Introducing Mavacamten for the Treatment of NYHA Class II and III Symptomatic Obstructive HCM in Adult Patients

Mavacamten is a First-in-Class Therapy and as a Pioneering Therapeutic Approach, Addresses the Fundamental Pathophysiology of Obstructive HCM

Mavacamten significantly improved symptom control (NYHA class) and exercise capacity (pVO2) versus placebo

Percentage of patients achieving primary composite endpoint at Week 30*

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Treatment difference: 19%; 95% CI: 8.67–30.13; p=0.0005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mavacamten</td>
<td>37%</td>
</tr>
<tr>
<td>+/- blocker (n=45/123)</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>17%</td>
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</tbody>
</table>

*92% of patients in the mavacamten and placebo treatment arms also remained on background therapy. Primary composite endpoint defined as a ≥2.5 mL/kg/min increase in pVO2 if NYHA class reduction, or a ≥2.0 mL/kg/min increase in pVO2 and no worsening in NYHA class.

Mavacamten significantly reduced the proportion of patients who proceeded or remained guideline-eligible for SRT vs placebo

Percentage of patients achieving primary composite endpoint vs. placebo

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Treatment difference: 59%; 95% CI: 44–74; p&lt;0.0001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mavacamten</td>
<td>82%</td>
</tr>
<tr>
<td>+/− blocker (n=56)</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>23%</td>
</tr>
</tbody>
</table>

*4x more patients were no longer guideline-eligible for SRT

The Safety Profile of Mavacamten is Comparable Between the EXPLORER-HCM and VALOR-HCM Trials

Most commonly reported adverse reactions with mavacamten:

Nervous system disorders:

- Dizziness (17%)
- Syncope (5%)

Cardiac disorders:

- Respiratory, thoracic, and mediastinal disorders:
  - Systolic dysfunction* (5%)
  - Dyspnoea (12%)

No patients discontinued treatment permanently due to a LVEF <50%.

Mavacamten reduces LVEF and may cause heart failure due to systolic dysfunction defined as symptomatic LVEF <50%. Patients with a serious intercurrent illness, such as infection or arrhythmia (including atrial fibrillation or other uncontrolled tachyarrhythmia), or those undergoing major cardiac surgery, may be at greater risk of systolic dysfunction and progress to heart failure.

Obstructive HCM Represents a Chronic and Progressive Disease, Posing Challenges in Both Diagnosis and Treatment

SRTs are complex, invasive procedures with significant risks. Following SRT, up to 30% of patients still require treatment for symptoms.

There is an unmet need for an approved non-invasive treatment that targets obstructive HCM.

Obstructive HCM is characterised by LV hypertrophy that cannot be explained by another cardiac or systemic disease.

Variable disease presentation and non-specific symptoms can make diagnosis difficult.

Current pharmacologic therapies, β-blockers, and calcium channel blockers address symptoms, but may not alter natural history of HCM.

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Therapeutic Indication: Mavacamten is indicated for the treatment of symptomatic (New York Heart Association, NYHA, class II-III) obstructive hypertrophic cardiomyopathy (oHCM) in adult patients.

Key

C1 confidence interval; CYP2C19: cytochrome P450 2C19; LV: left ventricular; LVOT: left ventricular outflow tract; NYHA: New York Heart Association; QD: once daily; SRT: septal therapies.

References