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Preserving renal function: gliflozins, GLP1 agonists, and antialdosterones

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For a long time, a prognostic and therapeutic fatalism accompanied even the most motivated clinicians when they had to deal with a progressive decline in renal function; the modest successes were nullified by an increasingly aggressive syndrome whose therapy had remained the same for more than 30 years. In the meantime, the increased understanding of the physiopathological mechanisms connected to it had not been accompanied by an equal development of drugs capable of counteracting it, and this, also due to the progressive aging of the population, had rapidly made 'chronic kidney disease' (CKD) a problem of World Public Health due to its incidence, prevalence, and exponentially increasing costs in every part of the world. The progressive reduction of glomerular filtration rate, as has been known for some time, is accompanied by an increase in cardiovascular risk, understood as fatal and non-fatal heart attack, stroke, heart failure, and mortality. Therefore, every effort must be aimed at preventing or slowing the decline of renal function to reduce not only critical renal events (the need for dialysis or transplant among the most feared) but also the incidence of cardiovascular events. Since the disease is asymptomatic for a long time (it is often detected occasionally and with culpable delay), it is essential to make a correct and early assessment of renal function with appropriate methods. Once CKD was identified, clinicians, to slow its progression, could rely for a long time only on strict control of those risk factors most responsible for worsening it, such as diabetes and its complications, on the optimization of high blood pressure values and the mandatory use of drugs blocking the renin-angiotensin-aldosterone system, particularly in the presence of albuminuria. This strategy has proven to be only partially effective over time, and most patients still showed a progressive worsening of renal function. Only in the last few years have we had access to two classes of innovative drugs, such as gliflozins and incretins, that have imposed themselves on the therapeutic scene because they have shown that they can slow the progression of CKD, first in patients with Type 2 diabetes and subsequently in patients with CKD regardless of the presence or absence of diabetes. Unexpectedly and convincingly, they have also shown a significant impact on cardiovascular prognosis. Initially antidiabetic drugs, their efficacy has forced the reviewers of both cardiology and nephrology guidelines to indicate them among the drugs to use. Lately, the class of mineralocorticoid receptor antagonist drugs has been enriched by finerenone. This molecule has favourable pharmacokinetic characteristics compared with previous medications of the same class and tested in Phase 3, randomized, placebo-controlled trials (FIDELIO-DKD and FIGARO-DKD) which has been shown to significantly reduce the risk of cardiovascular and renal disease in diabetic patients compared with placebo.

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'Chronic kidney disease' (CKD) has long been a global public health problem and shows an ever-increasing incidence and prevalence with worrying epidemiological data. It is estimated that more than 730 million individuals worldwide suffer from it and that in 2017 alone (latest reliable data), the disease caused more than 1 600 000 deaths and 37 million individuals with disabilities attributable to it.[1] In Italy, recent data estimate that approximately 10% of the population, therefore approximately 6 million, is affected by renal dysfunction; of these, according to data from the Italian Dialysis and Transplant Registry dating back to 2008-2012, approximately 42 000 are on extracorporeal dialysis, just over 4500 are on peritoneal dialysis, and over 27 000 had kidney transplant.

CKD (*Figure 1*) encompasses the definition and subdivision into stages of the disease trajectory.

Although only in the presence of a filtrate <60/mL/m', by convention, we can officially speak of kidney disease; the utmost attention should be paid to those individuals, not yet patients, who, even in the absence of renal structural alterations, present only microalbuminuria defined as urinary excretion of albumin between 30 and 300 mg/day or as *urine albumin-creatinine ratio* (UACR), even on spot urine, between 30 and 300 mg/g. This finding, far from being a simple indicator of kidney damage as long believed, has revealed itself to be a formidable marker of endothelial dysfunction and systemic organ damage, capable of impacting cardiovascular prognosis even more than the progression of CKD, regardless of the extent of the decline in the filtrate, even in the general population.[2] All this is to confirm if there was still any need and how much CKD can increase cardiovascular risk [intended as fatal and non-fatal heart attack, stroke, disability-related, heart failure (HF)].

