Finerenone for Cardiorenal Protection in Diabetic CKD: Impact on Renal Function Decline and Heart Failure

Introduction:

The parallel rise in chronic kidney disease (CKD) and type 2 diabetes mellitus (T2D) has emerged as a major global health challenge, contributing substantially to premature mortality and reduced quality of life.[1,2] Epidemiological data suggest that the age-standardized mortality rate attributable to diabetic CKD more than doubled between 1990 and 2013, while individuals with early-stage CKD and T2D may experience a reduction in life expectancy of up to sixteen years.[3,4] Cardiovascular (CV) events remain the predominant cause of death in this population, with estimates indicating a sixfold increase in CV mortality compared with the general population. Among these, sudden cardiac death frequently accounts for a considerable proportion of overall CV fatalities. Declines in estimated glomerular filtration rate (eGFR) and the persistence of albuminuria have been independently associated with heightened risks of both all-cause and CV mortality, emphasizing the clinical importance of maintaining renal function.[5] In addition, infections and certain malignancies appear to contribute, albeit to a lesser extent, to the overall mortality burden among patients with diabetic kidney disease.[6,7]

Pharmacologic interventions targeting the renin–angiotensin–aldosterone system (RAAS), such as angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), have long been established as standard therapy for slowing CKD progression and controlling hypertension in individuals with T2D.[8] However, despite their renoprotective effects, these agents have shown limited capacity to reduce all-cause mortality.[9] Mineralocorticoid receptor antagonists (MRAs) offer additional cardiorenal benefits, yet the clinical use of traditional

steroidal MRAs, including spironolactone and eplerenone, is frequently constrained by adverse effects such as hyperkalaemia, breast tenderness, and gynaecomastia[10].

Finerenone, a newer nonsteroidal MRA, has been developed to address these limitations. Its higher receptor selectivity and favorable safety profile enable effective cardiorenal protection with a reduced risk of hyperkalaemia and the absence of hormonal side effects. Evidence from the pivotal Phase III trials—FIDELIO-DKD and FIGARO-DKD—demonstrated that finerenone significantly reduces the risk of kidney disease progression and CV events when added to optimized ACEI or ARB therapy. Subsequent analyses indicated that these clinical benefits are largely independent of changes in metabolic or hemodynamic parameters, with only modest blood pressure reduction contributing to the observed outcomes. The pooled FIDELITY analysis, encompassing more than 13,000 participants across the CKD spectrum, provided comprehensive evidence supporting finerenone's efficacy in reducing both renal and cardiovascular mortality. Collectively, these findings underscore finerenone's emerging role as an evidence-based therapeutic option in the integrated management of diabetic CKD.[11,12]

This study, therefore, seeks to evaluate the clinical effectiveness and safety of finerenone in routine practice, providing context-specific evidence to guide therapeutic decision-making and to strengthen the continuum of cardiorenal protection in diabetic kidney disease.

OBJECTIVE:

To assess the effect of Finerinone on slowing renal function decline and improving cardiovascular outcomes, particularly heart failure risk, in patients with diabetic CKD.

OPERATIONAL DEFINITIONS:

- **Chronic Kidney Disease (CKD):**

  Defined by an **estimated glomerular filtration rate (eGFR)** of **25–<75 mL/min/1.73 m²** and/or **albuminuria**, quantified as a **urine albumin-to-creatinine ratio (UACR) ≥30 mg/g**.

- **Renal Function Decline:**

  Progressive worsening of kidney function is defined as a **sustained ≥40% reduction in eGFR from baseline**, **progression to kidney failure (ESKD)**, or **renal death**.

- **End-Stage Kidney Disease (ESKD):**

  Defined as **initiation of chronic dialysis or kidney transplantation**, or a sustained **eGFR <15 mL/min/1.73 m²**.

- **Heart Failure (HF) Event:**

  Defined as **hospitalization for new or worsening heart failure**, confirmed by clinical evidence of fluid overload and the requirement for intravenous therapy or hemodynamic support.

- **Cardiovascular (CV) Event:**

  Includes **CV death, non-fatal myocardial infarction, non-fatal stroke, or hospitalization for heart failure (HHF)** — forming the composite cardiovascular outcome measure in the finerenone studies.

