Emerging Treatments in Diabetic Kidney Disease (DKD)

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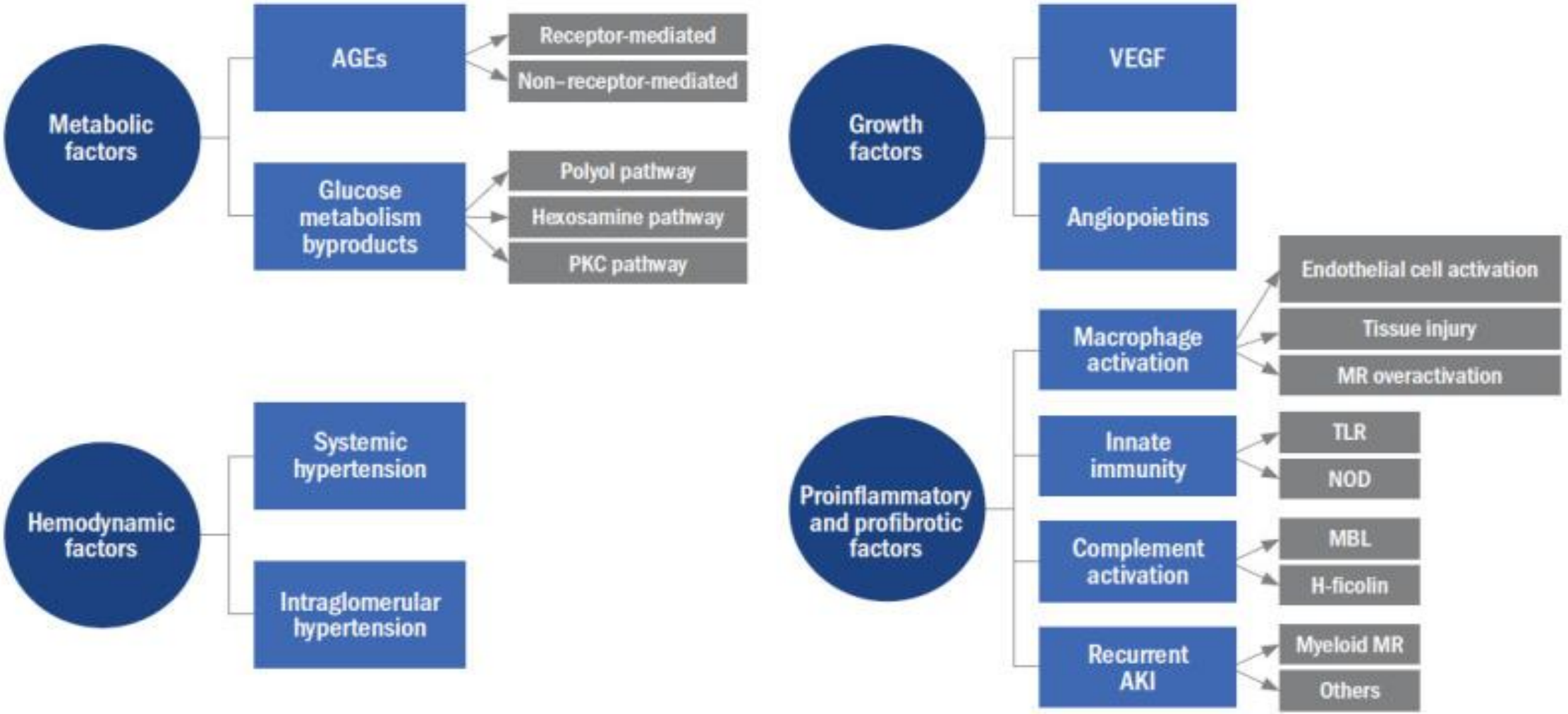
The Drivers of Diabetic nephropathy



The pathogenesis of diabetic nephropathy

- These pathogenetic factors produce lesions in various kidney compartments:

1. Glomeruli
2. Tubuli
3. Interstitium
4. Vasculature

Pathological Classification of Diabetic Nephropathy

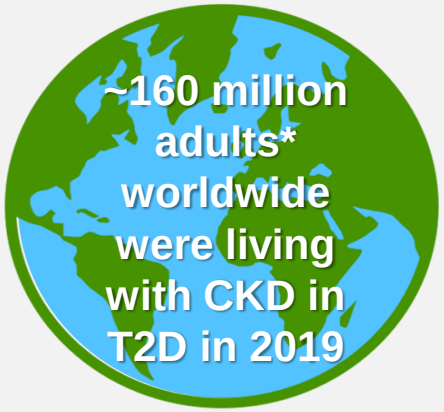
Class I	GBM thickening on electron microscopy; minimal, non-specific, or no changes on light microscopy	Patients may have such thickening but have no increase in urine albumin excretion rate or impairment of glomerular filtration rate observed within 2–8 years after the onset of diabetes
Class II	•Increase in mesangial matrix	
Class IIa	•Mesangial expansion ≤25%	**kidney enlargement**; kidneys are often 11 cm or larger on kidney ultrasound. Urine albumin excretion is often increased in these patients.
Class IIb	•Mesangial expansion >25%	
Class III	•Nodular **glomerulosclerosis**: •Kimmelstiel-Wilson lesion	An increase in mesangial matrix is followed by **mesangial sclerosis.**
Class IV	•Advanced **glomerulosclerosis**; •>50% glomeruli sclerotic	sclerosis in >50% of the glomeruli Loss of kidney function at the time of biopsy

Proinflammatory and Profibrotic Factors

- Inflammation and fibrosis are important causes of diabetic nephropathy
- Macrophages are activated to the proinflammatory (M1) phenotype by reactive oxygen species (ROS), angiotensin II, and the activation of **mineralocorticoid receptors** (MRs).
- Mineralocorticoid receptors (MRs) activation, particularly in the myeloid cells, may be important in mediating inflammation and **fibrosis** in CKD and after AKI in individuals with type 2 diabetes.

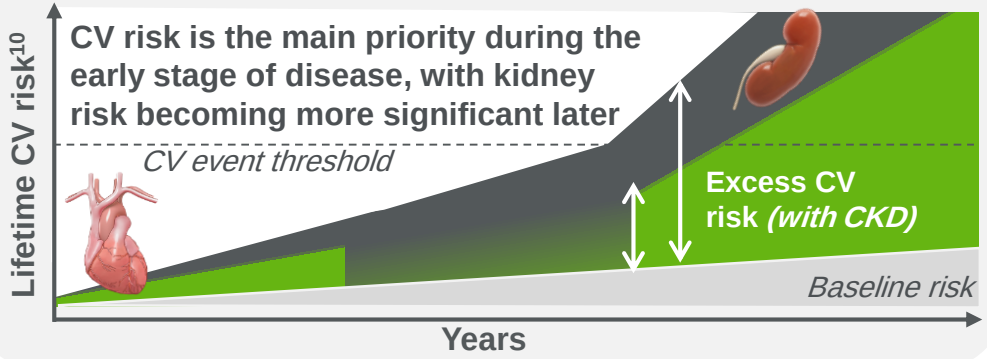
Global burden of disease[1,2]

CKD affects ~2 in 5 patients with T2D

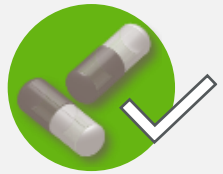


CKD progression and CV risk[3–6]

- Compared with T2D alone, comorbid CKD increases CV mortality
- CVD is a leading cause of death in patients with any stage of CKD
- CV mortality risk increases with eGFR decline and increased albuminuria



Unmet needs[7–9]



Recent treatment options in the field have led to a decline in diabetes-related CV complications

However, there remains unaddressed residual risk of CKD progression and CV events

