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

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Background

- Chronic obstructive pulmonary disease (COPD) is associated with worse outcomes in heart failure (HF) and mildly reduced or preserved ejection fraction (HFmrEF/HFpEF).
- A history of COPD does not appear to modify the beneficial effects of guideline-recommended therapies in patients with HF with reduced ejection fraction (HFrEF), or SGLT2 inhibitors in HFmrEF/HFpEF.
- A post hoc analysis of the TOPCAT trial suggested that the effectiveness of the steroidal mineralocorticoid-receptor antagonist (MRA), spironolactone, may be modified by pulmonary disease, with a greater benefit in patients with COPD/asthma.

Purpose

- To investigate the effects of the non-steroidal MRA, finerenone, compared to placebo, according to COPD status in a pre-specified analysis of the FINEARTS-HF trial.

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; history of primary pulmonary arterial hypertension or severe pulmonary disease requiring home oxygen or chronic oral steroid therapy.
- **Participants:** 6,001 patients, of whom 773 (12.9%) had a history of COPD.
- **History of COPD:** Investigator-reported.
- **Primary outcome:** Cardiovascular death and total worsening HF events (HF hospitalization or urgent HF visit requiring intravenous diuretics).
- **Statistics:**
  Total events: Semiparametric proportional-rates models.
  Time-to-event outcomes: Cox proportional hazard models.
  Improvement in NYHA class to 12 months: Logistic regression models.
  Change in KCCQ-TSS to 12 months: Linear regression models.

Results

Table 1. Baseline characteristics according to COPD status

	No COPD N=5228	COPD N=773	P-value
Age (years), mean	72	73	<0.001
Female sex, %	47	37	<0.001
BMI (kg/m^2), median	29	30	0.004
eGFR (mL/min/1.73m^2), mean	62	61	0.11
NT-proBNP (pg/mL), median	1037	1067	0.10
High-sensitivity troponin T (ng/L), median	17	20	<0.001
LVEF (%), mean	53	53	0.51
NYHA class III/IV, %	29	41	<0.001
KCCQ-TSS score (0-100), mean	68	61	<0.001
Current smoker, %	8	15	<0.001
Prior HF hospitalization, %	60	66	<0.001
Atrial fibrillation, %	55	59	0.033
Myocardial infarction, %	26	24	0.23
Peripheral arterial occlusive disease, %	8	13	<0.001
Hypertension, %	88	92	0.002
Type 2 diabetes, %	40	44	0.10
ACEi/ARB, %	71	68	0.063
ARNI, %	9	8	0.88
Beta-blocker, %	85	83	0.15
Beta-1 selective beta-blocker	71	70	0.47
Non-selective beta-blocker and alpha-blocker	13	13	0.75
Other non-selective beta-blocker	3	2	0.30
SGLT2i, %	14	13	0.48
Loop diuretic, %	87	91	0.001

Figure 1. Risk of primary outcome according to COPD status

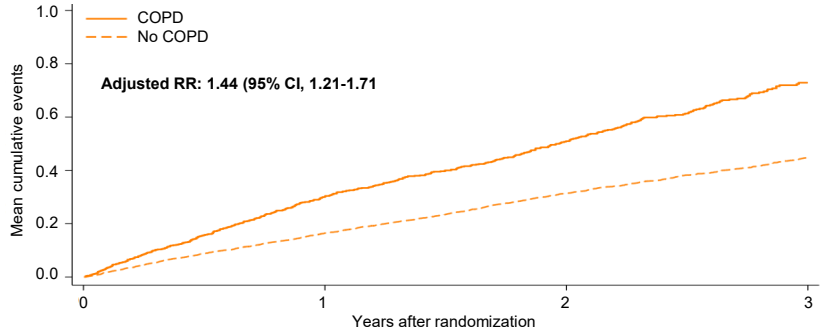

Figure 2. Effect of finerenone compared with placebo on clinical outcomes according to COPD status

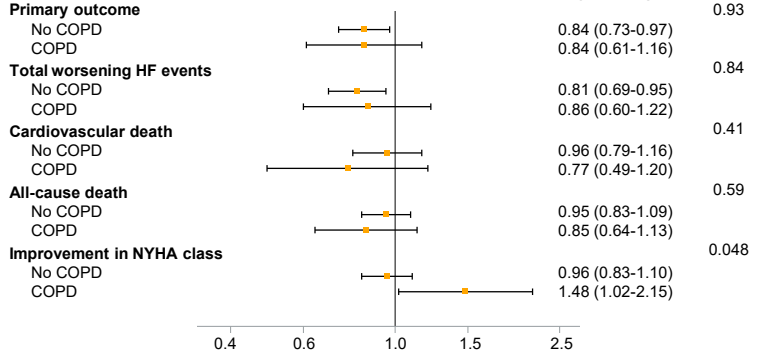

Figure 3. Effect of finerenone compared with placebo on change in KCCQ-TSS according to COPD status

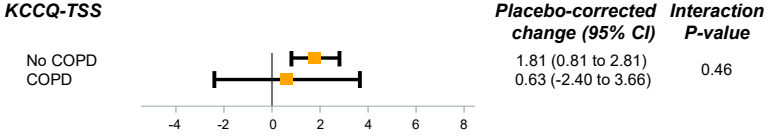

Table 2. Laboratory measures and systolic blood pressure according to treatment assignment and COPD status

	No COPD		COPD		Interaction
	Placebo	Fine	Placebo	Fine	P-value
Creatinine ≥2.5 mg/dL	4.6%	2.9%	6.6%	4.5%	0.82
Creatinine ≥3.0 mg/dL	2.0%	1.0%	1.9%	2.1%	0.22
Potassium >5.5 mmol/L	14.3%	6.9%	13.9%	6.9%	0.90
Potassium >6.0 mmol/L	2.9%	1.4%	3.3%	1.9%	0.70
Potassium <3.5 mmol/L	4.1%	10.0%	6.3%	7.7%	0.03
Systolic blood pressure <100 mmHg	18.5%	12.3%	18.4%	13.2%	0.52

Conclusions

In patients with HFmrEF/HFpEF, finerenone, compared with placebo, reduced the risk of clinical events, improved health status, and was well-tolerated, independent of a history of COPD.