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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 persons with type 2 diabetes and chronic kidney disease (CKD). The efficacy and safety of finerenone in persons with type 1 diabetes and CKD are unknown.

METHODS

We conducted a phase 3 trial involving adults who had type 1 diabetes, CKD (estimated glomerular filtration rate [eGFR], 25 to <90 ml per minute per 1.73 m^2 of body-surface area), and albuminuria (urinary albumin-to-creatinine ratio [with albumin measured in milligrams and creatinine measured in grams], 200 to <5000) and were receiving an angiotensin-converting–enzyme (ACE) inhibitor or an angiotensin-receptor blocker. Participants were randomly assigned to receive finerenone (10 or 20 mg per day, depending on the eGFR) or matching placebo. The primary outcome was the relative change in the urinary albumin-to-creatinine ratio over a period of 6 months.

RESULTS

A total of 242 participants underwent randomization. The median urinary albumin-to-creatinine ratio decreased from 574.6 at baseline to 373.5 at 6 months among all the participants assigned to receive finerenone and from 506.4 to 475.6 among those assigned to receive placebo. Over a period of 6 months, the urinary albumin-to-creatinine ratio decreased by 34% with finerenone (geometric mean ratio to baseline, 0.66; 95% confidence interval [CI], 0.60 to 0.73) and 12% with placebo (geometric mean ratio to baseline, 0.88; 95% CI, 0.79 to 0.98), which corresponded to a 25% greater reduction with finerenone than with placebo (geometric mean ratio for finerenone vs. placebo, 0.75; 95% CI, 0.65 to 0.87; P<0.001). The most common adverse event was hyperkalemia (in 12 participants [10.1%] with finerenone and in 4 [3.3%] with placebo); 2 participants (1.7%) discontinued finerenone because of hyperkalemia. At 6 months, the change in the eGFR was –5.6 ml per minute per 1.73 m^2 with finerenone and –2.7 ml per minute per 1.73 m^2 with placebo (difference, –2.9 ml per minute per 1.73 m^2; 95% CI, –5.1 to –0.7); eGFR values approached baseline levels during the washout period.

CONCLUSIONS

In adults with type 1 diabetes and CKD, finerenone resulted in a significantly greater decrease in the urinary albumin-to-creatinine ratio than placebo. (Funded by Bayer; FINE-ONE ClinicalTrials.gov number, NCT05901831.)

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Type 1 diabetes affects approximately 9.5 million persons 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 persons with type 2 diabetes, those with type 1 diabetes have two to four times the risk of cardiovascular disease as the general population.[4]

Therapies for the management of kidney and cardiovascular disease have emerged for persons 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 (GLP-1) receptor agonist semaglutide.[5] However, these agents have not been evaluated in rigorous clinical outcome trials involving persons with type 1 diabetes and CKD. To date, the treatment of CKD in persons with type 1 diabetes has focused on optimizing lifestyle, blood glucose levels, and blood pressure,[5] preferably with renin–angiotensin system (RAS) inhibitors on the basis of studies conducted more than three decades ago.[6] Although these interventions are effective in reducing CKD progression, they do not fully halt it.[6] Thus, new therapeutic approaches for persons 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 proinflammatory and profibrotic pathways, and contribute to albuminuria development and CKD progression in persons with either type 1 or 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 persons 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 persons with type 1 diabetes and CKD, with albuminuria as a surrogate outcome.

Methods

Trial Design and Oversight

We undertook a phase 3, international, prospective, double-blind, randomized trial of finerenone as compared with placebo in adults with type 1 diabetes and CKD. The trial design was published previously[14]; the trial protocol is available with the full text of this article at NEJM.org. The trial was designed by the steering committee and Bayer (the sponsor). An independent data and safety 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 Council for 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 access to the data. All the authors reviewed and revised subsequent drafts, approved the final version, and, together with the sponsor, agreed to submit the manuscript for publication. The 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 or older with type 1 diabetes and CKD, defined as an estimated glomerular filtration rate (eGFR) of 25 to less than 90 ml per minute per 1.73 m^2 of body-surface area, and albuminuria, defined as a urinary albumin-to-creatinine ratio (with albumin measured in milligrams and creatinine measured in grams) of 200 to less than 5000, with documentation of frank albuminuria or proteinuria for at least 3 months before screening. Participants had a glycated hemoglobin level of less than 10% and a serum potassium level of 4.8 mmol per liter or less at screening, and they had received a stable dose of an angiotensin-converting–enzyme (ACE) inhibitor or an angiotensin-receptor blocker for at least 4 weeks before screening. Exclusion criteria were CKD with a known cause other than type 1 diabetes, or previous kidney transplantation. Participants with symptomatic heart failure with a reduced ejection fraction and those who had received an SGLT2 inhibitor or a GLP-1 receptor agonist within 8 weeks before or at screening were also excluded. Full inclusion and exclusion criteria are shown in Table S1 in the Supplementary Appendix, available at NEJM.org.

