# Number of hospitalizations and effect of Finerenone in FINEARTS-HF

Shingo Matsumoto, MD, PhD[1], Alasdair D. Henderson, PhD[1], Brian L. Claggett, PhD[2], Akshay S. Desai, MD MPH[2], Carolyn S.P. Lam, MBBS PhD[3], Michele Senni, MD[4], Adriaan A. Voors, MD[5], Faiez Zannad, MD[6], Bertram Pitt, MD[7], Andrea Lage, MD[8], Katharina Mueller, MSc[8], Katja Rohwedder, MD[8], Paul Mernagh, MCom[8], Muthiah Vaduganathan, MD, MPH[2], Scott D. Solomon, MD[2], Pardeep S. Jhund, MBChB, MSc, PhD[1], John J.V. McMurray, MD[1]

1. British Heart Foundation Cardiovascular Research Centre, University of Glasgow, Glasgow, United Kingdom. 2. Cardiovascular Division, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA.
3. National Heart Centre Singapore and Duke-National University of Singapore, Singapore. 4. University of Milano-Bicocca, Papa Giovanni XXIII Hospital, Bergamo, Italy. 5. University of Groningen, Groningen, the Netherlands.
6. Université de Lorraine, Inserm Clinical Investigation Center at Institut Lorrain du Coeur et des Vaisseaux, University Hospital of Nancy, Nancy, France. 7. University of Michigan School of Medicine, Ann Arbor, MI, USA. 8. Bayer, Research & Development, Pharmaceuticals.

## Background

Heart failure hospitalization (HFH) represents an important event in the natural history of heart failure (HF) regardless of left ventricular ejection fraction (LVEF), with a worse subsequent disease trajectory than in patients not hospitalized. However, these high-risk patients often do not have treatment intensified, possibly because of concerns about tolerability and safety of HF therapy. It is important to know whether a new HF treatment is effective and safe in patients with prior HFH episodes.

## Purpose

To examine the association between the number of HFHs and outcomes in patients with heart failure and mildly reduced or preserved ejection fraction (HFmrEF/HFpEF).

## Methods

In this *post-hoc* analysis of FINEARTS-HF, we examined the efficacy and safety of finerenone in patients with HFmrEF/HFpEF, according to the number of prior HFHs within the last 1 year before randomization (no HFH, 1 HFH, and ≥2 HFHs).

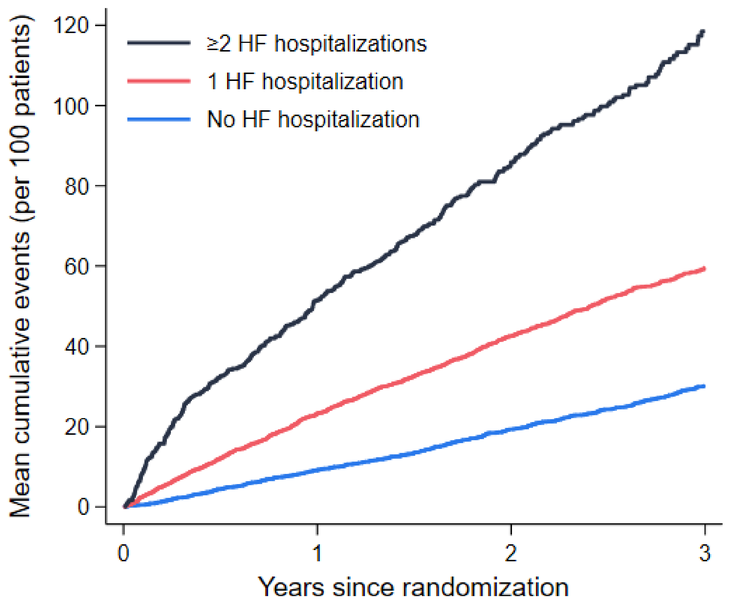
**Key inclusion criteria:** NYHA functional class II-IV, LVEF ≥40%, evidence of structural heart disease, and elevated natriuretic peptides

