The Implementation of Pharmacists in Outpatient Specialist care: Cardio-renal-metabolic involvement

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University Hospitals

OPA Annual Conference & Trade Show
April 5-7, 2024

OHIO PHARMACISTS ASSOCIATION

1 VOICE VISION TEAM

Disclosure Statement

- Brayden Dunn, Ebne Rafi, and Matthew Nennstiel have no relevant financial relationship(s) with ineligible companies to disclose.

  and

- None of the planners for this activity have relevant financial relationships with ineligible companies to disclose.

Learning Objectives

At the completion of this activity, the participant will be able to:

1) Explain the cardiac and potential renal benefits of GLP1ra agents
2) List the cardiac and renal benefits of SGLT2i agents
3) Recognize different work flow models where pharmacists can be involved in outpatient care

Epidemiology

- In 2021, diabetes was the eighth leading cause of death in the United States
- Individuals with diabetes have a 13-14 year-shorter life span compared to those without diabetes
- Men and women older than 40 years old with eGFR >60 have >20 year-shorter life expectancy compared to those with CKD stage4

Swamy S, et al. *J Clin MeD*. 2023 Nov 8;12(22):6984.
Ndumele CE, et al. *Circulation*. 2023 Nov 14;148(20):1606-1635.

CDC 2023: Top Conditions Leading to Mortality

Data in this table is from time period:Year/Month: 2023 (provisional); UCD - 15 Leading Causes of Death: 52 categories selected

UCD - 15 Leading Causes of Death	Deaths	Population	Crude Rate Per 100,000
#Diseases of heart (I00-I09,I11,I13,I20-I51)	674,773	333,287,557	202.5
#Malignant neoplasms (C00-C97)	612,227	333,287,557	183.7
#Cerebrovascular diseases (I60-I69)	162,190	333,287,557	48.7
#Chronic lower respiratory diseases (J40-J47)	144,703	333,287,557	43.4
#Accidents (unintentional injuries) (V01-X59,Y85-Y86)	141,253	333,287,557	42.4
#Alzheimer disease (G30)	113,951	333,287,557	34.2
#Diabetes mellitus (E10-E14)	94,507	333,287,557	28.4
#Nephritis, nephrotic syndrome and nephrosis (N00-N07,N17-N19,N25-N27)	55,107	333,287,557	16.5
#Chronic liver disease and cirrhosis (K70,K73-K74)	51,852	333,287,557	15.6
#COVID-19 (U07.1)	49,659	333,287,557	14.9
#Influenza and pneumonia (J09-J18)	44,705	333,287,557	13.4
#Essential hypertension and hypertensive renal disease (I10,I12,I15)	42,222	333,287,557	12.7
#Septicemia (A40-A41)	41,515	333,287,557	12.5
#Parkinson disease (G20-G21)	40,148	333,287,557	12.0
#Intentional self-harm (suicide) (*U03,X60-X84,Y87.0)	31,451	333,287,557	9.4

Cardiovascular-Kidney-Metabolic (CKM) Syndrome

- CKM is a health disorder connected to the presence of obesity, diabetes, chronic kidney disease, and cardiovascular disease
- CKM includes those with existing CVD and those at risk for CVD
- Similar to the staging of heart failure and CKD, CKM also is staged based on risk factor stratification and underlying comorbid conditions

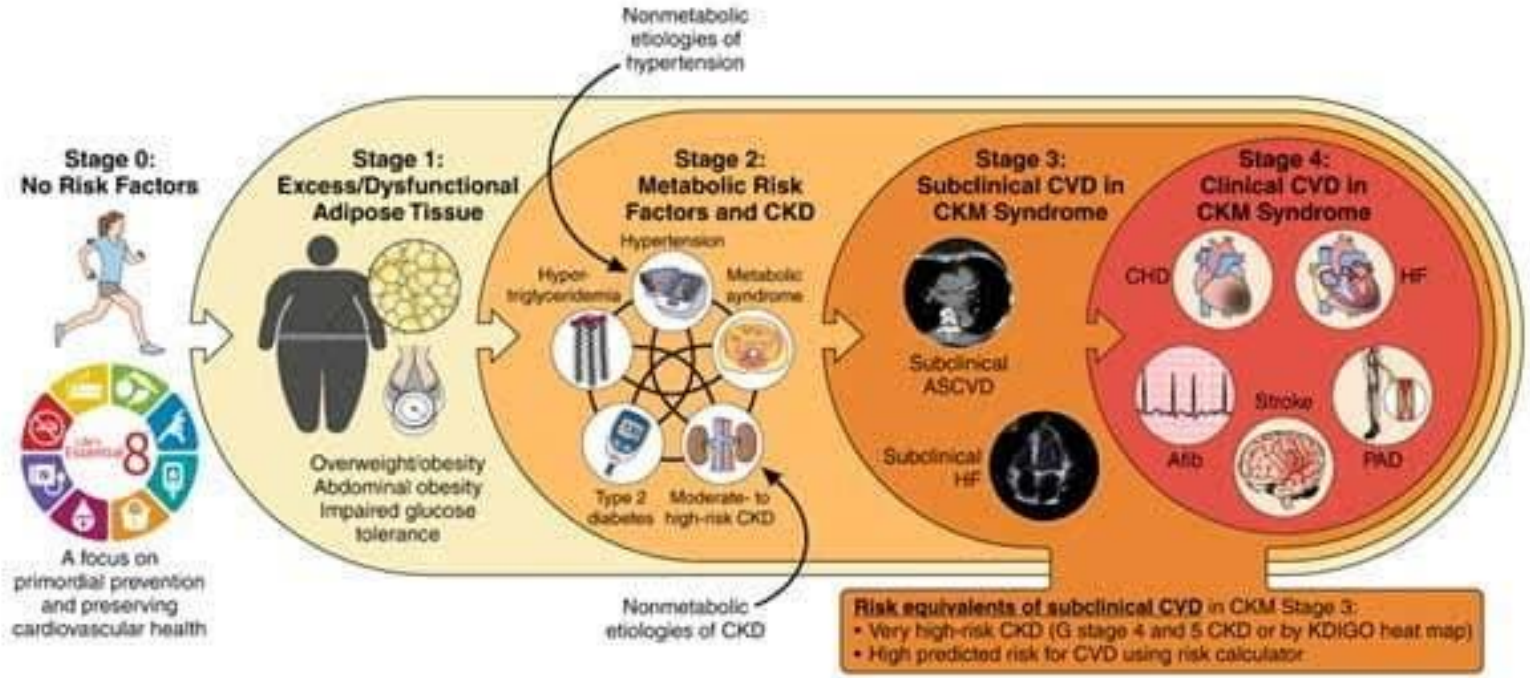
Ndumele CE, et al. *Circulation*. 2023 Nov 14;148(20):1606-1635.

CKM Stages

- Stage 0 – No Risk factors
- Stage 1 – Excess or Dysfunctional adiposity
- Stage 2 - Metabolic risk factors and CKD
- Stage 3 – Subclinical CVD in CKM Syndrome
- Stage 4- Clinical CVD in CKM Syndrome

Ndumele CE, et al. *Circulation*. 2023 Nov 14;148(20):1606-1635.

Stages of Cardiovascular-Kidney-Metabolic Syndrome



Abbreviations: AFib indicates atrial fibrillation; ASCVD, atherosclerotic cardiovascular disease; CHD, coronary heart disease; CKD, chronic kidney disease; CKM, cardiovascular-kidney-metabolic; CVD, cardiovascular disease; HF, heart failure; KDIGO, Kidney Disease Improving Global Outcomes; and PAD, peripheral artery disease.

Ndumele, C.E. et al., Cardiovascular Kidney Metabolic Health: A Presidential Advisory From the American Heart Association. 2023. Circulation

American Heart Association.

Ndumele CE, et al. *Circulation*. 2023 Nov 14;148(20):1606-1635.

CKD Definition and Scales of Illness

- CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health
- CKD is classified based on cause, GFR category (G1–G5), and Albuminuria category (A1–A3)

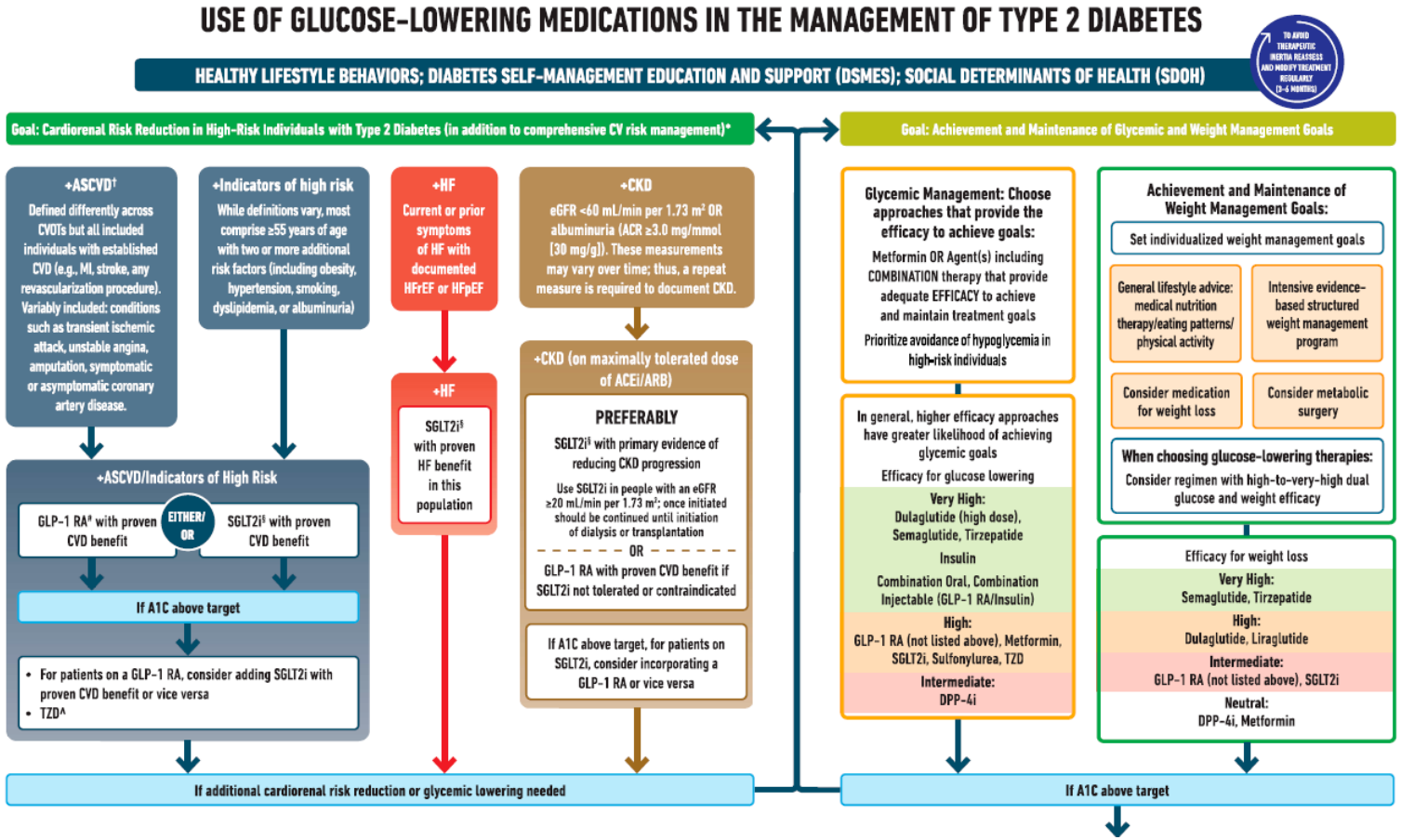
Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