- **Finerenone Therapy:**

  Finerenone is a **selective, non-steroidal mineralocorticoid receptor antagonist (ns-MRA)** administered **orally at 10–20 mg once daily**. The dose is titrated based on serum potassium and eGFR, and therapy is used **in addition to a maximally tolerated ACE inhibitor or ARB**.

- **Hyperkalaemia:**

  Defined as a **serum potassium level >5.5 mmol/L**, which served as a safety threshold for dose adjustment or discontinuation in the parent trial data.

- **Albuminuria:**

  Measured as **urinary albumin-to-creatinine ratio (UACR)**, with categories of **moderately increased (30–300 mg/g)** and **severely increased (>300 mg/g)** albuminuria, per KDIGO classification used in the trial protocols.

- **eGFR Measurement:**

  Estimated glomerular filtration rate calculated using the **CKD-EPI formula**, standardized for body surface area (mL/min/1.73 m²).

MATERIALS AND METHODS:

Study Design: Single Arm Before/After Trial.

Study setting: Department of Medicine Unit Nishtar Medical University & Hospital Multan.

Duration of Study: 06 months after approval of synopsis.

Sampling technique: Non-probability consecutive sampling.

Sample Size: 88

The sample size was calculated using the paired *t*-test formula for a within-subject continuous outcome, taking mean change in estimated glomerular filtration rate (eGFR) as the primary variable. Assuming an expected mean paired difference of 3 mL/min/1.73 m² with a standard deviation of 10 mL/min/1.73 m², a two-sided significance level (α) of 0.05, and a statistical power of 80 %, a minimum of 88 evaluable patients would be required. To compensate for an anticipated 20–25 % attrition rate and to improve precision of estimates, the target enrolment will

be **120 patients**. This sample size is considered adequate for detecting a clinically meaningful change in eGFR over 12 months in patients with type 2 diabetes and chronic kidney disease receiving finerenone in addition to standard renin–angiotensin system inhibition.

SAMPLE SELECTION:

Inclusion Criteria:

- Adults aged ≥18 years.
- Diagnosed cases of type 2 diabetes mellitus.
- Chronic kidney disease with eGFR 25–90 mL/min/1.73m² and/or UACR ≥30 mg/g.
- On stable ACE inhibitor or ARB therapy for at least 4 weeks.
- Serum potassium ≤4.8 mmol/L.
- Provided written informed consent.

Exclusion Criteria:

- Symptomatic heart failure (NYHA class II–IV).
- eGFR <25 mL/min/1.73m² or on maintenance dialysis.
- Known non-diabetic kidney disease.
- Recent major cardiovascular event (within 30 days).
- Serum potassium >4.8 mmol/L or history of severe hyperkalaemia.
- Contraindication or hypersensitivity to finerenone.
- Pregnancy or lactation.
- Any condition limiting compliance or follow-up.

DATA COLLECTION:

After approval of the synopsis, patients fulfilling the inclusion criteria will be enrolled from the nephrology and cardiology departments. Baseline data including demographic details

(age, gender, BMI), duration of diabetes, blood pressure, comorbid conditions, and current medications will be recorded. Laboratory investigations such as serum creatinine, eGFR, urine albumin-to-creatinine ratio (UACR), serum potassium, HbA1c, and lipid profile will be obtained at baseline and at each follow-up visit. Patients will be followed at 1, 3, and 6 months for reassessment of renal function and occurrence of heart failure events. All data will be documented on a structured proforma specifically designed for this study. (Annexure-I).

DATA ANALYSIS PLAN:

Data will be analyzed using SPSS version 29. Continuous variables including age, systolic and diastolic blood pressure, eGFR, urine albumin-to-creatinine ratio (UACR), serum potassium, and HbA1c will be expressed as mean ± standard deviation, while categorical variables such as gender, presence of hypertension, and occurrence of heart-failure hospitalization will be presented as frequency and percentage. The primary outcome will be the mean change in eGFR from baseline to 6 months. Paired *t*-test or repeated-measures ANOVA will be applied for within-subject comparisons of continuous variables, and logistic regression will be used to explore predictors of renal function decline. Correlation analyses will assess relationships between change in eGFR, UACR, and serum potassium. Kaplan–Meier survival analysis and Cox proportional hazards regression will be performed for time to first heart-failure hospitalization where applicable. A p-value < 0.05 and 95 % confidence intervals will be considered statistically significant.

