Efficacy and Safety of Finerenone in Heart Failure with Preserved Ejection Fraction: A FINE-HEART Analysis

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FINEHEART

Background

- Heart failure (HF) with mildly reduced or preserved ejection fraction (HFmrEF/HFpEF) is a highly heterogeneous population
- Finerenone, a nonsteroidal mineralocorticoid receptor antagonist, has been evaluated in three large-scale outcomes trials to date: FINEARTS-HF, FIDELIO-DKD, and FIGARO-DKD
- Given the important pathophysiological intersection between HF, CKD, and T2D, studies leveraging the totality of trial experience with finerenone may enhance understanding of its efficacy and safety in these clinically-relevant populations

Study Aims

- In this prespecified, participant-level pooled analysis of 3 phase III, global, double-blind, randomized clinical trials of finerenone (FINE-HEART), we evaluated the efficacy and safety of finerenone vs. placebo on clinical outcomes in participants with HFmrEF/HFpEF

Methods

- Participant-level data from the FIDELIO-DKD, FIGARO-DKD, and FINEARTS-HF trials were pooled with harmonized data elements
- Participants from FINEARTS-HF, as well as those from FIDELIO-DKD and FIGARO-DKD with an investigator reported history of HF (symptomatic HFrEF exclusionary in these trials) were included
- Treatment effects of finerenone on the following outcomes were evaluated through Cox proportional hazards regression models
  - Cardiovascular death (excluding deaths with undetermined causes) or HF hospitalization
  - Cardiovascular death (excluding deaths with undetermined causes)
  - HF hospitalization
  - All-cause death
  - New-onset atrial fibrillation

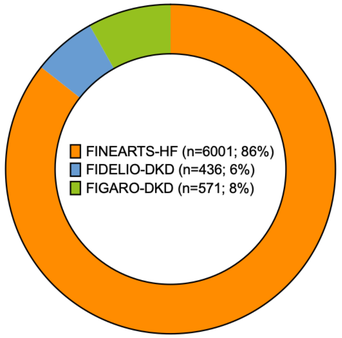
Baseline Characteristics

FINE-HEART
FIDELIO-DKD
FIGARO-DKD
FINEARTS-HF

7,008 individuals with HFmrEF/HFpEF

Mean age: 71 ± 10 years
Female sex: 44%
Mean HbA_{1c}: 6.6 ± 1.3%
Mean eGFR: 61 ± 20 mL/min/1.73 m²
Median UACR: 27 [8, 145] mg/g

FINE-HEART: Participants with HFmrEF/HFpEF by Trial



Treatment Effects of Finerenone vs. Placebo on Clinical Outcomes

Outcomes	Finerenone (n=3488) # of Patients with Event (%)	Finerenone (n=3488) IR (per 100 py)	Placebo (n=3520) # of Patients with Event (%)	Placebo (n=3520) IR (per 100 py)	Finerenone vs. Placebo HR (95% CI)	*P* value
Cardiovascular death* or HF hospitalization	677 (19.4)	8.4	775 (22.0)	9.7	0.87 (0.78, 0.96)	0.008
Cardiovascular death*	273 (7.8)	3.1	299 (8.5)	3.4	0.92 (0.78, 1.08)	0.32
HF hospitalization	502 (14.4)	6.2	597 (17.0)	7.5	0.84 (0.74, 0.94)	0.003
All-cause death	562 (16.1)	6.5	608 (17.3)	7.0	0.93 (0.83, 1.04)	0.21
New-onset atrial fibrillation	100 (2.9)	1.8	134 (3.8)	2.4	0.75 (0.58, 0.97)	0.030

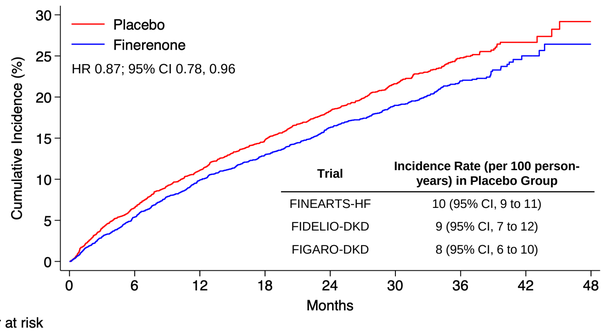
*: Excludes deaths with undetermined causes.
HRs (and 95% CIs) estimated through Cox proportional hazards regression models, stratified by trial.
Abbreviations: HF = heart failure; HR = hazard ratio; IR = incidence rate; py = person-years

