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Mineralocorticoid Receptor Antagonism for Treatment of CKD

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Disclosures

- Advisory fees received from:
  - Travere Therapeutics
  - Boehringer Ingelheim
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  - Novartis Pharma AG
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  - Vantive
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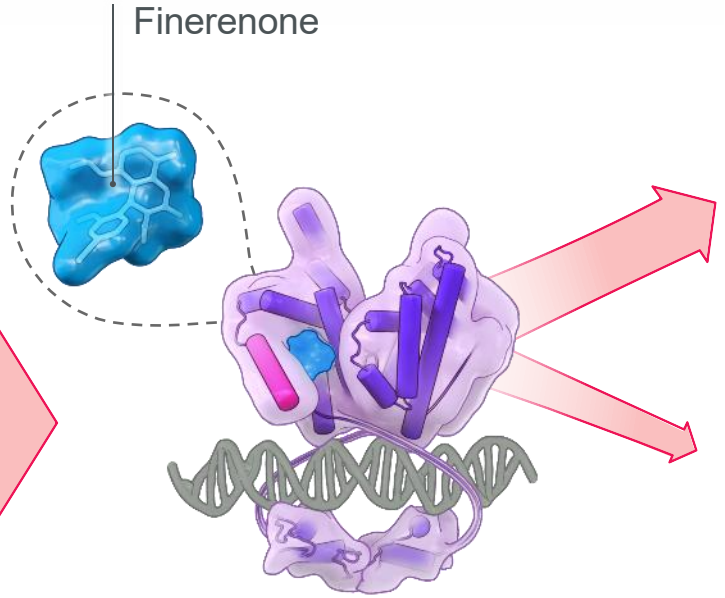
- KDIGO Executive Committee 2020-2023
  - Core member of IgAN and IgAV Clinical Practice Guideline Work Group 2025

Finerenone, a nonsteroidal, highly selective MRA, blocks MR overactivation, which slows kidney and CV disease progression in patients with type 2 diabetes[1–7]

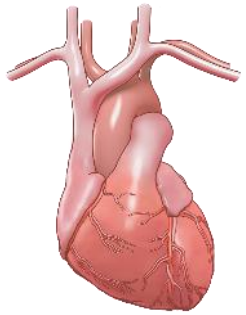
- Hyperglycaemia[1]
- High salt load[1]
- Oxidative stress[1]



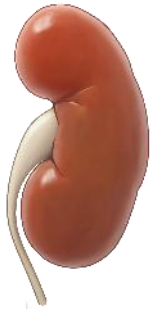
MR overactivation blockade and homeostatic action

Drivers[1,6,7]

- **Inflammation and fibrosis**
- **Haemodynamic factors**



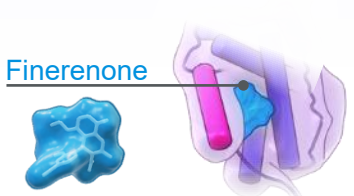
Heart and kidney protection



CV, cardiovascular; MR, mineralocorticoid receptor; MRA, mineralocorticoid receptor antagonist

1. Bauersachs J, *et al. Hypertension* 2015;65:257–263; 2. Kintscher U, *et al. Br J Pharmacol* 2021;179:3220–3234; 3. Agarwal R, *et al. Eur Heart J* 2021;42:152–162; 4. Amazit L, *et al. J Biol Chem* 2015;290:21876–21889; 5. Agarwal R, *et al. Nephrol Dial Transplant* 2020;37:1014–1023; 6. Alicic RZ, *et al. Clin J Am Soc Nephrol* 2017;12:2032–2045; 7. Mora-Fernández C, *et al. J Physiol* 2014;18:3997

Finerenone and steroidal MRAs have key pharmacodynamic and pharmacokinetic differences[1–3]

	Aldosterone antagonists		Finerenone
			
Structural properties	Flat (steroidal)	Flat (steroidal)	Bulky (nonsteroidal)
Potency against MR	+++	+	+++
Selectivity for MR	+	++	+++
CNS penetration	+	+	–
Sexual side effects	++	(+)	–
Half-life	>20 hours*	4–6 hours*	2–3 hours#
Active metabolites	++	–	–
Effect on BP	+++	++	+
Indication	**Congestive HF[4]**	**HF and LVEF ≤40% or ≤30%[5]**	**CKD (with albuminuria) associated with T2D[6]**

*In patients with HF
#In healthy volunteers
CNS, central nervous system; LVEF, left ventricular ejection fraction

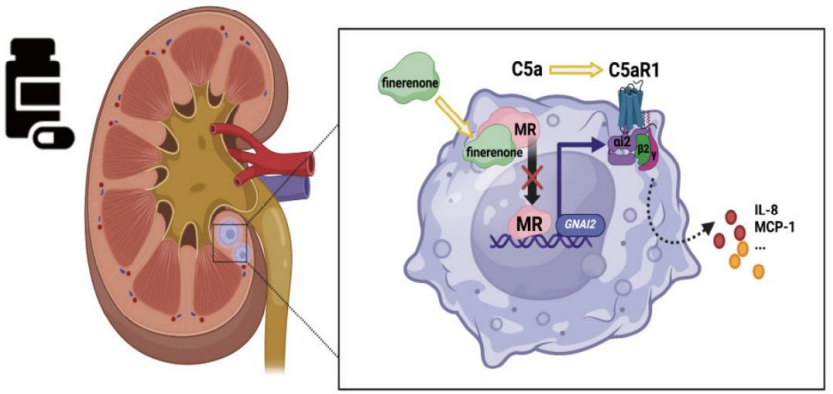
1. Kintscher U, *et al*. *Br J Pharmacol* 2021; doi: 10.1111/bph.15747; 2. Schwabe JW, *et al. Cell* 1993;75:567–578; 3. Tanenbaum DM, *et al. Proc Natl Acad Sci USA* 1998;95:5998–6003;
4. Pfizer Ltd. Aldactone (spironolactone) Summary of Product Characteristics. 2019. https://www.medicines.org.uk/emc/product/2899/smpc [accessed 28 Mar 2022];
5. Zentiva Pharma UK Limited. Eplerenone Summary of Product Characteristics. 2021. https://www.medicines.org.uk/emc/product/3665/smpc#INDICATIONS [accessed 28 Mar 2022];
6. Bayer AG. KERENDIA® (finerenone) Hong Kong Prescribing Information.

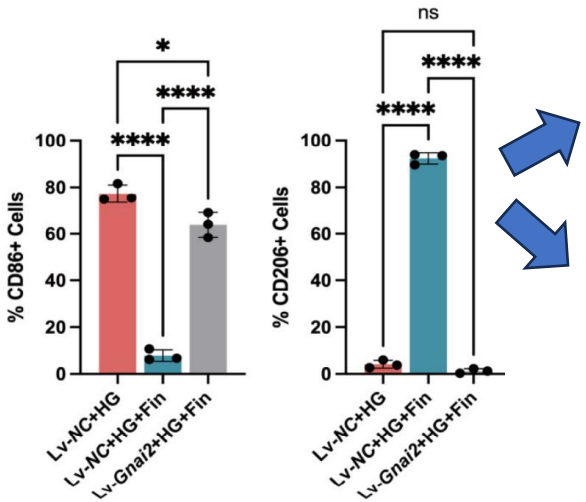
Finerenone Alleviates Over-Activation of Complement C5a-C5aR1 Axis of Macrophages by Regulating G Protein Subunit Alpha i2 to Improve Diabetic Nephropathy

Zi-Han Li [1,2,3,4], Zi-Jun Sun [1,2,3,4,5,6], Sydney C. W. Tang [7], Ming-Hui Zhao [1,2,3,4,5,6], Min Chen [1,2,3,4,5,6,*] and Dong-Yuan Chang [1,2,3,4,5,6,*]

Cells 2025

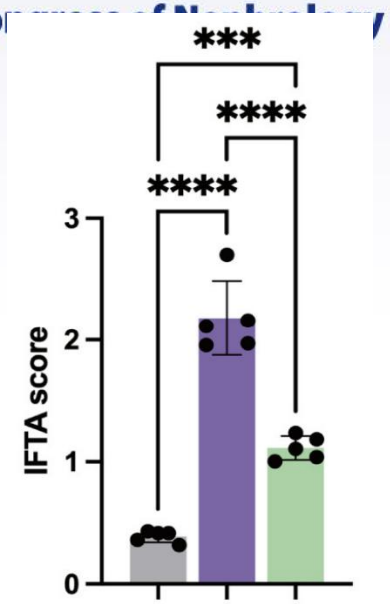
In macrophages

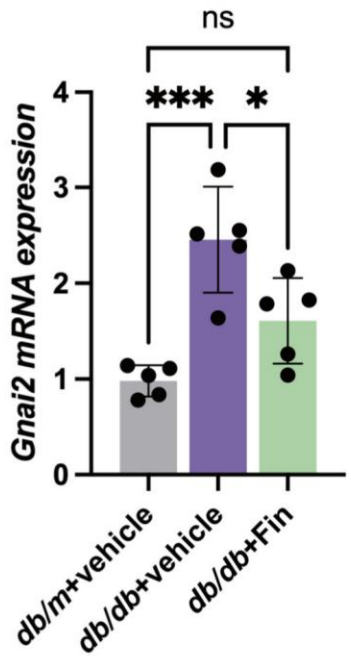


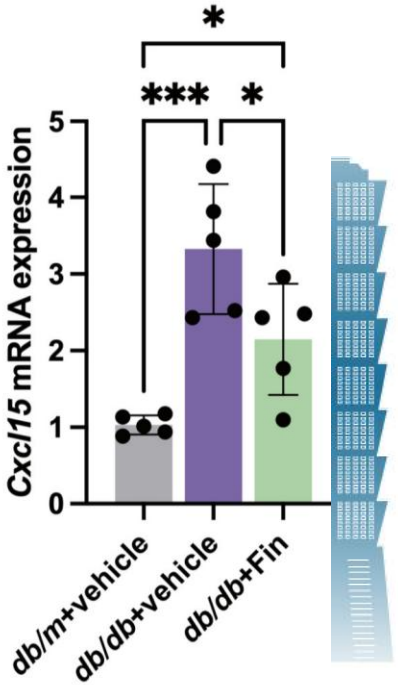


Finerenone alleviated HG-induced injuries and M1 polarization of macrophages via inhibiting Gnαi2

In db/db mice







FIDELIO-DKD and FIGARO-DKD assessed prespecified kidney & CV outcomes in patients across the spectrum of CKD severity

