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Tale of three services: early UK experience with mavacamten treatment for hypertrophic cardiomyopathy with left ventricular outflow tract obstruction

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ABSTRACT

Background Hypertrophic cardiomyopathy (HCM) is characterised by abnormal thickening of ventricular myocardium. Left ventricular outflow tract (LVOT) obstruction occurs in up to 70% of patients, causing progressive symptoms, heart failure and mortality. Mavacamten, the first targeted therapy for obstructive HCM (oHCM), was approved for use in the UK in 2024. We present data from the early experience with mavacamten treatment for oHCM in three UK centres and describe different clinical pathways.

Methods All patients with symptomatic oHCM eligible for mavacamten therapy were included. Eligibility criteria included New York Heart Association (NYHA) class II–III symptoms and LVOT gradients >30 mm Hg with normal left ventricular ejection function (LVEF >55%), as per National Institute for Health and Care Excellence guidelines and product literature. Patients underwent CYP2C19 genotyping before treatment, and dosing was adjusted accordingly. Echocardiographic assessments, clinical reviews and biomarker analyses were conducted at weeks 0, 4, 8 and 12.

Results 93 patients were initiated on mavacamten (mean age: 60±13 years; 72% male). The Valsalva LVOT gradient significantly decreased during treatment, from 88.9±31 mm Hg at baseline to 43.8±32.6 mm Hg by week 12, and further to 27.7±22.3 mm Hg on the maintenance dose. NT-proBNP levels also improved markedly, from 689 ng/L (IQR 343-1684 ng/L) at baseline to 171 ng/L (IQR 116-335 ng/L) on the maintenance dose. By week 12, 74% of patients experienced an improvement of at least one NYHA class, increasing to 91% on the maintenance dose. Temporary treatment interruptions occurred in 13 patients; however, no patients required permanent discontinuation of treatment due to a reduced LVEF (<50%). Outcomes were comparable across the three care pathways.

Conclusions Mavacamten treatment was associated with significant symptomatic improvement, reduced LVOT gradients and improved biomarker profiles in patients with oHCM. The implementation of clinical services to deliver mavacamten in the UK should not follow a 'one-size-fits-all' approach but rather leverage the unique strengths of each specific centre.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Phase III randomised control trials of cardiac myosin inhibitor mavacamten versus placebo for treatment of symptomatic obstructive hypertrophic cardiomyopathy (HCM) (EXPLORER-HCM and VALOR-HCM) demonstrated efficacy in left ventricular outflow tract (LVOT) obstruction, exercise tolerance and symptom improvements. Mavacamten has been approved for use in the UK.

WHAT THIS STUDY ADDS

⇒ Real-world data for mavacamten treatment outcomes from the UK have not previously been published. We demonstrate symptomatic improvement, reduction of LVOT obstruction and biomarker normalisation comparable to clinical trial data.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Mavacamten use requires intensive clinical monitoring, which challenges clinical services. We compare different but effective clinical pathways used at three UK centres which can be adapted for use by other centres to develop their own protocols.

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is a relatively common inherited cardiac condition (1 in 200–500 people)[1 2] characterised by abnormal thickening of the myocardium. It is associated with pathogenic variants in sarcomere genes often inherited in an autosomal dominant pattern. HCM results in the decreased super-relaxed state of myosin and increased actin-myosin cross-bridging, culminating in hypercontractility.[3 4] These biomechanical changes are the catalyst for pathological changes, including ventricular hypertrophy, microvascular myocardial ischaemia and myocyte disarray and fibrosis, resulting in adverse clinical outcomes.[5]

Left ventricular outflow tract (LVOT) obstruction occurs in up to 70% of patients and is associated with progressive symptoms, increased risk of heart failure and mortality.[6 7] Obstructive HCM (oHCM) is defined by the presence of outflow tract obstruction with peak outflow tract gradient >30 mm Hg, with a threshold for invasive intervention of >50 mm Hg.[8 9] Historically, pharmacological management for symptomatic patients with oHCM was confined to non-targeted therapies supported by relatively limited evidence.[10 11] In patients with refractory symptoms, septal reduction therapy (SRT) using either surgical myectomy or alcohol septal ablation was recommended. SRT outcomes exhibit considerable variability, dependent on case volume and expertise of the treating centre.[12] The regulatory authorisation of mavacamten as the first targeted oral therapy for oHCM offers a paradigm shift in treatment and heralds the potential to improve patient outcomes throughout the UK.

We present our early experience with mavacamten treatment for oHCM, including clinical pathways from three UK centres and combined outcome data.

Current evidence and treatment guidelines

Mavacamten, a small molecule allosteric inhibitor of cardiac myosin ATPase, reduces actin-myosin cross bridging, attenuating the hypercontractile state seen in HCM.[13 14] Multicentre, phase III randomised controlled trials have demonstrated improved exercise capacity, symptoms and LVOT gradients in oHCM patients treated with Mavacamten versus placebo.[15 16]

EXPLORER-HCM included patients with significant LVOT obstruction (mean postexercise LVOT gradient 86±34 mm Hg) and New York Heart Association (NYHA) class II–III symptoms. At 30 weeks, there was significant improvement in exercise tolerance and symptom profile. 37% patients on mavacamten met the primary endpoint, a composite of improvement in NYHA class and pVO2 (37% mavacamten vs 17% placebo, p<0.0005).

