Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Study Sites and Investigators

Study site investigators	Names of study sites
Shuyang Zhang	Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
Zhuang Tian	Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
Yaling Han	General Hospital of Shenyang Military Region, Shenyang, Liaoning Province, China
Ling Tao	Xijing Hospital of Air Force Military Medical University, Xi'an City, Shaanxi Province, China
Liwen Li	Guangdong Provincial People's Hospital, Guangzhou, Guangdong Province, China
Fang Wang	Beijing Hospital, National Center of Gerontology; Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing, China
Ping Yang	China-Japan Union Hospital of Jilin University, Changchun, Jilin Province, China
Wei Jin	Ruijin Hospital, Shanghai Jiao Tong University, School of Medicine, Shanghai, China
Jinmin Zhou	Zhongshan Hospital, Fudan University, Shanghai, China
Jian'an Wang	The Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, Zhejiang Province, China
Qing Zhang	West China Hospital, Sichuan University, Sichuan, China
Zhanquan Li	The People's Hospital of Liaoning Province, Shenyang, Liaoning Province, China
Xiaoyan Li	Renmin Hospital of Wuhan University, Hubei General Hospital, Wuhan, Hubei Province, China
Wei Ma	Peking University First Hospital, Beijing, China
Meng Jiang	Renji Hospital, Shanghai Jiaotong University, School of Medicine, Shanghai, China
Jianzeng Dong	Beijing Anzhen Hospital, Capital Medical University, Beijing, China
Xiang Cheng	Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei Province, China
Daoquan Peng	The Second Xiangya Hospital of Central South University, Changsha, Hunan Province, China

eMethods.

Blind dose adjustments during the Double-Blinded Placebo-Controlled Treatment Period

PK/PD Criteria for Down-Titration (requires resting LVEF ≥50% regardless of Valsalva gradient[a])		
Time of Assessment	**Pre-dose Mavacamten Plasma Concentration (ng/mL)[a]**	**Time and Dose[b]**
Week 4	700 < Plasma concentration < 1000	Week 6: Dose reduces from 2.5 mg to 1 mg
Week 6	700 < Plasma concentration < 1000	Week 8: Dose reduces from 2.5 mg to 1 mg (if dose is reduced at Week 6, it should remain unchanged at Week 8)
Week 8[c]	700 < Plasma concentration < 1000	2 weeks later: Dose reduces from 5 mg to 2.5 mg or Dose reduces from 2.5 mg to 1 mg or Dose reduces from 1 mg to placebo (if dose is reduced at Week 8, it should remain unchanged 2 weeks later)
Week 12	700 < Plasma concentration < 1000	Week 14: Dose reduces from 5 mg to 2.5 mg or Dose reduces from 2.5 mg to 1 mg or Dose reduces from 1 mg to placebo
Week 18	700 < Plasma concentration < 1000	Week 20: Dose reduces from 10 mg to 5 mg or Dose reduces from 5 mg to 2.5 mg or Dose reduces from 2.5 mg to 1 mg or Dose reduces from 1 mg to placebo
Week 24	700 < Plasma concentration < 1000	Week 26: Dose reduces from 15 mg to 10 mg or Dose reduces from 10 mg to 5 mg or Dose reduces from 5 mg to 2.5 mg or Dose reduces from 2.5 mg to 1 mg or Dose reduces from 1 mg to placebo
Week 26	700 < Plasma concentration < 1000	2 weeks later: Dose reduces from 15 mg to 10 mg or Dose reduces from 10 mg to 5 mg or Dose reduces from 5 mg to 2.5 mg or Dose reduces from 2.5 mg to 1 mg or Dose reduces from 1 mg to placebo (if dose is reduced at Week 26, it should remain unchanged 2 weeks later)

At Week 6, Week 12 and Week 18: if PK/PD criteria for down-titration are not met, potential dose up-titration may proceed as follows:

Dose Titration (requires resting LVEF ≥ 50% and pre-dose mavacamten plasma concentration ≤ 700 ng/mL)

Time of Assessment	**Dose Titration Criteria** (based on the LVEF, Valsalva gradient and pre-dose mavacamten plasma concentration)	**Dose Titration[d]**	**Time and Dose[e]**

