Lipids, the Heart, and the Kidney

A New Triad in the Making

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CKD Burden and Severity Increase With Age

- More than 10% of adults in the United States have CKD[a]
  - Age 20-39: 4%
  - Age ≥ 70: 47%
  - Overall prevalence of CKD ≥ prevalence of diabetes
- In the VA health system, 10% to 15% of patients have CKD stages 3-5[b]
  - Higher incidence: in patients with diabetes or hypertension, in females, and in non-Hispanic whites and Native Hawaiians/Pacific Islanders[b]

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[b] CDC website. CKD surveillance system 2011.
CVD Risk Increases With Renal Impairment

- Independent, graded association between reduced eGFR and the risk for death, CV events,* and hospitalization among > 1 million ambulatory adults

### CV Mortality Is Higher in Patients With ESRD

<table>
<thead>
<tr>
<th>Estimated GFR</th>
<th>Death from Any Cause Adjusted Hazard Ratio (95% Confidence Interval)</th>
<th>Any Cardiovascular Event Adjusted Hazard Ratio (95% Confidence Interval)</th>
<th>Any Hospitalization Adjusted Hazard Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60 ml/min/1.73 m²</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>45–59 ml/min/1.73 m²</td>
<td>1.2 (1.1–1.2)</td>
<td>1.4 (1.4–1.5)</td>
<td>1.1 (1.1–1.1)</td>
</tr>
<tr>
<td>30–44 ml/min/1.73 m²</td>
<td>1.8 (1.7–1.9)</td>
<td>2.0 (1.9–2.1)</td>
<td>1.5 (1.5–1.5)</td>
</tr>
<tr>
<td>15–29 ml/min/1.73 m²</td>
<td>3.2 (3.1–3.4)</td>
<td>2.8 (2.6–2.9)</td>
<td>2.1 (2.0–2.2)</td>
</tr>
<tr>
<td>&lt;15 ml/min/1.73 m²</td>
<td>5.9 (5.4–6.5)</td>
<td>3.4 (3.1–3.8)</td>
<td>3.1 (3.0–3.3)</td>
</tr>
</tbody>
</table>

CV Mortality
General Population vs Dialysis or Transplant Patients

CV Mortality in the General Population (NCHS) and in Kidney Failure Treated by Dialysis or Transplant (USRDS)

Mechanism of CVD Development in Patients With Uremia

Uremia

Dyslipidemia (TG↑, apoB↑, apoA1↓, HDL↓)

Immunodeficiency (T and B cell, phagocytosis, Ig formation)

Atherogenic lipid fractions (ox-LDL, small dense LDL)

Oxidative stress (ROS, AGE, AOPP)

Inflammatory activity

Malnutrition

ADMA↑

Endothelial dysfunction

Accelerated atherosclerosis

Lipid-Lowering Therapy Should Be Used Routinely in Patients With CKD

Rationale for Lipid-Lowering Clinical Trials in the CKD Population

- Patients with CKD and ESRD are at increased risk for CV complications
- Patients with CKD and ESRD have abnormal lipid profiles
- Secondary analyses of lipid-lowering studies indicated statin treatment improved CV outcomes in patients with CKD
- Secondary analyses of these studies also demonstrated slowing of CKD progression
- Need for randomized placebo-controlled statin trials in patients with CKD and ESRD

SHARP Trial
Simvastatin Plus Ezetimibe in CKD and Dialysis Patients

- Randomized, double-blind trial in 9270 patients with CKD (one-third on dialysis) randomized to simvastatin 20 mg + 10 mg ezetimibe daily or placebo

**Major Atherosclerotic Events Over 5 Years***

- Rate reduction 17% (95% CI 6–26%)
- Log-rank p=0.0021

*Study supports LDL reduction in patients at high risk for ASCVD events*

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>Placebo</th>
<th>Simvastatin plus ezetimibe</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4620</td>
<td>4650</td>
</tr>
<tr>
<td>1</td>
<td>4204</td>
<td>4271</td>
</tr>
<tr>
<td>2</td>
<td>3849</td>
<td>3939</td>
</tr>
<tr>
<td>3</td>
<td>3469</td>
<td>3546</td>
</tr>
<tr>
<td>4</td>
<td>2566</td>
<td>2655</td>
</tr>
<tr>
<td>5</td>
<td>1269</td>
<td>1265</td>
</tr>
</tbody>
</table>

