ECHO Diabetes:

Finerenone

May 12th, 2022

Emily Castle, PharmD

Objectives

- Evaluate the 2022 ADA update
- Understand Finerenone
- Discuss primary literature
- Determine how to adjust our practice

1.

Introduction

Why Finerenone?

Finerenone

2022 ADA guidelines new statement:

- “In patients with chronic kidney disease who are at increased risk for cardiovascular events or chronic kidney disease progression or are unable to use a sodium–glucose cotransporter 2 inhibitor, a nonsteroidal mineralocorticoid receptor antagonist (finerenone) is recommended to reduce chronic kidney disease progression and cardiovascular events”

Standards of Medical Care in Diabetes—2022[1]

2.
Drug Information

Mechanism of Action

- Finerenone is a nonsteroidal, mineralocorticoid receptor antagonist

- Works by ↓ inflammation & fibrosis through receptor blocking

Finerenone: Drug information. UpToDate[2] Investigating new treatment. Nephrol Dial Transplant.[3]

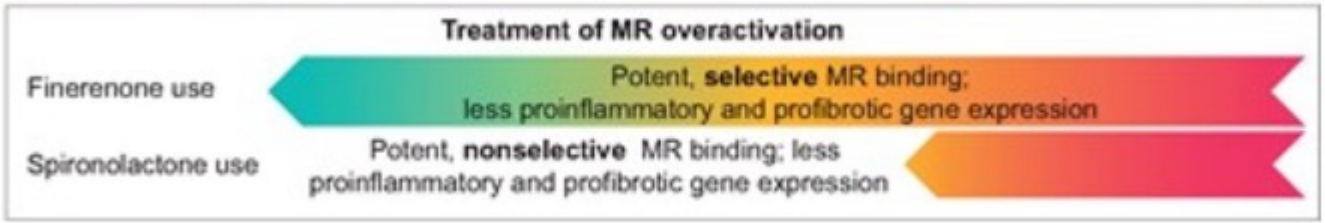
Mechanism of Action

- Mineralocorticoid receptors are normally activated by cortisol and aldosterone
- When activated, gene transcription is initiated
- Over activation of this receptor leads to inflammation and fibrosis -> in the kidneys leads to CKD development

Investigating new treatment. Nephrol Dial Transplant.[3]

Mechanism of Action

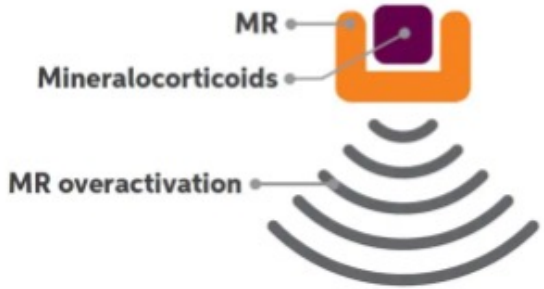
- Finerenone blocking these receptors prevents the inflammation and fibrosis from occurring



- Compared to spironolactone, it has *less* hyperkalemia and gynecomastia

Investigating new treatment. Nephrol Dial Transplant.[3]

MR overactivation may lead to inflammation and scarring in the kidneys, heart, and blood vessels



Finerenone attaches to the MR

Finerenone blocks MR overactivation

Kerenida Website. December 2021[4]

Indication

Indicated in patients with CKD and T2DM

- To **reduce the risk** of sustained eGFR decline, end-stage kidney disease, cardiovascular death, nonfatal myocardial infarction, and hospitalization for heart failure in adult patients with **chronic kidney disease associated with type 2 diabetes**.

