Poster 229

Effectiveness of finerenone in slowing CKD progression after hospitalization for heart failure: A FIDELITY subgroup analysis

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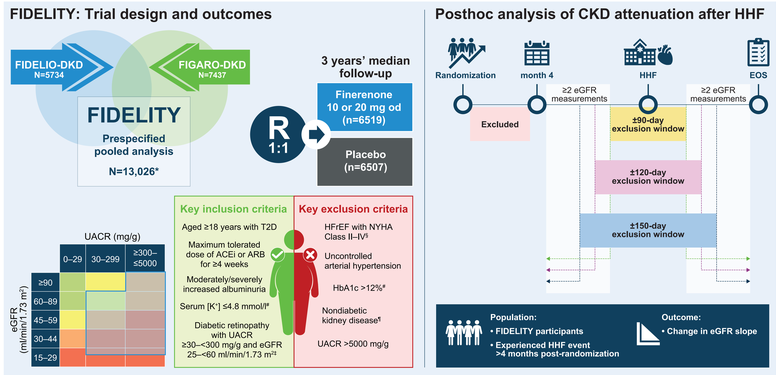
1. Background

- Chronic kidney disease (CKD) is a common complication of type 2 diabetes (T2D), affecting approximately 40% of patients with T2D[1]
- Cardiovascular complications and CKD are closely interlinked such that progression of one can lead to the worsening of the other[2]
- Patients with CKD hospitalized for HF have greater risk of CKD progression and death[3]
  - Moreover, in this patient population, higher rates of hospitalization have been observed in those with lower estimated glomerular filtration rate (eGFR) and higher urine albumin-to-creatinine ratio (UACR)[3]
- FIDELITY is a prespecified pooled analysis of the FIDELIO-DKD and FIGARO-DKD trials, which demonstrated that finerenone reduced the risk of cardiovascular and kidney outcomes versus placebo in patients with T2D and CKD[4]
- This post hoc analysis explored whether the benefit of finerenone on CKD progression persists in patients after discharge from a hospitalization for heart failure (HHF)

2. Study design and methods

- FIDELITY combined individual patient-level data from the two complementary phase III clinical trials, FIDELIO-DKD (NCT02540993) and FIGARO-DKD (NCT02545049), in patients with T2D and CKD receiving optimized renin–angiotensin system blockade randomized to finerenone or placebo
  - The designs and results of these studies have been published previously[5,6]
- This analysis included FIDELITY participants that experienced HHF >4 months after randomization
- A summary of the study design and patient population in FIDELITY and the assessment criteria for this post hoc analysis of CKD attenuation after HHF are shown in **Figure 1**

Figure 1. Study design and patient population in FIDELITY, and CKD attenuation after HHF post hoc analysis criteria



*Prospective exclusion of 145 patients; ‡at run-in or screening visit; §FIDELIO-DKD only; ¶run-in only; #known significant nondiabetic kidney disease, including clinically relevant renal artery stenosis
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; EOS, end of study; HbA1c, glycated hemoglobin; HFrEF, heart failure with reduced ejection fraction; HHF, hospitalization for heart failure; [K⁺], potassium concentration; NYHA, New York Heart Association; od, once daily; R, randomization; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio

- We used a mixed model for repeated measures to investigate changes in eGFR (eGFR slopes)
  - The primary eGFR slope analysis used a time-exclusion window of ±90 days before and after the adjudicated HHF event; set to exclude any measurements of serum creatinine that would have been modified due to the hospitalization event and thus not a true reflection of the treatment effect
    - Patients who had ≥1 post-baseline eGFR measurement that did not fall within the time-exclusion window were included in the analysis
  - Additional analyses were performed as above for time-exclusion windows of ±120 and ±150 days before and after the adjudicated HHF event
  - Sensitivity on-treatment analyses were also performed for each exclusion window
  - eGFR slopes from month 4 to an HHF event, and from an HHF event to the end of the study period were reported as least-squares (LS) mean changes in eGFR

3. Results

3.1. Baseline characteristics and medications

- Among patients who experienced an HHF event, baseline characteristics were generally balanced between finerenone (n=239) and placebo (n=311), and are outlined in **Table 1**

Table 1. Baseline (pre-randomization) characteristics and medications for patients who experienced an HHF event

