Finerenone in Clinical Practice

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Outline

1. Why MR overactivation is important in pathogenesis of DKD
2. What is Finerenone
3. Differences between Steroidal and Non steroidal MRA
4. Indications of Finerenone
5. Finerenone in guidelines
6. Finerenone in clinical trials
7. How to give finerenone,,Doses,Titration and monitorings
8. Side effects of Finerenone
9. 4 pillars of DKD
10. Is combinations is better
11. Can SGLT2 I combine with finerenone
12. Sequences of combinations Therapy

Combination Medical Therapy:
A New Standard of Cardio-Renal-Metabolic Care

HFrEF

"Quadruple Therapy"

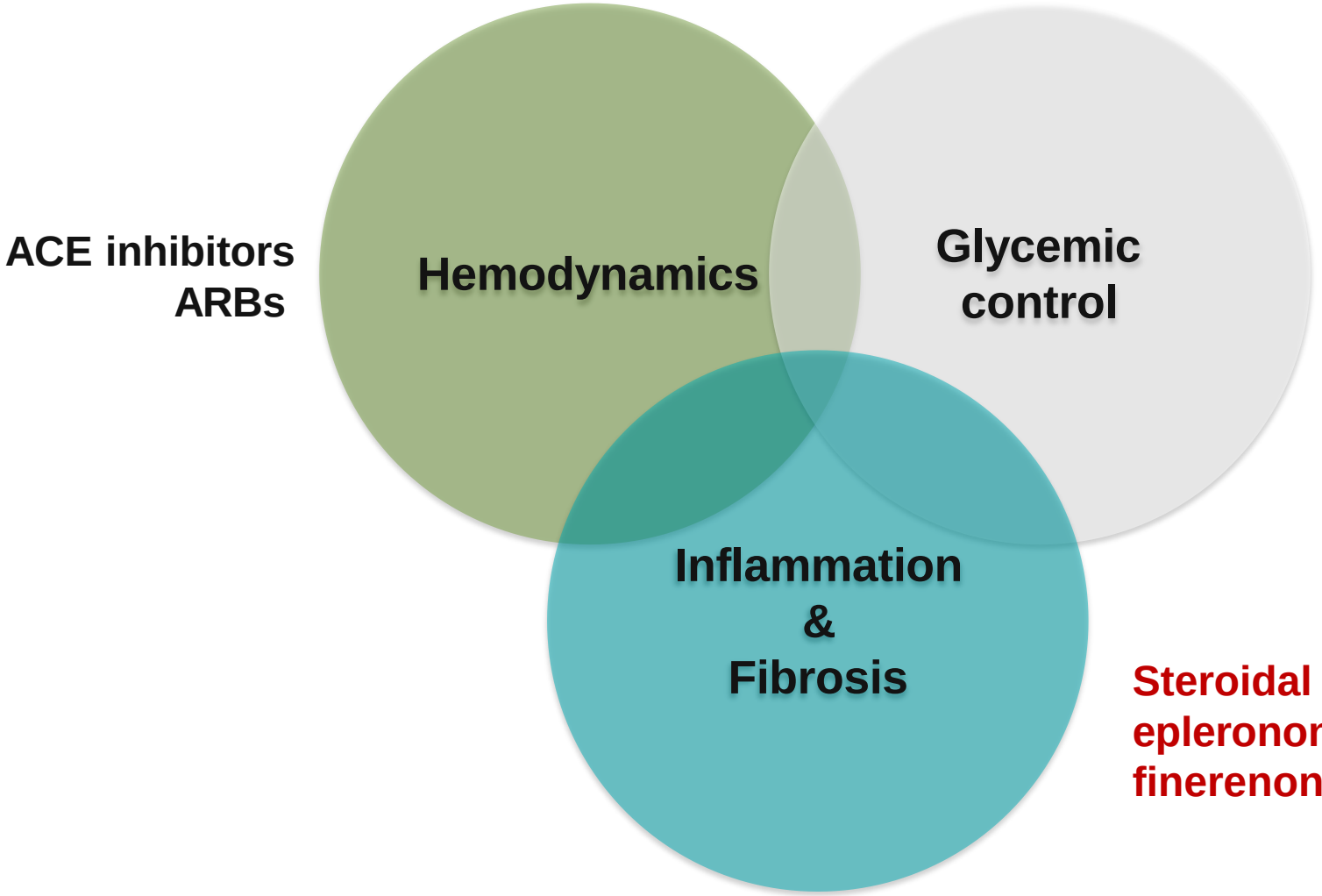
- **β-blocker**
- **ACEi/ARB/ARNI**
- ***Non-Steroidal* MRA**
- **SGLT-2 Inhibitor**

CKD

"Quadruple" Therapy

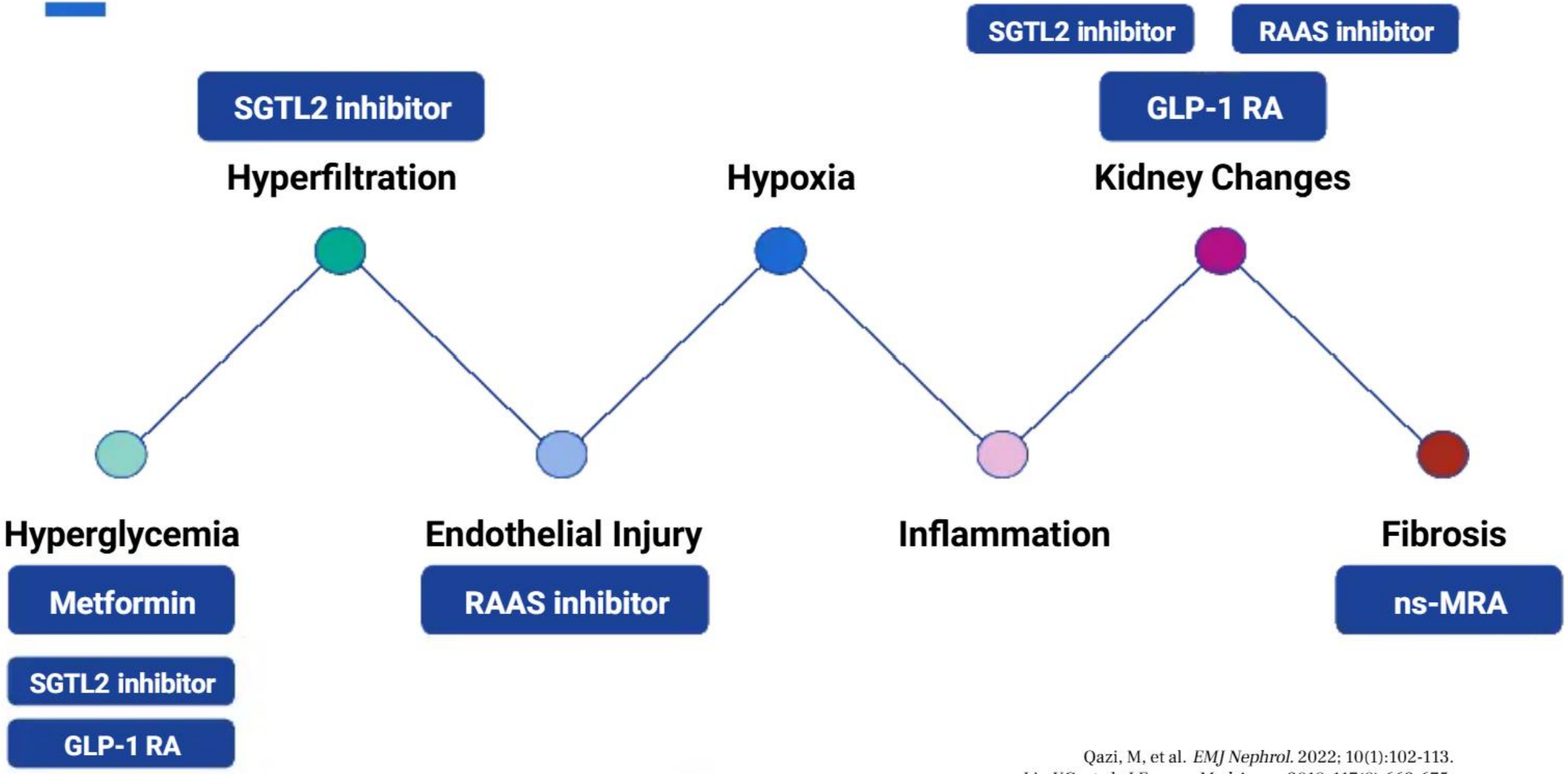
- **ACEi/ARB**
- ***Non-Steroidal* MRA**
- **SGLT-2 Inhibitor**
- **GLP-1RA**

Strategies to Slow Progression of CKD



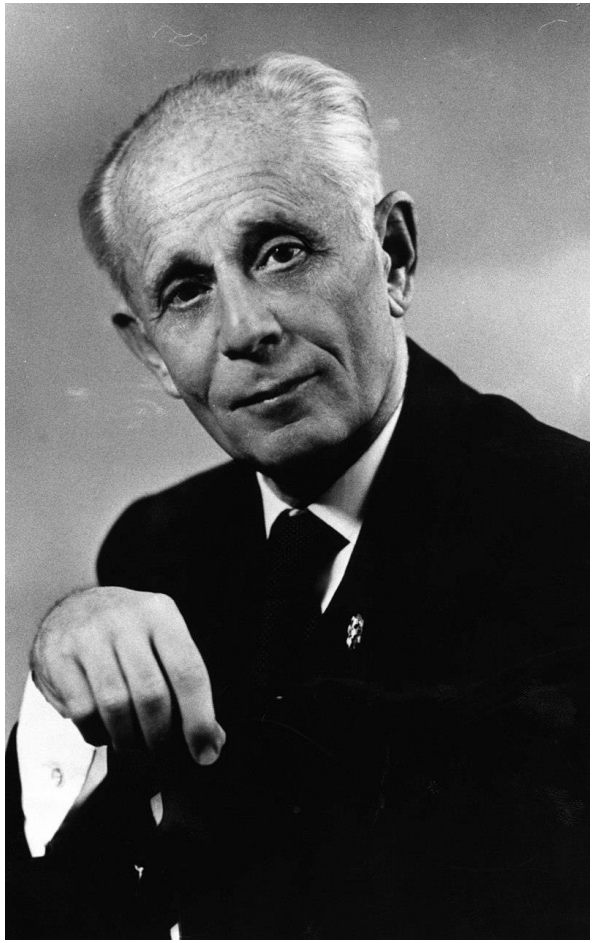
- Kolkhof P, et al. *Mol Cell Endocrinol*. 2012;350:310–317; Kolkhof P, et al. *J Endocrinol*. 2017;234:T125-T140.

DKD Overview – Treatment Targeting the Pathophysiology



Qazi, M, et al. *EMJ Nephrol.* 2022; 10(1):102-113.
Lin YC, et al. *J Formos Med Assoc.* 2018; 117(8):662-675.

MR Overactivation as a Central Driver of Inflammation and Fibrosis in the Heart and Kidneys



Hans Selye, 1907-1982,
Born Vienna, Austria-Hungary
Source: Wikipedia

MALIGNANT HYPERTENSION PRODUCED BY TREATMENT WITH DESOXYCORTICOSTERONE ACETATE AND SODIUM CHLORIDE*

By Hans Selye, M.D., Ph.D., D.Sc., F.R.S.C.,
C. E. Hall,† M.Sc. and E. M. Rowley, B.Sc.

Montreal

- Selye H, et al. *Can Med Assoc J*. 1943;49:88-92.

How MR Overactivation leads to Kidney Damage

Mineralocorticoid Receptor (MR) Overactivation: Key Driver of Kidney Damage

Mineralocorticoid receptors
regulate gene expression through cofactor recruitment[1]

In kidney disease, multiple factors overactivate the MR
including aldosterone, Rac1, cortisol, and others[2,3]

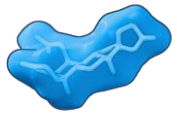
Overactivation of the MR signalling pathway drives inflammation and fibrosis
via proinflammatory cytokines and fibrotic proteins,
eg, TNF-α, IL-1b, and IL-6[1,2]

MR overactivation results in deleterious effects on the heart and kidney, promoting cardiac remodeling and progression of both kidney and cardiovascular disease[2]

1. Ong. J Mol Endocrinol. 2017;58:R33. 2. Bauersachs. Hypertension. 2015;65:257. 3. Bertocchio. Kidney Int. 2011;79:1051.

