Dr Abu-Alfa is a Professor of Medicine, Head of the Division of Nephrology and Hypertension at the American University of Beirut (AUB). He is the Director for the Human Research Protection Program and for Research Affairs. He joined AUB in 2010 after spending 2 decades at the Yale School of Medicine.

He is founding President of the Middle East Chapter of the International Society for Peritoneal Dialysis, is currently the President for the Lebanese Society of Nephrology and Hypertension, and Chair-Elect of the International Society of Nephrology (ISN)-Middle East Regional Board, and is serving as an ISN council member.

Dr Abu-Alfa’s scientific interests are in areas of CKD, Peritoneal Dialysis, complex hypertension, Mineral and Bone Disorder in CKD (CKD-MBD), imaging issues in renal patients and use of Gadolinium Based Contrast Agents. He is also very active in the sphere of research ethics.

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Head, Division of Nephrology & Hypertension
Director, Human Research Protection Program
American University of Beirut
Disclosures and Acknowledgements

- No financial or intellectual conflict of interest, or affiliations, of relevance to content.

KDIGO

- Dr Sara Jdiaa (Nephrology-AUB, Lebanon)
- Dr Imad Kibbe (Endocrinology-AUB, Lebanon)
- Dr Adrian Liew (Nephrology-Tan Tock Seng Hospital, Singapore)

Objectives

- Special issues in CKD:
  - Hypoglycemia
  - Reliability of HbA1C
  - Safety of commonly used hypoglycemic agents
- SGLT2 inhibitors and renal protection:
  - Major Trials of SGLT2i
  - CREDENCE trial in CKD patients
  - Use in transplant recipients
- GLP1-RA, DDP-4 inhibitors and renal protection
- Conclusions
**Hypoglycemia Risk in CKD**

- Retrospective cohort 243,222 patients who had 2,040,206 glucose measurements
- CKD defined as eGFR < 60 ml/min per 1.73 m²

![Graph showing hypoglycemia risk in CKD](image)

Moen MF et al: CJASN 2009: 4; 1121-1127

**Accuracy of HbA1c in CKD**

Scatterplots of HbA1c with fasting glucose or HbA1c by chronic kidney disease (CKD) category.

**Use of Metformin in CKD: Lactic Acidosis**

<table>
<thead>
<tr>
<th>Table 4—Recommended dose adjustments for metformin based on eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>≥60</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>&lt;60 and ≥45</td>
</tr>
<tr>
<td></td>
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<tr>
<td>&lt;45 and ≥30</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
</tr>
</tbody>
</table>

Adapted with permission from ADA (83).

Tuttle KR: Diabetes care 2014: 37; 2864-83

**Use of Sulphonylureas and other agents in CKD**

**Thiazolidinediones: Pioglitazone**
Increased risk for causing or aggravating CHF (water retention, edema, dyspnea, weight gain)

**DDP-4 inhibitors:**
- Linagliptin: No adjustment needed with CKD
- Saxagliptin: Adjustments needed with CKD

**GLP-1 Receptor Agonists:**
- Liraglutide: No adjustment needed
- Dulaglutide: No adjustments needed

### Objectives

- Special issues in CKD:
  - Hypoglycemia
  - Reliability of HbA1C
  - Safety of commonly used hypoglycemic agents
- SGLT2 inhibitors and renal protection:
  - Major Trials of SGLT2i
  - CREDENCE trial in CKD patients
  - Use in transplant recipients
- GLP1-RA, DDP-4 inhibitors and renal protection
- Conclusion

---

**Sodium-Glucose Co-transporter 2 (SGLT2) Inhibitors**
Renal Hemodynamic Effects of SGLT2 Inhibition

Mechanisms for SGLT2i Protective Effects

Wanner C. AM J Med 2017; 130; S63-S72

Heerspink HJL et al: Circulation 2016; 134; 752-772
## SGLT2 Inhibitors: 4 RCTs beyond Glucose Control

