INFINITY

Efficacy and safety of finerenone in patients with chronic kidney disease and cardiovascular diseases: An individual participant data pooled analysis (INFINITY)

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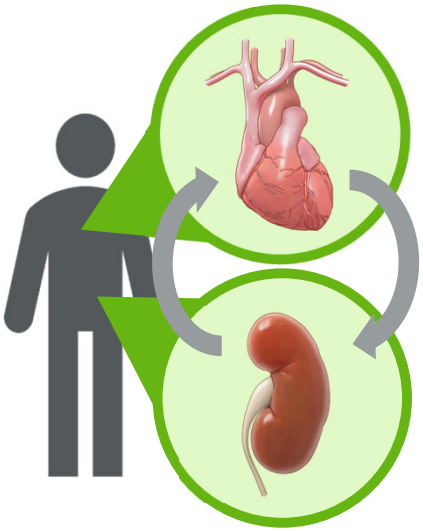
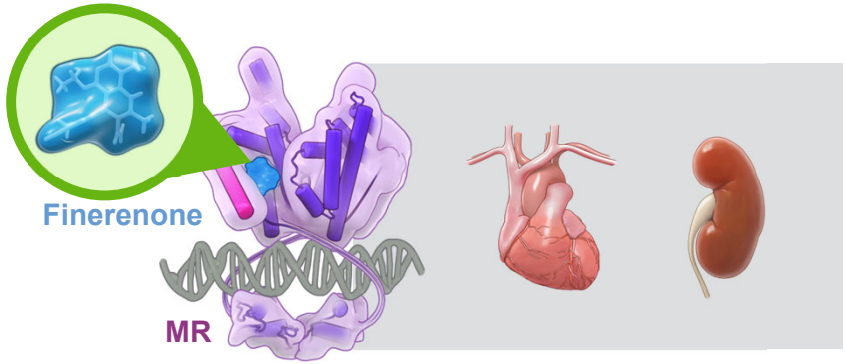
ESC
European Society of Cardiology

Introduction



- **CKD and CVD are closely intertwined**
  - CKD progression increases risk of primary and secondary CVD events and vice versa[1–4]
- **MR overactivation** represents a **shared mechanism** for CKD progression and CV complications[5,6]

Finerenone, a non-steroidal MR antagonist, was shown to **reduce the risk of CV and kidney events** in patients with CKD in the **INFINITY pooled analysis**[7]



This analysis examines the interrelationship between CV and kidney events, and the effect of finerenone on this relationship, in the pooled INFINITY dataset covering a broad spectrum of patients with CKD

CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; MR, mineralocorticoid receptor

1. Gansevoort RT, *et al. Lancet* 2013;382:339–352; 2. Vashistha V, *et al. Int J Cardiol* 2016;223:401–409; 3. Go AS, *et al. N Engl J Med* 2004;351:1296–1305; 4. Neuen BL, *et al. J Am Coll Cardiol* 2024;84:2246–2250; 5. Kolkhof P, *et al. J Cardiovasc Pharmacol* 2014;64:69–78; 6. Savarese G, *et al. Diabetologia* 2024;67:246–262; 7. Neuen BL, *et al. Lancet* 2026;407:2375–2386

INFINITY: individual participant data pooled analysis in a broad CKD population

FIGARO-DKD
FIDELIO-DKD
FIND-CKD N=1584
FIDELITY N=12,990
INFINITY N=14,574

R 1:1
- Finerenone 10 or 20 mg od* (n=7291)
- Placebo (n=7283)

Median follow-up of 3.1 years

CKD and CVD interrelationship

- **Time-updated (split-time) analyses** comparing incidence rates before and after non-fatal CV and kidney events
- **Estimation of all-cause mortality** from time of non-fatal CV and kidney events

Efficacy of finerenone on the INFINITY expanded CV composite

- Overall and by-component breakdown

Effect of CVD history on finerenone efficacy and safety

- Participants **with**/**without** a history of CVD
- **CVD was defined as**: ASCVD (coronary, cerebrovascular or peripheral arterial disease), HF, AF/flutter

Kidney events:
- CKD progression (sustained ≥40% decrease in eGFR or kidney failure*)

