Finerenone in mild to severe chronic kidney disease and type 2 diabetes: a FIDELITY subgroup analysis in patients with heart failure

Gerasimos Filippatos, MD, FESC, FHFA, FHFSA(h)
National and Kapodistrian University of Athens

FIDELITY
FInerenone in chronic kiDney diseasE and type 2 diabetes:
Combined FIDELIO-DKD and FIGARO-DKD Trial programme analYsis

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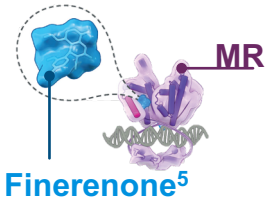
Finerenone targets MR overactivation, which may contribute to CV disease progression in patients with CKD associated with T2D



Finerenone is a novel, selective, nonsteroidal MRA that inhibits MR overactivation, which is thought to contribute to inflammation and fibrosis leading to kidney and CV damage[1–5]

FIDELIO-DKD

N=5734

Finerenone reducing **kidney failure and disease progression** in patients with CKD and T2D

Composite outcome:[4]
time to onset of kidney failure,* sustained ≥40% decrease in eGFR from baseline, or kidney death
RRR: 18%

Same as primary outcome in **FIGARO-DKD**

FIGARO-DKD

N=7437

Finerenone reducing **cardiovascular mortality and morbidity** in patients with CKD and T2D

Composite outcome:[5]
time to CV death, nonfatal MI, nonfatal stroke, or hospitalization for HF
RRR: 13%

Same as primary outcome in **FIDELIO-DKD**

Primary outcome

Secondary outcome

*Kidney failure defined as occurrence of ESKD (initiation of chronic dialysis for ≥90 days or kidney transplantation) or sustained eGFR <15 ml/min/1.73 m^2

CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HF, heart failure; MI, myocardial infarction; MR, mineralocorticoid receptor; MRA, mineralocorticoid receptor antagonist; RRR, relative risk reduction; T2D, type 2 diabetes

1. Agarwal R, *et al. Nephrol Dial Transplant* 2020; doi: 10.1093/ndt/gfaa294; 2. Agarwal R, *et al. Eur Heart J* 2021;42:152–161; 3. Khan NUA & Movahed A. *Rev Cardiovasc Med* 2004;5:71–81; 4. Bakris GL, *et al. N Engl J Med* 2020;383;2219–2229; 5. Pitt B, *et al. N Engl J Med* 2021; doi: 10.1056/NEJMoa2110956

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

13,171 patients randomised

3 years' median follow-up

48 countries

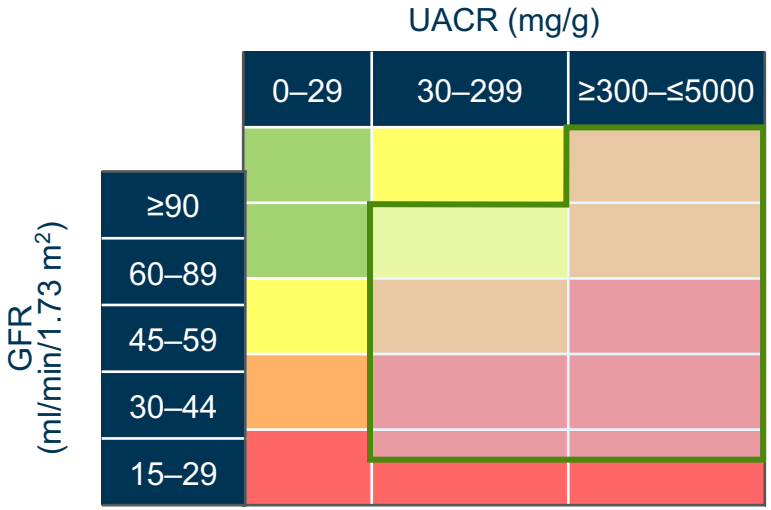
R

Finerenone 10 or 20 mg od*

Placebo

Key eligibility criteria

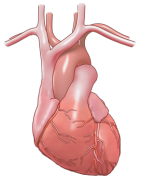
- ✓ **T2D**
- ✓ **CKD**
- ✓ On single RASi
- ✓ Serum [K^+] ≤4.8 mmol/l
- ✗ Symptomatic HFrEF