<table>
<thead>
<tr>
<th>Drug</th>
<th>Trial Name</th>
<th>Participants</th>
<th>Primary Reference(s)</th>
</tr>
</thead>
</table>
| Empagliflozin | CANVAS Trial (n=10,142)     |              | CANVAS Trial (n=10,142)  
| Canagliflozin | DECLARE-TIMI Trial (n=10,186) |              | DECLARE-TIMI Trial (n=10,186)  
| Dapagliflozin | EMPA-REG OUTCOME Trial (n=7,020) |              | EMPA-REG OUTCOME Trial (n=7,020)  

### Primary Outcome:
1. Composite of Death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke (EMPA-REG OUTCOME and CANVAS Trials)
2. MACE and a composite of cardiovascular death or hospitalization for heart failure. (DECLARE-TIMI Trial)

#### CREDENCE Trial - Canagliflozin

**Primary Outcome:**
1. Composite of end-stage kidney disease (dialysis, transplantation, or a sustained estimated GFR < 15 ml/min/1.73m²), doubling of serum creatinine, or death from renal or cardiovascular causes.

### SGLT2 Inhibitors RCTs: CKD Inclusivity

![Graphs showing eGFR distribution for DECLARE-TIMI, CANVAS, EMPA-REG OUTCOME, and CREDENCE trials](image)

Kluger et al. Cardiovasc Diabetol 2019: 18; 99
Empagliflozin and Progression of Kidney Disease in Type 2 Diabetes

Christoph Wanner, M.D., Silvio E. Inzucchi, M.D., John M. Lachin, Sc.D., David Fitchett, M.D., Maximilian von Eynatten, M.D., Michaela Mattheus, Dipl. Biomath., Odd Erik Johansen, M.D., Ph.D., Hans J. Woerle, M.D., Uli C. Broedl, M.D., and Bernard Zinman, M.D., for the EMPA-REG OUTCOME Investigators*

EMPA-REG: Change in GFR over time

EMPA-REG: Main Renal Outcomes

A Incident or Worsening Nephropathy

Hazard ratio, 0.61 (95% CI, 0.53–0.70)
P<0.001
### EMPA-REG: Detailed Renal Outcomes by Strata

<table>
<thead>
<tr>
<th>Event</th>
<th>Empagliflozin</th>
<th>Placebo</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>New or worsening nephropathy or cardiovascular death</td>
<td>675/4170 (16.2)</td>
<td>4972/102 (23.6)</td>
<td>95.9</td>
<td>0.61 (0.55–0.68)</td>
</tr>
<tr>
<td>New or worsening nephropathy</td>
<td>525/4124 (12.7)</td>
<td>388/2061 (18.8)</td>
<td>76.0</td>
<td>0.61 (0.53–0.70)</td>
</tr>
<tr>
<td>Progression to macroalbuminuria</td>
<td>4594/2091 (11.2)</td>
<td>330/2033 (16.2)</td>
<td>64.9</td>
<td>0.62 (0.54–0.72)</td>
</tr>
<tr>
<td>Doubling of serum creatinine (accompanied by eGFR [MDRD] &lt;45 ml/min/1.73 m²)</td>
<td>70/4645 (1.5)</td>
<td>60/2232 (2.6)</td>
<td>9.7</td>
<td>0.56 (0.39–0.79)</td>
</tr>
<tr>
<td>Initiation of renal replacement therapy</td>
<td>13/4687 (0.3)</td>
<td>14/2333 (0.6)</td>
<td>2.1</td>
<td>0.48 (0.21–0.97)</td>
</tr>
<tr>
<td>Doubling of serum creatinine (accompanied by eGFR [MDRD] &lt;45 ml/min/1.73 m²), initiation of renal replacement therapy or death due to renal disease</td>
<td>81/4645 (1.7)</td>
<td>71/2232 (3.1)</td>
<td>11.5</td>
<td>0.54 (0.40–0.75)</td>
</tr>
<tr>
<td>New onset of albuminuria in patients with normoalbuminuria at baseline</td>
<td>1430/2779 (51.5)</td>
<td>703/1374 (51.2)</td>
<td>286.0</td>
<td>0.98 (0.87–1.04)</td>
</tr>
</tbody>
</table>