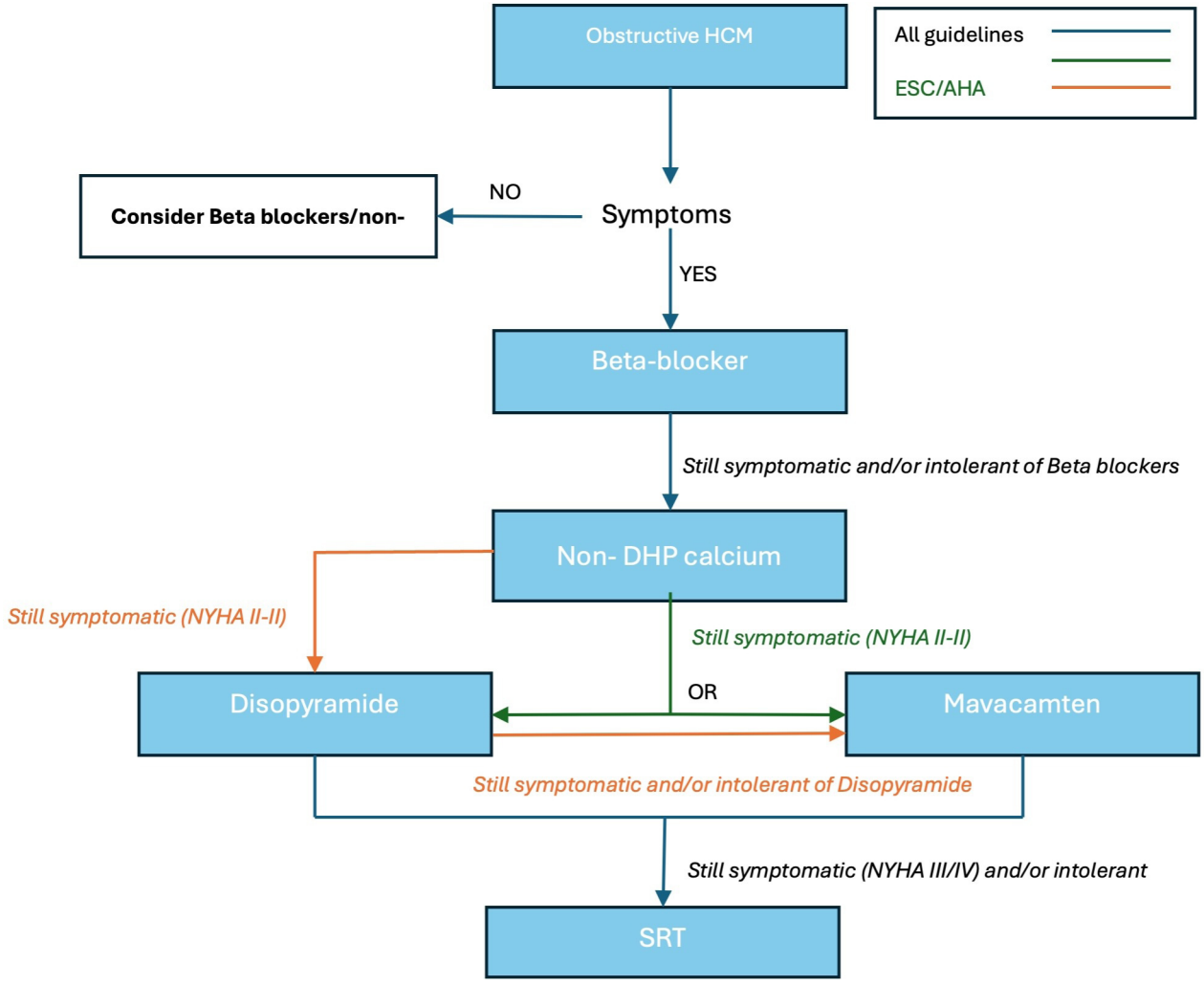

Figure 1 Flow chart for treatment of obstructive HCM (Adapted from ESC, AHA and NICE guidance). Non-DHP calcium, Non-dihydropyridine calcium channel blockers (eg, diltiazem or verapamil); HCM, hypertrophic cardiomyopathy; NICE, National Institute for Health and Care Excellence; NYHA, New York Heart Association functional classification; SRT, septal reduction therapy; ESC, European Society of Cardiology; AHA, American Heart Association.

More recent results from the long-term extension study (MAVA-LTE) have demonstrated sustained benefit to 180 weeks.[17 18]

VALOR-HCM assessed patients eligible for SRT. Participants were more symptomatic (93% NYHA class III–IV) than in EXPLORER-HCM but had similar baseline provokable LVOT gradients (84±35 mm Hg). After treatment, 17.9% of patients on mavacamten still met criteria for SRT at 16 weeks compared with 76.8% in the placebo group (p<0.001). These effects were sustained in a follow-up study to 32 weeks.[19]

In both studies, secondary endpoints demonstrated improved LVOT gradients, cardiac biomarkers and patient-reported symptom outcomes. Cardiac MRI and echocardiography substudies have suggested positive effects on cardiac remodelling, including changes in LV wall thickness, myocardial mass and markers of diastolic dysfunction.[20 21] Discontinuation of mavacamten results in rapid loss of symptomatic improvement as measured by the Hypertrophic Cardiomyopathy Symptom Questionnaire-Shortness of Breath Domain (HCMSQ-SoB).

