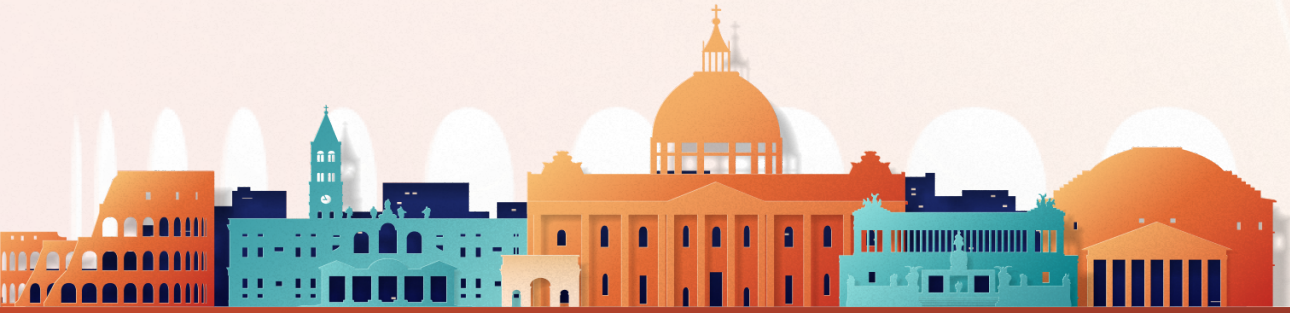
PLACE 2026
PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

CONGRESSO
ROMA, 25 - 27 Giugno 2026

IL CONTINUUM CARDIO-NEFRO-METABOLICO

Finerenone nel paziente con diabete di tipo2, malattia renale cronica ed albuminuria: quando il rischio si fa doppio



Maria Denitza Tinti
A. O. San Camillo - Forlanini

AGENDA

1. **Il rischio nel continuum cardio-nefro-metabolico**

2. **Finerenone nella CKD e nel diabete tipo 2**

   Le evidenze degli studi FIDELIO-DKD, FIGARO-DKD e dell'analisi pooled FIDELITY sugli esiti renali e cardiovascolari.

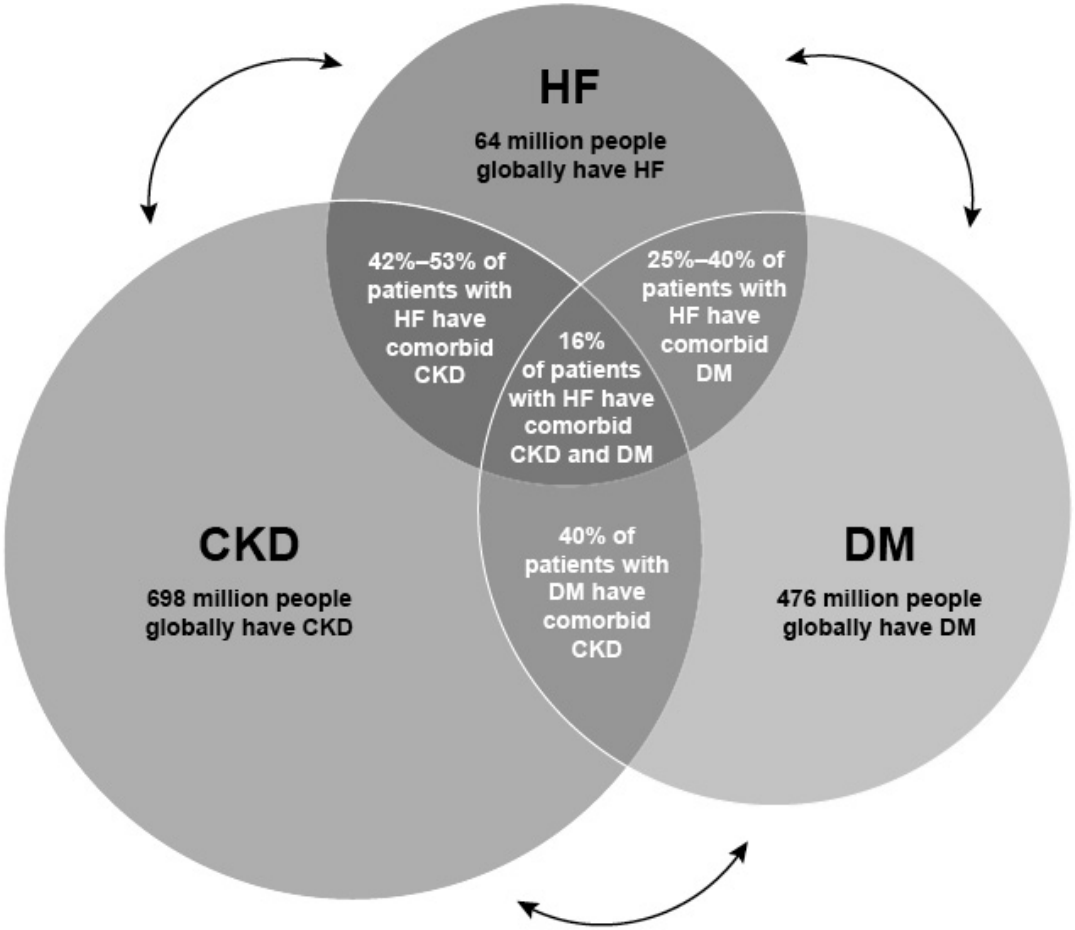
3. **Oltre il rene: lo scompenso cardiaco**

   Finerenone in HFmrEF/HFpEF (FINEARTS-HF)

4. **Oltre la nefropatia diabetica**

   I risultati dello studio FIND-CKD nella CKC non diabetica

MALATTIE CV, CKD E DIABETE SPESSO COESISTONO E SONO STRETTAMENTE CORRELATE

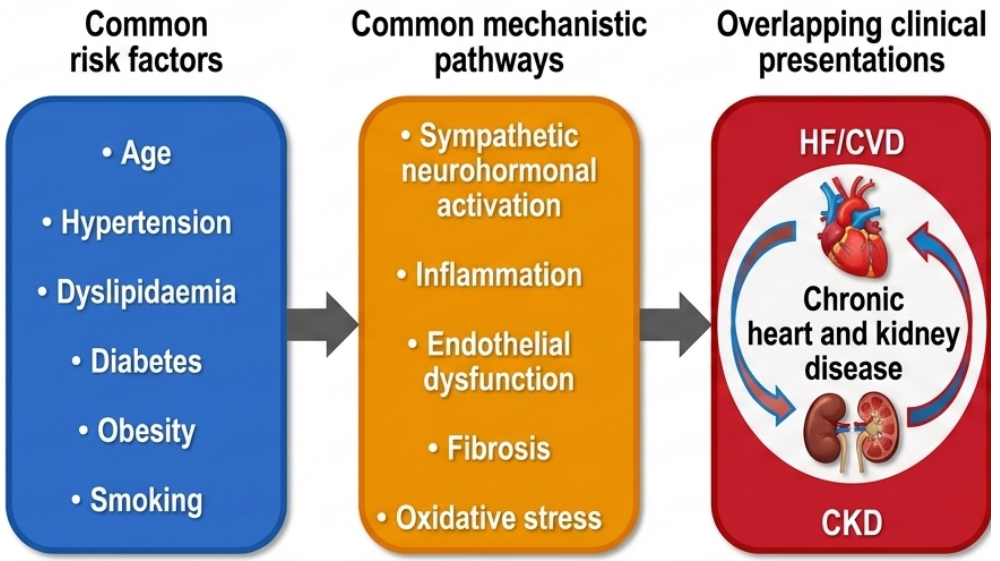


Common risk factors for HF, CKD, and DM:

- Obesity
- Inflammation
- Vascular disease

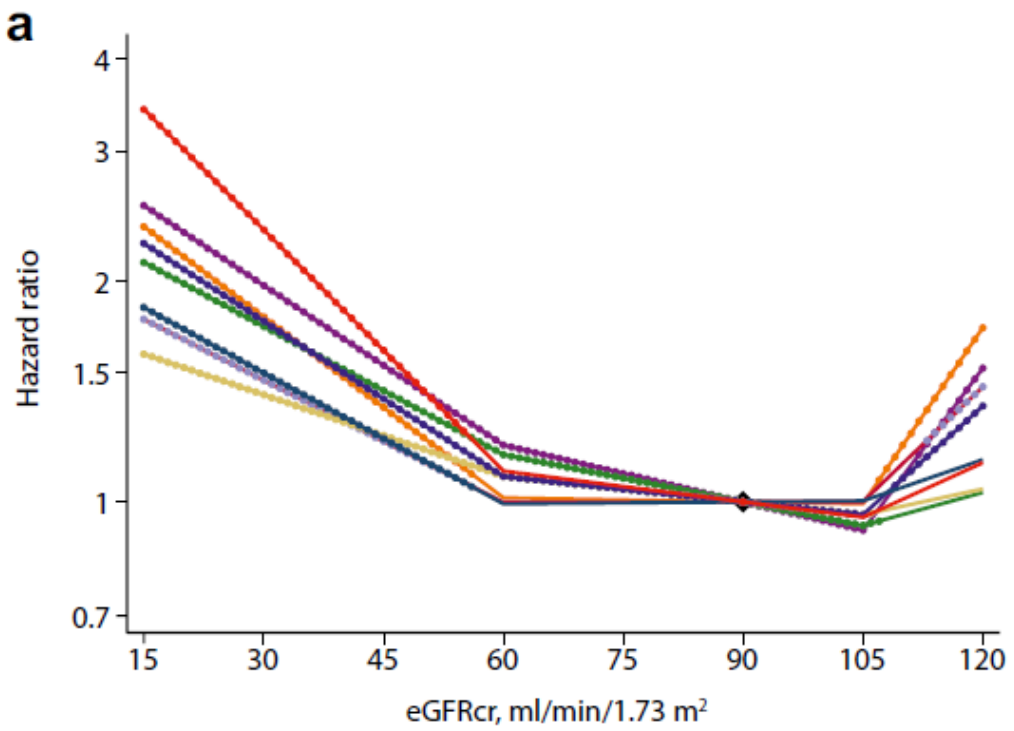
Common risk factors for DM and CKD:

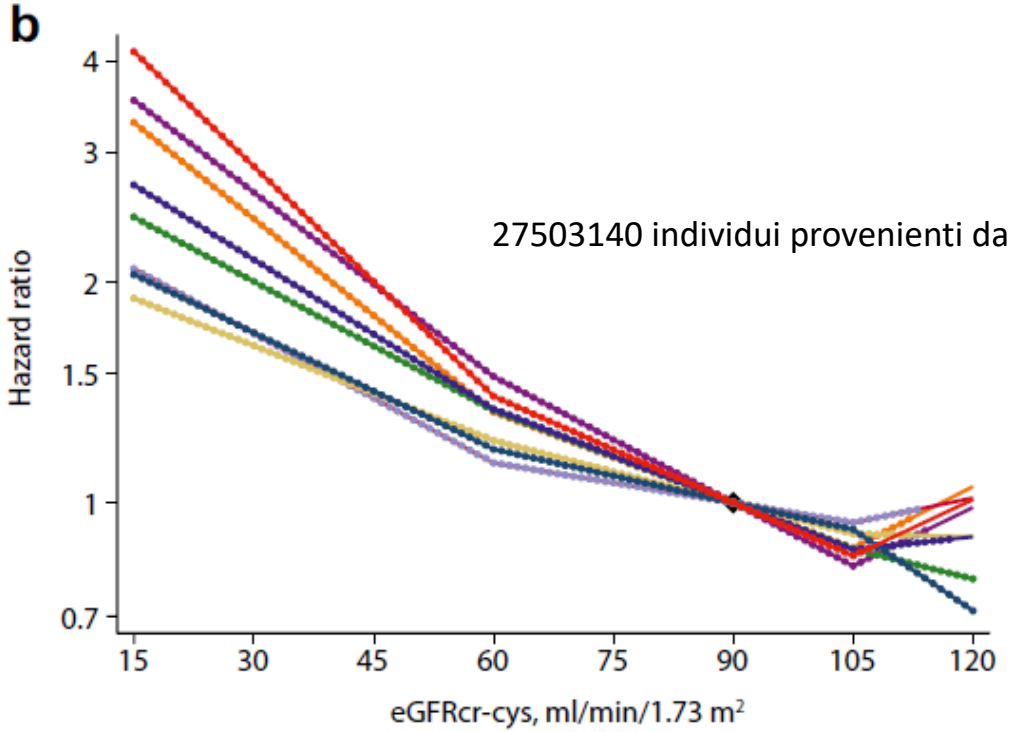
- Older age
- Male sex
- Hypertension
- Smoking



Kris Vijay et al, Cardiorenal Med 2022

HAZARD RATIOS FOR ADVERSE OUTCOMES USING THE CONTINUOUS MODEL OF EGFR





27503140 individui provenienti da 114 coorti,

- All-cause mortality, 721 394 participants; 102 910 events
- Cardiovascular mortality, 719 987 participants; 27 051 events
- All-cause hospitalization, 676 519 participants; 7862 events
- Myocardial infarction, 711 478 participants; 18 659 events
- Stroke, 711 293 participants; 17 609 events
- Heart failure, 674 255 participants; 28 530 events
- Atrial fibrillation, 653 507 participants; 38 224 events
- Peripheral artery disease, 660 412 participants; 4458 events
- Kidney failure with replacement therapy, 637 387 participants; 24 342 events
- Acute kidney injury, 632 452 participants; 466 201 events

Grams ME, , et al. JAMA. 2023

ALBUMINURIA AND HF RISK

UACR and HF risk

Continuous, graded risk with increasing UACR levels for new onset HF

RENAAL	2.7-fold	
SPRINT	2.6-fold	
UK biobank	3-fold	
ARIC study	<30 mg/g	1.9-fold
	30–299 mg/g	2.5-fold
T2DM cohort	30–300 mg/g	2.2-fold
	≥300 mg/g	6-fold
AF cohort	1.8-fold	
MESA study	2.7-fold	
FHS study	1.7-fold	

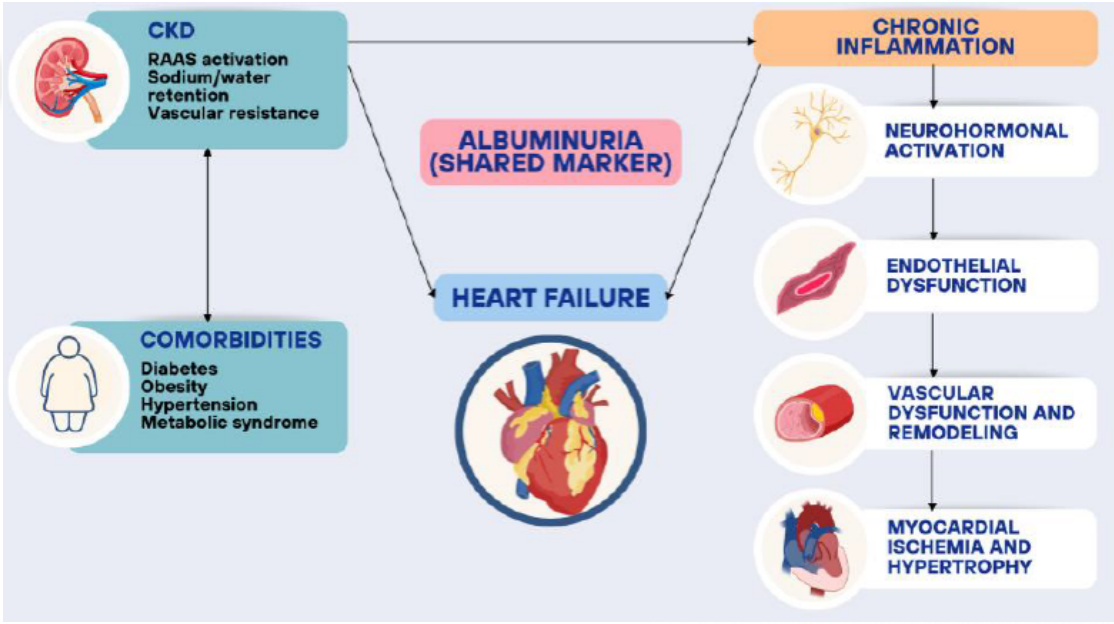
Risk marker for progression of HF

Albuminuria and HF

Risk marker for incident HF

Albuminuria independently predicts risk of hospitalizations for HF and mortality

CHARM	60–80%	higher mortality
	30–70%	higher HHF
SOLVD	1.8-fold	HHF risk
ASPREE	1.5-fold	HHF risk
	1.6-fold	mortality risk
	1.3-fold	HHF risk
EMPA-REG	2.2-fold	HHF/CV death risk increase with each 10-fold increment
Acute HF	1.47-fold	mortality risk
CHART-2	Independent predictor of mortality in HFpEF	
TOPCAT	Higher UACR linked to HF readmission	