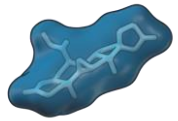
Mechanisms of MRA-Mediated Cardiovascular and Renal Protection via Inhibition of Aldosterone-Induced MR Overactivation

Generations of MRAs



Spironolactone

1st Generation



Eplerenone

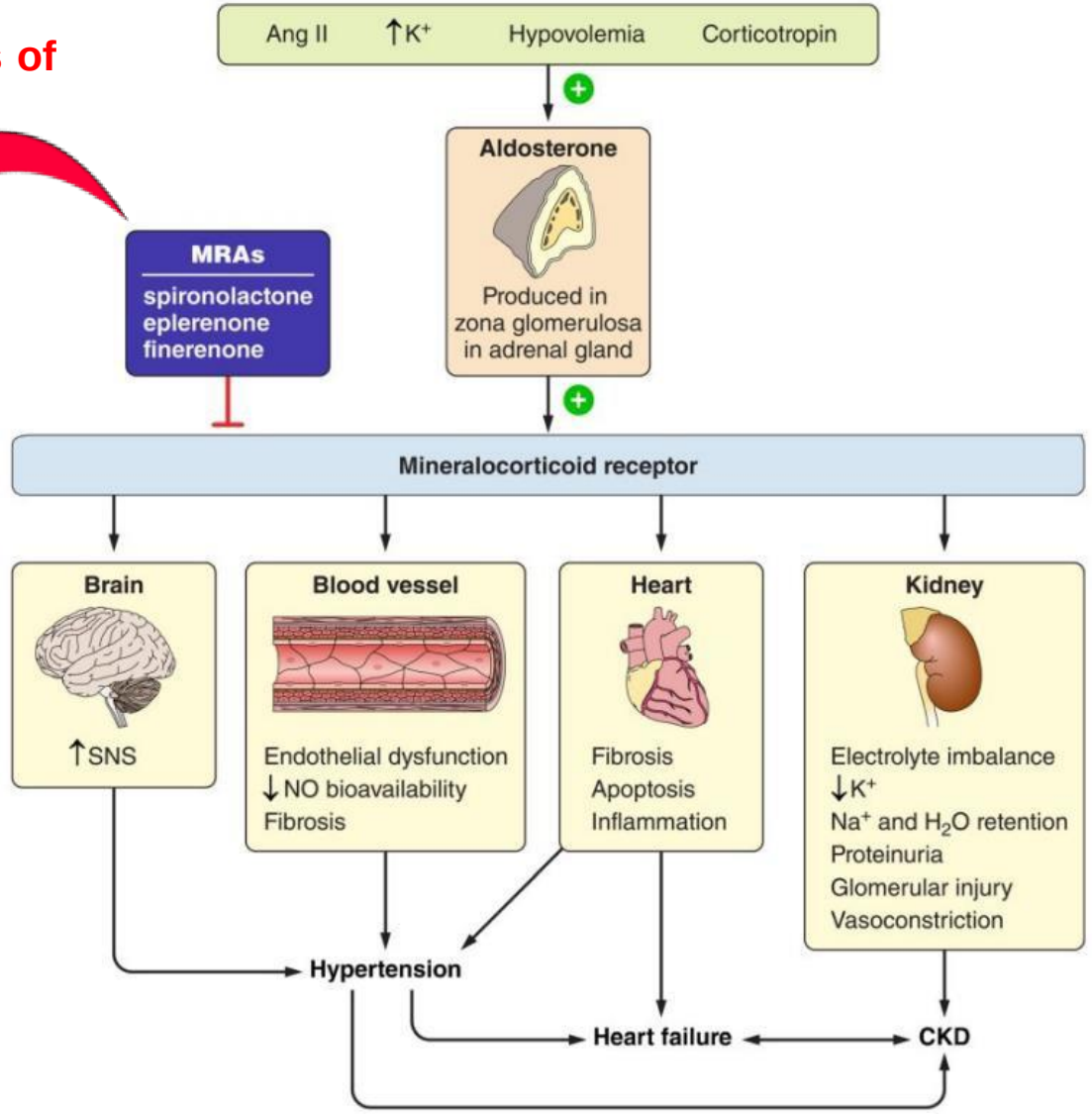
2nd Generation

Finerenone

3rd Generation

(1st Generation of ns-MRA)

FIDELIO-DKD

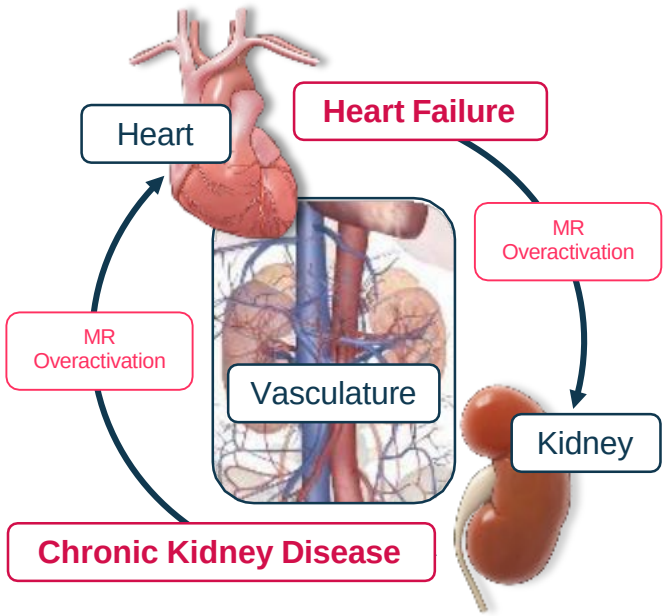


ns-MRA: non-steroidal Mineralocorticoid Receptor Antagonist

Curr Diab Rep. 2019 Jan 23;19(1):4.

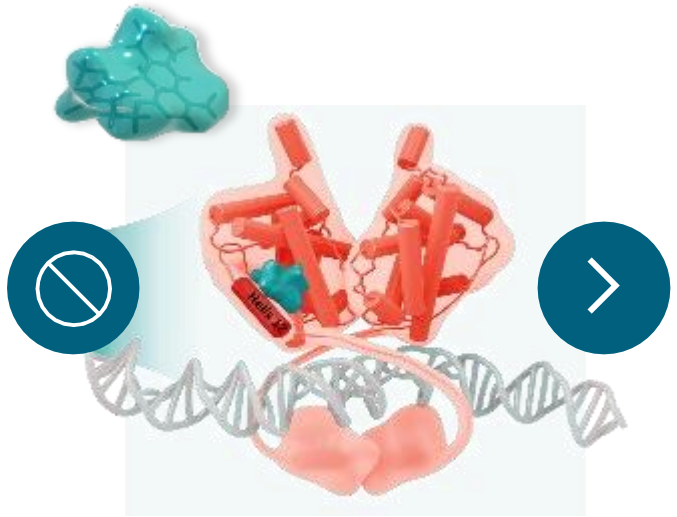
Highly Selective Inhibition of MR Overactivation With Finerenone to Address Fundamental Drivers of Disease Progression

Vicious Cycle of Worsening Disease



Pathophysiologic Heart-kidney Interplay

Finerenone



- Reduces Fibrosis
- Reduces inflammation
- Reduces Oxidative Stress
- Improves Endothelial Function

Halting the Vicious Cycle by Blocking MR Overactivation

- Highly selective inhibition of the MR receptor – reducing MR overactivation[1]
- Improved heart and kidney health[2]
- Improved patient outcomes[2]
- Breaking the MR-induced spiral of pathogenic heart-kidney damage [2,3]
- Address fundamental drivers of end-organ damage in HF and LVEF ≥40% [2,3]

HF: Heart failure; LVEF: Left ventricular ejection fraction; MR: Mineralocorticoid receptor
[1] Kolkhof P, et al. Handb Exp Parmacol 2017;243:271–305 [2] Kolkhof P, et al. Int J Mol Sci 2022, 23(16):9243 [3] Epstein M, et al. Am J Kidney Dis 2022;80(5):658-666

Due to Its Distinct Structural and Pharmacological Properties, Finerenone's Clinical Profile Significantly Differs from Other MRAs

Structural and pharmacological properties of MRAs[2]

	Spironolactone	Eplerenone	Finerenone
MRA Class	Steroidal	Steroidal	Non-steroidal
Potency	High	Low	High
Selectivity	Low	Medium	High
Metabolites	Multiple, active	No active	No active
Tissue distribution[3]	Kidney>>heart (>6-fold)	Kidney>heart (~3-fold)	Balanced (1:1)
Indication and key studies	HF with LVEF ≥40%: TOPCAT study failed[4] HF with LVEF <40%: class 1 recommendation[1-3] (RALES study)	HF with LVEF ≥40%: not tested HF with LVEF <40%: class 1 recommendation[1-3] (EPHESUS study)	Significant risk reduction in HF with LVEF ≥40% and patients with CKM
First launch	1960	2002	2021 in CKD/T2D

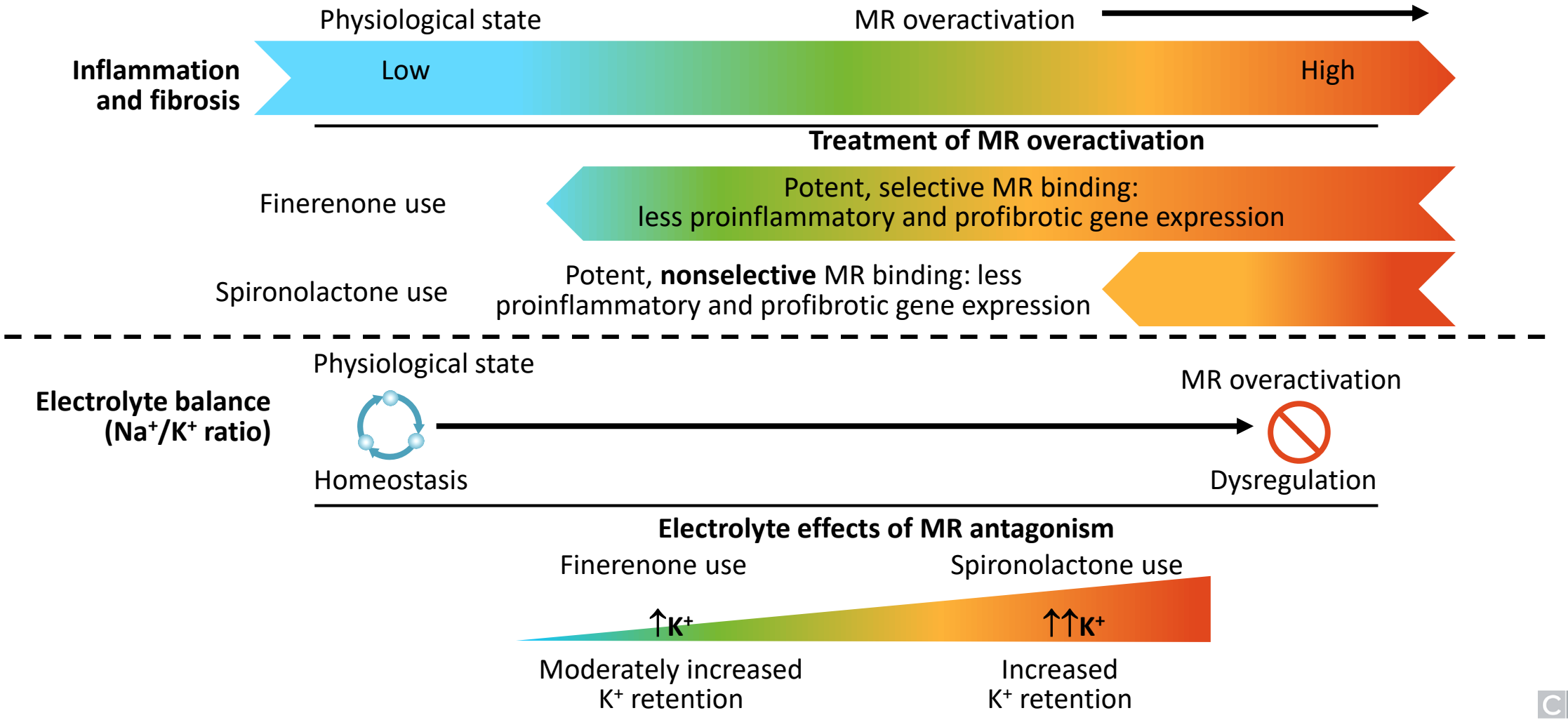
Characteristics of Finerenone

- Significant molecular and pharmacological differences that explain cardiorenal clinical effects[4]
- High selectivity for the MR over other steroid hormone receptors, which prevents antiandrogenic and progestational side effects[4]
- Balanced cardiac and kidney distribution
- Low incidence of hyperkalaemia-related adverse events with clinical impact and permanent treatment discontinuation[5]

CKM: Cardiovascular-kidney-metabolic; HFpEF: Heart Failure with preserved ejection fraction; HFrEF: Heart Failure with reduced ejection fraction; LVEF: Left ventricular ejection fraction; MRA: Mineralocorticoid receptor antagonist

[1] Kolkhof P, Nowack C, Eitner F. Curr Opin Nephrol Hypertens. 2015;24:417-424. [2] Modified from: Kolkhof B, Borden SA. Mol Cell Endocrinol. 2012;350:310-317. [3] Determined in rodents. [4] Kintscher U, Bakris GL, Kolkhof P. Novel non-steroidal mineralocorticoid receptor antagonists in cardiorenal disease. Br J Pharmacol. 2022 Jul;179(13):3220-3234. [5] Agarwal R, Filippatos G, Pitt B, Anker SD, Rossing P, Joseph A, Kolkhof P, Nowack C, Gebel M, Ruilope LM, Bakris GL; FIDELIO-DKD and FIGARO-DKD investigators. Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis. Eur Heart J. 2022 Feb 10; 43(6):474-484. doi: 10.1093/eurheartj/ehab777. Erratum in: Eur Heart J. 2022 May 21;43(20):1989.

