Long-Term Care Updates

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Finerenone - A Clinical Review

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Introduction

Finerenone is a novel, non-steroidal mineralocorticoid receptor (MR) antagonist approved by the FDA in 2021 that has shown substantial promise as a treatment option for patients with type 2 diabetes (T2D) to prevent cardiovascular and renal disease progression.[1] Early identification of diabetes-related cardiorenal complications and intervention with finerenone can mitigate the progression of these chronic conditions, leading to improved quality of life[2] and reduced healthcare costs[3] in the long-term care setting.

Indication and Mechanism of Action

Finerenone has been approved for patients 18 years or older with T2D and chronic kidney disease (CKD) stages 1-4 with albuminuria. It blocks the binding of aldosterone to the MR, which in turn, inhibits sodium reabsorption and overactivation of the MR. Finerenone has a balanced selectivity for MR in both kidney and heart tissue, and is thought to reduce fibrosis and inflammation of these tissues by blocking MR overactivation.[4] Finerenone is more selective than spironolactone (a non-selective steroidal MR antagonist) and has a stronger binding affinity for the MR receptor than eplerenone (a selective steroidal MR antagonist).[5] Finerenone has no relevant affinity for androgen, progesterone, estrogen, and glucocorticoid receptors, which greatly reduces the frequency of side effects like gynecomastia typically seen with spironolactone.

Place in Therapy

The American Diabetes Association Standards of Care recommends to consider finerenone in adults with T2D and CKD with albuminuria who are on the maximum tolerated dose of an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) to reduce the risk of cardiovascular events and CKD progression.[6,7] Finerenone reduces the urine albumin-to-creatinine ratio (UACR), reducing the risk of CKD progression and end-stage renal disease (ESRD), and also reduces major adverse cardiovascular events including non-fatal myocardial infarction, hospitalization for heart failure, and cardiovascular death.[8,9]

Clinical Research

The Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease (FIGARO-DKD) trial was a phase 3 randomized clinical trial that sought to establish cardiorenal efficacy and safety for less advanced chronic kidney disease. In this trial, 7352 patients with T2D, CKD, and albuminuria on maximum tolerated doses of ACEi or ARB therapy were randomized to receive finerenone once daily vs. placebo. Patients in the intervention group received an initial dose of finerenone according to their eGFR (10 mg once daily for eGFR 25 to <60 mL/min/1.73 m^2 and 20 mg once daily for eGFR ≥60 mL/min/1.73m^2) and were titrated to the target dose of 20 mg once daily after 30 days, provided their serum potassium level was ≤4.8 mmol/L. The primary outcome was a time-to-event analysis of a composite of death from any cause, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure with a median 3.4-year follow-up period. Finerenone significantly reduced the incidence of the primary composite outcome compared to placebo (finerenone 12.4% vs. placebo 14.2%, HR 0.87; 95% CI, 0.76 to 0.98; P = 0.03) with one primary outcome event prevented for every 47 patients treated with finerenone. Hyperkalemia was more common in patients receiving finerenone as compared to placebo (10.8% vs. 5.3%), but only 1.2% of those receiving finerenone and 0.4% of those receiving placebo discontinued therapy due to hyperkalemia. Overall, finerenone therapy resulted in greater improvement in cardiovascular outcomes as compared to placebo for patients with T2D, CKD, and albuminuria.[8]

In the companion trial to FIGARO-DKD, the Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (FIDELIO-DKD) trial sought to measure outcomes associated with CKD progression in patients with T2D and predominantly stage 3 or 4 CKD with severely increased albuminuria. In this trial, 5734 patients were randomized to receive finerenone once daily vs. placebo under the same treatment conditions as FIGARO-DKD. The primary outcome was a time-to-event analysis for a composite of kidney failure, sustained decrease in eGFR of 40% from baseline, or death from renal causes, with a mean follow-up time of 2.6 years. A primary event occurred significantly less frequently in patients receiving finerenone as compared to patients receiving placebo (17.8% vs. 21.1%, HR 0.82; 95% CI 0.73 – 0.93; P = 0.001), with all component events occurring less frequently in patients receiving finerenone. For every incidence of a primary event to be prevented, the number needed to treat with finerenone was 29. The incidence of hyperkalemia requiring discontinuation of the study drug was 2.3% in patients receiving finerenone and 0.9% in the placebo group. Overall, the FIGARO-DKD study showed benefits of slowing CKD progression and reduction of CVD mortality (a key secondary outcome) in patients with T2D and advanced CKD.[9]

