Finerenone Reduces New-Onset Atrial Fibrillation across the Spectrum of Cardio-Kidney-Metabolism: the FINE-HEART Pooled Analysis

Maria A. Pabon, MD[1]; Gerasimos Filippatos, MD[2]; Brian L. Claggett, PhD[1]; Michael Zi Miao, MS[1]; Akshay S. Desai, MD[1]; Pardeep S. Jhund, MD, PhD[3]; Alasdair Henderson, PhD[3]; Meike Brinker, MD4; Patrick Schloemer, PhD[4]; Lucas Hofmeister, PhD[4]; Li Li, MD, MPH, MBA[4], Carolyn S.P. Lam, MD, PhD[5]; Michele Senni, MD[6,7]; Sanjiv J. Shah, MD[8]; Adriaan A. Voors, MD, PhD[9]; Faiez Zannad, MD[10]; Peter Rossing, MD[11]; Luis M. Ruilope, MD[12]; Stefan D. Anker, MD[13]; Bertram Pitt, MD[14]; Rajiv Agarwal, MD[15]; John J.V. McMurray, MD[3]; Scott D. Solomon, MD[1]; Muthiah Vaduganathan, MD, MPH[1]

1. Cardiovascular Division, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA.
2. National and Kapodistrian University of Athens, School of Medicine, Attikon University Hospital, Athens, Greece. 3. British Heart Foundation Cardiovascular Research Centre, School of Cardiovascular and Metabolic Health, University of Glasgow, Glasgow, United Kingdom. 4. Bayer, Research & Development, Pharmaceuticals, Berlin, Germany. 5. National Heart Centre Singapore and Duke-National University of Singapore, Singapore. 6. University Bicocca Milan, Milan, Italy. 7. Papa Giovanni XXIII Hospital, Bergamo, Italy. 8. Northwestern University Feinberg School of Medicine, Chicago, IL, USA. 9. University Medical Center Groningen, Groningen, The Netherlands. 10. Université de Lorraine, Inserm Clinical Investigation Centre, CHU, Nancy, France. 11. Steno Diabetes Center Copenhagen and University of Copenhagen, Copenhagen, Denmark. 12. Hospital 12 de Octubre, Madrid, Spain. 13. Department of Cardiology (CVK) of German Heart Center Charité; German Centre for Cardiovascular Research (DZHK) partner site Berlin, Charité Universitätsmedizin, Berlin, Germany. 14. University of Michigan, Ann Arbor, MI, USA. 15. Indiana University School of Medicine, Indianapolis, IN, USA.

BACKGROUND

Mineralocorticoid receptor antagonists (MRA) modulate cardiac and systemic pathways such as fibrosis and inflammation, which may contribute to onset of atrial fibrillation (AF). In this participant-level pooled analysis of 3 large clinical trials, we evaluated the effect of the non-steroidal MRA finerenone on incident AF across the cardio-kidney-metabolic (CKM) spectrum.

METHODS

In this prespecified analysis, we pooled participants from 2 trials of chronic kidney disease and type 2 diabetes (FIDELIO-DKD and FIGARO-DKD) and a trial of heart failure (HF) with mildly reduced or preserved ejection fraction (FINEARTS-HF). Patients were randomized 1:1 to finerenone or placebo. New-onset AFF was prospectively adjudicated in all trials by blinded clinical event committees and required electrocardiographic confirmation on 12-lead ECG, electrophysiology study, telemetry, or short-term rhythm monitoring. The risk of new-onset AFF was evaluated using Cox regression models stratified by region and trial. The association between new-onset AFF and subsequent risk of clinical outcomes was assessed using time-updated Cox proportional hazards models.

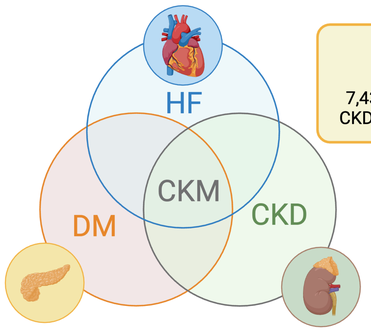
RESULTS

- Among 14,581 patients who were free from AFF at trial enrollment, 631 (4.3%) developed new-onset AFF during follow-up.
- Predictors of new-onset AFF included older age, history of HF, higher body mass index, geographic region, and higher levels of urine albumin creatinine ratio.
- Baseline characteristics were well-balanced between treatment arms (finerenone vs. placebo)(**Table 1**)
- During 2.9 years of median follow-up, new-onset AFF occurred in 286 (3.9%) participants receiving finerenone and 345 (4.7%) assigned to placebo (HR 0.83, 95% CI 0.71, 0.97, p=0.019) (**Central figure**). Risk reductions were consistent across major subgroups, irrespective of number of CKM conditions ($P_{interaction}$=0.87)and by trial ($P_{interaction}$ =0.57)(**Figure 1**).
- Participants with new-onset AFF were at significantly higher subsequent risk of cardiovascular death, HF hospitalization, and adverse kidney outcomes (**Central figure**).

CONCLUSION

The non-steroidal MRA finerenone reduced the risk of new-onset AFF across the CKM spectrum. Given the heightened risk of AFF in CKM syndrome, finerenone may be an important therapeutic option to help reduce AFF-related morbidity and improve outcomes across the CKM spectrum.