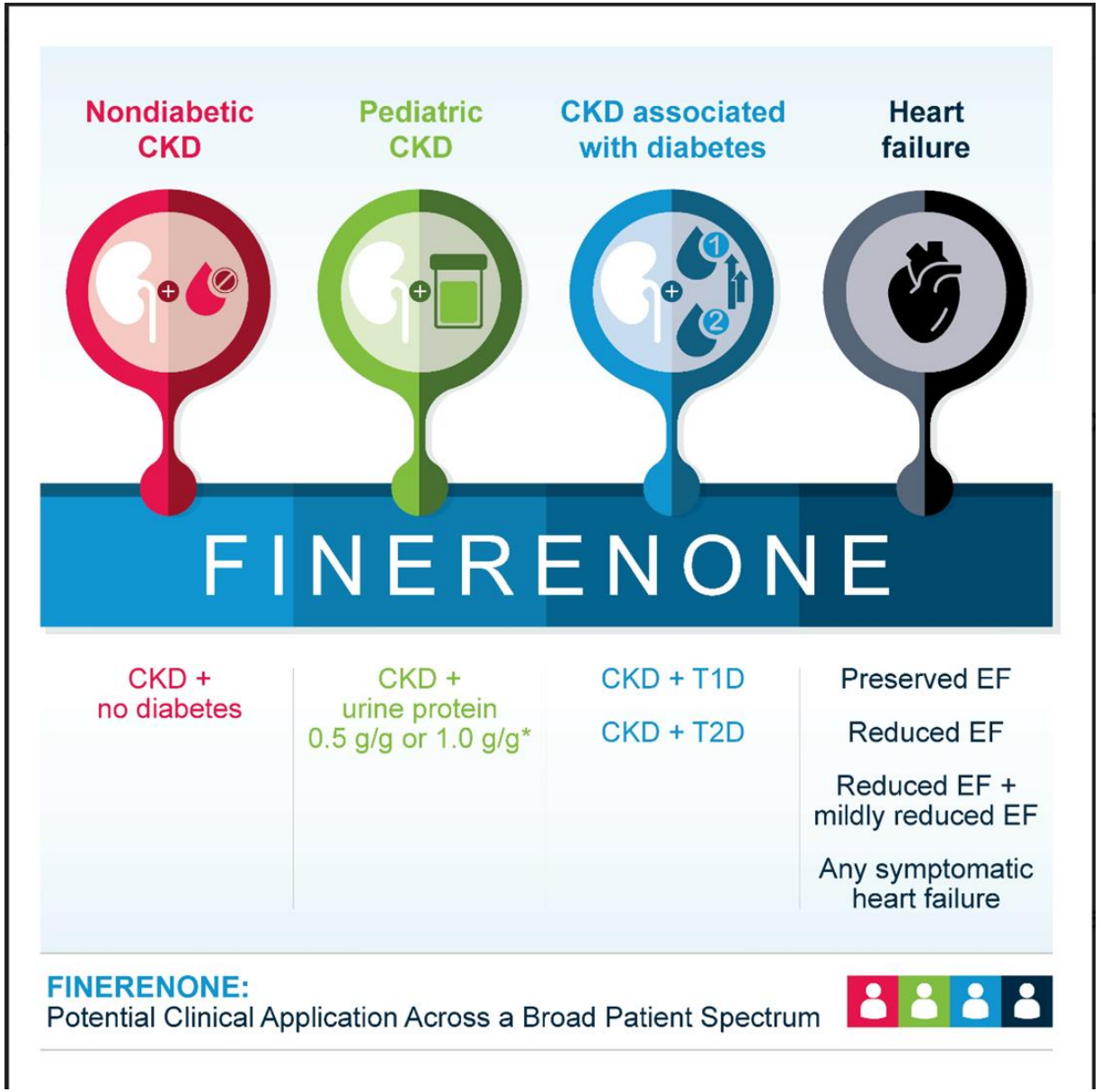
MRAs: Selectivity and Effects on Potassium



Agarwal. Nephrol Dial Transplant. 2022;37:1014.

Slide credit: clinicaloptions.com

Finerenone Indications and Guidelines



Finerenone: Indication

- **FDA approved in 2021**
- **Indication**
  - Indicated to reduce the risk of sustained eGFR decline, ESKD, CV death, nonfatal MI, and hospitalization for heart failure in adult patients with CKD associated with type 2 diabetes

In Europe, finerenone is indicated for the treatment of chronic kidney disease (stage 3 and 4 with albuminuria) associated with type 2 diabetes in adults.

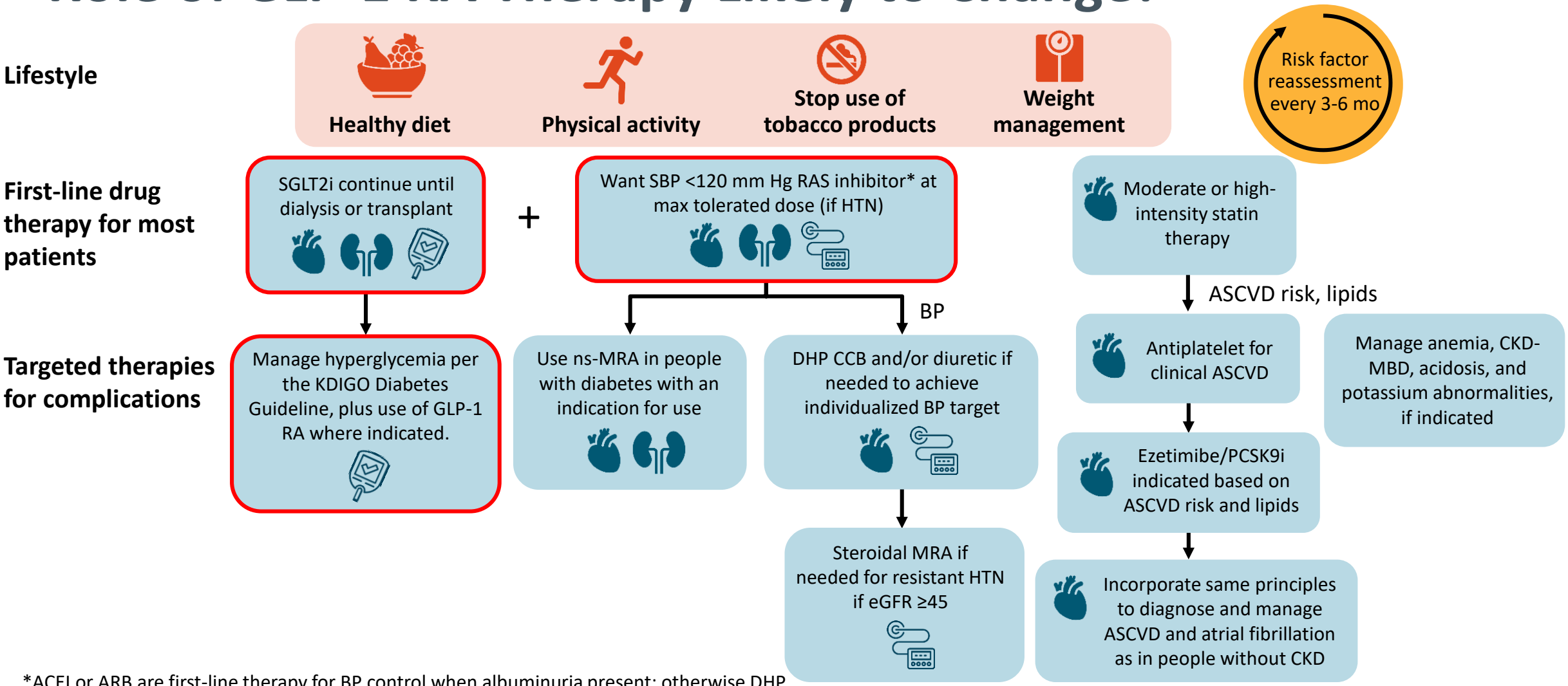
"In patients with chronic kidney disease who are at increased risk for cardiovascular events or chronic kidney disease progression or are unable to use a sodium-glucose cotransporter 2 inhibitor, a nonsteroidal mineralocorticoid receptor antagonist (finerenone) is recommended to reduce chronic kidney disease progression and cardiovascular events."

ADA Recommendation for Finerenone

Finerenone PI.

Slide credit: clinicaloptions.com

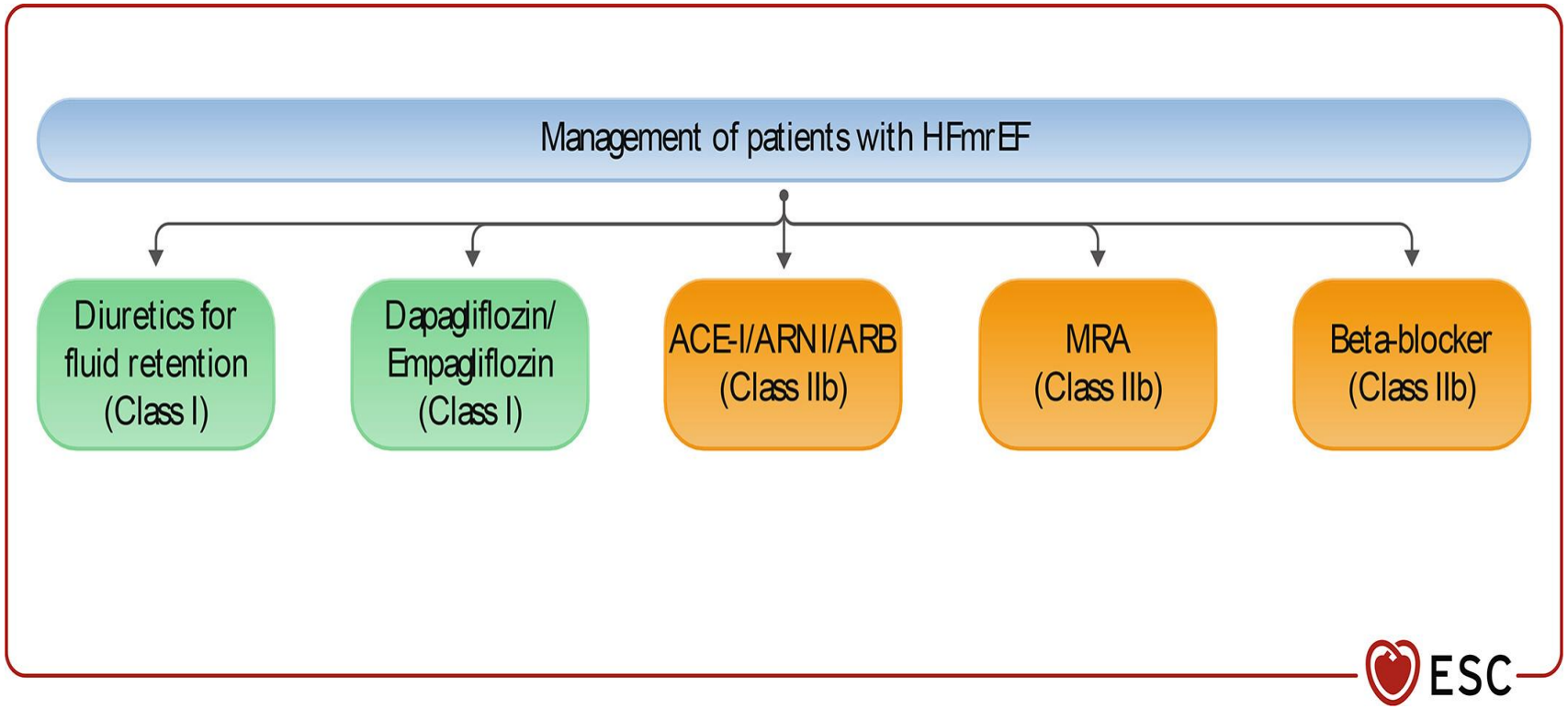
KDIGO 2024: RASi and SGLT2i First Line in CKD: Role of GLP-1 RA Therapy Likely to Change!



