Finerenone and New York Heart Association Functional Class in Heart Failure: The FINEARTS-HF Trial

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Background

- The New York Heart Association (NYHA) functional classification remains an important and widely used metric in heart failure (HF)-oriented clinical care and research.
- Whether the effect of finerenone varies according to NYHA class in HF with mildly reduced or preserved ejection fraction (HFmrEF/HFpEF) has not been evaluated.

Study Aims

- In this prespecified analysis of the FINEARTS-HF trial, we evaluated:
  1. Key cardiovascular and mortality outcomes according to baseline NYHA functional class
  2. Treatment effects of finerenone versus placebo on clinical outcomes and HF-related health status, by baseline NYHA functional class
  3. Treatment effects of finerenone versus placebo on change in NYHA functional class between baseline and 12 months

Methods

- FINEARTS-HF was an international, randomized, placebo-controlled, double-blind trial evaluating the efficacy and safety of finerenone in persons with symptomatic (NYHA class II-IV) chronic HFmrEF/HFpEF
  - Key exclusion criteria: eGFR <25 mL/min/1.73 m²; K >5.0 mmol/L
- FINEARTS-HF participants were categorized according to investigator-reported NYHA class (II or III/IV) at screening
- Assessment of NYHA functional classification was not required for participants who prematurely discontinued study treatment.
- Clinical outcomes and treatment effects of finerenone were evaluated using LWYY models (for recurrent events) and Cox proportional hazards regression models (for time to first events)
- The placebo-adjusted effect of finerenone on change in NYHA functional class was estimated using an ordinal logistic regression model, with results reported as an overall odds ratio (OR) and 95% CI for the likelihood of attaining a lower (better) or higher (worse) NYHA functional class.
- All analyses were performed using Stata, version 18.5 (StataCorp, LLC)

Baseline Characteristics According to NYHA Functional Class in FINEARTS-HF

NYHA II (n=4146; 69%)
NYHA III/IV (n=1854; 31%)
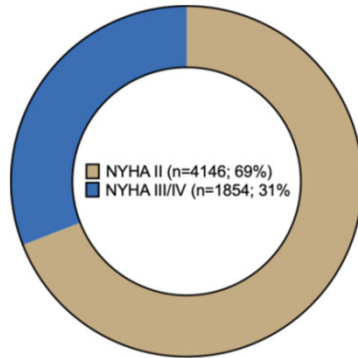
Worse NYHA functional class at baseline associated with:

- Older age
- Female sex
- Self-reported White race
- Recent HF events prior to randomization
- Prior HF hospitalization
- Worse patient-reported health status
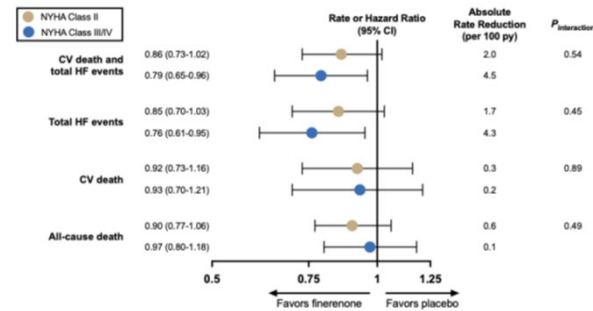- Higher burden of CV and non-CV comorbid conditions

Treatment Effects of Finerenone versus Placebo on Key Clinical Outcomes and HF-Related Health Status, by NYHA Functional Class

Treatment effects on clinical outcomes

Treatment effect estimates (and 95% CI) for recurrent events analyses (endpoints including total HF events) represent rate ratios, and others represent hazard ratios. All models were stratified by geographic region and left ventricular ejection fraction (<60% or ≥60%).
Abbreviations: CV = cardiovascular; HF = heart failure; NYHA = New York Heart Association; py = patient-years

Treatment effects on HF-related health status

Placebo-adjusted treatment effects of finerenone on mean change in KCCQ scores between baseline and 12 months, estimated through linear regression. Models adjusted for baseline values of each score, LVEF category (<60%, ≥60%), and geographic region. Interaction terms incorporated to evaluate for treatment effect modification by baseline NYHA class.