N=5,734

FIDELIO-DKD

+

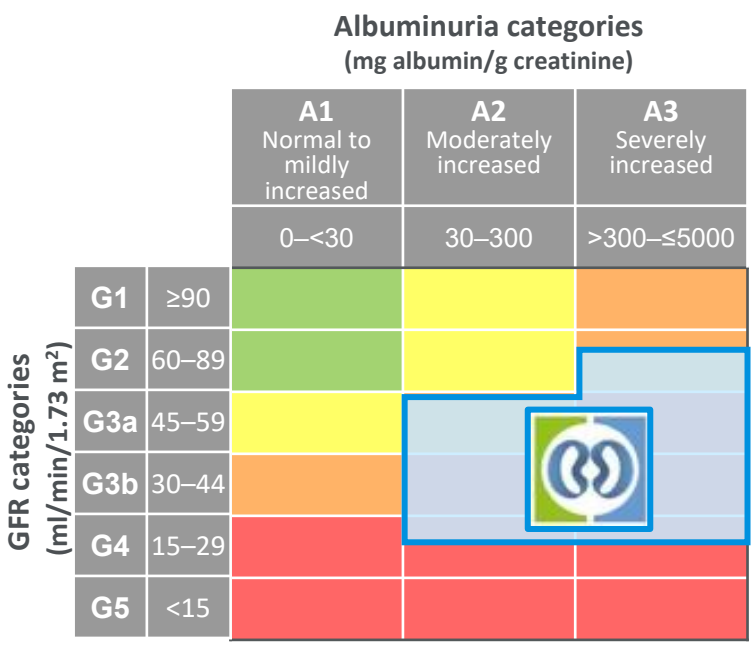
N=7,437

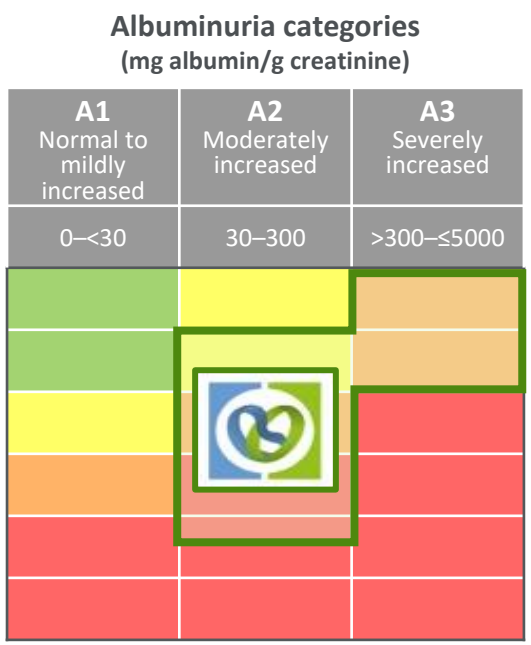
FIGARO-DKD

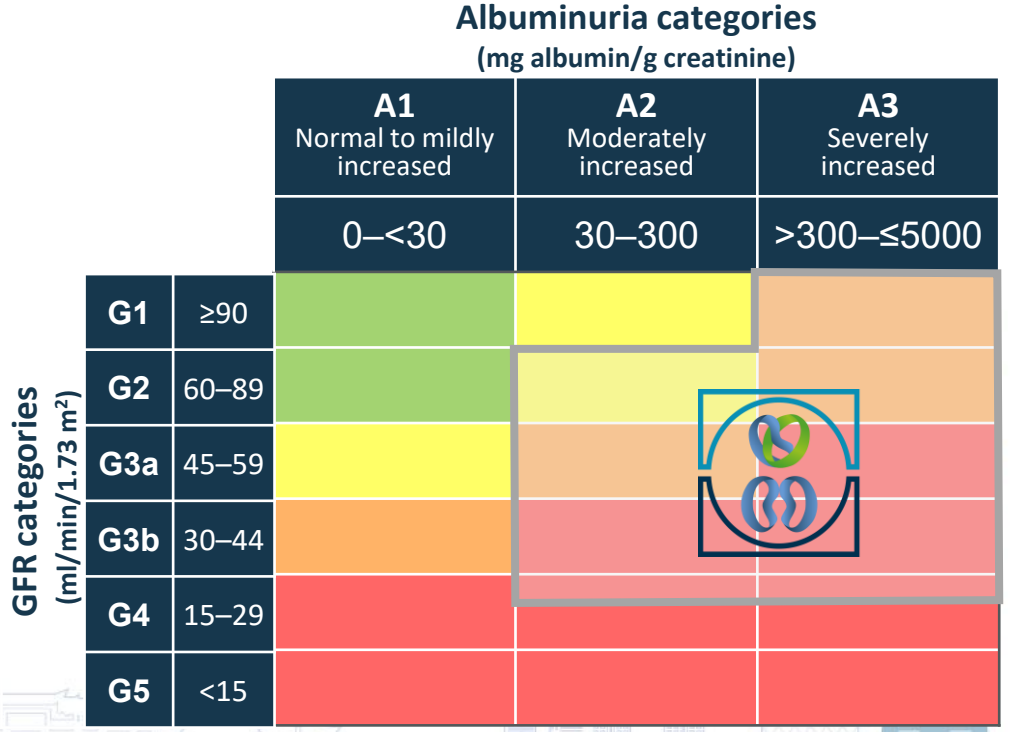
=

N=.13,000

FIDELITY (FIDELIO-DKD + FIGARO-DKD pooled)







1. Agarwal R, et al. European Heart Journal 2022;43, 474–484.

At baseline, patients in FIDELITY had well-controlled blood pressure and HbA1c, and CV medications were used by most patients[1]

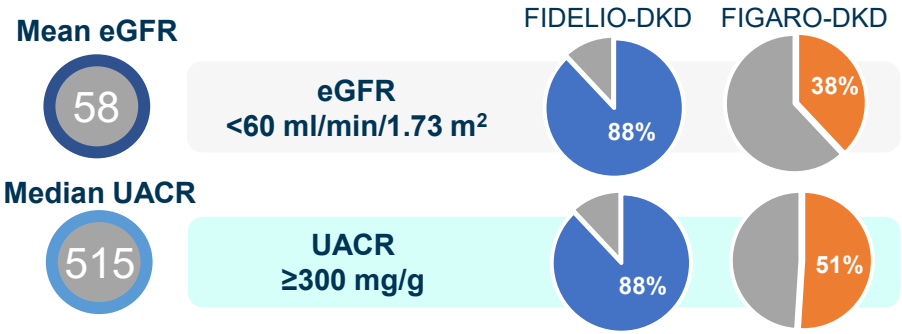
Key eligibility criteria[1–3]

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

99% of patients were treated with a **maximum tolerated dose of an ACEi or ARB**[1–3]

Blood pressure and **HbA1c** were well controlled at baseline[1–3]

A greater proportion of patients had **an eGFR of <60 ml/min/1.73 m² and severely increased UACR** (≥300 mg/g) **in FIDELIO-DKD versus FIGARO-DKD**[2,3]



Adherence to treatment **was high** (~92% in the finerenone and placebo groups)[2,3]

Numbers of permanent discontinuations were similar between treatment groups[2,3]

Median follow-up was **3.0 years**[1]

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin; HFrEF, heart failure with reduced ejection fraction; [K^+], potassium concentration; RASi, renin–angiotensin system inhibitor; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio

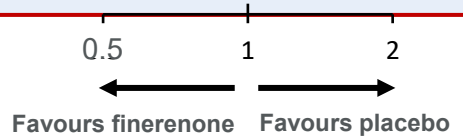
1. Agarwal R, *et al. Eur Heart J* 2022;43:474–484; 2. Bakris GL, *et al. N Engl J Med* 2020;383:2219–2229; 3. Pitt B, *et al. N Engl J Med* 2021;385:2252–2263

FIDELITY

Finerenone has demonstrated significant risk reductions in CV and kidney outcomes, in patients with CKD and T2D[1]

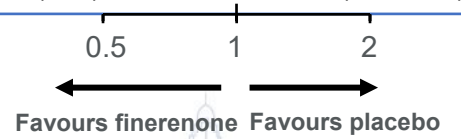
Composite CV outcome

Outcome	Finerenone (n=6519) n (%)	Placebo (n=6507) n (%)	HR (95% CI)	*p*-value
Composite CV outcome	**825 (12.7)**	**939 (14.4)**	**0.86 (0.78–0.95)**	**0.0018**
CV death	322 (4.9)	364 (5.6)	0.88 (0.76–1.02)	0.092
Non-fatal MI	173 (2.7)	189 (2.9)	0.91 (0.74–1.12)	0.36
Non-fatal stroke	198 (3.0)	198 (3.0)	0.99 (0.82–1.21)	0.95
First HHF*	256 (3.9)	325 (5.0)	0.78 (0.66–0.92)	0.0030



Composite kidney outcome

Outcome	Finerenone (n=6519) n (%)	Placebo (n=6507) n (%)	HR (95% CI)	*p*-value
≥57% eGFR kidney composite outcome	**360 (5.5)**	**465 (7.1)**	**0.77 (0.67–0.88)**	**0.0002**
Kidney failure*	254 (3.9)	297 (4.6)	0.84 (0.71–0.99)	0.039
ESKD#	151 (2.3)	188 (2.9)	0.80 (0.64–0.99)	0.040‡
Sustained decrease in eGFR to <15 ml/min/1.73 m^2	195 (3.0)	237 (3.6)	0.81 (0.67–0.98)	0.026‡
Sustained# ≥57% decrease in eGFR from baseline	257 (3.9)	361 (5.5)	0.70 (0.60–0.83)	<0.0001
Renal death‡	2 (<0.1)	4 (<0.1)	0.53 (0.10–2.91)	0.459