*Aged 20–79 years

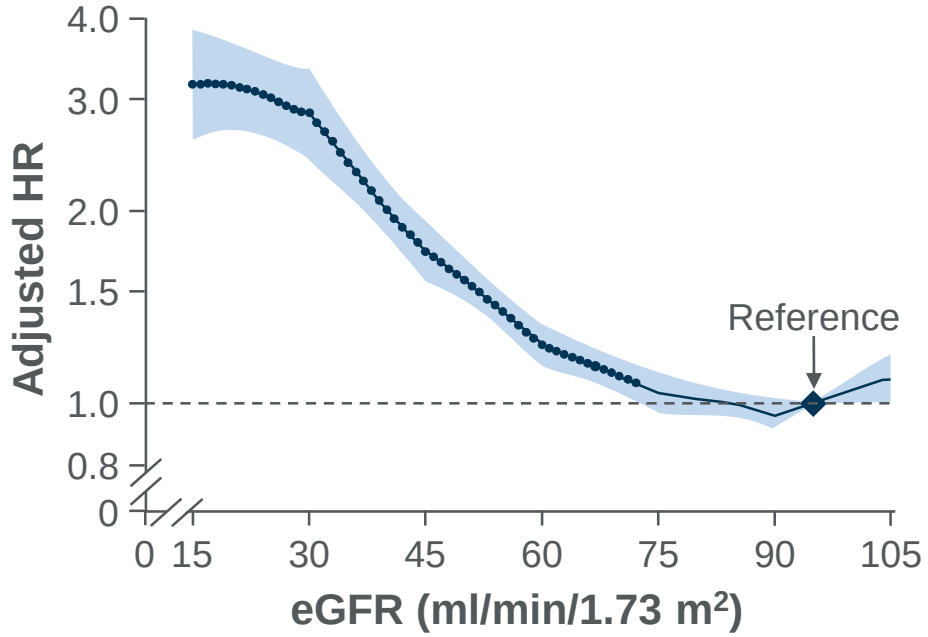
1. International Diabetes Federation. *IDF Diabetes Atlas,* 9th edn. 2019. https://diabetesatlas.org/en/ [accessed 28 July 2021]; 2. Wu B, *et al. BMJ Open Diabetes Res Care* 2016;4:e000154; 3. Afkarian M, *et al. J Am Soc Nephrol* 2013;24:302–308; 4. Gansevoort RT, *et al. Lancet* 2013;382:339–352; 5. Astor BC, *et al. Am J Epidemiol* 2008;167:1226–1234; 6. Sarnak MJ, *et al. J Am Coll Cardiol* 2019;74:1823–1838; 7. Brenner BM, *et al. N Engl J Med* 2001;345:861–869; 8. Lewis EJ, *et al. N Engl J Med* 2001;345:851–860; 9. Perkovic V, *et al. N Engl J Med* 2019;380:2295–2306; 10. Giorgino F, *et al. Cardiovasc Diabetol* 2020;18:196

CKD = eGFR <60 ml/min/1.73 m² for >3 months[1]

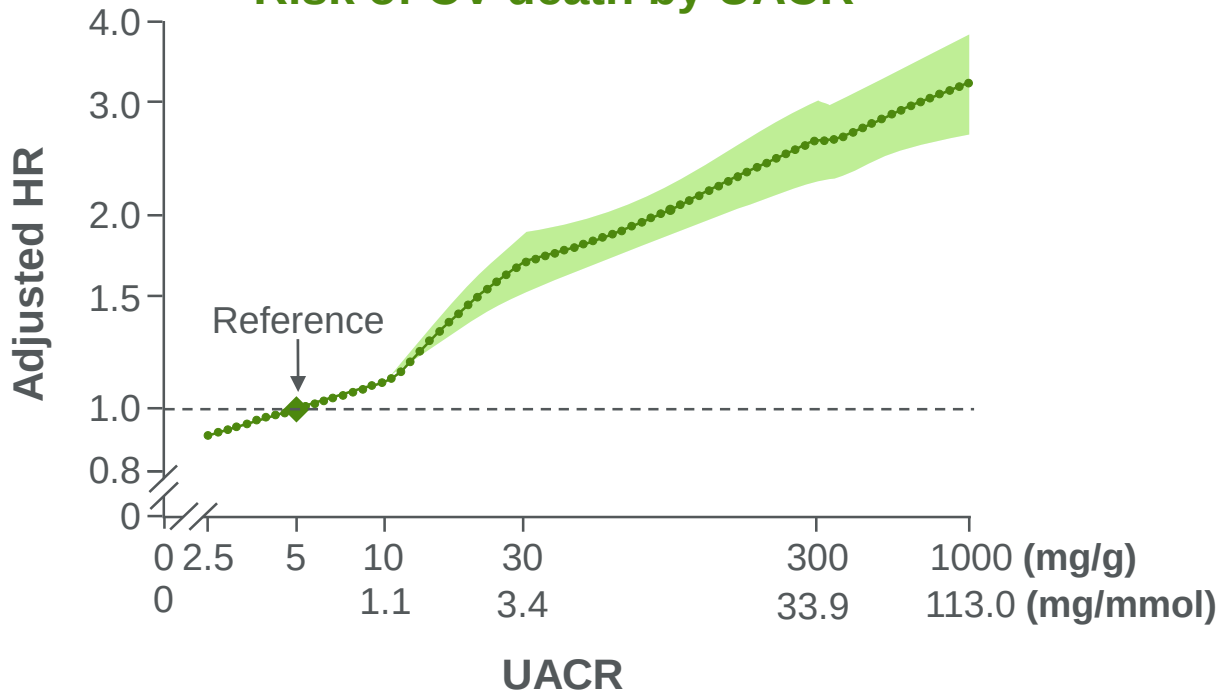
and
OR

CKD = UACR >30 mg/g (>3.4 mg/mmol) for >3 months[1]

Risk of CV death by eGFR*#,2



Risk of CV death by UACR*2

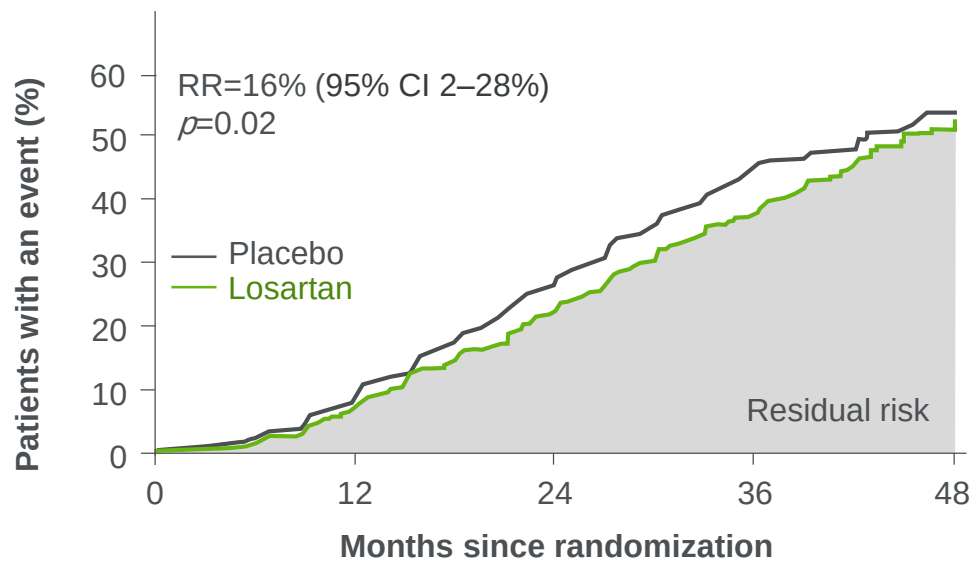


*Adjusted for age, sex, race or ethnic origin, smoking, SBP, antihypertensive drugs, diabetes, total and HDL cholesterol concentrations, and albuminuria (UACR or dipstick) or eGFR, as appropriate;
#figure adapted from Matsushita K, *et al.* 2015
CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HR, hazard ratio; SBP, systolic blood pressure; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio

1. Kidney Disease Improving Global Outcomes. *Kidney Int* 2013;3:1–150; 2. Matsushita K, *et al. Lancet Diabetes Endocrinol* 2015;3:514–525