And since most uraemic die of cardiovascular causes before even going on dialysis, it will not be enough to treat these patients, but it will be necessary to 'take care of them' by preventing and/or slowing down the progression of CKD in order to reduce the incidence of new cardiovascular events.

Correct and early assessment of renal function is the first step in impacting the prognosis. Once CKD is diagnosed, every effort must be made to prevent and/or slow down the decline of renal function to reduce not only critical renal events (the need for dialysis or transplant among the most feared) but also cardiovascular ones.

In general, the attempt to slow the decline of renal function for a long time could only rely on the control of hypertension and diabetes, on the inhibition of the renin-angiotensin-aldosterone system (RAAS), on changes in diet and lifestyle, and, as the disease progressed, on the correction of metabolic acidosis and the strict control of calcium-phosphorus balance. Careful monitoring of all nephrotoxic substances (a classic example is non-steroidal anti-inflammatory drugs or, dramatically, antineoplastic drugs) that one might be forced to administer was necessary. Given the complexity and breadth of the topic, it will be appropriate to concentrate, albeit briefly, on those conditions that the clinician most frequently encounters in his daily work.

Blood pressure control

While there is unanimous agreement on considering RAAS inhibitors as first-choice drugs in a therapy that will necessarily be an association, the discussion on the blood pressure target to be achieved in uraemic patients to slow the decline of CKD and impact the prognosis is very complex and sees different and debated positions.

The American College of Cardiology/American Heart Association (ACC/AHA) Task Force Guidelines recommend blood pressure values <130/80 mmHg for all patients with CKD.[3]

The recommendations of the Kidney Disease Improving Global Outcomes (K-DIGO) are different and complex, definable as a sort of nephrological 'BIBLE',[4] which suggests reaching blood pressure values <140/90 mmHg in the presence of UACR < 30 mg/day and 130/80 mmHg if UACR > 30 mg/day. The different recommendations[5] essentially arise from two fundamental trials [AASK trial (African American Study of Kidney Disease and Hypertension) and the Modification of Diet in Renal Disease (MDRD study)] that served as a reference. It was subsequently investigated whether reaching more aggressive blood pressure targets could be tolerated and better impact cardiovascular prognosis. The Systolic Blood Pressure Intervention Trial (SPRINT trial) compared two different blood pressure targets (<120 mmHg vs. <140 mmHg) in patients without diabetes but at high risk of cardiovascular events. Intensive control significantly impacted the risk of myocardial infarction, stroke, HF, and cardiovascular mortality but did not improve adverse renal events; in fact, a significant worsening of renal filtration was highlighted, especially in patients with more advanced stage CKD, probably due to haemodynamic changes rather than actual renal damage.[6]

Inhibition of the renin-angiotensin-aldosterone system

Multiple trials have shown that therapy with ACE inhibitors (ACEI) or sartans (ARB) can slow the decline of renal function, especially in the presence of albuminuria.

In the ramipril in non-diabetic renal failure (REIN trial), for example, patients with CKD randomized to ramipril vs. placebo showed a decline in renal function reduced in a highly significant way in the arm treated with ACEI, especially if proteinuria >3 g/day was present.[7] Similar results were obtained about sartans, for example, in the Irbesartan Diabetic Nephropathy Trial (IDNT) where irbesartan was compared with amlodipine. Finally, in the AASK trial, the use of ramipril was independently associated with a −22 and −38% composite risk (declining filtration rate >50% from baseline, the need for dialysis, or death) when compared with metoprolol and amlodipine, respectively.

Although still widely used in nephrology for their synergistic action on proteinuria, the combined use of an ACE inhibitor with an ARB is not supported by current literature in diabetics with CKD. The Veterans Affairs Nephropathy in Diabetes (VA NEPHRON-D study), which enrolled Type 2 diabetic patients with CKD randomized to losartan + lisinopril or losartan alone, was interrupted due to excess adverse events (hyperkalaemia and episodes of acute renal failure) in the arm treated with the combination compared with the monotherapy group.[8]