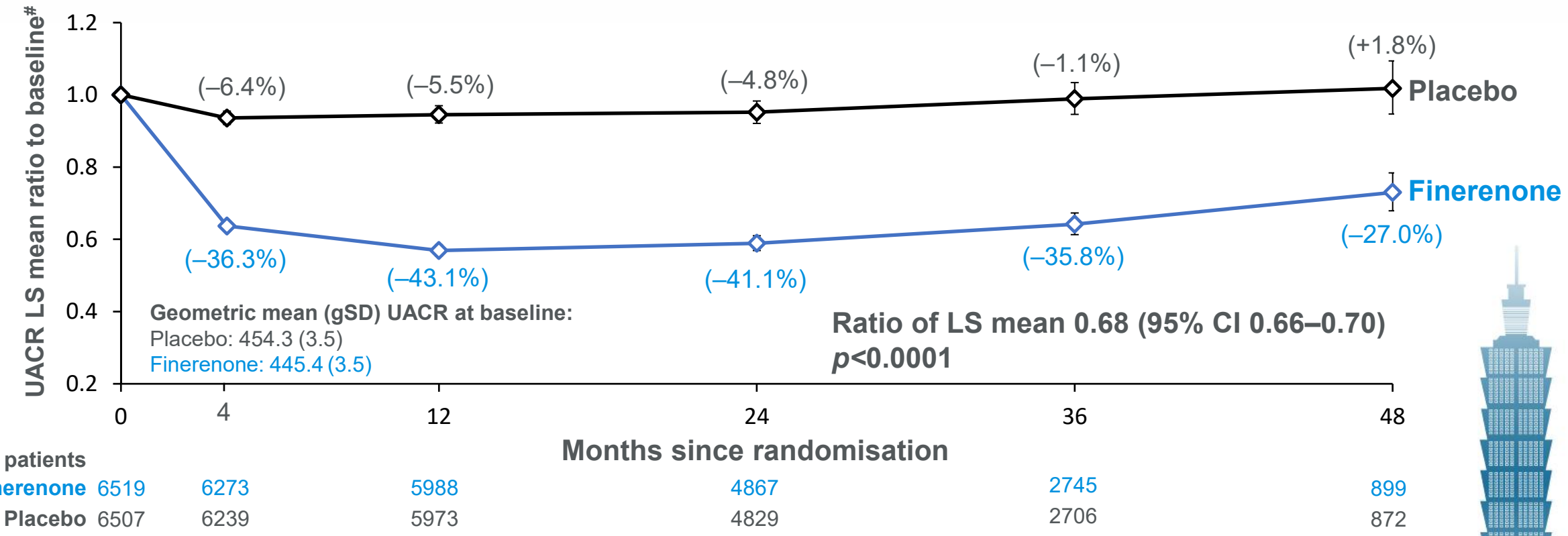


*First HHF defined as first event after randomisation; #ESKD or an eGFR <15 ml/min/1.73 m^2; events were classified as renal death if: (1) the patient died; (2) kidney replacement therapy had not been initiated despite being clinically indicated; and (3) there was no other likely cause of death; ‡Analyses for *p*-values not prespecified
CI, confidence interval; ESKD, end-stage kidney disease; HR, heart rate

1. Agarwal R, *et al. Eur Heart J* 2022;43:474–484; 2. Bayer AG. KERENDIA® (finerenone) Summary of Product Characteristics. 2023. https://www.ema.europa.eu/documents/product-information/kerendia-epar-product-information_en.pdf [accessed 03 July 2023]

Finerenone reduced UACR by 32% between baseline and month 4 vs placebo*

A lower mean UACR with finerenone vs placebo was maintained throughout the study



No. of patients						
Finerenone	6519	6273	5988	4867	2745	899
Placebo	6507	6239	5973	4829	2706	872

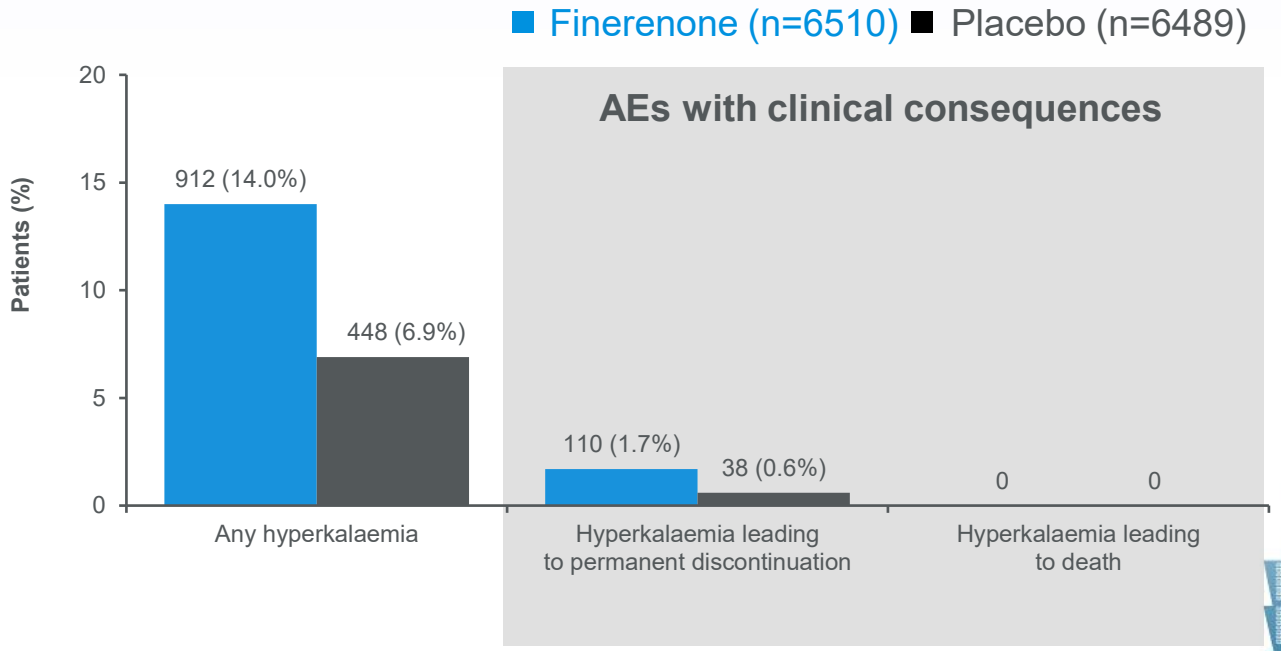
Data in parentheses are mean change from baseline
*Full analysis set. Mixed model with factors treatment group, region, eGFR category at screening, type of albuminuria at screening, CV disease history, time, treatment*time, study, study*treatment, log-transformed baseline value nested within type of albuminuria at screening and log-transformed baseline value*time as covariate. Separate unstructured covariance patterns are estimated for each treatment group; #data are LS mean/95% CI
CI, confidence interval; eGFR, estimated glomerular filtration rate; gSD, geometric standard deviation; LS, least-squares; UACR, urine albumin-to-creatinine ratio
Agarwal R, *et al. Eur Heart J* 2022;43(6):474–484

FIDELITY

Finerenone had a similar AE profile to placebo and an increased incidence of hyperkalaemia, but the clinical impact was minimal[1]

Incidence of AEs and changes in vital signs were similar between finerenone and placebo[1]

- **Any AE: 86.1% vs 86.4%**
- **AKI: 3.4% vs 3.6%**
- **Gynaecomastia: 0.1% vs 0.2%**
- **No change in HbA1c**



Maximum difference in mean serum [K⁺] between finerenone and placebo[1]

0.19 mmol/l at month 4

Hyperkalaemia risk factors[2]:
High baseline [K⁺], lower eGFR, higher UACR, beta blocker use

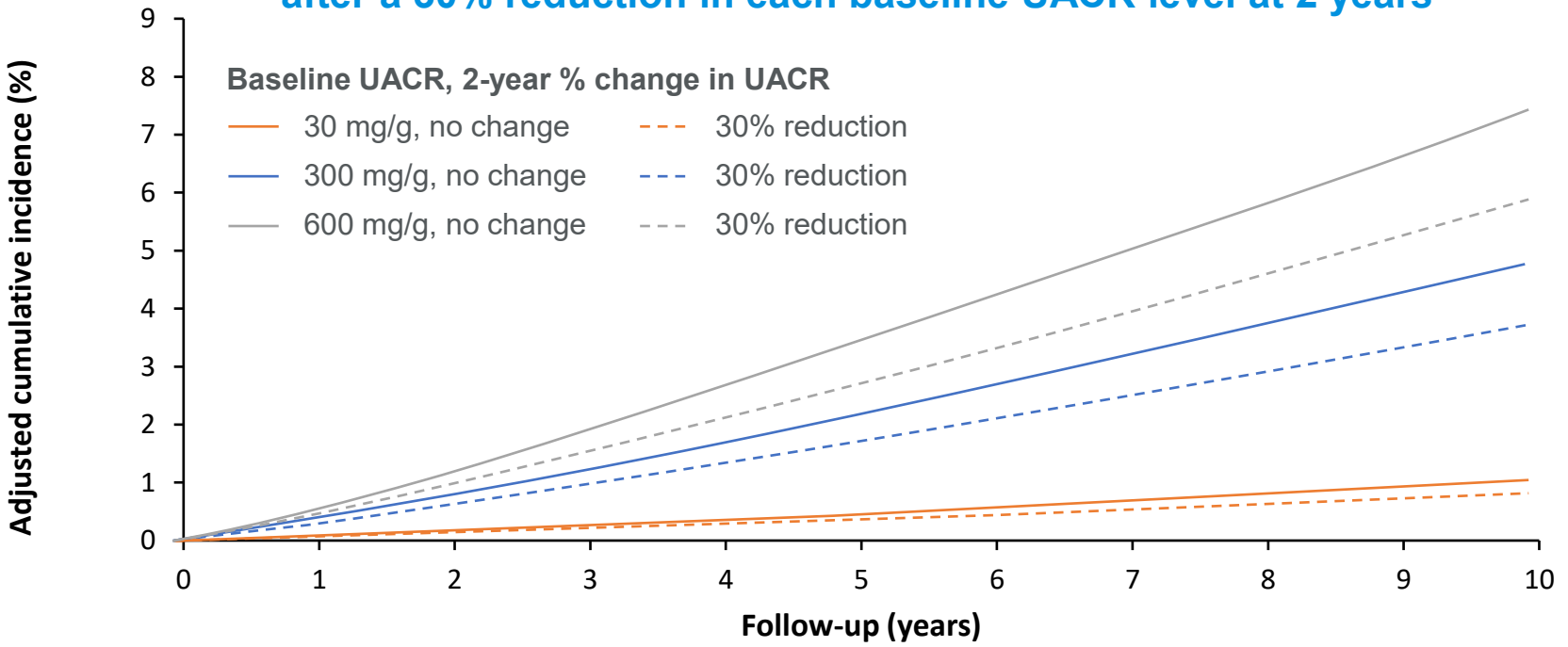
In FIDELITY, the total number of patients with an event in the finerenone group was n=6510, and n=6489 in the placebo group.
AE, adverse event; AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin; K, potassium; UACR, urine albumin-to-creatinine ratio.
1. Agarwal R, et al. *Eur Heart J.* 2022;43:474–484; 2. Agarwal R, et al. *J Am Soc Nephrol.* 2022;33:225–237.