Treatment algorithms for oHCM in Europe and North America recommend mavacamten for treatment of symptomatic patients with oHCM as a second line agent, once optimised on beta-blockers or non-dihydropyridine (DHP) calcium channel blockers.[8 9] In the UK, the National Institute for Health and Care Excellence (NICE) recommends mavacamten for oHCM patients who remain symptomatic on disopyramide or who are intolerant of this medication,[22] acknowledging low patient uptake for disopyramide, citing poor tolerance and/or supply chain difficulties (see figure 1).

Introducing mavacamten into UK clinical care: treatment requirements

Three major cautions for mavacamten use include (1) LV systolic dysfunction; (2) drug–drug interactions and (3) embryonic-fetal toxicity. As a result, intensive monitoring after initiating treatment, pretreatment CYP2C19 testing (in Europe) and pretreatment reproductive counselling is required.

Dosing regimen and monitoring requirements

A small decrease in LV systolic function is expected with mavacamten (mean left ventricular ejection fraction (LVEF) reduction 3.9% vs 0.1% with placebo in EXPLORER-HCM). Approximately 5% of patients experienced significant LV systolic dysfunction (LVEF <50%), which was reversible following mavacamten cessation within 4 weeks.[15] Greatest caution should be taken for patients

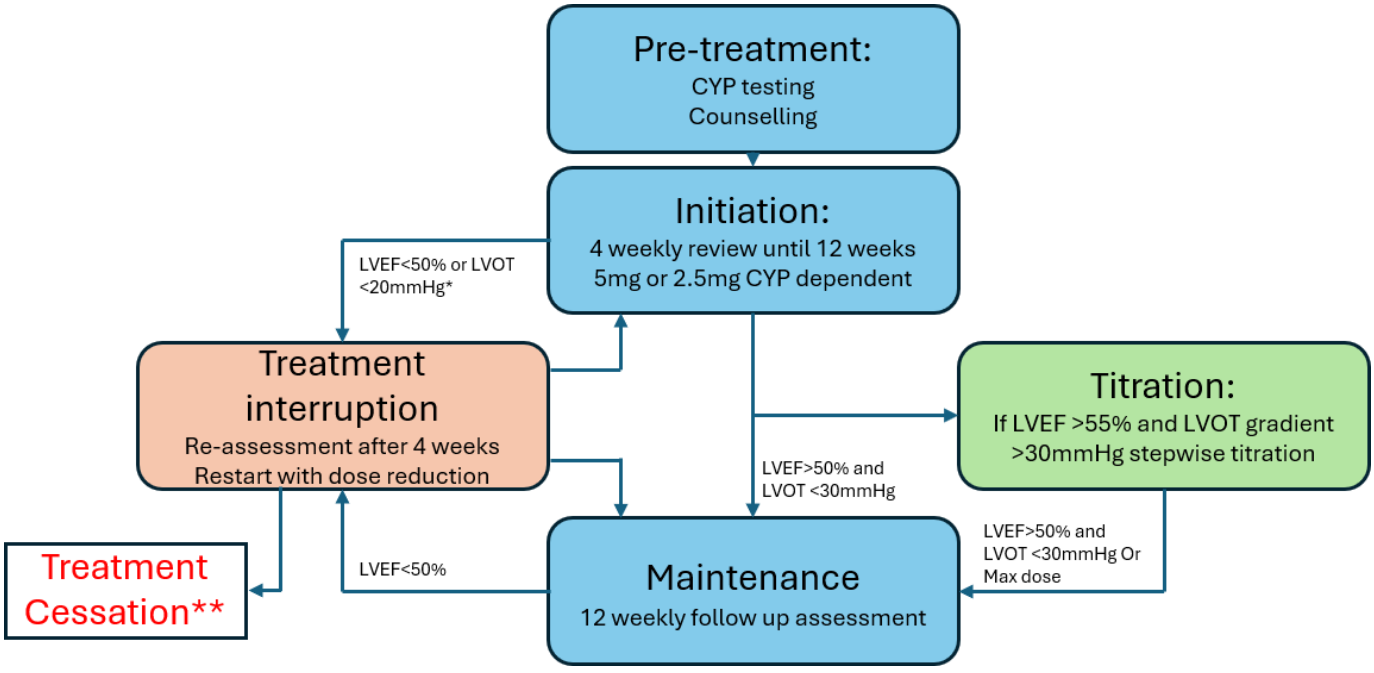

Figure 2 Summary of treatment Schedules. Initiation: Starting dose 5 mg or 2.5 mg (poor or unknown CYP2C19 metaboliser status). The initiation covers the first 12 weeks with clinical review and echocardiography required on a 4 weekly basis. *At weeks 4 and 8, if LVEF <50% or provokable LVOT gradient <20 mm Hg, dose reduction or treatment interruption occurs, with reassessment after 4 weeks. Dose titration: At week 12, if LVEF is >55% and the provokable LVOT gradient remains >30 mm Hg, mavacamten dose can be increased in a stepwise fashion to a maximum of 15 mg daily (5 mg in poor metabolisers). Maintenance: Patient enters maintenance with 12 weekly assessment once max LVOT gradient <30 mm Hg and/or at maximum dose for CYP2C19 status, providing LV ejection fraction remains >50%. Interruption or treatment cessation: If LVEF <50% at any stage, treatment should be interrupted, and reassessment at 4-week intervals is reinitiated. **Treatment cessation may be necessary if there are multiple interruptions for LV systolic dysfunction. LVEF, left ventricular ejection function; LVOT, left ventricular outflow tract.

with intercurrent illness or atrial arrhythmia who appear to be at greater risk of developing LV dysfunction.[23]

Treatment-related LV systolic impairment is minimised through a multistep dosing algorithm with frequent echocardiographic monitoring of LVEF and LVOT gradients. This includes three phases: initiation, titration and maintenance (see figure 2). Symptom assessment and echocardiography are performed at set intervals. Although these intervals appear predetermined, the speed of treatment response varies between patients and unpredictable dose reduction and/or treatment interruption may change the timing of subsequent appointments. Therefore, flexibility and resilience in service provision are vital to provide safe care.