References:

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1. I will abide by the declaration of World Medical Association (WMA) made at Helsinki regarding the ethical principles for medical research involving human subjects.
2. The health of the patients will be the prior consideration.
3. The procedure shall be explained to the subjects clearly and expressed consent shall be obtained.
4. All procedures shall be kept aseptic and painless.
5. The confidentiality of the information shall be assured and maintained.
6. Data shall be used for publication only.

Principal Investigator

Dr. Muhammad Awais Danish

Supervisor

Prof Dr. Muhammad Zafar Iqbal

CONSENT FORM

Finerenone for Cardiorenal Protection in Diabetic CKD: Impact on Renal Function Decline and Heart Failure

I---------- S/D/W/ of ---------- acknowledge that I have been informed in detail about the research titled "**Finerenone for Cardiorenal Protection in Diabetic CKD: Impact on Renal Function Decline and Heart Failure**" I am also informed regarding the purpose, nature, aims and objectives of the study. All the information in this study will be kept confidential and my name and other data will be utilized only for research purposes. I have been informed that I can be asked any type of question related to study. I have also been informed that this research is not just for the benefit of a single person but for the humanity at large. If after briefing I refuse to participate there will be no obligation on my side. I shall be treated in routine. I may withdraw my name anytime from study and I shall not be forced to continue. I give my consent and willingness to consider myself in this study.

Name of Patient; ----------

Signature / thumb impression; ----------

Date; ----------

Counseling Doctor;

Name;----------

Designation; - ----------

Signature; ----------

اجازت نامہ برائے تحقیق میں شرکت

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کمپیوٹرائزڈ شناختی کارڈ نمبر _____

میں _____ قبول کرتا/ کرتی ہوں کہ مجھے _____ نے اپنی تحقیق کے اغراض و مقاصد، ساخت اور اس میں شامل ہونے والے آپریشن کے فوائد و نقصانات سے آگاہ کر دیا ہے۔ اس سے منسلک تمام معلومات کو صیغہ راز میں رکھا جائے گا۔ میرا نام اور مجھ سے حاصل ہونے والی معلومات کو صرف تحقیق کے لیے استعمال کیا جائے گا۔ جس کی بدولت پوری انسانیت کی بھلائی ہو گی۔ میں جب چاہوں یعنی کے بعد از یا دوران تحقیق، اس تحقیق میں شمولیت سے انکار کر سکتا/ سکتی ہوں اور میری بیماری کا علاج پہلے کی طرح کیا جائے گا اور مجھ پر اس تحقیق میں شامل ہونے پر کسی طرح کا جبر نہیں کیا جائے گا اور میں اپنے پورے ہوش و حواس میں اس تحقیق میں شامل ہونے کا اظہار کرتا/ کرتی ہوں۔

دستخط/نشان انگوٹھا _____ دستخط/نشان انگوٹھا _____

مریض/مریضہ _____ گواہ _____

دستخط کنندہ _____

ڈاکٹر _____

ANNEXURE-I

Finerenone for Cardiorenal Protection in Diabetic CKD: Impact on Renal Function Decline and Heart Failure

Serial No.	Serial No.	Details / Units / Code	Baseline	1 Months	3 Months	6 Months
1	Study ID / Hospital No.					
2	Age (years)					
3	Gender	☐ Male ☐ Female				
4	Body Mass Index (kg/m²)					
5	Duration of Diabetes (years)					
6	Duration of CKD (years)					
7	Blood Pressure (mmHg)					
8	HbA1c (%)					
9	Serum Creatinine (mg/dL)					
10	Estimated GFR (mL/min/1.73 m²)	CKD-EPI				
11	Urine Albumin-to-Creatinine Ratio					

	(UACR) (mg/g)					
12	Serum Potassium (mmol/L)					
13	Lipid Profile (TC / LDL / HDL / TG)					
14	Finerenone Dose (mg/day)	10 mg ☐ 20 mg ☐				
15	Use of ACEi/ARB	☐ Yes ☐ No				
16	Use of SGLT2 inhibitor	☐ Yes ☐ No				
17	Presence of Hypertension	☐ Yes ☐ No				
18	History of Heart Failure	☐ Yes ☐ No				
19	Hospitalization for Heart Failure	☐ Yes ☐ No Date: ____				
20	Occurrence of Hyperkalaemia (K^+ > 5.5 mmol/L)	☐ Yes ☐ No				
21	Drug Discontinuation / Adverse Events	Specify: _____				
22	Remarks / Investigator Notes					