Selective Mineralocorticoid Receptor Antagonists for the **Treatment of Chronic** and **Diabetic Kidney Disease:** WHICH OF YOUR PATIENTS MAY BENEFIT?

This activity is provided by Med Learning Group.
This activity is co-provided by Ultimate Medical Academy/Complete Conference Management (CCM).
This activity has been supported by an educational grant from Bayer HealthCare Pharmaceuticals Inc.

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Program Agenda

I. Epidemiology and Implications for Increased Renal and CVD Risks in Patients with DKD

a. Case study
b. Definitions
c. Prevalence and mortality due to DKD in the US
d. Renal functional decline

II. Inflammation, Fibrosis and Activation of MRs Drive the Progression of CKD in Patients with DKD

a. Video 1: Mechanisms of fibrosis
b. Activation of RAAS
c. Adverse renal and CV effects of aldosterone
d. Pathogenesis of diabetic nephropathy

III. Screening Assessments for CKD that Assist in the Early Diagnosis of DKD in Clinical Practice

a. Importance of early recognition
b. Diagnosis and testing for DKD

IV. New and Emerging Renoprotective Agents for the Treatment of DKD

a. SGLT2 inhibitors
    - Mechanisms and clinical trials
b. Mineralocorticoid receptor antagonists
    - Mechanisms and clinical trials
    - *Video 2: role of MRAs in management of DKD*
c. Mechanisms of action and clinical profiles

V. Preventive Measures to Mitigate the Risk of Hyperkalemia

VI. Conclusions and Q/A

Selective Mineralocorticoid Receptor Antagonists for the Treatment of Chronic and Diabetic Kidney Disease: Which of Your Patients May Benefit?

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PROGRAM OVERVIEW

The case-based virtual live activity will cover the treatment and management of patients with chronic and diabetic kidney disease.

TARGET AUDIENCE

This educational activity is designed for US-based nephrologists and other healthcare professionals with an interest in treating patients with CKD, T2DM and CVD.

LEARNING OBJECTIVES

Upon the completion of this program, attendees should be able to:

- Specify the pathophysiological mechanisms underlying CKD that result in increased renal and CVD risks for patients with DKD
- Assess the roles of inflammation, fibrosis, and activation of MRs in the progression of CKD in patients with DKD
- Integrate evidence-based guideline screening assessments for CKD that may facilitate an earlier diagnosis of DKD into routine clinical practice
- Interpret data from clinical trials assessing the efficacy and safety of investigational renoprotective agents for the treatment of DKD
- Incorporate preventive measures to mitigate the risk of hyperkalemia in patients with DKD receiving MRA therapy

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Purpose: This program would be beneficial for nurses involved in the care of patients with chronic and diabetic kidney disease. **CNE Credits:** 1.0 ANCC Contact Hour.

CNE ACCREDITATION STATEMENT

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George Bakris, MD	Discloses that he has received Consulting fees from Merck, Novo-Nordisk, Bayer, Vascular Dynamics, and Ionis
Amy Freeth, MD	Has nothing to disclose
Mark Molitch, MD	Discloses that he worked as a Consultant for Janssen, Pfizer and Merck. He also received research grant funds from Bayer and Novartis
Dhiren Patel, PharmD, CDE, BC-ADM, BCACP	Discloses that he has worked as a Consultant for Amarin, Bayer, Dexcom, Lilly, Insulet, Novo-Nordisk and Sanofi. He has also worked on the Speakers' Bureau for Abbott, Amarin, Boehringer, Dexcom, Lilly, Merck, Novo-Nordisk, Xeris and Zealand
Richard Pratley, MD	Discloses that he has received Consulting fees from Corept Therapeutics Incorporated, Merck, Novo-Nordisk, Pfizer, Sanofi, Sochia Pharma Inc. and Sun Pharmaceutical Industries. He has also received research grant funding from Hanmi Pharmaceutical Co., Metavention, Novo-Nordisk, Poxel SA and Sanofi, and has been a paid speaker for Novo-Nordisk
Matthew Weir, MD	Discloses that he has received Consulting fees from Merck, Bayer, Vifor, Janssen, AstraZeneca, Novo-Nordisk and Boehringer-Ingelheim

CME Content Review

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The reviewer of this activity has nothing to disclose.

CNE Content Review

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2. Participate in the virtual live activity.
3. Complete the online post-test and evaluation.

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Accreditation

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Agenda

- Mechanisms of increased risk for renal and CV events in DKD
- Inflammation, fibrosis, and activation of MRs in CKD progression in patients with DKD
- CKD screening guidelines for early diagnosis of DKD
- Clinical trials on renoprotective agents for DKD
- Mitigation of hyperkalemia in patients with DKD on MRA therapy

CV = cardiovascular; DKD = diabetic kidney disease; MR = mineralocorticoid receptor; CKD = chronic kidney disease; MRA = MR antagonist.

Case Presentation

Case Presentation

- 68-year-old female with long-standing T2DM and HTN referred for rising serum creatinine and proteinuria
- Exam: BP = 138/73 mm Hg, HR = 86 bpm, weight = 66 kg, no retinopathy, pretibial edema
- Serum creatinine = 1.47 mg/dL, eGFR = 36 (stage 3b)
- Urinalysis: 2+ proteinuria, UACR = 528 mg/g
- Losartan-HCTZ, amlodipine, carvedilol, insulin
- Sonogram: no obstruction, kidneys 10 cm, increased echogenicity

T2DM = type 2 diabetes mellitus; HTN = hypertension; BP = blood pressure; HR = heart rate; bpm = beats per minute; eGFR = estimated glomerular filtration rate; UACR = urine albumin-to-creatinine ratio; HCTZ = hydrochlorothiazide.

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Clinical diagnosis: diabetic nephropathy

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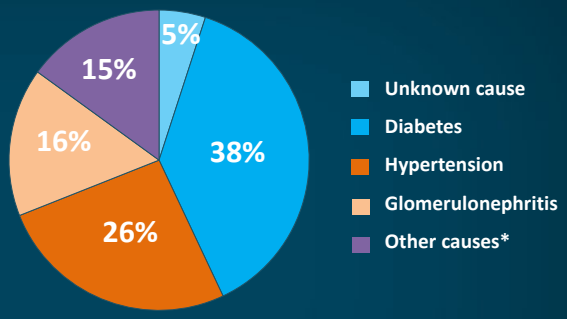
Epidemiology and Implications for Increased Renal and CVD Risks in Patients with DKD

Chronic Kidney Disease by the Numbers

- 37 million US adults are estimated to have CKD, and most are undiagnosed
- Kidney diseases are 9th leading cause of death in US
- 48% of people with severely reduced kidney function and not on dialysis are not aware of having CKD



N = 726,331 (all ages, 2016)
Source: US Renal Data System
*Includes polycystic kidney disease, among other causes

CDC. Chronic kidney disease basics, 2020 (www.cdc.gov/kidneydisease/basics.html).

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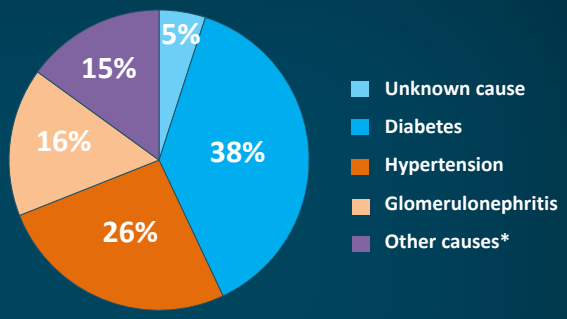

N = 726,331 (all ages, 2016)
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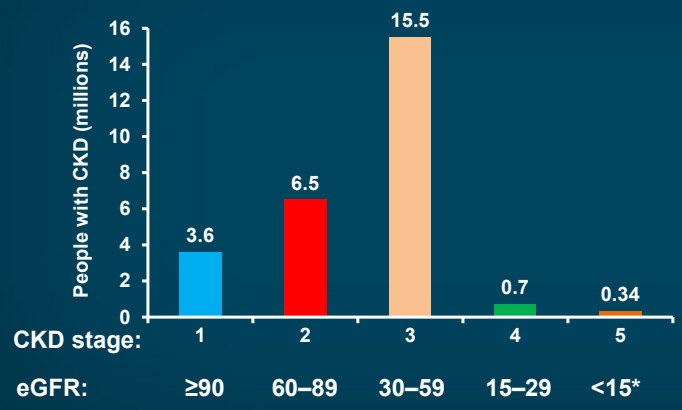
Diabetes is leading cause of ESRD

CDC. Chronic kidney disease basics, 2020 (www.cdc.gov/kidneydisease/basics.html).

Prevalence of CKD in United States

Cross-sectional data (NHANES 1999–2004)



*On dialysis.

NHANES = National Health and Nutrition Examination Survey.

Coresh J, et al. *JAMA*. 2007;298:2038-2047. United States Renal Data System (USRDS). (https://adr.usrds.org/2020/chronic-kidney-disease/1-ckd-in-the-general-population). Accessed 6/10/2021.

