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Finerenone in Chinese patients with type 2 diabetes and chronic kidney disease: A FIDELITY analysis

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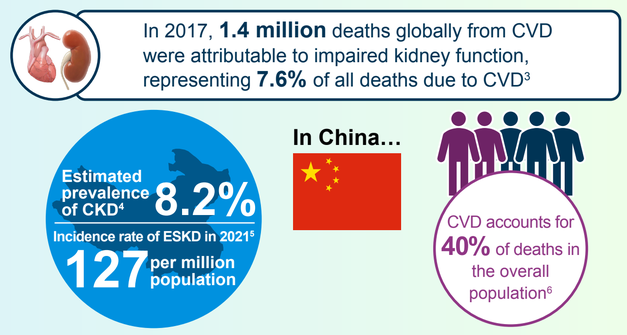
Background

- Globally, type 2 diabetes (T2D) is a leading cause of chronic kidney disease (CKD), and up to 40% of patients with T2D have CKD[1,2]
- The burden of CKD is high in the Chinese population (**Figure 1**)[3–6]
- In FIDELITY, a prespecified pooled analysis of two phase III trials, finerenone significantly improved heart and kidney outcomes in patients with CKD and T2D[7]
- This subanalysis of the FIDELITY dataset explores the efficacy and safety of finerenone in the Chinese patient subgroup

Figure 1. Burden of cardiovascular and kidney disease in the global and Chinese population

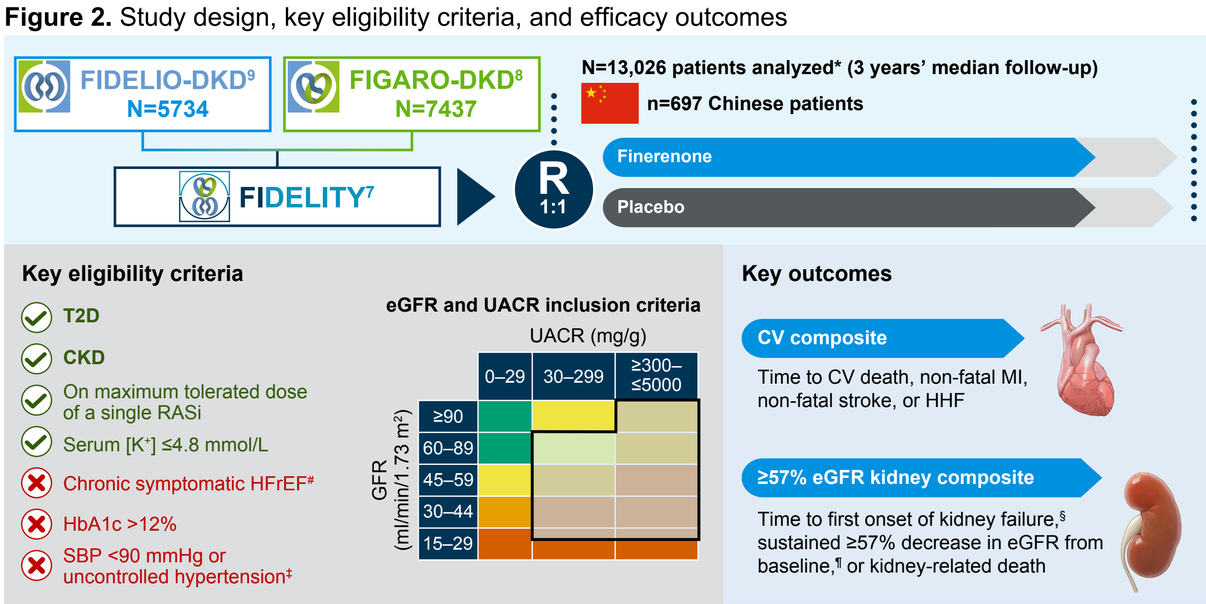


CKD, chronic kidney disease; CVD, cardiovascular disease; ESKD, end-stage kidney disease

Study design and methods

- FIDELITY combined individual patient-level data from the complementary phase III FIDELIO-DKD (NCT02540993) and FIGARO-DKD (NCT02545049) trials, which included a broad spectrum of patients with CKD and T2D who were using optimized renin–angiotensin system blockade (**Figure 2**)[7–9]
- Key eligibility criteria and efficacy outcomes are described in **Figure 2**;[7–9] other prespecified outcomes include:
  - A composite of time to first onset of kidney failure, sustained ≥40% decrease in estimated glomerular filtration rate (eGFR) from baseline over ≥4 weeks, or kidney-related death
  - The chronic eGFR slope (least-squares [LS] mean change in eGFR from month 4 to end of treatment)
  - Reduction in urine albumin-to-creatinine ratio (UACR) from baseline to month 4

