Relationship between cardiac biomarkers and major adverse cardiovascular events in DECLARE-TIMI 58


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Background

• Biomarkers of hemodynamic stress and myocardial injury are associated with the risk of CV death and heart failure (HF) in patients with atherosclerotic cardiovascular disease (ASCVD).

• Here, we explore the association between cardiac biomarkers (NT-proBNP and hsTnT) and ASCVD outcomes in patients with type 2 diabetes (T2DM).
Methods

• Nested biomarker study in DECLARE-TIMI 58
• Patients with T2DM and either multiple risk factors (MRF) (~60%) or established ASCVD (~40%)
• Serum levels of NT-proBNP and hsTnT (Roche Diagnostics) were measured in all patients with available blood samples at randomization (n = 14,565) in the TIMI Biomarker Laboratory
• **Primary Endpoint:** Major adverse cardiovascular events (MACE, i.e., the composite of myocardial infarction, ischemic stroke, and CV death)
• Multivariable adjusted Cox models & Spline regression models
# Baseline Biomarker Concentrations

<table>
<thead>
<tr>
<th></th>
<th>NT-proBNP</th>
<th></th>
<th>hsTnT</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Median (IQR)</td>
<td>&gt;125 pg/ml</td>
<td>≥450 pg/ml</td>
</tr>
<tr>
<td><strong>Total Population</strong></td>
<td>14,565</td>
<td>75 (35 - 165)</td>
<td>33%</td>
<td>8%</td>
</tr>
<tr>
<td><strong>ASCVD</strong></td>
<td>5,972</td>
<td>106 (48-241)</td>
<td>44%</td>
<td>13%</td>
</tr>
<tr>
<td><strong>MRF</strong></td>
<td>8,590</td>
<td>61 (30-122)</td>
<td>24%</td>
<td>5%</td>
</tr>
</tbody>
</table>
Baseline characteristics by biomarker quartiles

<table>
<thead>
<tr>
<th></th>
<th>NT-proBNP</th>
<th></th>
<th>hsTnT</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Q1</td>
<td>Q4</td>
<td>Q1</td>
<td>Q4</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>61</td>
<td>66</td>
<td>62</td>
<td>66</td>
</tr>
<tr>
<td>Duration of diabetes (yrs)</td>
<td>10</td>
<td>12</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>ASCVD (%)</td>
<td>28</td>
<td>58</td>
<td>32</td>
<td>52</td>
</tr>
<tr>
<td>Prior HF (%)</td>
<td>3</td>
<td>23</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td>Baseline eGFR (ml/min/1.73m²)</td>
<td>93</td>
<td>82</td>
<td>94</td>
<td>80</td>
</tr>
</tbody>
</table>

All P-trend <0.05
Relationship between cardiac biomarkers and MACE within the placebo arm

Clinical covariates: Adjusted for age, sex, race, smoking, baseline eGFR, BMI, T2DM duration, insulin use, history of CAD, MI, ischemic stroke, PAD, HF, dyslipidemia & hypertension
Multimarker Analysis

Adjusted for age, sex, race, smoking, baseline eGFR, BMI, T2DM duration, insulin use, history of CAD, MI, ischemic stroke, PAD, HF, dyslipidemia & hypertension
Risk of MACE by baseline biomarker levels and stratified by treatment arm

- **NT-proBNP**
  - Subgroup: ASCVD, MRF
  - Treatment: Placebo, Dapaglifozin

- **hsTnT**
  - Subgroup: ASCVD, MRF
  - Treatment: Placebo, Dapaglifozin

**Baseline Biomarker Levels**

- **Probability of MACE**
  - 0.0 to 0.3

**Graph Details**

- **X-axis**: Baseline Biomarker Levels
- **Y-axis**: Probability of MACE
Conclusion

• In patients with T2DM both with and without ASCVD, higher baseline NT-proBNP or hsTnT levels identified patients at increased risk of MACE.

• The difference in MACE rates between dapagliflozin and placebo tended to be more pronounced in ASCVD patients with higher baseline NT-proBNP or hsTnT levels.