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	• 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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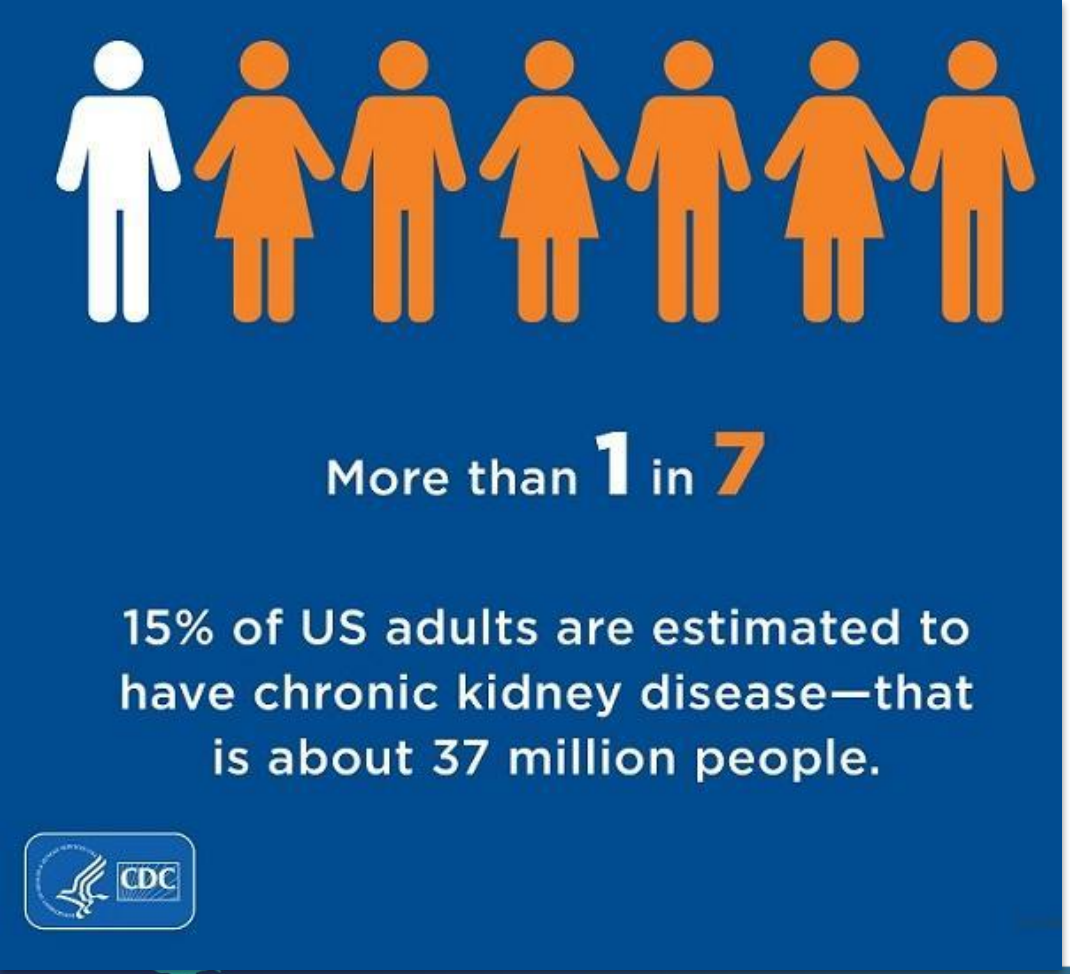
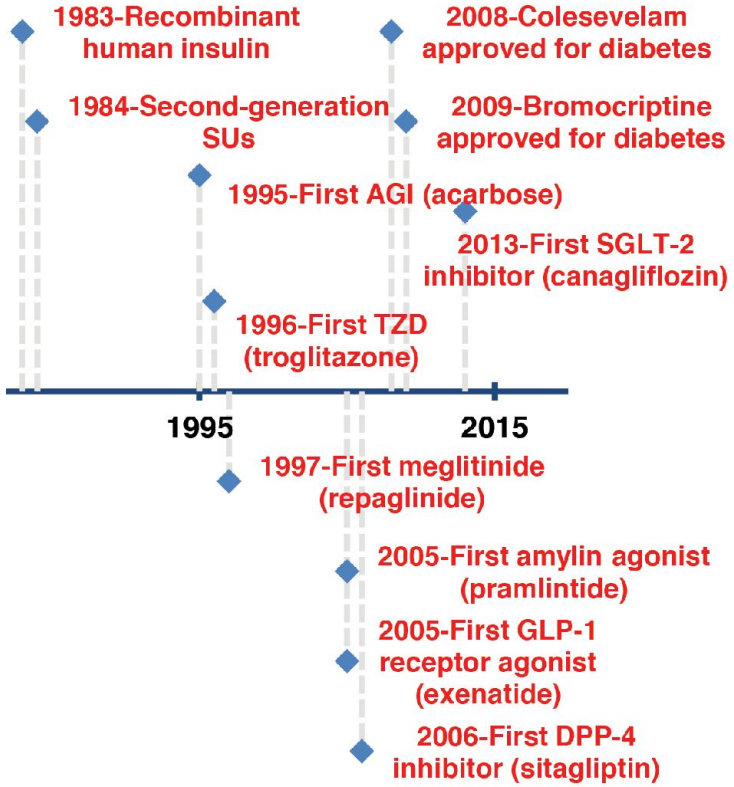


