Mass General Brigham

What's New, Innovative, and Controversial in Chronic Kidney Disease

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Disclosures

None

Objectives

- To highlight recent treatment innovations in chronic kidney disease
- To review recent controversies in chronic kidney disease
- To understand innovate strategies to eliminate disparities in kidney health

Case 1

A 61-year-old man of African descent presents for follow-up. He feels well and has no complaints. His 81-year-old mother has hypertension and end-stage kidney disease on hemodialysis.

Past Medical History

- Hypertension
- Gout
- Obstructive sleep apnea

Case 1-Medications

Amlodipine 5 mg daily

Lisinopril 20 mg daily

Allopurinol 100 mg daily

Case 1: Question

Which of the following diagnostic tests is/are appropriate in this patient?

A. Electrolytes
B. Serum creatinine
C. Urine albumin/creatinine
D. All of the above

Case 1: Answer

The correct answer is D.
This patient has hypertension and a first-degree relative with end-stage kidney disease. He is therefore at risk for chronic kidney disease, which is usually manifested first by albuminuria. Hence, measuring a serum creatinine and checking for the presence of albuminuria are appropriate. Because he is on an ACE-I, checking an electrolyte panel is also appropriate.

Controversy: Should we routinely screen for chronic kidney disease?

- Chronic kidney disease may remain asymptomatic until advanced
- Is there a role for routine screening of asymptomatic patients?

USPSTF Recommendations for screening asymptomatic adults for CKD

Population	Asymptomatic adults without diagnosed chronic kidney disease
Recommendation	No recommendation
	Grade: I (insufficient evidence)
Risk assessment	There is no generally accepted risk assessment tool for CKD. Diabetes and hypertension are well accepted risk factors with strong links to CKD. Other risk factors for CKD include older age, cardiovascular disease, obesity, and family history.
Screening tests	Although there is insufficient evidence to recommend routine screening, the tests often suggested for screening that are feasible in primary care include testing the urine for protein (microalbuminuria or macroalbuminuria) and testing the blood for serum creatinine to estimate glomerular filtration rate.
Balance of harms and benefits	The USPSTF could not determine the balance between the benefits and harms of screening for CKD in asymptomatic adults.

Moyer, VA Ann Intern Med. 2012;157:567-570

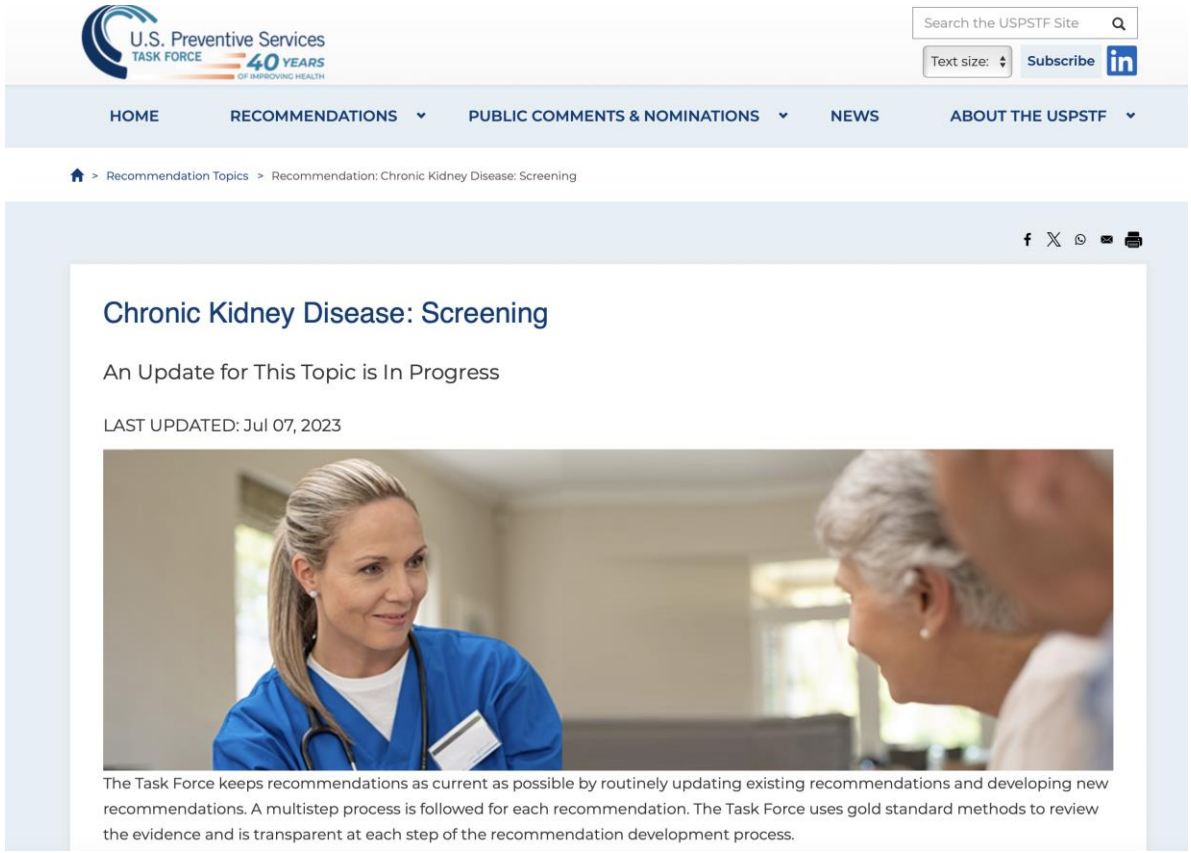
Statement from the National Kidney Foundation on Media Reports of USPSTF Considering Kidney Disease Screening

May 24, 2022, New York, NY —The National Kidney Foundation (NKF) is encouraged by reports the United States Preventative Services Task Force (USPSTF) may consider issuing new guidelines for kidney disease screening. NKF and the Coalition for Kidney Health have long been advocating for USPSTF to revise its CKD recommendations. A statement from Sylvia Rosas, MD, NKF President-elect and Associate Professor of Medicine, Harvard Medical School, and Joseph Vassalotti, MD, Chief Medical Officer for the NKF follows:

"Ultimately, CKD is a health equity issue – African Americans are 3 – 4 times more likely to develop kidney failure than Whites. If we can identify individuals with CKD earlier – at a more manageable stage of their disease – we can slow disease progression and help achieve better outcomes for all populations, but especially those at highest risk for kidney failure. The news that the USPSTF has agreed to review kidney disease screening again, is welcome. However, no timeline for future recommendations has been set. The USPSTF must act and act soon if we ever hope to adequately address inequity in CKD care."

- Sylvia Rosas, MD, NKF President-elect and Associate Professor of Medicine, Harvard Medical School

USPSTF Update for CKD Screening Still in Progress



ISN-KDIGO Early Identification and Intervention in Primary Care

Step 1: Identify those at risk

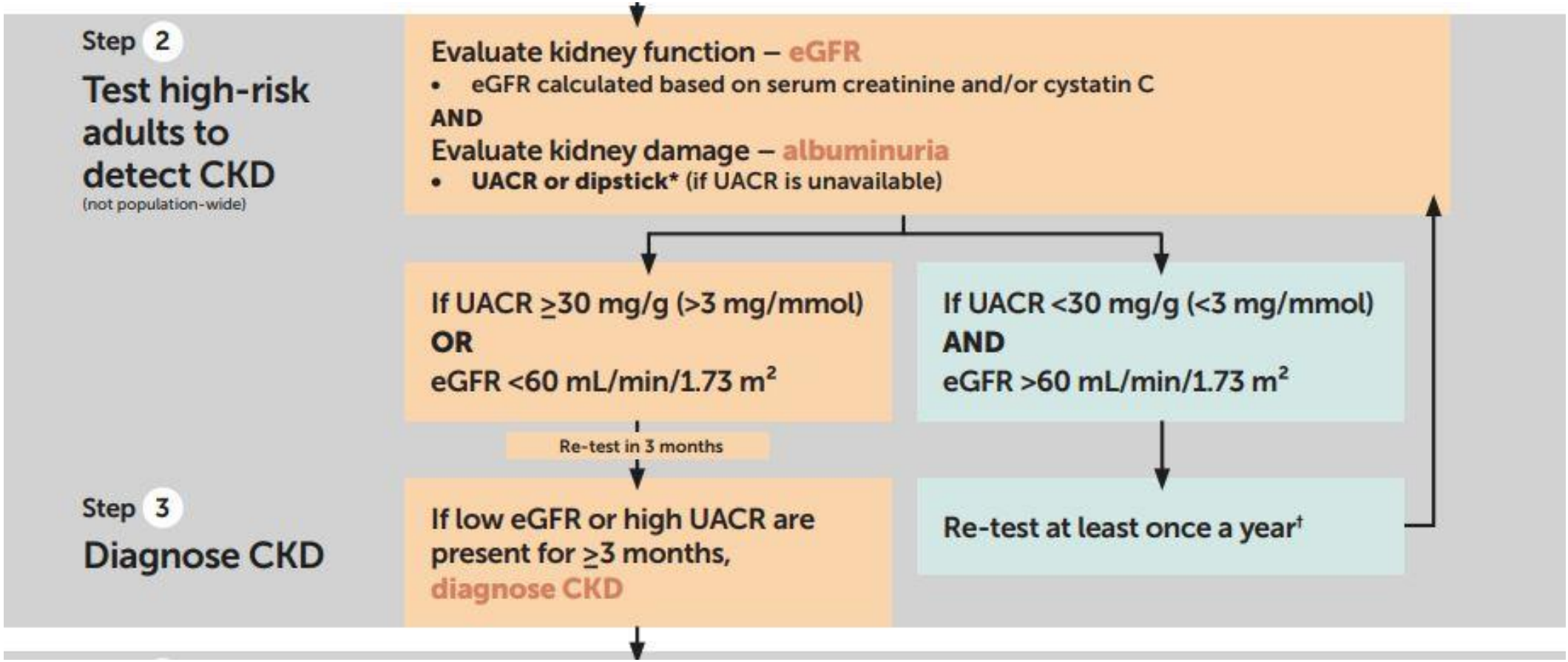
Main Clinical Risk Factors for CKD:

- Hypertension
- Diabetes
- CVD
- Family history of CKD

Consider Other Factors:

- Systemic diseases that may affect kidneys (SLE)
- Obesity
- Genetic Risk Factors
- Exposure to nephrotoxins
- Demographics (older age, race/ethnicity)
- History of AKI

ISN-KDIGO Early Identification and Intervention in Primary Care



International Society of Nephrology

ISN-KDIGO Early Identification and Intervention in Primary Care: Step 4, Stratify and Treat

Range	A1 <30 mg/g	A2 30-299 mg/g	A3 >300 mg/g
≥90 G1	Monitor	Treat	Treat and Consult
60-89 G2	Monitor	Treat	Treat and Consult
45-59 G3a	Treat	Treat	Treat and Consult
30-44 G3b	Treat	Treat and Consult	Treat and Consult
15-29 G4	Treat and Consult	Treat and Consult	Treat and Consult
< 15 G5	Treat and Consult	Treat and Consult	Treat and Consult

Treat to slow CKD progression, reduce mortality risk, and manage co-morbidities

- Lifestyle modification
  - Smoking cessation
  - Regular exercise
  - Well balanced diet
    - Avoiding excessive protein intake
    - Avoiding processed foods
    - Limiting sodium intake to < 2 grams/day
- Pharmacologic therapies

Monitor for CKD Progression and Comorbidities

CKD Progression and comorbidities	What to monitor
CKD Monitoring	eGFR, UACR, urinalysis (urine sediment)
CVD and Dyslipidemia	Blood pressure, cardiovascular risk stratification, lipid status
Diabetes	Blood glucose, hemoglobin A1C

International Society of Nephrology

Additional considerations for nephrology consultation

- Unexplained, progressive decline in eGFR ≥5 mL/min/1.73 m^2 over 12 months or sudden decline in eGFR over days to weeks
- Unexplained significant albuminuria/proteinuria or hematuria
- Persistent hyperkalemia, resistant hypertension (defined as uncontrolled hypertension on three antihypertensive agents, including a diuretic), recurring kidney stones, or hereditary kidney diseases (e.g. ADPKD)
- Other complications identified (anemia, mineral and bone disorders, metabolic acidosis, etc.)

Blood pressure control guidelines (KDIGO)

- Target systolic blood pressure of < 120 mm Hg when tolerated
- Start ACE-I or ARB in individuals with hypertension, CKD, and moderate to severe albuminuria with or without diabetes
- Avoid any combination of ACE-I, ARB, and direct renin inhibitor therapy in patients with CKD, with or without diabetes

Cheung AK et al 2021; Kidney Int 99: 559-569

Case 2

A 57-year-old woman with type 2 diabetes, hypertension, PAD, and CKD presents for follow-up.

