THE KIDNEY–HEART ALLIANCE:

FINERENONE AND THE EXPANDING CARDIORENAL LANDSCAPE

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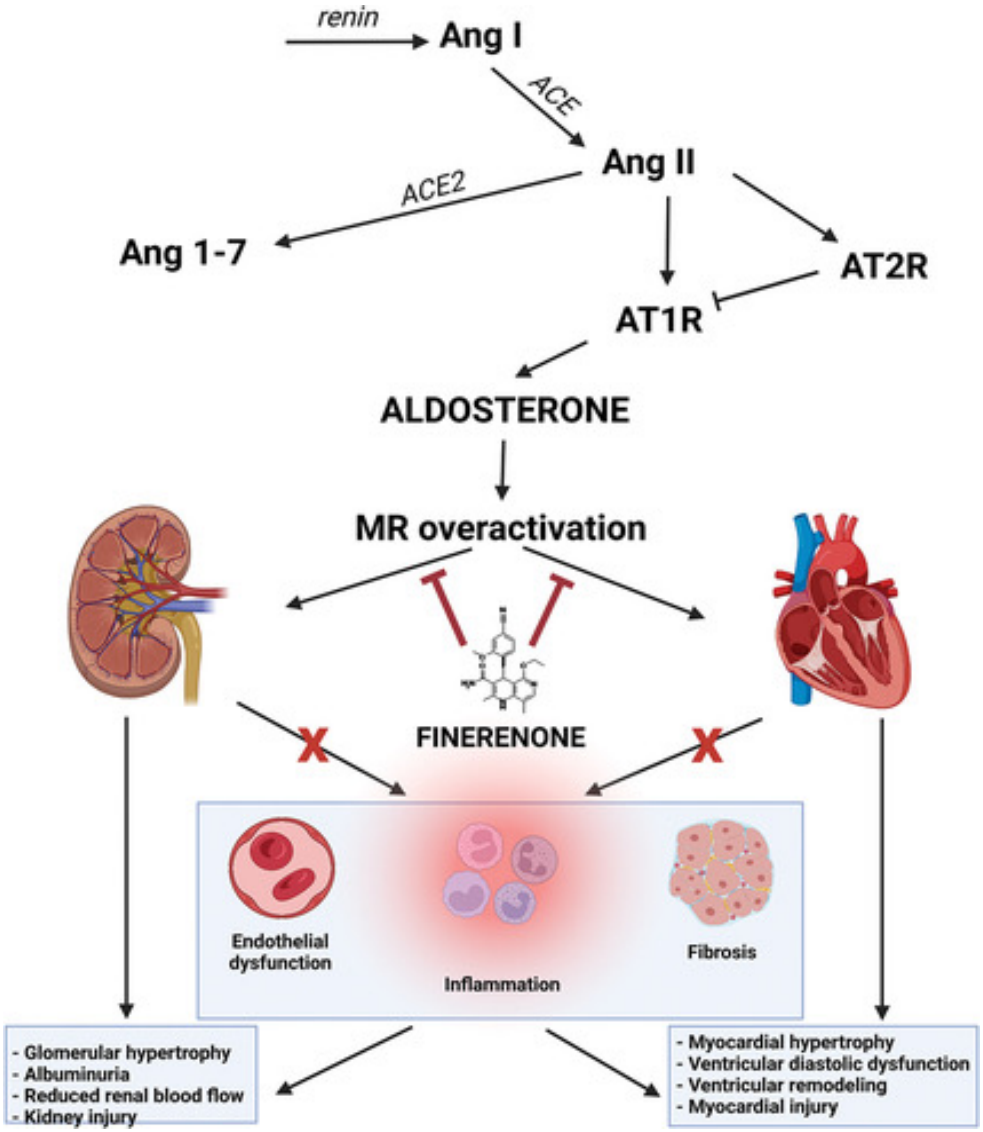
Northwell℠
Cardiovascular Institute

OBJECTIVES

- Describe the unique pharmacological characteristic of finerenone and how it therapeutically differentiates from traditional mineralocorticoid receptor antagonists (MRAs)
- Summarize the key clinical trial evidence demonstrating finerenone's efficacy in reducing cardiovascular and renal events in patients with chronic kidney disease (CKD) and type 2 diabetes (T2DM)
- Analyze the impact of finerenone in patients with HFmrEF and HFpEF
- Evaluate finerenone's complementary role alongside existing guideline-directed medical therapies within the contemporary cardio-kidney-metabolic (CKM) spectrum

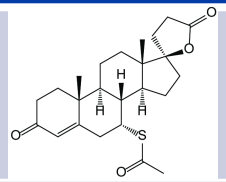
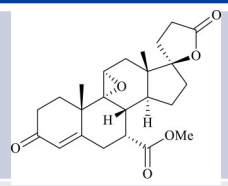
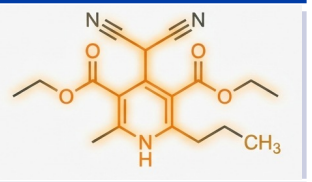
HOW DOES FINERENONE HELP WITH CARDIORENAL DISEASE?



MR: mineralocorticoid receptor

Expert Opinion on Drug Safety, *21*(9), 1161–1170.

