Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes With and Without Heart Failure: Analysis of the FIDELIO-DKD Study

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Heart Failure & World Congress on Acute Heart Failure 2021

Disclosures

- **Lecture Fees and/or Committee Member:** Of trials/registries sponsored by Amgen, Bayer, Boehringer Ingelheim, Novartis, Medtronic, Servier, Vifor
- **Research Grants:** European Union
- **Senior Consulting Editor:** *JACC: Heart Failure*
- **Past President:** Heart Failure Association of the ESC

Patients with CKD, T2D and HF have a high cardiorenal risk

CKD and **T2D** are **highly prevalent** among **patients with HF**[1,2]

- Patients with **all three conditions** have **unfavourable prognosis**[3–5]

Guidelines recommend patients with HFrEF are treated **with a steroidal MRA**[6,7]

- A **clear benefit** of MRAs in patients with **HFpEF** has **not been demonstrated** in **randomised trials**[8–10]

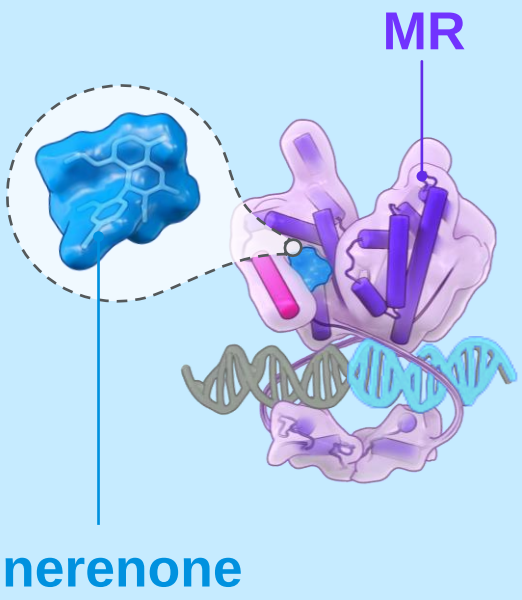
Finerenone is a novel, **selective, nonsteroidal MRA** that blocks MR overactivation[11]

- **MR overactivation** contributes to **inflammation and fibrosis**, which are **key drivers of CKD in T2D** progression[11]

CKD, chronic kidney disease; CVD, cardiovascular disease; HF, heart failure; HFpEF, heart failure with preserved ejection fraction HFrEF, heart failure with reduced ejection fraction; LV, left ventricular; MR, mineralocorticoid receptor; MRA, mineralocorticoid receptor antagonist; T2D, type 2 diabetes

1. Anker SD, *et al*. *Eur Heart J* 2020;22:2383–2392; 2. Solomon SD, *et al*. *Circ Heart Fail* 2018;11:e004962; 3. Seferovic PM, *et al*. *Eur J Heart Fail* 2018;20:853–872; 4. Filippatos G, *et al*. *Eur Heart J* 2014;35:416–418; 5. Hsu S, *et al*. *Curr Opin Nephrol Hypertens* 2019;28:262–266; 6. Ponikowski P, *et al. Eur Heart J* 2016; 37:2129–2200; 7.Yancy CW, *et al. Circulation* 2013;128:e240–327; 8. Pfeffer MA, *et al. Circulation* 2015;131:34 -42; 9. Pandey A, *et al. J Am Heart Assoc* 2015;4:e002137; 10. Pitt B, *et al. N Engl J Med* 2014;370:1383–1392; 11. Agarwal R, *et al. Eur Heart J* 2021;42:152–161

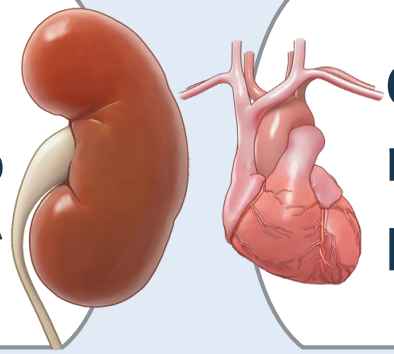
FIDELIO-DKD demonstrated kidney and CV benefits with finerenone in patients with CKD and T2D



In the **FIDELIO-DKD** patient population with **advanced CKD in T2D**, **finerenone** was well-tolerated and **significantly reduced**:[1]

CKD progression by **18%**

NNT=29*



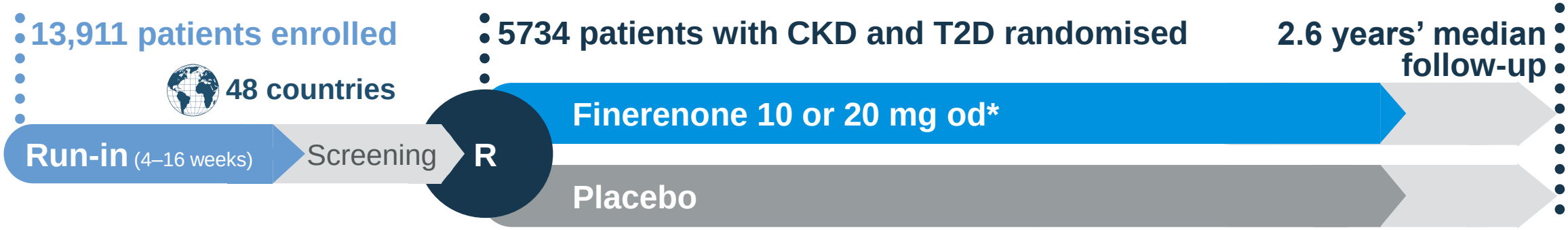
CV morbidity and **mortality** by **14%**

