

CLINICAL CASE:

Patient with T2D and Established CKD

52-year-old woman

- History
 - 12-year history of diabetes
 - 5-year history of hypertension
- Vitals
 - BP 138/86
 - HR 86
- Physical Exam
 - Unremarkable
- Labs
 - Hemoglobin A1c 7.6%
 - K⁺ 4.3 mmol/L
 - eGFR 47 mL/min/1.73 m²
 - UACR 176 mg/g

Medications (past 6 months)

- Telmisartan 80 mg/day
- Amlodipine 5 mg/day
- Metformin
 - 1 g in the morning
 - 0.5 g in the evening
- Canagliflozin 100 mg/day
- Atorvastatin 40 mg/day

FIDELITY¹: FIDELIO-DKD² + FIGARO-DKD³ Pooled Analysis

• 48 countries

• 13,171 patients randomized

• 3 years of median follow-up



Key Eligibility Criteria

- T2D
- CKD
- On single RAASi
- Serum [K⁺] ≤4.8 mmol/L
- No symptomatic HFrEF

Key Outcomes

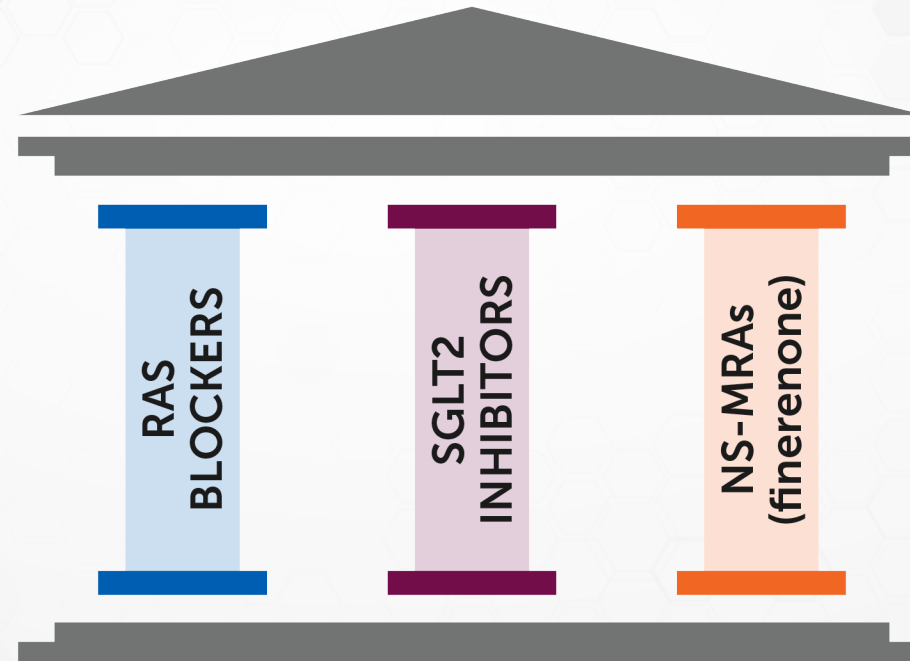
- CV composite
 - Time to CV death, nonfatal MI, nonfatal stroke, or HHF
- ≥40% and ≥57% eGFR kidney composites
 - Time to kidney failure, sustained ≥57% decrease in eGFR from baseline, or renal death

Albuminuria Categories (mg albumin/g creatinine)

		A1 Normal to mildly increased	A2 Moderately increased	A3 Severely increased
		0–29	30–299	≥300–≤5000
GFR Categories (mL/min/1.73 m ²)	G1	≥90		
	G2	60–89		
	G3a	45–59		
	G3b	30–44		
	G4	15–29		

*10 mg if screening eGFR 25–<60 mL/min/1.73 m²; 20 mg if ≥60 mL/min/1.73 m², up-titration encouraged from month 1 if serum potassium ≤4.8 mmol/L and eGFR stable.
 1. Agarwal R, et al. *Eur Heart J*. 2022;43(6):474-484; 2. Bakris GL, et al. *N Engl J Med*. 2020;383(23):2219-2229; 3. Pitt B, et al. *N Eng J Med*. 2021;385(24):2252-2263.

“Pillared Approach” to Therapy in Patients with Diabetic Kidney Disease for Cardiorenal Risk Reduction



Drug classes when used in combinations have been shown to slow kidney disease progression and reduce heart failure hospitalizations

NS-MRA, nonsteroidal mineralocorticoid receptor antagonist; RAS, renin angiotensin system; SGLT2, sodium-glucose transporter 2.
Blazek O, et al. *Amer Heart J Plus: Card Res and Prac.* 2022;19:100187.