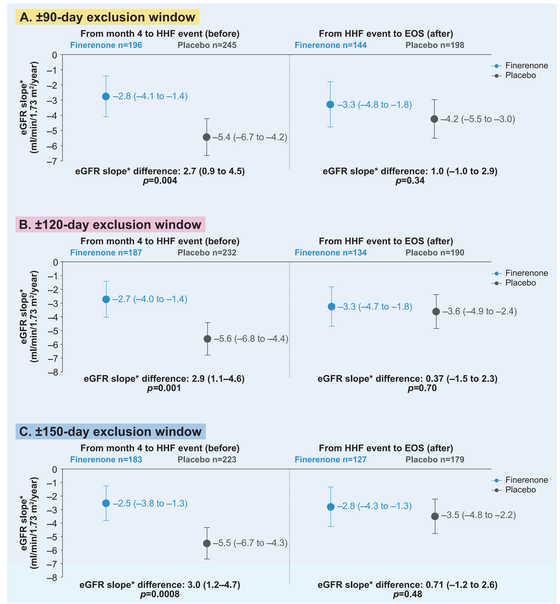
	Finerenone (n=239)	Placebo (n=311)
Baseline characteristics		
Age, years	66.7 ± 9.5	67.8 ± 8.9
Sex		
Male	150 (62.8)	233 (74.9)
Female	89 (37.2)	78 (25.1)
Duration of diabetes, years	18.0 ± 9.4	17.6 ± 8.9
HbA1c, %	7.8 ± 1.5	7.9 ± 1.5
Systolic blood pressure, mmHg	139.7 ± 15.5	139.8 ± 14.1
History of CV disease, yes	156 (65.3)	207 (66.6)
eGFR, ml/min/1.73 m²	50.7 ± 20.3	53.9 ± 20.7
UACR, mg/g, median (Q1–Q3)	840.4 (239.5–1725.9)	712.1 (257.0–1759.4)
Serum potassium, mmol/l	4.31 ± 0.47	4.28 ± 0.47
Baseline medications		
ACEis	97 (40.6)	131 (42.1)
ARBs	141 (59.0)	180 (57.9)
Beta blockers	168 (70.3)	216 (69.5)
Diuretics	172 (72.0)	221 (71.1)
Statins	174 (72.8)	242 (77.8)
Potassium supplements	11 (4.6)	22 (7.1)
Potassium-lowering agents	3 (1.3)	5 (1.6)
Glucose-lowering therapies	231 (96.7)	306 (98.4)
Insulin and analogs	162 (67.8)	223 (71.7)
Metformin	112 (46.9)	153 (49.2)
Sulfonamides	51 (21.3)	64 (20.6)
DPP-4 inhibitors	56 (23.4)	62 (19.9)
GLP-1RAs	15 (6.3)	22 (7.1)
SGLT-2is	10 (4.2)	20 (6.4)

Data are n (%) or mean ± SD unless stated otherwise
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CV, cardiovascular; DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated hemoglobin; HHF, hospitalization for heart failure; Q, quartile; SD, standard deviation; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; UACR, urine albumin-to-creatinine ratio

3.2. eGFR slope analysis before and after an HHF event

- For the primary analysis (±90-day exclusion window), the mean change in eGFR from month 4 to an HHF event showed a significantly slower decline in eGFR with finerenone (–2.8 ml/min/1.73 m²/year) compared with placebo (–5.4 ml/min/1.73 m²/year; between-treatment difference of 2.7 ml/min/1.73 m²/year; p=0.004) (**Figure 2A)**
  - A numerically slower decline in eGFR versus placebo was also observed with finerenone after an HHF event to the end of study (between-treatment difference 1.0 ml/min/1.73 m²/year; p=0.34) (**Figure 2A**)
- Similar results were observed with the ±120-day and ±150-day exclusion windows
  - Significant between-treatment eGFR slope differences of 2.9 ml/min/1.73 m²/year (p=0.001) and 3.0 ml/min/1.73 m²/year (p=0.0008) were observed from month 4 to an HHF for the ±120-day and ±150-day windows, respectively. The between-treatment eGFR slope differences were 0.37 ml/min/1.73 m²/year (p=0.70) and 0.71 ml/min/1.73 m²/year (p=0.48) after an HHF event, (**Figures 2B** and **2C**)
- Findings were similar for on-treatment sensitivity analyses for all exclusion windows

Figure 2. eGFR slope analysis with (A) ±90-, (B) ±120-, (C) ±150-day exclusion windows before and after HHF event



*eGFR slope data are presented as least-squares mean in ml/min/1.73 m²/year (95% CI)
CI, confidence interval; eGFR, estimated glomerular filtration rate; EOS, end of study; HHF, hospitalization for heart failure

3.3. Strengths and limitations

- There are several strengths to this analysis, and these include:
  - Data were reported from an international multicenter cohort that enrolled a diverse population, which increases the generalizability of results
  - HHF events were independently adjudicated to ensure accuracy and consistency of these reported events
  - Serum creatinine was measured routinely as part of the research protocol; therefore, results are not confounded by indication
- However, the benefits of the randomization process were invalidated by the use of post-baseline data (HHF events) to define subgroups
  - As such, the analysis may be susceptible to unmeasured confounding by introducing imbalances in the randomized groups that may have biased the efficacy outcome data

4. Conclusions

- Patients treated with finerenone tended to have lower eGFR decline after an HHF event when compared to placebo
- Our findings suggest that finerenone should be continued on discharge in patients experiencing an HHF event

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