



Welcome!

MCT2D Spring 2024 Regional Meeting

Dr. Lauren Oshman, MD, MPH
MCT2D Program Director

Dr. Heidi Diez, PharmD, BCACP
MCT2D Program Co-Director

Time	Presentation	Speaker
6:00 pm - 6:20 pm	Welcome & Quality Initiative Updates	Heidi Diez, PharmD, BCACP MCT2D Program Co-Director
6:20 pm - 6:35 pm	Updates from Nephrology	Mike Heung, MD, MS MCT2D Nephrology Program Director
6:35 pm-6:45 pm	Online Coverage Checker	Jackie Rau, MHSA, PMP MCT2D Program Manager
6:45 pm - 6:55pm	Break	
6:55 pm - 7:10 pm	Updates from Endocrinology	Kara Mizokami-Stout, MD, MS MCT2D Endocrinology Content Expert
7:10 pm - 7:50 pm	<ul style="list-style-type: none"> ● PCP Practices: QI Discussion ● Nephrology and Endocrinology Practices: Breakout discussion on care coordination 	Heidi Diez, PharmD, BCACP MCT2D Program Co-Director Mike Heung, MD, MS MCT2D Nephrology Program Director Kara Mizokami-Stout, MD, MS MCT2D Endocrinology Content Expert
7:50 pm - 8:00 pm	Looking Ahead for MCT2D	Jake Reiss, MHSA MCT2D Associate Program Manager

Recent Advances in Chronic Kidney Disease Management

MCT2D Regional Meetings

Spring 2024



Presented by
Mike Heung, MD, MS
MCT2D Nephrology
Program Director

Disclosures

- No relevant disclosures or conflicts of interest to report
- Employed by University of Michigan
- Grant funding: NIH, PCORI, CDC, Astute Medical Inc., Spectral Inc., CardioSounds Inc.
- Consultant: Wolters Kluwer Inc. (Lexicomp), Potrero Inc., CardioSounds Inc.

Learning Objectives

1. Describe recent literature expanding indications for SGLT2i in patients with CKD
2. Describe indications for non-selective MRA use
3. Describe potential emerging role of GLP-1 receptor agonists

Exciting Time to Be a Nephrologist!!

- New and emerging therapeutics
- With appropriate use, we may be able to change the epidemiology of kidney failure in the U.S.



*As captured at recent
nephrology faculty meeting*

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More than **1** in **7**

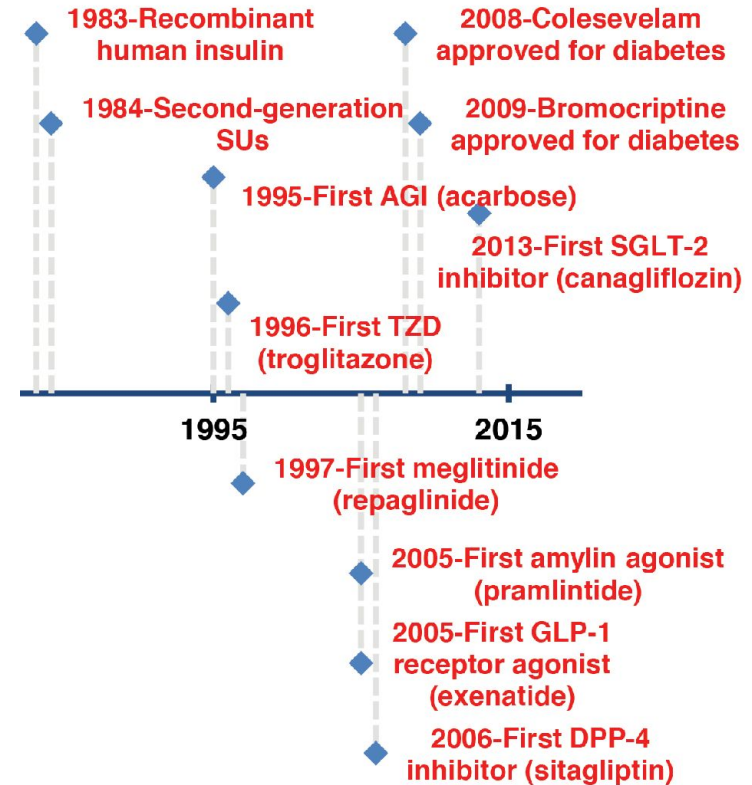
15% of US adults are estimated to have chronic kidney disease—that is about 37 million people.



