Effects of Finerenone on Heart Failure Outcomes According to Baseline Heart Failure Risk in Chronic Kidney Disease and Type 2 Diabetes

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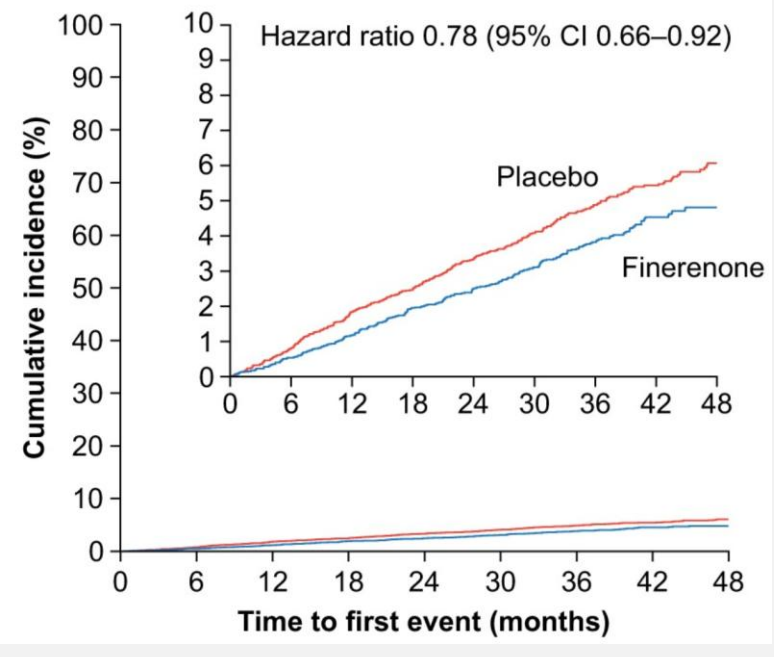
Background

- Persons with CKD and type 2 diabetes (T2D) experience substantial, but often underappreciated, risks of HF events
- As such, therapeutic strategies that reduce the HF risks in this population are important
- Finerenone has been shown to reduce HF hospitalization in persons with CKD and T2D
- <u>However, whether these benefits vary according to HF risk is uncertain</u>

HF Hospitalization in FIDELITY



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Objective and Study Population

In this secondary analysis of the FIDELITY program, we evaluated the relative and absolute effects of finerenone on HF outcomes according to baseline HF risk

FIDELITY n=12,990

FIDELIO-DKD

- Recruitment: 2015-2018
- Population: CKD and T2D, with albuminuria
- Primary outcome: kidney failure, sustained eGFR decrease ≥40%, or renal death

FIGARO-DKD

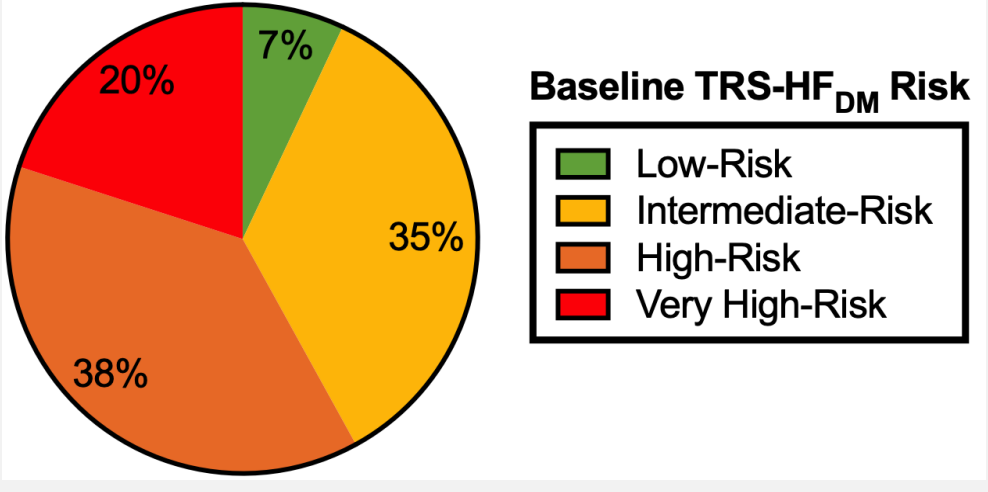
- Recruitment: 2015-2018
- Population: CKD and T2D, with albuminuria
- Primary outcome: CV death, non-fatal MI, non-fatal stroke, or HF hospitalization