SGLT-2 Inhibitors for Diabetic and Non-Diabetic Chronic Kidney Disease

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

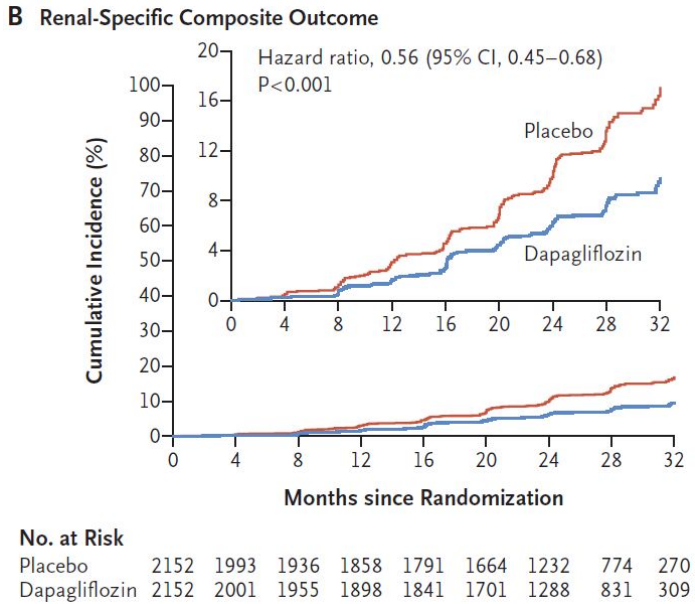


White, *Diab Spect* 2014;27:82-6

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 <u>plus</u> 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

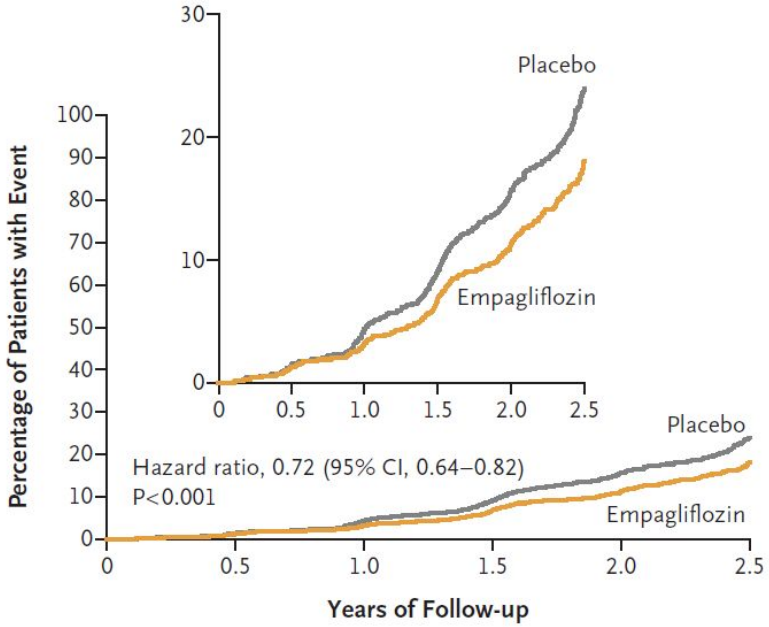


Type 2 DM	Dapa	Placebo	HR (95% CI)
Yes	152/1455	229/1451	0.64 (0.52-0.79)
No	**45/697**	**83/701**	**0.50 (0.35-0.72)**