- **Non-fatal CV events**:
  - MI, stroke, AF/flutter, HHF

Components:
- Non-fatal MI
- Non-fatal stroke
- HHF
- New onset AF/flutter
- CV death

- **Kidney composite:** Time to kidney failure* or sustained ≥57% decrease in eGFR
- **CV composite:** Time to HHF or CV death
- **Others**: Kidney–CV composite, dialysis or kidney transplantation, all-cause death
- **Safety outcomes:** TEAEs, SAEs and hyperkalaemia events

***Kidney failure defined as sustained eGFR <15 ml/min/1.73 m² or initiation of chronic dialysis or kidney transplantation**
AF, atrial fibrillation; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HF, heart failure; HHF, hospitalisation for heart failure; MI, myocardial infarction; SAE, serious adverse event; TEAE, treatment-emergent adverse event

Baseline demographics and clinical characteristics

Characteristic	With CVD (n=6822)	Without CVD (n=7752)
Age, years, mean ± SD	66.7 ± 8.7	61.0 ± 11.4
Sex, male, n (%)*	5031 (73.7)	5076 (65.5)
Race, n (%)		
White	5102 (74.8)	4415 (57.0)
Asian	1142 (16.7)	2586 (33.4)
Black	261 (3.8)	296 (3.8)
Medical history, n (%)		
Atherosclerotic CVD	6123 (89.8)	0 (0.0)
Heart failure	1042 (15.3)	0 (0.0)
Atrial fibrillation	1165 (17.1)	0 (0.0)
BMI, kg/m^2, mean ± SD	31.4 ± 5.9	30.5 ± 6.2
Obese, BMI ≥30 kg/m^2, n (%)	3752 (55.2)	3730 (48.2)

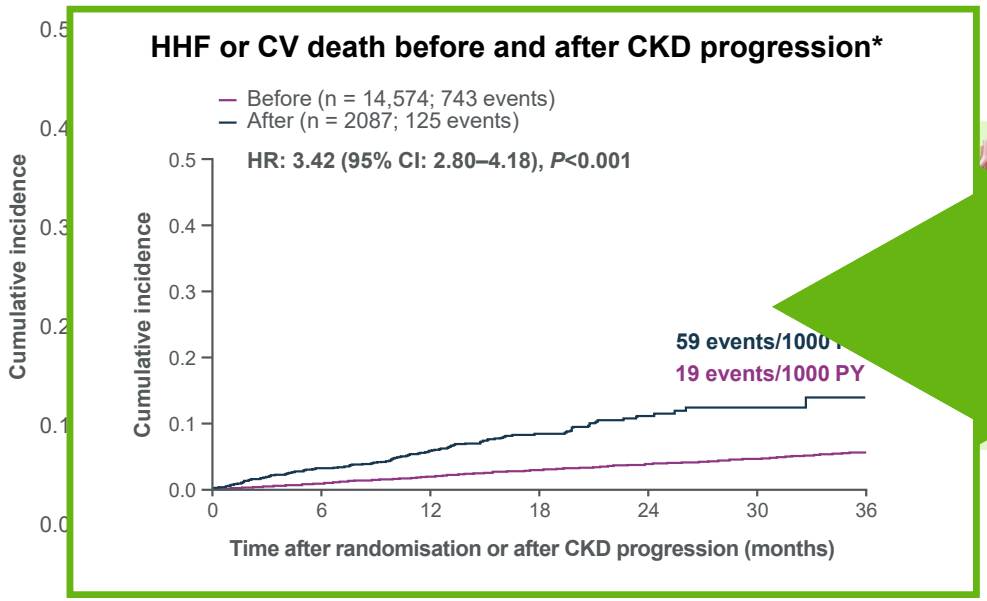
Characteristic	With CVD (n=6822)	Without CVD (n=7752)
SBP, mmHg, mean ± SD	136.6 ± 14.3	135.4 ± 14.4
HbA1c, %, mean ± SD	7.6 ± 1.4	7.3 ± 1.5
eGFR, ml/min/1.73 m^2, mean ± SD	54.0 ± 19.9	58.5 ± 22.4
UACR, mg/g, median (Q1–Q3)	482.7 (162.8–1104.3)	633.7 (310.8–1212.1)
Medication use, n (%)		
Statins	5417 (79.4)	4844 (62.5)
ARBs	4011 (58.8)	5038 (65.0)
ACEis	2803 (41.1)	2708 (34.9)
SGLT2is	474 (6.9)	668 (8.6)
Diuretics	3789 (55.5)	3202 (41.3)