NNT=42*

*NNT to prevent one event based on absolute risk reductions at 36 months
CV, cardiovascular; NNT, number needed to treat

1. Bakris GB, *et al. N Engl J Med* 2020;383:2219–2229

FIDELIO-DKD was a global, phase III, randomized controlled trial



Key endpoints

1. Kidney composite outcome

Time to kidney failure,[#] sustained ≥40% decrease in eGFR from baseline, or renal death

2. CV composite outcome

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

Aim of this subgroup analysis

To evaluate the **effect of finerenone on kidney and CV outcomes in patients with CKD and T2D with vs without a history of HF**

*10 mg if screening eGFR 25 to <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;
[#]defined as ESKD or an eGFR <15 ml/min/1.73 m^2
; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HHF, hospitalisation for heart failure; MI, myocardial infarction; od, once daily; R, randomisation

Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

Patients with HFrEF were excluded in the FIDELIO-DKD trial

Key inclusion criteria

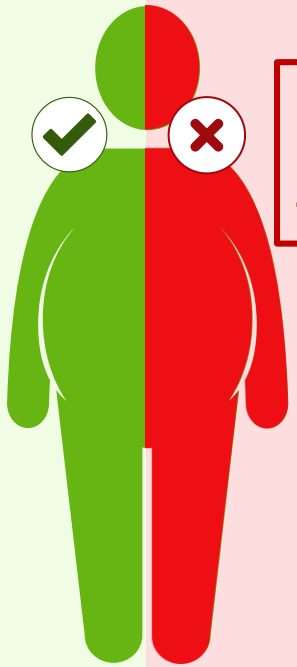
Aged ≥18 years with T2D

Treated with maximum tolerated dose of RASi for ≥4 weeks

eGFR ≥25–<75 ml/min/1.73 m^2

UACR ≥30–≤5000 mg/g*

Serum [K^+] ≤4.8 mmol/l at run-in and screening



Key exclusion criteria

HFrEF with NYHA Class II–IV (Class IA recommendation for treatment with an MRA)

Recent hospitalisation for worsening HF#

Uncontrolled arterial hypertension‡

HbA1c >12%

Other kidney disease

436 (7.7%) had a history of HF at baseline §

*Patients with moderately elevated albuminuria were required to also have diabetic retinopathy; #in the 30 days prior to the screening 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; § history of HF defined by investigators
DBP, diastolic blood pressure; HbA1c, glycated haemoglobin; NYHA, New York Heart Association; RASi, renin–angiotensin system inhibitor; SBP, systolic blood pressure; [K^+], potassium concentration; UACR, urine albumin-to-creatinine ratio
Bakris GL, et al. *N Engl J Med* 2020;383:2219–2229

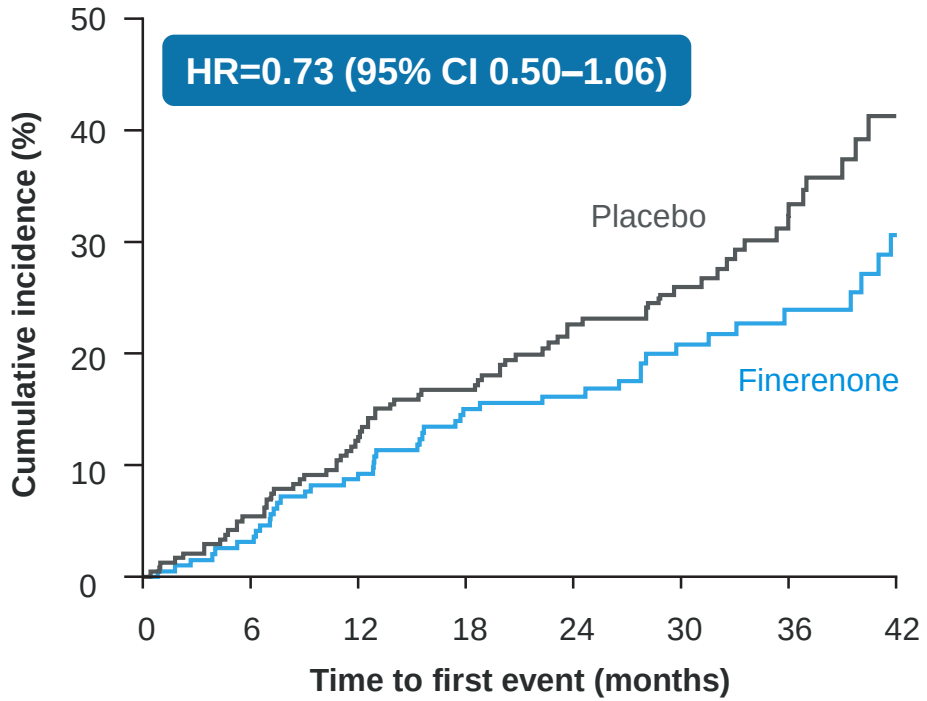
Patients with a history of HF had a lower eGFR, higher BMI and larger waist circumference than patients without HF