*Favor empagliflozin, favors placebo*

---

### Original Article

**Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy**


# CREDENCE: Design, Criteria and Outcomes

**Key inclusion criteria**
- ≥30 years of age
- T2DM and HbA1c 6.5% to 12.0%
- eGFR 30 to 90 mL/min/1.73 m²
- UACR 300 to 5000 mg/g
- Stable max tolerated labelled dose of ACEi or ARB for ≥4 weeks

**Key exclusion criteria**
- Other kidney diseases, dialysis, or kidney transplant
- Dual ACEi and ARB; direct renin inhibitor; MRA
- Serum K⁺ >5.5 mmol/L
- CV events within 12 weeks of screening
- NYHA class IV heart failure
- Diabetic ketoacidosis or T1DM

**Primary outcome**
A composite of ESRD, Doubling of creatinine, or Death from renal or CV causes

## 2-week placebo run-in

### Placebo

### Canagliflozin 100 mg

Follow-up at Weeks 3, 13, and 26 (Face to Face) then every 13 weeks (alternating phone/Face to Face)

**Participants** continued treatment if eGFR was <30 mL/min/1.73 m² until chronic dialysis was initiated or kidney transplant occurred


---

# CREDENCE: Changes in GFR and UACR

## A Urinary Albumin-to-Creatinine Ratio
- Median Baseline:
  - Canagliflozin: 913.5
  - Placebo: 918.0

## B Change from Baseline in Estimated GFR
- Baseline (mL/min/1.73 m²):
  - Canagliflozin: 56.4
  - Placebo: 56.0

CREDENCE: Non-Renal Outcomes

E. Death from Cardiovascular Cause
- Hazard ratio: 0.78 (95% CI, 0.61–1.00)
- P = 0.05

F. Death from Any Cause
- Hazard ratio: 0.83 (95% CI, 0.68–1.02)

No. at Risk
- Placebo: 2199, 2187, 2178, 2160, 2144, 2080, 1786, 1211, 646, 195
- Canagliflozin: 2202, 2181, 2144, 2080, 1786, 1211, 646, 195

Months since Randomization

CREDENCE: Renal-Specific Outcomes

B. Renal-Specific Composite Outcome
- Hazard ratio: 0.66 (95% CI, 0.53–0.81)
- P < 0.001

D. Dialysis, Kidney Transplantation, or Renal Death
- Hazard ratio: 0.72 (95% CI, 0.54–0.97)

No. at Risk
- Placebo: 2199, 2183, 2147, 2077, 1776, 1178, 653, 180
- Canagliflozin: 2202, 2184, 2148, 2100, 1811, 1236, 661, 199

Months since Randomization

Trial stopped at median follow-up of 2.62 years

### CREDENCE: Detailed Outcomes by Strata

**Primary composite outcome of ESKD, doubling of serum creatinine, or renal or CV death**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Canagliflozin</th>
<th>Placebo</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening estimated GFR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 to &lt;45 ml/min/1.73 m²</td>
<td>119/657</td>
<td>253/656</td>
<td>72.2</td>
<td>0.59-0.95</td>
</tr>
<tr>
<td>45 to &lt;60 ml/min/1.73 m²</td>
<td>56/640</td>
<td>102/638</td>
<td>13.4</td>
<td>63.1</td>
</tr>
<tr>
<td>60 to &lt;90 ml/min/1.73 m²</td>
<td>70/905</td>
<td>85/904</td>
<td>29.9</td>
<td>36.5</td>
</tr>
<tr>
<td>Baseline UACR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1000</td>
<td>69/1385</td>
<td>88/1163</td>
<td>22.0</td>
<td>28.8</td>
</tr>
<tr>
<td>&gt;1000</td>
<td>174/1017</td>
<td>252/1036</td>
<td>69.6</td>
<td>100.8</td>
</tr>
</tbody>
</table>

