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Finerenone: Time to Reconsider Mineralocorticoid Blockade in Heart Failure?

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Introduction

Mineralocorticoid receptor antagonists (MRA) have an established prognostic benefit in patients with heart failure with reduced ejection fraction (HFrEF)(1). In the TOPCAT trial, spironolactone for heart failure with preserved ejection fraction (HFpEF) failed to meet statistical significance for the primary outcome of a composite of cardiovascular death, aborted cardiac arrest and heart failure hospitalisation(2). However, post hoc analysis of the TOPCAT revealed geographical variation in treatment response, suggesting potential clinical benefit of MRA in HFpEF. Finerenone, a novel nonsteroidal MRA, has been shown to have prognostic benefit in patients with chronic kidney disease and type 2 diabetes (T2DM). This editorial reviews the emerging evidence for its use in heart failure patients.

Take Home Messages

- Finerenone is a nonsteroidal mineralocorticoid receptor antagonist (MRA) that differs from traditional steroidal MRAs in its structure, selectivity, and pharmacodynamic effects
- Emerging evidence is encouraging for reducing morbidity in the cardiovascular-kidney-metabolic syndrome
- Key challenges include the lack of a clear cardiovascular mortality benefit, integration into existing heart failure therapies, and its uncertain role in heart failure with reduced ejection fraction

How is it different?

Finerenone is a dihydropyridine-derived molecule with high affinity for mineralocorticoid receptors (MR) along with a balanced distribution between cardiac and renal tissues (**Table 1**). Overactivation of MR can result in endothelial dysfunction, pathological fibrosis, myocardial hypertrophy and end organ inflammation which can all influence the

development of heart failure. Whilst both steroid and non-steroidal MRAs can inhibit MR overactivation, finerenone has the added advantage of reduced metabolic (i.e. hyperkalaemia) and steroidal side effects (i.e. gynaecomastia) making it an attractive therapeutic option(3). Although no head-to-head trial exists, in the ARTS phase 2 trial finerenone had less hypokalaemia (5.3 vs. 12.7%; P=0.048) and a smaller blood pressure effect than spironolactone suggesting a safety advantage in patients with HFrEF and chronic kidney disease (CKD)(4).

Emerging indications

Phase III FIDELIO-DKD and FIGARO-DKD were contemporary trials assessing finerenone vs placebo in T2DM patients with chronic kidney disease for cardiovascular and renal outcomes(5,6). The FIDELITY pooled analysis combined both of these trials noting a benefit (HR 0.86, 95% CI:0.78–0.95) in composite cardiovascular outcomes (time to cardiovascular death, non-fatal myocardial infarction, non-fatal stroke and heart failure hospitalisation). The main driver for this was a reduction in heart failure hospitalisation with a 22% relative reduction with finerenone vs placebo. Chronic kidney disease (CKD) and diabetes are strongly linked to chronic heart failure, highlighting their importance for cardiologists, yet only 7.7% of the 13,026 FIDELITY trial patients had heart failure at baseline, emphasizing the need for a dedicated study.

Finerenone in heart failure

FINEARTS-HF is the latest randomised controlled trial looking at efficacy and safety of finerenone 20-40mg daily for patients with heart failure and left ventricular ejection fraction ≥40%(7). Over median follow of 32 months, finerenone significantly reduced primary composite endpoint of worsening heart failure events (unplanned or urgent admission for heart failure) and cardiovascular death (rate ratio 0.84, 95% CI 0.74-0.95). The results were driven mainly by reduced heart failure events as cardiovascular mortality was not statistically significant (HR 0.93; 95%CI 0.78-.11). The primary outcome was consistent across subgroups, including baseline NYHA classification, renal function and SGLT2 use (the only treatment to date option with prognostic benefit in HFpEF). Increase in serum creatine (2.0% vs 1.2%) and potassium >6mmol/l (3.0% vs 1.4%) were more common in finerenone group compared to placebo. Whilst the finerenone group has small increase in hyperkalaemia that led to hospitalisation (0.5% vs 0.2%) there were no death attributable to this in either groups.

