Finerenone Across the Spectrum of Kidney Risk in Heart Failure: The FINEARTS-HF Trial

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Background

- Estimated glomerular filtration rate (eGFR) and urine albumin-to-creatinine ratio (UACR) are complementary domains of kidney disease staging and independently associated with heart failure (HF) progression.
- However, whether treatment effects of finerenone vary according to kidney risk category in persons with HF with mildly reduced or preserved ejection fraction (HFmrEF/HFpEF) remains uncertain.

Study Aims

- In this prespecified analysis of the FINEARTS-HF trial, we evaluated:
  1. Cardiovascular, kidney, and mortality outcomes according to baseline Kidney Disease: Improving Global Outcomes (KDIGO) risk category
  2. Treatment effects of finerenone versus placebo according to baseline KDIGO risk category
  3. Changes in eGFR slope and UACR change according to baseline KDIGO risk category

Methods

- FINEARTS-HF was an international, randomized, placebo-controlled, double-blind trial evaluating the efficacy and safety of finerenone in persons with symptomatic chronic HFmrEF/HFpEF
  - Key exclusion criteria: eGFR <25 mL/min/1.73 m^2; K >5.0 mmol/L
- FINEARTS-HF participants were categorized according to KDIGO risk category using baseline eGFR and UACR values:
  - **Low risk:** eGFR ≥60 mL/min/1.73 m^2 and UACR <30 mg/g
  - **Moderately increased risk:** eGFR ≥60 mL/min/1.73 m^2 and UACR ≥30 to ≤300 mg/g or eGFR ≥45 to 59 mL/min/1.73 m^2 and UACR <30 mg/g
  - **High risk:** eGFR ≥45 to <60 mL/min/1.73 m^2 and UACR ≥30 to 300 mg/g, eGFR <45 mL/min/1.73 m2, or UACR >300 mg/g
- 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)
- Changes in eGFR and UACR were evaluating using mixed effects linear regression.
- All analyses were performed using Stata, version 18.5 (StataCorp, LLC)

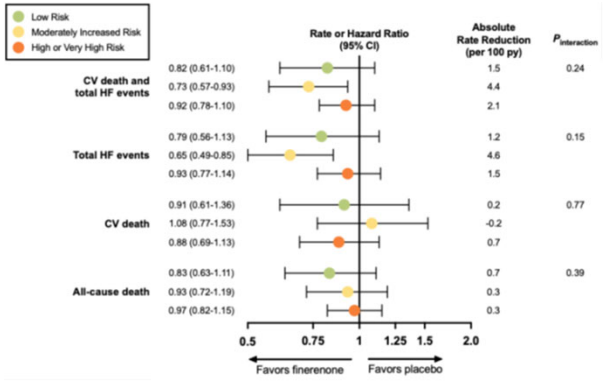
Distribution of Baseline KDIGO Risk Categories in FINEARTS-HF

eGFR (mL/min/1.73 m^2)			UACR (mg/g) A1 <30	A2 30-300	A3 >300
G1	≥90		6.3%	2.4%	0.5%
G2	60-89		28.5%	11.2%	2.8%
G3a	45-59		15.4%	8.2%	2.6%
G3b	30-44		8.7%	6.5%	3.0%
G4	15-29		1.6%	1.2%	0.9%
G5	<15		0.0%	0.0%	0.0%

KDIGO Risk Categories		
Low	Moderate	High or Very High
35%	29%	36%

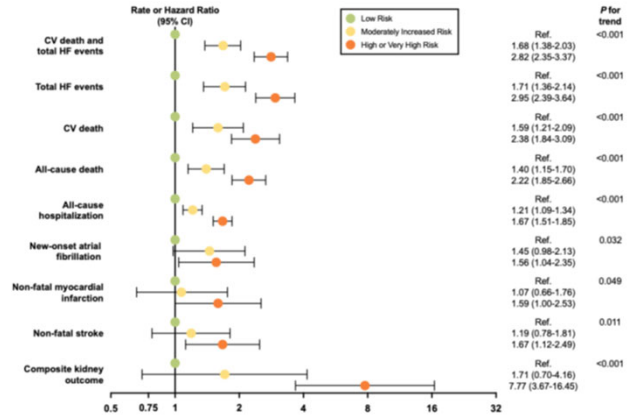
Participants with higher baseline KDIGO risk category were more likely to have older age, female sex, Asian race, worse HF-related health status, prior HF hospitalization, and a greater burden of comorbid cardiovascular and metabolic conditions.

Treatment Effects of Finerenone versus Placebo on Key Clinical Outcomes



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

KDIGO Risk Category and Cardiovascular, Kidney, and Mortality Outcomes in HFmrEF/HFpEF



Forest plot displays the covariate-adjusted association between KDIGO risk category and cardiovascular mortality, and kidney outcomes in FINEARTS-HF. All models adjusted for age, sex, race, timing of worsening HF events prior to randomization, New York Heart Association functional class, body mass index, atrial fibrillation, history of stroke, history of diabetes, history of myocardial infarction, smoking status, left ventricular ejection fraction, and randomized treatment.

Treatment Effects of Finerenone versus Placebo on UACR Change and eGFR Slope by Kidney Risk Category

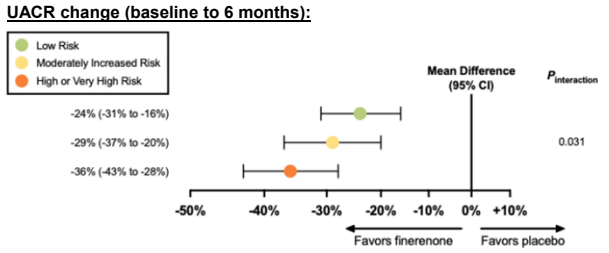


Figure displays placebo-adjusted treatment effects of finerenone on percentage change in UACR (geometric mean) between baseline to 6 months by KDIGO risk category at baseline, according to baseline diabetes status.
Abbreviations: UACR = urine albumin-to-creatinine ratio

Placebo-adjusted mean differences in acute initial eGFR change ($P_{interaction}$=0.71), chronic eGFR slope ($P_{interaction}$=0.49), and total eGFR slope ($P_{interaction}$=0.85) with finerenone were similar across KDIGO risk categories.

Key Findings

KDIGO risk category at baseline was associated with worse HF-related health status and a broad range of cardiovascular, kidney, and mortality outcomes in FINEARTS-HF

Finerenone reduced CV death and total HF events irrespective of baseline KDIGO risk category, with greater absolute benefits among those at moderately increased and high/very high kidney risk.

Participants with higher baseline kidney risk experienced relatively greater reductions in albuminuria; eGFR trajectories with finerenone versus placebo were similar across KDIGO risk categories.

Well-recognized higher odds of elevated serum creatinine levels and hyperkalemia with finerenone versus placebo were not enhanced with higher KDIGO kidney risk.

Severe kyperkalemia events with finerenone versus placebo, such as K >6.0 mmol/L (3.8% vs. 1.9%) and hyperkalemia leading to hospitalization (0.7% vs. 0.5%) were uncommon even among those with high/very high kidney risk.

Key limitations include eGFR-based exclusion criteria, lack of data on other serum and urinary biomarkers of kidney risk, and limited insights into individuals at very high kidney risk.

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These findings underscore the potential of comprehensive kidney screening to improve risk stratification in HFmrEF/HFpEF and support the use of finerenone to improve clinical outcomes across a broad range of kidney risk.