Poster No.: SA-PO273

# Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes: A Chinese subgroup analysis of the FIDELIO-DKD study


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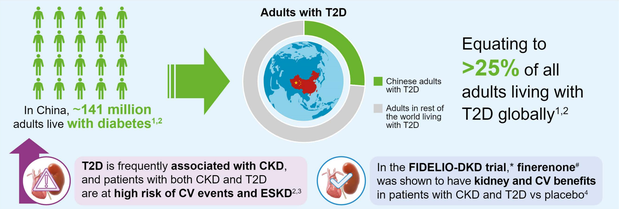
## 1. Background

- The background information for this analysis is presented in **Figure 1**[1-4]
- This subgroup analysis of the FIDELIO-DKD trial (NCT02540993) evaluated the efficacy and safety of finerenone in patients with chronic kidney disease (CKD) and type 2 diabetes (T2D) in China

**Figure 1.** Background



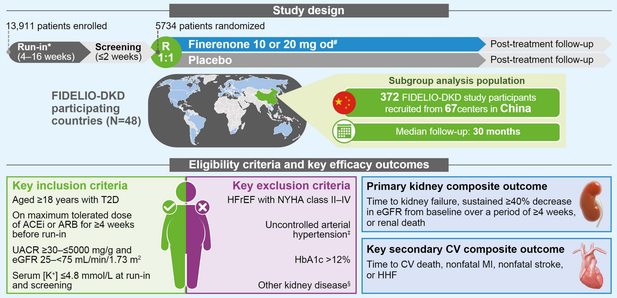

*A phase III, multicenter, randomized, double-blind trial (NCT02540993); #a selective, nonsteroidal mineralocorticoid antagonist
CKD, chronic kidney disease; CV, cardiovascular; ESKD, end-stage kidney disease; T2D, type 2 diabetes

## 2. Methods

### 2.1. Study design and participants

- In FIDELIO-DKD (N=5674), patients with CKD and T2D were randomized 1:1 to oral finerenone or placebo, and treated with a maximum tolerated dose of an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB), as shown in **Figure 2**[4]
- This analysis included a subset of the FIDELIO-DKD study population (n=372) recruited from 67 study sites in China (**Figure 2**)
- Key eligibility criteria and efficacy outcomes are described in **Figure 2**
- Safety analyses included assessment of investigator-reported adverse events (AEs)

**Figure 2.** FIDELIO-DKD study design and key efficacy endpoints




*Optimization of participant standard-of-care medical therapies including ensuring that patients were pretreated with a maximum tolerated labeled dose of either an ACEi or an ARB for ≥4 weeks prior to the screening visit; #10 mg if screening eGFR <60 mL/min/1.73 m²; 20 mg if eGFR ≥60 mL/min/1.73 m²; up-titration encouraged from month 1 if serum potassium ≤4.8 mmol/L and eGFR stable; a decrease in the dose from 20 to 10 mg od was allowed at any time after treatment initiation; sham dose adjustments were conducted in the placebo group; ‡mean sitting SBP ≥170 mmHg or mean sitting DBP ≥110 mmHg at the run-in visit, or mean sitting SBP ≥160 mmHg or mean sitting DBP ≥100 mmHg at the screening visit; §known significant nondiabetic kidney disease, including clinically relevant renal artery stenosis
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CV, cardiovascular; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; HFrEF, heart failure with reduced ejection fraction; HHF, hospitalization for heart failure; [K+], potassium concentration; MI, myocardial infarction; NYHA, New York Heart Association; od, once daily; R, randomization; SBP, systolic blood pressure; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio

### 2.2. Statistical analysis

- Efficacy analyses were conducted on the full analysis set
- Safety analyses were conducted on the safety analysis set (all patients from the full analysis set who received at least one dose of finerenone or placebo)
- Kaplan–Meier method and Cox proportional hazard models were used to analyze time-to-event variables
  - Treatment effects are expressed as hazard ratios (HRs) with corresponding 95% confidence intervals (CIs) and *p*-values
    - A two-sided $p<0.05$ was considered statistically significant

## 3. Results

### 3.1. Baseline characteristics

- Patient characteristics at baseline were generally balanced between groups. Patients in the placebo group had a longer mean duration of diabetes (14.17 years; standard deviation [SD] ± 8.40) and lower median urine albumin-to-creatinine ratio (1210.41 mg/g; interquartile range [IQR] 601.73–2329.66) compared with those in the finerenone group (13.31 years; SD ± 7.43, and 1326.61 mg/g; IQR 607.32–2148.56, respectively), as shown in **Table 1**
- At baseline, fewer patients were treated with diuretics in the finerenone group (n=29 [15.4%]) than in the placebo group (n=45 [24.5%]). All patients were treated with either an ACEi or an ARB, and >96% of patients were on glucose-lowering therapy (**Table 1**)

