



CONGRESSO

ROMA, 25 - 27 Giugno 2026

SEDE DEI LAVORI

A. Roma Lifestyle Hotel
Via Giorgio Zoega 59, Roma

**ISCRIZIONE
GRATUITA**

Cardiomiopatia ipertrofica: nuove terapie

Dott.C.Raineri

Divisione di Cardiologia

Città della Salute e della Scienza- Ospedale Molinette



HCM Clinical Spectrum

Prior to 2023, Guideline-Recommended Therapies for HCM

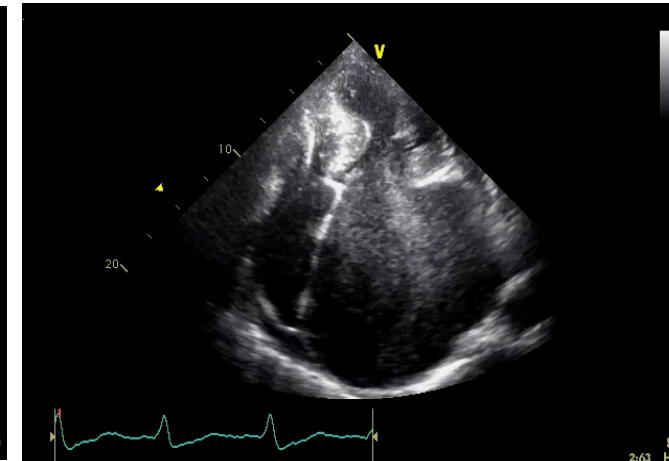
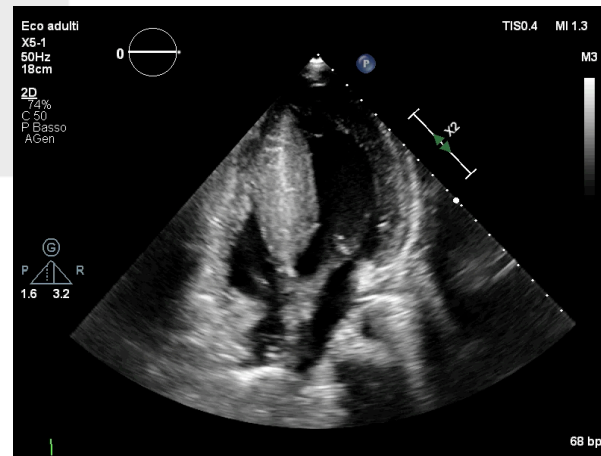
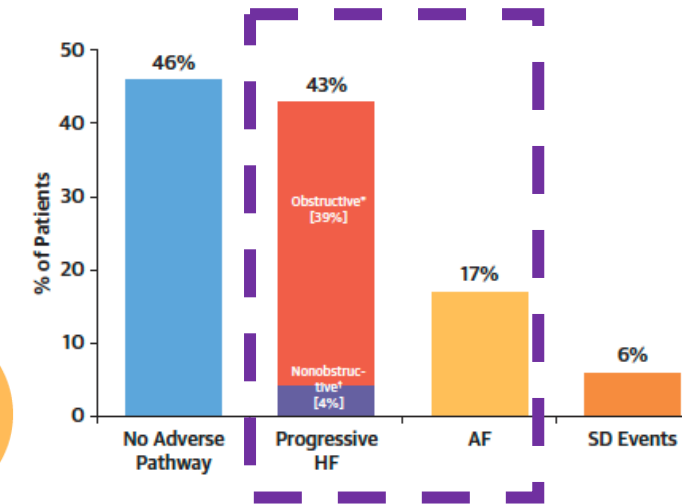
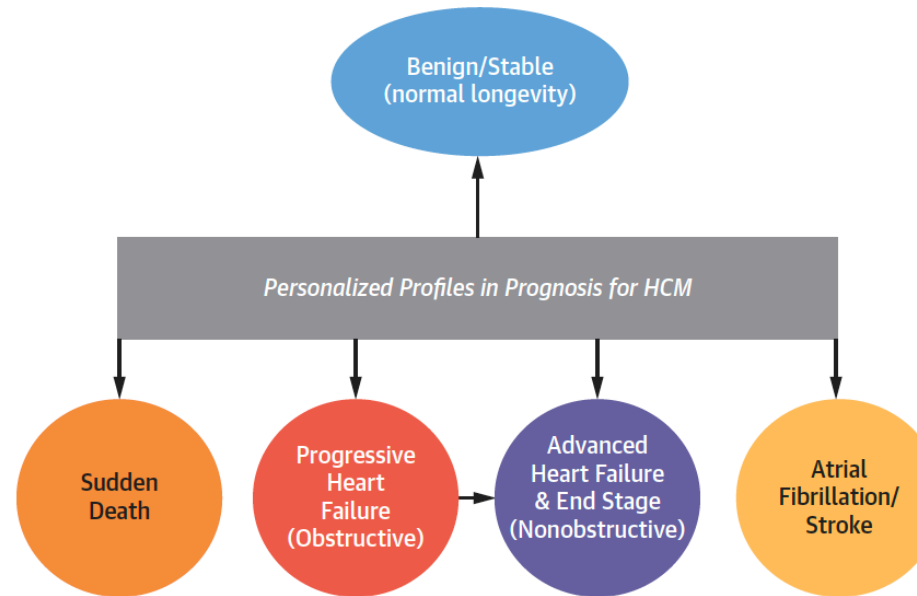
1960s-1970s
 β blockers

2000s-2010s
Disopyramide

1970s-1980s
Calcium channel
blockers

Conventional Medications for oHCM

- Do not target the disease process
- May not provide sufficient symptom relief
- Are often poorly tolerated
- Use is based on studies that are underpowered, not randomized, with short follow-up and mixed results



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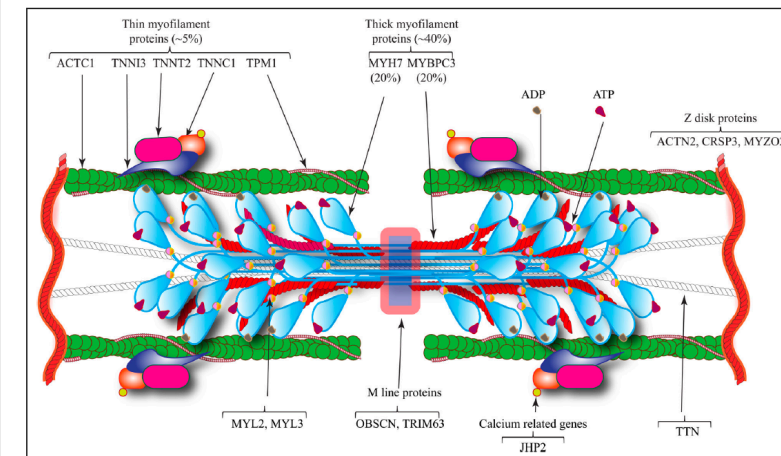
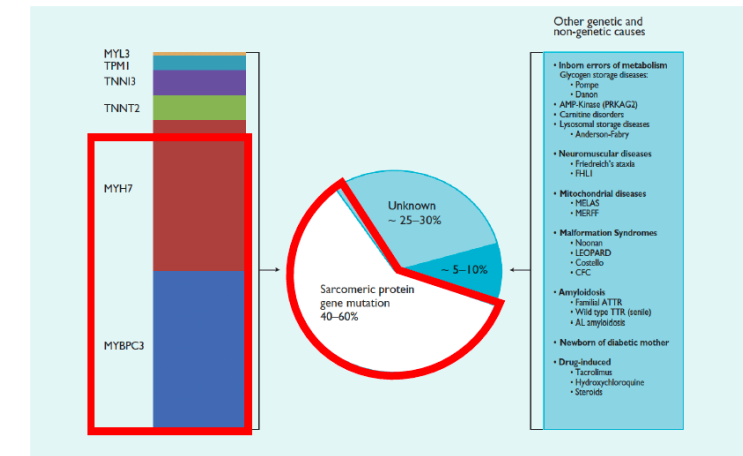
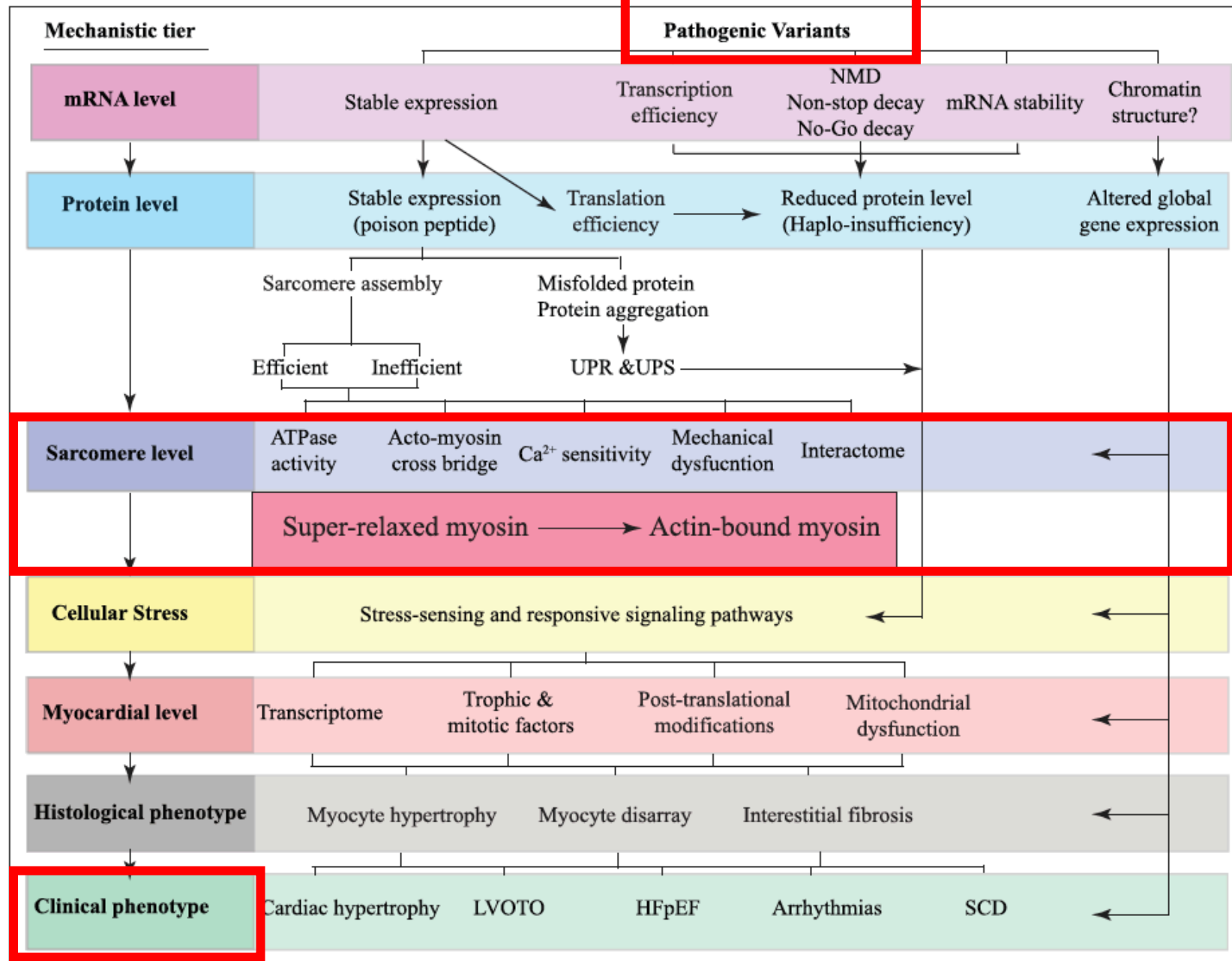
2020
**AHA/ACC HCM
guidelines**

2023
**ESC HCM
guidelines**

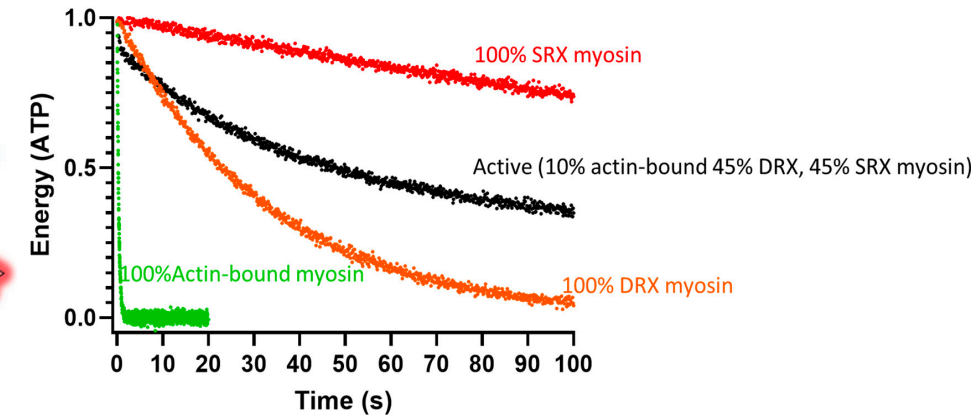
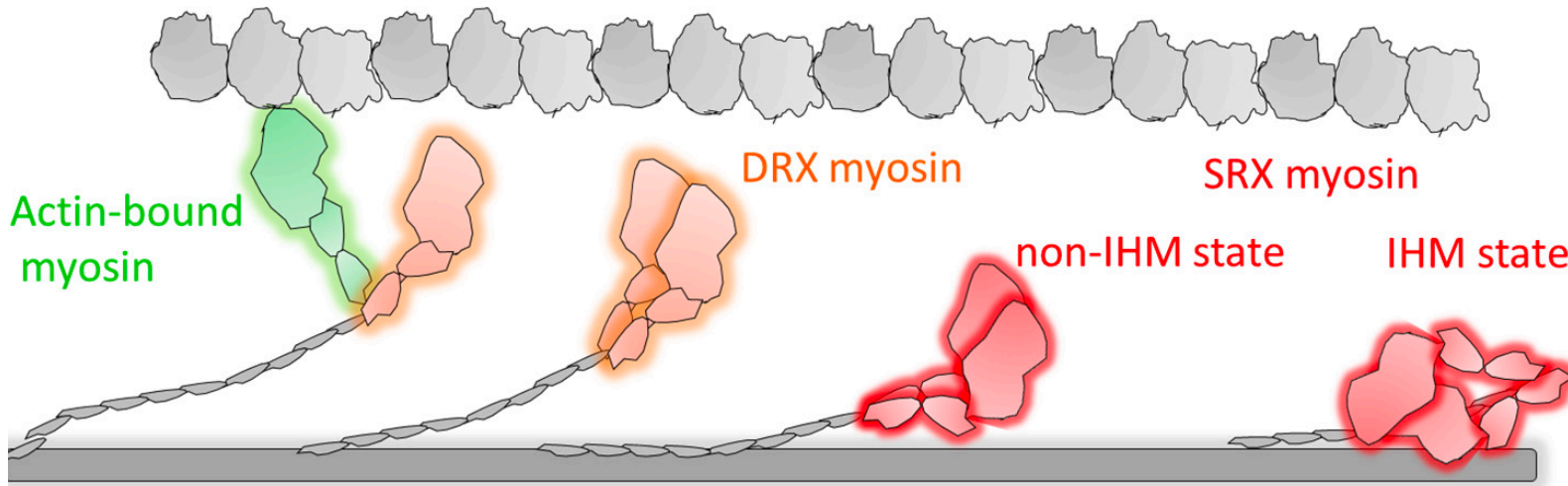
2024
**AHA/ACC HCM
guidelines**

2022
**First CMI,
mavacamten,
FDA-approved**

Pathogenesis of Hypertrophic Cardiomyopathy



"DIFFERENT" Myosin Configuration



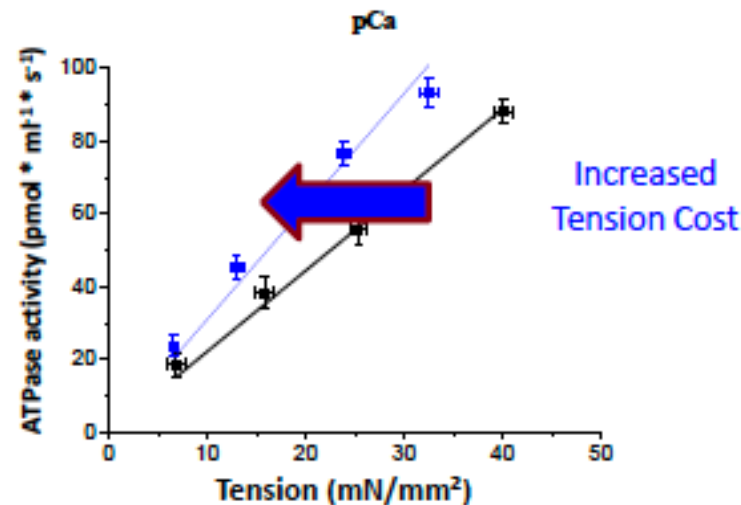
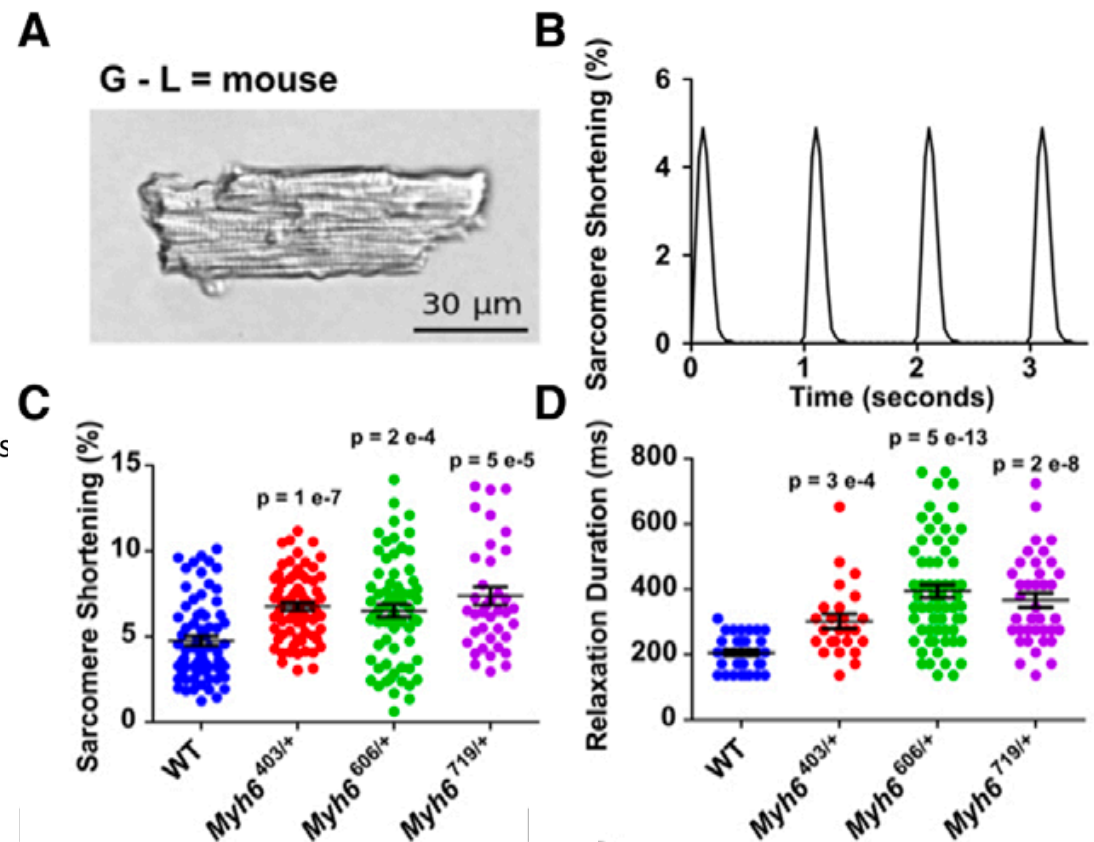
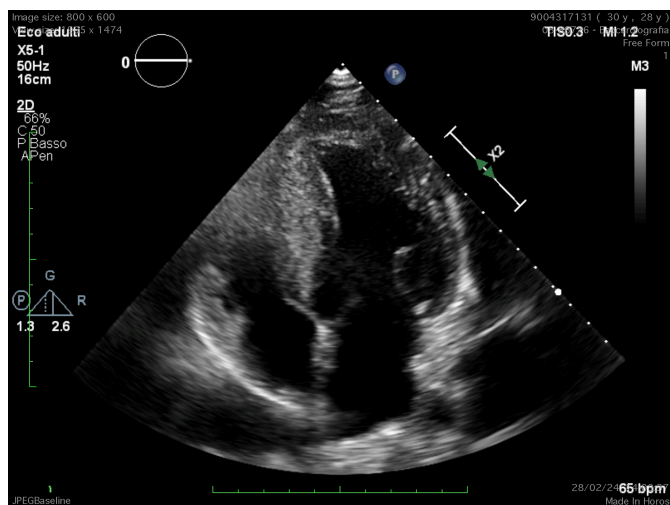
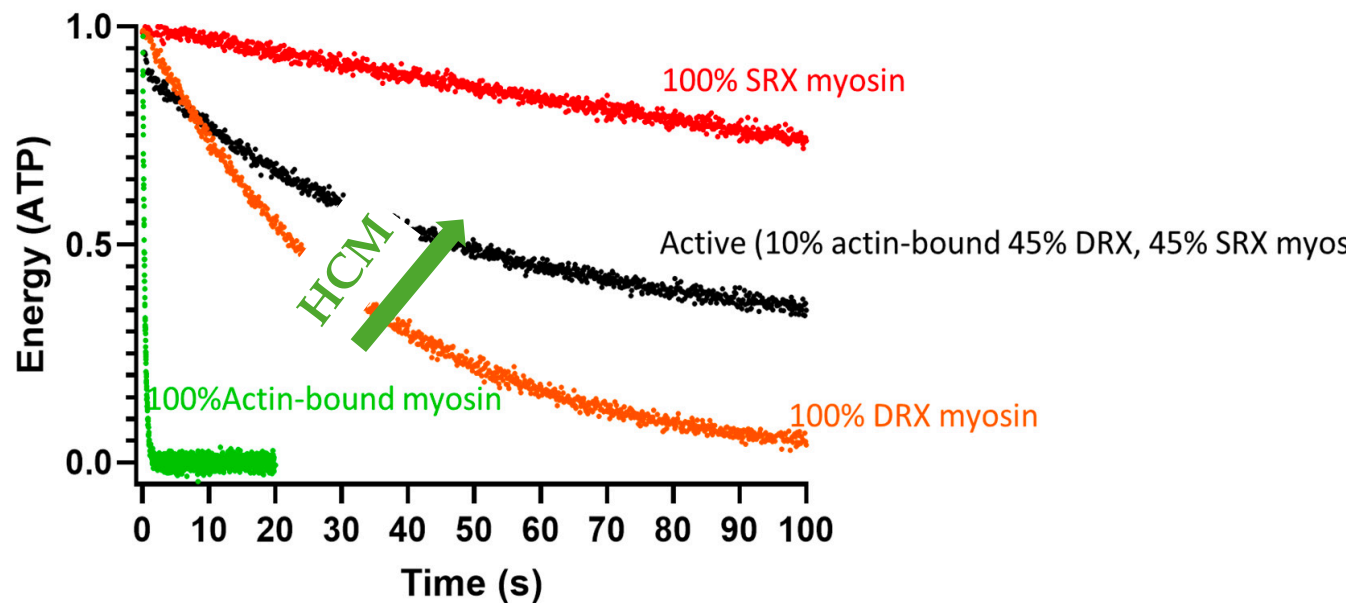
"Active"

Disordered-Relaxed (DRX)

Super-relaxed (SRX)



