International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	EFFICACY AND SAFETY OF MAVACAMTEN IN HYPERTROPHIC CARDIOMYOPATHY – A SYSTEMATIC REVIEW OF CURRENT CLINICAL STUDIES
DOI	https://doi.org/10.31435/ijitss.2(50).2026.5881
RECEIVED	18 March 2026
ACCEPTED	26 June 2026
PUBLISHED	30 June 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

EFFICACY AND SAFETY OF MAVACAMTEN IN HYPERTROPHIC CARDIOMYOPATHY – A SYSTEMATIC REVIEW OF CURRENT CLINICAL STUDIES

Wiktoria Szkatuła *(Corresponding Author, Email: wiktoria.szkatula@onet.pl)*
Provincial Specialist Hospital No. 2 in Jastrzębie-Zdrój, Ave. Jana Pawła II 7, 44-330 Jastrzębie-Zdrój, Poland
ORCID ID: 0009-0000-8206-3926

Marcin Schulz
II Department of Cardiology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Marii Skłodowskiej-Curie 10, 41-800 Zabrze, Poland
ORCID ID: 0009-0006-4466-5794

Agnieszka Morawa
Municipal Hospital in Zabrze, Zamkowa 4, 41-803 Zabrze, Poland
ORCID ID: 0009-0001-2325-7998

Dawid Studziński
Municipal Hospital in Zabrze, Zamkowa 4, 41-803 Zabrze, Poland
ORCID ID: 0009-0005-3834-716X

Karolina Osińska
Municipal Hospital in Kędzierzyn-Koźle, 24 kwietnia 5, 47-232 Kędzierzyn-Koźle, Poland
ORCID ID: 0009-0003-9731-0629

Michał Kulczak
School of Medicine, Medical University of Silesia, Poniatowskiego 15, 40-055 Katowice, Poland
ORCID ID: 0009-0006-4968-3318

Anna Kołcz
School of Medicine, Medical University of Silesia, Poniatowskiego 15, 40-055 Katowice, Poland
ORCID ID: 0009-0006-1446-2865

ABSTRACT

Introduction: Hypertrophic cardiomyopathy (HCM) is an inherited condition characterized by sarcomeric hypercontractility, leading to dynamic left ventricular outflow tract (LVOT) obstruction in approximately 70% of patients. Mavacamten, a first-in-class selective cardiac myosin inhibitor, addresses the underlying molecular cause by reducing excessive actin-myosin cross-bridge formation.
Aim: To evaluate the clinical efficacy and safety of mavacamten in symptomatic obstructive HCM (oHCM) using data from randomized trials and real-world studies.
Methods: A systematic search of PubMed, Embase, and Cochrane Library identified 110 publications. Following predefined criteria, 44 studies were included in the final analysis, including pivotal phase III trials (EXPLORER-HCM, VALOR-HCM) and long-term extensions.
Results: Mavacamten demonstrated a significant reduction in LVOT gradients (mean reduction of ~47 mmHg in EXPLORER-HCM) and improved quality of life, with KCCQ-CSS scores increasing by an average of 14.2 points. Between 60% and 80% of patients achieved ≥1 NYHA functional class improvement. In the VALOR-HCM trial, approximately 90% of patients avoided invasive septal reduction therapy (SRT) through 128 weeks. The primary safety concern was a transient reduction in LVEF (<50%) occurring in 5–14% of patients, which was typically reversible with dose titration.
Conclusion: Mavacamten is a transformative non-invasive therapy that shifts oHCM management from palliative care to mechanism-targeted treatment. While highly effective in improving hemodynamics and functional capacity, rigorous echocardiographic monitoring remains mandatory to ensure safety regarding systolic function.

KEYWORDS
Mavacamten; Cardiac Myosin Inhibitor; Hypertrophic Cardiomyopathy; LVOT Obstruction

CITATION
Wiktoria Szkatuła, Marcin Schulz, Agnieszka Morawa, Dawid Studziński, Karolina Osińska, Michał Kulczak, Anna Kołcz. (2026) Efficacy and Safety of Mavacamten in Hypertrophic Cardiomyopathy – a Systematic Review of Current Clinical Studies. *International Journal of Innovative Technologies in Social Science*. 2(50). doi: 10.31435/ijitss.2(50).2026.5881

Introduction

Hypertrophic cardiomyopathy (HCM) is widely regarded as the most prevalent inherited cardiac disorder, defined by otherwise unexplained left ventricular hypertrophy accompanied by characteristic myocardial fiber disorganization on histopathological examination [10,29]. The condition is most commonly transmitted in an autosomal dominant manner, with an estimated prevalence ranging from approximately 1:200 to 1:500 individuals worldwide [10,12,28]. HCM is a clinically and genetically heterogeneous disease, primarily driven by sarcomeric hypercontractility and impaired ventricular relaxation, which together contribute to the development of dynamic left ventricular outflow tract (LVOT) obstruction in nearly two-thirds of affected individuals [1,10,24]. From a clinical perspective, obstructive HCM is associated with substantial morbidity, as patients frequently present with exertional dyspnea, syncope, angina, and marked limitations in exercise capacity, all of which significantly impair quality of life [10,17]. In addition, the disease is linked to an increased incidence of arrhythmias, progressive heart failure, and an elevated risk of sudden cardiac death [10,29,40].

Despite its clinical impact, therapeutic strategies for HCM have long remained suboptimal. Traditional pharmacological approaches have primarily involved non-specific agents such as beta-adrenergic blockers, non-dihydropyridine calcium channel blockers, and disopyramide [10,24]. Although these medications may alleviate symptoms to some extent by influencing heart rate dynamics or intracellular calcium handling, they do not directly target the underlying molecular mechanisms of the disease. Moreover, their clinical utility is often constrained by limited efficacy, adverse effects, and a lack of disease-modifying potential [1,24,42]. In patients with persistent symptoms despite optimal medical therapy, invasive options namely septal reduction therapy (SRT), including surgical myectomy or alcohol septal ablation have traditionally been considered [6,10]. However, these procedures are associated with procedural risks, limited accessibility, and the requirement for specialized expertise typically available only in high-volume centers, thereby restricting their widespread use.

