhibitor to receive finerenone (10 or 20 mg per day) or matching placebo. The primary outcome was the relative change in uACR from baseline over 6 months.

Results: Median uACR decreased from 574.6 to 373.5 mg/g with finerenone and from 506.4 to 475.6 mg/g with placebo.. Over 6 months, the uACR fell by 34% with finerenone (geometric mean ratio 0.66; 95% CI 0.60, 0.73) and 12% with placebo (geometric mean ratio 0.88; 95% CI 0.79, 0.98) corresponding to a 25% greater uACR reduction with finerenone than placebo (geometric mean finerenone/placebo ratio 0.75; 95% CI 0.65, 0.87; P<0.001). The most common adverse event was hyperkalemia (12 [10.1%] with finerenone and 4 [3.3%] with placebo); two hyperkalemia events led to treatment discontinuations (2 [1.7%], finerenone; none, placebo). At 6 months, eGFR declined by −5 ml/minute/1.73 m^2 with finerenone and by −2.1 ml/minute/1.73 m^2 with placebo (difference –2.9 ml/minute/1.73 m^2 [95% CI: –5.1, –0.7]), returning toward baseline during washout.

Conclusion: In adults with type 1 diabetes and CKD, finerenone reduced the uACR compared with placebo.

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FINE-ONE Trial registration number: NCT05901831.

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Type 1 diabetes affects approximately 9.5 million people worldwide with prevalence projected to rise to nearly 15 million by 2040.[1] Chronic kidney disease (CKD) remains a common microvascular complication of type 1 diabetes despite many advances in diabetes care.[2,3] Similar to people with type 2 diabetes, those with type 1 diabetes also experience a two- to four-fold higher risk of cardiovascular disease compared with the general population.[4]

Therapies for the management of kidney and cardiovascular disease have emerged for people with type 2 diabetes and CKD, including sodium–glucose cotransporter 2 (SGLT2) inhibitors, the nonsteroidal mineralocorticoid receptor antagonist finerenone, and the glucagon-like peptide-1 receptor agonist (GLP1-RA) semaglutide.[5] However, these agents have not been evaluated in rigorous clinical outcome trials in people with type 1 diabetes and CKD. To date, the treatment of CKD in type 1 diabetes has focused on optimizing lifestyle, glycemia, and blood pressure,[5] preferably with renin–angiotensin-system inhibitors based on studies conducted over three decades ago.[6] While these interventions are effective in reducing CKD progression, they do not fully halt it.[6] Thus, new therapeutic approaches for people with type 1 diabetes and CKD would seem indicated.[7]

Studies have suggested that overactivation of the mineralocorticoid receptor and excess aldosterone in the kidneys promote sodium and water reabsorption, stimulate pro-inflammatory and pro-fibrotic pathways, and contribute to albuminuria development and CKD progression in people with both type 1 and type 2 diabetes.[8-10] The nonsteroidal mineralocorticoid receptor antagonist finerenone has been shown to decrease the risk of kidney failure and cardiovascular events in people with type 2 diabetes and CKD.[11-13] The current trial, FINE-ONE (FINErenone efficacy and safety in chronic kidney disease and type ONE diabetes), assessed the efficacy and safety of finerenone in people with type 1 diabetes and CKD with albuminuria as a surrogate outcome.

METHODS

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We undertook a randomized, prospective, double-blind, global, multicenter, phase 3 trial of finerenone versus placebo in adults with type 1 diabetes and CKD. The trial design was published previously;[14] the trial protocol is available at **NEJM.org**. The trial was designed by the steering committee and Bayer (the sponsor). An independent safety data monitoring committee oversaw the trial throughout. The trial followed the principles of the Declaration of Helsinki and the Council for International Organizations of Medical Sciences as well as the International Conference on Harmonisation Guidelines for Good Clinical Practice. Data were gathered by the investigators and analyzed by the sponsor. The first author prepared the initial draft of the manuscript and had full data access. All authors reviewed and revised subsequent drafts, approved the final version and, together with the sponsor, agreed to submit the manuscript for publication. All authors vouch for the completeness and accuracy of the data; the sponsor and the investigators vouch for the fidelity of the trial to the protocol.

