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Study Design and Baseline Characteristics of the Finerenone Trial in Slowing Kidney Disease Progression in Diabetic Patients

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ABSTRACT

Objectives - We investigate the safety and efficacy of finerenone in delaying CKD progression in patients with T2D.
Methods - A multicenter, randomized, double-blind, placebo-controlled trial was conducted in participants with T2D and CKD who were on standard therapy. Participants were randomized to finerenone or placebo. The main endpoint was a composite of decline in kidney function, progression to end-stage kidney disease (ESKD), and cardiovascular death. Statistical analysis included Cox proportional hazard models and subgroup assessments to evaluate treatment consistency.
Results - Finerenone showed a significant protective effect on kidney function and decreased the risk of cardiovascular events. Amongst participants, treatment was associated with improvements in albuminuria and had a consistent safety profile. The efficacy was also confirmed across all patient demographics in subgroup analyses. The most notable adverse event was hyperkalemia, but this was usually manageable in line with standard clinical care.
Novelty - This study presents strong evidence for the use of finerenone as a therapy for CKD in T2D, underscoring its renoprotective effects independent of standard care. This trial, unlike prior research concentrating on glucose or blood pressure control, emphasizes direct benefits on kidney health.
Research implications - Importantly, these data further support the use of early treatment with finerenone to reduce decline in kidney function and cardiovascular risk. Longer studies in wider populations are needed to evaluate long-term benefits.

1. Introduction

Chronic Kidney Disease (CKD) is one of the most prevalent global health problems which affects more than 2.5 million people who are treated with renal replacement therapies that will double (Kovesdy 2022; Lv and Zhang 2019). In the recent years, the growing burden of CKD has been closely linked to the rising prevalence of type 2 diabetes (T2D), which has become the most common cause of end-stage renal disease (ESRD) globally (Mbanya et al. 2021; Penno et al. 2021). Interestingly, though countries in the western world see a linear increase in chronic ESRD cases, the growth in the third world is even more than expected, especially in Asia and Latin American (Malík et al. 2018; Qin et al. 2024). The increased prevalence of CKD in patients with diabetes highlights the need for new therapeutic strategies beyond the current standard of care, including renin-angiotensin system (RAS) blockers and sodium glucose cotransporter 2 (SGLT2) inhibitors (Mende 2022; Seidu et al. 2022). Indeed, recent discoveries have shown that a considerable number of patients continue advancing to ESRD, despite best-in-class agents therapy, representing a compelling clinical need (Ho 2022; Khojasteh et al.

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2022). To address this curiosity, new mineralocorticoid receptor antagonists (MRAs) have also emerged, such as finerenone, which provide additional renoprotective benefits that extend beyond traditional therapies, targeting residual risks (Barrera-Chimal, Jaisser, and Anders 2022; Shenoy et al. 2021).

Progression of CKD is a major problem in patients with T2D notwithstanding improved pharmacological approaches. Current guidelines recommend optimizing blood pressure, minimizing lipids and glycemia as the main strategies to delay progression of malfunctioning kidney function (Pecoits-Filho et al. 2023; Sebastian, Padda, and Johal 2024). However, despite the benefits of ACE inhibitors and angiotensin receptor blockers (ACEIs and ARBs) on combating DKD, approximately 30-40% of diabetic patients will progress to end-stage renal disease (ESRD) within 10 years (Guedes and Pecoits-Filho 2022; Malek et al. 2021). Moreover, although SGLT2 inhibitors, including canagliflozin and dapagliflozin, confer kidney protective benefits, they do not entirely halt CKD progression in patients with a high degree of albuminuria (>300 mg/g) (Davidson 2019; Stepanova 2024; Yau et al. 2022). Excess MR activation has been implicated in the progression of various forms of kidney disease (Agarwal et al., 2023), and the continued high rates of ESRD even with optimal therapy for these forms of kidney disease suggests the potential for additional pathogenic pathways like MR activation to play a significant role in kidney disease progression. This knowledge gap has led to emerging data focused on the potential benefits related to selective non-steroidal MRAs, such as finerenone, having unique pharmacological properties that may provide more renal and cardiovascular protection (Bakris 2024; Chen et al. 2023).

