Finerenone and kidney outcomes in patients with chronic kidney disease and type 2 diabetes: Results from FIGARO-DKD

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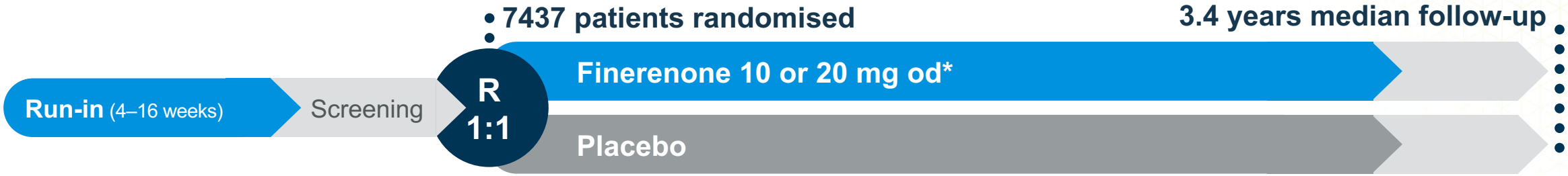
FIGARO-DKD

FIGARO-DKD was a randomised phase III trial of finerenone vs placebo in patients with early-stage CKD in T2D[1]



Key inclusion criteria

- Aged ≥18 years with T2D
- On max. tolerated dose of ACEi or ARB for ≥4 weeks
- UACR 30–<300 mg/g and eGFR 25–90 ml/min/1.73 m^2 or UACR 300–5000 mg/g and eGFR ≥60 ml/min/1.73 m^2
- Serum [K$^+$] ≤4.8 mmol/L at run-in and screening

Key exclusion criteria

- HFrEF with NYHA Class II–IV
- Uncontrolled arterial hypertension#
- HbA1c >12%
- Other kidney disease‡

Key endpoints

CV composite

Time to CV death, non-fatal MI, non-fatal stroke or HHF

Kidney composites

Time to kidney failure, sustained ≥40%/≥57% decrease in eGFR ≥4 weeks from baseline, or renal death

Albuminuria categories[2] (mg albumin/g creatinine)

GFR categories (ml/min/1.73 m^2)		A1 Normal to mildly increased (0–29)	A2 Moderately increased (30–299)	A3 Severely increased (≥300–≤5000)
G1	≥90			
G2	60–89			
G3a	45–59			
G3b	30–44			
G4	15–29			
G5	<15			

*10 mg if screening eGFR <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 potassium ≤4.8 mmol/L and eGFR stable; a decrease in the dose from 20 to 10 mg od was allowed any time after the initiation of finerenone or placebo; #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

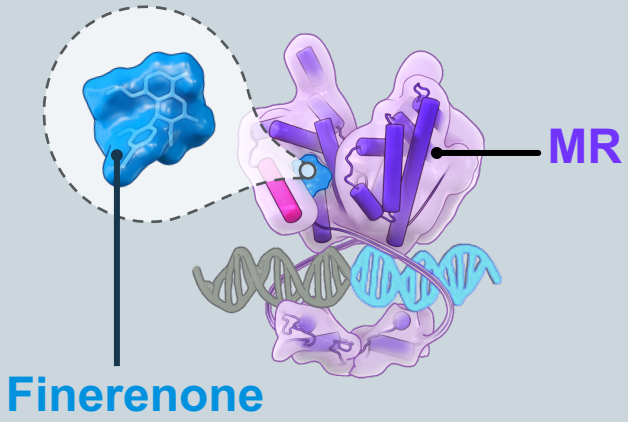
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; HbA1c, glycated haemoglobin; HFrEF, heart failure with reduced ejection fraction; [K$^+$], potassium concentration; MI, myocardial infarction; NYHA, New York Heart Association; od, once daily; R, randomisation; SBP, systolic blood pressure

1. Pitt B, *et al. N Engl J Med* 2021; doi: 10.1056/NEJMoa2110956; 2. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int* 2013;3:1–150