Key outcomes

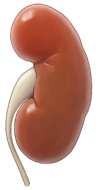
CV composite

Time to CV death, non-fatal MI, non-fatal 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 m²; 20 mg if ≥60 ml/min/1.73 m², 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 m²

GFR, glomerular filtration rate; HHF, hospitalisation for heart failure; HFrEF, heart failure with reduced ejection fraction; [K^+], potassium concentration; od, once daily; RASi, renin–angiotensin system inhibitor

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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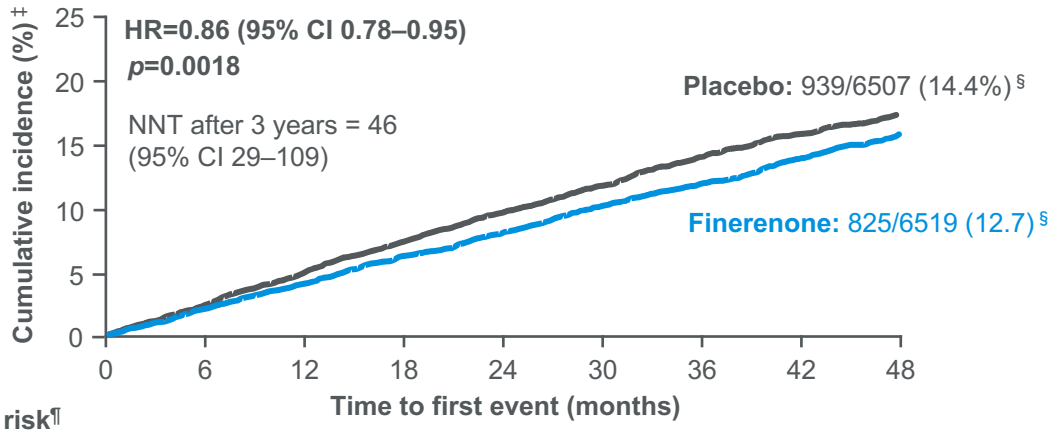
FIDELITY results overview

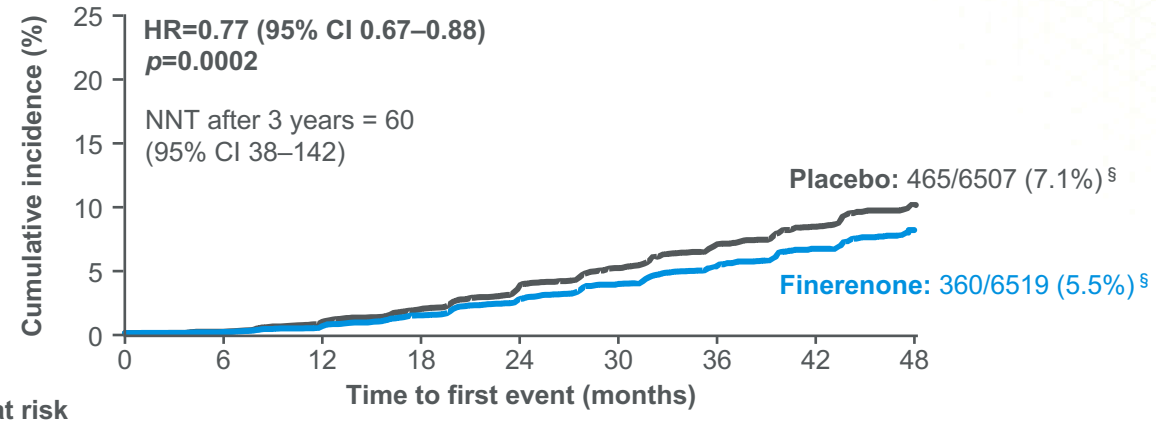
To evaluate the **efficacy and safety of finerenone across the spectrum** of patients with CKD associated with T2D and to provide insights into the relationship between CKD stage and the **effects of finerenone on composite cardiovascular- and kidney-specific endpoints**