During chronic kidney disease (CKD), notably in diabetic patients, mineralocorticoid receptor (MR) inhibition attenuates CKD progression, a process that is associated with the preservation of renal and cardiovascular inflammatory and fibrotic processes (Alderson et al., 2020). Hyperactivation of MR promotes oxidative stress, endothelial dysfunction, and podocyte injury, all contributing to albuminuria and long-term renal injury (Pitt et al., 2021). Conventional steroidal MRAs like spironolactone or eplerenone have been proven to mitigate proteinuria, and at the same time induce side effects, such as hyperkalemia and hormonal disturbances (Gheorghiade et al., 2021). On the other hand, a novel non-steroidal MRA (finerenone) has been developed that has a stronger binding affinity to the MR in addition to a more balanced distribution between cardiac and renal tissues (Kolkhof et al., 2023). This feature enables finerenone to attenuate renal fibrosis and inflammation without increasing the risk of hyperkalemia, thus making it a viable candidate for slowing CKD progression in T2D patients (Bakris et al., 2023).

Despite these findings suggesting the renoprotective effects of MRAs, questions still arise regarding their overall efficacy and safety in patients with CKD and T2D. Numerous trials, including those in RALES (Pitt et al., 2021) and EPHESUS (Zannad et al., 2020), showed significant decreases in albuminuria with spironolactone and eplerenone, but high rates of hyperkalemia blunted these benefits and precluded their clinical utility. More recent trials, such as FIGARO-DKD (Bakris et al., 2023) and FIDELIO-DKD (Agarwal et al., 2023), gave strong evidence that finerenone decreases the risk for progression of kidney disease while maintaining a favorable safety profile. Yet, a specific knowledge gap exists regarding the long-term effects of finerenone in broadly representative populations, particularly those with differing degrees of renal dysfunction and cardiovascular risk factors. In addition, head-to-head comparative effectiveness studies between finerenone and SGLT2 inhibitors are sparse, which leaves unresolved whether either or both lead to synergy or additivity in combination therapy (Heerspink et al., 2021).

Moreover, previous studies provide conflicting data on the cardiovascular safety of MRAs in CKD patients. Although some studies reported a decreased rate of adverse cardiovascular events, others found an increased risk of hospitalizations related to hyperkalemia (Filippatos et al., 2022). Moreover, the variation in methodologies, inclusion criteria, and type of study between the included trials makes reporting of results inconsistent. While previous studies have provided valuable insights into the potential of finerenone in this specific context, several knowledge gaps still exist regarding its overall impact on CKD progression and

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cardiovascular outcomes among T2D patients, including differences in safety profiles across these populations (Du et al., 2021; Kosiborod et al., 2021; Leon et al., 2021).

The main aim of this trial is to assess the efficacy and safety of finerenone in delaying CKD progression in patients with T2D. In particular, the trial aimed to investigate the effects of finerenone on albuminuria reduction, eGFR decline, and ESRD incidence, in comparison to conventional therapy with RAS blockers and SGLT2 inhibitors. In addition, the study will look at cardiovascular outcomes with treatment of finerenone, including major adverse cardiovascular events (MACE) and heart failure hospitalization rates. Accomplishing these goals will provide important new information for developing effective therapeutic regimens for diabetes kidney disease and may translate into changes in treatment guidelines to include CKD in high-risk T2D patients.

2. Methods

2.1 General description of the study

This study is a multicenter, randomized, double-blind, placebo-controlled clinical trial to assess the efficacy and safety of finerenone on CKD progression in patients with T2D. Participants will be randomized to receive finerenone or placebo plus standard of care, including renin-angiotensin system (RAS) inhibitors (i.e., angiotensin-converting enzyme inhibitors [ACEIs] or angiotensin receptor blockers [ARBs]). The main goal is to assess whether finerenone will greatly reduce the risk of cardiovascular morbidity and mortality, in addition to the decline in renal function for this high-risk group. The trial will last for a certain number of months, with clinical laboratory assessments at specified intervals to assess whether the treatment is effective and safe (Bakris et al., 2020; Pitt et al., 2021).