HCM Hypercontractility

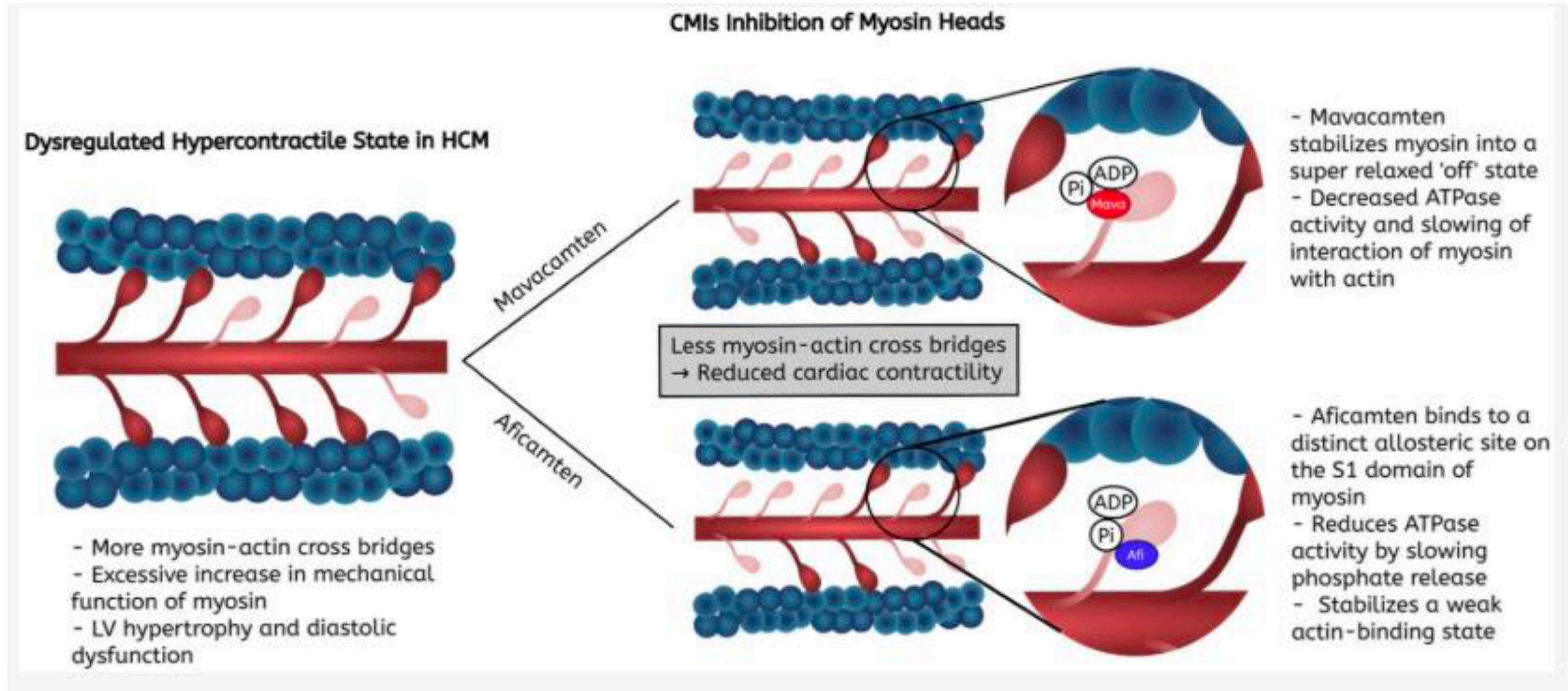


- Energy Profligation
- Mitochondrial Dysfunction
- Myocardial Hypertrophy
- Myocardial Fibrosis



Hypercontractility

Cardiac Myosin Inhibitor in HCM



Cardiac Myosin Inhibitor in HCM: clinical trial

MAVACAMTEN



EXPLORER-HCM

ValorHCM

- Improve oxygen consumption
- Gradient reduction 50 mmhg
- Improve at least one NYHA class in > 60% of pts
- Improve quality of life
- Reduce NT-proBNP
- Same effect in patients with oHCM regardless of the genetic testing results
- Satisfactory safety profile (aficamten > mavacamten)

AFICAMTEN

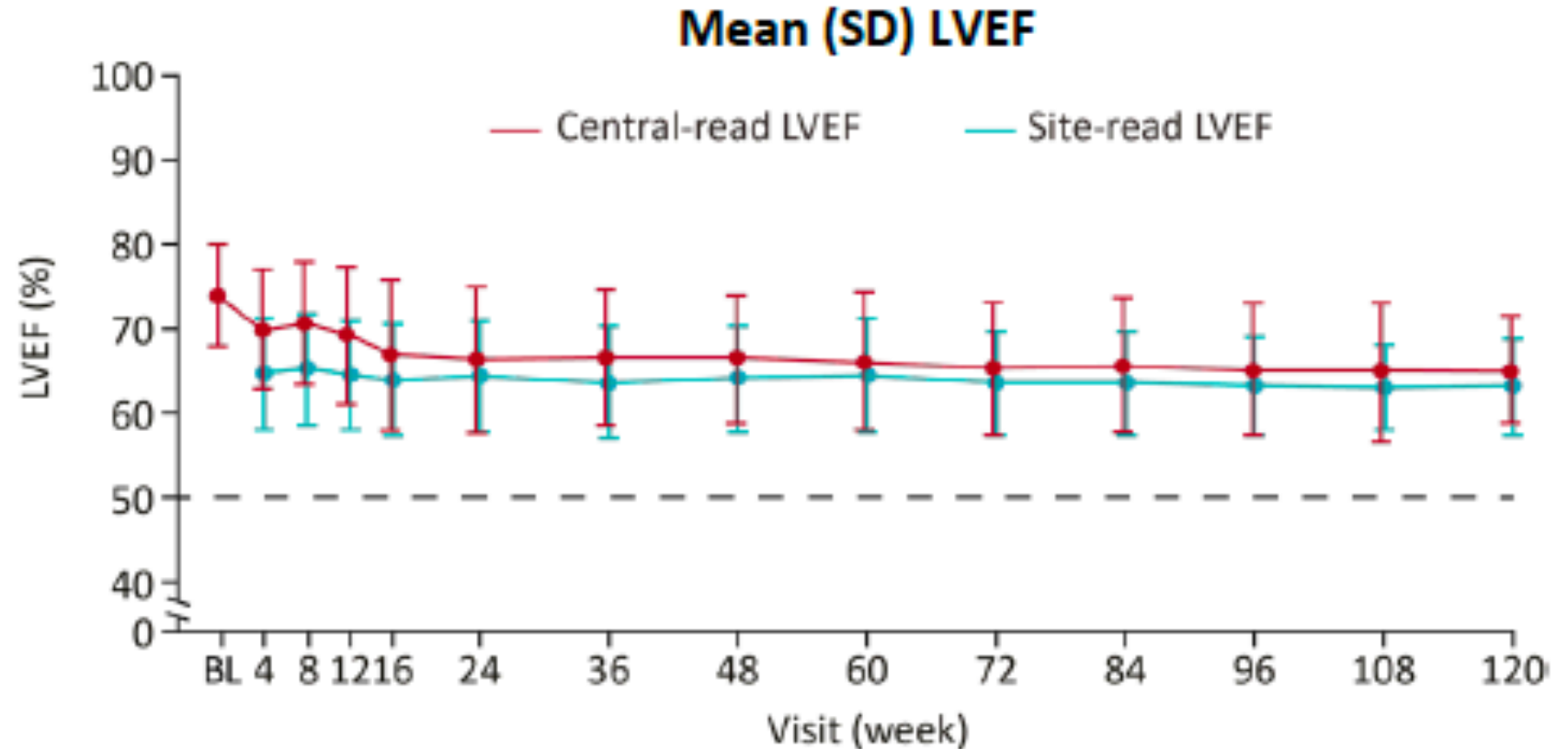


Olivotto I et al. EXPLORER-HCM. Lancet 2020
Desai MY et al. VALOR-HCM. J Am Coll Cardiol 2022
García-Pavia P et al, NEJM 2025

MAVA-LTE: Sustained Improvements in Cardiac Function and Symptoms at 3.5 Years With Mavacamten

Participants from EXPLORER-HCM (N = 231) sustained reductions at wk 180

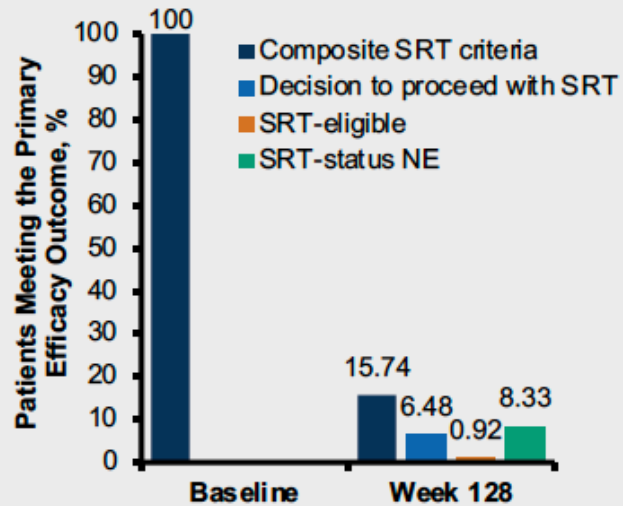
- LVOTG -40.3 mmHg
- vLVOTG -55.3 mmHg
- NT-proBNP -562
- EQ-5D-5L score 0.09
- LVEF decreased from 73.9% to 63.9%
- 77.9% improved by ≥ 1 NYHA class



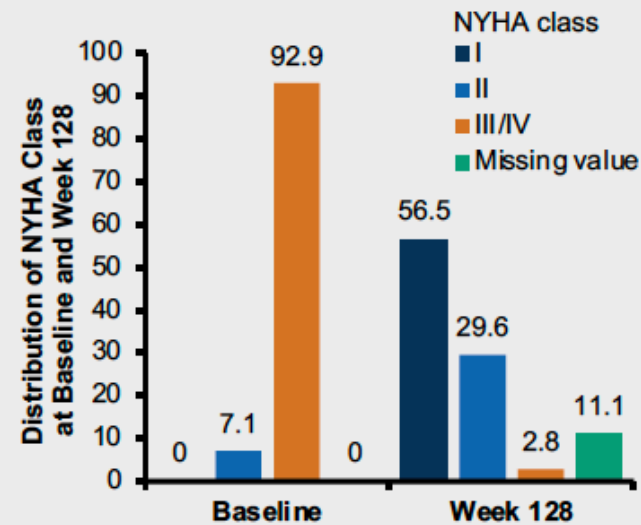
VALOR-HCM: Sustained Freedom From SRT Observed at 128 Weeks in Symptomatic Patients With oHCM

At week 128, 15.7% of patients met the composite endpoint (7 underwent SRT, 1 SRT-eligible, and 9 SRT-status unevaluable)

Primary Composite Endpoint

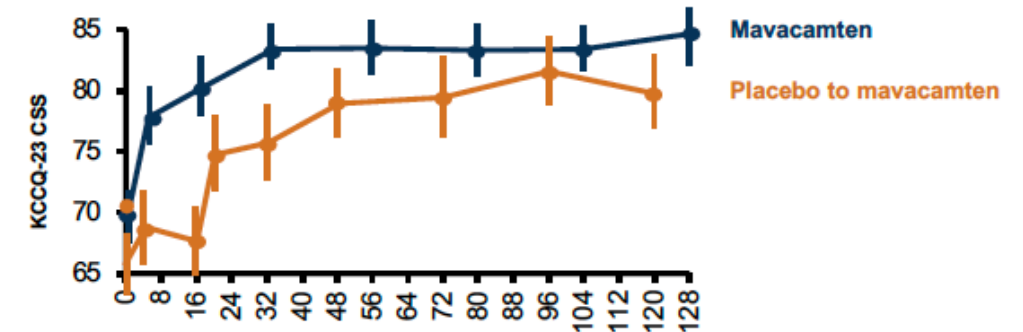


Improvement in NYHA Class

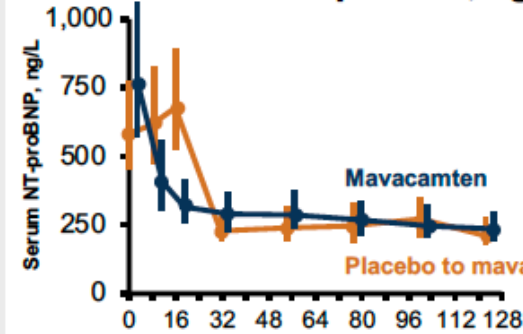


Changes in Health Status and Biomarkers

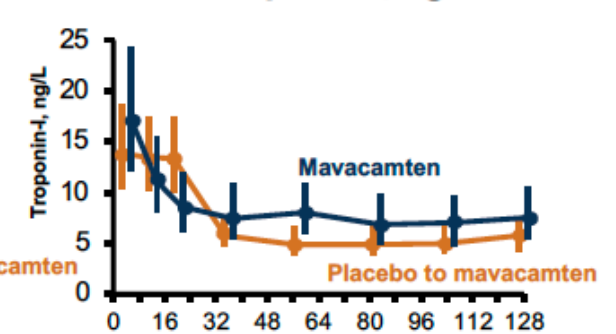
KCCQ-23 CSS



Serum NT-proBNP, ng/L

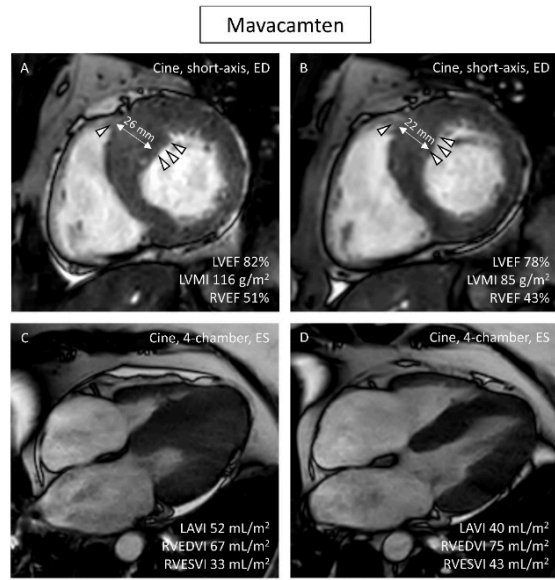


Troponin-I, ng/L



Time Since Randomization, wk

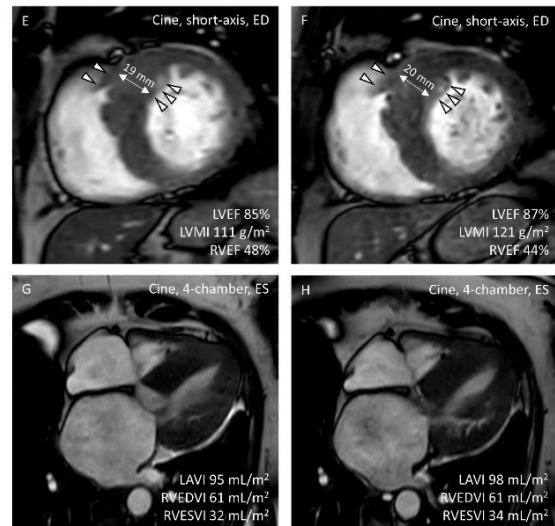
One-year functional and structural effects of mavacamten: CMR study



Baseline

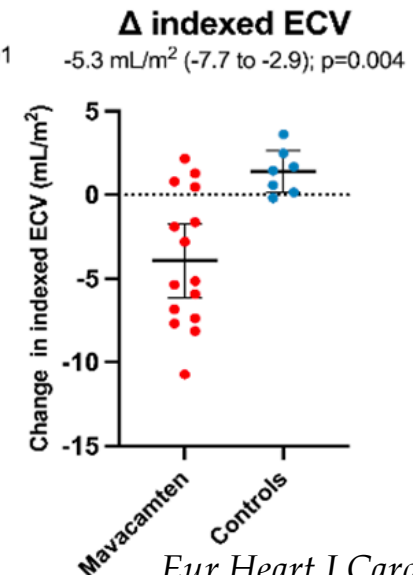
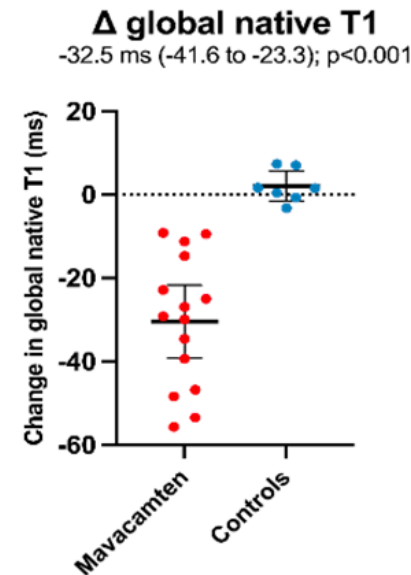
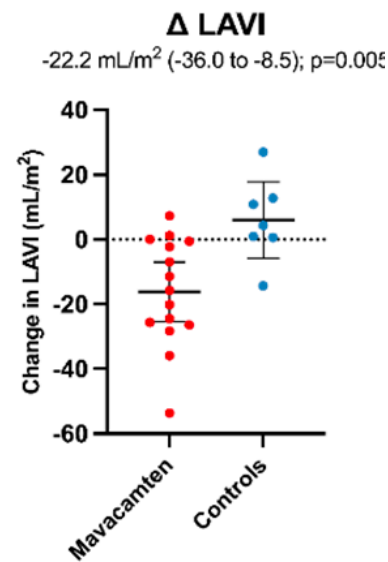
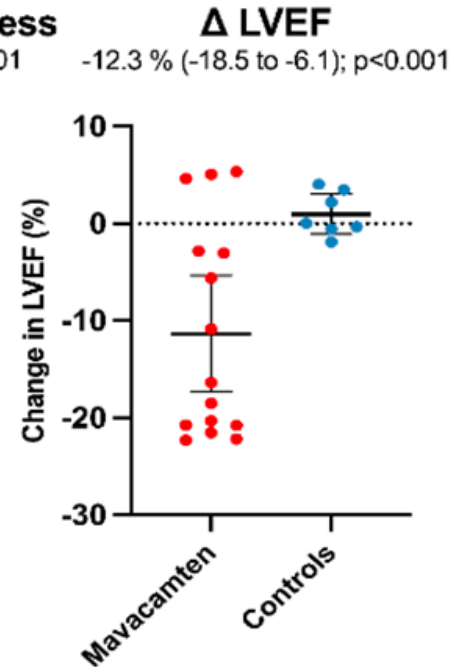
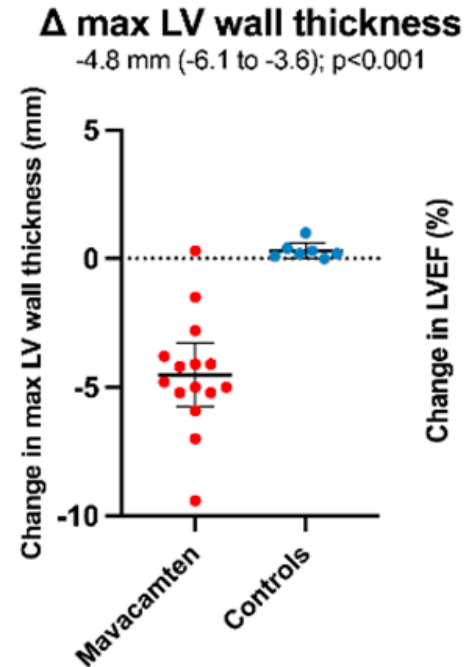
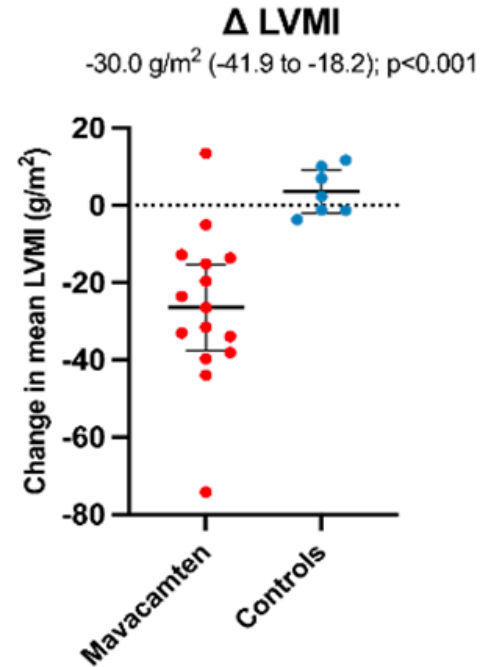
Follow-Up

Control

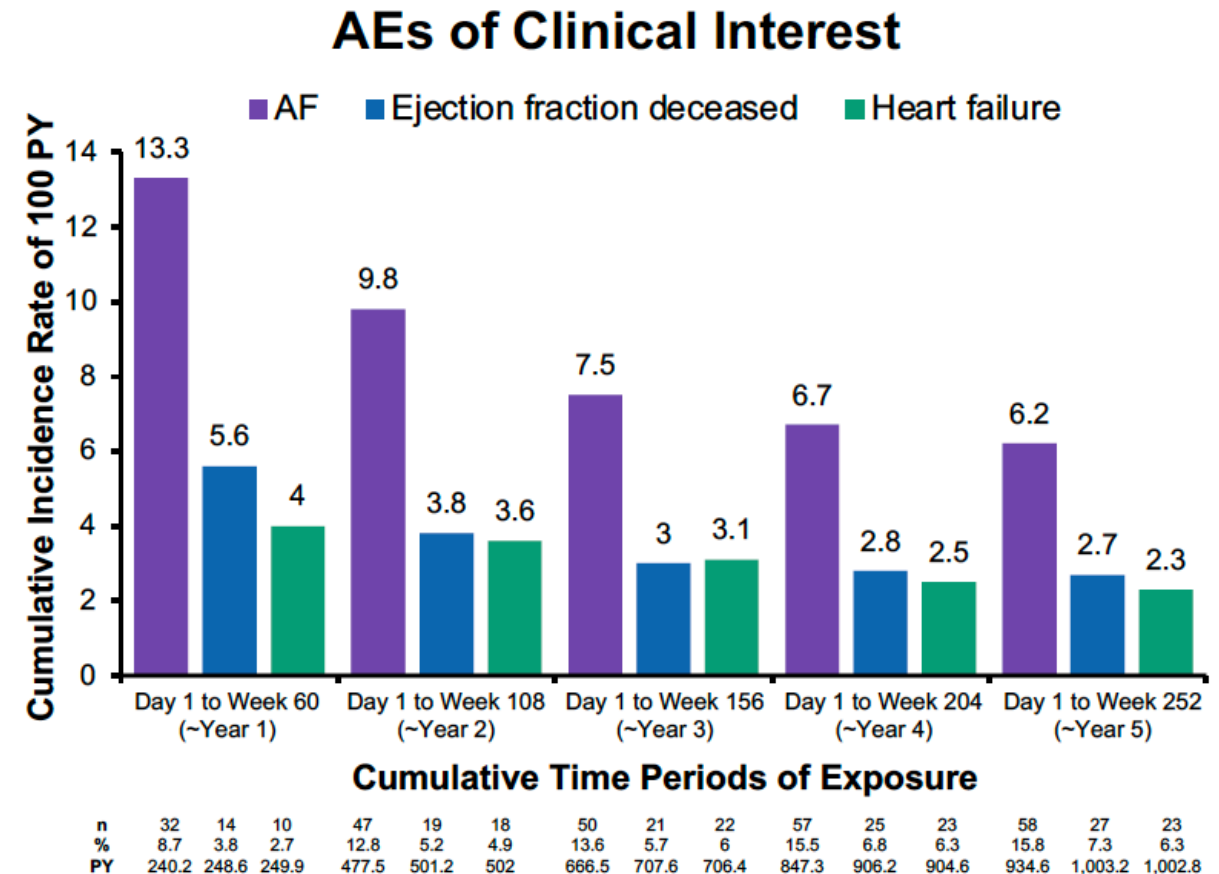
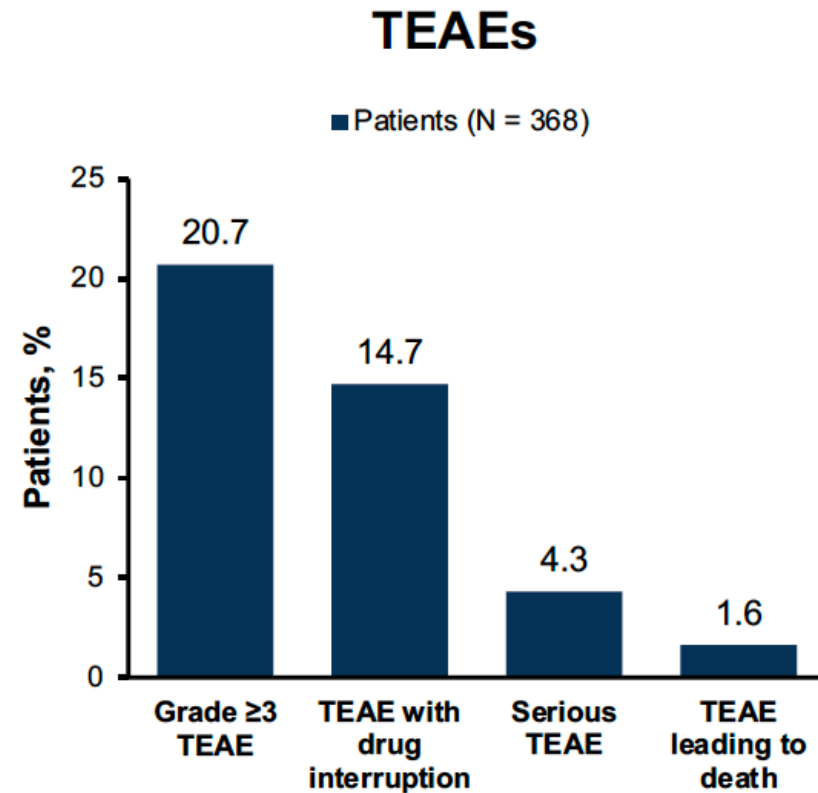