Time to CV death, non-fatal MI, non-fatal stroke, or hospitalisation for HF



No. at risk¶									
Finerenone	6519	6360	6202	6009	5273	4207	3065	2187	1087
Placebo	6507	6330	6125	5938	5184	4147	2969	2135	1082

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

FIDELITY showed significant **risk reductions** of **14%** in the **risk of CV morbidity and mortality** vs placebo (HR=0.86; 95% CI 0.78–0.95) and **23%** reduction in the **risk of CKD progression#** vs placebo (HR=0.77; 95% CI 0.67–0.88)[1]

*ESKD or an eGFR <15 ml/min/1.73 m^2; #events were classified as renal death if: (1) the patient died; (2) KRT 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; ¶at-risk subjects were calculated at start of time point
CI, confidence interval; HR hazard ratio; KRT, kidney replacement therapy; NNT, number needed to treat

1. Filippatos G, *et al*. ESC 2021 https://esc365.escardio.org/presentation/238815. Hot Line session 28 August 2021

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At baseline, patients had well-controlled blood pressure and HbA1c, and CV medications were used by most patients

Characteristic	Total (n=13,026)
Age, years	65
Male, %	70
Duration of T2D, years	15.4
HbA1c, %	7.7
SBP/DBP, mmHg	**137/76**
History of CV disease, n (%)	**5935 (46)**
History of HF, n %	**1007 (7.7)**
Serum [K^+], mmol/l	4.4

Medications, n (%)	Total (n=13,026)
CV medications	
RASi	**13,003 (100)**
Statins	**9399 (72)**
Beta-blockers	6504 (50)
Calcium antagonists	7358 (57)
Diuretics	6710 (52)
Glucose-lowering therapies	12,720 (98)
Metformin	7557 (58)
Insulin	7630 (59)
GLP-1RAs	**944 (7.2)**
SGLT-2is	**877 (6.7)**

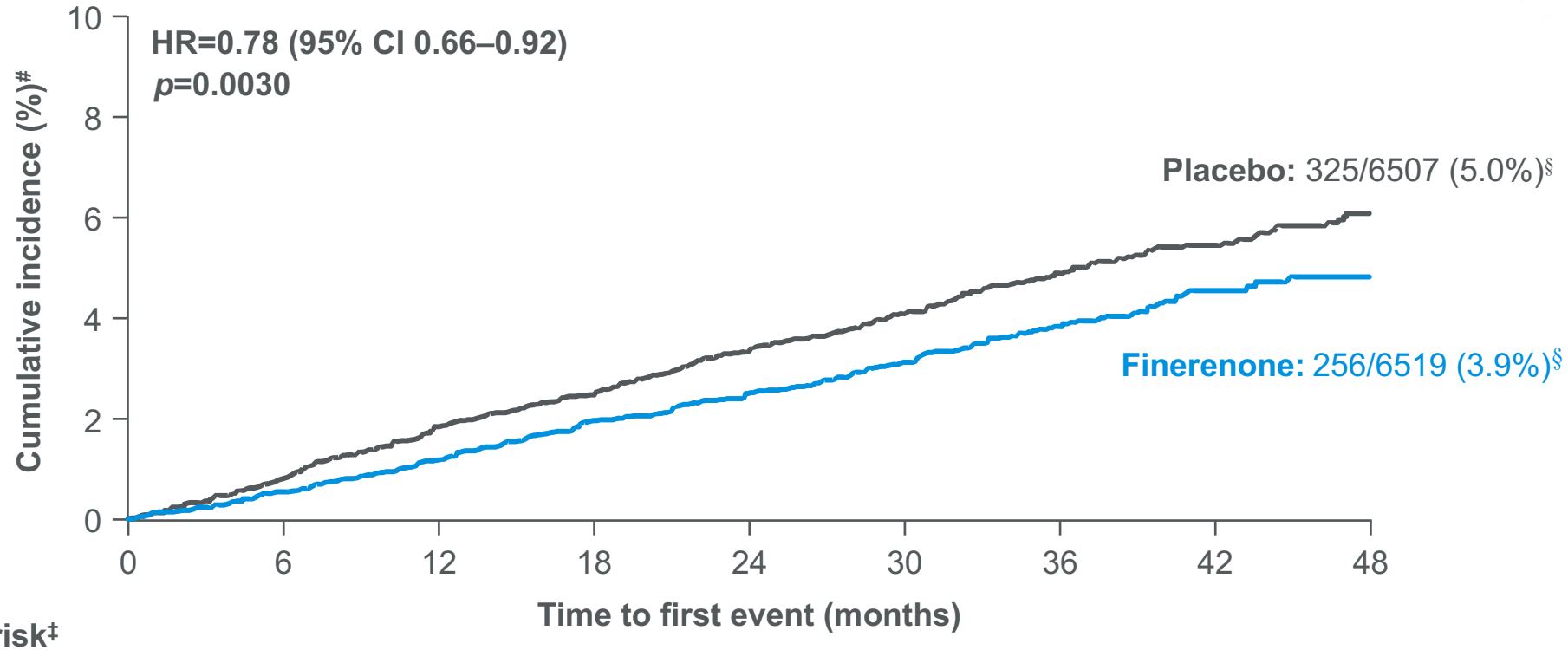
The aim of this subanalysis was to evaluate the effect of finerenone on HF-related outcomes in FIDELITY in the overall population, and across eGFR and UACR subgroups