Past Medical History

- Diabetes mellitus type 2
- Chronic kidney disease
- Hypertension
- Peripheral arterial disease

Case 2-Medications and Labs

- Amlodipine 10 mg daily
- Lisinopril 20 mg daily
- Chlorthalidone 25 mg daily
- Metformin 500 mg bid

- K^+ 4.8 mEq/L
- Bicarbonate 23 mmol/L
- Creatinine 1.2 mg/dL
- Hemoglobin A1C 8.0%
- Urine albumin/creatinine 400 mg/g

Case 2: Question

What additional medication(s) may be beneficial in improving her cardiorenal outcomes?

A. Glipizide
B. Saxtagliptin
C. Canagliflozin
D. Insulin

Case 2: Answer

The correct answer is C.
The only one of the medications listed with proven benefits in retarding progression of chronic kidney disease is canagliflozin.

Diabetes and Kidney Disease

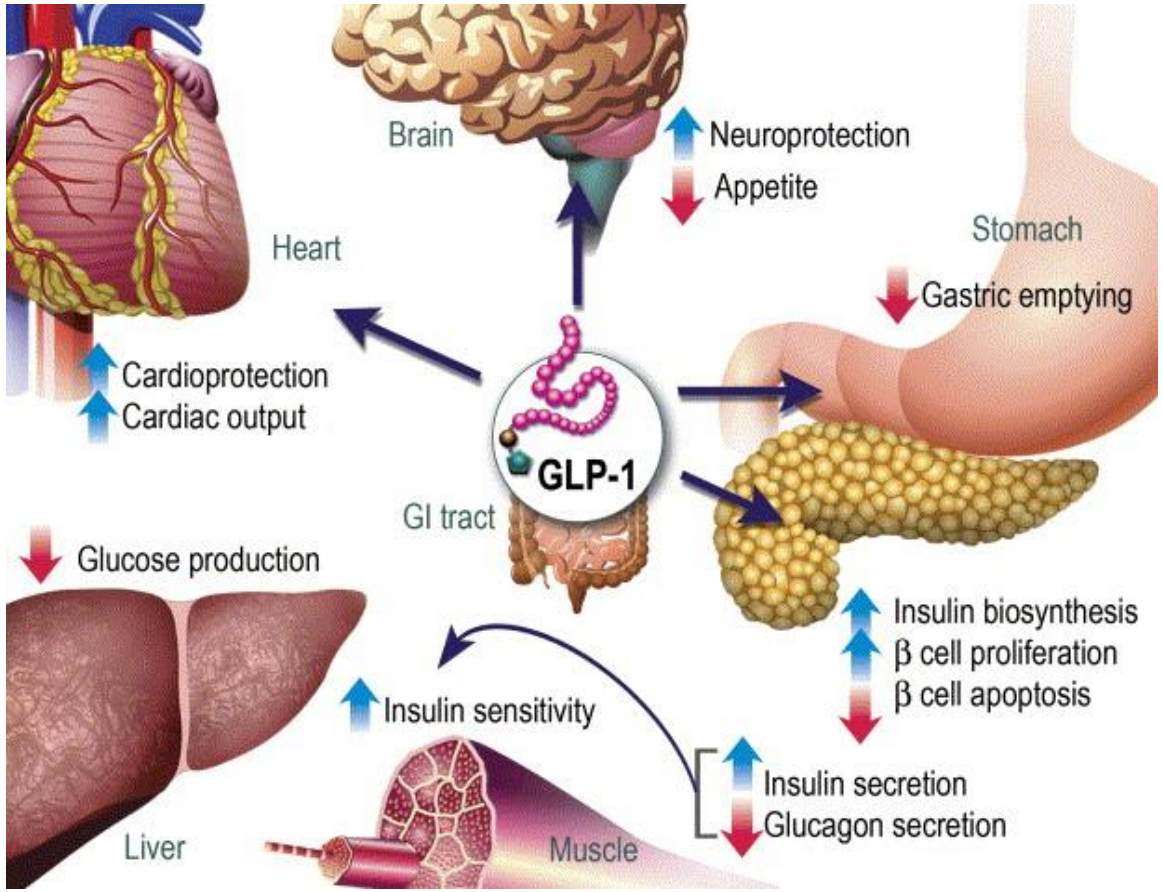
Treatment of diabetic kidney disease has focused on

- Blood pressure control
- Blockade of the renin/angiotensin system
  - –ACE-I
  - –ARB

Innovation: Drug class matters

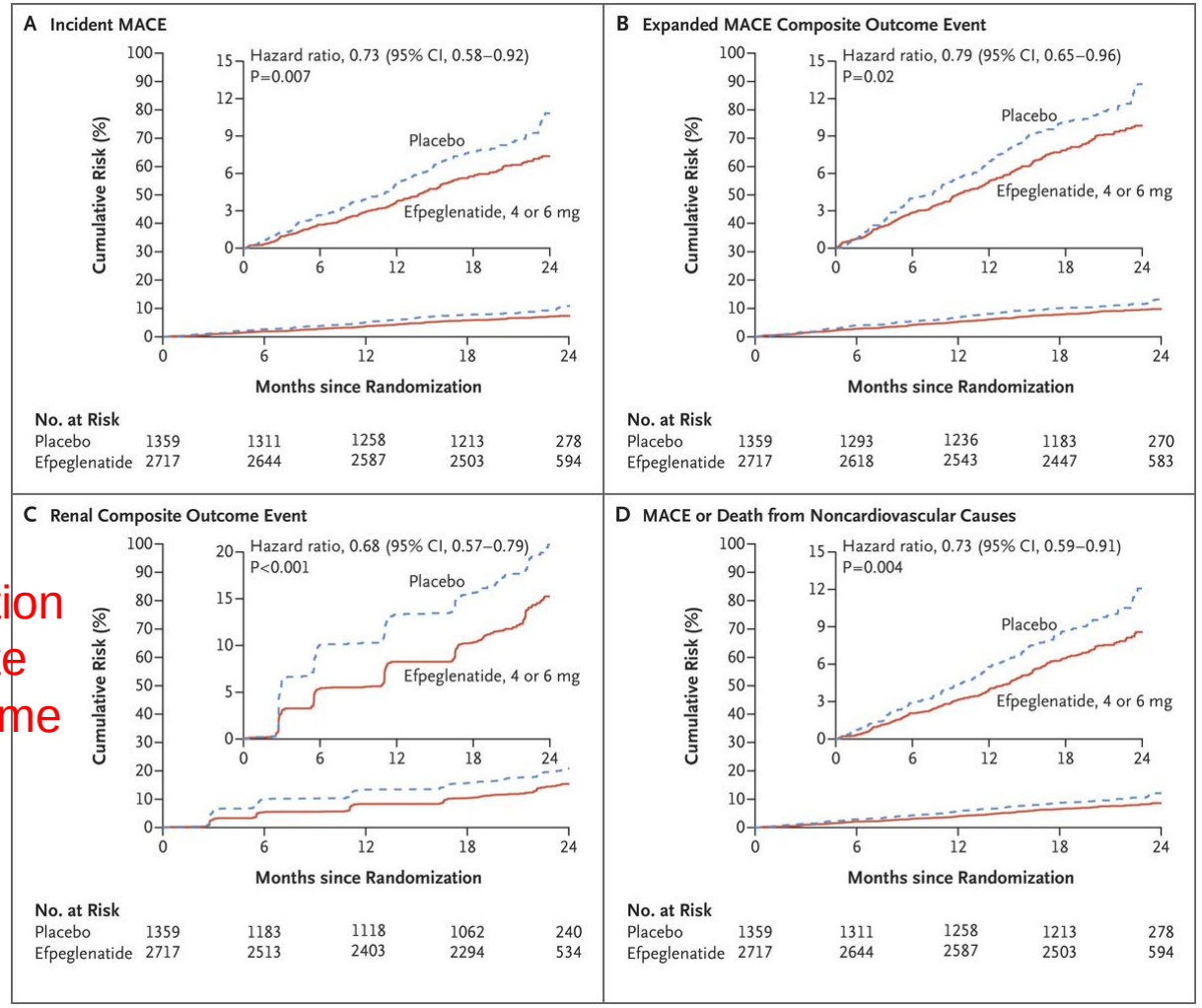
- Despite widespread use of RAS inhibitors, diabetes remains the leading cause of ESRD in the United States
- Some glucose-lowering agents appear to have glucose-independent effects on diabetic nephropathy and its progression
  –GLP-1 analogues
  –Sodium-glucose cotransporter-2 (SGLT-2) inhibitors

GLP-1 Agonists: Dulaglutide, Semaglutide and others



Drucker DJ Cell Metab 2006

Renal outcomes in AMPLITUDE-O



32% reduction in composite renal outcome

HC Gerstein *et al*. N Engl J Med 2021;385:896-907

GLP-1 Agonists and Renal Outcomes

- Awaiting trial data looking at GLP-1 agonists and other outcomes in a *kidney-focused* clinical trial
  - GFR
  - Progression to ESRD or transplantation

  - The Effect of Glucagon-like-peptide 1 (GLP-1) Receptor Agonism on Diabetic Kidney Disease
  - Effect of LIXIsenatide on the Renal System (ELIXIRS)
  - The FLOW study (Effect of semaglutide versus placebo on the progression of renal impairment in subjects with T2DM and CKD)

SGLT-2 Inhibitors

- Sodium-glucose transporter blockers
- Block the reabsorption of glucose at the proximal tubule
- Effective in individuals across stages of CKD
- Lower weight and blood pressure (diuretic effect)
- Low risk of hypoglycemia

CREDENCE: A game changer

Randomized trial of canagliflozin 100 mg daily versus placebo
4401 patients randomized
Inclusion criteria:

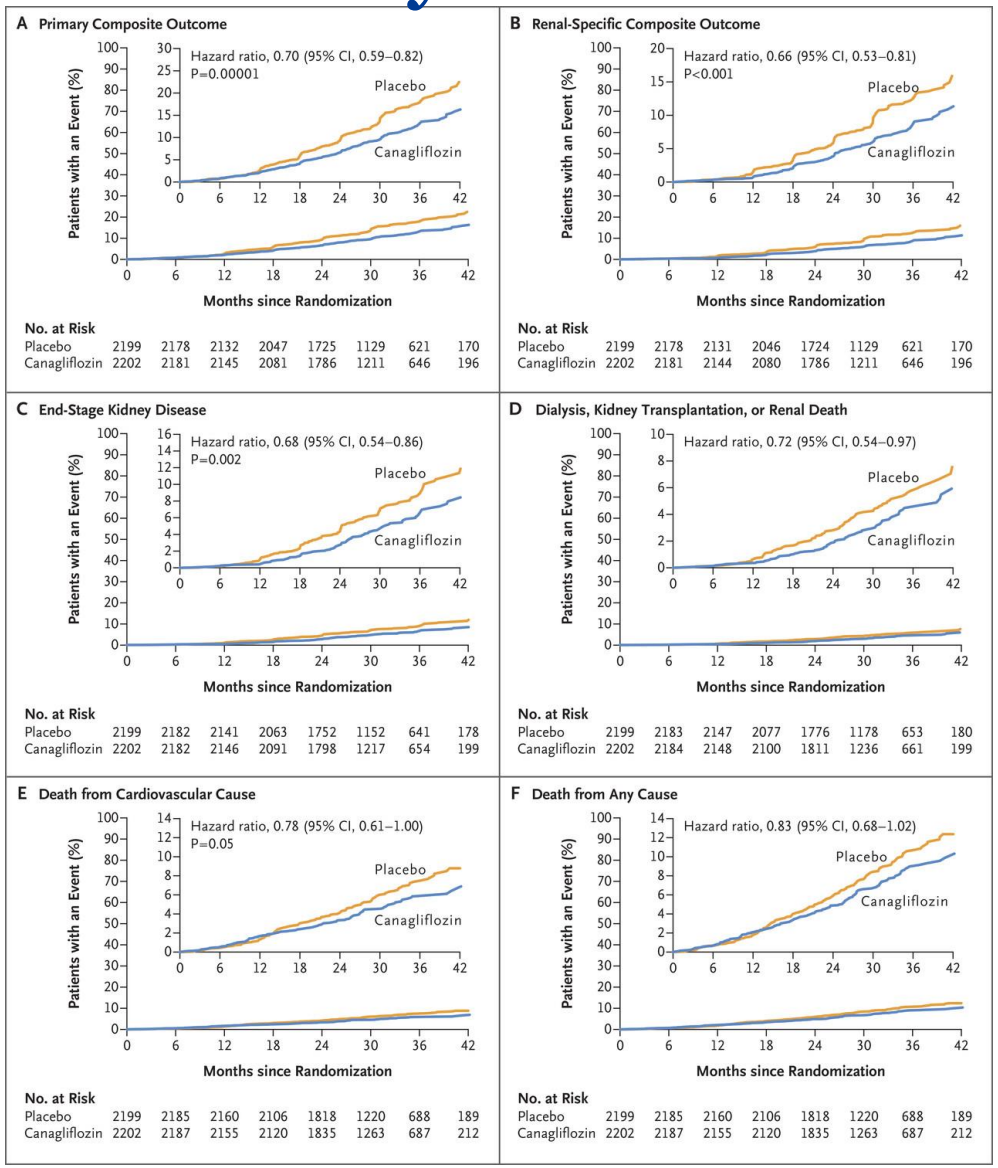
- Albumin/creatinine > 300 to 5000
- eGFR 30 to < 90
- Treatment with RAS blockade

