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

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

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.

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.

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:

Systolic dysfunction* (5%)

Respiratory, thoracic, and mediastinal disorders:

Dyspnoea (12%)

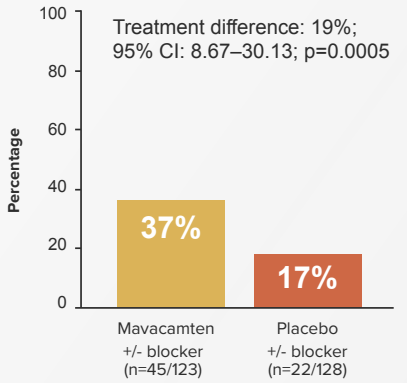
No patients discontinued treatment permanently due to a LVEF <50%.

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.

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*

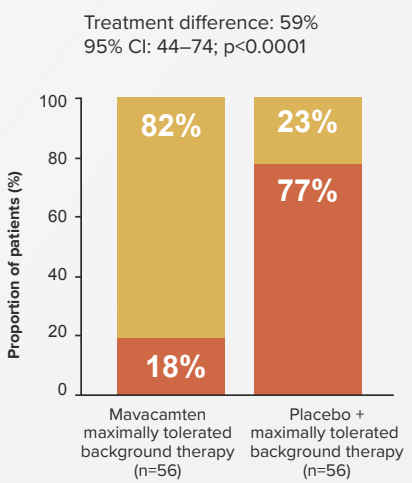


Twice as many patients achieved the primary composite endpoint vs. placebo

*92% of patients in the mavacamten and placebo treatment arms also remained on background therapy. †Primary composite endpoint defined as a ≥1.5 mL/kg/min increase in pVO2 and ≥1 NYHA class reduction, or a ≥3.0 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

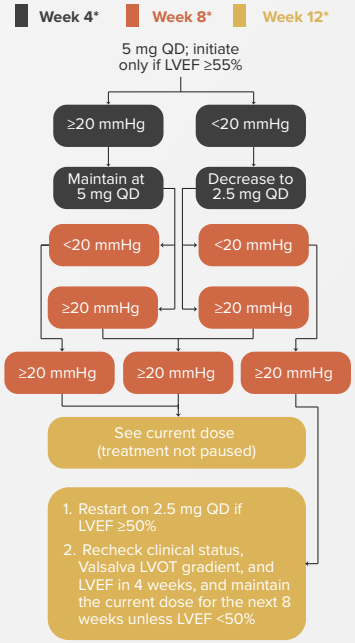
SRT eligibility at Week 16*

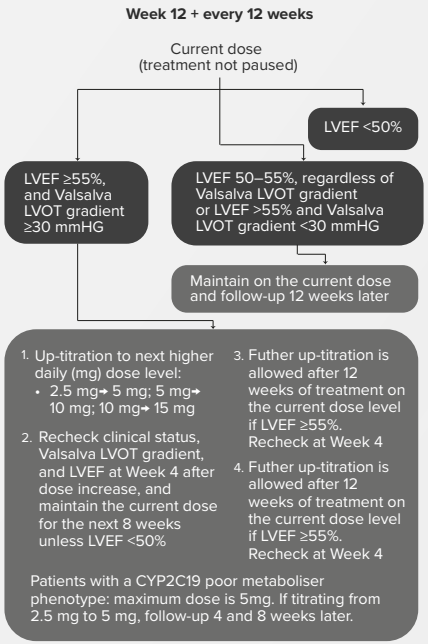


~4x more patients were no longer guideline-eligible for SRT

*In the mavacamten group, two patients chose to proceed with SRT prior to or at Week 16, and eight patients remained guideline-eligible for SRT after 16 weeks of treatment. In the placebo group, two patients chose to proceed with SRT prior to or at Week 16, and 39 patients remained guideline-eligible for SRT after 16 weeks. In two patients taking placebo, SRT status was not evaluable, and was imputed as meeting the primary endpoint.

Once-Daily Mavacamten Offers Individualised and Personalised Dosing to Achieve the Optimal Response





Dosing for patients with CYP2C19 intermediate, normal, rapid, and ultra-rapid metaboliser phenotypes

The incidence of patients with CYP2C19 intermediate, normal, rapid, and ultra-rapid metaboliser phenotypes ranges from approximately 98% in Caucasians to 82% in Asian populations

- The starting dose for patients with a CYP2C19 poor metaboliser phenotype is one 2.5-mg capsule orally, once daily.
- If treatment is initiated before CYP2C19 phenotype is determined, you should follow dosing instructions for CYP2C19 poor metaboliser phenotype until phenotype is determined.
- Maximum dose for patients with CYP2C19 poor metaboliser phenotype is 5 mg.

Mavacamten is available in 2.5 mg, 5 mg, 10 mg, and 15 mg

Prescribed doses should be taken in a single capsule

Treatment should be taken once daily at the same time each day, with or without food

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.

Confirm patient eligibility based on Summary of Product Characteristics before initiating treatment. The potential for drug interactions should be considered according to the Summary of Product Characteristics prior to initiation with mavacamten and throughout continued treatment.

References

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Key

CI: confidence interval; CYP2C19: cytochrome P450 2C19; HCM: hypertrophic cardiomyopathy; LV: left ventricular; LVEF: left ventricular ejection function; LVOT: left ventricular outflow tract; NYHA: New York Heart Association; QD: once daily; SRT: septal therapies.