Data are mean unless otherwise stated
DBP, diastolic blood pressure; GLP-1RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated haemoglobin; SBP, systolic blood pressure; SGLT-2, sodium-glucose co-transporter-2 inhibitor
Filippatos G, *et al*. *AHA* 2021; abstract 17139

FIDELITY

In FIDELITY, finerenone significantly reduced the risk of first hospitalisation for HF* by 22% vs placebo

Time to first hospitalisation for HF



No. at risk‡									
Finerenone	6519	6431	6313	6168	5450	4379	3203	2299	1143
Placebo	6507	6394	6246	6103	5379	4342	3138	2271	1144

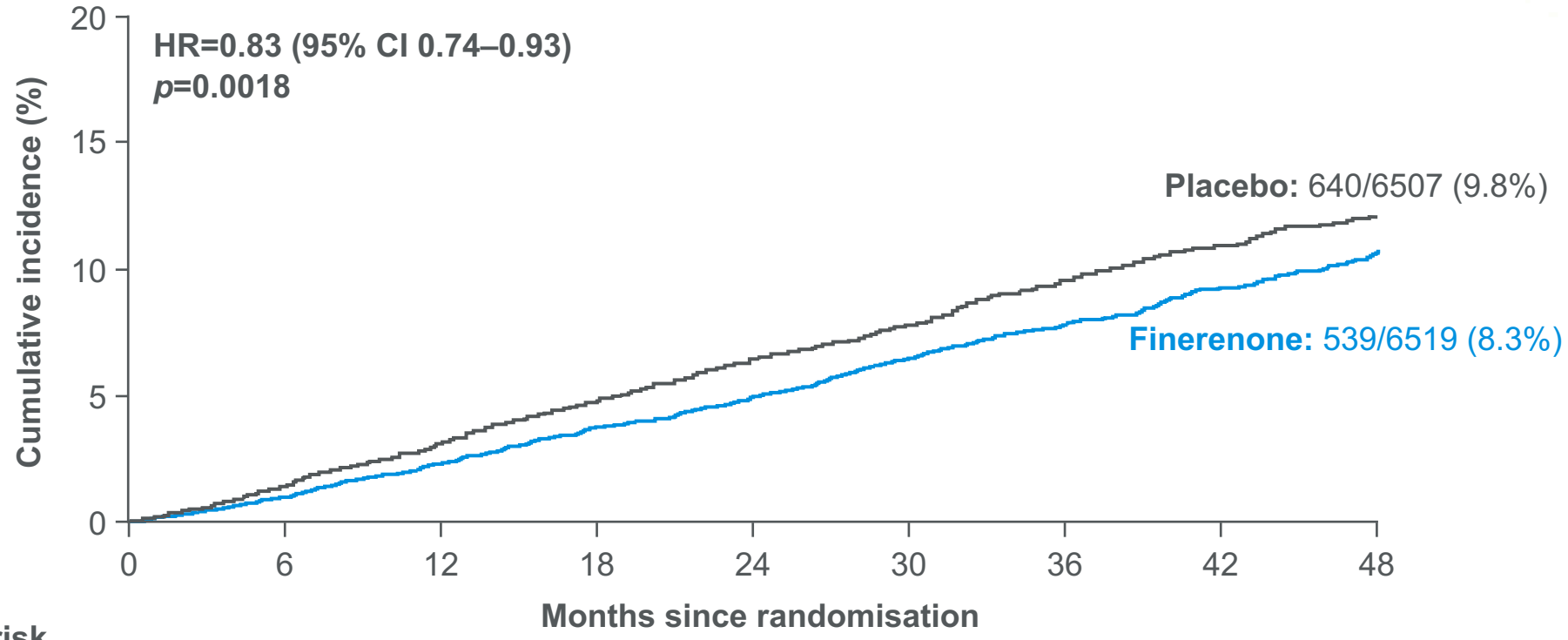
*First hospitalisation for HF defined as first event after randomisation; #cumulative incidence calculated by Aalen–Johansen estimator using deaths due to other causes as competing risk; ‡at-risk subjects were calculated at start of time point; §number of patients with an event over a median of 3.0 years of follow-up

