Prevention of Chronic Kidney Disease Progression

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Credentials

Oklahoma State University Medical Center

- Internal Medicine Residency, June 2016-2019
- Board Certified in Internal Medicine 2019

University of Oklahoma, School of Community Medicine

- Nephrology Fellowship, July 2019-2021
- Board Certified in Nephrology 2021

GlomCon Virtual Glomerular Disease Fellowship

- Glomerular Disease Fellowship, September 2020-June 2021

Disclosures

None

Goals and Objectives

Learn about medications used to treat chronic kidney disease

Review their different indications

Additional pearls on prevention of progression

Medications in Chronic Kidney Disease

In Order of Management:

1. ACE-I Inhibitors or Angiotensin Receptor Blockers
   - Consideration of potassium binding resin
2. SGLT 2 Inhibitors
3. Mineralocorticoid Receptor Antagonists
4. GLP-1 receptor agonists

SGLT 2 Inhibitors

CREDENCE Trial:

- Compared 4401 **diabetic** patients to canagliflozin (100 mg PO daily) to placebo
- Patient were already on ACE or ARB
- GFR ranges from 30 and 89 mL/min/1.73 m^2 and urine ACR >300 mg/g
- Results:
  - "30% reduction in primary outcome of a composite of:
  - end-stage kidney disease (dialysis, transplantation, or a sustained estimated GFR of <15 ml per minute per 1.73 m^2),
  - a doubling of the serum creatinine level,
  - or death from renal or cardiovascular causes" (NEJM 2019; 380:2295-2306)

Metanalysis of CREDENCE and three other trials showed that these benefits were more pronounced in those with severe albuminuria (>300 mg/day) (Lancet Diabetes Endocrinol. 2019;7(11):845)

SGLT 2 Inhibitors

DAPA CKD

- 4304 participants with CKD but with and without DM
- GFR of 25-75 mL/min/1.73 m^2 and a urinary albumin-to-creatinine ratio of 200 to 5000 to receive dapagliflozin (10 mg once daily) or placebo
- 98% were on ACE-I or ARB
- Results:
  - At 2.4 years, lowered all-cause mortality (4.7 versus 6.8 percent)
  - Decreased incidence of ESKD (5.1 versus 7.5 percent)
  - Reduced the risk of a 50 percent or greater decline in eGFR (5.2 versus 9.3 percent).

Benefits were similar in patients with DKD and non-Diabetic CKD, reinforcing the idea that benefits were independent of glycemic control

(NEJM 2023;388:117-127)

SGLT 2 Inhibitors

EMPA-KIDNEY

- 6609 CKD patients with and without proteinuria
- GFR 20-45 with or without albuminuria
- GFR 45-90 with >200 mg albuminuria
- About 46% of participants had diabetes
- Empagliflozin 10 mg daily vs placebo
- Results:
  - Follow up for 2 years
  - Reduced the incidence of ESKD (3.3 vs 4.8 %)
  - Reduced incidence of a sustained decline in eGFR to <10 mL/min/1.73 m^2 (3.5 vs 5.1 %)
  - Reduced incidence of sustained decrease in eGFR of >40% (10.9 vs 14.3%)
  - The benefit still larger in patients with albuminuria ≥300 mg/g and substantially less in patients with lower albumin excretion

(NEJM 2023;388:117-127)

MRAs

FIDELIO Trial

Phase 3, randomized, double-blind, placebo-controlled, multicenter clinical trial

- Type II DM and CKD

Finerenone was associated with a 31% greater reduction in the urinary albumin-to-creatinine ratio from baseline to month 4 than placebo