COMPARISON OF MINERALCORTICOIDS RECEPTOR ANTAGONISTS

Characteristics	Spironolactone	Eplerenone	Finerenone
Structural property	Steroidal 	Steroidal 	Non-steroidal 
MR affinity (nMol/L)	24.2 (high)	990 (low)	17.8 (high)
MR selectivity	Low (binds to MRA, progesterone + androgen receptors)	Medium	High
Metabolites	Hepatic, active metabolites	No active	No active
Half-life (hours)	> 20 (urinary levels present up to 3 weeks after discontinuation)	3 – 6	2 – 4
Hyperkalemia	High	Moderate	Low (milder impact on kidney electrolyte transport)
Tissue distribution	Kidney>>heart > 6-fold	Kidney>heart ~ 3-fold	Heart = Kidney, 1:1
BP-lowering effect	Strong	Weak	Weak (low lipophilic properties + short $t_{1/2}$)
Anti-fibrotic effect (animal studies)	Moderate	Moderate	High

Nephrol Dial Transplant 2024;39:1063-1072.

FINERENONE

- Finerenone is a nonsteroidal, selective mineralcorticoid receptor antagonist
- FDA approved for:

Chronic Kidney Disease associated with Type 2 Diabetes

Measure serum K+ and eGFR before dose initiation
DO NOT INITIATE if serum K+ is >5.0 mEq/L* or if eGFR is <25 mL/min/1.73 m²

	eGFR (mL/min/1.73 m²)	
	≥25 to <60	≥60
Starting dose	10 mg	20 mg
Target daily dose	20 mg	20 mg

The recommended starting dose and target daily dose is based on initial eGFR and serum K+ thresholds. Not actual size.

Heart Failure with Ejection Fraction ≥40%

Measure serum K+ and eGFR before dose initiation
DO NOT INITIATE if serum K+ is >5.0 mEq/L or if eGFR is <25 mL/min/1.73 m²

	eGFR (mL/min/1.73 m²)	
	≥25 to <60	≥60
Starting dose	10 mg	20 mg
Target daily dose	20 mg	40 mg

The recommended starting dose and target daily dose is based on initial eGFR and serum K+ thresholds. Not actual size.

FDA: Food and Drug Administration

Bayer Pharmaceuticals. Kerendia (finerenone) [package insert]. U.S. Food and Drug Administration.

A TIMELINE OF EVIDENCE

2020:
FIDELIO-DKD
(Renal Outcomes in CKD+T2DM)

2021:
FIGARO-DKD
(CV outcomes in CKD+T2DM)

2024:
FINEARTS-HF
(CV outcomes in HFmrEF/HFpEF)

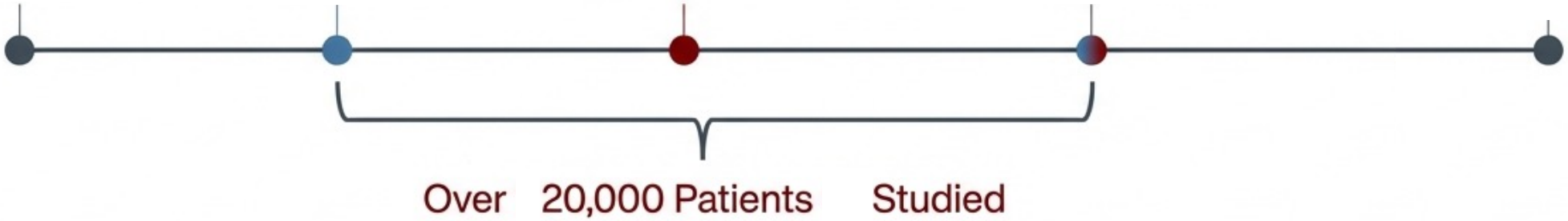
2025:
CONFIDENCE
(Renal Outcomes in CKD+T2DM – finerenone+empagliflozin)

Future:

CONFIRMATION-HF
(finerenone + SGLT2i in hospitalized HF)

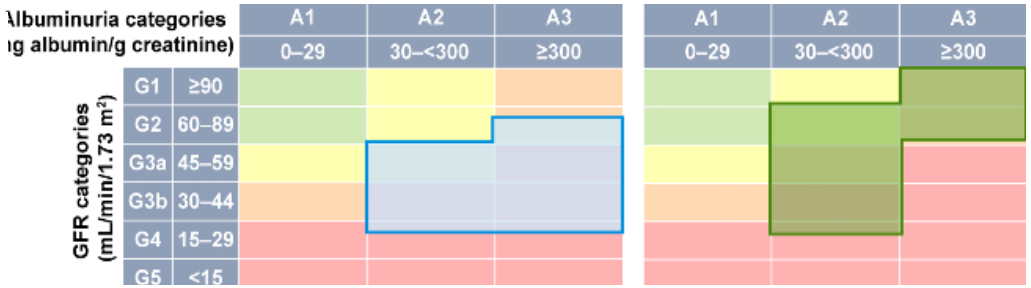
REDEFINE-HF
(ADHF, HFmrEF/HFpEF)

FINALITY-HF
(HFrEF)



HFmrEF: heart failure with mid-range ejection fraction; HFpEF: heart failure with preserved ejection fraction;
ADHF: acute decompensated heart failure; SGLT2i: sodium glucose cotransporter-2 inhibitors