*Sex and race were self-reported by the participants

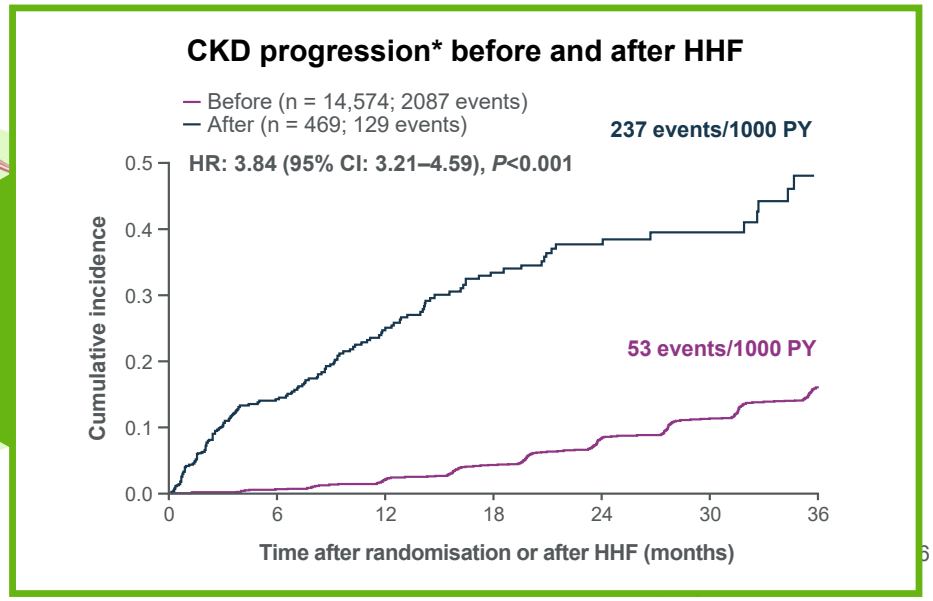
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin; SBP, systolic blood pressure; SGLT2i, sodium-glucose co-transporter-2 inhibitor; UACR, urine albumin-to-creatinine ratio

Event incidence before and after CV and kidney events

CKD progression* before and after a non-fatal CV event



Non-fatal CV events before and after CKD progression*

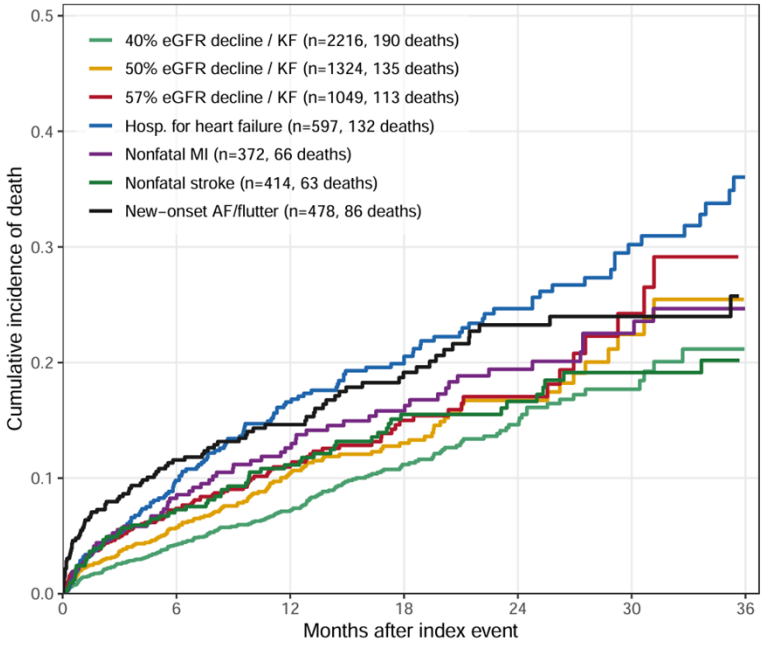


CKD progression was most strongly associated with subsequent HHF or CV death

*CKD progression in these analyses was defined as a sustained ≥40% decrease in eGFR relative to baseline or kidney failure, where kidney failure was defined as sustained eGFR <15 ml/min/1.73 m^2 or initiation of chronic dialysis or kidney transplantation. The eGFR threshold was chosen to allow time for event accumulation

CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HHF, hospitalisation for heart failure; PY, patient-years

Effect of non-fatal CV events and CKD progression on subsequent mortality



Event: n subsequent deaths per 1000 PY

HHF: **160**

57% eGFR decline or kidney failure: **119**

New onset AF/flutter: 136

50% eGFR decline or kidney failure: **104**

Non-fatal MI: **114**

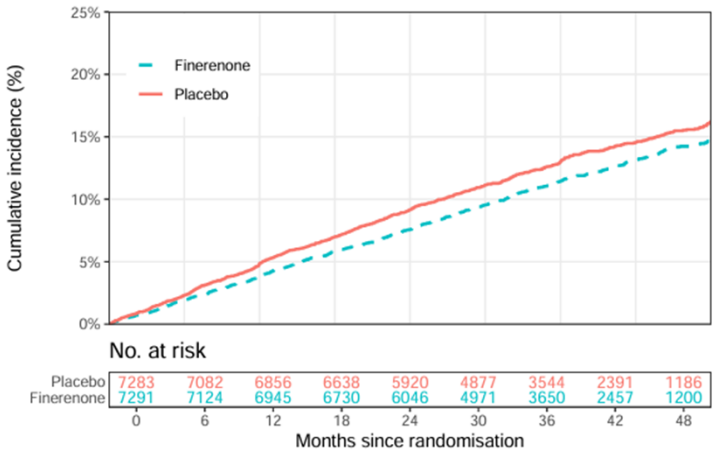
40% eGFR decline or kidney failure: **81**

Non-fatal stroke: **92**

Finerenone significantly reduced the risk of the expanded CV outcome versus placebo, supported by favourable HR estimates in most components

CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HHF, hospitalisation for heart failure; MI, myocardial infarction; PY, patient-years

Treatment effect on expanded CV outcome (non-fatal MI, non-fatal stroke, new onset AF/flutter, HHF and CV death)



Outcome	Finerenone (n=7291) n (%)	Finerenone (n=7291) n/1000 PY	Placebo (n=7283) n (%)	Placebo (n=7283) n/1000 PY	HR (95% CI)	*p*-value
Non-fatal MI	177 (2.4)	8.0	195 (2.7)	8.9	0.90 (0.73–1.10)	0.301
Non-fatal stroke	208 (2.9)	9.4	206 (2.8)	9.4	1.00 (0.83–1.22)	0.983
HHF	263 (3.6)	12.0	334 (4.6)	15.3	0.78 (0.66–0.92)	0.002
New onset AF/flutter*	223 (3.3)	11.0	255 (3.8)	12.6	0.87 (0.73–1.04)	0.128
CV death	182 (2.5)	8.1	220 (3.0)	9.9	0.82 (0.67–0.999)	0.049
Overall (expanded CV composite)	**887 (12.2)**	**41.7**	**995 (13.7)**	**47.5**	**0.88 (0.80–0.96)**	**0.004**

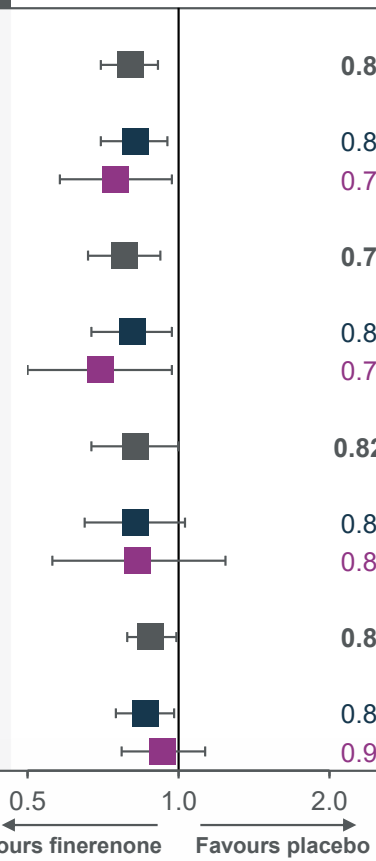
Finerenone significantly reduced the risk of the expanded CV outcome versus placebo, supported by favourable HR estimates in most components