GFR categories (ml/min/1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

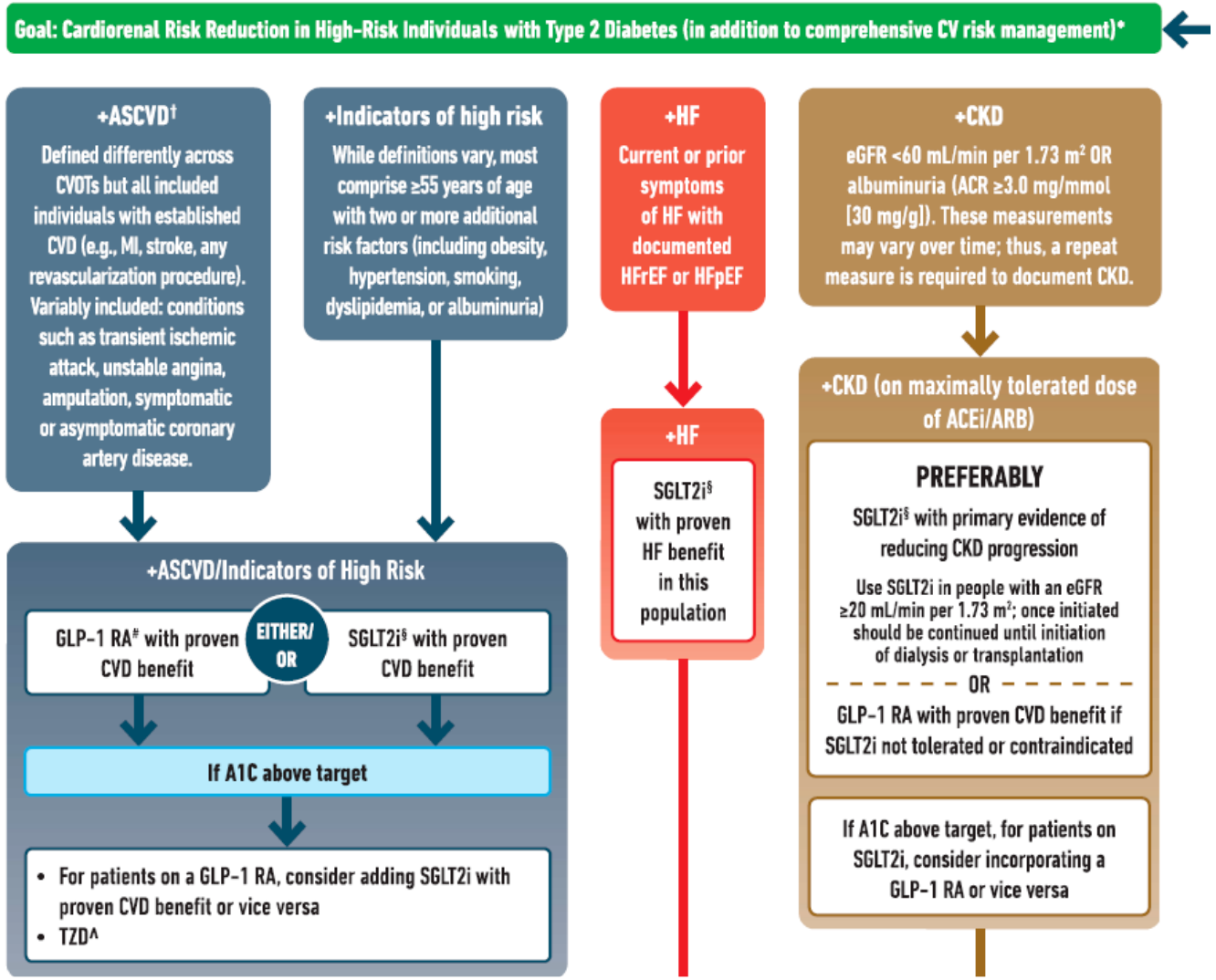
Green: low risk (if no other markers of kidney disease, no CKD); yellow: moderately increased risk; orange: high risk; red: very high risk.

Clinical Guidelines: ADA 2024, KDIGO 2022, 2022 AHA/ACC/HFSA

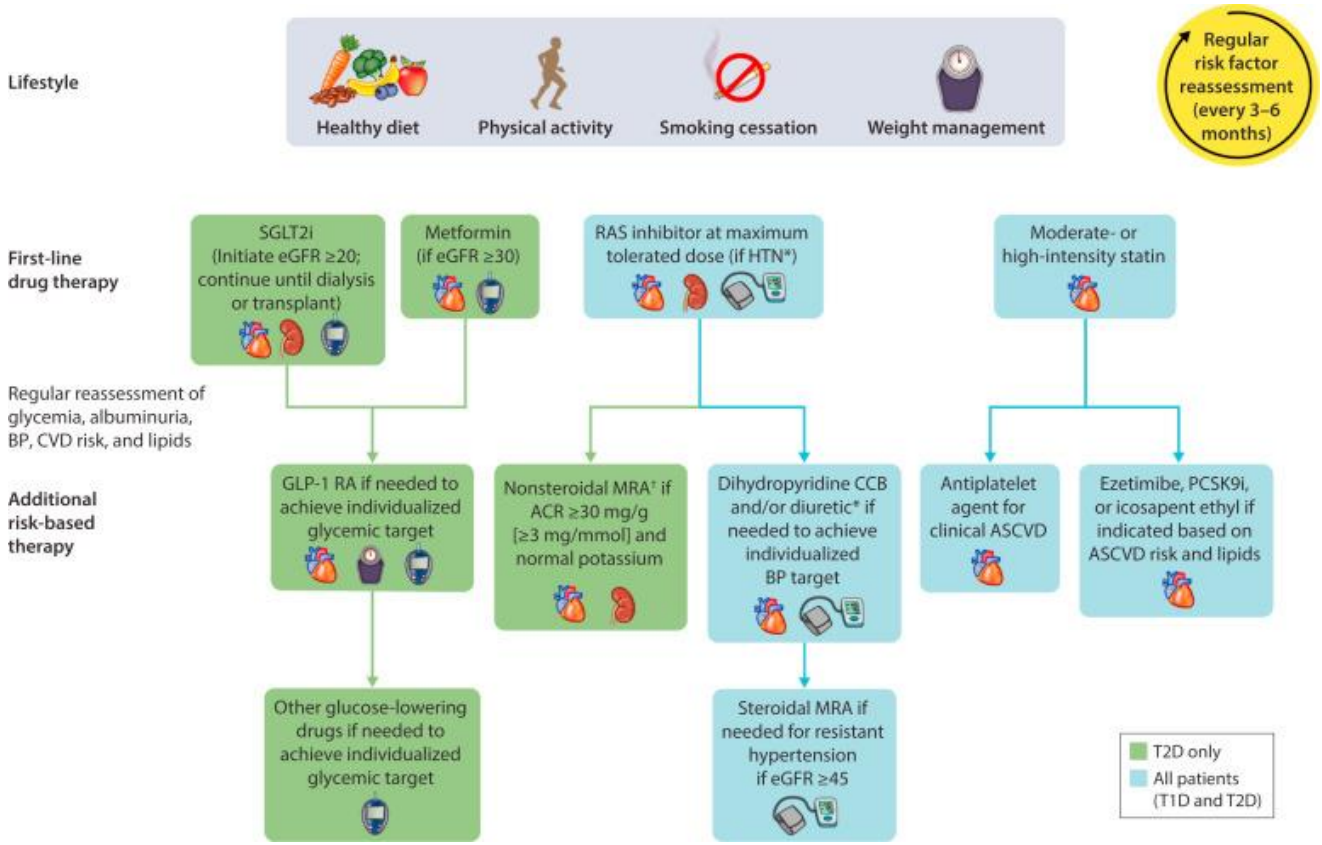
Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2024



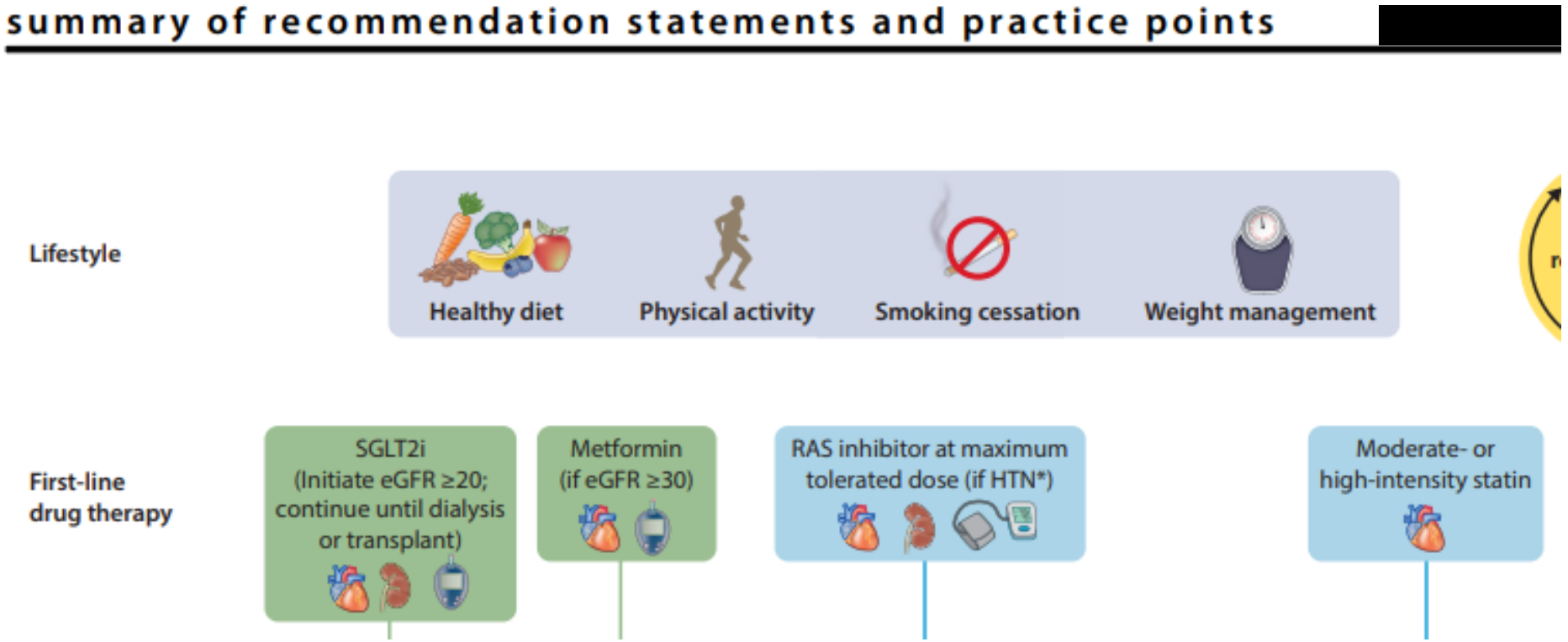
ADA 2024 Standards of Medical Care: Emphasis in Cardio-Renal Protection