FINERENONE IN CKD AND T2DM

	FIDELIO-DKD	FIGARO-DKD
Study Design	Phase III, multicenter, randomized, double-blind, placebo-controlled trial	
Population	5,734 patients over 2.6 years	7,437 patients over 3.4 years
	Age ≥18 years with T2DM and CKD treated with ACEi or ARB (max tolerated dose) Serum potassium <4.8 mEq/L at screening visit. Excluded HFrEF patients.	
	➢ eGFR 25-<60 mL/min + UACR 30-<300 mg/g and presence of diabetic retinopathy ➢ eGFR 25 –<75 mL/min + UACR ≥300-5,000 mG/g		➢ eGFR 25-90 mL/min + UACR 30-<300 mG/g ➢ eGFR ≥60 mL/min + UACR ≥300-5,000 mG/g *Enrolled patients with less advanced CKD (higher eGFR and lower albuminuria) than FIDELIO-DKD*
Objectives	To assess the effect of finerenone on **CKD progression** and CV outcomes in patients with T2DM	To evaluate **CV mortality and morbidity** with finerenone in a broad spectrum of CKD and T2DM
Interventions	Finerenone vs. placebo	
Primary endpoint	**Primary composite renal outcome** (kidney failure, ≥40% ↓ eGFR, renal death): 17.8% vs. 21.1% (HR 0.82; 95% CI 0.73-0.93, P=0.001) – Sustained decrease of ≥40% ↓ eGFR from baseline: 16.9% vs. 20.3% (HR 0.81; 95% CI 0.72-0.92) **Secondary CV composite outcome** (CV death, non-fatal MI/Stroke, HFF): 13.0% vs. 14.8% (HR 0.86; 95% CI 0.75-0.99, P=0.03)	**Primary composite CV outcome** (CV death, non-fatal MI/ stroke, HHF): 12.4% vs 14.2% (HR 0.87; 95% CI 0.76–0.98; P=0.03) – Driven by a 29% reduction in HHF (HR 0.71) **Secondary kidney composite outcome** (kidney failure, ≥40% ↓ eGFR, renal death): N/S – End-stage kidney disease HR 0.64; 95% CI 0.41-0.995 – Kidney-composite outcome with ≥57% ↓ eGFR: HR 0.77; 95% CI 0.60-0.99
Conclusion	In patients with CKD and T2DM, finerenone therapy resulted in lower risks of kidney failure and disease progression than placebo	Finerenone reduced CV mortality and morbidity across a wide spectrum of CKD and T2DM

UACR: urinary albumin to creatinine ratio; eGFR: estimated glomerular filtration rate H: hazard ratio; CI: confidence interval; HHF: heart failure hospitalization

N Engl J Med. 2020;383:2219-2229;
N Engl J Med 2021; 385:2252-2263.

FIDELIO-DKD SAFETY OUTCOMES

Event	Finerenone (N=2827)	Placebo (N=2831)
	no. of patients (%)	
Any adverse event	2468 (87.3)	2478 (87.5)
Adverse event related to trial regimen	646 (22.9)	449 (15.9)
Adverse event leading to discontinuation of trial regimen	207 (7.3)	168 (5.9)
Any serious adverse event†	902 (31.9)	971 (34.3)
Serious adverse event related to trial regimen†	48 (1.7)	34 (1.2)
Serious adverse event leading to discontinuation of trial regimen†	75 (2.7)	78 (2.8)
Investigator-reported hyperkalemia‡	516 (18.3)	255 (9.0)
Hyperkalemia related to trial regimen	333 (11.8)	135 (4.8)
Serious hyperkalemia†	44 (1.6)	12 (0.4)
Hospitalization due to hyperkalemia	40 (1.4)	8 (0.3)
Permanent discontinuation of trial regimen due to hyperkalemia	64 (2.3)	25 (0.9)
Investigator-reported hypokalemia	28 (1.0)	61 (2.2)
Investigator-reported renal-related adverse events		
Acute kidney injury§	129 (4.6)	136 (4.8)
Hospitalization due to acute kidney injury§	53 (1.9)	47 (1.7)
Discontinuation of trial regimen due to acute kidney injury§	5 (0.2)	7 (0.2)
Hospitalization due to acute renal failure¶	70 (2.5)	71 (2.5)
Discontinuation of trial regimen due to acute renal failure¶	31 (1.1)	36 (1.3)
Adverse events affecting ≥5% of patients in either group§		
Hyperkalemia	446 (15.8)	221 (7.8)
Nasopharyngitis	241 (8.5)	250 (8.8)
Hypertension	212 (7.5)	273 (9.6)
Anemia	209 (7.4)	191 (6.7)
Peripheral edema	186 (6.6)	304 (10.7)
Diarrhea	184 (6.5)	189 (6.7)
Upper respiratory tract infection	181 (6.4)	189 (6.7)
Glomerular filtration rate decreased	179 (6.3)	133 (4.7)
Urinary tract infection	179 (6.3)	192 (6.8)
Back pain	175 (6.2)	175 (6.2)
Hypoglycemia	151 (5.3)	194 (6.9)
Dizziness	146 (5.2)	153 (5.4)
Arthralgia	142 (5.0)	149 (5.3)
Bronchitis	134 (4.7)	151 (5.3)
Constipation	131 (4.6)	163 (5.8)
Pneumonia	128 (4.5)	181 (6.4)