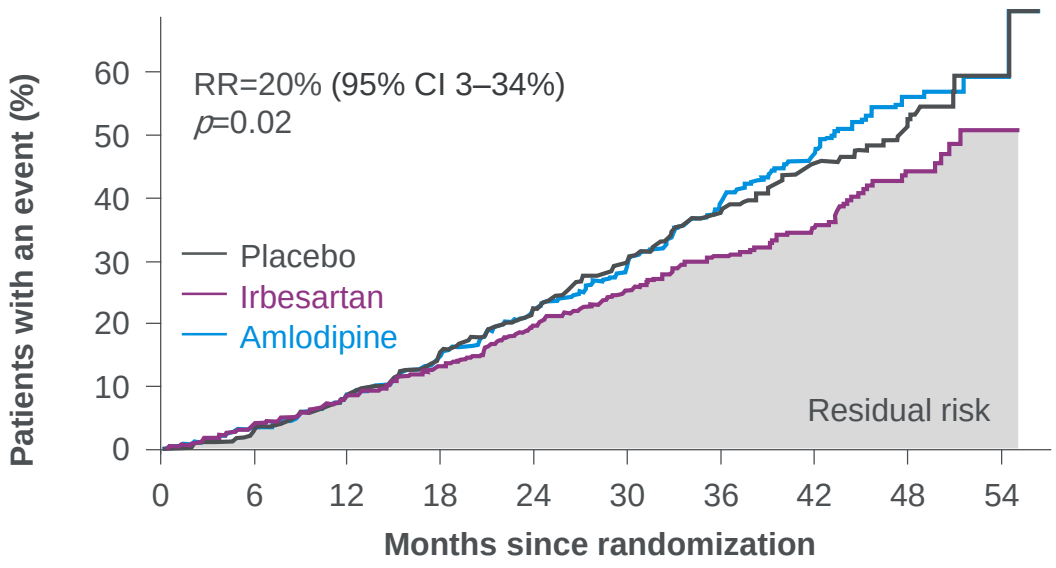
Despite RAS blockade, patients with CKD and T2D are at high risk of CKD progression

RENAAL: Losartan vs placebo[1]



Primary composite endpoint:
Doubling of SCr, kidney failure*, or death

IDNT: Irbesartan vs amlodipine vs placebo[2]



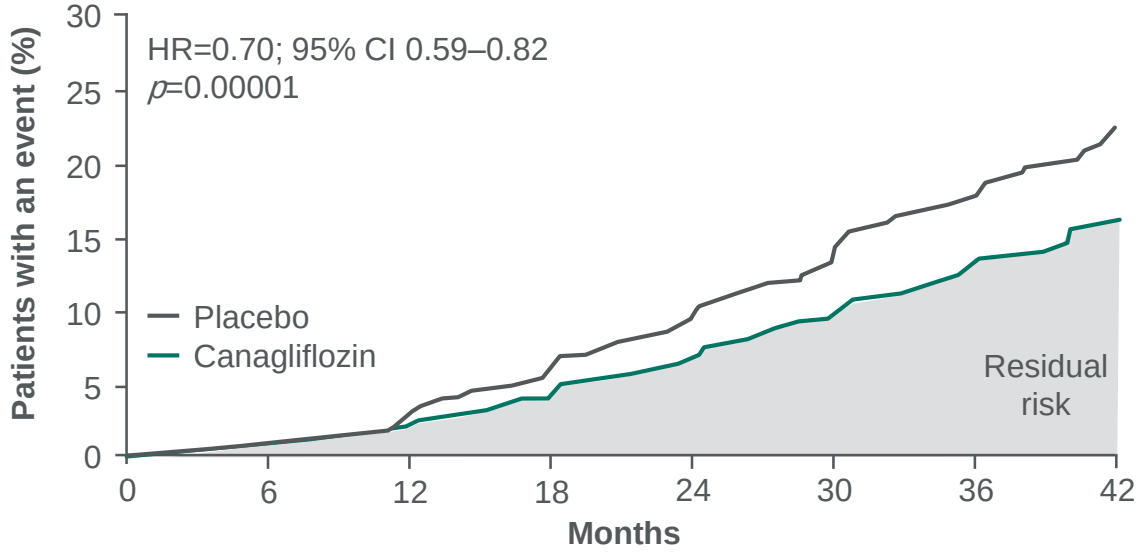
Primary composite endpoint:
Doubling of SCr, kidney failure,# or death

*Kidney failure defined as need for long-term dialysis or kidney transplantation
#Kidney failure defined as initiation of dialysis, kidney transplantation or a SCr ≥6.0 mg/dl (530 µM/l)

1. Brenner BM, *et al. N Engl J Med* 2001;345:861–869; 2. Lewis EJ, *et al. N Engl J Med* 2001;345:851–860

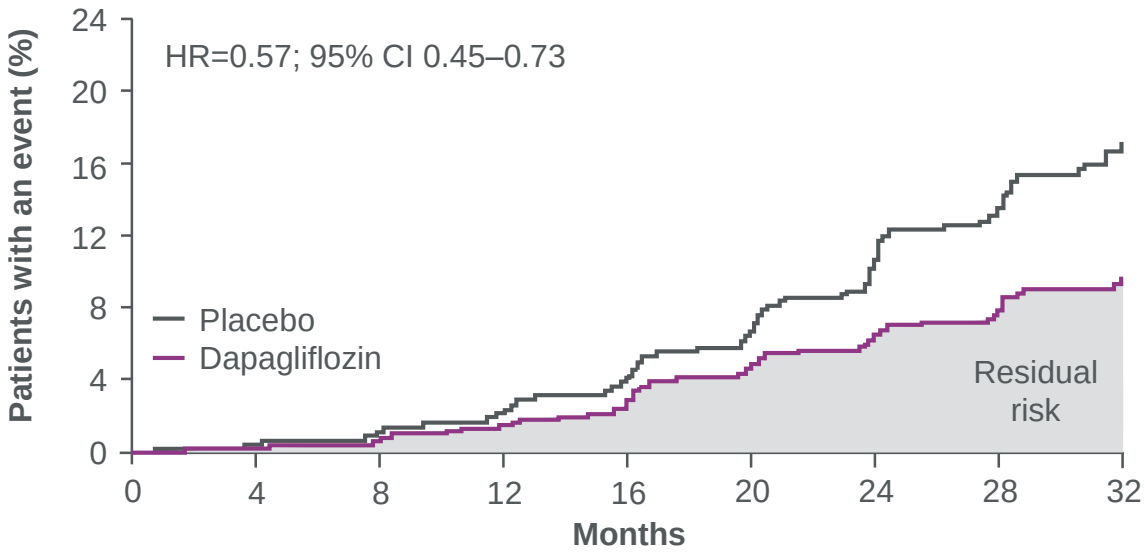
Despite SGLT-2i treatment being recommended for patients with CKD and diabetes,[1] further treatment options are needed

CREDENCE: Canagliflozin (+ RASi) vs placebo[2]



Primary composite outcome:
Kidney failure, doubling of SCr or death from kidney/CV causes

DAPA-CKD: Dapagliflozin (+ RASi) vs placebo (T2D subgroup)[3,4]



Secondary composite renal outcome:
Sustained ≥50% eGFR decline, ESKD or renal death

CREDENCE and DAPA-CKD have shown that **SGLT-2is offer kidney protection and lower the risk of CV events**; however, in these studies, **CKD progression or kidney failure still occurred in ~7% of patients and CV events in ~5–8% of patients** after a median follow-up of ~2.5 years[2,3]

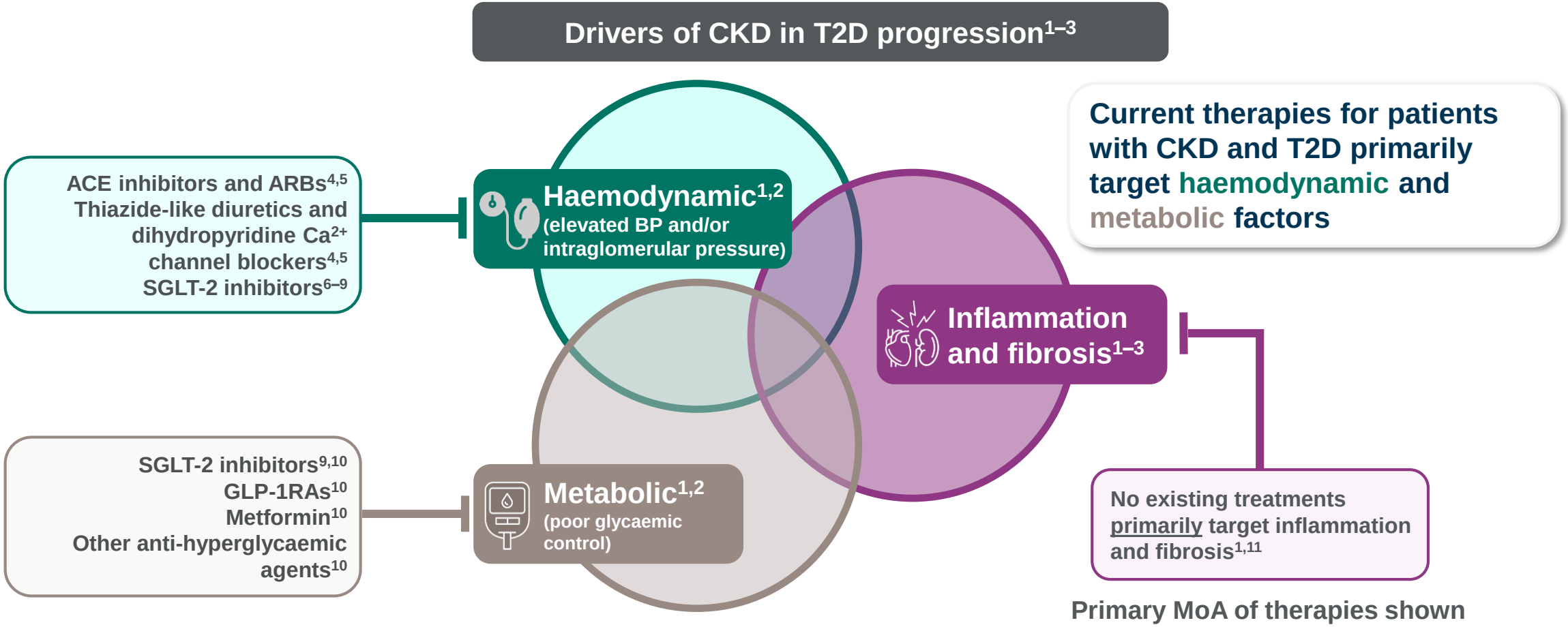
CI, confidence interval; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HR, hazard ratio; RASi, renin–angiotensin system inhibitor; SCr, serum creatinine

1. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. *Kidney Int.* 2020;98:S1–S115; 2. Perkovic V, *et al. N Engl J Med.* 2019;380:2295–2306; 3. Heerspink HJL, *et al. N Engl J Med.* 2020;383:1436–1446; 4. Wheeler DC, *et al. Lancet Diabetes Endocrinol.* 2021;9:22-31

An Introduction to Finerenone

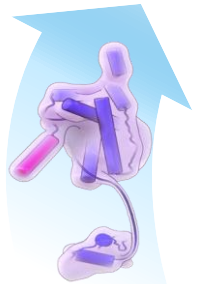
Mechanism of Action

CKD in T2D progression, associated with increased CV risk, is driven by the combined effects of metabolic, haemodynamic, inflammatory and fibrotic factors

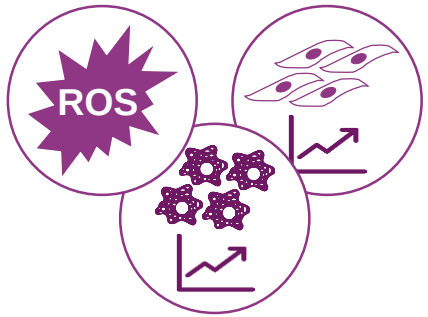


1. Alicic RZ, *et al. Clin J Am Soc Nephrol* 2017;12:2032–2045; 2. Mora-Fernández C, *et al. J Physiol* 2014;18:3997; 3. Bauersachs J, *et al. Hypertension* 2015;65:257–263; 4. American Diabetes Association. *Diabetes Care* 2022;45:S175–184; 5. American Diabetes Association. *Diabetes Care* 2022;45:S144–174; 6. Kidokoro K, *et al. Circulation* 2019:140;303–315; 7. Zelniker TA & Braunwald E. *J Am Coll Cardiol* 2018;72:1845–1855; 8. Heerspink HJ, *et al. Circulation* 2016;134:752–772; 9. Zelniker TA & Braunwald E. *J Am Coll Cardiol* 2020;75:422–434; 10. American Diabetes Association. *Diabetes Care* 2022;45:S125–S143; 11. Alicic RZ, *et al. Adv Chronic Kidney Dis* 2018;25:181–191

MR overactivation causes kidney and cardiovascular damage through inflammation and fibrosis



In kidney and heart diseases, the **MR pathway becomes overactivated** through multiple mechanisms[1,2]



Increased gene expression of NADPH oxidase, pro-inflammatory cytokines, and pro-fibrotic mediators[1–8]

Inflammation and fibrosis

Kidney damage[3,7]
- Glomerular damage
- Proteinuria
- Tubular injury
- Reduced renal blood flow
- Kidney injury

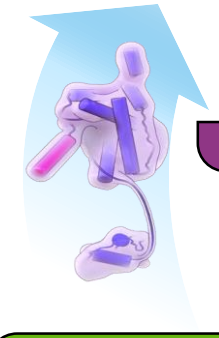
Vascular damage[1,6]
- Vascular remodeling
- Endothelial dysfunction
- Increased vascular stiffness

Heart damage[1,3]
- Myocardial hypertrophy
- Ventricular remodeling/fibrosis
- Reduced coronary blood flow
- Ischaemia/infarction
- Myocardial injury

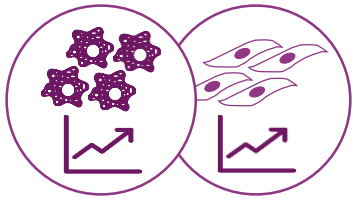
1. Buonafine M, *et al. Am J Hypertension* 2018;31:1165–1174; 2. Kolkhof P, *et al. Handb Exp Pharmacol* 2017;243:271–305; 3. Bauersachs J, *et al. Hypertension* 2015;65:257–263; 4. Gomez-Sanchez E & Gomez-Sanchez CE. *Compr Physiol* 2014;4:965–994; 5. Brown NJ. *Nat Rev Nephrol* 2013;9:459–469; 6. Biwer LA, *et al. Am J Hypertension* 2019;32:123–134; 7. Barrera-Chimal J, *et al. Kidney Int* 2019;96:302–319; 8. van de Heijden CDCC, *et al. Cardiovasc Res* 2018;114:944–953

MR overactivation, which contributes to inflammation and fibrosis, is a potential treatment target to slow CKD progression

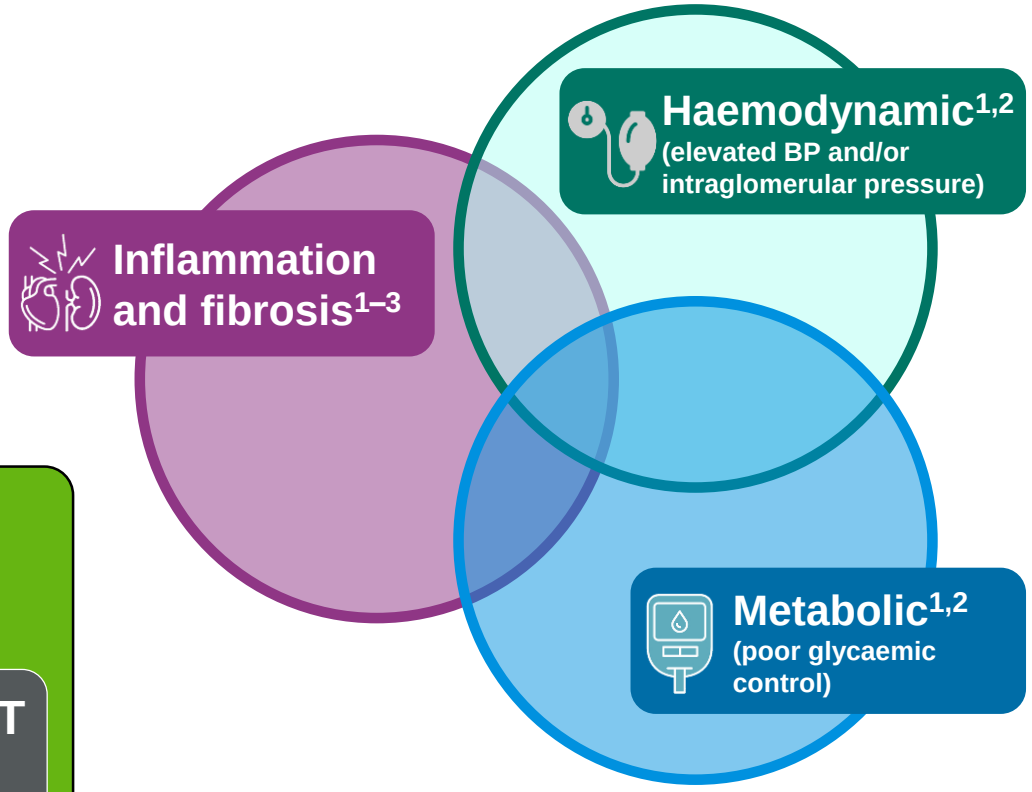
Kidney and heart diseases are associated with MR overactivation [4,7,8]