Safety

	Finerenone (n=3477)	Placebo (n=3515)
Any serious adverse event	1324 (38.1%)	1403 (39.9%)
Any potassium >5.5 mmol/L[a]	506 (15.0%)	257 (7.6%)
Any potassium >6.0 mmol/L[a]	99 (2.9%)	52 (1.5%)
Any potassium <3.5 mmol/L[a]	154 (4.6%)	319 (9.4%)
Hyperkalemia[b]	351 (10.1%)	159 (4.5%)
Hyperkalemia leading to hospitalization[b]	20 (0.6%)	8 (0.2%)
Acute kidney injury[b]	138 (4.0%)	95 (2.7%)
Acute kidney injury leading to hospitalization	60 (1.7%)	36 (1.0%)
Any systolic blood pressure <100 mm Hg	573 (16.9%)	387 (11.3%)
Gynecomastia	9 (0.3%)	3 (0.1%)

[a]: Based on central laboratory measurements of potassium levels
[b]: Based on investigator-reported adverse events
Treatment-emergent adverse events are defined as any adverse event occurring in any patient who has received at least one dose of study drug and within 3 days of permanent discontinuation. There were no instances of death due to hyperkalemia.

Treatment Effects of Finerenone vs. Placebo on CV Death or HF Hospitalization

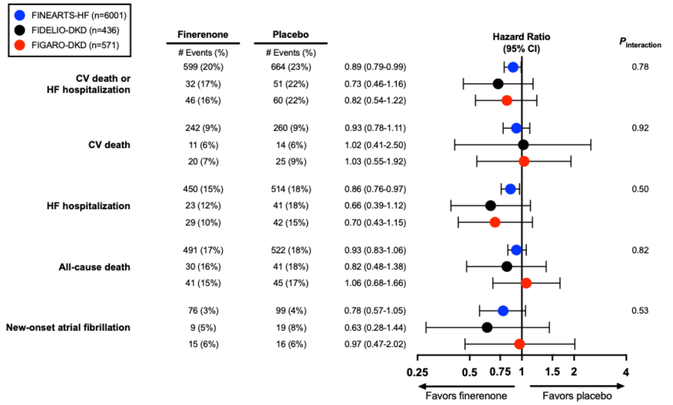


Trial	Incidence Rate (per 100 person-years) in Placebo Group
FINEARTS-HF	10 (95% CI, 9 to 11)
FIDELIO-DKD	9 (95% CI, 7 to 12)
FIGARO-DKD	8 (95% CI, 6 to 10)

Number at risk

Placebo	3520	3245	3044	2737	2311	1737	913	136	52
Finerenone	3488	3259	3051	2752	2326	1784	921	145	55

Treatment Effects of Finerenone vs. Placebo on Clinical Outcomes were Consistent Across Trials



Key Findings

In this prespecified participant-level pooled analysis representing the totality of outcomes trial experience with finerenone in HFmrEF/HFpEF, treatment benefits of finerenone on cardiovascular death or HF hospitalization observed in FINEARTS-HF were consistent in an expanded population of >1,000 participants enrolled in the adjacent FIDELIO-DKD and FIGARO-DKD trials.

Finerenone additionally reduced HF hospitalization and new-onset atrial fibrillation, but not mortality outcomes

No new safety signals with finerenone were identified.

However, some data elements were not consistently available for pooling (or assessed in all trials), and the primary endpoint of CV death was narrowly missed in the overall FINE-HEART analysis.

Funding

FIDELIO-DKD, FIGARO-DKD, and FINEARTS-HF were sponsored by Bayer AG.

These findings support the use of finerenone to reduce adverse clinical outcomes in individuals with HFmrEF/HFpEF across a broad range of cardiovascular-kidney-metabolic risk.