FIDELIO-DKD and FIGARO-DKD Clinical Trials

Albuminuria Categories¹
(mg albumin/g creatinine)

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	G2	60–89		
	G3a	45–59		
	G3b	30–44		
	G4	15–29		
	G5	<15		

FIDELIO-DKD² (5,674 randomized patients)

Primary outcome: Kidney composite



Finerenone significantly **slowed CKD progression by 18%** vs placebo in patients with advanced CKD in T2D, irrespective of baseline use of SGLT2is and GLP-1RAs

FIGARO-DKD^{3,4} (7,437 randomized patients)

Primary outcome: CV composite



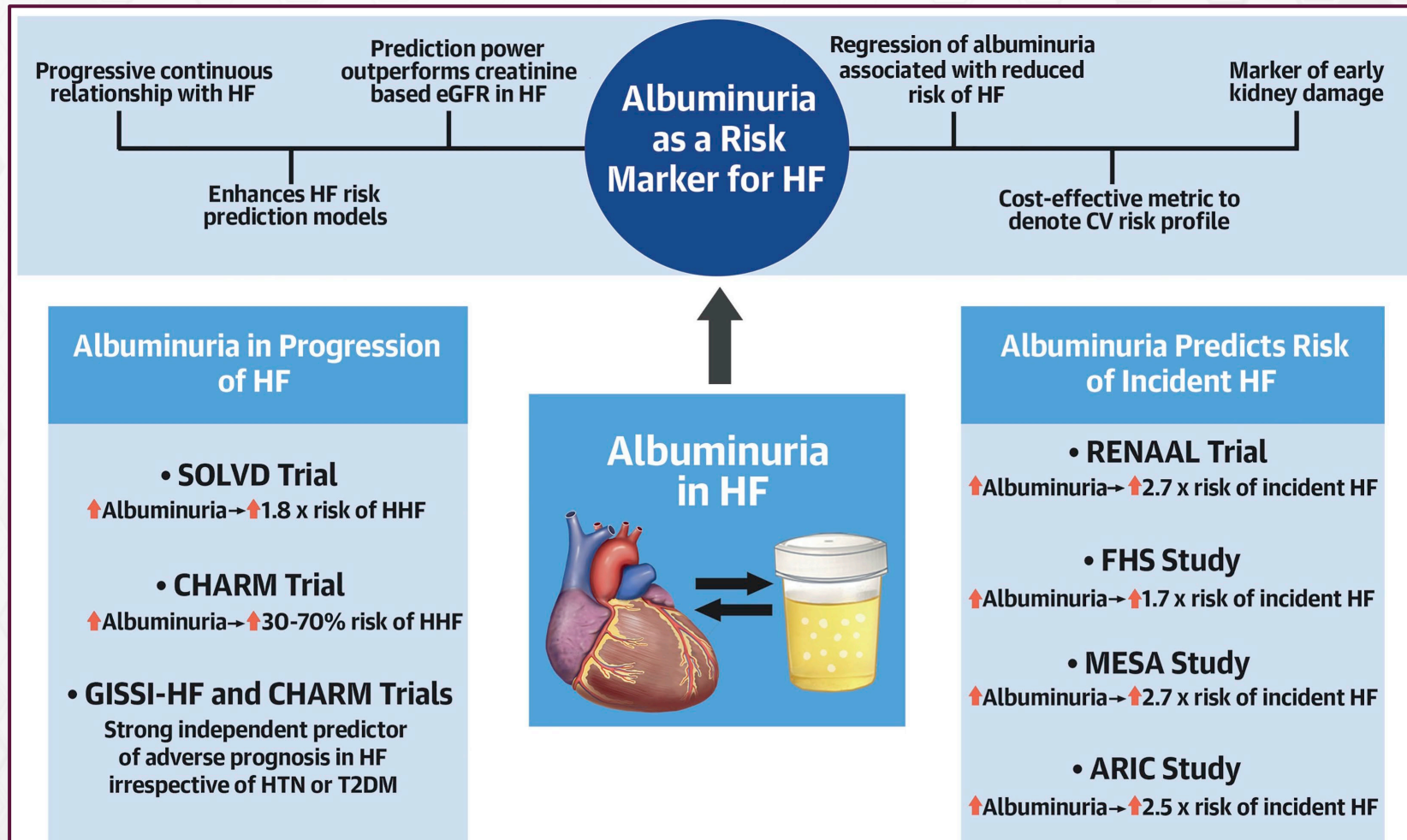
Finerenone significantly **reduced the risk of the primary CV outcome by 13%** vs placebo in patients with CKD in T2D on top of optimized RAAS blockade

RAAS, renin-angiotensin-aldosterone system.