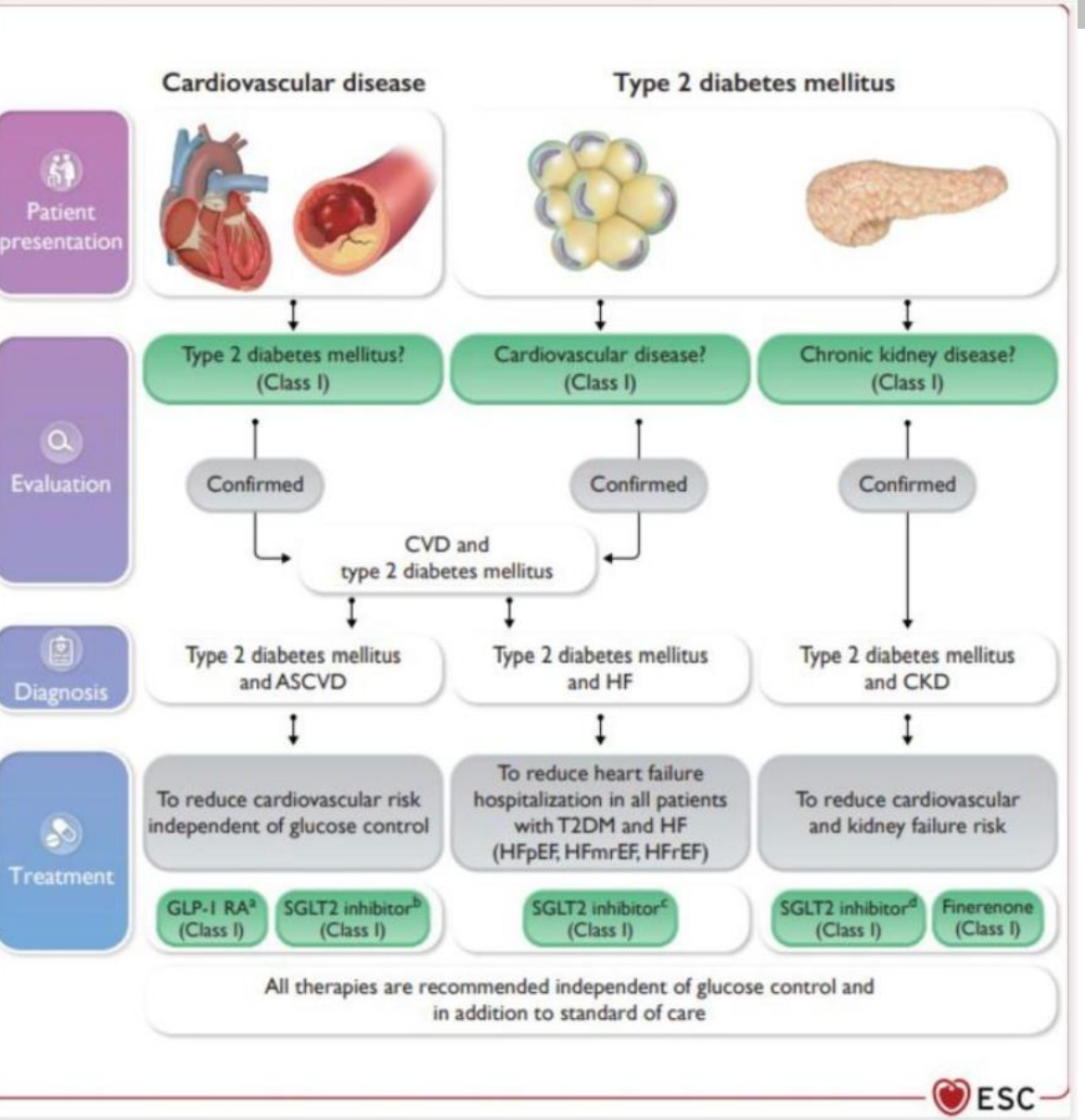
*ACEI or ARB are first-line therapy for BP control when albuminuria present; otherwise DHP CCB or diuretic can be considered

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. Kidney Int. 2024;105:S117.

2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure



European J of Heart Fail, Volume: 26, Issue: 1, Pages: 5-17, First published: 03 January 2024, DOI: (10.1002/ejhf.3024)



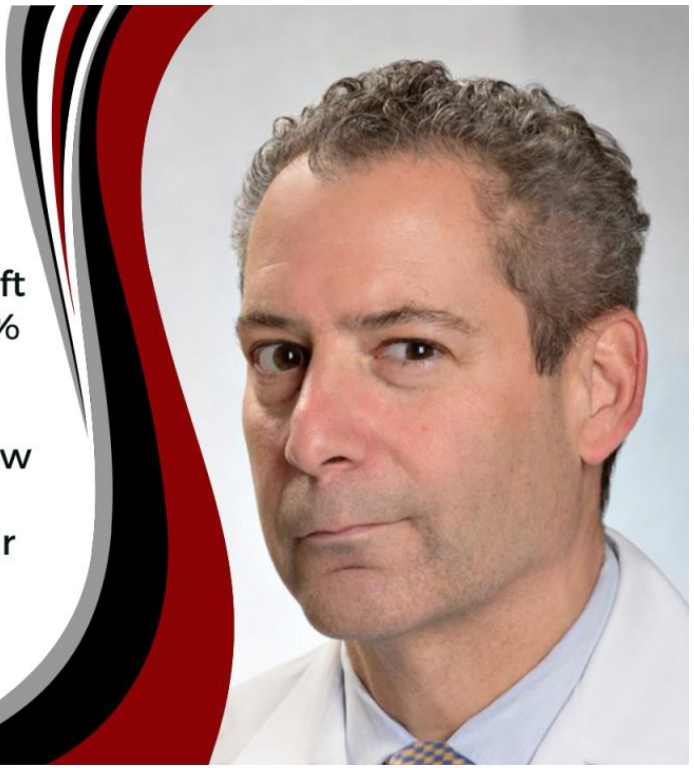
escardio.org • 1 min read

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes

HCP Live®

"The FDA's approval of finerenone expands treatment options for patients with heart failure with a left ventricular ejection fraction of ≥40% – a large and growing group of patients with a poor prognosis. Based on the clinical efficacy we saw in the FINEARTS-HF study, finerenone can become a new pillar of comprehensive care."

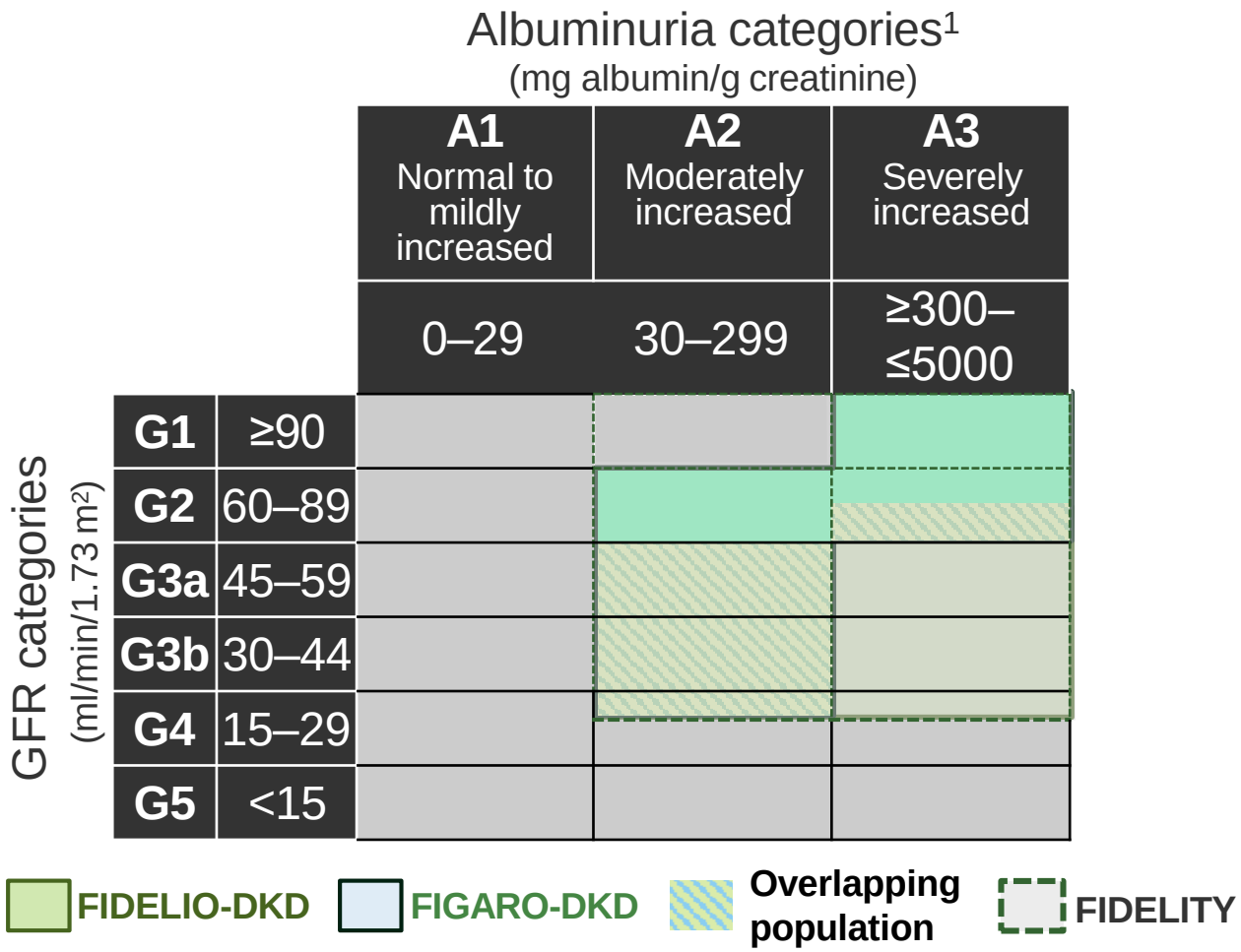
Scott D. Solomon, MD
Harvard Medical School, Mass General Brigham



Trials of MR Antagonism in HF and CKD

	SPIRIT-HF	SPIRRIT	FINEARTS-HF	FIND-CKD
Therapy	Spironolactone	Spironolactone	Finerenone	Finerenone
Sample Size	1300	3200	5500	1500
Population	HF and LVEF ≥ 40%	HF and LVEF ≥ 40%	HF and LVEF ≥ 40%	Non-diabetic CKD
Primary Endpoint	CV Death + Total HF Hospitalization	CV Death + Total HF Hospitalizations	CV Death + Total HF Events	Change in eGFR Slope
Estimated Completion Date	2024	2022	2024	TBD

Evaluation of Finerenone Across the Spectrum of Kidney Disease in Type 2 Diabetes(Finerenone in Clinical Trials)