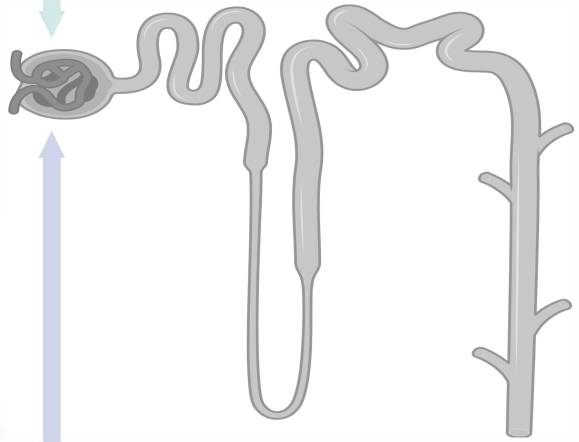


Butler J et al, Eur Heart J 2026

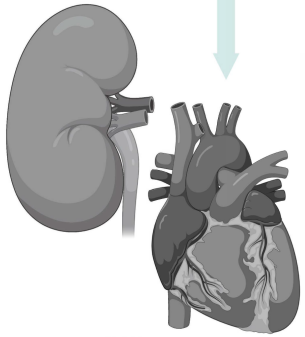
GDMT COMPLIMENTARY EFFECTS IN CKM

POTENTIAL PILLAR 4: GLP- 1RAs
- Decrease weight
- Decrease dyslipidemia
- Decrease oxidative stress
- Decrease endothelial dysfunction

PILLAR 1: RAS blockers
- Decrease efferent arteriole tone
- Decrease hyperfiltration
- Decrease endothelial dysfunction
- Decrease cardiac remodeling



Metabolic Dysregulation



Hemodynamic Perturbations

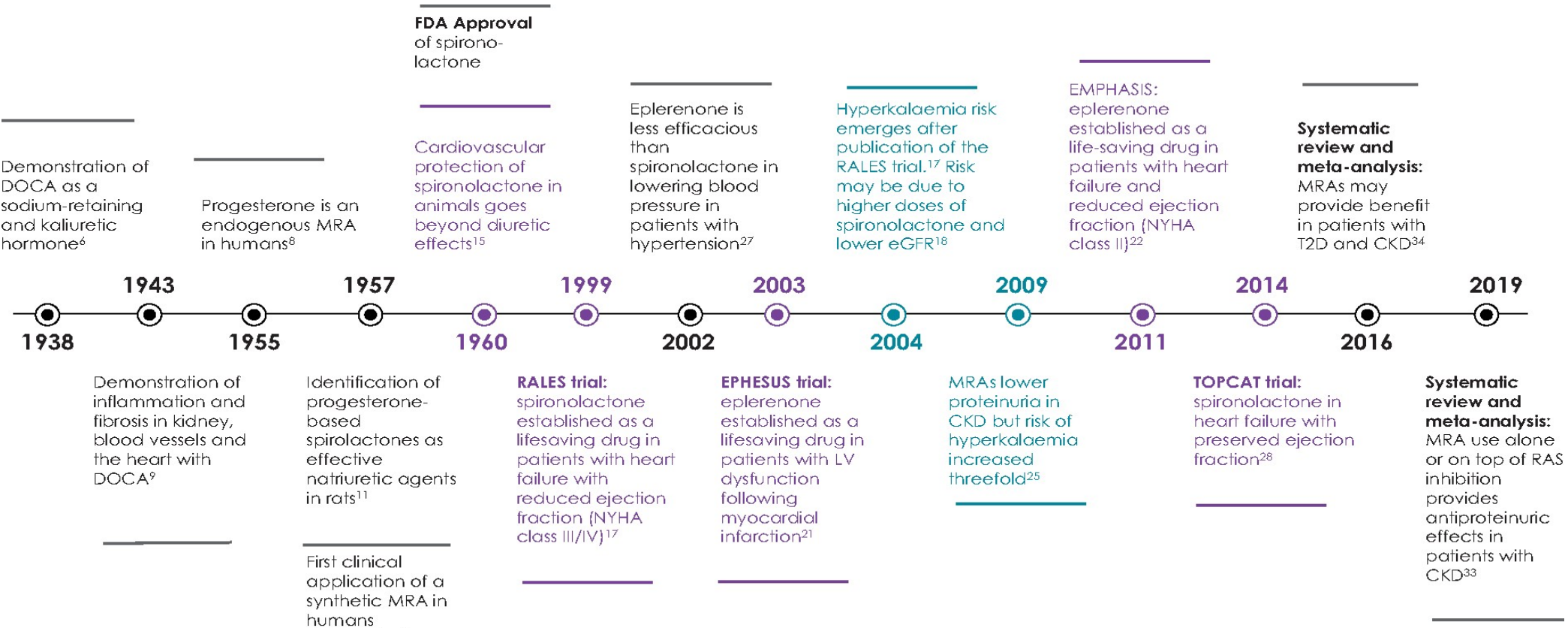
Inflammation

PILLAR 3: Finerenone
- Decreases inflammation
- Decreases fibrosis
- Decreases endothelial dysfunction
- Decreases tissue remodeling
- Decreases proteinuria

PILLAR 2: SGLT2 inhibitors
- Increase afferent arteriole tone
- Improve tubuloglomerular feedback
- Decrease hyperfiltration
- Decrease proteinuria
- Decrease oxidative stress
- Increase anti–inflammatory and anti–fibrotic effects

Naaman SC et al, Diabetes Care 2023

KEY STUDIES IN THE HISTORY OF MRAs



TEXT = Milestones

TEXT = Cardiac effects

TEXT = Risk of hyperkalaemia

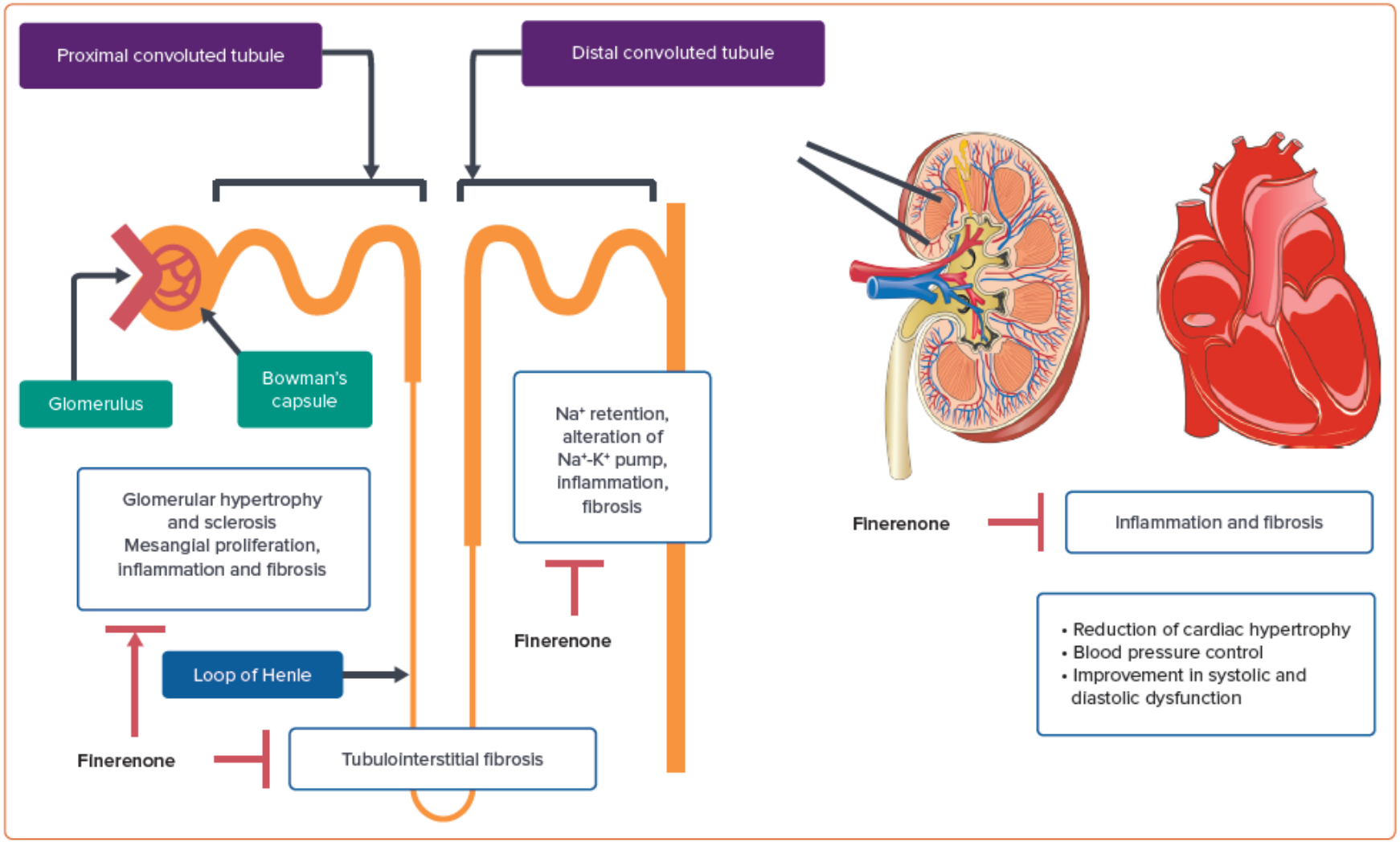
Eur Heart J, Volume 42, Issue 2, 7 January 2021

STEROIDAL VS NON-STEROIDAL MRAS

Steroidal MRA	Nonsteroidal MRA
• Spironolactone and eplerenone	• Finerenone, esaxerenone, balcinerenone
• Function as partial agonists	• Function as inverse agonists or partial antagonists
• Lower potency	• Higher potency
• Dose-related increase in potassium	• Lower rates of hyperkalemia
• Less selectivity	• Greater selectivity
• More sexual side effects	• Minimal to no sexual side effects

Chang J, et al. JACC Heart Fail. 2024

MECCANISMO D'AZIONE DEL FINERENONE



- Antagonista non steroideo del recettore dei mineralcorticoidi (MR)
- Blocco selettivo dell'attivazione patologica mediata da aldosterone e cortisolo
- Riduzione dell'infiammazione e della fibrosi a livello renale, cardiaco e vascolare
- Potenza superiore rispetto agli MRA steroidei con migliore selettività

Khullar D, Gupta AK, Singh K. Citation: Cardiac Failure Review 2024;10:e19.

2020

FIDELIO-DKD

Primary renal outcome: ≥40% sustained decline in eGFR, kidney failure or renal death.

DM CKD.

FIDELIO-DKD

2021

FIGARO-DKD

Secondary renal outcome: ≥40% sustained decline in eGFR, kidney failure or renal death.

DM CKD.

FIGARO-DKD

2024

FINEARTS-HF

Secondary renal outcome: ≥40% sustained decline in eGFR, kidney failure or renal death. ***HFpEF, HFmrEF.***

2026

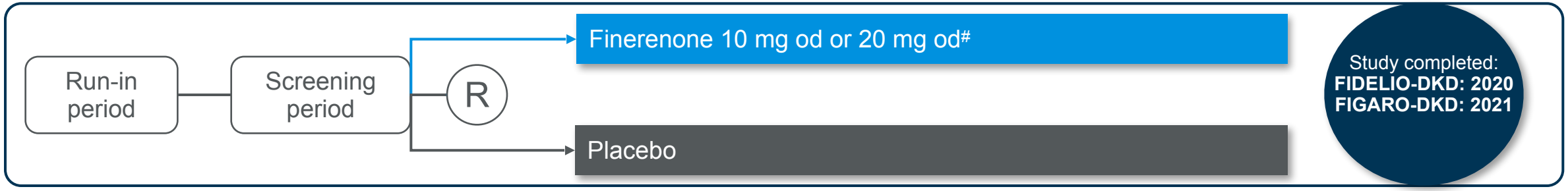
FIND-CKD

Primary renal outcome: Mean annual rate of change in eGFR from baseline to Month 32.

Non-diabetic CKD.

FIND-CKD

FIDELIO-DKD and FIGARO-DKD : effects of finerenone on kidney and CV outcomes in patients with CKD and T2D

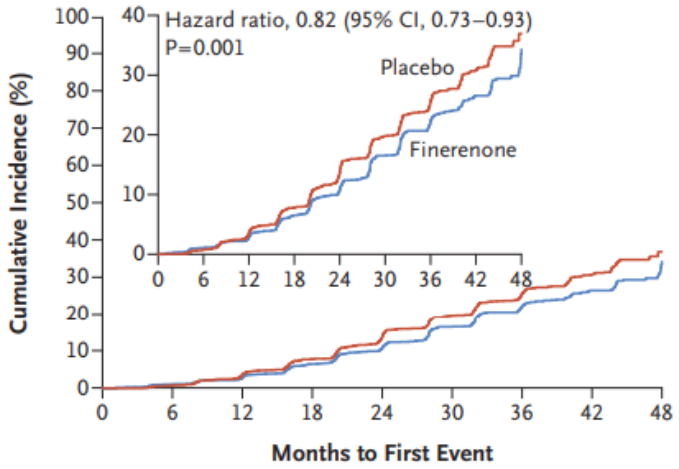


	FIDELIO-DKD[1]	FIGARO-DKD[2]
Clinical efficacy primary endpoint	Composite endpoint: time to onset of kidney failure* or decrease of eGFR ≥40% from baseline or death due to kidney disease	Composite endpoint: time to CV death, non-fatal MI, non-fatal stroke or hospitalisation for HF
Key secondary endpoints	Same as primary endpoint in FIGARO-DKD	Same as primary endpoint in FIDELIO-DKD
Enrolled patients	5734 patients with: • ACR 30-300 mg/g and eGFR 25-60 mL/min/1.73 m². • ACR 300-5000 and eGFR 25-75 mL/min/1.73 m².	7437 patients with: • ACR 30-300 mg/g and eGFR 25-90 mL/min/1.73 m². • ACR 300-5000 and eGFR >60 mL/min/1.73 m².