FIGARO-DKD SAFETY OUTCOMES

Event	Finerenone (N=3683)	Placebo (N=3658)
Investigator-reported adverse events — no. (%)		
Any adverse event	3134 (85.1)	3129 (85.5)
Adverse event related to finerenone or placebo	560 (15.2)	413 (11.3)
Adverse event leading to discontinuation of trial regimen	207 (5.6)	183 (5.0)
Any serious adverse event	1158 (31.4)	1215 (33.2)
Serious adverse event related to finerenone or placebo	35 (1.0)	27 (0.7)
Serious adverse event leading to discontinuation of trial regimen	70 (1.9)	76 (2.1)
Adverse event with outcome of death	79 (2.1)	100 (2.7)
Hyperkalemia†	396 (10.8)	193 (5.3)
Hyperkalemia related to finerenone or placebo	240 (6.5)	114 (3.1)
Serious hyperkalemia	25 (0.7)	4 (0.1)
Hospitalization due to hyperkalemia	21 (0.6)	2 (0.1)
Permanent discontinuation of trial regimen due to hyperkalemia	46 (1.2)	13 (0.4)
Hypokalemia	42 (1.1)	88 (2.4)
Renal-related adverse events		
Acute kidney injury‡	91 (2.5)	98 (2.7)
Hospitalization due to acute kidney injury‡	32 (0.9)	39 (1.1)
Discontinuation of trial regimen due to acute kidney injury‡	9 (0.2)	3 (0.1)
Hospitalization due to acute renal failure§	45 (1.2)	49 (1.3)
Discontinuation of trial regimen due to acute renal failure§	26 (0.7)	12 (0.3)
Covid-19–related adverse event¶		
Any adverse event	84 (2.3)	116 (3.2)
Serious adverse event	38 (1.0)	63 (1.7)
Central laboratory assessments — no./total no. (%)		
Serum potassium level		
>5.5 mmol/liter	495/3677 (13.5)	233/3655 (6.4)
>6.0 mmol/liter	86/3677 (2.3)	43/3655 (1.2)

N Engl J Med. 2020;383:2219-2229; N Engl J Med 2021; 385:2252-2263.

MONITORING HYPERKALEMIA ON FINERENONE

Chronic Kidney Disease associated with Type 2 Diabetes

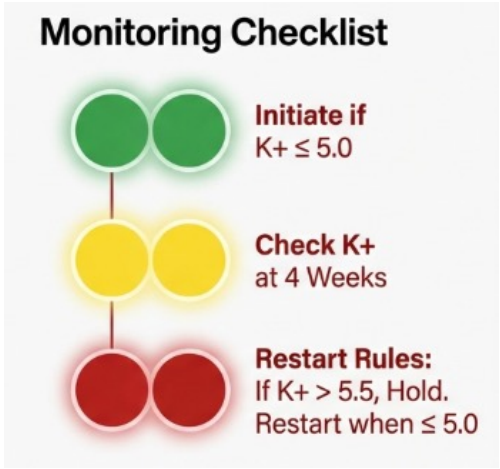
Measure serum K+ and eGFR levels 4 weeks after initiation, restart, or dose adjustment
WITHHOLD TREATMENT if serum K+ is >5.5 mEq/L and consider restarting at 10 mg once serum K+ is ≤5.0 mEq/L

Serum K+ level	Dose adjustment
≤4.8 mEq/L	Increase to† or maintain at target dose
>4.8 to 5.5 mEq/L	Maintain current dose

Heart Failure with Ejection Fraction ≥40%

Measure serum K+ and eGFR levels 4 weeks after initiation, restart, or dose adjustments
WITHHOLD TREATMENT if serum K+ is ≥6.0 mEq/L and restart at 10 mg once serum K+ is <5.5 mEq/L*

Serum K+ level	Dose adjustment
<5.0 mEq/L	Increase to† or maintain at target dose
≥5.0 to <5.5 mEq/L	Maintain current dose
≥5.5 to <6.0 mEq/L	Decrease dose to previous strength‡



Bayer Pharmaceuticals. Kerendia (finerenone) [package insert]. U.S. Food and Drug Administration.

THE FIDELITY ANALYSIS: POOLED EFFICACY AND SAFETY

13,026 Patients (FIDELIO + FIGARO)

Results

Time to CV death, non-fatal MI/ Stroke, or HHF

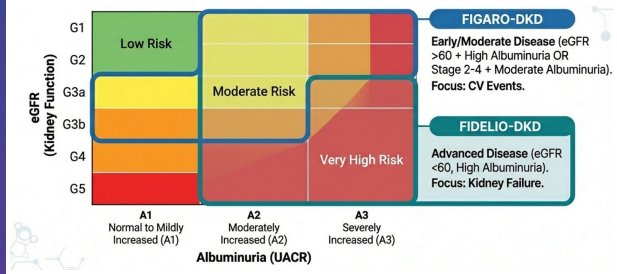
	HR (95% CI)	p-value	Risk ↓
Endpoint CV composite	0.86 (0.78 – 0.95)	0.0018	14%
HHF	0.78 (0.66 – 0.92)	0.0030	22%

