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Cardiorenal outcomes with finerenone in Asian patients with chronic kidney disease and type 2 diabetes: Prespecified sub-analysis from FIDELITY

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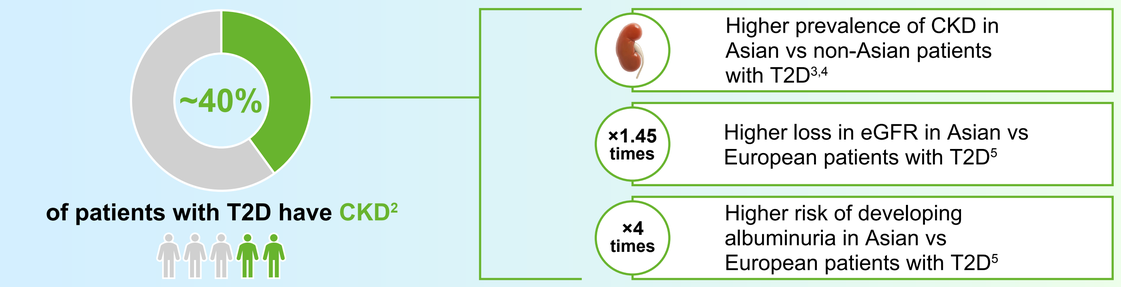
Background

- In FIDELITY, the prespecified pooled analysis of the complementary phase III trials FIDELIO-DKD and FIGARO-DKD, finerenone significantly improved cardiorenal outcomes in patients with chronic kidney disease (CKD) and type 2 diabetes (T2D)[1]
- **Figure 1** shows the background of CKD and T2D and the burden of disease in Asian patients[2–5]
- This prespecified sub-analysis of the FIDELITY dataset explores the cardiorenal effects of finerenone in Asian patients

