VA U.S. Department of Veterans Affairs
Veterans Health Administration
Minneapolis VA Health Care System

#AHA24

FINERENONE AND RISK OF HYPERKALEMIA IN PATIENTS WITH HEART FAILURE WITH MILDLY REDUCED OR PRESERVED EJECTION FRACTION

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On behalf of the FINEARTS-HF Investigators

American Heart Association.

FINEARTS-HF

FINerenone trial to investigate **E**fficacy and s**A**fety superio**R** to placebo in pa**T**ient**S** with **H**eart **F**ailure

University of Glasgow

American Heart Association. 100 YEARS Bold Hearts

DISCLOSURES

Dr. Vardeny reports receiving research support to her institution from AstraZeneca, Bayer, & Cardurion, and personal consulting fees from AstraZeneca, Bayer, Cardior, Cytokinetics, and Moderna.

BACKGROUND

- Mineralocorticoid receptor antagonists (MRA) are a key component of guideline directed medical therapy (GDMT) for heart failure with reduced ejection fraction (HFrEF) and may also be used in patients with heart failure with mildly reduced or preserved ejection fraction (HFmrEF/HFpEF)
- Steroidal MRAs are underutilized in HFrEF, in part due to the perceived risk of hyperkalemia
- Potassium levels **< 3.5mmol/l** are associated with an increased risk for adverse clinical outcomes in patients with heart failure, and MRAs mitigate the risk of hypokalemia
- **In the FINEARTS-HF trial, the nonsteroidal MRA finerenone reduced the risk of cardiovascular death and total worsening heart failure (HF) events in patients with HFmrEF/HFpEF**
- We investigated the frequency and predictors of serum potassium level **> 5.5 and < 3.5 mmol/l** and the treatment effect of finerenone, relative to placebo, on clinical outcomes based on post-randomization potassium levels.

FINEARTS-HF STUDY DESIGN

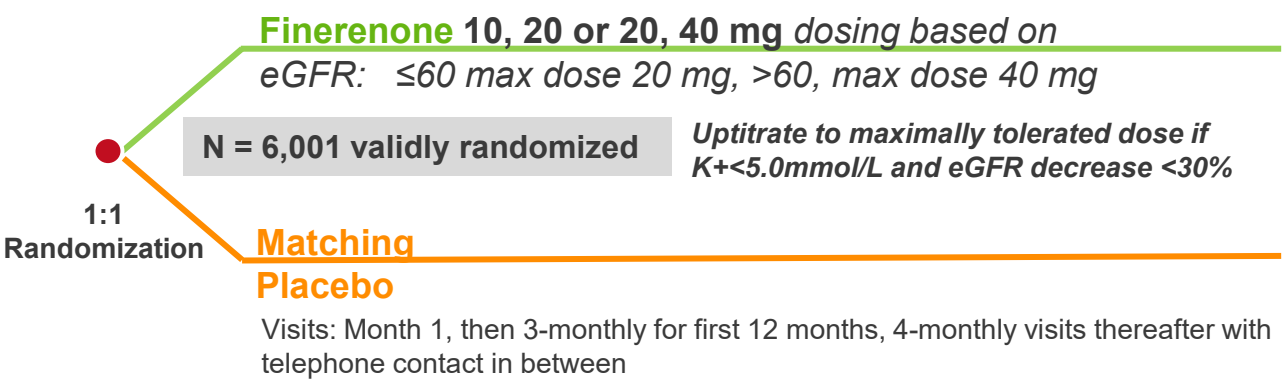
Randomized, double-blind, placebo-controlled trial testing the hypothesis that finerenone would reduce cardiovascular death and total worsening heart failure events in patients with heart failure and mildly reduced or preserved ejection fraction

Key Inclusion Criteria

- **Symptomatic HF (NYHA class II-V) with LVEF ≥ 40%**
- **Hospitalized, recently hospitalized, or ambulatory**
- **Elevated natriuretic peptide levels**
- **Structural heart disease (LA Enlargement or LVH)**
- **Diuretics in the 30d prior to randomization**

Key Exclusion Criteria

- **Potassium > 5.0 mmol/L; eGFR <25 mL/min/1.73 m²**
- **MRA use 30d prior to randomization**
- **History of peripartum, chemotherapy induced, or infiltrative cardiomyopathy (e.g., amyloidosis)**
- **Alternative causes of signs or symptoms**