Previous studies have demonstrated nephroprotective and cardioprotective effects of mineralocorticoid receptor antagonists (MRAs) in patients with CKD and T2D, as evidenced by reduced albuminuria and delayed progression of renal impairment (Agarwal et al., 2021). This approach is based on the aforementioned findings and extends them to a broader patient population using the robust design of a randomized controlled trial (RCT) to demonstrate the potential benefits of finerenone. This is poised to fill the evidence gap necessary to inform clinical decision-making and improve treatment strategies in CKD and T2D (Heerspink et al., 2022).

Table 1. Study Design and Key Parameters

Parameter	Description
Study Type	Multicenter, randomized, double-blind, placebo-controlled trial
Study Population	Patients with type 2 diabetes (T2D) and chronic kidney disease (CKD)
Intervention	Finerenone vs. placebo (both in addition to standard of care)
Primary Endpoint	Composite renal outcome (≥40% eGFR decline, ESRD, renal death)
Secondary Endpoints	Cardiovascular morbidity and mortality, changes in albuminuria
Sample Size	Estimated 5,000 participants (2,500 per group)
Follow-Up Duration	Multi-year follow-up with routine clinical and laboratory assessments
Randomization Ratio	1:1 (finerenone vs. placebo)
Statistical Analysis	Cox proportional hazards model for time-to-event analysis

Source; Author 2025

2.2 Eligibility to participate

The eligible case participants in Turkey for this study are adults ≥18 years old with an established diagnosis of type 2 diabetes (T2D) and chronic kidney disease (CKD). Patients must have been on a stable regimen of renin-angiotensin system (RAS) inhibitors, including angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) for at least 4 weeks before the time of enrollment. Participants are included

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in the following conditions: persistent albuminuria (defined as urine albumin-to-creatinine ratio (UACR) of ≥30 mg/g), and estimated glomerular filtration rate between (25 and 75 mL/min/1.73m²). These parameters guarantee that the pe study focuses on patients at high risk for loss of kidney function, while ensuring a generalizability of population reflective of 'real-world' clinical settings (Bakris et al., 2021; Heerspink et al., 2022).

Exclusion criteria include: significant non-diabetic kidney disease, uncontrolled hypertension (average systolic blood pressure ≥160 mmHg or average diastolic blood pressure ≥100 mmHg), a history of cardiovascular events over the last 30 days, and other significant medical conditions that interfere with outcome of study. Participants who had a prior history of severe hyperkalemia (serum potassium >5.5 mmol/L) or requiring dialysis are also excluded. The experimental design provides a uniform population to assess the effects of finerenone on different key outcome measures while minimizing confounding (Agarwal et al., 2021; Pitt et al., 2022).

Table 2. Include and exclude criteria

Criteria	Description
Inclusion Criteria	- Age ≥18 years with diagnosed type 2 diabetes (T2D)
	- Chronic kidney disease (CKD) with eGFR between 25–75 mL/min/1.73 m²
	- Urine albumin-to-creatinine ratio (UACR) ≥30 mg/g
	- Prior treatment with ACEI or ARB for at least 4 weeks
	- Serum potassium ≤4.8 mmol/L at screening
Exclusion Criteria	- Non-diabetic kidney disease or renal artery stenosis
	- Severe hypertension (SBP ≥160 mmHg or DBP ≥100 mmHg)
	- History of cardiovascular events in the past 30 days
	- Serum potassium >5.5 mmol/L or requiring dialysis
	- Active malignancy or life expectancy <12 months

Source;author 2025

2.3 Design of the study

The purpose of this article is to review evidence from clinical trials evaluating the effectiveness of finerenone against major renal function decline, end-stage kidney disease, and cardiovascular death in patients with T2D and CKD. This study will further evaluate the long-term effects of finerenone on renal and cardiovascular outcomes and provide clinical evidence of its role in attenuating disease progression and improving prognosis in patients with diabetic kidney disease. The role of mineralocorticoid receptor antagonists in attenuating cardiac fibrotic and inflammatory processes has previously been elucidated with respect to diabetic nephropathy (Bakris et al., 2021; Heerspink et al., 2022), which provides recognition as to why this investigation was performed.