**Renal-specific composite outcome of ESKD, doubling of serum creatinine, or renal death**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Canagliflozin</th>
<th>Placebo</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening estimated GFR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 to &lt;45 ml/min/1.73 m²</td>
<td>85/657</td>
<td>115/656</td>
<td>51.6</td>
<td>71.7</td>
</tr>
<tr>
<td>45 to &lt;60 ml/min/1.73 m²</td>
<td>33/640</td>
<td>66/639</td>
<td>19.7</td>
<td>40.8</td>
</tr>
<tr>
<td>60 to &lt;90 ml/min/1.73 m²</td>
<td>35/905</td>
<td>41/904</td>
<td>14.9</td>
<td>38.5</td>
</tr>
<tr>
<td>Baseline UACR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1000</td>
<td>29/1385</td>
<td>31/1163</td>
<td>9.2</td>
<td>10.2</td>
</tr>
<tr>
<td>&gt;1000</td>
<td>124/1017</td>
<td>193/1036</td>
<td>49.1</td>
<td>77.2</td>
</tr>
</tbody>
</table>

### CREDENCE: Detailed Outcomes by Strata

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Canagliflozin vs Placebo</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary composite outcome of ESKD, doubling of serum creatinine, or renal or CV death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening estimated GFR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 to &lt;45 mL/min/1.73 m²</td>
<td>119/657 vs 256/656</td>
<td>95.4</td>
</tr>
<tr>
<td>45 to &lt;60 mL/min/1.73 m²</td>
<td>96/640 vs 192/656</td>
<td>63.1</td>
</tr>
<tr>
<td>Baseline UACR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1000</td>
<td>69/1185 vs 88/1163</td>
<td>32.0</td>
</tr>
<tr>
<td>Renal-specific composite outcome of ESKD, doubling of serum creatinine, or renal death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening estimated GFR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 to &lt;45 mL/min/1.73 m²</td>
<td>119/657 vs 256/656</td>
<td>71.7</td>
</tr>
<tr>
<td>45 to &lt;60 mL/min/1.73 m²</td>
<td>96/640 vs 192/656</td>
<td>40.8</td>
</tr>
<tr>
<td>Baseline UACR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1000</td>
<td>69/1185 vs 88/1163</td>
<td>10.2</td>
</tr>
</tbody>
</table>

**NNT in patients with eGFR 30 to < 45 mL/min/1.73 m²**


### SGLT2 Inhibitors: Meta-analysis | Renal Outcomes

<table>
<thead>
<tr>
<th>Events</th>
<th>Patients</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialysis, transplantation, or death due to kidney disease</td>
<td>252 38723</td>
<td>0.67 (0.52-0.86)</td>
</tr>
<tr>
<td>ESKD</td>
<td>335 38723</td>
<td>0.65 (0.53-0.81)</td>
</tr>
<tr>
<td>Substantial loss of kidney function, ESKD, or death due to kidney disease</td>
<td>967 38671</td>
<td>0.58 (0.51-0.66)</td>
</tr>
<tr>
<td>Substantial loss of kidney function, ESKD, or death due to cardiovascular or kidney disease</td>
<td>2323 38676</td>
<td>0.71 (0.63-0.82)</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>943 38684</td>
<td>0.75 (0.66-0.85)</td>
</tr>
</tbody>
</table>

**Figure 4: Summary of the effects of SGLT2 inhibition on major kidney outcomes**

ESKD = end-stage kidney disease. SGLT2 = sodium-glucose co-transporter 2. RR = relative risk.

### SGLT2 Inhibitors: Adverse Events

**Table 2** Adverse events in the Dapagliflozin Effect on Cardiovascular Outcomes (DECLARE-TIMI 58), CANagliflozin Cardiovascular Assessment Study (CANVAS) Program, Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients—Removing Excess Glucose ( EMPA-REG OUTCOME), and Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) trials.

