Finerenone and atrial fibrillation in heart failure: a prespecified analysis of FINEARTS-HF

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Background

Atrial fibrillation (AF) is a common comorbidity in patients with heart failure (HF), especially in HF and mildly reduced or preserved ejection fraction (HFmrEF/HFpEF). Given that AF is associated with attenuated efficacy of some therapies, such as beta-blockers, in patients with HF and reduced ejection fraction (HFrEF), it is important to evaluate the efficacy of new treatments according to AF status in patients with HF.

Methods

We examined the efficacy and safety of finerenone compared to placebo according to the absence or presence of AF, and type of AF (paroxysmal or persistent/permanent).

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

Atrial fibrillation

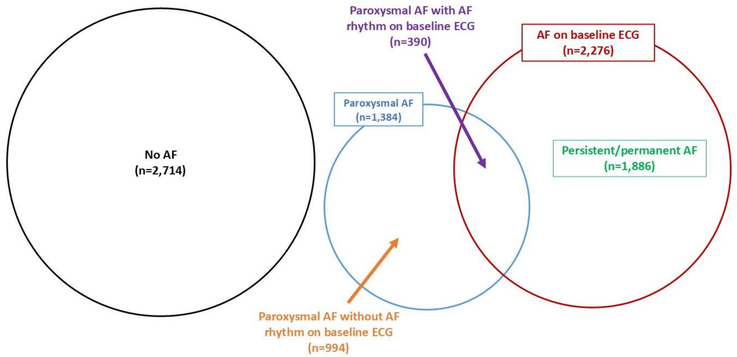
In FINEARTS-HF, the history of AF and its type were collected through the trial case report forms. Also, an electrocardiogram at enrolment was recorded, and investigators specified the heart rhythm from among the following options: sinus rhythm, AF, and other.

Outcome

The primary outcome was total (first and recurrent) HF hospitalizations and cardiovascular death. New-onset AF was a prespecified exploratory outcome and adjudicated.

AF status in FINEARTS-HF

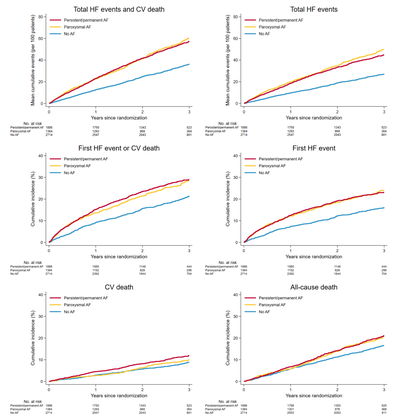
Results



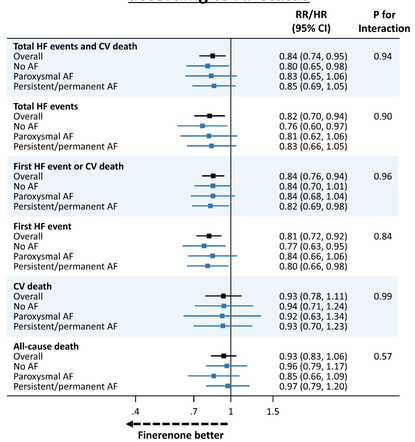
Baseline characteristics

	No AF	Paroxysmal	Persistent/ permanent	
	N=2,714	N=1,384	N=1,886	P-value
Age (years)	69.5±10.2	73.9±8.8	74.1±8.6	<0.001
Male	1,526 (56.2)	700 (50.6)	1,034 (54.8)	<0.01
NYHA Ⅲ or Ⅳ	723 (26.6)	440 (31.8)	689 (36.5)	<0.001
LVEF (%)	52.3±8.1	52.9±7.5	52.7±7.6	0.03
eGFR (ml/min/1.73m^2)	65.6±20.6	59.1±19.1	59.3±18.1	<0.001
NT-proBNP (pg/ml)	540 (286-1185)	1033 (480-1927)	1712 (1144-2809)	<0.001
Type 2 diabetes mellitus	1,230 (45.5)	535 (38.7)	667 (35.4)	<0.001
Hypertension	2,423 (89.3)	1,231 (88.9)	1,656 (87.8)	0.29
ACE-I or ARB	1,998 (73.6)	931 (67.3)	1,306 (69.2)	<0.001
ARNI	272 (10.0)	112 (8.1)	126 (6.7)	<0.001
Beta-blocker	2,254 (83.1)	1,166 (84.2)	1,660 (88.0)	<0.001
SGLT2 inhibitor	374 (13.8)	194 (14.0)	241 (12.8)	0.51

Outcomes according to AF status



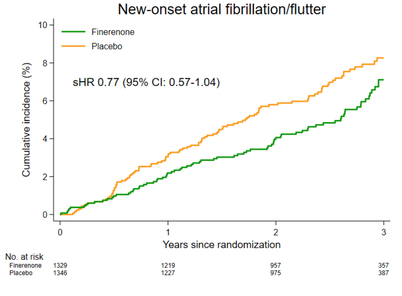
Effects of finerenone compared to placebo according to AF status