Finerenone: Drug information. UpToDate[2]

Contraindications

- Adrenal insufficiency
- Use with strong CYP3A4 inhibitors (a CY3A4 substrate)

Finerenone: Drug information. UpToDate[2]

Adverse Events

- Hyperkalemia:18%
- Hypotension: 5%
- Hyponatremia: 1%
- Initiation may cause a decrease in eGFR within the first four weeks of treatment, before stabilizing

Finerenone: Drug information. UpToDate[2]

Adverse Events: Hyperkalemia

Risk factors:

- Have higher baseline potassium
- Taking other potassium raising drugs
- Having diabetes, reduced renal function, or proteinuria

Finerenone: Drug information. UpToDate[2]

Formulations

- 10 mg tablet
- 20 mg tablet

- Dosing based on **renal function** and **potassium levels**

Finerenone: Drug information. UpToDate[2]

Dosing Process

Finerenone: Drug information. UpToDate[2]

Dosing Initial: Renal Adjustments

Renal Function	Dose
eGFR ≥60 mL/minute/1.73 m^2	20 mg once daily
eGFR ≥25 to <60 mL/minute/1.73 m^2	10 mg once daily
eGFR <25 mL/minute/1.73 m^2	Not recommended for use

Finerenone: Drug information. UpToDate[2]

Dosing Maintenance: Potassium Adjustments

	10 mg Initial Dose	20 mg Initial Dose
≤ 4.8 mEq/L	↑ to 20 mg daily ***	Continue dose
>4.8 to 5.5 mEq/L	Continue dose	Continue dose
>5.5 mEq/L	Pause therapy May consider restarting at 10 mg daily when potassium drops below 5 mEq/L	Pause therapy Restart at 10 mg daily when potassium drops below 5 mEq/L

*** If eGFR ↓ more than 30% from baseline, stay with 10 mg daily dosing

Finerenone: Drug information. UpToDate[2]

Pricing

DESCRIPTION	EST. NET PRICE	PURCHASE PRICE	UNIT PRICE	PRICE IND	DC QTY	ORD QTY
KERENDIA TB 10MG 90	$1124.95	$1124.95	$12.4994	GRP2	4	
KERENDIA TB 10MG 30	$370.69	$370.69	$12.3563	GRP2	34	
KERENDIA TB 20MG 90	$1119.05	$1119.05	$12.4339	GRP2	2	
KERENDIA TB 20MG 30	$366.93	$366.93	$12.2310	GRP2	17	

3.

Clinical Studies

What evidence is there?

Clinical Studies

- FIDELIO-DKD: published December 3rd, 2020
- FIGARO-DKD: published December 9th, 2021

The NEW ENGLAND JOURNAL of MEDICINE

Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes

Effect of finerenone. N Engl J Med.[5]

FIDELIO-DKD

Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (FIDELIO-DKD)

- Study of finerenone vs placebo
- Hypothesis that finerenone could potentially slow the progression of CKD and reduce cardiovascular morbidity and mortality in patients with T2DM and CKD

Effect of finerenone. N Engl J Med.[5]

Study Design

- Double blind randomized, placebo-controlled, multicenter clinical trial with 5700+ patients
- Inclusion Criteria:
  - 18+ years old with T2DM and CKD
  - 4-week pretreatment period with either ACEI or ARB at maximal tolerated labeled dose
  - Serum potassium ≤4.8 mmol/L.

Effect of finerenone. N Engl J Med.[5]

Study Design

- Exclusion Criteria:
  - Renal artery stenosis, dialysis, or renal allograft
  - Clinically diagnosed symptomatic heart failure
  - A1C above 12%
  - Uncontrolled arterial hypertension

Effect of finerenone. N Engl J Med.[5]

Study Design

- **Primary Composite Outcome:** kidney failure, a sustained decrease of at least 40% in the eGFR from baseline, or death from renal causes

- **Secondary Composite Outcome:** death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure

Effect of finerenone. N Engl J Med.[5]

Study Results

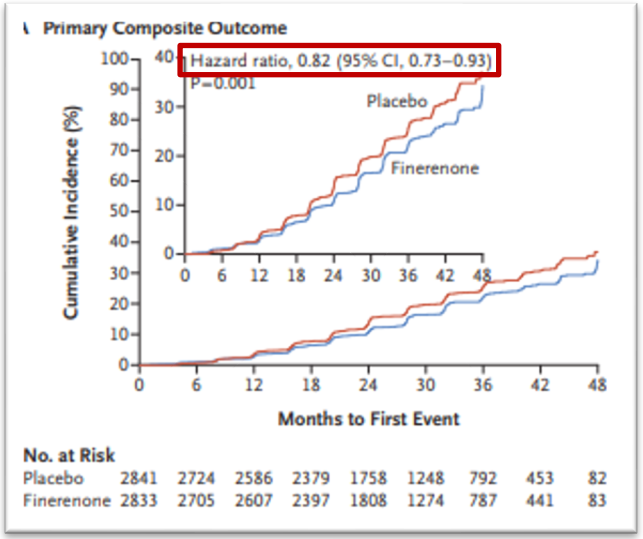
- **Primary Composite Outcome:** kidney failure, a sustained decrease of at least 40% in the eGFR from baseline, or death from renal causes
  - 17.8% (finerenone group) and 21.1% (placebo group)
  - Hazard ratio, 0.82; 95% confidence interval [CI], 0.73 to 0.93; P=0.001