The emergence of mavacamten, a selective and reversible inhibitor of cardiac myosin, represents a significant advancement in the therapeutic landscape of obstructive HCM [1,3,24]. By directly modulating sarcomeric function and reducing excessive actin–myosin cross-bridge formation, mavacamten targets the fundamental pathophysiological mechanism responsible for LVOT obstruction and facilitates beneficial cardiac remodeling [7,24]. Initial evidence supporting its efficacy and safety was provided by pivotal trials such as EXPLORER-HCM and VALOR-HCM, while more recent long-term extension studies and real-world data from heterogeneous patient populations offer further insights into its clinical performance [1,10,18]. Accordingly, this systematic review aims to comprehensively and critically evaluate the current body of evidence concerning the efficacy and safety of mavacamten in patients with symptomatic obstructive hypertrophic cardiomyopathy, integrating findings from randomized controlled trials, extension studies, and real-world clinical data.

Methodology

This systematic review was conducted to provide a rigorous and clearly structured evaluation of the current clinical evidence regarding the efficacy and safety of mavacamten in patients with symptomatic obstructive hypertrophic cardiomyopathy (oHCM). The literature selection process was designed to identify high-quality studies enabling a comprehensive assessment of the drug's impact on hemodynamic parameters, functional capacity, and patient-reported quality of life. An initial pool of 110 scientific publications was identified through systematic searches of major biomedical databases, including PubMed, Embase, and the Cochrane Library. The selection process followed predefined inclusion and exclusion criteria to ensure methodological rigor and reliability of the synthesized evidence.

Studies were considered eligible if they were conducted exclusively in human populations and represented clinical trials, including pivotal phase II and III studies such as EXPLORER-HCM and VALOR-HCM, as well as observational studies and experimental investigations providing primary clinical data. Publications were excluded if they did not provide original clinical evidence or failed to meet required methodological standards. In total, 66 studies were excluded, including 19 review articles due to their secondary nature, 24 case reports because of their limited generalizability and low level of evidence, 7 reviews and expert opinions lacking primary data, 5 editorial letters without sufficient methodological detail, 4 animal studies in line with the restriction to human populations, 3 cost analyses not addressing clinical efficacy or safety outcomes, and 3 preprints due to the absence of peer review, along with a small number of additional records excluded because of unavailable full text or content not aligned with the scope of the review.

After applying these criteria, 44 studies were included in the final analysis and constituted the basis for evaluating the therapeutic profile of mavacamten. The selected body of evidence enabled a comprehensive assessment of key clinical endpoints, including reduction in left ventricular outflow tract gradient, improvement in New York Heart Association functional class, and changes in cardiac biomarkers.

Pathophysiology of Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is primarily an inherited myocardial disorder, most often transmitted in an autosomal dominant fashion [10,12,26]. Its underlying cause lies in pathogenic variants affecting genes that encode components of the cardiac sarcomere or related structural elements [12,14,22]. Although the genetic background of HCM is highly heterogeneous, mutations in MYBPC3 (encoding myosin-binding protein C) and MYH7 (encoding β-myosin heavy chain) are the most commonly identified and together account for a substantial proportion of genetically confirmed cases [14,17,37]. These molecular abnormalities initiate a cascade of biomechanical and structural changes, ultimately leading to characteristic histopathological features such as myocyte disarray, interstitial fibrosis, and compensatory myocardial hypertrophy [3,22,26].

At the molecular level, sarcomeric mutations disrupt the finely regulated processes governing myocardial contraction, resulting in a hypercontractile phenotype [1,7,18]. A central feature of this dysregulation is an increased availability of myosin heads capable of interacting with actin, which enhances the formation of actin–myosin cross-bridges [12,13,22]. Under physiological conditions, approximately 40–50% of myosin heads remain in the energy-conserving "super-relaxed" (SRX) state, characterized by minimal ATP consumption and reduced actin binding [12,24,25]. In contrast, in HCM this proportion is markedly reduced to around 15–20%, with a corresponding increase in myosin heads transitioning into the active, force-generating state [24,25]. This shift leads to excessive cross-bridge cycling, contributing to energetic inefficiency, impaired ventricular relaxation, and increased myocardial stiffness [7,12,13,24].

The clinical phenotype of obstructive HCM (oHCM) reflects the interaction between these molecular abnormalities and structural remodeling at the organ level. Dynamic left ventricular outflow tract (LVOT) obstruction defined as a pressure gradient of at least 30 mmHg at rest or following provocation is observed in roughly 70% of patients [3,12,22,39]. The principal mechanism underlying this obstruction is systolic anterior motion (SAM) of the mitral valve, in which the anterior mitral leaflet abuts the hypertrophied interventricular septum during systole [3,15,38]. Additional anatomical factors, such as elongation of the anterior mitral valve leaflet (AMVL) and abnormalities of the papillary muscles (including displacement or bifid morphology), further contribute to narrowing of the outflow tract [3,15,44].

Hemodynamic factors also play a critical role in the development and exacerbation of LVOT obstruction. Flow-related forces, including the Venturi effect and drag forces within the narrowed outflow tract, promote anterior displacement of the mitral valve apparatus [3,44]. During systole, the hyperdynamic contraction of the left ventricle generates early and forceful ejection, creating a suction effect that draws the mitral leaflets

toward the septum [3,44]. The resulting dynamic obstruction leads to elevated intracavitary pressures and increased myocardial wall stress, which further contribute to subendocardial ischemia and progressive hypertrophic remodeling [12,17,18]. In addition, SAM frequently induces secondary mitral regurgitation, which together with the LVOT gradient underlies the characteristic clinical manifestations, including exertional dyspnea, angina, and syncope [3,17,18].

Current Treatment Strategies

The traditional therapeutic strategy for symptomatic obstructive hypertrophic cardiomyopathy (oHCM) has historically been based on a stepwise algorithm, primarily focused on alleviating symptoms through the reduction of myocardial contractility and modulation of heart rate [10,20,40]. Beta-adrenergic blockers constitute the cornerstone of first-line pharmacological treatment, as they decrease myocardial oxygen consumption and enhance diastolic filling time by reducing heart rate [14,24,28]. In individuals who do not tolerate beta-blockers or in whom these agents are contraindicated, non-dihydropyridine calcium channel blockers most notably verapamil and diltiazem are commonly employed as alternative therapies to reduce the left ventricular outflow tract (LVOT) gradient [4,22,24]. When symptom control remains insufficient, disopyramide, a Class IA antiarrhythmic agent, is frequently added to the treatment regimen [3,22]. Its mechanism involves attenuation of intracellular calcium influx and stabilization of the ryanodine receptor, thereby reducing myocardial contractile force and contributing to the mitigation of dynamic LVOT obstruction [3].

