Initial decline (dip) in estimated glomerular filtration rate with initiation of finerenone in patients with mildly reduced or preserved ejection fraction: A prespecified analysis of FINEARTS-HF

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Background

An initial decline in estimated glomerular filtration rate (eGFR) often leads to reluctance to continue the life-saving therapy in patients with heart failure (HF). However, this early decrease in eGFR has been shown to predict a favourable response to several HF therapies. We have analyzed the early change in eGFR and outcomes in patients treated with the non-steroidal mineralocorticoid receptor antagonist (MRA) finerenone.

Purpose

To examine the association between initial decline in eGFR with finerenone and subsequent outcomes in patients with heart failure and mildly reduced or preserved ejection fraction (HFmrEF/HFpEF)

Methods

In this prespecified analysis of FINEARTS-HF, we examined the association between initial decline in eGFR (≥15%) from randomization to 1 month (compared to no decline ≥15% - hereafter referred to as "no decline in eGFR") and subsequent outcomes, in patients assigned to finerenone or placebo. Other definitions of decline in kidney function were also examined (Table 2 and Figure 2).

Key inclusion criteria: NYHA functional class II-IV, LVEF ≥40%, evidence of structural heart disease, and elevated natriuretic peptides

Key exclusion criteria: eGFR <25 ml/min/1.73m^2, potassium >5.0 mmol/L

Primary outcome
Total (first and recurrent) HF hospitalizations and cardiovascular death

Results

Table 1. Baseline characteristics

	No decline in eGFR N=4,569	Initial decline in eGFR ≥15% N=1,018	P-value
Age (years)	71.7±9.7	72.9±9.5	<0.001
Male	2,542 (55.6)	535 (52.6)	0.07
BMI (kg/m^2)	29.9±6.1	29.9±6.1	0.97
NYHA class III/IV	1,361 (29.8)	350 (34.4)	<0.01
KCCQ-CSS	66.2±22.3	62.6±23.0	<0.001
Systolic blood pressure (mmHg)	129.0±15.2	131.2±15.4	<0.001
eGFR (ml/min/1.73m^2)	62.2±20.0	62.6±18.2	0.58
eGFR<60 ml/min/1.73m^2	2,214 (48.5)	459 (45.1)	0.05
UACR (mg/g)	17 (6-61)	23 (8-90)	<0.001
UACR category			<0.001
<30	2,756 (62.3)	540 (54.7)	
30-299	1,251 (28.3)	333 (33.7)	
≥300	418 (9.4)	115 (11.6)	
NT-proBNP (pg/ml)	997 (425-1865)	1185 (560-2318)	<0.001
- No atrial fibrillation	559 (299-1223)	746 (385-1560)	<0.001
- Atrial fibrillation	1694 (1124-2721)	1833 (1212-2952)	0.02
LVEF (%)	52.5±7.8	52.9±8.0	0.11
LVEF ≥50%	2,883 (63.2)	673 (66.1)	0.08

Figure 1. The primary outcome according to initial decline ≥15% in eGFR and randomized treatment assignment