Trial Visits

The trial included six prespecified visits: at screening, baseline, month 1, month 3, month 6 (end of treatment period), and follow-up (30 days

after the last dose of finerenone or placebo). At all prespecified visits, except month 1, three first-morning void urine samples were collected for assessment of the urinary albumin-to-creatinine ratio at the central laboratory. Blood samples were collected to centrally assess the serum potassium levels and eGFR at every prespecified trial visit.

TRIAL PROCEDURES

Participants were randomly assigned in a 1:1 ratio to receive oral finerenone (10 or 20 mg per day) or matching placebo with the use of interactive response technology. Finerenone was initiated at 20 mg per day if the screening eGFR was at least 60 ml per minute per 1.73 m^2 and at 10 mg per day if the screening eGFR was 25 to less than 60 ml per minute per 1.73 m^2. An increase in the dose of finerenone from 10 mg per day to the target dose of 20 mg per day was permitted from month 1 onwards in participants with a serum potassium level of 4.8 mmol per liter or less and a decrease in the eGFR of less than 30% below the value at the last visit. A reduction in the dose was allowed at any time for safety reasons. If the serum potassium level exceeded 5.5 mmol per liter, the trial regimen was withheld for 72 hours and was restarted at 10 mg per day once the serum potassium level decreased to 5.0 mmol per liter or less. All the investigators, treating physicians, participants, and trial personnel were unaware of the trial-group assignments throughout.

OUTCOMES

The primary efficacy outcome was the relative change in the urinary albumin-to-creatinine ratio from baseline (ratio to baseline) over a period of 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 subgroups defined according to baseline urinary albumin-to-creatinine ratio and eGFR. Other exploratory efficacy outcomes included the change in the urinary albumin-to-creatinine ratio from baseline to months 3 and 6 and the occurrence of a relative decrease in the urinary albumin-to-creatinine ratio of at least 30% and at least 50% from baseline at month 6. Secondary safety outcomes were the number of participants with adverse events and serious adverse events that emerged or worsened after the first dose of finerenone or placebo up to 3 days after any temporary or permanent interruption of the trial regimen. Prespecified adverse events of special interest included hyperkalemia, which was defined as any investigator-reported adverse event with *Medical Dictionary for Regulatory Activities* codes corresponding to the preferred term hyperkalemia or blood potassium increased. Other secondary outcomes included changes in eGFR, blood pressure, and the serum potassium level over time.

STATISTICAL ANALYSIS

We calculated that a sample size of 214 participants would provide 90% power with a two-sided significance level of 5% to detect a mean percentage change in the urinary albumin-to-creatinine ratio from baseline that was 30% greater with finerenone than with placebo, assuming a standard deviation in log-transformed urinary albumin-to-creatinine ratio of 0.8. To account for potential discontinuation from participation in the trial, at least 220 participants were required to achieve the desired power.

Continuous data are expressed as mean and standard deviation or median and interquartile range, and categorical data are expressed as number and percent. Efficacy analyses were conducted in the full analysis population, which included all the participants who underwent randomization. The analysis of the urinary albumin-to-creatinine ratio was performed on log-transformed values, with a back transformation to the original scale to obtain the equivalent geometric mean percentage change. The primary efficacy outcome was analyzed with the use of a mixed model for repeated measures that included the following factors: trial group, visit, trial-group-by-visit interaction, and log-transformed baseline urinary albumin-to-creatinine ratio as covariates 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 of less than 0.05 was considered to indicate statistical significance. Changes in the eGFR, serum potassium level, and blood pressure (systolic and diastolic) were analyzed with the use of a mixed model for repeated measures with the following factors included as covariates: trial group, visit, trial-group-by-visit interaction, baseline value of variable of interest, and baseline-value-by-visit interaction.

Because no provision for correction for multiplicity was planned when tests for the secondary or other outcomes were conducted, results are reported as point estimates and 95% confidence intervals. The widths of the confidence intervals 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 effect of missing data, control-based multiple imputation was performed with the use of multiple-imputation methods. Further details are provided in the Supplementary Appendix. Safety outcomes were analyzed in the safety analysis population (all the participants in the full analysis population who received at least one dose of finerenone or placebo). Measurements of serum potassium levels of more than 5.5 mmol per liter and more than 6.0 mmol per liter were based on central laboratory data. Analyses were performed with the use of SAS software, version 9.4 or higher (SAS Institute).