<table>
<thead>
<tr>
<th>Event</th>
<th>DECLARE/TIMI 58</th>
<th>CANVAS Program</th>
<th>EMPA-REG OUTCOME</th>
<th>CREDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive procedure resulting in death</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any AE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious AE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major adverse renal events</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major AE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major hypoglycemic reaction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major proteinuria</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
- * Indicates increased, ** indicates decreased, --- indicates no difference in risk associated with study drug compared to placebo.
- KDIGO: KDIGO did not differentiate post-transplant by sex.
- ** Indicates statistical significance at the 0.05 level.

---

### SGLT2 Inhibitors: Use post-Transplantation

**Table 2—Outcomes presented as median (IQR)**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Baseline</th>
<th>Week 24</th>
<th>P value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA&lt;sub&gt;1c&lt;/sub&gt; (%)</td>
<td>6.9 (6.5, 8.2)</td>
<td>6.7 (6.3, 7.5)</td>
<td>0.0525</td>
</tr>
<tr>
<td>HbA&lt;sub&gt;1c&lt;/sub&gt; (mmol/mol)</td>
<td>52 (48, 56)</td>
<td>50 (45, 58)</td>
<td>0.0525</td>
</tr>
<tr>
<td>FPG (mmol/L)</td>
<td>8.0 (7.3, 8.6)</td>
<td>7.2 (5.9, 8.1)</td>
<td>0.0525</td>
</tr>
<tr>
<td>FPG (mg/dL)</td>
<td>14.6 (13.3, 17.7)</td>
<td>14.2 (12.4, 15.6)</td>
<td>0.0525</td>
</tr>
<tr>
<td>2-h glucose after OGGT (mmol/L)</td>
<td>92 (80.8, 104.5)</td>
<td>88 (78.0, 100.0)</td>
<td>0.0525</td>
</tr>
<tr>
<td>BMI (kg/m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>28.8 (26.3, 32.4)</td>
<td>28.1 (25.8, 33.8)</td>
<td>0.0525</td>
</tr>
<tr>
<td>VAD (%)</td>
<td>7.0 (4.7, 8.5)</td>
<td>7.0 (4.7, 8.5)</td>
<td>0.0525</td>
</tr>
<tr>
<td>Mean 24-h SBP (mmHg)</td>
<td>136 (131, 147)</td>
<td>142 (126, 148)</td>
<td>0.0525</td>
</tr>
<tr>
<td>Mean 24-h DBP (mmHg)</td>
<td>76 (71, 82)</td>
<td>76 (70, 82)</td>
<td>0.0525</td>
</tr>
<tr>
<td>Mean 24-h pulse</td>
<td>74 (66, 79)</td>
<td>74 (63, 78)</td>
<td>0.0525</td>
</tr>
<tr>
<td>Median creatinine (mg/dL)</td>
<td>66 (57, 68)</td>
<td>65 (56, 67)</td>
<td>0.0525</td>
</tr>
<tr>
<td>Renal glucose excretion (g/24 h)</td>
<td>0.45 (0.20, 1.48)</td>
<td>0.46 (0.68, 6.84)</td>
<td>0.0525</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>13.9 (13.1, 14.4)</td>
<td>14.5 (13.5, 15.2)</td>
<td>0.0525</td>
</tr>
<tr>
<td>Hematuria</td>
<td>0.43 (0.39, 0.45)</td>
<td>0.45 (0.40, 0.46)</td>
<td>0.0525</td>
</tr>
<tr>
<td>Uric acid (μmol/L)</td>
<td>490 (434, 465)</td>
<td>527 (495, 596)</td>
<td>0.0525</td>
</tr>
<tr>
<td>Tacrolimus (C&lt;sub&gt;0&lt;/sub&gt;)</td>
<td>5.4 (4.6, 6.9)</td>
<td>5.2 (4.5, 6.3)</td>
<td>0.0525</td>
</tr>
</tbody>
</table>

**Notes:**
- * Indicates increased, ** indicates decreased, --- indicates no difference in risk associated with study drug compared to placebo.
- KDIGO did not differentiate post-transplant by sex.
- ** Indicates statistical significance at the 0.05 level.

