Finerenone and Blood Pressure in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

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FINEARTS-HF

Background

- Blood pressure (BP) optimization is a guideline-recommended priority of heart failure (HF) care
- Finerenone, a selective and potent nonsteroidal mineralocorticoid receptor antagonist, has been shown to improve clinical outcomes in individuals with heart failure (HF) with mildly reduced or preserved ejection fraction (HFmrEF/HFpEF)
- However, the BP effects of finerenone in this population, and whether they account for its treatment benefits, have not been rigorously evaluated

Study Aims

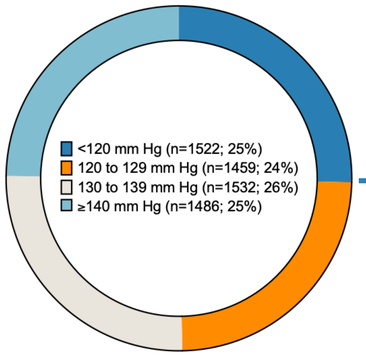
- In this prespecified analysis of the international, randomized FINEARTS-HF (FINerenone trial to investigate Efficacy and sAfety superioR to placebo in paTientS with Heart Failure) trial we evaluated:
  1. Treatment effects of finerenone vs. placebo on clinical outcomes according to baseline systolic BP (SBP)
  2. Treatment effects of finerenone vs. placebo on SBP

Methods

- Participants were categorized according to SBP at baseline (<120 mm Hg, 120 to 129 mm Hg, 130 to 139 mm Hg, and ≥140 mm Hg)
- Participants were additionally categorized according to BP status (controlled BP, non-resistant hypertension, and apparent treatment-resistant hypertension [aTRH]) according to clinical guidelines
- Treatment effects of finerenone vs. placebo on key clinical outcomes were evaluated using a semiparametric proportional hazards regression (for recurrent events outcomes) or Cox proportional hazards regression (for first event outcomes)
  - Interactions terms between treatment and BP category were included to evaluate for effect modification by baseline SBP
- Treatment effects of finerenone were evaluated across the continuous spectrum of baseline SBP using restricted cubic splines (estimated through Poisson regression) with 3 knots

Baseline Characteristics in FINEARTS-HF, by Baseline SBP Category

Distribution of Baseline SBP in FINEARTS-HF

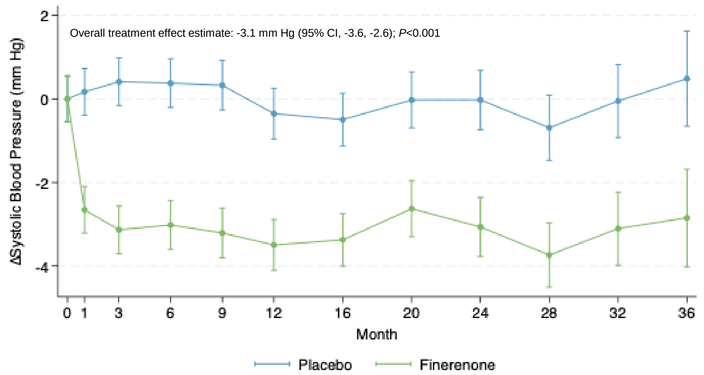


Compared to those with lower SBP, FINEARTS-HF participants with higher SBP:

↓ Asian race, prior HF hospitalization, NT-proBNP, AF, and background β-blockers, ARNI, SGLT2i, and loop diuretics

↑ Age, female sex, BMI, waist circumference, LVEF, UACR, T2D, background calcium channel blockers

Finerenone Significantly Reduced SBP vs. Placebo



Overall treatment effect estimated through mixed model linear regression incorporating baseline SBP as a fixed effect and patient-level intercept terms as random effects.

