CLINICAL CASE: Patient with T2D and Established CKD

52-year-old woman

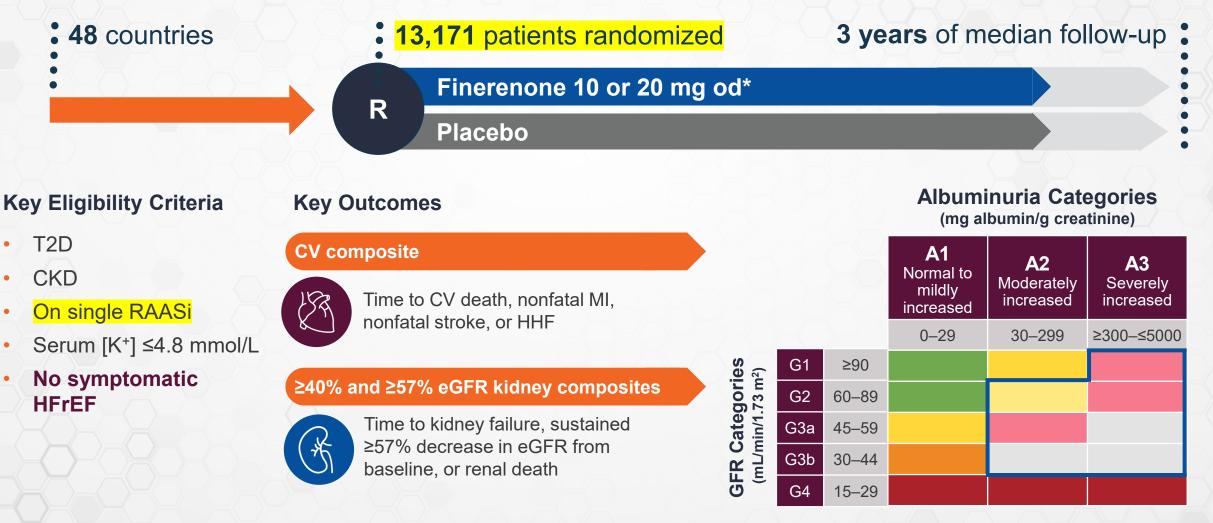
- History
 - 12-year history of diabetes
 - 5-year history of hypertension
- Vitals
 - BP 138/86
 - HR 86
- Physical Exam
 - Unremarkable
- Labs

- Hemoglobin A1c 7.6%
- K⁺ 4.3 mmol/L
- eGFR 47 mL/min/1.73 m²
- UACR 176 mg/g

Medications (past 6 months)

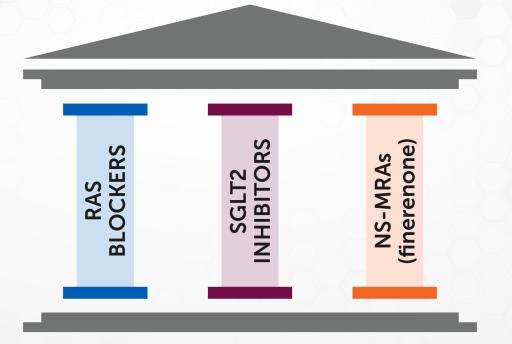
- Telmisartan 80 mg/day
- Amlodipine 5 mg/day
- Metformin
 - 1 g in the morning
 - 0.5 g in the evening
- Canagliflozin 100 mg/day
- Atorvastatin 40 mg/day

FIDELITY¹: FIDELIO-DKD² + FIGARO-DKD³ Pooled Analysis



*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)

			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			
$\mathbf{\tilde{\mathbf{A}}}$	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