In patients who continue to experience severe symptoms alongside significant hemodynamic obstruction despite optimal medical therapy, septal reduction therapy (SRT) represents the principal interventional option [10,22,28]. This approach includes two main techniques: surgical septal myectomy and alcohol septal ablation (ASA) [3,22]. Surgical myectomy, long regarded as the reference standard, entails the resection of hypertrophied segments of the interventricular septum and may be combined with correction of coexisting mitral valve abnormalities [1,11,22]. In contrast, alcohol septal ablation is a catheter-based procedure in which absolute alcohol is selectively injected into a septal perforator branch, inducing a controlled myocardial infarction that leads to septal thinning and subsequent reduction of LVOT obstruction [3,22]. Both modalities have demonstrated significant benefits in terms of long-term survival and improvement in quality of life when applied in appropriately selected patients [1].

Notwithstanding their clinical effectiveness, current therapeutic options exhibit important limitations that leave a considerable proportion of patients insufficiently treated [1,10,17]. Pharmacological therapies remain largely non-specific and primarily palliative, as they predominantly influence intracellular calcium handling rather than directly addressing the fundamental sarcomeric abnormalities responsible for hypercontractility [10,24,42]. Additionally, their use is often constrained by adverse effects, limited tolerability, and issues related to long-term adherence [1,10,32]. Invasive approaches, while effective, are not universally available and are associated with procedural risks, including conduction disturbances and the potential requirement for permanent pacemaker implantation [1,5,10]. Moreover, the outcomes of SRT are highly dependent on operator experience and institutional expertise, with notable variability in success rates and mortality across centers [1,3,24]. As a result, a substantial number of symptomatic patients are either unsuitable candidates for invasive procedures or lack access to specialized high-volume centers, underscoring a persistent therapeutic gap in the management of oHCM [1,22].

Mechanism of Action of Mavacamten

Mavacamten is a first-in-class, selective, and reversible inhibitor of cardiac myosin that directly targets the fundamental molecular mechanisms underlying hypertrophic cardiomyopathy (HCM) [1,3,10,12,13,17,24,42]. In contrast to conventional negative inotropic therapies such as beta-blockers or non-dihydropyridine calcium channel blockers which primarily act through modulation of heart rate or intracellular calcium handling, mavacamten exerts its effect at the level of the sarcomere [3,42]. Mechanistically, the drug functions as an allosteric inhibitor of β-cardiac myosin adenosine triphosphatase (ATPase) [3,12,13,20,22,24]. Under physiological conditions, myosin ATPase hydrolyzes ATP to adenosine diphosphate (ADP), enabling the interaction between myosin heads and actin filaments and initiating the contractile power stroke [3,42]. By attenuating this enzymatic activity, mavacamten reduces the frequency of cross-bridge cycling, thereby mitigating the hypercontractile phenotype characteristic of HCM [3,25,42].

At the cellular level, inhibition of myosin ATPase activity results in a redistribution of myosin head states, favoring the energy-conserving super-relaxed (SRX) conformation while decreasing the proportion of heads in the active, force-generating state [8,12,18,24,25,42]. This shift is of central importance, as HCM is

associated with an increased availability of myosin heads for actin interaction, leading to excessive cross-bridge formation and elevated energetic demand [7,13,18,22,24,25,32]. By limiting the number of active cross-bridges, mavacamten reduces contractile force, enhances myosin detachment from actin, and alleviates the persistent hypercontractility and increased myocardial stiffness observed in affected patients [3,13,14,22,24].

These molecular effects translate into clinically relevant hemodynamic improvements, most notably a marked reduction in dynamic left ventricular outflow tract (LVOT) obstruction [1,2,7,12,13,14,15,17,20,22,24,25]. By decreasing myocardial contractility, mavacamten delays the onset of systolic ejection and diminishes the flow-related forces responsible for systolic anterior motion (SAM) of the mitral valve, thereby relieving obstruction and improving forward flow [13,14,24,28,44]. Additionally, the reduction in excessive cross-bridge formation enhances diastolic relaxation, lowers ventricular stiffness, and decreases left-sided filling pressures [2,10,13,14,17,18,24,25,26,36]. Over time, these effects contribute to favorable cardiac remodeling, including regression of septal hypertrophy, reduction in left ventricular mass, and normalization of left atrial size [1,7,10,12,13,17,22,24]. Although treatment with mavacamten is associated with a modest decrease in left ventricular ejection fraction (LVEF), this change is generally interpreted as a physiological normalization of previously elevated contractility rather than an indicator of impaired systolic function [1,3,7,10,11,22,24].

Clinical Trials Characteristics of Mavacamten

The clinical development program for mavacamten is grounded in a series of well-structured, multicenter trials that collectively underpin its current therapeutic role. Among these, the phase 3 EXPLORER-HCM and VALOR-HCM studies represent the key registrational trials that formed the basis for regulatory approval [1,18,24]. These pivotal investigations have been complemented by additional studies, including EXPLORER-CN, which specifically evaluated outcomes in Asian populations, and earlier phase 2 trials such as MAVERICK-HCM, designed to explore safety and extend evaluation to alternative phenotypic presentations of the disease [12,24].

From a methodological perspective, the core trials were predominantly designed as randomized, double-blind, placebo-controlled, multicenter studies, ensuring a high level of internal validity and robustness of results [1,13,24]. In trials such as EXPLORER-HCM and VALOR-HCM, patients were typically randomized in a 1:1 ratio, with stratification based on key baseline characteristics, including New York Heart Association (NYHA) functional class, concomitant beta-blocker therapy, and eligibility for invasive interventions [1,23,24]. Control groups consistently received placebo alongside standard-of-care therapy at maximally tolerated doses [1]. The selection of endpoints was carefully aligned with both physiological and clinically meaningful outcomes. For example, VALOR-HCM employed a composite primary endpoint assessing the proportion of patients undergoing septal reduction therapy (SRT) or remaining eligible for such intervention at 16 weeks [1,24]. In contrast, EXPLORER-HCM utilized a functional composite endpoint defined by improvements in peak oxygen consumption (pVO2), requiring either an increase of ≥ 1.5 mL/kg/min with at least one NYHA class improvement or a ≥ 3.0 mL/kg/min increase in the absence of clinical deterioration [23,24].