PARTICIPANTS

Eligible participants were ≥18 years of age with type 1 diabetes and CKD, defined as estimated glomerular filtration rate (eGFR) between 25 and 90 ml/minute/1.73 m^2 of body surface area, and albuminuria, defined as a urinary albumin-to-creatinine ratio ([uACR] with albumin measured in milligrams and creatinine measured in grams) between 200 and 5000, and documentation of frank albuminuria or proteinuria for ≥3 months prior to screening. Participants had glycated hemoglobin levels <10% and serum potassium ≤4.8 mmol/liter at screening, and had received a stable dose of an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker for ≥4 weeks prior to screening. Exclusion criteria were CKD with known cause other than type 1 diabetes, or prior kidney transplantation. Participants with symptomatic heart failure with reduced ejection fraction and those treated with an SGLT2 inhibitor or GLP1-RA within 8 weeks prior to or at screening were also excluded. Full inclusion and exclusion criteria are shown in **Table S1**.

TRIAL VISITS

The trial included six prespecified visits: at screening, baseline, month 1, month 3, and month 6 (end of treatment), and at follow-up (30 days after last dose of study drug). At all

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prespecified visits, except month 1, three first morning void urine samples were collected for uACR assessment at the central laboratory. Blood samples were collected to centrally assess serum potassium and eGFR levels at every prespecified trial visit.

TRIAL PROCEDURES

Participants were randomly assigned 1:1 to oral finerenone (10 or 20 mg/day) or matching placebo using an Interactive Response Technology. Finerenone was initiated at 20 mg/day if screening eGFR was ≥60 ml/minute/1.73 m^2, and at 10 mg/day when the eGFR was between 25 and 60 ml/minute/1.73 m^2. Up-titration of finerenone from 10 mg/day to the target dose of 20 mg/day was permitted from month 1 onwards in those with serum potassium ≤4.8 mmol/liter and an eGFR decrease of <30% below the value at the last visit. Down-titration was allowed at any time for safety reasons. If serum potassium levels exceeded 5.5 mmol/liter, study treatment was withheld for 72 hours and was restarted at 10 mg/day once serum potassium levels decreased to ≤5.0 mmol/liter. All investigators, treating physicians, participants, and study personnel were blinded to the trial-group assignments throughout.

OUTCOMES

The primary efficacy outcome was the relative change in uACR from baseline (ratio to baseline) over 6 months, which represents the average in relative change across the 6 months. In an exploratory analysis, the primary outcome was also assessed in participant subgroups, which included baseline uACR and eGFR subgroups. Other exploratory efficacy outcomes included the change in uACR from baseline to months 3 and 6, and the occurrence of a relative decrease in uACR of ≥30% and ≥50% from baseline at month 6. Secondary safety outcomes were the number of participants with treatment-emergent adverse events and treatment-emergent serious adverse events, including hyperkalemia as a prespecified adverse event of special interest. Hyperkalemia was defined as any investigator reported adverse event with MedDRA codes corresponding to the preferred

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terms hyperkalemia or blood potassium increased. Other secondary outcomes included changes in eGFR, blood pressure, and serum potassium over time.

STATISTICAL ANALYSIS

We calculated that a sample size of 214 participants provided 90% power with a two-sided significance level of 5% to detect a mean percentage change in the uACR from baseline that was 30% lower with finerenone compared with placebo, assuming a standard deviation in log-transformed uACR of 0.8. To account for potential study discontinuation, at least 220 participants were required to achieve the desired power. Continuous data are expressed as mean ± standard deviation or median and interquartile range, and categorical data are expressed as n (%). Efficacy analyses were conducted in the full analysis set, comprising all randomized participants. The analysis of uACR was performed on log-transformed values, followed by a back transformation to the original scale to obtain the equivalent geometric mean percent change. The primary efficacy outcome was analyzed using a mixed model for repeated measures including the following factors: treatment group, visit, treatment by visit interaction, log-transformed baseline uACR as covariate and log-transformed baseline value by visit interaction to characterize baseline-specific response over time. Missing data were imputed as described in the Supplementary Appendix. A two-sided P value <0.05 was considered statistically significant. Changes in eGFR, serum potassium and blood pressure (systolic and diastolic) were analyzed using a mixed model for repeated measures with the following factors: treatment group, visit, treatment by visit interaction, baseline value of parameter of interest, and baseline value by visit included as covariates.

Since no provision for correcting multiplicity was planned when conducting tests for the secondary or other outcomes, results are reported as point estimates and 95% confidence intervals (CIs). The widths of the CIs have not been adjusted for multiplicity and should not be used to infer definitive treatment effects for secondary outcomes.