*Participants with a history of AF/flutter at baseline were excluded from this analysis: 6697 participants were included in the finerenone arm and 6712 in the placebo arm

AF, atrial fibrillation; CI, confidence interval; CV, cardiovascular; HHF, hospitalisation for heart failure; HR, hazard ratio; MI, myocardial infarction; PY, patient-years

Treatment effect on CV and mortality outcomes by CVD history

Outcome	Finerenone n/n (%)	Finerenone n/1000 PY	Placebo n/n (%)	Placebo n/1000 PY	HR (95% CI)	*p*-interaction
HHF or CV death						
Overall	**420/7291 (5.8)**	**19.1**	**520/7283 (7.1)**	**23.9**	**0.80 (0.70–0.91)**	
History of CVD						
With	316/3413 (9.3)	32.4	382/3409 (11.2)	39.8	0.82 (0.70–0.95)	0.574
Without	104/3878 (2.7)	8.5	138/3874 (3.6)	11.3	0.75 (0.58–0.97)	
HHF						
Overall	**263/7291 (3.6)**	**12.0**	**334/7283 (4.6)**	**15.3**	**0.78 (0.66–0.92)**	
History of CVD						
With	201/3413 (5.9)	20.6	246/3409 (7.2)	25.6	0.81 (0.67–0.97)	0.446
Without	62/3878 (1.6)	5.1	88/3874 (2.3)	7.2	0.70 (0.50–0.97)	
CV death						
Overall	**182/7291 (2.5)**	**8.1**	**220/7283 (3.0)**	**9.9**	**0.82 (0.67–0.999)**	
History of CVD						
With	137/3413 (4.0)	13.6	166/3409 (4.9)	16.7	0.82 (0.65–1.03)	0.950
Without	45/3878 (1.2)	3.6	54/3874 (1.4)	4.4	0.83 (0.56–1.24)	
All-cause death						
Overall	**569/7291 (7.8)**	**25.4**	**642/7283 (8.8)**	**28.8**	**0.88 (0.79–0.99)**	
History of CVD						
With	375/3413 (11.0)	37.2	433/3409 (12.7)	43.5	0.86 (0.75–0.98)	0.477
Without	194/3878 (5.0)	15.7	209/3874 (5.4)	17.0	0.93 (0.77–1.13)	



CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; HHF, hospitalisation for heart failure; HR, hazard ratio; PY, patient-years

