JACC: HEART FAILURE VOL. 13, NO. 8, 2025

ORIGINAL RESEARCH

HEART FAILURE

Efficacy and Safety of Finerenone in Heart Failure With Preserved Ejection Fraction

A FINE-HEART Analysis

John W. Ostrominski, MD,[a] Gerasimos Filippatos, MD,[b] Brian L. Claggett, PhD,[a] Zi Michael Miao, MS,[a] Akshay S. Desai, MD, MPH,[a] Pardeep S. Jhund, MBChB, PhD, MSc,[c] Alasdair D. Henderson, PhD,[c] Markus F. Scheerer, PhD,[d] Katja Rohwedder, MD,[d] Flaviana Amarante, MD,[e] Meike Brinker, MD,[f] James Lay-Flurrie, MSc,[g] Carolyn S.P. Lam, MBBS, PhD,[h] Michele Senni, MD,[i] Sanjiv J. Shah, MD,[j] Adriaan A. Voors, MD PhD,[k] Faiez Zannad, MD,[l] Peter Rossing, MD,[m,n] Luis M. Ruilope, MD PhD,[o] Stefan D. Anker, MD,[p] Bertram Pitt, MD,[q] Rajiv Agarwal, MD,[r] John J.V. McMurray, MD,[c] Scott D. Solomon, MD,[a] Muthiah Vaduganathan, MD, MPH[a]

ABSTRACT

BACKGROUND Pooling data from participants with heart failure with mildly reduced ejection fraction (HFmrEF) or heart failure with preserved ejection fraction (HFpEF) from all completed outcomes trials evaluating finerenone to date may enhance understanding of its safety and efficacy in this high-risk and heterogeneous population.

OBJECTIVES In this prespecified participant-level pooled analysis of the FIDELIO-DKD, FIGARO-DKD, and FINEARTS-HF trials (FINE-HEART), we evaluated the safety and efficacy of finerenone in individuals with HFmrEF/HFpEF.

METHODS The treatment effects of finerenone vs placebo on cardiovascular death or heart failure hospitalization were evaluated using Cox proportional hazards regression models stratified by trial. Additional endpoints included cardiovascular death, HF hospitalization, new-onset atrial fibrillation, and all-cause death.

RESULTS Among 18,991 pooled trial participants, 7,008 (36.9%) had HFmrEF/HFpEF (mean age, 71 ± 10 years; 44% female). Over a median follow-up of 2.5 years, finerenone reduced cardiovascular death or heart failure hospitalization compared with placebo (HR: 0.87 [95% CI: 0.78-0.96]; $P = 0.008$). Consistent effects were observed across trials ($P_{interaction} = 0.24$), key subgroups, and baseline estimated glomerular filtration rate ($P_{interaction} = 0.47$), urine albumin-to-creatinine ratio ($P_{interaction} = 0.62$), and glycated hemoglobin ($P_{interaction} = 0.93$). Finerenone additionally appeared to reduce heart failure hospitalization (HR: 0.84 [95% CI: 0.74-0.94]; $P = 0.003$) and new-onset atrial fibrillation (HR: 0.75 [95% CI: 0.58-0.97]; $P = 0.030$), but did not statistically significantly decrease cardiovascular death or all-cause death. Hyperkalemia was more common, and hypokalemia was less common, with finerenone vs placebo. Serious adverse events were similar between the treatment arms.

CONCLUSIONS This participant-level pooled analysis of 3 large-scale outcomes trials supports the use of finerenone in individuals with HFmrEF/HFpEF across a broad range of cardiovascular-kidney-metabolic risk. (FINE-HEART: An Integrated Pooled Analysis of Finerenone across 3 Phase III Trials of Heart Failure and Chronic Kidney Disease and Type 2 Diabetes; CRD42024570467) (JACC Heart Fail. 2025;13:102497) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

ISSN 2213-1779 https://doi.org/10.1016/j.jchf.2025.03.041

ABBREVIATIONS AND ACRONYMS

CKD = chronic kidney disease

EF = ejection fraction

eGFR = estimated glomerular filtration rate

HF = heart failure

HFmrEF = heart failure with mildly reduced ejection fraction

HFpEF = heart failure with preserved ejection fraction

IR = incidence rate

T2D = type 2 diabetes

UACR = urinary albumin-to-creatinine ratio

Finerenone, a nonsteroidal mineralocorticoid receptor antagonist, was recently demonstrated in the FINEARTS-HF (FINerenone trial to investigate Efficacy and sAfety superioR to placebo in paTientS with Heart Failure) trial to reduce cardiovascular death and heart failure (HF) events among individuals with heart failure with mildly reduced ejection fraction (HFmrEF) or heart failure with preserved EF (HFpEF).[1] Prior large-scale trials evaluating treatment effects of finerenone on cardiovascular and kidney outcomes in persons with chronic kidney disease (CKD) and type 2 diabetes (T2D), namely, the FIDELIO-DKD (Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease) and FIGARO-DKD (Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease) trials,[2-4] also included individuals with HFmrEF/HFpEF.

Given the important pathophysiological intersection between HF, CKD, and T2D,[5] and the rising frequency with which these conditions coexist,[6] studies leveraging the totality of advanced-phase trial experience with finerenone may enhance understanding of the safety and efficacy of finerenone in these growing and clinically relevant populations with cardiovascular-kidney-metabolic multimorbidity. In this participant-level pooled analysis of 3 international, randomized, placebo-controlled, outcomes trials (FINE-HEART),[7] we evaluated the safety and efficacy of finerenone among individuals with HFmrEF/HFpEF. Given the apparent consistency of treatment benefits of finerenone according to T2D and kidney status in FINEARTS-HF,[1] we hypothesized that finerenone would reduce cardiovascular events in the broader FINE-HEART population.

METHODS

THE INTEGRATED FINE-HEART PROGRAM, PATIENT POPULATION, AND TRIAL CHARACTERISTICS. The rationale, design, and primary results of FINE-HEART have been described previously.[7] Briefly, FINE-HEART is a prespecified participant-level pooled analysis (CRD42024570467) of 3 global, multicenter, double-blind, placebo-controlled, randomized clinical trials evaluating the safety and efficacy of finerenone in adults with CKD and T2D or HFmrEF/HFpEF with or without T2D. Smaller randomized clinical trials evaluating finerenone that excluded individuals with HFmrEF/HFpEF (eg, ARTS [NCT01345656] and ARTS-HF [NCT01807221]),[8,9] were active controlled, or did not include ≥100 individuals with HFmrEF/HFpEF were excluded. The design, baseline characteristics, and primary results of each of the trials included in FINE-HEART have been reported previously.[1-3,10-13]

The FIDELIO-DKD and FIGARO-DKD trials enrolled adults (≥18 years of age) with T2D and CKD across 48 countries. FIDELIO-DKD required a urinary albumin-to-creatinine ratio (UACR) of 30 to <300 mg/g, an estimated glomerular filtration rate (eGFR) of 25 to <60 mL/min/1.73 m^2, and a history of diabetic retinopathy or a UACR of 300 to 5,000 mg/g and eGFR of 25 to <75 mL/min/1.73 m^2. FIGARO-DKD required either a UACR of 30 to <300 mg/g with an eGFR of 25 to 90 mL/min/1.73 m^2 or a UACR of 300 to 5,000 mg/g with an eGFR of ≥60 mL/min/1.73 m^2. Both trials required a serum potassium of ≤4.8 mmol/L for enrollment. The use of renin-angiotensin system inhibitors and dosing was optimized prior to randomization during run-in phases (lasting 4-16 weeks) in both trials. Patients with a clinical diagnosis of symptomatic (NYHA functional class II-IV) heart failure with reduced ejection fraction (HFrEF) were

From the [a]Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA; [b]National and Kapodistrian University of Athens, School of Medicine, Attikon University Hospital, Athens, Greece; [c]University of Glasgow, Glasgow, Scotland, United Kingdom; [d]Bayer AG, Global Medical Affairs, Berlin, Germany; [e]Cardiology and Nephrology Clinical Development, Bayer SA, São Paulo, Brazil; [f]Bayer AG, Research and Development, Pharmaceuticals, Wuppertal, Germany; [g]Bayer plc, Research and Development, Pharmaceuticals, Reading, United Kingdom; [h]National Heart Centre Singapore and Duke-National University of Singapore, Singapore; [i]University of Milano-Bicocca ASST Papa Giovanni XXIII Hospital, Bergamo, Italy; [j]Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; [k]University of Groningen, Groningen, the Netherlands; [l]University of Lorraine, Nancy, France; [m]Steno Diabetes Center Copenhagen, Herlev, Denmark; [n]University of Copenhagen, Copenhagen, Denmark; [o]Hospital 12 de Octubre, Madrid, Spain; [p]Charité University, Berlin, Germany; [q]University of Michigan, Ann Arbor, Michigan, USA; and the [r]Indiana University School of Medicine, Indianapolis, Indiana, USA.