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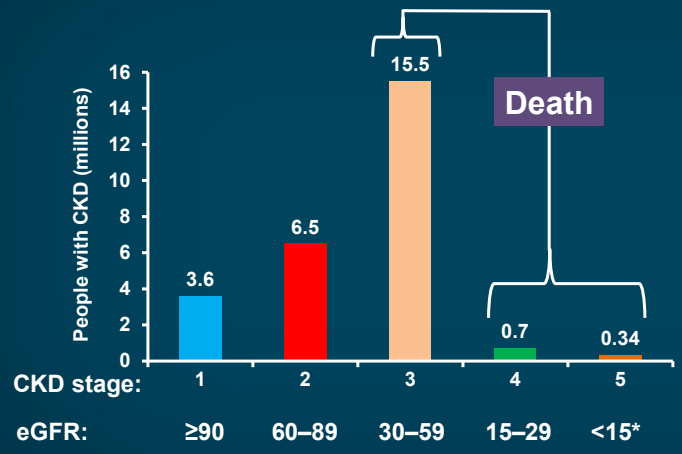

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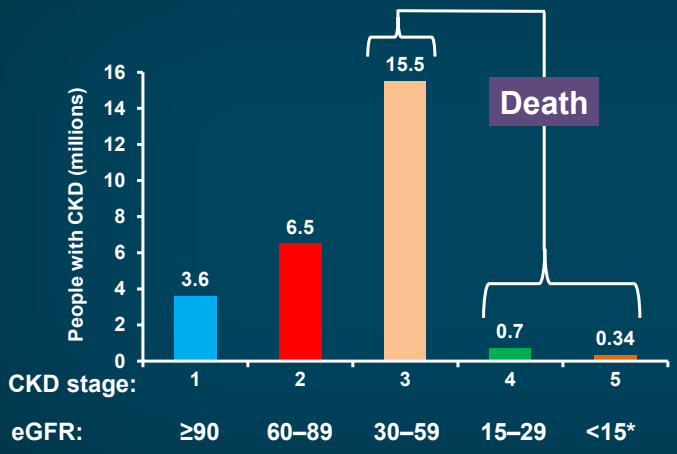


10% progress to ESRD

90% die from…
- CV events
- Infection
- Cancer
- Other

*On dialysis.

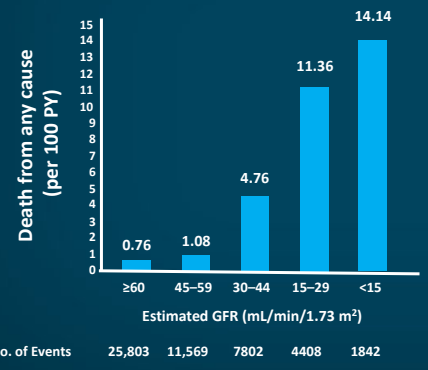
NHANES = National Health and Nutrition Examination Survey.

Coresh J, et al. *JAMA*. 2007;298:2038-2047. United States Renal Data System (USRDS). (https://adr.usrds.org/2020/chronic-kidney-disease/1-ckd-in-the-general-population). Accessed 6/10/2021.

Death and Cardiovascular Event Rates in CKD

1,120,295 ambulatory adults

Death



No. of Events	25,803	11,569	7802	4408	1842

PY = patient/person year(s)

Go AS, et al. *N Engl J Med*. 2004;351:1296-1305.

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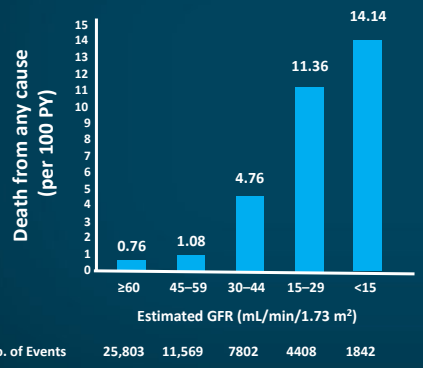
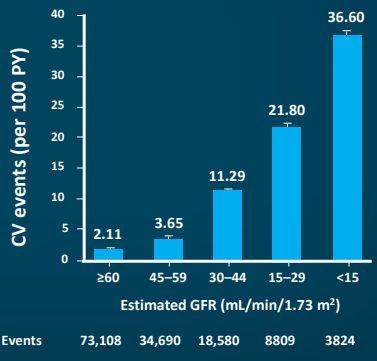


No. of Events	25,803	11,569	7802	4408	1842

CV events



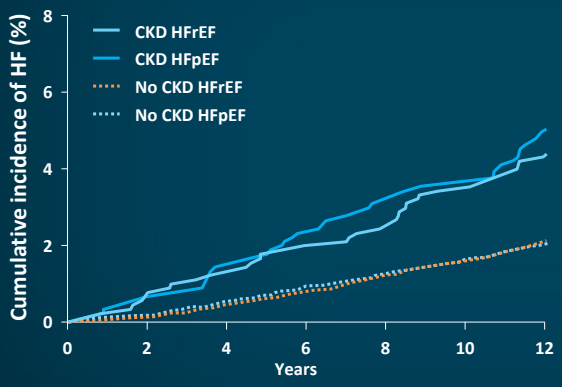
No. of Events	73,108	34,690	18,580	8809	3824

PY = patient/person year(s)

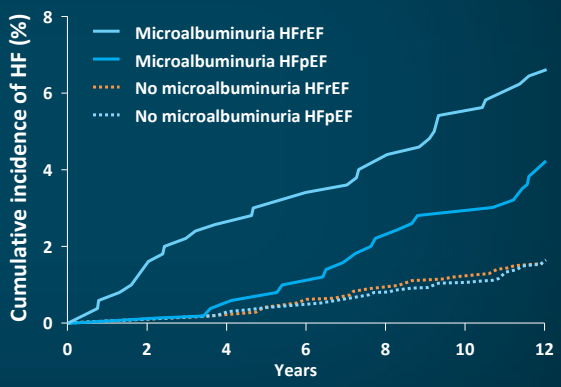
Go AS, et al. *N Engl J Med*. 2004;351:1296-1305.

Declining Renal Function Is Associated with Incident HF

Higher incidence rates of HF in patients with CKD compared with those without CKD



Higher incidence rates of HF in patients with microalbuminuria versus those without microalbuminuria

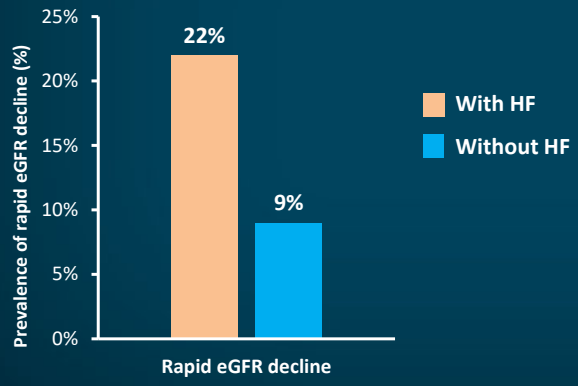


HF = heart failure; HFpEF = HF with preserved ejection fraction; HFrEF = HF with reduced ejection fraction.

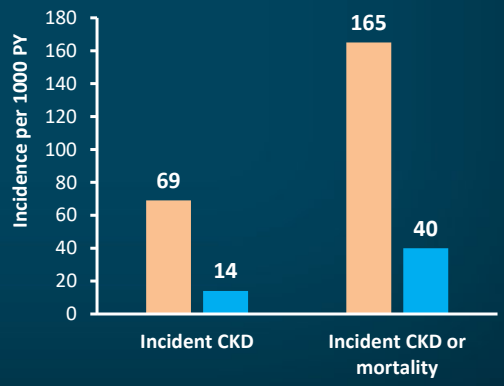
Nayor M, et al. *Eur J Heart Fail.* 2017;19:615-623.