CYP2C19 metaboliser testing

Mavacamten is primarily metabolised by liver enzymes CYP2C19 (74%), CYP3A4 (18%) and CYP2C9 (8%).[14] Plasma concentration of mavacamten is influenced by the genetically determined CYP2C19 metaboliser status. This is categorised into five metaboliser phenotypes: poor, intermediate, normal, rapid and ultra-rapid. There is a significant difference in the maximum plasma concentration in poor metabolisers compared with normal metabolisers (47%).

The European Medicines Agency and UK Medicines and Healthcare products Regulation Agency recommend CYP2C19 genotyping for patients prior to mavacamten treatment. The outcome of pharmacogenomic testing may influence other clinical care, for example, clopidogrel dosing following a stroke. Although guidance within the UK for reporting pharmacogenomic results has yet to be formalised, this discussion should form part of pretest counselling.

Pretreatment evaluation and counselling

Screening of concomitant medications prior to mavacamten initiation, and pre-emptive changes where

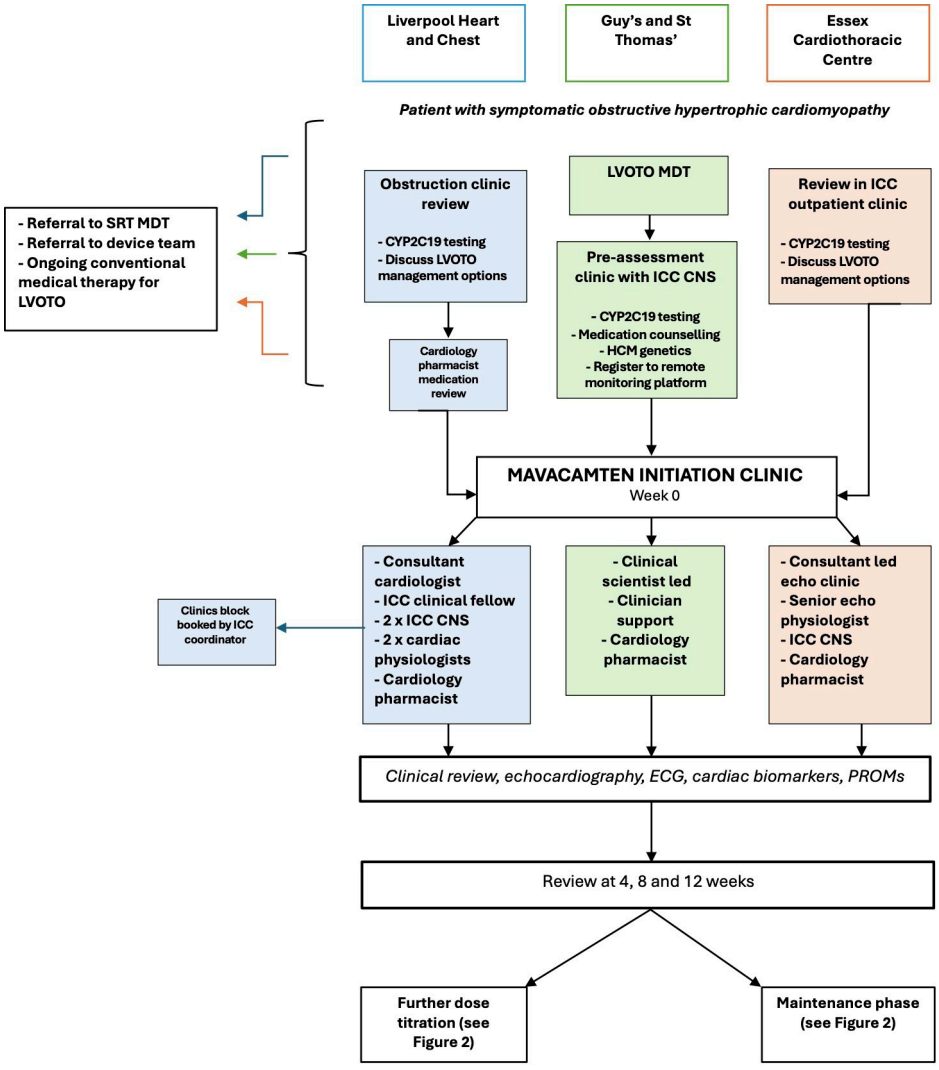

Figure 3 Example multidisciplinary clinical service for treatment with Mavacamten. Patient eligibility for treatment: symptomatic NYHA II or III, left ventricular ejection fraction >55%, left ventricular outflow tract gradient >30 mm Hg. Symptom assessment with both physician-assessed outcome (NYHA classification) and patient-reported outcome measures (PROMs). LVOTO, left ventricular outflow tract obstruction; MDT, multidisciplinary team; NYHA, New York Heart Association; SRT, septal reduction therapy; ICC CNS, Inherited cardiac conditions clinical curse specialist.

appropriate, emphasises the key role of cardiovascular pharmacists in the treatment pathway. Drug–drug interactions due to metabolism through the CYP2C19 or CYP3A4 pathways may affect mavacamten efficacy and exposure, and patients should understand which commonly used medications have the potential to interact.

