Finerenone and kidney outcomes in patients with CKD and T2D: Results from FIDELITY

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RATIONALE AND OBJECTIVE

- FIDELITY is a **prespecified pooled analysis** evaluating patient-level efficacy and safety data from the phase III FIDELIO-DKD (NCT02540993) and FIGARO-DKD (NCT02545049) trials
- Here, we report kidney outcomes with finerenone across a spectrum of patients with CKD and T2D

KEY FINDINGS

- Results of FIDELITY suggest that finerenone significantly **reduces progression of CKD by 23%** as well as the risk of **end-stage kidney disease by 20%**
- Moreover, finerenone slows CKD progression **across the spectrum of CKD severity**

1 CKD, chronic kidney disease; T2D, type 2 diabetes

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DISCLOSURES
Professor Bakris reports the following:

The University of Chicago Medicine
Consultant: Alnylam, AstraZeneca, Bayer, DiaMedica Therapeutics, Horizon, InRegen, Ionis, KBP Biosciences, Merck, Novo Nordisk, and Quantum Genomics
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FIDELITY

FIDELITY is a prespecified pooled analysis of patient-level data from FIDELIO-DKD[1] and FIGARO-DKD[2]

48 countries

13,171 patients randomized

3 years' median follow-up

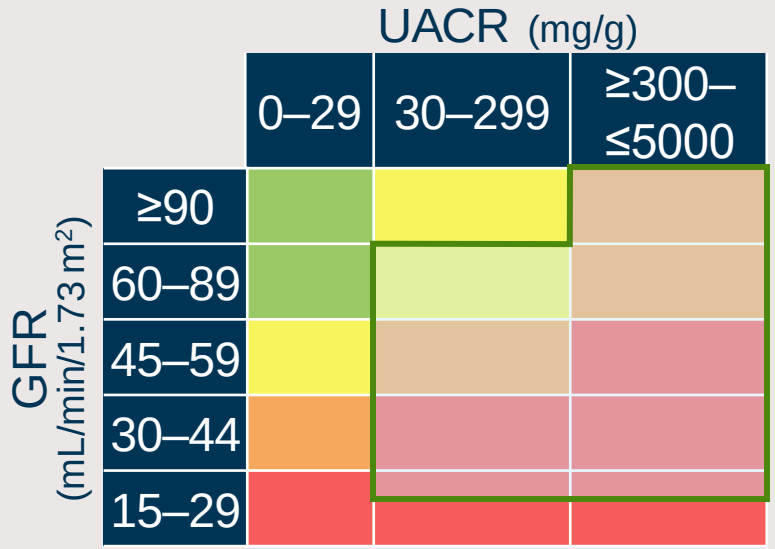
R

Finerenone 10 or 20 mg od*

Placebo

Key eligibility criteria

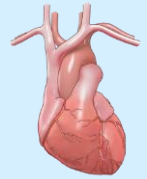
- ✓ T2D
- ✓ CKD
- ✓ Optimized RASi
- ✓ Serum [K^+] ≤4.8 mmol/L
- ✗ HFrEF (NYHA II–IV)



Key outcomes

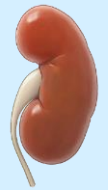
CV composite

Time to CV death, nonfatal MI, nonfatal stroke, or HHF



≥57% eGFR kidney composite

Time to kidney failure,[#] sustained ≥57% decrease in eGFR from baseline, or renal death



*10 mg if screening eGFR 25–<60 mL/min/1.73 m^2; 20 mg if ≥60 mL/min/1.73 m^2, up-titration encouraged from month 1 if serum [K^+] ≤4.8 mEq/L and eGFR stable; [#]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 m^2. CV, cardiovascular; ESKD, end-stage kidney disease; GFR, glomerular filtration rate; eGFR, estimated glomerular filtration rate; 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; RASi, renin–angiotensin system inhibitor; UACR, urine albumin-to-creatinine ratio

1. Bakris GB, *et al. N Engl J Med* 2020;383:2219–2229; 2. Pitt B, *et al. N Engl J Med* 2021; doi: 10.1056/NEJMoa2110956