To assess the results for the primary efficacy analysis with respect to the impact of missing data, control-based multiple imputation was performed utilizing multiple imputation methodology. Further details are provided in the Supplementary Appendix. Safety outcomes were analyzed in the safety analysis set (all full analysis set participants who took at least

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one dose of study drug). Measurements of serum potassium levels >5.5 and >6.0 mmol/liter were based on central laboratory data. Analyses were performed using SAS software, version 9.4 or higher (SAS Institute Inc., Cary, NC, USA).

RESULTS

From February 26, 2024, to February 14, 2025, 573 participants were assessed for eligibility, of whom 242 were randomly assigned to finerenone (n=120) or placebo (n=122), (see **Fig. S1, Supplementary Appendix**). During the 6-month double-blind treatment period, 8 (6.7%) participants in the finerenone and 10 (8.2%) in the placebo group discontinued treatment. uACR data for the primary outcome analysis was available in 233 (96.3%) participants. Baseline characteristics appeared to be well balanced between the two randomized treatment groups (**Table 1** and **Table S2**). The representativeness of the trial population is shown in **Table S3**. In the finerenone group, 98 (81.7%) participants were treated with a 20-mg dose and in the placebo group, 107 (87.7%) received matching placebo treatment.

PRIMARY OUTCOME

For placebo, the median uACR changed from 506.4 mg/g at baseline to 475.6 mg/g at the end of the 6-month treatment period. Respective values for finerenone were 574.6 mg/g and 373.5 mg/g. The geometric mean percentage changes from baseline over 6 months were 12% (least-squares mean ratio to baseline 0.88; 95% CI 0.79, 0.98) for placebo and 34% (least-squares mean ratio to baseline 0.66, 95% CI 0.60, 0.73) for finerenone (**Fig. 1**). Thus, the uACR over 6 months of finerenone treatment decreased by 25% compared with placebo (least-squares geometric mean finerenone/placebo ratio to baseline 0.75; 95% CI 0.65, 0.87, P<0.001). The uACR increased from the end of treatment to the end of follow-up in the finerenone group but did not increase in the placebo group (**Fig. 1**). uACR changes for finerenone versus placebo among pre-specified participant baseline subgroups are shown in **Figure 2**.

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At 6 months, the proportion of participants experiencing a reduction in uACR from baseline of ≥30% or ≥50% was 54.3% and 28.4% in the finerenone group, and 32.7% and 21.8% in the placebo group (**Fig. S2A** and **S2B**). Nine participants (3.7%) had missing uACR values, and prespecified control-based imputation and tipping point sensitivity analyses showed similar results (**Tables S4** and **S5**).

SAFETY OUTCOMES

The proportion of participants with treatment-emergent adverse events was 47.1% with finerenone and 49.2% with placebo (**Tables 2, S6**, and **S7)**. A similar proportion of patients also were reported to experience serious treatment-emergent adverse events (finerenone: 11.8%; placebo: 11.5%). Treatment-emergent adverse events leading to discontinuation were infrequent in both groups, and no fatal events were observed in the finerenone group.

Hyperkalemia was the most common adverse event: 12 (10.1%) participants with finerenone and 4 (3.3%) with placebo. Two (1.7%) participants in the finerenone group discontinued the study drug due to treatment-emergent hyperkalemia.

The increase in serum potassium with finerenone (0.14 mmol/liter [95% CI: 0.07, 0.21) was apparent after 1 month of treatment and was sustained throughout the treatment period. The respective increase in serum potassium with placebo was 0.07 mmol/liter (95% CI: 0.01, 0.14), corresponding to a least squares mean difference of 0.07 mmol/liter (95% CI: −0.03, 0.17). Serum potassium levels returned to baseline within 30 days after stopping finerenone (**Fig. 3A**). Two (1.7%) participants in the finerenone group and 1 (0.9%) participant in the placebo group experienced serum potassium levels >6.0 mmol/liter during the treatment period. Hypoglycemia occurred in 2 [1.7%] participants with finerenone and 7 [5.7%] with placebo. There were few events of hypotension and acute kidney injury for both treatment groups (**Table 2** and **Table S6**).