Baseline

Follow-Up



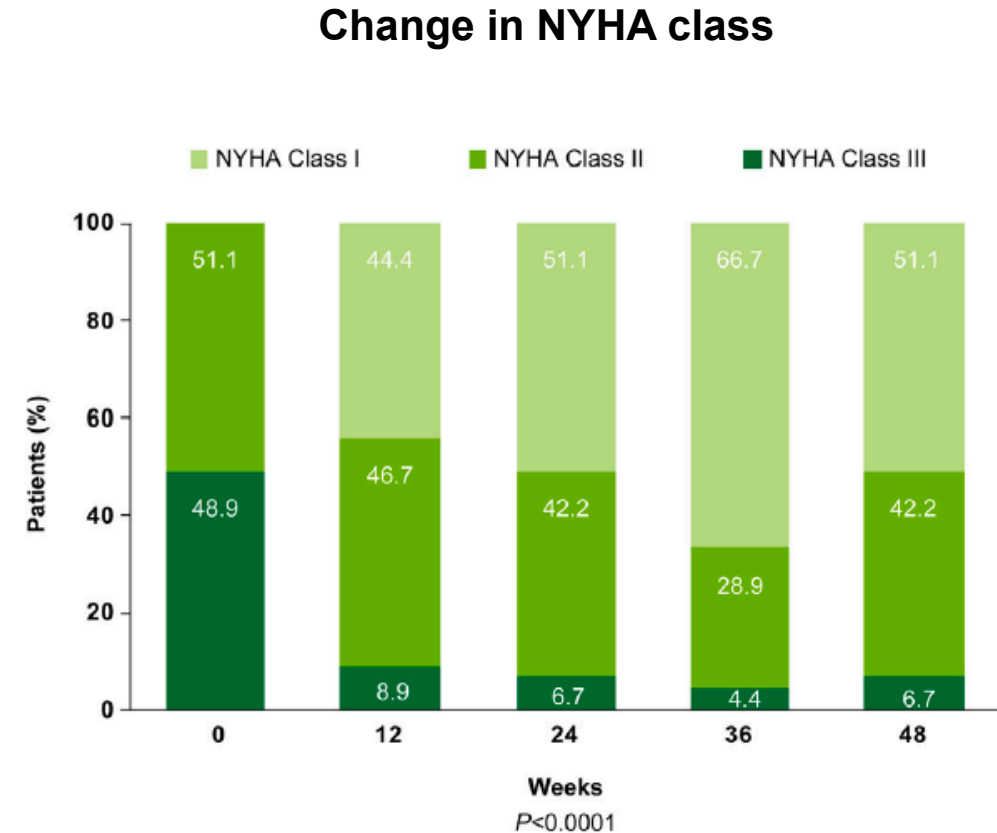
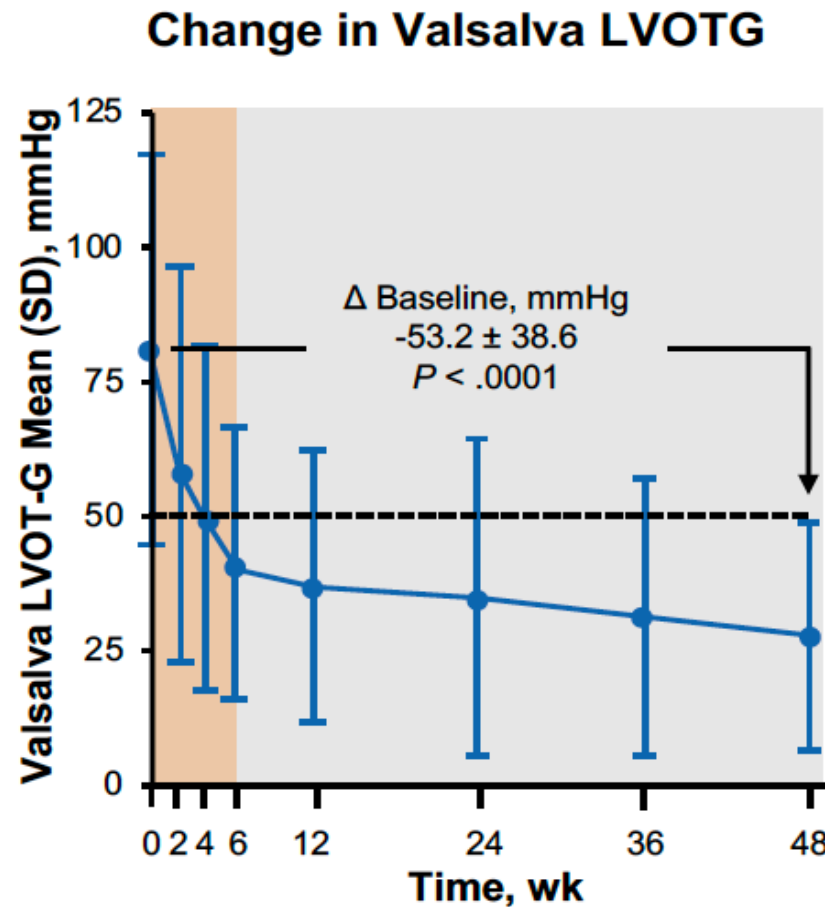
Pooled Safety Data for Mavacamten in oHCM Across 5 Trials Over 5 Years: Well Tolerated and TEAEs Decreased Over Time



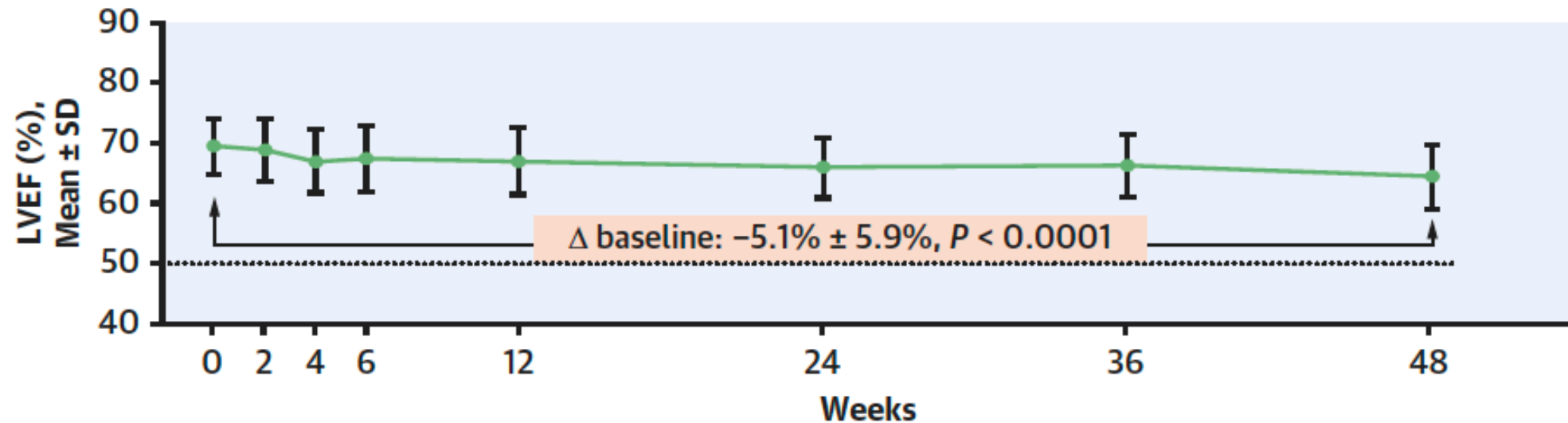
FOREST-HCM: Sustained 48-Week Efficacy in Symptoms and Cardiac Function With Aficamten in Patients with oHCM

Participants from REDWOOD-HCM and SEQUOIA-HCM could enroll (N = 213); 48-week data available for n = 46

- LVOTG -40 mmHg
- vLVOTG -53 mmHg
- NT-proBNP -63%

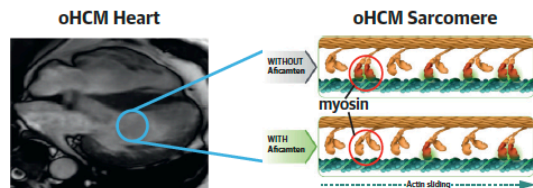


FOREST-HCM: Sustained 48-Week Efficacy in Symptoms and Cardiac Function With Aficamten in Patients with oHCM



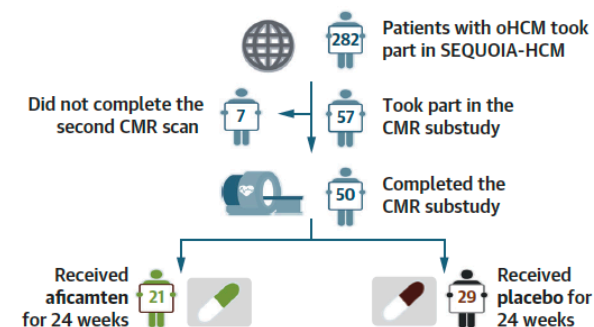
SEQUOIA-HCM CMR Substudy

Aficamten for Obstructive Hypertrophic Cardiomyopathy (oHCM)

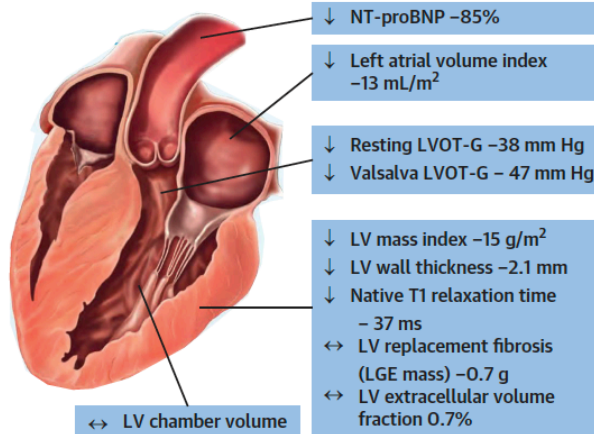


Aficamten decreases myocardial hypercontractility by reversibly binding to cardiac myosin and reducing excessive myosin-actin cross-bridges

SEQUOIA-HCM Cardiovascular Magnetic Resonance (CMR) Trial

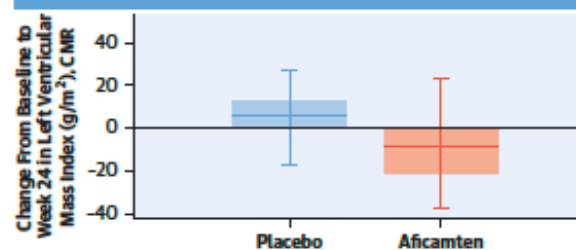


Placebo-Corrected Changes From Baseline to Week 24 in Patients Receiving Aficamten

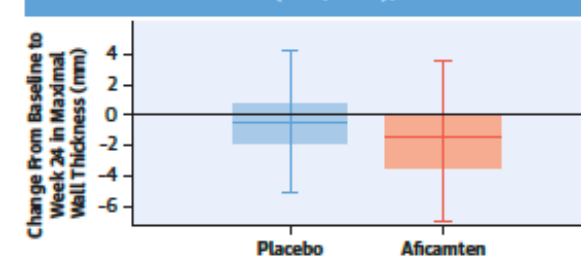


Down arrows indicate a statistically significant reduction from baseline. Data are the least squares mean.

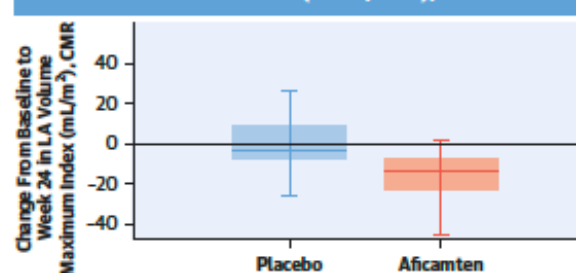
A Left Ventricular Mass Index (g/m²), CMR -15.4 (-24.5, -6.3); P = 0.001



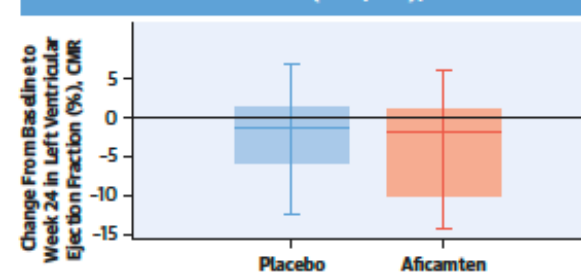
B Maximal Wall Thickness (mm) -1.2 (-1.8, -0.6); P < 0.001



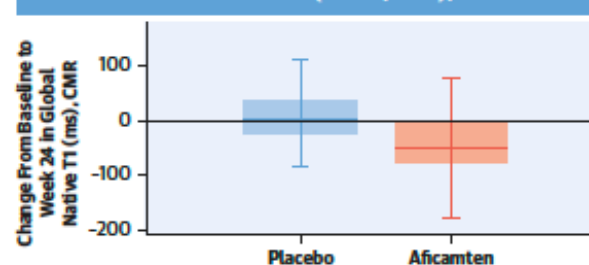
C LA Volume Maximum Index (mL/m²), CMR -12.8 (-19.0, -6.7); P < 0.001



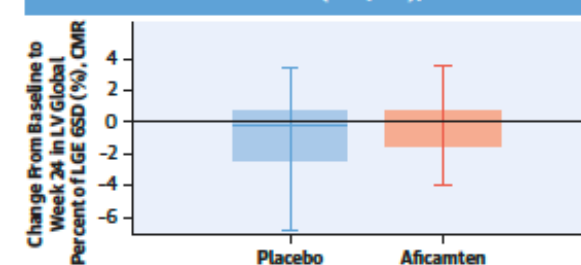
D Left Ventricular Ejection Fraction (%), CMR -2.6 (-5.9, 0.7); P = 0.122



E Global Native T1 (ms), CMR -36.8 (-68.8, -4.7); P = 0.026

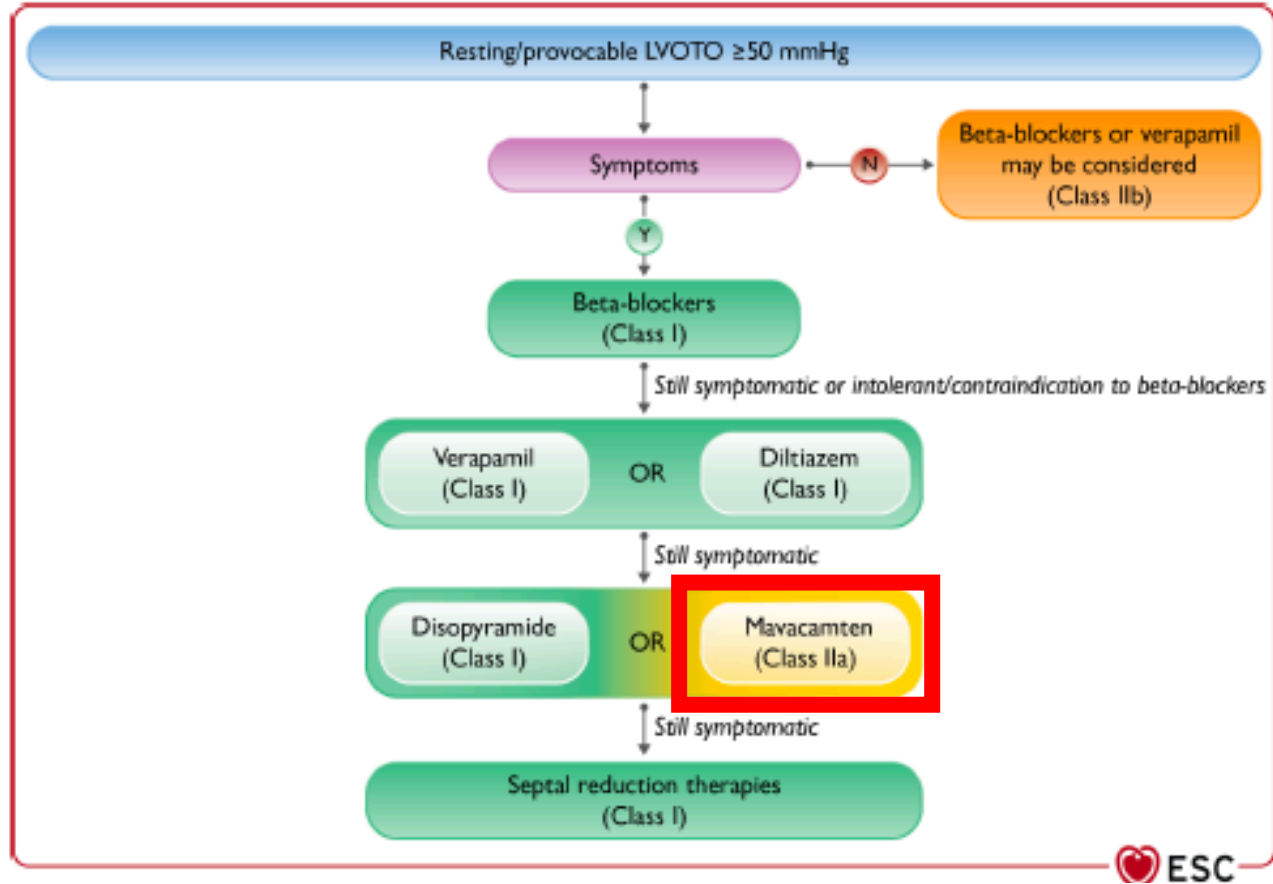


F LV Global Percent of LGE 6SD (%), CMR -0.4 (-2.1, 1.2); P = 0.60

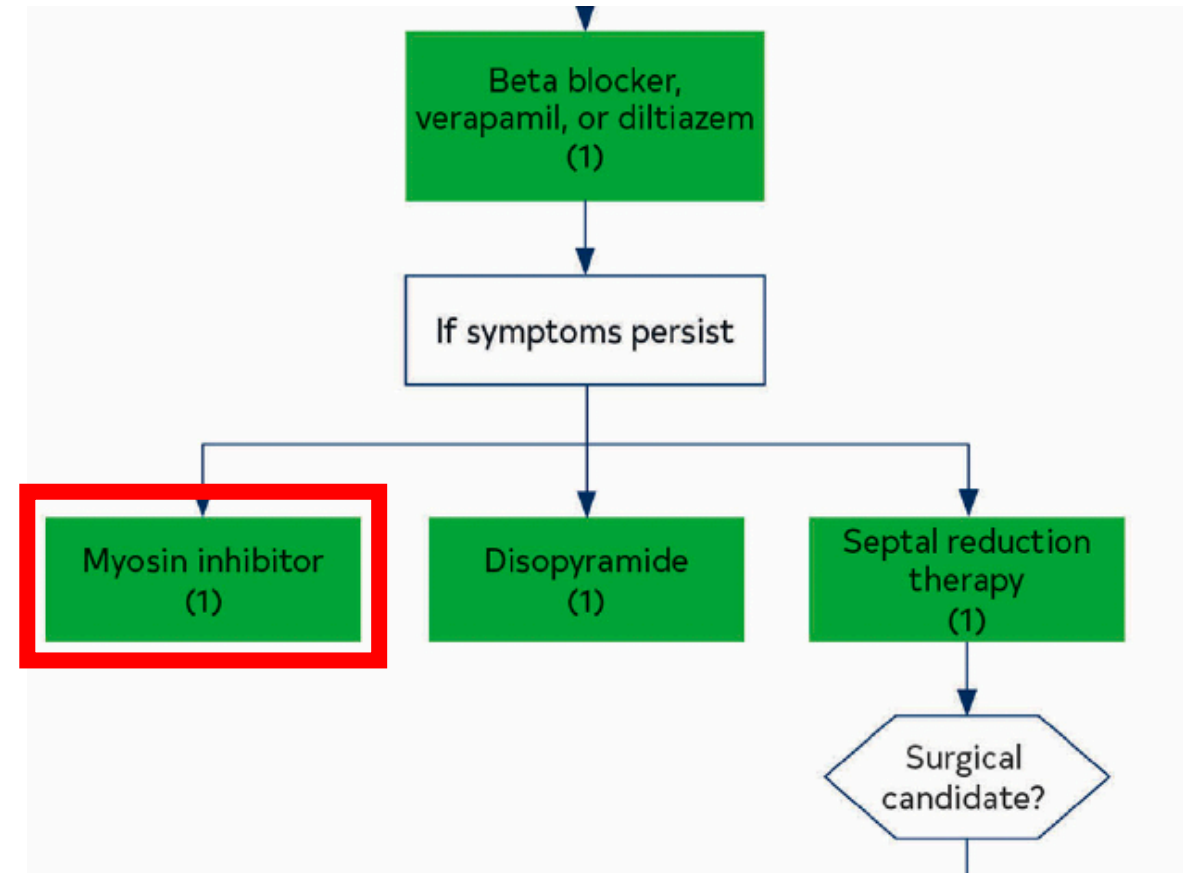


Management of LV outflow obstruction

2023 ESC HCM Guidelines



2024 AHA/ACC HCM Guidelines



Two Myosin Inhibitors APPROVED in Europe

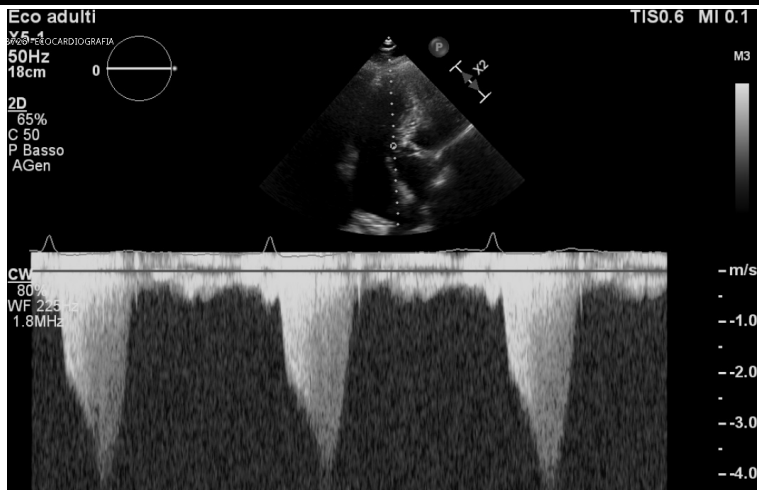
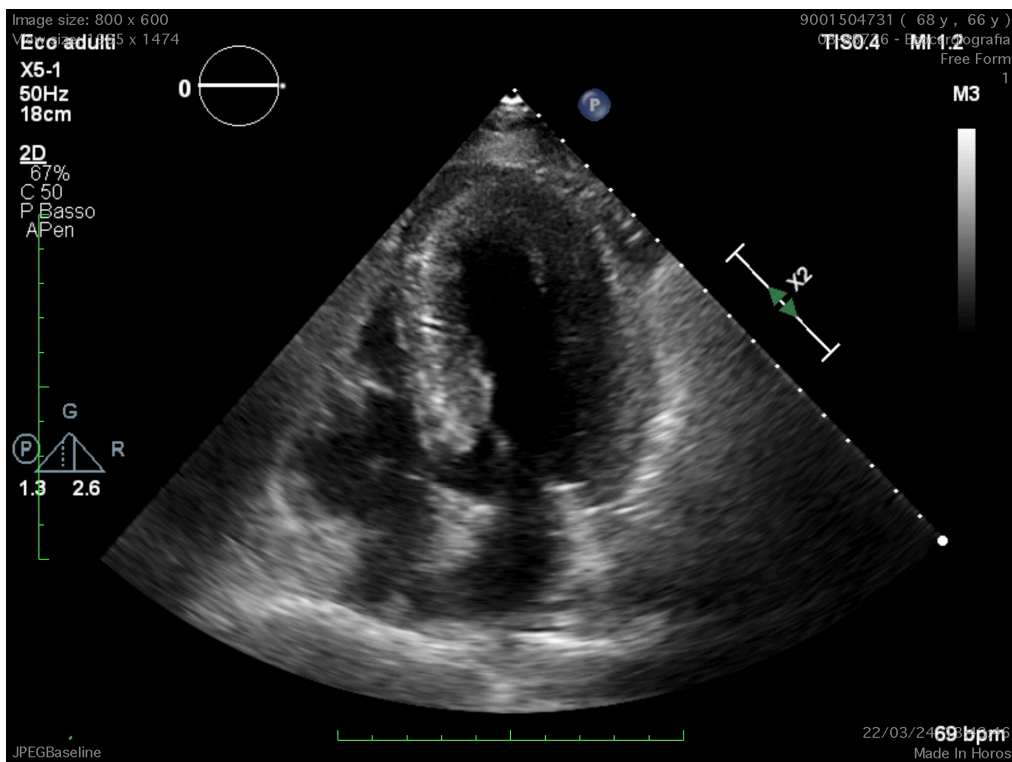
CAMZYOSTM
(mavacamten) 2.5, 5, 10, 15mg
capsules