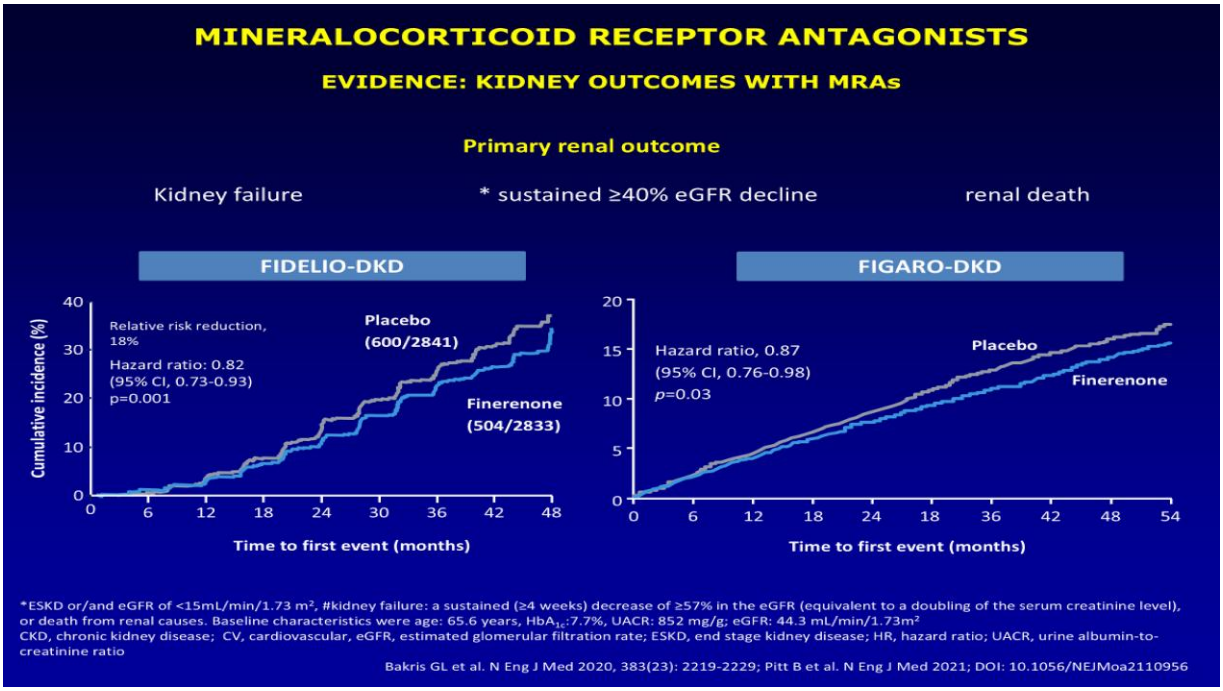

Figure 1 Definition and stage classification of chronic kidney disease.

The importance of reducing the daily sodium intake in the diet is also reiterated because this amplifies the nephroprotective effect of RAAS antagonist drugs. A vital meta-analysis (11 randomized controlled trials) shows that a low-sodium diet alone reduces urinary albumin excretion by 32%. The reduction in albuminuria becomes even more significant if accompanied by anti-RAAS therapy (−41 vs. −17%, respectively), suggesting a synergistic effect between a low-sodium diet and ACEI or ARB therapy.[9] Therefore, all patients taking RAAS inhibitors for albuminuria therapy should be encouraged to follow a low-sodium diet (−3 g/day).

Finally, the use of antialdosterone drugs [mineralocorticoid receptor antagonists (MRAs)] can be considered in patients intolerant to ACEI and ARB. This is because a recent meta-analysis of 31 randomized controlled trials aimed at evaluating the efficacy and tolerability of different MRAs (spironolactone, eplerenone, canrenone, and finerenone) in reducing albuminuria compared with placebo or active drug confirmed the effectiveness of these drugs in reducing albuminuria vs. placebo but did not show a superior effect when compared with ACEI or ARB in the face of a highly significant risk of hyperkalaemia.[10] More recently, much discussion has been generated by the data from the Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (FIDELIO-DKD) study. Although the reduction of albuminuria is not universally accepted as a surrogate endpoint of the 'need for dialysis', finerenone has been shown in Type 2 diabetic patients with CKD and treated with ACEI or ARB, to reduce by 18% the composite risk of renal events such as a decline in filtration rate, the need for dialysis, and CKD-related deaths when compared with placebo.[11] Ultimately, MRAs reduce albuminuria and slow the progression of CKD but carry an increased risk of hyperkalaemia, which requires careful monitoring in daily practice.