Conversely, HF Increases Risk of Renal Function Decline and Adverse Renal Outcomes

HF is associated with a more rapid decline in eGFR
(defined as slopes steeper than –5 mL/min/1.73m^2/year)



HF is associated with significantly higher risk of incident CKD and incident CKD or mortality
(defined as 2 eGFR values of <60 mL/min/1.73m^2 occurring ≥3 mos apart and a decrease from BL eGFR ≥25%)

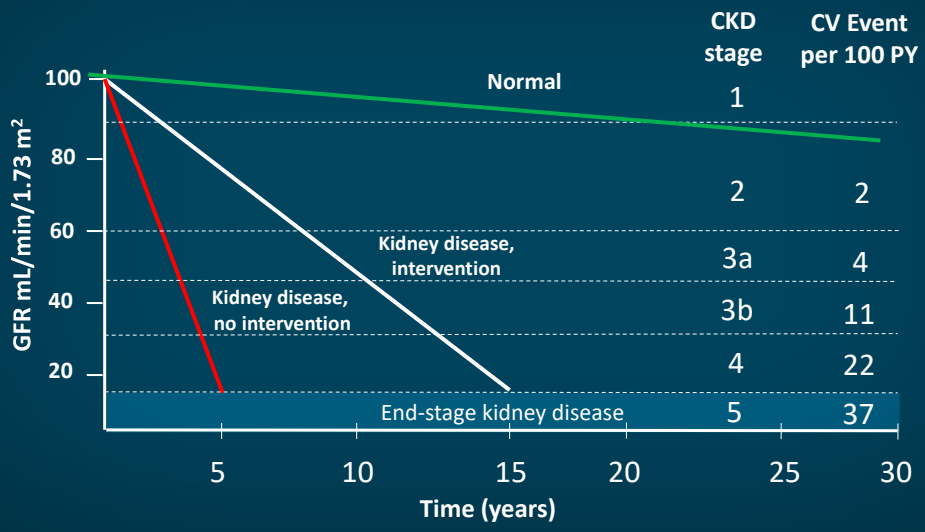


BL = baseline.

George LK, et al. *Circ Heart Fail.* 2017;10:e003825.

Potential Benefit of Slowing Progression of CKD

Lower CV Event Rate



Go AS, et al. *N Engl J Med.* 2004;351:1296-1305. Levey AS, et al. *Am J Kidney Dis.* 1998;32:853-906.

Inflammation, Fibrosis, and Activation of MRs Drive the Progression of CKD in Patients with DKD

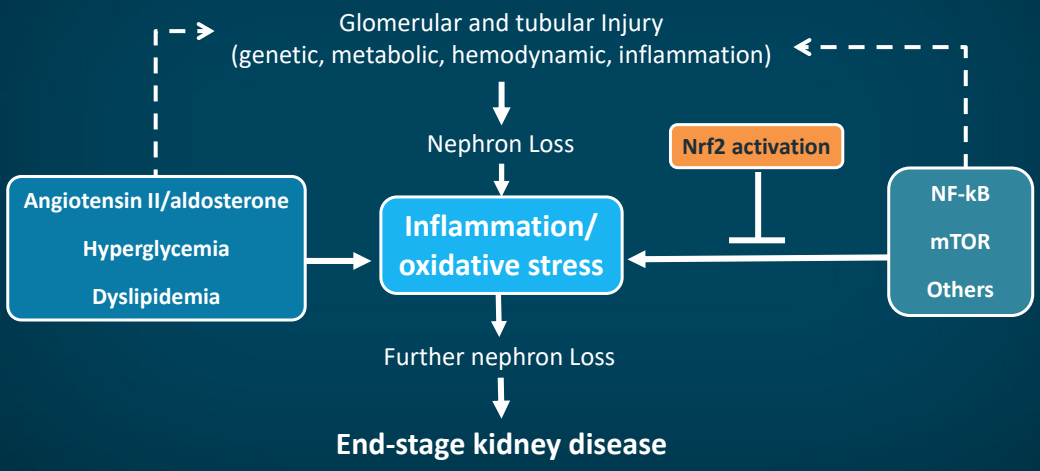
Inflammation, Fibrosis, and Activation of MRs Drive the Progression of CKD in Patients with DKD

Animation

Scan below to watch a brief animation exploring the Pathogenesis of Diabetic Nephropathy

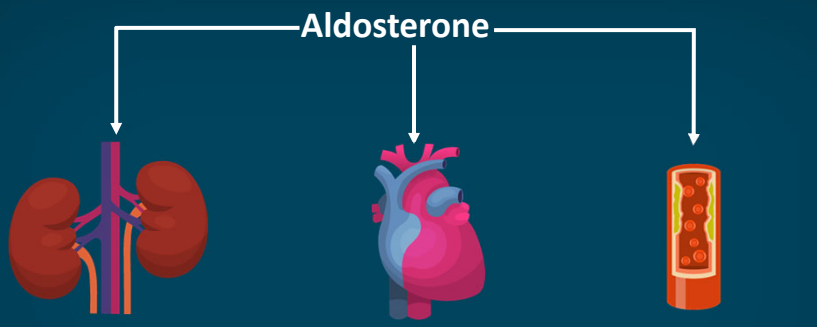
Pathogenesis of Diabetic Nephropathy

Focus on Inflammation and Oxidative Stress



nrf2 = nuclear factor-erythroid 2-related factor 2; NF-kB = nuclear factor-kappa B; mTOR = mammalian target of rapamycin.

Adverse Renal and CV Effects of Aldosterone



Glomerulosclerosis
Interstitial fibrosis
Proteinuria
Renal failure

Ventricular hypertrophy
Cardiac fibrosis
Contractile dysfunction
Heart failure

Endothelial dysfunction
Inflammation
Oxidative stress

Screening Assessments for CKD That Assist in the Early Diagnosis of DKD in Clinical Practice

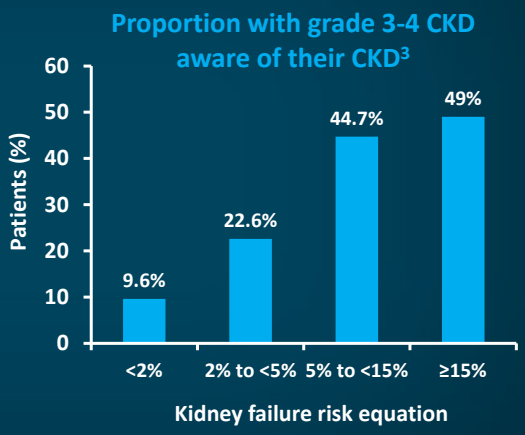
Early Recognition and Treatment of CKD Is Important, Although Identification Is Still Low

40.7%
of patients with 2 eGFR measurements <60 mL/min/1.73m² had diagnostic coding for CKD[1]

1/3
of incident ESKD patients had received little or no pre-ESKD nephrology care[2]

43.2%
of Medicare beneficiaries with DM and HTN, but without CKD, had a urine albumin test in 2017[2]

20.5%
of those with a CKD diagnosis were prescribed an ACEi or ARB[1]



ESKD = end-stage kidney disease; ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin-receptor blocker.

1. Tuttle KR, et al. *JAMA Netw Open*. 2019;2:e1918169. 2. Saran R, et al. *Am J Kidney Dis.* 2020;75(suppl 1):A6-A7. 3. Chu CD, et al. *Am J Kidney Dis.* 2020;76:174-183.

Diagnosis of Diabetic Kidney Disease

The clinical diagnosis of DKD in a patient with diabetes is based on[1,2]

Presence of albuminuria
(UACR ≥300 mg/g, **OR**
UACR 30–299 mg/g **with**:
- Diabetic retinopathy, and/or
- T1DM ≥10 years' duration

OR

Reduced kidney function
(eGFR <60 mL/min/1.73 m²)

In the absence of signs or symptoms of other primary causes of kidney damage

While the natural history of DKD varies, most patients eventually progress to end-stage kidney disease[2]

1. National Kidney Foundation. Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines. *Am J Kidney Dis*. 2007;49(suppl 2):S12-S154. 2. Alicic RZ, et al. *Clin J Am Soc Nephrol.* 2017;12:2032-2045.

Testing For DKD

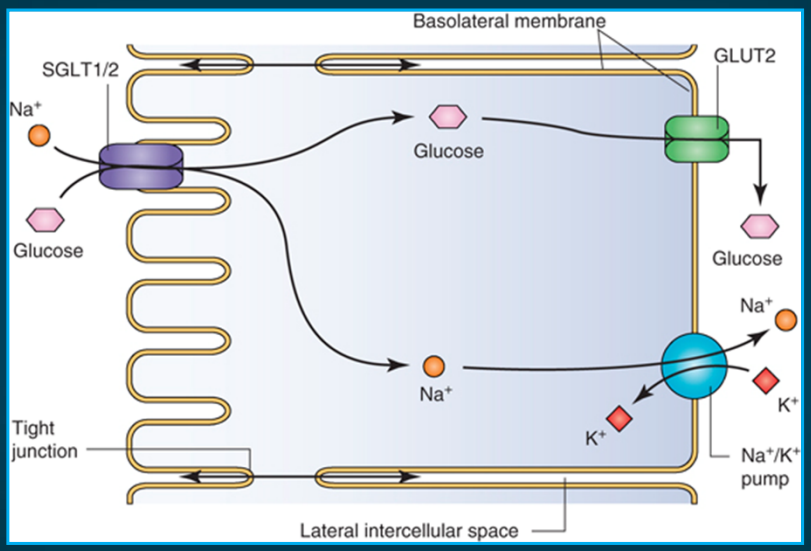
- Annual screening for urinary albumin and eGFR
  - Beginning 5 years after T1DM diagnosis
  - For all patients with T2DM
- Measure UACR and serum creatinine to estimate GFR
- Confirmation of albuminuria or low eGFR requires 2 abnormal measurements ≥3 months apart