Increased gene expression of pro-inflammatory and pro-fibrotic factors [3–8]



Drivers of CKD in T2D progression[1–3]



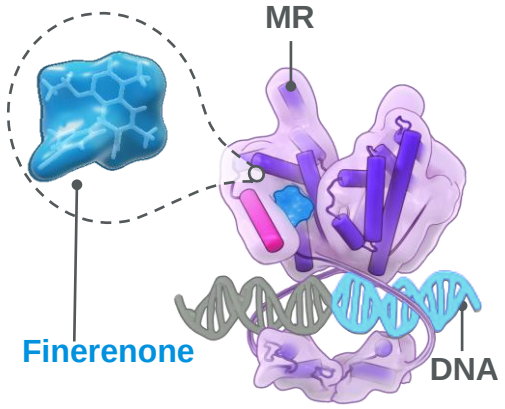
Blocking MR overactivation may slow CKD progression mediated through inflammatory and fibrotic pathways,[3,7] **which are largely unaddressed by current therapies**[1,9]

KIDNEY AND HEART PROTECTION

1. Alicic RZ, *et al. Clin J Am Soc Nephrol* 2017;12:2032–2045; 2. Mora-Fernández C, *et al. J Physiol* 2014;18:3997; 3. Bauersachs J, *et al. Hypertension* 2015;65:257–263;
4. Buonafine M, *et al. Am J Hypertension* 2018;31:1165–1174; 5. Brown NJ. *Nat Rev Nephrol* 2013;9:459–469; 6. Biwer LA, *et al. Am J Hypertension* 2019;32:123–134;
7. Barrera-Chimal J, *et al. Kidney Int* 2019;96:302–319; 8. Kolkhof P, *et al. Handb Exp Pharmacol* 2017;243:271–305; 9. Alicic RZ, *et al. Adv Chronic Kidney Dis* 2018;25:1941–191

Differences in chemical structure may explain the properties of finerenone versus steroidal MRAs

Due to its **nonsteroidal nature** and **bulky molecular structure**, **finerenone** binds to the MR with **high selectivity** and induces **conformational changes** that are different from those observed with **steroidal MRAs**[1,2]



As a result, **finerenone** and **steroidal MRAs** have **distinct gene expression patterns**,[3–5] **preclinical properties** and **clinical effects**[6–9]

- **Risk of sexual side effects**
- **Risk and manageability of hyperkalaemia**
- **Effect on blood pressure**

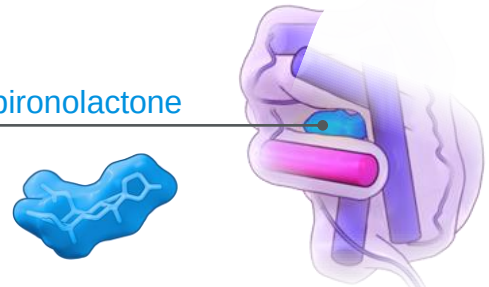
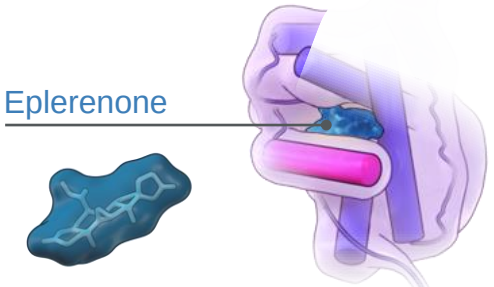
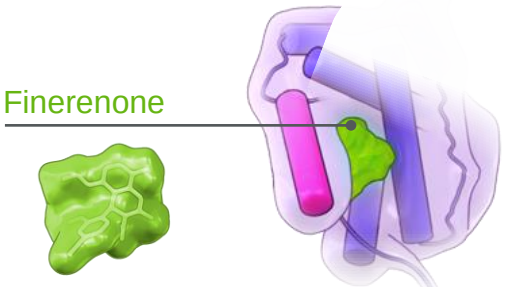
1. Amazit L, *et al. J Biol Chem* 2015;290:21876–21889; 2. Bärfacker L, *et al. ChemMedChem* 2012;7:1385–1403; 3. Grune J, *et al. Hypertension* 2018;71:599–608;
4. Kolkhof P, *et al. J Cardiovasc Pharmacol* 2014;64:69–78; 5. Kolkhof P, *et al. Curr Opin Nephrol Hypertens* 2015;24:417–424; 6. Bakris GL, *et al. N Engl J Med* 2020;383:2219–2229;
7. Pitt B, *et al. Eur Heart J* 2013;34:2453–2463; 8. Pitt B, *et al. N Engl J Med* 1999;341:709–717; 9. Agarwal R, *et al. Lancet* 2019;394:1540–1550

Differential MR binding of steroidal MRAs vs finerenone results in distinct effects on gene expression (1)

Finerenone has a shorter half-life ~2-3 hours

No active metabolites

Modest effect on BP

	Aldosterone antagonists		Finerenone
			
Structural properties	Flat (steroidal)	Flat (steroidal)	Bulky (nonsteroidal)[1,5]
Potency to MR	High[4,10]	Moderate[1,4,10]	High[1,2,10]
Selectivity to MR	Low[4,10]	Moderate[4,10]	High[1,2,10]
CNS penetration	Yes	Yes	No based on preclinical data[3]
Sexual side effects	Yes (gynecomastia)[4]	Less than spironolactone[4]	No signal in phase II studies[7-9]
Hyperkalaemia	Yes[4]	Yes[4]	Moderately increased*[,7-9]
Tissue distribution	Kidney > heart (at least 6-fold)[6,10]	Kidney > heart (~3-fold)[6,10]	Balanced kidney : heart (1:1)[6,10]

Based on preclinical data and ARTS phase II programme

MR, mineralocorticoid receptor

1. Bärfacker L, *et al. ChemMedChem* 2012;7:1385–1403; 2. Pitt B, *et al. Eur J Heart Fail* 2012;14:668–675; 3. Kolkhof P, *et al. J Cardiovasc Pharmacol* 2014;64:69–78; 4. Sica DA. *Heart Fail Rev* 2005;10:23–29; 5. Amazit L, *et al. J Biol Chem* 2015;290:21876–21889; 6. Kolkhof P, *et al. Curr Opin Nephrol Hypertens* 2015;24:417–424; 7. Pitt B, *et al. Eur Heart J* 2013;34:2453–2463; 8. Bakris GL, *et al. JAMA* 2015;314:884–894; 9. Filippatos G, *et al. Eur Heart J* 2016;37:2105–2114; 10. kolkhof P, *et* al. *Handb Exp Pharmacol*. 2017;243:271-305

*Hyperkalaemia was moderately increased in Phase 2 studies of finerenone

FIDELITY: A prespecified meta-analysis of FIDELIO-DKD and FIGARO-DKD data

FIDELIO-DKD; Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes

FIGARO-DKD: Cardiovascular Events with Finerenone in Kidney Disease and Type 2 Diabetes

FIDELITY is a large prespecified individual patient-data meta-analysis of the FIDELIO-DKD and FIGARO-DKD phase III trials[1–3] including CV- and kidney-specific composite outcomes across the spectrum of CKD stages

Kidney composite outcome

Time to first occurrence of:

- Onset of kidney failure:
  - ESKD (initiation of chronic dialysis for ≥90 days or kidney transplantation)
  - Sustained eGFR <15 ml/min/1.73 m$^{2\#}$
- A sustained ≥57% decrease of eGFR from baseline*
- Renal death‡

CV composite outcome

Time to first occurrence of:

- CV death*
- Non-fatal MI
- Non-fatal stroke
- Hospitalisation for HF

*Please refer to the slide notes section for footnotes

1. Bakris GL, *et al. Am J Nephrol* 2019;50:333–344; 2. Ruilope LM, *et al. Am J Nephrol* 2019;50:345–356; 3. Filippatos G, *et al. ESC* 2021; abstract 7161

Eligible patients in the FIDELITY prespecified meta-analysis included those with CKD and T2D, treated with an optimised dose of ACEi/ARB[1,2]