Study Endpoints

Primary Endpoint

- CV death and total HF events (hospitalizations/urgent visits)

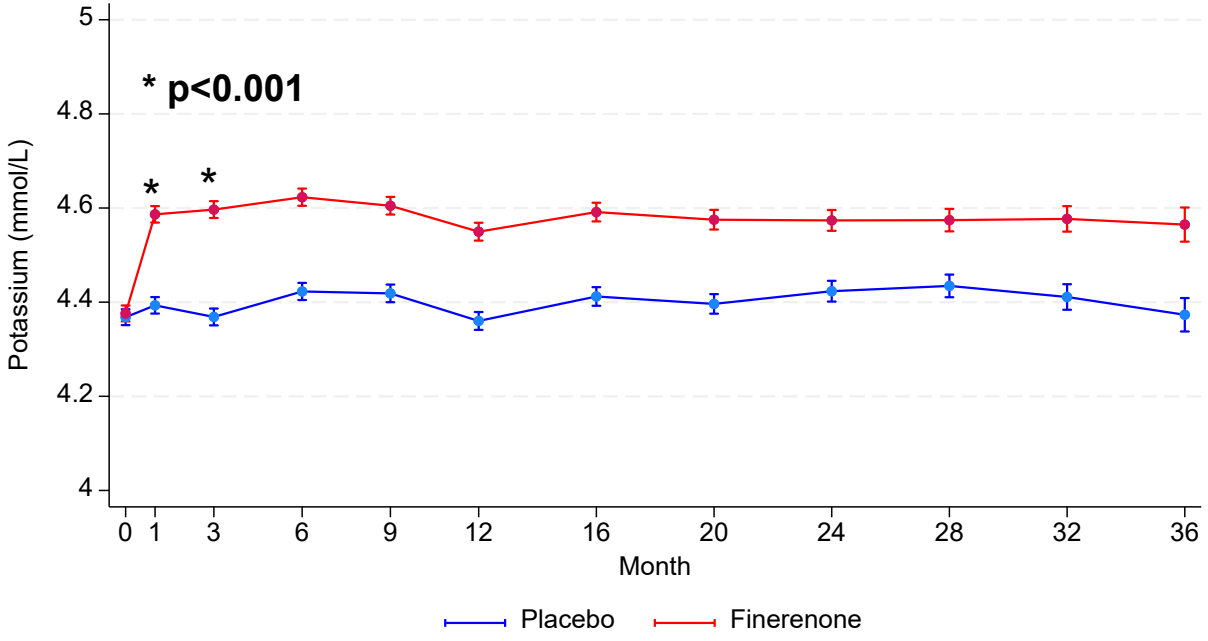
Secondary Endpoints

- Total HF events
- KCCQ-TSS at 6,9, and 12 months
- NYHA class at 12 months
- Renal composite endpoint
- All-cause mortality

METHODS

- Study medication dose adjustments
  - If potassium ≥ 5.5mmol/L, study medication dose was down-titrated if possible, or interrupted. If ≥ 6.0mmol/L, study medication was interrupted, and potassium rechecked in 72 hours
  - If repeat potassium was <5.5mmol/L, could restart at low dose
- Cox proportional hazards regression models were used to examine associations between baseline characteristics and time to post-baseline potassium > 5.5 mmol/L and potassium <3.5 mmol/L, adjusting for treatment assignment & clinical covariates
- Treatment-specific Poisson regression models used in landmark and time updated analyses, estimating via cubic spline models the rate of the primary outcome based on potassium levels

POTASSIUM LEVELS DURING THE STUDY BY TREATMENT



- One-month PL corrected potassium change: **0.19 (0.17-0.21)mmol/L**
- Three-month PL corrected potassium change: **0.23 (0.21-0.25)mmol/L**