RESULTS

PARTICIPANTS

From February 26, 2024, to February 14, 2025, a total of 573 participants in nine countries were assessed for eligibility, of whom 242 were randomly assigned to receive finerenone (120 participants) or placebo (122 participants) (Fig. S1). During the 6-month double-blind treatment period, 8 participants (6.7%) in the finerenone group and 10 (8.2%) in the placebo group discontinued the trial regimen. Data on the urinary albumin-to-creatinine ratio for the primary outcome analysis were available in 233 participants (96.3%). The baseline characteristics of the participants appeared to be well balanced between the two groups (Table 1 and Table S2). The representativeness of the trial population is shown in Table S3. In the finerenone group, 98 participants (81.7%) received a dose of 20 mg per day; in the placebo group, 107 (87.7%) received a placebo equivalent of the 20-mg-per-day dose.

PRIMARY OUTCOME

In the finerenone group, the median urinary albumin-to-creatinine ratio changed from 574.6 at baseline to 373.5 at the end of the 6-month treatment period. Respective values in the placebo group were 506.4 and 475.6. The geometric mean percentage changes from baseline over a period of 6 months were –34% (least-squares geometric mean ratio to baseline, 0.66; 95% confidence interval [CI], 0.60 to 0.73) with finerenone and –12% (least-squares geometric mean ratio to baseline, 0.88; 95% CI, 0.79 to 0.98) with placebo (Fig. 1). Thus, the urinary albumin-to-creatinine ratio over 6 months of finerenone treatment decreased by 25% more than with placebo (least-squares geometric mean ratio for finerenone vs. placebo, 0.75; 95% CI, 0.65 to 0.87; P<0.001). The urinary albumin-to-creatinine ratio increased from the end of the treatment period to the end of follow-up in the finerenone group but did not increase in the placebo group (Fig. 1). Changes in the urinary albumin-to-creatinine ratio with finerenone as compared with placebo in prespecified subgroups are shown in Figure 2.

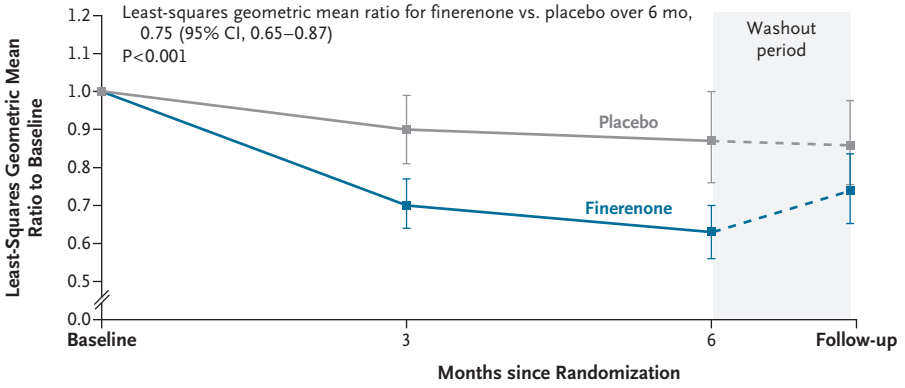
Table 1. Demographic and Clinical Characteristics of the Participants at Baseline.*

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 or ethnic group — no. (%)†		
White	85 (70.8)	90 (73.8)
Black	9 (7.5)	6 (4.9)
Asian	23 (19.2)	25 (20.5)
Other or missing	3 (2.5)	1 (0.8)

Table 1. (Continued.)

Characteristic	Finerenone (N=120)	Placebo (N=122)
Body-mass index‡	27.7±5.4	27.3±6.6
Blood pressure — mm Hg		
Systolic	136.5±15.8	134.2±17.7
Diastolic	78.5±10.4	76.7±11.2
Biochemical measurements		
Glycated hemoglobin		
Mean — %§	7.8±1.1	7.5±1.0
Distribution — no. (%)		
≤7.5%	54 (45.0)	70 (57.4)
>7.5%	66 (55.0)	50 (41.0)
Data missing	0	2 (1.6)
Urinary albumin-to-creatinine ratio¶		
Median (IQR)	574.6 (315.8–1224.9)	506.4 (288.2–1182.3)
Distribution — no. (%)		
<300	29 (24.2)	35 (28.7)
300 to 1000	57 (47.5)	54 (44.3)
>1000	34 (28.3)	33 (27.0)
Estimated glomerular filtration rate		
Mean — ml/minute/1.73 m^2	59.0±19.5	58.8±19.0
Distribution — no. (%)		
<45 ml/minute/1.73 m^2	32 (26.7)	31 (25.4)
45 to <60 ml/minute/1.73 m^2	32 (26.7)	30 (24.6)
≥60 ml/minute/1.73 m^2	56 (46.7)	61 (50.0)
Mean serum potassium — mmol/liter	4.6±0.4	4.6±0.4
Medical history		
Duration of diabetes — yr	32.0±14.1	32.0±14.4
History of cardiovascular disease — no. (%)‖	35 (29.2)	26 (21.3)
History of hypertension — no. (%)	104 (86.7)	103 (84.4)
Medication use — no./total no. (%)**		
ACE inhibitor	59/119 (49.6)	52/122 (42.6)
Angiotensin-receptor blocker	60/119 (50.4)	68/122 (55.7)
Diuretic	43/119 (36.1)	45/122 (36.9)