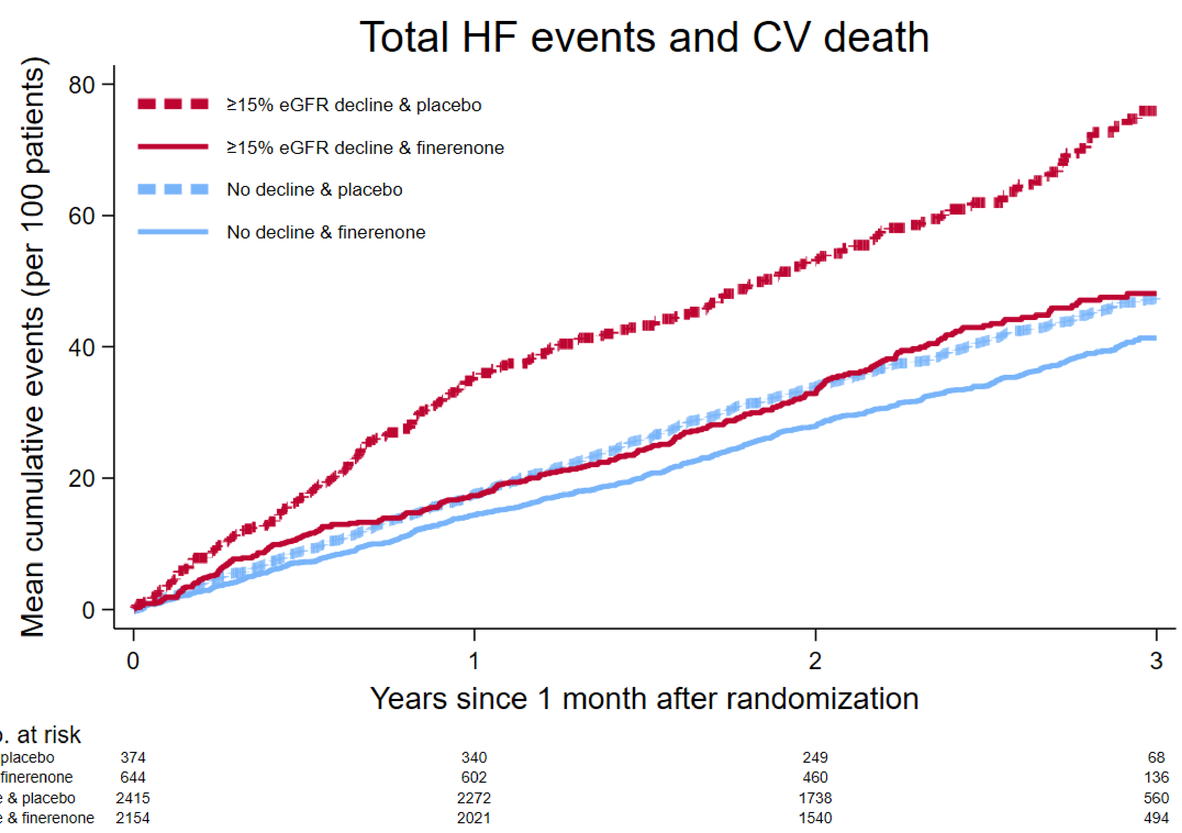
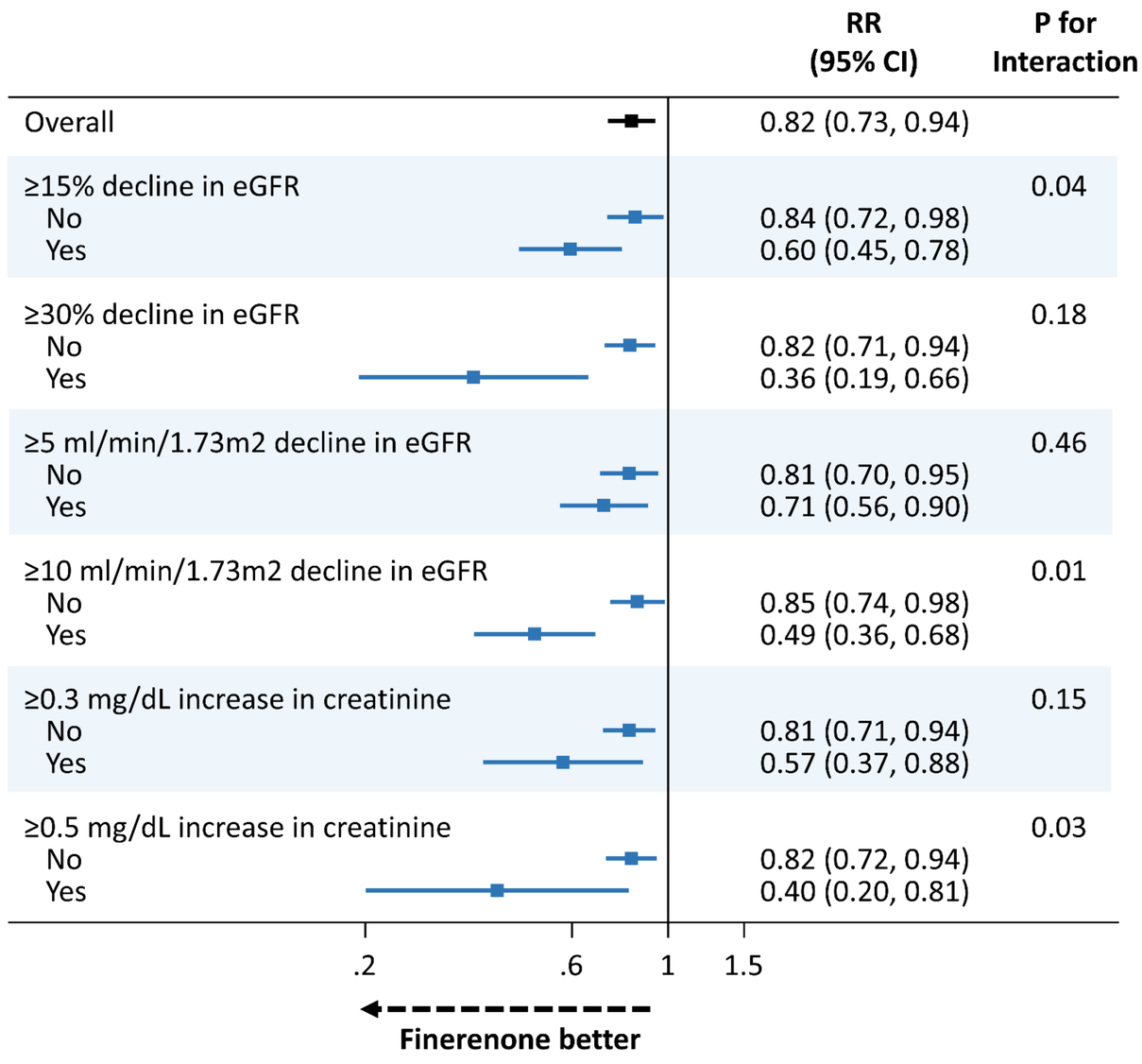