Characteristic*	With history of HF (n=436)	Without history of HF (n=5238)
Age, years	66±9	66±9
Gender, male, n (%)	280 (64)	3703 (71)
Mean SBP, mmHg	138±14	138±14
BMI, kg/m^2	33±7	31±6
Duration of T2D, years	17±9	17±9
HbA1c, %	7.8±1.3	7.7±1.3
Serum [K^+], mmol/l	4.4±0.5	4.4±0.5
eGFR, ml/min/1.73 m^2	42±13	45±13
Waist circumference, cm	111±16	106±15
CRP, mg/l	7±13	4±9
Heart rate, bpm	70±10	72±11
With a history of CVD, n (%)	328 (75)	2277 (44)

*Data expressed as mean ± SD unless otherwise stated
BMI, body mass index; bpm, beat per minute; CRP, C-reactive protein; SBP, systolic blood pressure; SD, standard deviation

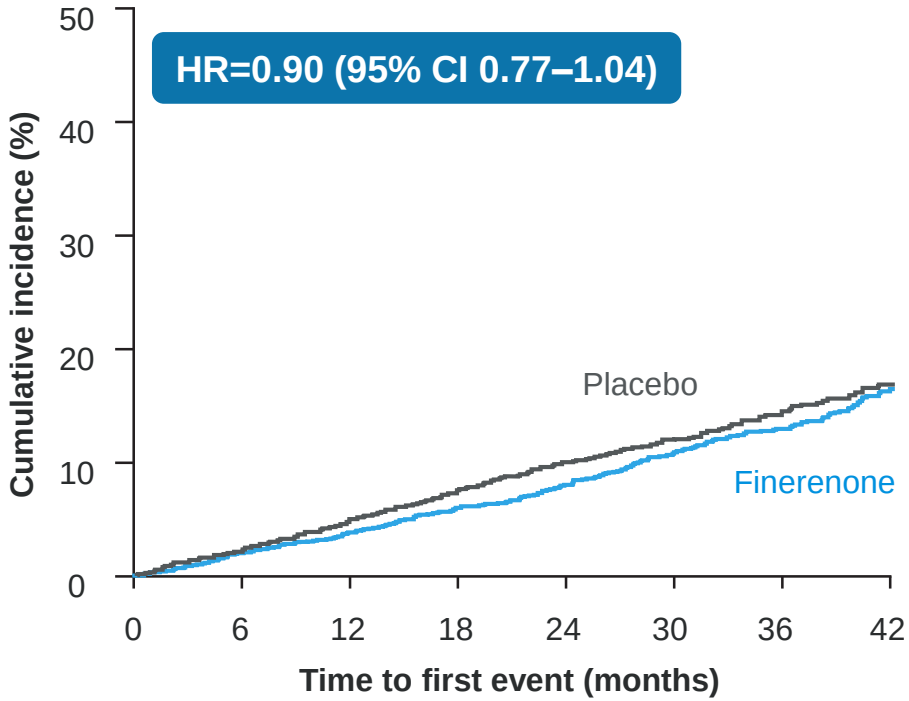
Finerenone reduced the risk of composite CV outcome* irrespective of history of HF

Patients with history of HF



No. at risk								
Finerenone	195	189	175	160	128	93	62	40
Placebo	241	227	208	195	140	99	62	25

Patients without history of HF



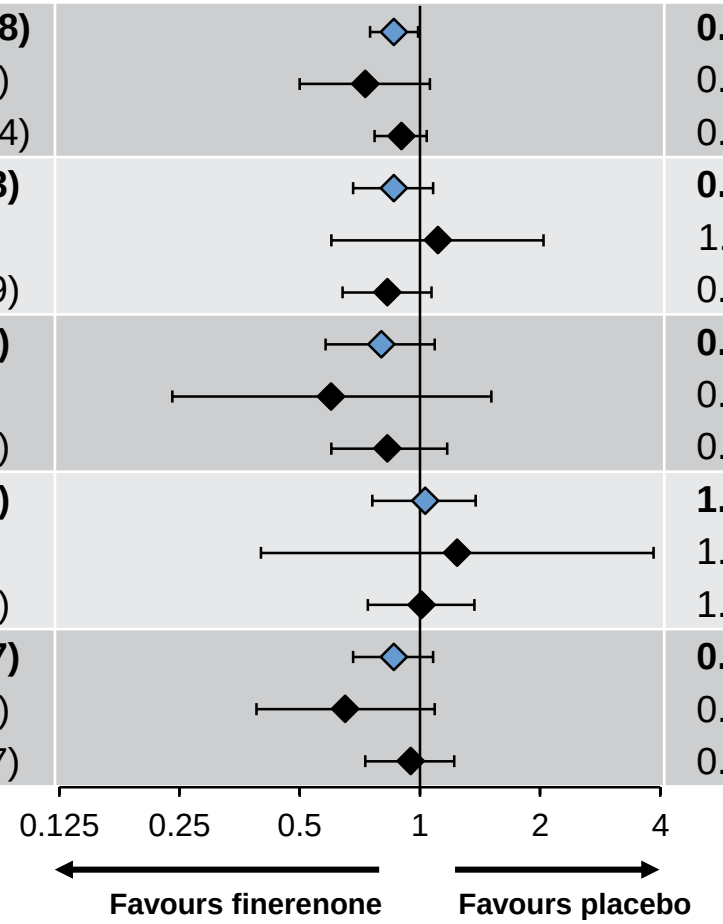
No. at risk								
Finerenone	2638	2571	2513	2422	1889	1395	922	497
Placebo	2600	2526	2445	2354	1829	1376	889	511