KDIGO 2022 CLINICAL PRACTICE GUIDELINE FOR DIABETES MANAGEMENT IN CKD



KDIGO 2022 Clinical Practice for Diabetes: Emphasis in Cardio-Renal Protection



KDIGO 2022 Clinical Practice for Diabetes: Emphasis in Cardio-Renal Protection

1.3. Sodium–glucose cotransporter-2 inhibitors (SGLT2i)

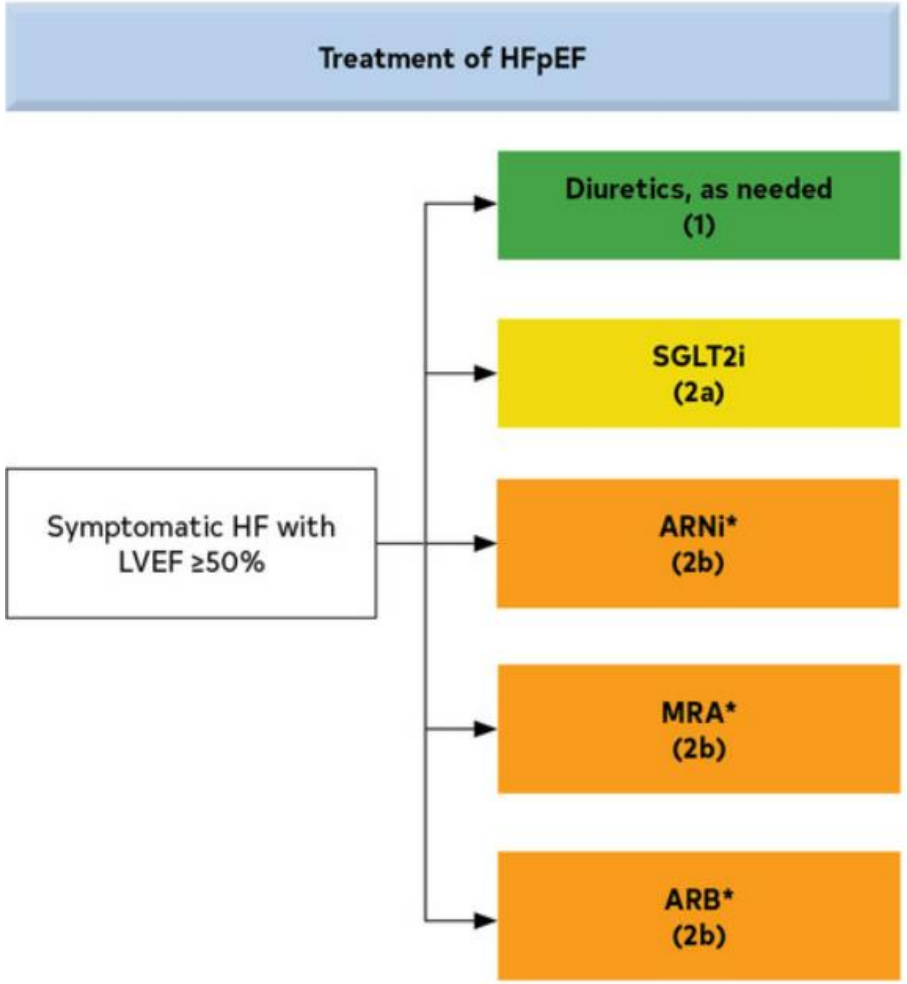
Recommendation 1.3.1: We recommend treating patients with type 2 diabetes (T2D), CKD, and an eGFR ≥20 ml/min per 1.73 m^2 with an SGLT2i *(1A)*.

Practice Point 1.3.1: The recommendation for SGLT2i is for kidney and cardiovascular protection and SGLT2i have been shown to have safety and benefit in CKD patients, even for those without T2D. Thus, if patients are already being treated with other glucose-lowering agents, an SGLT2i can be added to the current treatment regimen (Figure 6).

Practice Point 1.3.2: The choice of an SGLT2i should prioritize agents with documented kidney or cardiovascular benefits and take eGFR into account.

Practice Point 1.3.3: It is reasonable to withhold SGLT2i during times of prolonged fasting, surgery, or critical medical illness (when patients may be at greater risk for ketosis).

2022 AHA/ACC/HFSA Guidelines: Emphasis in Cardio-Renal Protection



COR	LOE	Recommendation
1	A	1. In patients with symptomatic chronic HFrEF, SGLT2i are recommended to reduce hospitalization for HF and cardiovascular mortality, irrespective of the presence of type 2 diabetes.[1,2]
Value Statement: Intermediate Value (A)		2. In patients with symptomatic chronic HFrEF, SGLT2i therapy provides intermediate economic value.[3,4]

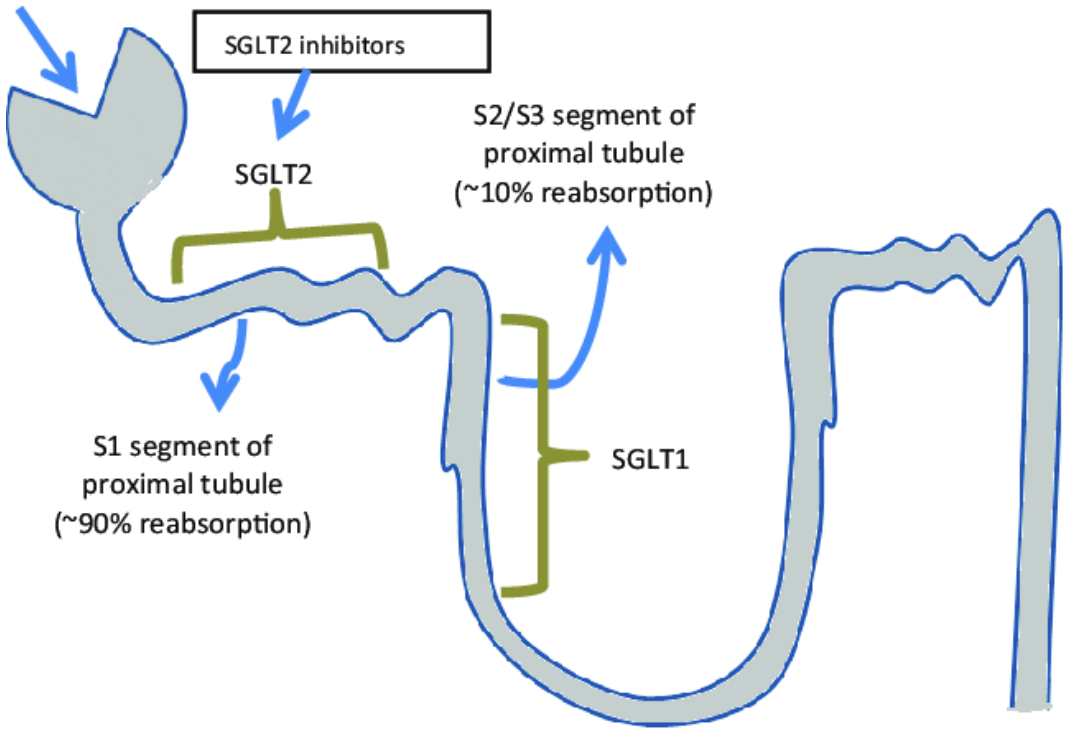
Comprehensive Guideline Directed Medical Therapy

- Therapy based on glycemic, hemodynamic and lipid concerns:
  - RAS inhibitor at maximally tolerated dose
  - Statin therapy
  - SGLT2i if eGFR ≥ 20 ml/min/1.72 m2
  - GLP1-RA
- Further Considerations:
  - Nonsteroidal MRA if ACR ≥ 30 mg/g and normal potassium

Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors

Review of Physiology

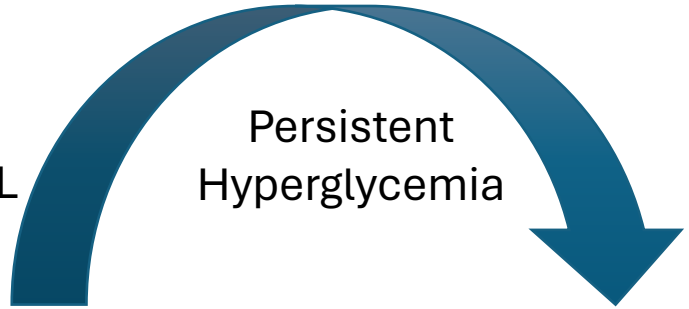
- Two main sodium-glucose cotransporters: SGLT1 and SGLT2
- SGLT2: exclusively in renal tissue
  - Major role is reabsorption
- SGLT1: renal, intestine, heart, and skeletal
  - Major role is intestinal absorption



Review of Physiology

SGLT2 Normal Physiology

- Renal reabsorption to a maximum of 180-200 mg/dL
- Limited protein expression



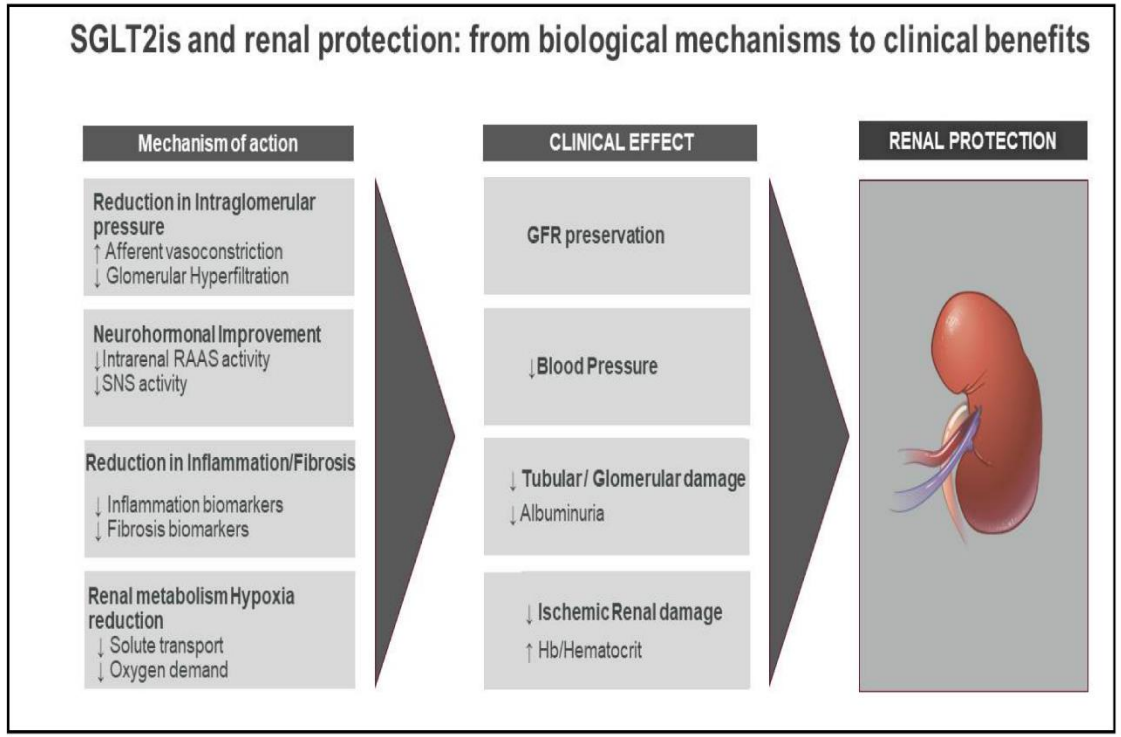
SGLT2 Pathophysiology

- Renal reabsorption increases to a maximum of 240 mg/dL
- Upregulation of SGLT2 expression in proximal tubule
- Increased energy expenditure from reabsorption

Bailey CJ, Day C, Bellary S. Renal Protection with SGLT2 Inhibitors: Effects in Acute and Chronic Kidney Disease. *Curr Diab Rep*. 2022;22(1):39-52. doi:10.1007/s11892-021-01442-z

Sodium Glucose Cotransporter 2 Inhibitors: Mechanism of Action

- Direct inhibition of the SGLT2 protein located in the proximal tubule of the nephron
- Inhibition leads to reabsorption targeting a blood glucose ~80 mg/dL



Fonseca-Correa JI, et al. *Front Med (Lausanne)*. 2021;8:777861.
Leoncini G, et al. *Int J Mol Sci*. 2021 Apr 23;22(9):4441.

Sodium Glucose Cotransporter 2 Inhibitors: Immediate Benefits

Immediate Effects	Secondary Effects
Glycosuria	Improvements in albuminuria
A1C improvement	Weight loss and lipid metabolism
Natriuresis	Improved renal oxygen delivery and consumption

Fonseca-Correa JI, et al. *Front Med (Lausanne)*. 2021;8:777861.