Primary outcomes:

- Composite of ESRD and
- Doubling of the serum creatinine
- Death from renal or cardiovascular causes

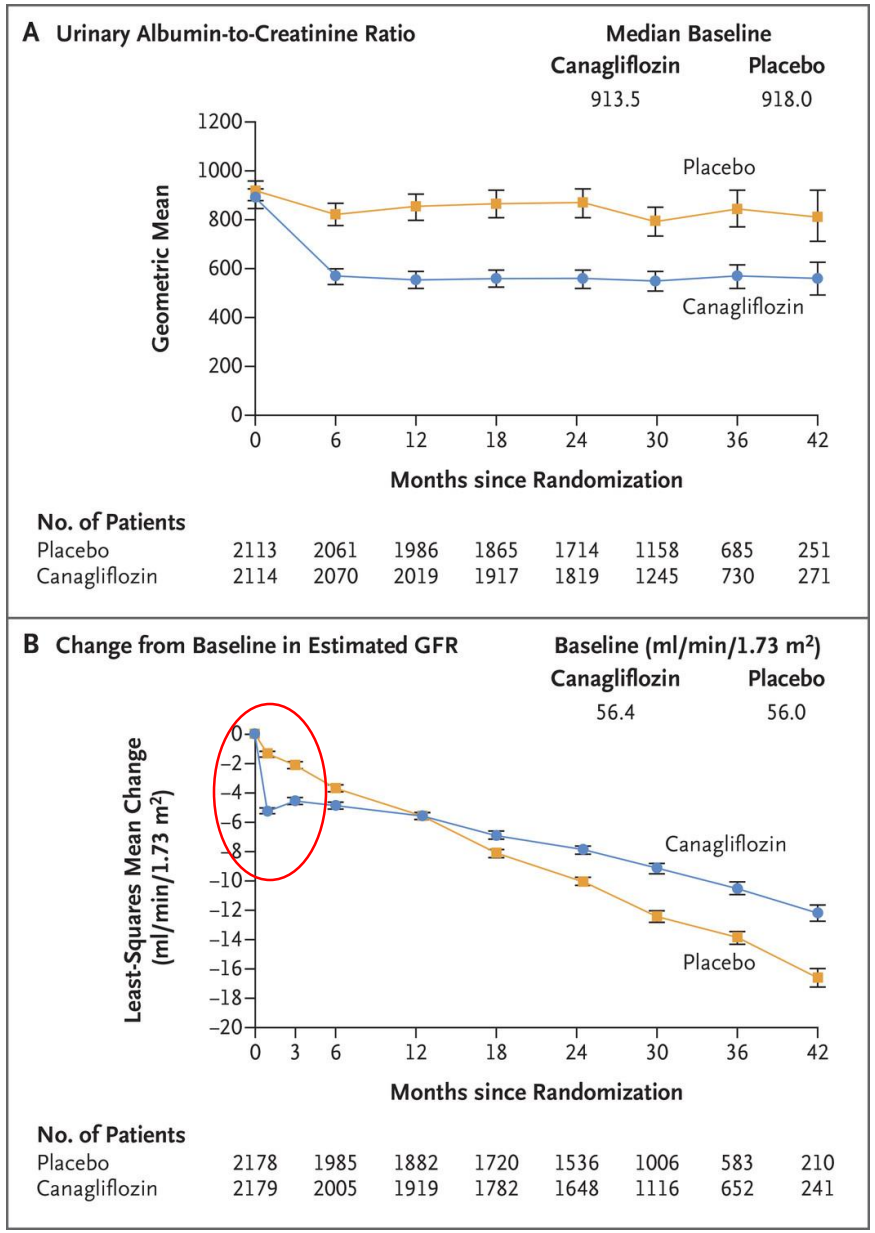
Primary Composite, Renal, and Mortality Outcomes

30% reduction in risk of primary outcome



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

Effects on Albuminuria and Estimated GFR



Note the acute drop in GFR

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

SGLT-2 inhibitors in non-diabetic kidney disease

Newer trials have shown SGLT-2 inhibitors to retard progression in *non-diabetic* kidney disease

- DAPA-CKD
- EMPA-KIDNEY

DAPA-CKD

- Randomized trial of dapagliflozin 10 mg daily versus placebo
- 4304 subjects *with or without diabetes* randomized
- Inclusion criteria:
  - Albumin/creatinine > 200 to 5000
  - eGFR 25-75 mL/min/1.73 m^2
  - Treatment with RAS blockade
- Primary outcomes:
  - Composite of sustained decline in eGFR of at least 50% and
  - End-stage kidney disease and
  - Death from renal or cardiovascular causes

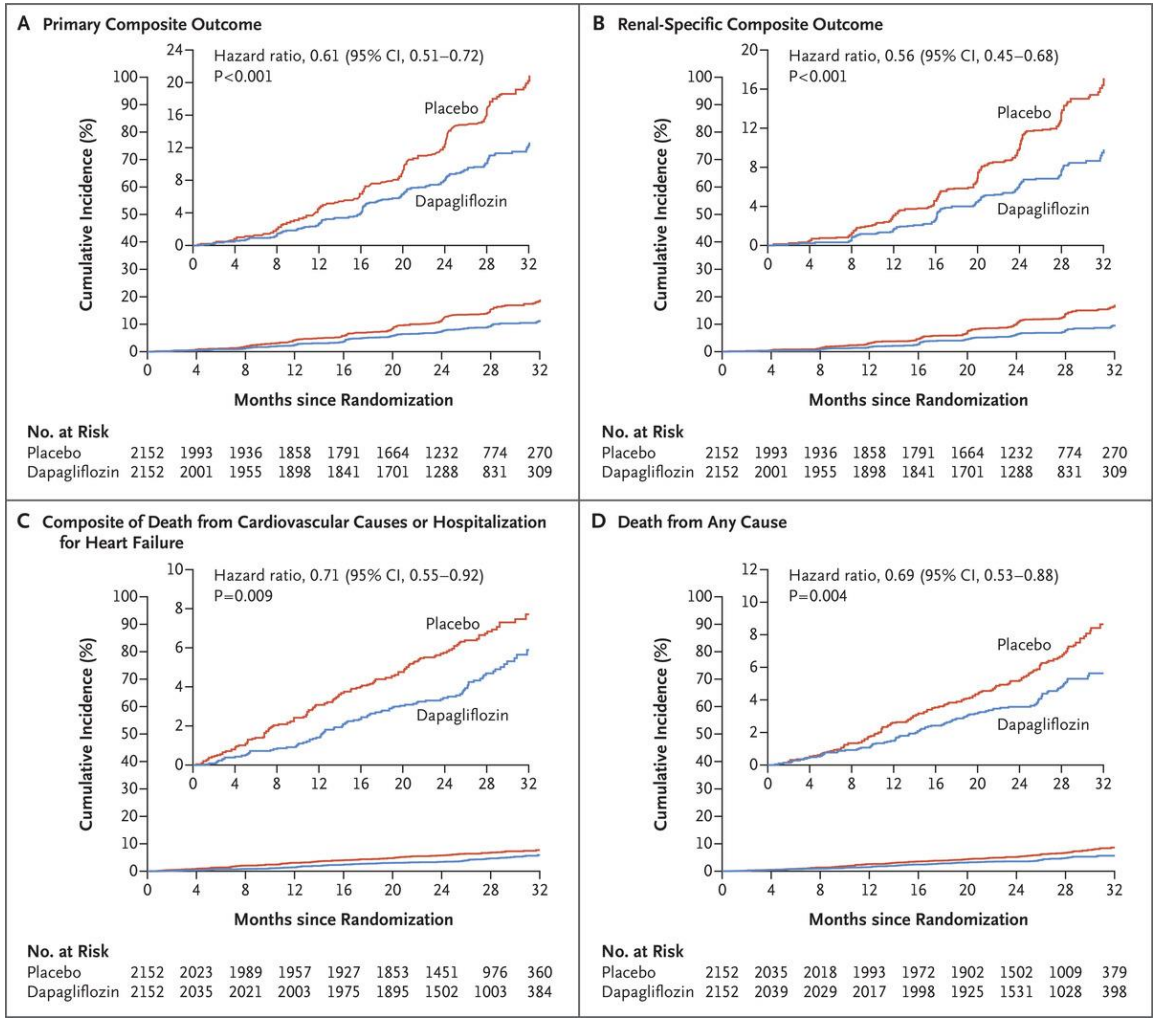
Demographic and Clinical Characteristics of the Participants at Baseline

Table 1. Demographic and Clinical Characteristics of the Participants at Baseline.*

Characteristic	Dapagliflozin (N=2152)	Placebo (N=2152)
Age — yr	61.8±12.1	61.9±12.1
Female sex — no. (%)	709 (32.9)	716 (33.3)
Race — no. (%)†		
White	1124 (52.2)	1166 (54.2)
Black	104 (4.8)	87 (4.0)
Asian	749 (34.8)	718 (33.4)
Other	175 (8.1)	181 (8.4)
Weight — kg	81.5±20.1	82.0±20.9
Body-mass index‡	29.4±6.0	29.6±6.3
Current smoker — no. (%)	283 (13.2)	301 (14.0)
Blood pressure — mm Hg		
Systolic	136.7±17.5	137.4±17.3
Diastolic	77.5±10.7	77.5±10.3
Estimated GFR		
Mean — ml/min/1.73 m^2	43.2±12.3	43.0±12.4
Distribution — no. (%)		
≥60 ml/min/1.73 m^2	234 (10.9)	220 (10.2)
45 to <60 ml/min/1.73 m^2	646 (30.0)	682 (31.7)
30 to <45 ml/min/1.73 m^2	979 (45.5)	919 (42.7)
<30 ml/min/1.73 m^2	293 (13.6)	331 (15.4)
Hemoglobin — g/liter	128.6±18.1	127.9±18.0
Serum potassium — mEq/liter	4.6±0.5	4.6±0.6
Urinary albumin-to-creatinine ratio§		
Median (interquartile range)	965 (472–1903)	934 (482–1868)
>1000 — no. (%)	1048 (48.7)	1031 (47.9)
Type 2 diabetes — no. (%)	1455 (67.6)	1451 (67.4)
Cardiovascular disease — no. (%)¶	813 (37.8)	797 (37.0)
Heart failure — no. (%)	235 (10.9)	233 (10.8)
Previous medication — no. (%)		
ACE inhibitor	673 (31.3)	681 (31.6)
ARB	1444 (67.1)	1426 (66.3)
Diuretic	928 (43.1)	954 (44.3)
Statin	1395 (64.8)	1399 (65.0)

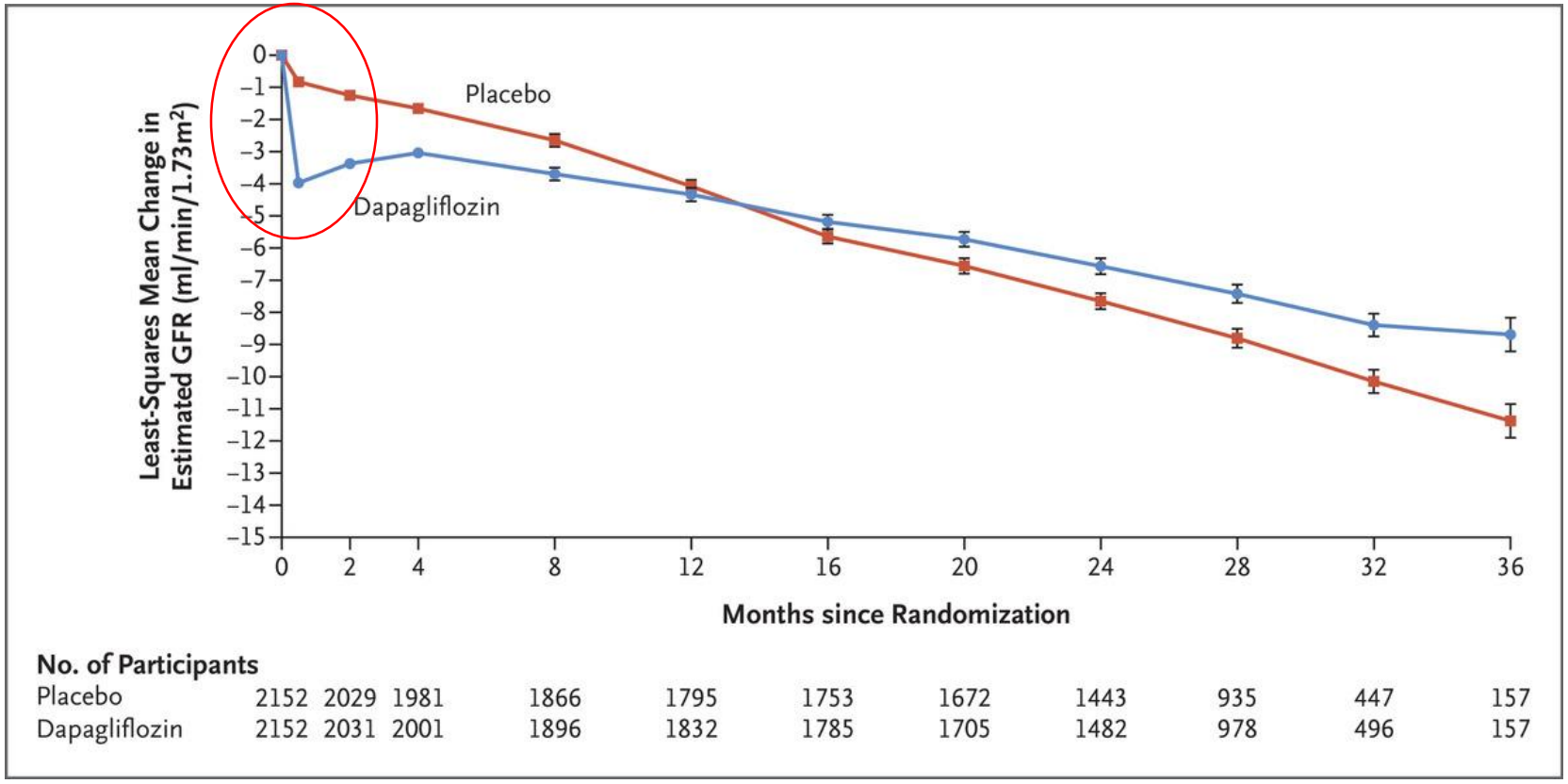
HJ Heerspink *et al*. N Engl J Med 2020;383:1436-1446