American Diabetes Association (ADA). Standards of medical care in diabetes-2021. *Diabetes Care*. 2021;44(suppl 1):S151-S167

New and Emerging Renoprotective Agents for the Treatment of DKD

Sodium Glucose Transporter 2 (SGLT-2) Inhibitors

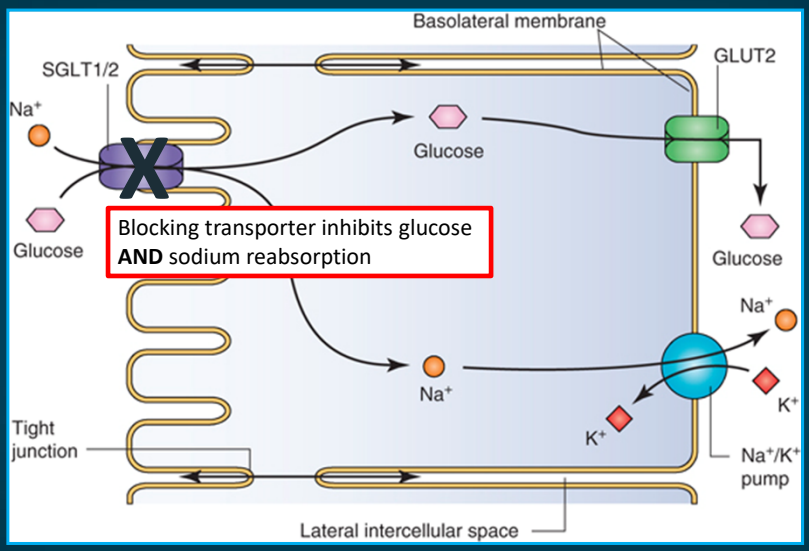
Glucose Transport in Proximal Tubule



SGLT = sodium-glucose cotransporter; Na+ = sodium ion; GLUT = glucose transporter isoform; K+ = potassium ion.

Bakris GL, et al. *Kidney Int*. 2009;75:1272-1277.

Glucose Transport in Proximal Tubule



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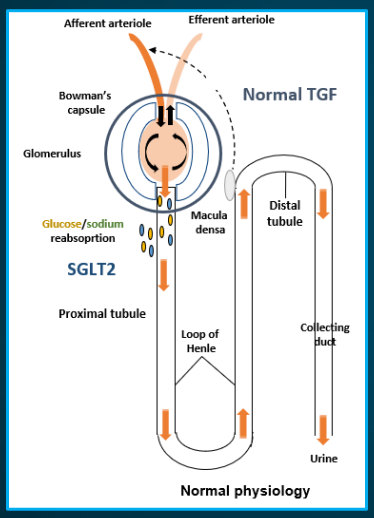
Alterations in Proximal Sodium Reabsorption Modulate Tubuloglomerular Feedback (TGF)



Modified from Cherney DZ, et al. *Circulation*. 2014;129:587–597

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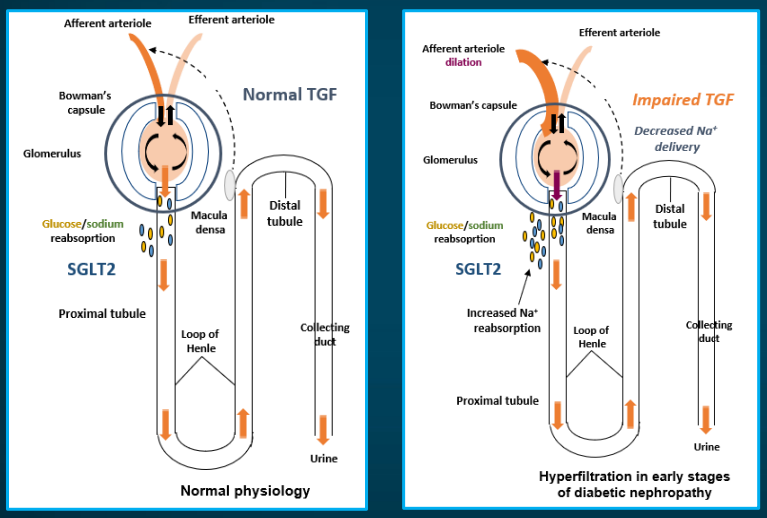
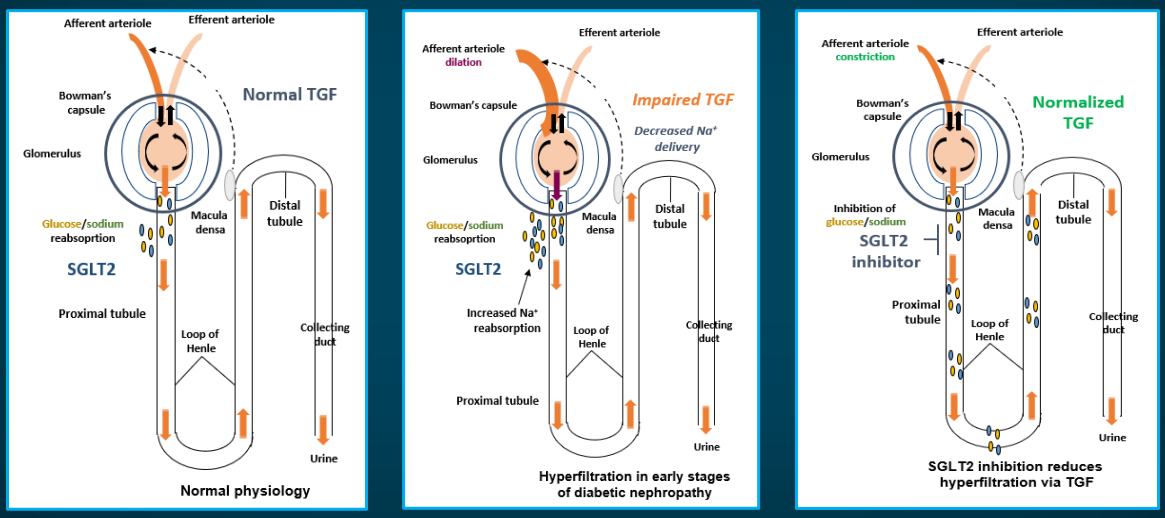


Modified from Cherney DZ, et al. *Circulation.* 2014;129:587–597

Alterations in Proximal Sodium Reabsorption Modulate Tubuloglomerular Feedback (TGF)

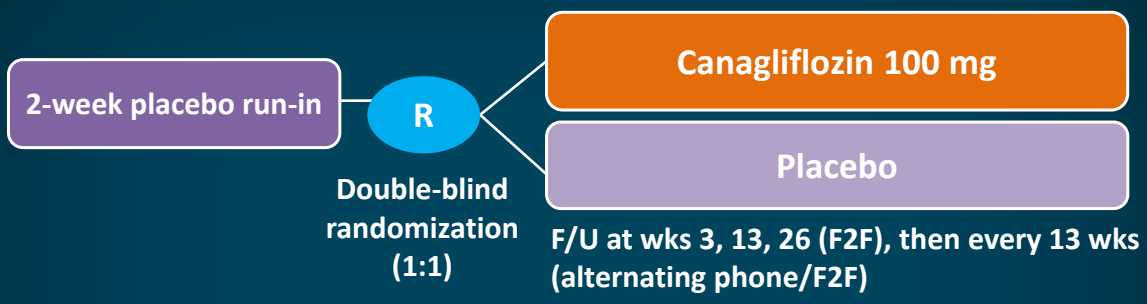


Modified from Cherney DZ, et al. *Circulation.* 2014;129:587–597

Recent Clinical Trials in DKD

SGLT-2 Inhibitors

CREDENCE Trial Design

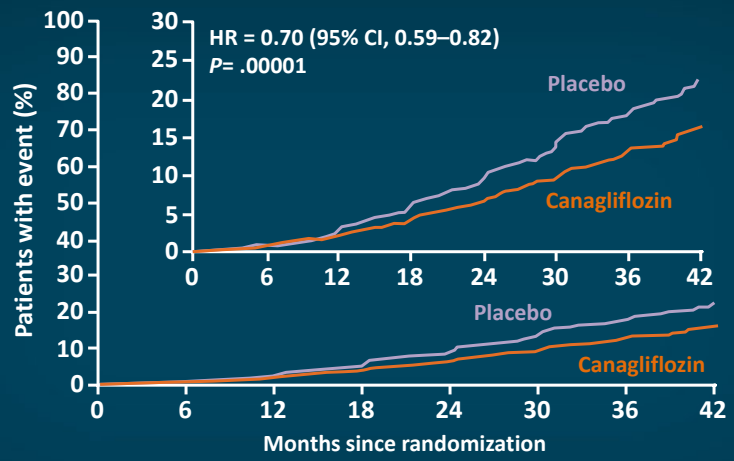


Participants continued Tx if eGFR was <30 until chronic dialysis started or kidney transplant occurred

Primary composite outcome: ESKD, doubling of SCr, renal or CV death

Key inclusion: ≥30 years of age, T2DM eGFR 30-90 mL/min/1.73 m^2, UACR 300 to 5000 mg/g, taking ACEi or ARB
Key exclusion: Other kidney diseases, dialysis, or Tx; CV events w/in 12 wks of screening , NYHA class IV HF
F2F = face-to-face; HbA1c = glycosylated hemoglobin; NYHA = New York Heart Association; SCr = serum creatinine.
Jardine MJ, et al. *Am J Nephrol.* 2017;46:462-472.