Heerspink, *NEJM* 2020;383:1436-46

EMPA-Kidney

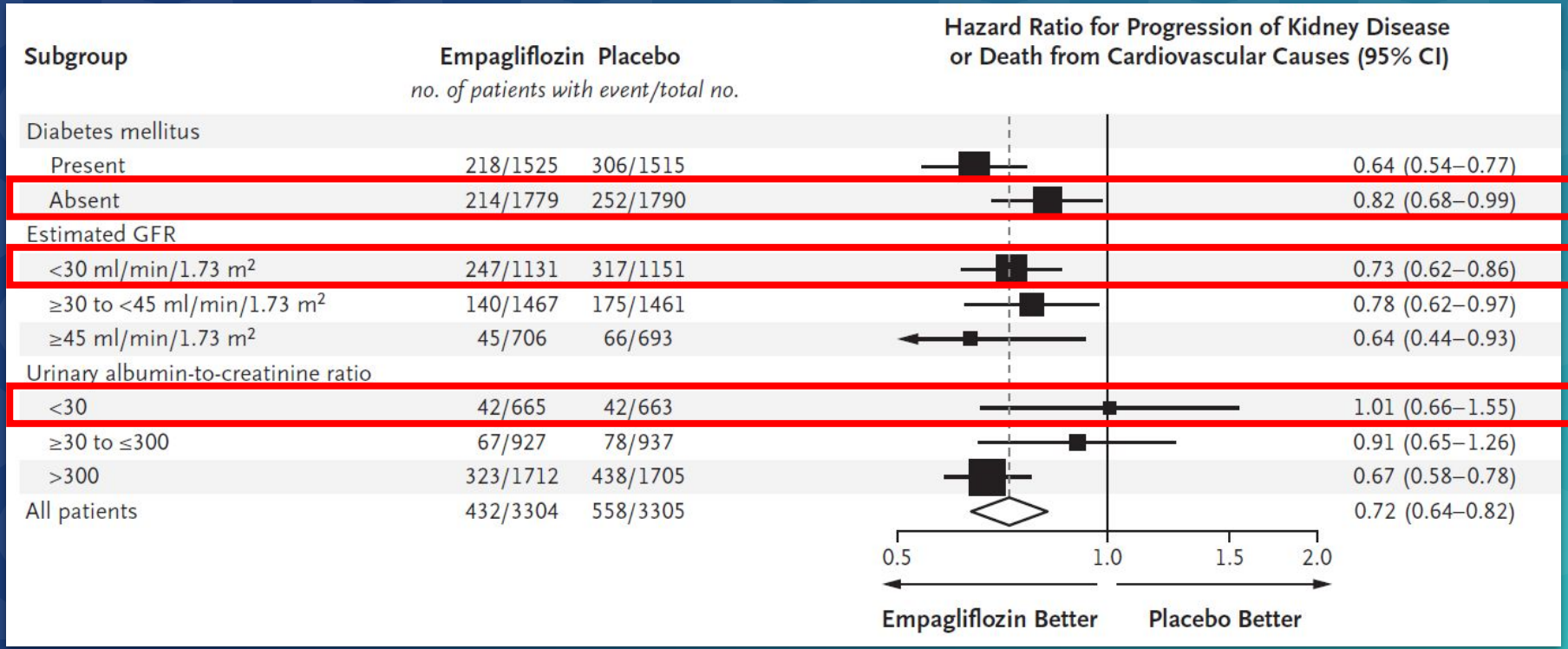
- RCT (n=6609) of empagliflozin vs placebo in patients with (46%) or without (54%) DM
  - eGFR **20**-45, or 45-90 with albuminuria (ACR>200)
- Primary outcome: composite of ≥40% reduction in eGFR, ESRD, death from renal or CV causes