DAPA-CKD Outcomes



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

Change in GFR from Baseline



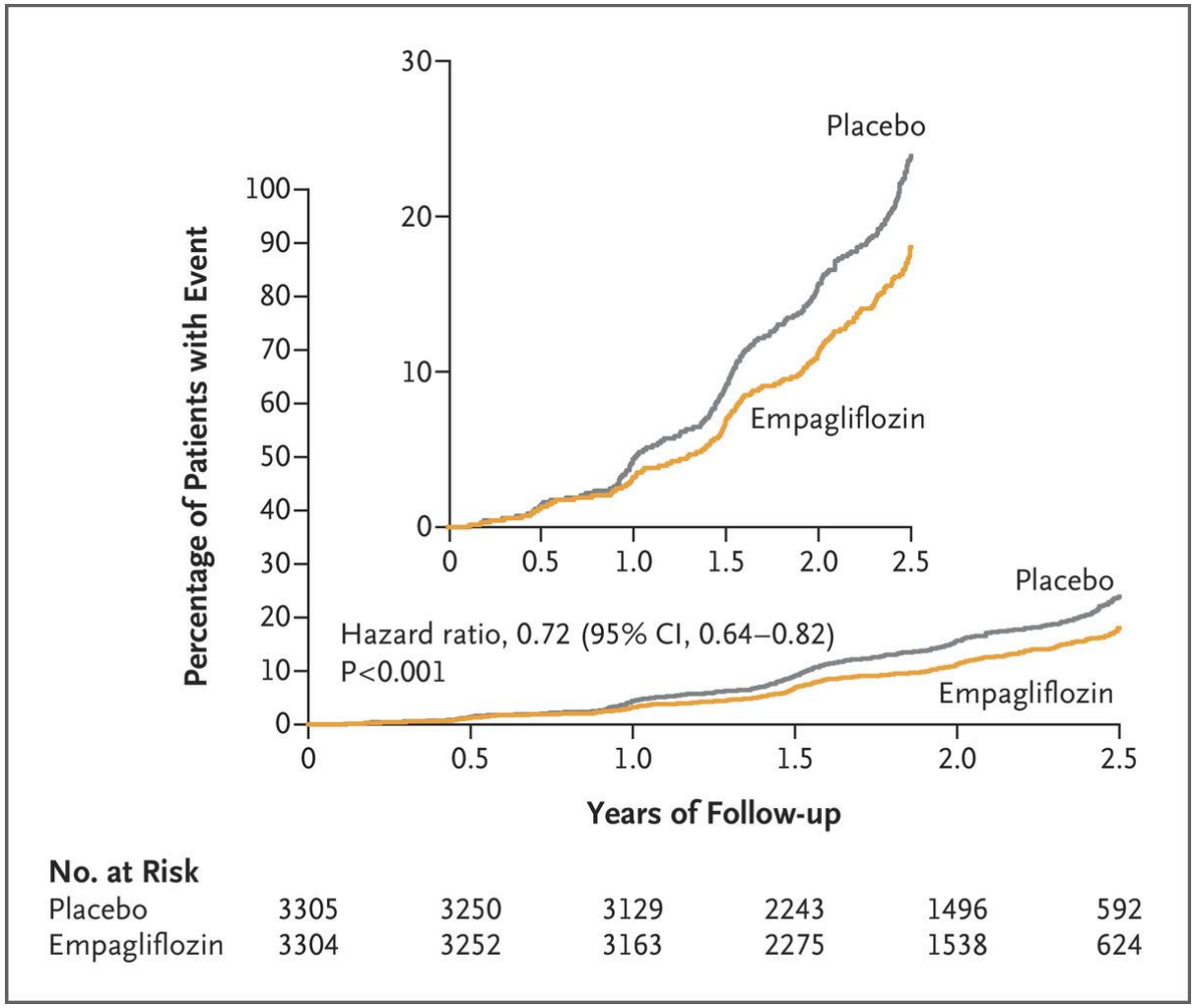
Acute drop in GFR

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

EMPA-KIDNEY

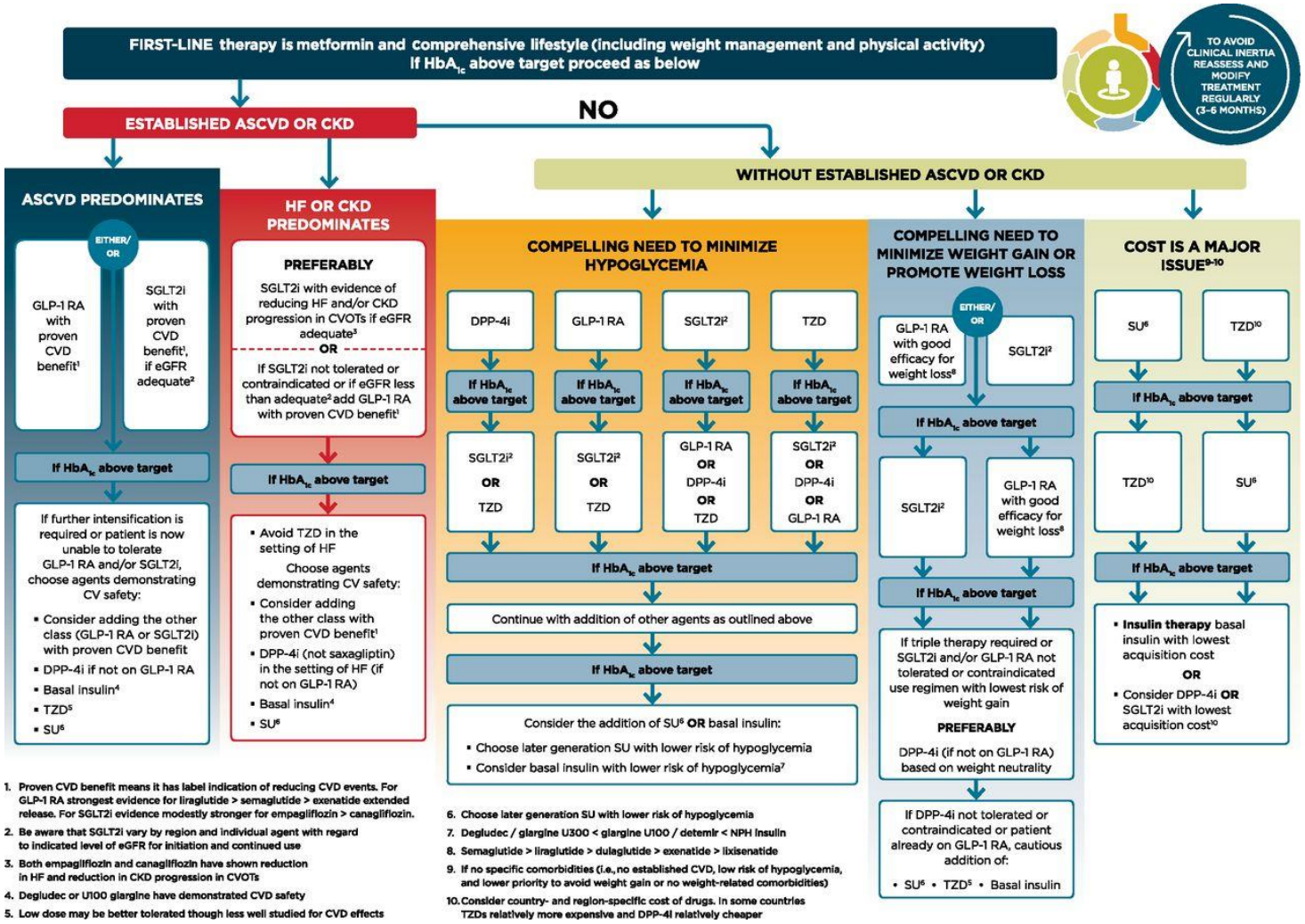
- Randomized trial of empagliflozin 10 mg daily versus placebo
- 6609 subjects *with or without diabetes* randomized
- Inclusion criteria:
  - Albumin/creatinine > 200 to 5000
  - eGFR $\geq$ 20 < 45 mL/min/1.73 m^2 regardless of level of albuminuria
  - eGFR $\geq$ 45 < 90 mL/min/1.73 m2 with UACR at least 200
  - Treatment with RAS blockade
- Primary outcomes:
  - Progression of kidney disease
  - Death from cardiovascular causes

EMPA-KIDNEY Outcomes



The EMPA-KIDNEY Collaborative Group. N Engl J Med 2023;388:117-127

Glucose-lowering medication in type 2 diabetes: overall approach



American Diabetes Association Dia Care 2019;42:S90-S102

Mineralocorticoid receptor blockade

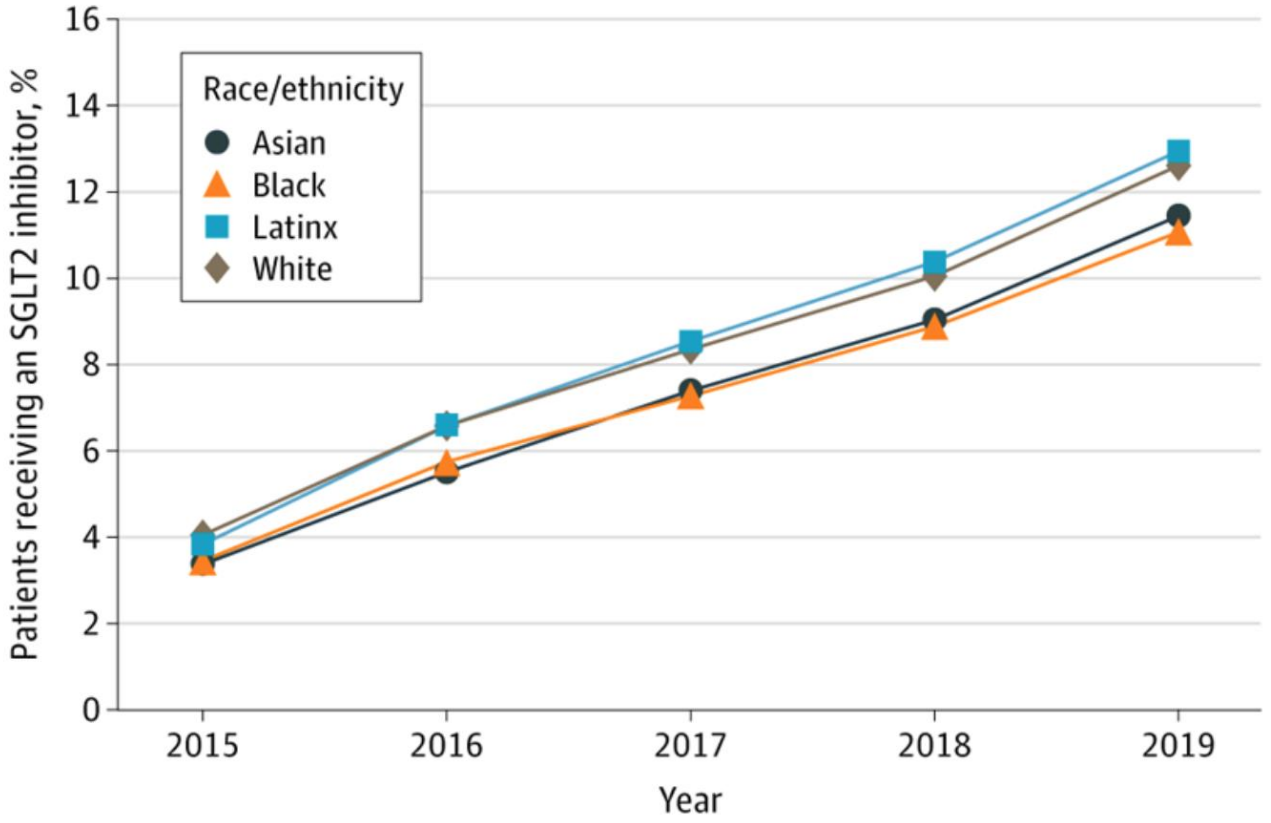
- Among patients with type 2 diabetes and urine albumin/creatinine 30-300 mg/g, eGFR 25-60 and diabetic retinopathy, *or* urine albumin/creatinine 300-5000 mg/g and eGFR 25-75
  - Finerenone lowered risk of CKD progression and cardiovascular events compared to placebo (FIDELIO-DKD)
- Among patients with type 2 diabetes and urine albumin/creatinine 30-300 mg/g and an eGFR 25-90 mL/min or a urine albumin/creatinine of 300-5000 mg/g and an eGFR $\geq$ 60 mL/min:
  - Finerenone improved cardiovascular outcomes compared to placebo (FIGARO-DKD)

