Cost-Effectiveness Analysis of Canagliflozin (CANA) Versus Dapagliflozin (DAPA) as an Add-On to Metformin (MET) in Patients With Type 2 Diabetes Mellitus (T2DM) in the United States

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BACKGROUND

Type 2 diabetes mellitus (T2DM) is a chronic and progressive disease characterized by beta-cell dysfunction, insulin resistance, and hyperglycemia. Maintaining near-normal blood glucose levels combined with lifestyle interventions that include weight loss and control of blood pressure and lipid levels is recommended to reduce the risk of micro- and macrovascular complications, and hence costs.

Unlike other oral classes, sodium-glucose co-transporter 2 (SGLT2) inhibitors are novel drugs that work in an insulin-independent manner, and are thereby complementary to other antihyperglycemic classes, including insulin. By inhibiting SGLT2, this class of drugs leads to inhibition of glucose reabsorption and urinary glucose excretion, thereby reducing blood glucose, weight, and blood pressure (due to ACE inhibition), and blood pressure (from weight loss and diastolic dysfunction).

Two compounds with SGLT2 activity, canagliflozin (CANA) and dapagliflozin (DAPA), are currently available in the US to treat T2DM as an adjunct to diet and exercise. CANA 100 mg, unlike DAPA 10 mg, also transiently blocks SGLT1 in the intestine, reducing glucose absorption.

Economic simulation modeling is a widely used tool (endorsed by the American Diabetes Association (ADA) Consensus Panel) that generates economic evidence to help make informed decisions on outcomes, associated costs, and quality adjusted life years (QALYs) of alternative treatment algorithms.

OBJECTIVE

To evaluate the cost-effectiveness of using CANA 300 mg versus DAPA 10 mg in patients whose AIC is inadequately controlled with MET (MT) monotherapy.

METHODS

Overview of Simulations

A validated health economic model, Economic and Health Outcomes (ECHO); T2DM (Box), was used to estimate the outcomes and costs over 10 years associated with using CANA 300 mg versus DAPA 10 mg as second-line therapy for the treatment of T2DM.

The base case simulation was performed on 1,000 cohorts of hypothetical individuals, whose characteristics reflect those of individuals inadequately controlled with MET monotherapy who participated in the DECLARE-T2D study.

Patients entered the model and received either CANA 300 mg or DAPA 10 mg.

Treatment was intensified when AIC >7.5%, first by adding basal insulin and then by adding prandial insulin.

In the first year, patients discontinued CANA and DAPA according to the rate observed in a pooled analysis of the MET add-on trials. To be conservative, the same rate was assumed for DAPA.

Consistent with the labels in the US, patients also discontinued CANA when simulated estimated glomerular filtration rate (eGFR) fell below 60 mL/min/1.73 m². CANA was not discontinued until eGFR fell below 45 mL/min/1.73 m².

For those with moderate renal impairment (eGFR 45–60 mL/min/1.73 m²), AIC, SBP, and BMI-lowering effects of CANA 300 mg were adjusted based on the percentage of renal function preserved.

Deterministic probabilities for CANA 300 mg and DAPA 10 mg were adjusted based on age (e.g., duration of disease, A1C, BMI), and comorbidities. The same probabilities were also used for the control arm.

RESULTS

The projected AIC curves are presented in Figure 1 - After the initial lowering, AIC resumes its upward drift, putting individual simulated patients at risk for needing rescue medication.

The AIC curves converge over time, reaching a plateau. This reflects the simulated intensity of insulin to the prespecified treatment goal (7.0%)

Subjects treated with CANA stayed on the drug longer before going on insulin rescue therapy and used a lower insulin dose over time compared with subjects treated with DAPA (Figure 2).

In the base case, CANA 300 mg (bNMA 10 mg) was associated with both cost offsets (USD 4,417) and more QALYs (0.22) compared with DAPA 10 mg (USD 1,389).

In the sensitivity analyses, CANA remained dominant (Figure 4).

DISCUSSION

The results suggest that the use of CANA 300 mg versus DAPA 10 mg as an add-on to MET, monotherapy can lead to gains in QALYs and cost offsets.

These results are driven by better simulated glucose control for CANA 300 mg versus DAPA 10 mg, which is attributable to the clinical evidence

Specifically, CANA 300 mg has better AIC reduction and can be used in patients with moderate renal impairment

The cost offsets associated with micro- and macrovascular complications are likely to be conservative in these simulations as insulin titration is simulated to maintain glucose control

Real-world data demonstrates insulin resistance is often less ideal.

As in any modeling study in T2DM, results should be interpreted appropriately as treatment effects and A1C rates were taken from short-term studies and extrapolated to long time horizons.

CONCLUSIONS

- CANA 300 mg produces a greater AIC reduction, body weight, and blood pressure, and thus the risk of micro- and macrovascular complications.

- Simulation estimates suggest that CANA 300 mg is likely to provide more QALYs at lower cost than DAPA 10 mg in dual therapy with a background of MET in the US.

Table 1. Clinical Inputs for CANA and DAPA

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Fasting Plasma Glucose (mg/dL)</th>
<th>A1C (Lower Limit)</th>
<th>SBP (mmHg)</th>
<th>BMI (kg/m²)</th>
<th>Lower limit of normal range SAFER study</th>
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</thead>
<tbody>
<tr>
<td>CANA 300 mg</td>
<td>192.3</td>
<td>6.7</td>
<td>132.1</td>
<td>29.1</td>
<td>3.8</td>
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<tr>
<td>DAPA 10 mg</td>
<td>218.5</td>
<td>7.7</td>
<td>130.1</td>
<td>30.1</td>
<td>4.0</td>
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</tbody>
</table>

Table 2. Summary of Key Results for CANA and DAPA: Head-to-Head Results

<table>
<thead>
<tr>
<th>Treatment</th>
<th>AIC (Year 10)</th>
<th>GLOM</th>
<th>LYs gained</th>
<th>Cost (USD)</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>CANA 300 mg</td>
<td>7.0</td>
<td>0.22</td>
<td>14.28</td>
<td>111,992</td>
<td>Dominant</td>
</tr>
<tr>
<td>DAPA 10 mg</td>
<td>7.2</td>
<td>-0.04</td>
<td>14.26</td>
<td>116,585</td>
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</tr>
</tbody>
</table>

Table 3. Summary of Sensitivity Analyses

<table>
<thead>
<tr>
<th>Treatment</th>
<th>AIC (Year 10)</th>
<th>GLOM</th>
<th>LYs gained</th>
<th>Cost (USD)</th>
<th>ICER</th>
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Figure 1. AIC over Time

Figure 2. Treatment Intensification Target

Figure 3. Cost-Effectiveness Plan

Figure 4. AIC over Time