Bakris GL, *et al. Am J Nephrol* 2019;50:333–344; Ruilope LM, *et al. Am J Nephrol* 2019;50:345–356;

Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes

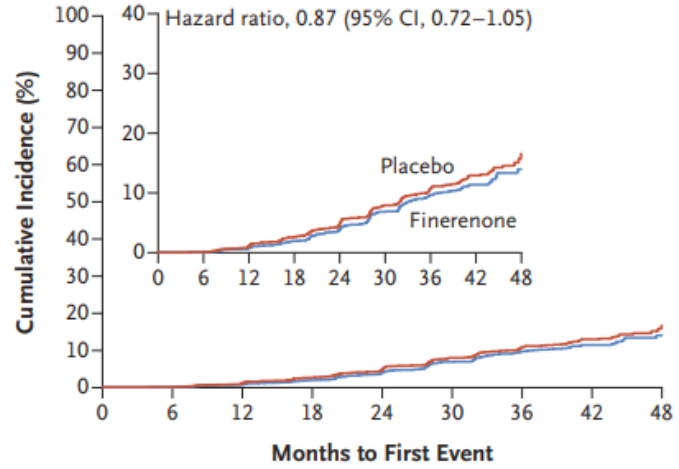
A Primary Composite Outcome



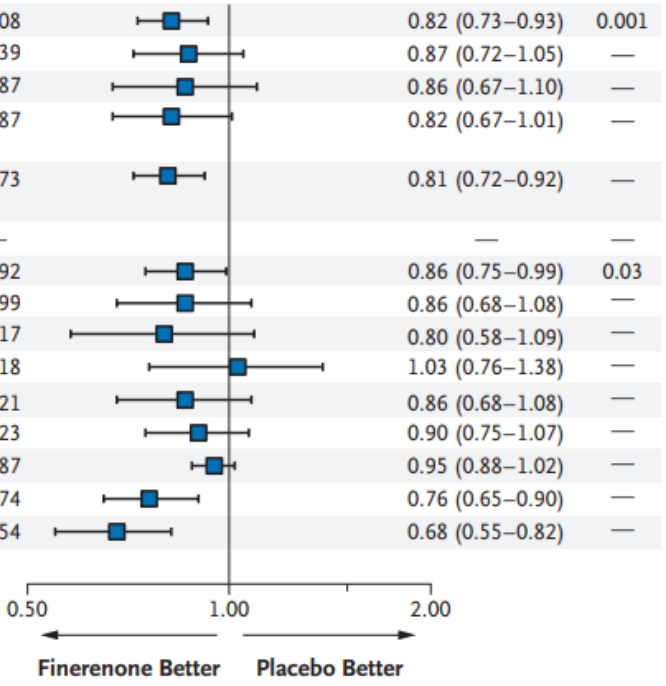
No. at Risk

Placebo	2841	2724	2586	2379	1758	1248	792	453	82
Finerenone	2833	2705	2607	2397	1808	1274	787	441	83

C Kidney Failure



Outcome	Finerenone (N=2833)	Placebo (N=2841)	Finerenone (N=2833)	Placebo (N=2841)	Hazard Ratio (95% CI)	P Value
	no. of patients with event (%)		*no. of patients with event per 100 patient-yr*			
Primary composite outcome	504 (17.8)	600 (21.1)	7.59	9.08	0.82 (0.73–0.93)	0.001
Kidney failure	208 (7.3)	235 (8.3)	2.99	3.39	0.87 (0.72–1.05)	—
End-stage kidney disease	119 (4.2)	139 (4.9)	1.60	1.87	0.86 (0.67–1.10)	—
Sustained decrease in eGFR to <15 ml/min/1.73 m^2	167 (5.9)	199 (7.0)	2.40	2.87	0.82 (0.67–1.01)	—
Sustained decrease of ≥40% in eGFR from baseline	479 (16.9)	577 (20.3)	7.21	8.73	0.81 (0.72–0.92)	—
Death from renal causes	2 (<0.1)	2 (<0.1)	—	—	—	—
Key secondary composite outcome	367 (13.0)	420 (14.8)	5.11	5.92	0.86 (0.75–0.99)	0.03
Death from cardiovascular causes	128 (4.5)	150 (5.3)	1.69	1.99	0.86 (0.68–1.08)	—
Nonfatal myocardial infarction	70 (2.5)	87 (3.1)	0.94	1.17	0.80 (0.58–1.09)	—
Nonfatal stroke	90 (3.2)	87 (3.1)	1.21	1.18	1.03 (0.76–1.38)	—
Hospitalization for heart failure	139 (4.9)	162 (5.7)	1.89	2.21	0.86 (0.68–1.08)	—
Death from any cause	219 (7.7)	244 (8.6)	2.90	3.23	0.90 (0.75–1.07)	—
Hospitalization for any cause	1263 (44.6)	1321 (46.5)	22.56	23.87	0.95 (0.88–1.02)	—
Secondary composite kidney outcome	252 (8.9)	326 (11.5)	3.64	4.74	0.76 (0.65–0.90)	—
Sustained decrease of ≥57% in eGFR from baseline	167 (5.9)	245 (8.6)	2.41	3.54	0.68 (0.55–0.82)	—



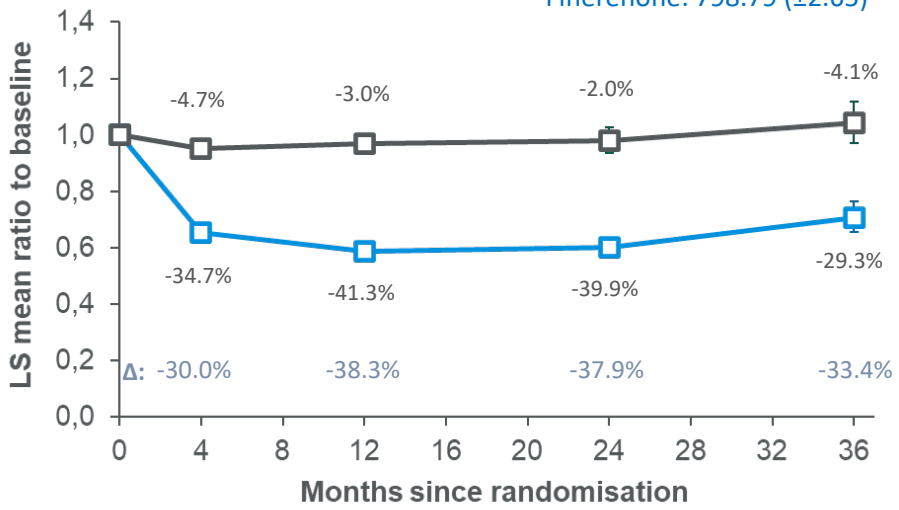
Nei pazienti affetti da CKD e DM tipo 2, il trattamento con finerenone ha determinato un rischio inferiore di progressione della malattia renale cronica e di eventi cardiovascolari rispetto al placebo.

Bakris et al- N Engl J Med 2020;383:2219-29.

FINERENONE RIDUCE L'UACR A PARTIRE DAL 4 MESE E IL PEGGIORAMENTO DELL' EGFR

uACR

At baseline:
Placebo: 814.74 (±2.67)
Finerenone: 798.79 (±2.65)

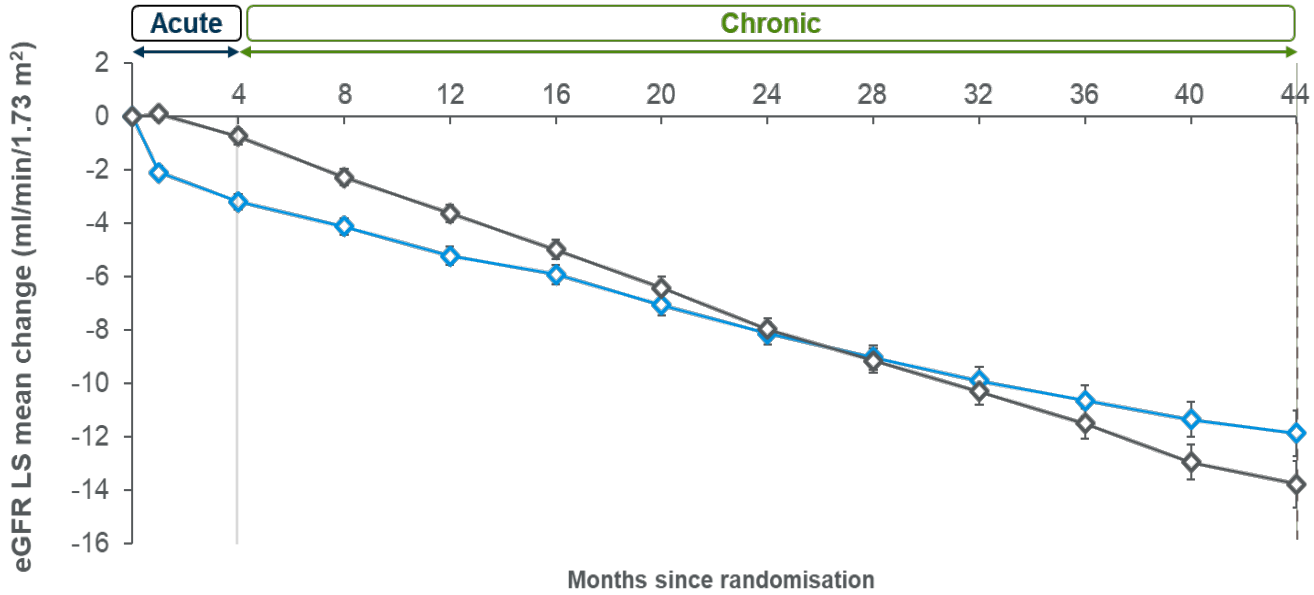


No. of patients				
Finerenone 2831	2582	1841	856
Placebo 2840	2598	1825	834

Ratio of least-squares mean change from baseline [Finerenone vs placebo]= **0.69; 95% CI 0.66–0.71**

eGFR

FIDELIO-DKD



Finerenone	2799	2722	2613	1870	867	336
Placebo	2800	2720	2611	1846	844	339

At baseline:
Placebo: 44.3 (±12.6)
Finerenone: 44.4 (± 12.6)

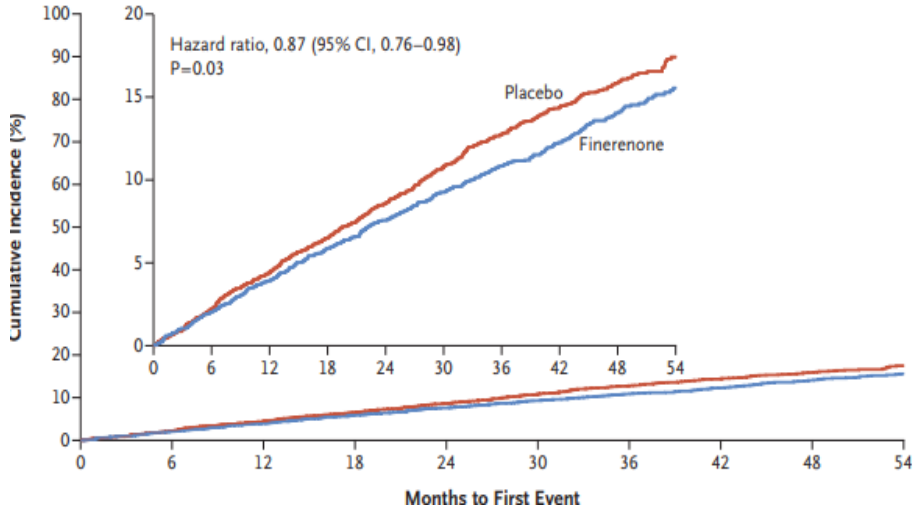
→

Acute eGRF change:
Placebo: -0.73 (-1.03 to -0.44)
Finerenone: -3.18 (-3.44 to -2.91)

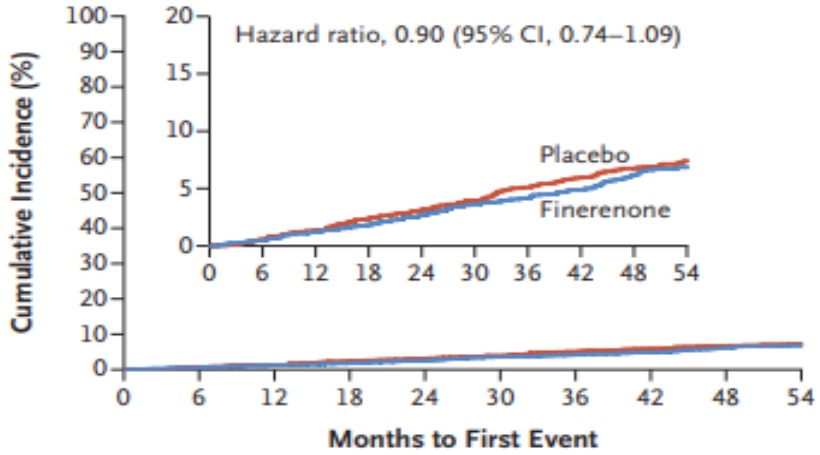
Chronic annulised eGRF change:
Placebo: -3.97 (-4.27 to -3.66)
Finerenone: -2.66 (-2.96 to -2.36)

Bakris et al- N Engl J Med 2020;383:2219-29.

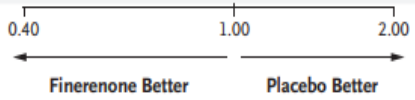
Cardiovascular Events with Finerenone in Kidney Disease and Type 2 Diabetes



Death from Cardiovascular Causes



Outcome	Finerenone (N=3686)	Placebo (N=3666)	Finerenone (N=3686)	Placebo (N=3666)	Hazard Ratio (95% CI)	P Value
	no. of patients with event (%)		*no. of patients with event per 100 patient-yr*			
Primary composite outcome	458 (12.4)	519 (14.2)	3.87	4.45	0.87 (0.76–0.98)	0.03
Death from cardiovascular causes	194 (5.3)	214 (5.8)	1.56	1.74	0.90 (0.74–1.09)	—
Nonfatal myocardial infarction	103 (2.8)	102 (2.8)	0.85	0.85	0.99 (0.76–1.31)	—
Nonfatal stroke	108 (2.9)	111 (3.0)	0.89	0.92	0.97 (0.74–1.26)	—
Hospitalization for heart failure	117 (3.2)	163 (4.4)	0.96	1.36	0.71 (0.56–0.90)	—
Kidney composite outcome with ≥40% decrease in eGFR	350 (9.5)	395 (10.8)	3.15	3.58	0.87 (0.76–1.01)	—
Kidney failure	46 (1.2)	62 (1.7)	0.40	0.54	0.72 (0.49–1.05)	—
End-stage kidney disease	32 (0.9)	49 (1.3)	0.26	0.40	0.64 (0.41–0.995)	—
Sustained decrease in eGFR of <15 ml/min/1.73 m^2	28 (0.8)	38 (1.0)	0.24	0.33	0.71 (0.43–1.16)	—
Sustained ≥40% decrease in eGFR from baseline	338 (9.2)	385 (10.5)	3.04	3.49	0.87 (0.75–1.00)	—
Death from renal causes	0	2 (0.1)	—	—	—	—
Hospitalization for any cause	1573 (42.7)	1605 (43.8)	16.9	17.5	0.97 (0.90–1.04)	—
Death from any cause	333 (9.0)	370 (10.1)	2.68	3.01	0.89 (0.77–1.04)	—
Kidney composite outcome with ≥57% decrease in eGFR	108 (2.9)	139 (3.8)	0.95	1.23	0.77 (0.60–0.99)	—
Sustained ≥57% decrease in eGFR from baseline	90 (2.4)	116 (3.2)	0.79	1.02	0.76 (0.58–1.00)	—

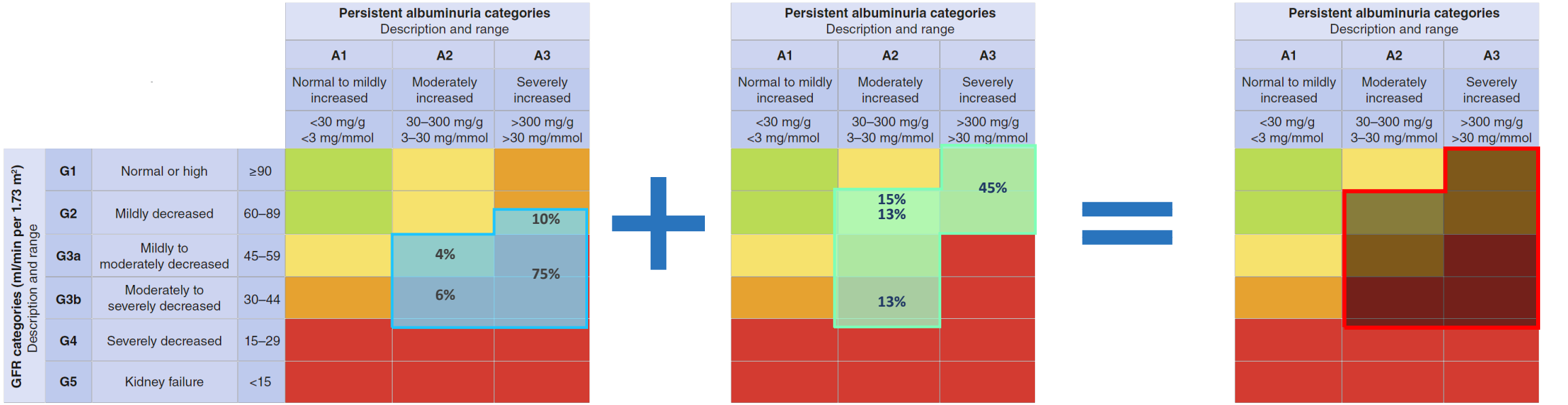


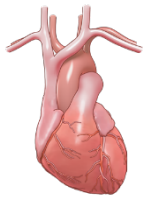
Nei pazienti con DM tipo 2 e CKD stadio da 2- 4 con albuminuria moderatamente elevata o CKD stadio 1 o 2 con albuminuria elevata, la terapia con finerenone ha migliorato gli endpoint cardiovascolari rispetto al placebo.