Filippatos G, *et al*. *AHA* 2021; abstract 17139

FIDELITY

In FIDELITY, finerenone reduced the risk for CV death and first hospitalisation for HF* by 17% vs placebo

Time to CV death and first hospitalisation for HF



No. at risk									
Finerenone	6519	6431	6313	6167	5449	4379	3202	2299	1143
Placebo	6507	6394	6246	6102	5379	4342	3138	2271	1144

*First hospitalisation for HF defined as first event after randomisation

Filippatos G, *et al*. *AHA* 2021; abstract 17139

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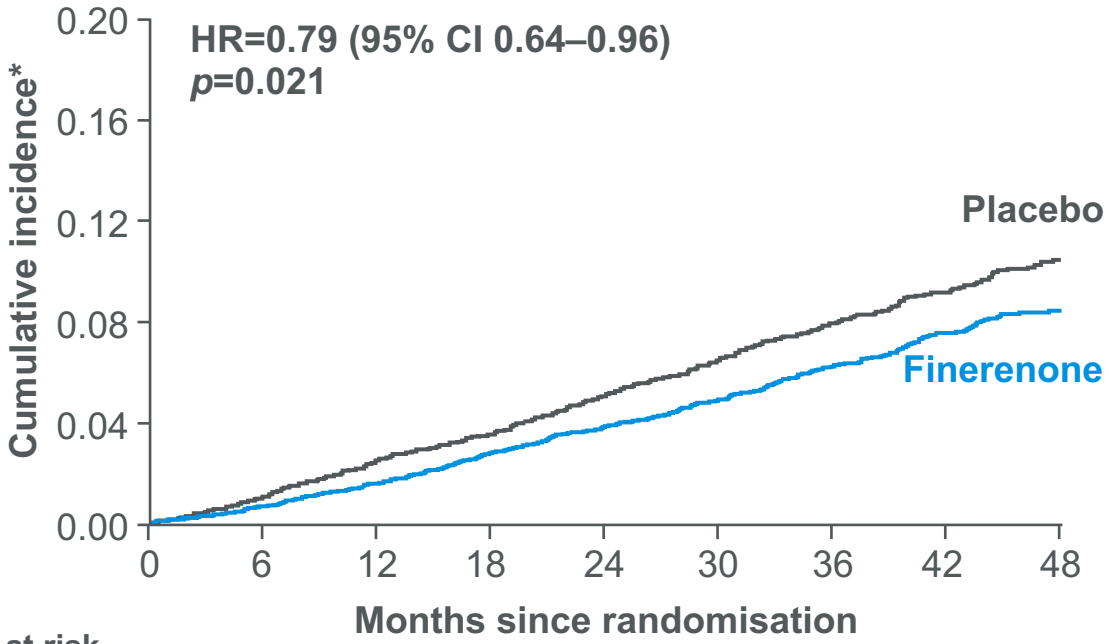
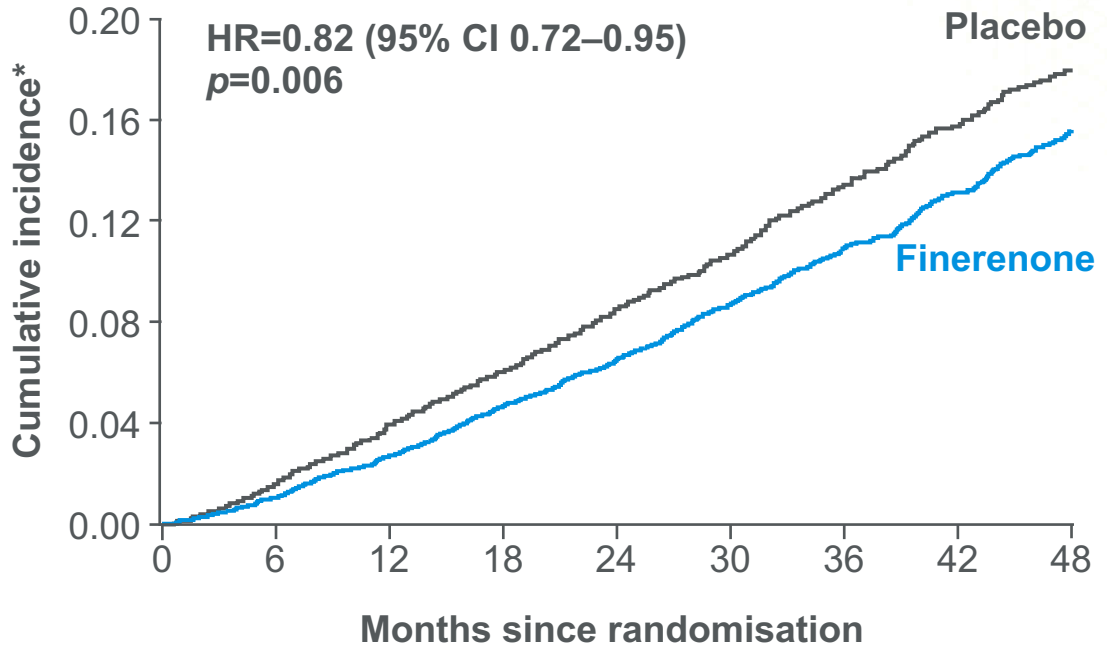
In FIDELITY, finerenone reduced risk of total hospitalisation for HF and CV death and total hospitalisation for HF