Optimal therapies for patients with (type 2) diabetic kidney disease

- ACE-I/ARB
- SGLT-2 Inhibitors
- GLP-1 agonists
- Finerenone
- Loop or thiazide diuretics
- Statins
- β-blockers

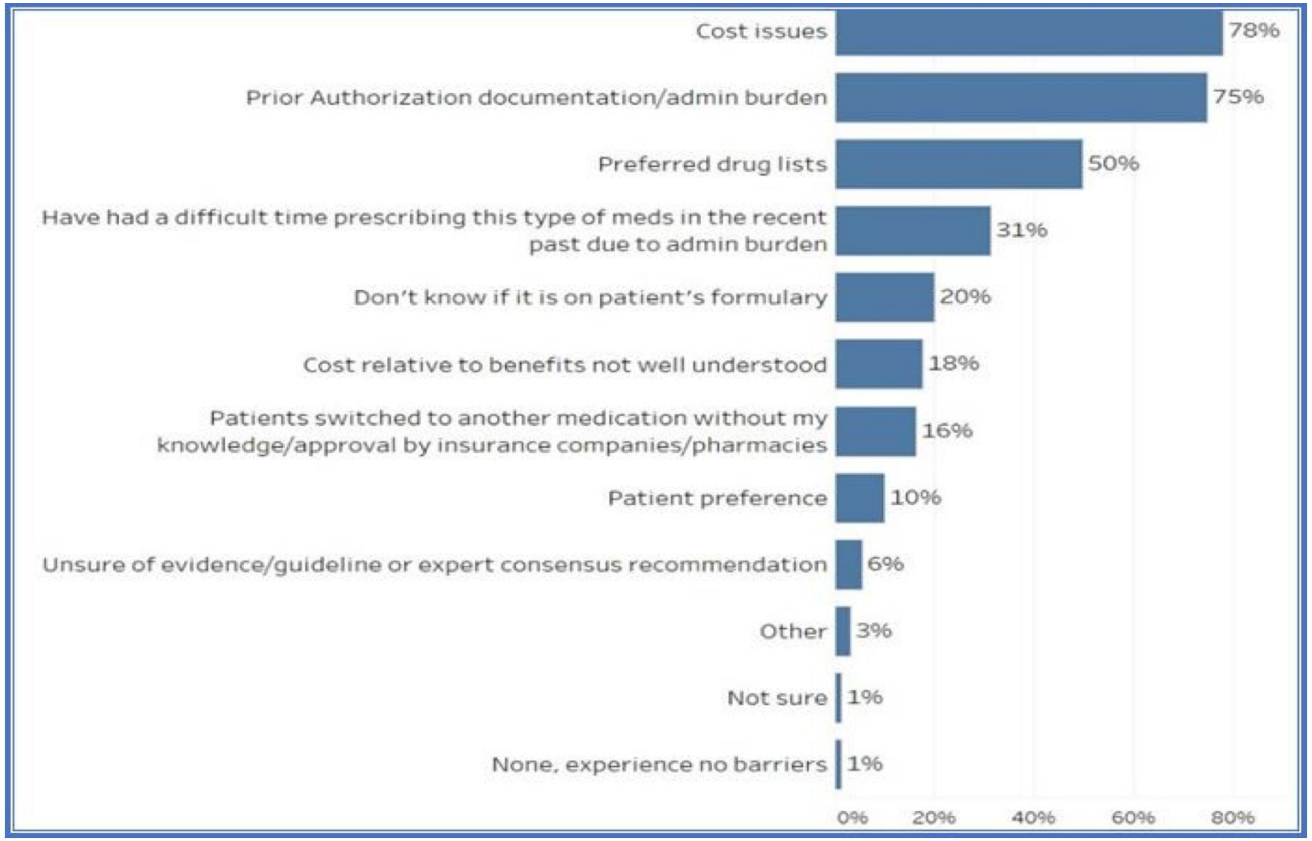
Are all patients offered advanced therapies at the same rates?

Racial/ethnic differences in use of SGLT-2 inhibitors among patients with diabetes in the United States



Eberly LA et al. JAMA Network Open 2021; 4(4):e216139. doi:10.1001/jamanetworkopen.2021.6139

Barriers to prescribing newest evidence based cardiovascular care



Association of Black Cardiologists, 2019

Case 3

A 45-year-old man with chronic kidney disease secondary to biopsy-proven IgA nephropathy presents for follow-up. He feels generally well and has no complaints. He has been followed by a nephrologist for several years, and despite treatment with an ACE-I and SGLT-2 inhibitor has persistent proteinuria.

Past Medical History/Medications

- Chronic kidney disease due to IgA nephropathy
- Hypertension

- Lisinopril 40 mg daily
- HCTZ 25 mg daily
- Dapagliflozin 10 mg daily

Physical Examination/Labs

- BP 129/77 mm Hg
- HR 70, regular
- Clear lungs
- RRR, normal S1 and S2
- Abdomen soft and nontender
- No lower extremity edema

- K^+ 4.1 mEq/L
- Creatinine 1.3 mg/dL
- 24-hour urine protein: 1.1 g
- Hemoglobin 13.5 g/dL

Case 3: Question

Which of the following additional therapies should be considered for this patient?

A. Cyclophosphamide
B. Prednisone
C. Tacrolimus
D. Budesonide

Case 3: Answer

The correct answer is D.

Innovation: Budesonide as new therapy for IgA nephropathy

While immunosuppressive therapies such as cyclophosphamide, prednisone, and tacrolimus have been used in rapidly progressive glomerulonephritis due to IgA nephropathy, they are not indicated in mild cases such as this one. Budesonide has recently been FDA approved for treatment of IgA nephropathy.

IgA nephropathy

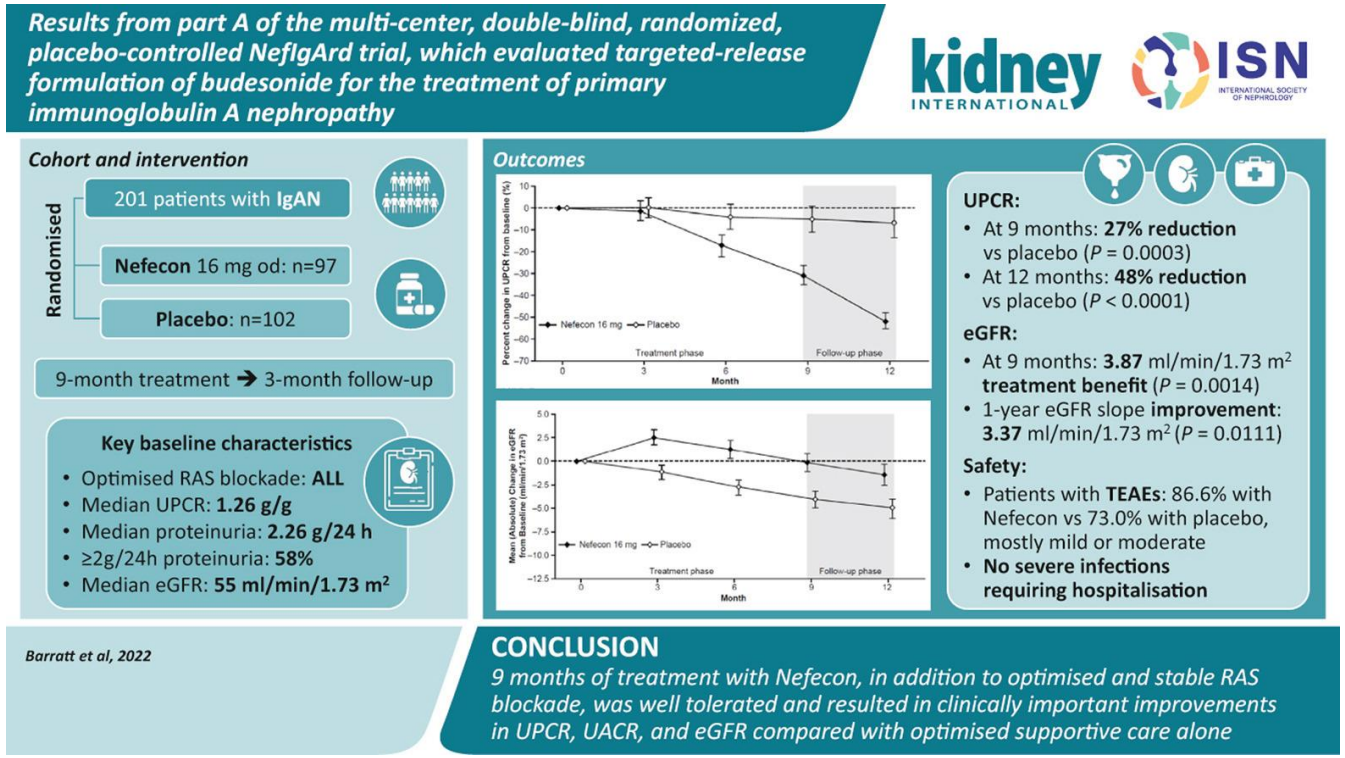
- Also known as Berger’s disease
- Worldwide is the most common glomerulonephritis
- Typically presents with microscopic hematuria and proteinuria
- Hematuria often becomes apparent (gross hematuria) in the setting of an upper respiratory infection
- In patients with persistent disease (proteinuria > 1 g/day), the risk of ESKD may be 50% at 20 years
- Treatment has focused on blood pressure control and blockade of the renin-angiotensin system

Pathology and Pathogenesis

- Mesangioproliferative glomerulonephritis characterized by mesangial deposition of galactose-deficient IgA1 (Gd-IgA1) immune complexes
- Immune complexes initiate a cascade of inflammatory events, eventually causing irreversible glomerulosclerosis and tubulointerstitial inflammation and fibrosis with loss of kidney function
- Accumulating evidence for the gut mucosal immune system and mucosal-derived Gd-IgA1 in the pathogenesis of primary IgAN
- New formulation of the oral glucocorticoid budesonide targets Gd-IgA1 production within the ileum.