Week 6	LVEF ≥ 55%	Valsalva gradient ≥ 30 mmHg AND plasma concentration < 350 ng/mL	Increase	**Week 8:** Dose increases from 2.5 mg to 5 mg
	LVEF ≥ 55%	Valsalva gradient < 30 mmHg and plasma concentration < 350 ng/mL OR 350 ≤ plasma concentration ≤ 700 ng/mL (regardless of Valsalva gradient)	No change	**Week 8:** Dose remains at 2.5 mg or 1 mg
	50% ≤ LVEF < 55%	Regardless of Valsalva gradient and plasma concentration		
Week 12	LVEF ≥ 55%	Valsalva gradient ≥ 30 mmHg AND plasma concentration < 350 ng/mL	Increase	**Week 14:** Dose increases from 5 mg to 10 mg or Dose increases from 2.5 mg to 5 mg
	LVEF ≥ 55%	Valsalva gradient < 30 mmHg and plasma concentration < 350 ng/mL OR 350 ≤ plasma concentration ≤ 700 ng/mL (regardless of Valsalva gradient)	No change	**Week 14:** Dose remains at 5 mg or 2.5 mg or 1 mg
	50% ≤ LVEF < 55%	Regardless of Valsalva gradient and plasma concentration		
Week 18	LVEF ≥ 55%	Valsalva gradient ≥ 30 mmHg AND plasma concentration < 350 ng/mL	Increase	**Week 20:** Dose increases from 10 mg to 15 mg or Dose increases from 5 mg to 10 mg or Dose increases from 2.5 mg to 5 mg
	LVEF ≥ 55%	Valsalva gradient < 30 mmHg and plasma concentration < 350 ng/mL OR 350 ≤ plasma concentration ≤ 700 ng/mL	No change	**Week 20:** Dose remains at 10 mg, 5 mg, 2.5 mg or 1 mg

		(regardless of Valsalva gradient)		
	50% ≤ LVEF < 55%	Regardless of Valsalva gradient and plasma concentration		

Abbreviations: IxRS = interactive response system; LVEF = left ventricular ejection fraction; PD = pharmacodynamics; PK = pharmacokinetics; TTE = transthoracic echocardiography.

[a] LVEF and pre-dose mavacamten plasma concentration will be communicated directly to the IxRS from the core/central laboratories based on assessments so that it is blinded to the investigator, study site personnel, and the Sponsor. Note: LVEF will not be performed at Week 8 (see also footnote c).
[b] Dose reduction applies if pre-dose PK criterion is met.
[c] Week 8 assessment for dose reduction will be based solely on pre-dose mavacamten plasma concentration value, there will be no TTE performed at Week 8, and therefore, no LVEF result.

[d] Titration adjustments will also be communicated directly to the IxRS based on Week 6, 12 and 16 including measures of peak Valsalva gradient reported by the core laboratory so that blinding is maintained.

[e] If the mavacamten dose is decreased at any time during the study, then the participant will continue on the reduced dose to Week 30 unless safety concerns or intolerability arise requiring further dose reduction or dose discontinuation.

Valsalva maneuver

To standardize the Valsalva maneuver, all participants were required to undergo and pass trainings such that they were able to produce a qualified and reproducible Valsalva maneuver. The training also ensured that the participants understand the effort and compliance required for the maneuver.

In addition, all sonographers in the study were rigorously trained to perform echocardiographic assessments, check the adequacy of the Valsalva maneuver and ensure that the Valsalva maneuver performed was qualified and reproducible according to standards detailed in echocardiographic manuals. Standardized training of sonographers also contributes towards making sure that Valsalva maneuver was uniformly applied to all study sites.

eTable 1. Study Eligibility Criteria

Inclusion criteria
Participants who met the following criteria were included in this study:
1) At least 18 years old at screening.
2) Body weight was greater than 45 kg at screening.
3) Had adequate acoustic windows to enable accurate transthoracic echocardiographies (TTEs) (refer to echocardiography related manual).
4) Diagnosed with obstructive hypertrophic cardiomyopathy (oHCM) consistent with current American College of Cardiology Foundation/American Heart Association, European Society of Cardiology, and Chinese Society of Cardiology guidelines, ie, satisfy criteria below (criteria to be documented by the echocardiography core laboratory):
A. Had unexplained left ventricular (LV) hypertrophy with nondilated ventricular chambers in the absence of other cardiac (eg, hypertension, aortic stenosis) or systemic disease and with maximal LV wall thickness ⩾15 mm (or ⩾13 mm with positive family history of hypertrophic cardiomyopathy), as determined by core laboratory interpretation, and
B. Had left ventricular outflow tract (LVOT) peak gradient ⩾50 mm Hg during screening as assessed by echocardiography at rest or after Valsalva maneuver (confirmed by echocardiography core laboratory interpretation).
5) Had documented LV ejection fraction (LVEF) ⩾55% by echocardiography core laboratory read of screening TTE at rest.
6) Had a valid measurement of Valsalva LVOT peak gradient at screening as determined by echocardiography core laboratory.
7) Had New York Heart Association (NYHA) class II or III symptoms at screening.
8) Had documented oxygen saturation at rest ⩾90% at screening.
9) Female participants should not be pregnant or lactating and, if sexually active at enrollment, had agreed upon using 1 of the following acceptable birth control methods from the screening visit through 5 months after the last dose of study treatment.
a) Estrogen- and progestogen-containing hormonal contraception associated with inhibition of ovulation or progestogen-only hormonal contraception associated with inhibition of ovulation by oral, implantable, or injectable route of administration.
b) Intrauterine device.
c) Intrauterine hormone-releasing system.
d) Bilateral tubal occlusion.
e) Female: surgically sterile for 6 months or postmenopausal for 1 year. Permanent sterilization included hysterectomy, bilateral oophorectomy, bilateral salpingectomy, and/or documented bilateral tubal occlusion at least 6 months prior to screening. Females were considered postmenopausal if they have had amenorrhea for ⩾1 year after cessation of all exogenous hormonal treatments, and follicle-stimulating hormone levels were in the postmenopausal range.
f) Male partners of female participants must also agree to use a contraceptive (eg, barrier, condom, or vasectomy) from screening through 5 months after the last dose of study drug.
10) Study participants were able to understand and comply with the study procedures, understand the risks involved in the study, and provided written informed consent according to national, local, and institutional guidelines before the first study-specific procedure.