CREDENCE: Primary Composite Outcome*

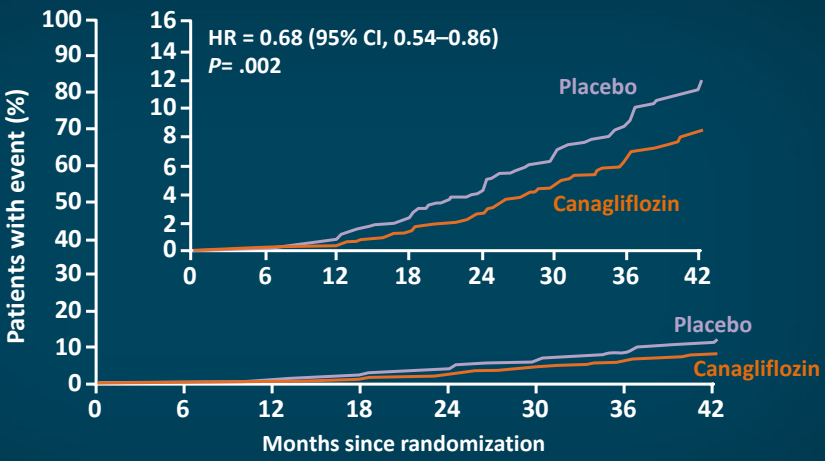


No. at risk								
Placebo	2199	2178	2132	2047	1725	1129	621	170
Canagliflozin	2202	2181	2145	2081	1786	1211	646	196

*ESKD, doubling of serum creatinine, renal or CV death.
HR = hazard ratio.

Perkovic V, et al. *N Engl J Med.* 2019;380:2295-2306.

CREDENCE: End-Stage Kidney Disease Events

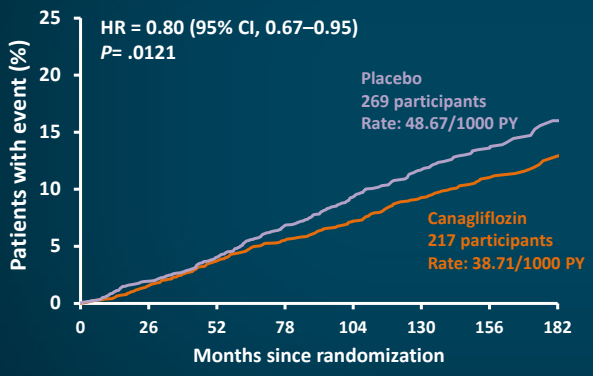


No. at risk								
Placebo	2199	2182	2141	2063	1752	1152	641	178
Canagliflozin	2202	2182	2146	2091	1798	1217	654	199

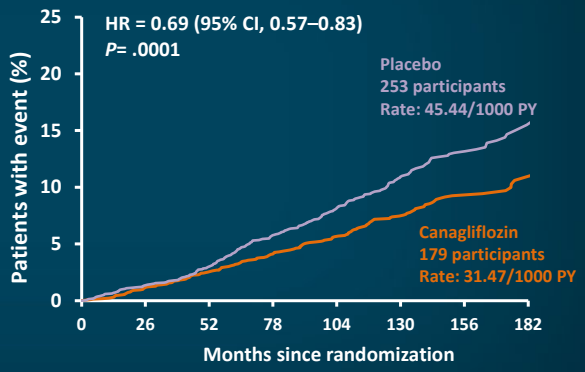
Perkovic V, et al. *N Engl J Med.* 2019;380:2295-2306.

CREDENCE: Other Endpoints

CV death, nonfatal MI, or nonfatal stroke



CV death or HF hospitalization

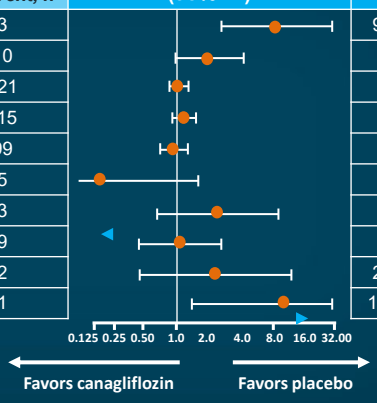


MI = myocardial infarction.

Perkovic V, et al. *N Engl J Med*. 2019;380:2295-2306.

CREDENCE: Adverse Events (AEs)* of Interest

AE	Canagliflozin (n = 2200)	Placebo (n = 2197)	Hazard ratio (95% CI)	HR (95% CI)
	Participants with an event, n			
Male genital mycotic infections	28	3		9.30 (2.83–30.60)
Female genital mycotic infections	22	10		2.10 (1.00–4.45)
Urinary tract infections	245	221		1.08 (0.90–1.29)
Volume depletion-related AEs	144	115		1.25 (0.97–1.59)
Malignancies	8	99		0.98 (0.74–1.30)
Renal cell carcinoma	1	5		0.20 (0.02–1.68)
Breast	8	3		2.59 (0.69–9.76)
Bladder	10	9		1.10 (0.45–2.72}
Acute pancreatitis	5	2		2.44 (0.47–12.59)
Diabetic ketoacidosis	11	1		10.80 (1.39–83.65)



No difference in amputations: HR = 1.11 (95% CI, 0.79–1.56)

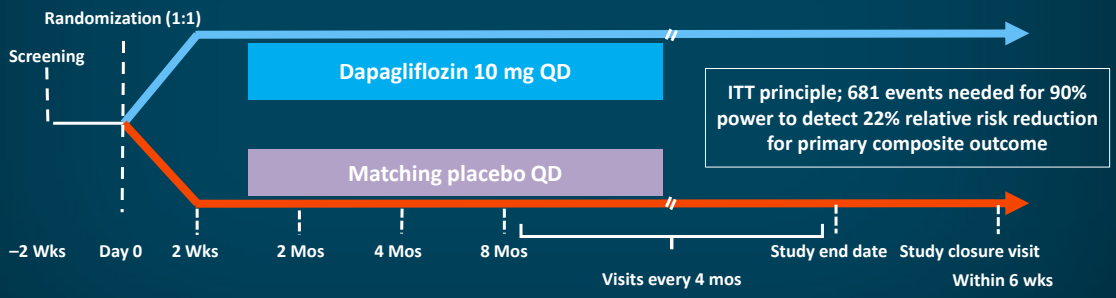
*Includes all treated participants through 30 days after last dose except cancer, which includes all treated patients through end of trial.

Adapted from Perkovic V, et al. *N Engl J Med*. 2019;380:2295-2306.

DAPA-CKD Study Design

Key inclusion criteria:
- ≥18 years of age , eGFR 25 to 75 mL/min/1.73 m^2 ,UACR 200 to 5000 mg/g (22.6 to 565 mg/mmol)
- Stable maximum tolerated labelled dose of ACEi or ARB for ≥4 weeks (if not contraindicated)

Key exclusion criteria:
- Type 1 diabetes, PKD, SLE, ANCA+ vasculitis, Immunosuppressive Rx within 6 months of enrollment



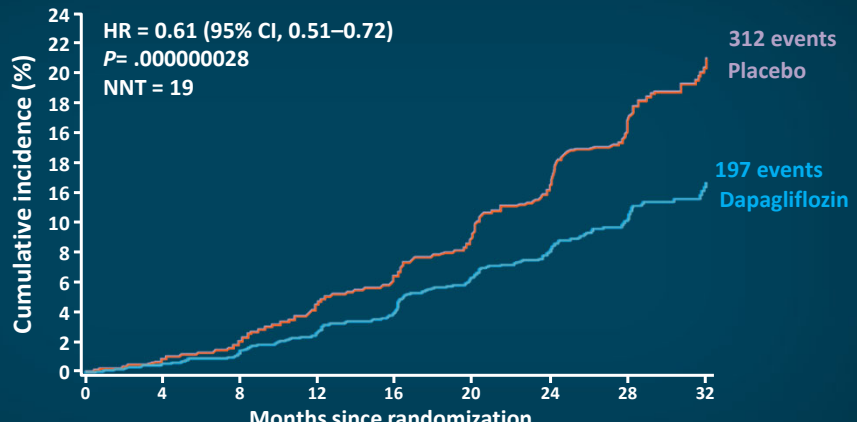
Outcome analysis based on Cox proportional hazard model stratified by T2DM and UACR and adjusted for eGFR

ANCA = anti-neutrophil cytoplasmic antibody; ITT = intention-to-treat; wk(s) = week(s); QD = once daily.

