Efficacy and safety of finerenone in patients with heart failure and mildly reduced or preserved ejection fraction: A prespecified anemia-specific analysis of the FINEARTS-HF trial

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BACKGROUND

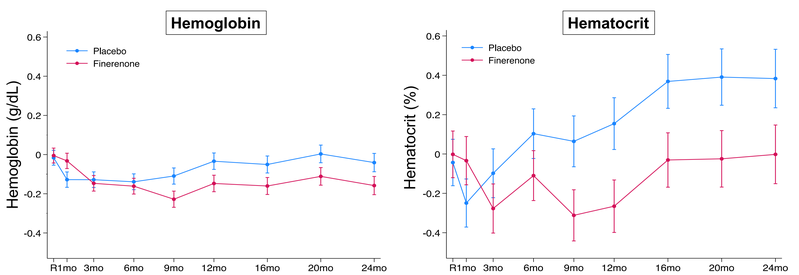
- Anemia is common in HFmrEF/HFpEF and associated with poor clinical outcomes.
- While renin-angiotensin system blockers reduce hemoglobin and sodium-glucose co-transporter 2 inhibitors (SGLT2i) increase hemoglobin, little is known about the effects of mineralocorticoid receptor antagonists (MRAs) on hemoglobin levels and in patients with anemia.
- We evaluated the efficacy and safety of finerenone based on anemia status in patients with HFmrEF/HFpEF enrolled in the FINEARTS-HF trial. Additionally, we examined the impact of finerenone on hemoglobin levels, new-onset anemia, and anemia resolution during follow-up.

METHODS

- FINEARTS-HF was a randomized, double-blind, multicenter, event-driven trial, investigating the efficacy and safety of the non-steroidal MRA finerenone, compared to placebo in patients with HFmrEF/HFpEF.
- Key inclusion criteria were NYHA functional class II-IV, treatment with a diuretic for ≥30 days before randomization, a LVEF ≥40% with evidence of structural heart disease and an elevated natriuretic peptide level (NT-proBNP >300 pg/mL [or BNP >100 pg/mL] for patients in sinus rhythm or NT-proBNP >900 pg/mL or BNP >300 pg/mL for patients in atrial fibrillation).
- The primary outcome was the composite of cardiovascular death and total (first and recurrent) HF events.
- Anemia was defined as hemoglobin <12 g/dL in women and <13 g/dL in men.
- New-onset anemia after randomization was defined as the occurrence of two consecutive hemoglobin measurements meeting the criteria for anemia at any time during follow-up.
- Correction of anemia after randomization was defined as the occurrence of two consecutive hemoglobin measurements exceeding the anemia threshold at any time during follow-up.

RESULTS

Figure : Change in hemoglobin and hematocrit from baseline according to treatment assignment



Mean placebo-corrected decrease from baseline to
12 months 0.11 (95%CI 0.06, 0.17) p<0.001
24 months 0.12 (95%CI 0.05, 0.18) p=0.001

Mean placebo-corrected decrease from baseline to
12 months 0.41 (95%CI 0.24, 0.59) p<0.001
24 months 0.39 (95%CI 0.17, 0.60) p<0.001

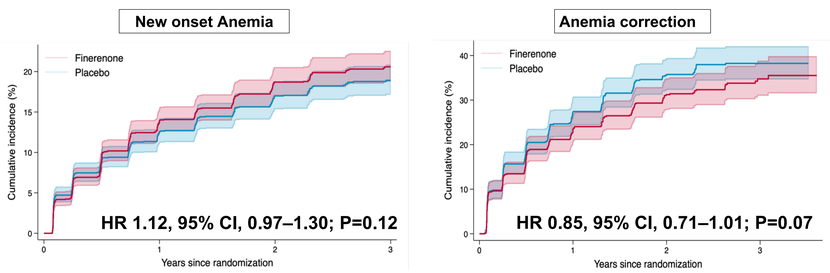
RESULTS

- Of 5,665 patients analysed, 1,584 (28.0%) had anemia at baseline.

Table : Baseline characteristics according to anemia status in the FINEARTS-HF

	Anemia (n = 1584)	No anemia (n = 4081)	p-value
Age (years)	76 (69 - 81)	72 (65 - 78)	<0.001
Male – no (%)	910 (57.5)	2,186 (53.6)	0.008
NYHA functional class III/IV – no (%)	554 (35.0)	1,181 (29.0)	<0.001
LVEF (%)	54 (48 - 58)	52 (45 - 58)	<0.001
KCCQ total symptom score	67 (48 - 84)	72 (52 - 88)	<0.001
Physiological and laboratory measurements			
Systolic blood pressure (mmHg)	130 (118 - 141)	130 (120-140)	0.57
Heart rate (bpm)	69 (62 - 77)	71 (63 - 80)	<0.001
Body mass index (kg/m^2)	29 (25 - 33)	29 (26 - 34)	<0.001
eGFR (ml/min/1.73m^2)	53 (40 - 69)	64 (49 - 80)	<0.001
NT-proBNP (pg/mL)	1371 (630-2622)	935 (404-1734)	<0.001
Hemoglobin (g/dL)	11.5 ± 0.9	14.1 ± 1.2	-
Hematocrit (%)	36 (34 - 38)	42 (40 - 45)	-
Medical history – no (%)			
Hypertension	1,413 (89.2)	3,615 (88.6)	0.51
Diabetes mellitus	794 (50.1)	1,519 (37.2)	<0.001
Myocardial infarction	367 (23.2)	1,079 (26.4)	0.01
AF (history)	885 (55.9)	2,218 (54.4)	0.30
Any prior hospitalization for HF	1,017 (64.2)	2,394 (58.7)	<0.001
Treatments – no (%)			
Beta-blocker	1,315 (83.0)	3,505 (85.9)	0.007
ACEi or ARB	1,073 (67.7)	2,930 (71.8)	0.003
ARNI	112 (7.1)	380 (9.3)	0.007
SGLT2i	215 (13.6)	552 (13.5)	0.96
Loop diuretic	1,438 (90.8)	3,508 (86.0)	<0.001
Anticoagulant	775 (48.9)	1,948 (47.7)	0.42
Antiplatelet	228 (14.4)	547 (13.4)	0.33