Outcomes according to new onset AF/AFL

	No AF/AFL	AF/AFL at baseline	New onset AF/AFL
	N=2,500	N=3,309	N=175
Total HF events and CV death			
Adjusted RR (95% CI)	Reference	1.12 (0.96-1.31)	3.65 (2.57-5.18)
Total HF events			
Adjusted RR (95% CI)	Reference	1.16 (0.96-1.39)	2.57 (1.65-4.01)
First HF event or CV death			
Adjusted HR (95% CI)	Reference	1.04 (0.91-1.18)	2.76 (1.80-4.22)
First HF event			
Adjusted HR (95% CI)	Reference	1.02 (0.88-1.18)	2.12 (1.21-3.72)
CV death			
Adjusted HR (95% CI)	Reference	1.01 (0.81-1.25)	7.13 (4.75-10.7)
All cause death			
Adjusted HR (95% CI)	Reference	0.88 (0.75-1.02)	4.23 (3.09-5.79)

Cumulative incidence of new-onset AF/AFL in patients assigned to finerenone or placebo



Effects of finerenone according to AF status

	No AF		Paroxysmal AF		Persistent/permanent AF	
	Placebo (N=1,367)	Finerenone (N=1,347)	Placebo (N=685)	Finerenone (N=699)	Placebo (N=940)	Finerenone (N=946)
Total HF events and CV death						
Event rate (95% CI)	13.2 (11.4-15.3)	10.6 (9.1-12.4)	22.2 (18.6-26.5)	18.5 (15.5-22.3)	21.3 (18.5-24.4)	18.3 (15.6-21.5)
RR (95% CI)*	0.80 (0.65-0.98)		0.83 (0.65-1.06)		0.85 (0.69-1.05)	
Total HF events						
Event rate (95% CI)	10.2 (8.6-12)	7.8 (6.5-9.4)	18.6 (15.3-22.6)	15.3 (12.5-18.7)	16.9 (14.4-19.7)	14.2 (11.8-17.1)
RR (95% CI)	0.76 (0.60-0.97)		0.81 (0.62-1.06)		0.83 (0.66-1.05)	
First HF event or CV death						
Event rate (95% CI)	8.5 (7.6-9.6)	7.2 (6.3-8.2)	12.8 (11.0-14.9)	10.9 (9.3-12.7)	13.7 (12.1-15.5)	11.3 (9.9-12.9)
HR (95% CI)	0.84 (0.70-1.01)		0.84 (0.68-1.04)		0.82 (0.69-0.98)	
First HF event						
Event rate (95% CI)	6.7 (5.8-7.6)	5.2 (4.5-6.1)	10.6 (9.0-12.6)	9.0 (7.6-10.7)	10.8 (9.4-12.4)	8.7 (7.4-10.1)
HR (95% CI)	0.77 (0.63-0.95)		0.84 (0.66-1.06)		0.80 (0.66-0.98)	
CV death						
Event rate (95% CI)	3.0 (2.5-3.7)	2.8 (2.3-3.4)	3.6 (2.8-4.6)	3.3 (2.5-4.3)	4.4 (3.6-5.4)	4.1 (3.4-5.1)
HR (95% CI)	0.94 (0.71-1.24)		0.92 (0.63-1.34)		0.93 (0.70-1.23)	
All-cause death						
Event rate (95% CI)	6.1 (5.3-7.0)	5.8 (5.0-6.7)	8.4 (7.1-10.0)	7.1 (5.9-8.5)	7.9 (6.9-9.2)	7.8 (6.7-9.0)
HR (95% CI)	0.96 (0.79-1.17)		0.85 (0.66-1.09)		0.97 (0.79-1.20)	

Discussion

In this prespecified analysis of FINEARTS-HF, we found that AF was common and both paroxysmal and persistent/permanent AF were associated with a higher risk of HF outcomes in patients with HFmrEF/HFpEF compared to no AF.

The effects of finerenone, compared to placebo, were consistent irrespective of the presence of AF or type of AF in patients with HFmrEF/HFpEF. This finding is in keeping with analyses of prior trials testing the steroidal MRAs spironolactone and eplerenone in HFrEF where there was no suggestion of attenuated benefit in patients with AF at baseline.

New-onset AF was associated with a higher risk of subsequent HF outcomes in HFmrEF/HFpEF (e.g., compared to no AF/AFL, the adjusted hazard ratio for the primary outcome was 1.12 (95% CI: 0.96–1.31) in patients with any AF/AFL and 3.65 (95% CI: 2.57–5.18) in those with new-onset AF/AFL).

Finerenone appeared to reduce the incidence of new-onset AF/AFL, although this effect was not statistically significant.

Conclusion

The effects of finerenone compared to placebo were consistent, regardless of the presence of AF and type of AF at baseline. New-onset AF/AFL was associated with a higher risk of subsequent outcomes. Finerenone appeared to reduce the incidence of new-onset AF/AFL, although this effect was not statistically significant.

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