Figure 2. Study design, key eligibility criteria, and efficacy outcomes



*Prospective exclusion of 145 randomized patients due to critical Good Clinical Practice violations; #NYHA class II–IV at run-in visit; ‡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; §kidney failure defined as either ESKD (initiation of chronic dialysis for ≥90 days or kidney transplant) or sustained decrease in eGFR <15 mL/min/1.73 m²; ¶over ≥4 weeks

CKD, chronic kidney disease; CV, cardiovascular; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; GFR, 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; R, randomization; RASi, renin–angiotensin system inhibitor; SBP, systolic blood pressure; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio

- This subanalysis presents results from a self-identified Chinese patient subgroup, exclusively enrolled from 67 sites across mainland China (N=697)

Statistical analysis

- Efficacy analyses were performed in the full analysis set[7–9]
- Time-to-event treatment outcomes were analyzed using a stratified Cox proportional hazards model estimated within each level of the subgroup variable; results are expressed as hazard ratios with corresponding 95% confidence intervals (HR [95% CI])[7–9]
- Patients included in the safety analysis had undergone randomization and had taken ≥1 dose of study drug or placebo[7–9]

Results

Baseline characteristics

- Of the 697 patients included in the Chinese subset of FIDELITY, 350 were randomized to receive finerenone compared with 347 assigned to placebo; demographic and baseline characteristics across treatment arms were generally similar (**Table 1**)

Table 1. Baseline characteristics and medications

	Chinese subgroup	
Baseline characteristics	**Finerenone (n=350)**	**Placebo (n=347)**
Age, years, mean ± SD	60.2 ± 10.2	58.9 ± 10.9
Sex, female, n (%)	85 (24.3)	73 (21.0)
Systolic blood pressure, mmHg, mean ± SD	135.9 ± 13.9	132.9 ± 15.8
Duration of diabetes, years, mean ± SD	13.3 ± 7.1	13.5 ± 7.8
Serum potassium, mmol/L, arithmetic mean ± SD	4.2 ± 0.4	4.2 ± 0.4
eGFR, mL/min/1.73 m², arithmetic mean ± SD	59.5 ± 21.0	60.4 ± 22.2
eGFR, mL/min/1.73 m², n (%)		
<25	1 (0.3)	3 (0.9)
25–<45	98 (28.0)	98 (28.2)
45–<60	101 (28.9)	92 (26.5)
≥60	150 (42.9)	154 (44.4)
UACR, mg/g, median	938.3	991.1
UACR, mg/g, mean ± SD	829.0 ± 3.0	856.9 ± 3.0
UACR, mg/g, n (%)		
<30	3 (0.9)	2 (0.6)
30–<300	53 (15.1)	52 (15.0)
≥300	294 (84.0)	293 (84.4)
Medical history at baseline, n (%)		
History of CV disease	131 (37.4)	123 (35.4)
Hypertension	329 (94.0)	325 (93.7)
Coronary artery disease	81 (23.1)	93 (26.8)
Peripheral arterial occlusive disease	68 (19.4)	60 (17.3)
Ischemic stroke	72 (20.6)	66 (19.0)
Heart failure	5 (1.4)	8 (2.3)
Medication use at baseline, n (%)		
Angiotensin-converting enzyme inhibitors	36 (10.3)	48 (13.8)
Angiotensin receptor blockers	312 (89.1)	299 (86.2)
Beta blockers	94 (26.9)	87 (25.1)
Diuretics	50 (14.3)	70 (20.2)
Statins	185 (52.9)	174 (50.1)
Potassium supplements	4 (1.1)	1 (0.3)
Potassium-lowering agents	0	2 (0.6)
Glucose-lowering therapies	342 (97.7)	338 (97.4)
Insulin and analogues	269 (76.9)	259 (74.6)
GLP-1RAs	7 (2.0)	9 (2.6)
SGLT-2 inhibitors	1 (0.3)	0

CV, cardiovascular; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide-1 receptor agonist; SD, standard deviation; SGLT-2, sodium-glucose co-transporter-2; UACR, urine albumin-to-creatinine ratio