FIGARO-DKD

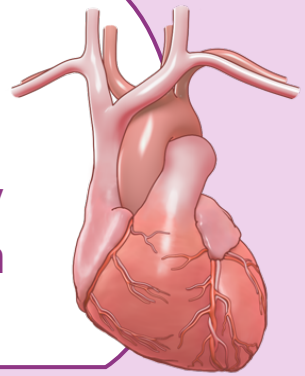
The FIGARO-DKD trial demonstrated CV benefits with finerenone in patients with CKD and T2D[1]

Finerenone is a **novel, nonsteroidal, selective MRA** that **inhibits MR overactivation in preclinical models**[2]



In FIGARO-DKD, finerenone:[1]

Significantly reduced the risk of **CV morbidity** and **mortality** by **13% (NNT=47*), predominantly driven** by a **29% reduction** in **HHF risk**



This analysis examines additional renal outcomes in FIGARO-DKD, and cardiorenal outcomes by baseline UACR, because the trial enrolled patients with both moderately and severely increased albuminuria

*NNT to prevent one event based on absolute risk reductions at 3.5 years

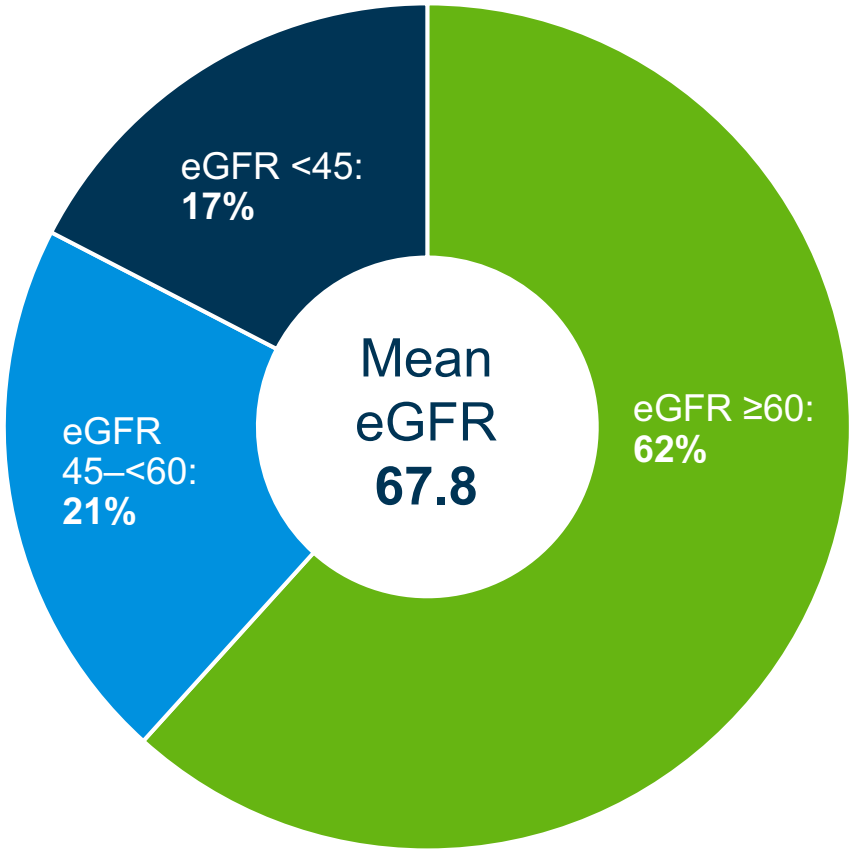
CKD, chronic kidney disease; CV, cardiovascular disease; HHF, hospitalisation for heart failure; MR, mineralocorticoid receptor; MRA, mineralocorticoid receptor antagonist; NNT, number needed to treat; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio

1. Pitt B, *et al. N Engl J Med* 2021; doi: 10.1056/NEJMoa2110956; 2. Agarwal R, *et al. Eur Heart J* 2021;42:152–161

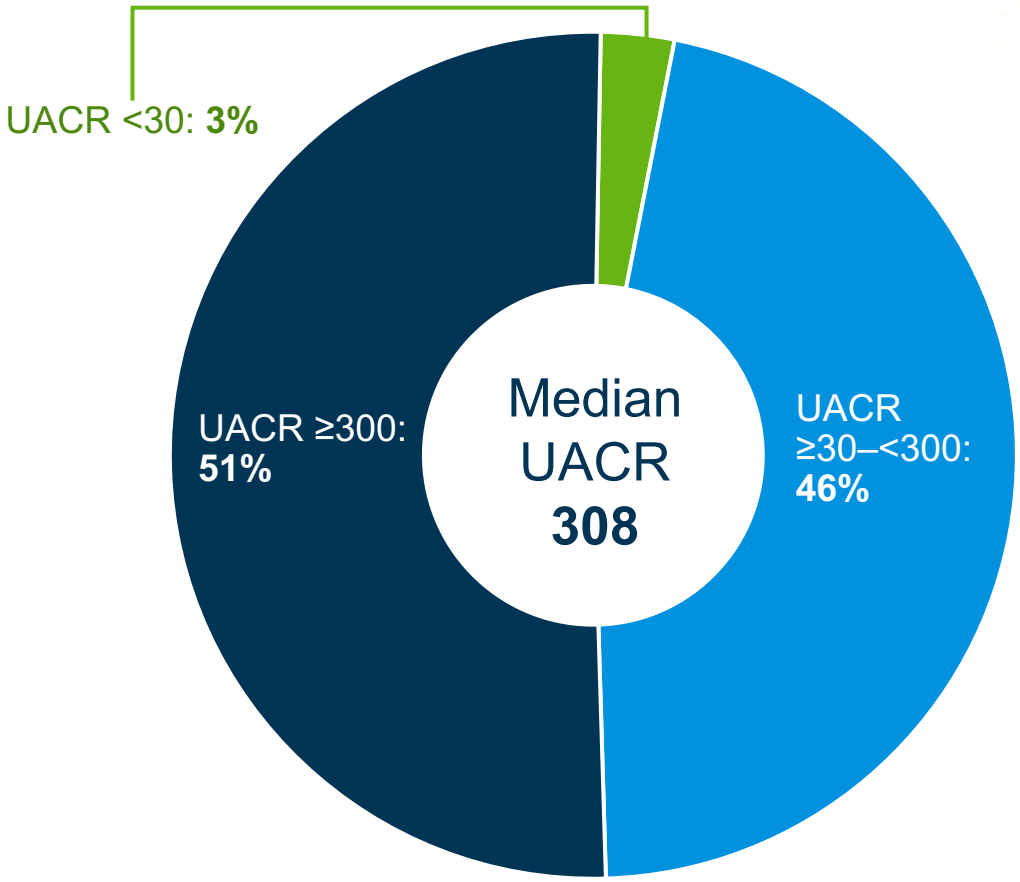
FIGARO-DKD

At baseline, 62% of patients had CKD with an eGFR ≥60 ml/min/1.73 m²

eGFR (ml/min/1.73 m²)



UACR (mg/g)