***p*-value for interaction = 0.33**

*Time to CV death, nonfatal MI, nonfatal stroke, or hospitalisation for heart failure
CI, confidence interval; HR, hazard ratio

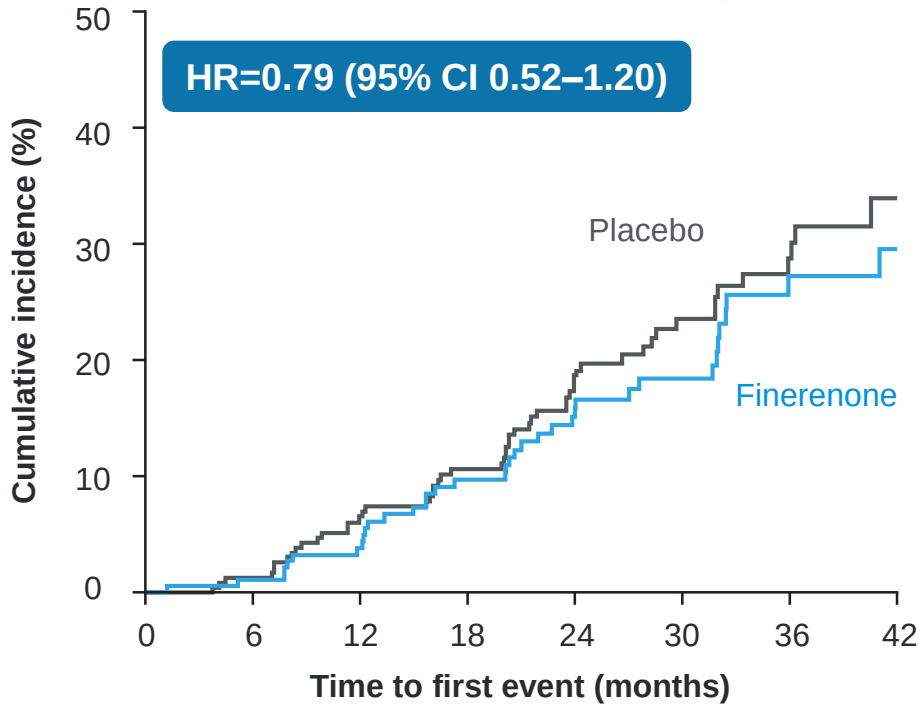
The effect of finerenone on the components of the composite CV outcome was consistent across subgroups of history of HF

Endpoint	Finerenone (N=2833) n (%)	Placebo (N=2841) n (%)	Hazard ratio (95% CI)	*p*-value for interaction
Composite CV Outcome	**367/2833 (13.0)**	**420/2841 (14.8)**	**0.86 (0.75–0.99)**	
With HF	46/195 (23.6)	71/241 (29.5)	0.73 (0.50–1.06)	0.33
Without HF	321/2638 (12.2)	349/2600 (13.4)	0.90 (0.77–1.04)	
CV death	**128/2833 (4.5)**	**150/2841 (5.3)**	**0.86 (0.68–1.08)**	
With HF	20/195 (10.3)	22/241 (9.1)	1.11 (0.60–2.04)	0.39
Without HF	108/2638 (0.7)	128/2600 (4.9)	0.83 (0.64–1.07)	
Nonfatal MI	**70/2833 (2.5)**	**87/2841 (3.1)**	**0.80 (0.58–1.09)**	
With HF	7/195 (3.6)	12/241 (5.0)	0.60 (0.24–1.51)	0.51
Without HF	63/2638 (2.4)	74/2600 (2.8)	0.83 (0.60–1.17)	
Nonfatal stroke	**90/2833 (3.2)**	**87/2841 (3.1)**	**1.03 (0.76–1.38)**	
With HF	6/195 (3.1)	6/241 (2.5)	1.24 (0.40–3.85)	0.73
Without HF	84/2638 (3.2)	81/2600 (3.1)	1.01 (0.74–1.37)	
First HHF	**139/2833 (4.9)**	**162/2841 (5.7)**	**0.86 (0.68–1.08)**	
With HF	23/195 (11.8)	41/241 (17.0)	0.65 (0.39–1.09)	0.20
Without HF	116/2638 (4.4)	121/2600 (4.7)	0.95 (0.73–1.22)	