Sodium Glucose Cotransporter 2 Inhibitors: Side Effects

Common	Severe
Genital mycotic infections	Ketoacidosis
Urinary tract infections	Volume depletion
Increased urination	Fournier's Gangrene

Padda IS, Mahtani AU, Parmar M. Sodium-Glucose Transport Protein 2 (SGLT2) Inhibitors. [Updated 2023 Jun 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan

Sodium Glucose Cotransporter 2 Inhibitors: Side Effects

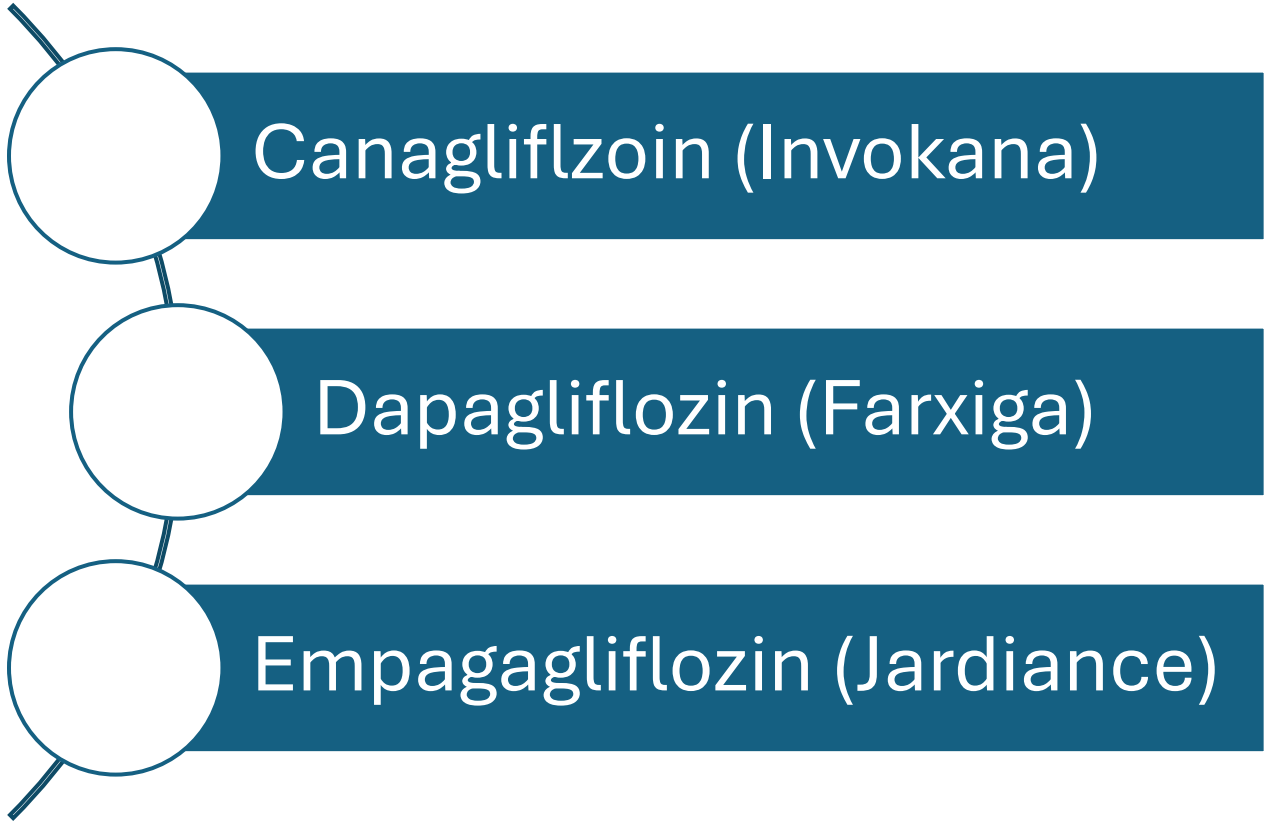
- Lower limb amputation
- Increased risk associated with:
  - Peripheral vascular disease
  - Neuropathy
  - History of diabetic foot ulcer
- Can consider holding SGLT2i during foot ulcers/limb infections
- Canagliflozin and ertugliflozin more associated with amputation

Padda IS, Mahtani AU, Parmar M. Sodium-Glucose Transport Protein 2 (SGLT2) Inhibitors. [Updated 2023 Jun 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan

Sodium Glucose Cotransporter 2 Inhibitors: Products on the Market

Medication	Renal benefit	Cardiac Benefit
Canagliflozin (Invokana)	✓	✓
Dapagliflozin (Farxiga)	✓	✓
Empagliflozin (Jardiance)	✓	✓
Ertugliflozin (Steglarto)		
Bexagliflozin (Brenzavvy)		
Sotagliflozin (Inpefa)		✓

Sodium Glucose Cotransporter 2 Inhibitors: Cardiac Benefits



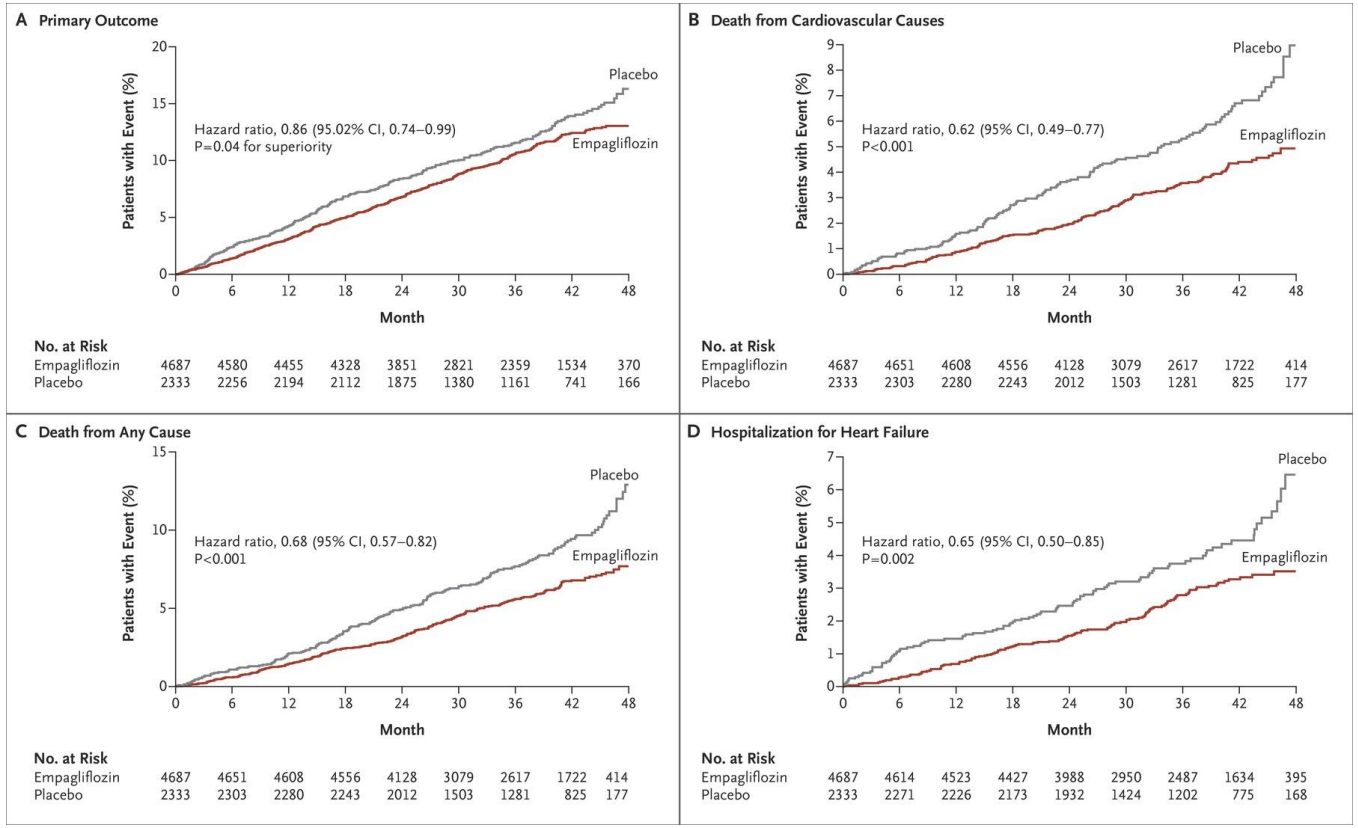
EMPA-REG OUTCOME Trial – Empagliflozin in T2DM

- Purpose: To demonstrate cardiovascular safety
- Population:
  - T2DM with cardiovascular disease
  - GFR > 30 mL/min
- Primary outcome: composite death from cardiovascular cause, nonfatal MI, nonfatal stroke
- Secondary outcome: composite of the primary outcome plus hospitalization for unstable angina

Zinman B, et al. *N Engl J Med.* (2015) 373:2117–28.

EMPA-REG OUTCOME Trial - Empagliflozin

- 7020 patients were enrolled and followed for 3 years
- Clinical benefits seen within 6 months therapy start



Zinman B, et al. *N Engl J Med.* (2015) 373:2117–28.

EMPA-REG OUTCOME Trial - Empagliflozin

Table 1. Primary and Secondary Cardiovascular Outcomes.

Outcome	Placebo (N=2333)		Empagliflozin (N=4687)		Hazard Ratio (95% CI)	P Value
	no. (%)	*rate/1000 patient-yr*	*no. (%)*	*rate/1000 patient-yr*		
Death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke: primary outcome*	282 (12.1)	43.9	490 (10.5)	37.4	0.86 (0.74–0.99)	
Noninferiority						<0.001†
Superiority						0.04†
Death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for unstable angina: key secondary outcome*	333 (14.3)	52.5	599 (12.8)	46.4	0.89 (0.78–1.01)	
Noninferiority						<0.001†
Superiority						0.08†
Death						
From any cause	194 (8.3)	28.6	269 (5.7)	19.4	0.68 (0.57–0.82)	<0.001
From cardiovascular causes	137 (5.9)	20.2	172 (3.7)	12.4	0.62 (0.49–0.77)	<0.001
Fatal or nonfatal myocardial infarction excluding silent myocardial infarction	126 (5.4)	19.3	223 (4.8)	16.8	0.87 (0.70–1.09)	0.23

Zinman B, et al. *N Engl J Med.* (2015) 373:2117–28.

SGLT2- Kidney Outcome Trials

	CREEDENCE	DAPA-CKD	EMPA-KIDNEY
Study Population	Type 2 DM ≥4 weeks stable on ACE-i/ARB therapy eGFR: ≥30-90 UACR: >300-≤5000	With or without diabetes ≥4 weeks stable on ACE-i/ARB therapy eGFR: ≥25-75 UACR: ≥200-≤5000	With or without diabetes Stable on ACE-i/ARB therapy eGFR: ≥20-45 OR eGFR: ≥45-90 UACR: ≥200
N	N=4401	N=4304	N=6009
Primary Endpoint	Composite: •ESKD •Doubling of sCr from baseline •Renal/CV death	Composite: •≥50% eGFR decrease •ESKD •Renal/CV death	Composite: •ESKD •eGFR ≤10 •≥40% eGFR decrease •Renal/CV death
Key Secondary Endpoints	**•CV death or HF hosp.** **•CV death, MI, or stroke** **•HF hosp.** **•ESKD, doubling of sCr, renal death**	**•≥50% eGFR decrease, ESKD, Renal Death** **•CV death or HF hosp.** **•All-cause Death**	•CV death or HF hosp. **•All-cause hosp.** •All-cause death

Yau K, et al. *Kidney Int Rep*. 2022 May 5;7(7):1463-1476.