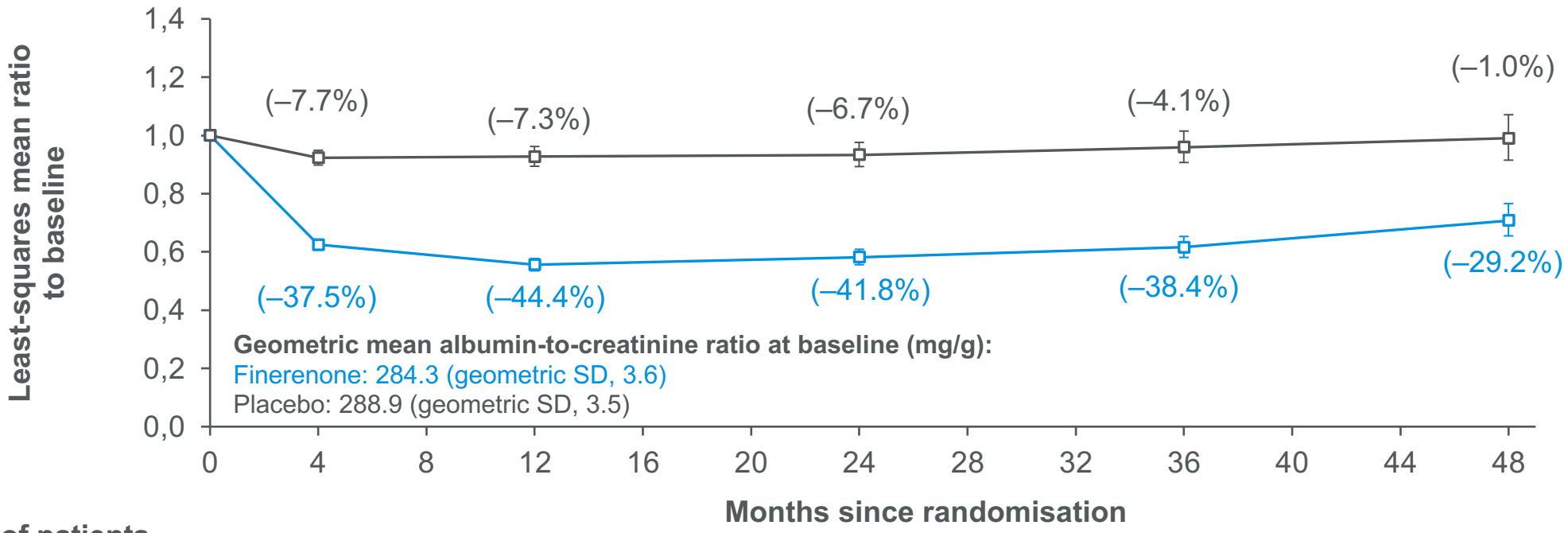


Pitt B, *et al. N Engl J Med* 2021; doi: 10.1056/NEJMoa2110956

FIGARO-DKD

In the overall population, finerenone reduced UACR by month 4 and increased the incidence of albuminuria regression vs placebo

UACR change from baseline[1]



Placebo-corrected 32% UACR reduction with finerenone at month 4 (p<0.0001)[2]

No. of patients						
Finerenone	3686	3548	3406	3026	1889	831
Placebo	3664	3513	3375	3004	1872	811