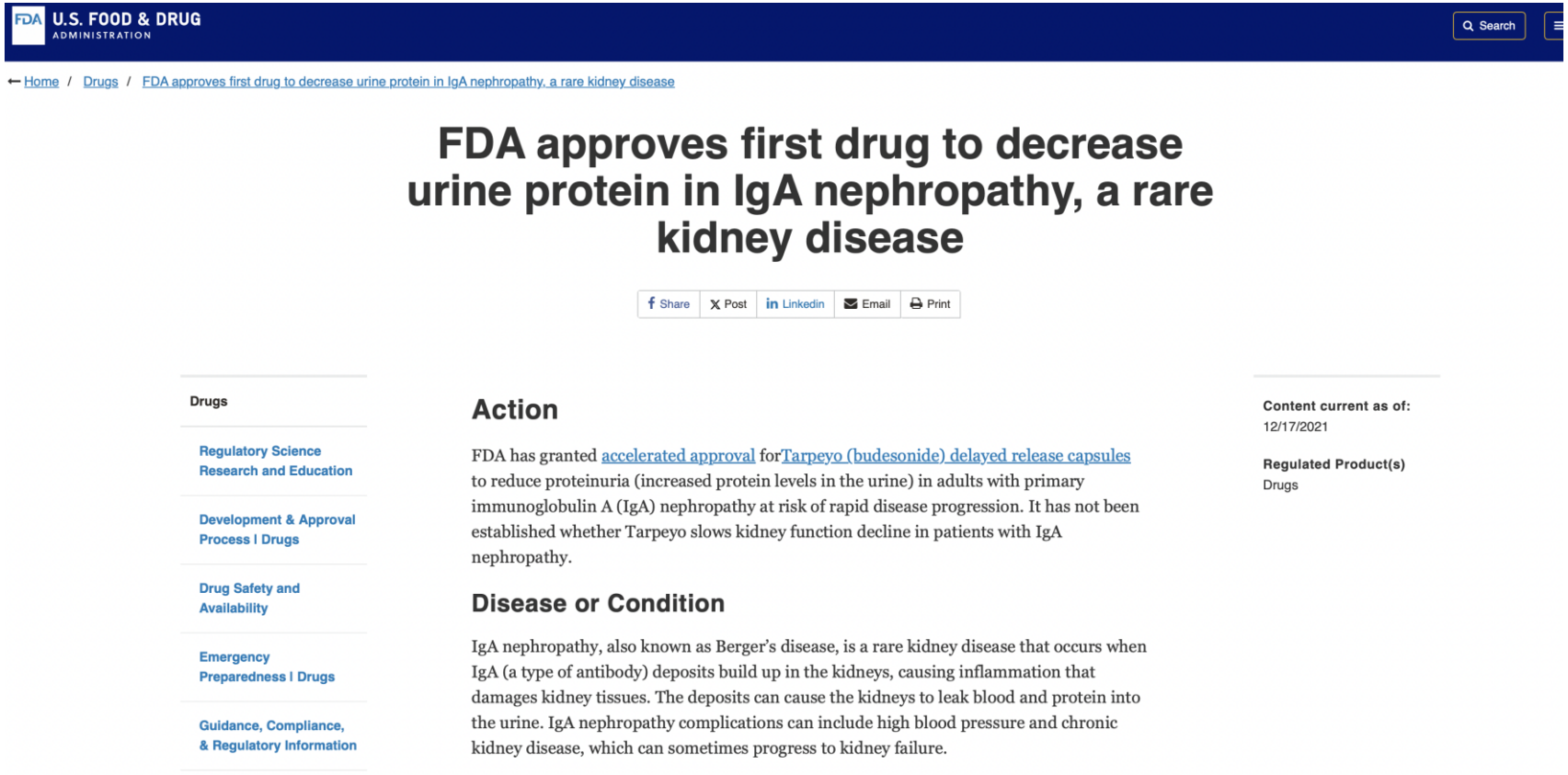
Barratt J *et al*. Kidney International 2023; 103: 391-402

Neflgard Trial



Barratt J *et al*. Kidney International 2023; 103: 391-402

FDA approves budesonide for decreasing proteinuria in IgA nephropathy



FDA U.S. FOOD & DRUG ADMINISTRATION

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FDA approves first drug to decrease urine protein in IgA nephropathy, a rare kidney disease

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Drugs

- Regulatory Science Research and Education
- Development & Approval Process | Drugs
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Action

FDA has granted accelerated approval forTarpeyo (budesonide) delayed release capsules to reduce proteinuria (increased protein levels in the urine) in adults with primary immunoglobulin A (IgA) nephropathy at risk of rapid disease progression. It has not been established whether Tarpeyo slows kidney function decline in patients with IgA nephropathy.

Disease or Condition

IgA nephropathy, also known as Berger's disease, is a rare kidney disease that occurs when IgA (a type of antibody) deposits build up in the kidneys, causing inflammation that damages kidney tissues. The deposits can cause the kidneys to leak blood and protein into the urine. IgA nephropathy complications can include high blood pressure and chronic kidney disease, which can sometimes progress to kidney failure.

Content current as of:
12/17/2021

Regulated Product(s)
Drugs

Case 4

A 72-year-old man with ESRD on HD, diabetes mellitus type 2, and peripheral arterial disease is admitted with a diabetic foot ulcer. He has a hemoglobin of 7.8 g/dL on admission. He has had no evidence of GI bleeding.

Case 4
Past Medical History

- ESRD
- Diabetes mellitus type 2
- Hypertension
- Colon cancer s/p partial colectomy 5 year prior; no metastatic disease
- TIA

Case 4
Outpatient Medications

- Amlodipine 10 mg daily
- ASA 81 mg daily
- Calcitriol 0.25 ug 3x/weekly
- Labetalol 300 mg bid
- Lisinopril 10 mg daily
- Pravastatin 40 mg daily
- Nephrocaps 1 daily
- Iron gluconate 125 mg weekly

Anemia Labs

- Hemoglobin 7.8 g/dL
- T-sat 13%
- Ferritin 602 ug/L

Case 4 Question 1

What would you do next in managing this patient's anemia?

A. Do nothing. The patient is asymptomatic.

B. Add an ESA.

C. Transfuse to a hemoglobin of 10-11 g/dL.

D. Give intravenous iron.

Case 4 Question 1 Answer

The patient is anemic but also iron deficient. The goal transferrin saturation in a hemodialysis patient is 30-40%. The first step in management of this patient would be to administer IV iron.

Follow-up

The patient is treated with a course of intravenous iron. His transferrin saturation rises to 35% and his hemoglobin rises to 8.1 g/dL. The patient complains of fatigue with minimal exertion.

Case 4 Question 2

What would you do next in managing this patient's anemia?

A. Do nothing. The patient is asymptomatic.

B. Add an ESA.

C. Transfuse to a hemoglobin of 10-11 g/dL.

D. Refer to hematology.

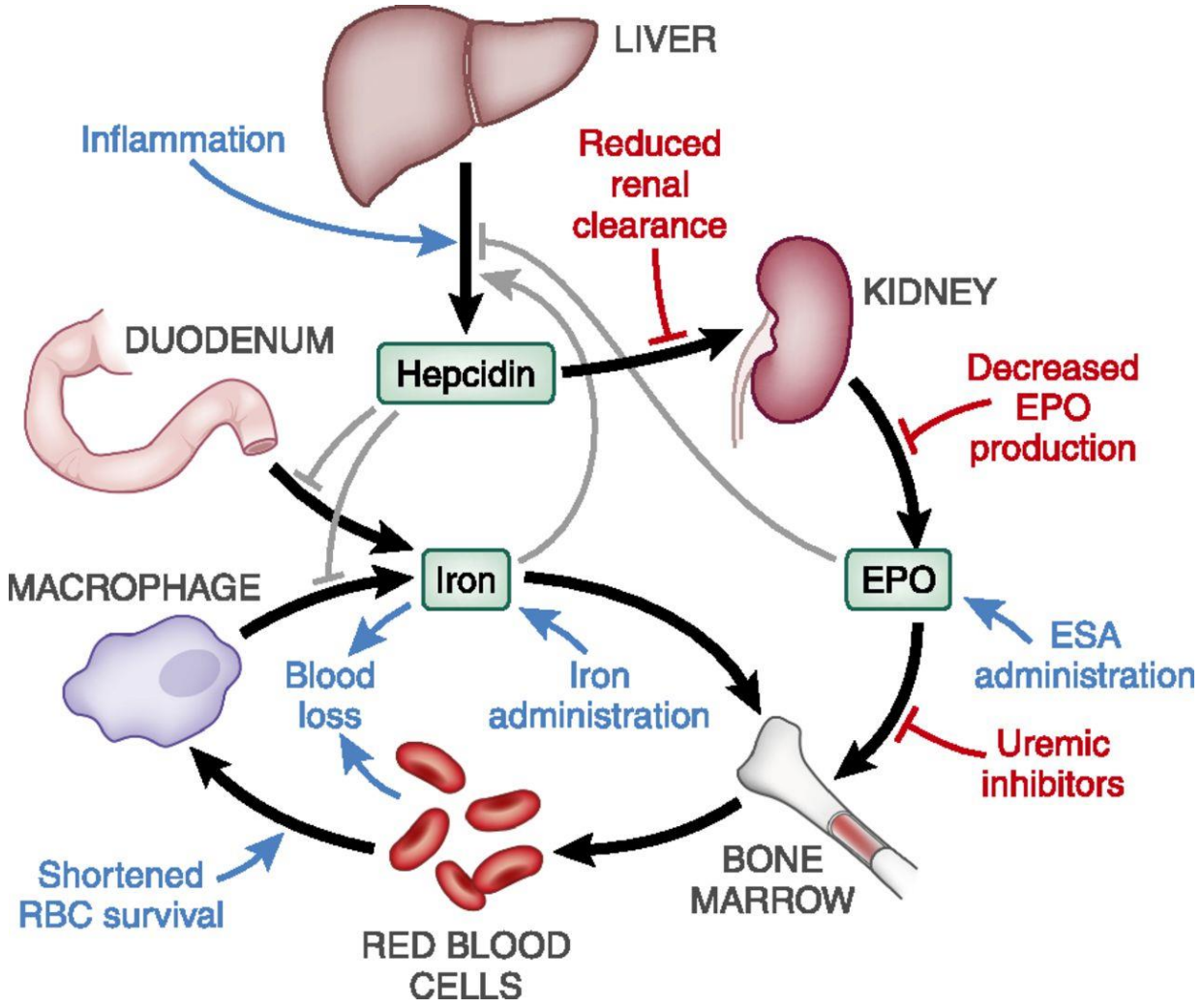
Case 4 Question 2 Answer

The patient has symptomatic anemia with an adequate transferrin saturation. The next best step would be to add an ESA.

Controvery: Use of ESAs in patients with a history of cancer and recent cardiovascular events

Over the last twenty years or so, there has been increasing evidence of the risks of ESAs, particularly in the setting of cancer and recent cardiovascular events, but those studies must be put into the context of how anemia was being managed at the time of those studies.

Mechanisms underlying anemia of chronic kidney disease



Jodie L. Babitt, and Herbert Y. Lin JASN 2012;23:1631-1634

KDIGO Recommendations

In initiating and maintaining ESA therapy, we recommend balancing the potential benefits of reducing blood transfusions and anemia-related symptoms against the risks of harm in individual patients (e.g., stroke, vascular access loss, hypertension). (1B)

Special considerations with ESAs in dialysis

- Cancer
- Stroke
- Vascular access thrombosis

ESAs and Cancer

Beginning in 2010, the FDA required that ESAs be prescribed to cancer patients under its risk evaluation and mitigation strategy program

- Requires additional education for healthcare providers who prescribe and dispense ESAs
- Requires documentation that patients understand ESA-related risks

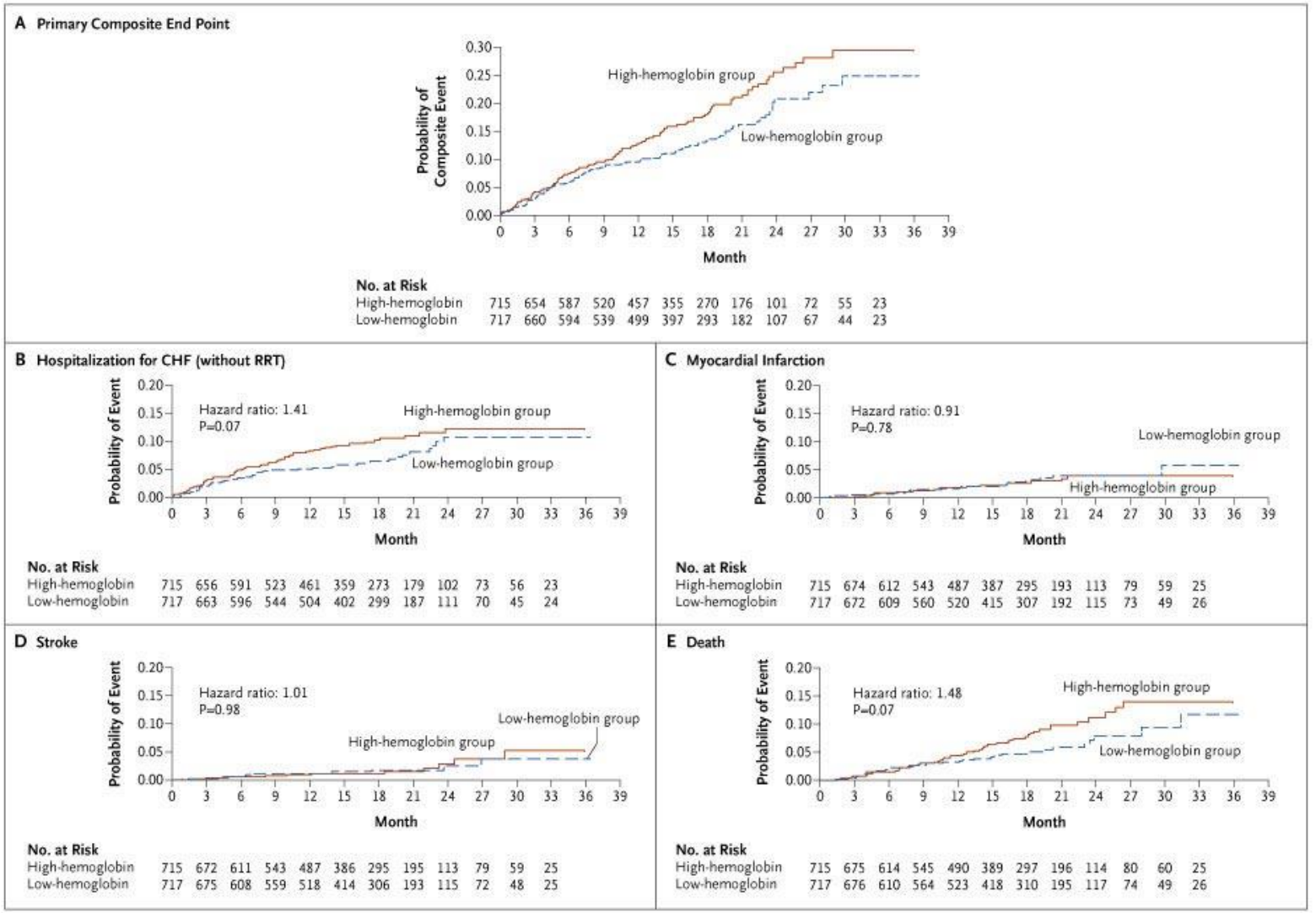
Source	Cancer Type	Concomitant Therapy	# of patients randomized	ESA Treatment	Hemoglobin Stopping Value g/dL	Adverse Outcome
Henke et al 2003	Head and neck	Radiotherapy	351	Epoetin beta (300 IU/kg 3x/week)	≥ 14 (women) ≥ 15 (men)	Locoregional progression
Hedenus et al 2003	Lympho-proliferative cancers	Chemotherapy	349	Darbepoietin alfa (2.25 ug/kg/week)	≥ 14 (women) ≥ 15 (men)	Shortened overall survival
Leyland-Jones et al 2005	Metastatic breast cancer	Chemotherapy	939	Epoetin alfa (40000 U/wk)	> 14	Overall survival vs placebo
Overgaard et al 2007	Locally advanced head and neck	Radiotherapy	522	Darbepoietin alfa (150 ug/week)	> 15.5	Increased risk in local-regional failure
PREPARE	Breast cancer	Chemotherapy	733	Darbepoietin alfa (4.5 ug/kg/2 wk)	≥ 13	Shortened overall survival