Key Cardiovascular and Mortality Outcomes According to Baseline NYHA Functional Class

	NYHA Functional Class II (n= 4146)	NYHA Functional Class III/IV (n=1854)
Primary composite outcome (CV death and total HF events)		
Number of events	1387	979
Event rate, per 100 py	13.6	22.8
Unadjusted RR (95% CI)	Ref.	1.67 (1.47, 1.90); P<0.001
Adjusted RR (95% CI)*	Ref.	1.28 (1.11, 1.46); P<0.001
Total HF events		
Number of events	1096	770
Event rate, per 100 py	10.7	17.9
Unadjusted RR (95% CI)	Ref.	1.66 (1.43, 1.92); P<0.001
Adjusted RR (95% CI)*	Ref.	1.25 (1.08, 1.46); P=0.004
CV death		
Number of events	291	211
Event rate, per 100 py	2.8	4.9
Unadjusted HR (95% CI)	Ref.	1.73 (1.45, 2.06); P<0.001
Adjusted HR (95% CI)*	Ref.	1.36 (1.12, 1.64); P=0.002
All-cause death		
Number of events	594	419
Event rate, per 100 py	5.8	9.7
Unadjusted HR (95% CI)	Ref.	1.68 (1.49, 1.91); P<0.001
Adjusted HR (95% CI)*	Ref.	1.36 (1.18, 1.55); P<0.001

*: Models adjusted for age, sex, race, body mass index, systolic blood pressure, diastolic blood pressure, smoking status, history of diabetes, history of stroke, history of myocardial infarction, history of atrial fibrillation, history of chronic obstructive pulmonary disease, estimated glomerular filtration rate, log-transformed N-terminal pro–B-type natriuretic peptide, left ventricular ejection fraction, prior HF hospitalization, and assigned treatment.
Abbreviations: CV = cardiovascular; HF = heart failure; HR = hazard ratio; NYHA = New York Heart Association; py = person-years; RR = rate ratio
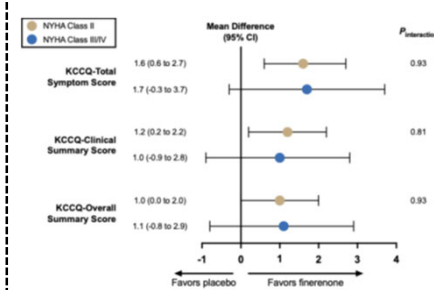
Treatment Effects of Finerenone on Change in NYHA Functional Class Between Baseline and 12 Months

OR for improvement: 1.11 (95% CI, 0.95 to 1.31) P=0.19
OR for improvement: 1.13 (95% CI, 0.98 to 1.31) P=0.09
OR for improvement: 1.04 (95% CI, 0.90 to 1.19) P=0.61
OR for improvement: 1.02 (95% CI, 0.89 to 1.17) P=0.80
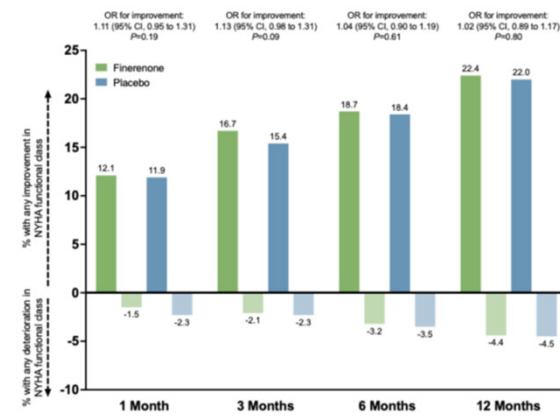
Finerenone
Placebo

Figure displays the percentage of participants with ≥1 improvement (i.e., to any lower class) and ≥1 deterioration (i.e., to any higher class) in NYHA functional class between baseline and 1-, 3-, 6-, and 12-months post-randomization, using all available data at each timepoint, without imputation for missing values. ORs, reflecting the overall likelihood of improvement or deterioration of NYHA functional class, and 95% CI estimated through ordinal logistic regression.

Key Findings

Finerenone reduced CV death and total HF events irrespective of baseline NYHA class, with greater absolute benefits among those with NYHA class III/IV vs. II.

Benefits of finerenone on HF-related health status were also consistent irrespective of baseline NYHA functional class; NYHA functional class improved similarly with finerenone versus placebo.

Baseline NYHA functional class did not appear to modify the safety profile of finerenone.

Key limitations include known inter-rater variability of NYHA class and limited enrollment of persons with NYHA functional class IV.

Funding

These findings support the use of finerenone in HFmrEF/HFpEF irrespective of NYHA functional class and provide important reassurance regarding the balance of benefit and risk in persons with more advanced symptoms and functional impairments.

Brigham and Women's Hospital — Founding Member, Mass General Brigham

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