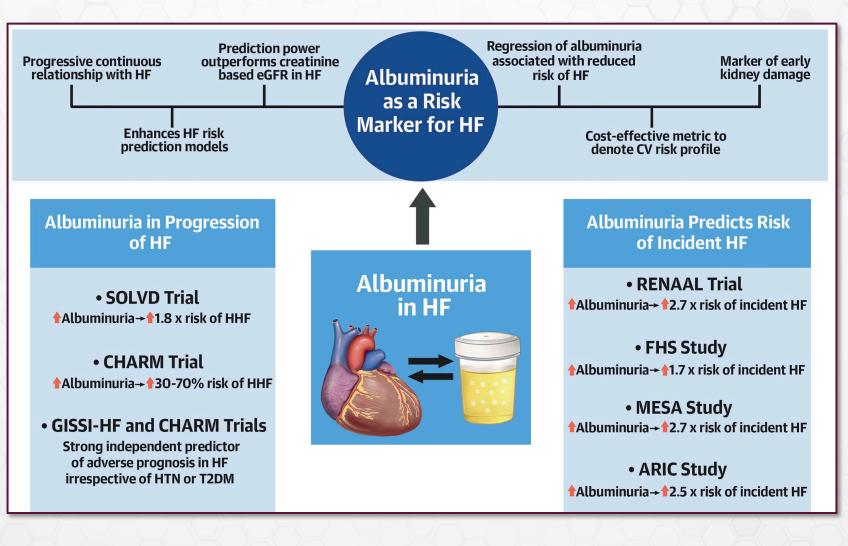
Finerenone significantly reduced the risk of the primary CV outcome by 13% vs placebo in patients with CKD in T2D on top of optimized RAAS blockade

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.

Takeaways for Clinicians from the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in CKD Top



Comprehensive care

Patients with diabetes and CKD have multisystem disease that requires treatment including a foundation of lifestyle intervention (healthy diet, exercise, weight management, no smoking) and drug therapy that improves kidney and cardiovascular outcomes (glucose, lipids, blood pressure).

Nutrition intake

Patients should consume a balanced, healthy diet that is high in vegetables, fruits, whole grains, fiber, legumes, plant-based proteins, unsaturated fats, and nuts; and lower in processed meats, refined carbohydrates, and sweetened beverages. Sodium (<2 g/day) and protein intake (0.8 g/kg/day) in accordance with recommendations for the general population.

SGLT2i

SGLT2i should be initiated for patients with T2D and CKD when eGFR is ${\geq}20$ ml/min/1.73 m² and can be continued after initiation at lower levels of eGFR. SGLT2i markedly reduce risks of CKD progression, heart failure, and atherosclerotic cardiovascular diseases, even when blood glucose is already controlled.

Metformin

Metformin should be used for patients with T2D and CKD when eGFR is ≥30 ml/min/1.73 m². For such patients, metformin is a safe, effective, and inexpensive drug to control blood glucose and reduce diabetes complications.

Glycemic monitoring and targe

HbA1c should be measured regularly. Reliability decreases with advanced CKD, particularly for patients treated with dialysis, and results should be interpreted with caution. CGM or SMBG may also be useful, especially for treatment associated with risk of hypoglycemia. Targets for glycemic control should be individualized, ranging from <6.5% to <8.0%.

GLP-1 RA

In patients with T2D and CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2i, or who are unable to use those medications, a long-acting GLP-1 RA is recommended as part of the treatment.

RAS blockade

Patients with T1D or T2D, hypertension, and albuminuria (persistent ACR ≥30 mg/g) should be treated with a RAS inhibitor (ACEi or ARB), titrated to the maximum approved or highest tolerated dose. Serum potassium and creatinine should be monitored.

Non-steroidal mineralocorticoid antagonists (ns-MRA)

ns-MRA reduce risks of CKD progression and cardiovascular events for people with T2D and residual albuminuria. They are suggested for patients with T2D, urine ACR ≥30 mg/g, and normal serum potassium on other standard of care therapies. Serum potassium and creatinine should be monitored.

Approaches to management

A team-based and integrated approach to manage these patients should focus on regular assessment, control of multiple risk factors, and structured education in self-management to protect kidney function and reduce risk of complications.