N Engl J Med 2021;385:2252-63.

FIDELITY POOLED ANALYSIS

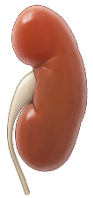
FIDELIO-DKD + **FIGARO-DKD** = **FIDELITY** (FIDELIO-DKD + FIGARO-DKD pooled)





PRIMARY CV ENDPOINT

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



KEY SECONDARY KIDNEY ENDPOINT

Time to kidney failure (initiation of chronic dialysis for ≥90 days, kidney transplantation or sustained eGFR <15 ml/min/1.73 m²), **sustained ≥57% decrease in eGFR from baseline, or renal death**

30≤UACR<300 mg/g and
25≤eGFR<90 mL/min/1.73m²

or

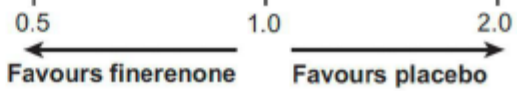
300≤UACR≤5000 mg/g and
eGFR≥25 mL/min/1.73m²

1. KDIGO. *Kidney Int* 2020;98:S1–S115; 2. Rutkowski M, *et al*. *Am J Nephrol* 2019;50:345–356; 3. Bakris GL, *et al*. *Am J Nephrol* 2019;50:333–344 4. Agarwal R et al. *Eur Heart J* 2021. DOI: 10.1093/eurheartj/ehab777/6423104

Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis

FIDELITY
(FIDELIO-DKD + FIGARO-DKD pooled)

Outcome	Finerenone (n = 6519)		Placebo (n = 6507)		Hazard ratio (95% CI)	*P*-value[a]
	Number of patients with event (%)	Number of patients with event per 100 patient-years	Number of patients with event (%)	Number of patients with event per 100 patient-years		
Composite cardiovascular outcome[b]	825 (12.7)	4.34	939 (14.4)	5.01	0.86 (0.78–0.95)	0.0018
Death from cardiovascular causes	322 (4.9)	1.61	364 (5.6)	1.84	0.88 (0.76–1.02)	0.092
Non-fatal myocardial infarction	173 (2.7)	0.88	189 (2.9)	0.97	0.91 (0.74–1.12)	0.36
Non-fatal stroke	198 (3.0)	1.01	198 (3.0)	1.02	0.99 (0.82–1.21)	0.95
Hospitalization for heart failure	256 (3.9)	1.31	325 (5.0)	1.68	0.78 (0.66–0.92)	0.0030
eGFR ≥57% composite kidney outcome[c]	360 (5.5)	1.96	465 (7.1)	2.55	0.77 (0.67–0.88)	0.0002
Kidney failure	254 (3.9)	1.38	297 (4.6)	1.62	0.84 (0.71–0.99)	0.039
End-stage kidney disease[d]	151 (2.3)	0.76	188 (2.9)	0.96	0.80 (0.64–0.99)	0.040[e]
Sustained decrease in eGFR to <15 mL/min/1.73 m²	195 (3.0)	1.06	237 (3.6)	1.29	0.81 (0.67–0.98)	0.026[e]
Sustained ≥57% decrease in eGFR from baseline	257 (3.9)	1.40	361 (5.5)	4.03	0.70 (0.60–0.83)	< 0.0001
Renal death	2 (<0.1)	0.01	4 (<0.1)	0.02	0.53 (0.10–2.91)	0.46[e]
eGFR ≥40% composite kidney outcome[f]	854 (13.1)	4.81	995 (15.3)	5.64	0.85 (0.77–0.93)	0.0004
Sustained ≥40% decrease in eGFR from baseline	817 (12.5)	4.60	962 (14.8)	5.45	0.84 (0.76–0.92)	0.0002
Death from any cause	552 (8.5)	2.76	614 (9.4)	3.10	0.89 (0.79–>1.00[g])	0.051[e]
Hospitalization for any cause	2836 (43.5)	19.04	2926 (45.0)	19.91	0.96 (0.91–1.01)	0.087[e]

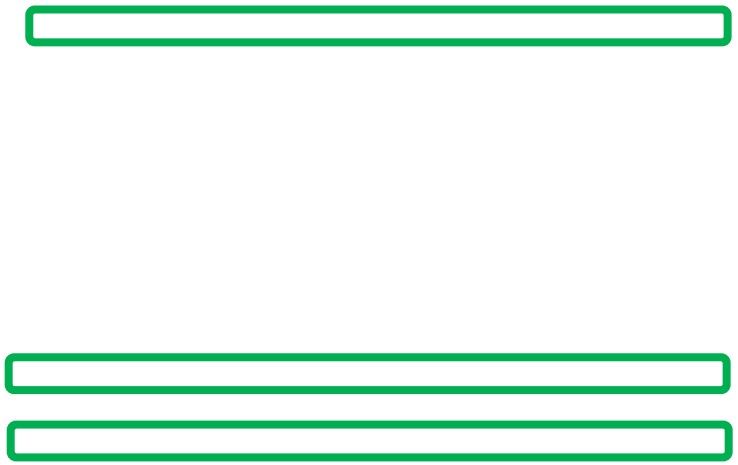


Agarwal R, *et al. Eur J Heart* 2022;43:474–484

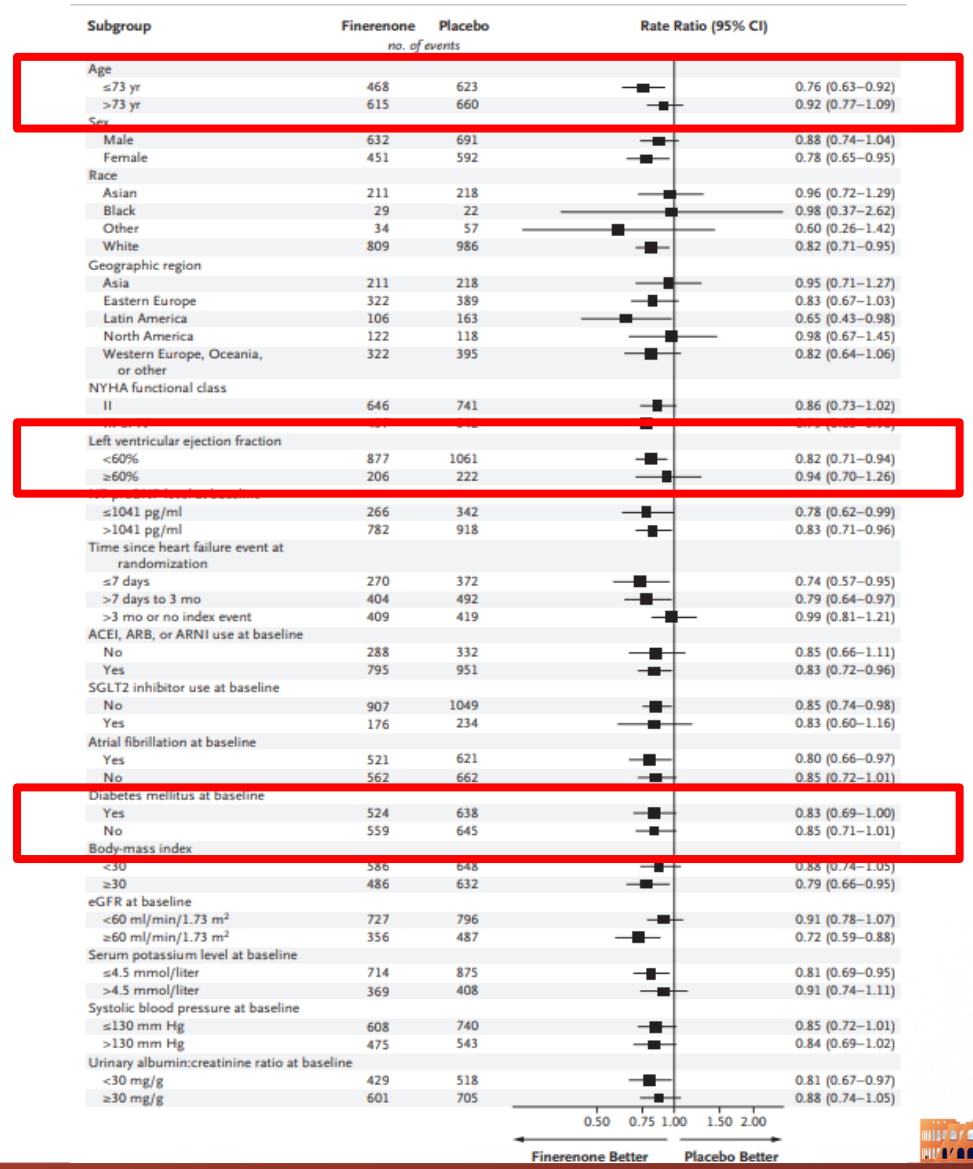
Efficacy and safety profile of finerenone in patients with symptomatic HF (vs placebo; N=6016)

Population:
Patients with HF (NYHA class II–IV) and LVEF ≥40%)

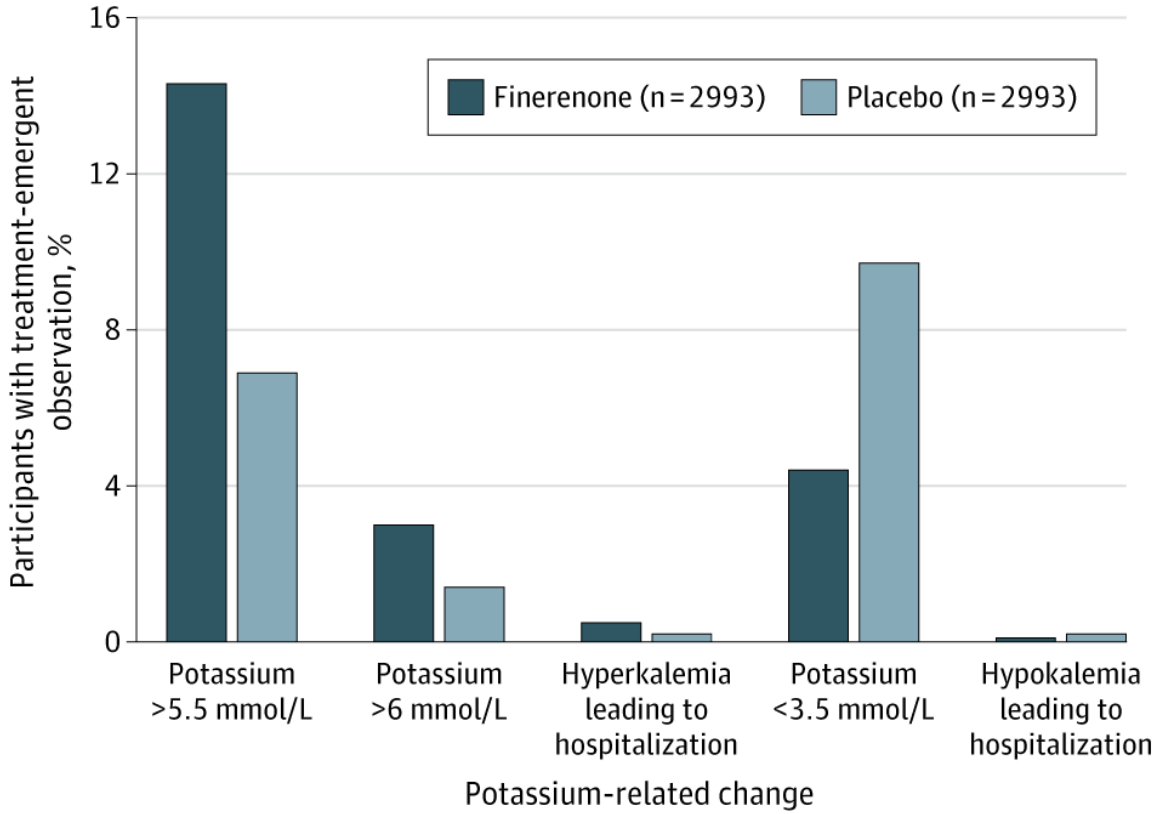
Primary outcome:
Total number of CV deaths and HF events



Solomon S et al. N Engl J Med 2024;391:1475-85



Solomon S et al. N Engl J Med 2024;391:1475-85



Solomon S et al. N Engl J Med 2024;391:1475-85. Vardeny O. et al. JAMA Cardiol. 2025

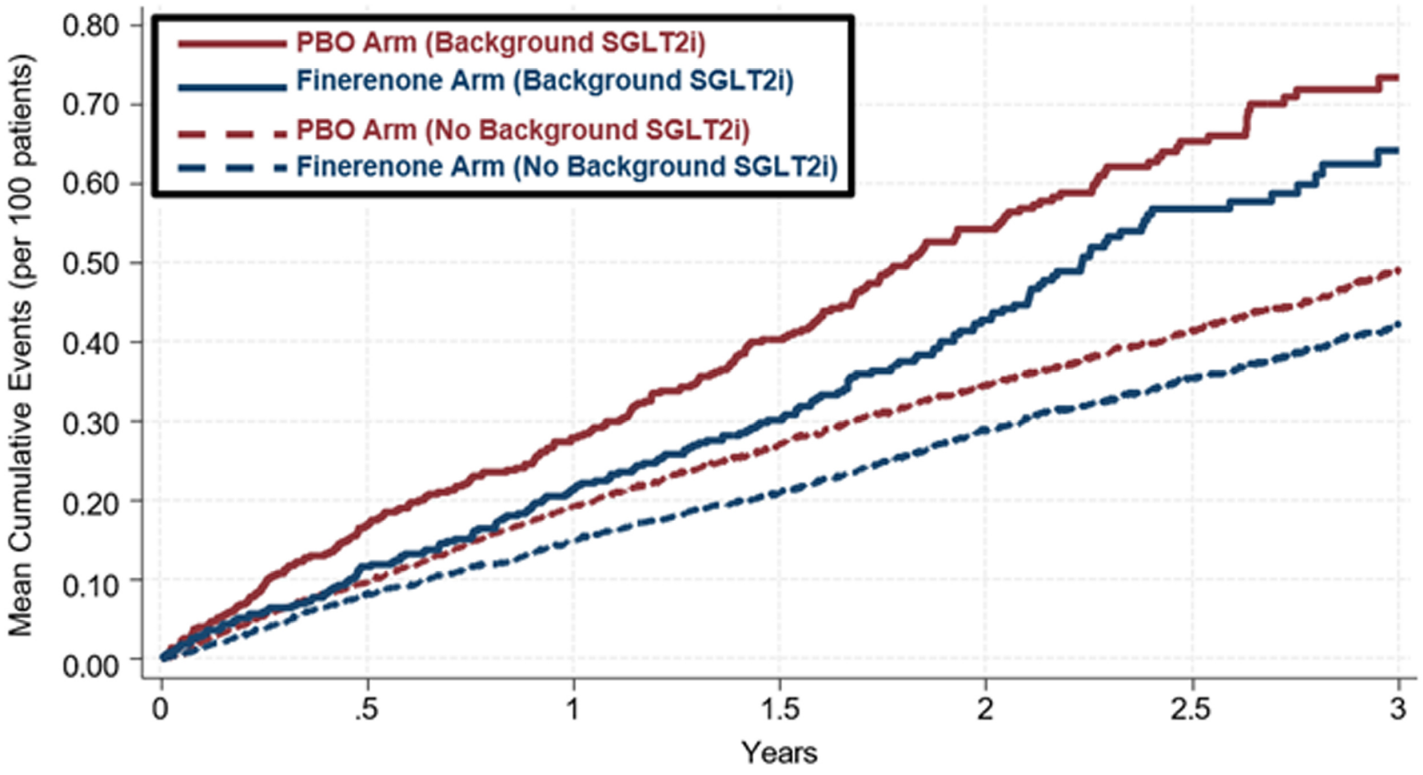
Lower risk population: baseline UACR <<< FIDELIO-DKD/FIGARO-DKD