---

**Halden TAS et al: Diabetes Care 2019: 42; 1067-1074**
**Objectives**

- Special issues in CKD:
  - Hypoglycemia
  - Reliability of HbA1C
  - Safety of commonly used hypoglycemic agents
- SGLT2 inhibitors and renal protection:
  - Major Trials of SGLT2i
  - CREDENCE trial in CKD patients
  - Use in transplant recipients
- GLP1-RA, DDP-4 inhibitors and renal protection
- Conclusion

---

**Glucagon-like Peptide Receptor Agonists (GLP1-RA)**

---

**KDIGO**
LEADER Trial: Liraglutide

- Randomized 9,340 patients with high cardiovascular risks.
- Median Follow-up of 3.84 years.
- Pre-specified secondary renal outcomes which was a composite of new-onset persistent albuminuria, doubling of serum creatinine, ESRD or death to renal causes.


AWARD-7 Trial: Dulaglutide in CKD Stages 3-4

Tuttle KR: *Lancet Diabetes Endocrinol* 2018; 6; 605-617
AWARD-7 Trial: Dulaglutide | Albuminuria

DPP-4 (dipeptidyl peptidase-4) Inhibitors
SAVOR-TIMI 53: Saxagliptin

Figure 1—Difference in mean change in ACR (mg/g) as continuous variable among treatment arms by eGFR baseline categories. The change in ACR as a continuous variable by baseline eGFR categories was analyzed using repeated-measures ANOVA, with baseline CV risk group (previous CVD or MRF) and treatment arm as model terms. SAXA, saxagliptin.

Mosenzon et al: Diabetes Care 2017; 40; 69–76

CARMELINA: Linagliptin in CKD

Figure 2. Time to Primary and Secondary Outcomes

A. Time to primary 3-point MACE outcome

B. Time to secondary kidney outcome

EURECA-m and DIABESITY: ERA-EDTA Consensus

Patients with type 2 DM and CKD (eGFR <60 ml/min/1.73m² or eGFR >60 ml/min/1.73m² and micro- or macroalbuminuria) not on HbA1c target (HbA1c >7%) on recommended metformin dose or not on HbA1c target (HbA1c >7%) and metformin is not tolerated or is contraindicated

Use SGLT-2 inhibitor with evidence for cardio- and nephroprotection¹

If HbA1c remains above target or SGLT-2 inhibitor is not tolerated or is contraindicated

Use GLP-1 receptor agonist with evidence for cardio- and nephroprotection²

If HbA1c remains above target or GLP-1 receptor agonist is not tolerated or is contraindicated

Use another antidiabetic agent (DPP-4 i, TZD, SU, or basal insulin) according to current recommendations for Type 2 DM³


EURECA-m and DIABESITY: ERA-EDTA Consensus

Patients with type 2 DM and CKD (eGFR <60 ml/min/1.73m² or eGFR >60 ml/min/1.73m² and micro- or macroalbuminuria) on HbA1c target (HbA1c <7%) on therapy with metformin and additional recommended agents

If not on SGLT-2 inhibitor, consider switching one of additional agents to a SGLT-2 inhibitor with evidence for cardio- and nephroprotection¹

If HbA1c remains above target or SGLT-2 inhibitor is not tolerated or is contraindicated

If not on a GLP-1 receptor agonist, consider switching one of additional agents to a GLP-1 receptor agonist with evidence for cardio- and nephroprotection²

Reassess HbA1c in 3-months interval and adjust the treatment if above target³

Summary and Conclusion

• Management of diabetes mellitus in CKD patients, especially in advanced stages, requires close coordination between nephrologist and endocrinologist.

• Newer classes of agents with reno-protective and cardio-protective attributes are important to include in regimens when feasible and indicated.

• SGLT2 inhibitors have had consistent outcomes among various RCTs with CREDECE trial lending strong support for their safe and beneficial use in CKD.

• The use of SGLT2 inhibitors GLP-1 receptor inhibitors need to be advocated for by the nephrologist in diabetic CKD patients as a reno-cardio-protective drugs, besides RAS blockade, even if glycemic control is being achieved.