Heerspink HJL, et al. *Nephrol Dial Transplant*. 2020;35:274-282.

DAPA-CKD: Primary Outcome

Sustained ≥50% eGFR Decline, ESKD, Renal or CV Death



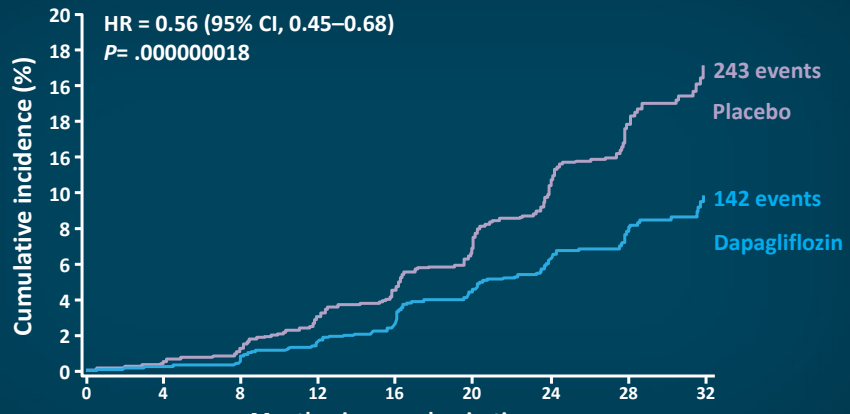
No. at risk									
Dapagliflozin	2152	2001	1955	1898	1841	1701	1288	831	309
Placebo	2152	1993	1936	1858	1791	1664	1232	774	270

NNT = number needed to treat.

Heerspink HJL, et al. *N Engl J Med*. 2020;383:1436-1446.

DAPA-CKD: Secondary Outcome

Sustained ≥50% eGFR Decline, ESKD, Renal Death

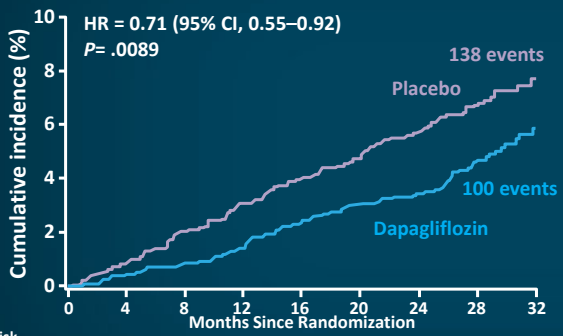


No. at risk									
Dapagliflozin	2152	2001	1955	1898	1841	1701	1288	831	309
Placebo	2152	1993	1936	1858	1791	1664	1232	774	270

Heerspink HJL, et al. *N Engl J Med*. 2020;383:1436-1446.

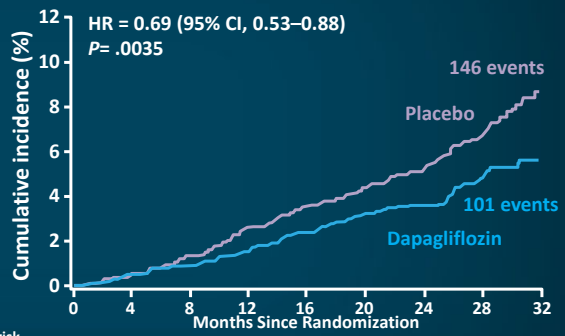
DAPA-CKD: Other Secondary Outcomes

CV death or HF hospitalization



No. at risk									
Dapagliflozin	2152	2035	2021	2003	1975	1895	1502	1003	384
Placebo	2152	2023	1989	1957	1927	1853	1451	976	360

All-cause mortality

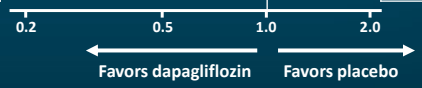


No. at risk									
Dapagliflozin	2152	2039	2029	2017	1998	1925	1531	1028	398
Placebo	2152	2035	2018	1993	1972	1902	1502	1009	379

Heerspink HJL, et al. *N Engl J Med*. 2020;383:1436-1446.

DAPA-CKD: Primary and Secondary Outcomes by Diabetes Status

	Dapagliflozin	Placebo	Hazard ratio (95% CI)	*P*-value for interaction
	No. of participants/total no.			
Primary outcome				
Overall	197/2152	312/2152	0.61 (0.51–0.72)	0.24
With T2DM	152/1458	229/1451	0.64 (0.52–0.79)	
Without T2DM	45/697	83/701	0.50 (0.35–0.72)	
Renal-specific outcome				
Overall	142/2152	2439/2152	0.56 (0.45–0.68)	
CV death or heart failure				
Overall	1100/2152	138/2152	0.71 (0.55–0.92)	
All-cause mortality				
Overall	101/2152	146/2152	0.69 (0.53–0.88)	



Heerspink HJL, et al. *N Engl J Med*. 2020;383:1436-1446.

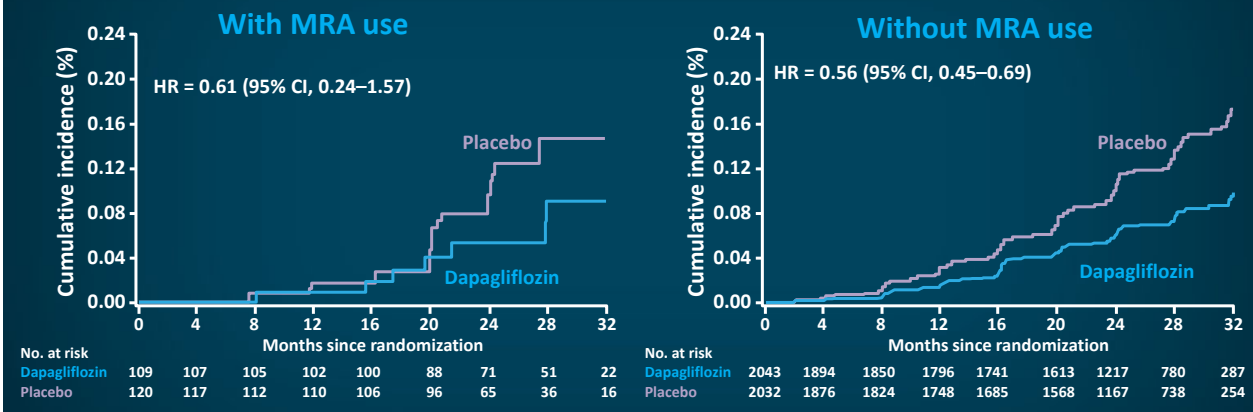
DAPA-CKD: Safety

Safety outcomes*, n (%)	Dapagliflozin (n = 2149)	Placebo (n = 2149)
Discontinuation of study drug	274 (12.8)	309 (14.4)
Discontinuation due to AE	118 (5.5)	123 (5.7)
Any serious AE	633 (29.5)	729 (33.9)
AEs of interest		
Amputation†	35 (1.6)	39 (1.8)
Any definite/probable diabetic ketoacidosis	0	2 (0.1)
Fracture	85 (4.0)	69 (3.2)
Renal-related AE	155 (7.2)	188 (8.7)
Major hypoglycemia‡	14 (0.7)	28 (1.3)
Volume depletion	127 (5.9)	90 (4.2)
Serious AEs of volume depletion	22 (1.0)	18 (0.8)

*Safety outcomes reported in participants on and off treatment; †surgical or spontaneous/nonsurgical amputation, excluding amputation due to trauma; ‡AE with following criteria confirmed by investigator: a) symptoms of severe impairment in consciousness or behavior, b) need of external assistance, c) intervention to treat hypoglycaemia, and d) prompt recovery of acute symptoms following the intervention.

Heerspink HJL, et al. *N Engl J Med*. 2020;383:1436-1446 and supplement.

DAPA-CKD: Renal Composite Outcome* in Patients ± MRA Use at BL



*Sustained ≥50% eGFR decline, ESKD, renal death.

Heerspink HJL, et al. *N Engl J Med*. 2020;383:1436-1446.

Recent Clinical Trials in DKD

Mineralocorticoid Receptor Antagonist

Animation

Scan below to watch a brief animation exploring the MOAs of Diabetic Nephropathy

Mineralocorticoid Receptors (MRs)

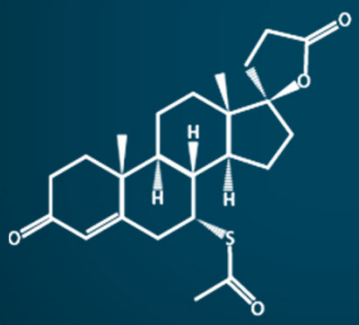
- Receptor for mineralocorticoid hormones such as aldosterone
- Expressed in CV system and are major determinant of endothelial function, smooth muscle tone, vascular remodeling, fibrosis, and BP
- Play an important role in immune cells and damage to heart, kidneys, and vasculature
- Play a role in insulin resistance

Belden Z, et al. *Am J Nephrol*. 2017;46:298-314.