METHODS

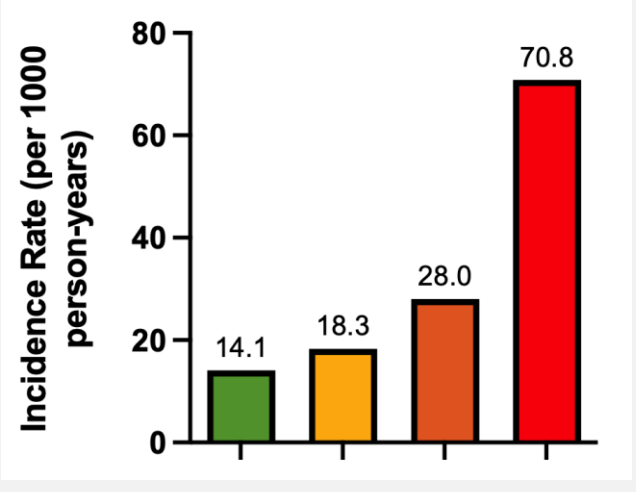
- **Exposure:** HF risk
  - Based on the validated Thrombolysis in Myocardial Infarction Risk Score for Heart Failure in Diabetes (TRS-HF_{DM})
    - TRS-HF_{DM} = history of **HF** (2 points) + history of **atrial fibrillation** (1 point) + history of **CAD** (1 point) + **eGFR** <60 mL/min/1.73 m^2 (1 point) + **UACR** 30-300 mg/g (1 point) or >300 mg/g (2 points)
      - **Low-risk:** 0-1 points
      - **Intermediate-risk:** 2 points
      - **High-risk:** 3 points
      - **Very high-risk:** ≥4 points
- **Main outcome:** cardiovascular death or HF hospitalization
- Analyses included the 12,990 participants validly randomized at sites without critical Good Clinical Practice violations, and followed intention-to-treat principles