* Plus–minus values are means ±SD. Percentages may not total 100 because of rounding. ACE denotes angiotensin-converting enzyme, and IQR interquartile range.
† Race or ethnic group was reported by the participants. Two participants in the finerenone group were Native American or Native Alaskan, and race or ethnic group was not reported for one participant in each group.
‡ The body-mass index is the weight in kilograms divided by the square of height in meters. Data were missing for one participant in each group.
§ Data were missing for two participants in the placebo group.
¶ Albumin was measured in milligrams, and creatinine was measured in grams.
‖ A history of cardiovascular disease was determined by the presence of one of the following in the medical history: myocardial infarction, coronary-artery stenosis, stroke, 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 trial.



No. of Patients				
Placebo	122	122	122	106
Finerenone	120	120	120	114
Least-Squares Geometric Mean Percentage Difference vs. Placebo		21	28	14

Figure 1. Change in the Urinary Albumin-to-Creatinine Ratio.

Up to three daily measures of the urinary albumin-to-creatinine ratio (with albumin measured in milligrams and creatinine measured in grams) were combined into a geometric mean urinary albumin-to-creatinine ratio before the analysis of the ratio to the baseline value. The least-squares geometric mean ratio for finerenone as compared with placebo over the trial period was an average of the geometric mean of the treatment effect at the month 3 visit and the month 6 visit. Assessment of data for the washout period was conducted with the use of an analysis-of-covariance model for the ratio to baseline at follow-up, with the model including trial group and log-transformed baseline urinary albumin-to-creatinine ratio. Follow-up was at 30 days (with a window of ±7 days) after the last dose of finerenone or placebo. I bars indicate 95% confidence intervals. Confidence intervals are unadjusted and should not be used for inference.

At 6 months, the percentage of participants having a reduction in the urinary albumin-to-creatinine ratio from baseline of at least 30% or at least 50% was 54.3% and 28.4%, respectively, in the finerenone group and 32.7% and 21.8% in the placebo group (Fig. S2A and S2B). Nine participants (3.7%) had missing values for the urinary albumin-to-creatinine ratio, and prespecified control-based imputation and tipping-point sensitivity analyses showed similar results (Tables S4 and S5).

SAFETY OUTCOMES

The percentage of participants with adverse events was 47.1% with finerenone and 49.2% with placebo (Table 2). The percentage of participants who were reported to have serious adverse events was also similar in the two groups (11.8% with finerenone and 11.5% with placebo). Adverse events leading to discontinuation of the trial regimen were infrequent in both groups, and no fatal events were observed in the finerenone group.

Hyperkalemia was the most common adverse event, reported in 12 participants (10.1%) who received finerenone and in 4 (3.3%) who received placebo. Two participants (1.7%) in the finerenone group discontinued the drug owing to hyperkalemia.

The increase in the serum potassium level with finerenone (0.14 mmol per liter; 95% CI, 0.07 to 0.21) was apparent after 1 month of treatment and was sustained throughout the treatment period. The increase in the serum potassium level with placebo was 0.07 mmol per liter (95% CI, 0.01 to 0.14), which corresponded to a least-squares mean difference of 0.07 mmol per liter (95% CI, −0.03 to 0.17). Serum potassium levels returned to baseline within 30 days after stopping finerenone (Fig. 3A). A total of 2 of 119 participants (1.7%) in the finerenone group and 1 of 117 participants (0.9%) in the placebo group had serum potassium levels of more than 6.0 mmol per liter during the treatment period (Table 2). Hypoglycemia occurred