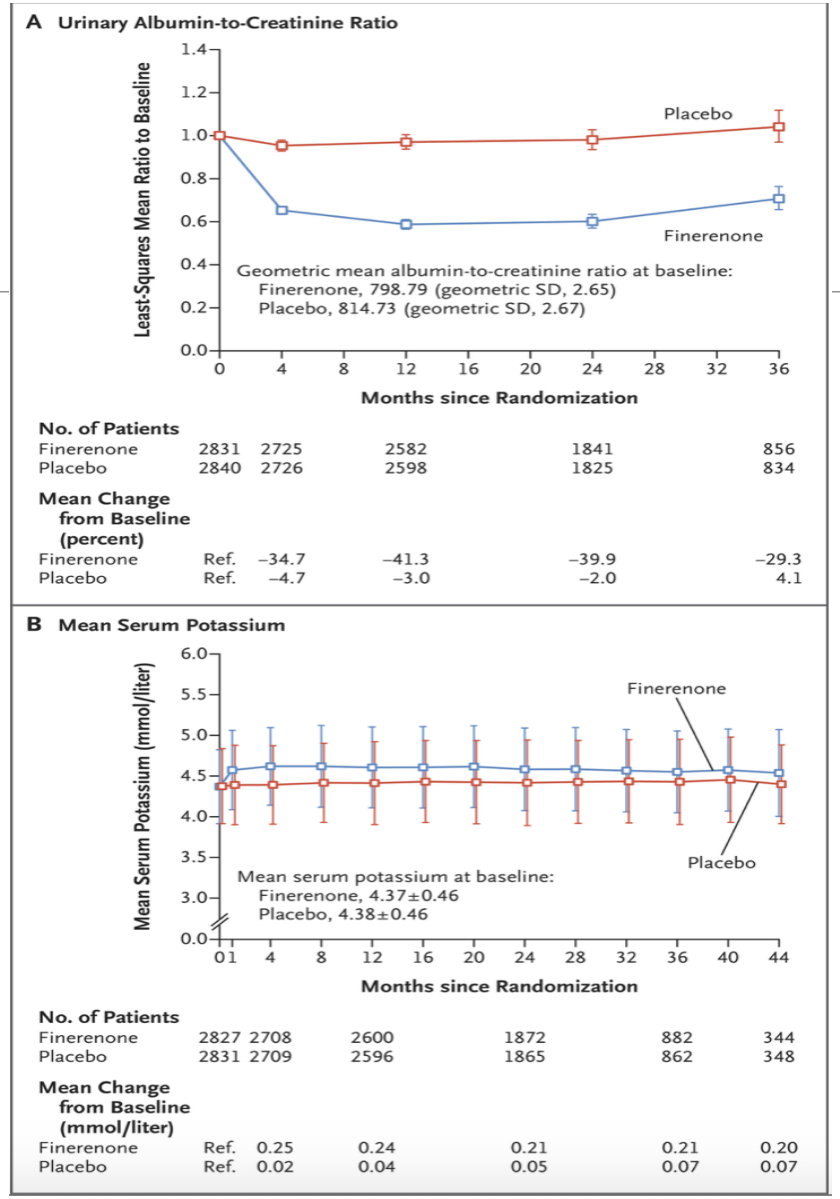
Lower mean urinary albumin-to-creatinine ratio with finerenone than with placebo was maintained thereafter

A total of 252 patients (8.9%) who received finerenone and 326 patients (11.5%) who received placebo had a secondary composite kidney outcome event (kidney failure, a sustained decrease of ≥57% in the eGFR from baseline, or death from renal causes)

Overall hyperkalemia-related adverse events were twice as frequent with finerenone as with placebo (18.3% and 9.0%, respectively)

The frequency of hyperkalemia leading to discontinuation of the trial regimen was also higher with finerenone (2.3% and 0.9% in the respective groups)

- However no fatal hyperkalemia results were reported

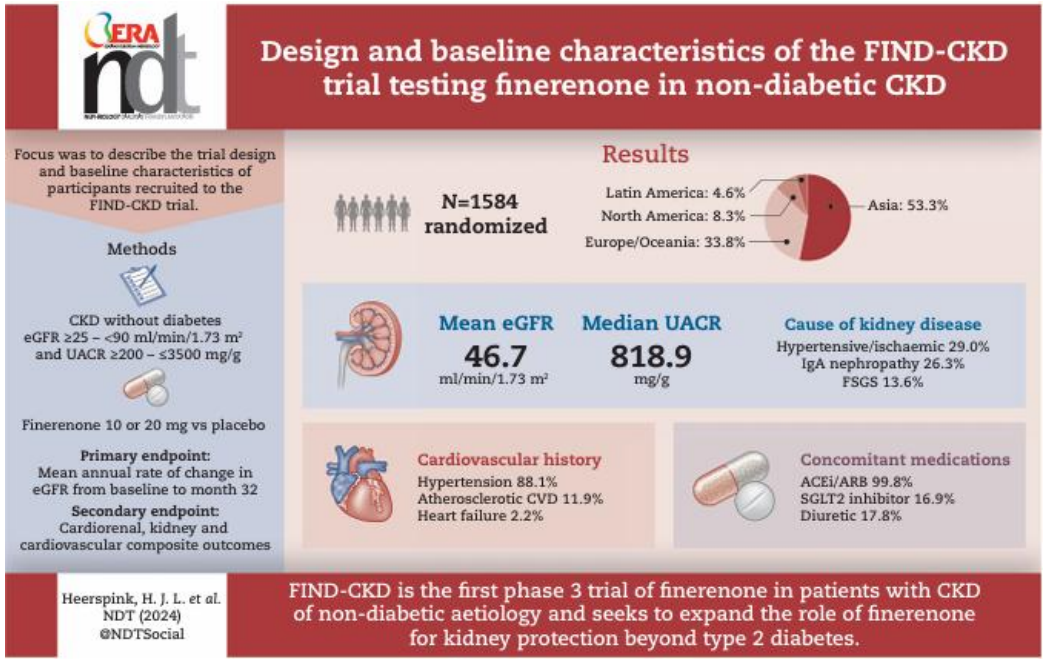


(NEJM 2020;383:2219-2229)