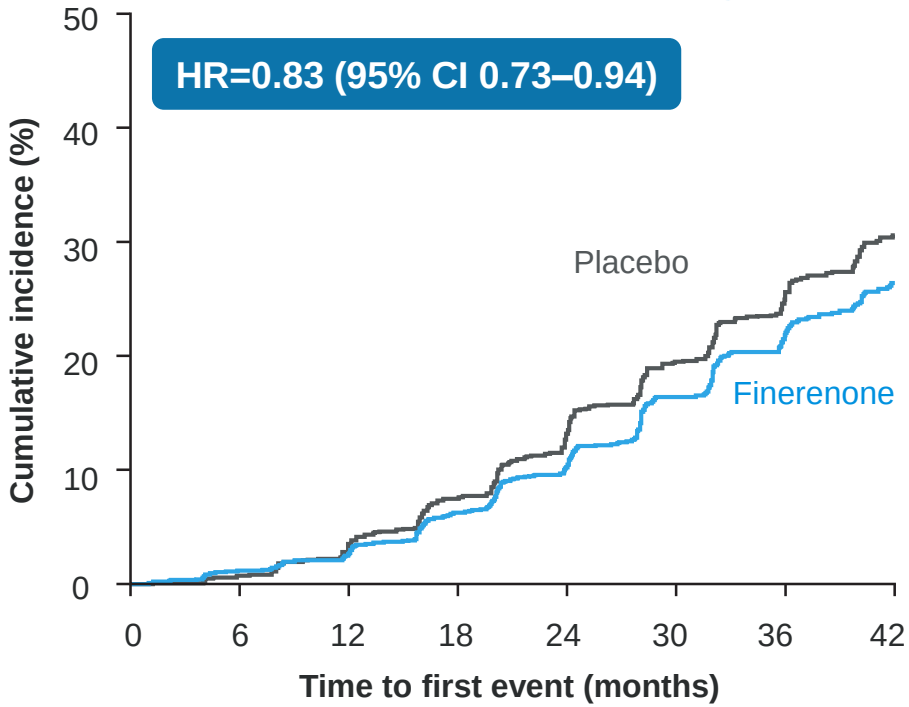
Finerenone slowed CKD progression irrespective of history of HF

Patients with history of HF



No. at risk								
Finerenone	195	185	170	149	114	79	45	28
Placebo	241	232	211	195	140	90	53	24

Patients without history of HF



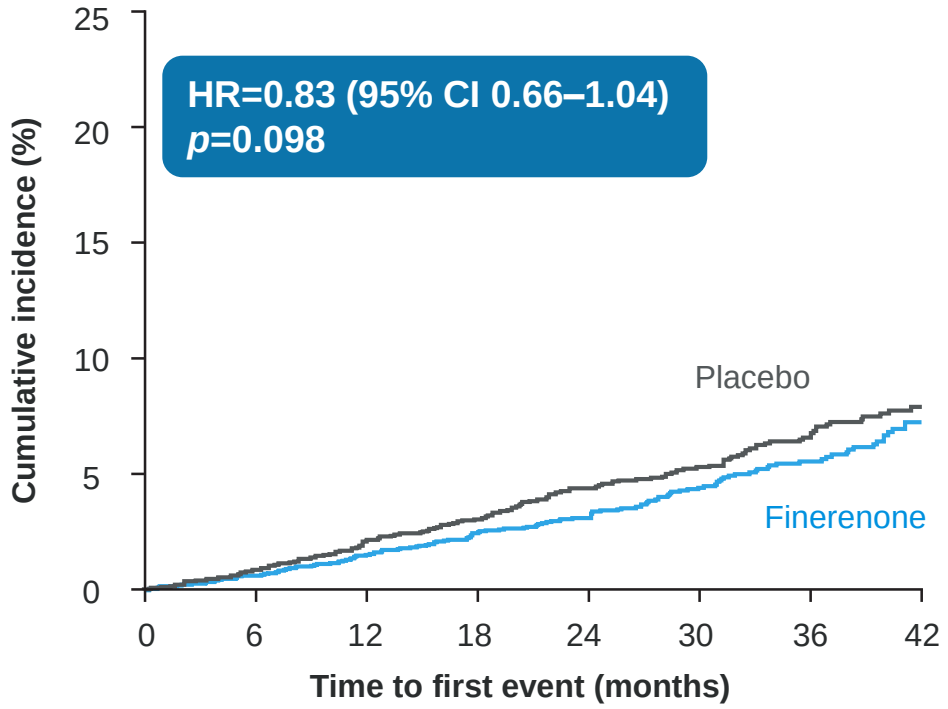
No. at risk								
Finerenone	2638	2520	2437	2248	1694	1195	742	413
Placebo	2600	2492	2375	2184	1618	1158	739	429

