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Changes in albuminuria and the effect of finerenone on cardiovascular outcomes: Insights from FINEARTS-HF

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INTRODUCTION

- Albuminuria is a potent predictor of adverse cardiovascular and kidney outcomes.[1,2]
- Albuminuria reduction accounted for a modest proportion of the effect of finerenone in reducing adverse cardiovascular outcomes among patients with chronic kidney disease (CKD) and type 2 diabetes mellitus (T2DM).[3]
- Whether this is similar among patients with heart failure (HF) is not clear.

AIM

- Explore the proportion of the treatment effect of mediated by the change in urine albumin/creatinine ratio from baseline to 3 months among participants of the Finerenone Trial to Investigate Efficacy and Safety Superior to Placebo in Patients with Heart Failure (FINEARTS-HF[4]; a randomized trial of finerenone vs. placebo among patients with HF with mildly reduced or preserved ejection fraction.

METHODS

- We performed a post hoc mediation analysis of 5,086 participants with available data from the FINEARTS-HF trial.
- Using accelerated failure time models, we explored the proportion of risk reduction mediated by a change in urine albumin/creatinine ratio (UACR; log-transformed and >30% decline) between baseline and 3 months on the subsequent risk of: 1) the composite of cardiovascular death or first HF event; 2) first worsening HF event.

METHODS

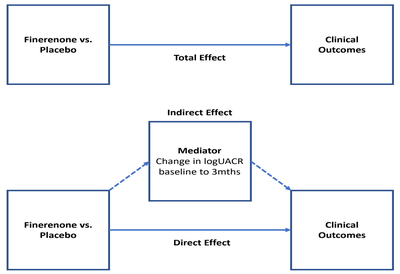

Figure 1. Directed acyclic graph illustrating the proposed mediation model. In the upper panel, the effect of the exposure (finerenone vs. placebo) on clinical outcomes is represented as a solid line between the two boxes (Total Effect).

In the lower panel, the treatment effect is considered as two parts: 1) the effect that is independent of the mediator (Direct Effect), and 2) the effect mediated by a reduction in UACR (Indirect Effect).

The percent mediated represents the percent of the total effect of finerenone on the outcome that is due to the effect mediated by the reduction in UACR.

RESULTS

Table 1. Mediation analyses according to changes in UACR from baseline to month 3

	Total Effects	Direct Effects	Indirect Effects	% Direct	% Mediated
Relative mean survival (95%CI) (log-UACR as mediator)					
CV death or first Heart Failure event	1.20 (1.04, 1.37)	1.13 (0.98, 1.29)	1.06 (1.04, 1.09)	66 (-31, 85)	34 (15, 131)
Heart Failure event	1.28 (1.08, 1.52)	1.19 (1.01, 1.41)	1.07 (1.04, 1.11)	71 (14, 86)	29 (14, 86)
Relative mean survival (95%CI) (≥30% vs. <30% decline in UACR as mediator)					
CV death or first Heart Failure event	1.20 (1.04, 1.37)	1.17 (1.01, 1.34)	1.03 (1.01, 1.05)	85 (42, 95)	15 (5, 58)
Heart Failure event	1.28 (1.08, 1.52)	1.24 (1.06, 1.47)	1.03 (1.01, 1.05)	90 (66, 97)	10 (3, 34)

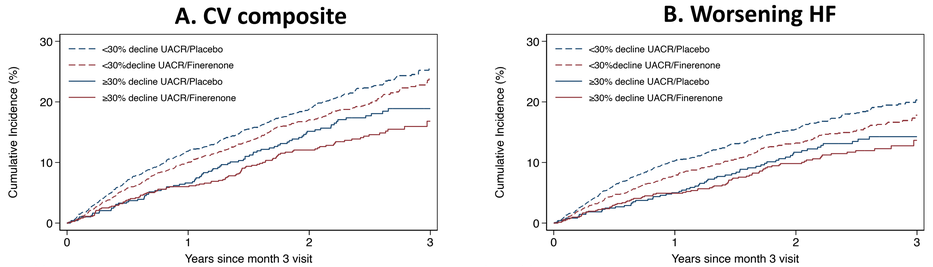

Fig 2. Kaplan-Meier analyses showing CV composite (A) and HF events (B) after 3 months, according to randomized treatment and 30% decline in UACR from baseline to 3 months

CONCLUSIONS

- Among participants of FINEARTS-HF, those who experienced >30% decline in UACR (vs. ≤30%) had lower risks of adverse cardiovascular outcomes.
- Despite relatively low levels of baseline albuminuria, early changes in UACR accounted for a modest proportion of the effect of finerenone on reducing cardiovascular outcomes.
- These findings highlight the importance of measuring UACR among patients with heart failure.

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