T2DM: 41% pts

Shorter duration of follow-up

FR McCausland et al, JACC 2025

CV Death and Total Worsening HF Events

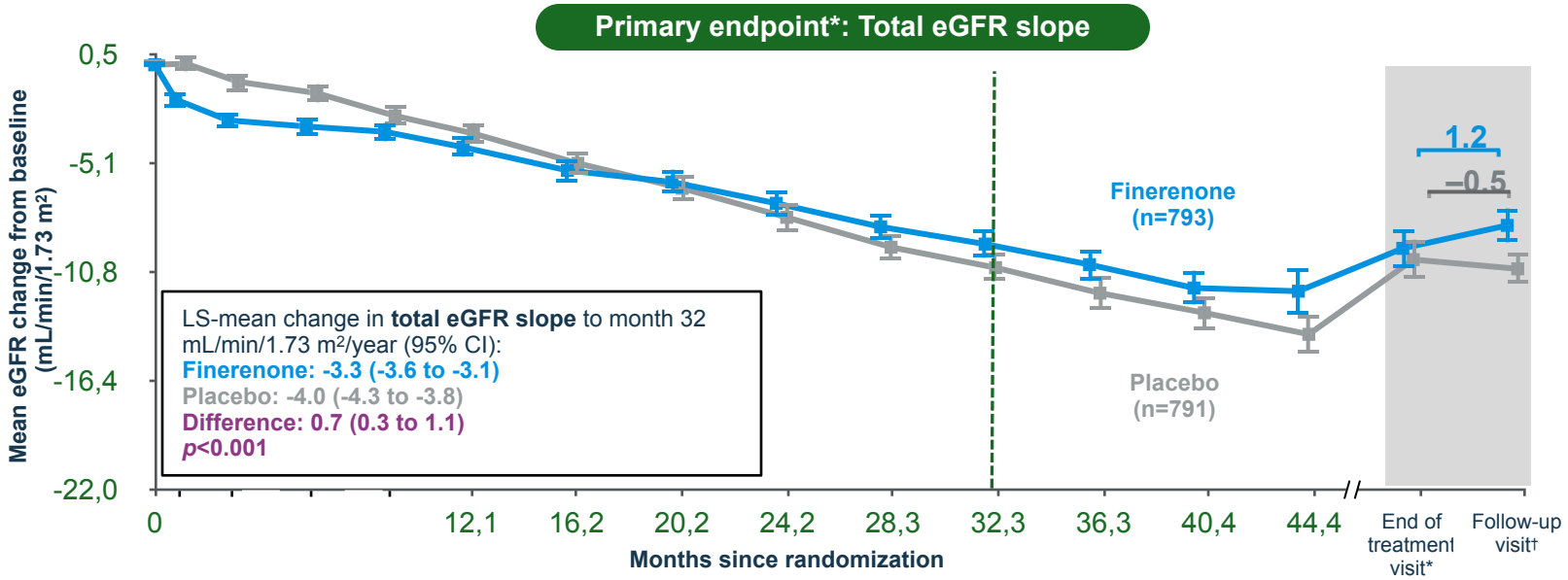


SGLT2i Subgroup (n=817):
RR 0.83; 95% CI 0.60-1.16
ARR 4.7 per 100py

No SGLT2i Subgroup (n=5,184):
RR 0.85; 95% CI 0.74-0.98
ARR 2.5 per 100py

$p_{interaction}$ = 0.76

Vaduganathan M et al, Circulation



Finerenone was associated with a statistically significant reduction in total eGFR slope versus placebo (0.7mL/min/1.73 m²/year [95% CI 0.3–1.1]; *p*<0.001) over 32 months of treatment

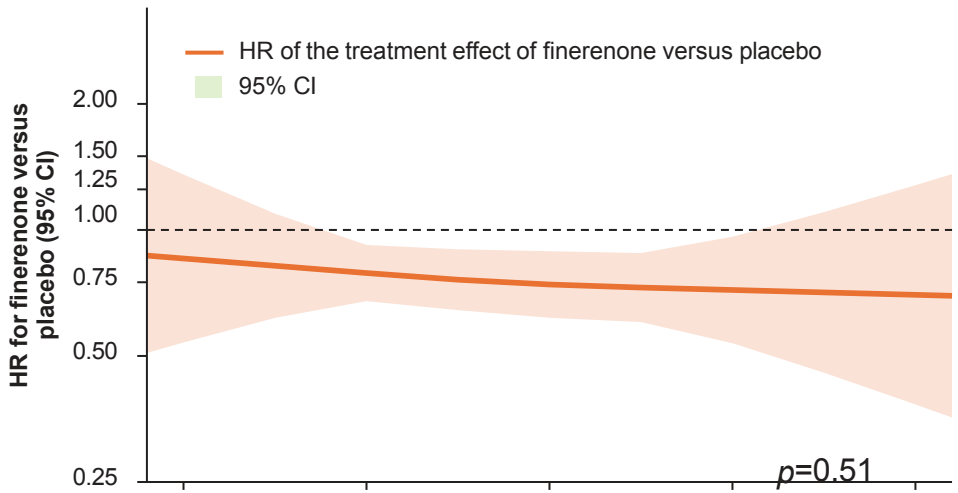
Pts with nd-CKD at risk of progression despite optimized ACEi/ ARB therapy

Finerenone 10/20 mg vs/placebo

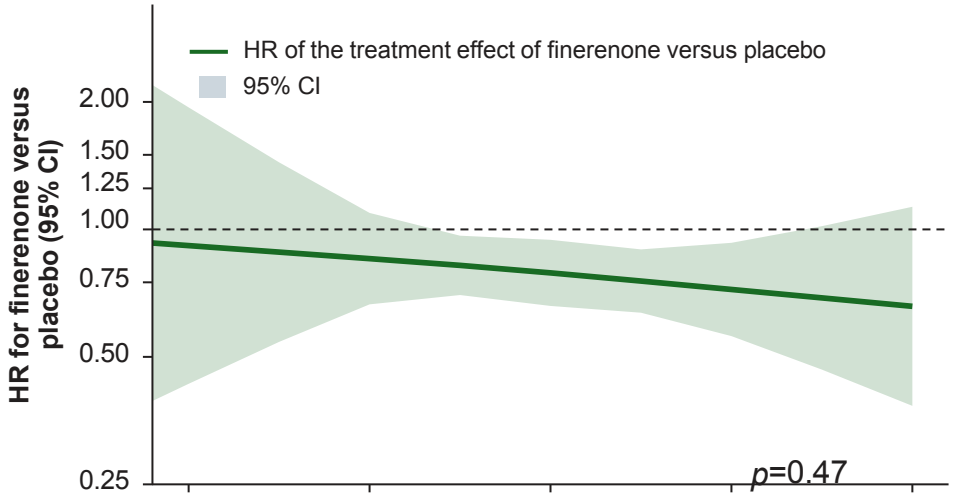
Primary endpoint – Total eGFR slope
Secondary efficacy outcomes
Combined cardio–kidney endpoint

COMPOSITE KIDNEY CARDIOVASCULAR OUTCOME

Composite kidney outcome*

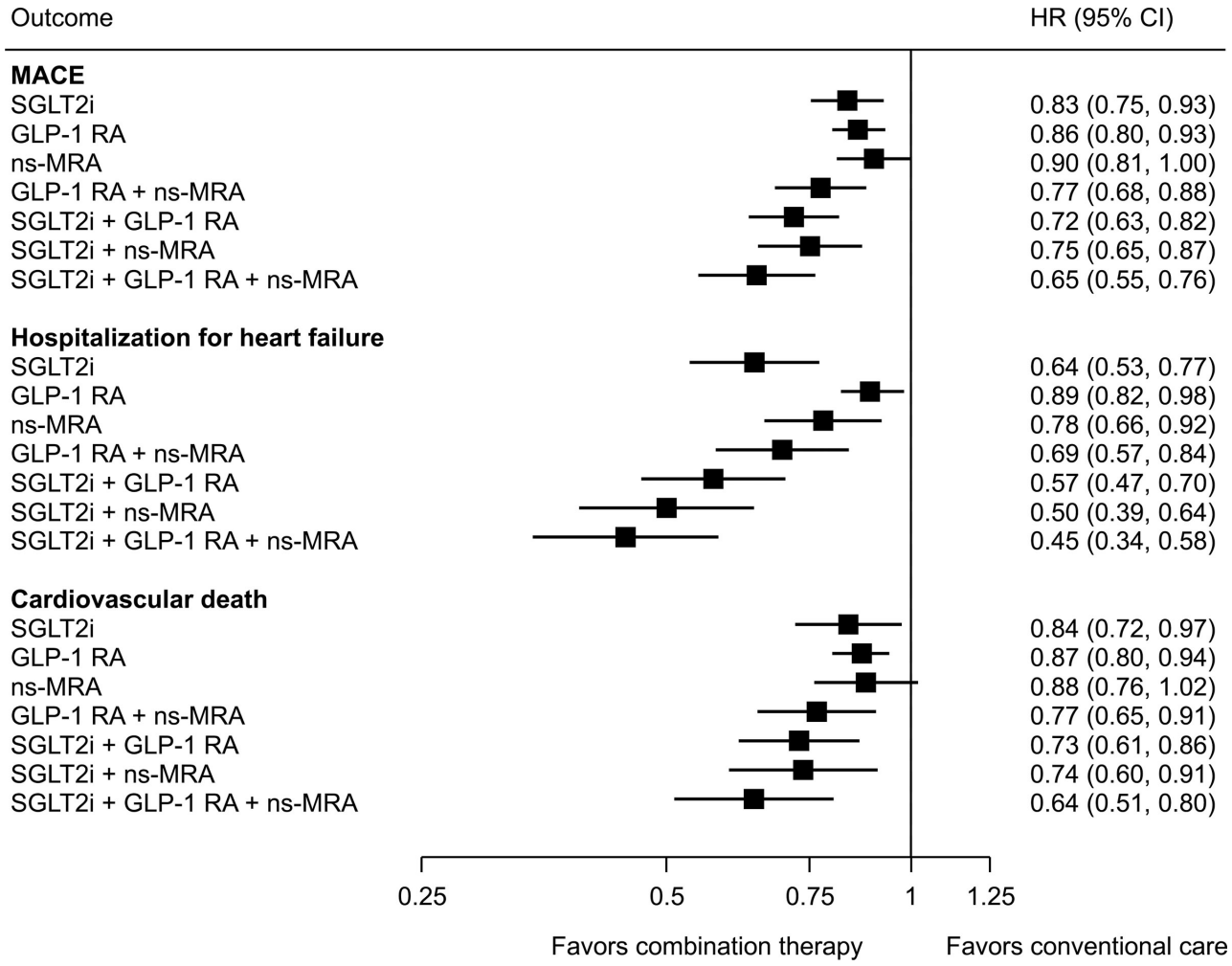


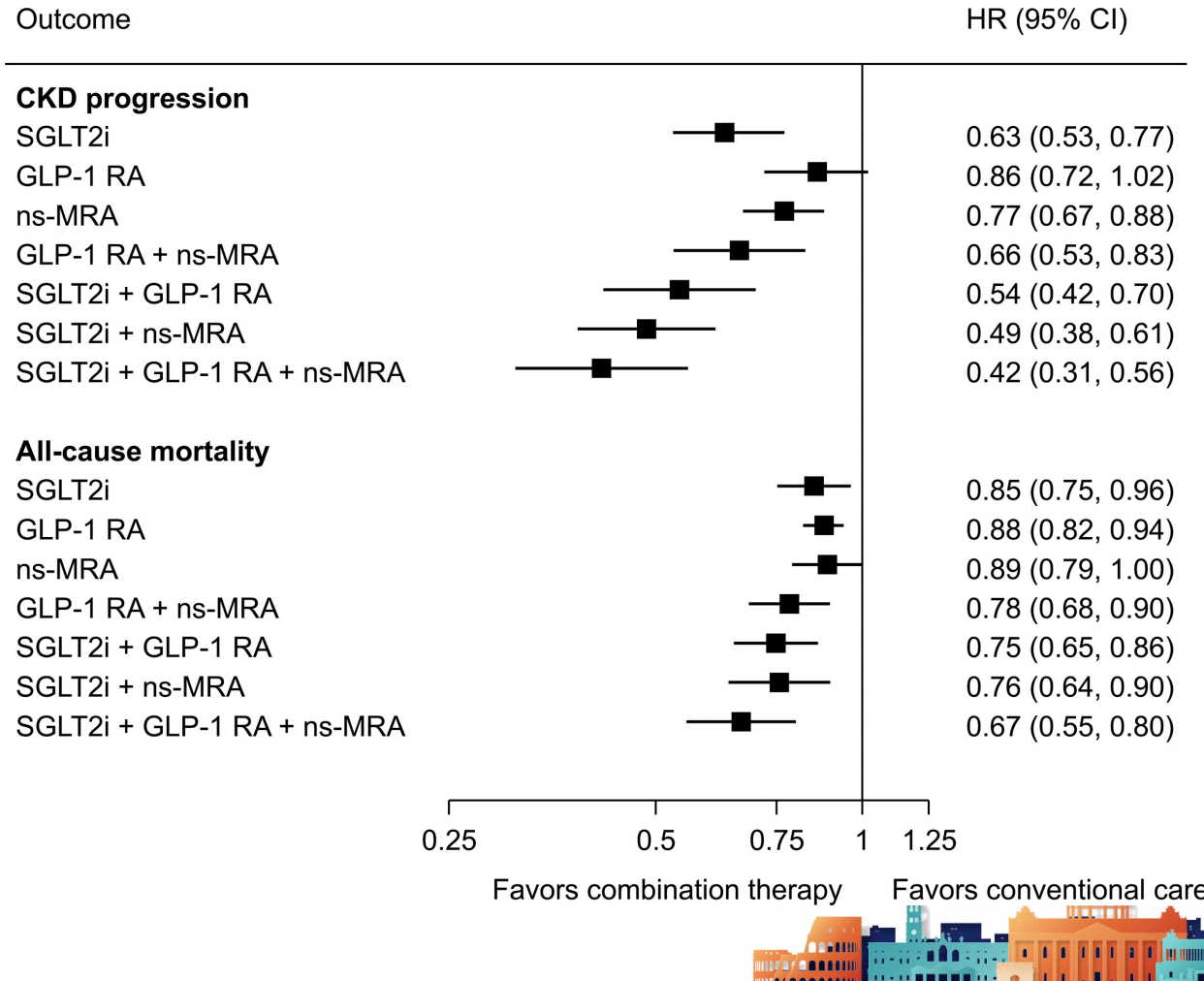
Composite CV outcome†



*A sustained ≥57% decline in eGFR or kidney failure (sustained eGFR <15 mL/min/1.73 m², chronic dialysis, or kidney transplantation); †HHF or CV death.
CI, confidence interval; CV, cardiovascular; HbA1c, glycated hemoglobin; HF, heart failure; HHF, hospitalization for heart failure; HR, hazard ratio.
Neuen BL, et al. *Lancet*. 2026; doi: 10.1016/S0140-6736(26)01009-3

Effetti stimati del trattamento sugli outcome con SGLT2i, GLP-1 RA e ns-MRA, da soli e in combinazione, in aggiunta al blocco del sistema renina-angiotensina nei pazienti con diabete di tipo 2





Neuen BL et al, Circulation 2023

MAJOR GUIDELINES AND SCIENTIFIC STATEMENTS USED IN THE CKM HEALTH CROSSWALK

La torre di Babele

Prevention and Management of ASCVD
2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease
2021 ESC Guidelines on Cardiovascular Disease Prevention in Clinical Practice
2023 Standards of Medical Care in Diabetes
2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults
2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol
2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults
2022 AHA Scientific Statement: Comprehensive Management of Cardiovascular Risk Factors for Adults With Type 2 Diabetes
2021 AHA Scientific Statement on Weight-Loss Strategies for Prevention and Treatment of Hypertension
2022 KDIGO Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease[69]
2013 KDIGO Clinical Practice Guideline for Lipid Management in Chronic Kidney Disease[70]
Prevention and Management of HF
2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure[71]
2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure[72]
2023 Standards of Medical Care in Diabetes[64]
2022 AHA Scientific Statement: Comprehensive Management of Cardiovascular Risk Factors for Adults With Type 2 Diabetes[61]
2022 KDIGO Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease[69]
Management of CKM Health in CKD
2022 KDIGO Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease[69]
2023 Standards of Medical Care in Diabetes[64]
2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure[71]
2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure[72]

Le raccomandazioni per la CKD e DM tipo 2 includono una combinazione di tre classi di farmaci per ridurre il rischio di MCV, HF e CKD