Most patients starting mavacamten are established on at least one other pharmacological agent to treat LVOT obstruction. Caution is advised for those using a beta-blocker and either calcium channel blocker or disopyramide due to concerns over concomitant use of negative inotropes and increased risk of LV systolic dysfunction. Many centres, therefore, discontinue disopyramide, with some also discontinuing non-DHP calcium channel blockers. Despite limited evidence,[24] there is currently no guidance for how patients should be transitioned to mavacamten in this setting, and consideration should be given for a centre-specific protocol.

Studies in animal models have demonstrated fetal teratogenicity, and mavacamten use is, therefore, contraindicated in human pregnancy.[23] Female patients of childbearing age should be advised to use effective contraception before treatment and offered a pregnancy test at treatment initiation. Patients in EXPLORER-HCM were advised to take 'acceptable highly effective contraceptive methods', which included the combined or progesterone only contraceptive pill, injectable or implantable hormonal contraception, intrauterine devices, intrauterine hormone releasing systems, bilateral tubal occlusion, surgical sterilisation (from 6 months after the

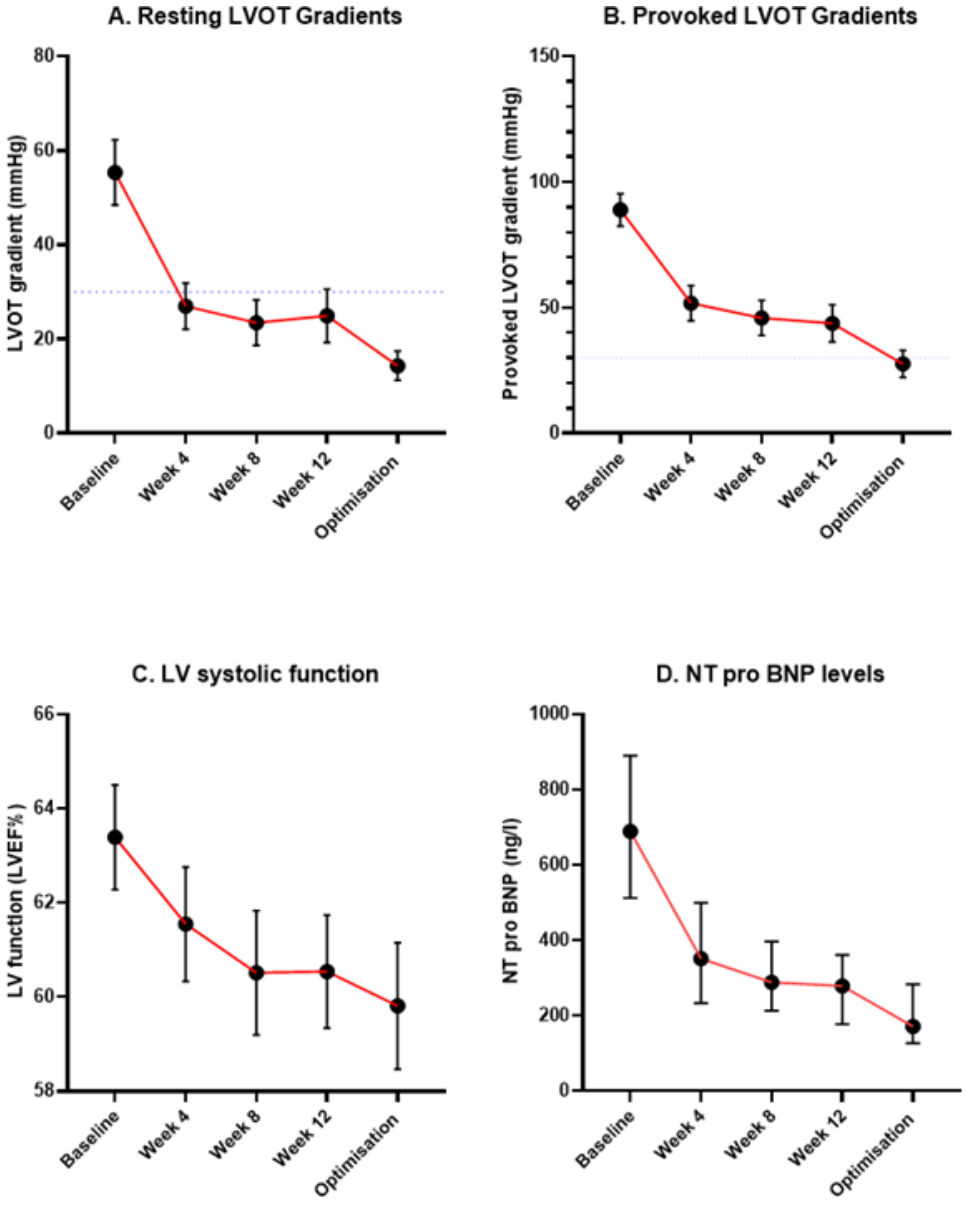

Figure 4 Change in echocardiographic and biomarker parameters from baseline. (A) Change in resting LVOT gradient. (B) Change in provoked LVOT gradient. (C) Change in LV systolic function. (D) Change in median NT-proBNP level. Intersection line on graphs A and B at 30 mm Hg (threshold for LVOT obstruction). Error bars 95% CI limits. LVEF, left ventricular ejection function; LVOT, left ventricular outflow tract.