Exclusion criteria	
A participant who met any of the following exclusion criteria was excluded from this study:	
1)	Participated in a clinical trial in which the participant received any investigational drug (or was currently using an investigational device) within 30 days prior to screening, or at least 5 times the respective elimination half-life (if known), whichever was longer.
2)	Known infiltrative or storage disorder causing cardiac hypertrophy that mimics oHCM, such as Fabry disease, amyloidosis, or Noonan syndrome with LV hypertrophy.
3)	Had a history of syncope within 6 months prior to screening or sustained ventricular tachyarrhythmia with exercise within 6 months prior to screening.
4)	Had a history of resuscitated sudden cardiac arrest (at any time) or known history of appropriate implantable cardioverter-defibrillator (ICD) discharge for life-threatening ventricular arrhythmia within 6 months prior to screening.
5)	Had paroxysmal, intermittent atrial fibrillation with atrial fibrillation present per the investigator's evaluation of the participant's electrocardiogram (ECG) at the time of screening.
6)	Had persistent or permanent atrial fibrillation not on anticoagulation for at least 4 weeks prior to screening and/or not adequately rate-controlled within 6 months prior to screening (note: participants with persistent or permanent atrial fibrillation who were anticoagulated and adequately rate-controlled were allowed).
7)	Previously participated in a clinical study with mavacamten.
8)	Hypersensitivity to any of the components of the mavacamten formulation.
9)	Current treatment (within 14 days prior to screening) or planned treatment during the study with disopyramide, cibenzoline, or ranolazine.
10)	Current treatment (within 14 days prior to screening) or planned treatment during the double-blinded treatment with a combination of beta-blockers and verapamil or a combination of beta-blockers and diltiazem.
11)	For individuals on beta-blockers, verapamil, or diltiazem, any dose adjustment of that medication within14 days prior to screening or any anticipated change in treatment regimen using these medications during the double-blind treatment.
12)	Had been successfully treated with invasive septal reduction (surgical myectomy or percutaneous alcohol septal ablation [ASA]) within 6 months prior to screening or planned to have either of these treatments during the study (note: individuals with an unsuccessful myectomy or percutaneous ASA procedure performed >6 months prior to screening were enrolled if study eligibility criteria for LVOT gradient criteria were met).
13)	ICD placement within 2 months prior to screening or planned ICD placement during the study.
14)	Had QTcF >500 msec when QRS interval <120 msec or QTcF >520 msec when QRS $\geqslant$120 msec or any other ECG abnormality considered by the investigator to pose a risk to participant safety (eg, second-degree atrioventricular block type II).
15)	Had documented obstructive coronary artery disease (>70% stenosis in 1 or more epicardial coronary arteries) or history of myocardial infarction.
16)	Had known moderate or severe (as per investigator's judgment) aortic valve stenosis, constrictive pericarditis, or clinically significant congenital heart disease at screening.
17)	Had any acute or serious comorbid condition (eg, major infection or hematologic, renal, metabolic, gastrointestinal, or endocrine dysfunction) that, in the judgment of the investigator, could lead to premature termination of study participation or interfere with the measurement or interpretation of the efficacy and safety assessments in the study.
18)	History of malignant disease within 10 years of screening:

	a) Participants who had been successfully treated for nonmetastatic cutaneous squamous cell or basal cell carcinoma or had been adequately treated for cervical carcinoma in situ or breast ductal carcinoma in situ were included in the study.
	b) Participants with other malignancies who were cancer free for more than 10 years before screening were included in the study.
19)	Had safety laboratory parameters (chemistry, hematology, coagulation, and urinalysis) outside normal limits (according to the local laboratory reference range) at screening as assessed by the local laboratory; however, a participant with safety laboratory parameters outside normal limits might be included if he or she met all of the following criteria:
	a) The safety laboratory parameter outside normal limits was considered by the investigator to be clinically not significant.
	b) If there was an alanine aminotransferase or aspartate aminotransferase result, the value must be <3× the upper limit of the laboratory reference range.
	c) The body size–adjusted estimated glomerular filtration rate was $\geqslant$30 mL/min/1.73 m^2.
20)	Had a positive serologic test at screening for infection with human immunodeficiency virus, hepatitis C virus, or hepatitis B virus surface antigen.
21)	Known uncured COVID-19 (coronavirus disease 2019) infection or with severe complication before screening.
22)	Had a history or evidence of any other clinically significant disorder, condition, or disease that, in the opinion of the investigator, would pose a risk to participant safety or interfere with the study evaluation, procedures, or completion.
23)	Was currently taking, or had taken within 14 days prior to screening, a prohibited medication, such as a cytochrome CYP2C19 inhibitor (eg, omeprazole or esomeprazole), a strong CYP3A4 inhibitor, or St. John's Wort. Alternatives, such as pantoprazole were allowed and could be discussed with the medical monitor.
24)	Prior treatment with cardio toxic agents such as doxorubicin or similar.
25)	Unable to comply with the study requirements, including the number of required visits to the clinical site.
26)	Was a first-degree relative of personnel directly affiliated with the study at the clinical study site, any study vendor, or the study sponsor.
27)	Was currently taking, or had taken within 14 days prior to screening, biotin supplements (multivitamins that contain <1000 mg biotin were allowed during the study, but should be stopped 24 hours prior to each study visit).
28)	Identified as alcohol addicts.
Cardiac magnetic resonance (CMR) exclusion criteria:	
A participant was to be excluded from the CMR assessments if he or she has any of the following:	
1)	An ICD or pacemaker, or another contraindication for CMR or conditions not suitable for CMR in the judgment of the investigator.
2)	Atrial fibrillation at the time of screening (participant who was in atrial fibrillation at the time of imaging was asked to return later within the screening period, and if the participant was still in atrial fibrillation, the participant was disqualified from the CMR assessments).
3)	Allergy or contraindication to contrast medium.
Removal of participants from therapy or assessment	
Study drug was permanently discontinued if any of the following criteria were met:	
The following reasons would lead to permanent treatment discontinuation or withdrawal from study:	
1)	If all the criteria are met for possible drug-induced liver injury.

2)	Pregnancy.
3)	LVEF ⩽30% as determined by site laboratory.
4)	New or worsening heart failure associated with systolic dysfunction.
5)	Any breaking of the study blind requested by the investigator.
6)	Continued administration of study drug is considered by the investigator to be detrimental to the participant's safety or well-being.
7)	The participant requests to discontinue study drug.
8)	The sponsor requests that the participant permanently discontinues study drug.
If a participant permanently discontinues treatment prior to week 30, the participants were asked to undergo an early termination visit as soon as possible after stopping study drug and were encouraged to participate in posttreatment visits (phone visit and the onsite visits) and the week 30 visit.	

eTable 2. Primary and Secondary Efficacy End Points

	Mavacamten group (n = 54)	Placebo group (n = 27)	Difference (95% CI)[a]	*P* value[b]
Primary endpoint				
Change from baseline to week 30 in Valsalva LVOT peak gradient, mm Hg, LSM (SE)	−51.05 (6.15)	19.23 (8.54)	−70.29 (−89.64 to −50.94)	<.001[c]
Secondary endpoints				
Change from baseline to week 30 in resting LVOT peak gradient, mm Hg, LSM (SE)	−49.04 (4.64)	5.95 (6.31)	−54.99 (−69.13 to −40.86)	<.001
Proportion of patients with Valsalva LVOT peak gradient <30 mm Hg at week 30, No. (%)	26 (48.1)	1 (3.7)	40.9% (24.4 to 57.5%)	<.001
Proportion of patients with Valsalva LVOT peak gradient <50 mm Hg at week 30, No. (%)	32 (59.3)	2 (7.4)	46.9% (29.6 to 64.2%)	<.001
Proportion of participants with ≥1 class improvement in NYHA functional classification from baseline to week 30, No. (%)	32 (59.3)	4 (14.8)	39.0% (19.89 to 58.12%)	<.001
Change from baseline to week 30 in KCCQ−CSS, LSM (SE)	4.99 (2.06)	−5.25 (2.75)	10.24 (4.35 to 16.13)	<.001
Change from baseline to Week 30 in NT-proBNP, ng/L, GMR (%CV)	0.18	0.93	0.18 (0.13 to 0.24)[d]	<.001
Change from baseline to Week 30 in cardiac troponin, ng/L, GMR (%CV)	0.42	1.24	0.34 (0.27 to 0.42)[d]	<.001
Change from baseline to Week 30 in LVMI evaluated by CMR imaging, g/m^2, mean (SD)[f]	−26.37	4.43	−30.80 (−41.55 to −20.05)	<.001[e]