Glycaemic control

The KDIGO guidelines for diabetes in CKD, at least until 2020, were limited to recommending individualizing the levels of glycated haemoglobin (HbA1c) to be achieved based on the severity of the kidney disease, comorbidities, and the individual risk of hypoglycaemia. This is because the most commonly used drugs at the time, such as insulin, sulfonylureas, and glinides, were often responsible for hypoglycaemic crises when the filtration rate worsened. The recent availability of innovative antidiabetic drugs characterized by a negligible or absent risk of hypoglycaemic episodes and a conception of diabetes itself less fossilized to glycaemic control alone has in fact overturned the entire therapeutic algorithm of diabetic patients with CKD.[12] All this is of great importance since most of the randomized trials suggested that intensive glycaemic control was necessary to slow down the decline in renal function and albuminuria in a highly significant way. In fact, the most important meta-analysis[13] confirmed that intensive glycaemic control was associated with a −20% risk of composite renal endpoints (worsening of filtration rate, UACR, and the need for dialysis) essentially driven by a reduction in the risk of albuminuria. This reduction was proportional to the degree of UACR and significant for each value investigated and present at baseline.[13] Finally, it should be emphasized that in daily therapeutic management, dose adjustments, usually necessary and frequent as the disease progresses, have become less demanding thanks to drugs such as gliflozins and incretins, which are easy to use and capable of

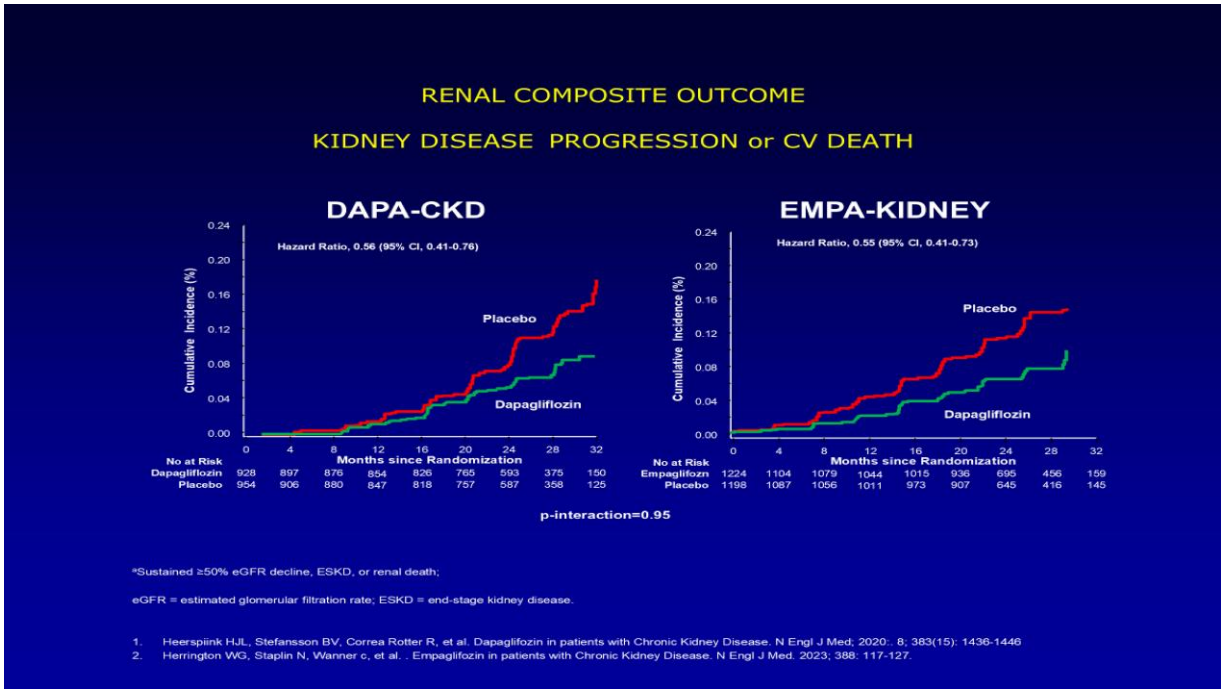

Figure 2 Primary composite outcome. The primary outcome was a composite of sustained decline in the estimated glomerular filtration rate of at least 50%, end-stage kidney disease, or death from renal or cardiovascular causes.