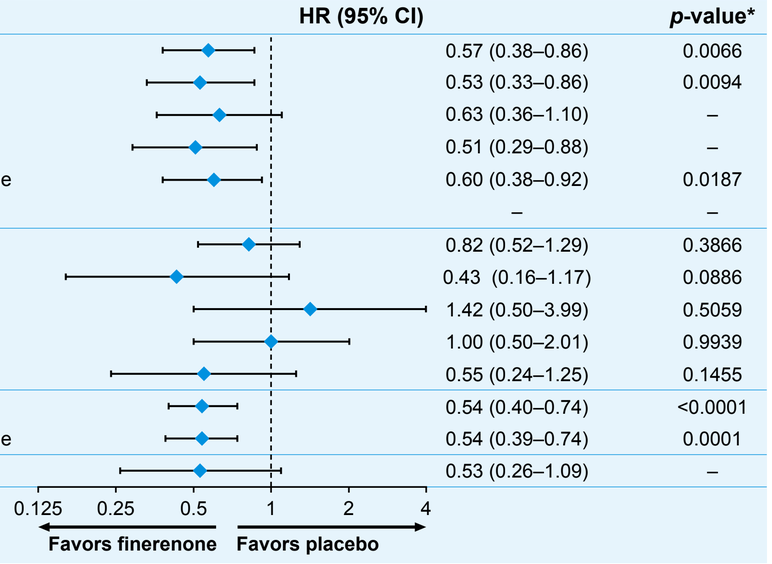
Key outcomes

- In the Chinese subgroup, finerenone significantly reduced the risk of the ≥57% kidney composite outcome by 43% versus placebo (HR=0.57; 95% CI 0.38–0.86; *p*=0.0066; **Figure 3**)
  - The relative risk reduction for kidney failure was 47% (HR=0.53; 95% CI 0.33–0.86; *p*=0.0094)
- The risk of the cardiovascular composite outcome versus placebo was numerically reduced (HR=0.82; 95% CI 0.52–1.29; *p*=0.3866; **Figure 3**)

Other prespecified outcomes

- In the Chinese subgroup, finerenone significantly reduced the risk of the ≥40% kidney composite outcome by 46% versus placebo (HR=0.54; 95% CI 0.40–0.74; *p*<0.0001; **Figure 3**)

Figure 3. Efficacy outcomes in the pooled Chinese populations

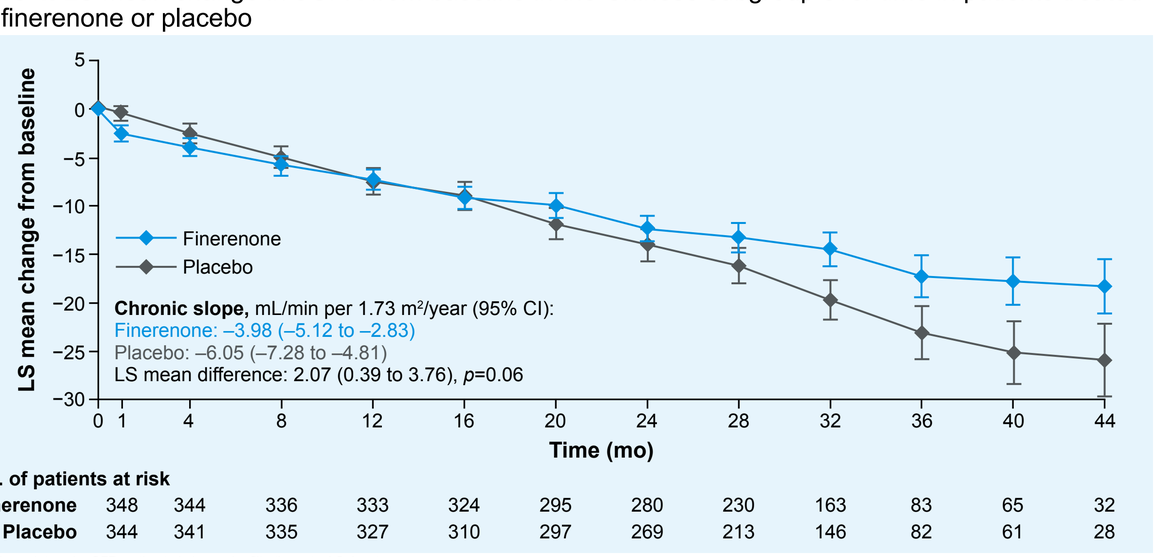


*Statistical tests where *p*-values are provided were exploratory in nature; therefore, no adjustment for multiplicity was performed; #the composite of time to first onset of kidney failure, sustained ≥57% decrease in eGFR from baseline over ≥4 weeks, or kidney-related death; ‡the composite of time to first onset of CV death, non-fatal myocardial infarction, non-fatal stroke, or hospitalization for heart failure; §the composite of time to first onset of kidney failure, sustained ≥40% decrease in eGFR from baseline over ≥4 weeks, or kidney-related death