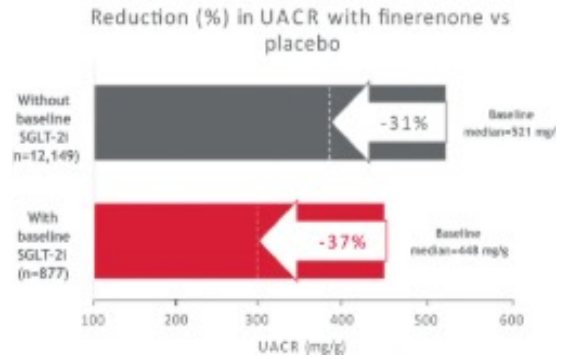
Time to kidney failure, sustained ≥57% ↓ eGFR, or renal death

	HR (95% CI)	p-value	Risk ↓
Kidney composite	0.77 (0.67 – 0.88)	0.0002	23%
Dialysis	0.80 (0.64 – 0.99)	0.040	20%

Conclusion

Finerenone on top of standard of care reduces the risk of clinically meaningful cardiovascular and kidney outcomes in patients with type 2 diabetes over a broad spectrum of chronic kidney disease



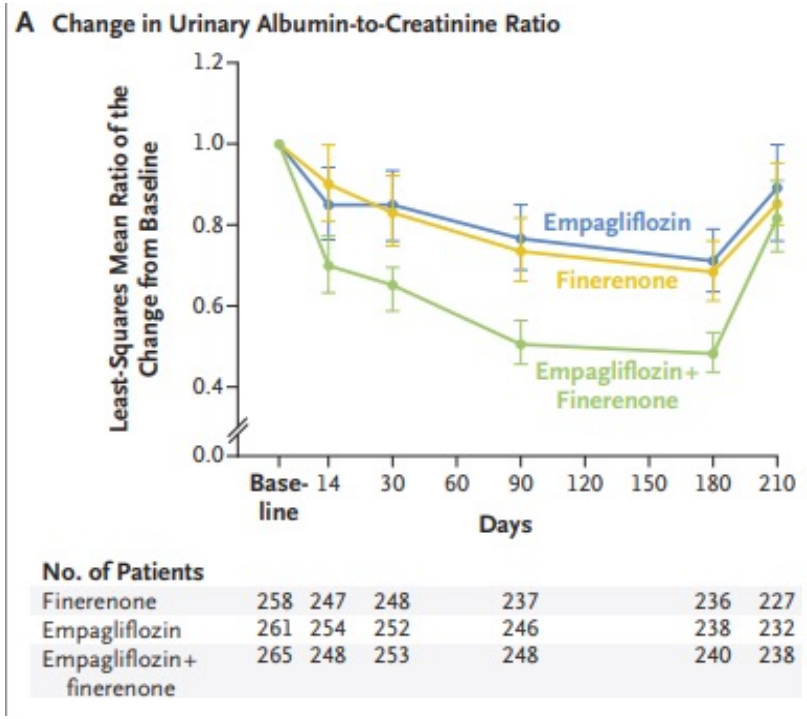


Effects of finerenone on cardiorenal outcomes are consistent regardless of SGLT2i

Eur Heart J. 2022 Feb 10;43(6):474-484.

SHOULD WE START FINERENONE AND SGTL2I TOGETHER?

	CONFIDENCE Trial N Engl J Med 2025;393:533-543
Study Design	Phase II, international, randomized, double-blind, 3-arm, active-controlled trial
Population	800 patients with T2DM (HbA1c<11%) and CKD (eGFR 30-90 mL/min + albuminuria (defined as UACR 100 – 5000 mg/g), already on ACEI/ARB for >1 month and K≤4.8
Interventions	1:1:1 ratio of finerenone (and empagliflozin-matching placebo) vs empagliflozin (and finerenone-matching placebo) vs combination
Primary endpoint	**Change in UACR baseline to day 180**: Combination therapy showed a 52% reduction in UACR at 180 days, significantly more effective, 29% greater reduction than finerenone alone and 32% greater than empagliflozin alone (P<0.001 for both) 70% of patients achieved >30% UACR reduction within 14 days vs. 52.1% for finerenone and 51.7% for empagliflozin



UACR: urinary albumin to creatinine ratio

N Engl J Med 2025;393:533-543

Table 3. Adverse Events and Safety Assessments after Treatment Initiation (Safety Analysis Population).*

Event or Assessment	Finerenone plus Empagliflozin (N=268)	Finerenone (N=264)	Empagliflozin (N=266)	Total (N=798)
	number (percent)			
Investigator-reported adverse events†				
Any adverse event	144 (53.7)	136 (51.5)	135 (50.8)	415 (52.0)
Adverse event leading to treatment discontinuation	12 (4.5)	9 (3.4)	9 (3.4)	30 (3.8)
Any serious adverse event	19 (7.1)	16 (6.1)	17 (6.4)	52 (6.5)
Serious adverse event leading to treatment discontinuation	3 (1.1)	3 (1.1)	2 (0.8)	8 (1.0)
Adverse event with death as the outcome	3 (1.1)	0	3 (1.1)	6 (0.8)
Hyperkalemia‡	25 (9.3)	30 (11.4)	10 (3.8)	65 (8.1)
Safety assessments				
>30% Decline in eGFR from baseline to 30 days§	17 (6.3)	10 (3.8)	3 (1.1)	30 (3.8)
Serum potassium level — no./total no.(%)¶				
>5.5 mmol/liter	40/262 (15.3)	48/258 (18.6)	25/257 (9.7)	113/777 (14.5)
>5.5 to ≤6.0 mmol/liter	34/262 (13.0)	43/258 (16.7)	21/257 (8.2)	98/777 (12.6)
>6.0 mmol/liter	12/263 (4.6)	12/262 (4.6)	7/262 (2.7)	31/787 (3.9)