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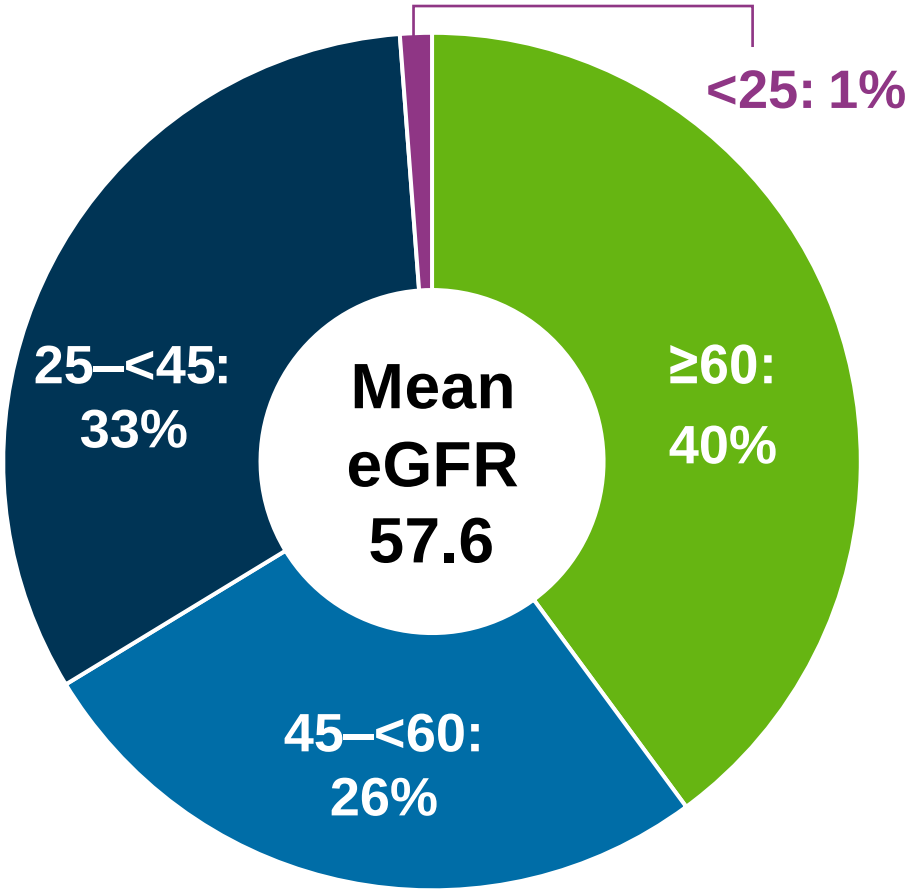
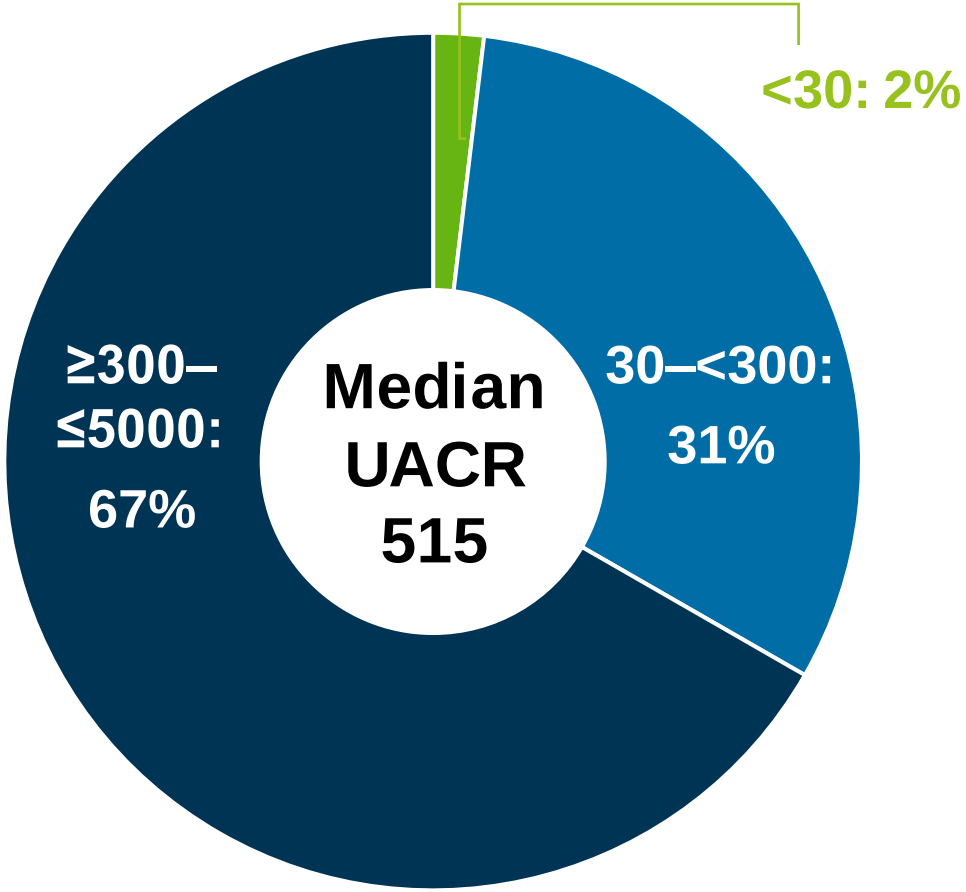
40% of patients had albuminuric CKD with preserved kidney function (eGFR ≥60 mL/min/1.73 m²)