Figure 1. Background and burden of disease in Asian patients with CKD in T2D

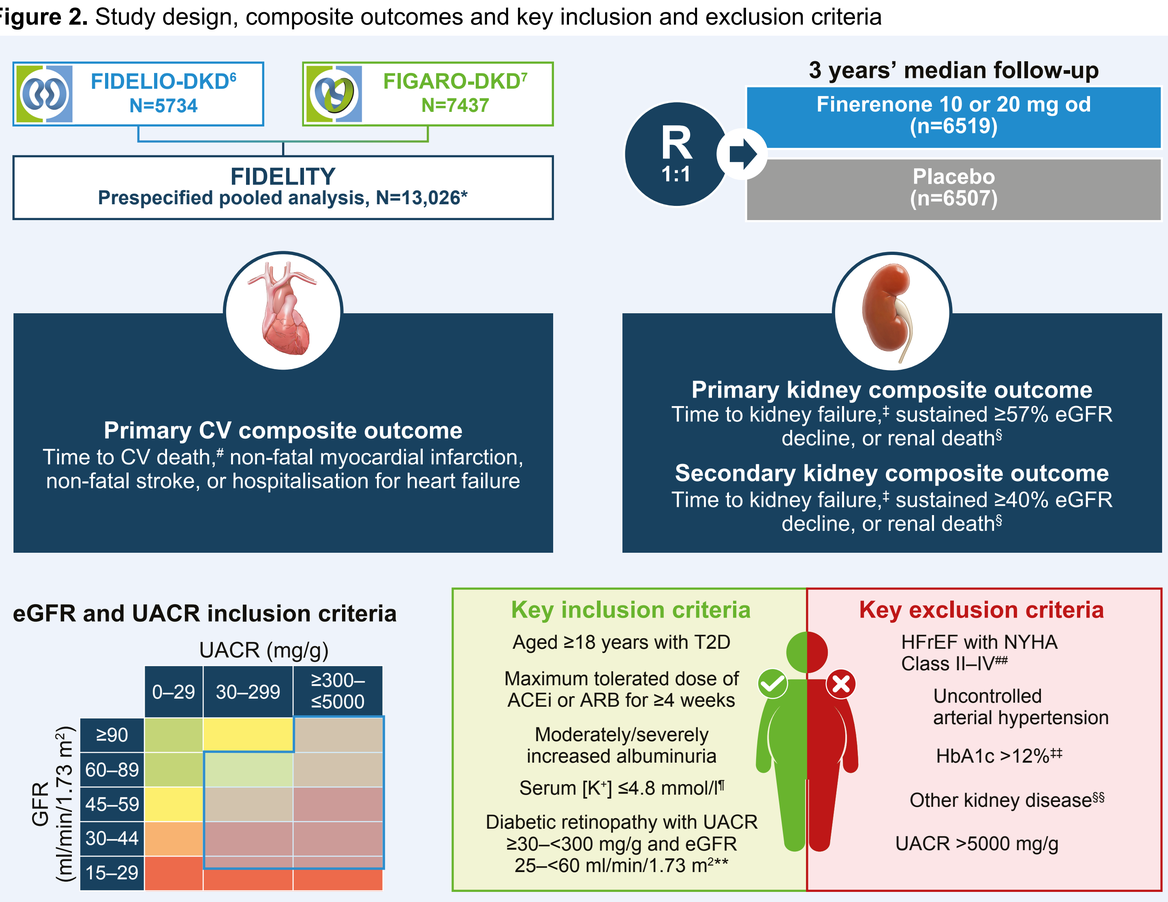


CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; T2D, type 2 diabetes

Study design and methods

- This analysis combines individual patient-level data from the two phase III clinical trials, FIDELIO-DKD (NCT02540993) and FIGARO-DKD (NCT02545049)[6,7]
- Adult patients with CKD and T2D were randomised (1:1) to finerenone or placebo (**Figure 2**)
- Patients were asked to self-identify their race, and for the current analysis patients were categorised as Asian or non-Asian (constituting patients who identified as Black or African American, White, American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, or multiple races)

Figure 2. Study design, composite outcomes and key inclusion and exclusion criteria



*Prospective exclusion of 145 patients; #events were classified as CV death if they were: (1) death due to acute myocardial infarction; (2) sudden cardiac death; (3) undetermined death; (4) death due to heart failure; (5) death due to stroke; (6) death due to CV procedures; or (7) death due to other CV causes; ‡confirmed by a second measurement, at the earliest 4 weeks after the initial measurement; §events were classified as renal death if: (1) the patient died; (2) kidney replacement therapy had not been initiated despite being clinically indicated; and (3) there was no other likely cause of death; ¶at run-in or screening visit; **FIDELIO-DKD only; ##run-in only; ‡‡at the run-in or screening visit; §§known significant non-diabetic kidney disease, including clinically relevant renal artery stenosis
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CV, cardiovascular; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; HbA1c, glycated haemoglobin; HFrEF, heart failure with reduced ejection fraction; [K+], potassium concentration; NYHA, New York Heart Association; od, once daily; R, randomisation; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio

Statistical analysis

- Efficacy analyses were performed in the full analysis set (all randomised patients without critical Good Clinical Practice violations)
- Safety analyses were performed in the safety analysis set (all randomised patients without critical Good Clinical Practice violations who took at least one dose of study drug)
- Time-to-event treatment outcome were analysed using a stratified Cox proportional hazards model; results are expressed as hazard ratios (HRs) with corresponding confidence intervals (CIs) and a *p*-value for interaction

Results

Baseline characteristics (Table 1)

- Of the 13,026 patients in FIDELITY (full analysis set), 2894 (22%) self-identified as Asian, and of these 1432 (49%) received finerenone

Table 1. Baseline characteristics and medications

Characteristic	Asian subgroup (n=2894)	Non-Asian subgroup (n=10,132)
Age, years, mean ± SD	62.2±10.3	65.5±9.2
Sex, female, n (%)	758 (26.2)	3180 (31.4)
Duration of diabetes, years, mean ± SD	15.0±8.5	15.5±8.7
HbA1c, %, mean ± SD	7.6±1.3	7.7±1.4
Systolic blood pressure, mmHg, mean ± SD	134.2±14.7	137.5±14.0
History of CV disease, yes, n (%)	1892 (65.4)	5199 (51.3)
eGFR, ml/min/1.73 m², mean ± SD	55.5±20.2	58.2±22.0
UACR, mg/g, median (IQR)	626.8 (257–1349)	491.7 (185–1096)
Serum potassium, mmol/l, mean ± SD	4.3±0.4	4.4±0.5
Baseline medications, n (%)		
Angiotensin-converting enzyme inhibitors	487 (16.8)	4592 (45.3)
Angiotensin receptor blockers	2404 (83.1)	5533 (54.6)
Beta blockers	879 (30.4)	5625 (55.5)
Diuretics	778 (26.9)	5932 (58.5)
Statins	1987 (68.7)	7412 (73.2)
Potassium supplements	413 (14.3)	2739 (27.0)
Potassium-lowering agents	62 (2.1)	120 (1.2)
Glucose-lowering therapies	2820 (97.4)	9900 (97.7)
Insulin and analogues	1546 (53.4)	6084 (60.0)
Biguanides	1468 (50.7)	6089 (60.1)
Sulfonamides	922 (31.9)	2467 (24.3)
Dipeptidyl peptidase-4 inhibitors	1164 (40.2)	2114 (20.9)
Glucagon-like peptide-1 receptor agonists	151 (5.2)	793 (7.8)
Sodium-glucose co-transporter-2 inhibitors	185 (6.4)	692 (6.8)