The least squares mean change in eGFR from baseline to month 1 was –2.8 ml/minute/1.73 m^2 (95% CI: –4.2, –1.4) with finerenone compared with –0.8 ml/minute/1.73

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m^2 (95% CI: –2.2, 0.7) with placebo, corresponding to a least squares mean difference from baseline of –2.0 ml/minute/1.73 m^2 (95% CI: –4.0, –0.0). The maximum difference between both treatment groups was seen at month 6 (–2.9 ml/minute/1.73 m^2 [95% CI: –5.1, –0.7]). The eGFR decrease was no longer appreciable 30 days after discontinuation of study medication in the finerenone group (**Fig. 3B**). The number of participants with a ≥30% decline in eGFR was 11 (9.2%) with finerenone and 9 (7.4%) with placebo (**Table S8**).

At month 6, the difference in change from baseline in systolic and diastolic blood pressure between finerenone and placebo was −0.9 mmHg (95% CI −4.3, 2.6) and −1.3 mmHg (95% CI −3.4, 0.9), respectively (**Fig. 3C** and **3D**).

No substantial changes in glycated hemoglobin or body weight were observed in either group, and between-group differences were small (**Table S9**).

DISCUSSION

In this randomized, placebo-controlled, double-blind clinical trial in participants with type 1 diabetes and CKD, finerenone treatment resulted in a larger reduction in uACR compared with placebo when administered in addition to guideline-directed medical therapy, including ACE inhibitors or angiotensin receptor blockers. These effects appeared similar across subgroup participants with lowest eGFR or highest uACR, participants who are at very high risk of adverse kidney and cardiovascular outcomes. Finerenone had modest effects on potassium concentrations with more instances of hyperkalemia than placebo.

Two previous clinical trials in participants with type 2 diabetes and CKD reported that finerenone reduced albuminuria and decreased the risk of kidney and cardiovascular events.[11,12] Analyses from those trials indicated that the geometric mean reduction in uACR of 32% with finerenone accounted for more than 80% of the benefit of finerenone in reducing kidney function decline or risk of kidney failure.[14,15] Based on these findings and with regulatory endorsement, the current study used reduction in albuminuria as a primary outcome.[14] The observed reduction in uACR of 25% over 6 months in the current study was similar to that previously observed in patients with type 2 diabetes and CKD,[13] a population

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with similar baseline risk profiles to the present population.[16] A meta-analysis of 41 clinical trials reported that each 30% decrease in the geometric mean albuminuria in treatment compared with control was associated with an average 27% lower hazard for the clinical endpoint.[17] Collectively, these studies may be taken to suggest that finerenone therapy may improve kidney outcomes in people with type 1 diabetes and CKD.

Modest reductions in systolic and diastolic blood pressure were observed in both the finerenone and placebo groups. Given the small alterations in blood pressure in this trial, we speculate that the observed reduction in uACR is most likely due to intrarenal factors rather than systemic hemodynamic effects.

Finerenone caused an acute reduction in eGFR after 1 month and was maximal at 6 months. This effect reversed in part during the 30-day wash-out period. We speculate that this finding is consistent with hemodynamic glomerular changes with finerenone, similar to those reported in people with type 2 diabetes and CKD and with other kidney-protective therapies.[18,19] However, larger and longer studies are required to evaluate kidney protective effects of finerenone as this study was not powered to determine effects on eGFR decline or clinical kidney outcomes The incidence of a ≥30% eGFR decline or acute kidney injury was low and similar between treatment groups. The overall incidence of hyperkalemia was higher with finerenone than placebo. None of these events led to death, although they led to discontinuation of finerenone in two participants.

Since studies in the early 1990s introduced RAS inhibitors for renoprotection, other agents have long been anticipated. The present study with finerenone suggests a favorable benefit-risk profile for people with type 1 diabetes and CKD. Although other therapies for CKD such as SGLT2 inhibitors and GLP1-RAs have been studied in people with type 2 diabetes,[20-23] treatment for CKD in people with type 1 diabetes remains to be evaluated in clinical trials. A trial assessing the efficacy and safety of SGLT2 inhibitors in people with type 1 diabetes and CKD is ongoing (NCT06217302).[24]

The 6-month follow-up and the use of a surrogate biomarker for the primary outcome are limitations related to challenges of conducting large long-term studies in this population.

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Although the trial had a geographically diverse study population with type 1 diabetes and CKD, the population consisted predominantly of male participants. Thus, the findings are only applicable to people who share the characteristics of the studied cohort and cannot be generalized.