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

Herrington, *NEJM* 2023;388(2):117-27

EMPA-Kidney



Herrington, *NEJM* 2023;388(2):117-27

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

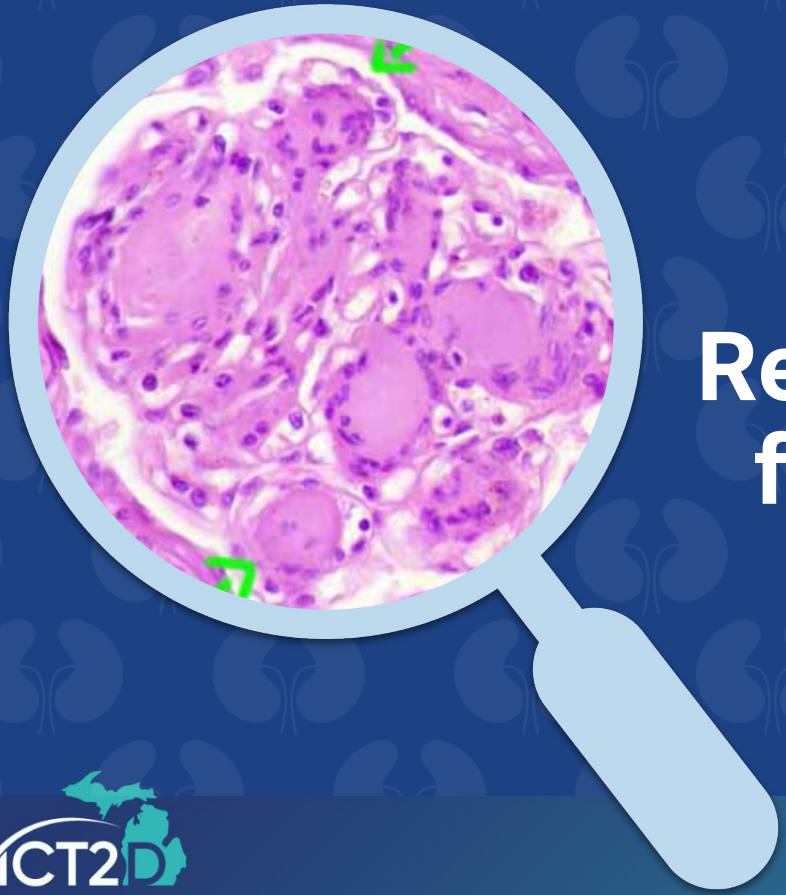
- Non-diabetic CKD without albuminuria

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

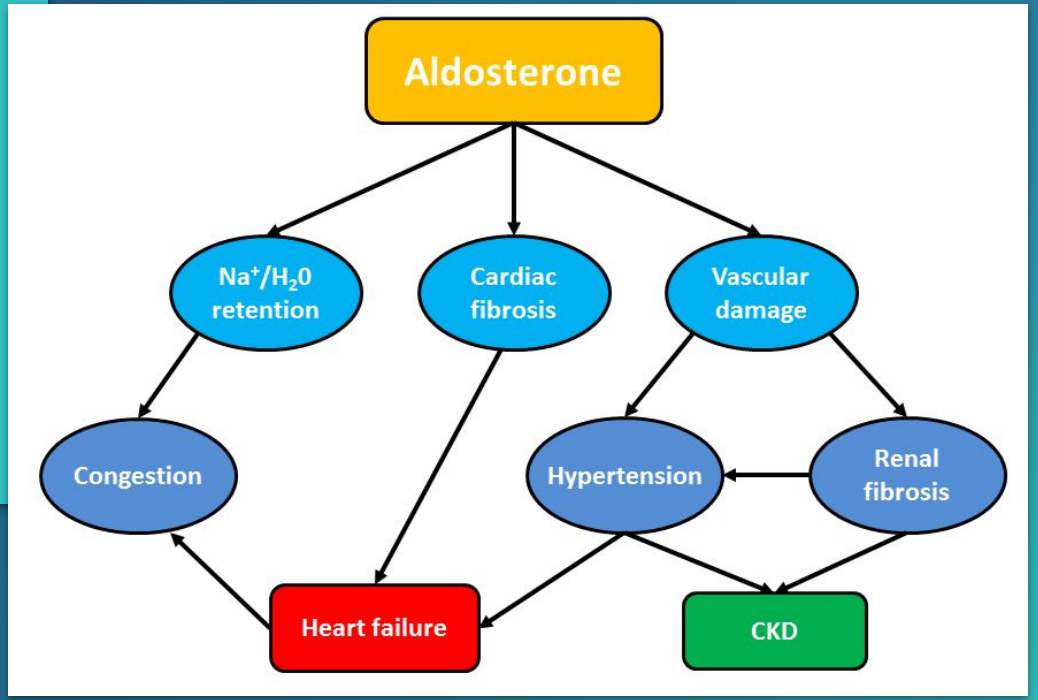
mct2d.org/resource-library/patient-handout-on-slgt2-glp1



