Latest Treatment Strategies for Type 2 Diabetes and Chronic Kidney Disease
Faculty

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Introduction

- Diabetic Kidney Disease (DKD) is the leading cause of end stage renal disease (ESRD) in the U.S.
- DKD occurs in approximately 40% of patients with T2D
- Most excess risk of all cause and CV mortality for T2D patients is related to DKD
- Natural history of DKD
  - Glomerular hyperfiltration
  - Progressive albuminuria
  - Declining GFR
  - ESRD/dialysis
Prevalence of Chronic Kidney Disease in Diagnosed Diabetes

Diabetic Kidney Disease Is the Leading Cause of Kidney Failure in the United States

*Pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

<table>
<thead>
<tr>
<th>NKF Stage</th>
<th>Description</th>
<th>GFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage* with normal or ↑ GFR</td>
<td>≥90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage* with mild ↓ GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure or ESRD</td>
<td>&lt;15 or dialysis</td>
</tr>
</tbody>
</table>

ESRD, end-stage renal disease; GFR, glomerular filtration rate (mL/min/1.73 m²);

Diagnosis of Diabetic Kidney Disease

The clinical diagnosis of Diabetic Kidney Disease (DKD) in a patient with diabetes is based on\(^1,2\):

- Presence of albuminuria (UACR $\geq 300$ mg/g, OR UACR 30-299 mg/g with:
  - Diabetic retinopathy, and/or
  - T1D $\geq$ 10 years’ duration)
- Reduced kidney function (eGFR $< 60$ mL/min/1.73 m\(^2\))

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\(^2\)

UACR: urine albumin:creatinine ratio

National Kidney Foundation. KDOQI Guidelines Executive Summary. 2007

Development of Diabetic Nephropathy

Genetically susceptible individuals

- Hyperglycemia
- Hypertension
- Angiotensin II

Hyperfiltration
- Enlarged kidneys

Breakdown of glomerular filtration barrier

Microalbuminuria

Protein reabsorption and accumulation in renal epithelial cells

Capillary occlusion

Decreasing GFR

Macroalbuminuria

Release of vasoactive and inflammatory cytokines

Tubule and podocyte damage

Tubular atrophy and fibrosis, podocyte destruction

Renal failure

## Staging and Monitoring of Renal Function and Albuminuria in Diabetes

**Persistent albuminuria categories**

<table>
<thead>
<tr>
<th>Description and range</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal to mildly increased</td>
<td>&gt;30 mg/g</td>
<td>&lt;3 mg/mmol</td>
<td>30-300 mg/g</td>
</tr>
<tr>
<td>Moderately increased</td>
<td>30-300 mg/g</td>
<td>&lt;3 mg/mmol</td>
<td>&gt;30 mg/mmol</td>
</tr>
<tr>
<td>Severely increased</td>
<td>&gt;300 mg/g</td>
<td>&gt;3 mg/mmol</td>
<td></td>
</tr>
</tbody>
</table>

### Guide to frequency of monitoring (number of times per year) by GFR and albuminuria category

<table>
<thead>
<tr>
<th>Category</th>
<th>GFR</th>
<th>Numbers</th>
<th>Monitoring frequency (times/year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>Normal or high</td>
<td>&gt;90</td>
<td>1 if CKD</td>
</tr>
<tr>
<td>G2</td>
<td>Mildly decreased</td>
<td>60-89</td>
<td>1 if CKD</td>
</tr>
<tr>
<td>G3a</td>
<td>Mild to moderately decreased</td>
<td>45-59</td>
<td>1</td>
</tr>
<tr>
<td>G3b</td>
<td>Moderately to severely decreased</td>
<td>30-44</td>
<td>2</td>
</tr>
<tr>
<td>G4</td>
<td>Severely decreased</td>
<td>15-29</td>
<td>3</td>
</tr>
<tr>
<td>G5</td>
<td>Kidney failure</td>
<td>&lt;15</td>
<td>4+</td>
</tr>
</tbody>
</table>

**Numbers = recommended monitoring frequency (times/year)**

**Increasing color intensity = higher risk of progression of DKD**

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CKD = chronic kidney disease; GFR = glomerular filtration rate

Pharmacologic Treatment Options for T2D with Renoprotection

Two classes of newer agents for T2D have added renal benefits beyond glycemic control.

- Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors
- Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

Each will be reviewed for:

- Mechanism
- Summary of CV outcome trials (CVOT)
- Benefits
- Adverse effects
Currently Available Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors

- Canagliflozin (Invokana)
- Dapagliflozin (Farxiga)
- Empagliflozin (Jardiance)
- Ertugliflozin (Steglatro)
SGLT2 inhibitors: Physiologic Actions

- Selectively blocks the transporter responsible for > 90% of glucose reabsorption in the nephron (SGLT2).
- This results in reduced absorption of glucose and sodium, leading to glycosuria and natriuresis.
- Greatest rate of glycosuria occurs during periods of hyperglycemia.
- Low risk of hypoglycemia.

Figure 1. The sodium-glucose cotransporter 2 (SGLT2) mechanism in the proximal tubule. Modified from Bakris et al\textsuperscript{6} with permission of the publisher. Copyright © 2009, Elsevier.
SGLT2 inhibitors: Mechanism of Action

SGLT2 inhibition

Mechanism

Possible cardio-renal effects

CV/renal outcomes

↑ Glucose removal  
↑ Na⁺ removal

Osmotic diuresis  
Metabolism  
Sodium

↑ Glucose removal  
↑ Na⁺ removal

Cardiac function
Preload
Afterload
↑ Cardiometabolic efficiency

Arrhythmia

Arterial wall structure/function

Glomerular pressure
Albuminuria

CV death
↓ Sudden death
↓ Fatal HF/stroke
↓ Hospitalization for heart failure
↓ Renal events

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SGLT2 inhibitors: Mechanisms of Renoprotection

• Glycosuria
• Natriuresis
• Reduced albuminuria
• Decreased glomerular pressure through restoration of tubuloglomerular feedback
• Decreased glomerular perfusion and hyperfiltration
• Decreased tubular workload and hypoxia
### Improved Renal Outcomes in GLP-1 RA and SGLT2i Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEADER&lt;sup&gt;1, a&lt;/sup&gt;</td>
<td>Liraglutide</td>
<td>0.78 (0.67, 0.92)</td>
<td>0.003</td>
</tr>
<tr>
<td>SUSTAIN 6&lt;sup&gt;2, b&lt;/sup&gt;</td>
<td>Semaglutide</td>
<td>0.64 (0.46, 0.88)</td>
<td>0.005</td>
</tr>
<tr>
<td>EMPA-REG OUTCOME&lt;sup&gt;3, c&lt;/sup&gt;</td>
<td>Empagliflozin</td>
<td>0.61 (0.53, 0.70)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CANVAS&lt;sup&gt;4, d&lt;/sup&gt;</td>
<td>Canagliflozin</td>
<td>0.60 (0.47, 0.77)</td>
<td></td>
</tr>
<tr>
<td>DAPA-CKD&lt;sup&gt;5, e&lt;/sup&gt;</td>
<td>Dapagliflozin</td>
<td>0.56 (0.45, 0.68)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CREDEENCE&lt;sup&gt;6, f&lt;/sup&gt;</td>
<td>Canagliflozin</td>
<td>0.70 (0.59, 0.82)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

**Composite Renal Outcomes:**

- <sup>a</sup>Macroalbuminuria, doubling of serum creatinine, and eGFR ≤45 mL/min/1.73 m<sup>2</sup>, ESRD, or renal death;
- <sup>b</sup>Macroalbuminuria, doubling of serum creatinine, and eGFR ≤45 mL/min/1.73 m<sup>2</sup> or need for continuous renal replacement therapy;
- <sup>c</sup>Macroalbuminuria, doubling of serum creatinine level, eGFR ≤45 mL/min/1.73 m<sup>2</sup>, initiation of renal-replacement therapy or renal death;
- <sup>d</sup>40% reduction in eGFR, ESRD, or renal death;
- <sup>e</sup>sustained decline in eGFR ≥ 50%, ESRD, or death from renal causes;
- <sup>f</sup>doubling of serum creatinine, ESRD (GFR ≤15 mL/min/1.73 m<sup>2</sup>, dialysis or transplant), renal death or CV death.