Time to total HHF (first and recurrent)



No. at risk									
Finerenone	6519	6464	6385	6280	5573	4507	3312	2395	1182
Placebo	6507	6444	6351	6240	5542	4495	3259	2364	1184

Time to CV death and total HHF (first and recurrent)



	6519	6464	6385	6280	5573	4507	3312	2395	1182
	6507	6444	6351	6240	5542	4495	3259	2364	1184

*Cumulative incidence based on mean cumulative function

Filippatos G, *et al*. *AHA* 2021; abstract 17139

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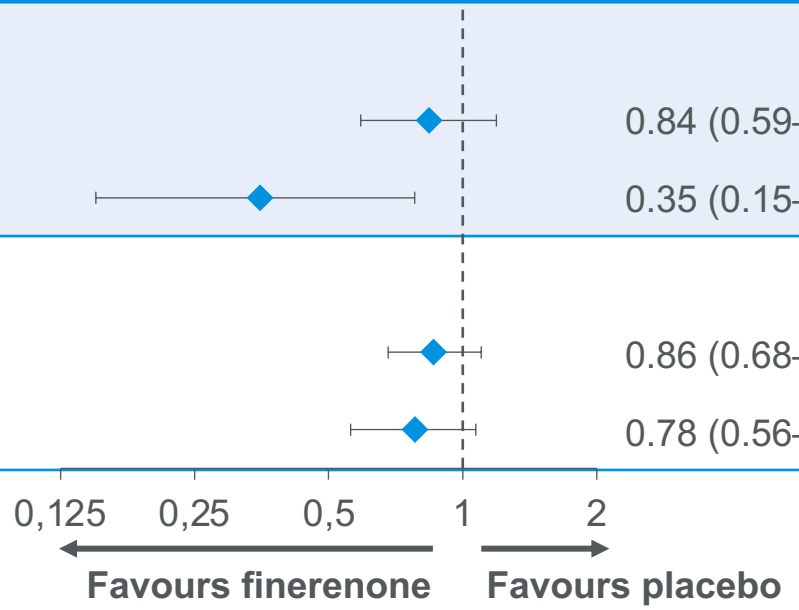
In FIDELITY, finerenone reduced the risk of first hospitalisation for HF vs placebo across the eGFR and UACR spectrum