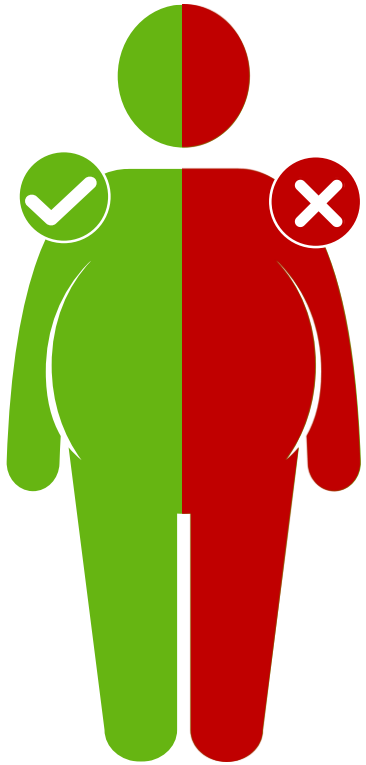
Key inclusion criteria

eGFR: 25–90 ml/min/1.73 m^2
+ UACR: 30–<300 mg/g (3.39–33.9 mg/mmol) #
or
eGFR: ≥25 ml/min/1.73 m^2
+ UACR: ≥300 mg/g (33.9 mg/mmol)

Aged ≥18 years with T2D

On maximum tolerated dose of ACEi or ARB for ≥4 weeks

Serum [K^+] ≤4.8 mmol/l at run-in and screening visit



Key exclusion criteria

HFrEF with NYHA Class II–IV

Uncontrolled arterial hypertension#

HbA1c >12%

Non-diabetic kidney disease, including clinically relevant renal artery stenosis

Stroke, transient ICA, ACS or HHF‡

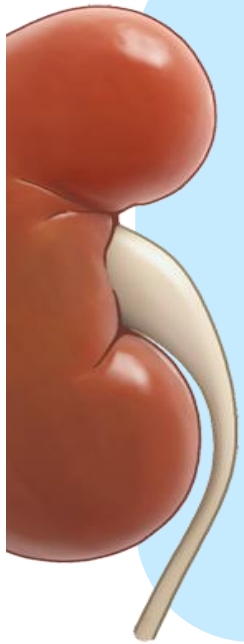
UACR >5000 mg/g

*Patients with moderately elevated albuminuria were required to also have diabetic retinopathy in FIDELIO-DKD as part of the study inclusion criteria[1], this was not specified in the eligibility criteria in FIGARO-DKD, but patients in FIGARO-DKD had diabetic retinopathy at baseline[2]; #mean sitting SBP ≥170 mmHg or mean sitting DBP ≥110 mmHg at the run-in visit, or mean sitting SBP ≥160 mmHg or mean sitting DBP ≥100 mmHg at the screening visit[1,2]; ‡in the last 30 days prior to the screening visit[1,2]

1. Ruilope LM, *et al. Am J Nephrol* 2019;50:345–356; 2. Bakris GL, *et al. N Engl J Med* 2020;383:2219–2229

Kidney composite outcome*: Summary

- In patients with CKD stage 1–4 with moderate-to-severely elevated albuminuria and T2D treated with optimised RAS therapy:



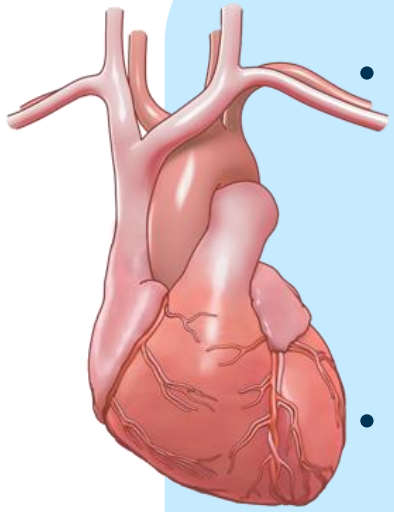
- **Finerenone significantly reduced the risk of kidney composite outcome*** by **23% (equivalent to an HR of 0.77)**
  vs placebo
  - With consistent effects on the components of the kidney composite outcome
  - Absolute risk reduction = **1.7%** at 3 years
- **Kidney benefits of finerenone were clinically relevant**
  - NNT to prevent one kidney outcome event over 3 years = **60**

*Time to kidney failure, sustained ≥57% decrease in eGFR from baseline, or renal death

Filippatos G, *et al. ESC* 2021; abstract 7161

CV composite outcome: Summary

- In patients with CKD stage 1–4 with moderate-to-severely elevated albuminuria and T2D treated with optimised RAS therapy :



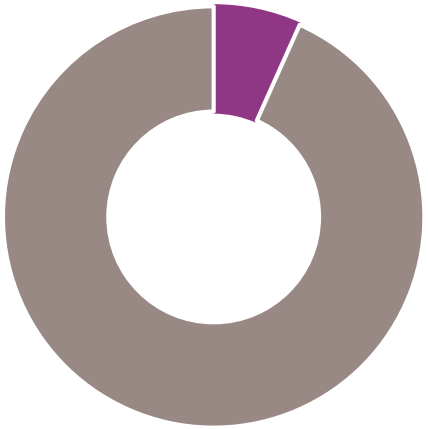
- **Finerenone significantly reduced** the **risk of CV morbidity and mortality** by **14% (equivalent to an HR of 0.86)** vs placebo
  - With consistent effects irrespective of region, baseline CKD severity, blood pressure, HbA1c and serum [K^+]
  - Absolute risk reduction = **2.2%** at 3 years
- **CV benefits of finerenone were clinically relevant**
  - NNT to prevent one CV outcome event over 3 years = 46

Filippatos G, *et al. ESC* 2021; abstract 7161

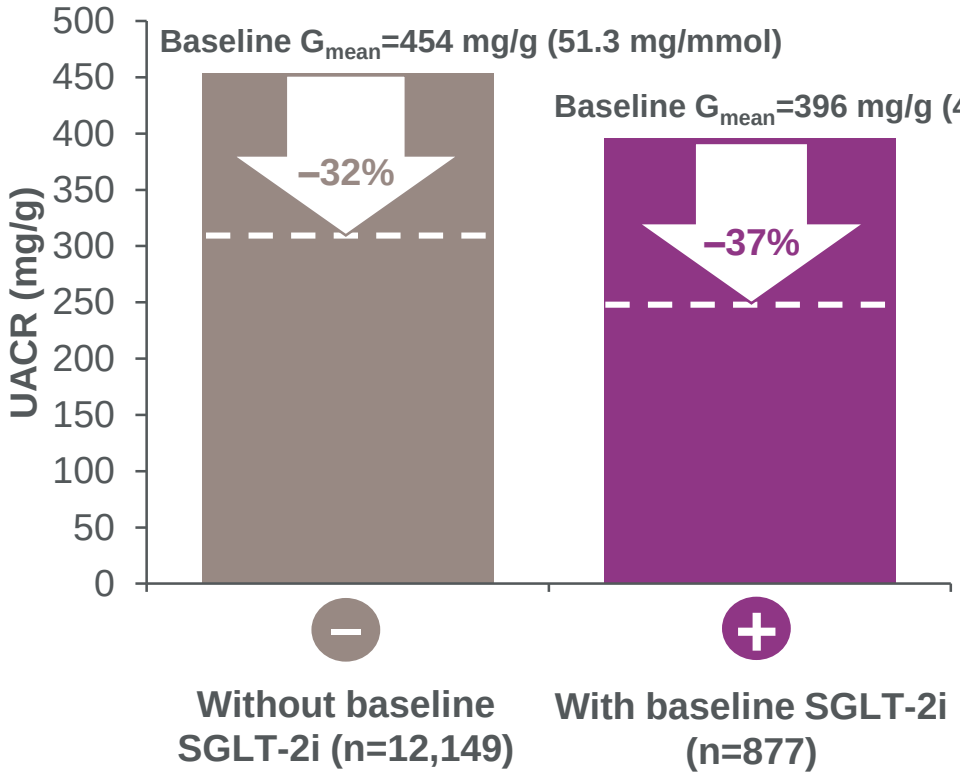
Many patients with T2D and CKD are already on an SGLT2i. Can finerenone be used in combination with an SGLT2i?