MRAs

FIND CKD TRIAL

TO BE PUBLISHED SOMETIME AFTER NOV. 2025



KEY LEARNING POINTS

What was known:

- Finerenone reduced the risk of kidney failure and improved cardiovascular outcomes in patients with chronic kidney disease (CKD) associated with type 2 diabetes (T2D) in the phase 3 FIDELIO-DKD and FIGARO-DKD outcome trials.
- Finerenone acts by targeting pathways of pathophysiological sodium retention, inflammation and fibrosis mediated by mineralocorticoid receptor overactivation in the vasculature, heart and kidney.
- Based on its properties, finerenone may also be beneficial in improving kidney and cardiovascular outcomes in patients with CKD without diabetes. This hypothesis is being tested in the ongoing FIND-CKD trial.

This study adds:

- The FIND-CKD trial is the first phase 3 trial studying the efficacy of finerenone in patients with CKD of non-diabetic aetiology, including hypertension and chronic glomerulonephritis (e.g. immunoglobulin A nephropathy and focal segmental glomerulosclerosis), who are at risk of progression.
- The primary endpoint in FIND-CKD is the estimated glomerular filtration rate slope at 32 months.
- The utilization of a hybrid decentralized clinical trial model is an added novelty that offers study participants and sites increased flexibility in trial conduct. This model integrates telemedicine technology into certain parts of the clinical research process and supports management of research activities, including remote data collection.

Potential impact:

- The FIND-CKD trial will determine the efficacy of finerenone for slowing kidney disease progression in patients with CKD without diabetes, providing a potential expanded role for finerenone for the treatment of CKD beyond T2D.

(Nephrol Dial Transplant , 2025, 40 , 308–319)

GLP 1 Agonists

Liraglutide and Renal Outcomes in Type 2 Diabetes

- significantly lower rates of renal outcomes driven mainly by a lower incidence of macroalbuminuria in the liraglutide group than in the placebo group
- Lower risks of the doubling of the serum creatinine level and of end-stage renal disease with liraglutide than with placebo during up to 5 years of follow-up but this was found to be non-significant

(NEJM 2017;377(9):839)

REWIND TRIAL

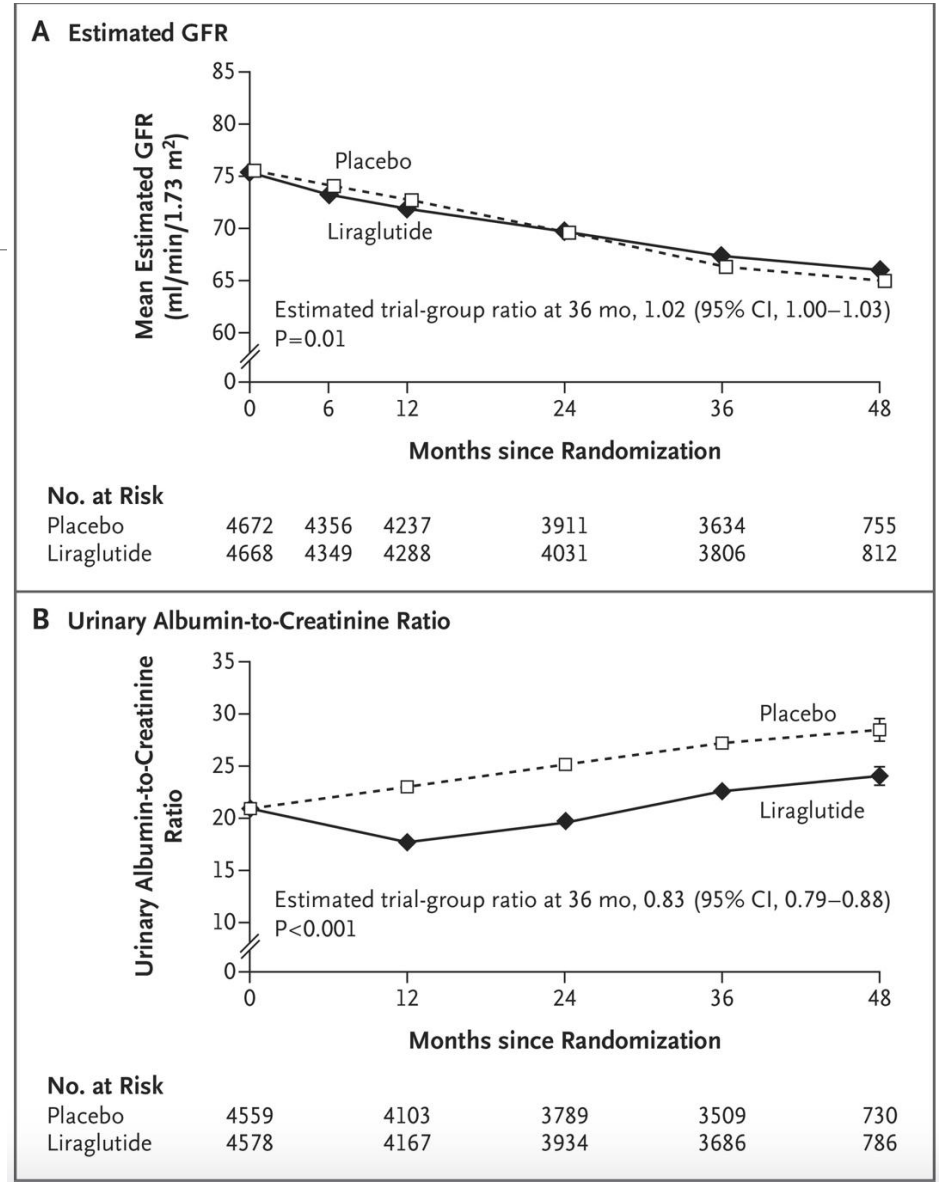
- Similar findings of decrease rates of new onset macroalbuminuria