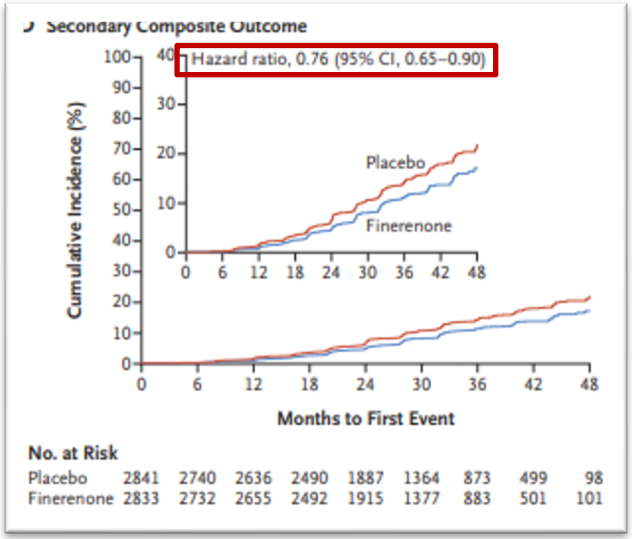
Effect of finerenone. N Engl J Med.[5]

Study Design

- **Secondary Composite Outcome:** death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure
  - 13.0% (finerenone group) vs 14.8%(placebo group)
  - Hazard ratio, 0.86; 95% confidence interval [CI], 0.75 to 0.99; P=0.03

Effect of finerenone. N Engl J Med.[5]





Effect of finerenone. N Engl J Med.[5]

Conclusion

- The use of finerenone in patients with T2DM and CKD who are also treated with an ACEi/ARB resulted in:
  - Lower risks of CKD progression vs placebo
  - Lower risks of cardiovascular events vs placebo

Effect of finerenone. N Engl J Med.[5]

The NEW ENGLAND JOURNAL of MEDICINE

Cardiovascular Events with Finerenone in Kidney Disease and Type 2 Diabetes

Cardiovascular events with finerenone. N Engl J Med[6]

FIGARO-DKD

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

- Study of finerenone vs placebo
- Difference from FIDELIO-DKD: focused on cardiovascular events as the primary outcome with patients with less severe CKD (patients in stages 1 and 2 with severe albuminuria)

Cardiovascular events with finerenone. N Engl J Med[6]

Study Design

- Double blind randomized, placebo-controlled, multicenter clinical trial with 7400+ patients
- Inclusion Criteria:
  - 18+ years old with T2DM and CKD
  - 4-week pretreatment period with either ACEI or ARB at maximal tolerated labeled dose
  - Serum potassium ≤4.8 mmol/L.

Cardiovascular events with finerenone. N Engl J Med[6]

Study Design

- Exclusion Criteria:
  - Renal artery stenosis, dialysis, or renal allograft
  - Clinically diagnosed symptomatic heart failure
  - A1C above 12%
  - Uncontrolled arterial hypertension