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EMPA-REG Trial: Slower Progression of Renal Disease Over Time

EMPA-REG and Effect on GFR

Change in GFR over 192 weeks

No. at Risk:
- PBO
- EMPA 10mg
- EMPA 25mg

<table>
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<tr>
<th></th>
<th>2323</th>
<th>2295</th>
<th>2267</th>
<th>2205</th>
<th>2121</th>
<th>2064</th>
<th>1927</th>
<th>1981</th>
<th>1763</th>
<th>1479</th>
<th>1262</th>
<th>1123</th>
<th>977</th>
<th>731</th>
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<td>PBO</td>
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<td></td>
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<tr>
<td>EMPA 10mg</td>
<td>2322</td>
<td>2290</td>
<td>2264</td>
<td>2235</td>
<td>2162</td>
<td>2114</td>
<td>2012</td>
<td>2064</td>
<td>1839</td>
<td>1540</td>
<td>1314</td>
<td>1180</td>
<td>1024</td>
<td>785</td>
<td>513</td>
</tr>
<tr>
<td>EMPA 25mg</td>
<td>2322</td>
<td>2288</td>
<td>2269</td>
<td>2216</td>
<td>2156</td>
<td>2111</td>
<td>2006</td>
<td>2067</td>
<td>1871</td>
<td>1563</td>
<td>1340</td>
<td>1207</td>
<td>1063</td>
<td>838</td>
<td>524</td>
</tr>
</tbody>
</table>

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CREDENCE: Canagliflozin in T2DM and Nephropathy

- ≥ 30 years old
- T2DM (HbA1c 6.5% to 12.0%)
- CKD (eGFR 30 mL/min/1.73 m² to < 90 mL/min/1.73 m², UACR > 300 mg/g to 5000 mg/g)
- Stable on max tolerated dose ACE inhibitor or ARB for ≥ 4 weeks

Double-blind randomization (1:1)

Canagliflozin 100 mg

Placebo

Treatment continued if eGFR < 30 mL/min/1.73 m² until initiation of RRT

Trial stopped early after planned interim analysis showed RR of the primary outcome was 30% lower in the canagliflozin group than in the placebo group

Dapagliflozin Improves Renal Outcomes: DAPA-CKD Trial (2/3 Type 2DM and 1/3 Non-DM)

- N = 4304 with eGFR 25-75 mL/min/1.73m² and ACR 200-5000 mg/g
- 1° outcome: Sustained decline in eGFR ≥ 50%, end-stage kidney disease, or death from renal or CV causes
  - 9.2% DAPA vs. 14.5% PBO
  - HR 0.61
  - NNT = 19
- Composite renal outcome:
  - HR 0.56 (95% CI, 0.45-0.68; P < 0.001)

SGLT2 Inhibitors: Adverse Effects

- Genital mycotic infections (women > men)
- Urinary tract infections
- Polyuria
- Volume depletion/hypotension/dizziness
- ↑ LDL-C
- ↑ Creatinine (transient)
- DKA/ euglycemic DKA
- Increased rate of lower extremity amputations (seen in CANVAS, not CREDENCE)
- CANVAS: numerically low numbers but statistically significant; 6.3 vs. 3.4%, HR 1.97 (95%CI 1.41-2.75)
- Side effect of Fournier’s gangrene
- Increased risk of bone fractures
Glucagon-Like Peptide 1 Receptor Agonists (GLP-1 RA)

Currently Available Drugs

• Exenatide (Byetta, Bydureon)
• Liraglutide (Victoza)
• Lixisenatide (Adlyxin, component of Soliqua)
• Semaglutide (Ozempic, Rybelsus)
• Dulaglutide (Trulicity)
GLP-1 RAs: Mechanism of Action