In conclusion, in this trial among adults with type 1 diabetes and CKD, finerenone decreased the uACR compared with placebo over 6 months of treatment.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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Tables and Figures:

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Figure 1: *Changes in uACR*

*Up to 3 daily uACR measures are combined into a geometric mean uACR prior to the analysis of the ratio to baseline of geometric mean uACR; †Geometric mean ratio of treatment group ratios to baseline over the study period (i.e. average of geometric mean of treatment effect at Month 3 and Month 6 visits); ‡Assessment of data for the washout period was conducted using an ANCOVA model for the ratio to baseline in uACR at follow-up with the model including treatment group and log baseline uACR; §30 days after last dose of study intervention with a ± 7-day window permitted.

I bars indicate 95% confidence intervals. Confidence intervals are unadjusted and should not be used for inference.

CI, confidence interval; LSGM, least squares geometric mean; uACR, urinary albumin-to-creatinine ratio.

Figure 2: *Change in uACR from Baseline over 6 months by Subgroups*

*Race was not reported in 1 participant in the placebo and finerenone groups; 2 participants in the finerenone group were Native American or Native Alaskan.

CI, confidence interval; eGFR, estimated glomerular filtration rate; LSGM, least squares geometric mean; uACR, urinary albumin-to-creatinine ratio.

I bars indicate 95% confidence intervals. Confidence intervals are unadjusted and should not be used for inference.

Figure 3: *Changes from Baseline* in Serum Potassium level, eGFR, SBP, and DBP*

* Analyzed using a mixed model for repeated measures with the following factors: treatment group, visit, treatment by visit interaction, baseline value of parameter of interest, and

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baseline value by visit included as covariates;†30 days after last dose of study intervention with a ±7-day window permitted.

I bars indicate 95% confidence intervals. Confidence intervals are unadjusted and should not be used for inference.

DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; LS, least squares; SBP, systolic blood pressure.

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Table 1 *Demographic and Clinical Characteristics of the Participants at Baseline*

Characteristic	Finerenone (N=120)	Placebo (N=122)
Age* — yr	51.3±14.2	51.9±13.2
Sex — no. (%)		
Female	41 (34.2)	43 (35.2)
Male	79 (65.8)	79 (64.8)
Race — no. (%)		
White	85 (70.8)	90 (73.8)
Black	9 (7.5)	6 (4.9)
Asian	23 (19.2)	25 (20.5)
Other†	3 (2.5)	1 (0.8)
BMI*‡ — kg/m^2	27.7±5.4	27.3±6.6
Clinical measurements		
Systolic blood pressure* — mmHg	136.5±15.8	134.2±17.7
Diastolic blood pressure* — mmHg	78.5±10.4	76.7±11.2
Biochemical measurements		
HbA1c*§ — %	7.8±1.1	7.5±1.0
HbA1c category percent§ — no. (%)		
≤7.5	54 (45.0)	70 (57.4)
>7.5	66 (55.0)	50 (41.0)

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Characteristic	Finerenone (N=120)	Placebo (N=122)
uACR¶ (Q1–Q3) — mg/g	574.6 (315.8–1224.9)	506.4 (288.2–1182.3)
uACR category, mg/g, no. (%)		
<300	29 (24.2)	35 (28.7)
300–≤1000	57 (47.5)	54 (44.3)
>1000	34 (28.3)	33 (27.0)
eGFR*— ml/minute/1.73 m^2	59.0±19.5	58.8±19.0
eGFR category, ml/minute/1.73 m^2 — no. (%)		
<45	32 (26.7)	31 (25.4)
45–<60	32 (26.7)	30 (24.6)
≥60	56 (46.7)	61 (50.0)
Mean serum potassium* — mmol/liter	4.6±0.4	4.6±0.4
Medical history		
Duration of diabetes* — y	32.0±14.1	32.0±14.4
History of CVD‖ — no. (%)	35 (29.2)	26 (21.3)
History of hypertension — no. (%)	104 (86.7)	103 (84.4)
Medication use** — no. (%)		
ACEis	59 (49.6)	52 (42.6)
ARBs	60 (50.4)	68 (55.7)
Diuretics	43 (36.1)	45 (36.9)

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* Presented as mean ±SD.

† Race was not reported in 1 participant in the placebo and finerenone groups; 2 participants in the finerenone group were Native American or Native Alaskan.

