Hospitalization for Heart Failure and Death in New Users of SGLT-2 Inhibitors in Subjects With and Without Cardiovascular Disease – CVD-REAL Study

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A prior study, EMPA-REG OUTCOME, has shown that treatment with the SGLT-2 inhibitor (SGLT-2i) empagliflozin, reduced death and hospitalization for HF in patients with T2D and established cardiovascular disease (CVD).

The CVD-REAL study is an observational study that includes over 300,000 patients with T2D from six countries.

The main results from the CVD-REAL study found that initiation of an SGLT-2i was associated with a significant reduction in death and HF when compared to initiation of other glucose-lowering drugs.

It remains unknown whether the effectiveness of SGLT-2i differs based upon the presence or absence of established CVD.
Aims

Primary Aim
• To determine whether the association between SGLT-2i and death varied depending on the presence or absence of CVD at the time at which glucose-lowering therapy was initiated

Secondary Aims
• To determine whether the association between SGLT-2i and HF and the composite of death or HF varied depending on the presence or absence of CVD at the time at which glucose-lowering therapy was initiated
Data Sources: Health Records From Five Countries

New users of SGLT-2i or other glucose-lowering drugs (GLDs)

- Truven Health MarketScan Claims and Encounters and linked Medicare Supplemental databases
- National full-population registries
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- Clinical Practice Research Datalink (CPRD) and The Health Improvement Network (THIN)
Absolute Rates of CV Events in Patients Treated with SGLT-2i and oGLD

p<0.001 for all comparisons
Association Between SGLT-2i and Lower Risk of Cardiovascular Events in Pts With and Without Established Cardiovascular Disease

<table>
<thead>
<tr>
<th>Event</th>
<th>With Prior CVD*</th>
<th>Without Prior CVD*</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>30,153</td>
<td>185,469</td>
<td>0.47 (0.36, 0.61)</td>
</tr>
<tr>
<td></td>
<td>569</td>
<td>765</td>
<td></td>
</tr>
<tr>
<td>HF</td>
<td>39,293</td>
<td>266,863</td>
<td>0.69 (0.59, 0.80)</td>
</tr>
<tr>
<td></td>
<td>706</td>
<td>244</td>
<td></td>
</tr>
<tr>
<td>HF + death</td>
<td>30,153</td>
<td>185,469</td>
<td>0.59 (0.52, 0.67)</td>
</tr>
<tr>
<td></td>
<td>1084</td>
<td>899</td>
<td></td>
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</tbody>
</table>

Data are on treatment, unadjusted; CVD=cardiovascular disease; HF=heart failure; HR=hazard ratio; oGLD=other glucose-lowering drug; SGLT-2i=sodium-glucose co-transporter-2 inhibitor.
Conclusions

• The majority of patients treated with SGLT-2i in clinical practice in five countries do not have established CVD

• Both patients with and without established CVD are at lower risk of both death and HF in the first eight months after initiation of SGLT-2i

• Rates of CV events are lower in patients without established CVD; thus, the absolute risk reduction would be expected to be greater and the number needed to treat lower, in patients with known CVD

• These data suggests that SGLT-2i may benefit a broad population including patients with and without established CVD

• Data from ongoing randomized clinical trials will provide further evidence regarding the CV benefits of different SGLT-2i, including in patients without established CVD
Conclusions

• Progression of atherosclerosis, weight and LDL cholesterol were reduced by metformin in middle-aged adults with longstanding type 1 diabetes

• These data may suggest a wider role for metformin in cardiovascular risk management

• Our data do not support use of metformin to improve glycaemic control in adults with long-standing type 1 diabetes as suggested by current guidelines
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