Biykem Bozkurt, MD, PhD, served as acting Editor-in-Chief and main adjudicator for this paper.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received November 29, 2024; revised manuscript received March 10, 2025, accepted March 11, 2025.

excluded, but those with HF and higher left ventricular ejection fraction (LVEF) were eligible.

The FINEARTS-HF trial enrolled adults (aged ≥40 years) with symptomatic HFmrEF/HFpEF across 37 countries. Key inclusion criteria included LVEF ≥40%, elevated natriuretic peptides (adjusted based on atrial fibrillation status and clinical setting of screening), evidence of structural heart disease, and recent diuretic use for ≥30 days. Patients were required to have an eGFR ≥25 mL/min/1.73 m^2 and a serum potassium level ≤5.0 mmol/L for enrollment. Participants were eligible for enrollment regardless of T2D status and clinical care setting (whether hospitalized, recently hospitalized, or in ambulatory care).

TRIAL PROCEDURES. Participants in each of the 3 trials were randomly allocated to finerenone or placebo. The initial dose of study medication was 10 mg once daily for participants with a baseline eGFR of <60 mL/min/1.73 m^2 (FIDELIO-DKD and FIGARO-DKD) or ≤60 mL/min/1.73 m^2 (FINEARTS-HF), titrated to a target dose of 20 mg once daily as tolerated. For participants with a baseline eGFR of ≥60 mL/min/1.73 m^2 (FIDELIO-DKD and FIGARO-DKD) or >60 mL/min/1.73 m^2 (FINEARTS-HF), study medication was initiated at a dose of 20 mg once daily, but further titration to a target dose of 40 mg once daily occurred only in FINEARTS-HF; 20 mg once daily was the target dose in FIDELIO-DKD and FIGARO-DKD, irrespective of baseline eGFR. The trial protocols were approved by ethics committees or Institutional Review Boards at all participating sites, and all patients provided written informed consent.

FINE-HEART POOLED ANALYSIS ENDPOINTS. Individual participant-level data were accessed and pooled with harmonized data elements for baseline characteristics and clinical outcomes.[7] All participants with HFmrEF/HFpEF randomized in each of the 3 trials were considered for this pooled analysis; only those with critical Good Clinical Practice violations were excluded.[7] All efficacy outcomes were analyzed in randomized patients under intention-to-treat principles, and all safety outcomes were analyzed in randomized patients who had taken ≥1 dose of the study drug.

To contextualize with prior HF outcomes trials, including FINEARTS-HF, cardiovascular death or HF hospitalization was designated as the primary composite outcome in this pooled analysis. Cardiovascular death, HF hospitalization, new-onset atrial fibrillation, the kidney composite outcome (defined as a sustained decrease in eGFR to ≥50% from baseline, sustained decrease in eGFR to <15 mL/min/1.73 m^2, kidney failure, and death due to kidney failure), all-cause hospitalization, and all-cause death were also evaluated additionally. The kidney composite endpoint inclusive of a sustained decrease in eGFR to ≥57% from baseline (corresponding with a doubling of serum creatinine) was additionally reported.[7] The composite of all-cause death or all-cause hospitalization,[7] along with the nonprespecified endpoint of noncardiovascular death, was also reported to describe the total burden of morbidity and mortality.

Cardiovascular death in this analysis was exclusive of deaths due to undetermined causes. HF hospitalization, new-onset atrial fibrillation, and all deaths were adjudicated by independent clinical endpoint committees in each of the trials included in this analysis. Select treatment-emergent adverse events related to hyperkalemia, acute kidney injury, hypotension, and gynecomastia were also reported in the pooled population.

STATISTICAL ANALYSIS. Participants with chronic HFmrEF/HFpEF from the FINEARTS-HF trial, as well as participants from FIDELIO-DKD and FIGARO-DKD with an investigator-reported history of HF, were included in this pooled analysis. Baseline characteristics were compared according to randomized treatment using Student's *t*-tests or Wilcoxon rank-sum tests for comparison of continuous variables, as appropriate, and chi-square tests for comparison of categorical variables. All endpoints were analyzed as time-to-first endpoint using Cox proportional hazards models, stratified by geographic region and trial (account for differences in trial design). As prespecified in the FINE-HEART statistical analysis plan,[7] all treatment effect estimates were presented as unadjusted HRs with 95% CIs. Two sensitivity analyses were performed. First, competing risks of death were considered through Fine-Gray models, and subdistribution HRs—adjusted for geographic region and trial—with 95% CIs were reported. Second, dedicated Cox proportional hazards regression models were constructed with adjustment for key covariates and stratification for geographic region and trial.

Selected endpoints were displayed graphically by treatment arm using Kaplan-Meier methods. Treatment effects of finerenone on cardiovascular death or HF hospitalization were additionally evaluated across the continuous spectrum of baseline eGFR, UACR, and glycated hemoglobin using Poisson regression

TABLE 1 Baseline Characteristics of FINE-HEART Participants With HFmrEF or HFpEF, by Treatment Arm

	Overall (N = 7,008)	Finerenone (n = 3,488)	Placebo (n = 3,520)	*P* Value
Age, y	71.1 ± 9.8	71.1 ± 9.8	71.2 ± 9.8	0.58
Female	3,109 (44.4)	1,538 (44.1)	1,571 (44.6)	0.65
Race[a]				0.84
Asian	1,074 (15.3)	530 (15.2)	544 (15.5)	
Black	142 (2.0)	73 (2.1)	69 (2.0)	
Other	212 (3.0)	100 (2.9)	112 (3.2)	
White	5,580 (79.6)	2,785 (79.8)	2,795 (79.4)	
Region				0.94
Asia	1,056 (15.1)	525 (15.1)	531 (15.1)	
Eastern Europe	3,163 (45.1)	1,586 (45.5)	1,577 (44.8)	
Latin America	705 (10.1)	341 (9.8)	364 (10.3)	
North America	635 (9.1)	318 (9.1)	317 (9.0)	
Western Europe, Oceania, and others	1,449 (20.7)	718 (20.6)	731 (20.8)	
Baseline body mass index, kg/m^2	30.4 ± 6.2	30.4 ± 6.3	30.4 ± 6.2	0.97
Baseline systolic blood pressure, mm Hg	130.4 ± 15.4	130.5 ± 15.3	130.4 ± 15.4	0.75
Baseline potassium, mmol/L	4.4 ± 0.5	4.4 ± 0.5	4.4 ± 0.5	0.64
Baseline HbA_{1c}, %	6.6 ± 1.3	6.7 ± 1.4	6.6 ± 1.3	0.29
Baseline eGFR, mL/min/1.73 m^2	61.0 ± 20.1	61.0 ± 19.8	60.9 ± 20.4	0.84
eGFR category, mL/min/1.73 m^2				0.36
<25	53 (0.8)	28 (0.8)	25 (0.7)	
25 to <45	1,693 (24.2)	812 (23.3)	881 (25.0)	
45 to <60	1,810 (25.8)	918 (26.3)	892 (25.3)	
≥60	3,451 (49.3)	1,730 (49.6)	1,721 (48.9)	
Baseline UACR, mg/g	27 (8-145)	25 (8-143)	27 (8-151)	0.47
Baseline UACR category, mg/g				0.62
<30	3,537 (52.0)	1,779 (52.5)	1,758 (51.4)	
30 to <300	2,042 (30.0)	1,009 (29.8)	1,033 (30.2)	
≥300	1,225 (18.0)	598 (17.7)	627 (18.3)	
AF on electrocardiogram	2,394 (34.2)	1,219 (34.9)	1,175 (33.4)	0.17
Baseline CKD[b]	3,895 (55.6)	1,936 (55.5)	1,959 (55.7)	0.90
History of diabetes	3,446 (49.2)	1,702 (48.8)	1,744 (49.5)	0.53
Number of CKM conditions[c]				0.75
1 (HF only)	1,974 (28.2)	996 (28.6)	978 (27.8)	
2 (HF and CKD or diabetes)	2,727 (38.9)	1,346 (38.6)	1,381 (39.2)	
3 (HF, CKD, and diabetes)	2,307 (32.9)	1,146 (32.9)	1,161 (33.0)	
Background medication use				
Diuretic agents	6,605 (94.2)	3,292 (94.4)	3,313 (94.1)	0.64
ACEI/ARB/ARNI	5,765 (82.3)	2,863 (82.1)	2,902 (82.4)	0.69
Aspirin	2,538 (36.2)	1,240 (35.6)	1,298 (36.9)	0.25
Statin	4,813 (68.7)	2,388 (68.5)	2,425 (68.9)	0.70
SGLT2i	863 (12.3)	418 (12.0)	445 (12.6)	0.40
GLP-1RA	207 (3.0)	105 (3.0)	102 (2.9)	0.78
Potassium-lowering therapies[d]	27 (0.4)	11 (0.3)	16 (0.5)	0.35