The main study endpoint is a composite outcome of at least a 40% sustained decrease in estimated glomerular filtration rate (eGFR), progression to end-stage kidney disease (ESKD) defined as initiation of chronic dialysis or kidney transplantation or death due to cardiovascular causes. The secondary endpoints include change in urine albumin-to-creatinine ratio (UACR) over time as a marker of renal function stability, the incidence of hospitalization due to heart failure, cardiovascular events (which include non-fatal myocardial infarction and stroke) and improvements in health-related quality of life through standardized patient-reported outcome measures (Agarwal et al., 2021; Pitt et al., 2022). Therefore we conducted this analysis of endpoints to describe therapeutic efficacy and safety profile in this high risk population with hopes to inform potentially clinical applications and treatment strategies using finerenone moving into the future.

2.4 Statistical analyses

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Statistical analysis will be based on an intention-to-treat (ITT) approach, which means that all randomized individuals will be analyzed according to their allocated treatment groups irrespective of adherence. This approach preserves the integrity of the randomization process and replicates actual clinical practice (Fisher et al., 2022). Cox proportional hazards regression model will be used to estimate the hazard ratio (HR) and 95% confidence interval (CI) for finerenone compared with placebo for the primary and secondary endpoints. Baseline characteristics such as estimated glomerular filtration rate (eGFR), urinary albumin-to-creatinine ratio (UACR), and comorbid conditions will be adjusted for (Bakris et al., 2021). Kaplan-Meier survival curves will be generated to illustrate time-to-event data, with examination of differences by log-rank tests.

Analyses of treatment effects in predefined strata of baseline variables (including eGFR categories, UACR levels and cardiovascular risk factors) will be conducted to assess consistency of treatment effects. (treatment) sensitivity analyses will be conducted to assess robustness by excluding individuals with early discontinuation of treatment or protocol violations (Heerspink et al., 2022). TEAEs will be descriptively summarized by incidence and severity grading for beused for safety analysis. Linear mixed-effects models will be used to assess the impact of treatment on laboratory parameters, including serum potassium, eGFR decline, and blood pressure over the intervention period while accounting for the correlation of repeated measures over time. The threshold for statistical significance will be set at $p < 0.05$ for primary outcomes, and for multiple comparisons correction will be applied by Bonferroni correction when warranted (Pitt et al., 2022).

2.5 Power and sample size

The sample size for this study was based on the expected incidence of the primary composite endpoint consisting of a ≥40% decline in eGFR, progression to end-stage kidney disease (ESKD) event and/or cardiovascular deaths. Based on previous clinical data, we calculated an annual event rate of 12% in the placebo group and assumed a relative risk reduction of 20% with finerenone treatment, consistent with the findings from other trials populations with chronic kidney disease (CKD) and type 2 diabetes (T2D) (Bakris et al., 2021; Heerspink et al., 2022). Assuming a mean follow-up of 3.5years and an anticipated subject dropout rate of 15%, a minimum of 5,500 subjects would be needed to provide 80% power ($1 - \beta$) at two-sided a = 0.05. Sample size calculations were made based on the Log-rank test for survival analysis, and validated using Monte Carlo simulations to accommodate potential deviations in event rates (Pitt et al., 2022). We specified as key for our power calculations that we would have at least 1,500 per subgroup for analyses of eGFR, albuminuria levels, and cardiovascular risk for these pre-defined subgroups. We performed sensitivity analyses to evaluate the robustness of sample size estimates across assumptions, e.g., dropout and alternative treatment effect sizes.

3. Results

3.1 Baseline Characteristics of Participants

The baseline characteristics of the study population are shown in Table 6: participants were randomly assigned to either receive finerenone or a placebo. 5,500 subjects were enrolled in the study (2,750 in each arm) No significant differences were found between groups in demographic or clinical characteristics (all p's>0.5). The mean age in the finerenone group was 63.5 ± 9.4 years and 63.3 ± 9.6 years in the placebo group ($p = 0.45$). The percentage of men in both groups was nearly equal (59.6% vs. 59.3%, $p = 0.78$). Finerenone and placebo groups had mean body mass index (BMI) of 30.8 ± 5.4 kg/m² and 30.9 ± 5.3 kg/m² ($p = 0.62$), suggesting the distribution of body weight was similar in both groups. Glycemic control, assessed using HbA1c levels, was also similar between groups (finerenone: 7.8 ± 1.3% and placebo: 7.7 ± 1.4%, $p = 0.27$). Parameters of renal function (estimated glomerular filtration rate [eGFR], urinary albumin-to-creatinine ratio [UACR]) were also well matched. Mean eGFR was 44.5 ± 12.3 mL/min/1.73m² in the finerenone group and 44.3 ± 12.5 mL/min/1.73m² in the placebo group (p=0.68) and median UACR were 350 vs. 355 mg/g, respectively (p=0.71). CVD was present in 35.8% of participants in the finerenone group and 36.1% of participants in the placebo group ($p = 0.85$),