SGLT-2 Inhibitors for Diabetic and Non-Diabetic Chronic Kidney Disease

Diabetic Kidney Disease

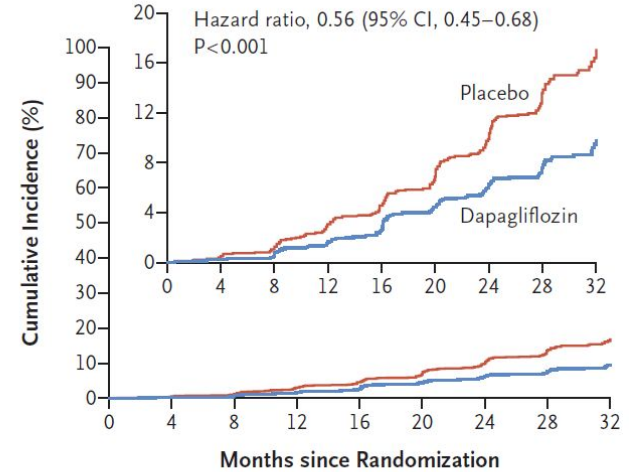
- **The good news:** Decrease in CKD among patients with DM, from 44% (2001-4) to 36% (2013-16)
 - Emphasis on glycemic control, ACEI/ARB use
- **The bad news:** Most common cause of ESRD in U.S.
 - 44% of incident cases; 60,112 in 2021
- Proliferation of DM management options



Beyond DM: DAPA-CKD

- RCT (n=4304) of dapagliflozin vs placebo in patients with CKD *with or without* (n=1398) DM2
 - High risk: **eGFR 25-75 plus albuminuria** (ACR 200-5000)
 - On standard therapy (65% statin, 98% ACEI/ARB)
- Primary outcome: composite of 50% decrease in eGFR, ESRD, death from renal or CV cause
 - 9.2% in dapa vs 14.5% in placebo over median 2.4y follow-up

B Renal-Specific Composite Outcome



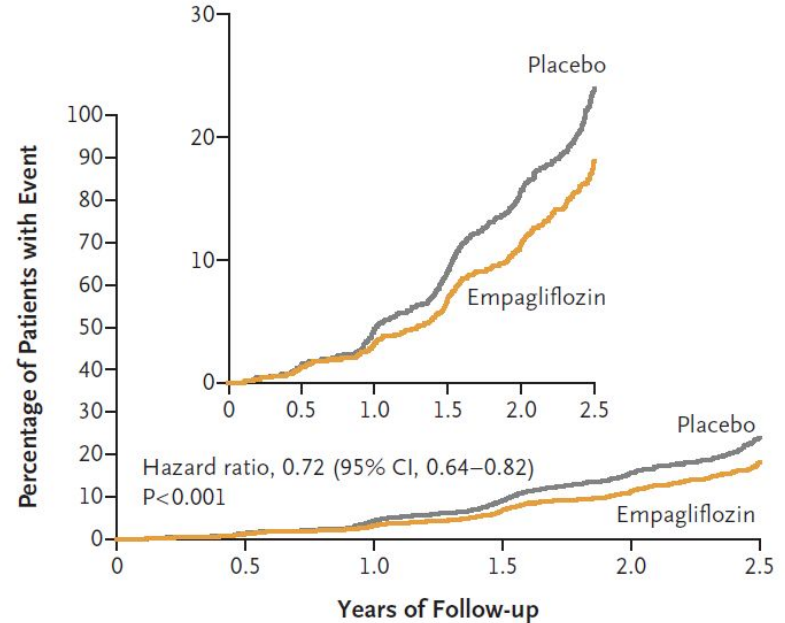
No. at Risk

Placebo	2152	1993	1936	1858	1791	1664	1232	774	270
Dapagliflozin	2152	2001	1955	1898	1841	1701	1288	831	309

Type 2 DM	Dapa	Placebo	HR (95% CI)
Yes	152/1455	229/1451	0.64 (0.52-0.79)
No	45/697	83/701	0.50 (0.35-0.72)