NKF KDOQI Guidelines and the 2010 CVD and CKD Core Curriculum

Management of Dyslipidemia

All patients with CKD, even in the absence of known CVD, should be considered at high risk for CVD outcomes\[a\]

Goal lipid levels (LDL-C and non-HDL-C)

- LDL-C < 100 mg/dL (< 2.59 mmol/L) (Level B evidence)\[a,b\]
- LDL-C < 70 mg/dL is a therapeutic option in patients with CKD and diabetes (Level B evidence)\[a-c\]
- Non-HDL-C < 130 mg/dL (< 3.36 mmol/L) (Level B evidence)\[a,b\]

Special attention should be made to patients with CKD and diabetes

- Patients with stages 1 to 4 should be treated with a statin (Level B evidence)\[a,b\]
- Patients with stage 5 on hemodialysis should not be initiated on a statin unless there is a specific CV indication (Level A evidence)\[a,b\]

## CKD Is a Risk Enhancer for CVD

**ACC/AHA 2018 Guidelines**

### Family history of premature ASCVD
- Males, age < 55 years
- Females, age < 65 years

### Primary hypercholesterolemia
- LDL-C 160-189 mg/dL (4.1-4.8 mmol/L)
- Non-HDL-C 190-219 mg/dL (4.9-5.6 mmol/L)

### Metabolic syndrome (total: 3)
- Increased waist circumference
- TGs > 175 mg/dL
- Low HDL-C (< 40 mg/dL [men], < 50 mg/dL [women])
- Elevated BP
- Elevated glucose

### Conditions specific to women
- Premature menopause (before age 40 years)
- Pre-eclampsia

### CKD
- eGFR 15-59 mL/min/1.73 m² with or without albuminuria
- Not treated with dialysis or transplant

### Chronic inflammatory conditions
- Psoriasis, rheumatoid arthritis, HIV/AIDS

### High-risk race/ethnicities
- South Asian

### Lipid/biomarkers
- hs-CRP ≥ 2.0 mg/L
- Lp(a) ≥ 50 mg/dL (≥ 125 nmol/L)
- apoB ≥ 130 mg/dL
- ABI < 0.9

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*Optimally, 3 determinations.*

*No established ASCVD or DM.*


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**Presence of risk-enhancing factors may affect the threshold for statin initiation or intensification in primary prevention of CVD**
CKD Is a Disease Multiplier

Distribution of NHANES participants with diabetes, self-reported cardiovascular disease, and single-sample markers of CKD, 2007-2012

- 76.5% None
- 13.6% DM only
- 3.9% CVD only
- 1% CKD only
- 5% DM and CKD
- 8.1% CVD and CKD
- 1.5% All 3 conditions
- 1.7% Significant risk for CV events

Almost 50% of individuals with CKD have diabetes and self-reported CVD

Statin AEs

Muscle symptoms
- Double-blind RCTs: 0.1% to 0.2%
- Nonblinded observational studies: 7% to 29%

Statin therapy

Dysglycemia, new-onset diabetes
- RCTs: ~0.1 per year; individuals with metabolic syndrome or prediabetes are at greater risk

Effect on liver
- Clinically relevant effects are very rare (~1 per 100,000

IMPROVE-IT Subanalysis of Outcomes and AEs in Patients With DM

- IMPROVE-IT enrolled 18,144 patients after ACS with LDL-C 50 to 125 mg/dL
  - Randomized to 40 mg ezetimibe/simvastatin or 40 mg placebo/simvastatin
- Primary composite endpoint: CV death, major coronary events, and stroke
- DM was a prespecified subgroup (N = 4933)

Subanalysis: Primary Endpoint in Patients With DM by Age Group (HR, CI, and P Value)*

<table>
<thead>
<tr>
<th>Age Group</th>
<th>HR (CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 75 years old</td>
<td>0.87 (0.78, 0.96); P = .008</td>
<td></td>
</tr>
<tr>
<td>≥ 75 years old</td>
<td>0.80 (0.65, 0.99); P = .039</td>
<td></td>
</tr>
</tbody>
</table>

*Medical history included: hypertension, current smoker, MI, PCI, CABG, CHF, PAD. On aspirin, ACE inhibitor/ARB, and β-blocker before and at randomization. *KM event at 7 years when comparing both simvastatin treatment arms.