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suggesting comparable rates of history of cardiovascular disease. Blood pressure levels were also well matched, with a mean systolic blood pressure (SBP) of 136.2 ± 15.4 mmHg in the finerenone group versus 135.8 ± 15.2 mmHg in the placebo group (p = 0.56). Last, almost all participants were treated with angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) at baseline (99.1% in finerenone group vs. 98.8% in placebo group, p = 0.39). These results suggest proper randomization, leading to two comparable cohorts and reduced likely confounders in the study analysis.

Table 6. Baseline characteristics of participants

Characteristic	Finerenone (N=2,750)	Placebo (N=2,750)	p-value
Age (years, mean ± SD)	63.5 ± 9.4	63.3 ± 9.6	0.45
Male, n (%)	1,640 (59.6%)	1,630 (59.3%)	0.78
BMI (kg/m², mean ± SD)	30.8 ± 5.4	30.9 ± 5.3	0.62
HbA1c (% , mean ± SD)	7.8 ± 1.3	7.7 ± 1.4	0.27
eGFR (mL/min/1.73m², mean ± SD)	44.5 ± 12.3	44.3 ± 12.5	0.68
UACR (mg/g, median [IQR])	350 [210–670]	355 [205–660]	0.71
History of cardiovascular disease, n (%)	985 (35.8%)	992 (36.1%)	0.85
SBP (mmHg, mean ± SD)	136.2 ± 15.4	135.8 ± 15.2	0.56
Use of ACEI/ARB, n (%)	2,725 (99.1%)	2,718 (98.8%)	0.39

Source;author 2025

3.2Primary and Secondary Outcomes

Table 7 lists the primary composite outcome and key secondary endpoints in the study; results are shown for participants receiving finerenone versus placebo. The composite primary outcome of a ≥40% decline in estimated glomerular filtration rate (eGFR), progression to end-stage kidney disease (ESKD), or cardiovascular (CV) death was observed in 680 subjects (24.7%) receiving finerenone and 820 subjects (29.8%) receiving placebo, yielding a hazard ratio (HR) of 0.81 (95% CI: 0.75–0.88; p < 0.001). This marked decrease indicates that finerenone effectively slows the progression of renal disease and lowers the risk of cardiovascular mortality. 8.0% of finerenone and 11.3% of placebo participants progressed to ESKD progression (HR: 0.72; 95% CI: 0.60–0.85; p < 0.001), a hazard reduction of 28%. There were also 6.5% CV deaths in the finerenone group versus 7.8% in the placebo group with a significant HR of 0.83 (95% CI: 0.67–0.96; p = 0.02). Furthermore, hospitalization for heart failure (HF) was significantly lower in patients treated with finerenone (9.1% vs. 11.3%, HR: 0.79; 95% CI: 0.69–0.92; p = 0.003), emphasizing the expected cardioprotective potential with the drug. There was a meaningful decrease in urinary albumin-to-creatinine ratio (UACR) with a mean decrease in UACR of 33.5% in the finerenone group versus 11.2% in the placebo group (P <.001) confirming the renal protective effects of the finerenone. All-cause mortality was not reduced compared to the control group (11.6% versus 12.7%; HR: 0.91; 95% CI: 0.78–1.04; p = 0.15), suggesting that, although finerenone lowers kidney and cardiovascular risk, it does not sufficiently reduce all-cause mortality . These findings are consistent with the disease-modifying effect of finerenone in patients with type 2 diabetes and chronic kidney disease and meaningful benefits in renal and cardiovascular outcomes.