Can be safely combined with SGTL2i which may further mitigate hyperkalemia risk

FINERENONE IN HEART FAILURE WITH EJECTION FRACTION ≥40%

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 24, 2024 VOL. 391 NO. 16

Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

S.D. Solomon, J.J.V. McMurray, M. Vaduganathan, B. Claggett, P.S. Jhund, A.S. Desai, A.D. Henderson, C.S.P. Lam, B. Pitt, M. Senni, S.J. Shah, A.A. Voors, F. Zannad, I.Z. Abidin, M.A. Alcocer-Gamba, J.J. Atherton, J. Bauersachs, M. Chang-Sheng, C.-E. Chiang, O. Chioncel, V. Chopra, J. Comin-Colet, G. Filippatos, C. Fonseca, G. Gajos, S. Goland, E. Goncalvesova, S. Kang, T. Katova, M.N. Kosiborod, G. Latkovskis, A.P.-W. Lee, G.C.M. Linssen, G. Llamas-Esperón, V. Mareev, F.A. Martinez, V. Melenovský, B. Merkely, S. Nodari, M.C. Petrie, C.I. Saldarriaga, J.F.K. Saraiva, N. Sato, M. Schou, K. Sharma, R. Troughton, J.A. Udell, H. Ukkonen, O. Vardeny, S. Verma, D. von Lewinski, L. Voronkov, M.B. Yilmaz, S. Zieroth, J. Lay-Flurrie, I. van Gameren, F. Amarante, P. Kolkhof, and P. Viswanathan, for the FINEARTS-HF Committees and Investigators*

OBJECTIVES

Primary Objective: Reducing Composite Cardiovascular Risk

The trial measures the impact of finerenone on total worsening heart failure events (hospitalizations and urgent visits) and death from cardiovascular causes.

PATIENT POPULATION

Global Population: 6,001 Randomized Patients

Participants were aged ≥ 40 years with symptomatic heart failure (NYHA Class II–IV) and evidence of structural heart disease.

Target Phenotype: HFmrEF and HFpEF

LVEF ≥ 40% NT-proBNP/BNP ↑

Eligible patients must have an LVEF ≥ 40% and elevated natriuretic peptides (NT-proBNP ≥ 300 pg/mL or BNP ≥ 100 pg/mL).

STUDY DESIGN

Randomized, Dose-Optimized Phase 3 Design

Finerenone 20/40mg | Placebo | Usual Therapy

Patients received finerenone (20 mg or 40 mg daily, adjusted for baseline eGFR) or placebo on top of usual therapy.

Rigorous Clinical Exclusion Criteria

<25 eGFR | K* > 5.0 mmol/L | Recent MRA Use

The study excluded patients with severe kidney disease (eGFR < 25), high potassium (> 5.0 mmol/L), or recent MRA use.

FINEARTS-HF OUTCOMES

Endpoint	Finerenone (n=3,003)	Placebo (N=2,998)	Effect	P-Value
Primary Outcome				
Total worsening of HF events + CV death	1,083 events	1,283 events	Rate ratio 0.84 (95% CI 0.74-0.95)	0.007
Worsening HF events, total	842	1,024	Rate ratio 0.82 (95% CI 0.71-0.94)	0.006
Death from CV causes, total	242 (8.1%)	260 (8.7%)	Rate ratio 0.93 (95% CI 0.78-1.11)	
Secondary Outcomes				
Change from baseline in KCCQ total symptom score (6, 9, 12 months)	+8.0± 0.3	+6.4± 0.3	Difference 1.6 (95% CI 0.8-2.3)	<0.001
Improvement in NYHA functional class at 12 months	18.6%	18.4%	Odds ratio 1.01 (95% CI 0.88-1.15)	
Kidney composite outcome	75 (2.5%)	55 (1.8%)	Hazard ratio 1.33 (95% CI 0.94-1.89)	
Death from any cause	491 (16.4%)	522 (17.4%)	Hazard ratio 0.93 (95% CI 0.83-1.06)	
1st worsening HF event or death from CV causes	624 (20.8%)	719 (24.0%)	Hazard ratio 0.84 (95% CI 0.76-0.94)	

CARDIOLOGY GUIDELINES

2021 ESC Guidelines For The Management Of Cardiovascular Disease In Patients With Diabetes

- Finerenone is recommended in addition to an ACEi or ARB when eGFR ≥60 mL/min/$^{1.73\ m2}$ with a UACR ≥30 mg/mmol, or an eGFR 25–60 mL/min/$^{1.73\ m2}$ and UACR ≥3 mg/mmol **(Grade IA recommendation)**