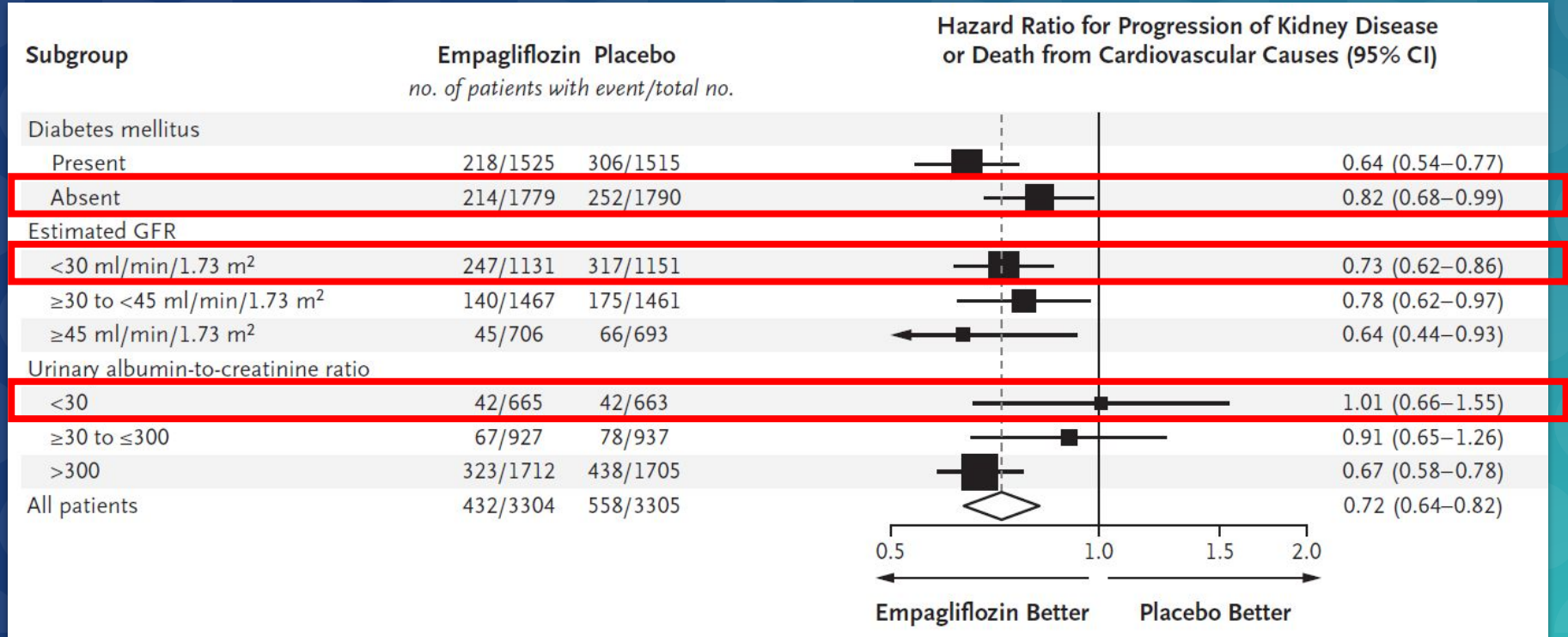
EMPA-Kidney

- RCT (n=6609) of empagliflozin vs placebo in patients with (46%) or without (54%) DM
 - eGFR **20-45**, or 45-90 with albuminuria (ACR>200)
- Primary outcome: composite of $\geq 40\%$ reduction in eGFR, ESRD, death from renal or CV causes



No. at Risk						
Placebo	3305	3250	3129	2243	1496	592
Empagliflozin	3304	3252	3163	2275	1538	624

EMPA-Kidney



SGLT2i's for Everybody???

Clear Outcome Benefits

- DM2 with known or high risk for CV disease
- HFrEF or HFpEF
- Diabetic CKD with **eGFR >20**
- **Non-diabetic CKD** with eGFR >20 and albuminuria

Uncertain Benefit

- Non-diabetic CKD without albuminuria



FDA Labeling

- **Dapagliflozin:** Approved for CKD indication 4/30/21 (“adults with chronic kidney disease at risk of progression”)
 - Limitations: Not for T1DM, PKD, recent immunosuppressive therapy for kidney disease
- **Empagliflozin:** Approved for CKD indication. 09/22/2023 “To reduce the risk of sustained decline in eGFR, end-stage kidney disease, cardiovascular death, and hospitalization in adults with chronic kidney disease at risk of progression.”
 - Limitations: Not for T1DM, PKD, recent immunosuppressive therapy for kidney disease, concomitant high dose prednisone use



The Benefits of Newer Diabetes Medications

Sodium-Glucose Transport Protein 2 Inhibitors (SGLT2)



Have you been prescribed one of these medications?

- Dapagliflozin (Farxiga)
- Canagliflozin (Invokana)
- Empagliflozin (Jardiance)
- Ertugliflozin (Steglatro)
- Bexagliflozin (Brenzavvy)

SGLT2s help your body lower blood sugar by causing glucose to be removed through your urine.