Values are n (%), mean ± SD, or median (Q1-Q3), unless otherwise indicated. *P* values reflect comparisons between treatment arms. [a]Represents self-reported race. Participants choosing not disclose race or who self-identified as multiple races are included in the "Other" category for descriptive purposes. [b]CKD includes all participants in the primary CKD outcomes trials (FIDELIO-DKD, FIGARO-DKD) and participants in FINEARTS-HF with baseline eGFR of <60 mL/min/1.73 m^2. [c]CKM conditions include heart failure, CKD, and diabetes. [d]Includes patiromer, sodium polystyrene sulfonate, calcium polystyrene sulfonate.

ACEI = angiotensin converting enzyme inhibitor; AF = atrial fibrillation; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor neprilysin inhibitor; CKD = chronic kidney disease; CKM = cardiovascular-kidney-metabolic; eGFR = estimated glomerular filtration rate; GLP-1RA = glucagon-like peptide-1 receptor agonist; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; SGLT2i = sodium-glucose cotransporter 2 inhibitor; UACR = urinary albumin-to-creatinine ratio.

models, allowing for potentially nonlinear relationships using restricted cubic splines. The number of knots was selected to minimize the Akaike information criterion. Statistical analyses were conducted using Stata, version 18 (StataCorp, LLC), with 2-sided values of $P < 0.05$ considered statistically significant. No adjustment for multiplicity was performed as this study was considered exploratory.

TABLE 2 Treatment Effects of Finerenone vs Placebo Among FINE-HEART Participants With HFmrEF or HFpEF

	Finerenone (n = 3,488)		Placebo (n = 3,520)		Finerenone vs Placebo		$P_{interaction}$ by Trial
	n (%)	IR (per 100 py)	n (%)	IR (per 100 py)	HR (95% CI)	*P* Value	
Primary composite outcome							
CV death[a] or HF hospitalization	677 (19.4)	8.4	775 (22.0)	9.7	0.87 (0.78-0.96)	0.008	0.24
Secondary cardiovascular outcomes							
CV death[a]	273 (7.8)	3.1	299 (8.5)	3.4	0.92 (0.78-1.08)	0.32	0.80
HF hospitalization	502 (14.4)	6.2	597 (17.0)	7.5	0.84 (0.74-0.94)	0.003	0.15
New-onset atrial fibrillation	100 (2.9)	1.8	134 (3.8)	2.4	0.75 (0.58-0.97)	0.030	0.51
Secondary kidney outcomes							
Composite kidney outcome (eGFR ≥50%)	112 (3.2)	1.5	108 (3.1)	1.4	1.09 (0.84-1.43)	0.51	0.06
Composite kidney outcome (eGFR ≥57%)	67 (1.9)	0.9	70 (2.0)	0.9	1.04 (0.74-1.46)	0.82	0.15
Secondary morbidity and mortality outcomes							
All-cause death	562 (16.1)	6.5	608 (17.3)	7.0	0.93 (0.83-1.04)	0.21	0.56
All-cause hospitalization	1,684 (48.3)	26.9	1,764 (50.1)	28.7	0.94 (0.88-1.01)	0.09	0.65
All-cause death and all-cause hospitalization	1,795 (51.5)	28.6	1,898 (53.9)	30.9	0.93 (0.88-1.00)	0.038	0.48
Exploratory outcome							
Non-CV death	289 (8.3)	3.3	309 (8.8)	3.5	0.94 (0.80-1.10)	0.42	0.57

HR (95% CI) estimated through Cox proportional hazards regression models, stratified by trial and geographic region. [a]Excludes deaths with undetermined causes.
CV = cardiovascular; HF = heart failure; IR = incidence rate; py = person-years.

RESULTS

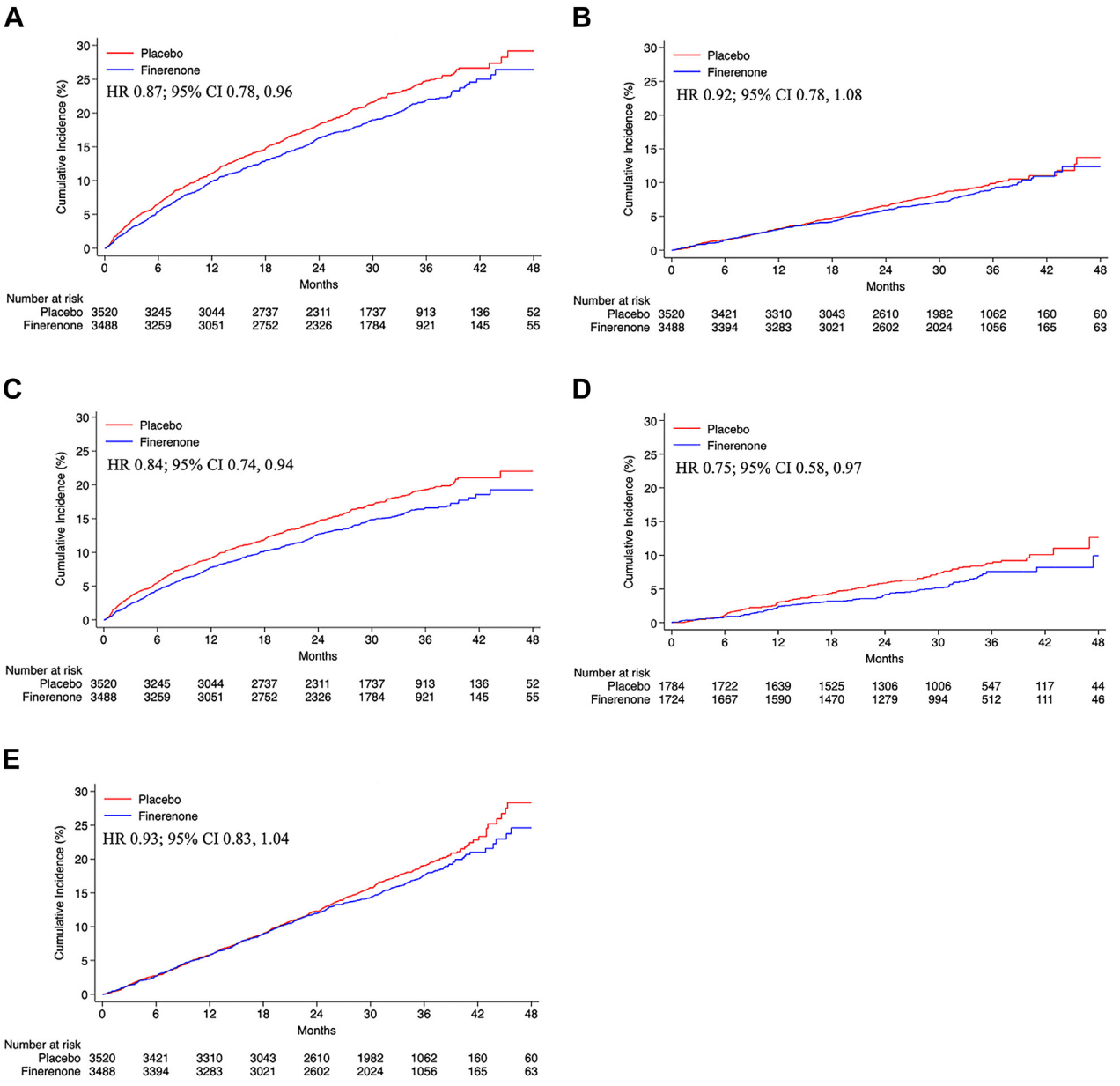
PATIENT POPULATION. Of 18,991 participants in the 3 trials, 7,008 (36.9%) had HFmrEF/HFpEF at baseline (mean age, 71 ± 10 years; 44% female; 80% White). Of these, 6,001 (85.6%) were enrolled in FINEARTS-HF, 436 (6.2%) were enrolled in FIDELIO-DKD, and 571 (8.1%) were enrolled in FIGARO-DKD. Baseline characteristics and background pharmacotherapies were well-balanced between treatment arms in the pooled HFmrEF/HFpEF population (**Table 1**), which exhibited a broad range of kidney risk (Supplemental Figure 1) and substantial cardiovascular-kidney-metabolic morbidity (72% with CKD and/or T2D in addition to HF).