**Table 1.** Baseline characteristics and medication use

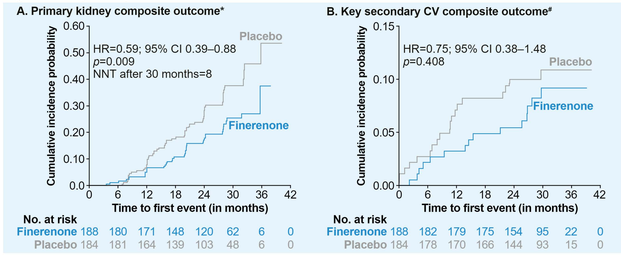
| | Total participants from China (N=372) | |
|---|---|---|
| **Characteristic** | **Finerenone (n=188)** | **Placebo (n=184)** |
| Age, years | 59.85 ± 10.16 | 60.68 ± 10.13 |
| Sex, male | 145 (77.1) | 145 (78.8) |
| Duration of diabetes, years | 13.31 ± 7.43 | 14.17 ± 8.40 |
| HbA1c, % | 7.47 ± 1.37 | 7.44 ± 1.33 |
| Systolic blood pressure, mmHg | 135.83 ± 14.6 | 132.89 ± 15.88 |
| eGFR, mL/min/1.73 m² | 45.88 ± 11.37 | 45.25 ± 11.22 |
| ≥60 | 21 (11.2) | 19 (10.3) |
| 45–<60 | 78 (41.5) | 70 (38.0) |
| 25–<45 | 88 (46.8) | 92 (50.0) |
| <25 | 1 (0.5) | 3 (1.6) |
| UACR, mg/g, median (IQR) | 1326.61 (607.32–2148.56) | 1210.41 (601.73–2329.66) |
| UACR, mg/g | | |
| 30–<300 | 18 (9.6) | 14 (7.6) |
| ≥300 | 170 (90.4) | 170 (92.4) |
| Serum [K+], mmol/L | 4.29 ± 0.44 | 4.28 ± 0.42 |
| **Baseline medications** | | |
| ACEis | 21 (11.2) | 23 (12.5) |
| ARBs | 167 (88.8) | 161 (87.5) |
| Diuretics | 29 (15.4) | 45 (24.5) |
| Statins | 104 (55.3) | 93 (50.5) |
| Potassium-lowering agents* | 0 | 2 (1.1) |
| Glucose-lowering therapies | 181 (96.3) | 179 (97.3) |
| Insulin | 147 (78.2) | 141 (76.6) |
| GLP-1 receptor agonists | 2 (1.1) | 4 (2.2) |
| SGLT-2 inhibitors | 0 | 0 |

All values are shown as either mean ± standard deviation or n (%), unless otherwise specified
*Including sodium polystyrene sulfonate, calcium polystyrene sulfonate, and potassium-binding agents
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; GLP-1, glucagon-like peptide-1; IQR, interquartile range; [K+], potassium concentration; SGLT-2, sodium-glucose co-transporter-2; UACR, urine albumin-to-creatinine ratio

### 3.2. Efficacy outcomes

- After a median follow-up of 30 months, the finerenone group showed a relative risk reduction (RRR) of 41% (HR=0.59; 95% CI 0.39–0.88; $p=0.009$) for the primary kidney composite outcome (kidney failure, sustained ≥40% decrease in estimated glomerular filtration rate [eGFR] from baseline over ≥4 weeks, or renal death) compared with the placebo group (**Figures 3A and 4**)
  - The benefit of finerenone was consistent across the primary kidney composite outcome components (**Figure 4**)
  - Finerenone also significantly reduced the risk of the primary kidney composite outcome versus placebo in the overall FIDELIO-DKD population (HR=0.82; 95% CI 0.73–0.93; $p=0.001$)[4]
- Based on an absolute between-group difference of 12.2% after 30 months, 8 patients (95% CI 4–84) needed to be treated with finerenone to prevent one primary kidney composite outcome event
- Similarly, for the key secondary cardiovascular (CV) composite outcome (CV death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure), finerenone showed an RRR of 25% (HR=0.75; 95% CI 0.38–1.48; $p=0.408$) compared with placebo, but the observed difference did not reach statistical significance (**Figure 3B**)
- In the overall FIDELIO-DKD population, a significant reduction in the risk of the key secondary CV composite outcome was reported with finerenone versus placebo (HR=0.86; 95% CI 0.75–0.99; $p=0.03$)[4]

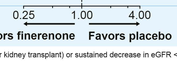
**Figure 3.** Key kidney and CV outcomes