The study populations across these trials were intentionally diverse in both size and clinical severity to capture a broad representation of disease burden. EXPLORER-HCM enrolled 251 participants, whereas VALOR-HCM focused on a smaller, more severely affected cohort of 112 patients who were already considered candidates for SRT [1,24]. Inclusion criteria were generally consistent and required adult patients with a confirmed diagnosis of HCM, symptomatic status (typically NYHA class II–III), and preserved left ventricular ejection fraction (LVEF), commonly ≥ 55–60% [12,13,18,23]. While most available data pertain to obstructive HCM (oHCM), defined by a dynamic left ventricular outflow tract (LVOT) gradient of ≥ 30 mmHg or ≥ 50 mmHg, the non-obstructive phenotype (nHCM) has also been investigated, notably in the MAVERICK-HCM trial [24,36]. Geographic and ethnic diversity was specifically addressed in EXPLORER-CN, which included 81 patients from China and incorporated adjusted dosing strategies (initiating at 2.5 mg) to account for differences in body mass and CYP2C19 metabolic profiles [12,13,24].

Assessment of therapeutic efficacy was multidimensional, incorporating clinical, functional, hemodynamic, and patient-reported outcomes. Symptomatic improvement was primarily evaluated using the NYHA functional classification, with emphasis on achieving at least one or two class improvements [1,12,24]. Objective exercise capacity was measured through peak oxygen consumption (VO2 max) obtained during cardiopulmonary exercise testing, a key indicator of aerobic performance [23,24]. Hemodynamic response was assessed by measuring the LVOT gradient via echocardiography, both at rest and under provocation (e.g., Valsalva maneuver or exercise), to determine the degree of obstruction relief [1,12]. Additionally, patient-

reported outcomes were captured using the Kansas City Cardiomyopathy Questionnaire (KCCQ), particularly the Clinical Summary Score (CSS) and Overall Summary Score (OSS), which provide validated insights into symptom burden and functional limitations from the patient's perspective [1,13,24]. Collectively, these measures enabled a comprehensive evaluation of mavacamten's clinical efficacy in modifying the disease trajectory of hypertrophic cardiomyopathy.

Clinical trial results

The clinical efficacy and safety profile of mavacamten has been established through an extensive and methodologically rigorous development program, encompassing early-phase exploratory trials, pivotal phase 3 studies, and subsequent long-term extension analyses. Collectively, these investigations have consistently demonstrated the drug's capacity to directly modulate the core pathophysiological mechanisms of obstructive hypertrophic cardiomyopathy (oHCM), primarily by reducing myocardial hypercontractility and alleviating left ventricular outflow tract (LVOT) obstruction responsible for symptom burden [24].

Early-phase studies, including the phase II PIONEER-HCM and MAVERICK-HCM trials, provided essential insights into dosing, safety, and preliminary efficacy. The open-label PIONEER-HCM study showed that mavacamten induced a rapid and clinically meaningful reduction in resting LVOT gradients, observable within the first week of therapy [43]. In contrast, the MAVERICK-HCM trial extended investigation to patients with symptomatic non-obstructive HCM (nHCM) [24]. Although the primary functional composite endpoint was not achieved, mavacamten demonstrated an acceptable safety profile, and exploratory analyses suggested potential benefits in selected subgroups, particularly those with elevated baseline filling pressures or increased troponin levels [3,24]. These findings underscored that the therapeutic effect of mavacamten is most pronounced in the obstructive phenotype, where sarcomeric hypercontractility directly contributes to dynamic LVOT obstruction [3].

The phase 3 EXPLORER-HCM trial provided the pivotal evidence supporting mavacamten's clinical efficacy in symptomatic oHCM [24,36]. In this randomized, double-blind, placebo-controlled study involving 251 patients, the primary endpoint was a composite measure integrating improvements in exercise capacity and functional status. Specifically, patients were required to achieve either an increase in peak oxygen consumption (pVO2) of ≥ 1.5 mL/kg/min accompanied by at least one New York Heart Association (NYHA) class improvement, or a ≥ 3.0 mL/kg/min increase in pVO2 without clinical deterioration [24]. At 30 weeks, the primary endpoint was met by 37% of patients receiving mavacamten, compared with 17% in the placebo group [24,32]. In addition, treatment resulted in substantial reductions in post-exercise LVOT gradients (mean decrease of 47 mmHg) and significant improvements in health-related quality of life, as reflected by increases in the Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS) [24,27]. Imaging substudies further demonstrated evidence of reverse cardiac remodeling, including reductions in left ventricular mass index and left atrial volume index [7,24].

The VALOR-HCM trial further strengthened the evidence base by focusing on patients with more advanced disease who were already being considered for septal reduction therapy (SRT) [1,24]. The primary composite endpoint evaluated the proportion of patients who either proceeded to SRT or remained eligible for the procedure after 16 weeks [1]. Mavacamten significantly reduced the need for invasive intervention, with only 17.9% of treated patients meeting this endpoint compared with 76.8% in the placebo arm [22,24]. Secondary outcomes consistently favored mavacamten, including improvements in NYHA functional class and sustained reductions in both resting and provoked LVOT gradients [24,25]. These findings established mavacamten as a potential non-invasive therapeutic alternative for patients who would otherwise require surgical or catheter-based septal reduction procedures [24,33].

Long-term extension studies, including MAVA-LTE (EXPLORER-LTE cohort) and extended follow-up analyses from VALOR-HCM, have confirmed the durability of these clinical benefits. Interim data from MAVA-LTE demonstrated sustained improvements in both symptomatic status and hemodynamic parameters for up to 180 weeks of follow-up [17,24]. Similarly, extended results from VALOR-HCM at 128 weeks indicated that nearly 90% of patients remained free from the need for SRT [1,24]. Durable symptomatic improvement was also observed, with more than 80% of patients maintaining at least a one-class improvement in NYHA functional status [1]. From a safety perspective, transient reductions in left ventricular ejection fraction (LVEF) below 50% were reported in approximately 9–14% of patients; however, these changes were generally reversible with dose adjustment or temporary discontinuation, and rates of permanent treatment cessation remained low [1,9,24]. Taken together, these findings support the role of mavacamten as a disease-specific, long-term therapeutic option that substantially alters the clinical course of obstructive hypertrophic cardiomyopathy [8,24].