Abbreviations: CI, confidence interval; CMR, cardiac magnetic resonance; CV, coefficient of variation; GMR, geometric mean ratio; KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire Clinical Summary Score; LSM, least-squares mean; LVMI, left ventricular mass index; LVOT, left ventricular outflow tract; NT-proBNP, N-terminal pro B-type natriuretic peptide; NYHA, New York Heart Association; SD, standard deviation; SE, standard error.

[a] Model estimated least-squares mean differences were reported for continuous variables. Common risk difference with 95% CI based on the stratified Miettinen-Nurminen method were reported for category variables.

[b] The *P* values generated for secondary endpoints are considered as descriptive purpose, with no multiplicity adjustment.

[c] One-sided *P* value.

[d] Proportion of GMR mavacamten/placebo (95% CI).

[e] Based on Wilcoxon signed-rank test.

[f] Based on subset of 58 patients (n = 39 in mavacamten group, n = 19 in placebo group) eligible for CMR.

eTable 3. Mean Valsalva LVOT Peak Gradients Over Time

Mean (SD), mm Hg	**Mavacamten group (n = 54)**	SD	**Placebo group (n = 27)**	SD
Baseline	106.78	43.225	99.79	41.100
Week 4	79.65	38.883	106.96	43.021
Week 6	89.62	44.121	111.62	47.553
Week 12	68.18	45.437	109.74	42.200
Week 18	45.45	35.650	114.38	54.935
Week 24	37.41	27.193	111.99	40.506
Week 26	43.45	37.774	119.89	46.636
Week 30	48.85	40.419	116.31	52.225
Change from baseline to Week 30	-57.93	45.614	20.65	46.448

Abbreviations: SD, standard deviation

eTable 4. Change From Baseline in Valsalva LVOT Peak Gradient for ITT and Per-Protocol Analyses Across Time Points

	ITT analysis[b]	Per-protocol analysis[c]
LS mean difference between groups in change from baseline in Valsalva LVOT peak gradient, mm Hg (95% CI); *P* value[a]		
Week 4	−29.42 (−46.18 to −12.67); *P* < .001	−35.16 (−54.12 to −16.20); *P* < .001
Week 6	−24.28 (−43.06 to −5.51); *P* = .006	−25.75 (−47.09 to −4.41); *P* = .009
Week 12	−45.44 (−62.43 to −28.44); *P* < .001	−49.94 (−69.61 to −30.27); *P* < .001
Week 18	−72.27 (−92.48 to −52.05); *P* < .001	−68.29 (−89.59 to −47.00); *P* < .001
Week 24	−74.83 (−91.34 to −58.33); *P* < .001	−68.85 (−84.70 to −53.00); *P* < .001
Week 26	−74.71 (−94.24 to −55.18); *P* < .001	−71.23 (−91.85 to −50.61); *P* < .001
Week 30	−70.82 (−90.29 to −51.35); *P* < .001	−72.24 (−92.87 to −51.60); *P* < .001

Abbreviations: CI, confidence interval; ITT, intent-to-treat; LS, least-squares; LVOT, left ventricular outflow tract.

[a] One-sided *P* value.

[b] Based on ITT population: mavacamten (n = 54); placebo (n = 27); stratification factor was beta-blocker use based on case report form.

[c] Based on per-protocol set (ie, patients who completed all efficacy assessments without important protocol deviation affecting primary efficacy endpoint): mavacamten (n = 52); placebo (n = 20).

eTable 5. Mean Resting LVOT Peak Gradients Over Time

Mean (SD), mm Hg	**Mavacamten group (n = 54)**	SD	**Placebo group (n = 27)**	SD
Baseline	74.62	35.045	73.41	32.228
Week 4	52.29	35.004	80.47	37.689
Week 6	58.24	41.225	81.31	38.725
Week 12	39.71	38.618	83.88	41.678
Week 18	22.79	22.122	92.91	47.787
Week 24	18.10	13.272	79.16	30.643
Week 26	23.60	28.919	91.26	40.770
Week 30	23.17	27.226	77.13	39.622
Change from baseline to Week 30	-51.45	35.985	6.38	34.356

Abbreviations: SD, standard deviation

eTable 6. Key Exploratory End Points for CMR Parameters

Mean change from baseline at week 30	Mavacamten (n = 39)	Placebo (n = 19)	Mean difference (95% CI)	*P* value[a]
LV mass, g	−46.30	6.34	−52.64 (−67.89 to −37.39)	<.001
LV maximal wall thickness, mm	−3.04	0.47	−3.52 (−4.65 to −2.38)	<.001
Maximum LAVI, mL/m^2	−17.31	0.96	−18.27 (−26.72 to −9.83)	<.001
Minimum LAVI, mL/m^2	-10.38	-0.06	-10.31 (-15.93, -4.70)	<.001

Abbreviations: CI, confidence interval; CMR, cardiac magnetic resonance; LAVI, left atrial volume index; LV, left ventricle.