- Kidney: ↑ Natriuresis, ↑ Diuresis
- Heart: ↑ Cardioprotection
- Blood vessel: ↓ Blood pressure
- Brain: ↓ Body weight
- Fats and other tissues: ↓ Inflammation
- Pancreas: ↓ Glucose, ↓ Hypoglycemia
- α-Cell: ↓ Glucagon secretion
- β-Cell: ↑ Insulin secretion, ↑ Insulin biosynthesis, ↓ Apoptosis
- Intestines: ↓ Postprandial lipids
- Platelets: ↓ Coagulation

Mechanisms for Renoprotection

- Increased natriuresis
- Increased diuresis
- Blood glucose lowering
- Blood pressure lowering effects
- Decreased insulin resistance
- Weight loss
GLP1 Receptor Agonists: Renal Outcome Trials

• LEADER
  • Liraglutide reduced new or worsening nephropathy by 22% (HR 0.74, 95%CI 0.60-0.91)
  • 26% reduction in macroalbuminuria

• SUSTAIN-6
  • Reduction in new or worsening nephropathy with semaglutide SC (HR 0.64, 95%CI 0.46-0.88, P=0.005)
  • 46% reduction in macroalbuminuria
GLP1 Receptor Agonists: Renal Outcome Trials

• EXSCEL
  • For a composite of 40% eGFR decline, renal replacement, renal death or new macroalbuminuria, significant reduction with Exenatide ER (HR 0.85, 95% CI 0.73-0.98), P=0.027).

• AWARD-7 / REWIND
  • Dulaglutide significantly attenuates eGFR decline compared to insulin glargine in DM2 patients with moderate to severe CKD. HR -0.05%, 95% CI, p<0.0001)
Renal Outcomes with GLP-1 RA

<table>
<thead>
<tr>
<th>GLP-1 receptor agonist</th>
<th>Placebo</th>
<th>Hazard ratio (95% CI)</th>
<th>NNT (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELIXA</td>
<td>17/1/264/7 (6%)</td>
<td>202/2629 (8%)</td>
<td>0.84 (0.68-1.02)</td>
<td>0.083</td>
</tr>
<tr>
<td>LEADER</td>
<td>268/46/68 (6%)</td>
<td>337/4672 (7%)</td>
<td>0.78 (0.67-0.92)</td>
<td>0.003</td>
</tr>
<tr>
<td>SUSTAIN-6</td>
<td>52/1648 (4%)</td>
<td>100/1649 (6%)</td>
<td>0.64 (0.46-0.88)</td>
<td>0.006</td>
</tr>
<tr>
<td>EXSCEL</td>
<td>366/6256 (6%)</td>
<td>407/6222 (7%)</td>
<td>0.88 (0.76-1.01)</td>
<td>0.065</td>
</tr>
<tr>
<td>REWIND</td>
<td>848/4949 (17%)</td>
<td>970/4982 (20%)</td>
<td>0.85 (0.77-0.93)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overall (F=0.08, p=0.413)</td>
<td>1716/20168 (9%)</td>
<td>2017/20134 (10%)</td>
<td>0.83 (0.78-0.89)</td>
<td>52 (48 to 96)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Worsening of kidney function</th>
<th>GLP-1 receptor agonist</th>
<th>Placebo</th>
<th>Hazard ratio (95% CI)</th>
<th>NNT (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELIXA</td>
<td>41/1301 (1%)</td>
<td>35/3032 (1%)</td>
<td>1.16 (0.74-1.83)</td>
<td>0.513</td>
<td></td>
</tr>
<tr>
<td>LEADER</td>
<td>87/4668 (2%)</td>
<td>97/4672 (2%)</td>
<td>0.89 (0.67-1.19)</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>SUSTAIN-6</td>
<td>18/1648 (1%)</td>
<td>14/1649 (1%)</td>
<td>1.28 (0.64-2.58)</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>EXSCEL</td>
<td>24/6456 (4%)</td>
<td>73/6458 (4%)</td>
<td>0.88 (0.74-1.05)</td>
<td>0.164</td>
<td></td>
</tr>
<tr>
<td>REWIND</td>
<td>169/4949 (3%)</td>
<td>237/4952 (5%)</td>
<td>0.70 (0.57-0.85)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Overall (F=0.42, p=0.137)</td>
<td>561/20752 (3%)</td>
<td>656/20763 (3%)</td>
<td>0.87 (0.73-1.03)</td>
<td>247 (119 to 10721)</td>
<td>0.098</td>
</tr>
</tbody>
</table>