Baseline eGFR (mL/min/1.73 m²)



Baseline UACR (mg/g)*



*Data were missing for 3 patients

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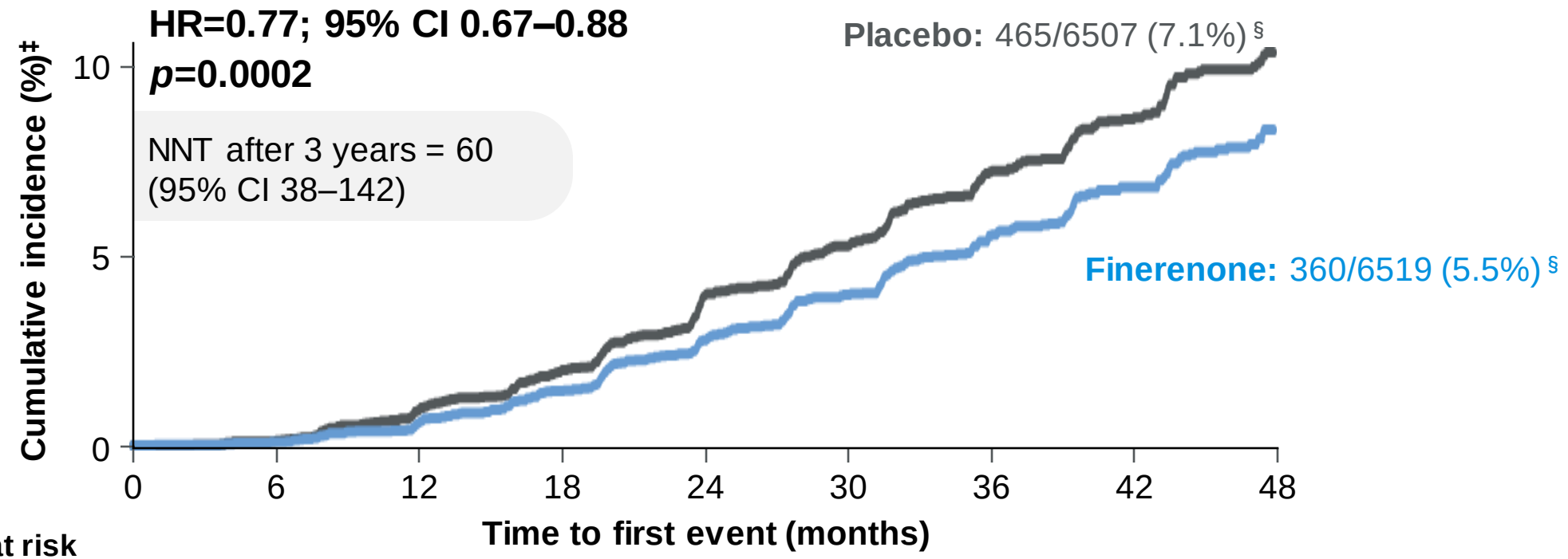
Finerenone significantly reduced the risk of the ≥57% eGFR kidney composite outcome by 23%

Time to kidney failure,* sustained ≥57% decrease in eGFR from baseline, or renal death#



No. at risk									
Finerenone	6519	6291	6107	5848	5027	3973	2815	2024	959
Placebo	6507	6292	6071	5815	4949	3932	2798	1988	962