Learning Question

VP is a 63 y/o female with stage 3b CKD. Other conditions include HTN, hyperlipidemia, and pre-DM. Current medications include atorvastatin 80mg qd, amlodipine 2.5mg qd, Lisinopril 20mg. The decision is made to start the patient on empagliflozin 10mg once daily.

Baseline labs: eGFR: 44 ml/min/1.73 m2, sCr: 1.33 mg/dL, UACR 350 mcg/mg.

Patient returns for a 1 month follow up and reports no significant adverse events.

Follow up labs show, eGFR: 34 ml/min/1.73 m2, sCr: 1.67 mg/dL.

What is the most appropriate therapy recommendation for this patient?

A) Discontinue empagliflozin 10mg due to worsening kidney function
B) Continue empagliflozin 10mg and continue to monitor symptoms and lab work
C) Increase empagliflozin to 25mg
D) Discontinue empagliflozin 10mg and start dapagliflozin 10mg

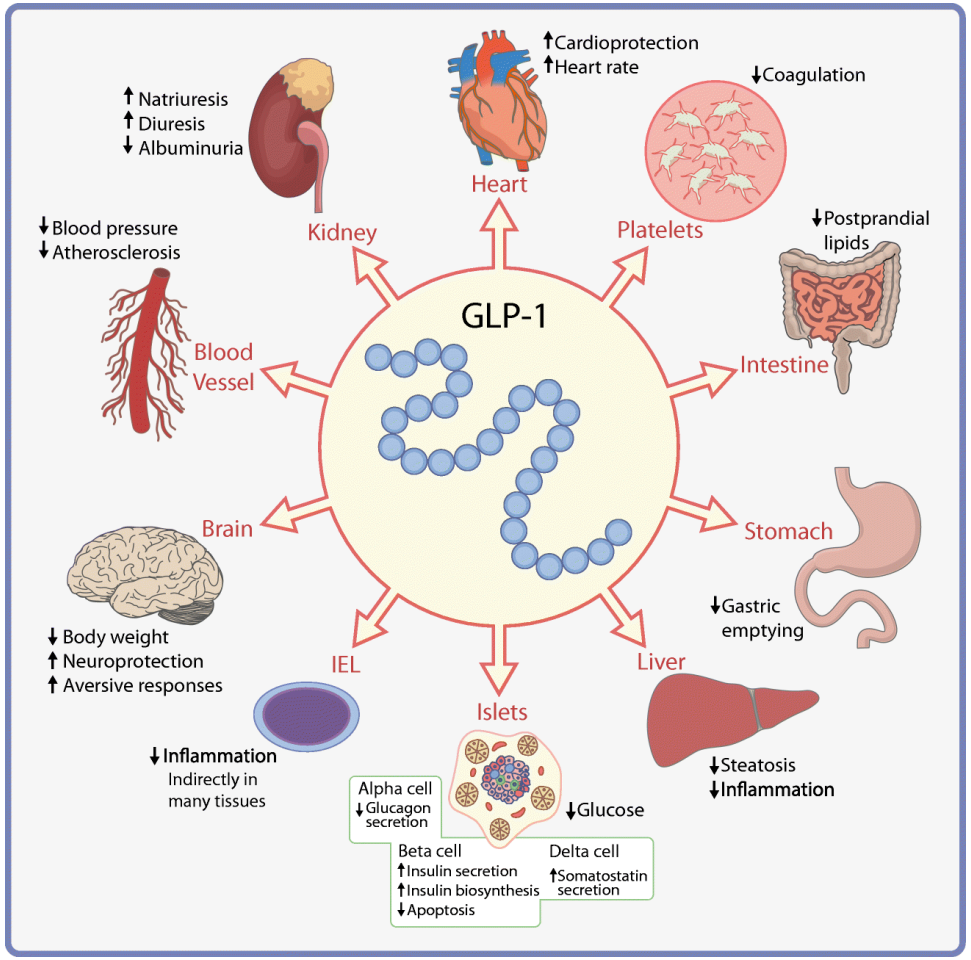
Incretin Based Therapies

Incretin Effect

- Oral glucose administration leads to greater stimulation of insulin secretory responses than does intravenous administration, despite a matched elevation in plasma glucose concentrations.
- The incretin effect is reported in individuals with normal oral glucose tolerance, however in individuals with diabetes it is reduced or may be absent

Incretin Hormones – Glucose-Like Peptide 1 (GLP-1)

- GLP-1
  - Peptide hormone released from gastrointestinal L cells upon nutrient ingestion.
  - GLP-1 effects upon binding to the GLP1-R include:
    - Glucose-dependent insulin secretion from pancreatic β cells
    - Inhibition of glucagon release from pancreatic α cells
    - The prolongation of gastric emptying

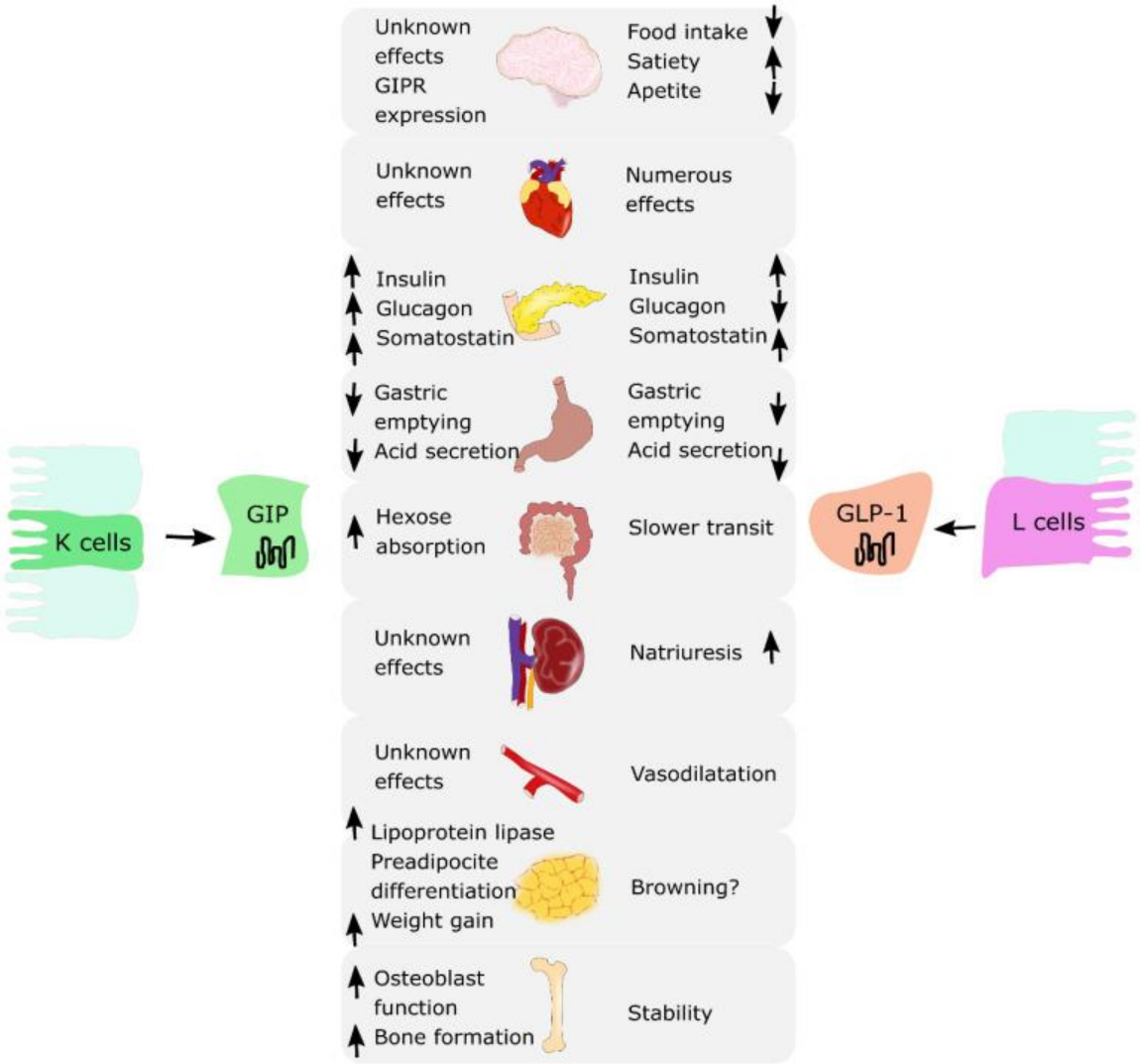


Marx N, et al. *Circulation*. 2022 Dec 13;146(24):1882-1894.

Incretin Hormones - Glucose-dependent insulinotropic polypeptide (GIP)

- GIP
  - Under hyperglycemic conditions, glucose-dependent insulinotropic polypeptide stimulates the release of insulin, thereby lowering glucagon levels
  - Under euglycemic or hypoglycemic conditions, glucagon levels are increased.
  - GIP-R are abundant in adipose tissue
    - GIP enhances both the postprandial lipid-buffering capacity of white adipose tissue and the sensitivity of adipose tissue to insulin, which may prevent ectopic fat deposition.

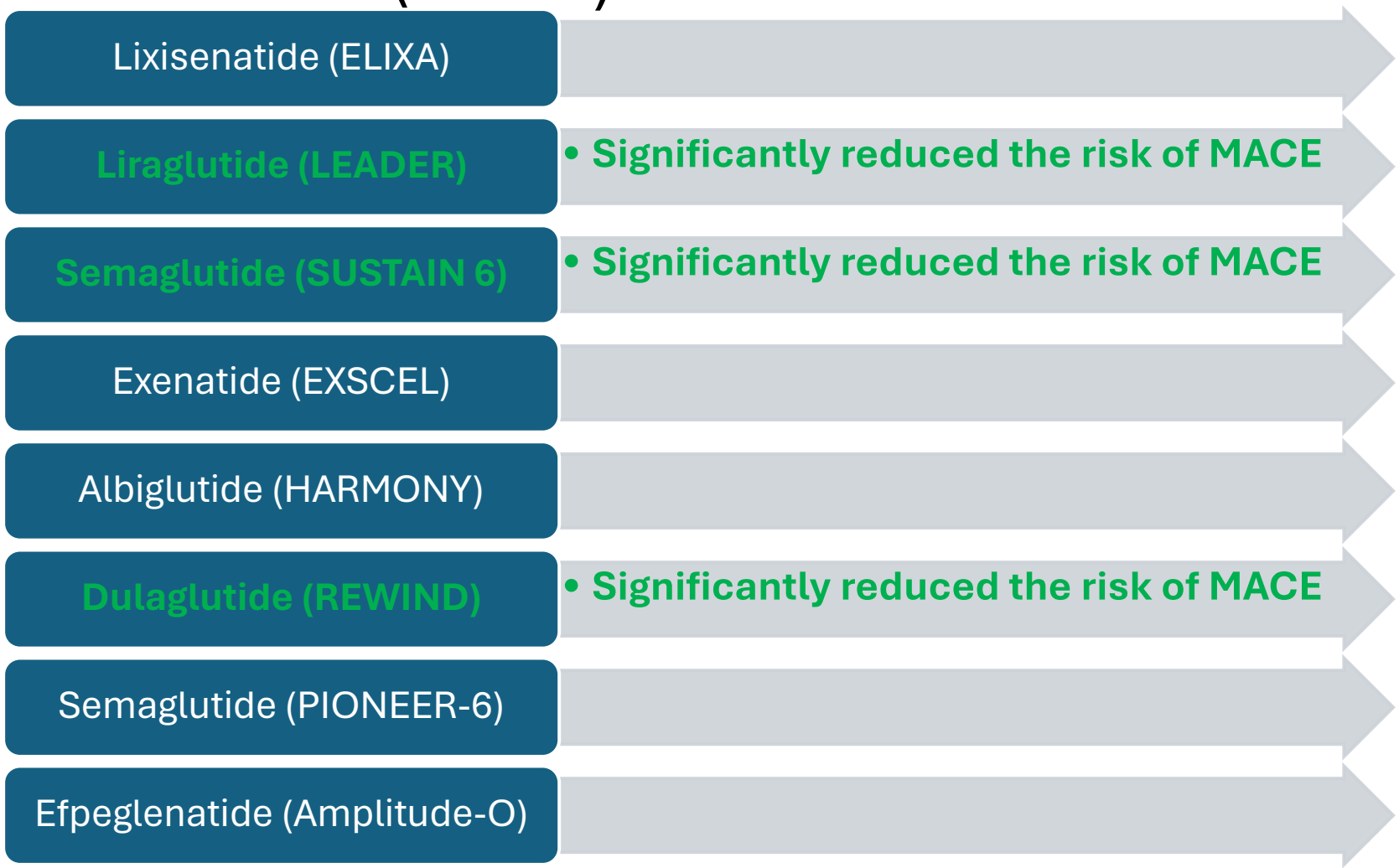
Incretin Therapies Mechanism of Action



Incretin hormone therapy: Contraindications/adverse Effects

- Contraindications:
  - Personal or family history of medullary thyroid carcinoma (MTC)
  - Personal history of multiple endocrine neoplasia type II (MEN-2)
- Common adverse effects:
  - Gastrointestinal
  - Fatigue
  - Headache
- Severe adverse effects:
  - Pancreatitis
  - Worsening diabetic retinopathy
  - Acute kidney injury
  - Gallbladder disease
  - Hypersensitivity reactions