***p*-value for interaction = 0.83**

*Kidney failure, sustained ≥40% decrease in eGFR from baseline, or renal death

Incidence of composite outcome of CV death or HHF in the overall population was lower in finerenone-treated patients

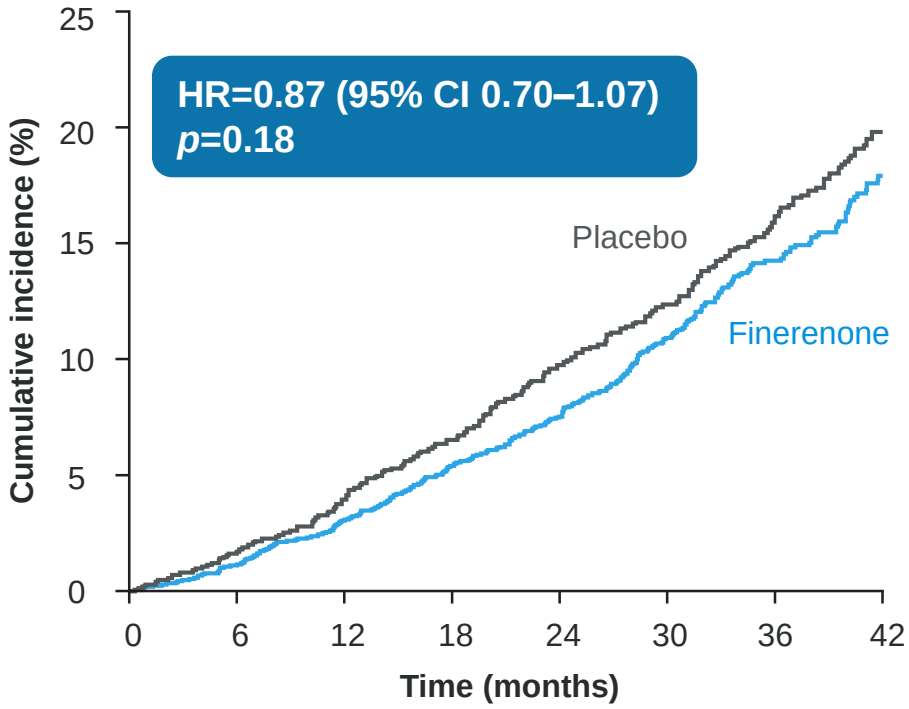
First event



No. at risk

Finerenone	2833	2791	2735	2653	2086	1553	1028	570
Placebo	2841	2784	2713	2632	2057	1550	1009	580

Total events

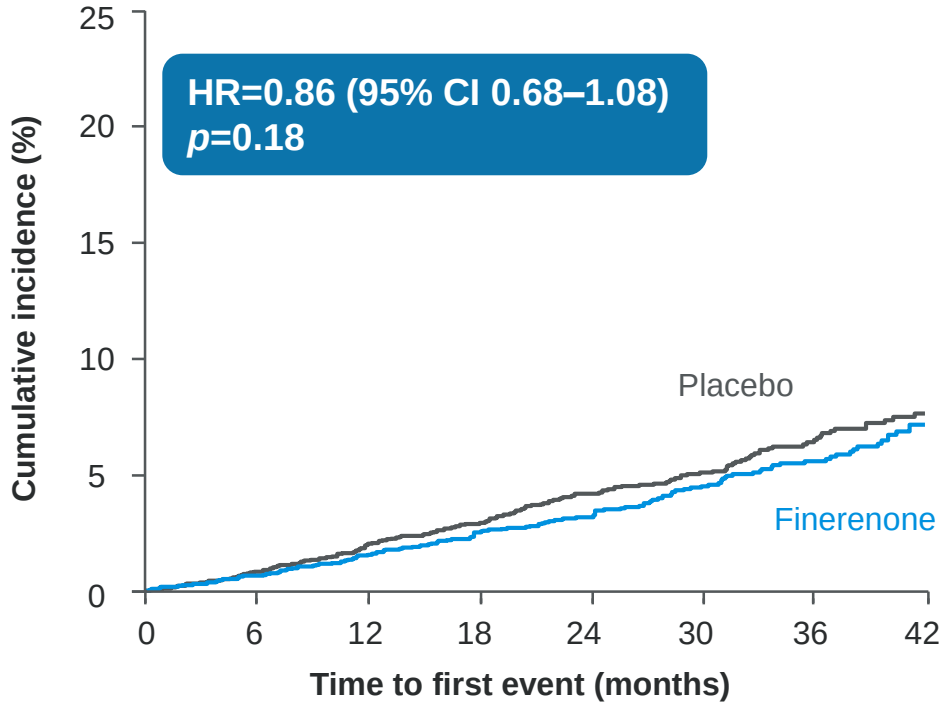


No. at risk

Finerenone	2833	2808	2774	2711	2146	1616	1083	616
Placebo	2841	2808	2768	2708	2140	1628	1064	618

