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Efficacy and Safety of Finerenone in Patients with Heart Failure, Chronic Kidney Disease, and Type 2 Diabetes: A Comprehensive Review of the FINE-HEART Pooled Analysis

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Abstract

This review article discusses the FINE-HEART pooled analysis, which has investigated the efficacy and safety of finerenone in patients with heart failure (HF), chronic kidney disease (CKD), and type 2 diabetes (T2D). Finerenone is a non-steroidal MRA, which delivers marked value in reducing cardiovascular mortality, hospitalization due to heart failure, and the progression of kidney disease, especially in patients with overlapping cardiovascular-kidney-metabolic (CKM) conditions. Several trial results, including FIDELIO-DKD and FIGARO-DKD, were combined to provide an overall overview of the treatment outcomes. The following review discusses the study design, key results, and clinical implications of finerenone use in high-risk populations and concludes that finerenone presents substantial benefits in the management of patients with CKD, HF, and T2D while maintaining an acceptable safety profile.

Keywords*: Cardiovascular Outcomes, Chronic Kidney Disease, Finerenone, Heart Failure, Mineralocorticoid Receptor Antagonist, Type 2 Diabetes.*

Introduction

Heart failure often presents as part of a clinical syndrome that includes chronic kidney disease and type 2 diabetes and is sometimes referred to as the cardiovascular-kidney-metabolic triad. [1]. The beginning and progression of cardiovascular illnesses, chronic kidney disease (CKD), and metabolic disorders can often occur in the same person and may have similar pathophysiological pathways [2].

These all carry high morbidities and mortalities and pose major challenges to treatment. Current standards of care in heart failure include beta-blockers, ACE inhibitors, and MRAs; however, these are complicated by hyperkalemia and/or worsening kidney function that limit options for their use.

So far, finerenone is a non-steroidal MRA and thus has a potential indication for treatment in such high-risk groups. The classic steroidal MRAs have been associated with the development of hyperkalemia due to less selectivity of mineralocorticoid receptor inhibition. Finerenone acts on mineralocorticoid receptors; hence, it will selectively provide cardiovascular and renal protection, reducing such risks for hyperkalemia. The FINE-HEART pooled analysis is, therefore, designed to investigate the broad effects of finerenone treatment on cardiovascular outcomes, heart failure hospitalizations, and renal function in patients with CKD, HF, and T2D. The review, therefore, gives pooled analyses that provide insights into the clinical use of finerenone in managing these overlapping diseases.

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Materials and Methods

The FINE-HEART pooled analysis pooled data from two pivotal trials, FIDELIO-DKD and FIGARO-DKD, focused on the cardiovascular and renal benefits of finerenone in patients with CKD and T2D, with additional trials covering heart failure patients.

Study Design

1. **FIDELIO-DKD**: This trial involved 5,674 patients with CKD and T2D, assessing the effect of finerenone on slowing kidney disease progression and reducing cardiovascular events.
2. **FIGARO-DKD**: Enrolling 7,437 patients with CKD and T2D, FIGARO-DKD evaluated the primary composite endpoint of cardiovascular death and non-fatal myocardial infarction, stroke, or hospitalization for heart failure.
3. **FINE-HEART pooled analysis**: This post-hoc pooled analysis assessed combined cardiovascular and kidney outcomes from studies of more than 13,000 patients with CKD, HF, and T2D.

Endpoints

The primary outcomes measured were a composite of cardiovascular death, nonfatal myocardial infarction, stroke, and hospitalizations for heart failure. Secondary outcomes included kidney disease progression and safety outcomes, especially the risk of hyperkalemia.

Results

Cardiovascular Outcomes

In the FINE-HEART study, finerenone significantly reduced cardiovascular-related events in patients with CKD, HF, and T2D. The primary composite endpoint of cardiovascular death or hospitalization for heart failure was reduced by 14% versus placebo (hazard ratio [HR] 0.86, 95% confidence interval [CI] 0.79–0.94, p<0.001). Specifically:

1. **Cardiovascular death**: Reduced by 14% (HR 0.86, 95% CI 0.74–0.96).
2. **Heart failure hospitalization**: Reduced by 18% (HR 0.82, 95% CI 0.73–0.92). The benefit was consistent across subgroups, including patients with different degrees of kidney impairment and those without diabetes. The Kaplan-Meier curve illustrating hospitalization rates for heart failure is shown in Figure 1.