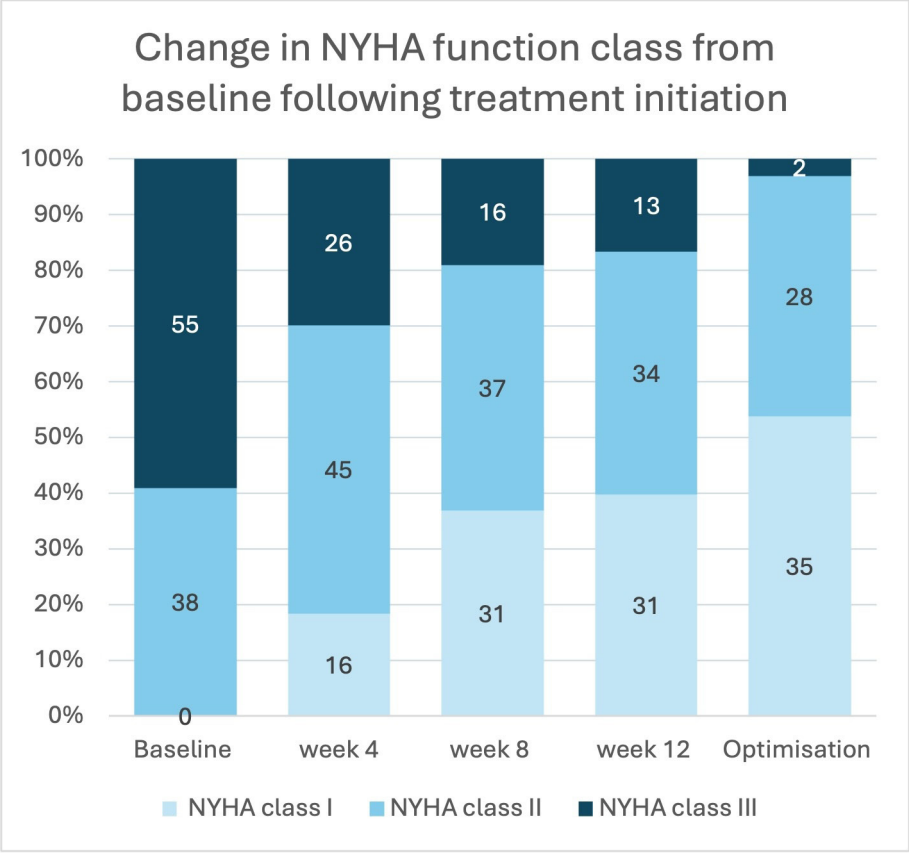

Figure 5 Change in patient New York Heart Association (NYHA) class from baseline to treatment optimisation. Numerical data on the chart represent patient numbers in each class.

procedure) or to be postmenopausal for 1 year.[25] While some constituents of oral contraceptives are metabolised by CYP3A4, no significant impact on efficacy when coadministered with mavacamten has been observed.[26] Patients should continue contraception use for 6 months after mavacamten discontinuation. This period relates to the time taken for elimination of the drug (approximately 5 half-lives: 45 days in normal CYP2C19 metabolisers and 115 days in poor metabolisers).

Overall, these requirements have ramifications for care provision, and thoughtful clinical service design is important.

Example models of care from three UK centres

Here, we present our experience of care models designed to meet the challenges outlined above from three centres: Guy's and St Thomas' Hospital London, Liverpool Heart and Chest Hospital and the Essex Cardiothoracic centre. Each centre has made use of local infrastructure and departmental experience to address the complex needs of this patient group (pathways presented in figure 3).

Across all three centres, a strong emphasis is placed on multidisciplinary working, with a team that encompasses physicians, clinical scientists/physiologists, specialist nurses, specialised cardiovascular pharmacists and clinical co-ordinators. Patients are often assessed for eligibility and alternative therapeutic options explored in specialised departmental multidisciplinary team (MDT) meetings.

Direct clinical assessment is carried out in either physician or clinical scientist led clinics depending on departmental strengths, with routine assessment common across all three pathways. This includes clinical assessment, ECG and focused echocardiography. Cardiac biomarkers (high sensitivity troponins, NT-proBNP) and patient-reported outcome measures are collected. Clinics are typically 'block booked' at weeks 0, 4, 8 and 12, with a more reactive approach for the titration and maintenance period.

Prescreening is either undertaken in specific clinics, using clinical nurse specialists or during routine cardiologist clinical review, with CYP2C19 testing performed ahead of treatment initiation. Early involvement of specialised cardiovascular pharmacists for medication review and to ensure appropriate National Health Service specialist commissioning reimbursement protocols are completed for eligible patients prior to Mavacamten initiation occurs in all three centres.

METHODS

Study design and setting

This retrospective study included patients with symptomatic oHCM treated with mavacamten at three UK

centres: Guy's and St Thomas' Hospitals, Essex Cardiothoracic Centre and Liverpool Heart and Chest Hospital between December 2023 and November 2024. The aim was to evaluate outcomes from mavacamten treatment in a real-world setting.

Patient selection

Eligible oHCM patients had NYHA class II–III symptoms, peak LVOT gradient >30 mm Hg and LVEF >55% LVEF was assessed by Simpson's Biplane Method, 3DEF or AutoEF (GE Healthcare). All were established on standard oHCM therapies (beta-blockers, calcium channel blockers or disopyramide). Mavacamten was introduced in accordance with NICE guidance.[22] Exclusion criteria included LVEF <55% and comorbid conditions that could interfere with required safety monitoring.