(Lancet 2019; 394:131-138)

FLOW TRIAL

- Semaglutide slowed eGFR loss by 1.16 mL/min/m^2 over a median follow-up of 3.4 years

(NEJM 2024;391:109-121)



GLP 1 Agonists

SELECT Trial

17,604 obese patients with CVD but without DM given once-weekly subcutaneous semaglutide 2.4 mg

- Showed at 20% reduction in MACEs compared to placebo

Post hoc-analysis done Looked at:

- death from kidney disease
- initiation of chronic kidney replacement therapy (dialysis or transplantation)
- onset of a persistent eGFR less than 15 persistent 50% or greater reduction in eGFR compared with baseline
- onset of persistent macroalbuminuria

Results after 104 weeks:

"1.8% of the semaglutide arm experienced…main kidney endpoint(s) compared with 2.2% of the placebo arm"

"eGFR had declined less (-0.86) in the semaglutide arm than in the placebo arm (-1.61)"

In those with a baseline eGFR less than 60%, eGFR increased with 5.28% vs 3.09% in placebo

All this to say, there is opportunity to study this medicine in CKD without DM

(Nature Med 2024; 30:2058–2066)

Potassium Binders Role

Because we have extensive data that prove the benefits of minimizing proteinuria in CKD, potassium binders are playing a role in treating hyperkalemia instead of stopping or decreasing an effective dose of ACE-I/ARB or MRA

The KDIGO 2020 Guideline for diabetes management in chronic kidney disease states*[1]:

- In patients with diabetes, hypertension, and albuminuria, ACEi or ARB treatment should be initiated and titrated to the maximum approved dose that is tolerated[1]
- ACEi or ARB treatment should only be reduced or discontinued if serum K^+ levels cannot be otherwise managed or if there is a greater than 30% increase in serum creatinine[1]
- Recommendations to manage hyperkalemia include review concurrent drugs, moderate K^+ intake, initiate diuretics or oral sodium bicarbonate in appropriate patients, and use of a gastrointestinal cation exchanger such as a K^+ binder[1]
- K^+ binders should be considered to decrease serum K^+ levels after other measures have failed, rather than decreasing or discontinuing ACEi or ARB treatment[1]

KDIGO 2020

It’s The Little Things That Matter Too

Counsel on tobacco cessation

Counsel on weight loss

Consider sodium bicarbonate tablets for a goal bicarb ~24
- Plant based diets

Limit contrast exposure

Limit nephrotic meds (ex. NSAIDs, Antibiotics, PPI’s, H2 Blockers)

Limit protein intake
- Protein intake of 0.8 g/kg body weight/d in adults with CKD G3–G5

Keep blood pressure in goal range

Keeping A1c controlled

Treat the underlying condition (refer if concern for glomerular disease)

KDIGO Guidelines 2024

Thank you!

Questions?