Finerenone, Coronary Heart Disease, and Heart Failure With Mildly Reduced or Preserved Ejection Fraction: A Prespecified Analysis of the FINEARTS-HF Trial

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Background

- Coronary heart disease (CHD) is prognostically important in heart failure (HF) with reduced ejection fraction, but its impact in HF with mildly reduced or preserved ejection fraction (HFmrEF/HFpEF) is less well understood.
- Given the high burden of cardiometabolic comorbidities in HFmrEF/HFpEF, atherothrombotic events may represent an important therapeutic target.

Purpose

- In a pre-specified analysis of the FINEARTS-HF trial, we investigated:
  - the effect of finerenone on atherothrombotic outcomes
  - the effect of finerenone on clinical outcomes according to history of CHD

Methods

- FINEARTS-HF was a randomized, double-blind, controlled trial in patients with HFmrEF/HFpEF, evaluating the efficacy and safety of finerenone compared with placebo.
- **Key inclusion criteria:** NYHA II-IV; LVEF ≥40%; structural heart disease; elevated natriuretic peptides.
- **Key exclusion criteria:** eGFR <25 mL/min/1.73m^2; potassium >5.0 mmol/L; MI or CABG in the 90 days before randomization; PCI in the 30 days before randomization.
- **Participants:** 6,001 patients, of whom 3,236 (53.9%) had a history of CHD.
- **History of CHD:** Investigator-reported.
- **Primary outcome:** Cardiovascular death and total HF events (HF hospitalization or urgent HF visit).
- **Statistics:**
  Total events: Semiparametric proportional-rates models.
  Time-to-event outcomes: Cox proportional hazard models.

Results

Table 1. Baseline characteristics according to a history of CHD

	No CHD N=2,765	CHD N=3,236	P-value
Age (years), mean	73	71	<0.001
Female sex, %	56	37	<0.001
BMI >30 kg/m^2, %	45	44	<0.001
eGFR (mL/min/1.73m^2), mean	61	63	0.002
NT-proBNP (pg/mL), median	1181	912	<0.001
High-sensitivity troponin T (ng/L), median	18	18	0.50
LVEF (%), mean	54	51	<0.001
NYHA class III/IV, %	29	33	0.002
Current smoker, %	7	9	<0.001
Prior HF hospitalization, %	61	60	0.54
Atrial fibrillation/flutter, %	66	46	<0.001
Stroke, %	11	16	<0.001
Myocardial infarction, %	N/A	48	N/A
PCI or CABG, %	N/A	63	N/A
Peripheral arterial occlusive disease, %	5	12	<0.001
Hypertension, %	86	91	<0.001
Type 2 diabetes, %	34	47	<0.001
Loop diuretic, %	88	86	0.02
ACEi/ARB, %	69	73	<0.001
ARNI, %	7	10	<0.001
SGLT2i, %	13	14	0.19
Beta-blocker, %	82	88	<0.001
Any lipid-lowering medication, %	51	84	<0.001
Antiplatelet, %	15	59	<0.001
Anticoagulant, %	63	42	<0.001

Figure 1. Effect of finerenone compared with placebo on first fatal/non-fatal stroke or MI

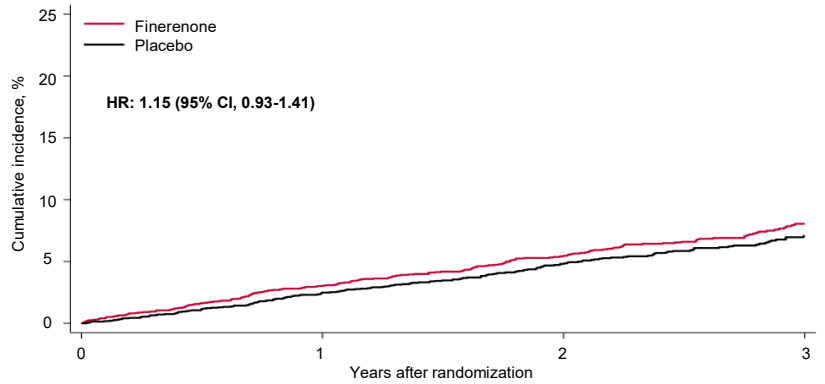

Figure 2. Effects of finerenone compared with placebo on outcomes according to a history of CHD

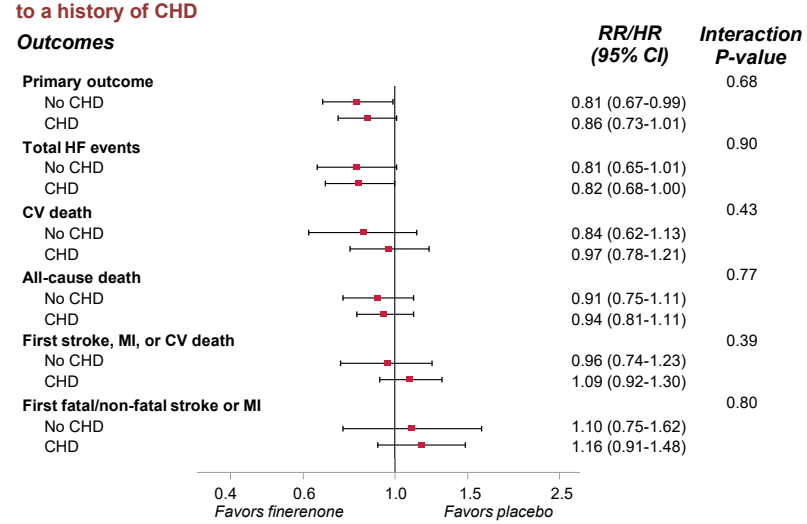

Table 2. Effects of finerenone compared with placebo on laboratory measures and systolic blood pressure according to a history of CHD

	No CHD		CHD		Interaction P-value
	Fine	Placebo	Fine	Placebo	
Creatinine >2.5 mg/dL	4.7%	2.5%	5.0%	3.6%	0.29
Creatinine >3.0 mg/dL	1.8%	0.8%	2.1%	1.5%	0.38
Potassium >5.5 mmol/L	12.1%	5.7%	16.0%	7.9%	0.97
Potassium >6.0 mmol/L	2.1%	1.4%	3.7%	1.4%	0.12
Potassium <3.5 mmol/L	5.1%	11.8%	3.8%	7.9%	0.54
Systolic blood pressure <100 mmHg	19.1%	12.9%	17.9%	12.1%	0.93

Conclusions

In patients with HFmrEF/HFpEF, compared with placebo, finerenone:

- reduced the risk of clinical events and was well-tolerated, independent of a history of CHD
- did not reduce the risk of atherothrombotic outcomes

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