**PCSK9 Inhibitor Therapy**

**FOURIER CKD Subanalysis**

**FOURIER**
- Randomized, double-blind, multinational study

Patients ages 40-85 y with ASCVD* and LDL ≥ 70 mg/dL on statin (N = 27,564)

Evocumb SC (140 mg every 2 weeks or 420 mg monthly)
- + Optimized statin therapy

Placebo SC

Baseline → 2.2 years

**Primary outcome:** composite of CV death, MI, stroke, hospitalization for UA, or coronary revascularization

**Secondary outcome:** composite of CV death, MI or stroke

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**FOURIER CKD Subgroup Methods**

- Stratification into preserved kidney function (eGFR ≥ 90 mL/min/1.73 m²); stage 2 or ≥ stage 3 CKD
- Time to event for binary endpoints (KM event-rate at 30 months)
- Changes in LDL-C and eGFR

**Analysis Hypotheses**

- Reduced risk for CV outcomes with PCSK9 inhibitor is maintained with more severe CKD compared with placebo
- Safety of evolocumab is preserved across CKD stages
- Evolocumab reduces the risk for CKD progression compared with placebo

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*Defined as a history of MI, nonhemorrhagic stroke, or symptomatic PAD, and additional characteristics that increased CV risk.

*Defined as preferably a high intensity statin but must have been equivalent to atorvastatin 20 mg daily, with or without ezetimibe.

## FOURIER CKD Subanalysis

### Baseline Characteristics by CKD Stage

<table>
<thead>
<tr>
<th>Characteristic, (%)</th>
<th>≥ Stage3 CKD (N = 4443)</th>
<th>Stage 2 CKD (N = 15,034)</th>
<th>Preserved Kidney Function (N = 8077)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>68.7</td>
<td>64.0</td>
<td>56.3</td>
</tr>
<tr>
<td>Male</td>
<td>65.0</td>
<td>75.7</td>
<td>80.6</td>
</tr>
<tr>
<td>Black/African American*</td>
<td>3.2</td>
<td>2.0</td>
<td>2.8</td>
</tr>
<tr>
<td><strong>CV Risk Factors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>46.4</td>
<td>33.0</td>
<td>37.8</td>
</tr>
<tr>
<td>Current smoker</td>
<td>15.8</td>
<td>24.5</td>
<td>42.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>89.3</td>
<td>79.9</td>
<td>75.5</td>
</tr>
<tr>
<td>MI</td>
<td>77.0</td>
<td>81.3</td>
<td>83.0</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>25.0</td>
<td>19.3</td>
<td>16.3</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>17.4</td>
<td>12.6</td>
<td>12.1</td>
</tr>
</tbody>
</table>

FOURIER CKD Subanalysis
Change in LDL

LDL-C at 48 Weeks: 58.2% (≥ Stage 3 CKD), 59.4% (Stage 2 CKD), and 58.7% (Preserved Kidney Function) Lower Compared With Placebo

### FOURIER CKD Subanalysis

**Baseline Characteristics by CKD Stage (cont)**

<table>
<thead>
<tr>
<th>Median (IQR) or %</th>
<th>≥ Stage 3 CKD (N = 4443)</th>
<th>Stage 2 CKD (N = 15,034)</th>
<th>Preserved Kidney Function (N = 8077)</th>
<th>P Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV Medications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-intensity statins</td>
<td>66.3</td>
<td>68.9</td>
<td>71.6</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>5.0</td>
<td>5.2</td>
<td>5.5</td>
<td>.23</td>
</tr>
<tr>
<td>Aspirin, P2Y12 inhibitor, or both</td>
<td>88.2</td>
<td>92.2</td>
<td>94.8</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>β-blocker</td>
<td>77.5</td>
<td>75.1</td>
<td>75.4</td>
<td>.04</td>
</tr>
<tr>
<td>ACE inhibitor, ARB, or AA</td>
<td>82.2</td>
<td>78.1</td>
<td>76.1</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Laboratory Measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL-C - mg/dL</td>
<td>91 (79-108)</td>
<td>92 (80-108)</td>
<td>93 (80-112)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Total cholesterol - mg/dL</td>
<td>168 (152-189)</td>
<td>168 (151-188)</td>
<td>168 (151-190)</td>
<td>.93</td>
</tr>
<tr>
<td>HDL-C - mg/dL</td>
<td>43 (36-53)</td>
<td>45 (38-54)</td>
<td>43 (36-51)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>TGs - mg/dL</td>
<td>141.0 (107.0-195.5)</td>
<td>130.5 (98.5-178.0)</td>
<td>133.5 (99.0-183.5)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Kidney Function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum creatinine - mg/dL</td>
<td>1.3 (1.2-1.5)</td>
<td>1.0 (0.9-1.1)</td>
<td>0.8 (0.7-0.9)</td>
<td>--</td>
</tr>
<tr>
<td>eGFR - ml/min/1.73m²</td>
<td>51.1 (43.6-56.2)</td>
<td>76.6 (69.3-83.5)</td>
<td>97.1 (93.3-101.8)</td>
<td>--</td>
</tr>
</tbody>
</table>