SGLT-2i use at baseline

877 (6.7%) patients on an SGLT-2i



Reduction in UACR (%) with finerenone vs placebo



Full analysis set. Mixed model with factors for treatment group, region, eGFR category at screening, type of albuminuria at screening, CV disease history; time, treatment*time, log-transformed baseline value nested within type of albuminuria at screening, and log-transformed baseline value*time as covariates

G_{mean}, geometric mean

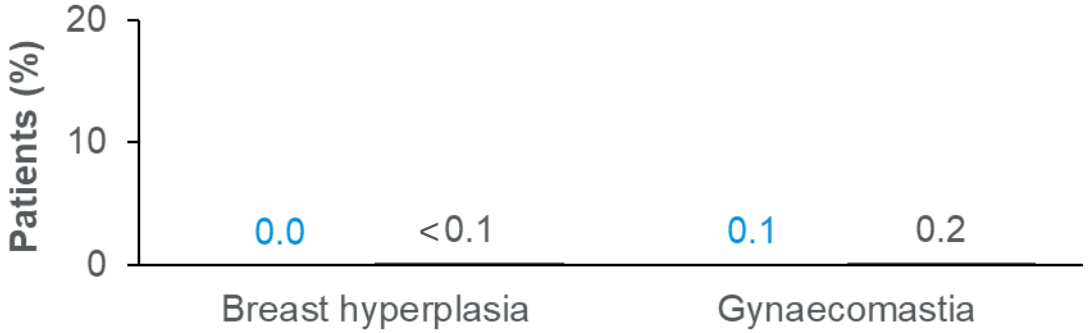
Rossing P, *et al. ASN* 2021; Abstract SA-OR22

Finerenone showed modest effects on SBP and no sexual side effects. Hyperkalemia was increased but clinical impact was low in this study

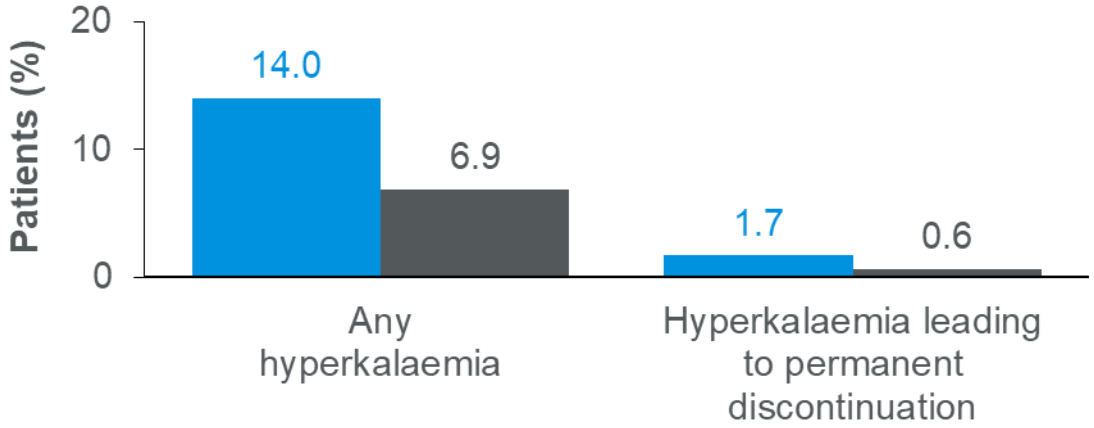
Modest effect on systolic blood pressure

Placebo-corrected change in mean SBP of **–3.7 mmHg** at 4 months

No sexual side-effects



Increased hyperkalaemia with minimal clinical impact in the study



Finerenone (n=6510)
Placebo (n=6489)

Filippatos G, *et al. ESC* 2021; abstract 7161

Safety and vital signs: Summary

In a patient population with advanced CKD in T2D, treated with a maximally tolerated dose of ACEi/ARB:

- **Finerenone was well-tolerated**
- The **overall incidence of treatment-emergent AEs and serious AEs was similar** between the finerenone and placebo groups

- **Finerenone** led to a mean **increase** in **serum [K^+]** of ~ **0.2 mmol/l** vs placebo
- Although hyperkalaemia was increased, by **temporarily withholding finerenone,** it was **manageable**
  - The clinical impact of hyperkalaemia was minimal

With the exception of temporary withdrawal of study drug, K^+ management was at the investigator's discretion

ACEi, angiotensin-converting enzyme inhibitor; AE, adverse event; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; HbA1c, glycated haemoglobin

Bakris GL, *et al.* 2020, N Engl J Med. DOI: 10.1056/NEJMoa2025845

Overall summary

The FIDELITY pre-specified meta-analysis of the FIDELIO-DKD and FIGARO-DKD studies comprises the largest cardiorenal outcome analysis of patients with CKD and T2D to date

In a broad patient population with CKD stage 1–4…

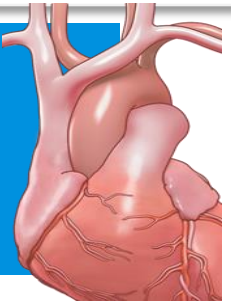
… with moderate-to-severely elevated albuminuria and T2D…

… well-controlled blood pressure and mildly elevated HbA1c…

… and treated with a maximum tolerated dose of an ACEi or ARB

Finerenone led to:

14% reduction in the risk of **CV morbidity and mortality** (HR=0.86; 95% CI 0.78–0.95)



23% reduction in the risk of **CKD progression*** (HR=0.77; 95% CI 0.67–0.88)

*Including time to first occurrence of: ≥57% decrease in eGFR; onset of kidney failure; ESKD (initiation of chronic dialysis for ≥90 days or kidney transplantation), sustained eGFR <15 ml/min/1.73 m^2; or renal death

Filippatos G, *et al. ESC* 2021; abstract 7161

Clinical practice guidelines

Current recommendations by scientific societies on treatment with finerenone

ADA Standards of Medical Care in Diabetes 2022[1,2]

In patients with **CKD** who are at **increased risk for CV events, CKD progression** or are **unable to use an SGLT-2i, finerenone** is recommended to **reduce CKD progression and CV events**. **[Evidence level: A]**

In patients with **CKD** and **T2D** treated with maximum tolerated doses of ACEi/ARB, **finerenone** should be considered to **improve CV outcomes** and **reduce risk of CKD progression**. **[Evidence level: A]**

KDIGO Clinical Practice Guideline for Diabetes Management in CKD[3]

We **suggest** a **nonsteroidal MRA** with **proven kidney or CV benefit** for patients with T2D, an **eGFR ≥25 ml/min/1.73 m²**, **normal serum [K⁺] and albuminuria** despite maximum tolerated dose of RASi **[Grade 2A]**

ADA and KDIGO consensus report 2022[4]

A **nonsteroidal MRA** with **proven kidney and CV benefit** is **recommended** for patients with **T2D, eGFR ≥25 ml/min/1.73 m², normal serum [K⁺] and albuminuria (≥30 mg/g)** despite maximum tolerated dose of RASi **[Level 2A]**

1. American Diabetes Association. *Diabetes Care* 2022;45(Suppl 1):S175–S184; 2. American Diabetes Association. *Diabetes Care* 2022;45(Suppl 1):S144–S174;
3. Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2022;102:S1–S128; 4. de Boer IH, et al. Diabetes Care 2022; doi: 10.2337/dci22-0027

Prior to initiation of treatment, serum [K^+] and eGFR must be measured

Measurement of serum [K^+] levels and eGFR:

If serum [K^+] ≤5.0 mmol/l*

If eGFR ≥25 ml/min/1.73 m^2

Finerenone can be initiated

Dosing:

Recommended target dose: **20 mg** od

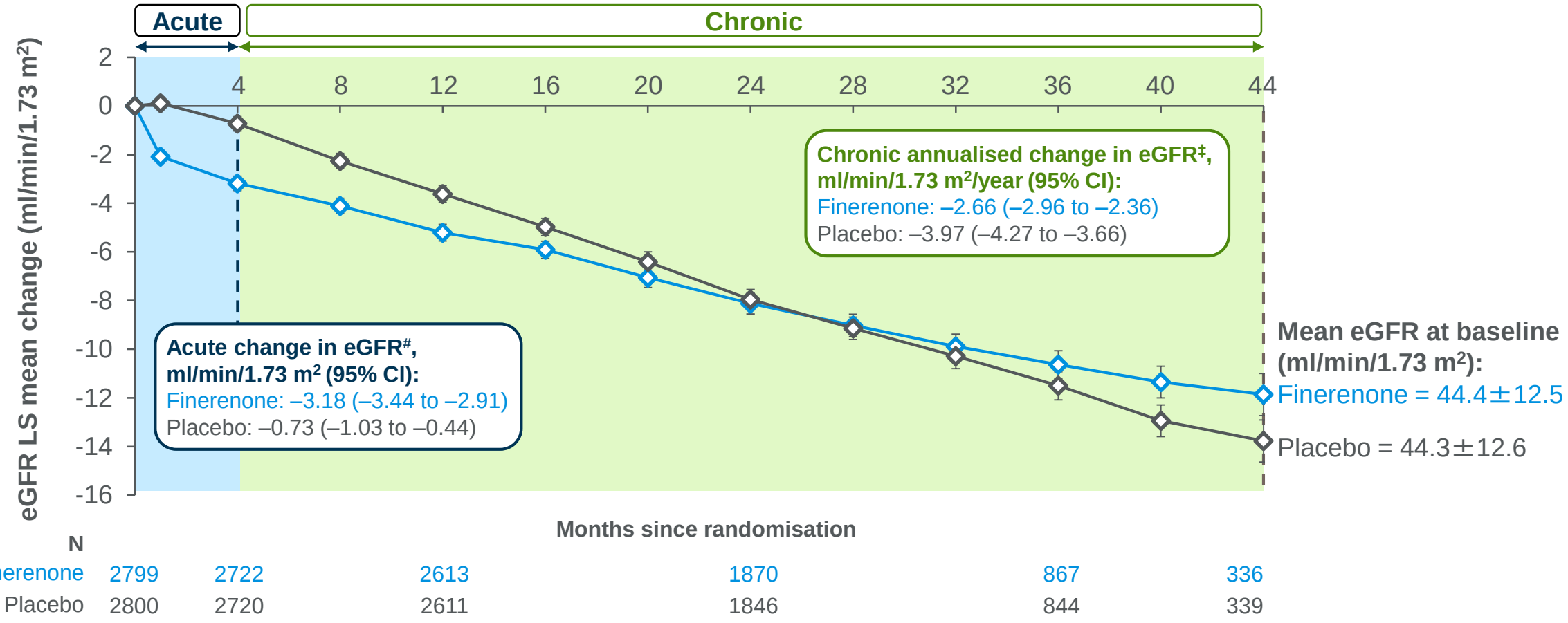
Starting dose:

if eGFR <60 ml/min/1.73) m^2 **10 mg** od

if eGFR ≥60 ml/min/1.73) m^2 **20 mg** od

*Initiation of finerenone may be considered with additional serum potassium monitoring within the first 4 weeks based on clinical judgement and serum potassium levels. Initiation of treatment is not recommended in patients with serum potassium > 5.0 mmol/L
In patients with eGFR < 15 mL/min/1.73m2, discontinue KERENDIA treatment as clinical experience is limited.
KERENDIA Product Monograph October 14th, 2022
https://www.bayer.com/sites/default/files/kerendia-pm-en.pdf

In an exploratory analysis, the acute effect of finerenone is a drop in eGFR but the long-term effect is a slowing of eGFR decline*



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

*Mixed model analysis of eGFR over time. Full analysis set; #LS mean change in eGFR slope from baseline to month 4; ‡LS mean change in eGFR slope from month 4 to the permanent discontinuation or end-of-study visit
CI, confidence interval; eGFR, estimated glomerular filtration rate; LS, least-squares
Bakris GL, *et al.* 2020, N Engl J Med. DOI: 10.1056/NEJMoa2025845

How do you monitor and adjust the dose for finerenone?

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***

Dose adjustments:

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

*Based on patient characteristics and serum [K+]; #If eGFR has decreased by more than 30% compared to previous measurement, maintain 10 mg dose

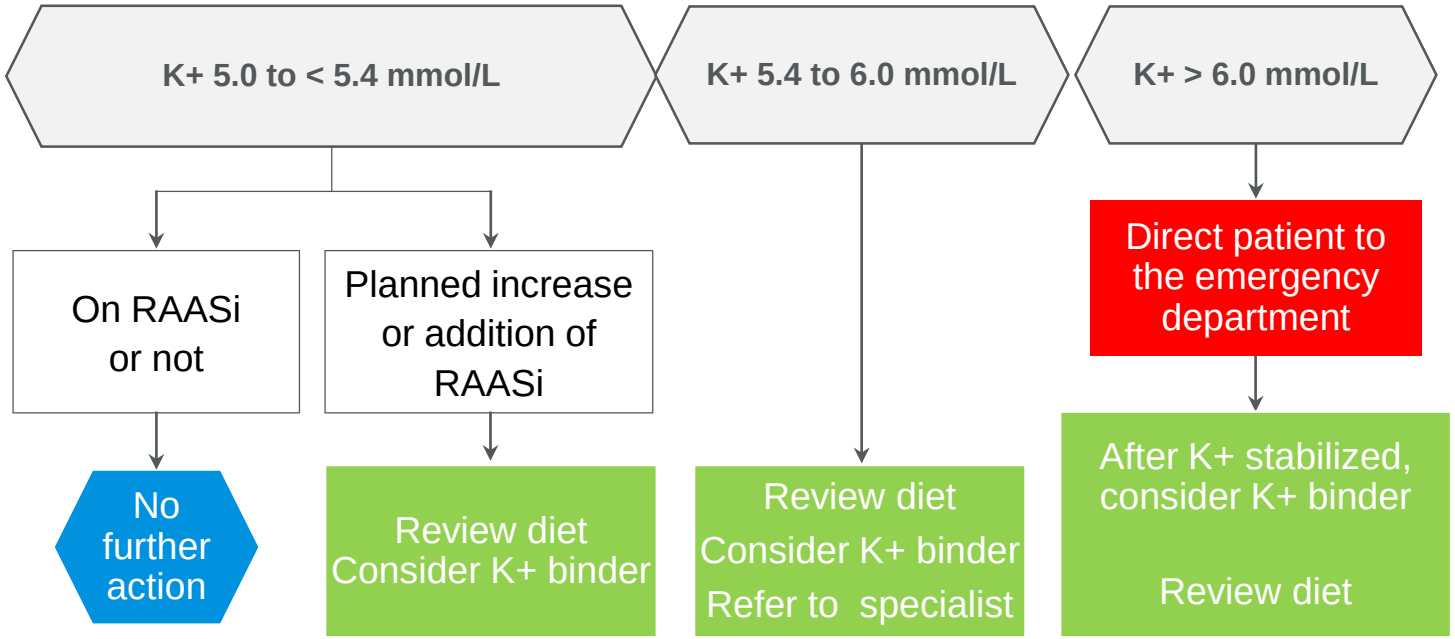
KERENDIA Product Monograph October 14th, 2022
https://www.bayer.com/sites/default/files/kerendia-pm-en.pdf

General strategies to reduce the risk of hyperkalemia

Mitigate hyperkalemia risk by:

- Reducing dietary potassium
- Use of loop or thiazide diuretics
- Use of potassium binders

- Organ protective (RAASi) agents should be prioritized for continuation/re-initiation when safe



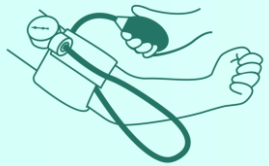
CKD, chronic kidney disease; HF, heart failure; K+, potassium; RAASi, renin-angiotensin aldosterone system inhibitor.
Adapted from: Weinstein J, Girard LP, Lepage S, et al. CMAJ. 2021 Dec 6;193(48):E1836-E1841.

Other important adverse events to consider[1,2]

Very common (≥10%)
- Hyperkalaemia

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

Hypotension



- Following a mild decrease in SBP (3 mmHg) and DBP (1–2 mmHg) after 1 month, it remained stable thereafter

Reductions in GFR

- The initial decrease in eGFR with finerenone attenuated over time, and was reversible with continuous treatment

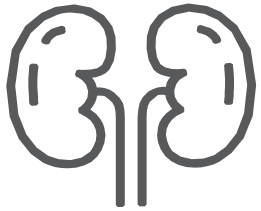
1. KERENDIA Product Monograph October 14th, 2022
https://www.bayer.com/sites/default/files/kerendia-pm-en.pdf

In summary

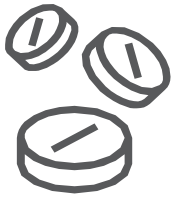
As an adjunct to standard treatment, Finerenone can help reduce residual renal and CV risks in patients with:

Type 2 diabetes

A serum K+ ≤ 4.8 mmol/L or
4.8 to 5.0 mmol/L (with closer monitoring)



Chronic kidney disease
(stages 2 to 4 : eGFR < 90 mL/ min/1.73 m2 to ≥ 25 mL/min/1.73 m^2)



Treatment with maximum dose of ACEI or ARB
± SGLT2i

KERENDIA Product Monograph October 14th, 2022
https://www.bayer.com/sites/default/files/kerendia-pm-en.pdf

Discussion and Q&A

Thanks