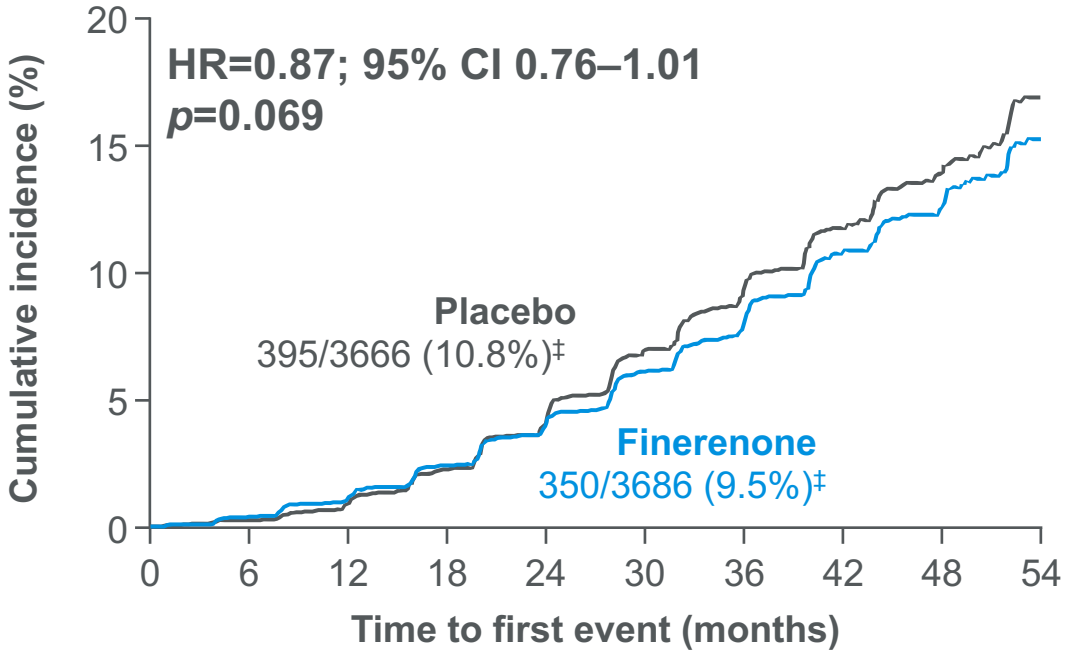
SD, standard deviation

1. Bakris G, *et al. ASN* 2021; Abstract SA-OR21; 2. Pitt B, *et al. N Engl J Med* 2021; doi: 10.1056/NEJMoa2110956

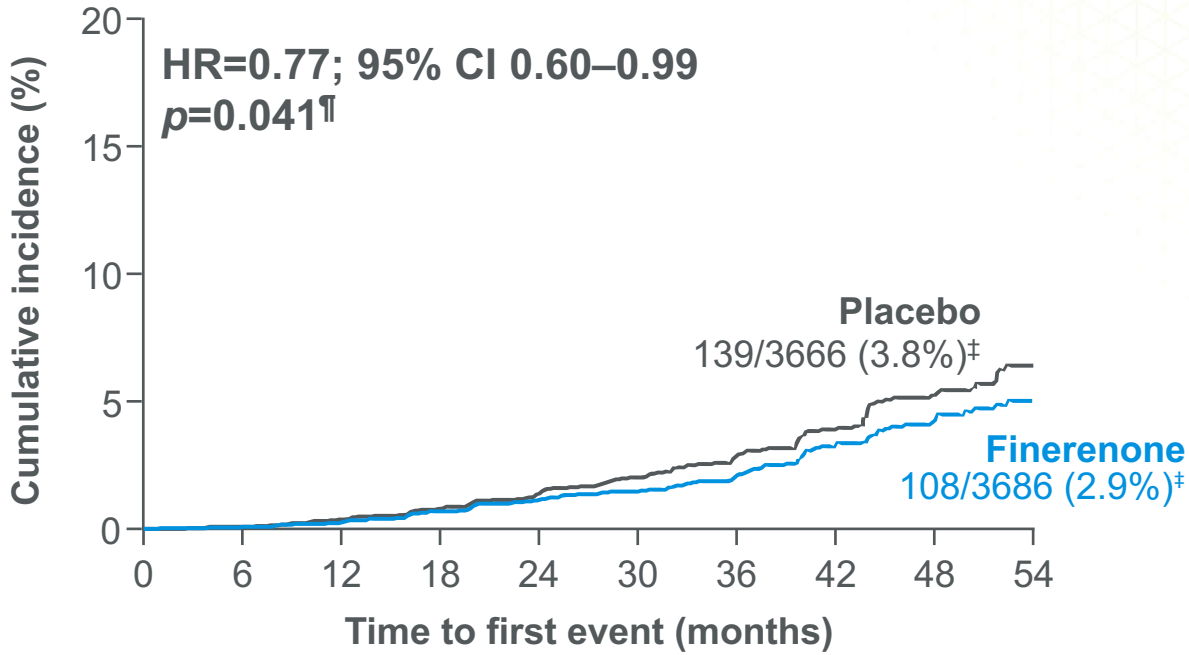
FIGARO-DKD

Finerenone on kidney outcomes

Kidney failure,* sustained ≥40% decrease in eGFR from baseline, or renal death# [1,2]



Kidney failure, sustained ≥57% decrease in eGFR from baseline,§ or renal death# [1,2]



ESKD occurred in 0.9% vs 1.3% of finerenone vs placebo recipients
(HR=0.64; 95% CI 0.41–0.995; *p*=0.046¶)

*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; ‡number of patients with an event over a median of 3.4 years of follow-up; §≥57% eGFR decline is equivalent to doubling of serum creatinine; ¶*p*-value is exploratory
CI, confidence interval; ESKD, end-stage kidney disease; HR, hazard ratio

1. Pitt B, *et al. N Engl J Med* 2021; doi: 10.1056/NEJMoa2110956; 2. Pitt B, presented at the ESC Congress 2021 Hot Line session 28 August 2021. https://esc365.escardio.org/presentation/238814