Incretin-Based Pharmacologic Therapies: Major Adverse Cardiovascular Event (MACE) Benefits



Marx N, et al. Circulation. 2022 Dec 13;146(24):1882-1894.
Ferhatbegović L, et al. *Front Clin Diabetes Healthc.* 2023 Dec 8:4:1293926.

GLP1 Clinical Trials Review: SUSTAIN-6 and REWIND

SUSTAIN-6 Trial – Semaglutide in T2DM

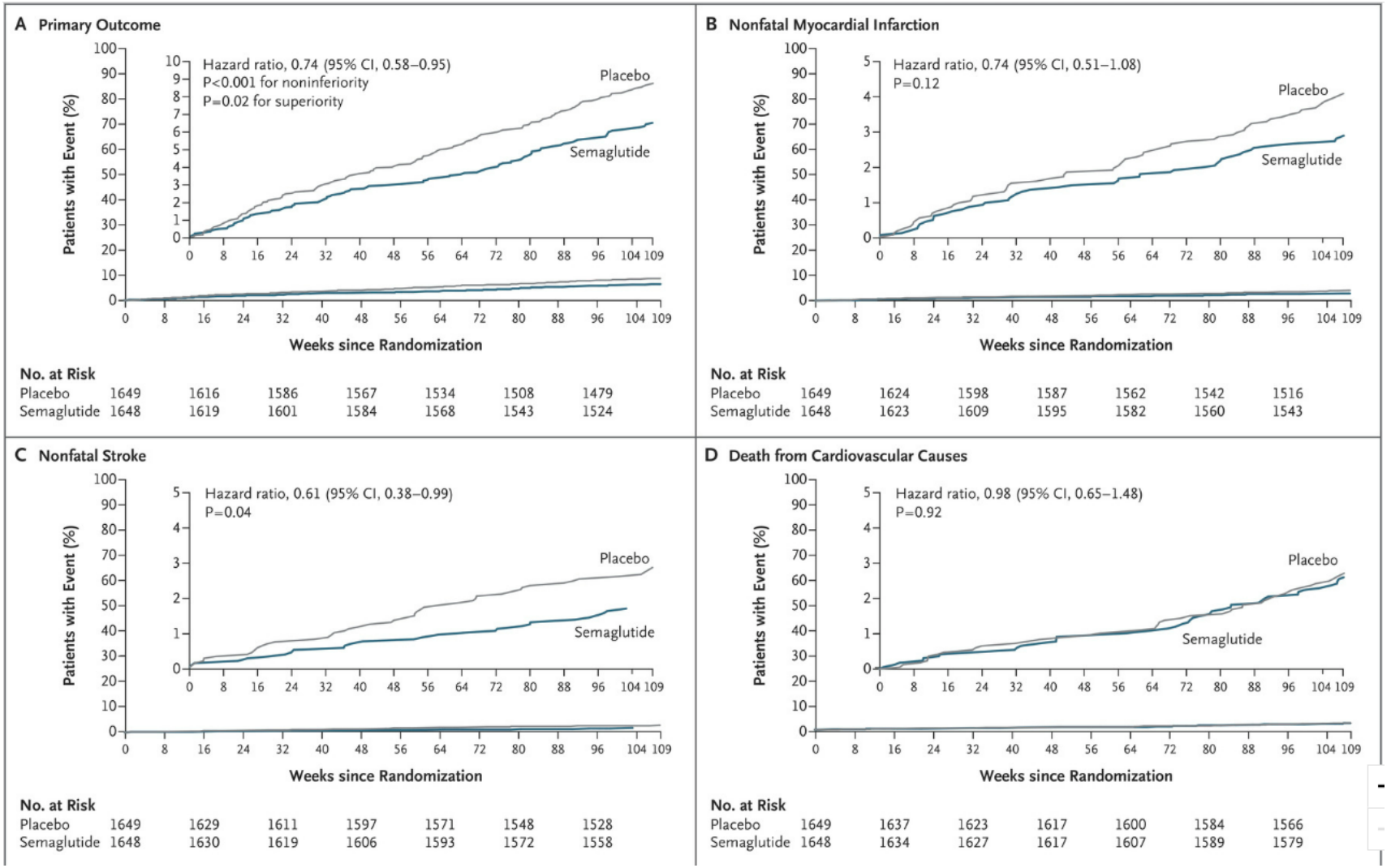
- Purpose: To compare the risk of MACE between once-weekly injectable semaglutide compared to placebo when used with standard of care treatments for diabetes and cardiovascular disease.
- Population:
  - T2DM with cardiovascular disease, CKD stage 3, OR CHF
- Primary outcome: Time to occurrence of MACE - A three-part composite outcome which included cardiovascular death, non-fatal myocardial infarction and non-fatal stroke

SUSTAIN-6 Trial – Semaglutide in T2DM

Table 2. Primary and Secondary Cardiovascular and Microvascular Outcomes.

Outcome	Semaglutide (N=1648)		Placebo (N=1649)		Hazard Ratio (95% CI)*	P Value
	no. (%)	*no./100 person-yr*	*no. (%)*	*no./100 person-yr*		
Primary composite outcome†	108 (6.6)	3.24	146 (8.9)	4.44	0.74 (0.58–0.95)	<0.001 for noninferiority; 0.02 for superiority
Expanded composite outcome‡	199 (12.1)	6.17	264 (16.0)	8.36	0.74 (0.62–0.89)	0.002
All-cause death, nonfatal myocardial infarction, or nonfatal stroke	122 (7.4)	3.66	158 (9.6)	4.81	0.77 (0.61–0.97)	0.03
Death						
From any cause	62 (3.8)	1.82	60 (3.6)	1.76	1.05 (0.74–1.50)	0.79
From cardiovascular cause	44 (2.7)	1.29	46 (2.8)	1.35	0.98 (0.65–1.48)	0.92
Nonfatal myocardial infarction	47 (2.9)	1.40	64 (3.9)	1.92	0.74 (0.51–1.08)	0.12
Nonfatal stroke	27 (1.6)	0.80	44 (2.7)	1.31	0.61 (0.38–0.99)	0.04
Hospitalization for unstable angina pectoris	22 (1.3)	0.65	27 (1.6)	0.80	0.82 (0.47–1.44)	0.49
Revascularization	83 (5.0)	2.50	126 (7.6)	3.85	0.65 (0.50–0.86)	0.003
Hospitalization for heart failure	59 (3.6)	1.76	54 (3.3)	1.61	1.11 (0.77–1.61)	0.57
Retinopathy complications§	50 (3.0)	1.49	29 (1.8)	0.86	1.76 (1.11–2.78)	0.02
New or worsening nephropathy¶	62 (3.8)	1.86	100 (6.1)	3.06	0.64 (0.46–0.88)	0.005

SUSTAIN-6 Trial – Semaglutide in T2DM



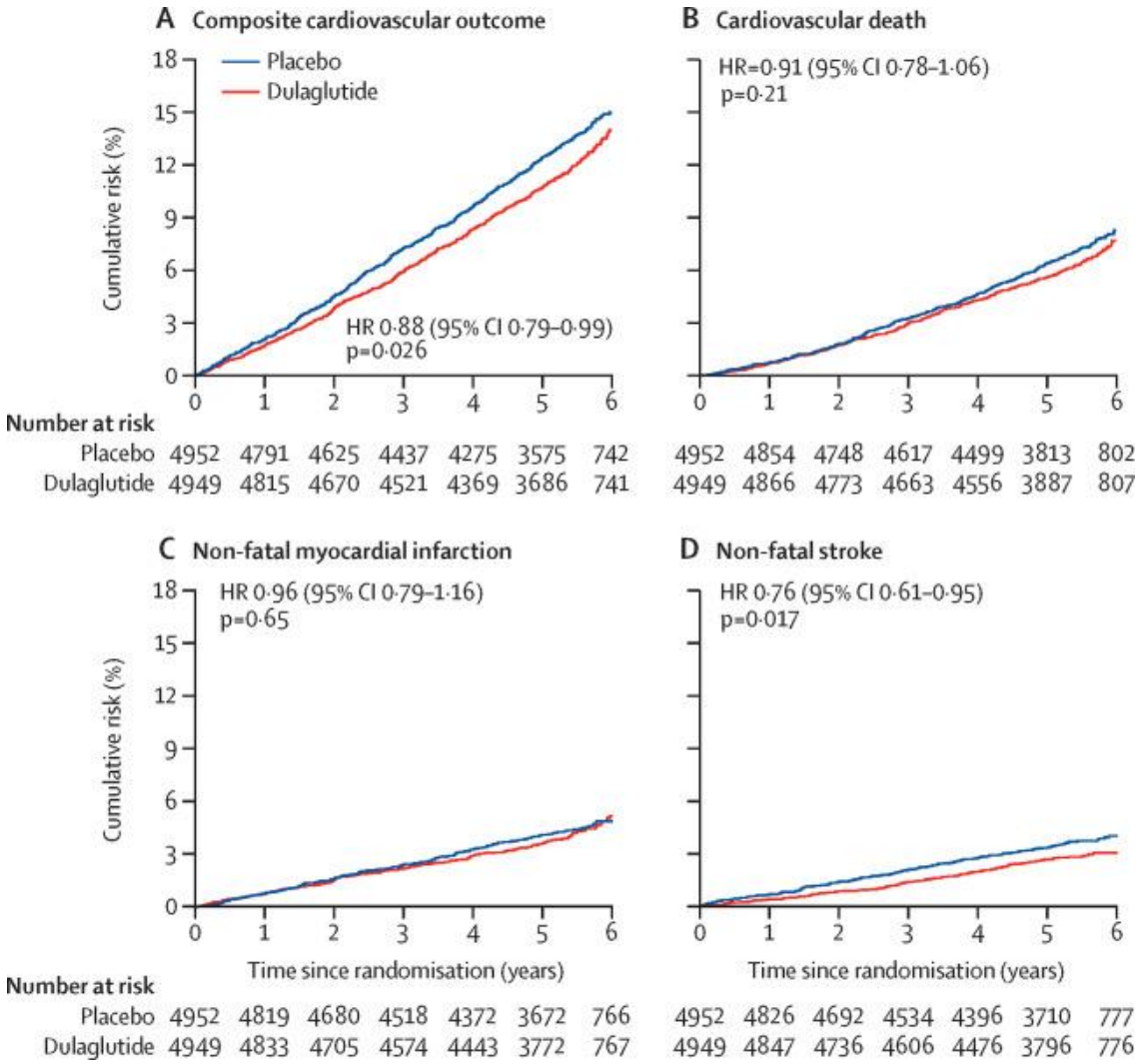
REWIND – Dulaglutide in T2DM

- Purpose: To compare the risk of MACE between once-weekly injectable dulaglutide compared to placebo when used with standard of care treatments for diabetes and cardiovascular disease.
- Population:
  - T2DM with a history of a cardiovascular event or cardiac risk factors
- Primary outcome: first occurrence of composite death from cardiovascular cause, nonfatal MI, nonfatal stroke

