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Fineronone- Favourable Cardio Renal Outcomes in Type 2 Diabetes Mellitus Patients

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ABSTRACT:

Though Mineralocorticoid receptors antagonist (MRAs)are in the markets since long ,such as spironolactone which is one of the basic and most proven MRA and also Eplerenone both known for there beneficial effects on congestive cardiac failures and chronic kidney diseases. There was not much enough evidence of its use in diabetic kidney diseases and in cardiac complications in patients with Diabetes mellitus. Recent introduction of Finerenone a novel MRA for the betterment in cardiac and kidney complications is being studied and was found to be potential game changer for Diabetic patients with reduced eGfR and Hfref. This review will make physicians analyse the efficacy of the recent MRA, Finerenone on cardiac and renal profiles of the Diabetic patients and will also guide on the current status of the drug.

Keywords: albuminuria, chronic kidney disease, estimated glomerular filtration rate, finerenone, heart failure, mineralocorticoid receptor antagonist

BACKGROUND:

For those with type 2 diabetes (T2D), declining kidney function (estimated glomerular filtration rate [eGFR]) and rising albuminuria enhance the chances of cardiovascular mortality and heart failure (HF). In FIDELITY (Finerenone in Chronic Kidney Disease and Type 2 Diabetes: Combined FIDELIO-DKD and FIGARO-DKD Trial Programme Analysis), a selective, nonsteroidal mineralocorticoid receptor antagonist, patients with CKD and T2D saw better cardio renal outcomes.

Aldosterone antagonists (also known as anti-mineralocorticoids) and mineralocorticoid receptor antagonists (MRAs) are a class of medications that prevent aldosterone's actions.(1) Multiple variables influence the synthesis of aldosterone, which is largely produced by the adrenal gland and can cause oxidative stress, inflammation, and organ fibrosis. Aldosterone

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binds to both epithelial and endothelial mineralocorticoid receptors. blood vessels, heart, and epithelial tissues, and it raises blood pressure by causing sodium reabsorption and potassium excretion. Examples of these tissues include kidneys. Over-activation of the mineralocorticoid receptor is a primary cause of kidney and cardiovascular disease. (1)

Aldosterone antagonists are a crucial component of the pharmacologic therapy used to block the neurohormones required for the treatment of hypertension and heart failure. Recent research has shown that mineralocorticoid receptor antagonists can avoid renal failure, proteinuria, and histopathological kidney abnormalities.

MRAs that are currently on the market include spironolactone, Eplerenone, and Finerenone. All medications in this class work in a similar way by competitively blocking the mineralocorticoid receptors in the distal convoluted tubule to enhance sodium and water excretion while maintaining potassium retention. (2)

Table 1: Mineralocorticoid receptor antagonists comparison, structure, chemistry, distribution, and receptors affinity.3, 4

*Lower values mean stronger inhibition.

	Spironolactone	Eplerenone	Finerenone
Chemistry	Steroidal		Non – steroidal, Dihydropyridine
Distribution	Higher concentrations in renal tissue in comparison to cardiac tissue.		Distributed relatively equally between the heart and the kidney.
Mineralocorticoid receptor	24	990	18
Glucocorticoid receptor	2400	22,000	>10,000
Androgen receptor	77	21,200	>10,000
Progesterone receptor	740	31,200	>10,000

Finerenone is a non-steroidal MRA, whereas Spironolactone and eplerenone are steroidal MRAs.

Eplerenone and finerenone are selective MRAs whereas spirolactone is a non-selective MRA. (3, 4)

In July 2021, the FDA approved finerenone, a nonsteroidal mineralocorticoid receptor antagonist based on dihydropyridine, to lower the risk of cardiovascular death, nonfatal heart attacks, kidney failure hospitalization, and kidney function decline in adults with chronic kidney disease (CKD) associated with type 2 diabetes mellitus.(5) It lowers albuminuria, fibrosis, and inflammation in diabetic individuals as well as the chance of developing kidney failure for the first time via binding to the MR receptor. (6)

To lower mortality and morbidity in individuals with chronic severe congestive heart failure and a low ejection fraction, finerenone inhibits the mineralocorticoid receptor.(7) It is divided comparatively evenly between heart and kidneys.

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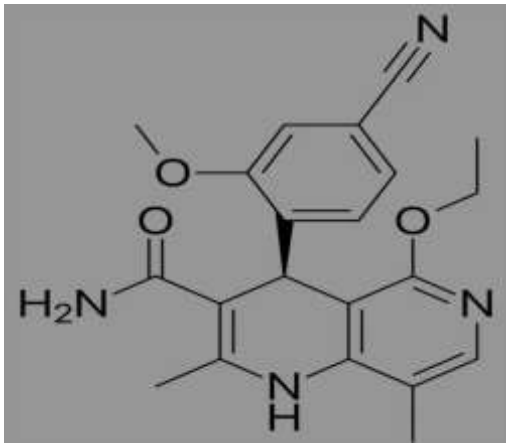
FINERONONE STRUCTURE:



Spironolactone and eplerenone concentrations in renal tissue are higher than those in cardiac tissue. (4) With regard to androgen, progesterone, estrogen, and glucocorticoid receptors, finerenone exhibits negligible affinity or activity.