Kaplan–Meier curves based on the full analysis set
*Time to kidney failure, sustained ≥40% decrease in eGFR from baseline over ≥4 weeks, or renal death; #time to CV death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure
CI, confidence interval; CV, cardiovascular; HR, hazard ratio; NNT, number needed to treat

**Figure 4.** Effect of finerenone on the components of the primary kidney outcome

| | Finerenone (n=188) | | Placebo (n=184) | | | |
|---|---|---|---|---|---|---|
| **Outcome** | **n (%)** | **n per 100 PY** | **n (%)** | **n per 100 PY** | **Hazard ratio (95% CI)** | ***p*-value** |
| **Primary kidney composite outcome** | **40 (21.3)** | **10.51** | **61 (33.2)** | **17.03** | **0.59 (0.39–0.88)** | **0.009** |
| Kidney failure* | 23 (12.2) | 5.79 | 30 (16.3) | 7.78 | 0.71 (0.41–1.23) | 0.219 |
| End-stage kidney disease | 16 (8.5) | 3.61 | 19 (10.3) | 4.37 | 0.83 (0.43–1.62) | 0.584 |
| Sustained# decrease in eGFR to <15 mL/min/1.73 m² | 19 (10.1) | 4.79 | 24 (13.0) | 6.24 | 0.73 (0.40–1.33) | 0.297 |
| Sustained# ≥40% decrease in eGFR from baseline | 38 (20.2) | 9.99 | 58 (31.5) | 16.21 | 0.59 (0.39–0.89) | 0.011 |
| Renal death | 0 | – | 1 (0.5) | – | – | – |

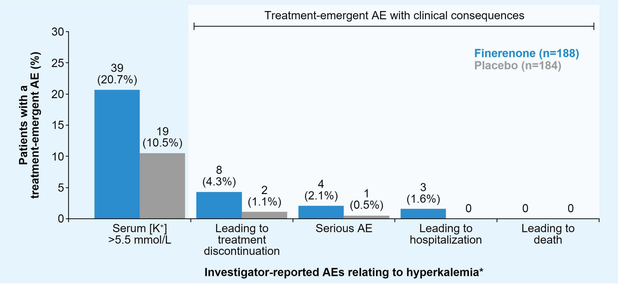



*Kidney failure defined as either end-stage kidney disease (initiation of chronic dialysis for ≥90 days or kidney transplant) or sustained decrease in eGFR <15 mL/min/1.73 m²;
#confirmed by two eGFR measurements ≥4 weeks apart
CI, confidence interval; eGFR, estimated glomerular filtration rate; PY, patient-years

### 3.3. Safety outcomes

- AEs were similar between the two groups. In the finerenone group, a modest reduction in blood pressure was observed from baseline to month 1 (–3.07 mmHg), to month 4 (–0.91 mmHg), and to month 12 (–1.15 mmHg), whereas an increase was observed with placebo (2.86, 3.00, and 1.82 mmHg from baseline to months 1, 4, and 12, respectively)
- There were no differences in the incidence of acute kidney injury between the finerenone and placebo groups (both n=3 [1.6%])
- No gynecomastia events or breast pain was reported in this subgroup analysis
- The incidence of serum potassium >5.5 mmol/L was higher with finerenone than with placebo (n=39 [20.7%] vs n=19 [10.5%], respectively)
- Hyperkalemia led to hospitalization and treatment discontinuation in 3 (1.6%) and 8 (4.3%) patients in the finerenone group, and 0 and 2 (1.1%) patients in the placebo group, respectively (**Figure 5**)
- No deaths due to hyperkalemia were reported in the study (**Figure 5**)

**Figure 5.** Key safety outcomes




*Investigator-reported AEs using the MedDRA preferred terms 'hyperkalemia' and 'blood potassium increased'
AE, adverse event; [K+], potassium concentration; MedDRA, Medical Dictionary for Regulatory Activities

## 4. Conclusions

- Among patients with CKD and T2D recruited for the FIDELIO-DKD trial in China, treatment with finerenone resulted in a reduced risk of CKD progression compared with placebo, with a number needed to treat of 8
- Although the incidence of hyperkalemia-related AEs was higher in the finerenone versus placebo group, hospitalizations and study drug discontinuations due to hyperkalemia were low
- The impact of finerenone on blood pressure was modest, and no differences were observed for acute kidney injury or breast-related side effects compared with placebo


## Acknowledgments

The FIDELIO-DKD trial was funded by Bayer AG. Medical writing assistance was provided by Chameleon Communications International with funding from Bayer AG.


## Disclosures

**HZ, JX, CH, XL, DZ, HZ, XX, ZM, WL, YL, CW, NT, LW,** and **ZL** report no conflicts of interest.

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**Poster #SA-PO273 presented at the American Society of Nephrology (ASN) 2022 (3–6 November, Orlando, Florida)**