Selective Mineralocorticoid Receptor Antagonists for Diabetic Kidney Disease

Background

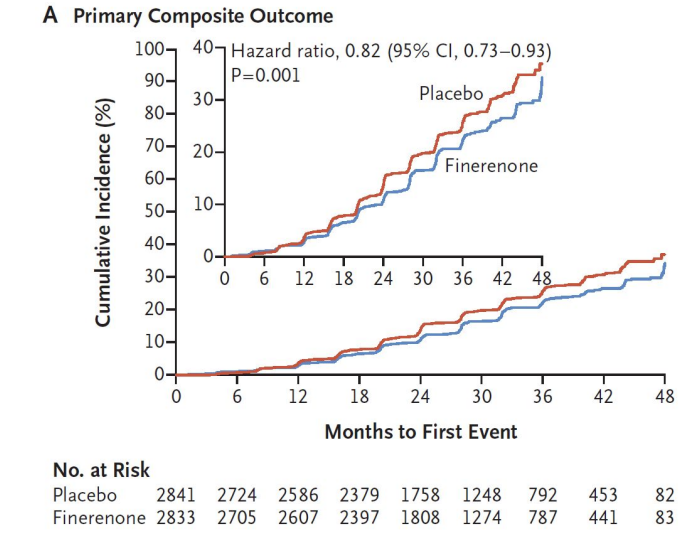
- Increasing recognition of role of aldosterone in promoting inflammation and tissue damage (fibrosis)
- Spironolactone and eplerenone shown to reduce albuminuria in animal models and small clinical trials

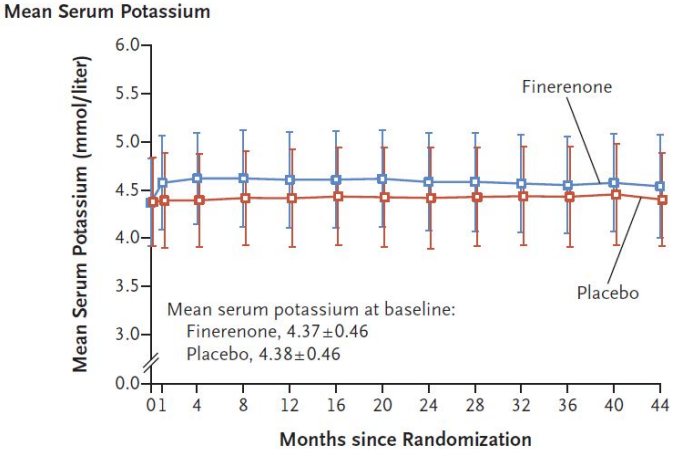


FIDELIO-DKD

- 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≤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