Interventions

Patients had CYP2C19 genotyping, and mavacamten dosing was guided by the metaboliser phenotype. Poor metabolisers or patients with unknown CYP2C19 status received an initial dose of 2.5 mg daily; other patients received 5 mg daily. The initiation phase comprised follow-up at weeks 0, 4, 8 and 12, including clinical assessment, echocardiography and biomarker testing. Treatment titration and maintenance were in accordance with recommendations from the summary of product characteristics.[23] Treatment optimisation was defined as the assessment where the patient entered the maintenance phase without further treatment titration.

Statistical analysis

Data were collected at each assessment and changes in clinical and echocardiographic parameters were analysed. Descriptive statistics were used to summarise baseline characteristics and paired t-tests to compare pretreatment and post-treatment values. Results were expressed as mean±SD or median and IQR with CIs.

RESULTS

93 patients (60±13 years; 72% male) from three sites started treatment with mavacamten between December 2023 and November 2024. 78 patients completed the 12-week initiation phase and 67 entered the maintenance phase by November 2024(table 1). All were eligible for treatment from referral data.

CYP2C19 metaboliser status was ascertained in 91 patients within 8 weeks of treatment, with delays occurring while establishing new pathways for CYP2C19 testing. Two patients (2%) were poor metabolisers.

Of 67 patients on maintenance therapy, the dose was 2.5 mg in 17% of patients, 5 mg in 32%, 10 mg in 43% and 15 mg in 7% of patients. The average time to treatment optimisation was 15.8 weeks.

13 patients required either temporary or permanent treatment interruption. Four patients had permanent discontinuation: one due to lack of symptom response; one due to intolerable side effects (headache) and two on safety grounds due to poor compliance with follow-up. Eight patients had treatment interruption during the initiation phase (weeks 4 or 8) due to LVOT gradient <20 mm Hg (5 patients) or LVEF <50% (3 patients). One patient had temporary interruption due to heart failure symptoms. All patients with temporary discontinuation were able to restart after 4 weeks. No patients experienced LV systolic impairment with LVEF <30% or

Table 1 Baseline demographic and pretreatment status

Baseline demographics	n=93 (SD or %)
Age at treatment initiation	60 (±13.0)
Sex	
Male	67 (72)
Female	26 (28)
Ethnicity	
White (British/European)	79 (85)
Black (African/Caribbean)	6 (6)
Asian	4 (4)
Other	4 (4)
Genetics	
Positive*	15 (16)
Negative	40 (43)
Not tested/awaiting outcome	38 (41)
CYP status	
Poor	2 (2)
Intermediate	28 (30)
Normal	39 (42)
Rapid	21 (23)
Ultra rapid	1 (1)
Not tested	2 (2)
Prior HCM treatment	
Beta blocker	73 (78)
Non-DHP calcium channel blockers	17 (18)
Disopyramide	34 (37)
Prior SRT	5 (5)
Comorbidity	
Hypertension	35 (38)
Coronary artery disease	18 (19)
Atrial fibrillation	21 (23)
History of syncope	8 (9)
Family history	
HCM	7 (8)
Sudden death	5 (5)

*Positive genetic result represents any sarcomeric variant detected on genetic testing (including American College of Medical Genetics and Genomics (ACMG) class 3 variant of unknown clinical significance/class 4 likely pathogenic/class 5 pathogenic).
DHP, dihydropyridine; HCM, hypertrophic cardiomyopathy; SRT, septal reduction therapy.

Table 2 Treatment outcomes at baseline, at completion of the initiation phase (12 weeks) and at treatment optimisation (maintenance phase)

Treatment outcomes	Baseline	Week 12	Treatment optimisation
LV function (LVEF; %)	63.4 (±5.4)	60.5 (±5.3)*	59.8 (±5.6)*
Resting LVOT gradient (mm Hg)	55.4 (±33.6)	25.0 (±24.0)†	14.4 (±12.2)†
Provoked LVOT gradient (mm Hg)	88.9 (±31)	43.8 (±32.6)‡	27.7 (±22.3)‡
NT pro-BNP (ng/L)§	689 (IQR 343–1684)	278 (IQR 141–568)	171 (IQR 116–335)
NYHA class			
I	0 (0%)	30 (40%)	35 (54%)
II	38 (41%)	34 (43%)	28 (43%)
III	55 (59%)	13 (17%)	2 (3%)

*Change in LV function from baseline p=0.0001 and p<0.0001 at 12 weeks and optimisation, respectively.
†Change in resting LVOT gradient compared with baseline p<0.0001 at 12 weeks and optimisation.
‡Change in provoked LVOT gradient compared with baseline p<0.0001 at 12 weeks and optimisation.
§NT-pro-BNP presented as median and IQR.
LVEF, left ventricular ejection function; LVOT, left ventricular outflow tract; NYHA, New York Heart Association.

required permanent discontinuation due to LV dysfunction. Two patients experienced transient asymptomatic rise in troponin levels, with no change in LV function or regional wall motion abnormality on echocardiography. One patient developed new atrial fibrillation on treatment and 0 patients reported syncope in the follow-up period.