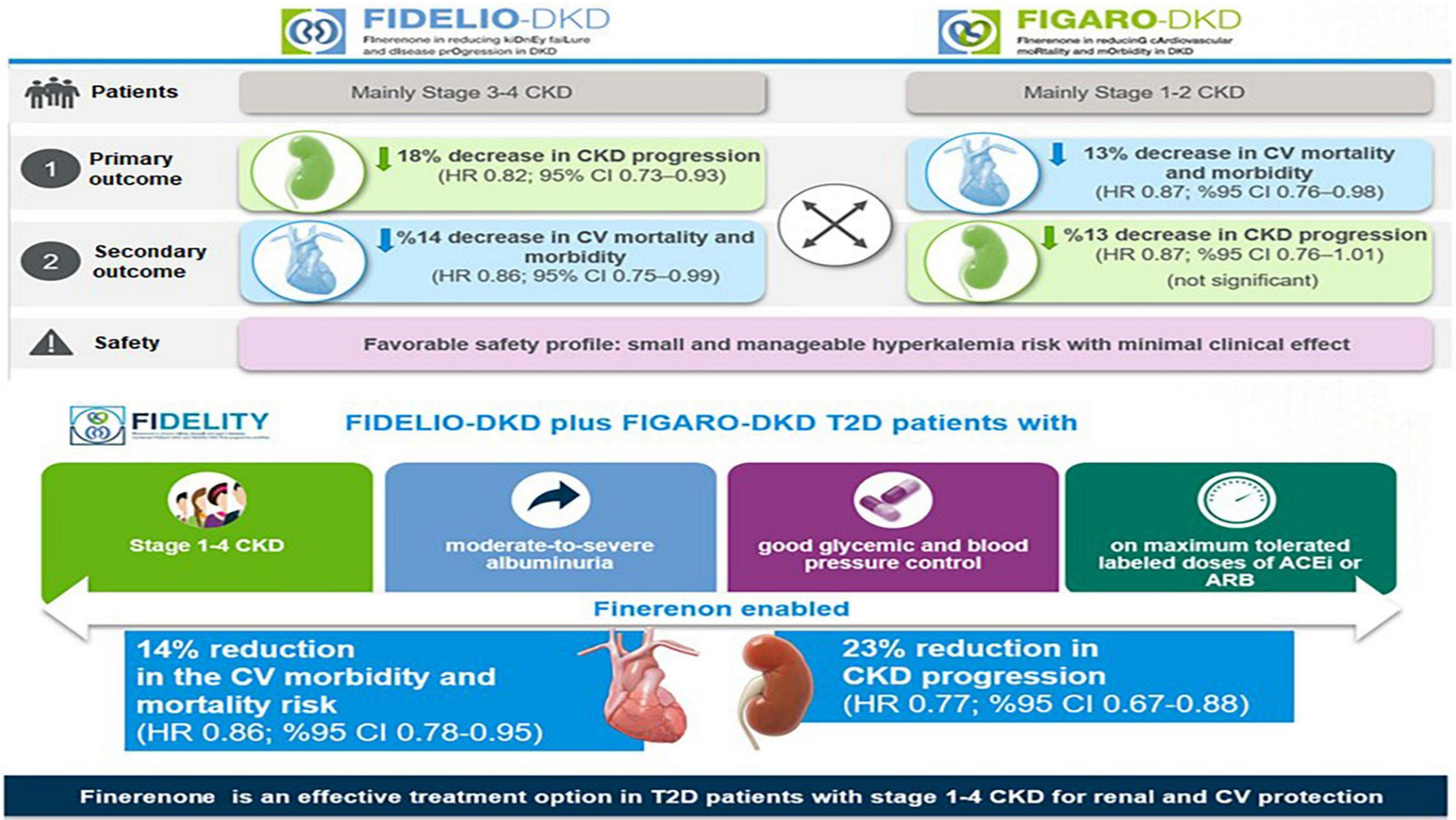
FIDELITY[4]
N=13,171

FIDELIO-DKD[2]
N=5734

FIGARO-DKD[3]
N=7437

1. *Kidney Int* 2013;3:1–150; 2. Bakris GB, *et al. N Engl J Med* 2020;383:2219–2229; 3.

Finerenone in Clinical Trials



Pooled Safety Data from 2 Pivotal RCTs of Finerenone in CKD

Finerenone had a modest effect on blood pressure

Overall difference in mean SBP between groups:

	Month 4	Month 12
FIDELIO-DKD[1]	–3.9 mmHg	–3.0 mmHg
FIGARO-DKD[2]	–3.5 mmHg	–3.0 mmHg
FIDELITY[3]	–3.7 mmHg	–3.0 mmHg

HbA1c levels and body weight were similar in both groups throughout the study

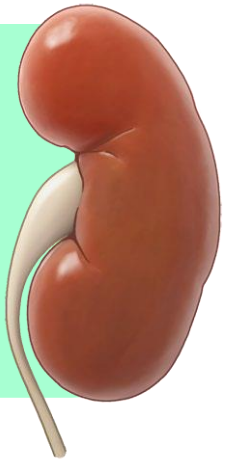
There were no differences in acute kidney injury between groups

Sexual side effects (e.g. gynaecomastia) were rare and balanced between groups

FIDELITY pooled analysis: NNT to prevent one kidney outcome event at 3 years

HR (95% CI)	ARR (95% CI) at 36 months	NNT (95% CI) at 36 months
0.77 (0.67–0.88)	–1.7% (–2.6 to –0.7)	60 (38–142)

- **Hazard ratio = 0.77** – equivalent to a **23% relative risk reduction**
- **Absolute risk reduction = 1.7%** at 3 years
- **NNT** to **prevent one kidney outcome event** was **60** at 3 years



FINEOVATE to Further Support Finerenone's Ambition as a Foundational Treatment Across the Spectrum of CKD and HF

THUNDERBALL | **FINEOVATE** | MOONRAKER

Paediatric CKD

FIONA OLE — September 2028*

FIONA — March 2027*

Nondiabetic CKD

FIND-CKD — February 2026*

CKD and T1D

FINE-ONE — October 2025*

CKD and T2D

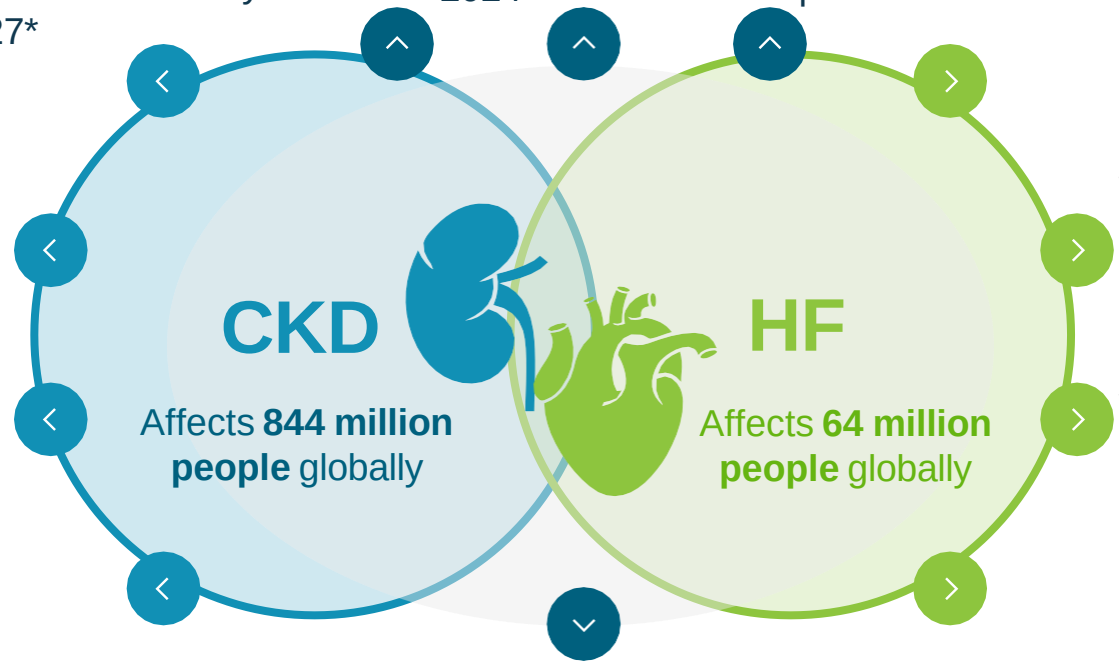
CONFIDENCE — February 2025*

Real-world evidence

FINE-REAL — January 2028*

FOUNTAIN — 2024#

WATERFALL-HF — Completion date tbc



HF (LVEF ≤40) not on or not eligible to steroidal MRAs

FINALITY-HF — January 2028*

Hospitalised for HF (LVEF ≥40%)

REDEFINE-HF — April 2026*

Hospitalised for HF independent of LVEF

CONFIRMATION-HF — SGLT2i combination therapy August 2025*

FIDELITY ✓ | FIDELIO-DKD ✓ | FIGARO-DKD ✓ | FINEHEART ✓

Symptomatic HF (LVEF ≥40%)

✓ FINEARTS-HF

CKD: Chronic kidney disease; HF: Heart failure; HFrEF: Heart failure with reduced ejection fraction; LVEF: Left ventricular ejection fraction; MRA: Mineralocorticoid receptor antagonist; SGLT2I: Sodium-glucose cotransporter-2 inhibitors; T1D: Type 1 diabetes mellitus; T2D: Type 2 diabetes mellitus
*Estimated study completion date; #estimated study completion dates for the FIRST-2 and FINEGUST studies are June 2024 and June 2025, respectively. All dates based on CT.gov – last accessed Aug 2024

Finerenone Dosing and Monitoring

1 INITIATE

Measure serum potassium

Do not initiate KERENDIA if serum potassium >5.0 mEq/L.

If >4.8 to 5.0 mEq/L, initiation may be considered with additional potassium monitoring within the first 4 weeks based on clinical judgment and serum potassium levels.

Measure eGFR to determine recommended starting dose

10 mg	eGFR ≥25 to <60 mL/min/1.73 m^2
20 mg	eGFR ≥60 mL/min/1.73 m^2
Not recommended	eGFR <25 mL/min/1.73 m^2

2 CHECK LABS

After initiation, restart, or dose adjustment of KERENDIA:

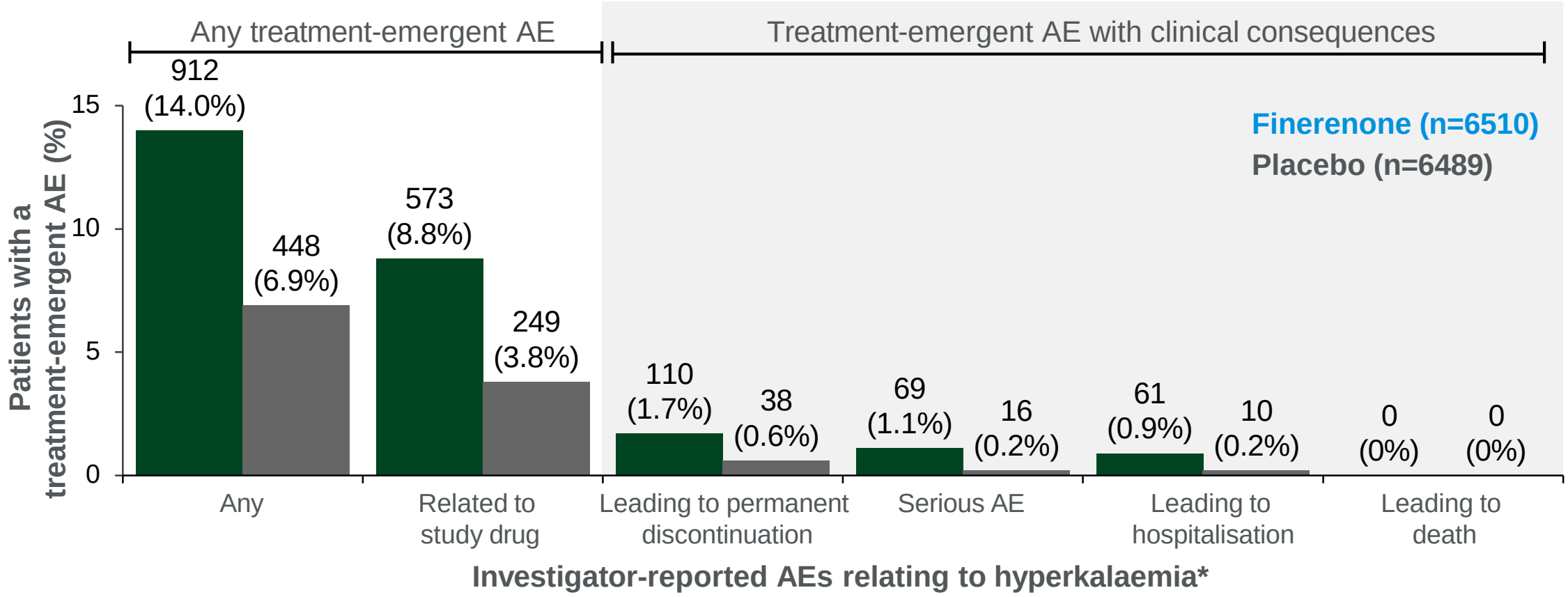
In 4 weeks, check serum potassium

3 ADJUST: Target daily dose of KERENDIA is 20 mg daily

Current serum potassium (mEq/L)	Current dose 10 mg once daily	Current dose 20 mg once daily
≤4.8	Increase the dose to 20 mg once daily*	Maintain 20 mg once daily
>4.8 to 5.5	Maintain 10 mg once daily	Maintain 20 mg once daily
>5.5	Withhold KERENDIA. Consider restarting at 10 mg once daily when serum potassium ≤5.0 mEq/L	Withhold KERENDIA. Restart at 10 mg once daily when serum potassium ≤5.0 mEq/L

*if eGFR has decreased by more than 30% compared to previous measurement, maintain 10 mg dose.