EUROPEAN COMMISSION APPROVAL
JUN 2023

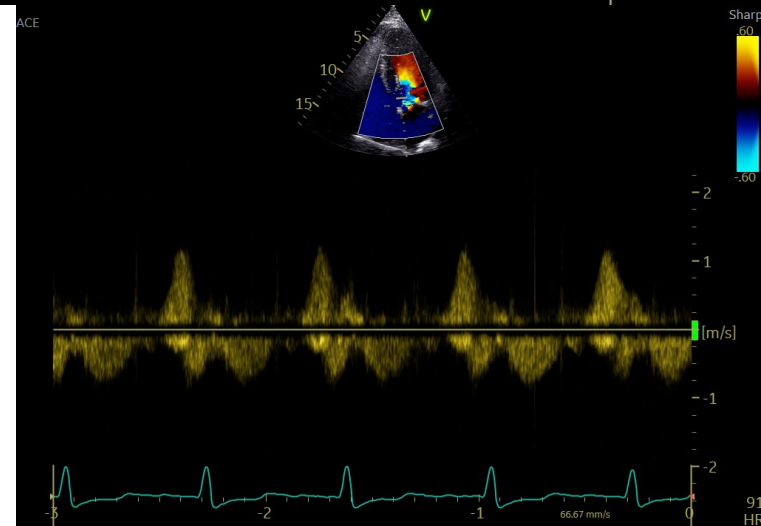
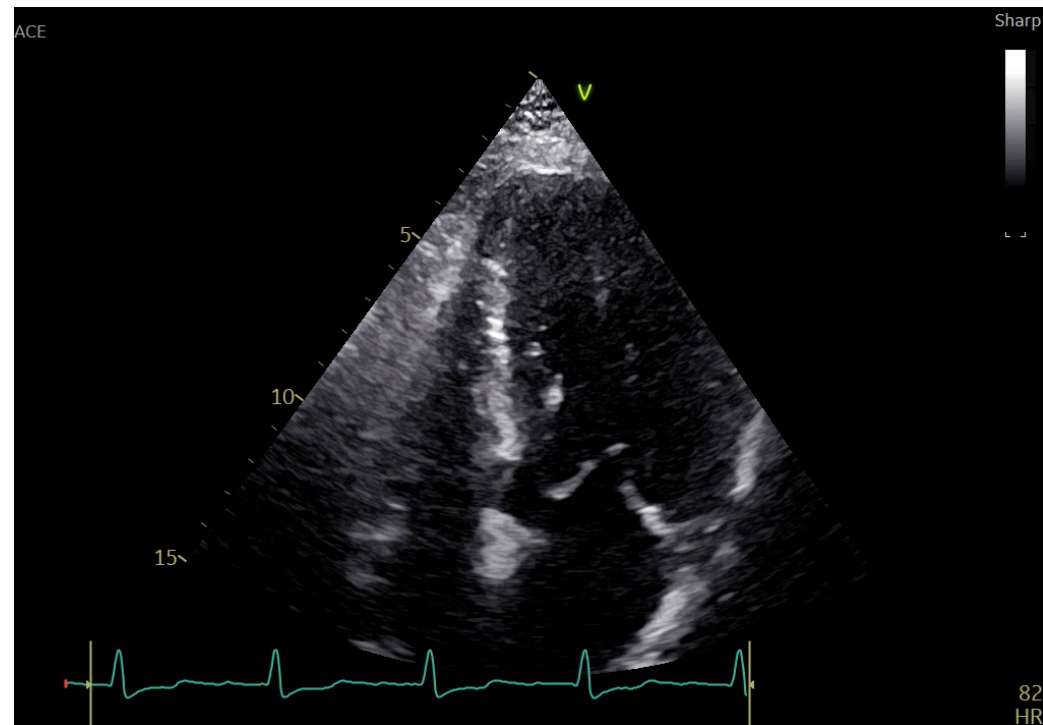
 **MYQORZO**TM
(aficamten) 5·10·15·20mg
tablets

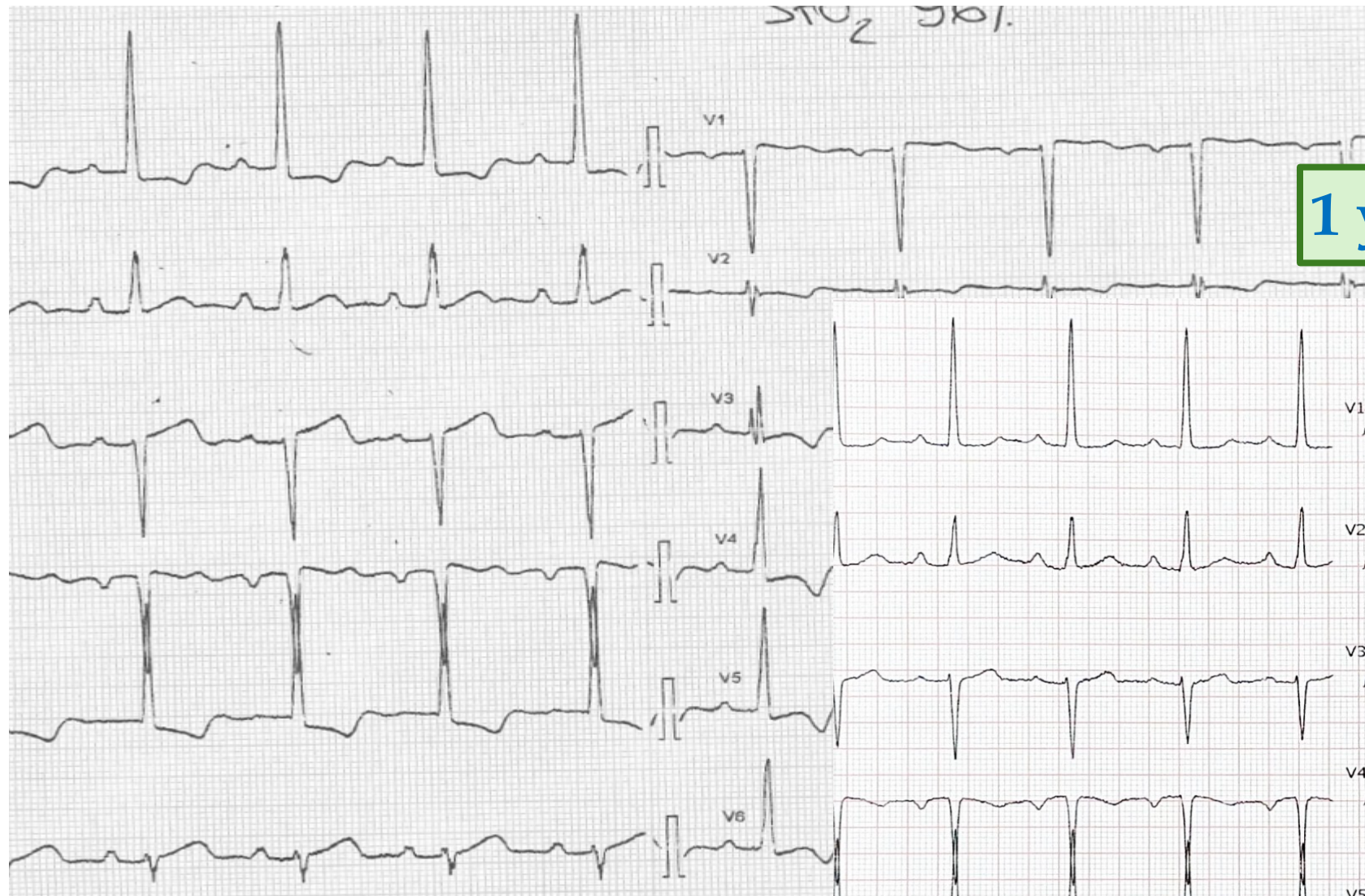
EUROPEAN COMMISSION APPROVAL
FEB 2026

Before -Mavacamten

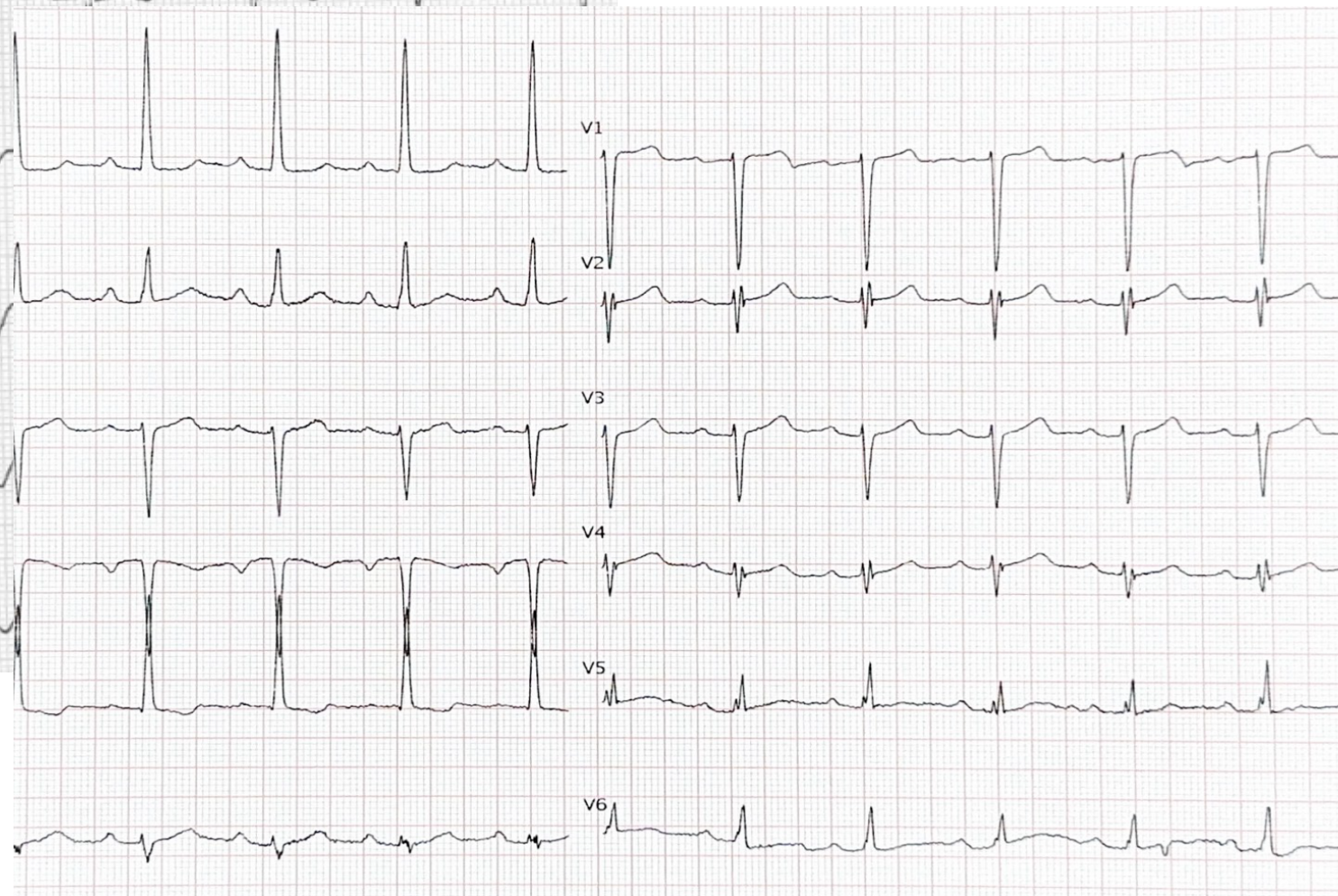


1 year on Macavacamten





1 year on Macavacamten



Before -Mavacamten

Reduced LVEF may occur

Mavacamten reversibly
reduces hypercontractility

Monitor LVEF

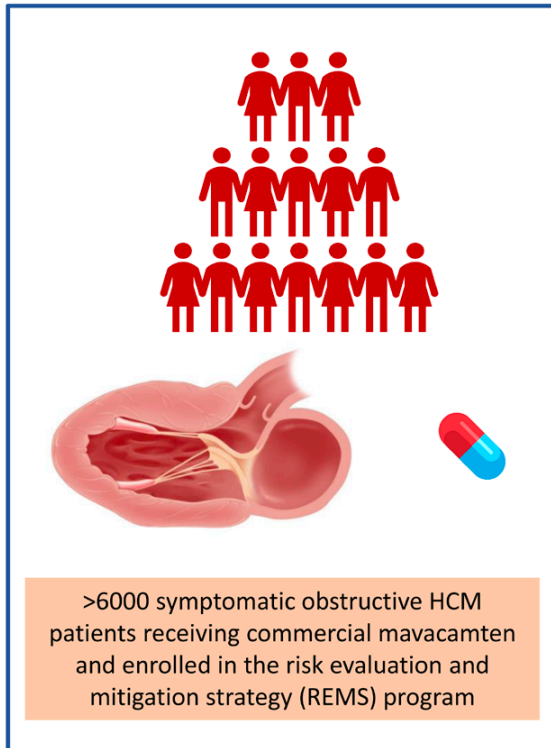
Don't initiate if LVEF <55%
Interrupt use if LVEF <50%,
HF sx, or worsening status

DDIs can increase the risk of HF

- Some CYP450 inhibitors or inducers
- Strong CYP2C19 inhibitors
- Mod-to-strong CYP2C19 inducers
- Mod-to-strong CYP3A4 inducers

- **Check** medication list at every visit
- **Review** DDIs before initiating any new Rx or OTC medication

Mavacamten REMS Program First 22 Months



CAMZYOS[®] REMS
Patient Status Form

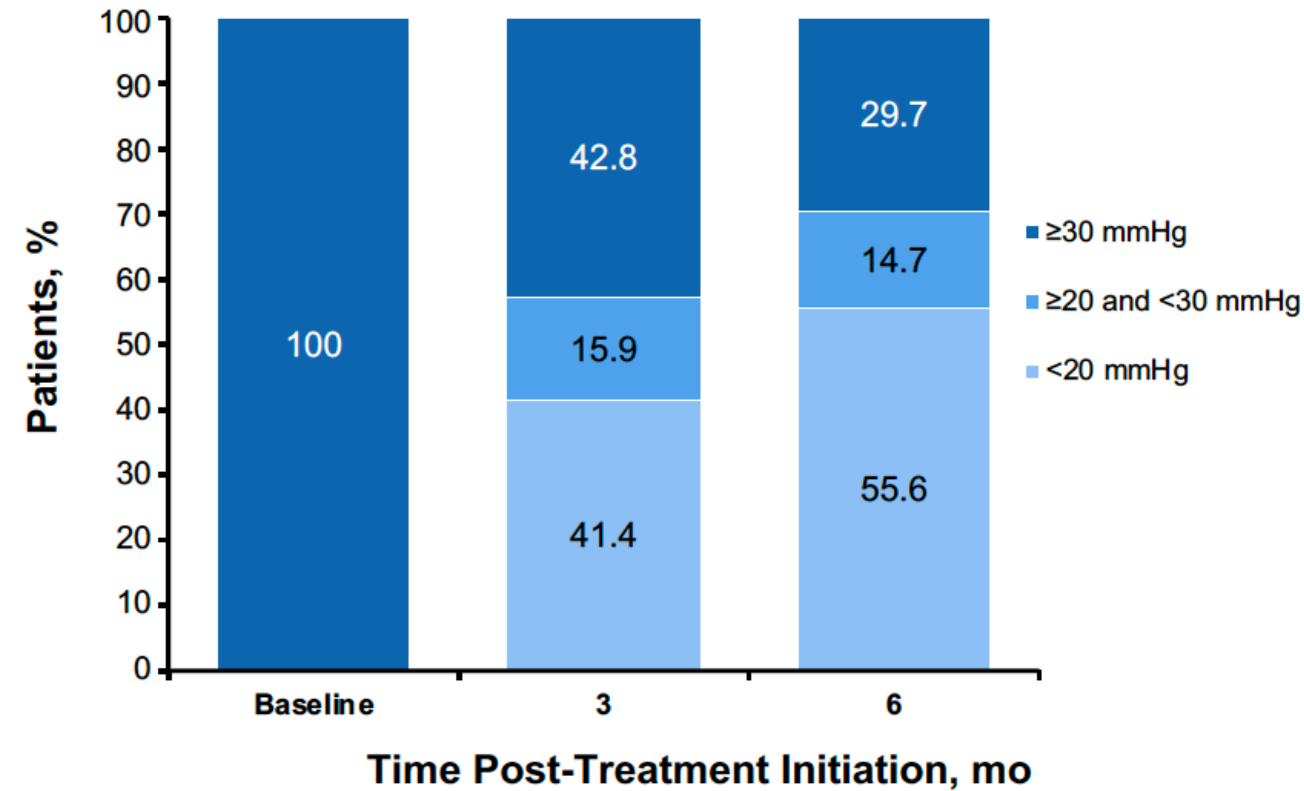
Patient Information
(Fields marked * are REQUIRED)
Patient First Name: _____ Middle Initial: _____ Last Name: _____
Birthdate (MM/DD/YYYY): _____ Phone: _____ Area Code/Telephone Number: _____

Healthcare Provider Information
(Fields marked * are REQUIRED)
Healthcare Provider First Name: _____ Last Name: _____
Healthcare Provider NPI #: _____ *Phone: _____ Area Code/Telephone Number: _____
*Fax: _____ *Email: _____

Healthcare Provider Agreement
☐ I acknowledge that I have counseled the patient on the:
• Risk of heart failure due to systolic dysfunction, including how to recognize and respond to the symptoms of heart failure due to systolic dysfunction
• Risk of drug-drug interactions with CYP2C9 and CYP3A4 inhibitors and inducers and the need to inform healthcare providers of all the prescription and nonprescription medication they take
☐ I acknowledge that the **Prescribing Information** states that the patient should receive echocardiograms.
☐ I acknowledge that I have assessed the patient's prescription and nonprescription medications and supplements for drug-drug interactions.

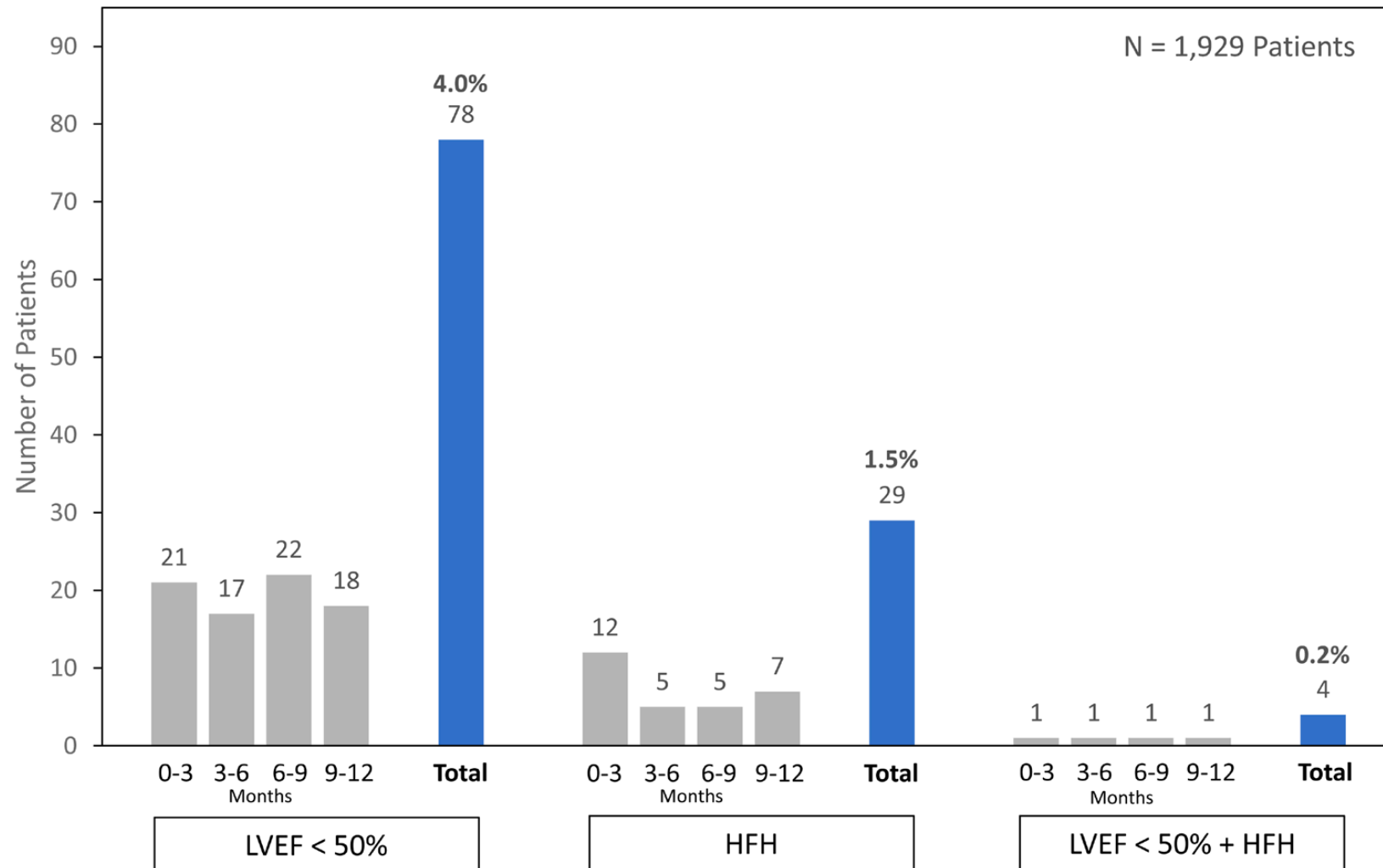
All patients underwent recommended echocardiograms following enrollment in the REMS program, followed by electronic submission of Patient Status Forms

Treatment With Mavacamten for 6 Months:
LVOT Gradients

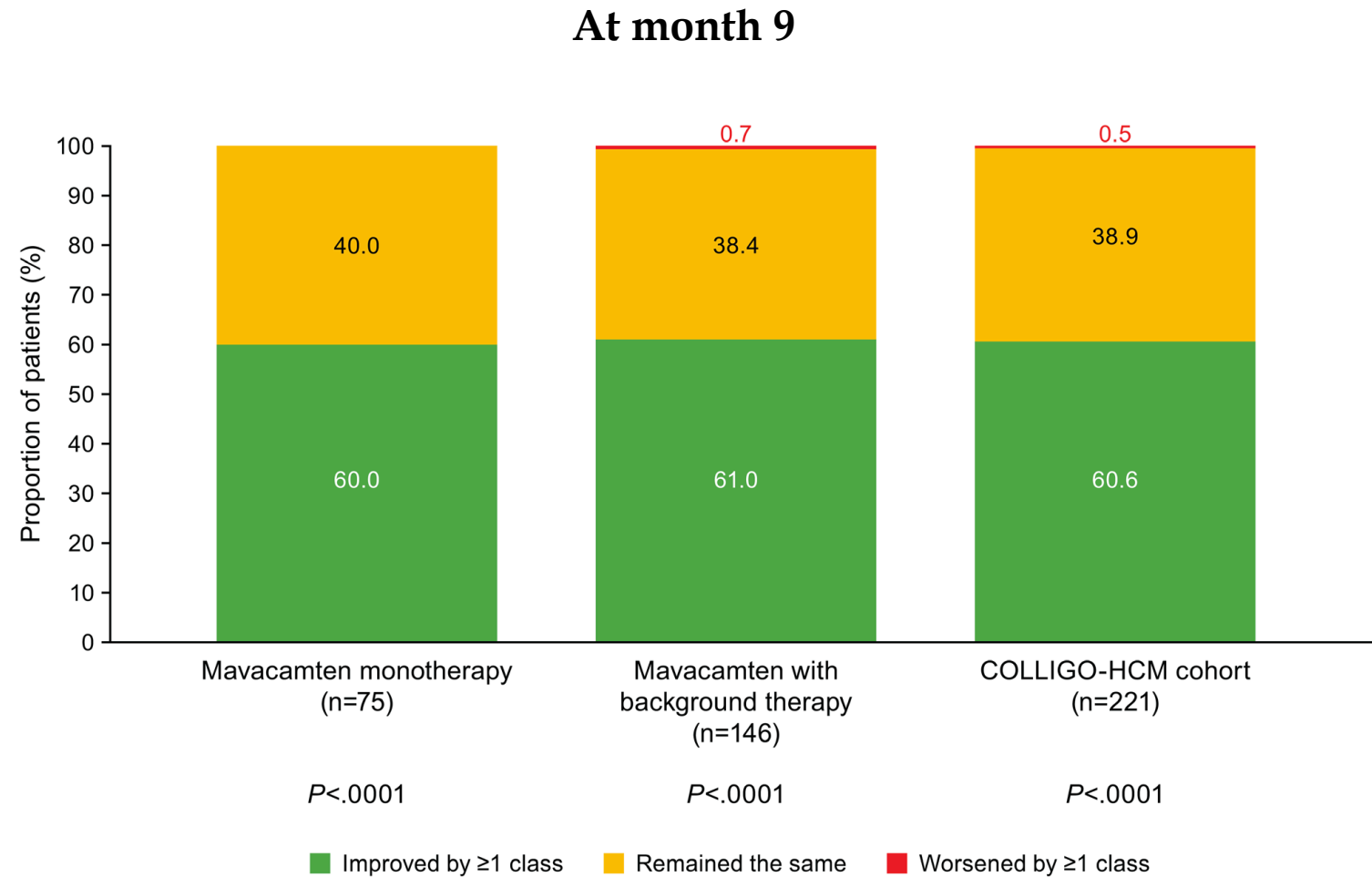
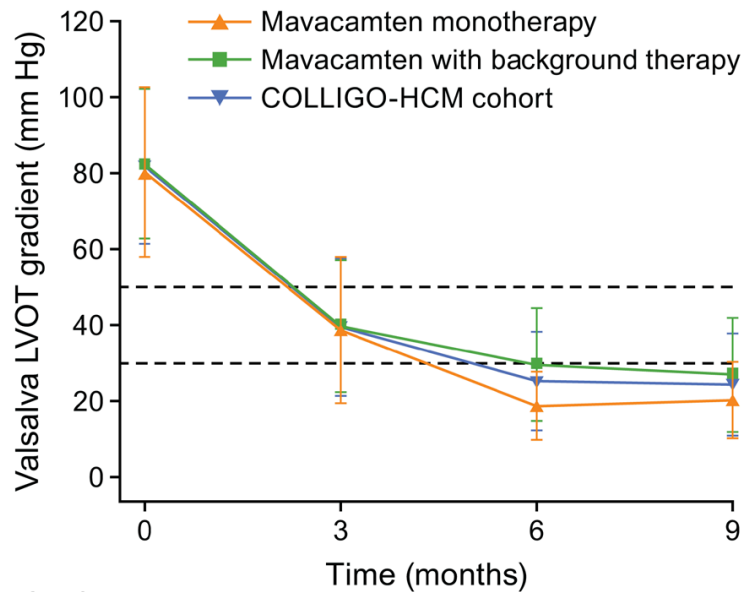
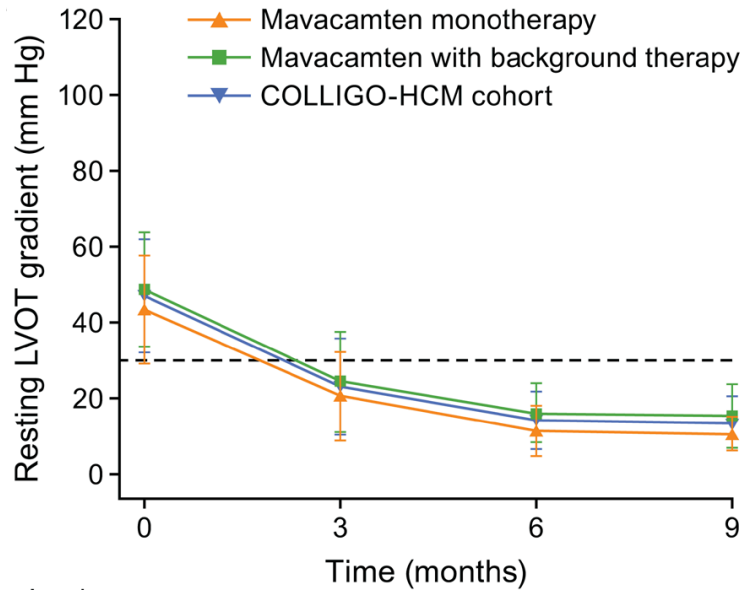