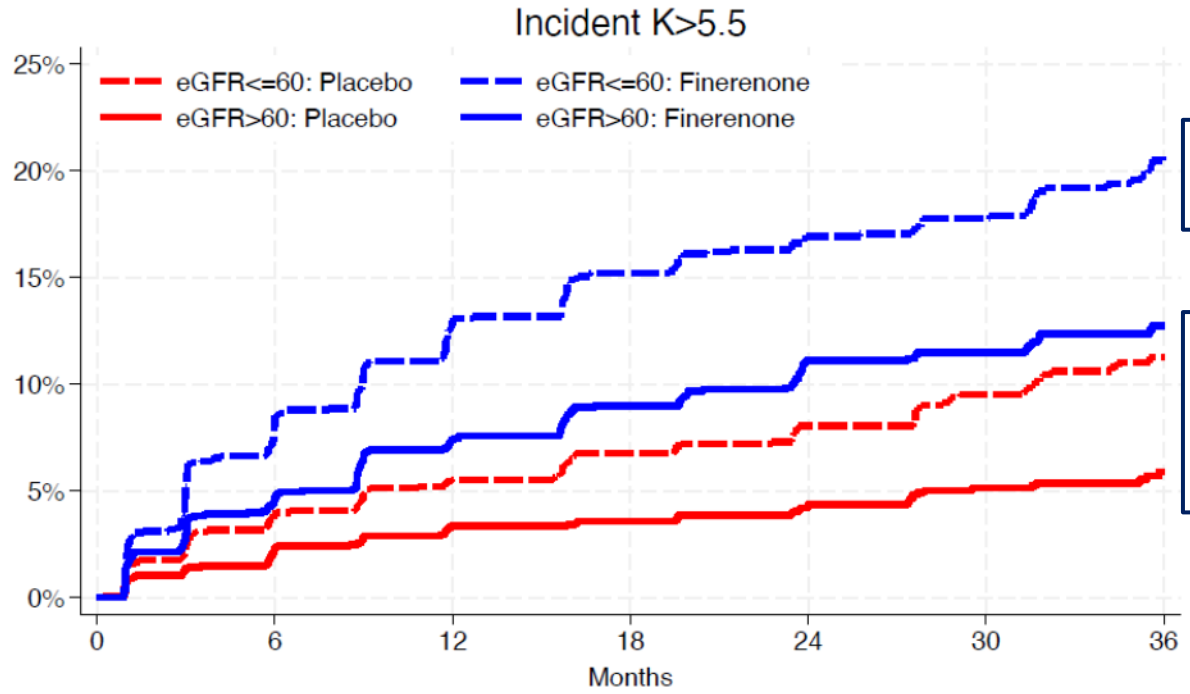
BASELINE CHARACTERISTICS (K > 5.5MMOL/L)

Characteristic		No potassium > 5.5 (n=5203)	Any potassium > 5.5 (n=633)	P value
Age, years		72.0 ± 9.7	71.6 ± 9.2	p=0.37
Women (%)		2382 (45.8%)	255 (40.3%)	p=0.009
Race (%)	White/Asian/Black/other	78 / 18 / 1.5 / 3.0	85 / 10 / 1.3 / 3.6	<0.001
History (%)	Type 2 diabetes	40	51	<0.001
	Myocardial infarction	25	31	0.003
	HF hospitalization	60	64	0.035
Body mass index, kg/m^2		30.0 ± 6.1	29.6 ± 5.7	p=0.18
Systolic blood pressure, mmHg		129.3 ± 15.4	130.4 ± 14.4	p=0.10
eGFR, mL/min/1.73 m^2		62.8 ± 19.7	57.6 ± 19.4	p<0.001
LVEF, %		52.6 ± 7.8	52.1 ± 7.7	p=0.10
NT-proBNP, pg/mL		1014 [441, 1901]	1163 [501, 2344]	p<0.001
NYHA class (%)	II/III/IV	70 / 29 / 0.7	67 / 32 / 0.3	0.18
Baseline potassium (mmol/l)		4.3 ± 0.5	4.7 ± 0.5	p<0.001
UACR (mg/G)		18 [7, 63]	22 [8, 102]	p<0.001

BASELINE CHARACTERISTICS (K <3.5MMOL/L)

Characteristic		No potassium < 3.5 (n=5392)	Any potassium < 3.5 (n=444)	P value
Age, years		71.9 ± 9.6	72.3 ± 10.5	p=0.37
Women (%)		2410 (44.7%)	227 (51.1%)	p=0.009
Race (%)	White/Asian/Black/other	80 / 16 / 1.4 / 3.1	67 / 29 / 2 / 2	<0.001
History (%)	Type 2 diabetes	2218 (41.1%)	161 (36.3%)	p=0.045
	Myocardial infarction	1420 (26.3%)	93 (20.9%)	p=0.013
	HF hospitalization	3212 (59.6%)	286 (64.4%)	p=0.045
Body mass index, kg/m^2		30.0 ± 6.1	29.5 ± 6.4	p=0.09
Systolic blood pressure, mmHg		129.4 ± 15.2	129.1 ± 16.3	p=0.61
eGFR, mL/min/1.73 m^2		62.3 ± 19.6	61.1 ± 20.6	p=0.23
LVEF, %		52.5 ± 7.8	53.4 ± 7.8	p=0.013
NT-proBNP, pg/mL		1014 [438, 1916]	1312 [616, 2264]	p<0.001
NYHA class (%)	II/III/IV	69 / 30 / 0.5	67 / 31 / 2.0	0.17
Baseline potassium (mmol/l)		4.4 ± 0.5	4.0 ± 0.5	p<0.001
UACR (mg/G)		18 [7, 65]	21 [9, 74]	p=0.012