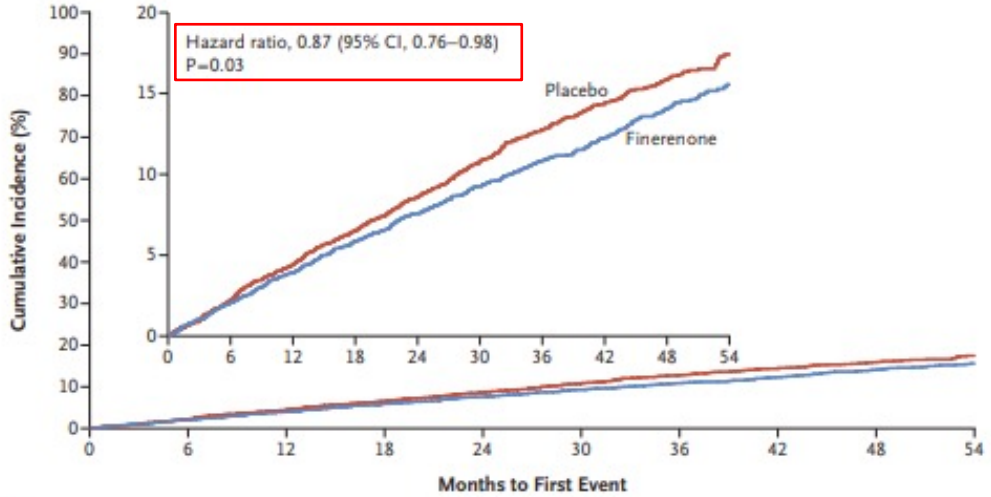
Cardiovascular events with finerenone. N Engl J Med[6]

Study Results

- **Primary Composite Outcome:** CV death, myocardial infarction (MI), stroke, hospitalization for HF
  - hazard ratio, 0.87; 95% confidence interval [CI], 0.76 to 0.98; P = 0.03

Cardiovascular events with finerenone. N Engl J Med[6]

A Primary Composite Outcome



No. at Risk										
Placebo	3666	3577	3479	3389	3267	2730	2125	1657	1076	585
Finerenone	3686	3600	3517	3427	3320	2781	2184	1712	1093	598

Cardiovascular events with finerenone. N Engl J Med[6]

Conclusions

In two different patient groups who have both CKD and T2DM: treated with Finerenone vs placebo…

- **Decreased occurrences of renal decline & cardiovascular and renal events**

Cardiovascular events with finerenone. N Engl J Med[6]

4.

Place in Practice

How can we best utilize this drug?

Finerenone

2022 ADA guidelines new statement:

- “In patients with chronic kidney disease who are at increased risk for cardiovascular events or chronic kidney disease progression or are unable to use a sodium–glucose cotransporter 2 inhibitor, a nonsteroidal mineralocorticoid receptor antagonist (finerenone) is recommended to reduce chronic kidney disease progression and cardiovascular events”

Standards of Medical Care in Diabetes—2022[1]

Finerenone

In two different patient groups who have both CKD and T2DM: treated with Finerenone vs placebo…

- **Decreased occurrences of renal decline & cardiovascular and renal events**
- **Benefit exists for patients with CKD and T2DM**

Finerenone

Additional Points

- Patients with pre-existing heart failure with persistent symptoms were excluded from both studies
- Patients who were already taking SGLT2-inhibitors were a small part of each study population
  - Unknown if patients already taking them would benefit extra or not

Thanks!

Any questions?

emily.castle@ihs.gov

References

1. Chronic Kidney Disease and Risk Management: Standards of Medical Care in Diabetes—2022 Diabetes Care 2022;45(Supplement_1):S175–S184
2. Finerenone: Drug information. In: Post TW, ed. UpToDate. UpToDate; 2020. Accessed March 16, 2022. https://www.uptodate.com/contents/finerenone-drug-information
3. Agarwal R, Anjer S, Bakris G, et al. Investigating new treatment opportunities for patients with chronic kidney disease in type 2 diabetes: the role of finerenone. Nephrol Dial Transplant. 2020 Dec 6; DOI: 10.1093/ndt/gfaa294
4. How can KERENDIA help? Kerenida Website. December 2021. Accessed March 16, 2022. https://www.kerendia-us.com/about-kerendiaFinerenone: Drug information. UpToDate; 2022. Accessed March 16, 2022. https://www.uptodate.com/contents/finerenone-drug-information
5. Bakris G, Agarwal R, Anker S, et al. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. N Engl J Med. 2020 Dec 3;383(23):2219-2229
6. Pitt B, Filippatos G, Agarwal R, et al. Cardiovascular events with finerenone in kidney disease and type 2 diabetes. N Engl J Med. 2021 Dec 9;385(24):2252-2263