Figure : New onset anemia and anemia correction according to treatment assignment

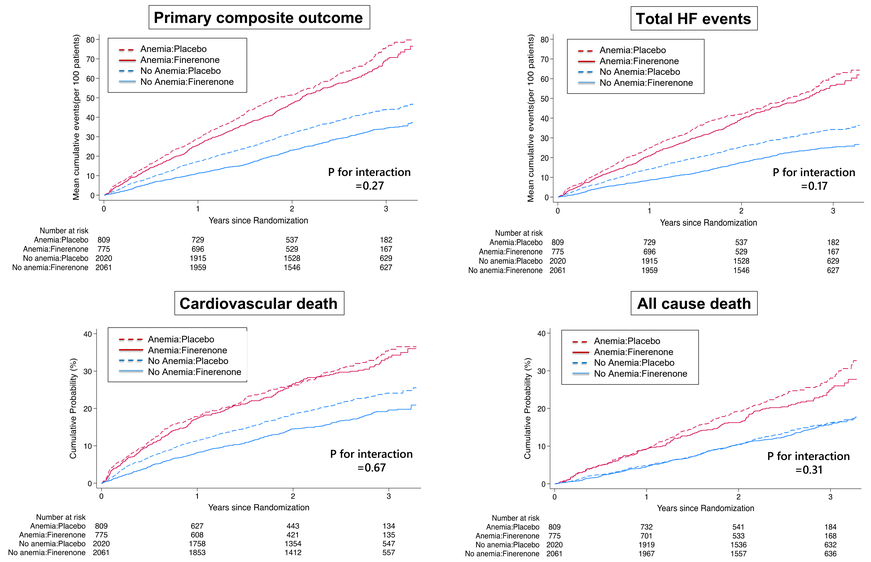


- Among patients who were not anemic at baseline, new-onset anemia occurred in
  18.8% (388/2061) of patients in the finerenone group
  17.3% (350/2020) of patients in the placebo group

- Among patients who were anemic at baseline, anemia correction occurred in
  30.3% (235/775) of patients in the finerenone group
  34.1% (276/809) of patients in the placebo group

Finerenone treatment did not increase the resolution of anemia or prevent new-onset anemia.

Figure : Kaplan-Meier curves for study outcomes according to anemia status at baseline and treatment



Patients with anemia experienced worse clinical outcomes; however, the treatment effect of finerenone on clinical outcomes remained consistent regardless of anemia status.

Table : Tolerability of treatment assignment according to anemia status at baseline

	Anaemia		No Anaemia		Interaction P value
	Placebo	Finerenone	Placebo	Finerenone	
Hypotension - no. (%)					
Systolic blood pressure<100 mmHg	112 (14.5)	143 (19.2)	231 (11.7)	367 (18.3)	
Odds ratio (95% CI)	1.42 (1.07-1.89)		1.80 (1.49-2.17)		0.20
Elevated serum creatinine - no. (%)					
≥ 2.5 mg/dl	45 (5.9)	69 (9.3)	39 (2.0)	65 (3.3)	
Odds ratio (95% CI)	1.64 (1.11-2.43)		1.67 (1.11-2.49)		0.97
≥ 3.0 mg/dl	20 (2.6)	35 (4.7)	13 (0.7)	20 (1.0)	
Odds ratio (95% CI)	1.85 (1.06-3.24)		1.52 (0.75-3.08)		0.65
Elevated serum potassium - no. (%)					
> 5.5 mmol/L	64 (8.4)	118 (15.9)	122 (6.2)	272 (13.6)	
Odds ratio (95% CI)	2.08 (1.50-2.88)		2.42 (1.93-3.04)		0.50
> 6.0 mmol/L	9 (1.2)	29 (3.9)	26 (1.3)	52 (2.6)	
Odds ratio (95% CI)	3.48 (1.63-7.42)		2.02 (1.25-3.25)		0.22
Decreased serum potassium – no. (%)					
< 3.5 mmol/L	76 (9.9)	36 (4.9)	187 (9.5)	81 (4.1)	
Odds ratio (95% CI)	0.45 (0.30-0.68)		0.40 (0.30-0.52)		0.56

Adverse events were similar regardless of anemia status.

CONCLUSION

In FINEARTS-HF, finerenone was efficacious and safe, irrespective of baseline anemia status, in patients with HFmrEF/HFpEF.

FINEARTS-HF
FINerenone trial to investigate Efficacy and sAfety superioR to placebo in paTientS with Heart Failure

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