REWIND – Dulaglutide in T2DM

	Dulaglutide (n=4949)		Placebo (n=4952)		Hazard ratio (95% CI)	p value
	Number of patients (%)	Incidence rate (number of events per 100 person-years)	Number of patients (%)	Incidence rate (number of events per 100 person-years)		
Primary composite outcome	594 (12·0%)	2·35	663 (13·4%)	2·66	0·88 (0·79–0·99) *	0·026
Myocardial infarction	223 (4·5%)	0·87	231 (4·7%)	0·91	0·96 (0·79–1·15)	0·63
Non-fatal myocardial infarction	205 (4·1%)	0·80	212 (4·3%)	0·84	0·96 (0·79–1·16)	0·65
Fatal myocardial infarction	26 (0·5%)	0·10	20 (0·4%)	0·08	1·29 (0·72–2·30)	0·40
Stroke	158 (3·2%)	0·61	205 (4·1%)	0·81	0·76 (0·62–0·94)	0·010
Non-fatal stroke	135 (2·7%)	0·52	175 (3·5%)	0·69	0·76 (0·61–0·95)	0·017
Fatal stroke	26 (0·5%)	0·10	33 (0·7%)	0·13	0·78 (0·47–1·30)	0·34
Cardiovascular death †	317 (6·4%)	1·22	346 (7·0%)	1·34	0·91 (0·78–1·06)	0·21
Non-cardiovascular death	219 (4·4%)	0·84	246 (5·0%)	0·95	0·88 (0·73–1·06)	0·18
All-cause death	536 (10·8%)	2·06	592 (12·0%)	2·29	0·90 (0·80–1·01)	0·067

REWIND – Dulaglutide in T2DM



FLOW (Kidney outcome trial)– Semaglutide in DKD

- Purpose: to demonstrate if once weekly semaglutide can reduce progression of CKD in patients with T2DM
- Population:
  - T2DM with CKD defined as:
    - eGFR: ≥50-75
    - UACR: >300-≤5000

    OR
    - eGFR: ≥25-50
    - UACR: >100-≤5000
- Primary outcome: composite ESKD, ≥50 eGFR decline, and renal/CV death
- Secondary outcome: Annual rate of change of eGFR, Time to first occurrence of 3-point MACE, Time to occurrence of all-cause death

Rossing P, et al. Nephrol Dial Transplant. 2023 Aug 31;38(9):2041-2051.

FLOW- Semaglutide in DKD

- Trial halted in October of 2023 due to early efficacy data
- March 2024 Novonordisk published a press release stating: “The trial achieved its primary endpoint by demonstrating a statistically significant and superior reduction in kidney disease progression as well as cardiovascular and kidney death of 24% for people treated with semaglutide 1.0 mg compared to placebo”
- Full trial publication still pending

Learning Question

- Which of the following is a contraindication for the use of GLP1a based medication
  a) History of medullary thyroid carcinoma
  b) History of acute kidney injury
  c) History of diabetic retinopathy
  d) History of gallbladder disease

Learning Question

Which of the following outcomes are not assessed in the composite MACE score?

a) Cardiovascular death
b) Non-fatal Stroke
c) Non-fatal MI
d) Hospitalization for heart failure

Learning Question

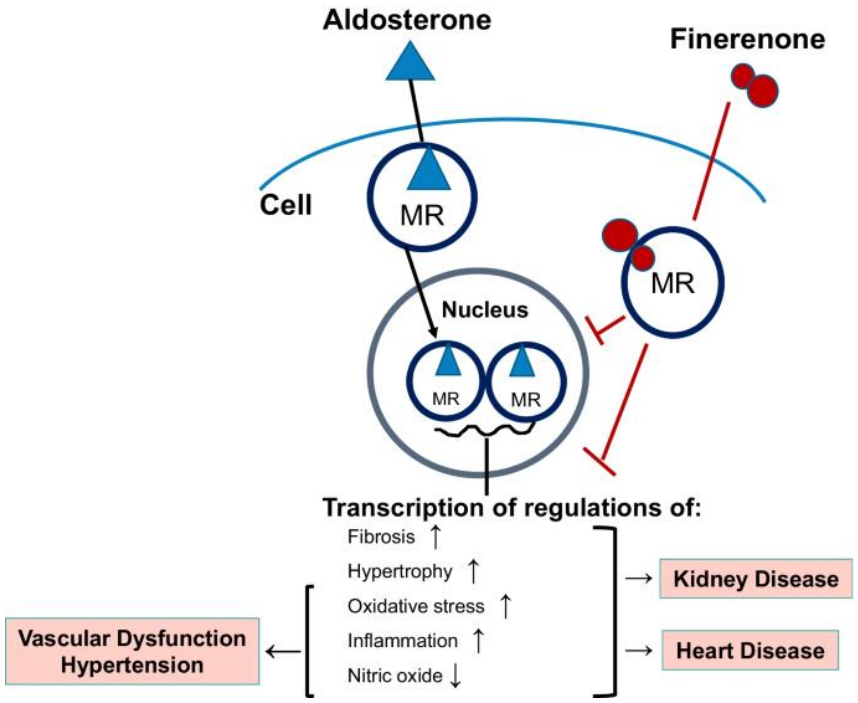
Which of the following GLP1 based medications was not shown to have improvements in MACE through a clinical trial?

a) Liraglutide
b) Semaglutide
c) Dulaglutide
d) Lixisenatide

Kerendia (Finerenone)

Finerenone: Mechanism of Action

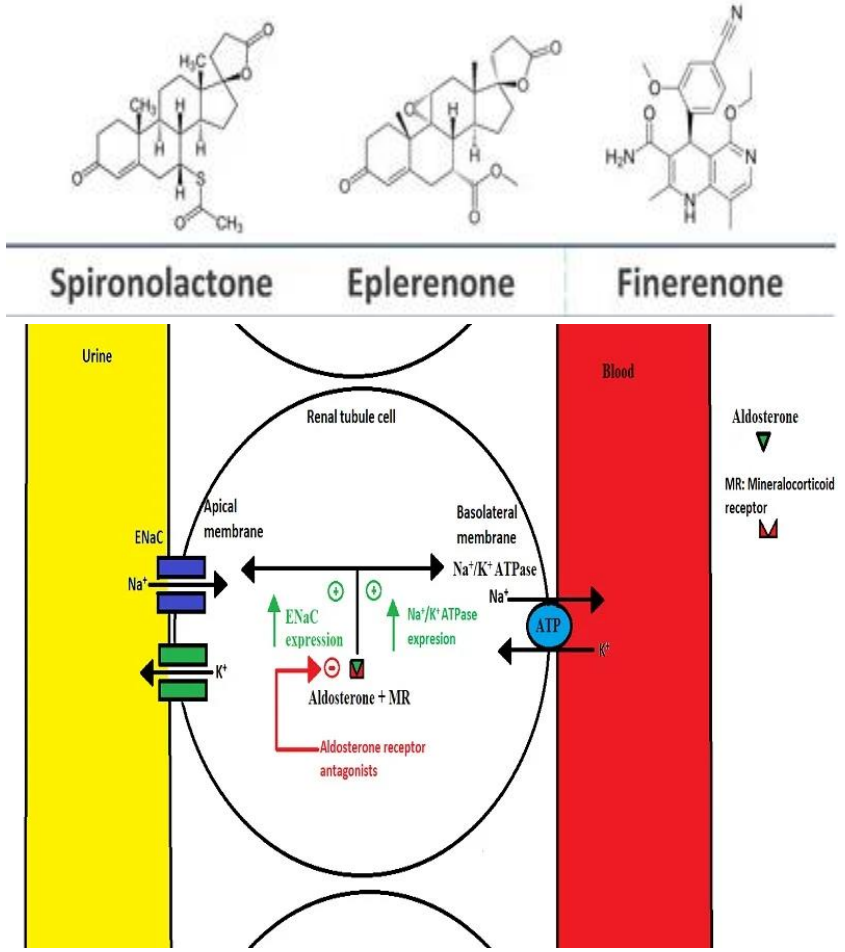
- FDA indication
  - To reduce the risk of sustained eGFR decline, ESRD, CV death, non-fatal MI, and hospitalization for HF in adult patients with CKD associated with T2DM
- Non-steroidal mineralocorticoid receptor antagonist (ns-MRA)
  - Inhibits MR-mediated sodium reabsorption
  - Inhibits MR overexpression
- Selective for heart/blood vessel/ kidney MRs



Ravid JD, et al. *Curr Cardiol Rep*. 2022 Oct;24(10):1251-1259.
Bakris GL, et al. N Engl J Med. 2020 Dec 3;383(23):2219-2229.

Contraindications/Adverse reactions

- Contraindications
  - Patients with adrenal insufficiency
  - Concomitant use with strong CYP3A4 inhibitors
  - Use not recommended in patients with eGFR <25
- Adverse Effects
  - Hyperkalemia
  - Hypotension
  - Hyponatremia



Antimineralocorticoid mechanism of action Retrieved from: https://commons.wikimedia.org/wiki/File:Antimineralocorticoid_mechanism_of_action.png

Finerenone (Kerendia) Clinical Trials Review: FIDELIO-DKD and FIGARO-DKD

Trial Protocol/Inclusion Criteria

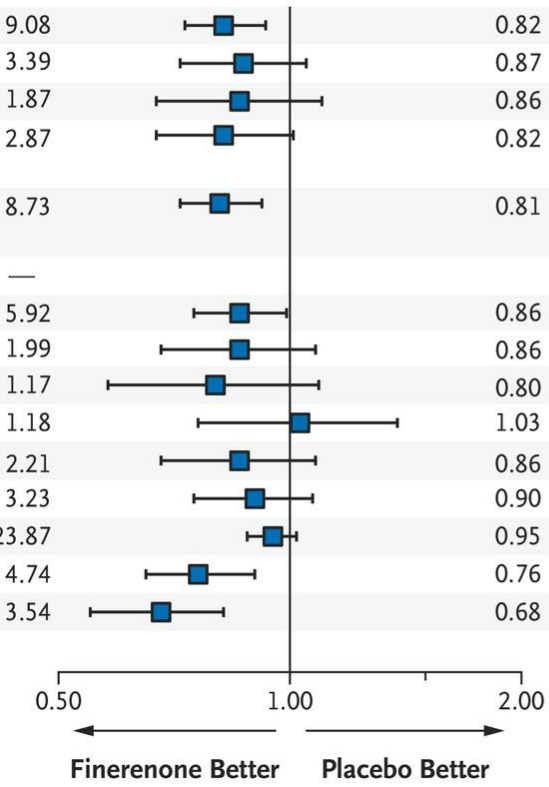
- All patients were to have a serum potassium ≤4.8 mEq/L at screening and be receiving standard of care background therapy
  - Maximally tolerated labeled dose of ACEi or ARB
- Kerendia initial dose:
  - eGFR of 25 to <60 mL/min/1.73 m^2: 10 mg once daily
  - eGFR ≥60 mL/min/1.73 m^2: 20 mg once daily in patients with an)
  - The dose of Kerendia could be titrated during the study, with a target dose of 20 mg daily.