Finerenone Impact on Hyperkalemia in Pivotal RCTs



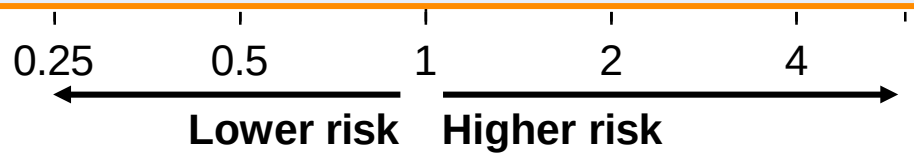
There were no deaths due to hyperkalaemia, and the incidences of treatment discontinuation or hospitalisation due to hyperkalaemia were low

*Investigator-reported AEs using the MedDRA preferred terms 'hyperkalemia' and 'blood potassium increased'.
MedDRA, Medical Dictionary for Regulatory Activities

Higher baseline [K⁺], lower eGFR and higher UACR were associated with higher risk of hyperkalaemia*

FIDELIO-DKD

Variable (%#)		HR (95% CI)	*p*-value
Baseline serum [K⁺], mmol/l	≤4.1 (30%)	0.44 (0.35–0.55)	<0.0001
	>4.1–≤4.5 (36%)	Reference	
	>4.5–≤4.8 (20%)	1.53 (1.29–1.82)	
	>4.8–≤5.0 (7%)	2.78 (2.25–3.44)	
	>5.0 (7%)	4.18 (3.45–5.05)	
Baseline eGFR, ml/min/1.73 m²	<25 (2%)	2.04 (1.35–3.07)	<0.0001
	25–<45 (53%)	1.51 (1.19–1.91)	
	45–<60 (34%)	1.02 (0.80–1.32)	
	≥60 (12%)	Reference	
Log2 of baseline UACR‡		1.12 (1.06–1.17)	<0.0001



After adjustment for age, sex, baseline UACR, baseline eGFR, baseline serum [K⁺], baseline medication use (diuretic use, βblocker use and SGLT-2i use) and treatment assignment (finerenone vs placebo); #

Frequency of potassium monitoring

Finerenone USPI label recommendations regarding potassium measurement[1]

- **Measure serum potassium** and **eGFR** in **all patients before initiation of treatment with finerenone** and **dose accordingly**. **Do not initiate finerenone** if **serum potassium is >5.0 mmol/l**
- **Measure serum potassium periodically** during **treatment with finerenone** and **adjust dose accordingly**
- **More frequent monitoring** may be necessary for patients at **risk for hyperkalaemia**, including those on **concomitant medications** that impair potassium excretion or increase serum potassium

		Current finerenone dose	
		10 mg once daily	20 mg once daily
Current serum potassium (mmol/l)	≤4.8	Increase the dose to 20 mg once daily*	Maintain 20 mg once daily
	>4.8 – 5.5	Maintain 10 mg once daily	Maintain 20 mg once daily
	>5.5	Withhold finerenone. Consider restarting at 10 mg once daily when serum potassium ≤5.0 mmol/l	Withhold finerenone. Restart at 10 mg once daily when serum potassium ≤5.0 mmol/l

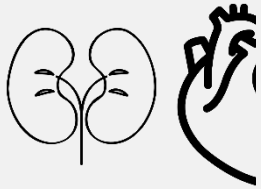
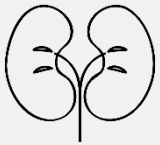
KDIGO practical guidance[2]

- Changes in **BP, serum creatinine, and serum potassium** should be checked **within 2–4 weeks of initiation** or increase in the dose of a RASi, depending on the current eGFR and serum potassium.
- In patients at **risk for hyperkalemia**, measuring **serum potassium before and at 1–2 weeks after initiation of RASi is recommended**

ESC guidance[3,4]

- Check **blood chemistry** at **1 and 4 weeks after starting/up-titrating MRA**
- **Potassium binders may be considered** in patients with **HF with or without CKD** to **manage hyperkalaemia**
- **Potassium binders** may be **considered** in selected **patients with HF with or without CKD** to allow **up-titration of MRAs** while avoiding hyperkalaemia

Finerenone : Less Serum K Change with Finerenone Compared to Spironolactone

Program	Patients	Comparator	Δ Serum K
ARTS[a] 	CKD and HF	Spironolactone	↓
ARTS-HF[b] 	HFrEF	Eplerenone	↔
ARTS-DN[c] 	CKD + A2/A3	Placebo	↑

- Bakris GL, et al. *JAMA.* 2015;314:884-894; Filippatos G, et al. *Eur Heart J*. 2016;37:2105-2114; Pitt B, et al. *Eur Heart* J. 2013;34:2453-2463.

Khullar D, Gupta AK, Singh K

Clinical Trials Evaluating the Safety and Efficacy of Finerenone in Patients with Heart Failure, Chronic Kidney Disease and/or Type 2 Diabetes

Citation: Cardiac Failure Review 2024;10:e19.
https://doi.org/10.15420/cfr.2024.11

Parameter	ARTS 2013[31]	ARTS-HF 2016[32]
Study population	HFrEF and mild to moderate CKD	HFrEF and T2D and/or CKD
Sample size, n	Part A: 65 Part B: 392	1,066
Mean age, years	Part A: 66.3 Part B: 72.1	71.2
Active arm	Part A: finerenone dose: 2.5, 5, or 10 mg once daily. Part B: finerenone dose: 2.5, 5, or 10 mg once daily or 5 mg twice daily.	Once daily finerenone dose: 2.5, 5, 7.5, 10, or 15 mg (on day 30, finerenone dose uptitrated to: 5, 10, 15, 20, or 20 mg respectively)
Control arm	Placebo (part A and B); or oral spironolactone (open-label) (once daily 25 or 50 mg) (Part B only)	Eplerenone (25 mg every other day, on day 30, titrated up to 25/day and on day 60, up to 50 mg/day)
Follow-up	28 days	90 days
Primary outcome	Change in serum potassium	Efficacy and safety of finerenone at different doses. The proportion of patients with reduction of plasma NT-proBNP (>30%) from baseline to day 90.
Findings	Finerenone demonstrated comparable efficacy to spironolactone 25 or 50 mg/day in diminishing of haemodynamic stressors while exhibiting fewer cases of hyperkalaemia	Finerenone was well tolerated and resulted in a comparable proportion of patients achieving a ≥30% decrease in NT-proBNP levels compared with eplerenone

CKD = chronic kidney disease; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; NT-proBNP = N-terminal pro-B-type natriuretic peptide; T2D = type 2 diabetes.

A Primary Care Guide to the Management of Chronic Kidney Disease in People Living With Type 2 Diabetes

American Diabetes Association®
ClinicalDIABETES

This review summarizes consensus recommendations for optimal screening and treatment of CKD in diabetes from an international group of experts representing multiple specialties.

Background — Diabetes is the leading cause of CKD worldwide; however CKD is underdiagnosed in people with diabetes.

People with CKD in the U.S. unaware they have the disease:

9 out of **10** people

Underdiagnosed CKD

People with diabetes who have CKD:

CKD

People with ESKD due to diabetes:

ESKD

CardioRenal Initiative Meeting — Primary care advisory board: 40 experts from around the globe

Developed recommendations for:

- Screening
- CKD management

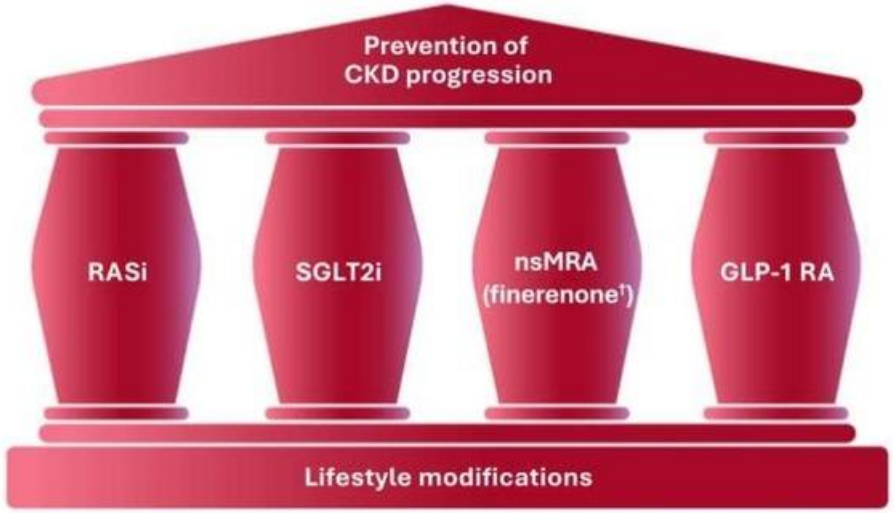
Based on:

- ADA and KDIGO guidelines

CKD screening recommendations

At-risk individuals should be screened regularly for impaired kidney function and kidney damage by measurement of eGFR and UACR.

Pillared approach for CKD management in T2D



†Finerenone is the only nsMRA approved for people with CKD and T2D.

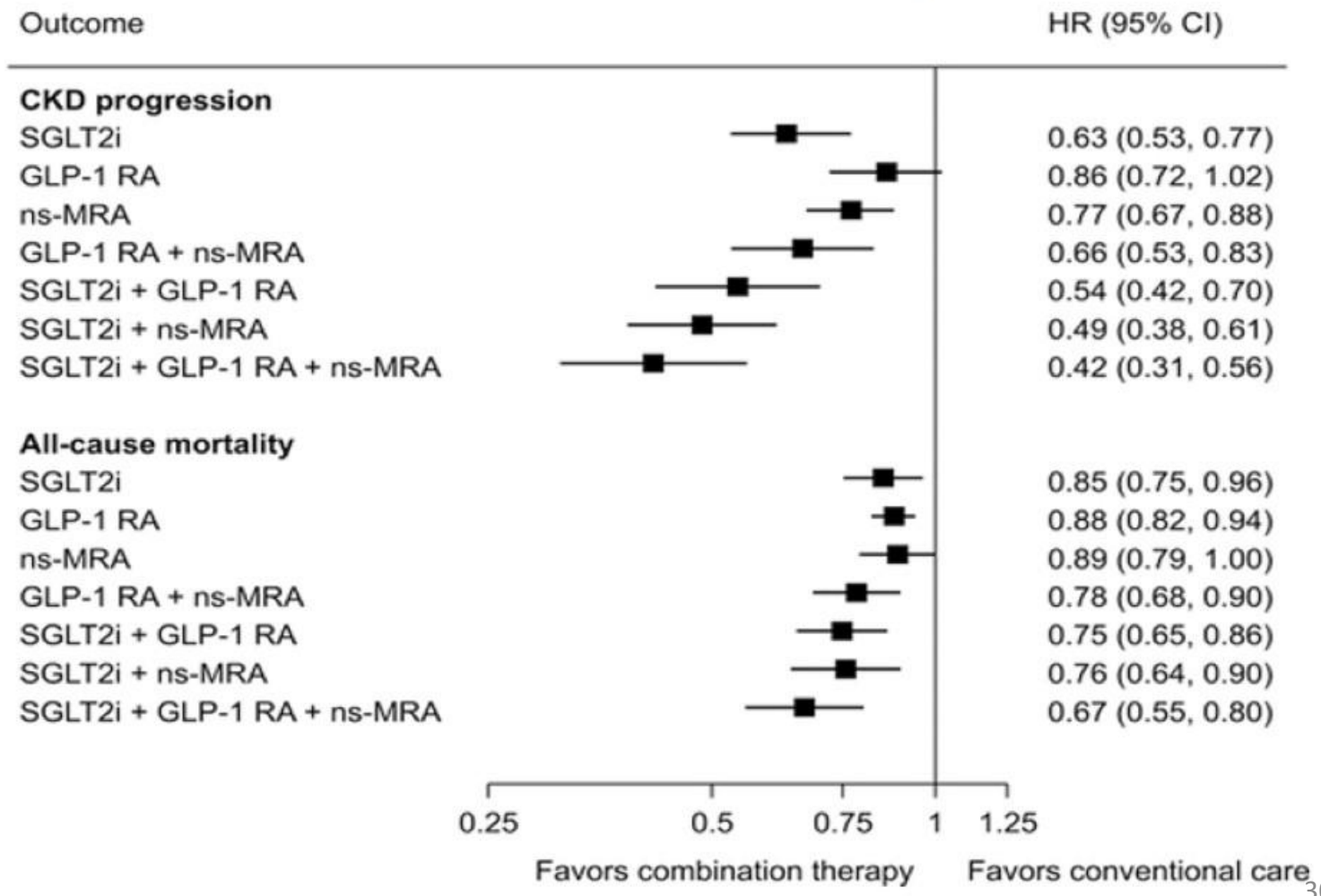
Wright E et al., Clinical Diabetes 2025.