Subgroup	No. of Patients		Least-Squares Geometeric Mean Ratio to Baseline		Least-Squares Geometric Mean Ratio for Finerenone vs. Placebo
	Finerenone (N=120)	Placebo (N=122)	Finerenone (N=120)	Placebo (N=122)	
Estimated GFR					
<45 ml/min/1.73 m^2	32	29	0.77	1.04	0.74 (0.57–0.97)
45 to <60 ml/min/1.73 m^2	32	27	0.63	0.93	0.67 (0.51–0.89)
≥60 ml/min/1.73 m^2	54	59	0.63	0.77	0.82 (0.67–1.00)
Urinary ACR					
<300	29	33	0.62	0.87	0.71 (0.54–0.93)
300 to 1000	55	50	0.63	0.87	0.72 (0.58–0.89)
>1000	34	32	0.77	0.85	0.91 (0.70–1.18)
Age					
<65 yr	92	94	0.69	0.89	0.78 (0.67–0.92)
≥65 yr	26	21	0.57	0.78	0.73 (0.54–1.00)
Sex					
Female	40	36	0.69	0.93	0.74 (0.58–0.94)
Male	78	79	0.65	0.84	0.78 (0.65–0.92)
Geographic region					
North America	36	40	0.73	0.89	0.82 (0.64–1.04)
Asia	16	23	0.90	1.02	0.88 (0.63–1.23)
Europe	66	52	0.59	0.79	0.74 (0.61–0.90)
Race or ethnic group					
White	84	84	0.61	0.85	0.72 (0.61–0.85)
Black	8	5	0.71	0.83	0.86 (0.47–1.59)
Asian	23	25	0.82	0.97	0.85 (0.63–1.14)
Other	3	1	1.23	0.53	2.32 (0.69–7.78)
Serum potassium					
<4.0 mmol/liter	10	7	0.60	0.58	1.04 (0.62–1.73)
4.0 to 4.8 mmol/liter	76	82	0.68	0.88	0.78 (0.65–0.92)
>4.8 mmol/liter	32	26	0.65	0.95	0.69 (0.52–0.91)
Systolic blood pressure					
<130 mm Hg	39	42	0.77	1.03	0.75 (0.59–0.94)
≥130 mm Hg	79	73	0.62	0.79	0.78 (0.66–0.93)
Glycated hemoglobin					
≤7.5%	53	67	0.74	0.92	0.80 (0.66–0.98)
>7.5%	65	46	0.61	0.80	0.76 (0.62–0.93)

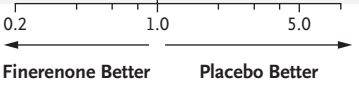


Figure 2. Change in the Urinary Albumin-to Creatinine Ratio According to Subgroup.

Race or ethnic group was reported by the participants. Two participants in the finerenone group were Native American or Native Alaskan, and race or ethnic group was not reported for one participant in each group. Confidence intervals are unadjusted and should not be used for inference. ACR denotes albumin-to-creatinine ratio, and GFR glomerular filtration rate.

in 2 of 119 participants (1.7%) with finerenone and 7 of 122 participants (5.7%) with placebo. There were few events of hypotension or acute kidney injury in either trial group (Table S6). Adverse events according to primary system organ class are shown in Table S7.

The least-squares mean change in the eGFR from baseline to month 1 was –2.8 ml per minute per 1.73 m^2 (95% CI, –4.2 to –1.4) with finerenone and –0.8 ml per minute per 1.73 m^2 (95% CI, –2.2 to 0.7) with placebo, which corresponded to a least-squares mean difference from baseline of –2.0 ml per minute per 1.73 m^2 (95% CI, –4.0 to 0.0). The maximum difference between the two trial groups was seen at month 6 (–2.9 ml per minute per 1.73 m^2; 95% CI, –5.1 to –0.7). The least-squares mean change in the eGFR from baseline to month 6 was –5.6 ml per minute per 1.73 m^2 (95% CI, –7.0 to –4.2) with finerenone and –2.7 ml per minute per 1.73 m^2 (95% CI, –4.5

Table 2. Summary of Adverse Events.*

Adverse Event	Finerenone (N=119)	Placebo (N=122)
	no. of participants (%)	
Any adverse event	56 (47.1)	60 (49.2)
Related to trial regimen	19 (16.0)	14 (11.5)
Leading to permanent discontinuation of trial regimen	3 (2.5)	3 (2.5)
Any serious adverse event	14 (11.8)	14 (11.5)
Related to trial regimen	3 (2.5)	0
Leading to permanent discontinuation of trial regimen	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¶	12 (10.1)	4 (3.3)
Related to trial regimen	11 (9.2)	4 (3.3)
Leading to permanent discontinuation of trial regimen	2 (1.7)	0
Any serious hyperkalemia	2 (1.7)	0
Related to trial regimen	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)