KDIGO · Kidney Disease Improving Global Outcomes

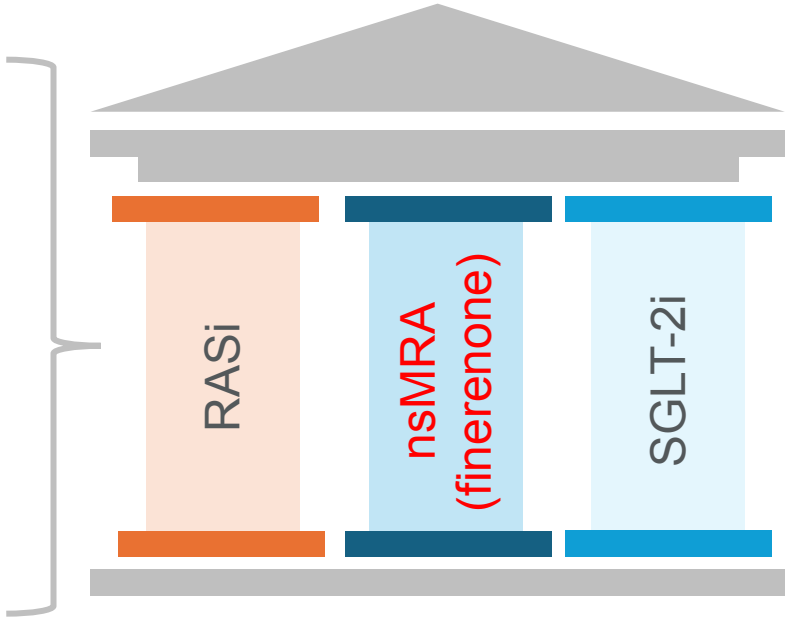
American Diabetes Association

ADA KDIGO Consensus 2022

ERA ERBP European Renal Best Practice

European Society of Hypertension (ESH)

ESC European Society of Cardiology



KDIGO guidelines (2022)

Recommendation 1.4.1:

Suggest a **nonsteroidal MRA with proven kidney or CV benefit for patients with T2D, eGFR ≥25 ml/min/1.73 m², normal serum [K⁺] and albuminuria** (≥30 mg/g) despite maximum tolerated dose of RASi

Grade 2A

L’iperattivazione del recettore dei mineralcorticoidi è un driver centrale della progressione delle malattie cardiache e renali

- Gli MRA steroidei (spironolattone ed eplerenone) rappresentano la terapia di base nei pazienti con HFrEF, ma possono favorire l’iperkaliemia
- Gli MRA non steroidei (finerenone) rallentano la progressione della malattia renale nella CKD e possono comportare un minor rischio di iperkaliemia
- Gli MRA possono essere facilmente combinati con altre terapie efficaci nello scompenso cardiaco e nella CKD
- Finerenone è inoltre il primo MRA non steroideo efficace nel ridurre la mortalità cardiovascolare e gli eventi correlati allo scompenso cardiaco nell’HFpEF
- Finerenone mostra evidenze iniziali di efficacia anche nella CKD non diabetica

FINERENONE VS PLACEBO IN PRESERVATION OF KIDNEY FUNCTION IN ND-CKD

Patients with nd-CKD at risk of progression despite optimized ACEi/ARB therapy were enrolled in the study

Study design

Primary endpoint – Total eGFR slope

Defined as the mean annual rate of change in eGFR from baseline to Month 32

Secondary efficacy outcomes†

- **Combined cardio–kidney endpoint:** A sustained **≥57% eGFR decline** from baseline over ≥4 weeks, **kidney failure**,‡ **HHF**, or **CV death**
- **Additional outcomes:** kidney composite outcome of a sustained ≥57% eGFR decrease or kidney failure;‡ CV composite endpoint of HHF or CV death

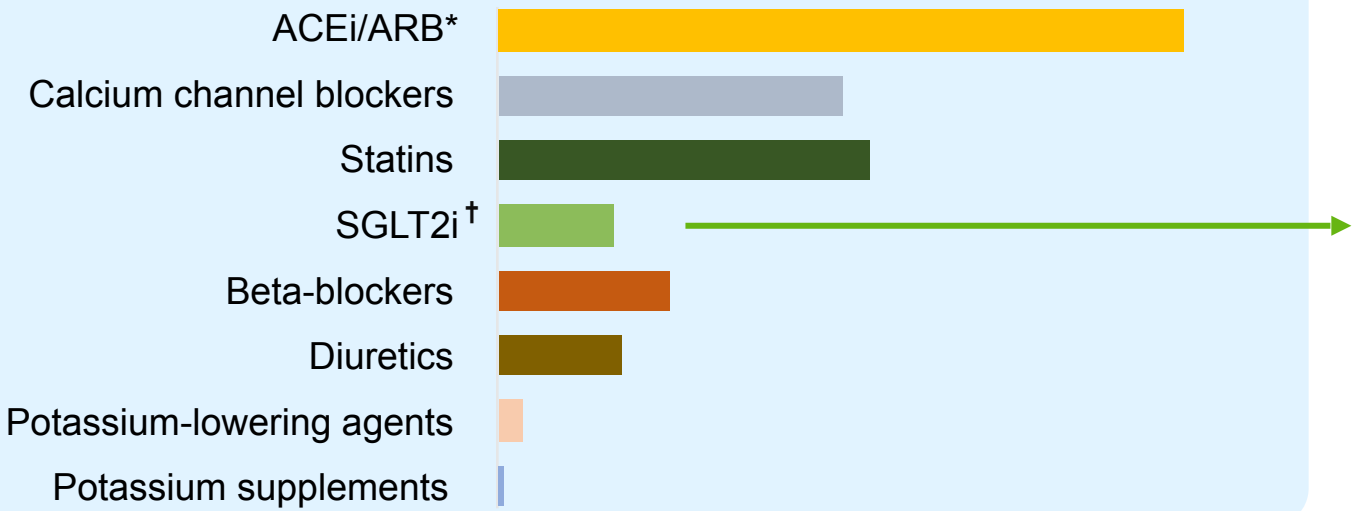
Safety outcomes

- TEAEs
- TESAEs
- AESI (specifically hyperkalemia)

Exploratory outcomes

- Change from baseline in UACR
- Change in health status score using EQ-5D-5L

Comedications (%)



	SGLT2i use at baseline		
	Overall	Yes	No
Mean UACR (mg/g)	818.9‡	871.9	808.3
Mean eGFR (mL/min/1.73 m²)	46.7	45.6	46.8

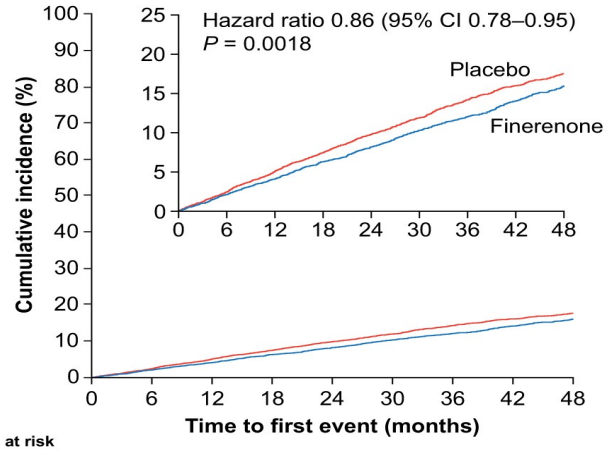
FIDELITY
(FIDELIO-DKD + FIGARO-DKD pooled)

Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis

Il finerenone ha ridotto il rischio di esiti cardiovascolari e renali clinicamente importanti rispetto al placebo nell'intero spettro della malattia renale cronica nei pazienti con diabete di tipo 2.

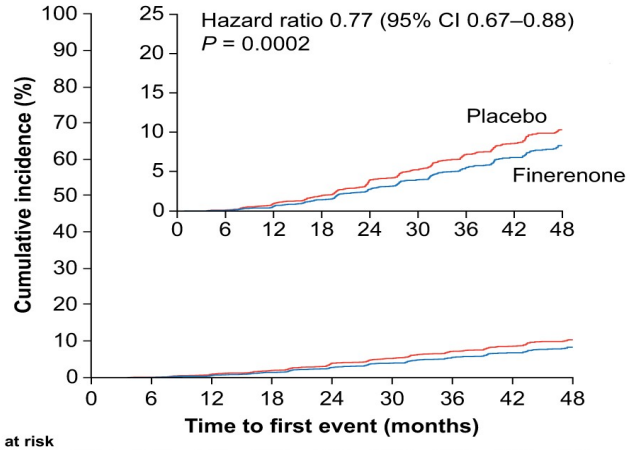
Placebo — Finerenone

A Composite cardiovascular outcome



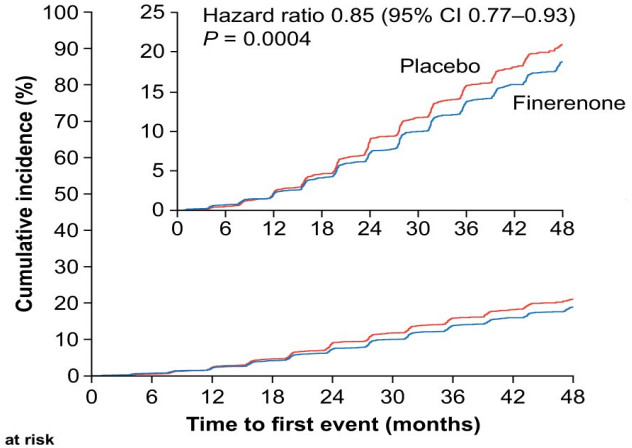
No. at risk									
Placebo	6507	6330	6125	5938	5184	4147	2969	2135	1082
Finerenone	6519	6360	6202	6009	5273	4207	3065	2187	1087

B eGFR ≥57% composite kidney outcome



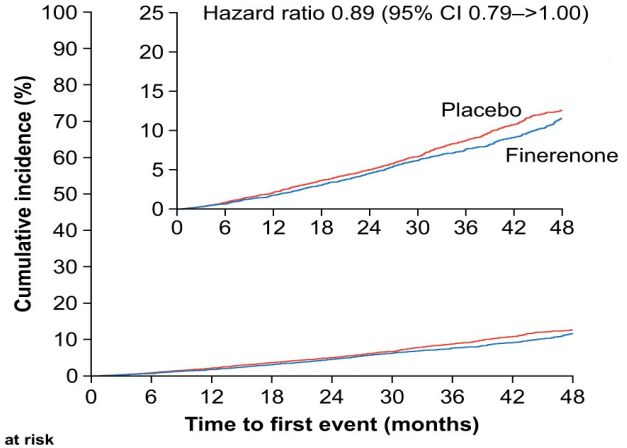
No. at risk									
Placebo	6507	6292	6071	5815	4949	3932	2798	1988	962
Finerenone	6519	6291	6107	5848	5027	3973	2815	2024	959

C eGFR ≥40% composite kidney outcome



No. at risk									
Placebo	6507	6270	5994	5661	4710	3709	2603	1850	891
Finerenone	6519	6255	6020	5698	4811	3764	2603	1868	882

D Death from any cause



No. at risk									
Placebo	6507	6448	6363	6253	5573	4588	3299	2389	1207
Finerenone	6519	6472	6396	6300	5592	4530	3358	2429	1198

Agarwal R, *et al. Eur J Heart* 2022;43:474–484

EFFECTS OF FINERENONE ON KIDNEY AND CV OUTCOMES IN >13,000 PATIENTS WITH CKD AND T2D

Run-in period → Screening period → R

- Finerenone 10 mg od or 20 mg od*
- Placebo

4–16 weeks
Maximum tolerated dose of ACEi/ARB

Symptomatic HFrEF excluded

Patients randomised	
FIDELIO-DKD[1]	5734
FIGARO-DKD[2]	7437

	FIDELIO-DKD	FIGARO-DKD
Clinical efficacy primary endpoint	Composite endpoint: Time to kidney failure,# sustained ≥40% eGFR decline, or kidney-related death	Composite endpoint: Time to CV death, non-fatal MI, non-fatal stroke, or hospitalisation for HF
Key secondary endpoint	Same as primary endpoint in FIGARO-DKD	Same as primary endpoint in FIDELIO-DKD

FIDELITY
Prespecified pooled analysis

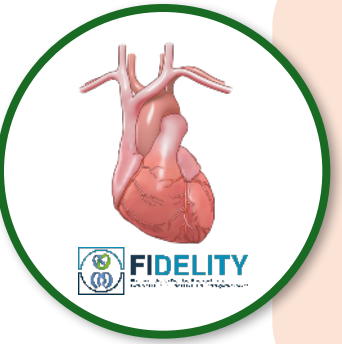
Key outcomes

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

57% kidney composite:
Time to kidney failure,# sustained ≥57% eGFR decline, or kidney-related death

Finerenone: efficacia su end-point CV e nella MRC in fase iniziale e avanzata

Relative risk reductions for composite outcomes vs placebo



14% relative risk reduction vs placebo for the CV composite*

CV death	Non-fatal MI	Non-fatal stroke	HHF
-12%	-9%	-1%	-22%

Relative risk reductions were also seen in the kidney composite* outcomes compared with placebo

Kidney failure	ESKD#	eGFR decrease to: <15 ml/min/1.73m²#	≥57%	Kidney death‡
-16%	-20%	-19%	-30%	0%

EFFECTS OF PHARMACOLOGIC THERAPIES ON ALBUMINURIA AND HF OUTCOMES

Butler J et al, Eur Heart J 2026

STUDIO FINEARTS-HF: DISEGNO

Randomized, double-blind, placebo-controlled trial testing the hypothesis that finerenone would reduce cardiovascular death and total worsening heart failure events in patients with heart failure and mildly reduced or preserved ejection fraction

Key Inclusion Criteria

- **Symptomatic HF (NYHA class II-V) with LVEF ≥ 40%**
- **Hospitalized, recently hospitalized, or ambulatory**
- **Elevated natriuretic peptide levels**
- **Structural heart disease (LA Enlargement or LVH)**
- **Diuretics in the 30d prior to randomization**

Key Exclusion Criteria

- **Potassium > 5.0 mmol/L; eGFR <25 mL/min/1.73 m²**
- **MRA use 30d prior to randomization**
- **History of peripartum, chemotherapy induced, or infiltrative cardiomyopathy (e.g., amyloidosis)**
- **Alternative causes of signs or symptoms**

Assessed for eligibility
N = 7463

1:1 Randomization

N = 6,001 validly randomized

Randomized to **finerenone**
N = 3011

Finerenone 10, 20 or 20, 40 mg *dosing based on eGFR: ≤60 max dose 20 mg, >60, max dose 40 mg*

Uptitrate to maximally tolerated dose if K+<5.0mmol/L and eGFR decrease <30%

Randomized to **placebo**
N = 3005

Matching Placebo

Visits: Month 1, then 3-monthly for first 12 months, 4-monthly visits thereafter with telephone contact in between

Study Endpoints

Primary Endpoint

- CV death and total HF events (hospitalizations/urgent visits)

Secondary Endpoints

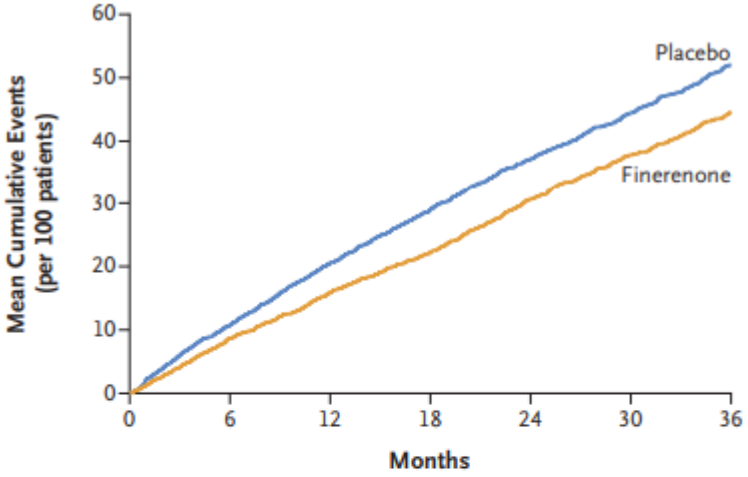
- Total HF events
- KCCQ-TSS at 6,9, and 12 months
- NYHA class at 12 months
- Renal composite endpoint
- All-cause mortality