Individuals with T2D should be screened regularly for CKD.
Lifestyle modifications and a pillared approach are recommended to manage CKD.

Combination Treatment Improves Renal and CV Prognosis in Patients With T2D

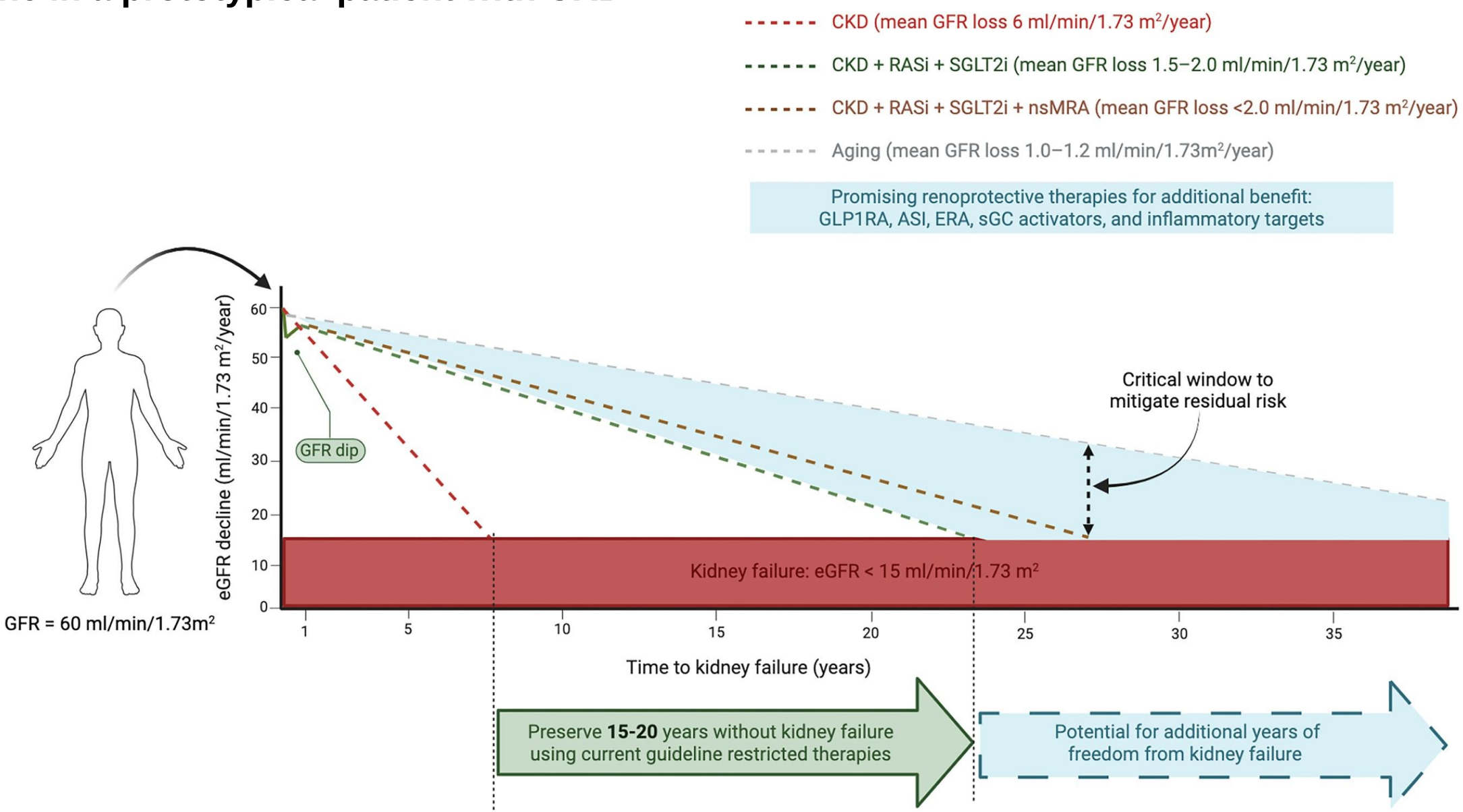
- **Pooled individual-level data of patients with T2D and UACR ≥ 30 mg/g**
- **2 SGLT2 inhibitor trials**
  - (N = 14,543); CANVAS and CREDENCE
- **2 ns-MRA trials**
  - (N = 13,026); FIDELIO-DKD and FIGARO-DKD
- **8 GLP-1 RA trials**
  - (N = 60,080)
- **Combination vs conventional care (RAS inhibitor)**

Estimated Treatment Effects on CKD Progression and All-Cause Mortality

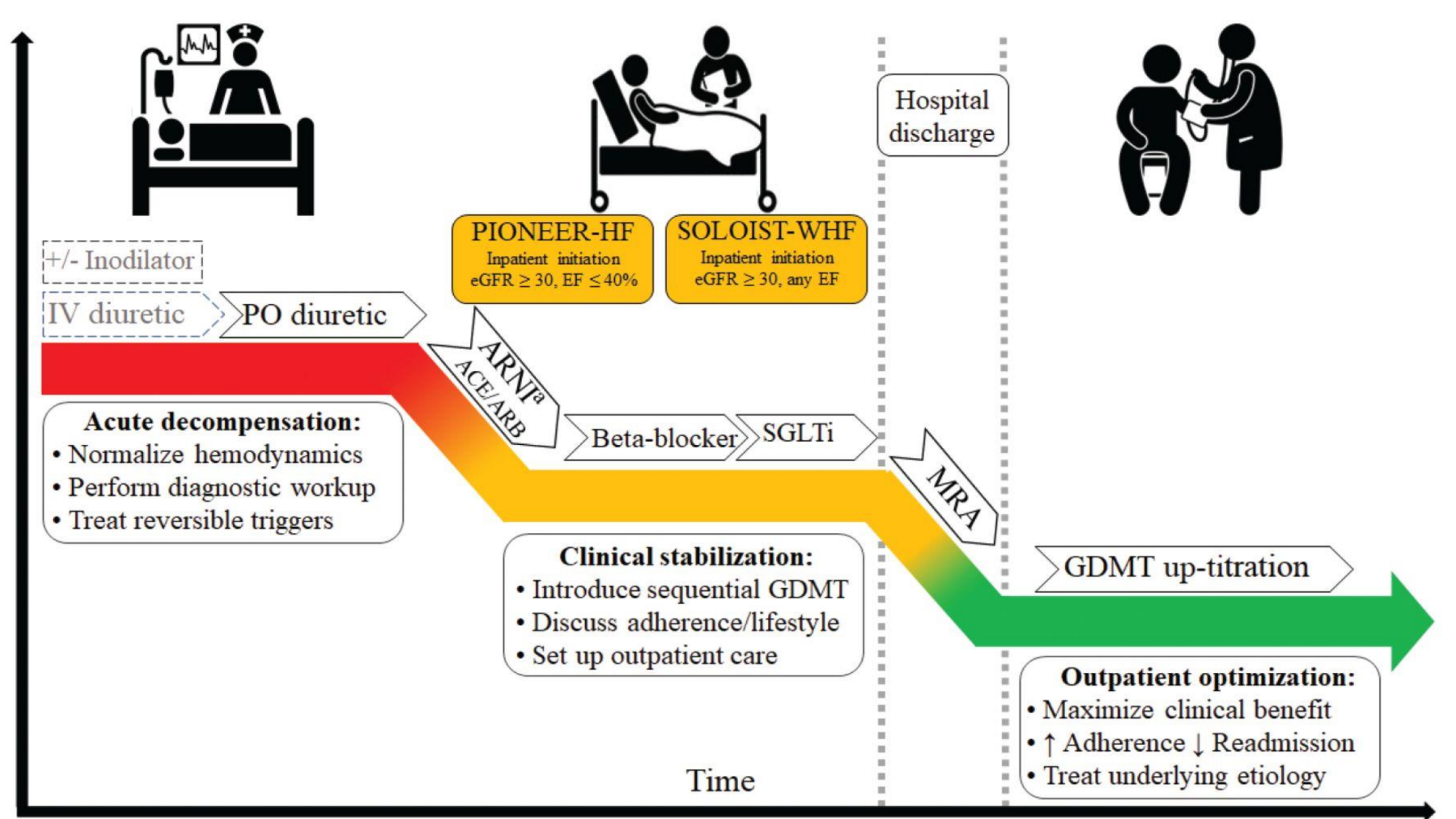


Neuen BL, et al. Circulation. 2024;149:450-462.

Effect of combination drug therapy on eGFR decline in a prototypical patient with CKD

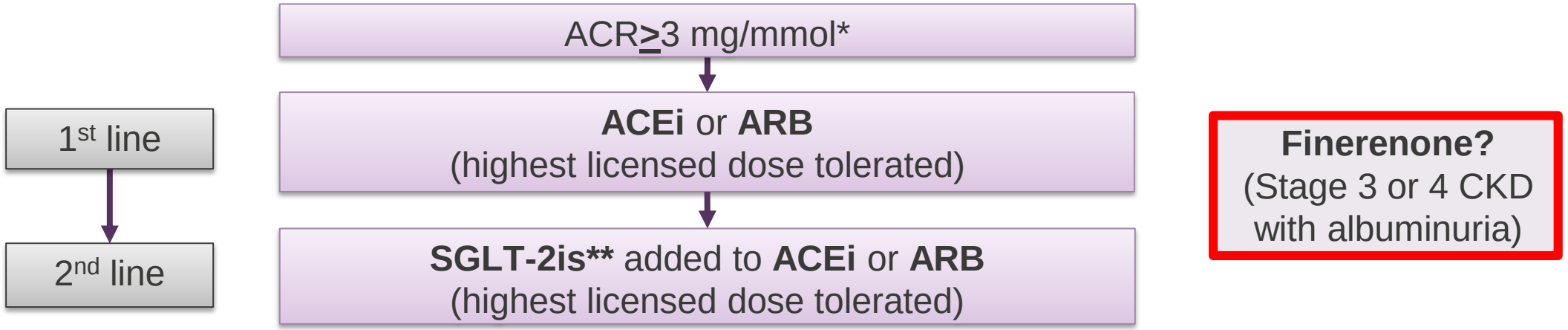


Nephrol Dial Transplant, Volume 40, Issue Supplement_1, January 2025, Pages i47–i58, https://doi.org/10.1093/ndt/gfae216


PIONEER-HF
Inpatient initiation
eGFR ≥ 30, EF ≤ 40%
SOLOIST-WHF
Inpatient initiation
eGFR ≥ 30, any EF
Hospital discharge
+/- Inodilator
IV diuretic
PO diuretic
ARNI[a]
ACE/ARB
Beta-blocker
SGLTi
MRA
GDMT up-titration
Acute decompensation:
• Normalize hemodynamics
• Perform diagnostic workup
• Treat reversible triggers
Clinical stabilization:
• Introduce sequential GDMT
• Discuss adherence/lifestyle
• Set up outpatient care
Outpatient optimization:
• Maximize clinical benefit
• ↑ Adherence ↓ Readmission
• Treat underlying etiology
Time

Treatment pathway – CKD & T2D

Finerenone as an add-on to existing treatment pathway and at a max dose angiotensin converting enzyme inhibitors (ACEi)/ angiotensin receptor blockers (ARBs)



- Does the treatment pathway reflect the expected positioning of finerenone in NHS clinical practice?
- Would finerenone be used instead of, or in combination with, an SGLT2i? Or both?