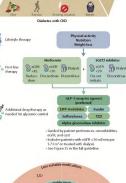
Research recommendations

medtelligence[™]

There is a paucity of data on optimal management of diabetes in kidney failure, including dialysis and transplantation, which should be one important focus for future studies.

ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin-creatinine ratio; ARB, angiotensin II receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA1c, hemoglobin A1c (glycated hemoglobin); RAS, renin-angiotensin system; SGLT2i, sodium-glucose cotransporter-2 inhibitor; SMBG, self-monitoring blood glucose; T1D, type 1 diabetes; T2D, type 2 diabetes

KDIGO. https://kdigo.org/wp-content/uploads/2022/10/KDIGO-2022-Diabetes-Management-in-CKD-Guideline-Top-10-Takeaways-for-Clinicians.pdf







1.2.

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
- **Physical Exam**
 - Unremarkable
- Labs

- Hemoglobin A1c 6.2%
- LDL-C 40 mg/dL
- eGFR 79 mL/min/1.73 m²
- UACR 874 mg/g

- BP 123/75

Furosemide 40 mg/day

Medications

Low-dose aspirin

High-intensity statin

Losartan 100 mg/day

Amlodipine 5 mg/day

- Empagliflozin 10 mg/day
- Semaglutide 2 mg/week (T2D)

ADA/KDIGO Consensus Statements 2022

- All patients with type 1 diabetes outlined and agreed by health ca cessation, and weight, upon which function and other therapies sele
- An ACE inhibitor (ACEi) or angio have hypertension and albuminu
- A statin is recommended for all p atherosclerotic cardiovascular di with multiple ASCVD risk factors
- Metformin is recommended for p mL/min/1.73 m²; the dose should some patients with eGFR 45–59
- A sodium-glucose cotransporter patients with T2D, CKD, and eGI eGFR
- A glucagon-like peptide 1 (GLP-T2D and CKD who do not meet to use these drugs.
- A nonsteroidal mineralocorticoid recommended for patients with 7 albuminuria (albumin-to-creatinin (RAS) inhibitor.

de Boer IH, et al. Diabetes Care. 2022;45(12):307



A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO) C.M. Rhee, S.E. Rosas, P. Rossina, and G. Bakris

Using Data to Improve the Management of Diabetes: The Tayside Experience M.K. Siddiqui, C. Hall, S.G. Cunningham, R. McCrimmor

Routine Islet Autoantibody Testing in Clinically Diagnosed Adult-Onset Type 1 Diabetes Can Help Identify Misclassification and the Possibility of Successful Insulin Cessation

R.J. Eason, N.J. Thomas, A.V. Hill, B.A. Knight, A. Carr, A.T. Hattersley, T.J. McDonald, B.M. Shields, and A.G. Jones, for the StartRight Study Group

Ten-Year Effectiveness of the Multidisciplinary Risk Assessment and Management Programme-Diabetes Mellitus (RAMP-DM) on Macrovascular and Microvascular Complications and All-Cause Mortality: A Population-Based Cohort Study

W.Y. Chin, D.V.K. Chao, W.W.S. Tsui, T.K.H. Ha, C.K.H. Wong, and



treated with a comprehensive plan, e nutrition, exercise, smoking

patients with T1D or T2D who nest tolerated dose.

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fit is recommended for patients with nd/or an SGLT2i or who are unable

nd cardiovascular benefit is ssium concentration, and dose of renin-angiotensin system

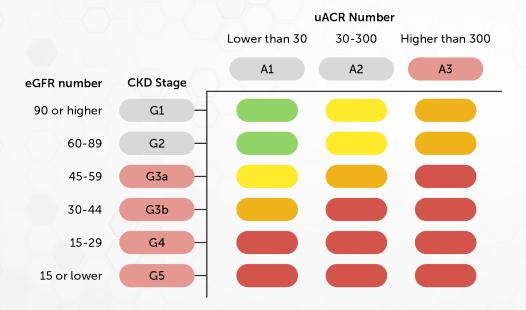
ADA/KDIGO Consensus Statements 2022

- 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.



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 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

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