‡ BMI values were missing for 1 participant for finerenone and 1 participant for placebo.

§ HbA1c values were missing for 2 participants for placebo.

¶ Presented as median.

‖ History of CVD was determined by the presence of one of the following in the medical history: myocardial infarction, coronary artery stenosis, cerebrovascular accident, transient ischemic attack, peripheral arterial occlusive disease, or cardiac failure.

** Use of sodium–glucose cotransporter-2 inhibitors and glucagon-like peptide-1 receptor agonists was not permitted in the FINE-ONE trial.

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; Q, quartile; SD, standard deviation; uACR, urinary albumin-to-creatinine ratio.

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Table 2: Treatment-Emergent Adverse Event Summary

Adverse event — no. (%)	**Finerenone**	**Placebo**
	(N=119)	**(N=122)**
Any treatment-emergent AE	56 (47.1)	60 (49.2)
Related to study drug	19 (16.0)	14 (11.5)
Leading to permanent discontinuation of study drug	3 (2.5)	3 (2.5)
Any treatment-emergent SAE	14 (11.8)	14 (11.5)
Related to study drug	3 (2.5)	0
Leading to permanent discontinuation of study drug	3 (2.5)	1 (0.8)
Leading to hospitalization	12 (10.1)	10 (8.2)
Life-threatening*	3 (2.5)†	1 (0.8)‡
Leading to death	0	1 (0.8)
Any hyperkalemia (treatment-emergent AESI)§	12 (10.1)	4 (3.3)
Related to study drug	11 (9.2)	4 (3.3)
Leading to permanent discontinuation of study drug	2 (1.7)	0
Any serious hyperkalemia	2 (1.7)	0
Related to study drug	2 (1.7)	0
Leading to hospitalization	2 (1.7)	0
Life-threatening	0	0
Leading to death	0	0
Serum potassium level — no./total no. (%)		
>5.5 mmol/liter¶	13/118 (11.0)	4/115 (3.5)
>6.0 mmol/liter‖	2/119 (1.7)	1/117 (0.9)

* None of the life-threatening treatment-emergent SAEs were related to study drug according to the investigators.

† Life-threatening events in the finerenone group included sarcoma, urinary tract infection with septic shock and stab wound with pneumothorax.

‡ The life-threatening event reported in the placebo group was suicidal intent.

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§ Hyperkalemia includes investigator-reported AEs with MedDRA codes hyperkalemia and blood potassium increased.

¶ Central laboratory assessment values were missing for 1 participant for finerenone and 7 participants for placebo.

‖ Central laboratory assessment values missing for 5 participants for placebo.

AE, adverse event; AESI, adverse event of special interest; SAE, serious adverse event.

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Figure 1: *Changes in uACR*¶

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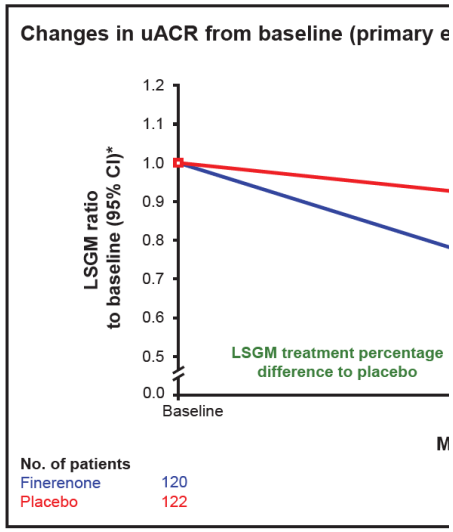

*Up to 3 daily uACR measures are combined into a geometric mean uACR prior to the analysis of the ratio to baseline of geometric mean uACR; †Geometric mean ratio of treatment group ratios to baseline over the study period (i.e. average of geometric mean of treatment effect at Month 3 and Month 6 visits); ‡Assessment of data for the washout period was conducted using an ANCOVA model for the ratio to baseline in uACR at follow-up with the model including treatment group and log baseline uACR; §30 days after last dose of study intervention with a ± 7-day window permitted.¶

I bars indicate 95% confidence intervals. Confidence intervals are unadjusted and should not be used for inference.¶

CI, confidence interval; LSGM, least squares geometric mean; uACR, urinary albumin-to-creatinine ratio.

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Figure 2: *Change in uACR from Baseline over 6 months by Subgroups*¶

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