* The relatedness of adverse events to the trial regimen was determined by the investigator.
† None of the life-threatening serious adverse events were considered to be related to the trial regimen by the investigator.
‡ 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.
¶ Hyperkalemia was an adverse event of special interest. Hyperkalemia includes investigator-reported adverse events with the *Medical Dictionary for Regulatory Activities* codes hyperkalemia and blood potassium increased.

to –1.0) with placebo. During the washout period, eGFR values approached baseline levels in the finerenone group (Fig. 3B and Table S8). The number of participants with a decrease in the eGFR of at least 30% was 11 (9.2%) with finerenone and 9 (7.4%) with placebo.

At month 6, the difference in change from baseline in systolic blood pressure between the finerenone and placebo groups was –0.9 mm Hg (95% CI, –4.3 to 2.6), and the difference in change in diastolic blood pressure was –1.3 mm Hg (95% CI, –3.4 to 0.9) (Fig. 3C and 3D). No substantial changes in glycated hemoglobin level or body weight were observed in either group, and between-group differences were small (Table S9).

DISCUSSION

In this double-blind, randomized, placebo-controlled clinical trial involving participants with type 1 diabetes and CKD, finerenone treatment resulted in a larger reduction in the urinary albumin-to-creatinine ratio than placebo when administered in addition to guideline-directed medical therapy, including ACE inhibitors or angiotensin-receptor blockers. These effects appeared to be similar across subgroups of participants with the lowest eGFR or highest urinary albumin-to-creatinine ratio — participants who are at very high risk for adverse kidney and cardiovascular outcomes. Finerenone had modest