Solomon S et al. N Engl J Med 2024;391:1475-85

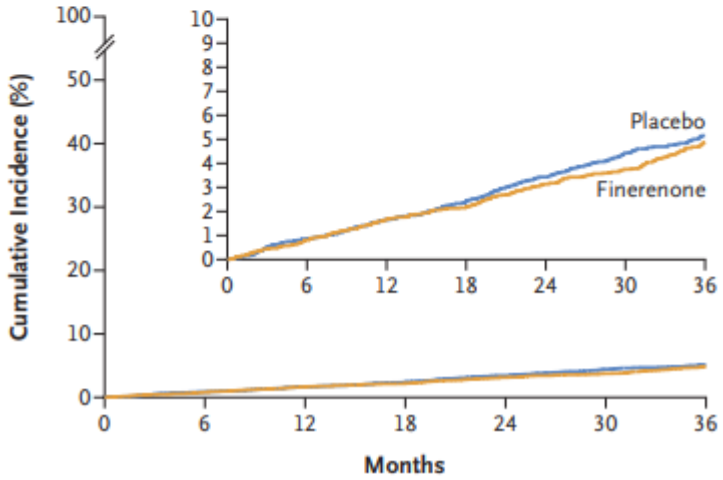
Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

FINEARTS-HF

A Total Worsening Heart Failure Events and Death from Cardiovascular Causes

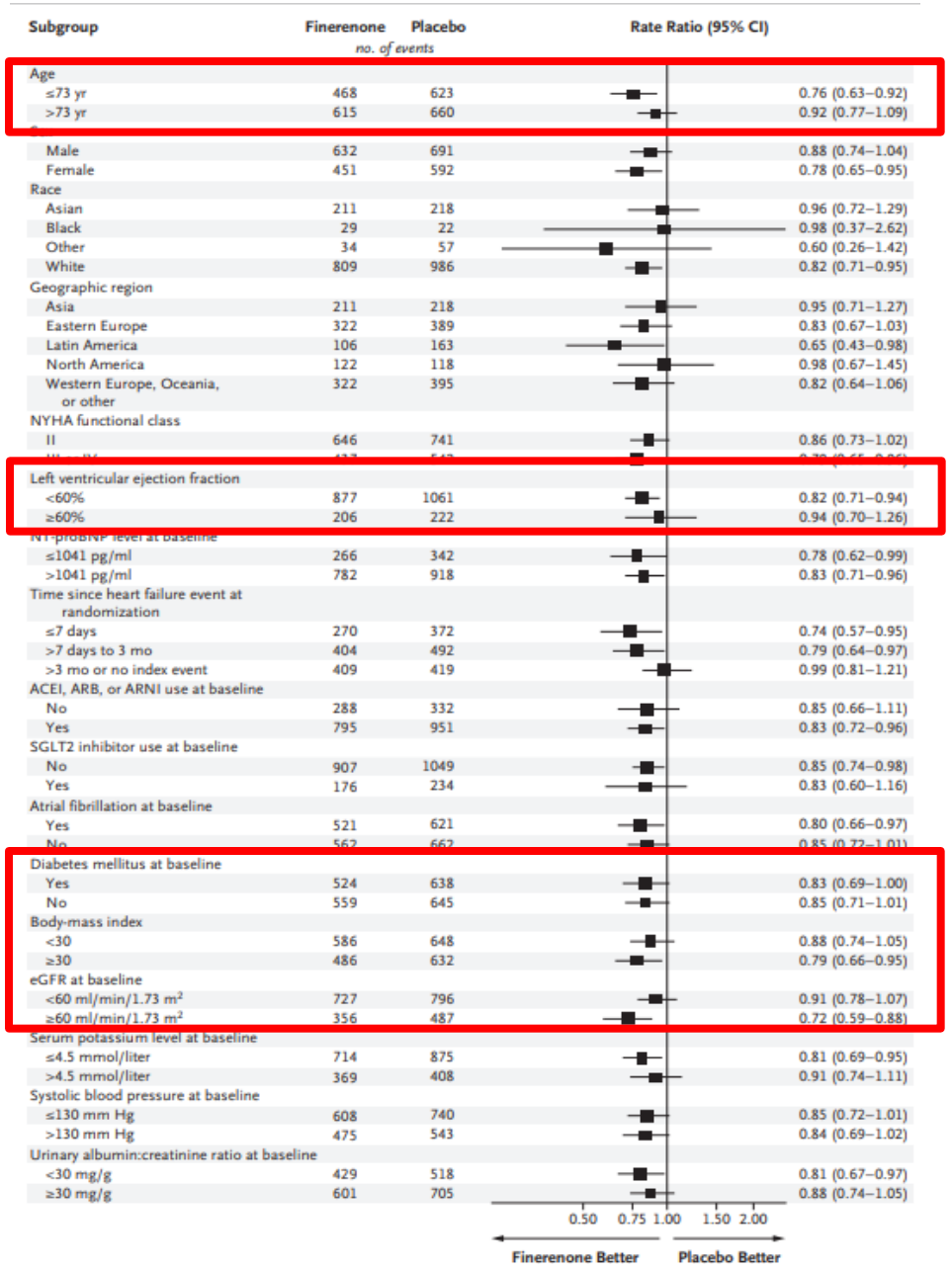


C Death from Cardiovascular Causes



Nei pazienti con HF FE lievemente ridotta o preservata, il finerenone ha determinato una riduzione dell'end-point primario (eventi WHF totali e decessi per cause CV) rispetto al placebo.

- Riduzione del 16% (RR 0.84, IC95% 0.74-0.95, p=0.007)
- Eventi HF totali ridotti del 18% (RR 0.82, p=0.006)
- Ospedalizzazioni HF ridotte del 14% (HR 0.86, p=0.02)



Solomon S et al. N Engl J Med 2024;391:1475-85

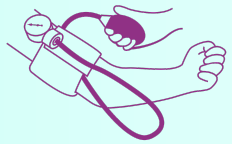
Quali eventi avversi sono associati al trattamento con finerenone?

Very common (≥10%)
- Hyperkalaemia

Common (≥1% to <10%)
- Hypotension
- eGFR decreased
- Hyponatraemia
- Pruritus
- Hyperuricaemia

Uncommon (≥0.1% to <1%)
- Haemoglobin decreased

Hypotension



- Most hypotension events in the finerenone group were mild or moderate in severity and resolved
- Following a mild decrease in SBP (2–4 mmHg) and DBP (1–2 mmHg) after 1 month, it remained stable thereafter

Hyperuricaemia

- All events were non-serious and did not result in permanent discontinuation in patients receiving finerenone
- The increase in serum uric acid (mean 0.3 mg/dL) with finerenone up to month 16 attenuated over time

Reductions in GFR

- The majority of GFR-decreased events in the finerenone group were mild or moderate in severity and were resolved
- The initial decrease in eGFR (mean 2 ml/min/1.73 m^2) with finerenone attenuated over time, and was reversible with continuous treatment

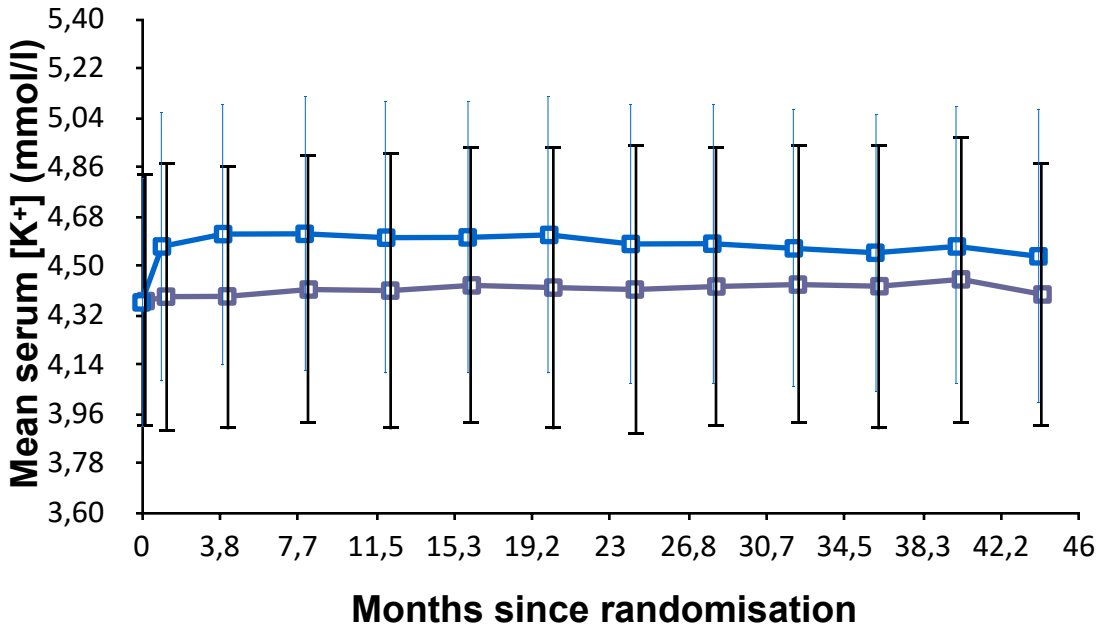
Reductions in haemoglobin

- Finerenone was associated with a mild decrease in haemoglobin and haematocrit after 4 months of treatment
- These changes were transient, and levels comparable with the placebo group were achieved after ~24–32 months

L'aumento medio del potassio è basso, gli eventi di iperkaliemia sono aumentati ma solo il 2,3% ha causato l'interruzione permanente del farmaco

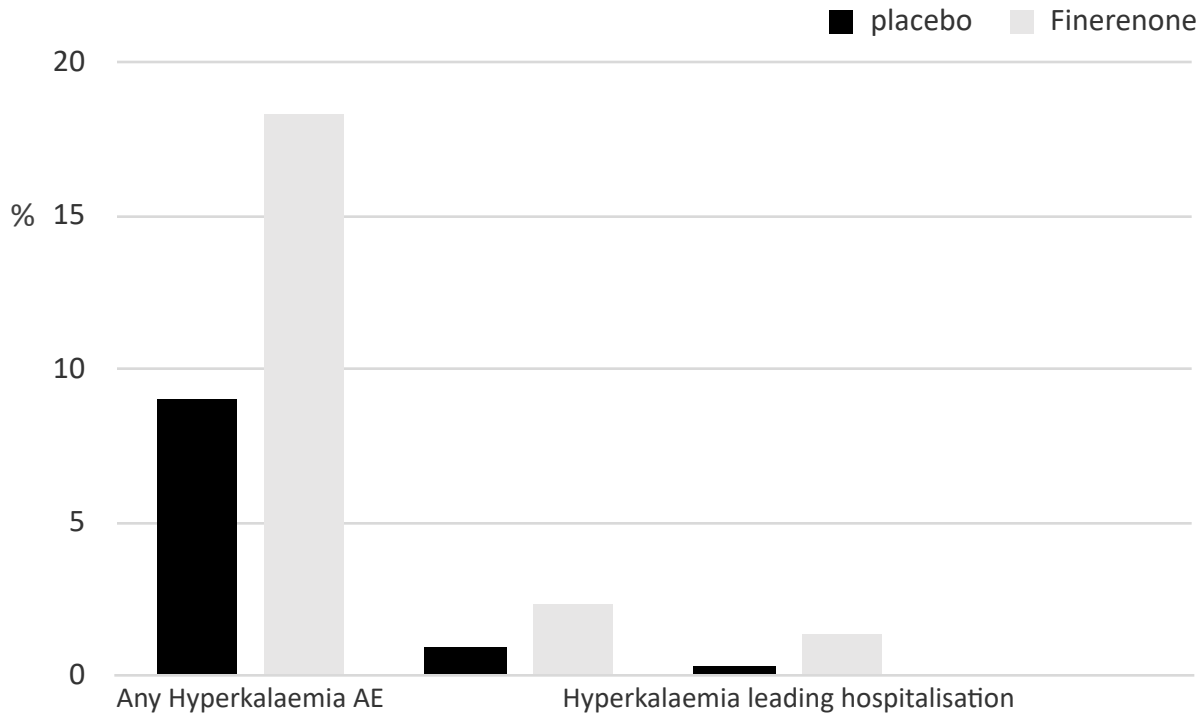
Mean serum potassium (mmol/L)

At baseline:
Placebo: 4.37 (±0.46)
Finerenone: 4.37 (±0.46)



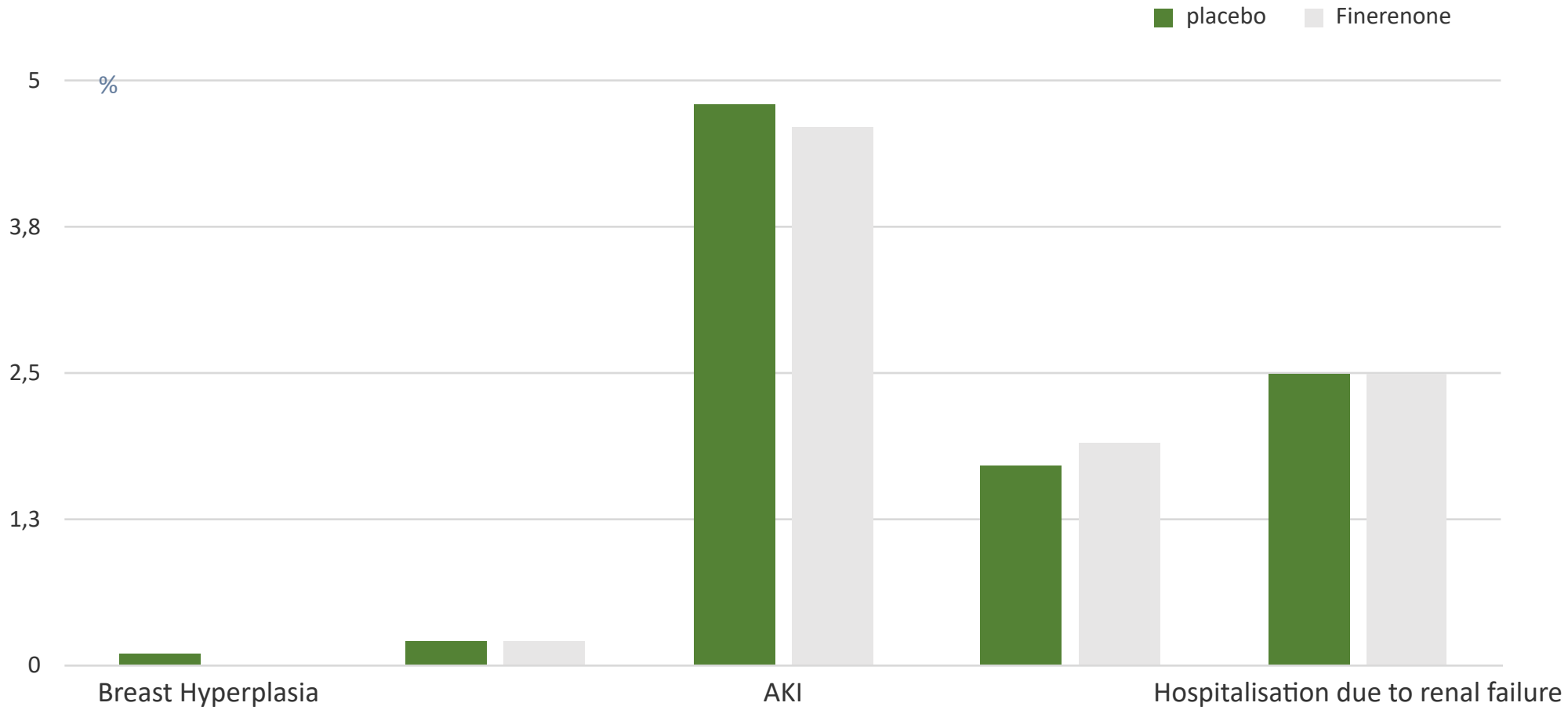
Maximum mean difference in serum potassium between groups= **0.23 mmol/l** at month 4

Patients with a treatment-emergent Hyperkalaemia AE (%)



Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes

Finerenone: Ginecomastia e AKI sovrapponibili al placebo



Bakris et al- N Engl J Med 2020;383:2219-29.

Profilo di Sicurezza e titolazione

Monitoraggio del potassio sierico durante il trattamento con un MRA non steroideo (finerenone).

