Effect of Omecamtiv Mecarbil in Patients With Heart Failure With Reduced Ejection Fraction and Atrial Fibrillation/Flutter: Results from COSMIC-HF

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OBJECTIVES

To characterize, in patients with and without atrial fibrillation or flutter, the effects of omecamtiv mecarbil (OM) on 20 weeks of change from baseline in:

- Systolic ejection time (SET)
- Stroke volume
- Left ventricular end-diastolic (endo) diameter (LVEDD; LVESD)
- Heart rate
- N-terminal pro-B-type natriuretic peptide (NT-proBNP)

METHODS

Study Design

COSMIC-HF (NCT01786512) was a multicenter, randomized, placebo-controlled, double-blind phase 2 study that enrolled patients with:

- Stable, optimally treated chronic heart failure (HF)
- New York Heart Association (NYHA) class II or III
- Left ventricular ejection fraction (LVEF) ≤ 40%
- Females and males
- Age, years, mean (SD) 65.8 (9.9) 70.3 (8.8) 63.1 (9.6) 60.6 (11.5)
- Sex, male, % 68.6 87.5 72.6 82.9
- Race, % 12.5 12.5 28.1 28.1
- Diabetes 46.9 28.1 39.3 39.3

- NT-proBNP, pg/mL, median (Q1,Q3) 2941 (1717, 5394) 2998 (1687, 4356) 1322 (647, 2483) 1564 (687, 2457)
- LVESD, cm, mean (SD) 5.4 (0.9) 5.1 (0.7) 5.3 (1.0) 5.5 (0.9)
- LVEDD, cm, mean (SD) 6.3 (0.9) 6.0 (0.8) 6.2 (1.0) 6.4 (0.9)
- Heart rate, bpm, median (Q1,Q3) 73 (65, 85) 72 (65, 85) 74 (65, 85) 71 (65, 85)
- Stroke volume, mL, mean (SD) 51.3 (13.3) 51.0 (14.0) 52.4 (15.4) 52.8 (15.1)
- SET, msec, mean (SD) 280.7 (30.7) 297.7 (28.5) 303.5 (37.2) 299.1 (33.9)

Mecamaltiv mecarbil dose-escalation from 25 mg BID to 50 mg BID based on MAP PK-titration group

- 25 mg BID
- 50 mg BID

- Placebo-corrected change from baseline at 20 weeks in OM PK-titration group

- NS = not statistically significant

CHANGE IN LVEF (≤ ≤ ≤) in patients with and without AF

- No AF
- AF

Table 2. Effects of Omecamtiv Mecarbil in Patients With HFrEF, With and Without AF

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No AF, n = 117</th>
<th>AF, n = 32</th>
<th>Interaction p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVESD, cm</td>
<td>5.1 (0.9)</td>
<td>5.0 (0.9)</td>
<td>0.84</td>
</tr>
<tr>
<td>LVEDD, cm</td>
<td>6.2 (0.9)</td>
<td>6.3 (0.9)</td>
<td>0.67</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>72 (65, 85)</td>
<td>73 (65, 85)</td>
<td>0.61</td>
</tr>
<tr>
<td>Stroke volume, mL</td>
<td>51.0 (14.0)</td>
<td>52.5 (14.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>SET, msec</td>
<td>280.7 (30.7)</td>
<td>288.3 (30.7)</td>
<td>0.38</td>
</tr>
<tr>
<td>NT-proBNP, pg/mL</td>
<td>2998 (1687)</td>
<td>2736 (1246)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

DISCLOSURES

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REFERENCES