The FInerenone in chronic kiDney diseasE and type 2 diabetes: Combined FIDELIO-DKD and FIGARO-DKD Trial programme analYsis (FIDELITY) was a pooled analysis of the complementary FIGARO-DKD and FIDELIO-DKD trials that included more than 13,000 patients to provide a robust assessment of safety and efficacy of finerenone in patients with T2D and CKD stages 1-4 with moderate to severe albuminuria. In the FIDELITY analysis, finerenone was shown to reduce the composite renal endpoint by 23% and reduce the risk of developing Stage 5 CKD requiring dialysis by 20%. There was also a 14% reduction in the cardiovascular composite endpoint and a 22% reduction in the risk of hospitalization for heart failure. The results of the FIDELITY analysis suggests that the pathogenesis of CKD and cardiovascular disease in patients with T2D and CKD is strongly connected to the overactivation of mineralocorticoid receptors by aldosterone, which can be mitigated with finerenone therapy.[1]

Two clinical trials are in progress with further implications for finerenone and its place in therapy for CKD and cardiovascular disease. The FINEARTS-HF trial has enrolled over 6,000 male and female patients 40 years and older suffering from heart failure with preserved ejection fraction (HFpEF), defined as heart failure with ejection fraction ≥40%. This study aims to evaluate the effect of finerenone compared to placebo in the reduction of cardiovascular death and total heart failure (HF) events, including HF hospitalization and urgent visits for HF in patients suffering from HFpEF with an estimated completion date of September 2024.[11] The CONFIDENCE trial has enrolled over 800 patients with T2D and CKD to study the safety and efficacy of the combination of empagliflozin and finerenone as compared to either drug alone in slowing the progression of CKD with an estimated completion date of June 2024.[12]

Safety

The most common adverse reactions seen with finerenone were hyperkalemia, hypotension, and hyponatremia, which occurred in <5% of patients in clinical trials.[4] In the FIDELITY pooled analysis of FIGARO and FIDELIO, only 1.7% of study participants had hyperkalemia requiring discontinuation of finerenone compared to 0.6% of participants receiving placebo.[1] Finerenone is contraindicated for use in patients with adrenal insufficiency. Providers should monitor estimated glomerular filtration rate (eGFR) and serum potassium 4 weeks after initiation and at each dose adjustment throughout treatment.[4] Because it is a substrate of CYP3A4, finerenone levels are affected by concomitant use of CYP3A4 inhibitors or inducers. The use of finerenone is contraindicated with strong CYP3A4 inhibitors. Finerenone levels increase with moderate or weak CYP3A4 inhibitors, increasing the risk of hyperkalemia. Serum potassium levels should be monitored in patients who are taking moderate or weak CYP3A4 inhibitors, and finerenone dosing adjusted accordingly. Finerenone efficacy may be reduced by strong or moderate CYP3A4 inducers, so concomitant administration should be avoided. Patients should avoid grapefruit and potassium-containing salt substitutes while taking finerenone. Patients who are taking potassium-sparing diuretics or other drugs that increase serum potassium levels should be monitored closely for hyperkalemia.[4]

Dosing and Administration

Finerenone is available as 10 mg and 20 mg tablets marketed by Bayer under the brand name Kerendia. Finerenone may be taken without regard to food and may crushed and mixed with water or soft foods to be administered immediately. Usual initial dose and subsequent dose adjustments are based on eGFR and current serum potassium (K) levels (Table 1).[4]

Table 1. Finerenone dosing and dose adjustments.[4]

		eGFR ≥25 to <60 mg/min/1.73m^2	eGFR ≥ 60 mg/min/1.73m^2
Initial Dose (serum potassium must be ≤ 5.0 mEq/L at initiation)		10 mg once daily	20 mg once daily
Dose adjustment based on current serum K level (mEq/L)	≤ 4.8	Increase to 20 mg once daily*	Continue 20 mg once daily
	> 4.8 – 5.5	Continue 10 mg once daily	Continue 20 mg once daily
	> 5.5	Hold until serum K ≤ 5.0 mEq/L, then consider restarting at 10 mg once daily	Hold until serum K ≤ 5.0 mEq/L, then restart at 10 mg once daily

*For patients with eGFR of ≥25 to <60 mg/min/1.73m^2 at initiation of finerenone, if eGFR has decreased by more than 30% from previous measurement, consider maintaining 10 mg once daily instead of increasing to 20 mg once daily.

Because the risk of hyperkalemia increases with decreasing renal function, finerenone should not be initiated in patients with eGFR <25 mg/min/1.73m^2. It should also be avoided in patients with severe hepatic impairment (Child Pugh class C). No dose adjustment is necessary for mild to moderate hepatic impairment (Child Pugh class A or B).

According to the FIDELITY pooled analysis of the FIDELIO-DKD and FIGARO-DKD trials, the mean age of study participants was 64.8 +/- 9.5 years old, with 55% of patients aged 65 years or older and 14% of patients aged 75 or older. There were no differences in safety or efficacy observed between these patients and younger patients, and as such, no dose adjustment is required.[7]

Nursing staff should be aware of the potential for hypotension in patients receiving finerenone, which could increase fall risk, especially in geriatric patients.

References

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