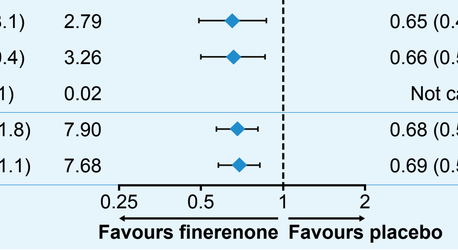
CV, cardiovascular; eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin; IQR, interquartile range; SD, standard deviation; UACR, urine albumin-to-creatinine ratio

Primary outcomes

- Reductions in the hazard of the cardiovascular (CV) composite outcome in the Asian subgroup (HR=0.90; 95% CI 0.70–1.15) were observed for finerenone versus placebo
  - Reductions in the Asian subgroup were consistent with the non-Asian subgroup ($p_{interaction}$=0.88) (**Figure 3**)
- Reductions in the hazard of the kidney composite outcome in the Asian subgroup (HR=0.66; 95% CI 0.52–0.84) were observed for finerenone versus placebo
  - Reductions in the Asian subgroup were consistent with the non-Asian subgroup ($p_{interaction}$=0.08) (**Figure 3**)

Figure 3. CV and kidney outcomes in Asian patients

Outcome	Finerenone (n=1432) n (%)	Finerenone (n=1432) n per 100 PY	Placebo (n=1462) n (%)	Placebo (n=1462) n per 100 PY	HR (95% CI)	$p_{interaction}$
Composite CV outcome	122 (8.5)	2.82	139 (9.5)	3.16	0.90 (0.70–1.15)	0.88
CV death	28 (2.0)	0.62	38 (2.6)	0.83	0.75 (0.46–1.23)	0.48
Non-fatal MI	25 (1.7)	0.56	26 (1.8)	0.57	1.19 (0.66–2.13)	0.71
Non-fatal stroke	45 (3.1)	1.02	44 (3.0)	0.98	1.03 (0.68–1.57)	0.87
Hospitalisation for HF	33 (2.3)	0.75	48 (3.3)	1.07	0.67 (0.43–1.05)	0.47
Composite kidney outcome	109 (7.6)	2.61	170 (11.6)	4.10	0.66 (0.52–0.84)	0.08
Kidney failure	77 (5.4)	1.83	118 (8.1)	2.79	0.65 (0.49–0.87)	0.02
≥57% eGFR decline	86 (6.0)	2.06	137 (9.4)	3.26	0.66 (0.50–0.86)	0.40
Renal death	0	0	1 (0.1)	0.02	Not calculable	
Secondary composite kidney outcome	222 (15.5)	5.50	318 (21.8)	7.90	0.68 (0.57–0.81)	0.01
≥40% eGFR decline	219 (15.3)	5.42	309 (21.1)	7.68	0.69 (0.58–0.82)	0.01

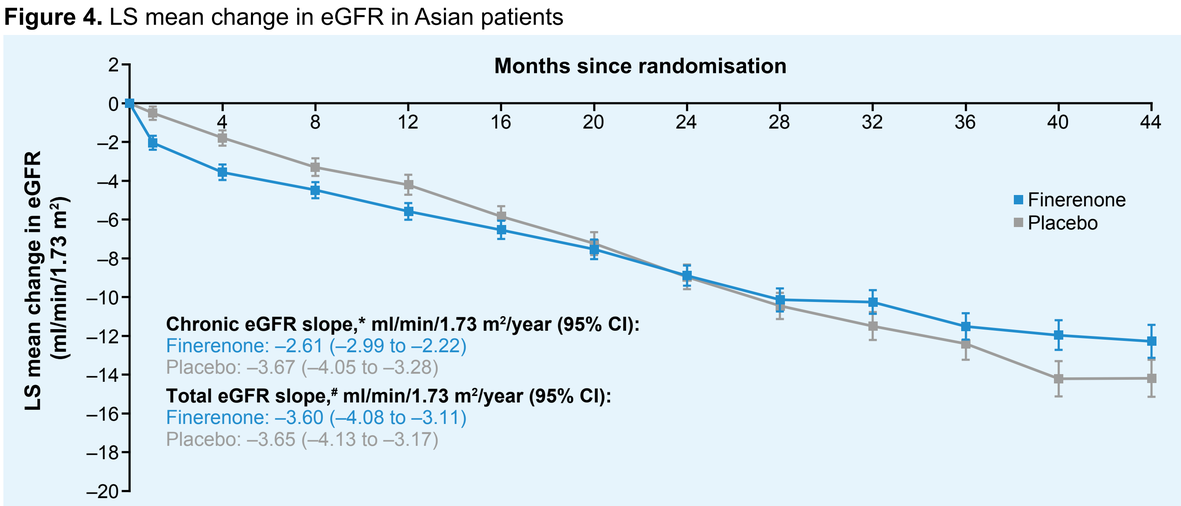


CI, confidence interval; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, hazard ratio; MI, myocardial infarction; PY, patient-years