modifying the entire course of CKD in diabetic patients. The 2022 American Diabetes Association (ADA) guidelines give precise indications for the use of sodium–glucose cotransporter Type 2 inhibitors (SGLT2i) and GLP1ra in diabetic patients with CKD and/or cardiovascular diseases.[14] Both classes are equivalent, diversifying the choice based on the comorbidities present along the course of the diabetic disease and suggesting SGLT2i in case of HF and CKD with proteinuria and GLP1a in case of heart attack or stroke.

Gliflozins

Recently, SGLT2i, commonly known as 'gliflozins', have become increasingly popular due to their ability to slow the progression of CKD, particularly in patients with Type 2 diabetes and albuminuria. The recent ADA and European Association for the Study of Diabetes guidelines recommend SGLT2i as first-choice drugs in all patients with Type 2 diabetes and risk of CKD progression regardless of the presence of cardiovascular disease.

The meta-analysis by Neuen *et al.* (38 723 patients enrolled) demonstrated that the use of SGLT2i involves a −33% composite renal risk (the need for dialysis or transplant and CKD-related death) compared with placebo. Of great importance is the fact that the benefits of SGLT2i were statistically significant regardless of the amount of filtration at enrollment.[15]

Finally, extraordinarily significant data are offered to us, specifically, by the Dapagliflozin in Patients with Chronic Kidney Disease (DAPA-CKD) and Empagliflozin in Patients with Chronic Kidney Disease (EMP-KIDNEY) trials (*Figure 2*).

The DAPA-CKD study (~4300 patients enrolled in optimized therapy, randomized to 10 mg dapagliflozin vs. placebo) demonstrated that in addition to optimal therapy, dapagliflozin reduced the risk of mortality from all causes by 31%, an extraordinary result in itself, and the composite relative risk of worsening of renal function, onset of end-stage renal disease, or death related to CKD by 39%. This study also enrolled non-diabetic uraemic patients (32%) and was interrupted prematurely due to the excess benefit of dapagliflozin vs. placebo on the composite renal outcome, regardless of the presence or absence of diabetes. The drug was well tolerated and easy to manage, and there was no significant difference in adverse events between the two arms of the study.[16]

More recently, the EMPA-KIDNEY study, the largest nephroprotection study ever conducted to date with >6600 patients enrolled, also confirmed an extraordinary efficacy and tolerability for empagliflozin, showing a −28% reduction in the progression of CKD and related cardiovascular mortality. The study was stopped ahead of schedule for evidence of the benefits demonstrated on renal endpoints and CKD-related mortality, even if it did not reach significance on the reduction of all-cause mortality.[17]

The depth of these data marks an epochal turning point in the treatment of CKD, a disease that, it is useful to point out, involves a very high mortality rate, which in dialysis patients at 5 years is 50% higher when compared with that of, for example, lymphomas or prostate cancer.

Incretins

GLP1 receptor agonists, an English acronym for 'glucagon-like peptide 1' commonly called incretins, are the other class of antidiabetic drugs that have recently been shown to be able to slow the decline of CKD and improve renal outcomes. In the meta-analysis by Kristensen *et al.*[18] including five trials, GLP1a showed a −17% reduction in the composite renal endpoint (new onset of UACR > 300 mg/g, doubling of serum creatinine,