Treatment effect on kidney and kidney–CV outcomes by CVD history

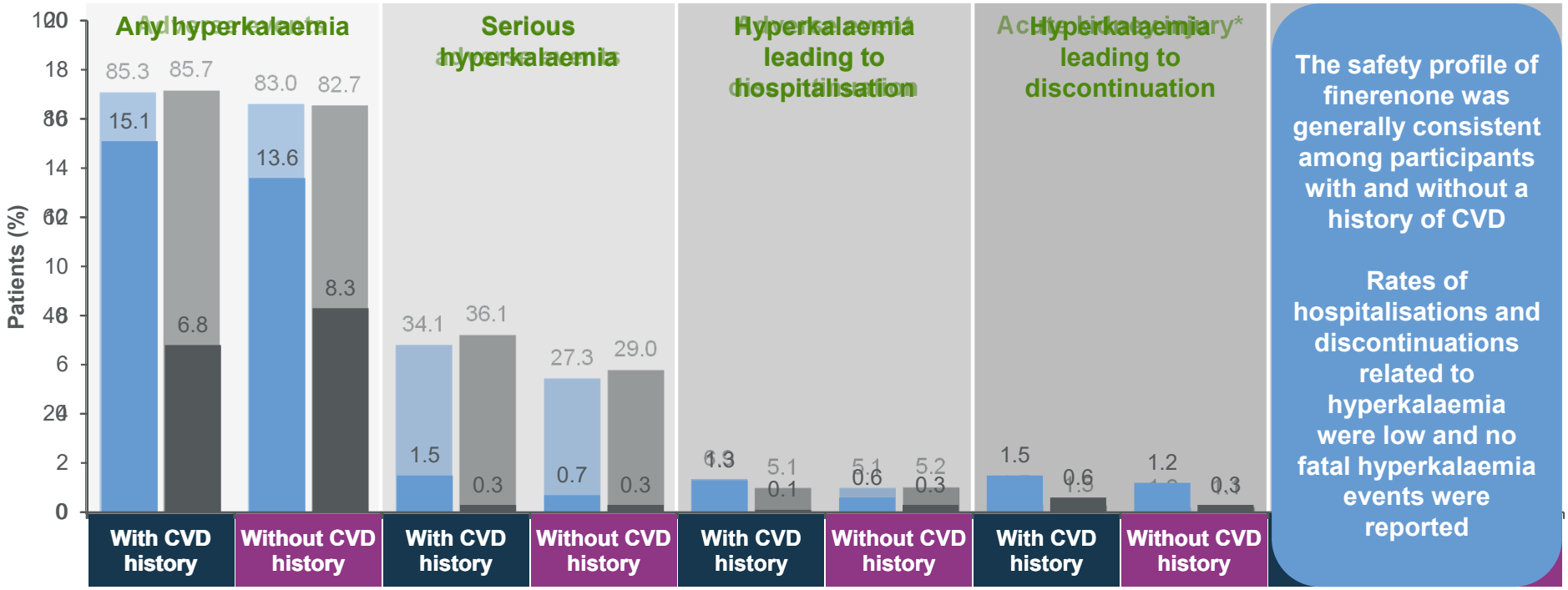
Outcome	Finerenone n/n (%)	Finerenone n/1000 PY	Placebo n/n (%)	Placebo n/1000 PY	HR (95% CI)	*p*-interaction
Kidney composite (≥57% decline in eGFR or kidney failure*)						
Overall	**460/7291 (6.3)**	**22.3**	**589/7283 (8.1)**	**28.8**	**0.76 (0.68–0.86)**	
History of CVD						
With	172/3413 (5.0)	18.7	232/3409 (6.8)	25.4	0.76 (0.63–0.93)	0.966
Without	288/3878 (7.4)	25.3	357/3874 (9.2)	31.6	0.76 (0.65–0.89)	
Kidney–CV composite (≥57% decline in eGFR, kidney failure,* HHF or CV death)						
Overall	**786/7291 (10.8)**	**38.6**	**997/7283 (13.7)**	**49.6**	**0.77 (0.70–0.85)**	
History of CVD						
With	424/3413 (12.4)	47.0	549/3409 (16.1)	61.8	0.77 (0.68–0.87)	0.971
Without	362/3878 (9.3)	32.0	448/3874 (11.6)	39.9	0.77 (0.67–0.88)	
Dialysis or kidney transplantation						
Overall	**189/7291 (2.6)**	**8.5**	**240/7283 (3.3)**	**10.9**	**0.77 (0.64–0.94)**	
History of CVD						
With	72/3413 (2.1)	7.2	98/3409 (2.9)	9.9	0.75 (0.55–1.02)	0.774
Without	117/3878 (3.0)	9.6	142/3874 (3.7)	11.7	0.79 (0.62–1.01)	

Finerenone consistently reduced the risk of CV, kidney and mortality outcomes in participants with and without a history of CVD

*Kidney failure was defined as sustained eGFR <15 ml/min/1.73 m^2, initiation of dialysis or kidney transplantation

CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HHF, hospitalisation for heart failure; HR, hazard ratio; PY, patient-years

Prespecified safety outcomes: Hyperkalaemia



The safety profile of finerenone was generally consistent among participants with and without a history of CVD

Rates of hospitalisations and discontinuations related to hyperkalaemia were low and no fatal hyperkalaemia events were reported

Patients with CVD history: finerenone n=3408, placebo n=3401. Patients without CVD history: finerenone n=3874, placebo n=3864
*Preferred term
CVD, cardiovascular disease

Summary

HF occupies a central position in the CV–kidney continuum:

- HHF was the CV event most strongly associated with subsequent CKD progression
- CKD progression was in turn most strongly associated with subsequent HHF or CV death

Among all non-fatal CV and kidney events, HHF identified patients at highest subsequent risk of death

Finerenone reduced HF, kidney and combined kidney–CV outcomes with no detected heterogeneity according to CVD history

CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; HF, heart failure; HHF, hospitalisation for heart failure

Thank you

We thank all participating patients and their families