Compared with FINEARTS-HF participants, FIDELIO-DKD and FIGARO-DKD participants with HFmrEF/HFpEF were younger, more often male, and had higher baseline body mass index, systolic blood pressure, glycated hemoglobin, and UACR (Supplemental Table 1). The baseline eGFR was lowest among FIDELIO-DKD participants. The mean daily dose of finerenone overall and according to trial is presented in Supplemental Table 2.

TREATMENT EFFECTS OF FINERENONE ON CLINICAL OUTCOMES. Over a median follow-up of 2.5 years, cardiovascular death or HF hospitalization occurred in 677 participants (19.4%) in the finerenone arm and in 755 participants (22.0%) in the placebo arm (HR: 0.87 [95% CI: 0.78-0.96]; $P = 0.008$) (**Table 2**, **Figure 1**). Incidence rates (IRs) per 100 person-years were similar in the placebo arms of each of the 3 trials: FINEARTS-HF (IR: 10.0 [95% CI: 9.3-10.8]), FIDELIO-DKD (IR: 9.2 [95% CI: 7.0-12.2]), and FIGARO-DKD (IR: 7.6 [95% CI: 5.9-9.8]) (**Figure 2**). Similar findings were observed in sensitivity analyses accounting for competing risks of death (Supplemental Table 3) and after adjustment for covariates listed in **Table 1** (Supplemental Table 4). Consistent effects of finerenone on cardiovascular death or HF hospitalization were observed across trials ($P_{interaction} = 0.24$) (**Table 2**, **Figure 2**), key subgroups (**Figure 3**), and across the range of baseline eGFR ($P_{interaction} = 0.47$), UACR ($P_{interaction} = 0.62$), and glycated hemoglobin ($P_{interaction} = 0.93$) (**Central Illustration**).

Finerenone additionally appeared to decrease the rate of HF hospitalization (HR: 0.84 [95% CI: 0.74-0.94]; $P = 0.003$) and new-onset atrial fibrillation (HR: 0.75 [95% CI: 0.58-0.97]; $P = 0.030$) compared with placebo, but did not statistically significantly decrease cardiovascular death (HR: 0.92 [95% CI: 0.78-1.08]; $P = 0.32$), either kidney composite outcome, or all-cause death (HR: 0.93 [95% CI: 0.83-1.04]; $P = 0.21$) (**Table 2**). However, finerenone appeared to statistically significantly decrease the summary morbidity and mortality endpoint of all-cause death and all-cause hospitalization (HR: 0.93 [95% CI: 0.88-1.00]; $P = 0.038$). The effects of finerenone on all key secondary endpoints were consistent across trials (**Figure 2**), although with potential

FIGURE 1 Cumulative Incidence of Primary and Selected Secondary Outcomes, by Treatment Arm

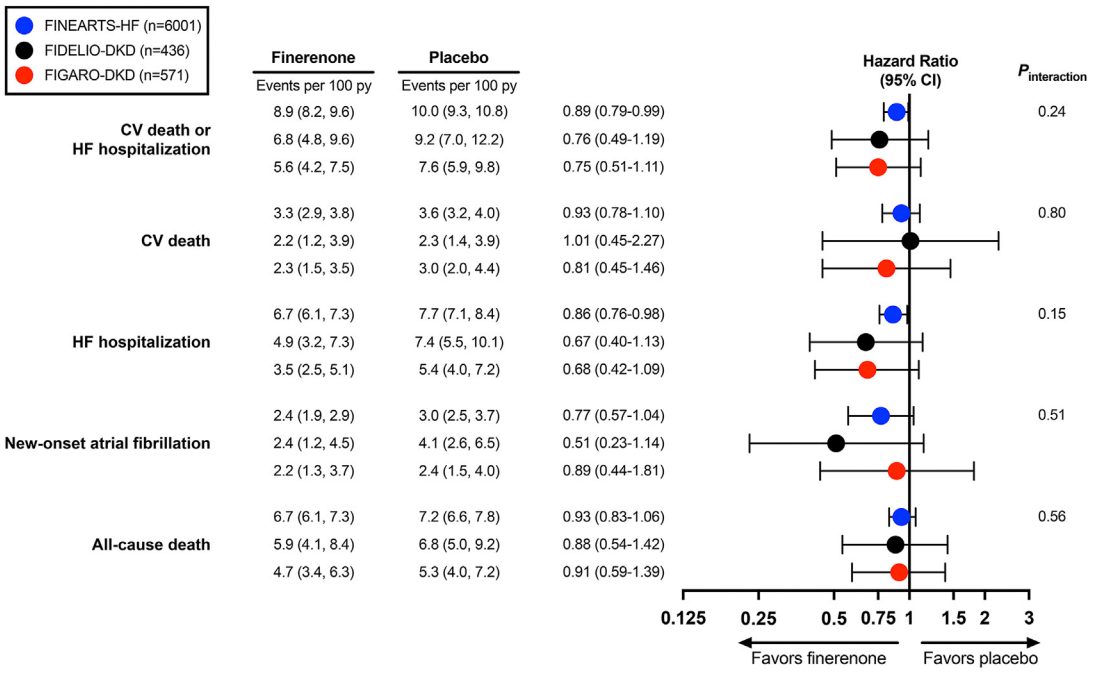


CV death or HF hospitalization (A), CV death (B), HF hospitalization (C), new-onset atrial fibrillation (D), and all-cause death (E). Cumulative incidence of each endpoint by treatment arm, estimated through Kaplan-Meier methods. CV death is exclusive of deaths owing to undetermined causes. CV = cardiovascular; HF = heart failure.

evidence of heterogeneity across trials for the composite kidney outcome inclusive of a sustained decrease in the eGFR to ≥50% from baseline ($P_{interaction} = 0.06$).