Clinical efficacy of Mavacamten

The therapeutic efficacy of mavacamten is principally reflected in its capacity to produce marked and sustained reductions in left ventricular outflow tract (LVOT) gradients [1,12]. In the pivotal EXPLORER-HCM trial, treatment with mavacamten resulted in a mean decrease in post-exercise LVOT gradients of 47 mmHg, with 27% of patients achieving a complete response defined as a gradient < 30 mmHg in conjunction with New York Heart Association (NYHA) class I status by week 30 [24]. These findings were corroborated by the VALOR-HCM study, in which a cohort with more advanced symptom burden exhibited durable reductions in both resting and Valsalva-provoked gradients, reaching 38.2 mmHg and 59.4 mmHg, respectively, over 128 weeks of follow-up [1]. Evidence derived from real-world clinical practice further supports these observations, demonstrating that significant hemodynamic improvement may occur as early as one week after treatment initiation, even among patients presenting with markedly elevated baseline gradients exceeding 100 mmHg [25].

Improvements in LVOT obstruction translate directly into meaningful clinical benefits, particularly in terms of functional capacity and symptom burden. Across clinical studies, approximately 80% of patients experience an improvement of at least one NYHA functional class, with these effects maintained over extended follow-up periods of up to 180 weeks [1,12,22]. Objective measures of exercise performance also demonstrate consistent gains; in EXPLORER-HCM, mavacamten was associated with a mean increase in peak oxygen consumption (pVO2) of 1.4 mL/kg/min [24]. Complementary real-world data using the 6-minute walk test similarly indicate clinically relevant improvements, with median increases exceeding 50 meters observed within the initial months of therapy [25].

Furthermore, mavacamten leads to a substantial enhancement in health-related quality of life, as measured by the Kansas City Cardiomyopathy Questionnaire (KCCQ). Patients report meaningful improvements in symptom frequency and physical limitations, with KCCQ Clinical Summary Scores increasing by an average of 14.2 points [1,24]. Ultimately, mavacamten provides a transformative non-invasive alternative to surgery; long-term data from VALOR-HCM show that nearly 90% of patients referred for septal reduction therapy (SRT) were able to avoid invasive procedures through week 128 [1].

Therapy safety

The safety profile of mavacamten is generally considered favorable; however, its use necessitates careful clinical monitoring due to its mechanism of action [2,10,12]. The most commonly reported non-cardiac adverse events across clinical trials and real-world registries include dizziness, fatigue, and headache. These events are typically mild, transient, and infrequently lead to permanent discontinuation of therapy [1,6,9,12]. Atrial fibrillation (AF), however, represents a clinically relevant concern. Real-world multicenter data indicate that approximately 5% of patients develop new-onset AF, while those with a prior history of the arrhythmia experience recurrence rates as high as 39% [21]. Long-term follow-up from the VALOR-HCM study reported an exposure-adjusted incidence of new-onset AF of 4.55 per 100 patient-years, suggesting that this risk may be more reflective of the underlying disease substrate rather than a direct proarrhythmic effect of mavacamten itself [1,9].

The principal safety consideration associated with mavacamten therapy is its negative inotropic effect, which results in a dose-dependent reduction in left ventricular ejection fraction (LVEF) [3,24]. Although this reduction is often interpreted as a normalization of the hypercontractile state characteristic of hypertrophic cardiomyopathy, excessive suppression of contractility may lead to clinically significant systolic dysfunction [7,22,36]. In the VALOR-HCM trial, 13.8% of patients experienced a decline in LVEF below 50%, with comparable rates ranging from approximately 5% to 14% reported in other clinical studies [1,9,11,15,21,22,24]. Importantly, these reductions are typically reversible; temporary interruption of treatment for 2–4 weeks generally results in recovery of LVEF to ≥50%, allowing therapy to be resumed at a lower dose in most cases [1,3,9,22,24]. Permanent discontinuation due to severe systolic impairment (LVEF ≤30%) or lack of recovery remains uncommon, occurring in approximately 1.1% to 2.8% of patients [1,8,9,10].

Given the risk of treatment-induced systolic dysfunction, structured and ongoing monitoring is essential for safe use of mavacamten [28]. In the United States, prescribing is regulated under the Risk Evaluation and Mitigation Strategy (REMS) program, which mandates serial echocardiographic evaluations every four weeks during the initial 12-week dose-titration phase, followed by assessments at longer intervals (e.g., every 12 weeks or up to every 6 months) [3,10,11,24,42]. In Europe and the United Kingdom, additional precautions include mandatory CYP2C19 genotyping prior to treatment initiation [2,32,42]. As mavacamten is primarily metabolized via the CYP2C19 pathway, individuals with poor metabolizer status are at increased risk of drug

accumulation and should be initiated on a reduced starting dose of 2.5 mg [2,32,42,43]. Careful consideration of potential drug–drug interactions is also required, particularly with strong inhibitors of CYP2C19 or CYP3A4. Furthermore, appropriate reproductive counseling is essential, as mavacamten is contraindicated during pregnancy due to evidence of embryo-fetal toxicity [22,24,42,43].

Discussion

The integration of available clinical data indicates that mavacamten constitutes a major advancement toward mechanism-based therapy in obstructive hypertrophic cardiomyopathy (oHCM) [1,24,27]. Evidence derived from multicenter trials demonstrates that inhibition of cardiac myosin leads to both rapid and sustained reductions in left ventricular outflow tract (LVOT) gradients detectable as early as one week after treatment initiation while also promoting reverse cardiac remodeling [1,7,24,25]. In contrast to conventional pharmacological strategies, which primarily offer symptomatic relief, mavacamten directly targets the underlying sarcomeric hypercontractility that drives disease progression [1,24]. Importantly, long-term observations indicate that the drug may function as an effective non-invasive alternative to septal reduction therapy (SRT), with approximately 90% of patients initially referred for invasive intervention able to defer such procedures during extended follow-up [1,27].

Subgroup analyses further suggest that the therapeutic benefits of mavacamten are consistent across diverse patient populations. Female patients achieve comparable and sustained improvements in symptom burden and quality of life relative to male counterparts, despite often presenting with more advanced baseline disease [16,34]. Similarly, studies conducted in Asian populations have demonstrated that lower initial dosing regimens (e.g., 2.5 mg) remain highly effective, likely reflecting interindividual and ethnic differences in body composition and pharmacokinetics [8,12,18,23]. The clinical relevance of these findings is reinforced by substantial improvements in health-related quality of life, as measured by Kansas City Cardiomyopathy Questionnaire (KCCQ) scores, as well as reductions in estimated 5-year sudden cardiac death (SCD) risk, largely attributable to favorable changes in modifiable hemodynamic and structural parameters [1,2,13,29].