GLP1 Receptor Agonists: Benefits

• ↓ Postprandial glucose excursions
• Weight loss: Average weight loss of 2-4 kg
• Increased satiety
• ↓ LDL-C and ↓ triglycerides
• Low rate of hypoglycemia
• Cardiac and renal protection
GLP1 Receptor Agonists: Adverse Effects

- Gastrointestinal side effects
  - Nausea, vomiting most common
  - Diarrhea
  - Association with acute gallstone disease
- ↑ Heart rate
- Acute pancreatitis
  - Risk not confirmed in CVOT
# AACE/ACE Comprehensive Type 2 Diabetes Management Algorithm

## Profiles of Anti-Hyperglycemic Medications

<table>
<thead>
<tr>
<th></th>
<th>MET</th>
<th>GLP1-RA</th>
<th>SGLT2i</th>
<th>DPP4i</th>
<th>AGi</th>
<th>TZD (moderate dose)</th>
<th>SU</th>
<th>GLIN</th>
<th>COLSUL</th>
<th>BCR-QR</th>
<th>INSULIN</th>
<th>PRAML</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYPO</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate/Severe</td>
<td>Mild</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate to Severe</td>
<td>Neutral</td>
</tr>
<tr>
<td>WEIGHT</td>
<td>Slight Loss</td>
<td>Loss</td>
<td>Loss</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Gain</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Gain</td>
<td>Loss</td>
<td></td>
</tr>
<tr>
<td>RENAL / GU</td>
<td>Contra-indicated if eGFR &lt;30 mL/min/1.73 m²</td>
<td>Excessive</td>
<td>Not Indicated</td>
<td>CRCL &lt;30</td>
<td>Not Indicated</td>
<td>CRCL &lt;30</td>
<td>Not Indicated</td>
<td>CRCL &lt;30</td>
<td>Dose Adjustment Necessary (Except Linagliptin)</td>
<td>Effective in Reducing Albuminuria</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td>GI, Sx</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Mild</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>CHF</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Prevent HF Hospitalization</td>
<td>Manage HF/See #2</td>
<td>See #4</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>CHF Risk</td>
<td>Neutral</td>
</tr>
<tr>
<td>CARDIAC</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Potential Benefit of MET</td>
<td>See #3</td>
<td>See #3</td>
<td>Neutral</td>
<td>May Reduce Stroke Risk</td>
<td>Possible ASCVD Risk</td>
<td>lowers LDL-C</td>
<td>Safe</td>
<td>Neutral</td>
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<td>ASCVD</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Fracture Risk</td>
<td>Neutral</td>
<td>Neutral</td>
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<td>Neutral</td>
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<tr>
<td>BONE</td>
<td>Neutral</td>
<td>Neutral</td>
<td>DKA Can Occur in Various Stress Settings</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
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</tr>
</tbody>
</table>

### Notes:

1. Canagliflozin indicated for eGFR ≥45 mL/min/1.73 m² in patients with CKD 3 + albuminuria.
2. Dapagliflozin—potential primary prevention of HF hospitalization & demonstrated efficacy in HFpEF.
3. Empagliflozin—SGLT2 inhibitor approved for reduce CV mortality, Canagliflozin—FDA approved to reduce MACE events.
4. Possible increased hospitalizations for heart failure with dapagliflozin and saxagliptin.

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Medication Access/Medication Cost

• Despite promising data described above, many patients are unable to utilize these classes of medications due to high cost involved and economic hardship.