SAFETY EVENTS. The incidence of any serious adverse event was similar between treatment arms (Table 3). Laboratory-defined hyperkalemia (any serum potassium >5.5 mmol/L) was increased (15.0% vs 7.6%), whereas laboratory-defined hypokalemia was reduced (4.6% vs 9.4%), with finerenone vs placebo. Investigator-reported hyperkalemia-related hospitalization (0.6% vs 0.2%), investigator-reported acute kidney injury (4.0% vs 2.7%), and acute

FIGURE 2 Treatment Effects of Finerenone vs Placebo on Primary and Selected Secondary Outcomes in FINE-HEART Participants With HFmrEF or HFpEF, by Trial



Forest plot shows treatment effects of finerenone vs. placebo on time-to-first clinical endpoints, estimated through Cox proportional hazards regression models stratified by trial and geographic region. CV death is exclusive of deaths with undetermined causes. HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; py = person-year; other abbreviations as in Figure 1.

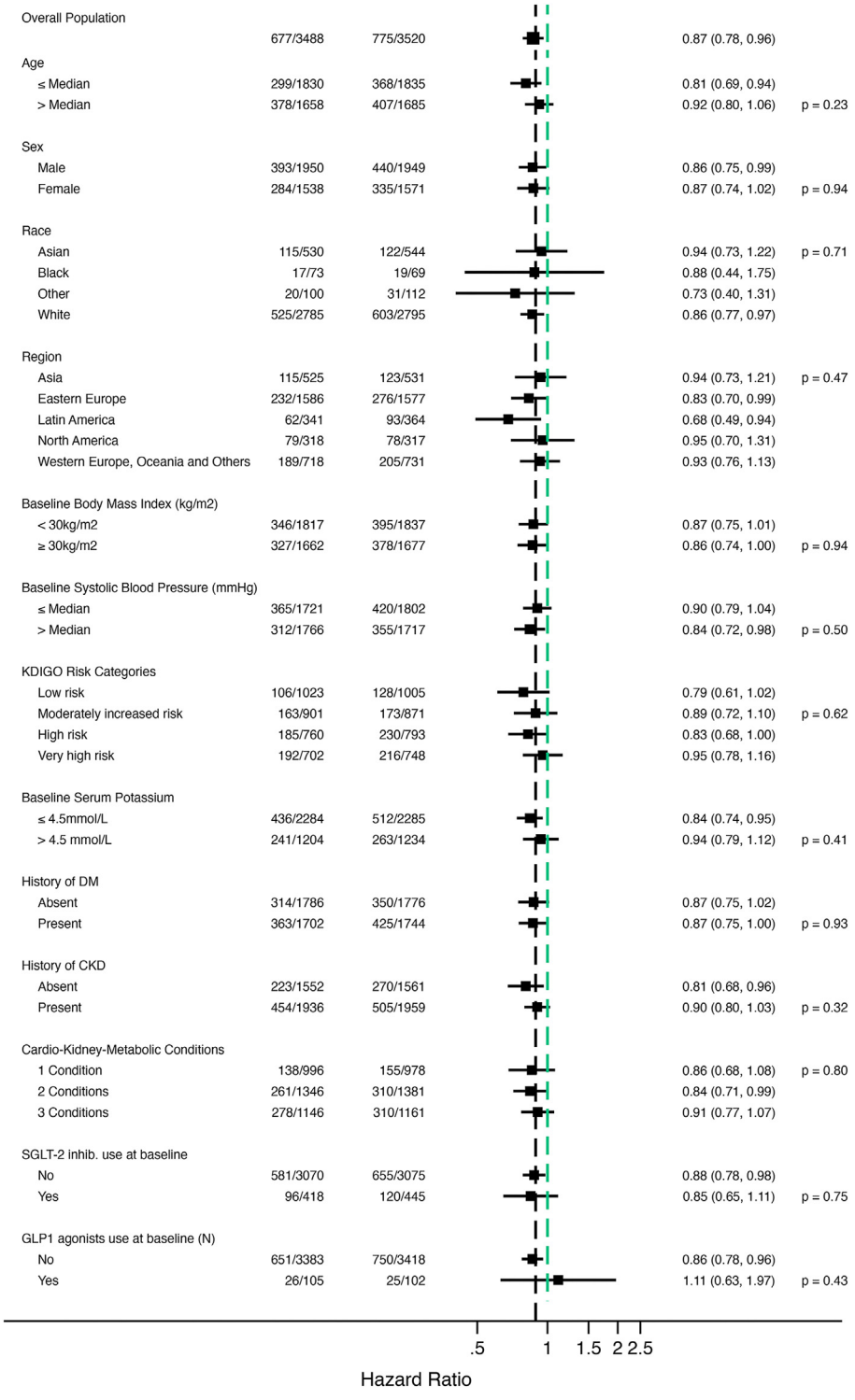
kidney injury leading to hospitalization (1.7% vs 1.0%) were increased with finerenone. However, there were no apparent between-group differences in treatment discontinuation because of hyperkalemia or acute kidney injury. There were no deaths related to hyperkalemia in either treatment arm.

DISCUSSION

In this participant-level pooled analysis representing the totality of outcomes trial experience with finerenone in individuals with HFmrEF/HFpEF, finerenone decreased cardiovascular deaths or HF hospitalizations across a wide spectrum of cardiovascular and kidney risk and in all clinically relevant subgroups. Finerenone additionally decreased HF hospitalization and new-onset atrial fibrillation in this pooled HFmrEF/HFpEF population, but did not significantly decrease cardiovascular death, the kidney composite outcome, or all-cause death. Treatment with finerenone modestly increased the risk of hyperkalemia and acute kidney injury compared with placebo, but decreased the risk of hypokalemia; there were no between-group differences in serious adverse events. Taken together, these findings enhance our understanding of the safety and efficacy of finerenone in individuals with HFmrEF/HFpEF.

Although the proportions of patients in the FIDELIO-DKD and FIGARO-DKD with HF were generally modest (~8% in both trials),[14-16] given these were large outcomes trials, >1,000 patients from these trials combined had investigator-reported HF. Furthermore, although the clinical profiles of participants with investigator-reported HF in FIDELIO-DKD and FIGARO-DKD modestly varied from those enrolled in the dedicated HF outcomes trial FINEARTS-HF, the placebo group event rates for cardiovascular death or HF hospitalization across the 3 trials among participants with HF were similar. These findings provide reassurance that the trials included in this analysis targeted populations at similar absolute risk. Pooling patients from these

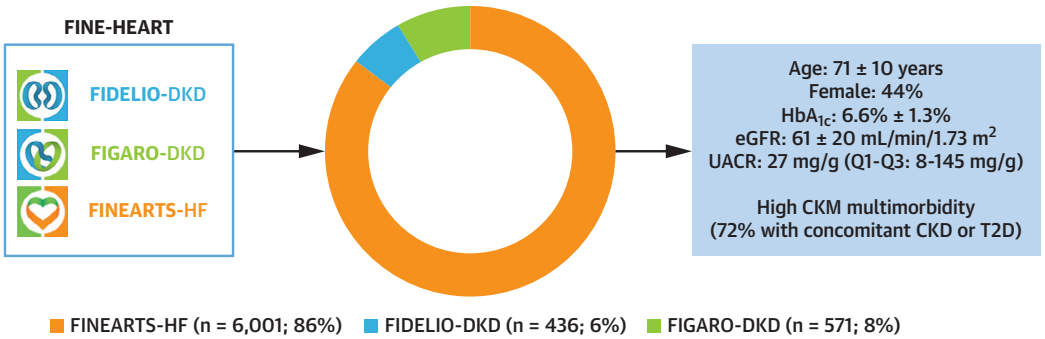
FIGURE 3 Treatment Effects of Finerenone vs Placebo on CV Death or HF Hospitalization in Fine-Heart Participants With HFmrEF or HFpEF, Overall and in Key Subgroups



Forest plot shows treatment effects of finerenone vs. placebo on CV death (exclusive of death due to undetermined causes) or HF hospitalization (HR and 95% CI) overall and in key subgroups. *P* values reflect *P* values for treatment-by-subgroup interaction. Cardio-kidney-metabolic conditions refer to HF, CKD, and DM. CKD = chronic kidney disease; DM = diabetes mellitus; GLP = glucagon-like peptide; KDIGO = Kidney Disease Improving Global Outcomes; SGLT2 = sodium-glucose cotransporter 2; other abbreviations as in Figures 1 and 2.