A meta-analysis of cohort data has revealed a lower risk of kidney failure with a 30% reduction in UACR over 2 years

Individual-level meta-analysis of 693,816 participants from 28 observational cohorts*

Over 2 years, a **30% reduction** in UACR reduced the risk of ESKD by
17%
regardless of baseline UACR
(adjusted# HR=0.83; 95% CI 0.74−0.94)

Incidence of ESKD at three baseline UACR levels and after a 30% reduction in each baseline UACR level at 2 years



*This meta-analysis included 18 cohorts with follow-up for ESKD and 16 cohorts that quantified albuminuria with UACR; †Adjusted for age, sex, race/ethnicity (Black vs non-Black), systolic blood pressure, total cholesterol, diabetes, history of CV disease, current smoking, former smoking, first eGFR and albuminuria.

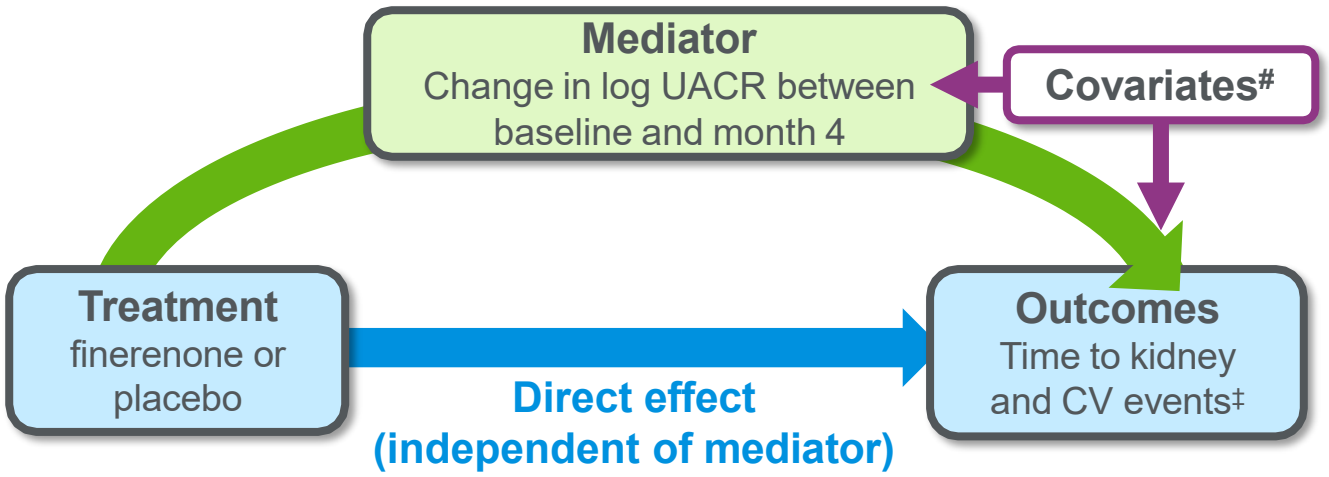
1 CI, confidence interval; CV, cardiovascular; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HR, hazard ratio; UACR, urine albumin-to-creatinine ratio.

1 Coresh J, et al. *Lancet Diabetes Endocrinol.* 2019;7:115−127.

Effect of finerenone on UACR, CV and kidney outcomes

Mediation model framework

Indirect effect (mediated by reduction in log UACR)



The **extent to which UACR reduction mediated the clinical benefits** observed with finerenone on the kidney and CV outcomes‡ was **determined by comparing** the relative magnitudes of the **direct** and **indirect effects**

UACR reduction at month 4 mediated:

84% of the effect of finerenone on the **kidney composite outcome**

37% of its treatment effect on the **CV composite outcome**

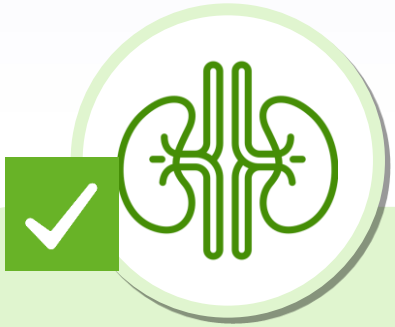
Agarwal R, *et al. Ann Intern Med* 2023;176:1606–1616

The ‘five 5s’ of finerenone treatment

Initiation and monitoring[1]

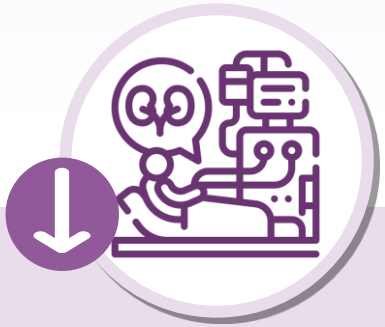
Initiate treatment when **serum [K+]** is **≤5** mmol/l*

Withhold treatment if **serum [K+]** is **>5.5** mmol/l



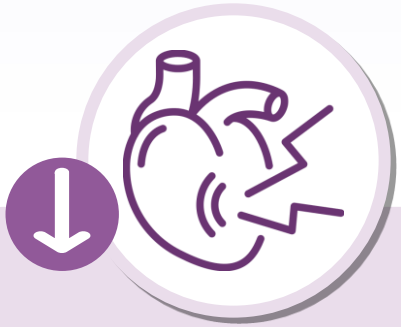
Initiate treatment when **eGFR** is **≥25** ml/min/1.73 m^2

Key treatment effects[2]



Finerenone reduced the risk of **ESKD#** by **1/5**

HR 0.80
(95% CI 0.64–0.99)



Finerenone reduced the risk of **HHF** by **>1/5**

HR 0.78
(95% CI 0.66–0.92)

*Finerenone can be started if serum [K+] is ≤4.8 mmol/l and initiation may be considered if serum [K+] is ≤5 mmol/l with additional serum potassium monitoring within the first 4 weeks based on patient characteristics and serum potassium levels; #ESKD defined as initiation of chronic dialysis for ≥90 days or kidney transplant. HHF, hospitalisation for heart failure; HR, hazard ratio

1. Kerendia (finerenone) Hong Kong Prescribing Information. 2. Agarwal R, *et al*. *Eur Heart J* 2022;43:474–484

Case Mr M

CKD G3a
CKM Stage 2

- M/78
- Known T2DM for >10 years, well controlled with A1C 6.5%, BMI 25
- Serum creatinine 130 µmol/L (eGFR 54)
- UACR ~ 600 mg/g, SBP 110-120 mmHg
- Medications: sitagliptin, olmesartan, amlodipine, simvastati
  Chol: 3.8 mmol/L
- Came to see me because of increased UACR

	Dec 2021	Dec 2022
UACR (mg/g)	603	1,519
eGFR (ml/min/1.73m^2)	54	54

eGFR categories (mL/min/1.73 m^2) Description and range	Albuminuria categories: A1 <30 mg/g <3 mg/mmol	A2 30-299 mg/g 3-29 mg/mmol	A3 ≥300 mg/g ≥30 mg/mmol
≥90 G1	Monitor (1)	Treat (1)	Treat & consult (3)
60-89 G2	Monitor (1)	Treat (1)	Treat & consult (3)
45-59 G3a	Treat (1)	Treat (2)	Treat & consult (3)
30-44 G3b	Treat (2)	Treat & consult (3)	Treat & consult (3)
15-29 G4	Treat & consult (3)	Treat & consult (3)	Treat & consult (4+)
<15 G5	Treat & consult (4+)	Treat & consult (4+)	Treat & consult (4+)

The American Heart Association PREVENT™ Online

Welcome to the American Heart Association **Predicting Risk of cardiovascular disease EVENTs** (PREVE
primary prevention patients (those without atherosclerotic cardiovascular disease or heart failure) only.

Sex ◉ Male ○ Female

Age
78 years

Total Cholesterol
150 mg/dL

HDL Cholesterol
40 mg/dL

SBP
120 mmHg

BMI
25

eGFR
54

Diabetes ○ No ◉ Yes

Current Smoking ◉ No ○ Yes

Anti-hypertensive medication ○ No ◉ Yes

Lipid-lowering medication ○ No ◉ Yes

The following three predictors are optional for further personalization of risk assessment. When they are clinically indicated or available, please click on yes and enter the value

UACR ○ No ◉ Yes
1500 mg/g

HbA1C ○ No ◉ Yes
6.5 %

Zip Code (for estimating social deprivation index [SDI]) ◉ No ○ Yes

Calculate Reset

◉ Risk of CVD ○ Risk of ASCVD ○ Risk of Heart Failure

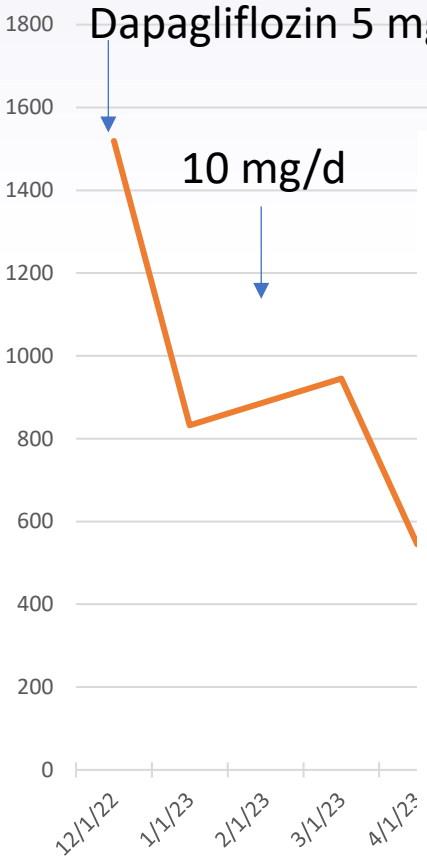
This individual has an estimated 10-year risk of CVD = 47.8%

10-y CVD Risk 48%

What would you do?

Current Medications: sitagliptin, olmesartan, amlodipine, simvastatin/ezetimibe, aspirin

Mr M



UACR Trend

→ 20 mg/d

At last FU
22/7/2025
UACR 609 mg/g

😁

Now 82 yo
Living better

Is this what you would also do if you have a similar patient?