FOURIER CKD Subanalysis

Event Rates by CKD Stage

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Evolocumab (N = 13,782)</th>
<th>Placebo (N = 13,772)</th>
<th>Evolocumab vs Placebo (N = 27,554)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>KM (%) at 30 Months</td>
<td>KM (%) at 30 Months</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>Primary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ Stage 3 CKD</td>
<td>14.6</td>
<td>16.1</td>
<td>0.89 (0.76, 1.05)</td>
</tr>
<tr>
<td>Stage 2 CKD</td>
<td>10.2</td>
<td>12.0</td>
<td>0.85 (0.77, 0.94)</td>
</tr>
<tr>
<td>Preserved kidney function</td>
<td>10.0</td>
<td>12.2</td>
<td>0.82 (0.71, 0.94)</td>
</tr>
<tr>
<td>Key Secondary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ Stage 3 CKD</td>
<td>10.3</td>
<td>12.8</td>
<td>0.79 (0.65, 0.95)</td>
</tr>
<tr>
<td>Stage 2 CKD</td>
<td>6.2</td>
<td>7.7</td>
<td>0.82 (0.72, 0.93)</td>
</tr>
<tr>
<td>Preserved kidney function</td>
<td>5.4</td>
<td>7.1</td>
<td>0.75 (0.62, 0.90)</td>
</tr>
</tbody>
</table>

## FOURIER CKD Subanalysis
### Additional Events by CKD Stage

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Evolocumab (N = 13,782)</th>
<th>Placebo (N = 13,772)</th>
<th>Evolocumab vs Placebo (N = 27,554)</th>
<th>P Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>KM (%) at 30 Months</td>
<td>KM (%) at 30 Months</td>
<td>HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>CV death</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ Stage 3 CKD</td>
<td>4.0</td>
<td>4.7</td>
<td>0.88 (0.64, 1.20)</td>
<td>.40</td>
</tr>
<tr>
<td>Stage 2 CKD</td>
<td>1.8</td>
<td>1.6</td>
<td>1.16 (0.89, 1.51)</td>
<td>--</td>
</tr>
<tr>
<td>Preserved kidney function</td>
<td>1.6</td>
<td>1.3</td>
<td>1.03 (0.70, 1.51)</td>
<td>--</td>
</tr>
<tr>
<td>MI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ Stage 3 CKD</td>
<td>5.5</td>
<td>7.4</td>
<td>0.70 (0.55, 0.91)</td>
<td>.40</td>
</tr>
<tr>
<td>Stage 2 CKD</td>
<td>3.8</td>
<td>4.8</td>
<td>0.78 (0.66, 0.91)</td>
<td>--</td>
</tr>
<tr>
<td>Preserved kidney function</td>
<td>3.0</td>
<td>4.9</td>
<td>0.64 (0.50, 0.81)</td>
<td>--</td>
</tr>
<tr>
<td>Hospitalization for UA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ Stage 3 CKD</td>
<td>2.2</td>
<td>1.8</td>
<td>1.20 (0.76, 1.89)</td>
<td>.68</td>
</tr>
<tr>
<td>Stage 2 CKD</td>
<td>1.7</td>
<td>1.9</td>
<td>0.96 (0.74, 1.23)</td>
<td>--</td>
</tr>
<tr>
<td>Preserved kidney function</td>
<td>2.1</td>
<td>2.1</td>
<td>0.95 (0.70, 1.31)</td>
<td>--</td>
</tr>
</tbody>
</table>