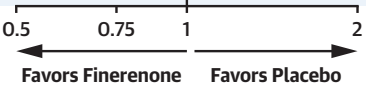
CENTRAL ILLUSTRATION **Effect of Finerenone on Cardiovascular Outcomes in HFmrEF or HFpEF in FINE-HEART**

A Baseline Characteristics of Participants in FINE-HEART Trials with HFmrEF/HFpEF (n = 7,008)

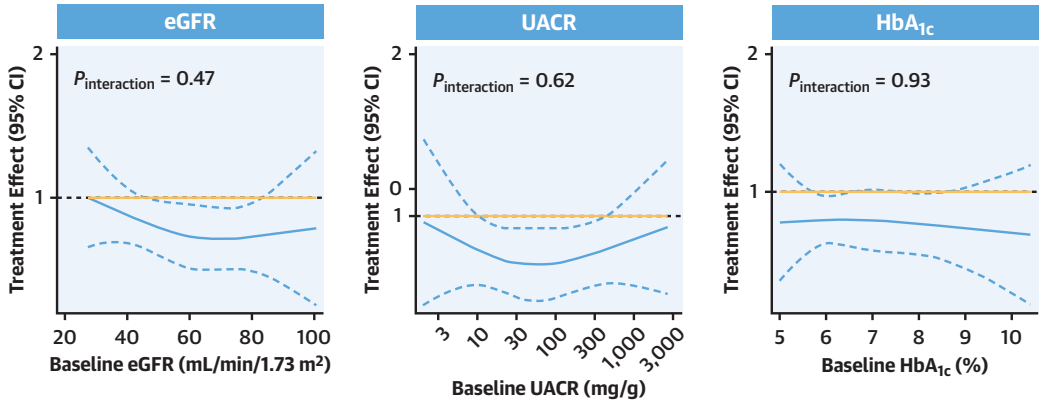


B Treatment Effects of Finerenone vs Placebo on Cardiovascular Outcomes

	Finerenone Events per 100 py	Placebo Events per 100 py	HR (95% CI)	*P* Value
CV death or HF hospitalization	8.4	9.7	0.87 (0.78-0.96)	0.008
CV death	3.1	3.4	0.92 (0.78-1.08)	0.32
HF hospitalization	6.2	7.5	0.84 (0.74-0.94)	0.003
New-onset atrial fibrillation	1.8	2.4	0.75 (0.58-0.97)	0.030



C Treatment Effects of Finerenone on CV Death or HF Hospitalization, by Baseline eGFR, UACR, and HbA_{1c}



Ostrominski JW, et al. JACC Heart Fail. 2025;13(8):102497.

Patient population and selected baseline characteristics of FINE-HEART trial participants with HFmrEF/HFpEF (A), treatment effects of finerenone vs placebo on selected CV outcomes in the pooled population with HFmrEF/HFpEF (B), and treatment effects of finerenone on CV death (exclusive of death due to undetermined causes) and HF hospitalization across the continuous spectrum of eGFR, UACR, and HbA_{1c} (C). Restricted cubic splines (C) estimated through Poisson regression with 3 knots. CKD = chronic kidney disease; CKM = cardiovascular-kidney-metabolic; CV = cardiovascular; eGFR = estimated glomerular filtration rate; HbA_{1c} = glycated hemoglobin; HF = heart failure; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; py = person-years; T2D = type 2 diabetes; UACR = urinary albumin-to-creatinine ratio.

TABLE 3 Safety Outcomes of FINE-HEART Participants With HFmrEF or HFpEF, by Treatment Arm

	Finerenone (n = 3,477)	Placebo (n = 3,515)	*P* Value
Any serious adverse event	1,324 (38.1)	1,403 (39.9)	0.12
Any adverse event leading to treatment discontinuation	122 (3.5)	111 (3.2)	0.41
Any potassium >5.5 mmol/L[a]	506 (15.0)	257 (7.6)	<0.001
Any potassium >6.0 mmol/L[a]	99 (2.9)	52 (1.5)	<0.001
Any potassium <3.5 mmol/L[a]	154 (4.6)	319 (9.4)	<0.001
Hyperkalemia[b]	351 (10.1)	159 (4.5)	<0.001
Hyperkalemia leading to treatment discontinuation	17 (0.5)	11 (0.3)	0.24
Hyperkalemia leading to hospitalization[b]	20 (0.6)	8 (0.2)	0.021
Acute kidney injury[b]	138 (4.0)	95 (2.7)	0.003
Acute kidney injury leading to treatment discontinuation	2 (0.1)	2 (0.1)	0.99
Acute kidney injury leading to hospitalization	60 (1.7)	36 (1.0)	0.012
Any systolic blood pressure <100 mm Hg	573 (16.9)	387 (11.3)	<0.001
Gynecomastia or breast hyperplasia	9 (0.3)	3 (0.1)	0.08

Values are n (%), unless otherwise indicated. Treatment-emergent adverse events are defined as any adverse event occurring in any patient who has received ≥1 dose of study drug and within 3 days of permanent discontinuation. There were no instances of death due to hyperkalemia. [a]Based on central laboratory measurements of potassium levels. [b]Based on investigator-reported adverse events.

Abbreviations as in Table 2.

3 trials confirmed the consistency of treatment benefits of finerenone on cardiovascular death or HF hospitalization in an enriched population with HFmrEF/HFpEF featuring a broad spectrum of cardiovascular-kidney-metabolic risk. This analysis has additionally underscored favorable but statistically insignificant trends from the FINEARTS-HF trial alone, such as a decrease in new-onset atrial fibrillation, extending findings from FIDELIO-DKD.[17] Although further clinical trial evidence related to finerenone in patients with HFmrEF/HFpEF is awaited (eg, REDEFINE-HF [A Study to Determine the Efficacy and Safety of Finerenone on Morbidity and Mortality Among Hospitalized Heart Failure Patients; NCT06008197]), the consistent effect sizes on key efficacy endpoints between FINEARTS-HF and patients with HF identified in FIDELIO-DKD and FIGARO-DKD bolsters the certainty of evidence.

This analysis has some limitations. First, certain data elements were not available across trials to allow for pooling. For instance, outpatient worsening HF events, which are frequent among individuals with HFmrEF/HFpEF[18] and included as a part of the FINEARTS-HF primary outcome, were not collected in FIDELIO-DKD and FIGARO-DKD. Hence, this analysis may have underestimated the totality of treatment effects of finerenone on HF events. Further, NYHA functional class, natriuretic peptide levels, and LVEF were not assessed systematically in FIDELIO-DKD and FIGARO-DKD. Second, this prespecified FINE-HEART analysis did not include smaller early-phase trials evaluating finerenone (eg, ARTS-DN [Safety and Efficacy of Different Oral Doses of BAY94-8862 in Subjects With Type 2 Diabetes Mellitus and the Clinical Diagnosis of Diabetic Nephropathy; NCT01874431]). However, the number of individuals with HFmrEF/HFpEF enrolled in these trials was small.[19] Third, although symptomatic HFrEF was exclusionary in FIDELIO-DKD and FIGARO-DKD, some individuals with asymptomatic or preclinical (eg, stage B) HFrEF or HFmrEF/HFpEF may have been reported by the study investigators of these trials to have HF. Indeed, the modestly lower event rates observed in FIDELIO-DKD and FIGARO-DKD may be related to trial-level differences in event adjudication and/or the lack of enrichment through selection of individuals with worse symptoms, elevated natriuretic peptides, and adverse cardiac remodeling, which is used commonly in HF outcomes trials, including FINEARTS-HF.[1] However, as has previously been suggested,[16] the baseline characteristics of these participants and the similarity of their event rates when compared with FINEARTS-HF are most consistent with stage C HFmrEF/HFpEF. Fourth, the impact of trial-level differences in dose of study medication was not considered explicitly in this analysis. Fifth, because the primary endpoint of cardiovascular death (exclusive of undetermined death) was narrowly missed in the overall FINE-HEART analysis,[7] further subgroup analysis should be interpreted in this context. Sixth, additional research efforts are needed to ascertain whether these findings apply to younger individuals, to community settings, and individuals with more diverse racial and ethnic backgrounds.