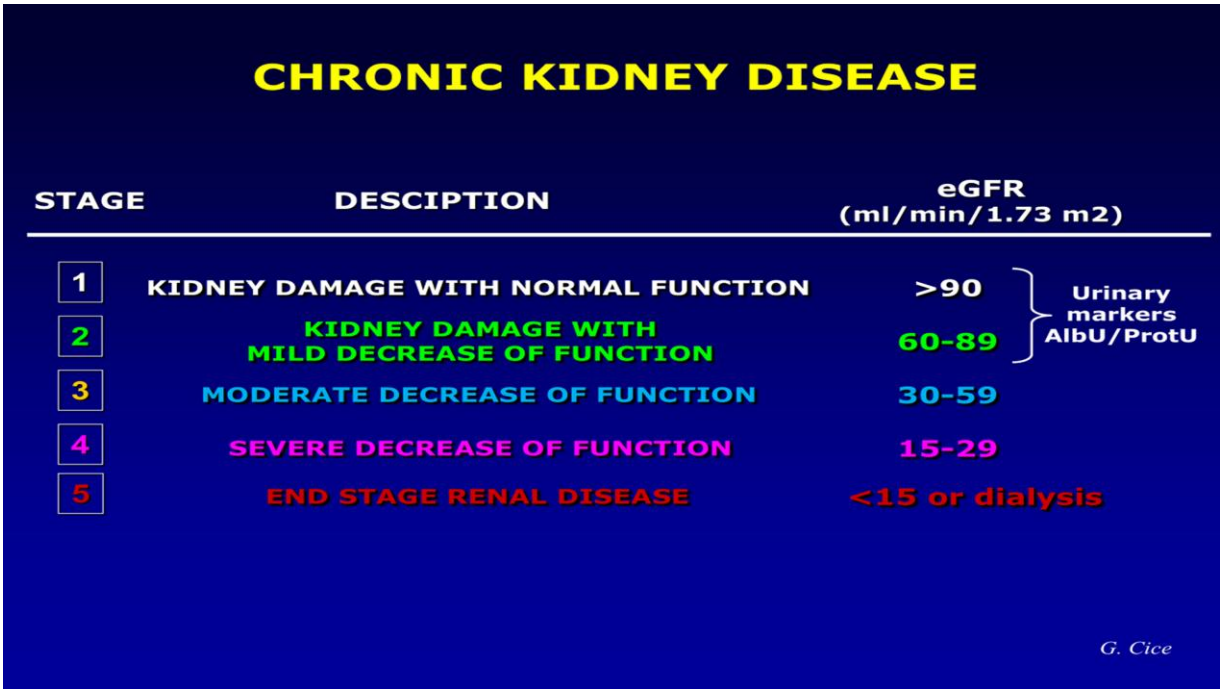

Figure 3 Primary composite outcome FIDELIO-DKD. The primary outcome was a composite of kidney failure, end-stage kidney disease, and a sustained decrease in estimated glomerular filtration rate to <15 mL/min/1.73 m'. Primary composite outcome FIGARO-DKD. The primary outcome was a composite of death from cardiovascular causes, non-fatal myocardial infarction, non-fatal stroke, or hospitalization for heart failure.

the need for dialysis, and CKD-related death) with a HR of 0.83 (95% CI, 0.78–0.89).

However, it has been noted that if only more specific and restrictive data on the worsening of renal function were considered, such as doubling of serum creatinine and the need for dialysis, the significance was not maintained (HR 0.87, 95% CI, 0.73–1.03). Although there are currently no trials directly comparing SGLT2i and GLP1a on renal outcomes, the Zelniker meta-analysis (including eight trials on renal and cardiovascular endpoints) highlights a −38% (HR 0.62, 95% CI, 0.58–0.67) reduction in the risk of worsening of renal function for SGLT2i vs. a −18% (HR 0.82, 95% CI, 0.75–0.89) highlighted by GLP1a.[19] In light of these data, SGLT2i appear more effective than GLP1a in reducing the progression of CKD and should be preferred.

Finally, very promising data are beginning to appear on the benefits of the combined use of these two classes of drugs in diabetic patients with atherosclerotic disease and HF. When GLP1ra were added to SGLT2i, a reduction in the risk of atherosclerotic events (all-cause mortality, heart attack, stroke) was demonstrated, but no effect on the risk of HF.[20]