## FOURIER CKD Subanalysis

### Safety by CKD Stage

<table>
<thead>
<tr>
<th>Event type (%)</th>
<th>( \geq \text{Stage 3 CKD (N = 4443)} )</th>
<th>( \text{Stage 2 CKD (N = 15,034)} )</th>
<th>( \text{Preserved Kidney Function (N = 8077)} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Evolocumab ( (n = 2302) )</td>
<td>Placebo ( (n = 2141) )</td>
<td>Evolocumab ( (n = 7456) )</td>
</tr>
<tr>
<td>Any AE</td>
<td>82.7</td>
<td>81.7</td>
<td>77.1</td>
</tr>
<tr>
<td>Serious AE</td>
<td>32.6</td>
<td>33.3</td>
<td>24.2</td>
</tr>
<tr>
<td>AE leading to discontinuation</td>
<td>6.1</td>
<td>5.9</td>
<td>4.4</td>
</tr>
<tr>
<td>AE related to therapy AND leading to discontinuation</td>
<td>1.9</td>
<td>2.0</td>
<td>1.7</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>6.3</td>
<td>5.6</td>
<td>6.4</td>
</tr>
<tr>
<td>Muscle related</td>
<td>13.6</td>
<td>14.2</td>
<td>13.7</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
<td>0.0</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Cataract</td>
<td>2.9</td>
<td>2.9</td>
<td>1.7</td>
</tr>
<tr>
<td>New-onset diabetes</td>
<td>8.8</td>
<td>9.1</td>
<td>8.3</td>
</tr>
<tr>
<td>Neurocognitive</td>
<td>2.5</td>
<td>2.7</td>
<td>1.9</td>
</tr>
<tr>
<td>Aminotransferase &gt; 3x ULN</td>
<td>1.7</td>
<td>1.4</td>
<td>1.6</td>
</tr>
<tr>
<td>CK &gt; 5x ULN</td>
<td>0.5</td>
<td>0.9</td>
<td>0.8</td>
</tr>
</tbody>
</table>

FOURIER CKD Subanalysis

**Key Secondary Endpoint**

**Absolute Risk Reduction at 30 Months**

- **≥ Stage 3 CKD**
  - HR 0.79
  - (95% CI: 0.65, 0.95)
  - ARR: -2.5%
  - KM Event Rate: 10.3% Evolocumab, 12.8% Placebo

- **Stage 3 CKD**
  - HR 0.82
  - (95% CI: 0.72, 0.93)
  - ARR: -1.5%
  - KM Event Rate: 6.2% Evolocumab, 7.7% Placebo

- **Preserved kidney function**
  - HR 0.75
  - (95% CI: 0.62, 0.90)
  - ARR: -1.7%
  - KM Event Rate: 5.4% Evolocumab, 7.1% Placebo

**ARR stage 3 vs stage 2:** \( P = .004 \)
**ARR stage 3 vs preserved:** \( P = .01 \)

N = 27554.
## FOURIER CKD Subanalysis

### Overall CKD Progression and Change in eGFR

<table>
<thead>
<tr>
<th></th>
<th>Evolocumab (N = 13,782)</th>
<th>Placebo (N = 13,772)</th>
<th>Evolocumab vs Placebo (N = 27,554)</th>
<th>Cox P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>KM (%)</td>
<td>KM (%)</td>
<td>HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>≥ 30% decline in eGFR</td>
<td>3.2</td>
<td>3.3</td>
<td>0.99 (0.86, 1.14)</td>
<td>.90</td>
</tr>
<tr>
<td>≥ 40% decline in eGFR</td>
<td>1.4</td>
<td>1.4</td>
<td>1.05 (0.84, 1.31)</td>
<td>.66</td>
</tr>
<tr>
<td>≥ 50% decline in eGFR</td>
<td>0.5</td>
<td>0.6</td>
<td>0.97 (0.69, 1.37)</td>
<td>.86</td>
</tr>
</tbody>
</table>

### Change in eGFR Over Time (Overall CKD Population)

![Graph showing change in eGFR over time](image_url)

Alirocumab

ODYSSEY Outcomes Trial Results

Percent of Patients Experiencing Specified Outcome

- **Primary endpoint**: 9.5% (HR: 0.85, 95% CI: 0.78, 0.93) *P* < .001
- **Nonfatal MI**: 6.6%
- **Stroke**: 1.2% (HR: NR) 1.6% (HR: NR)
- **Unstable angina**: 0.4% (HR: NR) 0.6% (HR: NR)
- **All-cause death**: 3.5% (HR: NS) 4.1% (HR: NS)
- **CHD death**: 2.2% 2.3%
- **CV death**: 2.5% 2.9%

Results support ADA recommendation to consider PCSK9 inhibitor therapy for individuals with DM and ASCVD\[b\]

*Composite of CHD death, nonfatal MI, ischemic stroke, UA requiring hospitalization.