The incorporation of mavacamten into routine clinical practice necessitates adaptation of existing care pathways, particularly with regard to structured monitoring protocols. Regular echocardiographic assessment is essential to detect and manage transient, dose-dependent reductions in left ventricular ejection fraction (LVEF) [2,22,24,28]. In European and United Kingdom settings, mandatory CYP2C19 genotyping prior to treatment initiation further supports an individualized treatment approach, enabling dose optimization based on metabolic capacity [2,22,32]. As clinical familiarity increases and monitoring strategies become more streamlined, mavacamten has the potential to substantially reshape the therapeutic landscape of oHCM, reducing dependence on non-specific pharmacotherapy and the need for invasive septal reduction procedures [2,5,22,24].

Conclusions

The current body of clinical evidence positions mavacamten as a first-in-class cardiac myosin inhibitor that fundamentally targets the molecular drivers of obstructive hypertrophic cardiomyopathy (oHCM) [24]. Across pivotal phase 3 trials as well as increasingly extensive real-world cohorts, treatment has consistently been associated with pronounced and sustained reductions in left ventricular outflow tract (LVOT) gradients, with measurable hemodynamic improvement often evident within the first week of therapy initiation [1,25]. These physiological changes are closely linked to clinically meaningful benefits, including improvements in functional capacity, with approximately 60–80% of patients achieving at least a one-class improvement in New York Heart Association (NYHA) status, alongside gains in exercise tolerance and health-related quality of life [1,10,12,17,24]. In longer-term extension studies with follow-up extending to 128 and 180 weeks, mavacamten has also been associated with favorable reverse remodeling of cardiac structure, including reductions in septal hypertrophy and left atrial volume [1,7,10,24]. Although dose-dependent and transient reductions in left ventricular ejection fraction (LVEF < 50%) remain the most important safety consideration, these events are typically reversible with temporary treatment interruption or dose adjustment, supporting an overall favorable long-term safety profile under structured monitoring [1,9,10,12].

The broader clinical relevance of mavacamten lies in its capacity to address a longstanding therapeutic gap by shifting oHCM management from predominantly symptomatic, non-specific approaches toward mechanism-based intervention [1,22,42]. By directly attenuating sarcomeric hypercontractility, the drug offers an effective non-invasive alternative for many patients who would otherwise be candidates for septal reduction therapy (SRT). In this context, long-term data from the VALOR-HCM trial indicate that nearly 90% of patients

initially considered for invasive intervention were able to avoid surgical or percutaneous procedures during follow-up [1,22,24]. Improvements in patient-reported outcomes, particularly Kansas City Cardiomyopathy Questionnaire (KCCQ) scores, are substantial and in many cases exceed those observed with conventional heart failure therapies [1,25]. Emerging evidence further suggests potential favorable effects on arrhythmic risk stratification, likely mediated through improvements in modifiable structural and hemodynamic determinants such as septal thickness and LVOT gradient, which contribute to established sudden cardiac death (SCD) risk models [29]. Collectively, these findings demonstrated across diverse populations in Europe, Asia, and other regions support a paradigm shift in the standard of care for oHCM [7,10,12,18,22].

Looking ahead, the clinical development of mavacamten and related cardiac myosin inhibitors continues to expand into new patient populations and technological frameworks for monitoring [23,24]. Ongoing studies, including SCOUT-HCM, are evaluating the safety and efficacy of mavacamten in adolescents with symptomatic disease, addressing an important unmet need in the pediatric population [23]. Although early phase 3 results in non-obstructive HCM (nHCM) did not meet primary endpoints, exploratory analyses have identified potential benefit in selected subgroups characterized by elevated filling pressures or biomarker profiles, warranting further investigation in this phenotype [19,24]. In parallel, next-generation cardiac myosin inhibitors such as aficamten, with shorter pharmacokinetic half-lives, are being explored to improve titration flexibility and safety management. Advances in imaging and monitoring including AI-assisted echocardiographic assessment and hemodynamic force analysis may further streamline long-term surveillance and reduce the burden on specialized centers [3,24,28,44]. Ultimately, large-scale registry data and real-world outcome studies will be essential to clarify the impact of mavacamten on hard clinical endpoints, including heart failure hospitalization and mortality, thereby defining its long-term position within the therapeutic algorithm of hypertrophic cardiomyopathy [24,25,29].

AI: In the study, AI was used to improve the language of the manuscript, ensuring consistency and compliance with scientific standards. After using this tool, the authors reviewed and edited the content as necessary, taking full responsibility for the substantive content of the publication.

Author Contribution:
Conceptualization: W.S, M.S, D.S, K.O, A.M, M.K, A.K
Methodology: W.S, M.S, D.S, K.O, A.M, M.K, A.K
Validation: W.S, M.S, D.S, K.O, A.M, M.K, A.K
Resources: W.S, M.S, D.S, K.O, A.M, M.K, A.K
Visualization: W.S, M.S, D.S, K.O, A.M, M.K, A.K
Writing-Rough Preparation: W.S, M.S, D.S, K.O, A.M, M.K, A.K
Writing-Review and Editing: W.S, M.S, D.S, K.O, A.M, M.K, A.K
Supervision: W.S, M.S, D.S, K.O, A.M, M.K, A.K

All authors have read and agreed with the published version of the manuscript.
Funding statement: The study received no financial support.