Did you know that these medications can do more than that help lower your blood sugar? Other benefits include:

- Protect kidney function and prevent the need for dialysis
- Lower risk of having or dying from a heart attack, stroke, or heart failure
- Lower blood pressure
- Mild weight loss

How is the medication taken?

These are oral medications that should be taken once a day. Because they make you urinate more, you should take them in the morning.

What should I expect after starting an SGLT2?

After starting this medicine, you may see a small drop in kidney function measured by blood tests. This is an expected short-term effect and may be associated with long-term improvement in kidney function. Your health care team may check your blood tests after 1-2 months to monitor.

What side effects might you experience?

- *Side effects are mild and may improve or go away in about 3-8 weeks.
- Increased urination
- Yeast infection
- Urinary tract infection
- Low blood pressure

How can I lessen or avoid side effects?

- Adequate hydration by drinking 6-8 glasses of water daily
- Avoid drinking water too close to bedtime
- Practice good genital hygiene (ensure you wipe yourself dry after urinating) and shower daily (in hot summer months, consider showering multiple times per day)
- Use cotton underwear
- Monitor your blood pressure at home
- Monitor your blood sugar at home if on insulin, glipizide, glyburide, or glimepiride
- Notify your doctor if another doctor/specialist starts you on a blood pressure medication

When should I call my health care team?

- If you experience:
- Unexplained fatigue, loss of appetite, or shortness of breath
 - Intense pain of genitals or rectum with a fever and/or feeling unwell
 - Unexplained falls
 - Being unable to eat
 - Unexplained, frequent low blood sugars (less than 70mg/dL)
 - If you are started on a new blood pressure medication
 - If you are scheduled for surgery and need to stop your medications
 - If you decide to start following a low carb diet (less than 100 grams of total carbohydrates daily)

*NOTE: These are the most common side effects. This list does not include all possible side effects. You may not experience any of these side effects. Please talk to your health care team if you have other concerns about side effects.

This handout should not be used as a substitute for medical advice from your health care team. It is your responsibility to review information provided by your pharmacy and consult with your doctor or health care team member prescribing these medications with any questions about your medication.

Understanding these medications

Commercial Insurance

SGLT2s are generally covered, but insurance may not cover all medications. Check with your insurance to see which are covered and tell your health care team. *MCT2D Coverage Guide: michmed.org/mkfm* out-of-pocket cost.

If you have a high deductible plan, you will have to pay the full cost of the medication until your deductible is met.

Medicare Part D

You may have a copay. Copay savings cards cannot be used with Medicare insurance. Talk to your doctor about Patient Assistance Programs. Patients with an annual income of less than \$50,000 may be able to get the medication for free.

Medicaid

At least one of these medications will be covered by your insurance. These medications do not have a generic version. Check with your insurance to see which medication is preferred. This will have the least out-of-pocket cost to you.

How much does the medication cost?

Not sure what the medication will cost contact your health care team or insurance company. Ask them the following questions:

- Do my plans preferred SGLT2s?
- Do I have any copay for this medication?
- Do I have a deductible for medications, and have I met it?
 - Currently met: \$ _____
- Are they available? Yes No
- Do I have a preferred local pharmacy? _____
- Do I have a preferred mail order pharmacy? _____
- Do I have any other medications I am on currently preferred? Yes No

Find your insurance company contact information on the back of your insurance card.

If you cannot locate your card, you can search the web for your insurance company's phone number.