2023 ESC Guidelines Focused Update Of The 2021 ESC Guidelines For The Diagnosis And Treatment Of Acute And Chronic Heart Failure

Recommendations	Class[a]	Level[b]
In patients with T2DM and CKD,[c] SGLT2 inhibitors are recommended to reduce the risk of HF hospitalization or CV death.[35]	I	A
In patients with T2DM and CKD,[c] finerenone is recommended to reduce the risk of HF hospitalization.[10,11,34,40]	I	A

ACC: American College of Cardiology; AHA: American Heart Association; HFSA: Heart Failure Society of America; ESC: The European Society of Cardiology

Eur Heart J. 2021;42(36):3599–3726; Eur Heart J. 2023;44(37):3627–3639.
J Am Coll Cardiol 2022;Apr 1:[Epub ahead of print]

KDIGO GUIDELINES

2024 KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

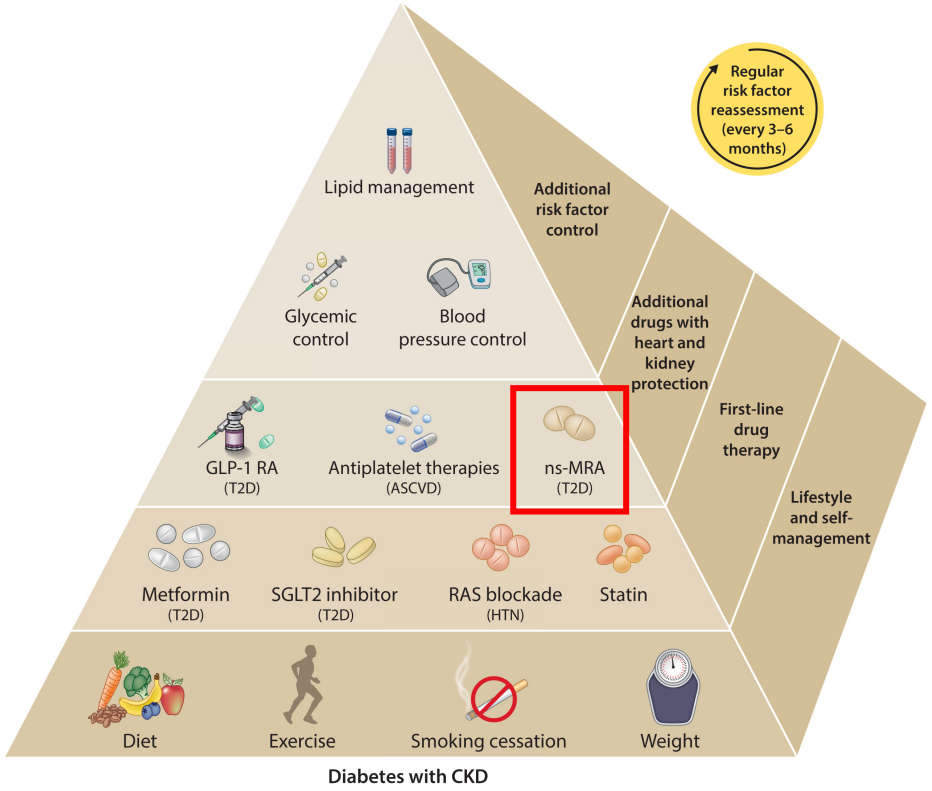
Recommendation 3.8.1: We suggest a nonsteroidal mineralocorticoid receptor antagonist with proven kidney or cardiovascular benefit for adults with T2D, an eGFR >25 ml/min per 1.73 m^2, normal serum potassium concentration, and albuminuria (>30 mg/g [>3 mg/mmol]) despite maximum tolerated dose of RAS inhibitor (RASi) *(2A)*.

Practice Point 3.8.1: Nonsteroidal MRA are most appropriate for adults with T2D who are at high risk of CKD progression and cardiovascular events, as demonstrated by persistent albuminuria despite other standard-of-care therapies.

Practice Point 3.8.2: A nonsteroidal MRA may be added to a RASi and an SGLT2i for treatment of T2D and CKD in adults.

Practice Point 3.8.3: To mitigate risk of hyperkalemia, select people with consistently normal serum potassium concentration and monitor serum potassium regularly after initiation of a nonsteroidal MRA (Figure 26).