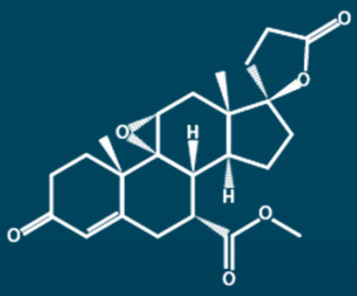
Steroidal vs Non-steroidal MRA

Steroidal MRAs

Spironolactone

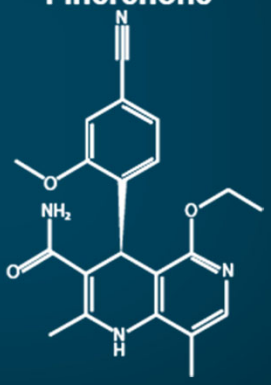


Eplerenone



Non-steroidal MRA

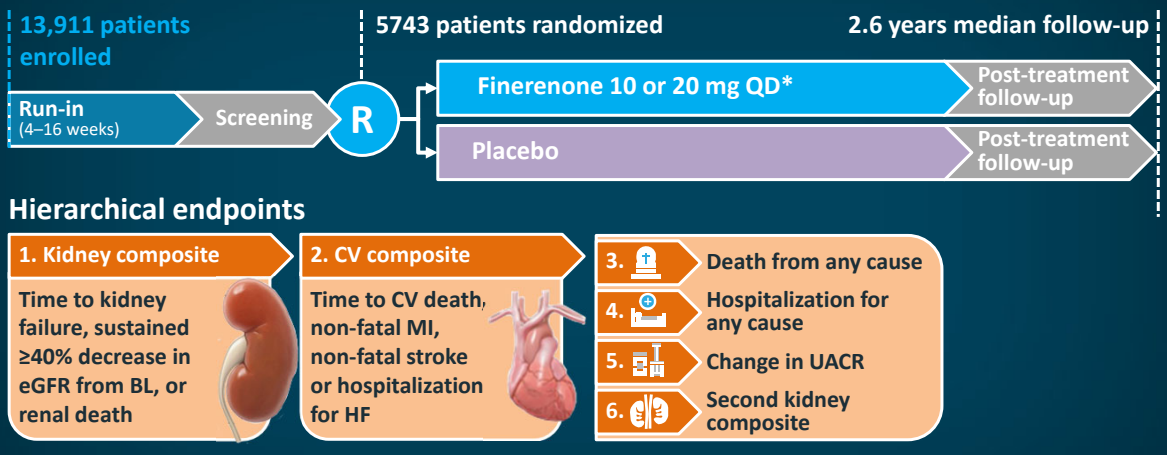
Finerenone



FDA approved July 9, 2021

MR expressed in kidney, colon, heart, and brain.

FIDELIO-DKD Study Design



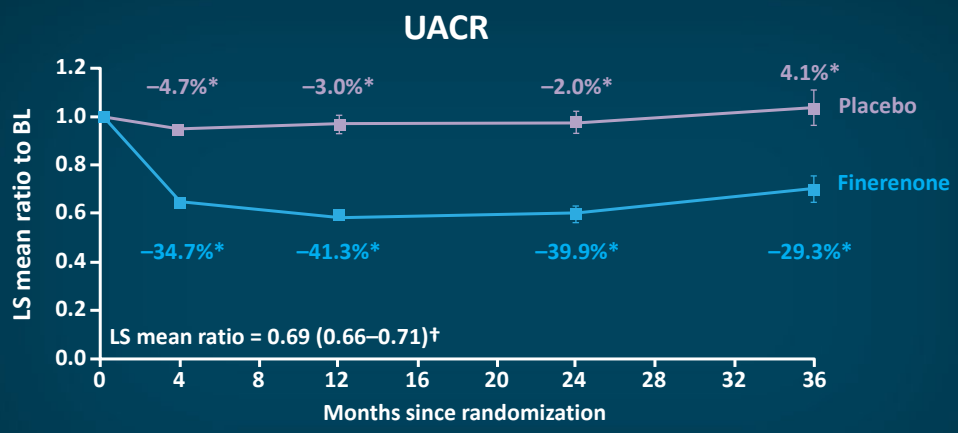
Hierarchical endpoints

1. **Kidney composite**: Time to kidney failure, sustained ≥40% decrease in eGFR from BL, or renal death
2. **CV composite**: Time to CV death, non-fatal MI, non-fatal stroke or hospitalization for HF
3. Death from any cause
4. Hospitalization for any cause
5. Change in UACR
6. Second kidney composite

*10 mg if screening eGFR <60 mL/min/1.73 m^2 and 20 mg if >60 mL/min/1.73 m^2, uptitration encouraged from month 1 if serum potassium <4.8 mEq/L and eGFR stable.

Bakris GL, et al. *N Engl J Med*. 2020;383:2219-2229.

FIDELIO-DKD: Albuminuria Change Over Time



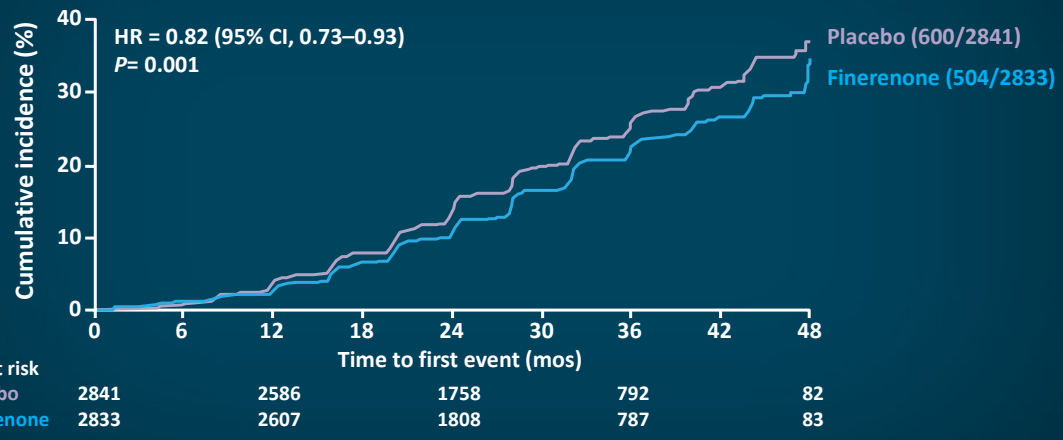
31% reduction in UACR at month 4 with finerenone vs placebo

*Mean change from baseline; †Between baseline and month 4 (prespecified secondary outcome).
LS = least-squares.

Bakris GL, et al. *N Engl J Med*. 2020;383:2219-2229.

FIDELIO-DKD: Primary Endpoint

Kidney Failure*, Sustained >40% Decrease in eGFR from BL, or Renal Death



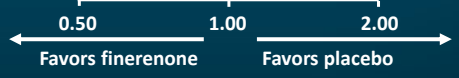
No. at risk					
Placebo	2841	2586	1758	792	82
Finerenone	2833	2607	1808	787	83

*ESKD or eGRF <15 mL/min/1.73 m²

Bakris GL, et al. *N Engl J Med*. 2020;383:2219-2229.

FIDELIO-DKD: Primary Kidney-Specific Composite Endpoint

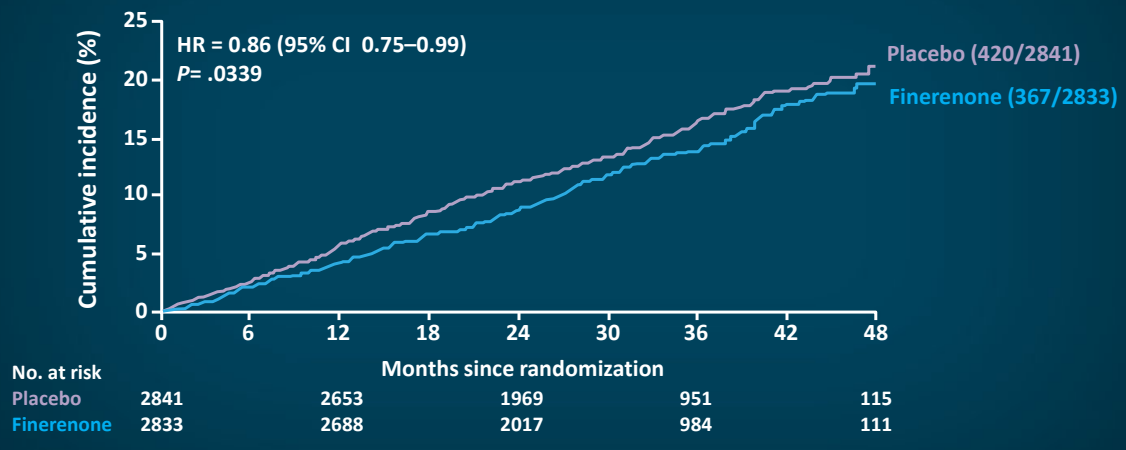
Endpoint	Finerenone (n = 2833) n (%)	Placebo (n = 2841) n (%)	Hazard ratio (95% CI)	*P*-value
Primary composite kidney endpoint	504 (17.8)	600 (21.1)	0.82 (0.73–0.93)	0.001
Kidney failure	208 (7.3)	235 (8.3)	0.87 (0.72–1.05)	—
ESKD	119 (4.2)	139 (4.9)	0.86 (0.67–1.10)	—
Sustained eGFR <15 mL/min/1.73 m^2	167 (5.9)	199 (7.0)	0.82 (0.67–1.01)	—
Sustained ≥40% decrease in eGFR from BL	479 (16.9)	577 (20.3)	0.81 (0.72–0.92)	—
Renal death	2 (<0.1)	2 (<0.1)	—	—



Bakris GL, et al. *N Engl J Med*. 2020;383:2219-2229.