My Savings Card
Copay Savings Guide
#K5

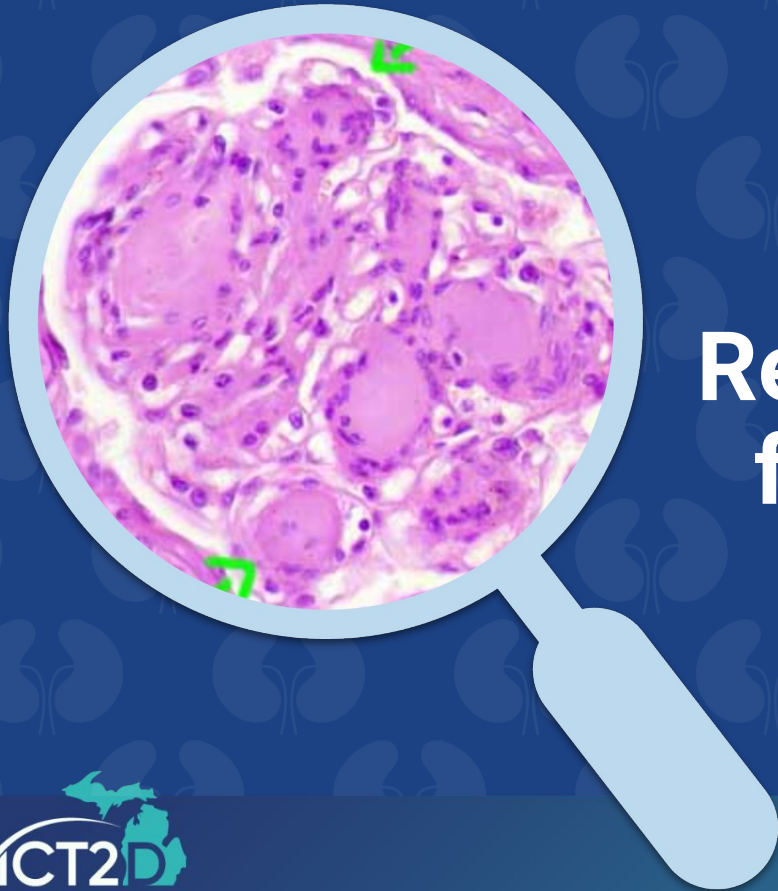


Patient Assistance Program
(PAP) Guide
michmed.org/kQQRy



For more diabetes resources for patients:
mct2d.org/patients

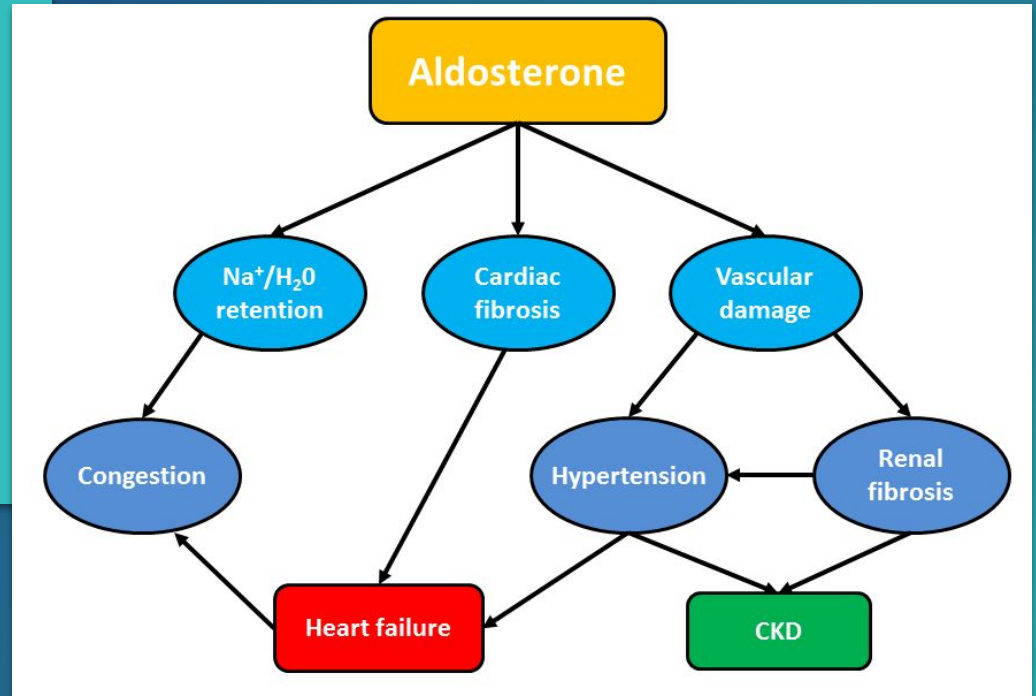




Selective Mineralocorticoid Receptor Antagonists for Diabetic Kidney Disease

Background

- Increasing recognition of role of aldosterone in promoting inflammation and tissue damage (fibrosis)
- Spironolactone and eplerenone shown to reduce albuminuria in animal models and small clinical trials

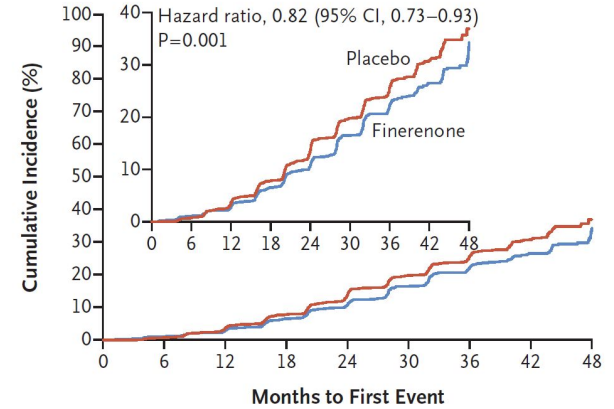


FIDELIO-DKD

- RCT (n=5734) of finerenone vs placebo in patients with DM2
 - eGFR 25-60 w ACR 30-300, or eGFR 25-75 w ACR 300-5000
 - On optimal doses of ACEI or ARB
 - Baseline $K \leq 4.8$
- Primary outcome: 40% decrease in eGFR, ESRD, death from renal causes
 - 17.8% in finerenone vs 21.1% in placebo
- Safety outcomes
 - Any hyperkalemia: 18.3% vs 9.0%
 - Hyperkalemia requiring discontinuation: 2.3% vs 0.9%