1. Kidney Disease Improving Global Outcomes. *Kidney Int Suppl.* 2013;3(1):1-150; 2. Bakris GB, et al. *N Engl J Med.* 2020;383(23):2219-2229;

3. Ruilope LM, et al. *Am J Nephrol.* 2019;50(5):345-356; 4. Pitt B, et al. *N Engl J Med.* 2021;385(24):2252-2263.

Albuminuria as a Risk Marker for Heart Failure



Khan MS, et al. *J Am Coll Cardiol.* 2023;81(3):270-282.

CLINICAL CASE:

Patient with T2D and Early-Stage CKD

50-year-old man

- History
 - 10-year history of diabetes
 - Multiple comorbidities
 - > Obesity BMI 42
 - > Hypertension
 - > Coronary disease (currently asymptomatic)
 - > PCI
 - Symptomatic HFpEF NYHA Class 2
- Vitals
 - BP 123/75
- Physical Exam
 - Unremarkable
- Labs
 - Hemoglobin A1c 6.2%
 - LDL-C 40 mg/dL
 - eGFR 79 mL/min/1.73 m²
 - UACR 874 mg/g

Medications

- Low-dose aspirin
- High-intensity statin
- Losartan 100 mg/day
- Amlodipine 5 mg/day
- Furosemide 40 mg/day
- Empagliflozin 10 mg/day
- Semaglutide 2 mg/week (T2D)

ADA/KDIGO Consensus Statements 2022

- All patients with type 1 diabetes should be treated with a comprehensive plan, including medical nutrition therapy, physical activity, smoking cessation, and weight, upon which other therapies selected.
- An ACE inhibitor (ACEi) or angiotensin receptor inhibitor (ARDi) is recommended for patients with hypertension and albuminuria.
- A statin is recommended for all patients with atherosclerotic cardiovascular disease (ASCVD) or with multiple ASCVD risk factors.
- Metformin is recommended for patients with type 2 diabetes (T2D) and eGFR ≥ 30 mL/min/1.73 m²; the dose should be adjusted for some patients with eGFR 45–59 mL/min/1.73 m².
- A sodium–glucose cotransporter inhibitor (SGLT2i) is recommended for patients with T2D, CKD, and eGFR ≥ 25 mL/min/1.73 m².
- A glucagon-like peptide 1 (GLP-1) receptor agonist is recommended for patients with T2D and CKD who do not meet criteria to use these drugs.
- A nonsteroidal mineralocorticoid receptor antagonist (MRA) is recommended for patients with T2D and albuminuria (albumin-to-creatinine ratio ≥ 30 mg/g) on a renin-angiotensin system (RAS) inhibitor.



treated with a comprehensive plan, including medical nutrition, exercise, smoking cessation, and weight, upon which other therapies selected.

for patients with T1D or T2D who do not meet criteria for the highest tolerated dose.

for primary prevention of cardiovascular disease (ASCVD) and some patients with T2D.

with an eGFR ≥ 30 mL/min/1.73 m² and in patients with eGFR 30–44 mL/min/1.73 m² and in patients with eGFR ≥ 30 mL/min/1.73 m².

cardiovascular benefit is recommended for patients with T2D and CKD who can be continued at lower levels of albuminuria.

cardiovascular benefit is recommended for patients with T2D and CKD and/or an SGLT2i or who are unable to use these drugs.

cardiovascular benefit is recommended for patients with T2D and albuminuria on a renin-angiotensin system (RAS) inhibitor.

de Boer IH, et al. *Diabetes Care*. 2022;45(12):3073–3084.