A. Yes, **starting with an SGLT2i** and if UACR does not improve to the desired level, **add a nsMRA sequentially**

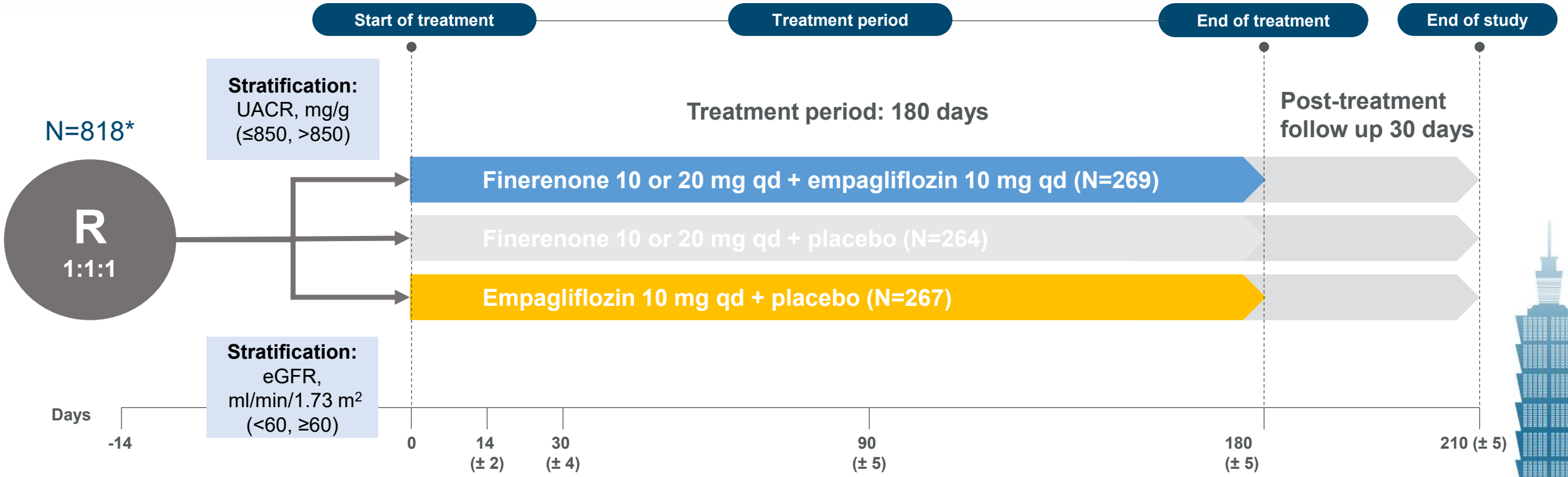
B. Yes, but starting with **a nsMRA** and if UACR does not improve to the desired level, **add an SGLT2i sequentially**

C. No, I would start an **SGLT2i + nsMRA simultaneously**

D. No, I would **increase** his **ARB dose** and not use **SGLT2i / nsMRA**

CONFIDENCE was a randomized, double-blind, double-dummy, multicenter, three-armed, parallel-group, phase II study[1–3]

Participants enrolled from 185 sites across multiple countries/regions: Belgium, Canada, Denmark, France, Germany, India, Israel, Italy, Japan, Republic of Korea, the Netherlands, Spain, Taiwan, and the USA



*Four participants underwent randomization twice in error and 14 participants from one site were excluded owing to historic violations of Good Clinical Practice guidelines not related to this study, and their data were not included. Therefore, 800 participants were included in the full analysis set for the efficacy analyses.[3]
eGFR, estimated glomerular filtration rate; qd, once daily; R, randomization; UACR, urine albumin-creatinine ratio.

1. Green JB, et al. *Nephrol Dial Transplant*. 2023;38:894–90. This figure is reproduced from Green JB, et al. under the terms of the Creative Commons Attribution-Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0/); 2. NCT05254002. Available at: https://clinicaltrials.gov/study/NCT05254002; 3. Agarwal R, et al. *N Engl J Med*. 2025; doi:10.1056/NEJMoa2410659.

CONFIDENCE aimed to determine the role of simultaneous finerenone and SGLT-2i initiation in people with CKD and T2D[1–3]

Key inclusion criteria

- Aged ≥18 years
- eGFR 30–90 mL/min/1.73m^{2*}
- UACR ≥100–<5000 mg/g
- T2D with HbA1c <11%
- Clinically maximum tolerated dose of ACEi/ARB for >1 month

Key exclusion criteria

- T1D
- Day 1 BP >160/100 or SBP <90 mmHg
- Serum K^+ >4.8 mmol/L
- HFrEF with NYHA Class II–IV
- Current treatment with finerenone and an SGLT-2i

Primary endpoint

Relative change in UACR from baseline to Day 180:

- **Combination** versus **empagliflozin**
- **Combination** versus **finerenone**

Secondary endpoints

Secondary efficacy outcomes

Relative change in UACR:

- Between end of treatment visit to 30 days after end of treatment visit
- Between 30 days after end of treatment visit and baseline
- Category (>30%, >40%, and >50%) at 180 days

Secondary safety outcomes

- Initial and longer-term changes in eGFR
- Acute kidney injury
- Treatment-related AEs: hyperkalemia, symptomatic hypotension, genital mycotic events

*Patients will require at least one value of eGFR <60 mL/min/1.73 m^2 within the previous 3 months or have registered diagnosis of CKD. Patients with an eGFR >75–90 mL/min/1.73 m² will be capped at 20%. Patients in Part A required to have eGFR 40–90 mL/min/1.73 m², expanded to 30–90 mL/min/1.73 m² in Part B following feedback from DMC and safety analysis.

ACEi, angiotensin-converting enzyme inhibitor; AE, adverse event; ARB, angiotensin receptor blocker; BP, blood pressure; CKD, chronic kidney disease; DMC, data monitoring committee; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; HFrEF, heart failure with reduced ejection fraction; NYHA, New York Heart Association; SBP, systolic blood pressure; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T1D, type 1 diabetes; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio.

1. Green JB, et al. *Nephrol Dial Transplant*. 2023;38(4):894–903; 2. NCT05254002. Available at: https://clinicaltrials.gov/study/NCT05254002 [accessed May 2025]; 3. Agarwal R, et al.

CONFIDENCE

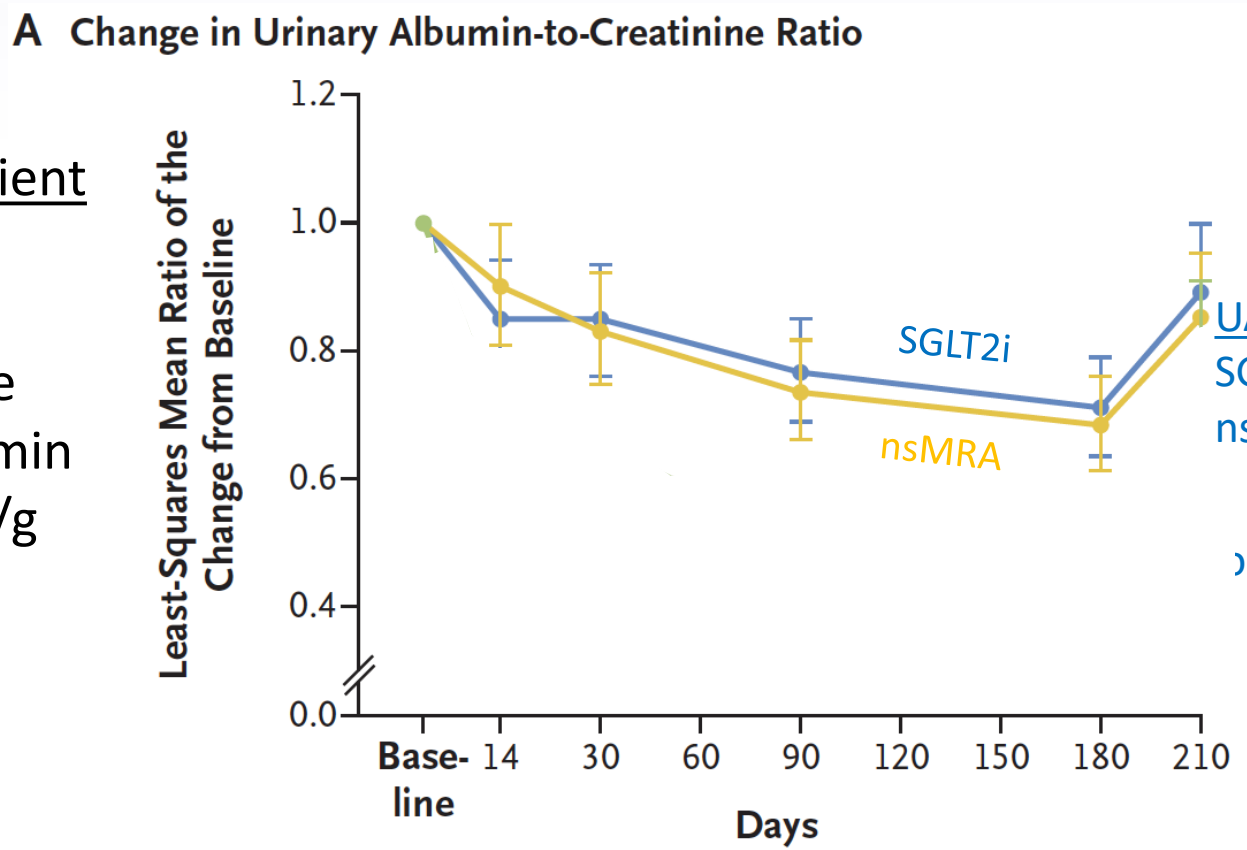
ERA Congress, Vienna, 5 Jun 2025

St. Stephen's Cathedral, built 1137,
Was where Wolfgang A. Mozart married
Constanze Weber in 1781

Agarwal R, et al, NEJM, ePub 5 Jun 2025

CONFIDENCE

Baseline	My patient
Age 67 78 y	
Male 75%	M
Asian 46%	Chinese
eGFR 54	54 ml/min
UACR 580	1500 g/g
BMI 29	25
A1C 7.3%	6.5
On RASi>98%	Y