Table 2. Early decline in kidney function at 1 month and the subsequent occurrence of the primary outcome in each treatment group (landmark analysis)

Definition of decline in kidney function	Placebo: No decline	Placebo: Decline in kidney function	Finerenone: No decline	Finerenone: Decline in kidney function	P for interaction
≥15% decline in eGFR					
RR (95% CI)	Reference	1.56 (1.22-1.99)	Reference	1.14 (0.90-1.43)	0.06
Adjusted RR (95% CI)	Reference	1.50 (1.20-1.89)	Reference	1.07 (0.84-1.35)	0.04
≥30% decline in eGFR					
RR (95% CI)	Reference	1.76 (1.13-2.75)	Reference	1.42 (0.90-2.23)	0.43
Adjusted RR (95% CI)	Reference	1.48 (0.91-2.41)	Reference	0.97 (0.58-1.63)	0.18
≥5 ml/min/1.73m^2 decline in eGFR					
RR (95% CI)	Reference	1.06 (0.87-1.29)	Reference	1.11 (0.90-1.36)	0.70
Adjusted RR (95% CI)	Reference	1.25 (1.02-1.53)	Reference	1.17 (0.94-1.45)	0.46
≥10 ml/min/1.73m^2 decline in eGFR					
RR (95% CI)	Reference	1.25 (0.97-1.61)	Reference	0.88 (0.68-1.15)	0.05
Adjusted RR (95% CI)	Reference	1.47 (1.13-1.91)	Reference	0.97 (0.73-1.28)	0.01

Figure 2. Association between finerenone use and adjusted risk of the primary outcome according to initial changes in kidney function



Conclusion

Although an initial decline in eGFR was associated with worse subsequent outcomes in patients assigned to placebo, this association was not as strong (or even absent) in those assigned to finerenone. An early decline in eGFR can be anticipated with finerenone and should not automatically lead to the discontinuation of finerenone, as with other effective treatments in patients with HF.

Simultaneous publication

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