**Key exclusion criteria:** eGFR <25 ml/min/1.73m$^2$, potassium >5.0 mmol/L

**Primary outcome**
Total (first and recurrent) HF hospitalizations and cardiovascular death

## Results

### The primary outcome according to the number of heart failure hospitalizations within the last 1 year

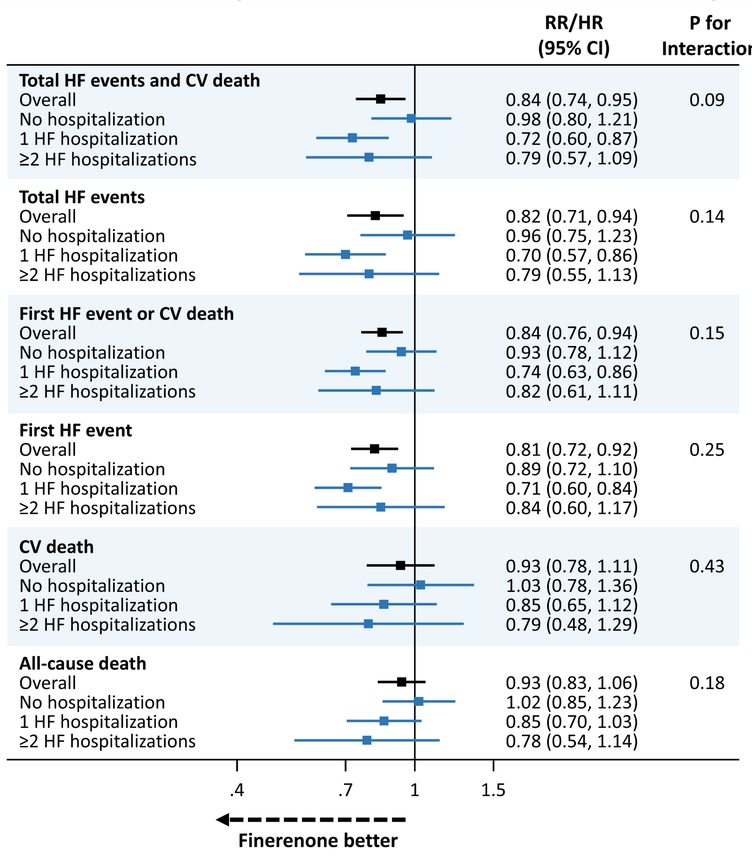



### Outcomes according to the number of heart failure hospitalizations within the last 1 year

| | No HFH in prior 12 months N=2,879 | 1 HFH in prior 12 months N=2,504 | ≥2 HFHs in prior 12 months N=421 |
|---|---|---|---|
| **Total HF events and CV death** | | | |
| Number of events | 732 | 1,170 | 375 |
| Event rate per 100 person-y (95% CI) | 9.9 (8.9-10.9) | 20.5 (18.6-22.5) | 41.3 (34.9-48.8) |
| RR (95% CI)* | Reference | 2.04 (1.77-2.36) | 3.96 (3.25-4.83) |
| Adjusted RR (95% CI)** | Reference | 1.76 (1.52-2.03) | 2.78 (2.26-3.41) |
| Adjusted RR (95% CI)*** | Reference | 1.53 (0.96-2.42) | 2.40 (1.50-3.84) |
| **Total HF events** | | | |
| Number of events | 528 | 962 | 308 |
| Event rate per 100 person-y (95% CI) | 7.1 (6.3-8.0) | 16.8 (15.2-18.7) | 33.9 (28.1-40.8) |
| RR (95% CI)* | Reference | 2.34 (1.98-2.76) | 4.46 (3.56-5.58) |
| Adjusted RR (95% CI)** | Reference | 2.02 (1.71-2.39) | 3.14 (2.49-3.96) |
| Adjusted RR (95% CI)*** | Reference | 1.69 (1.01-2.85) | 2.61 (1.55-4.40) |
| **CV death** | | | |
| Number of events | 204 (7.1%) | 210 (8.4%) | 67 (15.9%) |
| Event rate per 100 person-y (95% CI) | 2.7 (2.4-3.2) | 3.7 (3.2-4.2) | 7.4 (5.8-9.4) |
| HR (95% CI)* | Reference | 1.29 (1.06-1.58) | 2.67 (2.01-3.54) |
| Adjusted HR (95% CI)** | Reference | 1.08 (0.88-1.32) | 1.82 (1.36-2.45) |
| Adjusted HR (95% CI)*** | Reference | 1.01 (0.57-1.80) | 1.71 (0.91-3.21) |
| **All cause death** | | | |
| Number of events | 438 (15.2%) | 420 (16.8%) | 115 (27.3%) |
| Event rate per 100 person-y (95% CI) | 5.9 (5.4-6.5) | 7.3 (6.7-8.1) | 12.5 (10.4-15.0) |
| HR (95% CI)* | Reference | 1.26 (1.10-1.45) | 2.19 (1.77-2.69) |
| Adjusted HR (95% CI)** | Reference | 1.07 (0.93-1.24) | 1.58 (1.27-1.96) |
| Adjusted HR (95% CI)*** | Reference | 0.76 (0.50-1.16) | 1.11 (0.70-1.76) |