CONCLUSIONS

Treatment benefits of finerenone on cardiovascular death or HF hospitalization observed in FINEARTS-HF were consistent in an expanded population of >1,000 participants enrolled in the adjacent FIDELIO-DKD and FIGARO-DKD trials. This prespecified individual participant-level pooled analysis supports the use of finerenone to reduce cardiovascular death or HF hospitalization among individuals with HFmrEF/HFpEF across a broad range of cardiovascular-kidney-metabolic risk.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

FIDELIO-DKD, FIGARO-DKD, and FINEARTS-HF were funded by Bayer AG. Dr Ostrominski has received grant support from the National Institutes of Health (5T32HL007604-39). Dr Filippatos has received lecture fees and/or trial committee membership fees and/or consulting fees from Boehringer Ingelheim, Servier, Novartis, Bayer, Impulse Dynamics, Vifor, Medtronic, Cardior, and Novo Nordisk; and research grants from the European Union. Dr Claggett has received personal consulting fees from Alnylam, Bristol Myers Squibb, Cardior,

Cardurion, Corvia, CVRx, Eli Lilly, Intellia, and Rocket; and has served on a DSMB for Novo Nordisk. Dr Desai has received institutional research grants (to Brigham and Women's Hospital) from Abbott, Alnylam, AstraZeneca, Bayer, Novartis, and Pfizer; and personal consulting fees from Abbott, Alnylam, AstraZeneca, Bayer, Biofourmis, Boston Scientific, Medpace, Medtronic, Merck, Novartis, Parexel, Porter Health, Regeneron, River2Renal, Roche, Veristat, Verily, and Zydus. Dr Jhund has received speaker fees from AstraZeneca, Novartis, Alkem Metabolics, ProAdWise Communications, and Sun Pharmaceuticals; advisory board fees from AstraZeneca, Boehringer Ingelheim, and Novartis; and research funding from AstraZeneca, Boehringer Ingelheim, Analog Devices Inc, and Roche Diagnostics. Dr Jhund's employer, the University of Glasgow, has been remunerated for clinical trial work from AstraZeneca, Bayer AG, Novartis, and Novo Nordisk. Drs. Scheerer and Rohwedder are full-time employees of Bayer AG. Dr Amarante is a full-time employee of Bayer SA. Dr Brinker is a full-time employee of Bayer AG. Mr Lay-Flurrie is a full-time employee of Bayer plc, Research and Development, Pharmaceuticals, Reading, United Kingdom. Dr Lam has received research support from NovoNordisk and Roche Diagnostics; has received consulting fees from Alleviant Medical, Allysta Pharma, AnaCardio AB, Applied Therapeutics, AstraZeneca, Bayer, Biopeutics, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, CardioRenal, CPC Clinical Research, Eli Lilly, Impulse Dynamics, Intellia Therapeutics, Ionis Pharmaceutical, Janssen Research and Development LLC, Medscape/WebMD Global LLC, Merck, Novartis, Novo Nordisk, Prosciento Inc, Quidel Corporation, Radcliffe Group Ltd, Recardio Inc, ReCor Medical, Roche Diagnostics, Sanofi, Siemens Healthcare Diagnostics, and Us2.ai; and is a cofounder and nonexecutive director of Us2.ai. Dr Senni has served on advisory boards, has done consultancy, and has received honoraria from Novartis, Abbott, Merck, Merck Sharp & Dohme, Vifor, AstraZeneca, Cardurion, Novonordisk, Bayer, and Boehringer Ingelheim. Dr Shah has received research grants from NIH (U54 HL160273, X01 HL169712, R01 HL140731, R01 HL149423), AHA (24SFRNPCN1291224), AstraZeneca, Corvia, and Pfizer; and consulting fees from Abbott, Alleviant, AstraZeneca, Amgen, Aria CV, Axon Therapies, Bayer, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, Cyclerion, Cytokinetics, Edwards Lifesciences, Eidos, Imara, Impulse Dynamics, Intellia, Ionis, Lilly, Merck, MyoKardia, Novartis, Novo Nordisk, Pfizer, Prothena, Regeneron, Rivus, Sardocor, Shifamed, Tenax, Tenaya, and Ultromics. Dr Voors's employer has received consultancy fees and/or research support from Adrenomed, Anacardio, AstraZeneca, Bayer AG, BMS, Boehringer Ingelheim, Corteria, EliLilly, Merck, Moderna, Novartis, Novo Nordisk, Roche diagnostics, and SalubrisBio. Dr Zannad has received personal fees from 89Bio, Abbott, Acceleron, Applied Therapeutics, Bayer, Betagenon, Boehringer, BMS, CVRx, Cambrian, Cardior, Cereno pharmaceutical, Cellprothera, CEVA, Inventiva, KBP, Merck, NovoNordisk, Owkin, Otsuka, Roche Diagnostics, Northsea, and USa2; has stock options at G3Pharmaceutical; equities at Cereno, Cardiorenal and Eshmoun Clinical research; and is the founder of Cardiovascular Clinical Trialists. Dr Rossing has received grants and payment of honoraria for lectures, educational events, and steering group participation from AstraZeneca, Bayer, and Novo Nordisk (all to the Steno Diabetes Center Copenhagen); payment of honoraria for lectures and participation in advisory boards from Boehringer Ingelheim, Sanofi, Gilead, and Astellas (all to the Steno Diabetes Center Copenhagen); and has received study drugs for free for investigator initiated studies from Bayer, Novo Nordisk, and Lexicon. Dr Anker has received grants from Vifor Int and Abbott; has received consulting fees from CVRx, AstraZeneca, Bioventrix, Repairon, Novo Nordisk, Brahms, Novartis, Actimed Therapeutics, Faraday Pharmaceuticals, Cytokinetics, HeartKinetics, GlaxoSmithKline, Vectorious, Scirent, Sensible Medical. Edwards, Relaxera, Repairon, Regeneron Pharmaceuticals, and Cordio; has done steering or advisory committee work for Vifor Int, Bayer AG, Boehringer Ingelheim, Medtronic, Abbott, Impulse Dynamics, Cardior, V-Wave, Pfizer, Cardiac Dimensions, and Occlutech; and is a named co-inventor of 2 patent applications regarding MR-proANP (DE 102007010834 and DE 102007022367), but he does not benefit personally from the related issued patents. Dr Pitt has been a consultant for Bayer, AstraZeneca, Boehringer Ingelheim, Lexicon, Bristol Meyers Squibb, KBP Biosciences, Sarfez Pharmaceuticals, SQinnovations, G3 Pharmaceuticals, Sea Star Medical, Vifor, Prointel, Brainstorm Medical; and ha stock/stock options from KBP Biosciences, Sarfez Pharmaceuticals, SQinnovations, Sea Star Medical, Vifor, Prointel, and Brainstorm Medical. Dr Agarwal has received support from Bayer; royalties or licenses from UpToDate; consulting fees from Boehringer Ingelheim, Novartis, Akebia, Intercept Pharma, and Alnylam; support for meetings from Boehringer Ingelheim, Novartis, Akebia, and Vertex; and has participated on DSMB or Advisory Board for Vertex, Eloxx, and Chinook. Dr McMurray has received payments through Glasgow University from work on clinical trials, consulting, and grants from Amgen, AstraZeneca, Bayer, Cardurion, Cytokinetics, GlaxoSmithKline, and Novartis; personal consultancy fees from Alynylam Pharmaceuticals, Amgen, AnaCardio, AstraZeneca, Bayer, Berlin Cures, BMS, Cardurion, Cytokinetics, Ionis Pharmaceuticals, Novartis, Regeneron Pharmaceuticals, River 2 Renal Corporation, British Heart Foundation, NIH-NHLBI, Boehringer Ingelheim, SQ Innovations, and Catalyze Group; personal lecture fees from Abbott, Alkem Metabolics, AstraZeneca, Blue Ocean Scientific Solutions Ltd, Boehringer Ingelheim, Canadian Medical and Surgical Knowledge, Emcure Pharmaceuticals Ltd, Eris Lifesciences, European Academy of CME, Hikma Pharmaceuticals, Imagica Health, Intas Pharmaceuticals, J.B. Chemicals and Pharmaceuticals Ltd, Lupin Pharmaceuticals, Medscape/Heart.Org, ProAdWise Communications, Radcliffe Cardiology, Sun Pharmaceuticals, The Corpus, Translation Research Group, and Translational Medicine Academy; has DSMB membership for WIRB-Copernicus Group Clinical Inc; and he is a director of Global Clinical Trial Partners Ltd. Dr Solomon has received research grants from Alexion, Alnylam, AstraZeneca, Bellerophon, Bayer, BMS, Boston Scientific, Cytokinetics, Edgewise, Eidos, Gossamer, GlaxoSmithKline, Ionis, Lilly, MyoKardia, NIH/NHLBI, Novartis, NovoNordisk, Respicardia, Sanofi Pasteur, Theracos, and US2.AI; and has consulted for Abbott, Action, Akros, Alexion, Alnylam, Amgen, Arena, AstraZeneca, Bayer, Boehringer Ingelheim, BMS, Cardior, Cardurion, Corvia, Cytokinetics, Daiichi-Sankyo, GlaxoSmithKline, Lilly, Merck, Myokardia, Novartis, Roche, Theracos, Quantum Genomics, Janssen, Cardiac Dimensions, Tenaya, Sanofi-Pasteur, Dinaqor, Tremeau, CellProThera, Moderna, American Regent, Sarepta, Lexicon, Anacardio, Akros, and Valo. Dr Vaduganathan has received research grant support, served on advisory boards, or had speaker engagements with American Regent, Amgen, AstraZeneca, Bayer AG, Baxter Healthcare, BMS, Boehringer Ingelheim, Chiesi, Cytokinetics, Fresenius Medical Care, Idorsia Pharmaceuticals, Lexicon Pharmaceuticals, Merck, Milestone Pharmaceuticals, Novartis, Novo Nordisk, Pharmacosmos, Relypsa, Roche Diagnostics, Sanofi, and Tricog Health; and participates on clinical trial committees for studies sponsored by AstraZeneca, Galmed, Novartis, Bayer AG, Occlutech, and Impulse Dynamics. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Muthiah Vaduganathan, Cardiovascular Division, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, Massachusetts 02115, USA. E-mail: mvaduganathan@bwh.harvard.edu. X handle: @mvaduganathan.