Although aforementioned individual trials showed improvement in composite endpoints, they were not powered for assessment of key outcomes such as cardiovascular mortality or outcomes in overlapping cardiovascular-kidney-metabolic syndrome conditions. The FINE-HEART pooled analysis combined data from FIDELIO-DKD, FIGARO-DKD and FINEARTS-HF which included 18,991 participants with 2.9 years median follow-up(8). This pooled analysis signalled a reduction in cardiovascular mortality but this failed to meet statistical significance (HR 0.89, 95%CI 0.78-1.01). This is substantiated by outcome benefit in all-cause mortality, heart failure hospitalisation, new-onset atrial fibrillation, and kidney disease progression without any new safety concerns. More recently, prespecified analysis of the FINEARTS-HF trial has demonstrated that finerenone can reduce hazard of new-onset diabetes by 24% which provides an additional meaningful clinic benefit in the treatment of HFpEF(9).

Conclusion

Whilst finerenone represents a promising therapeutic option in HFpEF, its role and integration within existing therapies remains a work in progress. The absence of a strong cardiovascular mortality benefit underscores the need to refine patient selection and a longer follow up. Additionally, the high prevalence of CKD in HFpEF patients raises concerns around hyperkalaemia which may require dose adjustments and closer monitoring. Finally it is yet to be determined if finerenone has a role in HFrEF for patients who are intolerant of steroidal MRA.

Table 1: Comparison of mineralocorticoid receptor antagonists

Characteristics	Finerenone	Spironolactone	Eplerenone
Class	Non-steroidal	Steroidal	Steroidal
MRA selectivity	+++	+	++
Half-life (h)	~ 2-3	~ 24	~ 4-6
Distribution	Equal	Kidney>heart	Kidney>heart
Hyperkalaemia	++	+++	+++
Reduction in SBP	+	+++	++
Sexual side effects	-	+++	++

MRA= Mineralocorticoid receptor antagonists; SBP= systolic blood pressure; +=low; ++=moderate; +++ = high
Table adapted from Khullar et al(10) though CC-BY-NC 4.0 License

Disclosures: none

References

1. Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, et al. The Effect of Spironolactone on Morbidity and Mortality in Patients with Severe Heart Failure. N Engl J Med. 1999 Sep 2;341(10):709–17.

2. Pitt B, Pfeffer MA, Assmann SF, Boineau R, Anand IS, Claggett B, et al. Spironolactone for Heart Failure with Preserved Ejection Fraction. N Engl J Med. 2014 Apr 10;370(15):1383–92.

3. Arici M, Altun B, Araz M, Atmaca A, Demir T, Ecder T, et al. The significance of finerenone as a novel therapeutic option in diabetic kidney disease: a scoping review with emphasis on cardiorenal outcomes of the finerenone phase 3 trials. Front Med. 2024 Jun 14;11:1384454.

4. Pitt B, Kober L, Ponikowski P, Gheorghiade M, Filippatos G, Krum H, et al. Safety and tolerability of the novel non-steroidal mineralocorticoid receptor antagonist BAY 94-8862 in patients with chronic heart failure and mild or moderate chronic kidney disease: a randomized, double-blind trial. European Heart Journal. 2013 Aug 14;34(31):2453–63.

5. Pitt B, Filippatos G, Agarwal R, Anker SD, Bakris GL, Rossing P, et al. Cardiovascular Events with Finerenone in Kidney Disease and Type 2 Diabetes. N Engl J Med. 2021 Dec 9;385(24):2252–63.

6. Bakris GL, Agarwal R, Anker SD, Pitt B, Ruilope LM, Rossing P, et al. Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes. N Engl J Med. 2020 Dec 3;383(23):2219–29.

7. Solomon SD, McMurray JJV, Vaduganathan M, Claggett B, Jhund PS, Desai AS, et al. Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction. N Engl J Med. 2024 Oct 24;391(16):1475–85.

8. Vaduganathan M, Filippatos G, Claggett BL, Desai AS, Jhund PS, Henderson A, et al. Finerenone in heart failure and chronic kidney disease with type 2 diabetes: FINE-HEART pooled analysis of cardiovascular, kidney and mortality outcomes. Nat Med. 2024 Dec;30(12):3758–64.

9.Butt JH, Jhund PS, Henderson AD, Claggett BL, Desai AS, Viswanathan P, et al. Finerenone and new-onset diabetes in heart failure: a prespecified analysis of the FINEARTS-HF trial. The Lancet Diabetes & Endocrinology. 2025 Feb;13(2):107–18.

10.Khullar D, Gupta AK, Singh K. Finerenone: Will It Be a Game-changer? Card Fail Rev. 2024 Dec 23;10:e19.