*Adjusted for treatment assignment
**Adjusted for treatment assignment, age, sex, body mass index, eGFR, New York Heart Association functional classification, heart rate, systolic blood pressure, type 2 diabetes mellitus, atrial fibrillation, myocardial infarction, and log-transformed NT-proBNP
***Adjusted for recency of HFH in addition to model**

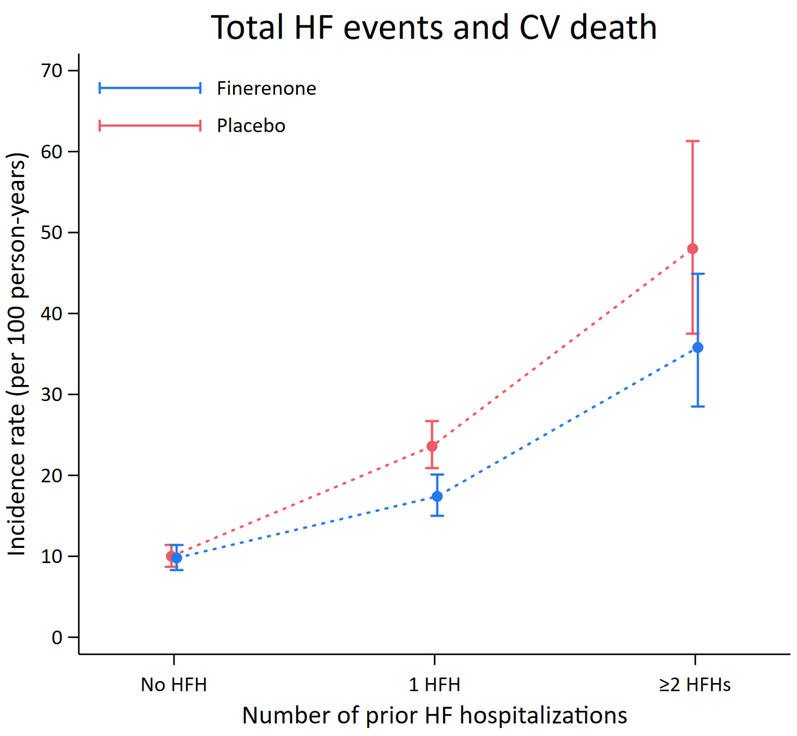
### Effect of finerenone compared to placebo according to the number of heart failure hospitalizations within the last 1 year




### Safety outcomes according to the number of heart failure hospitalizations within the last 1 year

| | No HFH in prior 12 months | | 1 HFH in prior 12 months | | ≥2 HFHs In prior 12 months | | P for interaction |
|---|---|---|---|---|---|---|---|
| | Placebo | Finerenone | Placebo | Finerenone | Placebo | Finerenone | |
| Any serious adverse events | 578 (39.9) | 511 (35.8) | 495 (40.0) | 498 (40.0) | 98 (50.8) | 115 (50.7) | 0.21 |
| Serum creatinine level | | | | | | | |
| Creatinine ≥2.5 mg/dL | 34 (2.4) | 61 (4.4) | 42 (3.5) | 62 (5.2) | 9 (5.0) | 11 (5.1) | 0.46 |
| Creatinine ≥3.0 mg/dL | 12 (0.9) | 30 (2.2) | 16 (1.3) | 20 (1.7) | 3 (1.7) | 4 (1.9) | 0.26 |
| Hyperkalemia | | | | | | | |
| Potassium >5.5 mmol/L | 91 (6.4) | 199 (14.3) | 89 (7.5) | 164 (13.7) | 12 (6.7) | 36 (16.6) | 0.38 |
| Potassium >6.0 mmol/L | 19 (1.3) | 43 (3.1) | 20 (1.7) | 34 (2.8) | 2 (1.1) | 7 (3.2) | 0.61 |
| Hypokalemia | | | | | | | |
| Potassium <3.5 mmol/L | 135 (9.5) | 44 (3.2) | 114 (9.6) | 62 (5.2) | 25 (13.9) | 16 (7.4) | 0.08 |
| Potassium <3.0 mmol/L | 42 (3.5) | 62 (5.2) | 9 (5.0) | 11 (5.1) | 4 (4.0) | 7 (7.9) | 0.40 |
| SBP <100 mmHg | 183 (12.9) | 257 (18.4) | 142 (11.8) | 228 (19.0) | 27 (14.9) | 46 (20.9) | 0.43 |

### Absolute risk reduction with finerenone according to the number of heart failure hospitalizations within the last 1 year




## Conclusion

Although a higher number of prior HFHs was associated with worse HF status and a substantially higher risk of HF outcomes, the efficacy and safety of finerenone compared to placebo were maintained, even in patients experiencing recurrent HFHs within the last 1 year. Consequently, the absolute rate reduction with finerenone was greater in these high-risk patients.