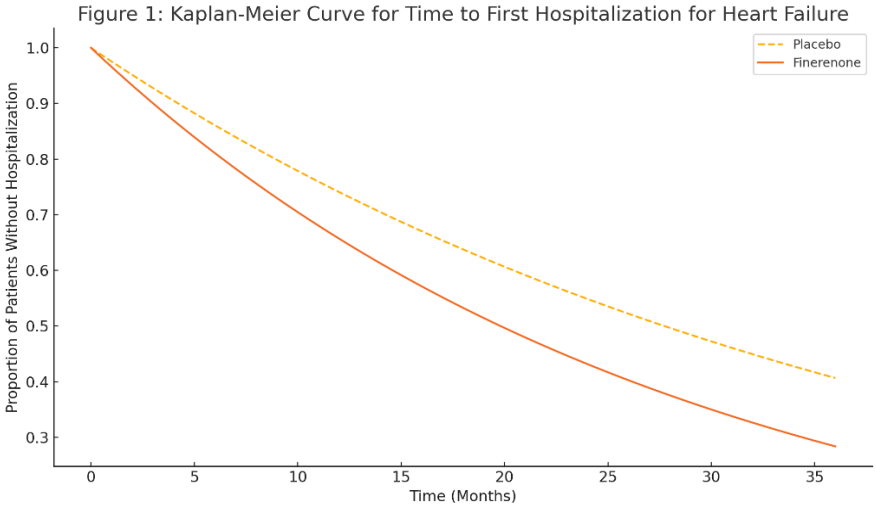

Figure 1. Kaplan-Meier Curve Showing the Time to First Hospitalization for Heart Failure in Patients Treated with Finerenone Compared to Placebo

Kidney Outcomes

Finerenone has provided important renal protection by reducing the progression of kidney disease in high-risk patients. The pooled analysis documented a 20% reduction in the risk of achieving the kidney composite endpoint: a sustained decline in eGFR, progression to end-stage kidney disease, or renal death (HR 0.80, 95% CI 0.71–0.91, p<0.001). Primary outcomes in the FINE-HEART pooled analysis are presented in Table 1.

Moreover, event rates for cardiovascular death and kidney disease progression are displayed in Figure 2.

Table 1. Primary Outcomes in FINE-HEART Pooled Analysis

Outcome	Finerenone (%)	Placebo (%)	HR (95% CI)
Cardiovascular Death	14	17	0.86 (0.74–0.96)
HF Hospitalization	18	22	0.82 (0.73–0.92)
Kidney Disease Progression	20	25	0.80 (0.71–0.91)

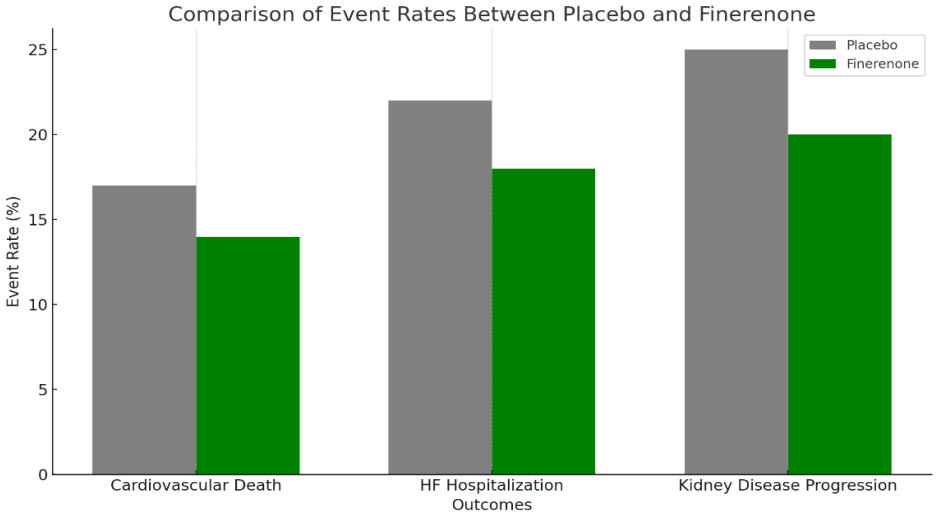

Figure 2. Graphical Comparison of Event Rates for Cardiovascular Death, HF Hospitalization, and Kidney Disease Progression Between Placebo and Finerenone

Safety Outcomes

The safety profile for finer enone was generally consistent with that observed in prior trials. The most notable side effect was hyperkalemia, which occurred in 1.3% of patients in the finerenone group versus 0.5% in the placebo group. However, it did not translate into significant differences in mortality or AKI related to hyperkalemia and was well-managed.

Discussion

Indeed, the FINE-HEART analysis provides strong evidence for the use of finerenone in those patients who present with typical combined cardiovascular, kidney, and metabolic conditions by targeting mineralocorticoid receptor pathways. [3] Finerenone exerts dual protective effects on both cardiovascular and renal events. This is relevant in settings where CKD and T2D coexist, considering that traditional MRAs have limited application because of safety concerns such as hyperkalemia.

It also demonstrated an improved safety and efficacy profile compared with the conventional treatment, mainly in heart failure hospitalization reduction and in the slowing of

kidney disease. The consistent benefit across subgroups points to the broad applicability of finerenone across a wide range of patient populations, extending from advanced CKD to mild-to-moderate heart failure [4].

Thus, finerenone was considered a backbone in the treatment of patients with CKD, and its positive benefit-to-risk ratio opens perspectives for its probable inclusion in future guidelines. The moderate increase in hyperkalemia is a concern but can be managed appropriately with monitoring and dose adjustment [5].

Conclusion

Finerenone has been highly valued in the management of patients with chronic kidney disease, heart failure, and type 2 diabetes [6]. The FINE-HEART pooled analysis provides evidence regarding the reduction in cardiovascular mortality, prevention of heart failure hospitalizations, and slowing of renal impairment. With a safety profile carrying some risk of hyperkalemia, it is still acceptable given the substantive benefits. These findings are important for clinical practice, as they outline how finerenone will be integrated into the current treatment approach for high-risk patients with CKD.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgements

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