LVOT gradients reduced from baseline (resting gradient 55.4±33.6 mm Hg; provoked gradient 88.9±31 mm Hg) to 12 weeks (resting gradient 25±24 mm Hg, p<0.0001; provoked gradient 43.8±32.6 mm Hg, p<0.0001) and further at dose optimisation (resting gradient 14.4±12.2 mm Hg, p<0.0001; provoked gradient 27.7±22.3 mm Hg, p<0.0001). LVEF reduced from 63.4%±5.4% at initiation to 60.5%±5.3% at 12 weeks and 59.8%±5.6% at dose optimisation. Average NT-pro BNP levels reduced from baseline 689 ng/L (IQR 343-17684ng/L) to 278 ng/L (IQR141-568ng/L) at 12 weeks and 171 ng/L (IQR 116-335 ng/L) at optimisation (table 2, figure 4).

NYHA class improved. At treatment initiation, 38 (41%) patients were NYHA class II and 55 (59%) NYHA class III. At 12 weeks, 58 (74%) patients experienced an improvement of at least 1 NYHA class. 59 (91%) of patients who reached treatment optimisation had improvement in NYHA class (figure 5). 28 patients (38%) who either completed the 12-week initiation or started maintenance therapy had a complete response, defined as NYHA class I symptoms and maximum resting or provoked LVOT gradients <30 mm Hg.

Learning from the early experience

These are the first real-world data from UK use of mavacamten for oHCM. The improvement in symptoms and echocardiographic outcomes was comparable to that seen in the EXPLORER-HCM and VALOR-HCM trials. At dose optimisation, mean LVOT gradients were <30 mm Hg, which is in keeping with resolution of LVOT obstruction. Similar to data from MAVA-LTE, over half of the patients were symptom-free (NYHA class I) at treatment optimisation.[18]

A modest reduction in LV function was expected and in keeping with that seen in trial data,[15 20] with LVEF reduction of approximately 4% seen in our population. No patients had permanent discontinuation due to left ventricular dysfunction, and temporary discontinuation due to LVEF <50% or heart failure symptoms occurred in 4.3% of patients, similar to that observed in trial data.[15] Patients initiated on mavacamten required a minimum of seven clinical assessments during the first 12 months of treatment, when mapped against the recommended follow-up intervals as of December 2024. Patients in our cohort were estimated to require eight assessments in the first year on average. This predominantly relates to patients who require higher treatment doses, with a longer initiation phase, and approximately 50% of patients in our cohort were optimised on 10–15 mg mavacamten. This impacts service requirements, and although early identification of those likely to require additional monitoring can help with resource allocation, services need flexibility, particularly in echocardiography provision.

One key area where clinical practice differs in the UK compared with North America is the need for CYP2C19 testing. Clinical service development to provide a pipeline for CYP testing can be challenging for new centres, particularly as routine pharmacogenetic testing is in its infancy during day-to-day clinical practice. In our population, mavacamten dose adjustment following CYP testing was rare (2% of patients were poor metabolisers), but recognising metaboliser status was helpful to guide dose adjustments for other potential drug–drug interactions.

Hypertension and atrial fibrillation were common comorbidities in our patients (present in 38% and 23% of patients, respectively). Importantly, however, other than non-DHP calcium channel blockers, most common

antihypertensive medications and anticoagulants are not known to have significant pharmacokinetic interactions with mavacamten via CYP2C19 or CYP3A4 pathways.[23]

There are several limitations to our retrospective analysis. In this real-world setting, patients were often referred for treatment following assessment in consultant clinics or after MDT consensus, where it was felt the patient was most likely to benefit from treatment, and this selection process introduces bias. In addition, despite a well-defined dosing regimen and follow-up framework, clinical practice differed in each site, for example, in echocardiography protocols, which may influence reported outcomes.

We have described three different but effective clinical pathways, which use local experience, whether through consultant or clinical scientist-led services. During service establishment, centres are encouraged to assess and leverage their local strengths to devise local protocols. Our pathways have evolved and developed over time to meet the clinical monitoring, CYP2C19 testing and patient counselling requirements.

There are similarities between pathways: (1) involvement of the MDT according to local strengths, (2) pretreatment assessment and (3) early involvement of cardiovascular pharmacists. Pretreatment assessment provides an opportunity for medication reconciliation, assessment of potential drug–drug interactions, instructions for transition to mavacamten, counselling for use of effective contraception where applicable and CYP2C19 testing. A pretreatment visit helps to minimise delays in treatment initiation and can be used to identify additional needs such as diagnostic HCM genomic testing if not previously performed. Involving cardiovascular pharmacists early in the patient journey is also important in managing the logistical aspects of drug stock and supporting local commissioning applications for mavacamten, which has 'high cost' drug restrictions.

Future pathway development

Recognising the importance of equitable patient access to treatment and long-term drug monitoring, the future for mavacamten is likely to require 'hub-and-spoke' networks and shared care prescribing agreements to facilitate provision of expert care and medication availability closer to patients' homes.[27 28] With increased real-world data to add to the existing trial data, we expect that knowledge and confidence around drug safety will increase, potentially leading to a reduction in the frequency of clinical and echocardiographic assessments.

CONCLUSIONS

Mavacamten, the first targeted treatment for oHCM, has compelling data from randomised controlled clinical trials which demonstrate efficacy in improvement of symptoms and physiological outcomes. Our early experience from three UK centres is comparable to trial data, with significant improvements in LVOT gradients, patient symptoms and NT-proBNP levels.

There are important considerations and challenges that influence service provision, including frequent and flexible clinical monitoring with echocardiography; CYP2C19 testing pathways; and pretreatment counselling. We have described three clinical pathways for mavacamten use operational in the UK. There is no 'one-size-fits-all' approach; however, all pathways require multidisciplinary input.

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