*ESKD or an eGFR <15 mL/min/1.73 m^2; #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; ‡cumulative incidence calculated by Aalen–Johansen estimator using deaths due to other causes as competing risk; § number of patients with an event over a median of 3.0 years of follow-up. CI, confidence interval; HR, hazard ratio; NNT, number needed to treat

Filippatos G. ESC 2021; abstract 7161

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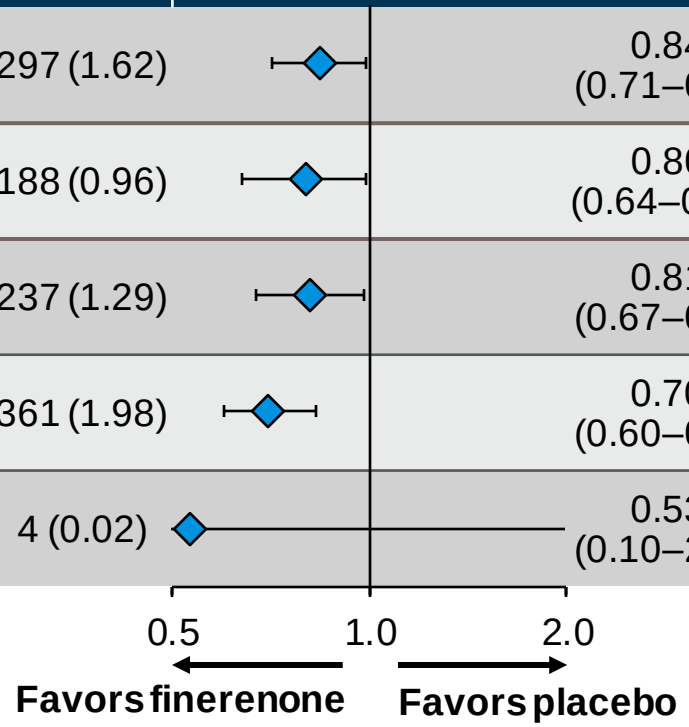
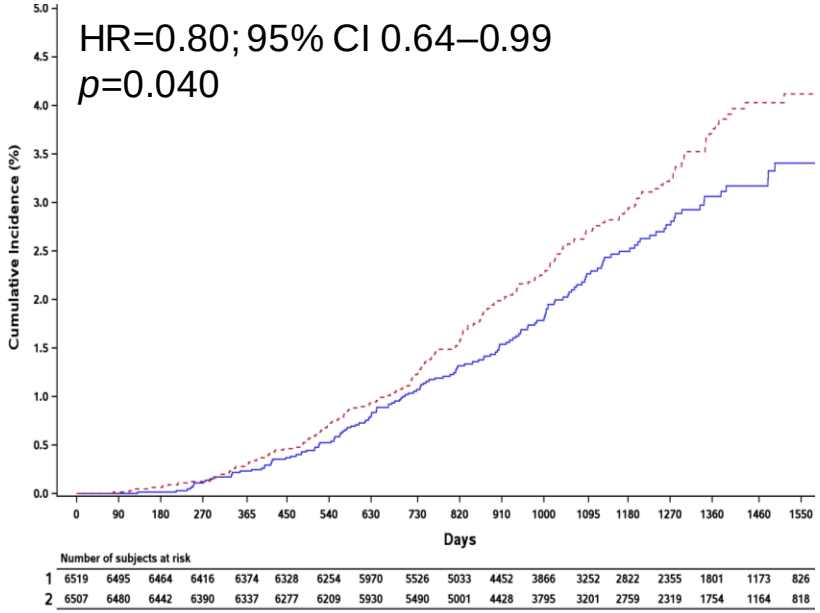
Finerenone significantly reduced the risk of all nonfatal components of the ≥57% eGFR kidney composite outcome

Component of ≥57% eGFR kidney composite	Finerenone (n=6519)	Placebo (n=6507)	HR (95% CI)	*p*-value
	n (n/100 PY)			
Kidney failure	254 (1.38)	297 (1.62)	0.84 (0.71–0.99)	0.039
ESKD*	151 (0.76)	188 (0.96)	0.80 (0.64–0.99)	0.040[#]
eGFR <15 mL/min/1.73 m^2[‡]	195 (1.06)	237 (1.29)	0.81 (0.67–0.98)	0.026[#]
≥57% decrease in eGFR[‡¶]	257 (1.40)	361 (1.98)	0.70 (0.60–0.83)	<0.0001
Renal death	2 (0.01)	4 (0.02)	0.53 (0.10–2.91)	–