• Uninsured patients, and even some insured patients, with high copays or deductibles may be limited in their ability to obtain diabetes medications with the best profiles for organ protection.

• Often a particular insurance company will only cover one agent within a particular class so ability to select a specific drug may be limited.

• Be aware of limitations when prescribing and consider options for cost-reduction or alternative medications if cost remains prohibitive.
Conclusions

Diabetes is a multifactorial disease

Many people with T2DM have ASCVD, kidney disease, and/or HF

Role for PCPs, cardiologists, nephrologists, and diabetologists in risk management for T2DM and CVD, or CKD, or risk factors

We can prevent progression of diabetes complications

Latest guidelines recommend SGLT2 inhibitors and GLP-1 RAs for organ protection in individualized diabetes care

Novel glucose-lowering drugs have a role beyond T2DM: in HF, ASCVD, and kidney disease
64-year-old male with DM2 is admitted to the hospital for dyspnea and lower extremity edema. Transthoracic echo demonstrates EF 15%. Patient is treated for congestive heart failure with diuretics, and initially required oxygen therapy which improved closer to discharge. He is found with newly diagnosed Type 2 DM, HbA1c 7.9%. His GFR is >45.

**Question**: Aside from lifestyle modifications, what diabetes therapy would you recommend for this patient at hospital discharge?

**Answer choices**
- Metformin
- Sulfonylurea
- DPP4 inhibitor
- SGLT2-inhibitor
Practice Patient Scenario 1

Correct Answer: SGLT2-inhibitor

Rationale: SGLT2-I can be utilized as first line therapy for DM in a high-risk patient, specifically in the setting of both HF and CKD for organ protection. Although metformin has traditionally been used for first line therapy, it would not be initiated for GFR < 45 and caution should be used for patients with severely reduced EF. Some DPP4 inhibitors have a neutral profile for HF but some in the class were associated with worse outcomes. Sulfonylureas would not confer any cardiac or renal benefit.
Practice Patient Scenario 2

A 59-year-old female presents for evaluation after a recent ischemic stroke. Her current diabetes therapy includes metformin 1000mg BID and Januvia 100mg daily. HBA1c 7.5%. Renal function and transthoracic echo are within normal limits.

**Question:** Which change in diabetes therapy would you recommend?

**Answer Choices**

- Stop Januvia and add a GLP1-RA
- Add a SGLT2 inhibitor
- Add basal insulin therapy
- No change is needed
Correct Answer: Stop Januvia and add a GLP1-RA

Rationale: Given the history of stroke the patient would benefit from addition of a GLP1-RA. Since Januvia, a DPP4 agent is in a related class this drug would need to be discontinued once starting a GLP1-RA. Given the absence of HF or CKD in this patient, GLP1-RA would be preferential over SGLT2-i.
70-year-old female with a history of DM2 but not currently on therapy, presents to the hospital with severe hyperglycemia to 600s, polyuria, polydipsia and weight loss, and is found with diabetic ketoacidosis (DKA), HbA1c 14%. She is treated with IV insulin therapy with resolution of DKA. She has a history of CKD but no prior known CAD. BMI 18.2.

**Question:** What diabetes therapy would you recommend for hospital discharge?

**Answer Choices**

- Basal and bolus insulin therapy
- SGLT2 inhibitor
- GLP1 RA
- Metformin + SGLT2 inhibitor
Correct Answer: Basal and bolus insulin therapy

Rationale: Although the patient has a history of CKD it would not be appropriate to initiate SGLT2-i in a patient with a recent diagnosis of DKA. Given the DKA, the severity of the HbA1c and the weight loss/BMI is low – this patient appears to be in an insulin deficient state and would benefit from insulin therapy at this time. Furthermore, drugs which cause weight loss such as GLP1-RA and SGLT2-I, would not be appropriate given the patient is currently underweight. She should be ruled out for LADA/ Type 1 DM as well.
References

Slide 4: National Kidney Foundation. KDOQI Guidelines Executive Summary. 2007
References


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