Efficacy and safety of Mavacamten in the treatment of Hypertrophic Cardiomyopathy: A Systematic Review

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Background

- The prevalence of hypertrophic cardiomyopathy (HCM) is 1 in 500 adults in the general population
- Genetic disorder of cardiac myocytes can be characterized as cardiac hypertrophy, specifically in the left ventricle. Depending on the extent of hypertrophy, patients can develop abnormalities such as left ventricular outflow tract (LVOT) obstruction, diastolic dysfunction, mitral regurgitation, and myocardial ischemia
- Multiple treatment modalities can be used, but pharmacologic treatments are the most common. Alternatively, there are other forms of treatment, such as surgical septal myomectomy or alcohol septal ablation. This review aims to compare the safety and efficacy of a novel pharmacologic agent, mavacamten, in comparison to the current standard pharmacological approach.
- The mechanism of action of Mavacamten is inhibition of phosphate release from cardiac myosin, leading to a decrease in sarcomere force production, ultimately reducing cardiac contractility and increasing the ventricular chamber size.
- In 2022, FDA approved mavacamten is now a drug of choice in the treatment of HCM, with a goal to avoid the need for surgical intervention.
- This systematic review aims to assess the safety and efficacy of mavacamten in the treatment of HCM.

Results

Efficacy of Mavacamten

- All studies found a statistically significant reduction in NYHA.
- When assessing net health benefits in this trial were life-years (LYs) and quality-adjusted life-years (QALYs); results demonstrated large increases in both LYs and QALYs from the use of mavacamten with or without BB or CCB monotherapy and placebo with or without BB or CCB monotherapy.
- An increase in mixed venous oxygen pressure (pVO_2) after mavacamten treatment, was seen in 3 out of 4 studies.

Safety of Mavacamten

- Each of these trials identified similar results with regards to the safety of mavacamten.
- Heitner et al. found the most common adverse events to be decreased LVEF and atrial fibrillation (Afib). Of the 5 total AFib events, three were intermittent, two resolved, and one had a history of paroxysmal AFib and had to drop out of the trial. However, there were no observed sustained arrhythmias and no evidence of QT prolongation.
- MAVERICK-HCM found five participants to have an LVEF ≤ 45% after receiving mavacamten but all five returned to their baseline after undergoing protocol directed dose adjustment[9].

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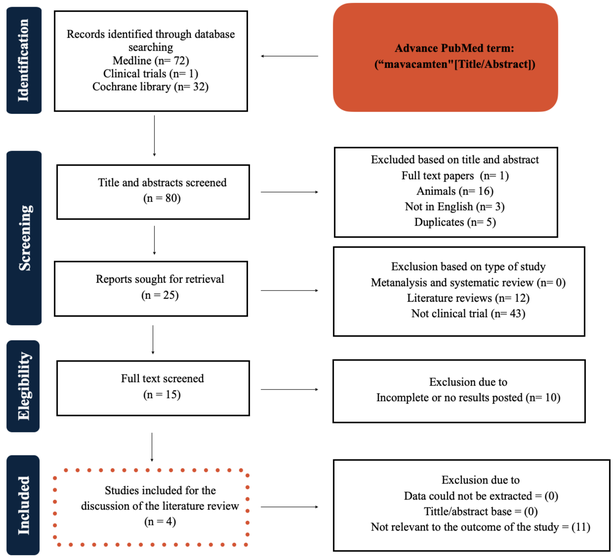

Figure 1. PRISMA flow chart demonstrating study selection.

Author, year of the publication	Country	Study design	Number of patients in treatment group	Number of patients in control group	Intervention	Time of outcome assessment
Heitner et al. 2019	USA	Open-label, nonrandomized, prospective, phase 2 trial	11	10	M: 15 mg/d M: 5 mg/d once a day orally	16 weeks
Ho et al. 2020 MAVERICK-HCM	USA	Multicenter, double-blind, placebo-controlled, dose-ranging phase II study	Group 1= 19 Group 2 = 21	Group 3 = 19	M1: 200 ng/ml M2: 500 ng/ml Placebo once a day orally	16 weeks
Olivotto et al. 2020 EXPLORER-HCM	Multiple countries	Phase 3, randomized, double-blind, placebo-controlled trial	123	128	M: 2.5 mg M: 5 mg M: 15 mg Placebo once a day orally	30 weeks
Desai et al. 2022 VALOR-HCM	USA	Multicenter, randomized, double-blind, placebo-controlled, phase 3 trial	56	56	M: 5 mg Placebo once a day orally	16 weeks

Figure 2. Shows the author, year, country, study design, number of patients in treatment and control group, intervention, and time of outcome assessment.

Discussion

- By binding allosterically to β-cardiac myosin, mavacamten reduces the hypercontractility of cardiac sarcomeres.
- This reduces the degree of hypertrophy and ultimately, the symptoms associated with HCM. The secondary endpoint, an increase in mixed venous oxygen pressure (pVO_2) after mavacamten treatment, was seen in 3 out of 4 studies.
- Peak oxygen consumption is measured using mixed venous blood samples were obtained from the inferior and superior vena cava and the heart.
- In patients with HCM, the hypertrophic tissue leads to an increased oxygen consumption thereby leading to a reduction in pVO_2.
- The trials looked at an elevation of pVO_2 as a primary endpoint after mavacamten use.
- The proposed mechanism acts by inhibiting myocardial cross-bridge formation, decreasing the energy requirements of cardiac muscle, thus, leading to a decrease in oxygen consumption.
- This should then be reflected by an increase in pVO_2. All 3 trials that measured pVO_2 as an endpoint, showed an increase in pVO_2 after treatment with mavacamten.

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