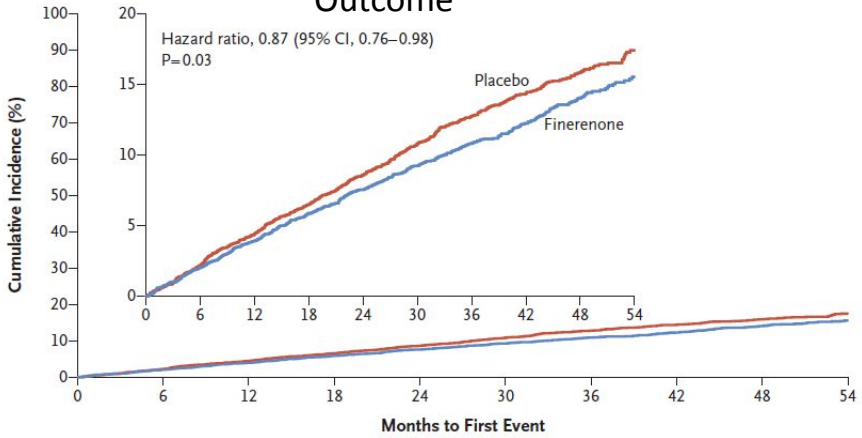




FIGARO-DKD

- 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

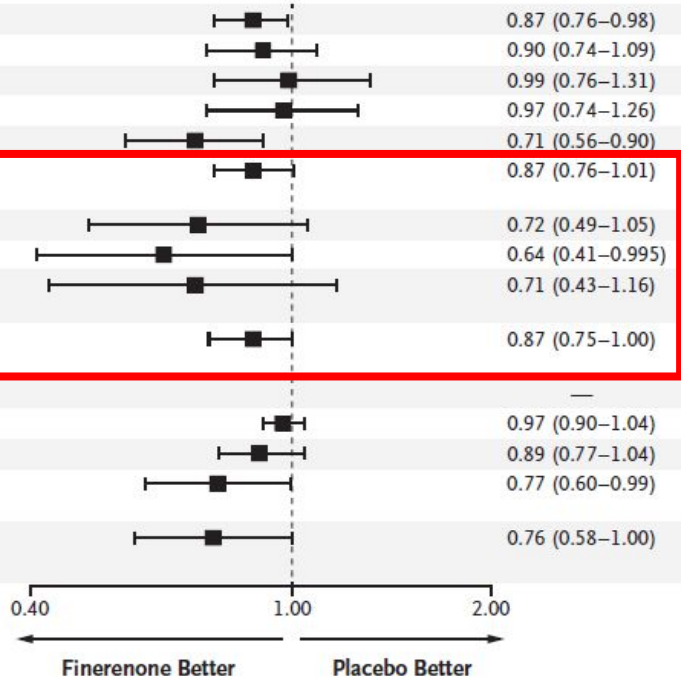
Primary Outcome



Pitt et al, *NEJM* 2021;385:2252-63

FIGARO-DKD

Outcome	Finerenone (N=3686)	Placebo (N=3666)	Finerenone (N=3686)	Placebo (N=3666)	Hazard Ratio (95% CI)
	no. of patients with event (%)		*no. of patients with event per 100 patient-yr*		
Primary composite outcome	458 (12.4)	519 (14.2)	3.87	4.45	0.87 (0.76–0.98)
Death from cardiovascular causes	194 (5.3)	214 (5.8)	1.56	1.74	0.90 (0.74–1.09)
Nonfatal myocardial infarction	103 (2.8)	102 (2.8)	0.85	0.85	0.99 (0.76–1.31)
Nonfatal stroke	108 (2.9)	111 (3.0)	0.89	0.92	0.97 (0.74–1.26)
Hospitalization for heart failure	117 (3.2)	163 (4.4)	0.96	1.36	0.71 (0.56–0.90)
Kidney composite outcome with ≥40% decrease in eGFR	350 (9.5)	395 (10.8)	3.15	3.58	0.87 (0.76–1.01)
Kidney failure	46 (1.2)	62 (1.7)	0.40	0.54	0.72 (0.49–1.05)
End-stage kidney disease	32 (0.9)	49 (1.3)	0.26	0.40	0.64 (0.41–0.995)
Sustained decrease in eGFR of <15 ml/min/1.73 m^2	28 (0.8)	38 (1.0)	0.24	0.33	0.71 (0.43–1.16)
Sustained ≥40% decrease in eGFR from baseline	338 (9.2)	385 (10.5)	3.04	3.49	0.87 (0.75–1.00)
Death from renal causes	0	2 (0.1)	—	—	—
Hospitalization for any cause	1573 (42.7)	1605 (43.8)	16.9	17.5	0.97 (0.90–1.04)
Death from any cause	333 (9.0)	370 (10.1)	2.68	3.01	0.89 (0.77–1.04)
Kidney composite outcome with ≥57% decrease in eGFR	108 (2.9)	139 (3.8)	0.95	1.23	0.77 (0.60–0.99)
Sustained ≥57% decrease in eGFR from baseline	90 (2.4)	116 (3.2)	0.79	1.02	0.76 (0.58–1.00)