Mavacamten REMS Program:

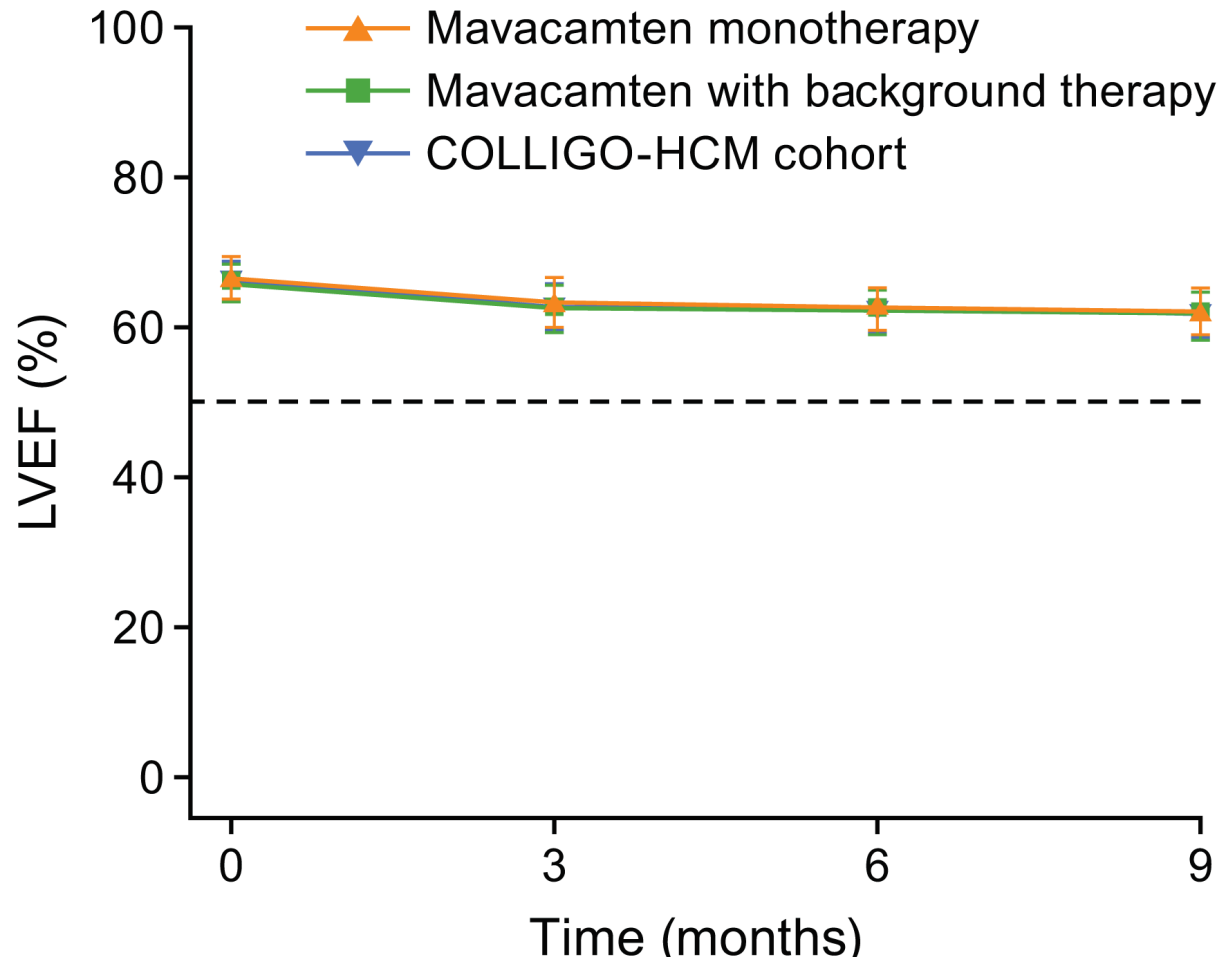
Pts treated with mavacamten for ≥ 1 year who experienced a decrease in LVEF $< 50\%$,
HF requiring hospitalization or both



Mavacamnten in real-world: Evidence From COLLIGO-HCM



Mvacamnten in real-world: Evidence From COLLIGO-HCM

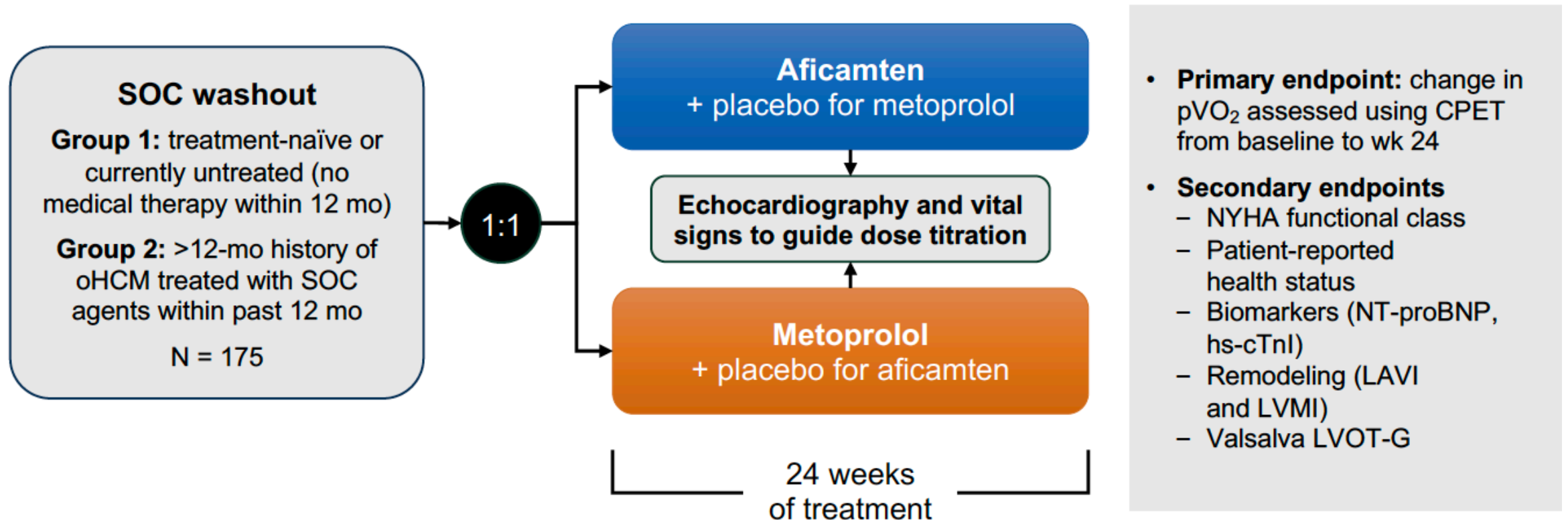


Two patients in the mavacamten monotherapy subgroup and **1 patient** in the mavacamten with background therapy subgroup **permanently discontinued treatment (LVEF <50%)**

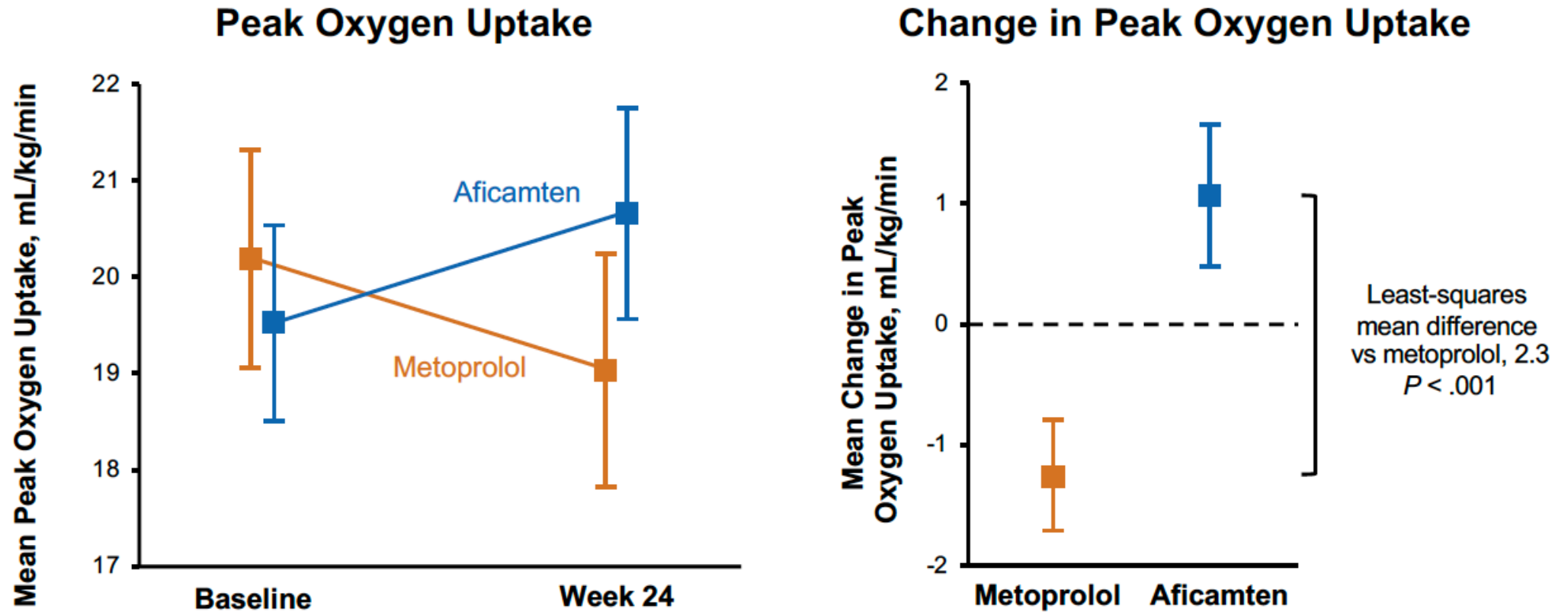
MAPLE-HCM:

Phase 3 Trial of Aficamten vs Metoprolol in Patients With oHCM

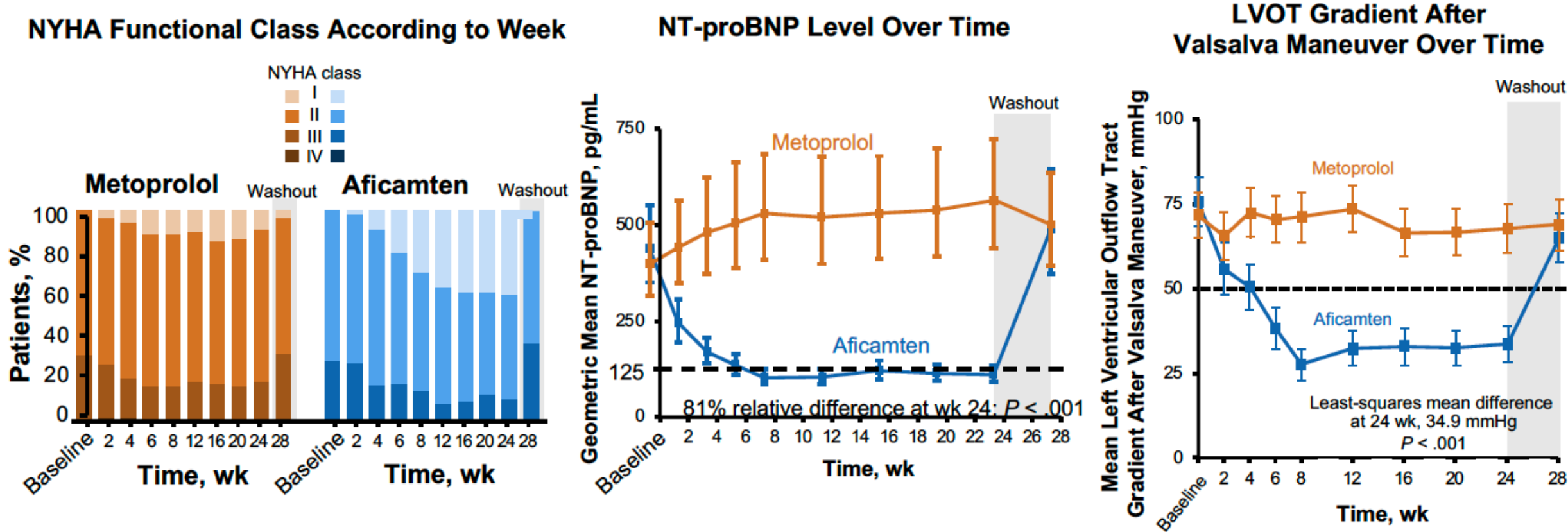
- First head-to-head study of a CMI (aficamten) vs a β blocker (metoprolol) for oHCM
- Aim: evaluate the safety and efficacy of aficamten as 1L treatment or as monotherapy for oHCM



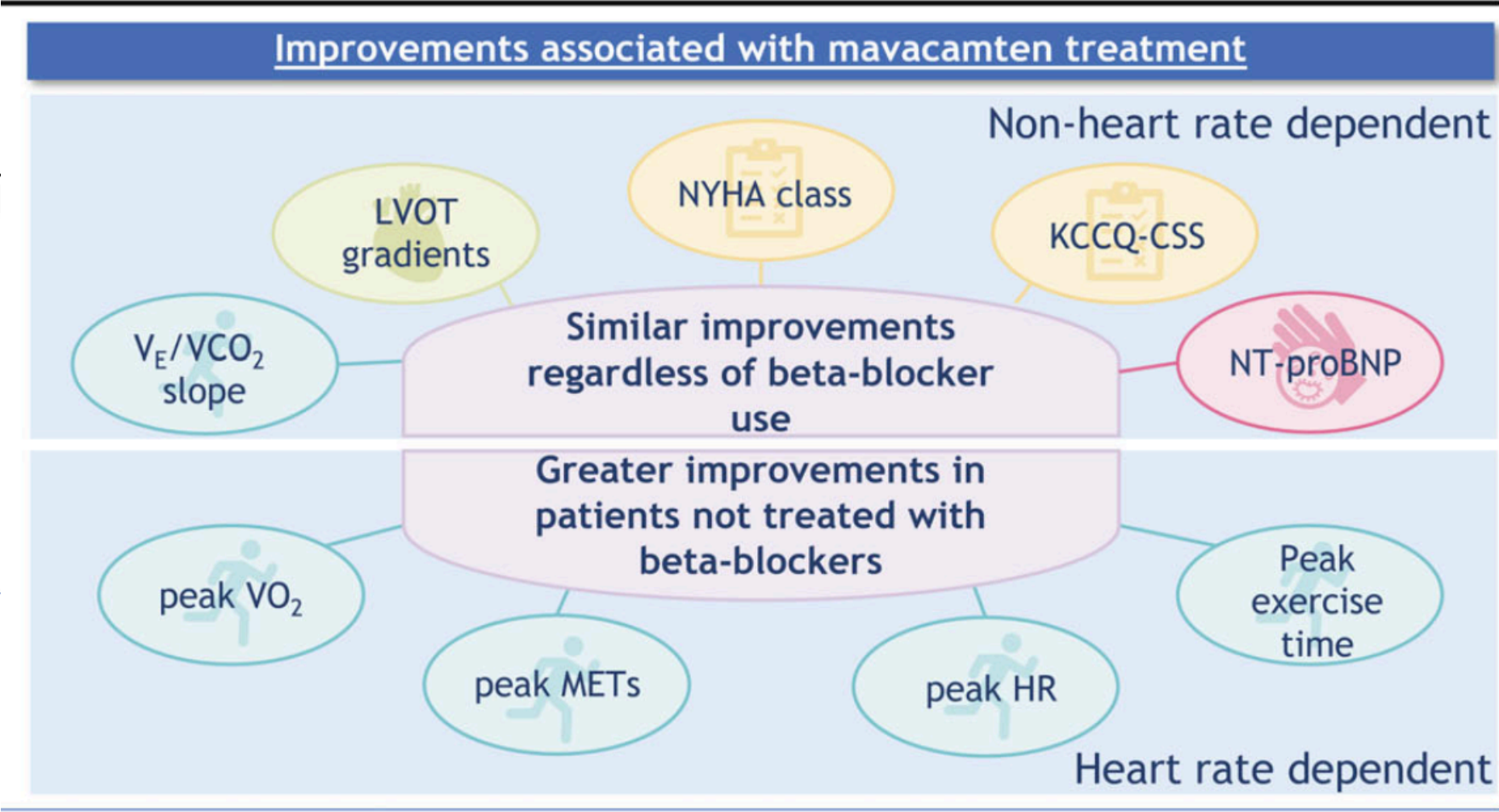
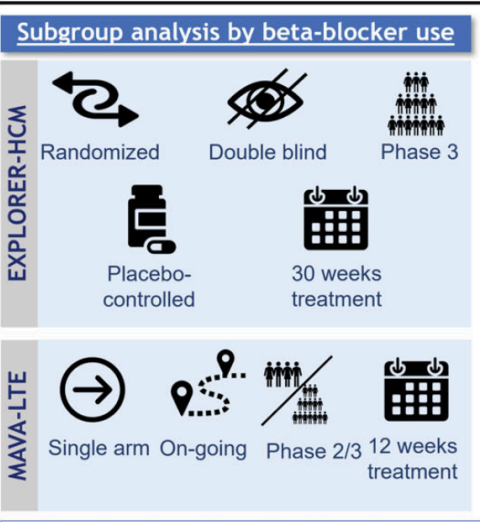
MAPLE-HCM: Aficamten Monotherapy Improves Peak Oxygen Uptake vs Metoprolol Monotherapy



MAPLE-HCM: Improvements in NYHA Class, NT-proBNP, and LVOT Gradient With Aficamten vs Metoprolol

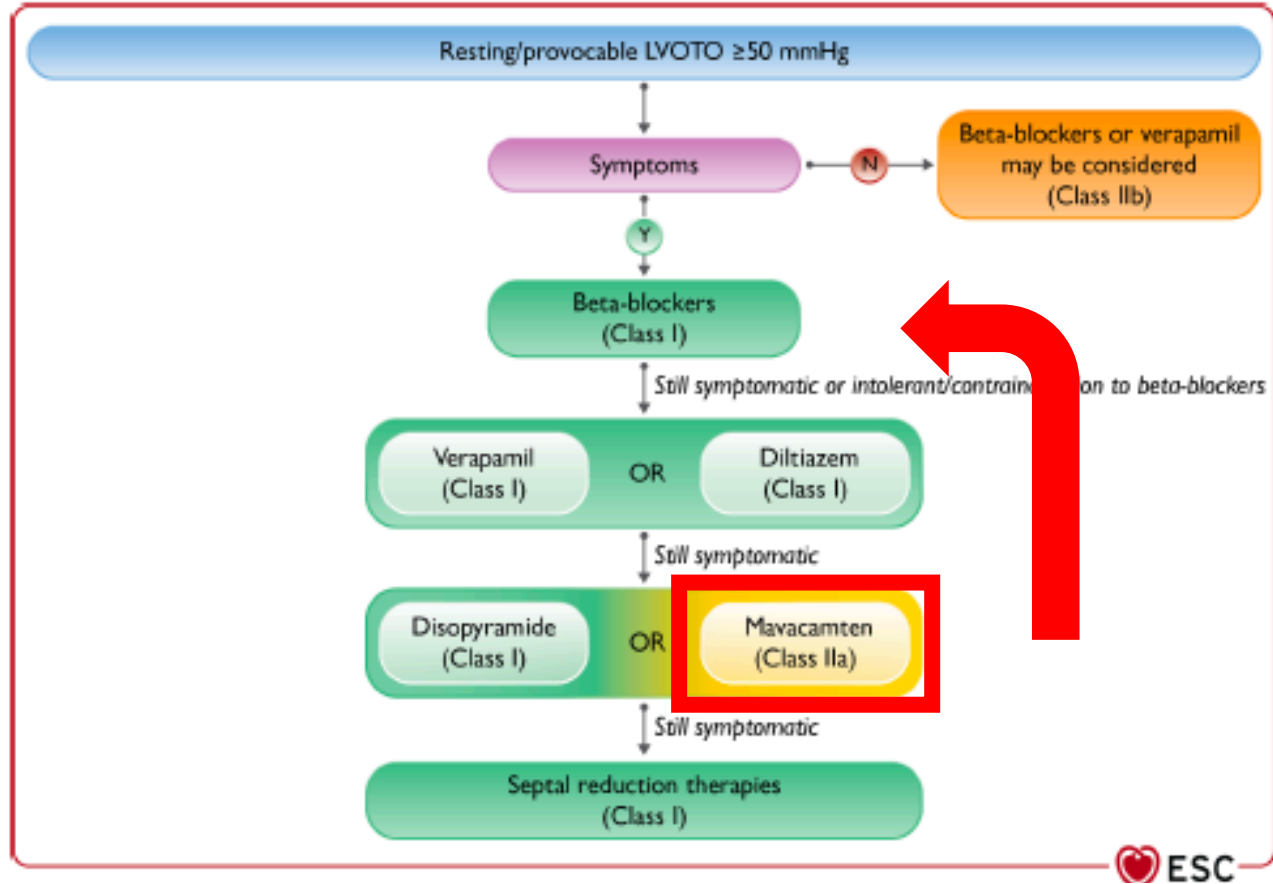


Effect of beta-blocker on the response to Mavacamten in patients with oHCM

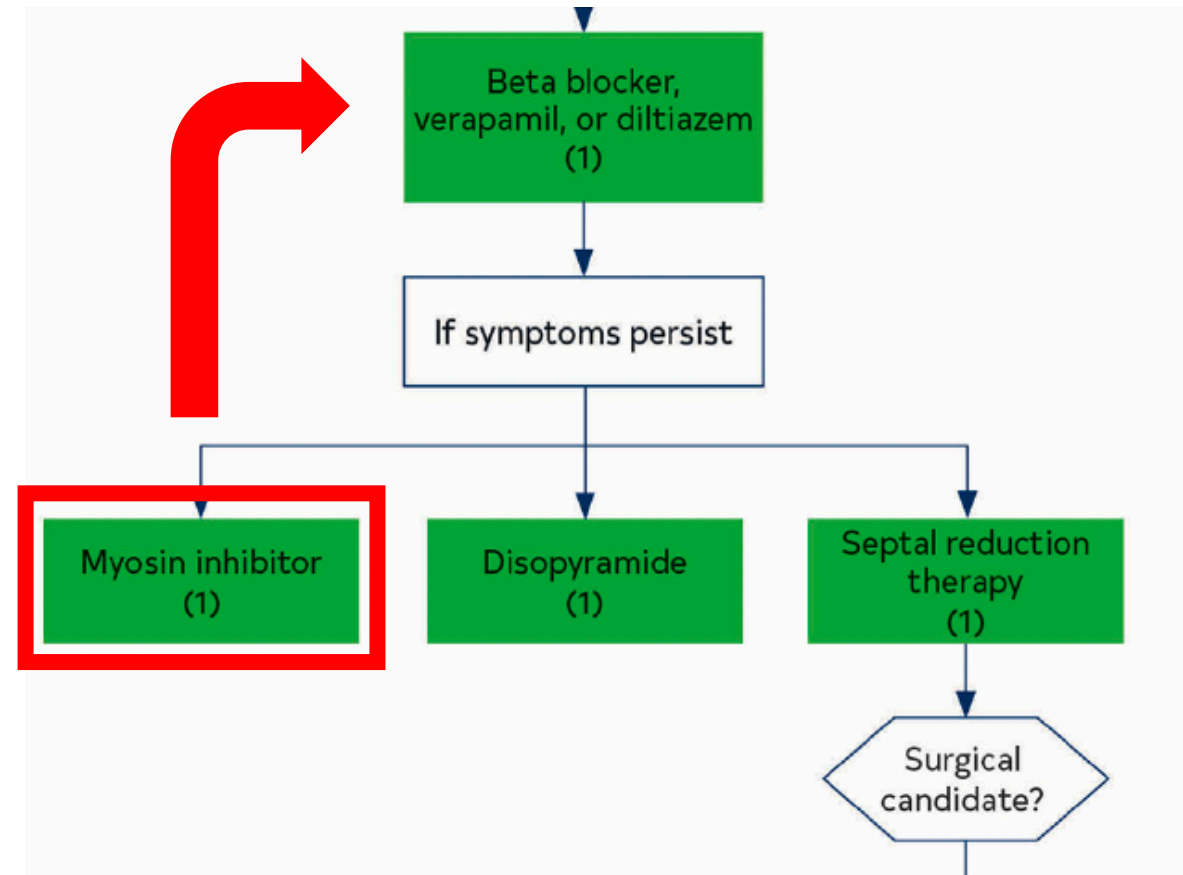


Myosin inhibitors in oHCM... "First line/class effect"?