Time to first hospitalisation for HF

Baseline UACR (mg/g) and eGFR (ml/min/1.73 m²)	Finerenone (n=6519) n/100PY	Placebo (n=6507) n/100PY	Hazard ratio (95% CI)	*p*-value for interaction
UACR <300				
eGFR <60	1.2	1.5	0.84 (0.59–1.19)	
eGFR ≥60	0.4	1.0	0.35 (0.15–0.78)	
UACR ≥300				**0.3011***
eGFR <60	2.0	2.3	0.86 (0.68–1.10)	
eGFR ≥60	1.1	1.5	0.78 (0.56–1.07)	



*Typically, a *p*-value <0.1 indicates a statistically significant subgroup effect
UACR, urine albumin-to-creatinine ratio
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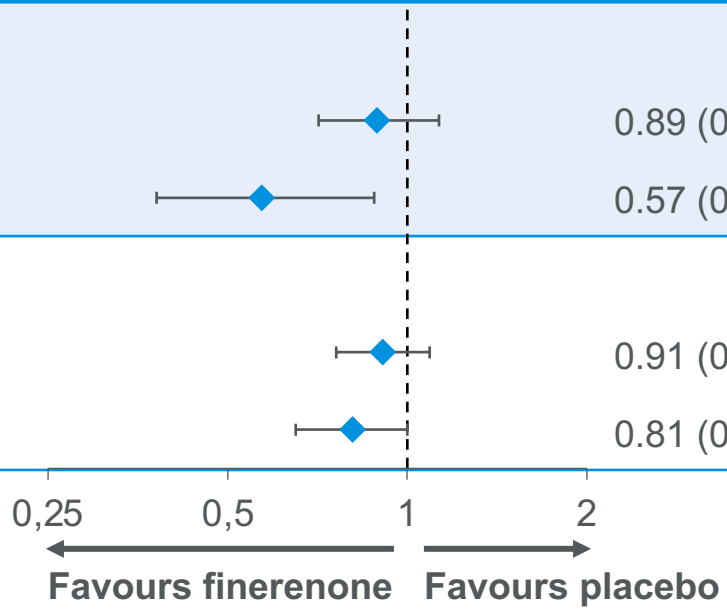
FIDELITY

In FIDELITY, finerenone also reduced the risk of CV death and first hospitalisation for HF vs placebo across the eGFR and UACR spectrum

Time to CV death and first hospitalisation for HF

Baseline UACR (mg/g) and eGFR (ml/min/1.73 m²)	Finerenone (n=6519) n/100PY	Placebo (n=6507) n/100PY	Hazard ratio (95% CI)	*p*-value for interaction
UACR <300				
eGFR <60	2.8	3.1	0.89 (0.71–1.13)	
eGFR ≥60	1.5	2.4	0.57 (0.38–0.88)	
UACR ≥300				0.3201*
eGFR <60	3.6	4.1	0.91 (0.76–1.09)	
eGFR ≥60	2.4	3.0	0.81 (0.65–1.00)	



*Typically, a *p*-value <0.1 indicates a statistically significant subgroup effect

Filippatos G, *et al*. *AHA* 2021; abstract 17139

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Summary and conclusion

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

Finerenone reduced the risk of first hospitalization for HF by 22%
(HR 0.78;
95% CI 0.66–0.92)

Finerenone reduced the risk of hospitalization for HF and CV death by 17%
(HR 0.83;
95% CI 0.74–0.93)

Finerenone reduced hospitalization for HF and CV death, irrespective of eGFR and UACR category

Filippatos G, *et al*. *AHA* 2021; abstract 17139