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LETTER TO THE EDITOR

Mavacamten's therapeutic impact: cardiac-specific myosin inhibition in obstructive hypertrophic cardiomyopathy

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Dear Editor,

Obstructive hypertrophic cardiomyopathy (oHCM) is a hereditary cardiac condition, affecting 1 in about 500 individuals, characterized by an atypical thickening of the heart muscle, specifically the interventricular septum.[1] It results from excessive cross-bridging of cardiac myosin and actin and enhanced sensitivity to calcium due to cardiac sarcomere dysfunction. Among the main pathophysiologic characteristics of HCM are myocardial fibrosis, diastolic dysfunction, microvascular ischemia, and left ventricular hypertrophy (LVH).[2]

There are currently few pharmaceutical alternatives for treating hypertrophic cardiomyopathy (HCM). These include beta-blockers, non-dihydropyridine Ca+2 channel blockers, and disopyramide, which are not specific to any particular illness. These medications, which frequently provide less than ideal clinical relief, are often constrained by adverse effects and do not address the primary pathologic abnormalities underlying the illness.[3]

Mavacamten is an entirely novel, FDA-approved cardiac myosin ATPase allosteric inhibitor that lowers cardiac contractility and decreases myocardial energy consumption in experimental cardiac failure models.[3] The heart performs poorly in both the systolic and diastolic phases due to restriction of the left ventricular outflow tract (LVOT) and enhanced ventricular filling pressure, respectively, which is the manifestation of the disease. Mavacamten causes the heart to become extremely relaxed, which in turn improves cardiac filling pressures and reduces LVOT obstruction. As a result, patients with obstructive cardiomyopathy or phase II and III symptoms according to the New York Heart Association (NYHA) report better functional ability and improved symptoms.[4]

A recent systematic review and meta-analysis, encompassing an international cohort of 524 patients, further underscores the efficacy and safety of mavacamten. The study showed that mavacamten significantly improved clinical outcomes, including NYHA class, reduced the need for septal reduction therapy, and enhanced patient-reported quality of life measures. Although it resulted in a small increase in adverse events, there was no significant rise in serious adverse events compared to placebo. However, mavacamten did not show a statistically significant improvement in peak oxygen consumption. These findings highlight Mavacamten as a safe and effective treatment option for HCM in the short term, with the potential for broader applications pending further research.[5]

Hegde *et al.* report that after 30 weeks, mavacamten was linked to a substantial decrease in the post-exercise LVOT gradient, and that reduction persisted for 48 weeks. Cardiac magnetic resonance imaging (CMR) discovered that mavacamten was associated with positive remodeling. Additionally, mavacamten enhanced several cardiopulmonary activity test metrics.[6]

In conclusion, patients with HCM now have a new therapeutic option in mavacamten, which provides an extra choice for those with chronic symptoms who had few other alternatives. Future long-term studies are essential to further elucidate its role in oHCM management, its interactions with other therapies, and its potential for altering the disease course beyond symptomatic improvement.

Contributions

AS, conceptualization, manuscript original drafting; LY, manuscript editing; EK, manuscript final version reviewing. All authors made a substantive intellectual contribution; read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflicts of interest

The authors declare no conflict of interest.

Availability of data and material

The content is based on existing literature and publicly available data.

Ethical approval

Not applicable.

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