[a] Based on Wilcoxon rank sum test.

eTable 7. Severity of TEAEs

	Mavacamten (n = 54)	Placebo (n = 27)
Total numbers of TEAEs	165	82
Mild	147	74
Moderate	15	8
Severe	1	0
Life-threatening	2	0
Fatal	0	0

Abbreviations: TEAE, treatment-emergent adverse event

Footnote:
One patient in the mavacamten group experienced 1 severe TEAE of ankle fracture and 2 life-threatening TEAEs of atrial fibrillation and hypotension. All events were not related to study medication. Other TEAEs were all mild or moderate.

eTable 8. Common TEAEs Reported in ≥5% of Patients by System Organ Class and Preferred Term

SOC PT	Mavacamten (n = 54) No. (%)	Placebo (n = 27) No. (%)	Total (N = 81) No. (%)
Number of patients with any TEAE	45 (83.3)	24 (88.9)	69 (85.2)
Infections and infestations			
COVID-19	20 (37.0)	11 (40.7)	31 (38.3)
Upper respiratory tract infection	8 (14.8)	4 (14.8)	12 (14.8)
Cardiac disorders			
Defect conduction intraventricular	5 (9.3)	0	5 (6.2)
Palpitations	3 (5.6)	2 (7.4)	5 (6.2)
Ventricular extrasystoles	2 (3.7)	3 (11.1)	5 (6.2)
Cardiac discomfort	3 (5.6)	0	3 (3.7)
Ventricular tachycardia	2 (3.7)	2 (7.4)	4 (4.9)
Metabolism and nutrition disorders			
Hyperuricemia	7 (13.0)	2 (7.4)	9 (11.1)
Hyperlipidemia	4 (7.4)	0	4 (4.9)
Nervous system disorders			
Dizziness	7 (13.0)	2 (7.4)	9 (11.1)
Hypoesthesia	3 (5.6)	0	3 (3.7)
Headache	1 (1.9)	2 (7.4)	3 (3.7)
Investigations			
Hepatic enzyme increased	3 (5.6)	0	3 (3.7)
Electrocardiogram QT prolonged	1 (1.9)	2 (7.4)	3 (3.7)
Respiratory, thoracic, and mediastinal disorders			
Cough	1 (1.9)	2 (7.4)	3 (3.7)
Hepatobiliary disorders			
Hepatic function abnormal	3 (5.6)	0	3 (3.7)
Vascular disorders			
Hypertension	3 (5.6)	0	3 (3.7)

Abbreviations: PT, preferred term; SOC, system organ class; TEAE, treatment-emergent adverse event.

eTable 9. Summary of QTcF Intervals (SAF)

	Mavacamten (n = 54)	Placebo (n = 27)	Total (N = 81)
QTcF category	**No. (%)**	**No. (%)**	**No. (%)**
Baseline QTcF			
>450 msec	18 (33.3)	14 (51.9)	32 (39.5)
>480 msec	2 (3.7)	4 (14.8)	6 (7.4)
>500 msec	1 (1.9)	0	1 (1.2)
>520 msec	0	0	0
>550 msec	0	0	0
Maximum postbaseline **QTcF**			
>450 msec	24 (44.4)	20 (74.1)	44 (54.3)
>480 msec	5 (9.3)	7 (25.9)	12 (14.8)
>500 msec	1 (1.9)	2 (7.4)	3 (3.7)
>520 msec	0	0	0
>550 msec	0	0	0
Maximum CFB			
>30 msec	5 (9.3)	8 (29.6)	13 (16.0)
>60 msec	0	0	0
Maximum % CFB			
>15%	0	0	0

Abbreviations: CFB, change from baseline; QTcF, QT Interval (milliseconds) corrected using Fridericia's formula; SAF, safety analysis set.

Safety baseline in double-blind, placebo-controlled period was defined as the last non-missing measurement taken prior to first dose date of double-blinded study treatment.

The categories were not mutually exclusive. A participant that was counted in the higher category was also counted in the lower category.

