Effects of Finerenone on Natriuretic Peptide Levels in Heart Failure with Mildly Reduced or Preserved Ejection Fraction: The FINEARTS-HF Trial

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FINEARTS-HF

Background

- N-terminal pro–B-type natriuretic peptide (NT-proBNP) levels are widely used for diagnosis and risk stratification in heart failure (HF).
- Changes in NT-proBNP with therapy have correlated with effects on HF hospitalizations in previous clinical trials.
- The non-steroidal mineralocorticoid receptor antagonist (MRA) finerenone reduced NT-proBNP by 18% in patients with type 2 diabetes and chronic kidney disease (Berger et al, *Circulation*, 2023).
- In patients with HF with mildly reduced or preserved ejection fraction (HFmrEF/HFpEF) in the FINEARTS-HF trial, finerenone reduced the primary outcome of total worsening HF events and CV death by 16% (Solomon et al, *NEJM*, 2024).
- The effect of finerenone on NT-proBNP in the HFmrEF/HFpEF population is unknown.

Study Aims

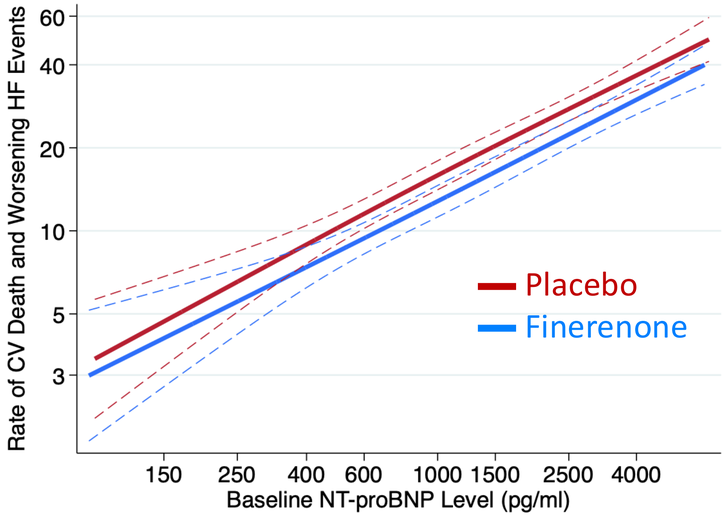
In patients with HFmrEF/HFpEF, we studied:

1. The treatment effect of finerenone on total HF hospitalization and cardiovascular death across baseline levels of NT-proBNP
2. The effect of finerenone on NT-proBNP levels

Methods

- FINEARTS-HF compared finerenone and placebo in 6001 patients with symptomatic HFmrEF/HFpEF (≥40%).
- NT-proBNP ≥300 pg/ml or BNP ≥100 pg/ml were required for inclusion. Thresholds were tripled in atrial fibrillation.

Clinical Benefit of Finerenone Across the Spectrum of Baseline NT-proBNP

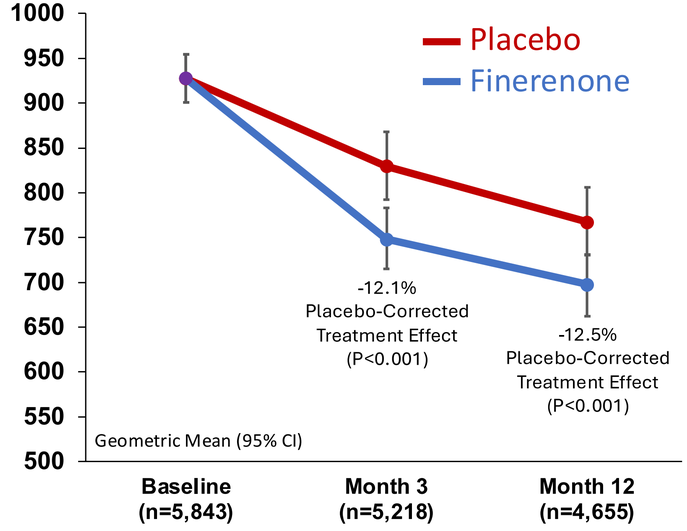


The restricted cubic spline displays the predicted rate of the primary outcome, total worsening heart failure events and cardiovascular death, by baseline NT-proBNP level in each treatment group. Dashed lines indicate 95% confidence intervals.

Methods (cont.)

- We evaluated associations between log-transformed baseline NT-proBNP and the primary outcome using semiparametric proportional rates models. We tested whether finerenone's effect on the primary outcome was modified by baseline NT-proBNP level.
- Models were adjusted for 12 covariates: age, sex, region, systolic blood pressure, body mass index, estimated glomerular filtration rate, ejection fraction, history of myocardial infarction, stroke, or hospitalization for HF, and diabetes mellitus or atrial fibrillation.
- We evaluated the placebo-corrected effect of finerenone on NT-proBNP levels at 3 and 12 months using linear regression, adjusted for the baseline value.

Treatment Effect of Finerenone on NT-proBNP



Geometric mean (95% confidence interval) NT-proBNP levels are shown at baseline and 3 and 12 months after randomization. Patients with missing NT-proBNP data at baseline were excluded at all three time points.

Results

- Among 5843 patients (97%) with available NT-proBNP data, median baseline NT-proBNP was 1041 [interquartile range 449,1946] pg/ml.
- NT-proBNP was strongly and independently associated with risk of the total worsening HF events and cardiovascular death (adjusted rate ratio 1.44 per doubling [95% CI 1.37-1.51], P<0.001).
- NT-proBNP was also associated with each component of the primary outcome alone: total worsening HF events (adjusted rate ratio 1.41 [95% CI 1.34-1.49], p<0.001) and cardiovascular death (adjusted hazard ratio 1.52 [95% CI 1.43-1.63], p<0.001]).

Results (cont.)

- Baseline NT-proBNP did not significantly modify the beneficial effects of finerenone on the primary outcome ($P_{interaction}$=0.92); finerenone reduced the primary outcome events across the spectrum of NT-proBNP levels.
- Finerenone reduced NT-proBNP by 12.1% (95% CI 8.5-15.4%) at 3 months and 12.5% (95% CI 8.1-16.7%) at 12 months, compared to placebo.
- The effect of finerenone on NT-proBNP levels at 3 months was not significantly modified by age, sex, race, atrial fibrillation, BMI, eGFR, or left ventricular ejection fraction.

Conclusions

- In this prespecified analysis of the FINEARTS-HF trial, NT-proBNP was strongly and independently associated with risk of worsening HF events and cardiovascular death.
- Finerenone appears to reduce worsening HF events and cardiovascular death in patients with HFmrEF/HFpEF with any degree of natriuretic peptide elevation.
- Finerenone reduced NT-proBNP by 12% compared to placebo. These reductions occurred rapidly (by 3 months after randomization) and were sustained through 12 months.

Funding

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