2023 ESC HCM Guidelines



2024 AHA/ACC HCM Guidelines



Pediatric patients with oHCM

MAVACAMTEN

adolescents (12 to <18 years of age)



AFICAMTEN

adolescents (12 to <18 years of age)

Children (6 to <12 yo)



"ON GOING"

Mavacamten in Adolescents with Obstructive Hypertrophic Cardiomyopathy

Joseph W. Rossano, M.D.,^{1,2} Charles Canter, M.D.,³ Cordula M. Wolf, M.D.,⁴
Andrew Papez, M.D.,⁵ Marta Gamba, M.D.,⁶ Randall M. Bryant, M.D.,⁷
Juan Alejos, M.D.,⁸ Michael McCulloch, M.D.,⁹
Georgia Sarquella Brugada, M.D., Ph.D.,¹⁰ Matthew J. Bock, M.D.,¹¹
Aamir Jeewa, M.B., B.Ch.,¹² F. Bennett Pearce, M.D.,¹³ Milind Y. Desai, M.D.,¹⁴
Nicholas Favatella, Pharm.D.,¹⁵ Atefeh Javidialsaadi, Ph.D.,¹⁵ Van Phung, B.S.,¹⁵
Thomas Rano, Ph.D.,¹⁵ Lin Zhu, Ph.D.,¹⁵ Joshua L. Dyme, M.D.,¹⁵
and Seema Mital, M.D.,¹² for the SCOUT-HCM Investigators*

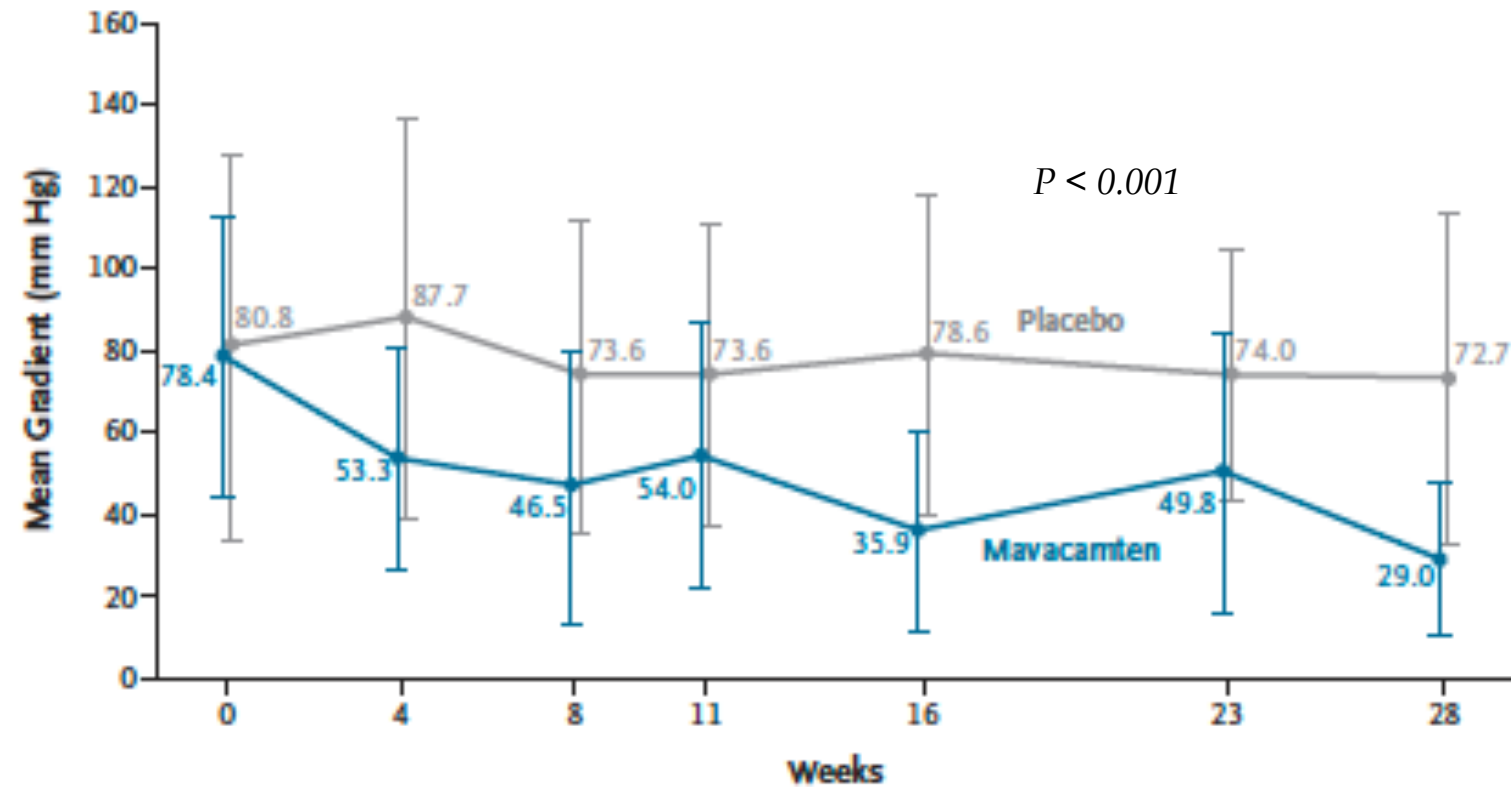
44 adolescent (12 to <18 years of age)

oHCM in NYHA class II-III

Starting dose:

- 5 mg in pts with a body weight $\geq$ 45 kg - - 2.5 mg
in pts with a body weight between 35Kg and 45 Kg

Valsalva LVOT Gradient over Time

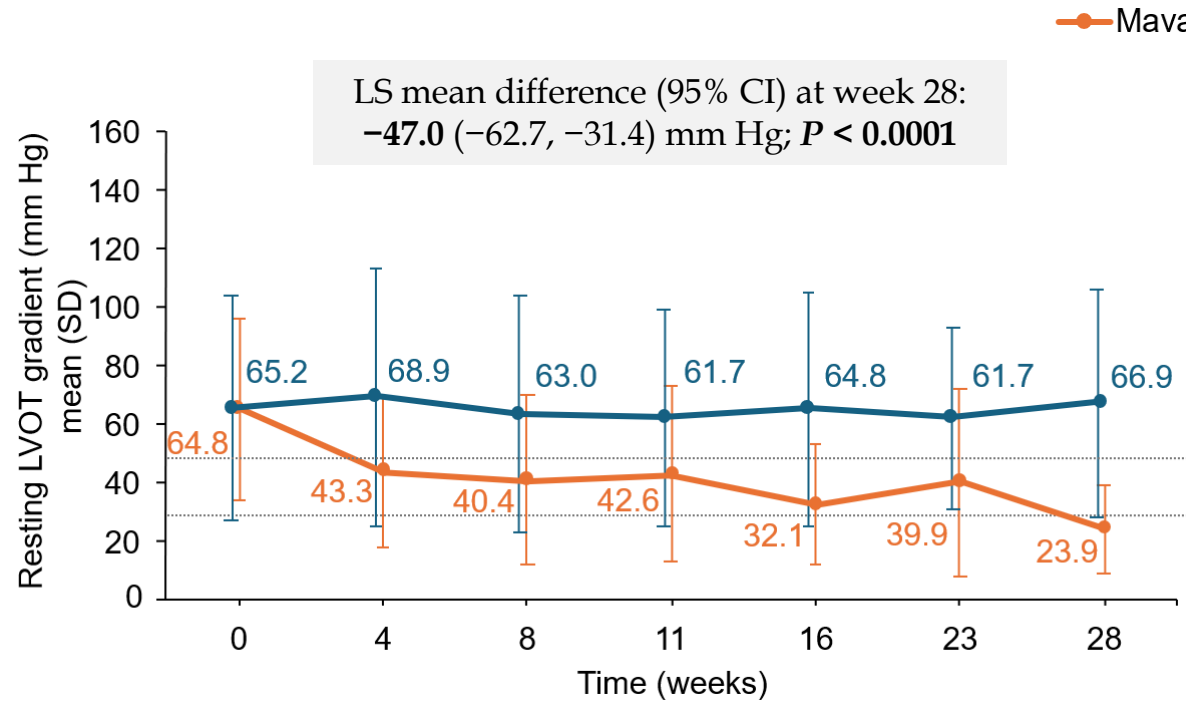


New Eng Med J 2026 (march)

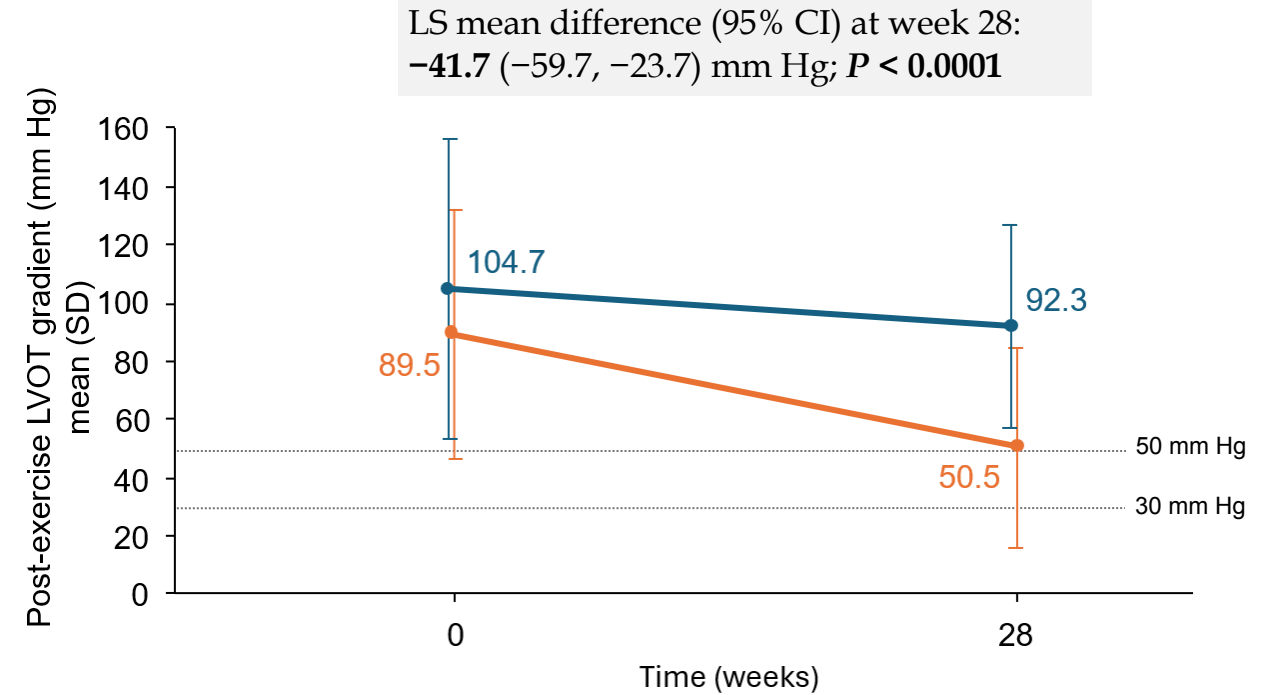
Mavacamten in Adolescents with Obstructive Hypertrophic Cardiomyopathy

Joseph W. Rossano, M.D.,^{1,2} Charles Canter, M.D.,³ Cordula M. Wolf, M.D.,⁴
Andrew Papez, M.D.,⁵ Marta Gamba, M.D.,⁶ Randall M. Bryant, M.D.,⁷
Juan Alejos, M.D.,⁸ Michael McCulloch, M.D.,⁹
Georgia Sarquella Brugada, M.D., Ph.D.,¹⁰ Matthew J. Bock, M.D.,¹¹
Aamir Jeewa, M.B., B.Ch.,¹² F. Bennett Pearce, M.D.,¹³ Milind Y. Desai, M.D.,¹⁴
Nicholas Favatella, Pharm.D.,¹⁵ Atefeh Javidialsadi, Ph.D.,¹⁵ Van Phung, B.S.,¹⁵
Thomas Rano, Ph.D.,¹⁵ Lin Zhu, Ph.D.,¹⁵ Joshua L. Dyme, M.D.,¹⁵
and Seema Mital, M.D.,¹² for the SCOUT-HCM Investigators*

Resting LVOT gradient



Post-exercise LVOT gradient

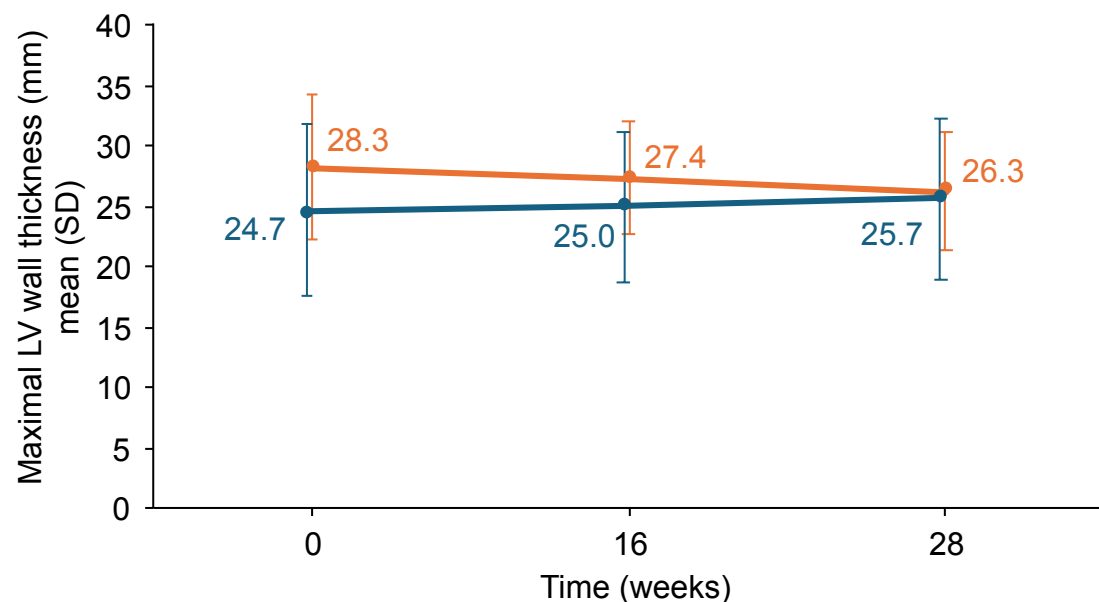


Mavacamten in Adolescents with Obstructive Hypertrophic Cardiomyopathy

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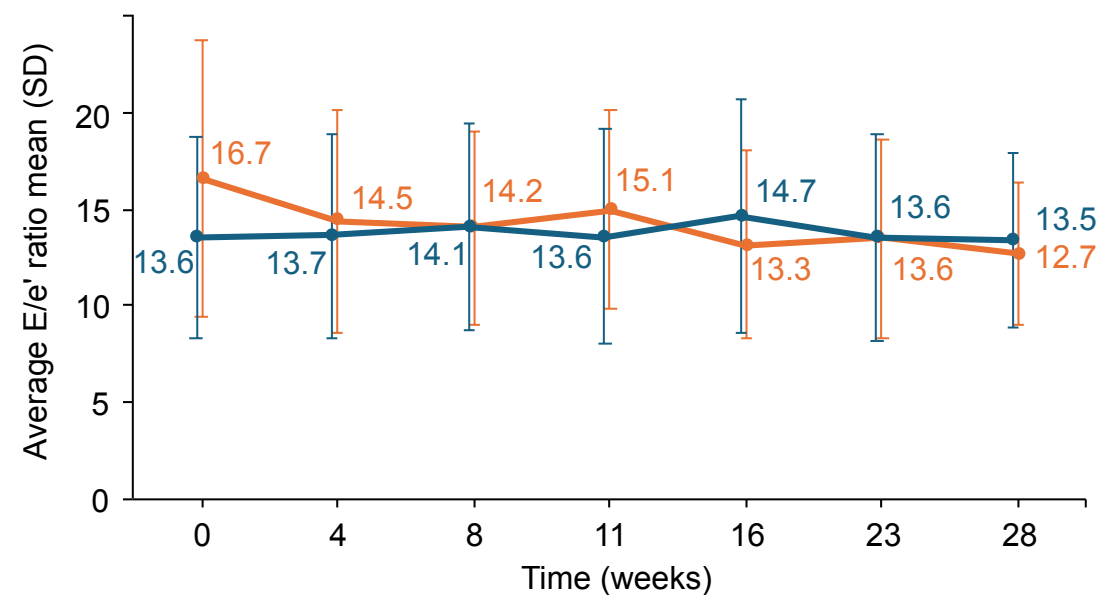
Maximal LV wall thickness

LS mean difference (95% CI) at week 28:
-1.8 (-3.4, -0.2) mm; $P = 0.0269$



Average E/e' ratio

LS mean difference (95% CI) at week 28:
-3.4 (-5.1, -1.6); $P = 0.0002$



Safety

Patients with an event, n (%)	Mavacamten (N = 23)	Placebo (N = 21)
TEAEs	18 (78.3)	17 (81.0)
Treatment-related TEAEs	2 (8.7)	3 (14.3)
TESAEs	2 (8.7)	2 (9.5)
Treatment-related TESAEs	1 ^a (4.3)	0
TEAEs leading to drug interruption	1 ^b (4.3)	1 (4.8)

- **No TEAE-related treatment discontinuations or deaths occurred, and no patient experienced an LVEF of < 50% or ≤ 30%**
- No cases of atrial fibrillation or symptomatic heart failure were reported

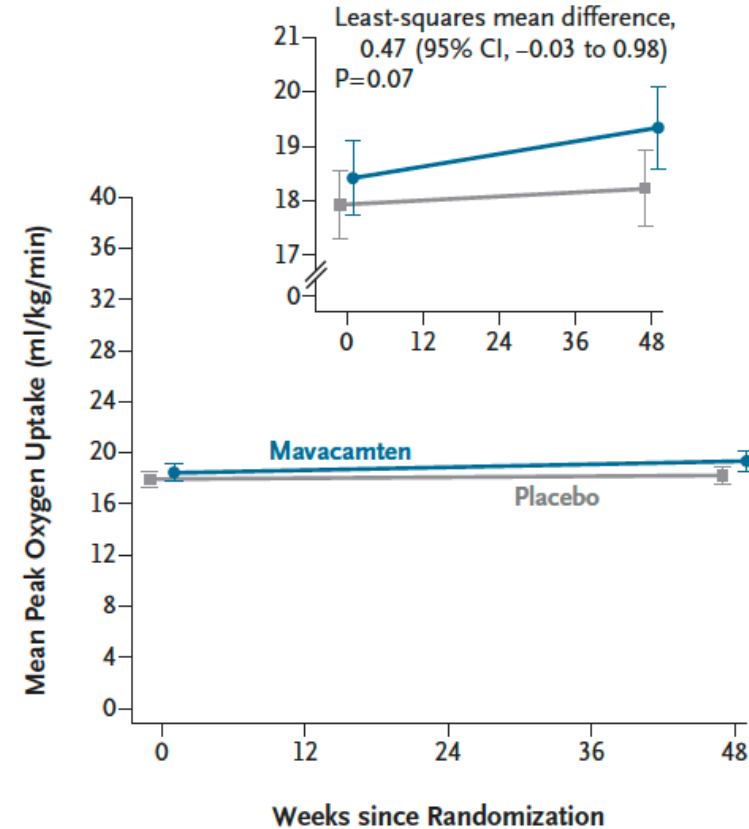
Mavacamten in Symptomatic Non obstructive HCM: ODYSSEY-HCM

590 pts HCM

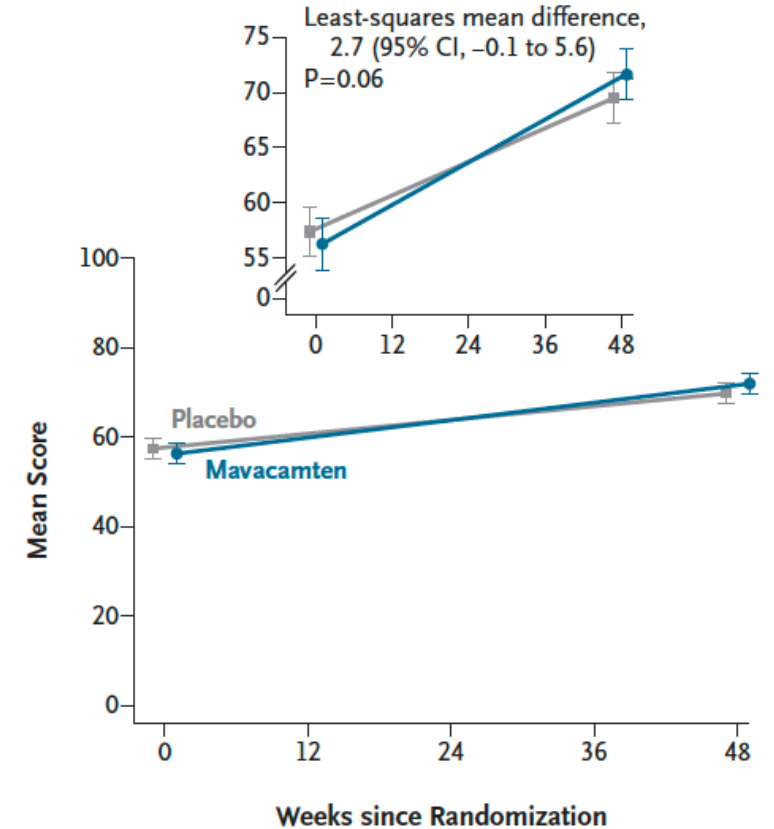
Background HCM therapy:

- 77.2% Beta-blocker
- 11.8% Calcium-channel blocker
- 9% Disopyramide

A Change in Peak Oxygen Uptake

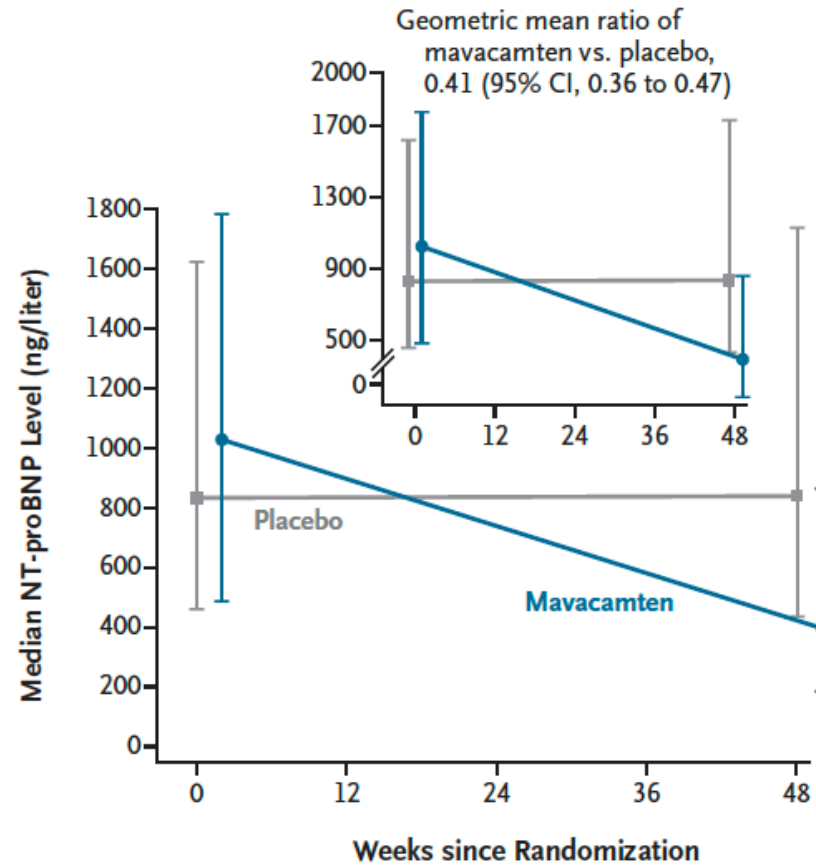


B Change in KCCQ-CSS

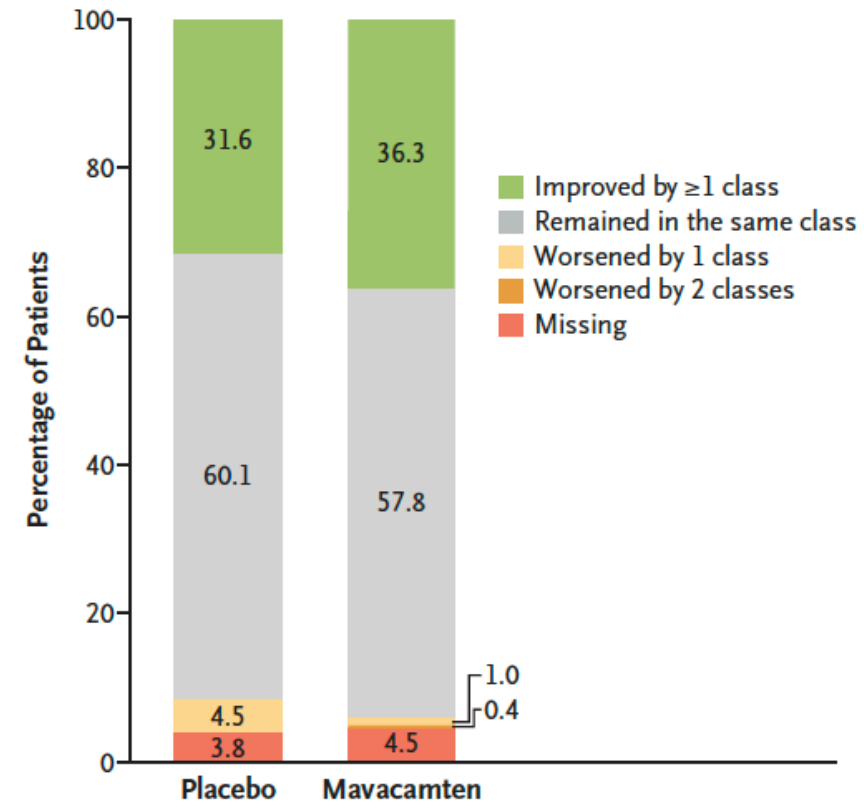


Mavacamten in Symptomatic Nonobstructive HCM: ODYSSEY-HCM

C NT-proBNP Level



D Change in NYHA Classification

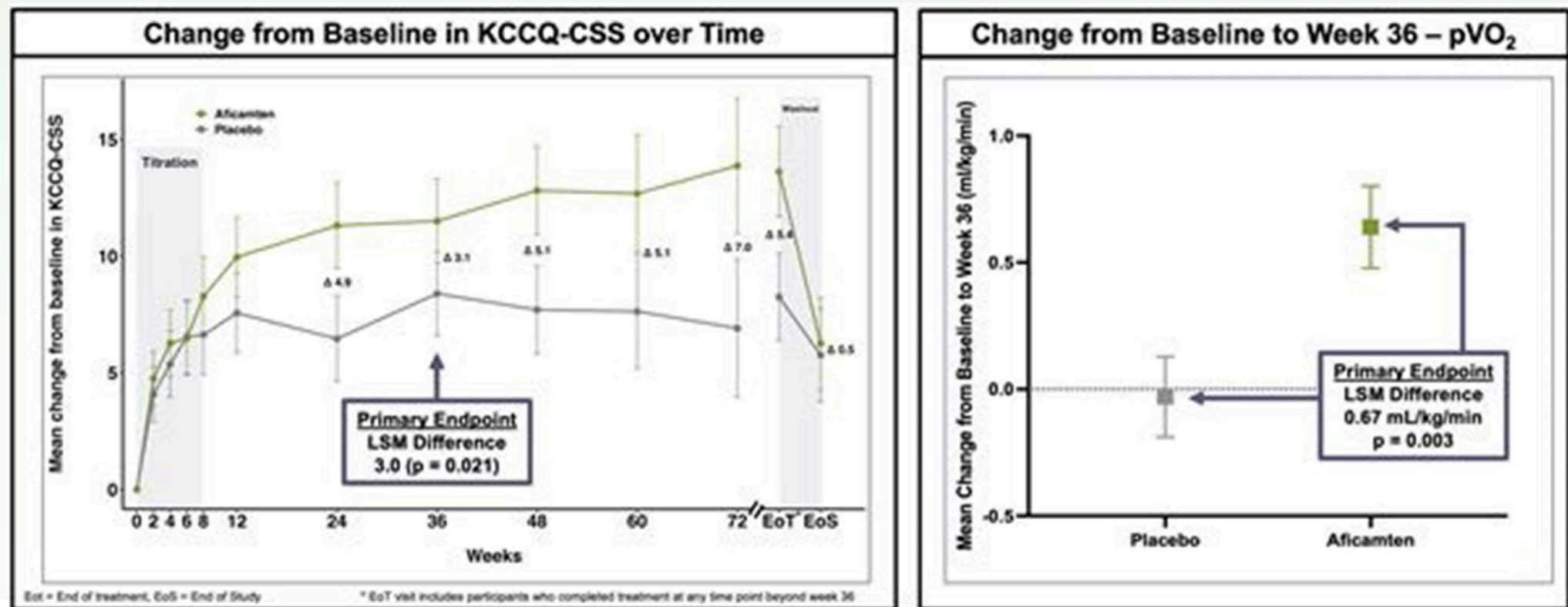


ODYSSEY-HCM : Safety

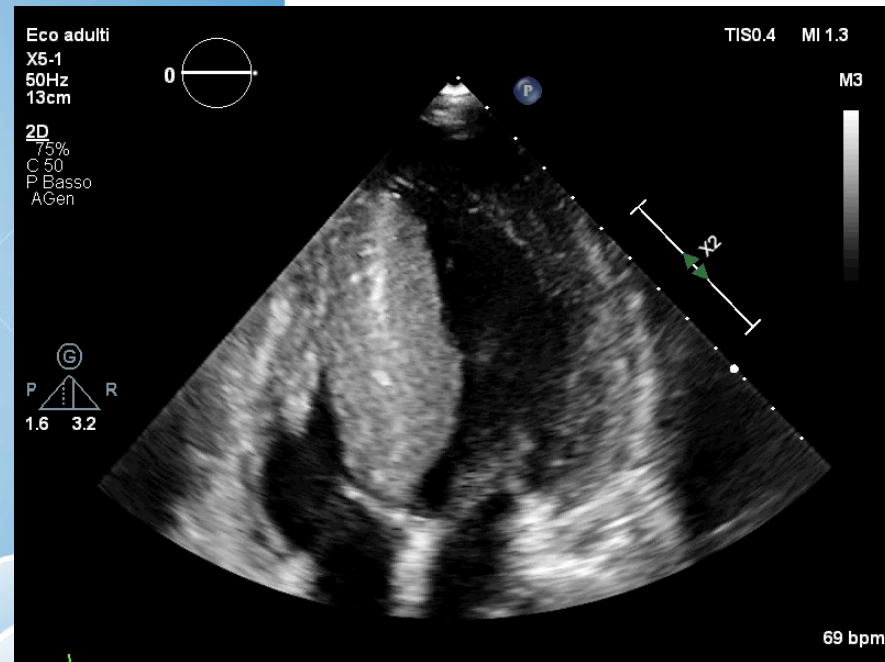
- Study drug interruption or permanent treatment discontinuation occurred in 42 (14.6%) and 15 (5.2%) pts assigned to mavacamten and 15 (5.2%) and 8 (2.8%) to placebo, respectively
- LVEF<50% occurred in 62 (21.5%) pts assigned to mavacamten vs 5 (1.7%) to placebo, while $\leq 30\%$ was observed in 7 (2.4%) pts in the mavacamten group and none in the placebo group
- During the placebo-controlled period, recovery of LVEF $\geq 50\%$ in all but 3 pts

Cytokinetics Announces Positive Topline Results from ACACIA-HCM, the Pivotal Phase 3 Clinical Trial of Aficamten in Patients with Non-Obstructive Hypertrophic Cardiomyopathy

May 5, 2026



<https://ir.cytokinetics.com/press-releases/press-release-details/2026/Cytokinetics-Announces-Positive-Topline-Results-from-ACACIA-HCM-the-Pivotal-Phase-3-Clinical-Trial-of-Aficamten-in-Patients-with-Non-Obstructive-Hypertrophic-Cardiomyopathy/default.aspx>



- Sarcomeric Modulation: EDG-7500 (CIRRUS-HCM)
- Metabolic Modulation:
 - NinerafaXstat (FORTITUDE-HCM)
 - Sotagliflozin (SONATA-HCM)



cloud.raineri@gmail.com
scompenso@cittadellasalute.to.it

Sarcomeric Modulators: EDG-7500



Targets when obstruction begins*

EDG-7500 slows the rate of acto-myosin **cross-bridge formation** during isovolumic contraction, **exactly where obstruction formation starts**



Improves diastolic dysfunction*

EDG-7500 speeds the rate of acto-myosin **cross-bridge detachment** to **improve relaxation rate and ventricular filling**

*Based on preclinical data with EDG-7500.

EDG-7500 parameters

Human T _{1/2}	30 hours
LVEF impact	Minimal
CYP inhibition (IC ₅₀)	>30 µM (all isoforms)
Dosing	Oral, once daily
Time to steady state	3-4 days
Substrate for transporters?	No

CIRRUS-HCM: Clinical Trial Design



PRIMARY OBJECTIVE

Safety & tolerability
in adults with HCM

KEY INCLUSION CRITERIA

Male and female patients
≥ 18 years of age with HCM
LVEF ≥ 60%

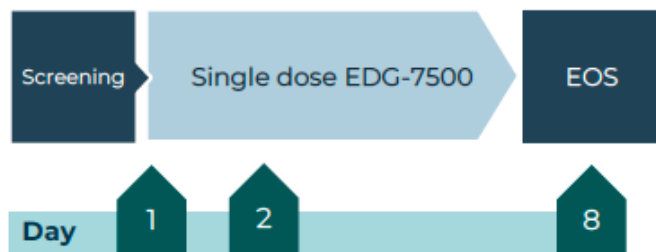
TARGET ENROLLMENT

~75

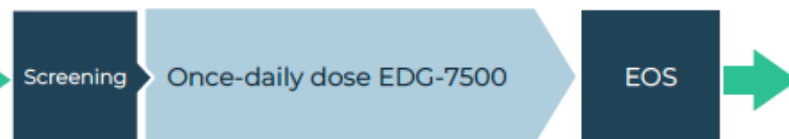
KEY OUTCOME MEASURES

Cardiovascular PD, LVEF,
Biomarkers, PK

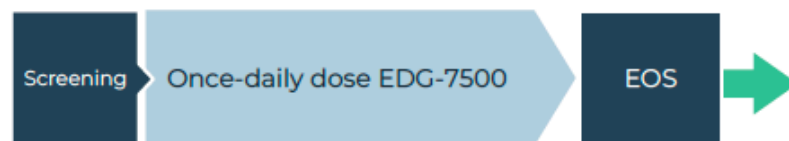
PART A: Single Dose ~15 oHCM patients



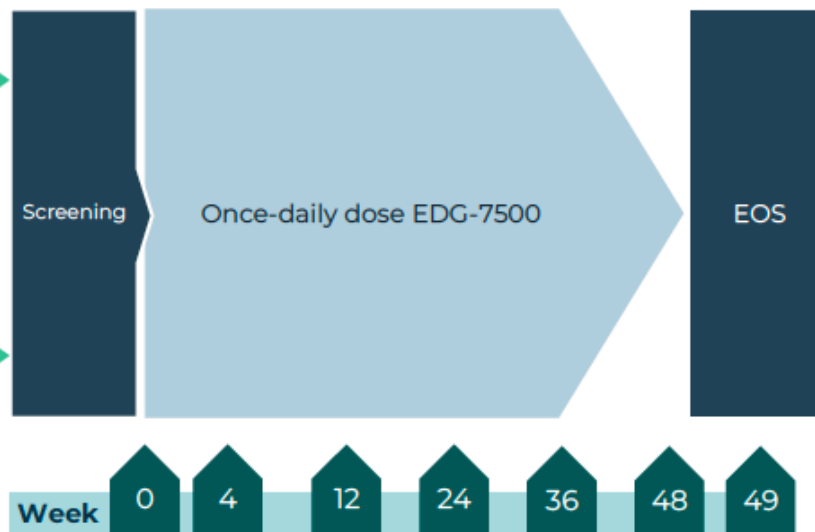
PART B: Multiple Dose ~30 oHCM patients



PART C: Multiple Dose ~30 nHCM patients



PART D: Extended Dose (Patients from Parts B/C)

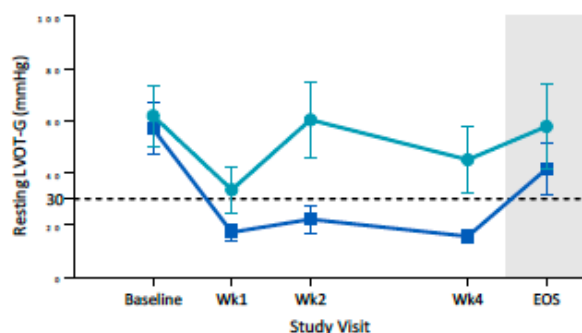




CIRRUS-HCM Part B summary: multiple-dose 4-week study in oHCM

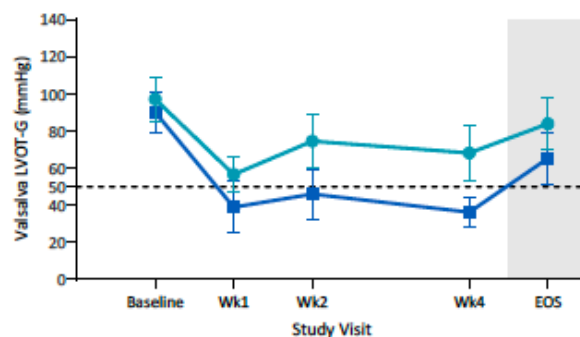


Resting LVOT-G*

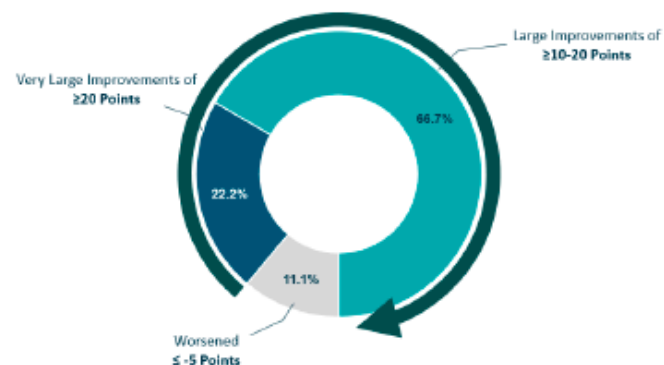


● 50mg (N=8) ■ 100mg (N=9)

Valsalva LVOT-G*

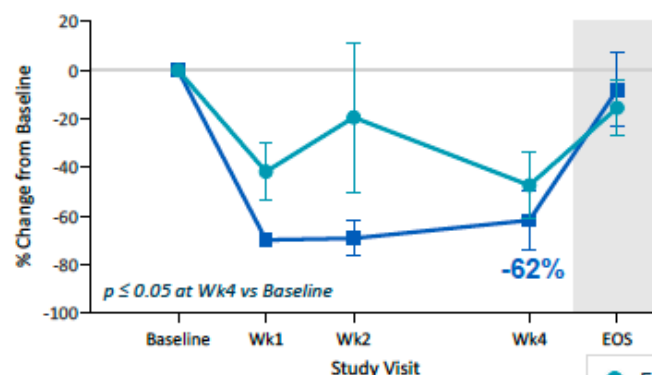


KCCQ-CSS (100mg)



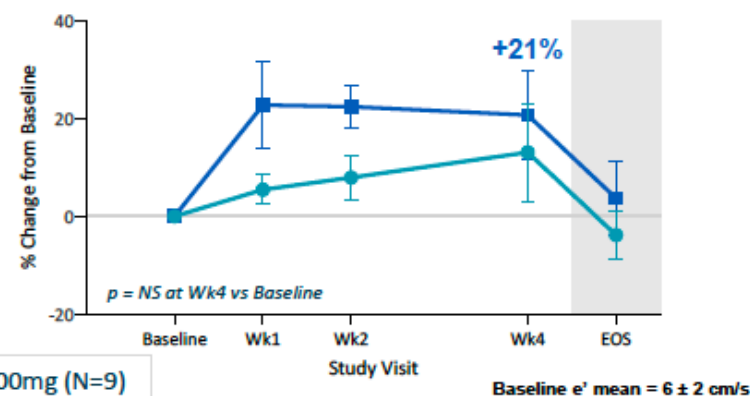
- 89% at 100mg reached resting LVOT <30mmHg and Valsalva LVOT <50mmHg
- 56% at 100mg achieved NT-proBNP <150 pg/mL
- 89% with clinical improvements in KCCQ-CSS (100mg) after 4 weeks
- 43% at 50mg and 78% at 100mg achieved ≥ 1 NYHA Class improvement at week 4

NT-proBNP



● 50mg (N=8) ■ 100mg (N=9)

Early diastolic mitral annular velocity (e')

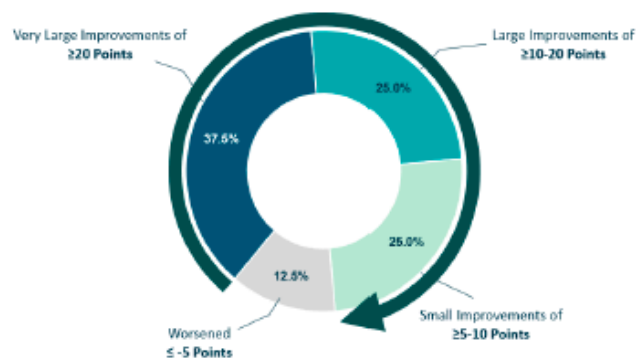




CIRRUS-HCM Part C summary: multiple-dose 4-week study in nHCM



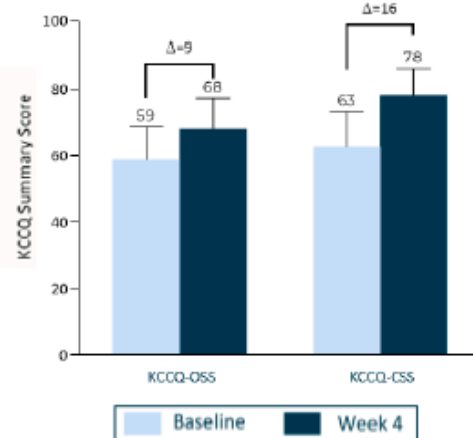
KCCQ-CSS (50mg and 100mg)



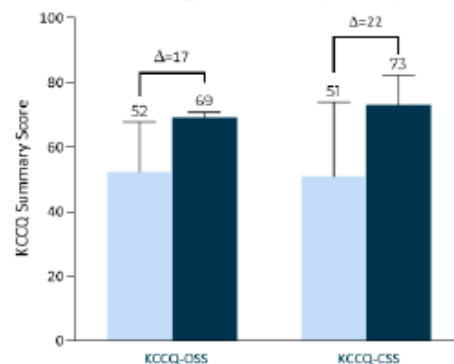
- **Rapid and robust reductions in NT-proBNP**
- **Mean e' changes in as early as one week following dosing**
- **88% with clinical improvements in KCCQ-CSS after 4 weeks (50mg/100mg combined)**

KCCQ-OSS and KCCQ-CSS

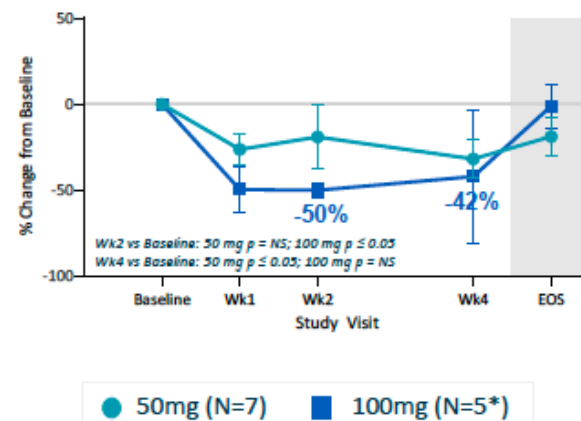
50mg Dose Group (N=6)



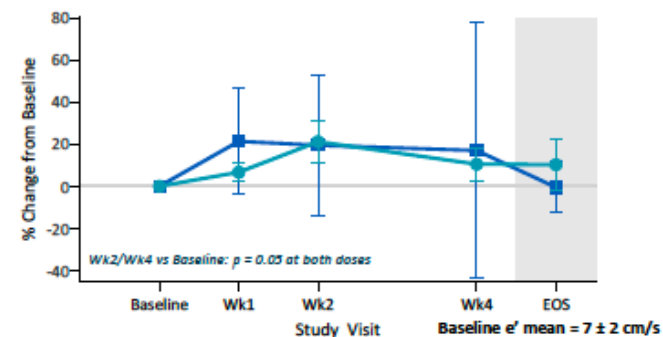
100mg Dose Group (N=2)



NT-proBNP



Early diastolic mitral annular velocity (e')

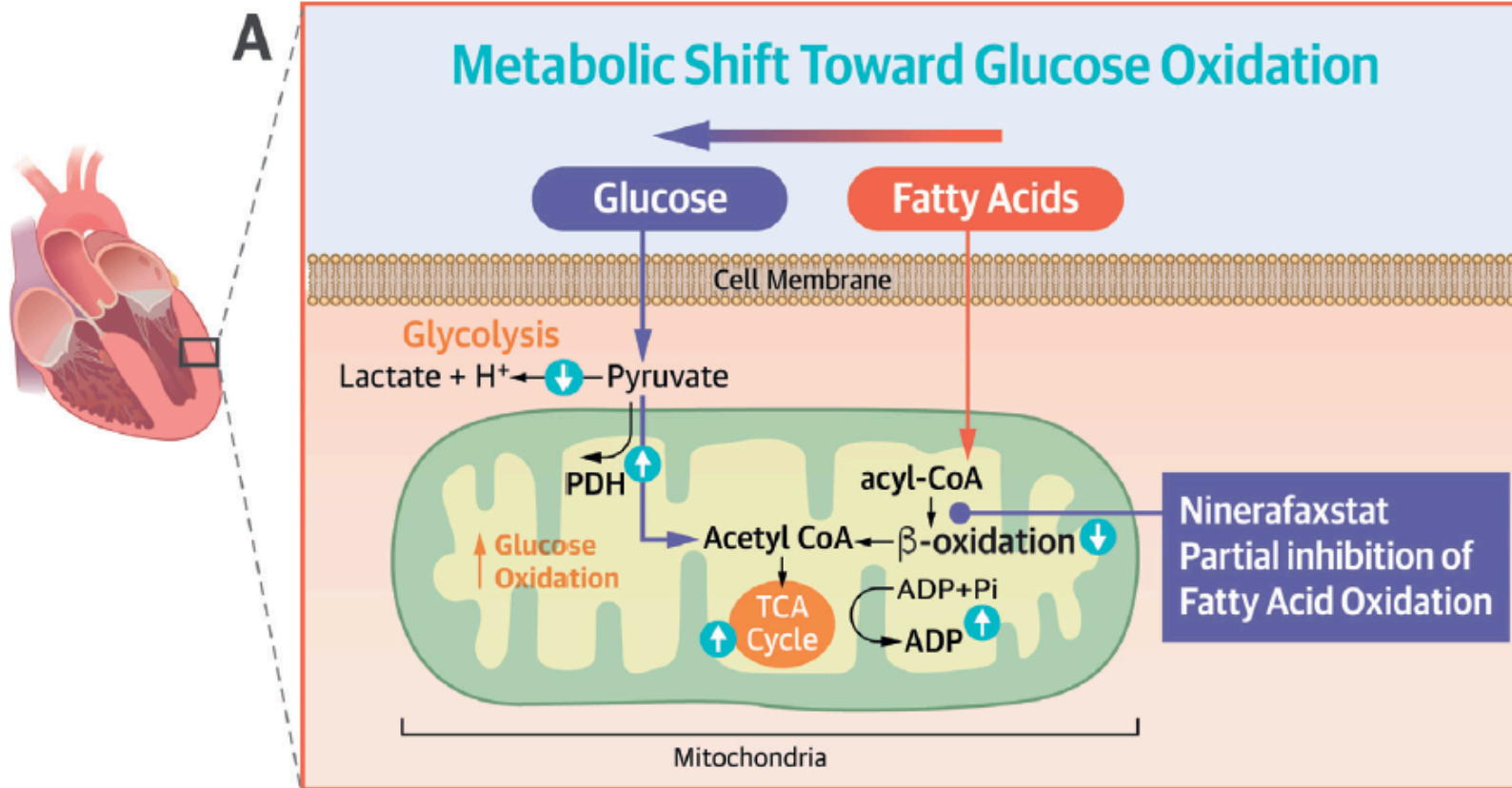


Mean $\pm$ SEM * Two participants at week 4

EOS, end of study; KCCQ, Kansas City Cardiomyopathy Questionnaire; KCCQ-CSS, KCCQ-Clinical Summary Score; KCCQ-OSS, KCCQ-Overall Summary Score; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association nHCM, nonobstructive hypertrophic cardiomyopathy.