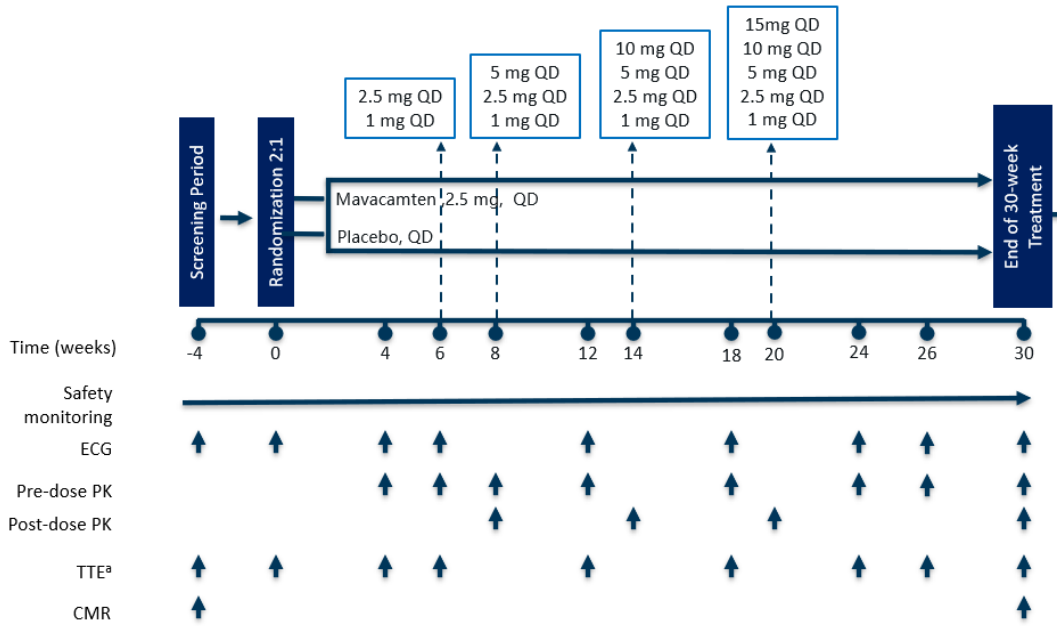
For the days with more than 1 electrocardiogram measurement, the average value of the day was used in the analysis.

eTable 10. Holter Monitoring Results

	Mavacamten	Placebo
Patients with AF, No. (%)		
Baseline	1/54 (1.9)	0/27 (0.0)
Week 12	2/52 (3.8)	0/24 (0.0)
Week 26	1/52 (1.9)	1/25 (4.0)
Patients with ≥1 episode of NSVT, No. (%)		
Baseline	14/54 (25.9)	4/27 (14.8)
Week 12	10/52 (19.2)	3/24(12.5)
Week 26	9/52 (17.3)	5/25 (20.0)

Abbreviations: AF, atrial fibrillation; NSVT, non-sustained ventricular tachycardia.

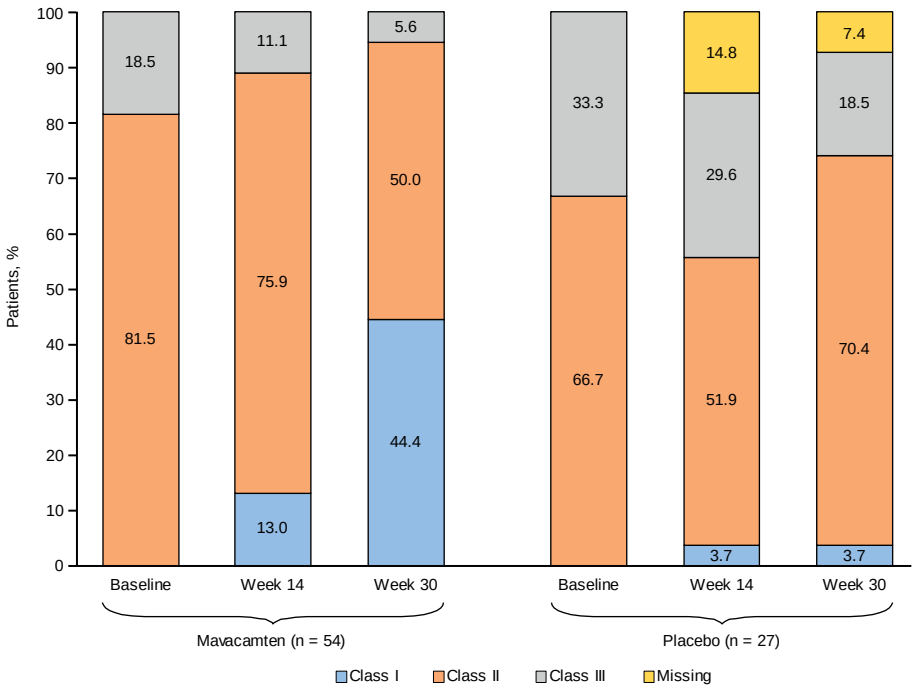
eFigure 1. Study Schema From Screening to Week 30



CMR indicates cardiac magnetic resonance; ECG, electrocardiogram; PK, pharmacokinetics; QD, once daily; TTE, transthoracic echocardiogram.