Mineralocorticoid receptor antagonists

The class of MRA drugs, long known for their effects in the therapeutic field of cardiology and/or nephrology (the best known are historically spironolactone and eplerenone), has recently been revitalized by the appearance of new non-steroidal molecules such as esaxerenone, apararenone, and finerenone.[21] The latter in particular has been differentiated by a more balanced pharmacokinetic distribution between the heart and kidney compared with the steroid precursors such as spironolactone and eplerenone, by having a shorter half-life and by the absence of active metabolites, which potentially reduces its long-term effects on sodium-potassium balance.[22] Furthermore, finerenone has significantly more powerful anti-inflammatory and antifibrotic effects compared with steroidal MRAs. Its effects have been highlighted in patients with CKD and Type 2 diabetes, known to be at high risk of cardiovascular morbidity and mortality.[19,23]

Finerenone has been shown to reduce albuminuria and N-terminal B-type pro-natriuretic peptide (NT-proBNP) and to cause a lower risk of hyperkalaemia compared with steroid MRAs. Two Phase 3 trials were conducted, FIDELIO-DKD and FIGARO-DKD, to evaluate its efficacy and safety (*Figure 3*). Both were double-blind, randomized, and placebo-controlled. The FIDELIO-DKD study involved patients with Type 2 diabetes and advanced CKD. The FIGARO-DKD study instead always involved Type 2 diabetic patients with less renal impairment but at high cardiovascular risk. Randomized patients were administered finerenone or placebo orally. In total, these studies included 13 026 patients, of whom 5935 had a history of atherosclerotic cardiovascular disease (ASCVD). It was demonstrated that the drug significantly reduced the risk of cardiovascular and renal disease compared with placebo regardless of the presence or absence of ASCVD, while proving well tolerated. These data led the US Food and Drug Administration to approve finerenone to reduce the progression of CKD, heart attack, cardiovascular death, and the risk of developing HF in Type 2 diabetics. KERENDIA, which is the commercial name, is the only MRA available for these indications. In light of these data, the effect of finerenone in patients with congestive heart failure (CHF) with preserved or moderately reduced function has recently been

investigated, since the efficacy of MRAs in CHF with depressed contractile function has been consolidated for some time. In the Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction (FINEARTS-HF) trial, an international, double-blind, placebo-controlled study that enrolled 6001 patients with CHF with preserved or moderately reduced contractile function, finerenone or placebo was randomly assigned in a 1:1 ratio. The primary outcome was a composite of total events of worsening of CHF and death from cardiovascular causes. Safety was also evaluated. In a median follow-up of 32 months, finerenone significantly reduced the composite of events of worsening of CHF and death from cardiovascular causes compared with placebo.[24] It resulted in an increased risk of hyperkalaemia. After gliflozins, finerenone is proposed in the therapy of preserved ischaemic cardiomyopathy which for many years has been a land of speculation rather than consolidated data.