CI, confidence interval; CV, cardiovascular; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HR, hazard ratio

- The chronic eGFR slope was −3.98 mL/min/1.73 m²/year for finerenone versus −6.05 mL/min/1.73 m²/year for placebo, with a difference in LS means of 2.07 mL/min/1.73 m² (95% CI 0.39−3.75; *p*=0.06; **Figure 4**)

Figure 4. LS mean change in eGFR from baseline in the Chinese subgroup over time in patients treated with finerenone or placebo



CI, confidence interval; eGFR, estimated glomerular filtration rate; LS, least-squares

- A reduction in UACR from baseline to month 4 was observed for finerenone versus placebo, with a placebo-corrected reduction of 33% [LS mean ratio=0.67; 95% CI 0.62–0.73]

Safety outcomes

- In the Chinese subgroup, the overall frequency of treatment-emergent adverse events was similar between the finerenone and placebo arms (**Table 2**)
- Investigator-reported hyperkalemia events and treatment-emergent serum potassium >5.5 mmol/L or >6.0 mmol/L (as measured by central laboratory) were higher with finerenone vs placebo; however, overall events that led to discontinuation of the study drug were low (**Table 2**)

Table 2. Treatment-emergent adverse and hyperkalemia events

	Chinese population			
TEAE	**Finerenone (n=350)**		**Placebo (n=346*)**	
	n (%)	**IR per 100 PY**	**n (%)**	**IR per 100 PY**
Any AE#	335 (95.7)	224.1	336 (97.1)	264.9
Any study drug-related AE	128 (36.6)	21.2	113 (32.7)	17.0
Any AE leading to discontinuation of study drug	19 (5.4)	2.3	11 (3.2)	1.3
Any SAE	173 (49.4)	30.2	184 (53.2)	33.6
Any study drug-related SAE	7 (2.0)	0.9	13 (3.8)	1.6
Any SAE leading to discontinuation of study drug	5 (1.4)	0.6	8 (2.3)	1.0
Any SAE with outcome of death	2 (0.6)	0.2	6 (1.7)	0.7
Treatment-emergent hyperkalemia				
Any hyperkalemia‡	101 (28.9)	–	77 (22.3)	–
Any study drug-related hyperkalemia	74 (21.1)	–	56 (16.2)	–
Any hyperkalemia leading to discontinuation of study drug	9 (2.6)	–	3 (0.9)	–
Any serious hyperkalemia	5 (1.4)	–	2 (0.6)	–
Any study drug-related serious hyperkalemia	4 (1.1)	–	2 (0.6)	–
Any serious hyperkalemia leading to discontinuation of study drug	0	–	2 (0.6)	–
Any serious hyperkalemia reported as life-threatening	0	–	2 (0.6)	–
Hospitalization due to serious hyperkalemia	4 (1.1)	–	0	–
Serum potassium >5.5 mmol/L§	54/349 (15.5)	–	33/342 (9.6)	–
Serum potassium >6.0 mmol/L§	15/349 (4.3)	–	8/343 (2.3)	–
Death due to hyperkalemia	0	–	0	–

*Of the 347 patients randomized in the placebo arm, one patient was never administered placebo; #this category contains any AEs reported during the study, including AEs that may occur between random grouping and first administration of the study drug in patients who did not receive their first dose on the day of random grouping; ‡investigator-reported AEs using the MedDRA preferred terms 'hyperkalemia' and 'blood potassium increased'; §the number of patient cases at risk with at least one treatment-emergent laboratory assessment meeting the criteria during the treatment. For evaluation during treatment, evaluation is only considered from the start of treatment to 3 days after temporary interruption or permanent discontinuation of the study drug

AE, adverse event; IR, incidence rate; MedDRA, Medical Dictionary for Regulatory Activities; PY, patient-years; SAE, serious adverse event; TEAE, treatment-emergent adverse event

Conclusions

- In the Chinese subpopulation of FIDELITY, patients with CKD and T2D who received finerenone demonstrated a significant reduction in the risk of CKD progression, as well as a trend towards lower risk of cardiovascular outcomes, compared with placebo; the safety profile was well balanced, with a manageable risk of hyperkalemia
- The findings in this analysis support the use of finerenone for the management of kidney and CV events across a spectrum of Chinese patients with CKD and T2D

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