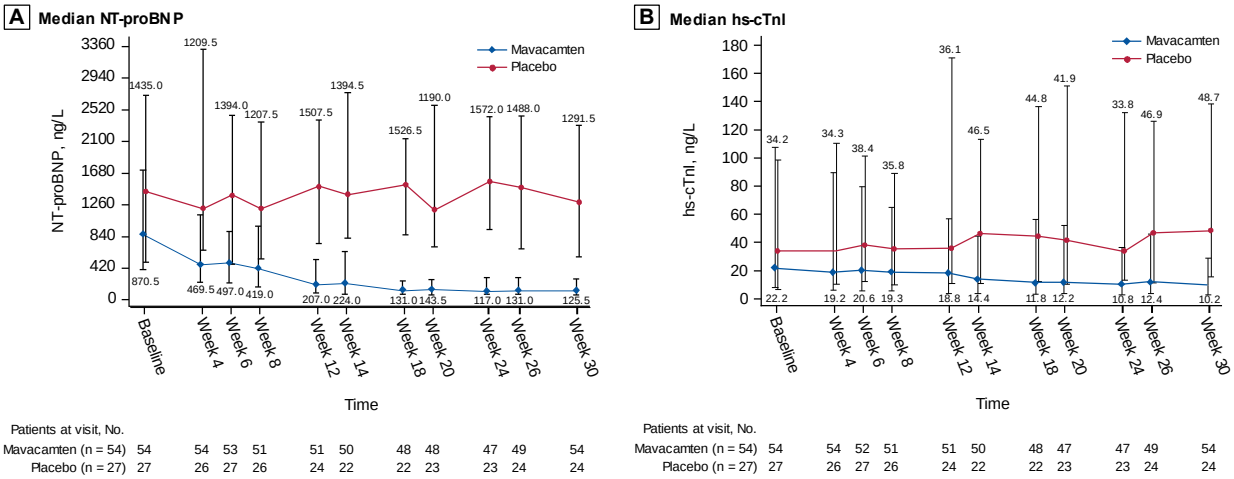
[a] Resting and Valsalva TTE.

eFigure 2. Proportion of Patients Across NYHA Functional Classes at Baseline, Week 14, and Week 30



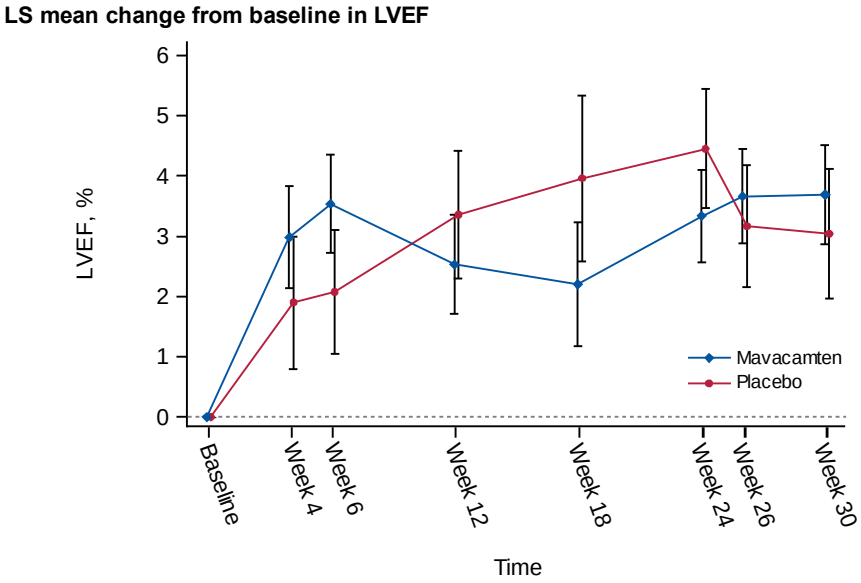
NYHA, New York Heart Association.

eFigure 3. Changes in NT-proBNP (A) and hs-cTnI (B) From Baseline to Week 30



Error bars indicate interquartile range. NT-proBNP, N-terminal pro B-type natriuretic peptide.

eFigure 4. LSM Change in LVEF From Baseline to Week 30



Patients at visit, No.								
Mavacamten (n = 54)	54	52	53	52	44	48	49	54
Placebo (n = 27)	27	25	26	24	21	22	22	24

Error bars indicate standard errors