Efficacy and safety of sodium glucose co-transporter-2 inhibitors at three clinics within an educational health system

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INTRODUCTION

• The American Diabetes Association recommends that pharmacologic therapy for Type 2 Diabetes, to be added in treatment to metformin, should be an agent proven to reduce major cardiovascular events and mortality.1
• Sodium-glucose co-transporter 2 inhibitors (SGLT2i) canagliflozin and empagliflozin have demonstrated atherosclerotic cardiovascular and heart failure (HF) benefit.1
• SGLT2i reduce the reabsorption of glucose in the proximal renal tubules, thereby lowering plasma glucose levels.

BACKGROUND

<table>
<thead>
<tr>
<th>EMPA-REG&lt;sup&gt;®&lt;/sup&gt;</th>
<th>CANVAS&lt;sup&gt;®&lt;/sup&gt;</th>
<th>CVD-REAL&lt;sup&gt;®&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>empagliflozin (n=7,020)</td>
<td>canagliflozin (n=4,330)</td>
<td>dapagliflozin (n=400,000)</td>
</tr>
<tr>
<td>CVD at baseline</td>
<td>99%</td>
<td>65.6%</td>
</tr>
<tr>
<td>Primary (3pt MACE)</td>
<td>0.86 (0.74-0.99)</td>
<td>0.86 (0.75-0.97)</td>
</tr>
<tr>
<td>CV death</td>
<td>0.62 (0.49-0.77)</td>
<td>0.96 (0.77-1.18)</td>
</tr>
<tr>
<td>HF hospitalization</td>
<td>0.65 (0.50-0.85)</td>
<td>0.67 (0.52-0.87)</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>0.68 (0.57-0.82)</td>
<td>0.87 (0.74-1.01)</td>
</tr>
<tr>
<td>Worsening nephropathy</td>
<td>0.61 (0.53-0.70)</td>
<td>0.60 (0.47-0.77)</td>
</tr>
<tr>
<td>Amputation</td>
<td>88 (1.9%)</td>
<td>37 (0.6%)</td>
</tr>
<tr>
<td>Genital Infection</td>
<td>301 (6.4%)</td>
<td>601 (10.4%)</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>492 (36.4%)</td>
<td>232 (4%)</td>
</tr>
<tr>
<td>Acute Kidney Injury</td>
<td>246 (5.2%)</td>
<td>17 (0.3%)</td>
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</table>

- The knowledge of SGLT2i is evolving, with variation seen between agents. Due to increased SGLT2i prescribing in our health system, an assessment of agents was conducted to ensure effective and safe practice.
- The objective of this study was to assess the efficacy and safety of SGLT2i in diabetic patients in terms of glycosylated hemoglobin (A1c), blood glucose (BG), blood pressure (BP), and weight (WI) reductions at three clinics within an educational health system.

METHODS

• Multi-clinic, retrospective medication use evaluation.
• Inclusion: Patients (n=139) at one of three clinics who were prescribed Invokana (canagliflozin), Farxiga (dapagliflozin), or Jardiance (empagliflozin) before March 9th, 2018.
• Exclusion: Patients (n=42) did not have at least one of the following: Post-A1c, Post-BG, Post-BP, or Post-WI due to loss of follow up or recent initiation.
• The primary analysis was a paired t-test of the means of two continuous data groups a with a null value of zero, presented as the change in outcome value with corresponding 95% confidence intervals, group mean and standard deviation.
• The primary outcome was also examined in three prespecified subgroups based on clinic stratification, SGLT2i agent, and strength.

RESULTS

- Efficacy:
  • Of 97 patients, 49 (50.52%) were prescribed canagliflozin, 25 (23.71%) empagliflozin, and 23 (23.71%) dapagliflozin.
  • Dapagliflozin showed the greatest reduction in A1c and BG (-1.44%, -91.83 mg/dL, followed by canagliflozin (-1.12%, -40.82 mg/dL).
  • Dapagliflozin showed comparable results at both strengths, 5mg (-1.14%, -102.00 mg/dL) and 10mg (-1.43%, -87.37 mg/dL).
  • Canagliflozin 300mg showed greater reduction in A1c (-1.12%) and BG (-40.82 mg/dL) than 100mg (-0.87%, -13.73 mg/dL).
  • Clinic 1 had the greatest reductions in A1c and BG (-1.5%, -71.18 mg/dL), followed by Clinic 2 (-0.92%, -86.63 mg/dL), and Clinic 3 (-0.28%, +8.92 mg/dL).
- Safety:
  • Eleven (11.34%) patients reported intolerable vaginosis, vaginitis, candidiasis or yeast infection.
  • Four (4.14%) had inappropriate renal function for SGLT2i use.

CONCLUSIONS

- There was a statistically significant reduction in A1c (-1.05%, p=0.0005) and blood glucose (-53.22 mg/dL, p=0.0001) among all agents reviewed.
- Dapagliflozin was found the most effective SGLT2i in terms of A1c and BG reductions.
- There was no significant difference in blood pressure ([systolic: -2.0mmHg, p=0.4605], [diastolic: -1.0mmHg, p=0.6644]) or weight (-1.19kg, p=0.7699) reductions after starting SGLT2i.

FUTURE IMPLICATIONS

- SGLT2i are recommended when glucose control is desired in patients with cardiovascular disease or risk factors.
- Future studies should reassess the amputation risk of SGLT2i.
- Investigation to assess most effective SGLT2i agent in a head to head comparison of agents is needed.

REFERENCES

3. Radhakrishnan, Arun et al. Gingival Infection in Type 2 Diabetes Mellitus. Results from the CANVAS Program (Canagliflozin Cardiovascular Assessment Study). Circulation (New York, N.Y.) 2018;137:177-187. DOI: 10.1161/CIRCULATIONAHA.118.034222

Disclosures: Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have direct or indirect interest in the subject matter of this presentation.
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