Bakris, *NEJM* 2020;383:2219-29

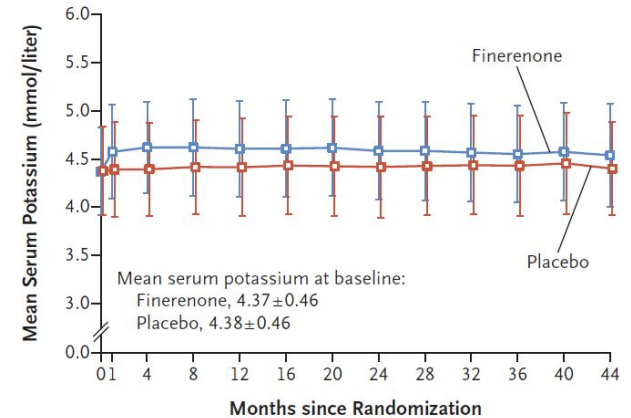
A Primary Composite Outcome



No. at Risk

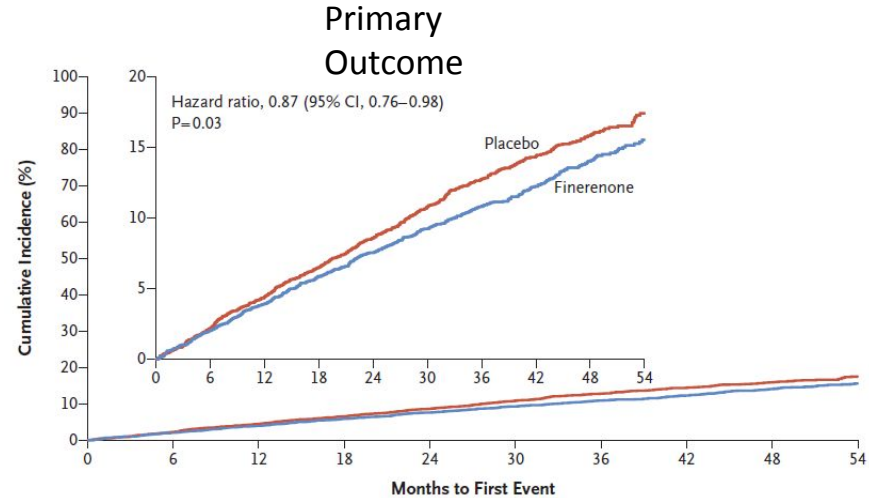
Placebo	2841	2724	2586	2379	1758	1248	792	453	82
Finerenone	2833	2705	2607	2397	1808	1274	787	441	83

