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Editorial

Finerenone: A Pillar for the Treatment of Diabetic Kidney Disease

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Abstract: Diabetic kidney disease[DKD] has the potential to progress to end stage kidney disease as well as increase the risk of cardiovascular disease.. Remarkable advances have occurred in management of DKD., This review highlights the role of finerenone a novel nonsteroidal minerallocorticoid receptor antagonist in DKD.

Keywords: Diabetic kidney disease, MRA, Proteinuria

1. Introduction

The number of individuals with Diabetes Mellitus (DM) increased from 200 million in 1990 to 830 million in 2022. This rise is prevalence is faster in low- and middle-income countries than in high-income ones [1]. Concurrently, there is a global increase in the incidence of chronic kidney disease [CKD] and a recent report showed that the clinical burden of CKD in Americas, Europe and Asia Pacific is expected to reach 436.6 million cases in the period from 2022 to 2027, corresponding to an increase of 5.8% [2]. NHANES data also show that 15% of US adults are affected by Cardiovascular-Kidney Metabolic syndrome of stages 3 and 4 [3]. Moreover, Diabetic kidney disease [DKD] has been reported to affect 20–40% of individuals diagnosed with DM. Diabetes Mellitus is the leading cause of end-stage renal disease worldwide, causing significant morbidity and reduced life expectancy [4].

Since 2019, numerous clinical studies have progressed our treatment of diabetic kidney disease. In 2022, Kidney Disease Improving Global Outcomes [KDIGO] released updated guidelines for managing diabetes and CKD [4]. Moreover, there are recommendations to consider four pillars of goal-directed medical management [GDMT] to optimize cardiorenal protection [5]. The American Society of Nephrology's Diabetic Kidney Disease Collaborative Initiative emphasized the importance of reducing the gap between knowledge and implementation [6].

Finerenone is a novel selective nonsteroidal mineralocorticoid receptor antagonists [MRA] that is recommended as one of the four pillars of GDMT. In this Editorial, we discuss the current state of knowledge of finerenone and its role in DKD and CKD is discussed.

2. Pharmacology

Mineralocorticoid receptors (MR) are intracellular steroid hormone receptors primarily expressed in the kidney and colon. They regulate electrolyte balance and blood pressure by influencing sodium, water, and potassium excretion. Studies have detected MR in the heart, blood vessels, macrophages, white adipose tissue, and brain regions such as the amygdala and hippocampus. They interact with glucocorticoid receptors to maintain homeostasis.

Overactivation of MR upregulates gene expression of pro-inflammatory and profibrotic factors, resulting in inflammation and fibrosis of cardiorenal tissue [7].

Mineralocorticoid Receptor Antagonists [MRA] inhibit the actions of aldosterone at the MR, thereby blocking their effects. Clinical trials have demonstrated the cardiorenal benefits of MRA, observing that it decreases proteinuria and ameliorates CHF.

Since the discovery of the first-generation Spironolactone, several advancements in MRA have been made. Spironolactone is a non-selective steroidal MRA that binds to androgen and progesterone inhibitors. It has a greater affinity to kidney tissues compared to cardiac tissues, but it is not indicated in the treatment of CKD. Eplerenone is a second-generation steroidal MRA that is a less potent, highly selective MRA with equal affinity for kidney and heart receptors. Finerenone is a novel third-generation nonsteroidal MRA with a "bulky" structure and strong affinity and selectivity for the mineralocorticoid receptor.

3. Clinical Studies

Preclinical studies have demonstrated reduced proteinuria, which formed the basis for the clinical studies discussed here. The ARTS-Diabetic Nephropathy [ARTS-DN] study was the pioneer placebo-controlled phase 2B study to evaluate the safety and efficacy of varying doses of finerenone in diabetics with kidney disease on baseline RASi [8]. A dose-dependent reduction in proteinuria independent of blood pressure changes was observed. Hyperkalemia resulting in discontinuation of the study occurred in 1.6% of the patients. Following the positive results, further Phase III trials were conducted. The inclusion criteria for phase III included a serum potassium ≤4.8 mmol/l and e-GFR ≥25 mL/min/1.73 m^2.

Phase III Studies

The Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (Fidelio-DKD) study which evaluated the efficacy of finerenone reported that patients had a baseline mean e-GFR of 44 ± 12.5 mL/min/1.73 m^2 and a median UACR of 852 mg/g, with 87.5% of patients having macroalbuminuria. The median follow-up period was 2.6 years and for patients who received RASI as background therapy, finerenone reduced the primary renal outcome by 18% and the cardiovascular outcome by 13% [9].

The Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease (Figaro-DKD) study enrolled 7434 patients with a mean estimated glomerular filtration rate (e-GFR) of 67.8 ± 21.7 mL/min/1.73 m^2 and a median urinary albumin-to-creatinine ratio (UACR) of 308 mg/g. Participants were assigned to receive either finerenone or a placebo. It was observed that finerenone resulted in a 13% reduction in the occurrence of the primary cardiovascular outcome. Moreover, there was a 23% reduction in key secondary renal endpoints.[10]

In the Fidelity Analysis of Finerenone in CKD and type 2 Diabetes Mellitus (combining FIDELIO DKD and Figaro DKD data), the mean e-GFR was 57.6 ± 21.7 mL/min/1.73 m^2, and the median UACR was 515 mg/g. Finerenone administration reduced the composite cardiovascular outcome by 14%, primarily by decreasing heart failure, and improved key secondary kidney outcomes by 23%. It also lowered the relative risk of a sustained >57% decrease in e-GFR from baseline by 30% and reduced the incidence of ESRD by 20%, with the exception of time to death from renal causes.[11]

4. Safety and Tolerability

The most frequently reported side effect is hyperkalemia. In the Fidelity analysis, the incidence of hyperkalemia (serum potassium above 5.5) was twice as high in patients treated with finerenone compared to those that received a placebo (14% vs. 6.9%). The risks of hyperkalemia increased with higher baseline serum potassium levels, lower estimated glomerular filtration rates (e-GFR), and higher urinary albumin-to-creatinine ratios (UACR). The study was discontinued due to hyperkalemia in 1.7% of patients treated with finerenone compared to 0.6% in the placebo group.

A post-hoc analysis of Fidelio-DKD explored the incidence and predictors of hyperkalemia (serum K of 5.5), and found that it occurred in 21% of patients treated with finerenone compared to 9.2% of those receiving a placebo. Baseline risk factors identified as potential risk factors included female sex, lower e-GFR, higher UACR, beta-blocker use, and the use of finerenone over placebo [12].

Similarly, in a recent FINEARTS-HF study, finerenone increased the risk of potassium levels above 5.5 mmol from 6.9% in the placebo arm to 14.3% in the finerenone group [13].

5. Finerenone in Combination with SGLT2 Inhibitors or GLP-1 Agonist

Fidelity pooled analysis showed that among 877 patients (6.7%) who received SGLT2 inhibitors and 944 patients (7.2%) administered with GLP-1 agonists, the benefit of finerenone on cardiovascular and kidney

outcomes was significant in patients treated with either SGLT2 inhibitors or GLP-1 agonists. Less frequent hyperkalemia adverse events and lower urinary albumin-to-creatinine ratio were detected in those receiving both finerenone and SGLT2 inhibitors compared to those who only received finerenone.

CONFIDENCE is a randomized, controlled study designed to investigate the effects of the combination therapy. Patients with Type 2 Diabetes, stage 2–3 CKD, and a urine albumin: creatinine ratio (UACR) between 300 and 5000 mg/g will be enrolled in this study. The primary objective is to determine whether a six-month dual therapy regimen of finerenone and the SGLT2 inhibitor empagliflozin can effectively reduce albuminuria compared to using either agent separately [14].

6. Other Studies in Progress

The Finerenone Non-Diabetic Chronic Kidney [FIND-CKD] is a randomized, double-blind, placebo-controlled Phase III trial for patients with CKD of non-diabetic origin. Adults with a UACR of 200–3500 mg/g and eGFR of 25–90 mL/min/1.73 m^2, on the highest tolerable dose of a renin-angiotensin system (RAS) inhibitor, were randomly assigned to receive finerenone (10 or 20 mg based on eGFR) or placebo daily. The trial aims to evaluate the efficacy and safety of adding finerenone to standard care in delaying CKD progression in non-diabetic patients [15].

FINE-ONE (NCT05901831) is a 7.5-month, randomized, placebo-controlled, double-blind phase III trial comprising 220 adults with type 1 diabetes. The enrolled participants have a UACR of 200–5000 mg/g (22.6–565 mg/mmol) and an eGFR of 25–90 mL/min/1.73 m^2. The trial aims to determine whether finerenone, in combination with a RAAS inhibitor, can slow kidney disease progression by evaluating changes in UACR from baseline to 6 months. The study will also monitor safety by recording adverse events for more than 7 months. Hyperkalaemia, a known side effect of finerenone, will be tracked as an adverse event of special interest [16].

7. Guidelines

Several global guidelines have recommended finerenone as a drug for preventing the progression of CKD and heart disease in patients with diabetic CKD who are already receiving RAS inhibitors.

Recently, the American Diabetes Association [ADA] standards of care [2025] recommended the application of a nonsteroidal MRA to reduce cardiovascular events and CKD progression in patients with CKD and albuminuria if eGFR is ≥25 mL/min/1.73 m^2 [17]. The guidelines also recommend that potassium levels should be monitored [Grade A recommendations]. This ADA recommendation is consistent with recommendations by the KDIGO [4].

8. Conclusion

In patients with T2DM and eGFR greater than 25 mL/min/1.73 m^2 accompanied by albuminuria, finerenone can reduce the progression of CKD and the incidence of end-stage kidney disease (ESKD), as well as decrease the occurrence of heart failure and cardiovascular events. It is advisable to regularly monitor serum potassium levels and make necessary dose adjustments to mitigate hyperkalemia. Alongside RAS inhibitors, SGLT2 inhibitors, and GLP-1 antagonists, finerenone is one of the four pillars in the optimal management of diabetic kidney disease. Its role in CKD and Type 1 diabetes mellitus (DM) is currently under investigation.

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Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

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