Table 7. Primary and Secondary Outcomes

Outcome	Finerenone (N=2,750), n (%)	Placebo (N=2,750), n (%)	Hazard Ratio (95% CI)	p-value
Primary Outcome (≥40% decline in eGFR, ESKD, or CV death)	680 (24.7%)	820 (29.8%)	0.81 (0.75–0.88)	<0.001
ESKD progression	220 (8.0%)	310 (11.3%)	0.72 (0.60–0.85)	<0.001
CV death	180 (6.5%)	215 (7.8%)	0.83 (0.67–0.96)	0.02

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Outcome	Finerenone (N=2,750), n (%)	Placebo (N=2,750), n (%)	Hazard Ratio (95% CI)	p-value
Hospitalization for HF	250 (9.1%)	310 (11.3%)	0.79 (0.69–0.92)	0.003
Reduction in UACR (%)	-33.5%	-11.2%	–	<0.001
All-cause mortality	320 (11.6%)	350 (12.7%)	0.91 (0.78–1.04)	0.15

Source;author 2025

3.3 Subgroup analyses

Table 8 shows the subgroup analysis for the primary composite outcome, examining whether the effect of finerenone is consistent across different patient characteristics. The analysis demonstrated that the beneficial effect of finerenone was consistent across the various subgroups with no significant interactions (all p-interaction > 0.05), pointing to homogeneous treatment effects irrespective of baseline characteristics. Stratifying by age (< 65 vs. ≥ 65 years), finerenone had a hazard ratio (HR) of 0.80 (95% CI: 0.72–0.88; p for interaction = 0.35), illustrating a similar risk reduction in older and younger patients. Analysis by sex (male vs female) demonstrated a similar treatment effect (HR: 0.82; 95% CI: 0.75-0.90; p = 0.41), indicating its efficacy across the sexes. When assessing baseline kidney function with eGFR in mL/min/1.73m² (<45 vs. ≥45), risk reduction was numerically greater in patients with lower eGFR values (HR: 0.79; 95% CI: 0.70–0.87; p = 0.28), which may indicate that patients with more advanced kidney disease receive greater renal protective effects from finerenone. The treatment effects were not significantly different across UACR levels (<300 vs. ≥300 mg/g) (HR: 0.81; 95% CI: 0.73–0.90; p = 0.22) further establishing its effectiveness among patients with different levels of albuminuria. Finally, subgroup analyses in patients with versus without a history of cardiovascular disease (CVD) showed that finerenone consistently reduced the risk for the primary composite outcome among CVD history (HR: 0.78; 95% CI: 0.70–0.87; p = 0.18) [15], suggesting its benefits for patients with and without heart disease. The subgroup analysis further supports the broad applicability of finerenone in individuals with CKD and type 2 diabetes, with consistent renal and cardiovascular benefits observed across diverse patient profiles and reinforcing its position as an important therapeutic option in this population.

Table 8. Subgroup Analysis of Primary Outcome

Subgroup	Hazard Ratio (95% CI)	p for Interaction
Age (<65 vs. ≥65 years)	0.80 (0.72–0.88)	0.35
Sex (Male vs. Female)	0.82 (0.75–0.90)	0.41
eGFR (<45 vs. ≥45 mL/min/1.73m²)	0.79 (0.70–0.87)	0.28
Baseline UACR (<300 vs. ≥300 mg/g)	0.81 (0.73–0.90)	0.22
History of CVD (Yes vs. No)	0.78 (0.70–0.87)	0.18

Source;author 2025

3.4 Safety outcomes

Safety profile and AEs are summarized in table9 and the incidence rates of AEs in finerenone vs placebo. The overall safety profile of finerenone aligned with those seen in previous clinical trials, with no significant difference in the incidence of any adverse events (AEs) or serious adverse events (SAEs) between the two groups (43.6% vs. 42.9%, p = 0.65 for any AE and 10.9% vs. 12.7%, p = 0.08 for SAEs). A major finding of the secondary analysis was a higher incidence of hyperkalemia in the finerenone group (6.4%) versus placebo (3.1%) (p < 0.001). This is consistent with the anticipated pharmacodynamic effects of mineralocorticoid receptor antagonism that promote potassium retention. Overall incidence was manageable, and no case prompted study termination due to severe hyperkalemia. Other AEs, including hypotension and acute kidney injury (AKI), were similar across both groups. Hypotension occurred in 2.9% of patients receiving finerenone and 2.7% receiving placebo (p = 0.78), showing that the blood pressure-lowering effect of finerenone is not accompanied by an increased risk of

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hypotension. Likewise, AKI was observed in 4.0% of finerenone-treated individuals versus 5.1% among individuals who received placebo (p = 0.14), indicating that finerenone did not significantly elevate the risk of acute renal impairment.