* **NICE guidelines 28 (NG28)** recommends SGLT2is *offered* if ACR >30 mg/mmol & *considered* if ACR is 3-30 mg/mmol, & meets licence criteria including eGFR thresholds. **Technology appraisal 775 (TA775)** recommends dapagliflozin (an SGLT-2i) as add-on if eGFR 25 to 75 ml/min/1.73 m^2 **and** T2D, **or** ACR ≤ 22.6 mg/mmol

NICE

ACR: Albumin to creatinine ratio; CKD: Chronic kidney disease; eGFR: estimated glomerular filtration rate; SGLT2is: Sodium-glucose co-transporter-2 inhibitors; T2D: Type 2 diabetes

Panel A

TRADITIONAL APPROACH
Maximise RAS blockade, add SGLT2i, re-assess in 3-6 months, add ns-MRA, consider GLP-1 RA
Limitations: Ignores excess early cardiovascular risk, very high risk of therapeutic inertia

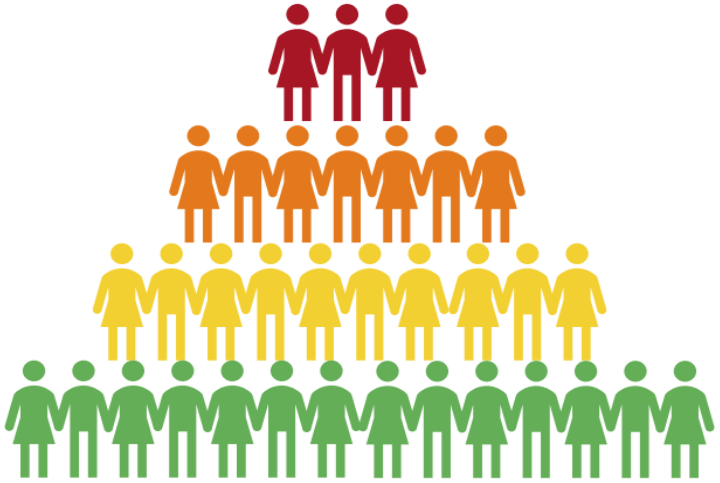
RAPID SEQUENCE APPROACH
Simultaneous or rapid implementation of GDMT for type 2 diabetes and CKD
Considerations: Assumes all patients with CKD are at equally high risk, cost-effectiveness and early safety uncertain

ACCELERATED RISK-BASED APPROACH
Identify patients at highest risk using validated risk score, prioritise accelerated implementation of GDMT for type 2 diabetes and CKD
Appeal: Match intensity of treatment to risk, prioritise patients likely to obtain greatest absolute benefits

Panel B

Accelerated risk-based implementation of GDMT for type 2 diabetes and CKD

Stratify risk using validated risk score
(e.g. KDIGO heat map or KFRE)



Very high/high risk

- Early nephrology referral
- Up-front, accelerated sequence combination therapy

Moderate/low risk

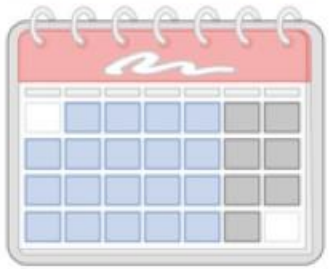
- Primary care management
- As needed specialist referral
- Traditional, sequential add-on therapy

Implementation of combination GDMT in Type 2 diabetes and CKD

Nephrol Dial Transplant, Volume 40, Issue Supplement_1, January 2025, Pages i59–i69, https://doi.org/10.1093/ndt/gfae258

Accelerated Implementation to Maximize Cardiokidney Benefits

Traditional/conservative approach



2 months → 3–6 months → 3–6 months → 2–3 months →

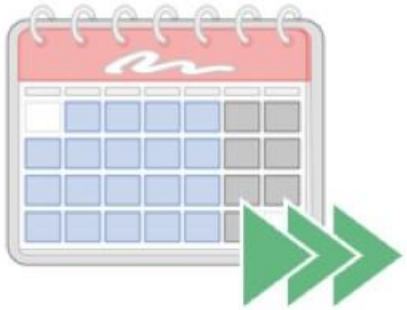
ACEi/ ARB	Titrate dose	SGLT2i	Re-evaluate albuminuria	nsMRA	Titrate dose and re-evaluated albuminuria	GLP-1 RA	Up titrate dose

Accelerated approach

2 months → 4 months → 3 months →

ACEi/ ARB	SGLT2i	nsMRA	GLP-1 RA	Titrate dose, reinforce adherence, Risk factor control

Rapid sequence approach



3 months → 2-3 months →

ACEi/ ARB	nsMRA	Titrate dose, reinforce adherence, Risk factor control
SGLT2i	GLP-1 RA	

It can take 12 to 18 months until guideline-directed medical therapy for T2D and CKD is fully implemented

Brendon N, et al. Clin J Am Soc Nephrol. 2024;19:1209-1211.

How will finerenone be used with SGLT2is?
Would finerenone be used in combination with an SGLT2i?
Would finerenone be used instead of an SGLT2i when an SGLT2i is contraindicated?
Would finerenone be used instead of an SGLT2i when an SGLT2i could be used instead?

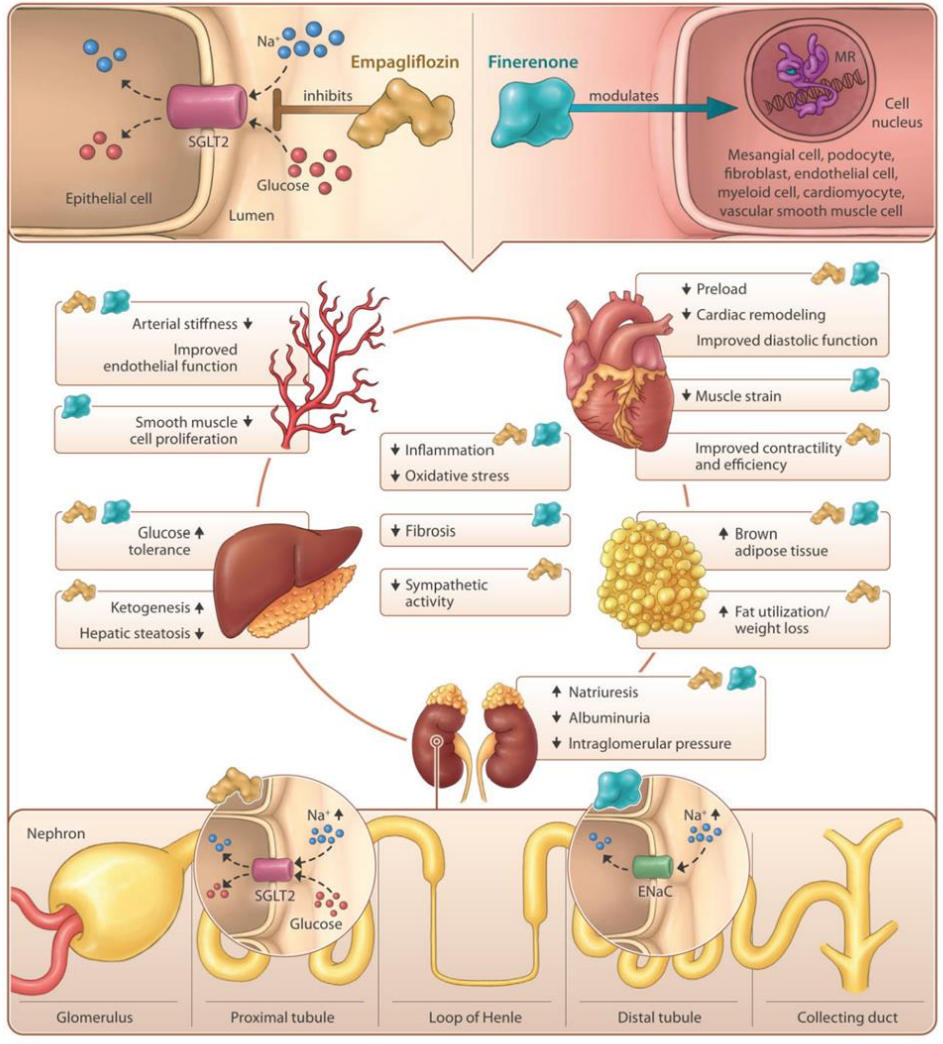


FIGURE 1: Proposed mechanisms for reducing adverse cardiovascular- and kidney-related outcomes based on preclinical and clinical studies

Design of the COmbinatioN effect of FInerenone anD EmpagliflOziN in participants with chronic kidney disease and type 2 diabetes using a UACR Endpoint study (CONFIDENCE)

Background

Both finerenone (nonsteroidal MRA) and empagliflozin (SGLT2i) can reduce kidney and cardiovascular events in people with CKD and T2D.

CONFIDENCE (NCT05254002) investigates whether dual therapy with finerenone and empagliflozin is superior to either agent alone in reducing albuminuria.

Participants

- 807 participants
- 125 centres
- 13 countries

✓
- ≥ 18 years
- T2D, CKD stage 2–3
- UACR ≥ 300 to < 5000 mg/g

✗
- T1D
- Serum K^+ > 4.8 mmol/L
- Treatment with SGLT1/2i or MRA

Treatment arms

R 1:1:1

- 269 — Finerenone (10 or 20 mg od) + Empagliflozin (10 mg od)
- 269 — Finerenone (10 or 20 mg od) + Placebo
- 269 — Empagliflozin (10 mg od) + Placebo

0 — Treatment period (days) — 180

Primary outcomes

Relative change in UACR from baseline to 180 days in:

- Dual therapy vs. Finerenone
- Dual therapy vs. Empagliflozin

Conclusion

Should an additive effect be shown, early and efficient intervention with dual finerenone and SGLT2i therapy could slow disease progression and provide long-term benefits for people with CKD and T2D.

ERA NDT NEPHROLOGY DIALYSIS TRANSPLANTATION

Green, J. et al. NDT (2022)
@NDTSocial

Finerenone and empagliflozin: is the combination better than either agent alone in CKD and Type 2 Diabetes?

#NephJC

Methods

- Randomized, double-blind trial
- CKD + T2D
- 14 countries
- 98% ACEi/ARB users
  23% GLP-1RA users
- Stratified according to eGFR and UACR

	UACR drop at day 180	Hyperkalemia	> 30% eGFR drop at day 30
Empagliflozin	29% ↓	3.8%	1.1%
Finerenone	32% ↓	11.4%	3.8%
Empagliflozin & Finerenone	52% ↓	9.3%	6.3%

No unexpected adverse events

Conclusion: Among persons with both chronic kidney disease and type 2 diabetes, initial therapy with finerenone plus empagliflozin led to a greater reduction in the urinary albumin-to-creatinine ratio than either treatment alone.

VA by Michelle Fravel

Agarwal R, Green JB, Heerspink HJL, et al; CONFIDENCE Investigators. Finerenone with Empagliflozin in Chronic Kidney Disease and Type 2 Diabetes. N Engl J Med. 2025 Jun 5.

Finerenone: Who Should Prescribe It for CKD? Physician Associates (PA) Perspectives

Becky M. Ness MPAS, PA-C, Assistant Professor of Medicine, Mayo Clinic College of Medicine, Department of Nephrology, Rochester, MN, USA; and Heidi Webb MMS, PA-C, CAQ-HM, Bahl & Bahl Medical Associates, Pittsburgh, PA, USA

BACKGROUND

30-40%

of all patients with diabetes are affected by **Diabetic Kidney Disease**

Finerenone

was approved by the FDA for adults with **CKD associated with T2D** to reduce the risk of **kidney** and **CV** outcomes.

Physician Associates

should be empowered in **GDMT prescription** and other **kidney protection strategies**

KEY MESSAGE

Physician associates play a vital role in **diagnosing, monitoring, and managing** chronic kidney disease, diabetes mellitus, and cardiovascular disease.

Finerenone Benefits in DKD

Efficacy and Safety
tested in FIDELIO-DKD and FIGARO-DKD

FDA Approval
to reduce the risk of sustained eGFR decline, ESKD, CV death, non-fatal MI, and hospitalization for HF

Independent Benefit
with other CKD-T2D GDMT

Role of Physician Associates

Early CKD Journey
identification and prevention

Late CKD Journey
routinely monitor CKD and its related conditions

Continuity of Care
ensuring treatment, information, communication, and management continuity

Barriers to Optimum Care

Insufficient Patient Engagement
need to continue discussing and educating

Cost and Lack of Referral Coordination
disparities are major challenges

Unstandardized Guidelines
consensus is increasing

CONCLUSION

Based on the proposed multidisciplinary guidelines, PAs should be more comfortable **implementing care and goal-directed therapies** to prevent the advancement of DKD.

Journal of NEPHROLOGY
official journal of the Italian Society of Nephrology

Conclusions

- **Mineralocorticoid receptor over-activation is a central driver of progression of heart and kidney disease**
- **Steroidal MRAs (spironolactone and eplerenone) form backbone therapy for patients with HFrEF, but do potentiate hyperkalemia**
- **Nonsteroidal MRAs (finerenone) slows kidney disease progression in CKD and may have lower risks of hyperkalemia**
- **MRAs can be easily combined with other effective therapies in HF and CKD**
- **Ongoing trials are underway evaluating finerenone in HFpEF and non-diabetic CKD**

Knowledge Check

Q7: Would you want to see a patient with CKD associated with T2DM on finerenone?

A) Yes, given they are on first-line standard-of-care therapy

B) No, I do not see enough benefit

C) Depends

Thank You For Kind Attention