Benefits of Finerenone on Outcomes were Independent of BP Effects

Efficacy Outcome	Model 1[a] RR (95% CI)	Model 1[a] *P* value	Model 2[b] RR (95% CI)	Model 2[b] *P* value
CV death and total worsening HF events	0.84 (0.74, 0.95)	0.007	0.85 (0.74, 0.97)	0.015
Total worsening HF events	0.82 (0.71, 0.94)	0.006	0.83 (0.71, 0.96)	0.014

[a]: Unadjusted semiparametric proportional rates model, stratified by LVEF category (<60% and ≥60%) and geographic region, comparing finerenone to placebo among the 5,999 participants with available systolic BP at baseline.
[b]: Semiparametric proportional rates model, stratified by LVEF category (<60% and ≥60%) and geographic region, landmarked at 1 month, with adjustment for systolic BP at baseline and 1 month.
Abbreviations: BP = blood pressure; CV = cardiovascular; HF = heart failure; RR = rate ratio

Treatment Effects of Finerenone vs. Placebo on CV Death and Worsening HF Events, by Baseline SBP

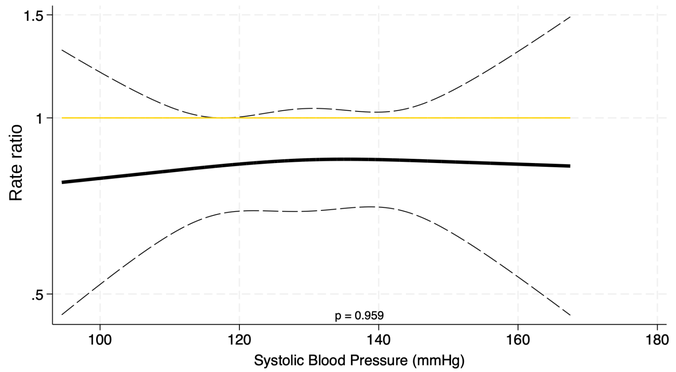


Figure displays the continuous flexible association between baseline SBP and treatment effects of finerenone vs. placebo on the primary composite endpoint. *P* value refers to *P* value for interaction by baseline SBP.

Finerenone Significantly Reduced SBP vs. Placebo, Including Among Participants with aTRH

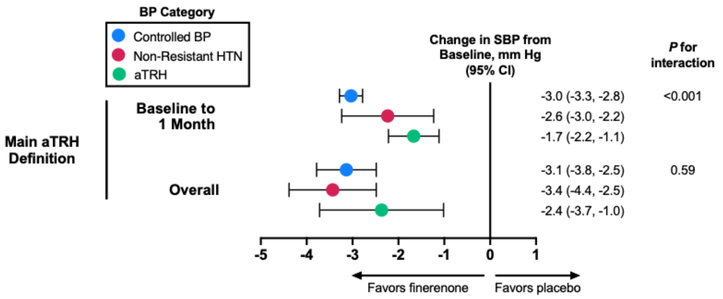


Figure displays placebo-adjusted changes in SBP, by BP category
Main aTRH definition: aTRH = BP ≥140/80 mm Hg (≥130/80 mm Hg if diabetes) and taking ACEI/ARB/ARNI + CCB + diuretic; non-resistant HTN = BP above threshold, but not meeting aTRH criteria; controlled BP = BP below threshold

Key Findings

In this prespecified analysis of the FINEARTS-HF trial, benefits of finerenone on CV death and total worsening HF events were consistent irrespective of SBP, including among those with aTRH

Finerenone significantly reduced systolic BP between baseline and 36 months, including among participants with aTRH, but these effects did not account for its benefits on clinical outcomes

Modestly higher odds of laboratory-defined hyperkalemia, elevated serum creatinine levels, and SBP <100 mm Hg with finerenone vs. placebo were not enhanced with higher or lower baseline SBP, or among participants with aTRH

Funding

FINEARTS-HF was sponsored by Bayer AG.

In the FINEARTS-HF trial, finerenone consistently reduced CV death and total worsening HF events irrespective of baseline SBP, and additionally resulted in early and sustained reductions in SBP, among individuals with HFmrEF/HFpEF.