FIGARO-DKD

The effect of finerenone on the composite kidney outcomes was reflected by a reduction in the risk of ESKD by 36% vs placebo

	Finerenone (n=3686)	Placebo (n=3666)	HR (95% CI)
≥40% secondary kidney outcome	350 (9.5)	395 (10.8)	0.87 (0.76–1.01)
Kidney failure*	46 (1.2)	62 (1.7)	0.72 (0.49–1.05)
ESKD	32 (0.9)	49 (1.3)	0.64 (0.41–0.995)
Sustained# decrease in eGFR to <15 ml/min/1.73 m^2	28 (0.8)	38 (1.0)	0.71 (0.43–1.16)
Sustained# ≥40% decrease in eGFR from baseline	338 (9.2)	385 (10.5)	0.87 (0.75–1.00)
Renal death	0	2 (<0.1)	0.87 (0.76–1.01)
≥57% secondary kidney composite‡	108 (2.9)	139 (3.8)	0.77 (0.60–0.99)
≥57% ↓ in eGFR	90 (2.4)	116 (3.2)	0.76 (0.58–1.00)

*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;
#confirmed by two eGFR measurements ≥4 weeks apart; ‡composite of kidney failure, sustained ≥57% decrease in eGFR from baseline, or renal death

Pitt B, *et al. N Engl J Med* 2021; doi: 10.1056/NEJMoa2110956

FIGARO-DKD

More AEs were reported in patients with moderately increased albuminuria; however, this group had lower eGFR by trial design

Treatment-emergent AE, n (%)	Moderately increased albuminuria (30–<300 mg/g) Mean baseline eGFR 56 (IQR 42–67) ml/min/1.73 m²		Severely increased albuminuria (≥300 mg/g) Mean baseline eGFR 80 (IQR 68–92) ml/min/1.73 m²	
	Finerenone (n=1724)	Placebo (n=1682)	Finerenone (n=1850)	Placebo (n=1877)
Any AE	**1507 (87.4)**	**1483 (88.2)**	**1532 (82.8)**	**1562 (83.2)**
AE related to study drug	327 (19.0)	241 (14.3)	210 (11.4)	161 (8.6)
AE leading to treatment discontinuation	133 (7.7)	104 (6.2)	69 (3.7)	72 (3.8)
Any serious AE	**607 (35.2)**	**616 (36.6)**	**516 (27.9)**	**571 (30.4)**
Any hyperkalaemia AE	**234 (13.6)**	**108 (6.4)**	**148 (8.0)**	**83 (4.4)**
Hyperkalaemia				
Related to study drug	142 (8.2)	64 (3.8)	89 (4.8)	48 (2.6)
Leading to hospitalisation	14 (0.8)	2 (0.1)	6 (0.3)	0
Leading to permanent discontinuation	32 (1.9)	9 (0.5)	12 (0.6)	4 (0.2)

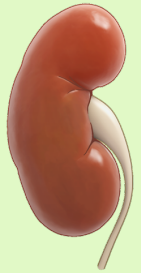
AE, adverse event; IQR, interquartile range

Bakris G, *et al. ASN* 2021; Abstract SA-OR21

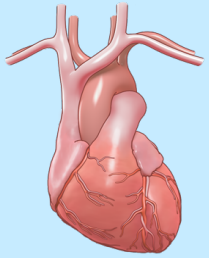
Summary and conclusions

In patients with CKD stage 1–4 with moderate-to-severely elevated albuminuria (UACR ≥30 mg/g), well-controlled SBP and HbA1c, and treated with optimised RAS blockade, finerenone:

- **Showed a trend towards a risk reduction for the ≥40% and ≥57% eGFR kidney composite outcomes**
  - **Kidney benefits were reflected in a 36% relative risk reduction in ESKD**



- **Significantly reduced the risk of CV morbidity and mortality by 13%**
  - **Results were consistent in patients with moderately increased and severely increased albuminuria**



RAS, renin–angiotensin system

Bakris G, *et al. ASN* 2021; Abstract SA-OR21

FIGARO-DKD

Thank you

48 countries, 19,381 patients enrolled, 7437 patients randomised

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FIGARO-DKD

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