Finerenone reduced the risk of ESKD* by 20% vs placebo



*Initiation of chronic dialysis for ≥90 days or kidney transplant; [#]analysis for *p*-values not prespecified; [‡]confirmed by two eGFR measurements ≥4 weeks apart; [¶]from baseline
PY, patient-years

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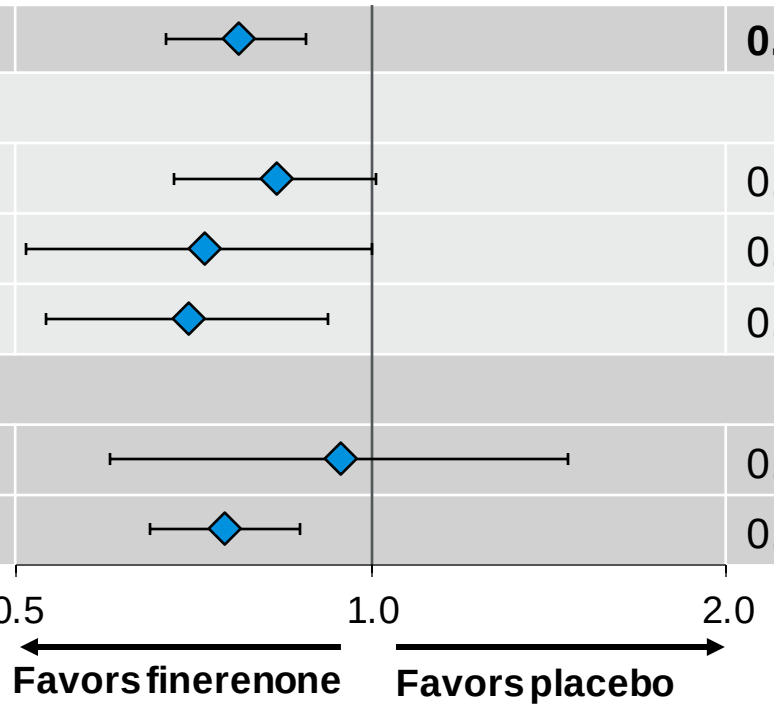
Finerenone reduced the risk of the ≥57% eGFR kidney composite outcome, irrespective of baseline eGFR or UACR

	Finerenone	Placebo	Hazard ratio (95% CI)	*p*-value for interaction
	n/N (n per 100 PY)			
Overall	**360/6519 (1.96)**	**465/6507 (2.55)**	**0.77 (0.67–0.88)**	
Baseline eGFR (mL/min/1.73 m²)*				
25–<45	188/2117 (3.42)	225/2115 (4.14)	0.83 (0.68–1.01)	0.6244
45–<60	62/1717 (1.31)	87/1717 (1.83)	0.72 (0.52–1.00)	
≥60	90/2603 (1.14)	130/2592 (1.66)	0.70 (0.53–0.92)	
Baseline UACR (mg/g)#				
30–<300	38/2076 (0.57)	40/2023 (0.62)	0.94 (0.60–1.47)	0.6673
≥300	321/4321 (2.85)	424/4371 (3.71)	0.75 (0.65–0.87)	



*P-values for interaction also includes data from eGFR <25 ml/min/1.73 m2 (HR 0.83 [0.42–1.61]); #p-values for interaction also includes data from UACR <30 mg/g categories (HR 0.78 [0.05–12.5])