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Data availability

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Disclaimer

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References

1. Saran R, Robinson B, Abbott KC, Bragg-Gresham J, Chen X, Gipson D *et al*. US renal data system 2019 annual data report: epidemiology of kidney disease in the United States. *Am J Kidney disease* 2020;**75**:S1–S64.
2. Chronic Kidney Disease Prognosis Consortium, Matsushita K, van der Velde M, Astor BC, Woodward M, Levey AS *et al*. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet* 2010;**375**:2073–2081.
3. Whelton PK, Carey RM, Aronow WS, Casey DE, Jr., Collins KJ, Dennison Himmelfarb C *et al*. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Hypertension* 2018;**71**:e13–e115.
4. Levin A, Stevens PE, Bilous RW, Coresh J, De Francisco AL, De Jong PE *et al*. Kidney disease: improving global outcomes (KDIGO) CKD work group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl* 2013;**3**:1–150.
5. Wright JT, Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J *et al*. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. *JAMA* 2002;**288**:2421–2431.
6. SPRINT Research Group, Wright JT, Jr., Williamson JD, Whelton PK, Snyder JK, Sink KM *et al*. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med* 2015;**373**:2103–2116.
7. Ruggenenti P, Perna A, Loriga G, Ganeva M, Ene-Iordache B, Turturro M *et al*. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease (REIN-2): multicentre, randomised controlled trial. *Lancet* 2005;**365**:939–946.
8. Fried LF, Emanuele N, Zhang JH, Brophy M, Conner TA, Duckworth W *et al*. Combined angiotensin inhibition for the treatment of diabetic nephropathy. *N Engl J Med* 2013;**369**:1892–1903.
9. D’Elia L, Rossi G, Schiano di Cola M, Savino I, Galletti F, Strazzullo P *et al*. Meta-analysis of the effect of dietary sodium restriction with or without concomitant renin-angiotensin-aldosterone system-inhibiting treatment on albuminuria. *Clin J Am Soc Nephrol* 2015;**10**:1542–1552.
10. Alexandrou ME, Papagianni A, Tsapas A, Loutradis C, Boutou A, Piperidou A *et al*. Effects of mineralocorticoid receptor antagonists in proteinuric kidney disease: a systematic review and meta-analysis of randomized controlled trials. *J Hypertens* 2019;**37**:2307–2324.
11. Bakris GL, Agarwal R, Anker SD, Pitt B, Ruilope LM, Rossing P *et al*. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. *N Engl J Med* 2020;**383**:2219–2229.
12. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 clinical practice guideline for diabetes management in chronic kidney disease. *Kidney Int* 2022;**102**:S1–S127.
13. Zougas S, Arima H, Gerstein HC, Holman RR, Woodward M, Reaven P *et al*. Effects of intensive glucose control on microvascular outcomes in patients with type 2 diabetes: a meta-analysis of individual participant data from randomised controlled trials. *Lancet Diabetes Endocrinol* 2017;**5**:431–437.
14. American Diabetes Association Professional Practice Committee. 9. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes-2022. *Diabetes Care* 2022;**45**:125–143.
15. Heerspink HJL, Stefansson BV, Correa-Rotter R. Dapagliflozin in patients with chronic kidney disease. *N Engl J Med* 2020;**383**:1436–1446.
16. EMPA-KIDNEY Collaborative Group, Herrington WG, Staplin N, Wanner C, Green JB, Hauske SJ *et al*. Empagliflozin in patients with chronic kidney disease. *N Engl J Med* 2023;**388**:117–127.
17. Kristensen S, Roth R, Jhund PS, Docherty KF, Sattar N, Preiss D *et al*. Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. *Lancet Diabetes Endocrinol* 2019;**7**:776–785.
18. Zelniker TA, Wiviott SD, Raz I, Im K, Goodrich EL, Furtado RHM *et al*. Comparison of the effects of glucagon-like peptide receptor agonists and sodium-glucose cotransporter 2 inhibitors for prevention of major adverse cardiovascular and renal outcomes in type 2 diabetes mellitus. *Circulation* 2019;**139**:2022–2031.
19. Pitt B, Filippatos G, Agarwal R, Anker SD, Bakris GL, Rossing P *et al*. Cardiovascular events with finerenone in kidney disease and type 2 diabetes. *N Engl J Med* 2021;**385**:2252–2263.
20. David Lopez PD, Bhatia K, Bhora C, Mahmood K, Baruch L, Eng C *et al*. Benefits of adding glucagon-like peptide 1 receptor agonists to sodium-glucose co-transporter 2 inhibitors in diabetic patients with atherosclerotic disease and heart failure. *AMj Cardiol* 2022;**181**:87–93.
21. Kolkhof P, Delbeck M, Kretschmer A, Steinke W, Hartmann E, Bärfacker L *et al*. Finerenone, a novel selective nonsteroidal mineralocorticoid receptor antagonist protects from rat cardiorenal injury. *J Cardiovasc Pharmacol* 2014;**64**:69–78.
22. Heining R, Kimmerskamp-Kirshbaum N, Halabi A, Lentini S. Pharmacokinetics of the novel nonsteroidal mineralocorticoid receptor antagonist finerenone (BAY 94-8862) in individuals with renal impairment. *Clin Pharmacol Drug Dev* 2016;**5**:488–501.
23. Bakris GL, Agarwal R, Anker SD, Pitt B, Ruilope LM, Rossing P *et al*. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. *N Engl J Med* 2020;**385**:2219–2229.
24. Solomon SD, Mc Murray J, Vaduganathan M, Claggett B, Jhund PS, Desai AS *et al*. Finerenone in heart failure with mildly reduced or preserved ejection fraction. *N Engl J Med* 2024;**39**:475–1485.