Finerenone lowered first and total HHF events in the overall study population

First event



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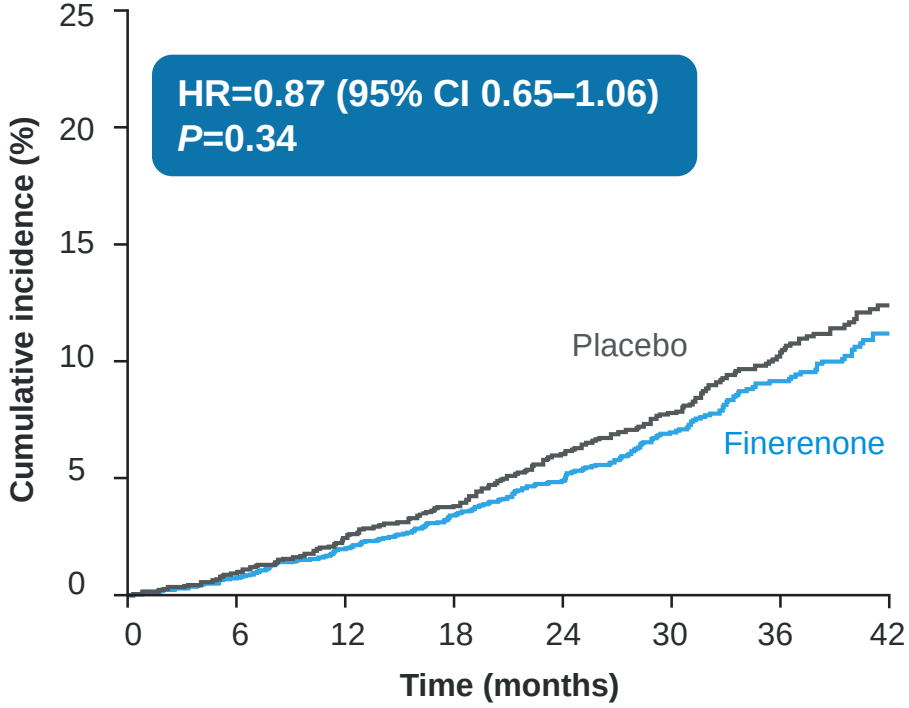
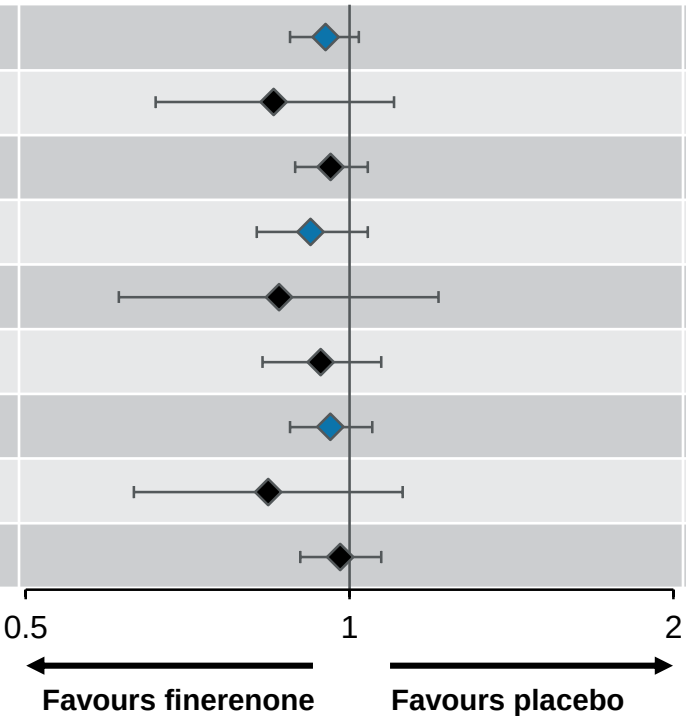
Total events