K^+ ≤4.8 mmol/l

- Initiate finerenone
  - 10 mg daily if eGFR 25–59 ml/min/1.73 m^2
  - 20 mg daily if eGFR ≥60 ml/min/1.73 m^2
- Monitor K^+ at 1 month after initiation and then every 4 months
- Increase dose to 20 mg daily, if on 10 mg daily
- Restart 10 mg daily if previously held for hyperkalemia and K^+ now ≤5.0 mmol/l

K^+ 4.9–5.5 mmol/l

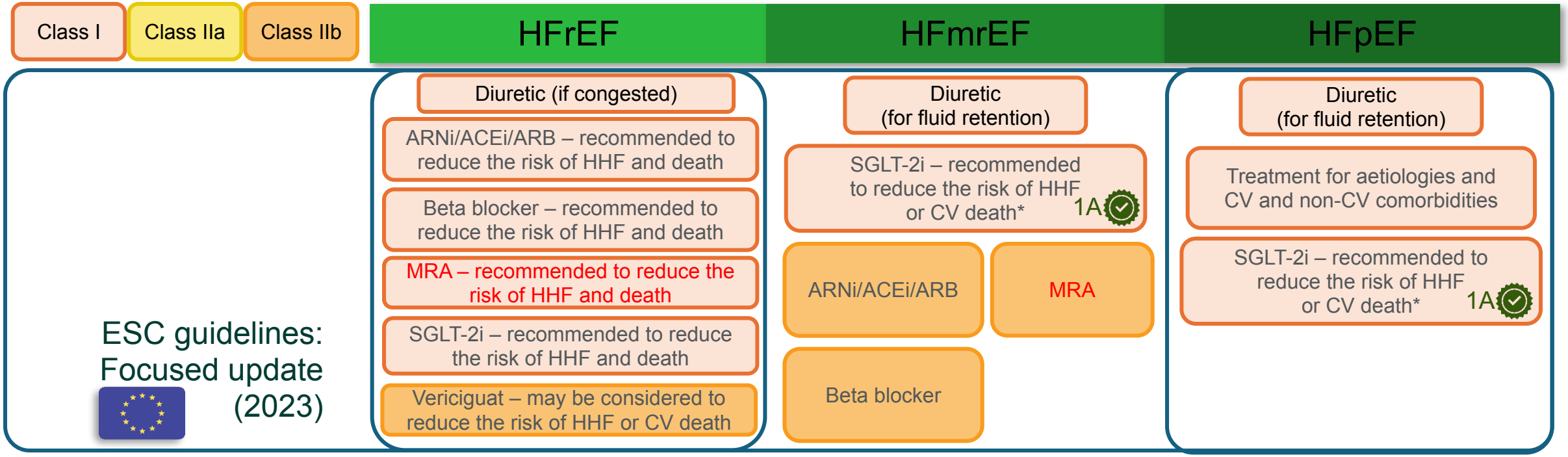
- Continue finerenone 10 mg or 20 mg
- Monitor K^+ every 4 months

K^+ >5.5 mmol/l

- Hold finerenone
- Consider adjustments to diet or concomitant medications to mitigate hyperkalemia
- Recheck K^+
- Consider reinitiation if/when K^+ ≤5.0 mmol/l

KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int. 2022;102:S1–S127.23

2023 focused update of the 2021 ESC guidelines for the management of HF

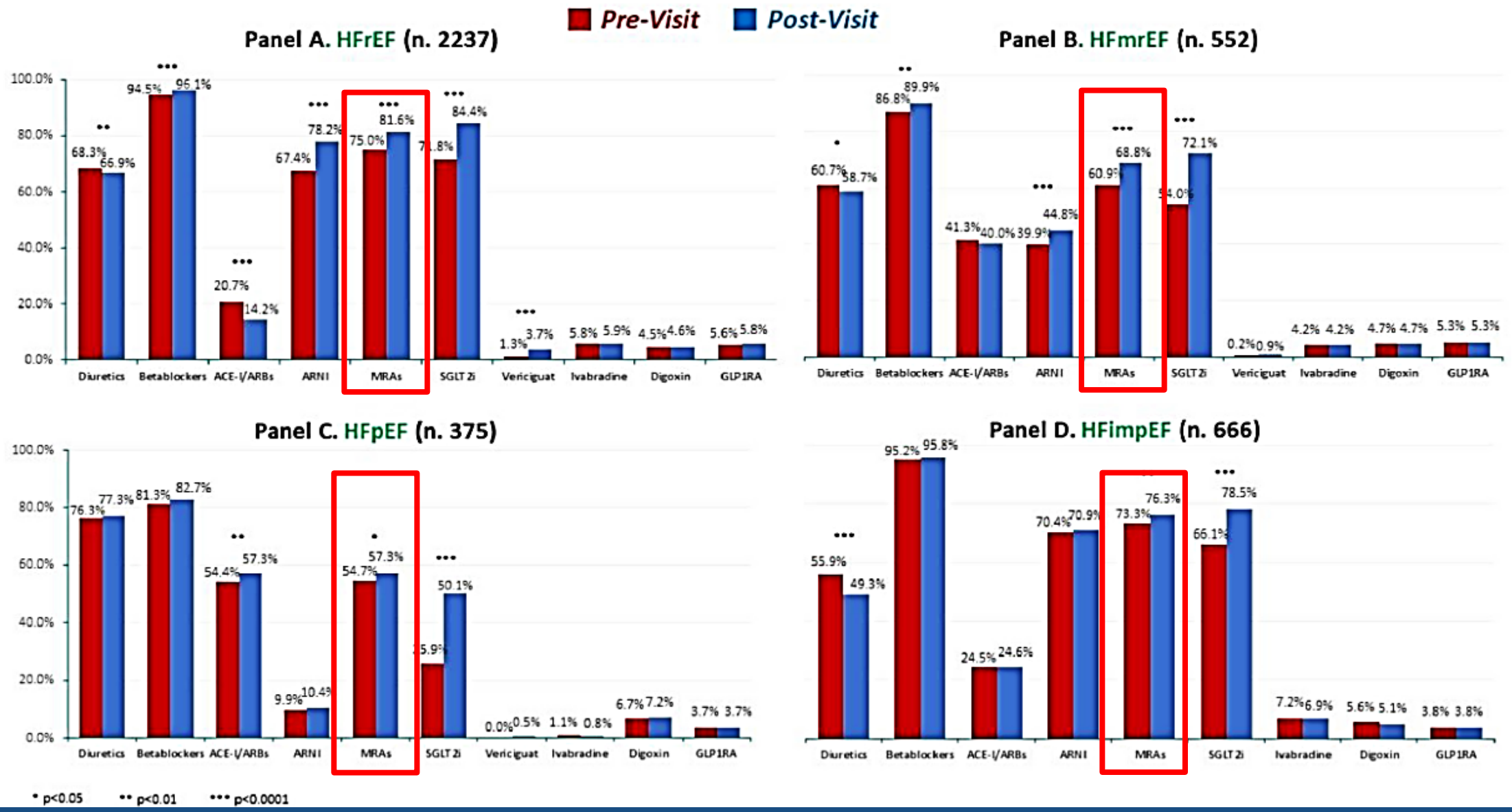


Prevention of HF in CKD and T2D

Finerenone – in patients with CKD and T2D, recommended to reduce the risk of HHF 1A

SGLT-2i – in patients with CKD and T2D, recommended to reduce the risk of HHF or CV death 1A

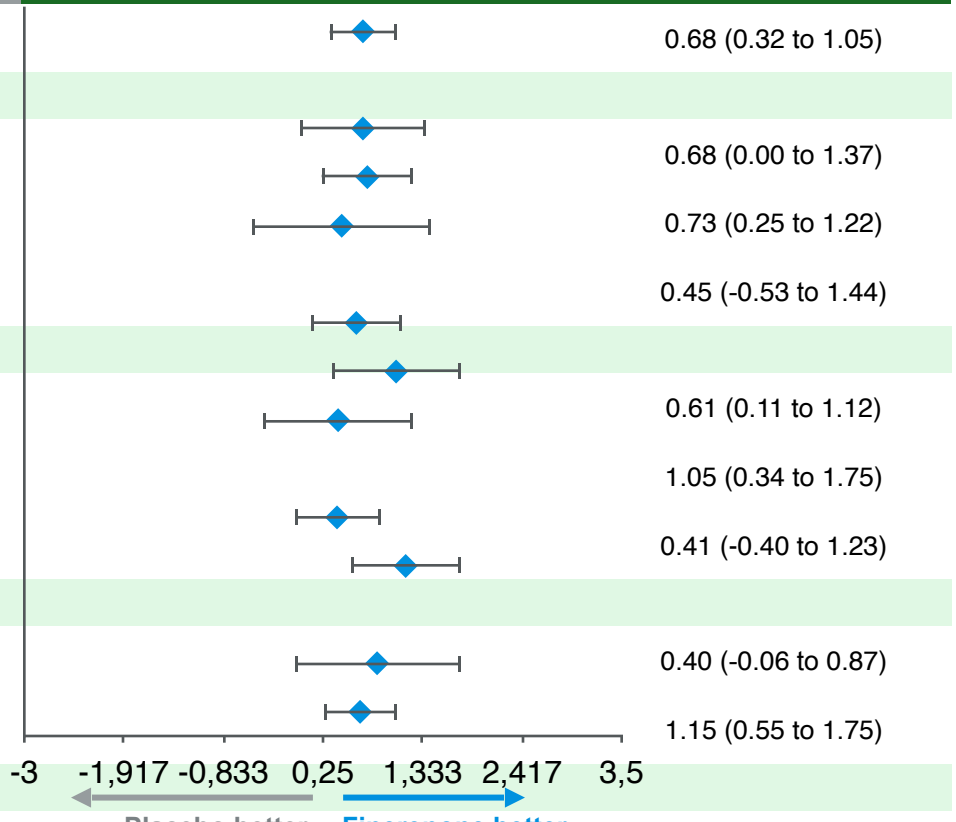
Medical Treatments in Patients With Ambulatory Heart Failure: First Data From the BRING-UP-3 Heart Failure Study



Oliva F et al. J Card Fail. 2025 Dec;31(12):1847-1857

Finerenone demonstrated consistent reduction in eGFR slope across prespecified subgroups

Outcomes according to baseline subgroups	Finerenone		Placebo		Difference in slopes (95% CI)
	n	eGFR slope*	n	eGFR slope*	
Overall	793	-3.34	791	-4.02	0.68 (0.32 to 1.05)
Primary cause of CKD					
Hypertension/ischemic nephropathy	234	-3.15	225	-3.83	0.68 (0.00 to 1.37)
Chronic glomerulonephritis	446	-3.49	457	-4.22	0.73 (0.25 to 1.22)
Other/unknown	113	-3.14	109	-3.59	0.45 (-0.53 to 1.44)
eGFR (mL/min/1.73 m²)					
<45	424	-3.16	420	-3.77	0.61 (0.11 to 1.12)
45–<60	207	-3.26	216	-4.31	1.05 (0.34 to 1.75)
≥60	162	-3.90	155	-4.31	0.41 (-0.40 to 1.23)
UACR (mg/g)					
≤1000	491	-2.68	491	-3.08	0.40 (-0.06 to 0.87)
>1000	302	-4.42	300	-5.57	1.15 (0.55 to 1.75)
SGLT2i use					
Yes	135	-3.15	135	-4.00	0.84 (-0.06 to 1.73)
No	658	-3.38	656	-4.03	0.65 (0.25 to 1.06)



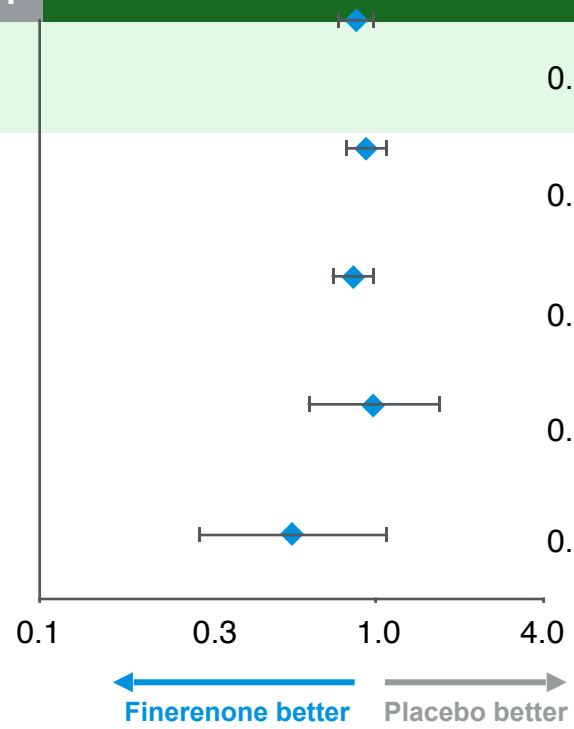
Calculated with the use of a 2-slope linear spline mixed-effect model. The square represents the estimate of the total slope difference at 32 months; the lower and upper ends of the whiskers indicate the limits of the 95% CI. *mL/min/1.73 m²/year.

CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; SGLT2i, sodium-glucose co-transporter 2 inhibitor; UACR, urinary albumin-to-creatinine ratio.

Heerspink HJL, et al. *N Eng J Med.* 2026; doi: 10.1056/NEJMoa2604625.

Finerenone demonstrated consistent benefits versus placebo across all components of the cardio–kidney endpoint

Outcome	Finerenone (N=793)		Placebo (N=791)		Hazard ratio (95% CI)
	n (%)	n per 100 PY	n (%)	n per 100 PY	
Composite kidney–CV	110 (13.9)	4.7	134 (16.9)	5.8	0.77 (0.60–0.99)
Kidney failure	95 (12.0)	4.0	102 (12.9)	4.4	0.88 (0.67–1.17)
Sustained decrease of eGFR ≥57%	77 (9.7)	3.2	98 (12.4)	4.2	0.74 (0.55–1.00)
HHF	8 (1.0)	0.3	9 (1.1)	0.4	0.97 (0.39–2.44)
CV death	3 (0.4)	0.1	9 (1.1)	0.4	0.32 (0.09–1.19)



Component tiers analyzed as separate time-to-event endpoints with endpoint-specific follow-up: eGFR-based components used the eGFR ascertainment window, whereas HHF and CV death used standalone follow-up censored at last contact or planned treatment end (while alive for non-CV death) and were not constrained by the eGFR window; counts and rates are not intended to sum to the composite.
CI, confidence interval; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HHF, hospitalization for heart failure; PY, patient-years.
Heerspink HJL, et al. *N Eng J Med.* 2026; doi: 10.1056/NEJMoa2604625.

FIND-CKD included a broad population, with common nd-CKD etiologies well represented

Kidney disease etiology,[1] n (%)	
Hypertensive/ ischemic nephropathy	460 (29)
Chronic glomerulonephritis	903 (57)
IgAN	417 (26)
FSGS	215 (14)
Membranous nephropathy	91 (6)
Mesangial proliferative glomerulonephritis*	17 (1)
Other glomerular disease	154 (10)
Unknown	164 (10)
Other	57 (4)

Hypertensive nephropathy is the **second most common** cause of **kidney failure**[2]

Most common primary glomerulonephritis globally[3]

Accounts for **~40% cases of adult cases** nephrotic syndrome[4]

CVD history , n (%)

Hypertension	1396 (88)
ASCVD	189 (12)
Atrial fibrillation	59 (4)
Heart failure	35 (2)

*Defined as occurrence of one of the following non-pre-specified terms: glomerulonephritis membranoproliferative, glomerulonephritis proliferative, mesangioproliferative glomerulonephritis.
ASCVD, atherosclerotic cardiovascular disease; CVD, cardiovascular disease; FSGS, focal segmental glomerulosclerosis; IgAN, immunoglobulin A nephropathy; nd-CKD, non-diabetic chronic kidney disease.
1. Heerspink HJL, et al. *Nephrol Dial Transplant.* 2025;40:308–319; 2. Lucero C, et al. *Int J Mol Sci.* 2022;23(24):15936; 3. Cheung CK, et al. *Nat Rev Nephrol.* 2025;21:9–23; 4. Rout P, et al. Focal segmental glomerulosclerosis. 2024. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026. https://www.ncbi.nlm.nih.gov/books/NBK532272/ [accessed May 2026].