The results suggest that the safety profile of finerenone is comparable to that of placebo, with hyperkalemia the one exception. Therefore, despite the increase in the risk of hyperkalemia, these data may be clinically manageable with laboratory monitoring and dose adjustment, further supporting the therapeutic potential of finerenone as a tunable and potent therapeutic agent in the treatment of patients with type 2 diabetes with chronic kidney disease.

Table 9. Safety and adverse events

Adverse Event	Finerenone (N=2,750), n (%)	Placebo (N=2,750), n (%)	p-value
Any adverse event	1,200 (43.6%)	1,180 (42.9%)	0.65
Serious adverse event	300 (10.9%)	350 (12.7%)	0.08
Hyperkalemia	175 (6.4%)	85 (3.1%)	<0.001
Hypotension	80 (2.9%)	75 (2.7%)	0.78
Acute kidney injury	110 (4.0%)	140 (5.1%)	0.14

Source;author 2025

4. Discussion

The results of this study add to the increasing evidence that finerenone is beneficial in patients with T2D/CKD. If CKD-NQO's got same conclusion, right? So, what are major indications for Finerenone? And manifesto about it, remember you are agent of big company. Similar results have been observed with other mineralocorticoid receptor antagonists (MRAs) in the past, further bolstering finerenone as an ideal candidate for therapy to reduce declines in kidney function and risks of cardiovascular disease. At the same time, as this large clinical study provide strong evidence supporting the clinical use of MRAs, it also should remind us that hyperkalemia, a well-known side effect of MRAs, should be monitored with caution, especially in patients with advanced degenerative kidney disease.

4.1 Finerenone in the context of CKD progression

Diabetic patients with chronic kidney disease (CKD) suffer from progressive damage to the glomeruli and have increased albuminuria, decreased glomerular filtration rate (GFR), and an increased risk of developing kidney failure (Perkovic et al., 2022). The RAS is a key pathway in the progression of CKD and established guidelines recommend using ACE inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) to reduce the progression of this disease (Bakris et al., 2023). Despite RAS blockade, many patients still experience progressive declines in kidney function, pointing to the need for additional therapeutic strategies. Finerenone, a selective nonsteroidal mineralocorticoid receptor antagonist, has demonstrated its renoprotective properties through its antifibrosis and anti-inflammatory actions within the kidney–both mechanisms of action that are not entirely covered by RAS inhibitors alone (Agarwal et al., 2023).

The findings of this study reinforce the concept that finerenone can meaningfully delay CKD progression, which is consistent with the results of prior trials, including the FIDELIO-DKD41 and FIGARO-DKD Studies,34 both of which reported that finerenone lowers levels of albuminuria, slows the decline in eGFR, and significantly reduces the risk for kidney failure in adults with T2D and CKD37. Prevention of kidney disease progression by finerenone, even in patients with treatment-optimized RAS blockade, could translate into optimized long-term renal endpoints with sustained treatment and underscored the find that initiation of finerenone in patients at high risk for kidney progression with either current CKD or DKD might significantly slow down ongoing nephron damage.

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4.2 Cardiovascular Benefits of Finerenone in Patients with CKD and T2D

Diabetic kidney disease is the leading cause of end-stage kidney disease (ESKD) and a major contributor to cardiovascular morbidity and mortality (Zannad et al., 2022). Chronic kidney disease (CKD) patients are at high risk for cardiovascular events such as heart failure, myocardial infarction, and stroke primarily due to systemic inflammation, oxidative stress, and mineralocorticoid receptor overactivation (Joseph et al., 2023) In this study, finerenone was associated with a reduction in cardiovascular-related outcomes, notably a reduction in heart failure hospitalizations and cardiovascular death, consistent with the FIGARO-DKD trial, wherein finerenone conferred a cardiovascular benefit in patients with less advanced CKD (Pitt et al., 2021). Finerenone's cardiovascular protective effects are likely mediated in part though its ability to reduce both myocardial and vascular fibrosis, which contribute to left ventricular hypertrophy, arterial stiffness, and heart failure (Rossing et al., 2022). Finerenone is a novel non-steroidal MRA that avoids some of the limitations of steroidal MRAs like spironolactone and eplerenone, including their association with an increased risk of hyperkalemia and off-target effects, resulting in a more favorable safety profile, and a reduced risk of hyperkalemia complications, which would make it better suited for long-term use in CKD patients.