Pitt et al, *NEJM* 2021;385:2252-63

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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 ≥25mL/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).

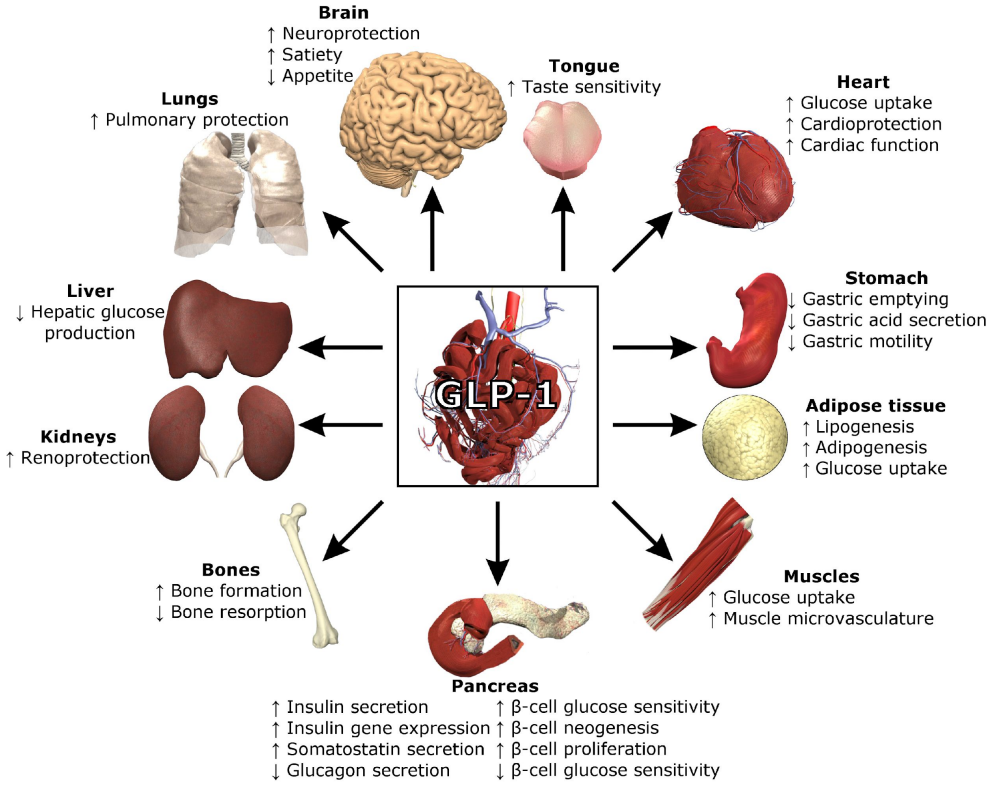
MRA Comparison

	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*

Rossing P, Baeres FMM, Bakris G, Bosch-Traberg H, Gislum M, Gough SCL, Idorn T, Lawson J, Mahaffey KW, Mann JFE, Mersebach H, Perkovic V, Tuttle K, Pratley R. The rationale, design and baseline data of FLOW, a kidney outcomes trial with once-weekly semaglutide in people with type 2 diabetes and chronic kidney disease. Nephrol Dial Transplant. 2023 Aug 31;38(9):2041-2051. doi: 10.1093/ndt/gfad009. Erratum in: Nephrol Dial Transplant. 2024 Mar 27;39(4):724. PMID: 36651820; PMCID: PMC10469096.

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.