Distribution of HF Risk in FIDELITY

Distribution of Baseline HF Risk in FIDELITY

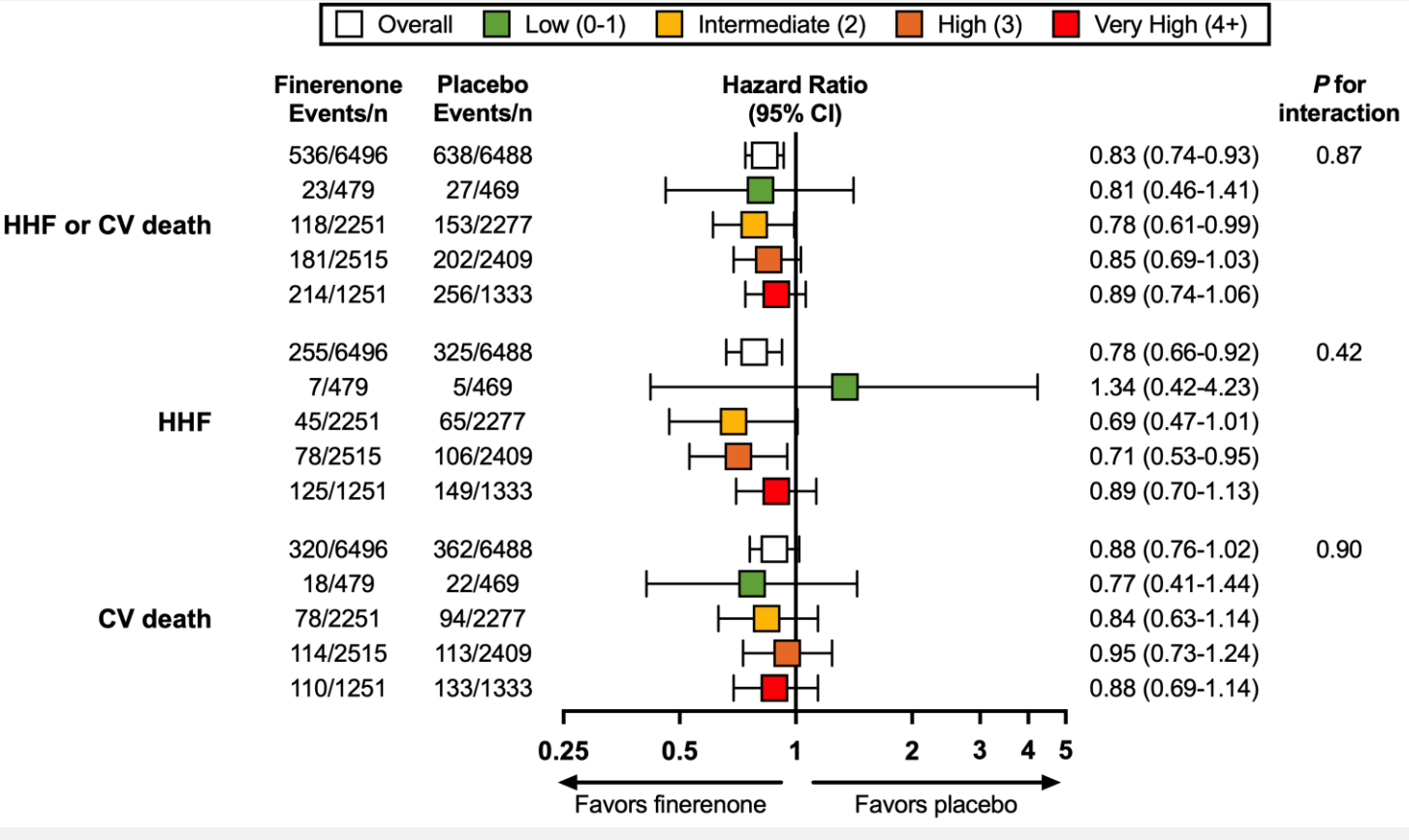


Incidence of CV Death or HF Hospitalization, by Baseline HF Risk



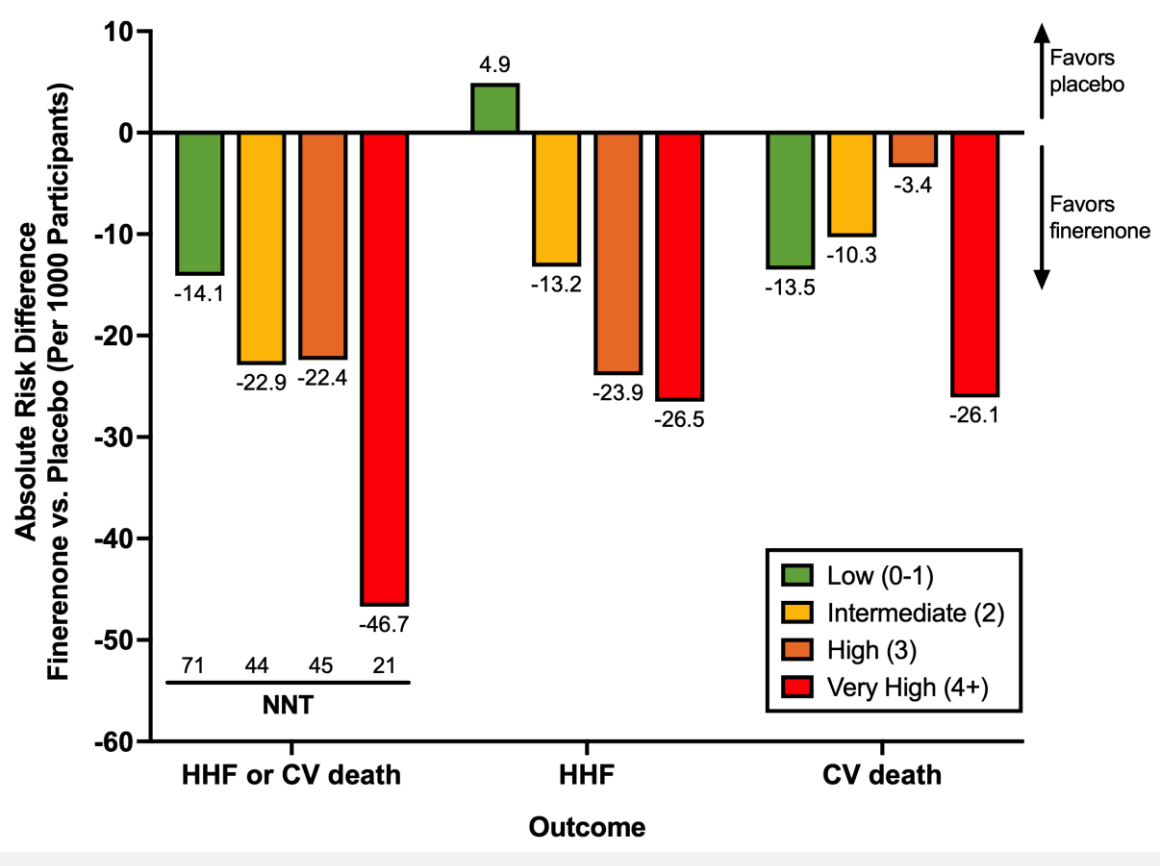
Most (58%) FIDELITY participants had a high or very high predicted risk of HF events; baseline TRS-HF$_{DM}$ score was incrementally associated with CV events

Relative Effects of Finerenone, by Baseline HF Risk



Treatment effects of finerenone vs. placebo on key cardiovascular outcomes, overall and by TRS-HF_{DM} risk category, estimated through Cox proportional hazards regression, stratified by trial and the trial-specific stratification factors

Absolute Benefits of Finerenone, by Baseline HF Risk



Absolute treatment effects of finerenone versus placebo on key cardiovascular outcomes, by TRS-HF_{DM} risk category. Absolute risk differences per 1,000 persons were estimated through Poisson regression.

Discussion and Conclusions

- Higher baseline TRS-HF_{DM} scores were associated with an incrementally higher rate of adverse cardiovascular outcomes in FIDELITY
- Relative benefits of finerenone on CV death or HF hospitalization were consistent, irrespective of baseline TRS-HF_{DM} score
- Due to higher baseline risk, absolute benefits of finerenone on CV death or HF hospitalization appeared greater in participants with highest baseline HF risk

These findings underscore the potential value of risk-based identification of persons with CKD and T2D who might benefit most from accelerated implementation of combination guideline-based medical therapies, including finerenone, to reduce the risk of HF events.