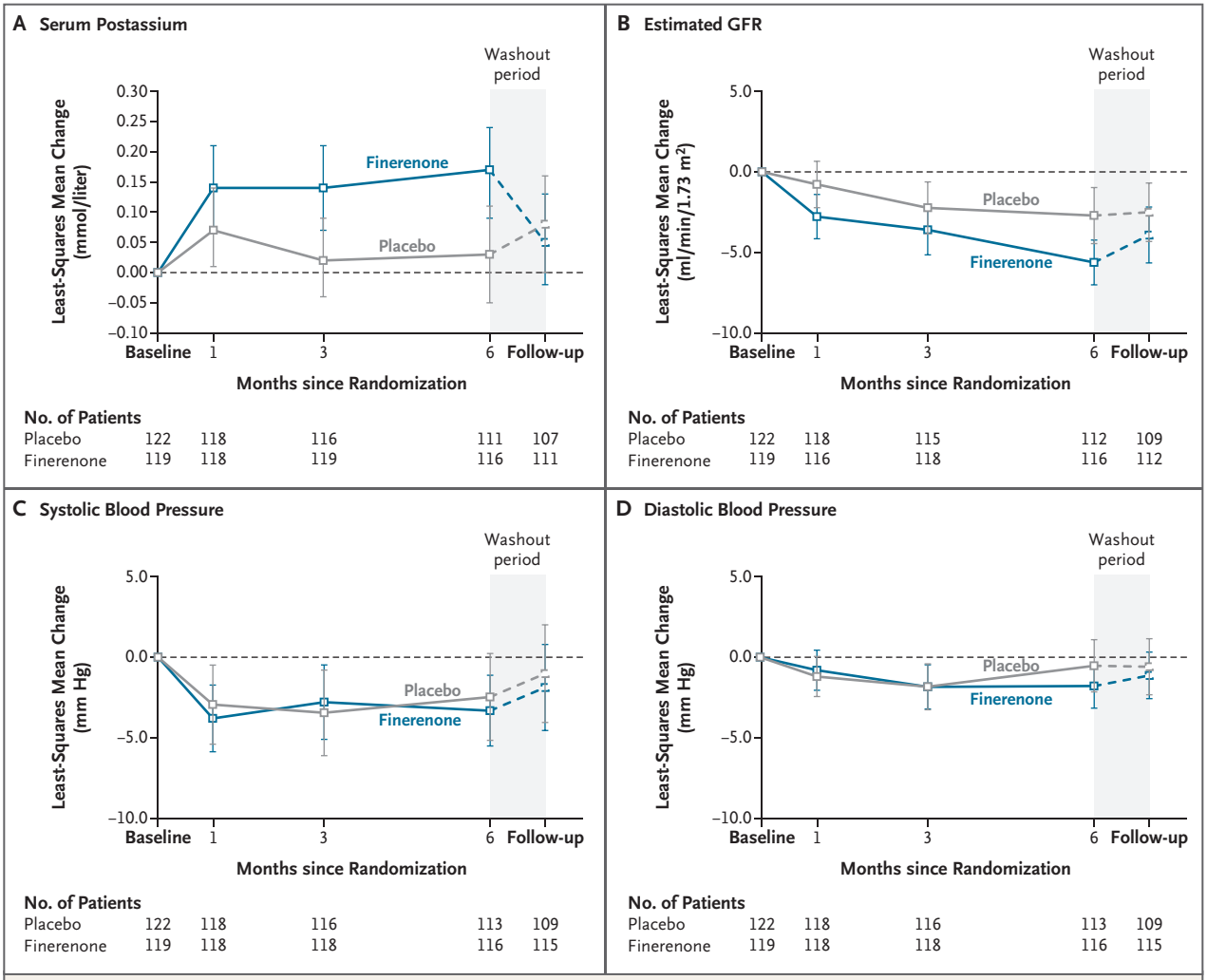


Figure 3. Changes in Serum Potassium Level, Estimated GFR, and Systolic and Diastolic Blood Pressure.

All variables were analyzed with the use of a mixed model for repeated measures with the following factors included as covariates: trial group, visit, trial-group-by-visit interaction, baseline value of variable of interest, and baseline-value-by-visit interaction. Follow-up was at 30 days (with a window of ±7 days) after the last dose of finerenone or placebo. I bars indicate 95% confidence intervals. Confidence intervals are unadjusted and should not be used for inference.

effects on potassium concentrations, with more instances of hyperkalemia than with placebo.

Two previous clinical trials involving participants with type 2 diabetes and CKD showed that finerenone reduced the urinary albumin-to-creatinine ratio and decreased the risk of kidney and cardiovascular events.[11,12] Analyses from those trials indicated that the geometric mean reduction in the urinary albumin-to-creatinine ratio 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] On the basis of these findings and with regulatory endorsement, the current trial used the change in the albumin-to-creatinine ratio as a primary outcome.[14] The 25% greater decrease in this ratio with finerenone than with placebo over a period of 6 months in the current trial was similar to that previously observed in patients with type 2 diabetes and CKD,[13] a population with baseline risk profiles similar to those in the present population.[16] A meta-analysis of 41 clinical trials concluded that each 30% decrease in the geometric mean albuminuria with treatment as compared with control was associated with an average 27% lower hazard for the

clinical end point.[17] Collectively, these trials may be taken to suggest that finerenone therapy may improve kidney outcomes in persons 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 the urinary albumin-to-creatinine ratio is most likely due to intrarenal factors rather than systemic hemodynamic effects.

Finerenone caused an acute reduction in eGFR after 1 month, and the effect was maximal at 6 months. This effect reversed in part during the 30-day washout period. We speculate that this finding is consistent with hemodynamic glomerular changes with finerenone, similar to those reported in persons with type 2 diabetes and CKD and with other therapies used for kidney disorders.[18,19] However, larger and longer studies are required to evaluate kidney-related effects of finerenone because this trial was not powered to determine effects on eGFR change or clinical kidney outcomes. The incidence of a decrease in the eGFR of at least 30% and the incidence of acute kidney injury were low, without substantial differences between the two groups. The overall incidence of hyperkalemia was higher with finerenone than with 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 trial of finerenone suggests a favorable benefit–risk profile for persons with type 1 diabetes and CKD. Although other therapies for CKD such as SGLT2 inhibitors and GLP-1 receptor agonists have been studied in persons with type 2 diabetes,[20-23] treatment for CKD in persons with type 1 diabetes remains to be evaluated in clinical trials. A trial assessing the efficacy and safety of SGLT2 inhibitors in persons with type 1 diabetes and CKD is ongoing (ClinicalTrials.gov number, NCT06217302).

The 6-month treatment period and the use of a surrogate biomarker for the primary outcome are limitations related to the challenges of conducting large, long-term trials in this population. Although the trial had a geographically diverse population of persons with type 1 diabetes and CKD, approximately two thirds of the trial population were men. Thus, the findings are applicable only to persons who share the characteristics of the studied cohort and cannot be generalized.

In this trial involving adults with type 1 diabetes and CKD, finerenone resulted in a significantly greater decrease in the urinary albumin-to-creatinine ratio than placebo over 6 months of treatment.

