Esaxerenone lowered BP and albuminuria with limited changes in potassium, but long-term studies with clinical end points are lacking (85). Finerenone was investigated in two complementary phase 3 studies of patients with T2D, kidney disease (defined primarily as ACR ≥30 mg/g), and potassium <4.8 mmol/L and is the only ns-MRA approved in the world for slowing CKD progression and reducing cardiovascular events. In Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (FIDELIO-DKD), both the primary kidney end point of progression of kidney disease (40% decline in eGFR or kidney failure) and the prespecified secondary composite cardiovascular end point (MACE or hospitalization for HF) were reduced with finerenone compared with placebo. Serum potassium was monitored regularly, and 2.6% of participants stopped treatment because of hyperkalemia with finerenone compared with 0.9% on placebo (86). In Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease (FIGARO-DKD), the primary composite cardiovascular end point (MACE or hospitalization for HF) was reduced with finerenone compared with placebo, with estimates of effect for kidney outcomes and hyperkalemia similar to those seen in FIDELIO-DKD (87).

Findings from the FIDELITY (Finerenone in Chronic Kidney Disease and Type 2 Diabetes: Combined FIDELIO-DKD and FIGARO-DKD Trial Programme Analysis) individual patient, prespecified combined analysis of both trials (13,191 total participants) demonstrated significant reductions of 18% for the composite cardiovascular outcome; 23% for a composite outcome of doubling of creatinine, kidney failure, or renal death; and 20% for dialysis initiation with a 22% reduction in HF hospitalizations (88). While <10% of participants were treated with an SGLT2i or a GLP-1 receptor agonist, results of subgroup analyses suggested that benefits of finerenone were similar with and without concomitant SGLT2i or GLP-1 receptor agonist treatment. Moreover, the risk of hyperkalemia was significantly reduced by the presence of an SGLT2i (89).

In summary, FIDELIO-DKD and FIGARO-DKD demonstrated cardiovascular and kidney benefits for finerenone among people with T2D who were treated with standard of care (including an RAS inhibitor at maximally tolerated doses and good control of glycemia and BP) who were at high residual risk, based largely on albuminuria (ACR ≥30 mg/g). These effects appear to be additive, based on preclinical studies, to those of SGLT2i and GLP-1 receptor agonists, though further clinical research on these combinations is needed. Therefore, it is reasonable to add finerenone to the treatment regimen of patients with T2D who have any level of persistent albuminuria despite current standard of care treatment with glucose-lowering and antihypertensive medications (Fig. 3).

Finerenone can be initiated with eGFR ≥25 mL/min/1.73 m^2 (as per trial eligibility) and serum potassium 4.8 mmol/L (per trial eligibility criteria) or ≤5.0 mmol/L (as per U.S. Food and Drug Administration label). As per trial protocols, finerenone should be started at a dose of 20 mg daily for eGFR >60 mL/min/1.73 m^2 and 10 mg for eGFR 25–60 mL/min/1.73 m^2 and uptitrated to 20 mg daily if possible. Potassium should be followed 4 weeks after dose change and regularly during treatment. With potassium <4.8 mmol/L, dose can be uptitrated to 20 mg and continued with potassium ≤5.5 mmol/L. If potassium increases to >5.5 mmol/L, finerenone should be withheld and can be restarted at 10 mg daily when potassium is ≤5.0 mmol/L. Finerenone can be continued with eGFR <25 mL/min/1.73 m^2 as long as potassium is acceptable and the drug is otherwise tolerated.

Consensus Statement

- An ns-MRA with proven kidney and cardiovascular benefit is recommended for patients with T2D, eGFR ≥25 mL/min/1.73 m^2, normal serum potassium concentration, and albuminuria (ACR ≥30 mg/g) despite maximum tolerated dose of RAS inhibitor.

CONCLUSIONS

The 2022 ADA Standards of Care and KDIGO 2022 guideline are aligned on issues of CKD screening and diagnosis, glycemia monitoring, lifestyle therapies, treatment goals, and pharmacologic management (1,2). Both recommend comprehensive care in which pharmacotherapy that is proven to improve clinical kidney and cardiovascular outcomes is layered upon a foundation of healthy lifestyle approaches. This consensus approach to management is based on high-quality evidence. Randomized clinical trial data are most abundant for drug therapies, and other professional societies have also made similar recommendations for use of these agents.

Implementation of proven therapies is paramount to improving health outcomes. There is a critical need for patients with diabetes and CKD to be treated in accord with the most up-to-date recommendations. The ADA and KDIGO, individually and now in combination, offer clear guidance on applying and prioritizing interventions. High cost, limited workforce, and other resource constraints in health care systems will limit implementation of some recommendations among individuals and populations, and efforts to improve accessibility are essential to maximizing benefit and minimizing disparities.

Investigation remains active in the fields of diabetes, CKD, and cardiovascular disease, and additional data on existing and novel approaches are anticipated. Clinical practice guidelines will continue to evolve. When possible, consensus approaches to diagnosis and management will help interpret new data in context and translate discoveries to improved outcomes for patients.

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