REFERENCES

1. Desai, M. Y., Wolski, K., Owens, A., et al. (2025). Mavacamten in patients with hypertrophic cardiomyopathy referred for septal reduction: Week 128 results from VALOR-HCM. *Circulation, 151*(19), 1378–1390. https://doi.org/10.1161/CIRCULATIONAHA.124.072445
2. Scholtz, S., Coppée, C., Mohemed, K., et al. (2025). Mavacamten maintenance dose determination: Insights into individualised therapy for hypertrophic cardiomyopathy. *Open Heart, 12*(1), e003192. https://doi.org/10.1136/openhrt-2025-003192
3. Patel, D., Bhargav, R., Mousa, A., & Bokhari, S. (2025). Hypertrophic cardiomyopathy: Current perspectives. *Reviews in Cardiovascular Medicine, 26*(9), 42824. https://doi.org/10.31083/RCM42824
4. Reza, N., Mahmud, N., Austin, M. A., et al. (2025). Hypertension in patients with obstructive hypertrophic cardiomyopathy treated with mavacamten. *JACC: Heart Failure, 13*(11), 102666. https://doi.org/10.1016/j.jchf.2025.102666
5. Samhan, A., Saleh, D., Kim, E. Y., et al. (2025). Comparison of alcohol septal ablation with mavacamten in obstructive hypertrophic cardiomyopathy. *The American Journal of Cardiology, 239*, 51–56. https://doi.org/10.1016/j.amjcard.2024.12.024
6. Massera, D., Adlestein, E., Frejat, S., et al. (2025). Mavacamten in symptomatic patients resistant to previous advanced therapy for obstructive hypertrophic cardiomyopathy. *Journal of the American Heart Association, 14*(15), e041565. https://doi.org/10.1161/JAHA.125.041565
7. Tian, Z., Li, L., Li, X., et al. (2025). Effects of mavacamten on cardiac magnetic resonance features in Chinese patients with obstructive hypertrophic cardiomyopathy. *JACC: Asia, 5*(8), 1064–1074. https://doi.org/10.1016/j.jacasi.2025.05.015
8. Bilen, O., Adler, A., Bastiaenen, R., et al. (2026). Mavacamten monotherapy in real-world patients with obstructive hypertrophic cardiomyopathy: Evidence from COLLIGO-HCM. *Circulation: Genomic and Precision Medicine, 19*(1), e005502. https://doi.org/10.1161/CIRCGEN.125.005502
9. Desai, M. Y., Wolski, K., Owens, A., et al. (2025). Correction to: Mavacamten in patients with hypertrophic cardiomyopathy referred for septal reduction: Week 128 results from VALOR-HCM. *Circulation, 151*(19), e1001. https://doi.org/10.1161/CIR.0000000000001339
10. Desai, M. Y., Gaballa, A., Okushi, Y., et al. (2025). Real-world observations in patients with obstructive hypertrophic cardiomyopathy treated with mavacamten: Evidence of favorable disease modification. *Journal of the American Heart Association, 14*(19), e044537. https://doi.org/10.1161/JAHA.125.044537
11. Mahana, I., Mejia, A. T., Elman, M. R., et al. (2025). Characteristics and outcomes of mavacamten use in 2440 patients with obstructive hypertrophic cardiomyopathy. *Journal of the American Heart Association, 14*(21), e042488. https://doi.org/10.1161/JAHA.125.042488
12. Yang, W., Shi, H., Chang, R. S., et al. (2026). Low-dose mavacamten initiation in obstructive hypertrophic cardiomyopathy: A real-world study in China. *Cardiovascular Therapeutics, 2026*, 5690104. https://doi.org/10.1155/cdr/5690104
13. Tian, Z., Li, X., Li, L., et al. (2025). Effect of mavacamten on echocardiographic features in Chinese patients with obstructive hypertrophic cardiomyopathy: Results from the EXPLORER-CN study. *Cardiology and Therapy, 14*(2), 267–282. https://doi.org/10.1007/s40119-025-00409-5
14. Badr, A., Roehl, K., Suppah, M., et al. (2025). Temporal patterns of Holter-detected arrhythmias in hypertrophic cardiomyopathy patients treated with mavacamten. *Biomedicines, 13*(4), 1005. https://doi.org/10.3390/biomedicines13041005
15. Saleh, D., Kim, E. Y., Hussain, K., et al. (2025). Anterior mitral valve leaflet length and response to mavacamten in obstructive hypertrophic cardiomyopathy. *European Heart Journal - Imaging Methods and Practice, 3*(2), qyaf081. https://doi.org/10.1093/ehjimp/qyaf081
16. Desai, M. Y., Saberi, S., Geske, J. B., et al. (2025). Long-term response of obstructive hypertrophic cardiomyopathy patients to mavacamten based on sex: Insights from the VALOR-HCM trial. *JACC: Heart Failure, 13*(6), 1037–1040. https://doi.org/10.1016/j.jchf.2025.02.005
17. Reza, N., Dubey, A., Mahmud, N., et al. (2025). Long-term real-world outcomes of mavacamten in symptomatic obstructive hypertrophic cardiomyopathy up to 108 weeks. *Journal of Clinical Medicine, 14*(22), 8181. https://doi.org/10.3390/jcm14228181
18. Lim, J., Cho, J. Y., Kwak, S., et al. (2025). Real-world experience of mavacamten for patients with obstructive hypertrophic cardiomyopathy in South Korea: A prospective multi-center observational study. *Korean Circulation Journal, 55*(4), 339–354. https://doi.org/10.4070/kcj.2024.0443
19. Wu, X., Puli, S., Chen, N., et al. (2025). Model-informed recommendation of mavacamten posology for Chinese adults with obstructive hypertrophic cardiomyopathy. *CPT: Pharmacometrics & Systems Pharmacology, 14*(4), 751–758. https://doi.org/10.1002/psp4.13312