Secondary outcomes

- Reductions in hazard were observed for finerenone versus placebo for the secondary composite kidney outcome in the Asian subgroup (HR=0.68; 95% CI 0.57–0.81); however, this effect was not consistent in the non-Asian subgroup ($p_{interaction}$=0.01) (**Figure 3**), but it was directionally consistent across subgroups ($p_{Gail\text{-}Simon}$=0.50)
- Time to all-cause mortality (HR=0.70; 95% CI 0.50–0.99) and time to all-cause hospitalisation (HR=0.93; 95% CI 0.84–1.04) were also reduced with finerenone compared with placebo in the Asian subgroup
- Change in chronic estimated glomerular filtration rate (eGFR) slope (least-squares mean change in eGFR from month 4 to end of treatment) was −2.61 ml/min/1.73 m²/year with finerenone versus −3.67 ml/min/1.73 m²/year with placebo in the Asian subgroup; the change in total eGFR slope (least-squares mean change in eGFR from baseline to end of treatment) was −3.60 ml/min/1.73 m²/year with finerenone versus −3.65 ml/min/1.73 m²/year with placebo in the Asian subgroup (**Figure 4**)

Figure 4. LS mean change in eGFR in Asian patients



*LS mean change in eGFR from month 4 to end of treatment; #LS mean change in eGFR from baseline to end of treatment
CI, confidence interval; eGFR, estimated glomerular filtration rate; LS, least-squares

Safety outcomes

- Overall, the incidences of any treatment-emergent adverse events (AEs) and serious AEs were higher in Asian patients than in non-Asian patients, irrespective of treatment group (**Table 2**)

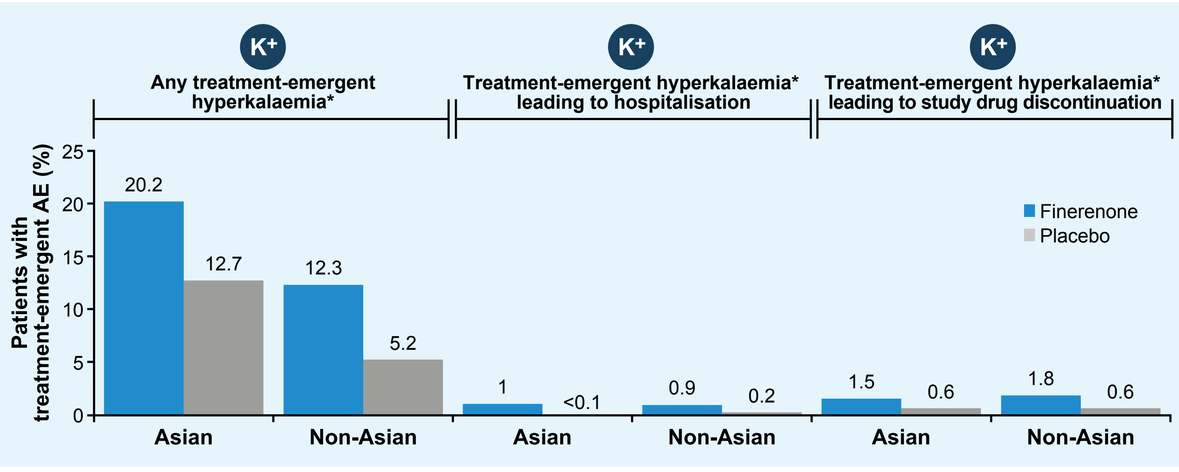
Table 2. Overall treatment-emergent AEs

Characteristic, n (%)	Asian subgroup		Non-Asian subgroup	
	Finerenone (n=1433)	Placebo (n=1457)	Finerenone (n=5077)	Placebo (n=5032)
Any AE	1335 (93.2)	1370 (94.0)	4267 (84.0)	4237 (84.2)
Related to study drug	327 (22.8)	246 (16.9)	879 (17.3)	616 (12.2)
Leading to discontinuation of study drug	84 (5.9)	83 (5.7)	330 (6.5)	268 (5.3)
Any serious AE	509 (35.5)	577 (39.6)	1551 (30.5)	1609 (32.0)
AE with outcome of death	20 (1.4)	25 (1.7)	90 (1.8)	126 (2.5)

AE, adverse event

- Overall, the incidence of investigator-reported treatment-emergent hyperkalaemia AEs was higher in patients treated with finerenone compared with placebo (**Figure 5**)

Figure 5. Treatment-emergent hyperkalaemia in Asian and non-Asian patients



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

Conclusions

- In Asian patients with CKD and T2D in the FIDELITY population, finerenone had beneficial effects on cardiorenal outcomes and a favourable safety profile; effects were consistent with non-Asian patients from the FIDELITY population
- These data support the use of finerenone in patients of Asian race to reduce the hazard of CV events and CKD progression

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