PERSPECTIVES

COMPETENCY IN PATIENT CARE: Finerenone, a nonsteroidal mineralocorticoid receptor antagonist, consistently reduced cardiovascular death or HF hospitalization irrespective of eGFR, UACR, and glycated hemoglobin among individuals with HFmrEF/HFpEF in the complementary FINEARTS-HF, FIDELIO-DKD, and FIGARO-DKD trials.

TRANSLATIONAL OUTLOOK: This analysis supports the use of finerenone to improve clinical outcomes among individuals with HFmrEF/HFpEF, across a broad range of cardiovascular-kidney-metabolic risk.

REFERENCES

1. Solomon SD, McMurray JJV, Vaduganathan M, et al. Finerenone in heart failure with mildly reduced or preserved ejection fraction. *N Engl J Med*. 2024;391:1475-1485.

2. Bakris GL, Agarwal R, Anker SD, et al. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. *N Engl J Med*. 2020;383:2219-2229.

3. Pitt B, Filippatos G, Agarwal R, et al. Cardiovascular events with finerenone in kidney disease and type 2 diabetes. *N Engl J Med*. 2021;385:2252-2263.

4. Filippatos G, Farmakis D. Non-steroidal mineralocorticoid receptor antagonists in heart failure. *Nat Rev Cardiol*. 2023;20:645-646.

5. Ndumele CE, Neeland IJ, Tuttle KR, et al. A synopsis of the evidence for the science and clinical management of cardiovascular-kidney-metabolic (CKM) syndrome: a scientific statement from the American Heart Association. *Circulation*. 2023;148:1636-1664.

6. Ostrominski JW, Arnold SV, Butler J, et al. Prevalence and overlap of cardiac, renal, and metabolic conditions in US adults, 1999-2020. *JAMA Cardiol*. 2023;8:1050-1060.

7. Vaduganathan M, Filippatos G, Claggett BL, et al. Finerenone in heart failure and chronic kidney disease with type 2 diabetes: FINE-HEART pooled analysis of cardiovascular, kidney and mortality outcomes. *Nat Med*. 2024;30:3758-3764.

8. Pitt B, Køber L, Ponikowski P, et al. Safety and tolerability of the novel non-steroidal mineralocorticoid receptor antagonist BAY 94-8862 in patients with chronic heart failure and mild or moderate chronic kidney disease: a randomized, double-blind trial. *Eur Heart J*. 2013;34:2453-2463.

9. Filippatos G, Anker SD, Böhm M, et al. A randomized controlled study of finerenone vs. eplerenone in patients with worsening chronic heart failure and diabetes mellitus and/or chronic kidney disease. *Eur Heart J*. 2016;37:2105-2114.

10. Bakris GL, Agarwal R, Anker SD, et al. Design and baseline characteristics of the finerenone in reducing kidney failure and disease progression in diabetic kidney disease trial. *Am J Nephrol*. 2019;50:333-344.

11. Ruilope LM, Agarwal R, Anker SD, et al. Design and baseline characteristics of the finerenone in reducing cardiovascular mortality and morbidity in diabetic kidney disease trial. *Am J Nephrol*. 2019;50:345-356.

12. Vaduganathan M, Claggett BL, Lam CSP, et al. Finerenone in patients with heart failure with mildly reduced or preserved ejection fraction: rationale and design of the FINEARTS-HF trial. *Eur J Heart Fail*. 2024;26:1324-1333.

13. Solomon SD, Ostrominski JW, Vaduganathan M, et al. baseline characteristics of patients with heart failure with mildly reduced or preserved ejection fraction: the FINEARTS-HF trial. *Eur J Heart Fail*. 2024;26:1334-1346.

14. Filippatos G, Anker SD, Pitt B, et al. Finerenone and heart failure outcomes by kidney function/albuminuria in chronic kidney disease and diabetes. *JACC Heart Fail*. 2022;10:860-870.

15. Filippatos G, Pitt B, Agarwal R, et al. Finerenone in patients with chronic kidney disease and type 2 diabetes with and without heart failure: a prespecified subgroup analysis of the FIDELIO-DKD trial. *Eur J Heart Fail*. 2022;24:996-1005.

16. Filippatos G, Anker SD, Agarwal R, et al. Finerenone reduces risk of incident heart failure in patients with chronic kidney disease and type 2 diabetes: analyses from the FIGARO-DKD trial. *Circulation*. 2022;145:437-447.

17. Filippatos G, Bakris GL, Pitt B, et al. Finerenone reduces new-onset atrial fibrillation in patients with chronic kidney disease and type 2 diabetes. *J Am Coll Cardiol*. 2021;78:142-152.

18. Chatur S, Vaduganathan M, Claggett BL, et al. Outpatient worsening among patients with mildly reduced and preserved ejection fraction heart failure in the DELIVER trial. *Circulation*. 2023;148:1735-1745.

19. Ruilope LM, Agarwal R, Chan JC, et al. Rationale, design, and baseline characteristics of ARTS-DN: a randomized study to assess the safety and efficacy of finerenone in patients with type 2 diabetes mellitus and a clinical diagnosis of diabetic nephropathy. *Am J Nephrol*. 2015;40:572-581.

KEY WORDS chronic kidney disease, finerenone, heart failure with preserved ejection fraction, mineralocorticoid receptor antagonists, outcomes, type 2 diabetes

APPENDIX For supplemental tables and figures, please see the online version of this paper