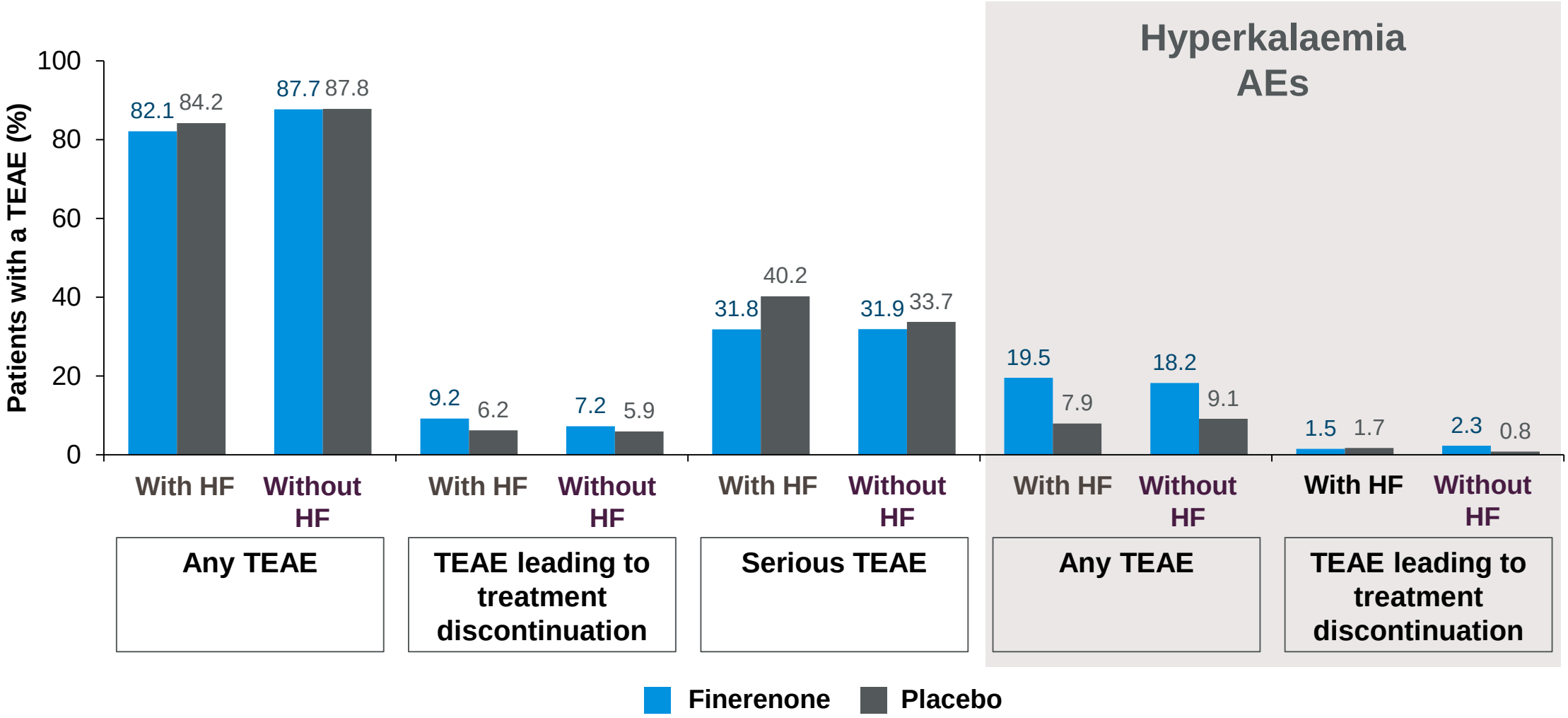
No. at risk								
Finerenone	2833	2808	2774	2711	2146	1616	1083	616
Placebo	2841	2808	2768	2708	2140	1628	1064	618

A history of HF did not modify the effect of finerenone on all-cause, CV and non-CV hospitalisation

Endpoint	Finerenone n/N (%)	Placebo n/N (%)	Hazard ratio (95% CI)	*P*-value for interaction
All-cause hospitalisation	**1263/2833 (44.6)**	**1321/2841 (46.5)**	**0.95 (0.88–1.02)**	**0.37**
With HF	101/195 (51.8)	139/241 (57.7)	0.85 (0.66–1.10)	
Without HF	1162/2638 (44.0)	1182/2600 (45.5)	0.96 (0.89–1.04)	
CV hospitalisation	**519/2833 (18.3)**	**561/2841 (19.7)**	**0.92 (0.82–1.04)**	**0.63**
With HF	56/195 (28.7)	78/241 (32.4)	0.86 (0.61–1.21)	
Without HF	463/2638 (17.6)	483/2600 (18.6)	0.94 (0.83–1.07)	
Non-CV hospitalisation	**1026/2833 (36.2)**	**1059/2841 (37.3)**	**0.96 (0.88–1.05)**	**0.31**
With HF	78/195 (40.0)	109/241 (45.2)	0.84 (0.63–1.12)	
Without HF	948/2638 (35.9)	950/2600 (36.5)	0.98 (0.90–1.07)	



Incidence of overall TEAEs was similar between treatment arms irrespective of HF history



AE, adverse event; TEAE, treatment-emergent adverse event

In FIDELIO-DKD, finerenone was well-tolerated and improved CV and kidney outcomes irrespective of pre-existing HF status

Finerenone consistently reduced the incidence of CV and kidney events in patients with CKD and T2D with and without a history of HF

- Due to the study design, patients with a history of HF in this analysis most likely had HFpEF

Overall, AEs were similar between treatment arms irrespective of history of HF

- In patients with a history of HF, fewer serious AEs were observed with finerenone than placebo
- There was no clinical significance in the higher incidence of hyperkalaemia with finerenone in patients with and without HF

Additional data from FIGARO-DKD and the ongoing FINEARTS-HF trial will provide the opportunity to further evaluate the efficacy and safety of finerenone in patients with HF

Thank you

FIDELIO-DKD
FInerenone in reducing kiDnEy faiLure and dIsease prOgression in DKD

The FIDELIO-DKD team would like to thank all participating investigators, the centres, the sponsor study team, and the patients and their families

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48 countries, 913 sites, 13,911* participants

*Number of patients who provided informed consent