UACR Δ at 180 d from baseline with:
SGLT2i alone: – 29%
nsMRA alone: – 32%

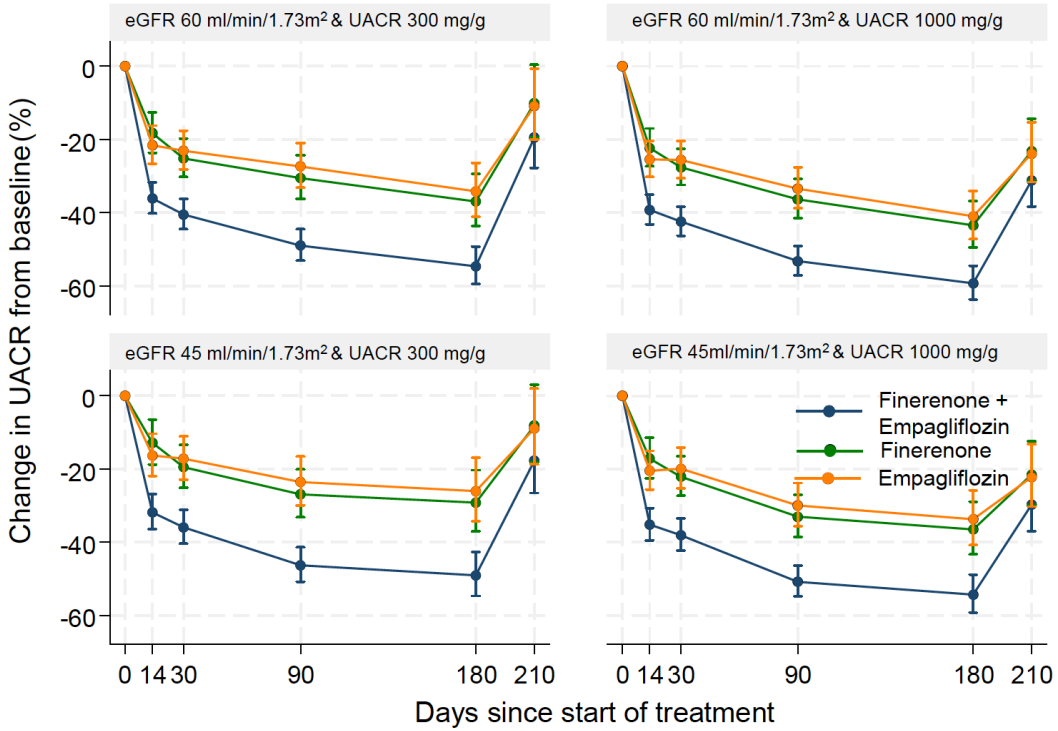
How about combination Rx?
ombination: – 52%

A. 31%
B. 38%
C. 45%
D. 52%

Posthoc analysis of CONFIDENCE

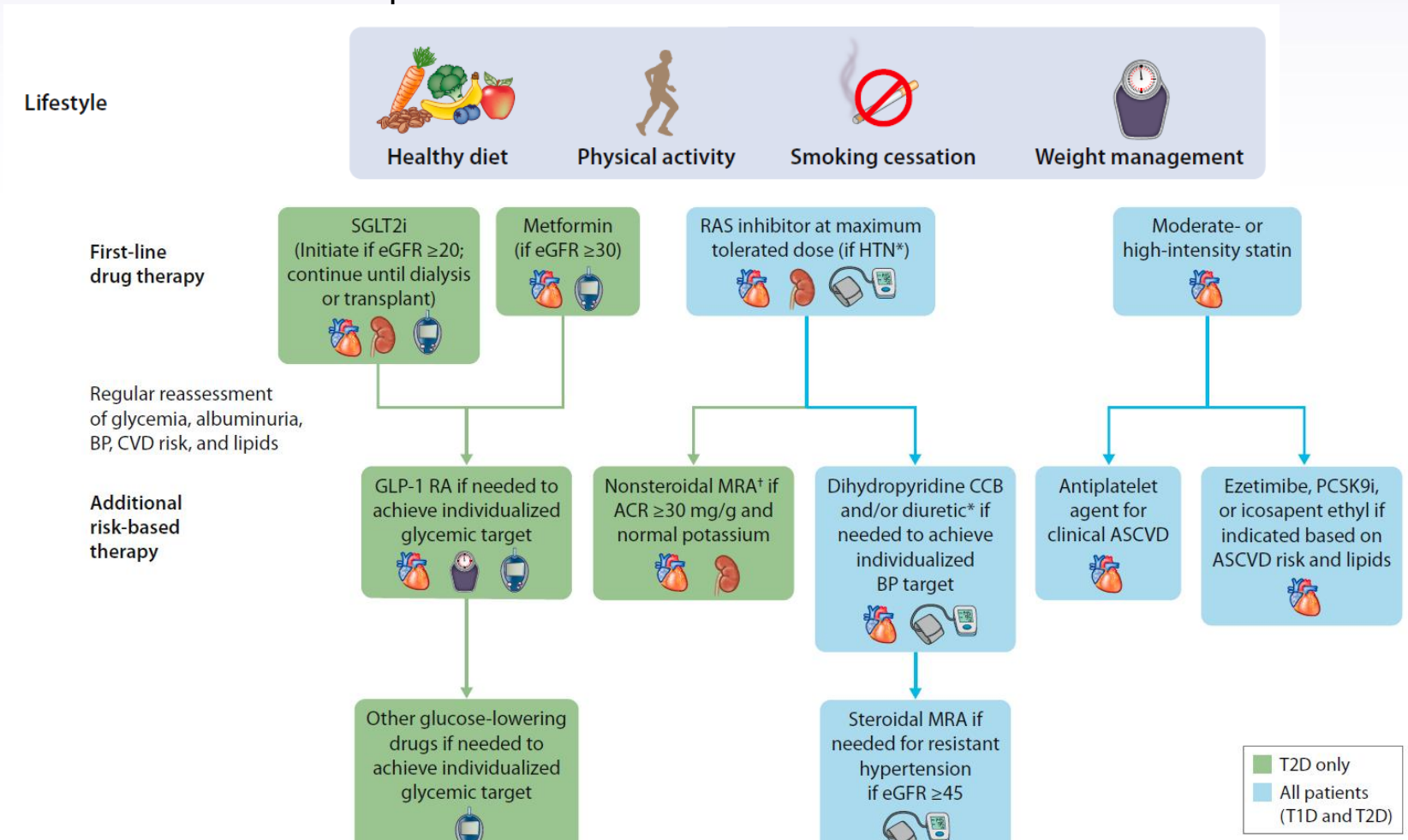
Table 2. Percent change in UACR from baseline at various timepoints by baseline eGFR and baseline log UACR, all three treatment groups combined

	Change in UACR per log baseline UACR Percent (95% CI)	Change in UACR per 10 mL/min/1.73 m^2 baseline eGFR Percent (95% CI)
Day 14	–4.2 [–7.7 to –0.5]	–4.2 [–6.3 to –2.2]
Day 30	–2.7 [–6.5 to 1.1]	–4.8 [–6.9 to –2.7]
Day 90	–7.1 [–11.4 to –2.5]	–3.3 [–5.9 to –0.7]
Day 180	–8.7 [–14.4 to –2.7]	–7.5 [–10.7 to –4.1]



Mottl A, et al. To be presented at the ASN Kidney Week, 6- 9 Nov 2025, Houston

The ADA/KDIGO consensus proposes a holistic approach for improving outcomes in patients with diabetes and CKD



The ADA/KDIGO consensus positions finerenone after treatment with RASis to protect against persistent cardiorenal risk in patients with diabetes and CKD (UACR ≥30 mg/g)

*ACEi or ARB (at maximal tolerated doses) should be first-line therapy for hypertension when albuminuria is present. Otherwise, dihydropyridine calcium channel blocker or diuretic can also be considered; all three classes are often needed to attain BP targets. †Finerenone is currently the only nonsteroidal MRA with proven clinical kidney and CV benefits

ACR, albumin-to-creatinine ratio; BP, blood pressure; CCB; calcium channel blocker; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; MRA, mineralocorticoid receptor antagonist; PCSK9I, proprotein convertase subtilisin/kexin type 9 inhibitor; RASi, renin–angiotensin system inhibitor; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T1D, type 1 diabetes; UACR, urine albumin-to-creatinine ratio

de Boer IH, *et al. Diabetes Care* 2022;doi:10.2337/dci22-0027

American Diabetes Association.

Management of chronic kidney disease: a Hong Kong consensus recommendation

Sydney CW Tang *, Kelvin KL Ho, Welchie WK Ko, Albert Lee, CB Leung, WK Lo, Ronald CW Ma, SL Pang, Kathryn CB Tan, MW Tsang, Martin CS Wong, William CW Wong, Francis KM Wong, CC Szeto

Hong Kong Med J 2024;30:478–87

9	In patients with diabetes and hypertension or albuminuria, ACEis or ARBs should be initiated as first-line pharmacological treatment for renal protection and blood pressure control, and the maximum tolerated dose should be titrated.	1	100% (A: 79%, B: 21%, C: 0%, D: 0%, E: 0%)
10	In patients with T2DM and CKD who have an eGFR of ≥20 mL/min/1.73 m^2, a SGLT2i can be initiated as first-line pharmacological treatment for glycaemic control, renal protection, and cardiovascular protection.	1	93% (A: 64%, B: 29%, C: 7%, D: 0%, E: 0%)
11	Patients with T2DM who have an eGFR of ≥25 mL/min/1.73 m^2, normal serum potassium concentration, and uACR of ≥30 mg/g (≥3 mg/mmol) despite receiving the maximum tolerated dose of a RAS inhibitor can be treated with a nonsteroidal MRA for renal and cardiovascular protection, depending on accessibility.	1	86% (A: 50%, B: 36%, C: 14%, D: 0%, E: 0%)
12	Patients with T2DM and CKD who have not achieved individualised glycaemic targets despite metformin and SGLT2i treatment or who cannot use those medications can be treated with GLP-1 RAs.	1	100% (A: 64%, B: 36%, C: 0%, D: 0%, E: 0%)

IDF Global Clinical Practice Recommendations for Managing Type 2 Diabetes – 2025 (Released 9 Apr)