The medication has a lower incidence of hyperkalemia and other adverse effects compared to both spironolactone and eplerenone, and it is at least as potent as spironolactone. It binds selectively to the mineralocorticoid receptor.(4)

In order to ascertain finerenone's effectiveness on albuminuria in individuals with diabetic nephropathy, it was previously investigated in the ARTS-DN randomised clinical trial. 8 In a different clinical trial, finerenone was found to be superior to eplerenone at lowering a composite end point of all-cause mortality and heart failure outcomes. (9)

The medication is currently being studied in studies FINEARTS-HF and FIGARO-DKD to determine how it affects heart failure with reduced ejection fraction and heart failure with preserved ejection fraction as well as how it affects cardiovascular mortality and morbidity in patients with less advanced stages of CKD and T2DM. (10,11)

Recent research has shown that mineralocorticoid receptor antagonists can avoid renal failure, proteinuria, and histopathological kidney abnormalities.(12) Despite guideline-directed therapy, there is still a significant unmet medical need among patients with CKD and T2DM, and the proportion of T2DM patients at risk for CKD is rising. (13)

According to the FIDELIO-DKD trial, finerenone both in individuals with and without a history of atherosclerotic cardiovascular disease lowered the risk of cardiovascular and kidney failure outcomes. The findings imply that finerenone may represent a significant advancement in cardiovascular care for patients with CKD and T2DM. (11)

It may be advised for persons with CKD and T2DM to lower their risk of long-term glomerular filtration rate decline, end-stage kidney disease, cardiovascular death, heart attacks, and hospitalisation for heart failure.

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For people with T2DM, finerenone protects the heart and kidneys and may be an alternative if SGLT2 inhibitors are not recommended. (13)

Conclusion- With all the research and proven efficacy of Spironolactone one of the oldest MRAs in improving cardiac functions and renal outcomes in non diabetic patients is being evolved and time tested.There's was always the need for the molecule to early intervene in the disease and also reduce the complications in the diabetes mellitus patients. With all the trials Finerenone seems to improve cardiac and renal outcomes with least side effects as compared to older generations MRAs and found is also improving patients health and postponing the complications.

REFERENCES:

1. Chrousos GP. Adrenocorticosteroids & Adrenocortical Antagonists. In: Katzung BG, Vanderah TW. eds. Basic & Clinical Pharmacology, 15e. McGraw Hill; 2021. https://accesspharmacy.mhmedical.com/content.aspx?bookid=2988&sectionid=250600694 Accessed March 09, 2022.
2. Sam R, Pearce D. Diuretic Agents. In: Katzung BG, Vanderah TW. eds. Basic & Clinical Pharmacology, 15e. McGraw Hill; 2021. https://accesspharmacy.mhmedical.com/content.aspx?bookid=2988&sectionid=250596112 Accessed March 9, 2022.
3. Schubert-Zsilavecz M, Wurglics M. Neue Arzneimittel Herbst. 2015.
4. Bärfacker L, Kuhl A, Hillisch A, et al. Discovery of bay 94-8862: A nonsteroidal antagonist of the mineralocorticoid receptor for the treatment of Cardiorenal diseases. Chemistry Europe. https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/cmdc.201200081. Published July 12, 2012. Accessed March 9, 2022
5. KERENDIA (finerenone) [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals, Inc.; July 2021.
6. Grune J, Beyhoff N, Smeir E, et al. Selective mineralocorticoid receptor cofactor modulation as molecular basis for finerenone's antifibrotic activity. Hypertension. 2018; 71:599-608.
7. Pitt B, Kober L, Ponikowski P, et al. Safety and tolerability of the novel nonsteroidal mineralocorticoid receptor antagonist BAY 94-8862 in patients with chronic heart failure and mild or moderate chronic kidney disease: a randomized, double-blind trial. Eur Heart J. 2013; 34:2453-63.
8. Bakris GL, Agarwal R, Chan JC, et al. Effect of finerenone on albuminuria in patients with diabetic nephropathy: a randomized clinical trial. JAMA 2015; 314:884-94.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 2, 2022

9. Filippatos G. et al. Finerenone and Cardiovascular Outcomes in Patients With Chronic. Kidney Disease and Type 2 Diabetes. Circulation. 2021;143:540–552. DOI: 10.1161/ CIRCULATIONAHA.120.051898.

10. U.S. National Library of Medicine. Study to Evaluate the Efficacy (Effect on Disease) and Safety of Finerenone on Morbidity (Events Indicating Disease Worsening) & Mortality (Death Rate) in Participants With Heart Failure and Left Ventricular Ejection Fraction (Proportion of Blood Expelled Per Heart Stroke) Greater or Equal to 40% (FINEARTS-HF). https://clinicaltrials.gov/ct2/show/NCT04435626 Accessed March 9, 2022.

11. U.S National Library of Medicine Clinical Trials. Efficacy and Safety of Finerenone in Subjects With Type 2 Diabetes Mellitus and Diabetic Kidney Disease (FIDELIO-DKD) https://www.clinicaltrials.gov/ct2/show/NCT02540993 Accessed March 9, 2022.

12. Haller H, et al. Finerenone: a New Mineralocorticoid Receptor Antagonist Without Hyperkalemia: an Opportunity in Patients with CKD? Curr Hypertens Rep. 2016;18: 41 DOI 10.1007/s11906-016-0649-2.

13. Bakris GL., et al. Design and Baseline Characteristics of the Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease Trial. Am J Nephrol. 2019;50:333–344 DOI: 10.1159/000503713.