Dapagliflozin and Changes in Metabolic Syndrome in Patients with Type 2 Diabetes: A DECLARE TIMI 58 Sub-analysis

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Background

- SGLT2 inhibitors reduce cardiovascular risk in a broad range of patients
- SGLT2 inhibitors have non-glycemic effects on blood pressure, weight, and lipid profile (components of metabolic syndrome)
- The significance of metabolic syndrome in patients with established cardiometabolic disease is not clear

Objectives

- Determine prognostic relevance of metabolic syndrome in patients with established type 2 diabetes.
- Investigate effect of dapagliflozin on metabolic syndrome and its key components.
Methods

DECLARE – TRIAL DESIGN

17,160 with Type 2 DM
Established CV Disease (6974) or
Multiple Risk Factors (10186)

RANDOMIZE 1:1
DOUBLE BLIND
All other DM Rx per treating MD

DAPAGLIFLOZIN
10 mg DAILY

PLACEBO

Follow-up visits
In Person Q 6 mo/ telephone Q 3 mo

Primary EPs
Safety: MACE (CVD/MI/Ischemic Stroke)
Dual Efficacy: CVD/HHF, MACE

Median follow up
4.2 years
IDF Metabolic Syndrome Criteria

BMI > 30 kg/m² or elevated waist circumference

+  
≥ 2 factors

- Raised triglycerides  
≥ 150 mg/dL

- Reduced HDL-C  
< 40 mg/dL (men)  
< 50 mg/dL (women)

- Raised blood pressure  
SBP ≥130 or DBP ≥85 mmHg

- Raised fasting plasma glucose  
≥ 100 mg/dL or history of DM

Methods
Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Full Trial Cohort N=17160</th>
<th>Metabolic Syndrome N=9121</th>
<th>No Metabolic Syndrome N=8030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Mean (SD)</td>
<td></td>
<td>64 (7)</td>
<td>64 (7)</td>
</tr>
<tr>
<td>Female, (%)</td>
<td></td>
<td>39</td>
<td>36</td>
</tr>
<tr>
<td>BMI, Mean (SD)</td>
<td></td>
<td>36 (5)</td>
<td>28 (4)</td>
</tr>
<tr>
<td>HbA1c, Mean (SD)</td>
<td></td>
<td>8 (1)</td>
<td>8 (1)</td>
</tr>
<tr>
<td>Duration of T2DM (years), Median (IQR)</td>
<td></td>
<td>10 (6, 16)</td>
<td>11 (6, 16)</td>
</tr>
<tr>
<td>History of hypertension, (%)</td>
<td></td>
<td>94</td>
<td>85</td>
</tr>
<tr>
<td>History of dyslipidemia, (%)</td>
<td></td>
<td>82</td>
<td>79</td>
</tr>
<tr>
<td>Current Smoker, (%)</td>
<td></td>
<td>13</td>
<td>17</td>
</tr>
<tr>
<td>Prior MI, (%)</td>
<td></td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>History of CHF, (%)</td>
<td></td>
<td>12</td>
<td>8</td>
</tr>
</tbody>
</table>
Outcomes in patients with metabolic syndrome

* Cox proportional hazards models adjusted for treatment, ACSVD status, age, sex, race (white vs. nonwhite), current smoker, prior MI, CHF history, duration of diabetes, ACE/ARB, BB, and MRA
Lower prevalence of metabolic syndrome in dapagliflozin group compared to placebo

Prevalence Of Metabolic Syndrome

![Graph showing prevalence of metabolic syndrome over months, with lower values in the dapagliflozin group compared to placebo.](image)

- **Placebo**
- **Dapagliflozin**

*\( p < 0.001 \)
Progression and regression of metabolic syndrome

**Progression of metabolic syndrome**

- Dapagliflozin
- Placebo

**Regression of metabolic syndrome**

- Dapagliflozin
- Placebo

*\(p<0.001\)
Changes in components of metabolic syndrome

**Prevalence of Elevated SBP or DBP**
- Dapagliflozin
- Placebo

* *p<0.001

**Prevalence of Low HDL**
- Dapagliflozin
- Placebo

* *p<0.001

**Prevalence of Elevated BMI (≥30 kg/m²)**
- Dapagliflozin
- Placebo

* *p<0.001

**Prevalence of Elevated Triglycerides (≥150 mg/dL)**
- Dapagliflozin
- Placebo
Summary

• The presence of metabolic syndrome is prognostically relevant even among patients with DM with higher rates of HHF and MI.

• In patients treated with dapagliflozin, there were lower rates of metabolic syndrome, higher rates of regression and fewer cases of new metabolic syndrome.
  
  • This was driven by favorable effects on blood pressure, weight/BMI, and the prevalence of low HDL
  • These differences were evident at 6 months and persisted through 48 months
THANK YOU