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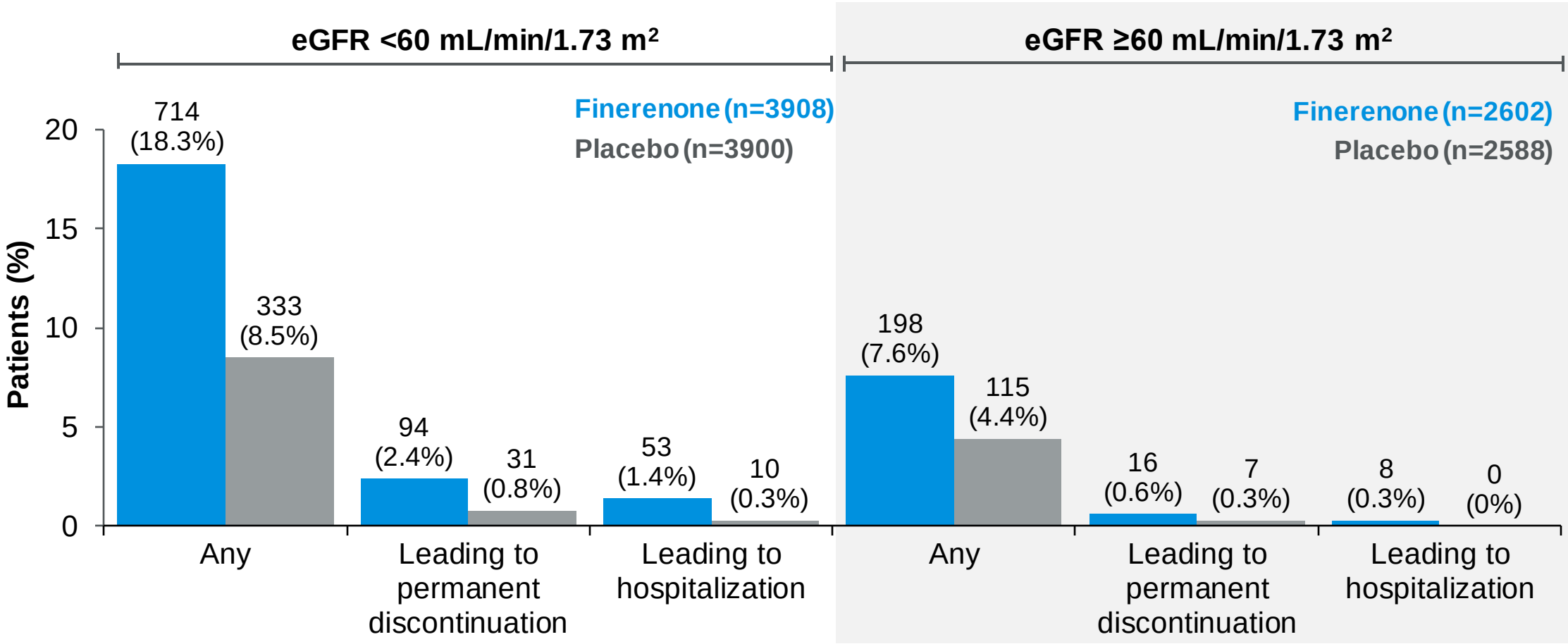
Overall safety outcomes and kidney AEs were similar between treatment arms across eGFR categories

Investigator-reported AEs, n (%)	eGFR <60 mL/min/1.73 m^2		eGFR ≥60 mL/min/1.73 m^2	
	Finerenone (n=3908)	Placebo (n=3900)	Finerenone (n=2602)	Placebo (n=2588)
Any AE	**3534 (90.4)**	**3507 (89.9)**	**2216 (85.2)**	**2210 (85.4)**
Leading to discontinuation	341 (8.7)	274 (7.0)	119 (4.6)	124 (4.8)
Any serious AE	**1609 (41.2)**	**1656 (42.5)**	**857 (32.9)**	**897 (34.7)**
Worsening renal function				
Leading to hospitalization	96 (2.5)	93 (2.4)	14 (0.5)	19 (0.7)
Leading to discontinuation	41 (1.0)	38 (1.0)	11 (0.4)	4 (0.2)
Acute kidney injury	**179 (4.6)**	**190 (4.9)**	**41 (1.6)**	**44 (1.7)**

AE, adverse event

Low incidence of hyperkalemia leading to discontinuation or hospitalization with finerenone across eGFR categories



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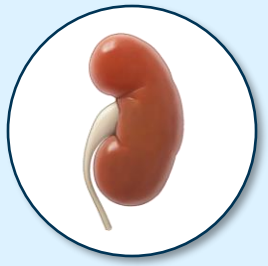
Summary



In patients with CKD and T2D, finerenone consistently reduced the risk of the kidney composite outcome by 23%

All nonfatal components of the kidney composite outcome were also reduced with finerenone versus placebo, and the benefits of finerenone were not modified by baseline eGFR and albuminuria

Overall safety was similar between the finerenone and placebo groups

Renal AEs were balanced between treatment groups, and the incidence of hyperkalemia AEs leading to discontinuation or hospitalization in the finerenone group was low

Results of FIDELITY suggest that finerenone slows CKD progression across the spectrum of CKD severity in patients with T2D