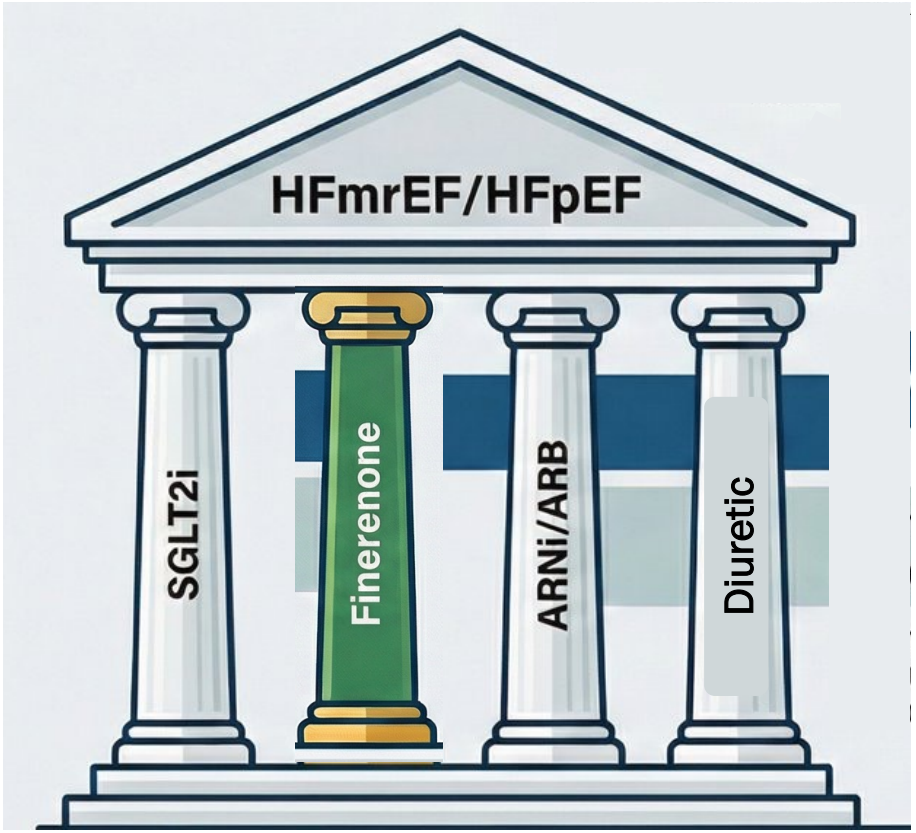
2022 KDIGO Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease

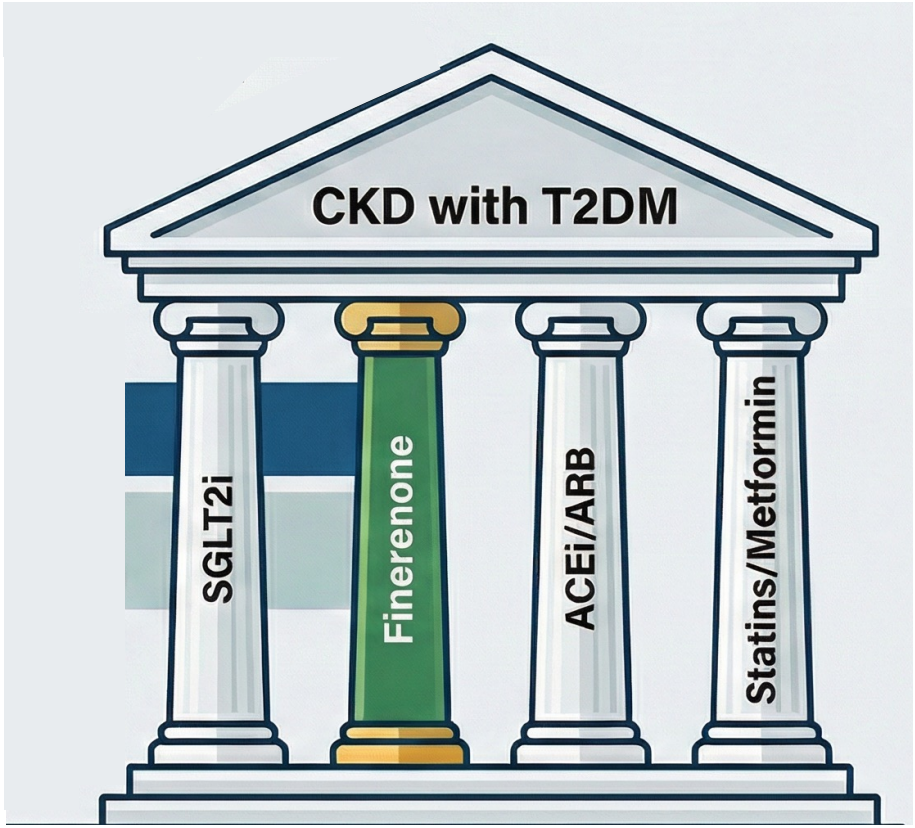


KDIGO: Kidney Disease: Improving Global Outcomes

Kidney Int. 2024;105(4S):S117–S314.
Kidney Int. 2022;102, S1-S127.

THE NEW FOUNDATIONAL PILLAR OF CARDIORENAL THERAPY





MRAs are underused –
Early implementation has the potential to significantly improve long-term cardio-renal outcomes

THE FUTURE OF FINERENONE

The therapeutic scope is rapidly expanding into other indications:

- **FINE-HEART**: pooled analysis of FIDELIO-DKD, FIGARO-DKD, FINEARTS-HF
  - 9% reduction in All-Cause Mortality; consistent cardio-kidney protection across the CKM spectrum
  - Significantly reduces sudden death and new-onset atrial fibrillation

- **FINE-CKD**: non-diabetic CKD
  - largest Phase III study
  - Met primary endpoint of a lower eGFR slope decline vs. placebo through Month 32

- **FINE-ONE**: T1DM and CKD
  - 25% reduction in albuminuria (UACR) within 6 months (p=0.0001)

T1DM: Type 1 diabetic

THANK YOU

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THE KIDNEY–HEART ALLIANCE:

FINERENONE AND THE EXPANDING CARDIORENAL LANDSCAPE

Karen Chen, PharmD, BCPS

April 16, 2026

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