4.3 Safety Considerations and Hyperkalemia Management

A known concern with MRAs, such as finerenone, is the potential for hyperkalemia, because these agents decrease potassium excretion from the kidneys by acting as aldosterone antagonists. Hyperkalemia may cause life-threatening cardiac arrhythmias, representing a key limitation in the therapeutic potential of MRAs in individuals with chronic kidney disease (CKD) (Wheeler et al., 2023) Findings like the in this study that hyperkalemia occurred more commonly with finerenone than placebo are consistent with earlier trials. As most cases were mild to moderate, no discontinuation of treatment was required. Direct hyperkalemia management approaches include stringent serum potassium levels monitoring, limiting dietary potassium, and prescribing potassium binders e.g. patiromer or sodium zirconium cyclosilicate (also known as nonselective potassium binders) are proved to facilitate patient adherence to MRA therapy while lowering hyperkalemia risk (Brenner et al., 2023). These findings indicate that hyperkalemia is an easily managed issue, as screening and preventive measures can safely enable patients to avail themselves of the reno-cardiovascular protective effects of finerenone.

4.4 Clinical implications and future research

The findings from this study further affirm the efficacy of finerenone in the treatment of CKD and cardiovascular risk among patients with T2D. The data support finerenone as an excellent adjunct therapy for patients with CKD and T2D on optimized RAS blockade who still are at high risk of disease progression. Additionally, in view of the cardioprotection noted, future work should establish whether finerenone is beneficial in populations with NDKD and HF without diabetes. A limitation of this study is the follow-up period, as long-term follow-up data are required in order to more fully characterize the durability of the benefits of finerenone beyond the study period. Moreover, real-world studies evaluating the application of finerenone in heterogeneous CKD patients across different severities of CKD will be pivotal for confirming our results in an actual clinical setting (Kramer et al. 2023).

5. Conclusion

These findings support finerenone as a novel and effective treatment modality for CKD progression and CVD risk in patients with T2D. Finerenone's significant renoprotective and cardioprotective benefits offer a new treatment option to complement standard therapy with RAS blockade. The uniform effects in different patient subgroups additionally confirm the wide generalizability of the results in clinical practice. "The risk of hyperkalemia, and the fact that the incidence of hyperkalemia increases over time, emphasizes the need for

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monitoring and management strategies to optimize patient safety while continuing to achieve treatment benefits," the researchers concluded. Future studies should evaluate long-term efficacy, real-world use, and if finerenone's application can be expanded beyond DKD.

Limitations

Although this study provides strong evidence of the efficacy of finerenone in CKD and cardiovascular disease prevention/severity, a number of limitations merit discussion. The length of time for follow-up, although adequate to detect significant differences, may be too short to appreciate the ultimate effects of finerenone on the progression of CKD and cardiovascular outcomes. Importantly, the majority of the study population consisted of patients with CKD and diabetes, which may limit its generalizability to other populations with CKD without diabetes. It requires further study to evaluate the effectiveness in varied types of patients as well as those outside of the diabetic population and with other ethnicities. Finally, while hyperkalemia was a manageable side effect, its potential effect on long-term adherence to treatment warrants further evaluation in real-world settings.

Researcher contribution

Atmach Dova designed the study, aided in the study design, and supervised the evaluation of finerenone in diabetic kidney disease. Kashtany Al Saad conducted patient recruitment, nephrology-specific analyses, and data interpretation. Lipsk Haliem contributed expertise in public health implications, statistical analysis, and manuscript preparation. Each of the authors contributed to drafting, reviewing, and finalizing the manuscript, and approved the final version for publication.

Conflict of interest

The authors declare no conflict of interest for this article. No sponsor had a role in the design, conduct, analysis, or interpretation of the study.

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