Patients at CKD levels 3-5 (including dialysis and transplant) are at high risk for CV events and should be considered for lipid-lowering therapy.

Strategies for Collaborative Patient-Centered Care in Patients With CKD

- Initiate lipid-lowering therapy in patients with CKD at highest risk for ASCVD events
  - Complex patient populations (eg, HIV, pregnancy)
- Team-based care (eg, nephrologist, internist, cardiologist, endocrinologist, diabetologist)
- Appropriate management of CV medications and comorbidities (eg, GERD, hypertension, mineral bone disease, anemia, diabetes)
  - Renal dosing of CV medications
  - Monitor for drug-drug interactions
- Patient education on risk-enhancing factors for CV events and CKD complications such as dialysis
Conclusion

- It is important to recognize CKD as a risk factor for CVD
- CV mortality remains high in CKD despite use of standard CV therapies, including statins
  - Highest in patients with ESRD
- Faculty recommends that patients with CKD (including those who are stage 5, are on dialysis, and are transplant recipients) can benefit from risk-based lipid-lowering treatment
- The ADA recommends PCSK9 inhibitor therapy for individuals with DM and ASCVD
### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>aldosterone antagonist</td>
</tr>
<tr>
<td>ABI</td>
<td>ankle-brachial index</td>
</tr>
<tr>
<td>ACC</td>
<td>American College of Cardiology</td>
</tr>
<tr>
<td>ACE</td>
<td>angiotensin-converting enzyme</td>
</tr>
<tr>
<td>ACS</td>
<td>acute coronary syndrome</td>
</tr>
<tr>
<td>ADA</td>
<td>American Diabetes Association</td>
</tr>
<tr>
<td>ADMA</td>
<td>asymmetric dimethylarginine</td>
</tr>
<tr>
<td>AE</td>
<td>adverse event</td>
</tr>
<tr>
<td>AGE</td>
<td>advanced glycation end product</td>
</tr>
<tr>
<td>AHA</td>
<td>American Heart Association</td>
</tr>
<tr>
<td>AOPP</td>
<td>advanced oxidation of plasma protein</td>
</tr>
<tr>
<td>ApoA1</td>
<td>apolipoprotein A1</td>
</tr>
<tr>
<td>ApoB</td>
<td>apolipoprotein B</td>
</tr>
<tr>
<td>ARB</td>
<td>angiotensin receptor blocker</td>
</tr>
<tr>
<td>ASCVD</td>
<td>atherosclerotic cardiovascular disease</td>
</tr>
<tr>
<td>BP</td>
<td>blood pressure</td>
</tr>
<tr>
<td>CABG</td>
<td>coronary artery bypass grafting</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>CHD</td>
<td>coronary heart disease</td>
</tr>
</tbody>
</table>
Abbreviations (cont)

CHF = congestive heart failure
CI = 95% confidence interval
CK = creatine kinase
CKD = chronic kidney disease
CPK = creatine phosphokinase
CV = cardiovascular
CVD = cardiovascular disease
DM = diabetes mellitus
ED = erectile dysfunction
eGFR = estimated glomerular filtration rate
Epi = epidemiology
ESRD = end-stage renal disease
Evo = evolocumab
GERD = gastroesophageal reflux disease
GFR = glomerular filtration rate
GP = general population
HDL = high-density lipoprotein
HDL-C = high-density lipoprotein cholesterol
HR = hazard ratio
Abbreviations (cont)

hs-CRP = high-sensitivity C-reactive protein
Ig = immunoglobulin
IQR = interquartile range
KDOQI = Kidney Disease Outcomes Quality Initiative
KM = Kaplan-Meier
LDL = low-density lipoprotein
LDL-C = low-density lipoprotein cholesterol
Lp(a) = lipoprotein (a)
MI = myocardial infarction
NCHS = National Center for Health Statistics
NICE = National Institute for Health and Care Excellence
NIDDK = National Institute of Diabetes and Digestive and Kidney Diseases
NKF = National Kidney Foundation
NR = not reported
NS = not significant
Ox = oxidized
PAD = peripheral artery disease
PCI = percutaneous intervention
PCSK9 = proprotein convertase subtilisin–kexin type 9
Abbreviations (cont)

RCT = randomized controlled trial
ROS = reactive oxygen species
SAMS = statin-associated muscle symptom
SC = subcutaneous
TG = triglyceride
UA = unstable angina
ULN = upper limit of normal
USRDS = United States Renal Data System
VA = Veterans Affairs