International Diabetes Federation

75 YEARS 1950 - 2025

Chapter 6

Cardio-renal protection in type 2 diabetes

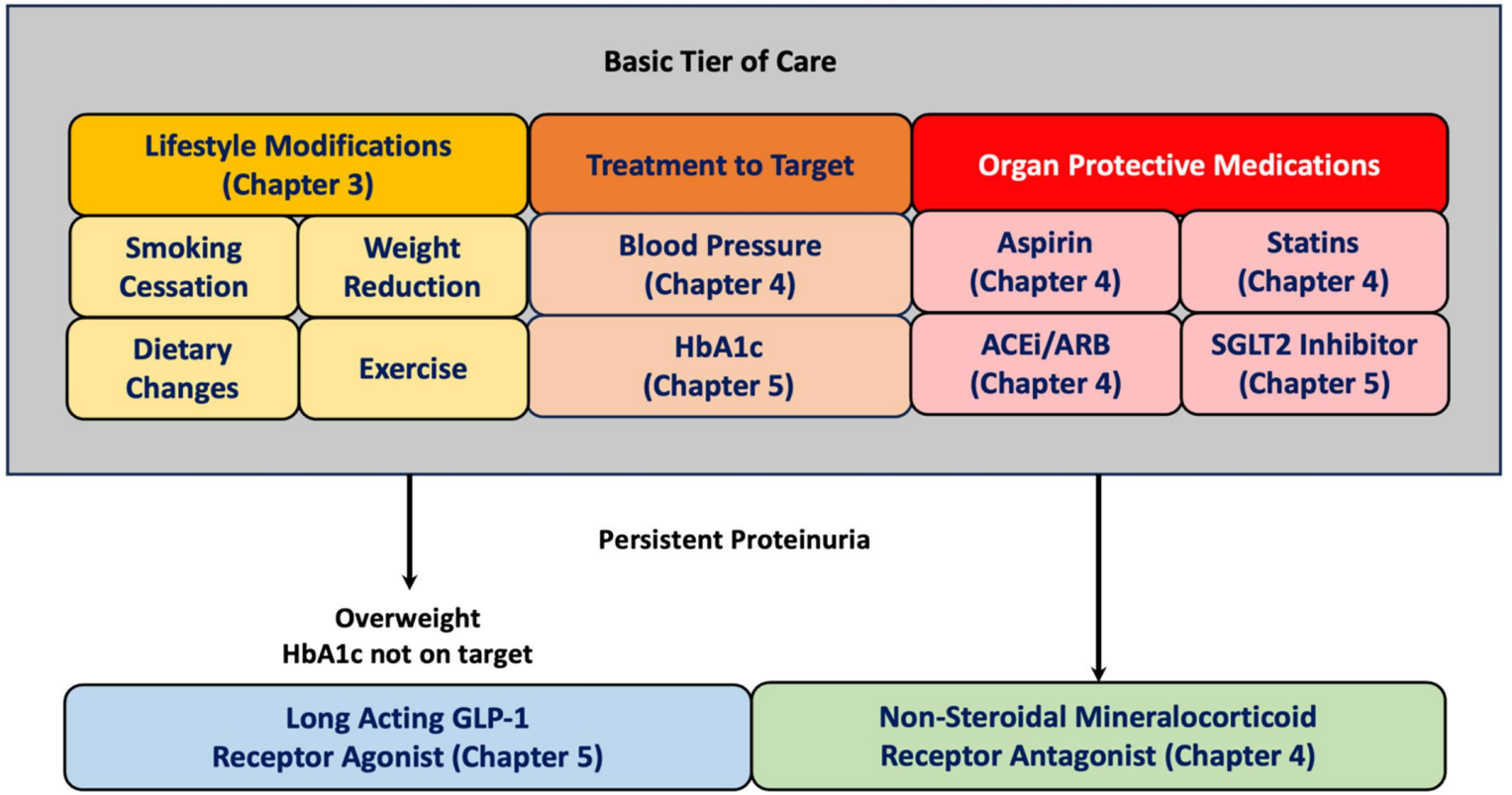
↓ major adverse CV events, all-cause mortality, and composite kidney outcomes

	Optimal Care	Basic Care
Atherosclerotic Cardiovascular Disease (ASCVD)		
Screening/risk assessment	• History of ASCVD • High-risk assessment - Age plus 2 risk factors - CVD risk score	
Management	• Glycaemic control • Risk factor control • Blood pressure/lipid control • Consider aspirin • SGLT2i or GLP-1RA • Consider SGLT2i and GLP-1RA • Finerenone	• Glycaemic control • Risk factor control • Blood pressure/lipid control • Consider aspirin • SGLT2i*

Asian Pacific Society of Nephrology Clinical Practice Guideline on Diabetic Kidney Disease—2025 Update

Adrian Liew ✉, Sunita Bavanandan, Chuan-Ming Hao, Soo Kun Lim, Narayan Prasad, Manisha Sahay, Paweena Susantitaphong, Veena Roberts, Eranga Wijewickrama, Muh Geot Wong, Sydney C. W. Tang

First published: 09 July 2025 | https://doi.org/10.1111/nep.70030



- ***The choice between a long acting GLP-1 receptor agonist and a non-steroidal mineralocorticoid receptor antagonists as the next therapeutic agent will depend on cost, availability, tolerability and therapeutic goal.***
- ***Where cost and accessibility are not issues, both agents can be used sequentially if proteinuria persists after the addition of the first drug.***

Design and baseline characteristics of the FIND-CKD trial testing finerenone in non-diabetic CKD

Focus was to describe the trial design and baseline characteristics of participants recruited to the FIND-CKD trial.

Methods

CKD without diabetes
eGFR ≥25 – <90 ml/min/1.73 m²
and UACR ≥200 – ≤3500 mg/g

Finerenone 10 or 20 mg vs placebo

Primary endpoint:
Mean annual rate of change in eGFR from baseline to month 32

Secondary endpoint:
Cardiorenal, kidney and cardiovascular composite outcomes

Results

N=1584 randomized

Mean eGFR
46.7
ml/min/1.73 m²

Median UACR
818.9
mg/g

Cause of kidney disease
Hypertensive/ischaemic 29.0%
IgA nephropathy 26.3%
FSGS 13.6%

Cardiovascular history
Hypertension 88.1%
Atherosclerotic CVD 11.9%
Heart failure 2.2%

Concomitant medications
ACEi/ARB 99.8%
SGLT2 inhibitor 16.9%
Diuretic 17.8%

Heerspink, H. J. L. *et al.*
NDT (2024)
@NDTSocial

FIND-CKD is the first phase 3 trial of finerenone in patients with CKD of non-diabetic aetiology and seeks to expand the role of finerenone for kidney protection beyond type 2 diabetes.

Baseline Demographics and Disease Characteristics†

Characteristic	Total (N=1584)
Age, years, mean (SD)	54.7 (14.3)
Sex, male, n (%)	1049 (66.2)
Race, n (%)	
Asian	866 (54.7)
White	648 (40.9)
Black	37 (2.3)
Other	33 (2.1)
Ethnicity, n (%)	
Non-Hispanic	1461 (92.2)
Hispanic	111 (7.0)
Region, n (%)	
Asia	844 (53.3)
Europe and Oceania	535 (33.8)
North America	132 (8.3)
Latin America	73 (4.6)

Characteristic	Total (N=1584)
eGFR, mL/min/1.73 m^2, mean (SD)	46.7 (16.1)
eGFR category, mL/min/1.73 m^2, n (%)	
<25	23 (1.5)
25 to <45	821 (51.8)
45 to <60	423 (26.7)
≥60	317 (20.0)
UACR, mg/g, median (IQR)	818.9 (577.4-1244.0)
UACR category, mg/g, n (%)	
<300	63 (4.0)
300 to ≤1000	929 (58.6)
>1000	592 (37.4)
BMI, kg/m^2, mean (SD)	27.6 (5.6)
SBP, mmHg, mean (SD)	129.5 (14.1)
DBP, mmHg, mean (SD)	80.0 (9.6)
HbA1c, % (SD)	5.5 (0.4)
Serum potassium, mmol/L, mean (SD)	4.5 (0.4)

Baseline Kidney Disease Etiology, CVD History, and Concomitant Medications

In FIND-CKD, historical kidney biopsies from patients were available for 787 (49.7%) patients.
Historical kidney biopsies were available for 42% and 36% of patients without diabetes in the EMPA-KIDNEY and DAPA-CKD trials, respectively.[1,2]

Kidney disease etiology, n (%)	Total (N=1584)
Hypertensive/ischemic nephropathy	460 (29.0)
Chronic glomerulonephritis	903 (57.0)
IgAN	417 (26.3)
FSGS	215 (13.6)
Primary FSGS	109 (6.9)
Secondary FSGS	106 (6.7)
Membranous nephropathy	91 (5.7)
Mesangial proliferative glomerulonephritis†	26 (1.6)
Other chronic glomerulonephritis	154 (9.7)
Other	57 (3.6)
Unknown	164 (10.4)

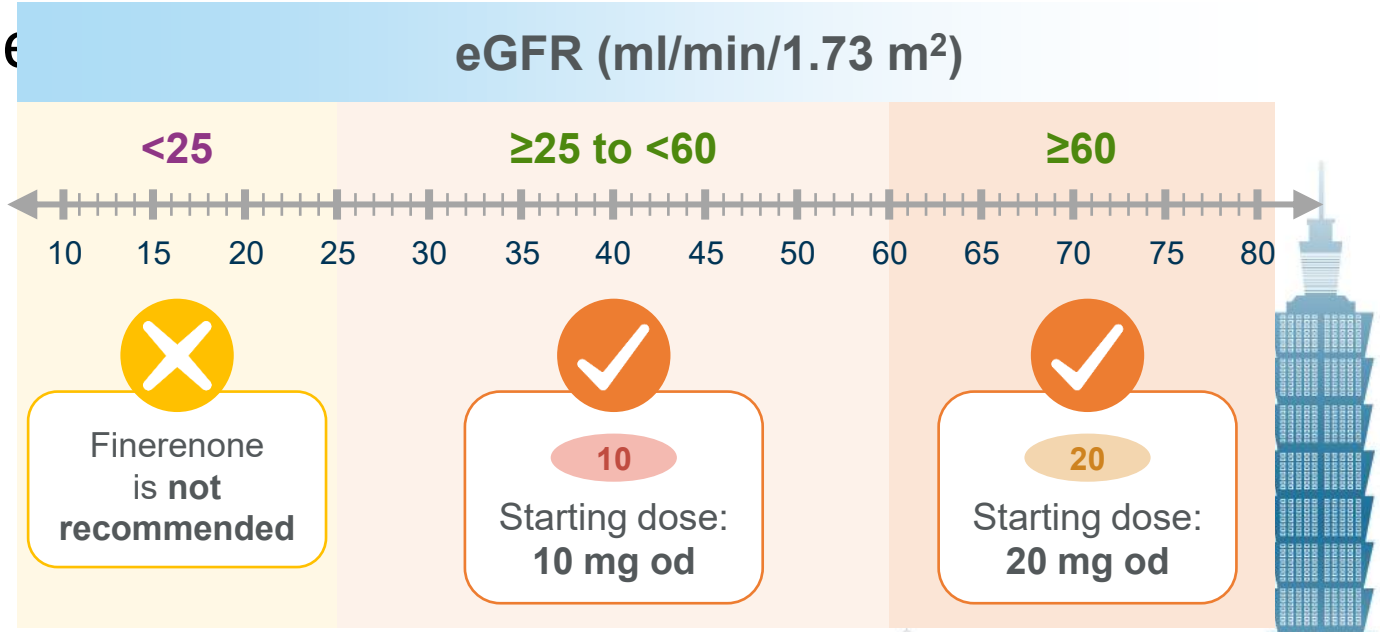
CVD history and concomitant medications, n (%)	Total (N=1584)
Hypertension	1396 (88.1)
Atherosclerotic CVD	189 (11.9)
Atrial fibrillation	59 (3.7)
Heart failure	35 (2.2)
RAASis‡	1581 (99.8)
ACEis‡	435 (27.5)
ARBs‡	1146 (72.3)
SGLT2 inhibitors	267 (16.9)
Potassium-lowering agents	58 (3.7)
Potassium supplements	20 (1.3)
Beta-blockers	403 (25.4)
Diuretics	282 (17.8)
Loop diuretics	128 (8.1)
Thiazide diuretics	116 (7.3)
Calcium channel blockers	794 (50.1)
Statins	851 (53.7)