FIDELIO-DKD: Key Secondary Endpoint

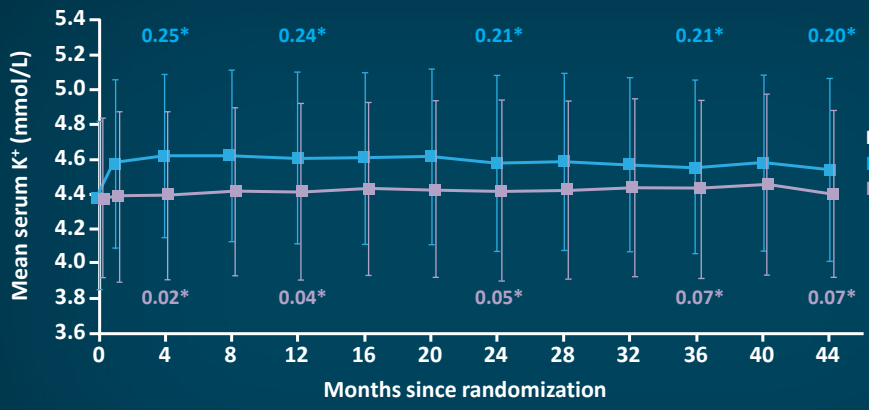
CV Death, Non-Fatal MI, Non-Fatal Stroke, or Hospitalization for HF



No. at risk					
Placebo	2841	2653	1969	951	115
Finerenone	2833	2688	2017	984	111

Bakris GL, et al. *N Engl J Med*. 2020;383:2219-2229.

FIDELIO-DKD: Change in Serum Potassium Over Time



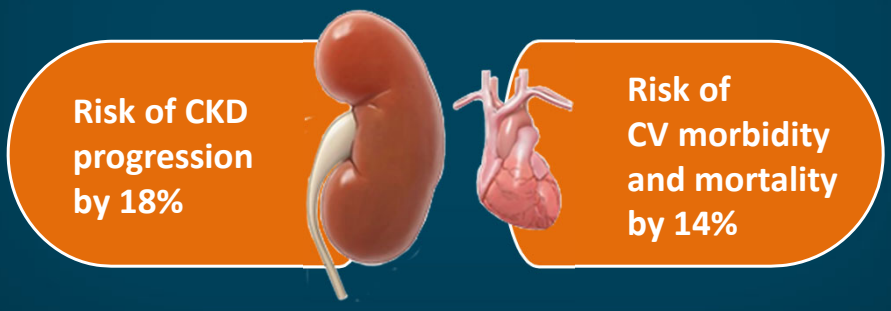
Maximum mean difference in serum potassium between groups = 0.23 mmol/L at month 4

*Mean change from baseline.

Bakris GL, et al. *N Engl J Med*. 2020;383:2219-2229.

FIDELIO-DKD: Summary and Conclusions

In patients with CKD and T2DM treated with optimized RAS therapy, finerenone was well-tolerated and significantly reduced:



RAS = renin-angiotensin system.

Bakris GL, et al. *N Engl J Med*. 2020;383:2219-2229.

Preventive Measures to Mitigate the Risk of Hyperkalemia

Strategies to Mitigate Hyperkalemia

- Dietary potassium restriction
- Avoid drugs that can cause or potentiate hyperkalemia
  - NSAIDs
  - K^+ sparing diuretics
  - Calcineurin inhibitors
  - Other
- Concomitant use of potassium binders such as patiromer, zirconium cyclosilicate, sodium polystyrene sulfonate

NSAIDs = non-steroidal antiinflammatory drugs.

Conclusions

- The pathophysiology of CKD is complex, as is its relationship with increased renal and CVD risk in patients with DKD
- Inflammation, fibrosis, and MR activation are significant drivers of CKD/DKD progression
- The ADA recommends annual screening for T1DM and T2DM by measuring UACR and serum creatinine to estimate GFR
- There are multiple new and emerging renoprotective agents with differing mechanisms of action for the treatment of DKD

CVD = cardiovascular disease

Thank You!

Q&A

Chronic and Diabetic Kidney Disease: Diagnosis and Management

Resource	Address
Akhtar M, et al. Diabetic kidney disease: Past and present. *Adv Anat Pathol*. 2020;27(2):87-97.	https://pubmed.ncbi.nlm.nih.gov/31876542/
Alicic RZ, et al. Diabetic kidney disease: Challenges, progress, and possibilities. *Clin J Am Soc Nephrol.* 2017;12:2032-2045.	https://pubmed.ncbi.nlm.nih.gov/28522654/
American Diabetes Association (ADA). 11. Microvascular complications and foot care: Standards of medical care in diabetes-2021. *Diabetes Care*. 2021;44(suppl 1):S151-S167.	https://pubmed.ncbi.nlm.nih.gov/33298422/
Anders HJ, et al. CKD in diabetes: Diabetic kidney disease versus nondiabetic kidney disease. *Nat Rev Nephrol*. 2018;14(6):361-377.	https://pubmed.ncbi.nlm.nih.gov/29654297/
Bakris GL, et al. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. *N Engl J Med*. 2020;383:2219-2229.	https://pubmed.ncbi.nlm.nih.gov/33264825/
Chu CD, et al. CKD awareness among US adults by future risk of kidney failure. *Am J Kidney Dis*. 2020;76:174-183.	https://pubmed.ncbi.nlm.nih.gov/32305206/
Fu H, et al. Diabetic kidney diseases revisited: A new perspective for a new era. *Mol Metab*. 2019;30:250-263.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6838932/
George LK, et al. Heart failure increases the risk of adverse renal outcomes in patients with normal kidney function. *Circ Heart Fail.* 2017;10(8):e003825.	https://pubmed.ncbi.nlm.nih.gov/28765150/
Heerspink HJL, et al. Dapagliflozin in patients with chronic kidney disease. *N Engl J Med*. 2020;383:1436-1446.	https://pubmed.ncbi.nlm.nih.gov/32970396/
McGrath K, et al. Diabetic kidney disease: Diagnosis, treatment, and prevention. *Am Fam Physician.* 2019;99(12):751-759.	https://www.aafp.org/afp/2019/0615/p751.html
Nayor M, et al. The association of chronic kidney disease and microalbuminuria with heart failure with preserved vs. reduced	https://pubmed.ncbi.nlm.nih.gov/28217978/

ejection fraction. *Eur J Heart Fail.* 2017;19:615-623.	
Perkovic V, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *N Engl J Med*. 2019;380:2295-2306.	https://pubmed.ncbi.nlm.nih.gov/30990260/
Persson F, et al. Diagnosis of diabetic kidney disease: State of the art and future perspective. *Kidney Int Suppl (2011)*. 2018;8(1):2-7.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6336222/
Saran R, et al. US Renal Data System 2019 Annual Data Report: Epidemiology of kidney disease in the United States. *Am J Kidney Dis.* 2020;75(suppl 1):A6-A7.	https://pubmed.ncbi.nlm.nih.gov/31704083/
Stephens JW, et al. Chronic kidney disease in type 2 diabetes: Implications for managing glycaemic control, cardiovascular and renal risk. *Diabetes Obes Metab*. 2020;22(suppl 1):32-45.	https://pubmed.ncbi.nlm.nih.gov/32267078/
Tuttle KR, et al. Clinical characteristics of and risk factors for chronic kidney disease among adults and children: An analysis of the CURE-CKD Registry. *JAMA Netw Open*. 2019;2:e1918169.	https://pubmed.ncbi.nlm.nih.gov/31860111/

Resources and Societies

Resource	Address
McGrath K, et al. Diabetic kidney disease: Diagnosis, treatment, and prevention. *Am Fam Physician.* 2019;99(12):751-759.	https://www.aafp.org/afp/2019/0615/p751.html
American Diabetes Association. Accessed June 28, 2021.	https://www.diabetes.org/
American Society of Nephrology. Diabetic Kidney Disease Collaborative (DKD-C). Accessed June 28, 2021.	https://www.asn-online.org/dkd-c/
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