Finerenone and New Onset Atrial Fibrillation/Flutter FINE-HEART



FIGARO-DKD

7,437 participants with CKD and type 2 diabetes

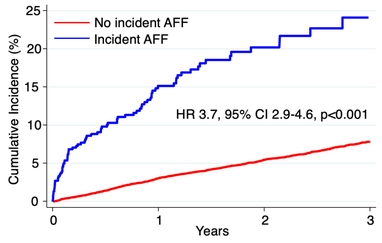
FIDELIO-DKD

5,674 participants with CKD and type 2 diabetes

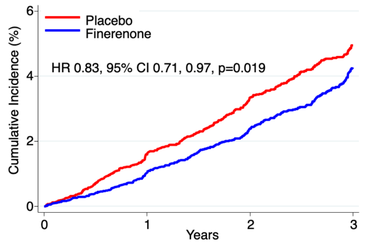
FINEARTS-HF

6,001 participants with HFmrEF HFpEF

New-Onset Atrial Fibrillation/Flutter and Subsequent Risk of HF hospitalization or CV death



Finerenone Reduces New-Onset Atrial Fibrillation/Flutter in the FINE-HEART program



Incident AFF was associated with significantly worse adverse CV outcomes in this high risk CKM population. The non-steroidal MRA finerenone reduced the risk of new-onset AFF across the CKM spectrum

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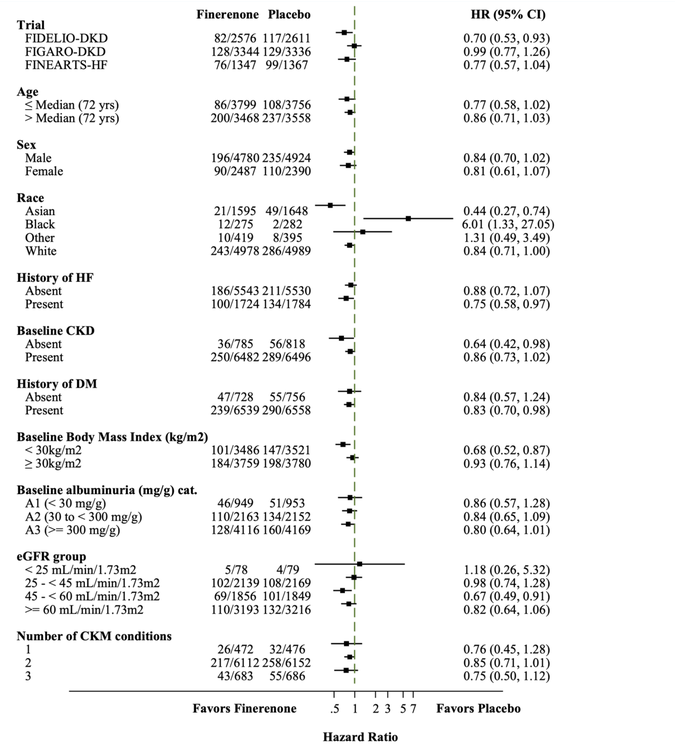
TABLE 1: Baseline characteristics by treatment arm

Characteristic	Placebo (N=7314)	Finerenone (N=7267)	Standardized Mean Differences
Age	65.4 ± 10	65.2 ± 9.7	0.02
Female Sex	2390 (32.7%)	2487 (34.2%)	-0.03
Race			-0.01
Asian	1648 (22.5%)	1595 (21.9%)	
Black	282 (3.9%)	275 (3.8%)	
Other	395 (5.4%)	419 (5.8%)	
White	4989 (68.2%)	4978 (68.5%)	
Region			0.008
Asia	1524 (20.8%)	1499 (20.6%)	
Eastern Europe	2063 (28.2%)	2103 (28.9%)	
Latin America	904 (12.4%)	896 (12.3%)	
North America	1035 (14.2%)	1016 (14.0%)	
Western Europe, Oceania and Others	1788 (24.4%)	1753 (24.1%)	
Baseline Body Mass Index (kg/m2)	30.9 ± 6.0	30.9 ± 6.0	0.0006
Baseline Systolic Blood Pressure (mmHg)	135.59 ± 14.56	135.72 ± 14.51	-0.01
Baseline potassium (mmol/L)	4.37 ± 0.45	4.37 ± 0.44	0.006
Baseline eGFR (mL/min/1.73m2)	59.50 ± 21.98	59.23 ± 21.71	0.01
Baseline UACR (mg/g)	399 [91, 1014]	401 [89, 1002]	0.003
Baseline Hemoglobin A1C (%)	7.5 ± 1.4	7.5 ± 1.4	-0.02
History of HF	1784 (24.4%)	1724 (23.7%)	0.02
Baseline CKD	6496 (88.8%)	6482 (89.2%)	-0.01
History of diabetes	6558 (89.7%)	6539 (90.0%)	-0.01
Diuretic use at baseline	4368 (59.7%)	4249 (58.5%)	0.03
ACEi/ARB/ARNI	7079 (96.8%)	7038 (96.8%)	-0.004
Aspirin	3814 (52.1%)	3802 (52.3%)	-0.004
SGLT-2 Inhibitors	594 (8.1%)	581 (8.0%)	0.005
GLP-1 Receptor Agonists	443 (6.1%)	491 (6.8%)	-0.03

FIGURE 1: Treatment effects of finerenone on new-onset atrial fibrillation/flutter across major clinical subgroups



DISCLOSURE INFORMATION

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