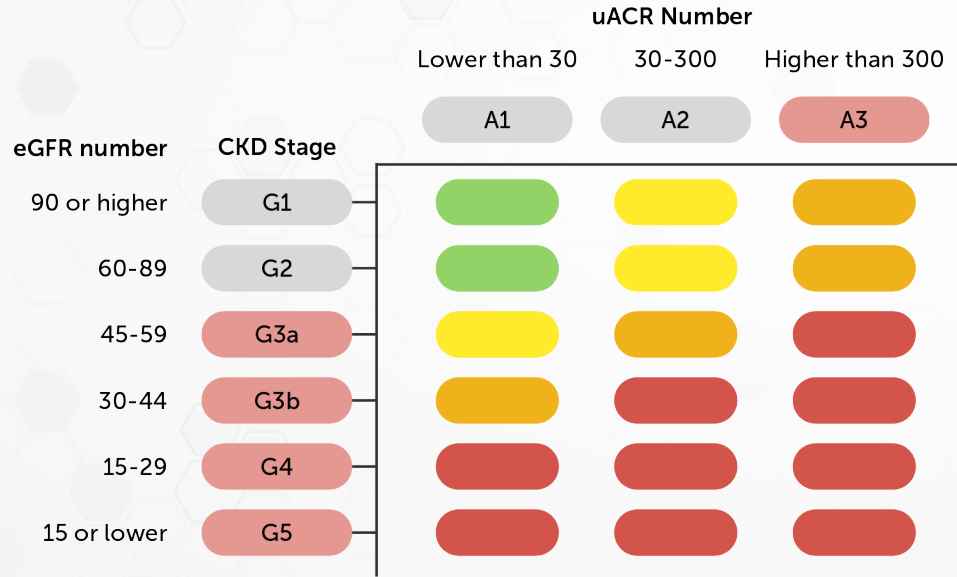
ADA/KDIGO Consensus Statements 2022

- All patients with type 1 diabetes (T1D) or type 2 diabetes (T2D) and CKD should be treated with a comprehensive plan, outlined and agreed by health care professionals and the patient together, to optimize nutrition, exercise, smoking cessation, and weight, upon which are layered evidence-based pharmacologic therapies aimed at preserving organ function and other therapies selected to attain intermediate targets for glycemia, blood pressure (BP), and lipids.
- An ACE inhibitor (ACEi) or angiotensin II receptor blocker (ARB) is recommended for patients with T1D or T2D who have hypertension and albuminuria, titrated to the maximum antihypertensive or highest tolerated dose.
- A statin is recommended for all patients with T1D or T2D and CKD, moderate intensity for primary prevention of atherosclerotic cardiovascular disease (ASCVD) or high intensity for patients with known ASCVD and some patients with multiple ASCVD risk factors.
- Metformin is recommended for patients with T2D, CKD, and estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m²; the dose should be reduced to 1,000 mg daily in patients with eGFR 30–44 mL/min/1.73 m² and in some patients with eGFR 45–59 mL/min/1.73 m² who are at high risk of lactic acidosis.
- A sodium–glucose cotransporter 2 inhibitor (SGLT2i) with proven kidney or cardiovascular benefit is recommended for patients with T2D, CKD, and eGFR ≥ 20 mL/min/1.73 m². Once initiated, the SGLT2i can be continued at lower levels of eGFR.
- A glucagon-like peptide 1 (GLP-1) receptor agonist with proven cardiovascular benefit is recommended for patients with T2D and CKD who do not meet their individualized glycemic target with metformin and/or an SGLT2i or who are unable to use these drugs.
- A nonsteroidal mineralocorticoid receptor antagonist (ns-MRA) with proven kidney and cardiovascular benefit is recommended for patients with T2D, eGFR ≥ 25 mL/min/1.73 m², normal serum potassium concentration, and albuminuria (albumin-to-creatinine ratio [ACR] ≥ 30 mg/g) despite maximum tolerated dose of renin-angiotensin system (RAS) inhibitor.

de Boer IH, et al. *Diabetes Care*. 2022;45(12):3075-3090.

Kidney Numbers and the CKD Heat Map

If you do have chronic kidney disease, then your doctor will use the **CKD Heat Map** to find out your risk for CKD getting worse and your risk for heart disease.



On *the left side* of the map, your eGFR number matches up with a CKD stage. A higher eGFR number is better because it means you have a lower CKD stage.

eGFR Number	CKD Stage
90 or higher	G1
60-89	G2
45-59	G3a
30-44	G3b
15-29	G4
15 or lower	G5

A **Green** box means you do NOT have chronic kidney disease, or that you are at the lowest risk for CKD getting worse. **Yellow** means increased risk for CKD getting worse. **Orange** means high risk for CKD getting worse. **Red** means the highest risk for CKD getting worse.

On the top of the map, your uACR number matches up with a uACR level. A lower uACR is better because that means less albumin in the urine

uACR Number	uACR Level
Lower than 30	A1, normal – mildly increased
30-300	A2, moderately increased
Higher than 300	A3, severely increased

CKD, chronic kidney disease; GFR, glomerular filtration rate; uACR, urine albumin-creatinine ratio. National Kidney Foundation. Kidney numbers and the CKD heat map - educate your patients. September 29, 2022. Accessed June 12, 2023. <https://www.kidney.org/content/kidney-numbers-and-ckd-heat-map-educate-your-patients>