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A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

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REFERENCES

1. Ogle GD, Wang F, Haynes A, et al. Global type 1 diabetes prevalence, incidence, and mortality estimates 2025: results from the International Diabetes Federation atlas, 11th edition, and the T1D index version 3.0. Diabetes Res Clin Pract 2025;225:112277.
2. Heerspink HJ, Cherney DZ, Groop P-H, et al. People with type 1 diabetes and chronic kidney disease urgently need new therapies: a call for action. Lancet Diabetes Endocrinol 2023;11:536-40.
3. Tuttle KR, Reynolds CL, Kornowske LM, et al. Prevalence and severity of chronic kidney disease in a population with type 1 diabetes from a United States health system: a real-world cohort study. Lancet Reg Health Am 2025;47:101130.
4. Jones TLZ, Kusmartseva I, Litovsky S, et al. The Cardiovascular Repository for Type 1 Diabetes (CaRe-T1D): an NIDDK initiative to advance understanding of mechanisms underlying cardiovascular disease in type 1 versus type 2 diabetes. Diabetes 2025;74:1078-88.
5. American Diabetes Association Professional Practice Committee. Chronic kidney disease and risk management: standards of care in diabetes — 2025. Diabetes Care 2025;48:Suppl 1:S239-S251.
6. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. N Engl J Med 1993;329:1456-62.
7. Tuttle KR, Ji L, Mathieu C, Rosen J. Addressing unmet needs for chronic kidney disease treatment in type 1 diabetes: a review. Diabetes Obes Metab 2026;28:16-26.
8. Mende CW, Samarakoon R, Higgins PJ. Mineralocorticoid receptor-associated mechanisms in diabetic kidney disease and clinical significance of mineralocorticoid receptor antagonists. Am J Nephrol 2023;54:50-61.
9. Luther JM, Fogo AB. The role of mineralocorticoid receptor activation in kidney inflammation and fibrosis. Kidney Int Suppl 2022;12:63-8.
10. Hollenberg NK, Stevanovic R, Agarwal A, et al. Plasma aldosterone concentration in the patient with diabetes mellitus. Kidney Int 2004;65:1435-9.
11. Bakris GL, Agarwal R, Anker SD, et al. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. N Engl J Med 2020;383:2219-29.
12. Pitt B, Filippatos G, Agarwal R, et al. Cardiovascular events with finerenone in kidney disease and type 2 diabetes. N Engl J Med 2021;385:2252-63.
13. Agarwal R, Filippatos G, Pitt B, et al. Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis. Eur Heart J 2022;43:474-84.
14. Heerspink HJL, Birkenfeld AL, Cherney DZI, et al. Rationale and design of a randomised phase III registration trial investigating finerenone in participants with type 1 diabetes and chronic kidney disease: the FINE-ONE trial. Diabetes Res Clin Pract 2023;204:110908.
15. Agarwal R, Tu W, Farjat AE, et al. Impact of finerenone-induced albuminuria reduction on chronic kidney disease outcomes in type 2 diabetes: a mediation analysis. Ann Intern Med 2023;176:1606-16.
16. Heerspink HJL, Agarwal R, Amor AJ, et al. Comparing CKD populations with T1D and T2D: a perspective based on the FINE-ONE and FIDELITY populations. Nephrol Dial Transplant 2025 September 15 (Epub ahead of print).
17. Heerspink HJL, Greene T, Tighiouart H, et al. Change in albuminuria as a surrogate endpoint for progression of kidney disease: a meta-analysis of treatment effects in randomised clinical trials. Lancet Diabetes Endocrinol 2019;7:128-39.
18. Navaneethan SD, Anker SD, Filippatos G, et al. Efficacy and safety of finerenone in patients with an acute change in estimated glomerular filtration rate in the prespecified FIDELITY pool analysis. Kidney Int 2025;108:136-44.
19. Kolkhof P, Lawatscheck R, Filippatos G, Bakris GL. Nonsteroidal mineralocorticoid receptor antagonism by finerenone — translational aspects and clinical perspectives across multiple organ systems. Int J Mol Sci 2022;23:9243.
20. Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. N Engl J Med 2019;380:2295-306.
21. Jongs N, Greene T, Chertow GM, et al. Effect of dapagliflozin on urinary albumin excretion in patients with chronic kidney disease with and without type 2 diabetes: a prespecified analysis from the DAPA-CKD trial. Lancet Diabetes Endocrinol 2021;9:755-66.
22. Cherney DZI, Zinman B, Inzucchi SE, et al. Effects of empagliflozin on the urinary albumin-to-creatinine ratio in patients with type 2 diabetes and established cardiovascular disease: an exploratory analysis from the EMPA-REG OUTCOME randomised, placebo-controlled trial. Lancet Diabetes Endocrinol 2017;5:610-21.
23. Perkovic V, Tuttle KR, Rossing P, et al. Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes. N Engl J Med 2024;391:109-21.