Mean Serum Potassium

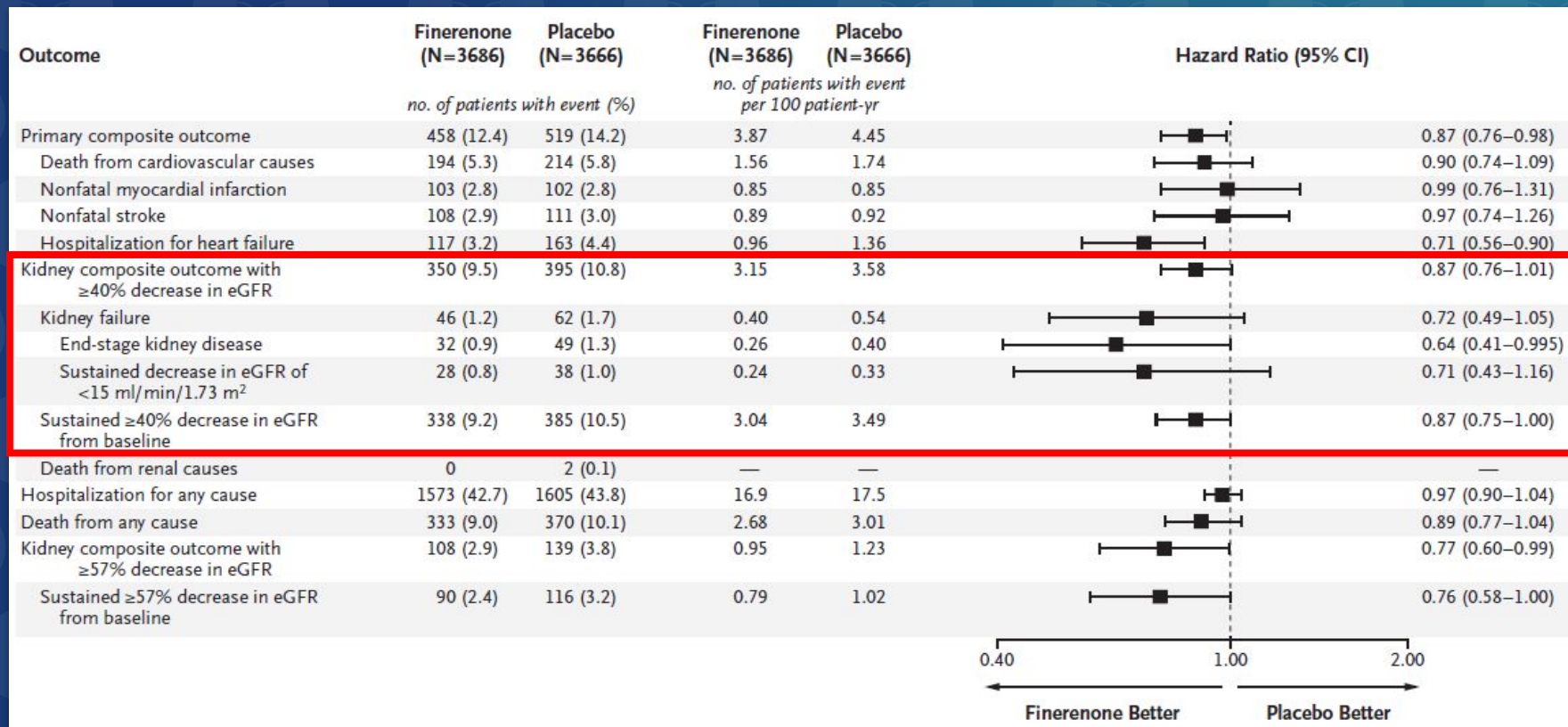


FIGARO-DKD

- RCT (n=7437) of finerenone vs placebo in pts with T2D and CKD
 - eGFR 25-90 plus UACR 30-300
 - **eGFR >60 plus UACR 300-5000**
 - Median follow-up 3.4yrs
- Primary outcome: composite of CV death, MI, CVA or CHF hospitalization
- Secondary outcome: composite of ESKD, 40% decrease in eGFR, renal death



FIGARO-DKD



Incorporation into Guidelines

- Finerenone approved 7/9/21
- ADA 2024, Recommendation 11.5d As people with CKD and albuminuria are at increased risk for cardiovascular events and CKD progression, a nonsteroidal mineralocorticoid receptor antagonist that has been shown to be effective in clinical trials is recommended to reduce cardiovascular events and CKD progression (if eGFR is ≥ 25 mL/min/1.73m²). Potassium levels should be monitored. (A)
- KDIGO 2022, Recommendation 1.3.1: We suggest a nonsteroidal MRA for pts with T2D, an eGFR ≥ 25 , normal serum potassium and albuminuria >30 despite maximum tolerated dose of RAS inhibitor (2A).