20. Buehning, F., Lerchner, T., Vogel, J., et al. (2025). ECG markers of left ventricular hypertrophy indicate response to mavacamten in hypertrophic obstructive cardiomyopathy. *Open Heart, 12*(2), e003611. https://doi.org/10.1136/openhrt-2025-003611
21. Nguyen, O., Wiedrick, J., Massera, D., et al. (2025). Incidence and outcomes of atrial fibrillation and systolic dysfunction in patients receiving mavacamten for obstructive hypertrophic cardiomyopathy: A multicenter study [Preprint]. *medRxiv*. https://doi.org/10.1101/2025.09.15.25335783
22. Burford, E., Kasolo, Y., Draper, J., et al. (2025). Tale of three services: Early UK experience with mavacamten treatment for hypertrophic cardiomyopathy with left ventricular outflow tract obstruction. *Open Heart, 12*(1), e003218. https://doi.org/10.1136/openhrt-2025-003218
23. Rossano, J., Canter, C., Wolf, C., et al. (2026). Mavacamten in symptomatic adolescent patients with obstructive hypertrophic cardiomyopathy: Design of the phase 3 SCOUT-HCM trial. *American Heart Journal, 292*, 107283. https://doi.org/10.1016/j.ahj.2025.107283
24. Lim, J., & Kim, H. K. (2025). Cardiac myosin inhibitors in hypertrophic cardiomyopathy. *Journal of Cardiovascular Imaging, 33*(1), 7. https://doi.org/10.1186/s44348-025-00052-7
25. Nagy, V., Rácz, G., Takács, H., et al. (2026). Mavacamten effectively reduces >100 mmHg left ventricular outflow tract gradients as early as one week of treatment in obstructive hypertrophic cardiomyopathy. *International Journal of Cardiology, 442*, 133882. https://doi.org/10.1016/j.ijcard.2025.133882
26. Saleh, D., Kim, E. Y., Hussain, K., et al. (2025). Comparison of diastolic function parameters after alcohol septal ablation and mavacamten therapy in obstructive hypertrophic cardiomyopathy. *Journal of Cardiovascular Development and Disease, 13*(1), 16. https://doi.org/10.3390/jcdd13010016
27. Ibrahim, R., Wang, W., Pham, H. N., et al. (2026). Impact of mavacamten approval on septal reduction therapy rates in hypertrophic cardiomyopathy. *Journal of the American Heart Association, 15*(6), e045649. https://doi.org/10.1161/JAHA.125.045649
28. Pearlman, A., Hellyer, R., Burns, C., Medi, C., & Gray, B. (2026). Focused transthoracic echocardiogram surveillance protocol for hypertrophic cardiomyopathy patients on mavacamten therapy. *Heart, Lung and Circulation, 35*(3), 432–435. https://doi.org/10.1016/j.hlc.2025.08.026
29. Usai, P., Cariou, E., Donal, E., et al. (2026). Effect of mavacamten on sudden cardiac death risk scores in obstructive hypertrophic cardiomyopathy. *ESC Heart Failure, 13*(1), xvag003. https://doi.org/10.1093/eschf/xvag003
30. Reza, N., Mahmud, N., Austin, M. A., et al. (2026). Association between baseline hypertension and longitudinal functional status in obstructive hypertrophic cardiomyopathy treated with mavacamten. *Journal of Cardiac Failure*. Advance online publication. https://doi.org/10.1016/j.cardfail.2025.12.010
31. Hundal, P., Abood, Z., Sanders, H., et al. (2025). Chemical myectomy with mavacamten in patients with obstructive hypertrophic cardiomyopathy with prior septal reduction therapy: A single-center experience. *JTCVS Open, 27*, 58–61. https://doi.org/10.1016/j.xjon.2025.07.007
32. Kasolo, Y., Burford, E., Obeidat, M., et al. (2026). CYP2C19 genotyping and mavacamten: Predicting outcomes in normal, intermediate and rapid metabolisers in obstructive hypertrophic cardiomyopathy. *European Journal of Clinical Pharmacology, 82*(3), 67. https://doi.org/10.1007/s00228-025-03991-8
33. Masri, A., Maron, M. S., Abraham, T. P., et al. (2026). Concomitant aficamten and disopyramide in symptomatic obstructive hypertrophic cardiomyopathy. *JACC: Heart Failure, 14*(2), 102441. https://doi.org/10.1016/j.jchf.2025.03.008
34. Wang, X., Pabon, M. A., Makuvire, T. T., et al. (2026). Effect of aficamten in women compared with men with obstructive hypertrophic cardiomyopathy in SEQUOIA-HCM. *Circulation: Heart Failure, 19*(1), e013918. https://doi.org/10.1161/CIRCHEARTFAILURE.125.013918
35. Hafeez, N., Claggett, B. L., Owens, A. T., et al. (2026). Social determinants of health and clinical outcomes in hypertrophic cardiomyopathy. *JAMA Cardiology, 11*(2), 165–174. https://doi.org/10.1001/jamacardio.2025.4869
36. Cohen, N., Lucas, C., Idini, C., et al. (2026). Effect of mavacamten on left ventricular diastolic function and left atrial remodelling in obstructive hypertrophic cardiomyopathy. *Archives of Cardiovascular Diseases*. Advance online publication. https://doi.org/10.1016/j.acvd.2026.01.006
37. Sadasivan, C., Gagnon, L. R., Hazra, D., et al. (2025). Early genetic screening and cardiac intervention in patients with cardiomyopathies in a multidisciplinary clinic. *ESC Heart Failure, 12*(3), 1942–1955. https://doi.org/10.1002/ehf2.15202
38. Park, J., Kim, J., Jeon, J., et al. (2025). Single-view echocardiographic analysis for left ventricular outflow tract obstruction prediction in hypertrophic cardiomyopathy: A deep learning approach. *Journal of the American Society of Echocardiography, 38*(12), 1115–1126. https://doi.org/10.1016/j.echo.2025.08.008
39. Merali, S., Sychterz, C., Perera, V., Gaohua, L., Florea, V., & Murthy, B. (2025). Drug-drug interaction potential of mavacamten with midazolam: Combined results from clinical and model-based studies. *Journal of Clinical Pharmacology, 65*(5), 598–606. https://doi.org/10.1002/jcph.6175
40. Seuthe, K., Feidakis, A., Nies, R., et al. (2026). Hemodynamic and symptomatic response in hypertrophic obstructive cardiomyopathy patients on myosin inhibitor therapy. *Frontiers in Cardiovascular Medicine, 12*, 1639855. https://doi.org/10.3389/fcvm.2025.1639855

41. Groeneweg, J. A., van Dalen, B. M., Cox, M. P. G. J., et al. (2025). 2023 European Society of Cardiology guidelines on the management of cardiomyopathies: Statement of endorsement by the NVVC. *Netherlands Heart Journal, 33*(5), 148–156. https://doi.org/10.1007/s12471-025-01955-2
42. Desai, M. Y., Michaud, V., Thacker, D., et al. (2025). CYP450 activity, drug interactions, and genetic polymorphisms: Clinical relevance for the new selective cardiac myosin inhibitors. *Expert Opinion on Drug Safety*. Advance online publication. https://doi.org/10.1080/14740338.2025.2596231
43. Merali, S., Bunn, H., Sychterz, C., et al. (2025). Exposure-response modeling and simulation to identify optimal mavacamten posology when coadministered with CYP3A4 and CYP2C19 inhibitors in patients with obstructive HCM. *Journal of Clinical Pharmacology, 65*(12), 1802–1814. https://doi.org/10.1002/jcph.70072
44. Zocchi, C., Milazzo, A., Panichella, G., et al. (2026). Non-invasive evaluation of left ventricular hemodynamic force abnormalities in hypertrophic cardiomyopathy: Implications for myosin inhibition. *International Journal of Cardiology, 448*, 134175. https://doi.org/10.1016/j.ijcard.2026.134175