INCIDENCE OF POTASSIUM > 5.5MMOL/L BY EGFR GROUP

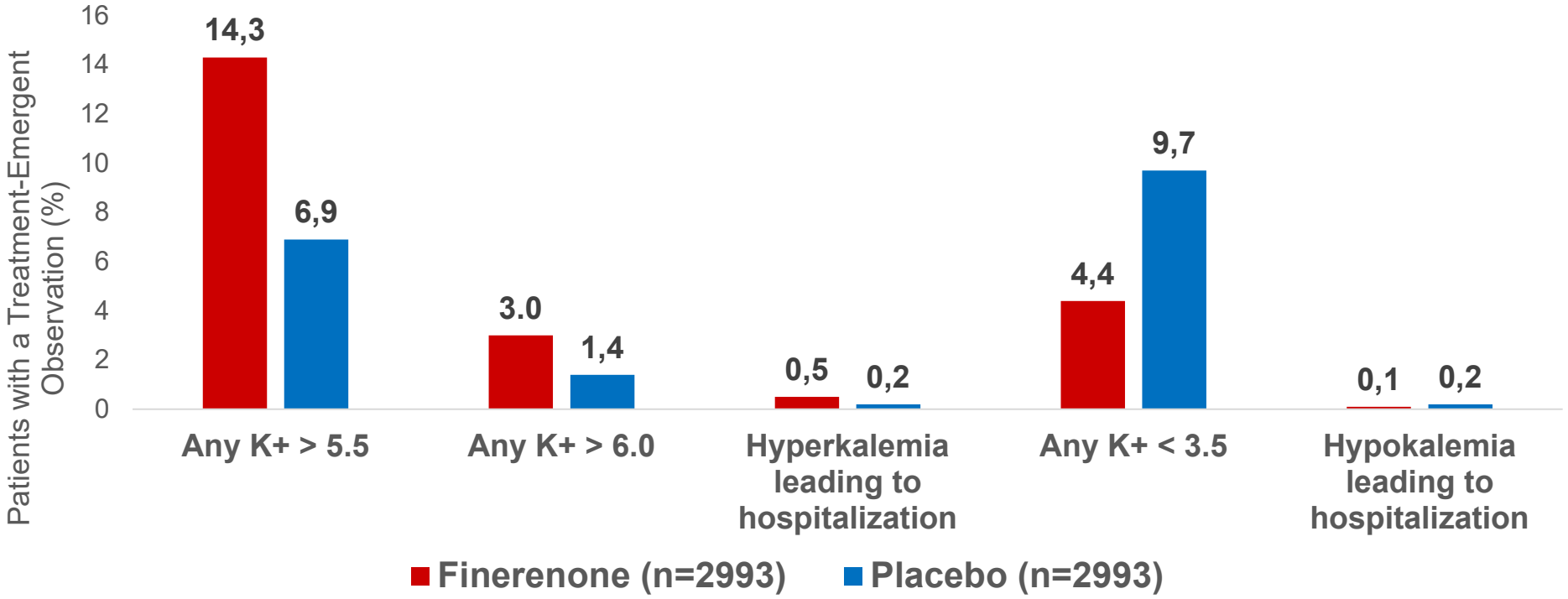


20mg, eGFR ≤60ml/min/1.73m^2
HR 2.02; 95% CI 1.63, 2.50

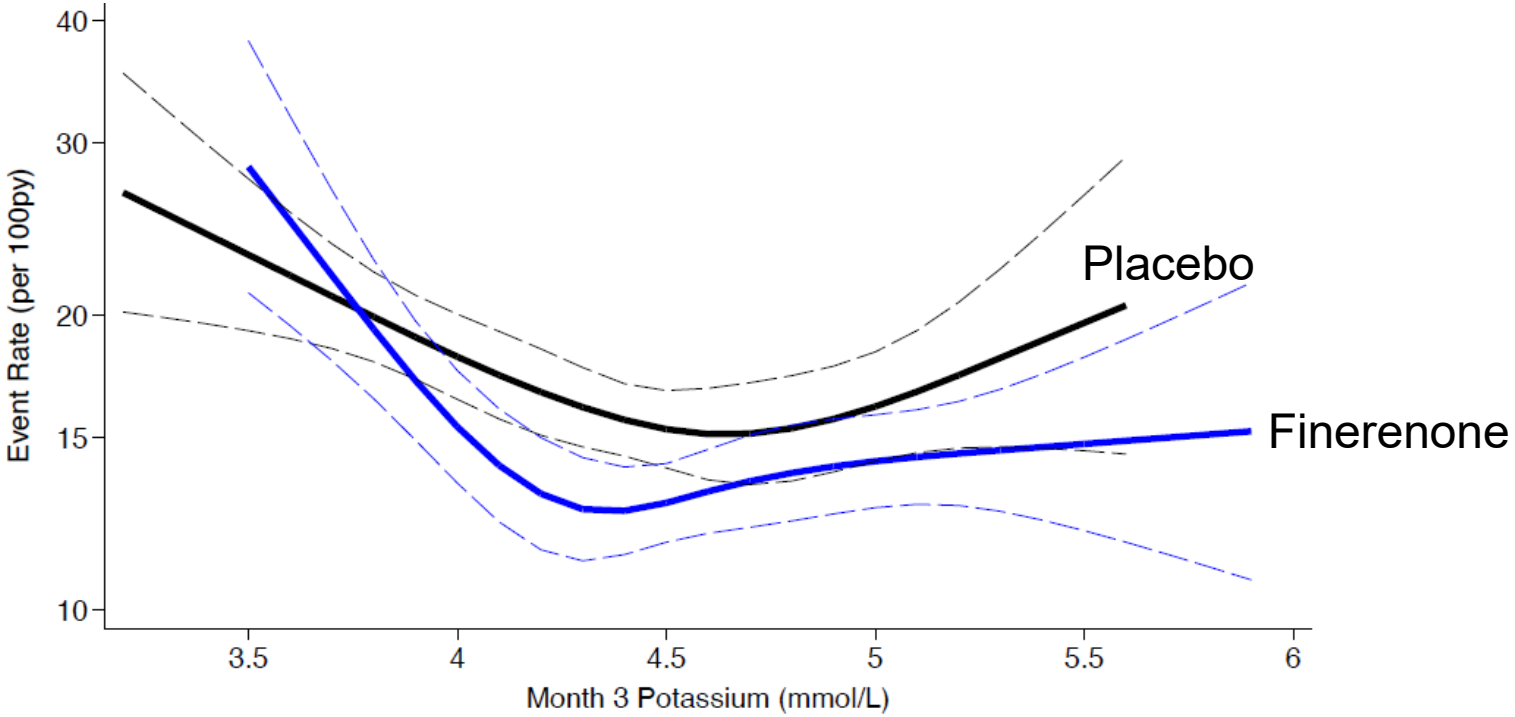
40mg, eGFR >60ml/min/1.73m^2
HR 2.35; 95% CI 1.80, 3.05

interaction p=0.39

SPECTRUM OF POTASSIUM-RELATED CHANGES



RATES OF CARDIOVASCULAR DEATH OR TOTAL WORSENING HEART FAILURE BY 3-MONTH POTASSIUM LEVELS



CONCLUSIONS

- In patients with heart failure and mildly reduced or preserved ejection fraction, finerenone resulted in early modest increases in potassium levels
- The clinical benefit associated with finerenone was maintained even in the setting of elevated potassium, and the risk of hypokalemia was reduced with finerenone
- Appropriate dose selection according to baseline renal function and dose adjustments in response to monitored potassium levels, may mitigate risks of serious hyperkalemia and optimize treatment continuation in clinical practice
- **These data suggest a favorable risk-to-benefit ratio for the use of finerenone in select patients with HFmrEF/HFpEF in the setting of protocolized surveillance and follow up**

THANK YOU

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Finerenone, Serum Potassium, and Clinical Outcomes in Heart Failure With Mildly Reduced or Preserved Ejection Fraction

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