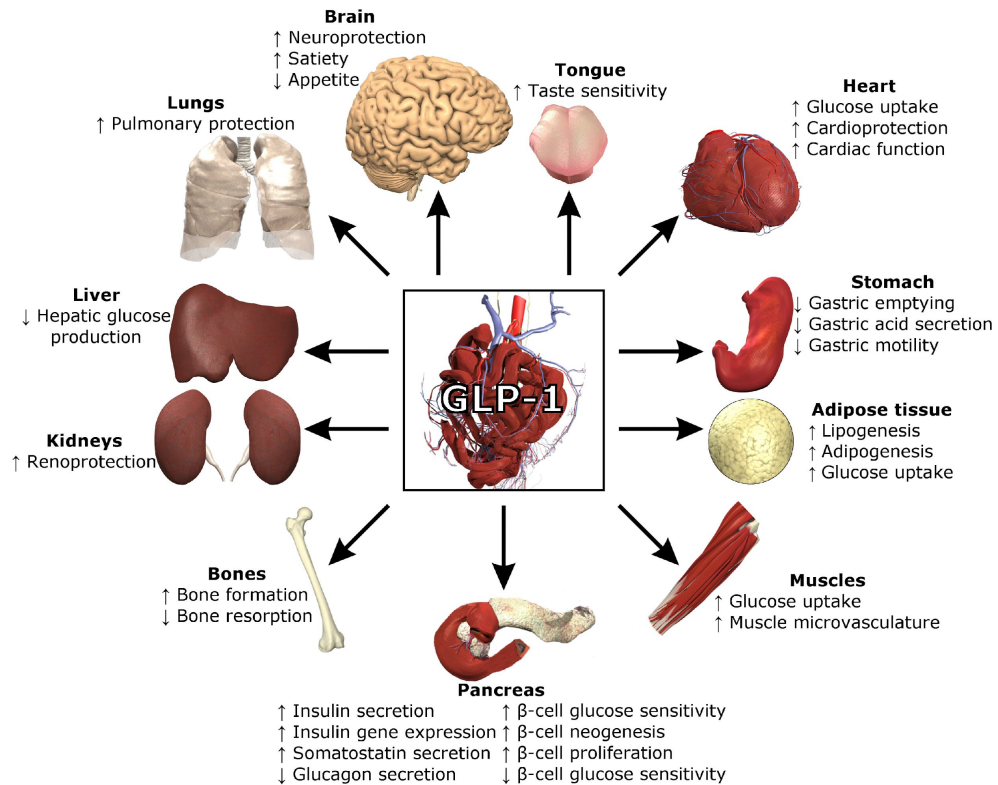
MRA Comparison

	Spironolactone (steroidal)	Eplerenone (steroidal)	Finerenone (non-steroidal)
Receptor Selectivity	Low	Medium	High
Tissue Distribution	Kidney>>Heart	Kidney>Heart	Kidney = Heart
Hyperkalemia	++	++	+
Effect on Lowering BP	++	+	Minimal
Anti-Androgenic	++	+	None
Clinical Evidence*	-	-	+
Cost	\$	\$\$	\$\$\$

* Demonstrated outcome benefit in patients with diabetic kidney disease

MRA Unanswered Questions

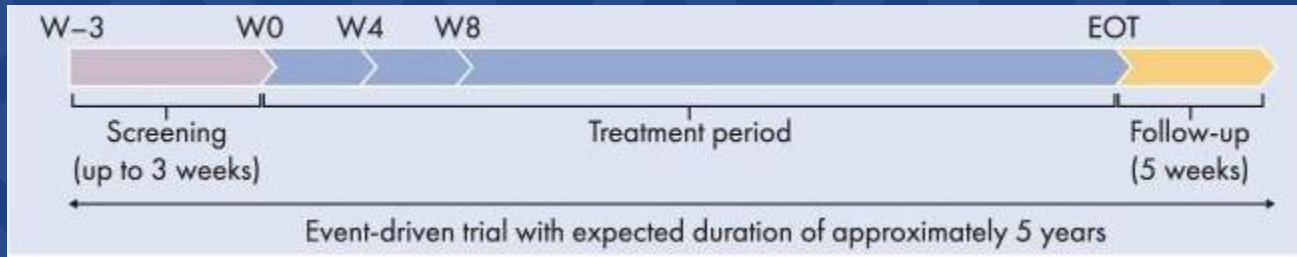
- Role in non-diabetic CKD?
 - Clinical trial initiated 2021 with estimated completion 2025
- Benefits compared to/in combination with SGLT2i?
 - Clinical trial of finerenone vs empagliflozin vs both in patients with diabetic kidney disease, initiated 2022 with estimated completion 2024
- Benefits compared to older MRA's (spironolactone, eplerenone)?



Updates on GLP-1 RA in Diabetic Kidney Disease

FLOW Trial

- RCT of semaglutide (8wk dose escalation from 0.25 to 1.0mg/wk) vs placebo (n=3534) in patients with T2D and CKD
- Primary outcome: composite of 50% decrease in eGFR, ESKD, renal death, CV death
- 10/10/23 new release: study stopped early due to recommendations from DSMB based on interim analysis *meeting efficacy criteria*



Summary

- SGLT2 inhibitors are beneficial in both diabetic and non-diabetic kidney disease
- Non-steroidal MRAs (finerenone) reduce CV risk and improve renal outcomes in patients with T2D and CKD
- There may be emerging evidence for improved renal outcomes with GLP-1 RA
- Likely change in guidelines for whether to use an SGLT2i or a GLP-1 RA and how to choose.