FIDELIO-DKD	FIGARO-DKD
Inclusion	
UACR 30-300 eGFR 25 to <75 and diabetic retinopathy	UACR of 30 to < 300 and an eGFR of 25 to 90
UACR of ≥ 300 and an eGFR of 25 to < 75	UACR ≥ 300 and an eGFR ≥ 60

Bakris GL, et al. N Engl J Med. 2020 Dec 3;383(23):2219-2229.
Filippatos G, et al. *JACC Heart Fail*. 2022 Nov;10(11):860-870.

FIDELIO-DKD: Efficacy Outcomes

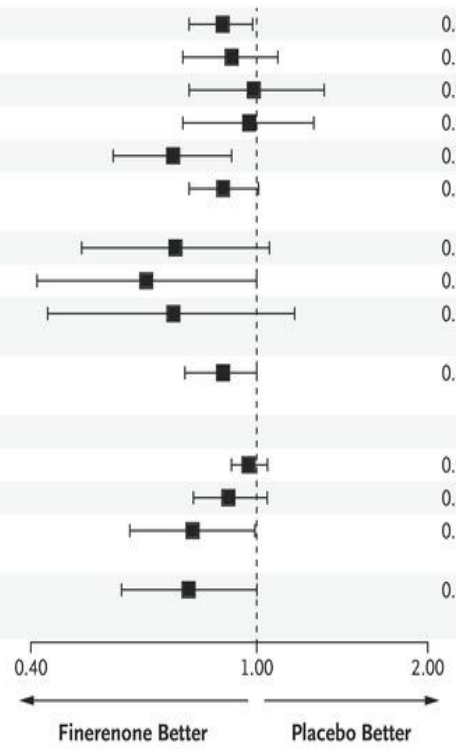
Outcome	Finerenone (N=2833)	Placebo (N=2841)	Finerenone (N=2833)	Placebo (N=2841)	Hazard Ratio (95% CI)	P Value
	no. of patients with event (%)		*no. of patients with event per 100 patient-yr*			
Primary composite outcome	504 (17.8)	600 (21.1)	7.59	9.08	0.82 (0.73–0.93)	0.001
Kidney failure	208 (7.3)	235 (8.3)	2.99	3.39	0.87 (0.72–1.05)	—
End-stage kidney disease	119 (4.2)	139 (4.9)	1.60	1.87	0.86 (0.67–1.10)	—
Sustained decrease in eGFR to <15 ml/min/1.73 m^2	167 (5.9)	199 (7.0)	2.40	2.87	0.82 (0.67–1.01)	—
Sustained decrease of ≥40% in eGFR from baseline	479 (16.9)	577 (20.3)	7.21	8.73	0.81 (0.72–0.92)	—
Death from renal causes	2 (<0.1)	2 (<0.1)	—	—	—	—
Key secondary composite outcome	367 (13.0)	420 (14.8)	5.11	5.92	0.86 (0.75–0.99)	0.03
Death from cardiovascular causes	128 (4.5)	150 (5.3)	1.69	1.99	0.86 (0.68–1.08)	—
Nonfatal myocardial infarction	70 (2.5)	87 (3.1)	0.94	1.17	0.80 (0.58–1.09)	—
Nonfatal stroke	90 (3.2)	87 (3.1)	1.21	1.18	1.03 (0.76–1.38)	—
Hospitalization for heart failure	139 (4.9)	162 (5.7)	1.89	2.21	0.86 (0.68–1.08)	—
Death from any cause	219 (7.7)	244 (8.6)	2.90	3.23	0.90 (0.75–1.07)	—
Hospitalization for any cause	1263 (44.6)	1321 (46.5)	22.56	23.87	0.95 (0.88–1.02)	—
Secondary composite kidney outcome	252 (8.9)	326 (11.5)	3.64	4.74	0.76 (0.65–0.90)	—
Sustained decrease of ≥57% in eGFR from baseline	167 (5.9)	245 (8.6)	2.41	3.54	0.68 (0.55–0.82)	—



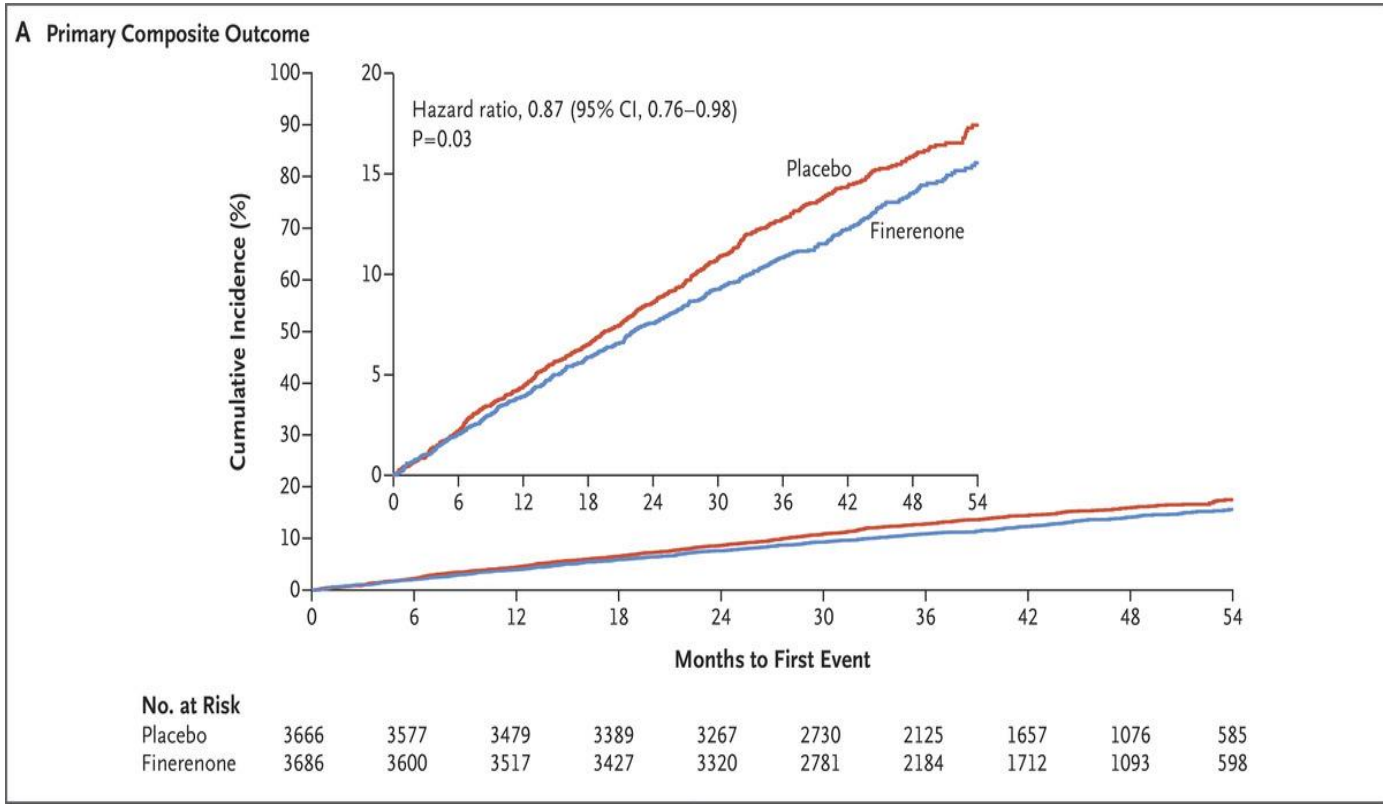
Bakris GL, et al. N Engl J Med. 2020 Dec 3;383(23):2219-2229.

FIGARO-DKD: Efficacy Outcomes

Outcome	Finerenone (N=3686)	Placebo (N=3666)	Finerenone (N=3686)	Placebo (N=3666)	Hazard Ratio (95% CI)	P Value
	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)	0.03
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)	—



FIGARO-DKD: Primary Composite Outcome



FIDELIO-DKD					FIGARO-DKD			
Time-to-event Endpoints	Event Rate 100 pt-yr)	Event Rate (100 pt-yr)	HR 95% CI)	p-value	Event Rate (100 pt-yr)	Event Rate (100 pt-yr)	HR (95% CI)	p-value
			0.82 0.73-0.93	**0.001**				
Kidney failure	3.0	3.4	0.87 0.72-1.05	-	0.4	0.5	0.72 0.49-1.05	-
Renal death	-	-	-	-	-	-	-	-
			0.86 0.75-0.99	**0.034**			**0.87 0.76-0.98**	**0.026**

Finerenone Practical Application

KERENDIA once-daily dosing can be an integral part of your treatment strategy[13]

1 Measure serum potassium to determine if KERENDIA is appropriate[13]*

If serum potassium ≤4.8 mEq/L	KERENDIA can be initiated
If serum potassium >4.8 to 5.0 mEq/L*	Initiation of Kerendia can be considered
If serum potassium >5.0 mEq/L	Do not initiate KERENDIA

*KERENDIA may be considered with additional serum potassium monitoring within the first 4 weeks based on clinical judgment and serum potassium levels.[13]

2 Measure eGFR to determine the appropriate starting dose of KERENDIA[13]

≥60 mL/min/1.73 m² The recommended target daily dose of KERENDIA is 20 mg	Initiate 20-mg starting dose
≥25 to <60 mL/min/1.73 m²	Initiate 10-mg starting dose
<25 mL/min/1.73 m²	Initiation not recommended

Not actual size.

3 Regularly monitor serum potassium to adjust doses appropriately[13]†

Serum potassium must be remeasured 4 weeks after:	• Initiation of treatment • Restarting treatment • Dose adjustment

†If serum potassium levels are >4.8 to 5.0 mEq/L, initiation may be considered with additional potassium monitoring within the first 4 weeks based on clinical judgment and serum potassium levels.

Dose adjustment[13]

Current serum potassium (mEq/L)	Current KERENDIA dose
≤4.8	Increase to or maintain **20 mg once daily**
>4.8-5.5	Maintain current dose
>5.5	**Withhold treatment** Restart at 10 mg once daily when [K+] is ≤5.0 mEq/L

If eGFR has decreased by more than 30% compared to previous measurement, maintain 10-mg dose.

Kerendia Retrieved from: https://www.kerendiahcp.com/about-kerendia/dosing

Learning Question

BD is a 68 y/o male with stage 3b CKD. Other conditions include HTN, Hyperlipidemia, and controlled DM. Current medications include atorvastatin 40mg qd,, lisinopril 40mg, metformin 1000mg bid, dapagliflozin 10mg. Pertinent baseline labs: eGFR: 44, sCr: 1.33 UACR: 350 mcg/mg K+: 4.7. The decision is made to initiate finerenone. What would be the most appropriate starting dose for this patient?

A) Do not initiate finerenone as it is currently contraindicated due to potassium level
B) Initiate finerenone 20mg qd
C) Initiate finerenone 10mg qd
D) Do not initiate finerenone as it is currently contraindicated due to eGFR

Pharmacist Role In Care: Nephrology and Cardiovascular clinic

- Collaborative Practice Agreements
  - Individualized CPA agreements are composed for each of our specialist clinics
  - Prescribe and titrate medication doses
    - More frequent follow up
- Comprehensive medication review
  - Appropriateness of dosing for renal/liver function
  - Review medication list for more effective agents
  - Provide detailed interpretation for drug-drug interactions
  - Medication access

Pharmacist Role In Care: Endocrinology clinic

- Scheduled patient appointments under a collaborative practice agreement (CPA)
  - Emphasis in diabetes technology: CGM and insulin pump management
  - New medication starts and adjustments
  - In office billing opportunities

Medication Access

- Benefits Investigation and Education
  - Type of plan
  - Where to fill
  - Formulary Preferences
  - Cost navigation
    - Deductible
    - Donut Hole
- Appropriate utilization of financial assistance
  - Copay cards
  - Free trials
  - Patient Assistance Programs
- Pharmacist to pharmacist problem solving

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