Initiation of treatment

Measurement of serum potassium levels and eGFR

- Serum potassium levels are measured to determine whether patients can initiate finerenone
- The recommended starting dose

Serum potassium levels	
mmol/l	Initiation of finerenone
≤4.8	✓ Can be started
>4.8–5.0	✓ May be considered*
>5.0	✗ Not recommended



Continuation of treatment and dose adjustment

Serum [K^+] and eGFR must be remeasured 4 weeks after:

- Initiation of treatment
- Restarting treatment
- Increase in dose

Thereafter, serum [K^+] should be **remeasured periodically** and **as needed***

Treatment can be **maintained** in patients with an **eGFR ≥15 ml/min/1.73 m²**. If **eGFR** falls below **15 ml/min/1.73 m²** **continue treatment with caution** regarding serum potassium levels as clinical experience is limited

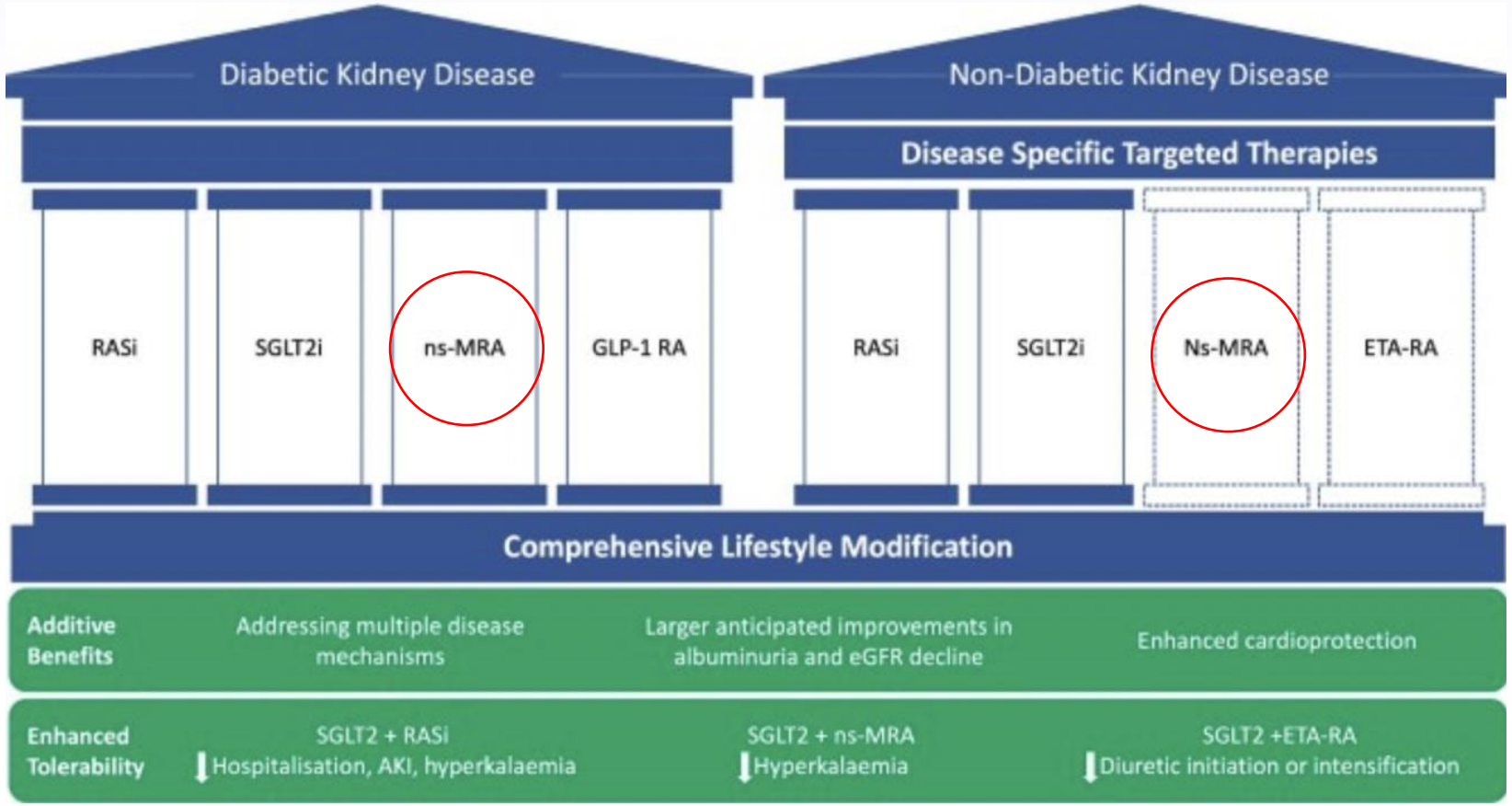
Dose adjustments:

Current serum potassium (mmol/l)	Current finerenone dose
≤4.8	10 → 20 ← 20 Increase to# or maintain **20 mg od**
4.9–5.5	**Maintain current dose**
>5.5	**Withhold treatment** Restart at 10 mg od when serum [K^+] is ≤5.0 mmol/l

The recommended target dose and maximum recommended dose of finerenone is 20 mg od

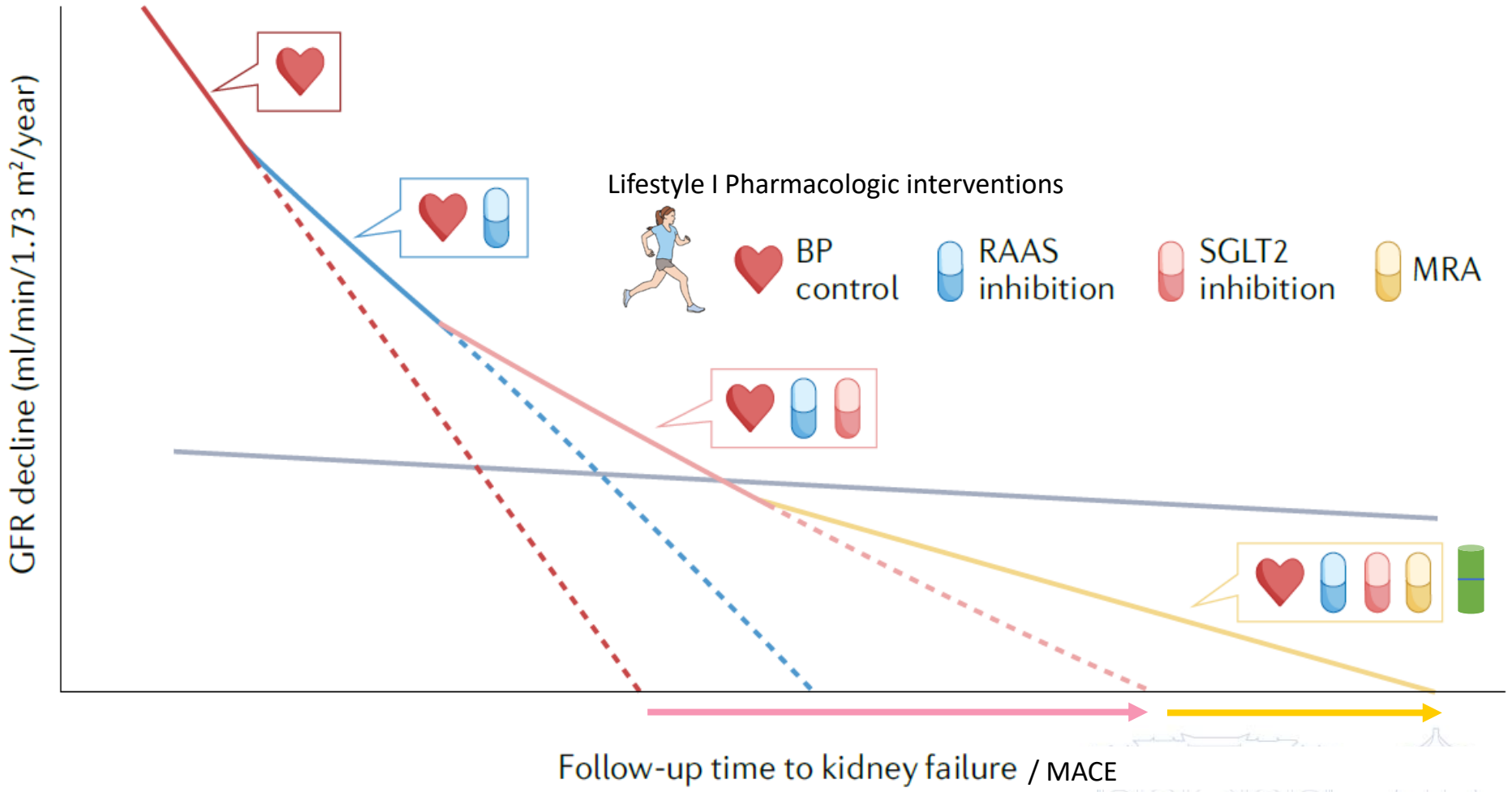
*Based on patient characteristics and serum [K^+]; #Maintain 10 mg od if eGFR has decreased >30% compared with the previous measurement

Mineralocorticoid Receptor Antagonism is a pillar for diabetic CKD care and may become one in nondiabtic CKD in due course



Neuen BL, et al. Nephrol Dial Transplant 2025

My Last Takeaway – Screen Early, Treat Better



Delays Dialysis by

N Years

Reduces MACE by

X %

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