Bennett CL *et al* JAMA 2008; 299: 914-924

What is the evidence for an increased risk of cardiovascular events?

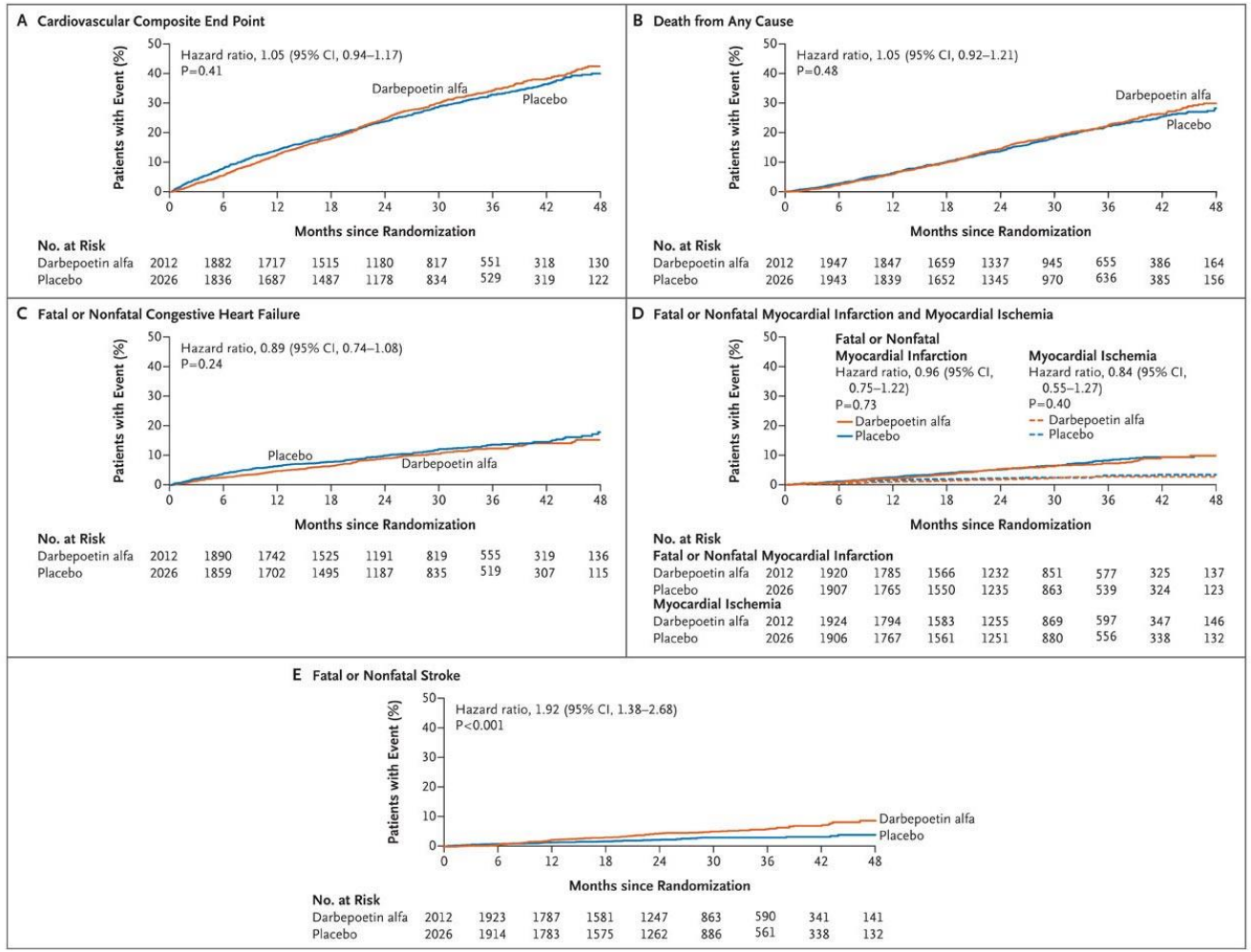
- CHOIR
  - Participants all had CKD and were randomized to two different hemoglobin targets
- TREAT
  - Participants all had CKD and diabetes and were randomized to darbepoietin versus placebo

CHOIR: Probabilities of the Primary and Secondary End Points



Singh AK *et al*. N Engl J Med 2006;355:2085-2098

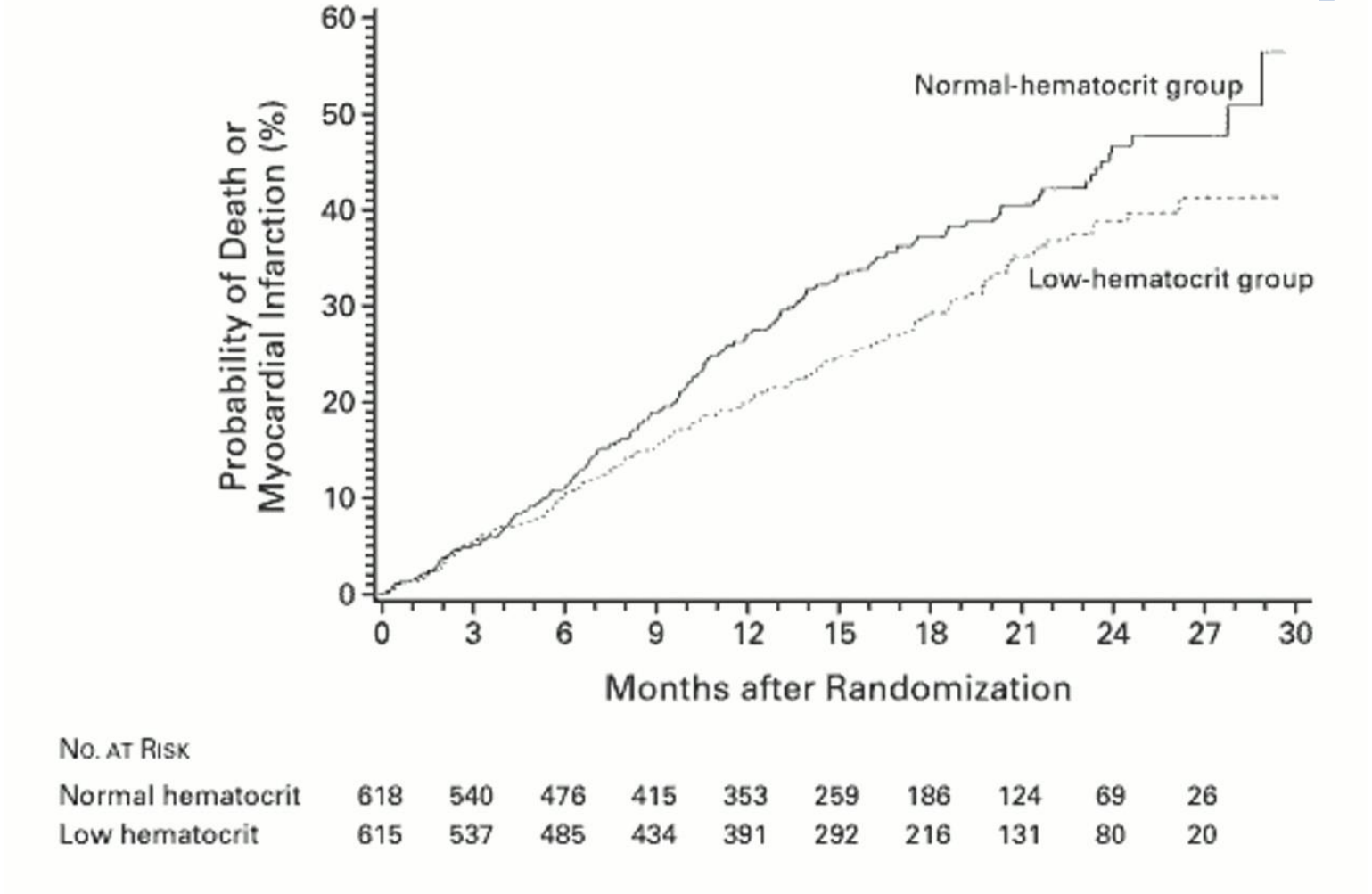
Treat: Kaplan-Meier Estimates of the Probability of the Primary and Secondary End Points (Note Panel E)



Pfeffer M *et al*. N Engl J Med 2009;361:2019-2032

Is a higher hemoglobin better in dialysis patients?

Probability of Death or a First Nonfatal Myocardial Infarction in the Normal-Hematocrit and Low-Hematocrit Groups



No. at Risk										
Normal hematocrit	618	540	476	415	353	259	186	124	69	26
Low hematocrit	615	537	485	434	391	292	216	131	80	20

Besarab A *et al*. N Engl J Med 1998;339:584-590

FDA changes to the ESA label June 2011

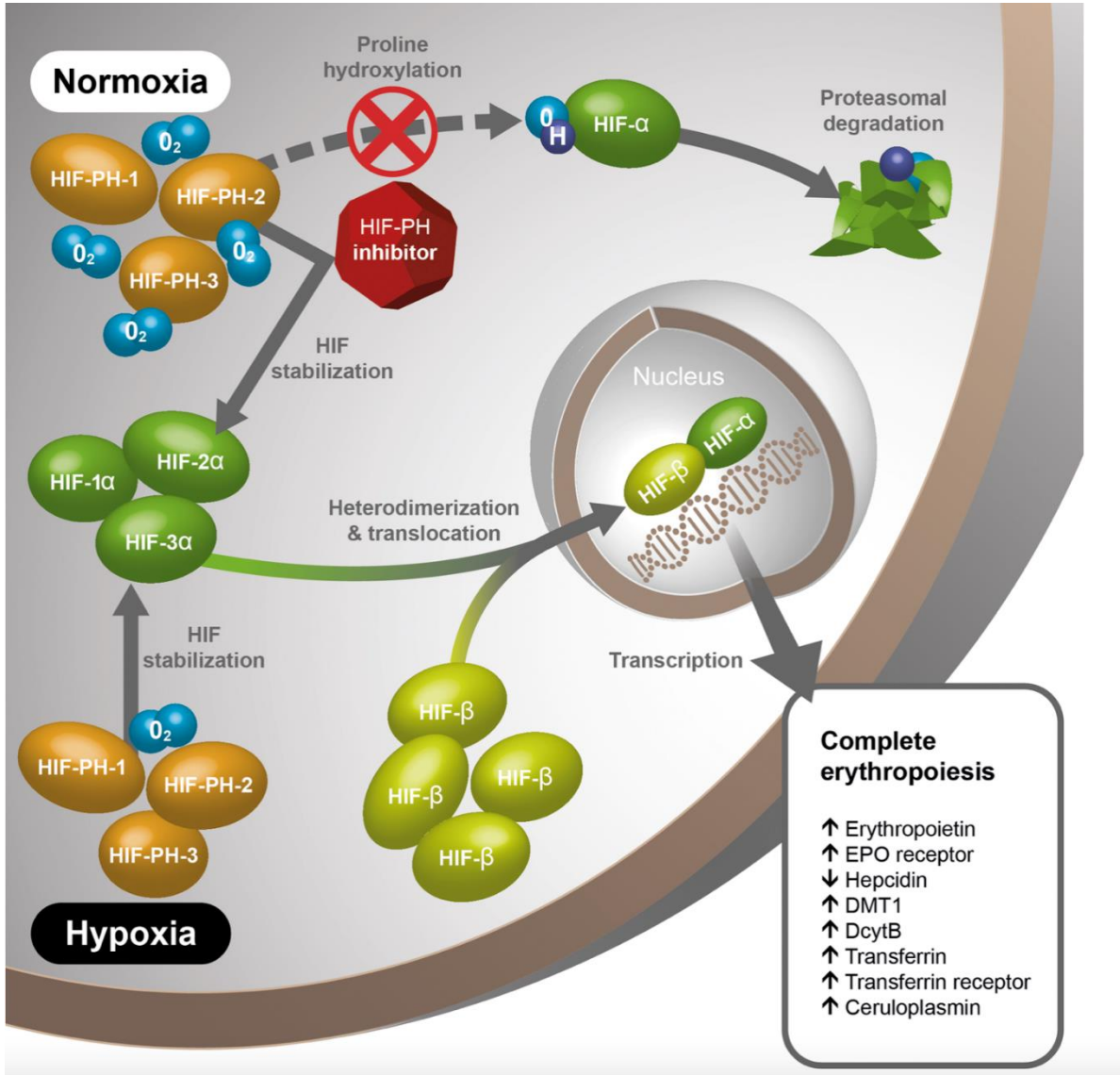
For patients with CKD on dialysis:

- Initiate ESA treatment when the hemoglobin level is less than 10 g/dL
- If the hemoglobin level approaches or exceeds 11 g/dL, reduce or interrupt the dose of ESA.
- When initiating or adjusting therapy, monitor hemoglobin levels at least weekly until stable, then monitor at least monthly.
- For patients who do not respond adequately over a 12-week escalation period, increasing the ESA dose further is unlikely to improve response and may increase risks.

Innovation: New drugs to treat anemia of chronic kidney disease

HIF prolyl hydroxylase inhibitors

- Stabilize the HIF complex
- Stimulate endogenous EPO production
- Orally administered



Gupta N and Wish JB. Am J Kidney Dis 2017; 69: 815-826

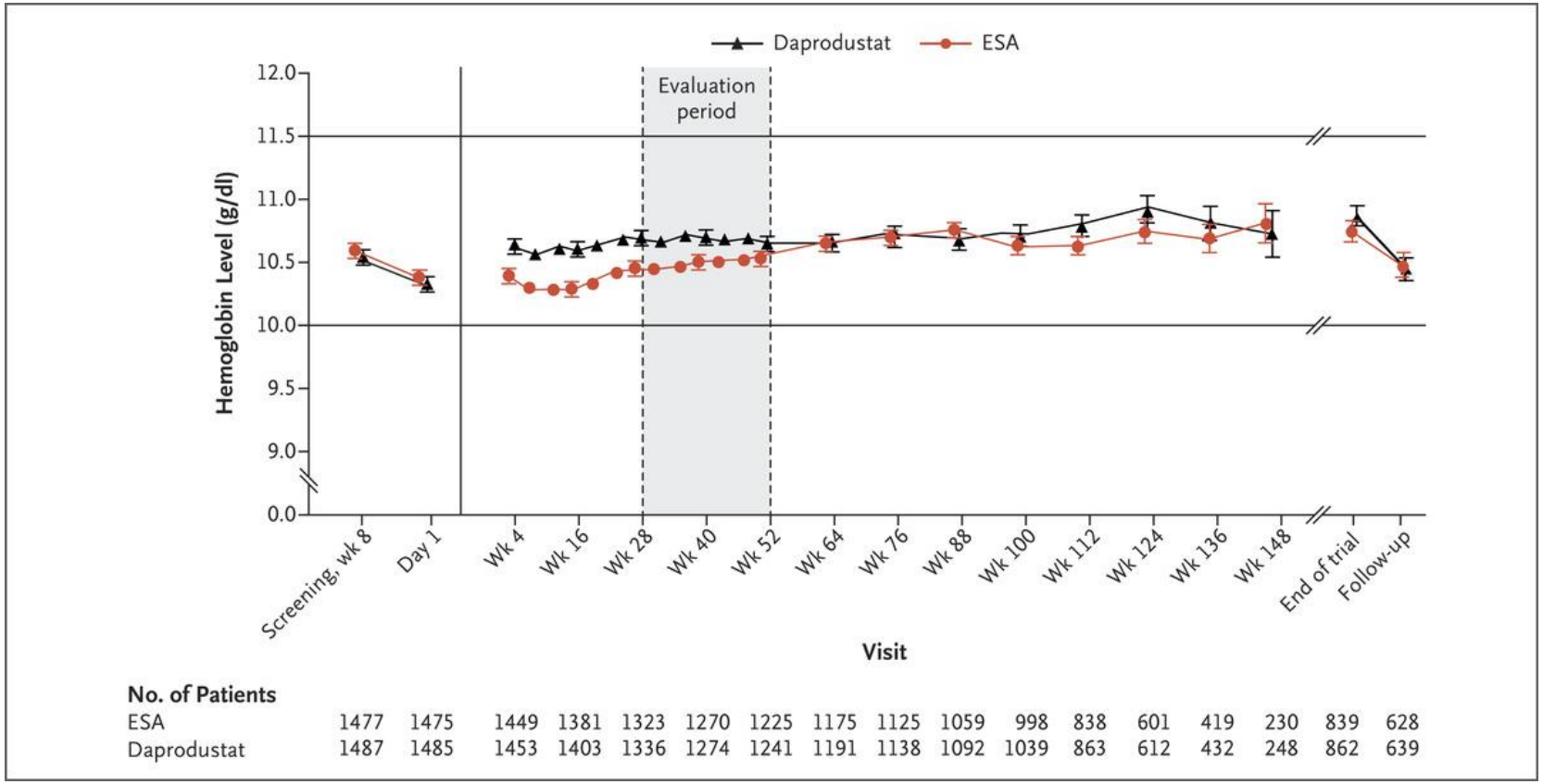
HIF-PH Inhibitors Under Development

Drug	Dosing Frequency
Roxadustat	3x/week
Vadadustat	Daily
Daprodustat	Daily
Molidustat	Daily

Why look for alternatives to erythropoietin?

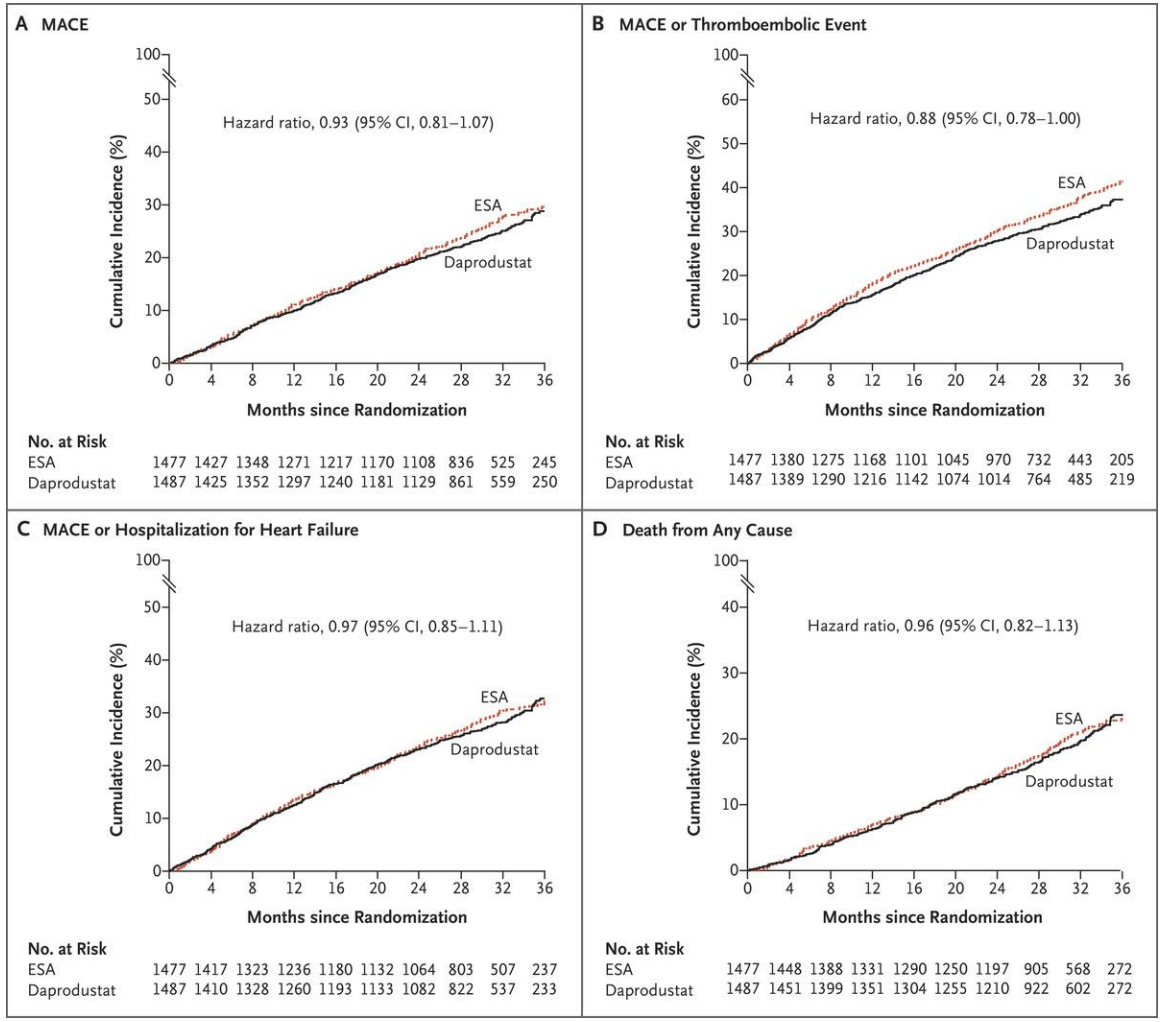
- Cost
- Intravenous or subcutaneous route of administration
- Adverse cardiovascular events
  - CHOIR study: erythropoietin: more CHF in high-hemoglobin group
  - TREAT study: diabetic subjects; more strokes in high hemoglobin group

Daprodustat vs ESA in treatment of anemia



AK Singh et al. N Engl J Med 2021;385:2325-2335.

Time to First Occurrence of Cardiovascular Events and Death



AK Singh et al. N Engl J Med 2021;385:2325-2335.

Summary of Daprodustat Trials

Dialysis-Dependent CKD

- Daprodustat was non-inferior to EPO with respect to correction of anemia
- Daprodustat was non-inferior with respect to cardiovascular safety

Non-Dialysis-Dependent CKD

- Daprodustat was non-inferior to EPO with respect to correction of anemia
- Daprodustat was non-inferior with respect to cardiovascular safety

FDA NEWS RELEASE

FDA Approves First Oral Treatment for Anemia Caused by Chronic Kidney Disease for Adults on Dialysis

More Press Announcements

For Immediate Release: February 01, 2023

Today, the U.S. Food and Drug Administration approved Jesduvroq tablets (daprodustat) as the first oral treatment for anemia (decreased number of red blood cells) caused by chronic kidney disease for adults who have been receiving dialysis for at least four months. Jesduvroq is not approved for patients who are not on dialysis. Other FDA-approved treatments for this condition are injected into the blood or under the skin.

"With an oral drug option in addition to the FDA-approved injection options, adults with chronic kidney disease on dialysis now have multiple ways to treat their anemia," said Ann Farrell, M.D., director of the Division of Non-Malignant Hematology in the FDA's Center for Drug Evaluation and Research. "This approval demonstrates the FDA's commitment to helping bring a range of therapeutic options to patients with chronic diseases. Patients can consult with their healthcare providers to select the option that is most appropriate."

Content current as of:
02/01/2023

Regulated Product(s)
Drugs

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Key Points

- Screen patients at high risk for kidney disease
- SGLT-2 inhibitors and GLP-1 agonists are key medications in retarding progression of diabetic kidney disease.
- SGLT-2 inhibitors may be useful in retarding progression of non-diabetic kidney disease
- Iron deficiency is common in CKD and should be corrected before starting an ESA.
- Daprodustat is the first FDA-approved HIF-PH inhibitor for treatment of anemia of CKD

Next best steps

- Endocrine consultation may be helpful in management of poorly controlled type 2 diabetic patients given the number of new diabetic medications and the complexity of some regimens.


Mass General Brigham