Preliminary data as of May 2025

Safety and Efficacy of Metabolic Modulation With Nineraxfaxstat in Patients With Nonobstructive Hypertrophic Cardiomyopathy



ATP yield per unit
of oxygen consumed

Glucose	+	+	+
Palmitate	+	+	

↑ Energy generation and
myocardial efficiency

↑ Diastolic function

Recruiting



A Trial to Evaluate the Efficacy and Safety of Ninerafaxstat in Patients With Symptomatic Non-obstructive Hypertrophic Cardiomyopathy (FORTITUDE-HCM)

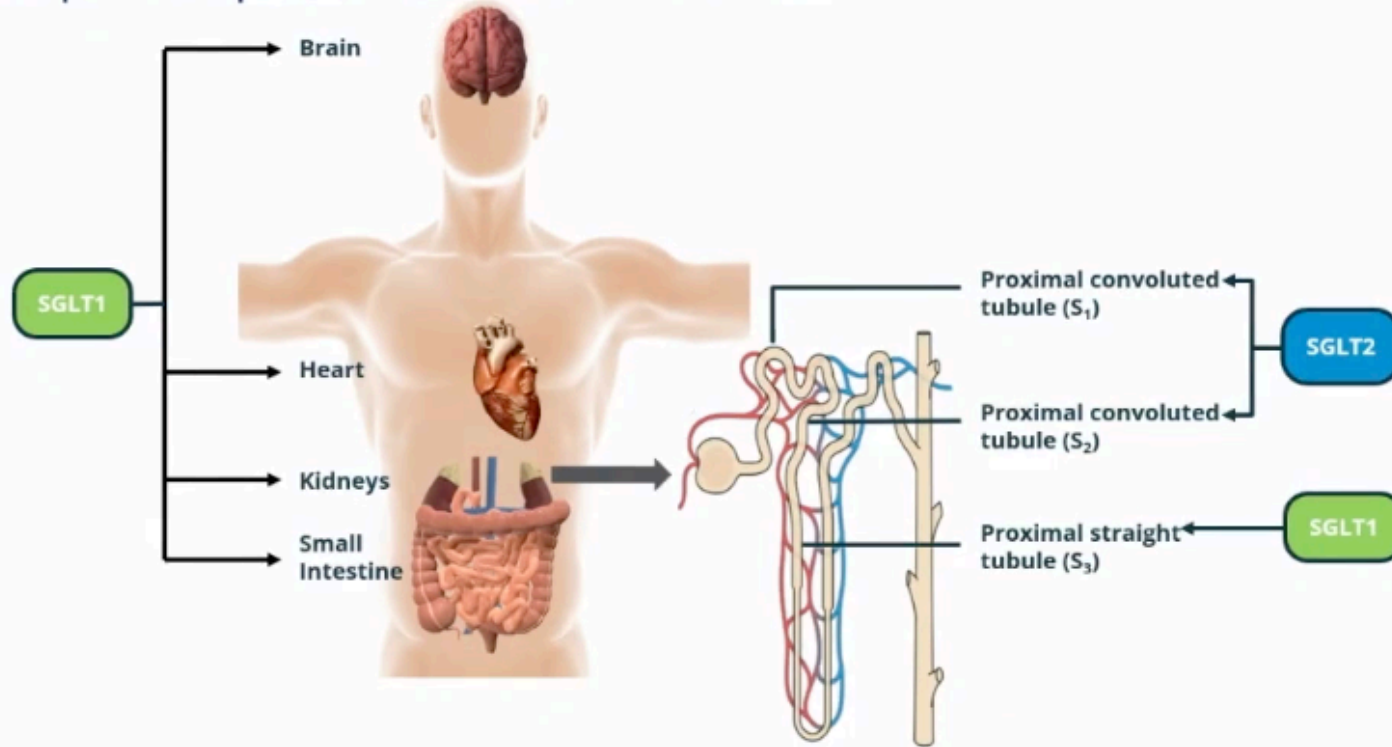
ClinicalTrials.gov ID  NCT07023614

Sponsor  Imbria Pharmaceuticals, Inc.

Sotagliflozin: Dual SGLT Inhibitor

Sodium-glucose Cotransporter-1 (SGLT1) and Sodium-glucose Cotransporter-2 (SGLT2)

Expression patterns of SGLT2 and SGLT1^{1,2}



SGLT2 is expressed in the **renal proximal tubule**

- Co-transport Na^+ and Glucose (1:1)
- High capacity / Low Affinity
- Reuptake of 90-97% glucose in the kidney

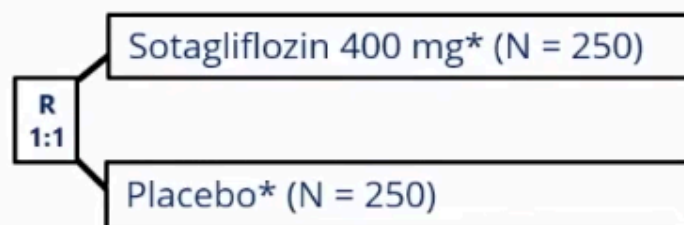
SGLT1 is expressed in the **kidney, intestine, heart, and vascular endothelium**

- Co-transport Na^+ and Glucose (2:1)
- Low capacity / High Affinity
- Primary transporter for absorption of glucose in the GI tract

SONATA-HCM

A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study to Evaluate the Efficacy and Safety of Sotagliflozin in Patients with Symptomatic obstructive And non-obstructive Hypertrophic Cardiomyopathy

- Adults with HCM (o/n)
- LVOT gradient per HCM type:
 - oHCM ≥ 30 mm Hg at rest OR with Valsalva
 - nHCM < 30 mm Hg at rest AND with Valsalva
- KCCQ CSS < 85
- NYHA Class II or III
- LVEF $\geq 50\%$



Primary endpoint:
Change from baseline
in KCCQ Clinical
Summary Scale (CSS)
score



*For patients not tolerating treatment, sotagliflozin or matching placebo down-titrated to 200 mg starting at Week 4.

130 sites in 20 countries (N = 500),
with 100 sites outside US (n = 375)

O = obstructive; NO = non-obstructive; LVOT = left ventricular outflow tract; NYHA = New York Heart Association; KCCQ = Kansas City Cardiomyopathy Questionnaire; R = randomization

[ClinicalTrials.gov: NCT06481891](https://clinicaltrials.gov/ct2/show/study/NCT06481891)



CIRRUS-HCM: Clinical trial design^{1,2}



Primary objective

Safety and tolerability
in adults with HCM

Key inclusion criteria

Male and female participants
≥18 years of age with HCM
LVEF ≥60%

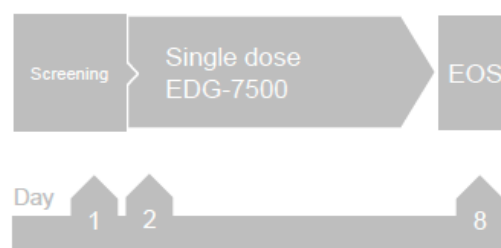
Target enrollment

≈75

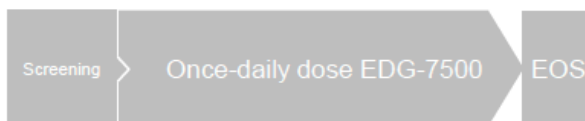
Key outcome measures

- Cardiovascular PD
- LVEF
- Biomarkers
- PK

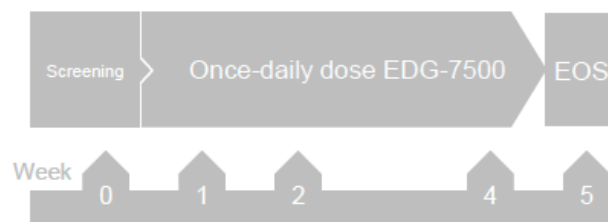
Part A: Single Dose Participants with oHCM



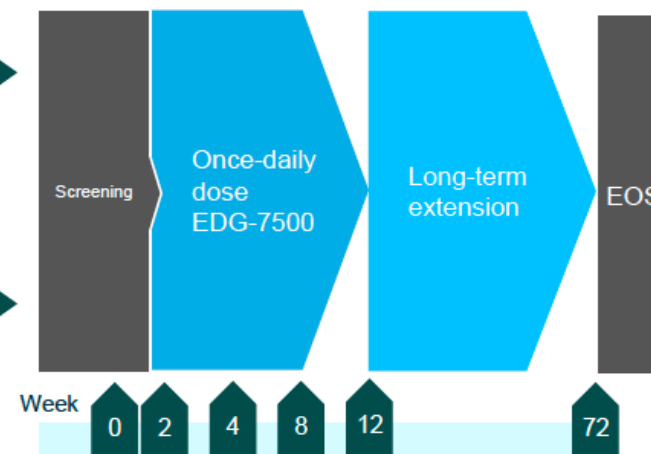
Part B: Multiple Dose Participants with oHCM



Part C: Multiple Dose Participants with nHCM



Part D: Extended Dose New participants plus from Parts B/C





↑ Improved ventilatory efficiency



↑ Improved KCCQ-CSS in patient with abnormal values at baseline

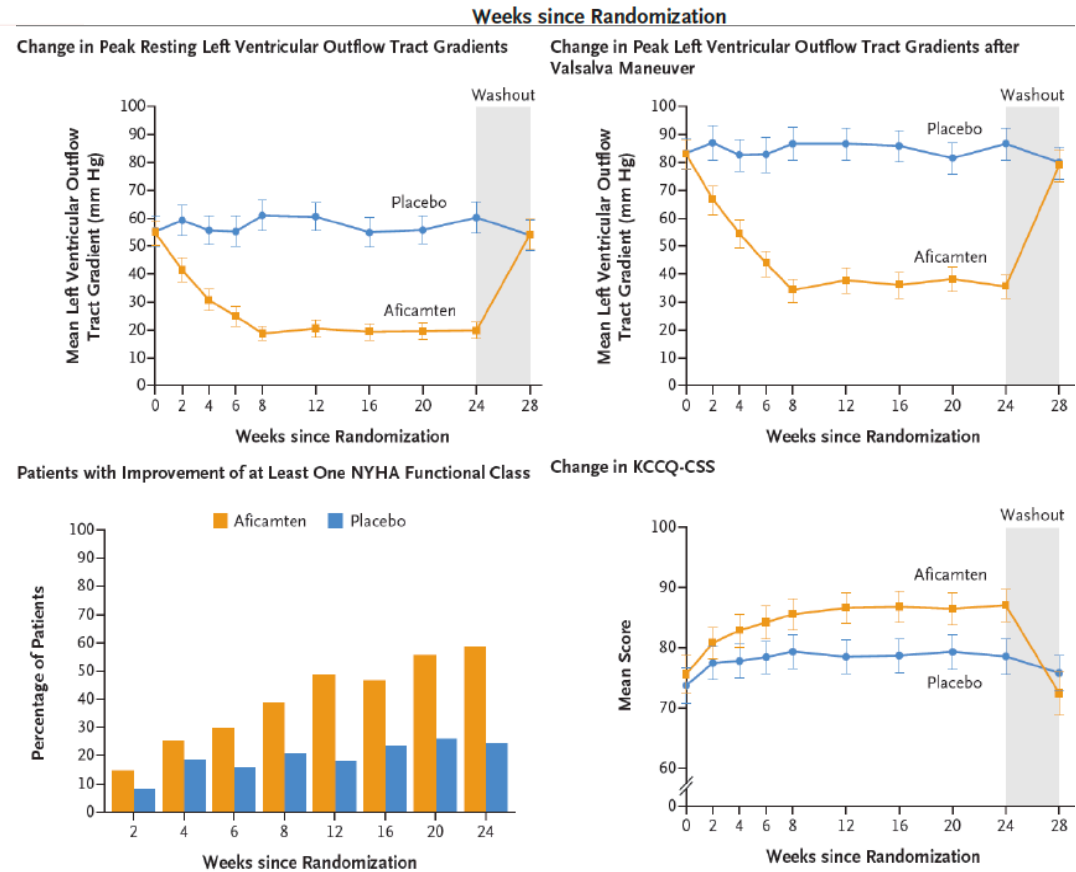
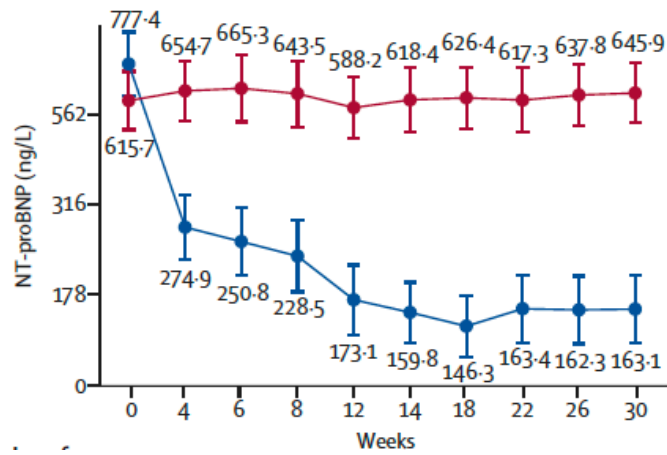
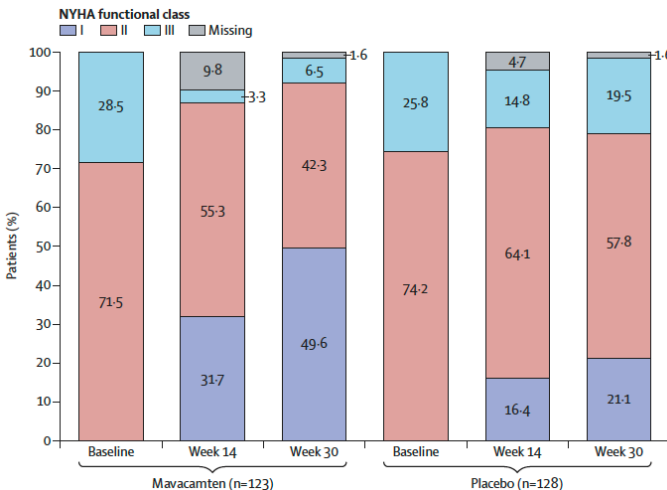
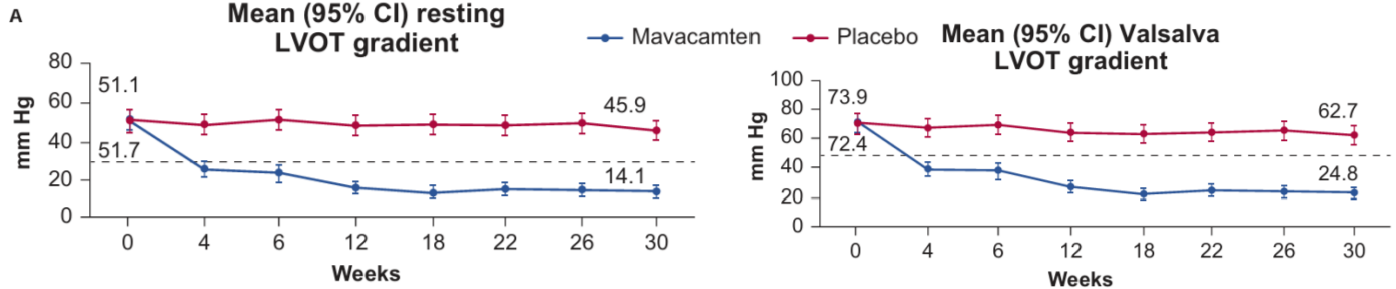
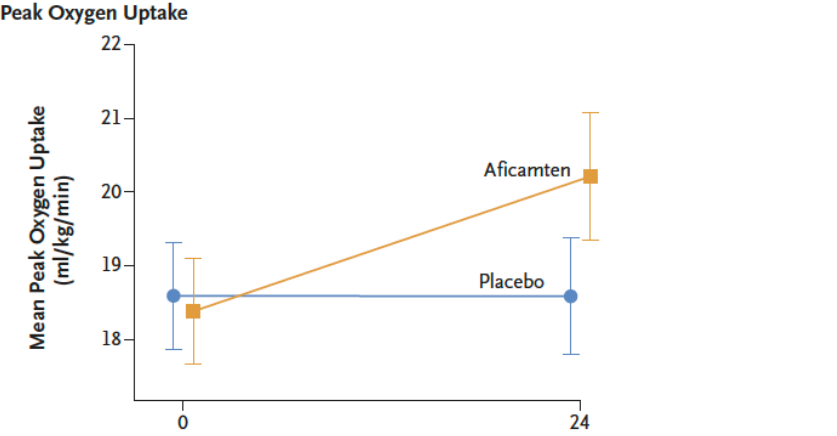
RESULTS A total of 67 patients with nHCM were enrolled at 12 centers (57 ± 11.8 years of age; 55% women). Serious adverse events occurred in 11.8% ($n = 4$ of 34) in the nineraxstat group and 6.1% ($n = 2$ of 33) of patients in the placebo group. From baseline to 12 weeks, nineraxstat was associated with significantly better V_E/V_{CO_2} (ventilatory efficiency) slope compared with placebo with a least-squares (LS) mean difference between the groups of -2.1 (95% CI: -3.6 to -0.6 ; $P = 0.006$), with no significant difference in peak VO_2 ($P = 0.90$). The Kansas City Cardiomyopathy Questionnaire Clinical Summary Score was directionally, though not significantly, improved with nineraxstat vs placebo (LS mean 3.2; 95% CI: -2.9 to 9.2 ; $P = 0.30$); however, it was statistically significant when analyzed post hoc in the 35 patients with baseline Kansas City Cardiomyopathy Questionnaire Clinical Summary Score ≤ 80 (LS mean 9.4; 95% CI: 0.3 - 18.5 ; $P = 0.04$).

Mavacamten

N Engl J Med 2024;390:1849-61.

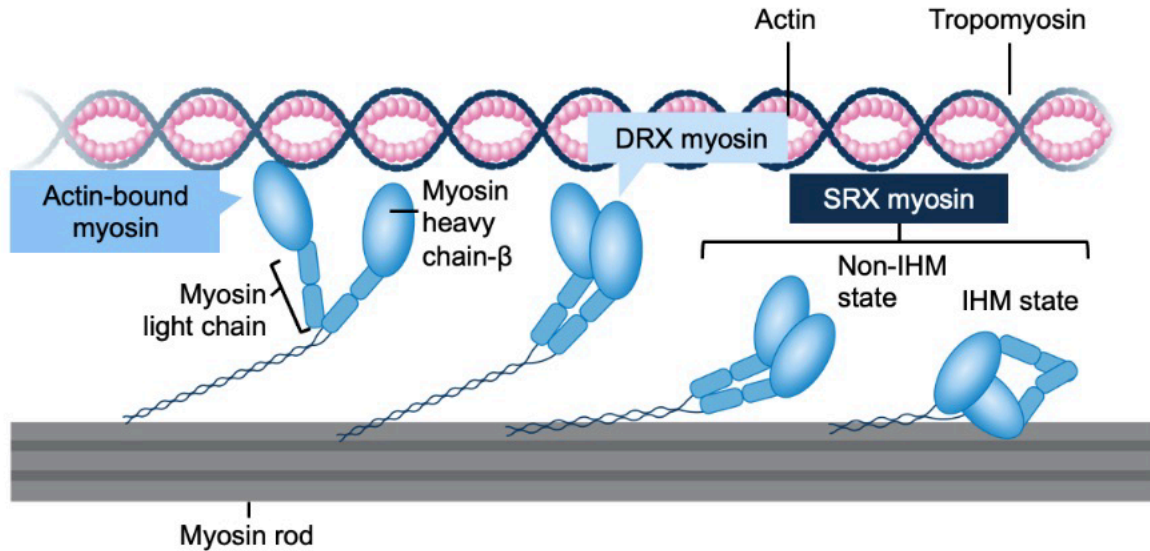
	Mavacamten group (n=123)	Placebo group (n=128)	Difference* (95% CI), p value
Primary endpoint†			
Either ≥1.5 mL/kg per min increase in pVO ₂ with ≥1 NYHA class improvement or ≥3.0 mL/kg per min increase in pVO ₂ with no worsening of NYHA class	45 (37%)	22 (17%)	19.4 (8.7 to 30.1; p=0.0005)
≥1.5 mL/kg per min increase in pVO ₂ with ≥1 NYHA class improvement	41 (33%)	18 (14%)	19.3 (9.0 to 29.6)
≥3.0 mL/kg per min increase in pVO ₂ with no worsening of NYHA class	29 (24%)	14 (11%)	12.6 (3.4 to 21.9)
Both ≥3.0 mL/kg per min increase in pVO ₂ and ≥1 NYHA class improvement	25 (20%)	10 (8%)	12.5 (4.0 to 21.0)

Aficamten



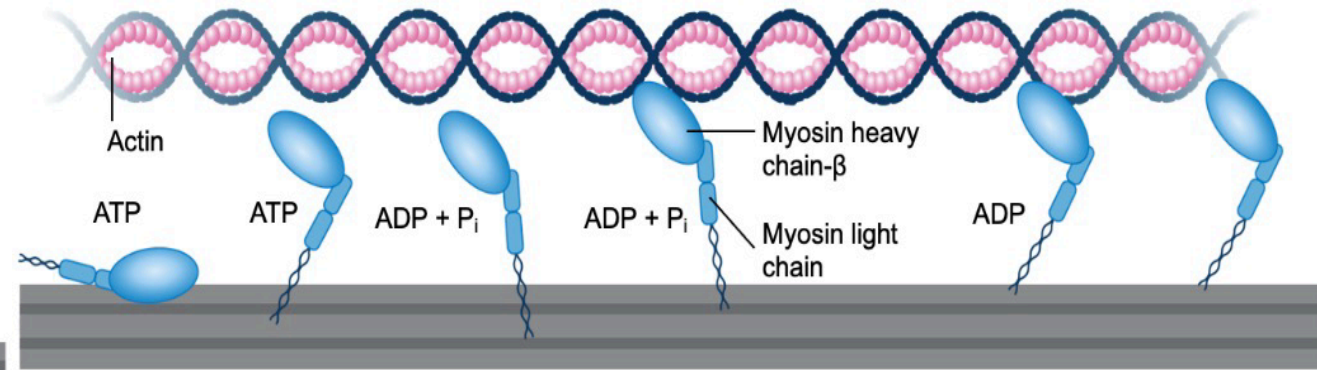
Small-Molecule Cardiac Myosin Inhibitors Targeting HCM

Mavacamten



Selective, reversible allosteric inhibitor of β -cardiac myosin ATPase, binding to a specific pocket within the myosin motor domain to reduce the rate of ATP hydrolysis and subsequent energy release available for actin–myosin cross-bridge formation.

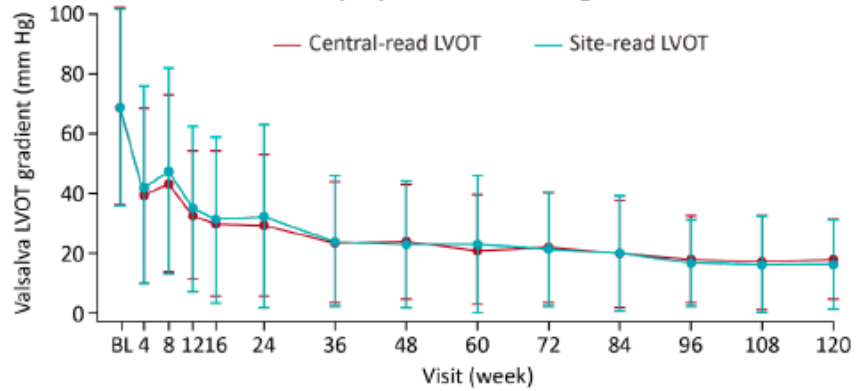
Aficamten



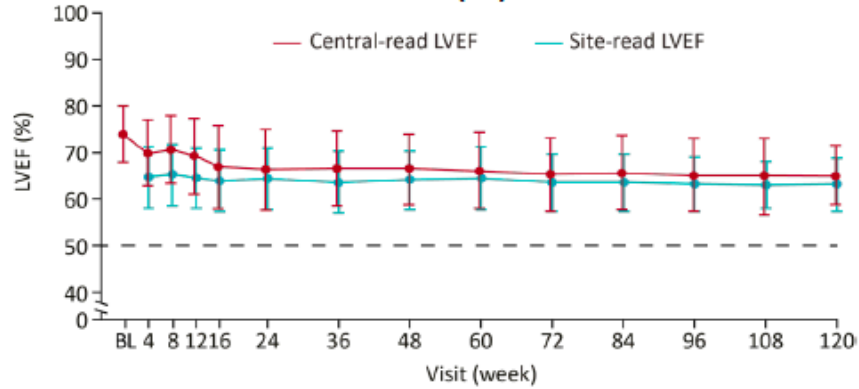
- Distinctive binding site
- Slows phosphate release from myosin
- Stabilizes weak actin-binding myosin conformation
- Shorter half-life
- Reach steady state in 2 weeks
- No substantial cytochrome P450 induction or inhibition

Mavacamten

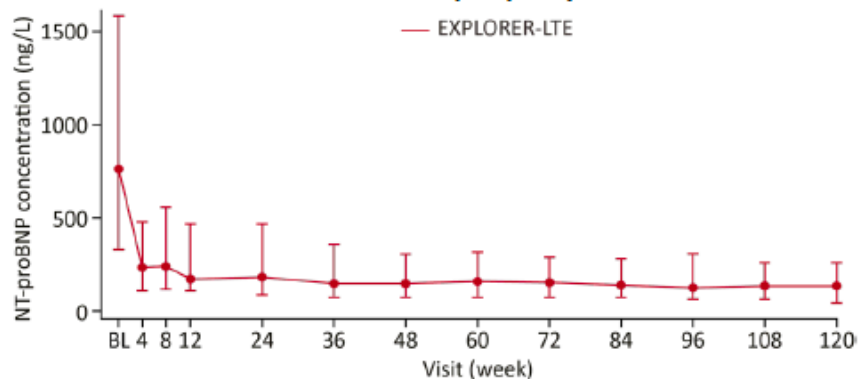
Mean (SD) Valsalva LVOT gradient



Mean (SD) LVEF



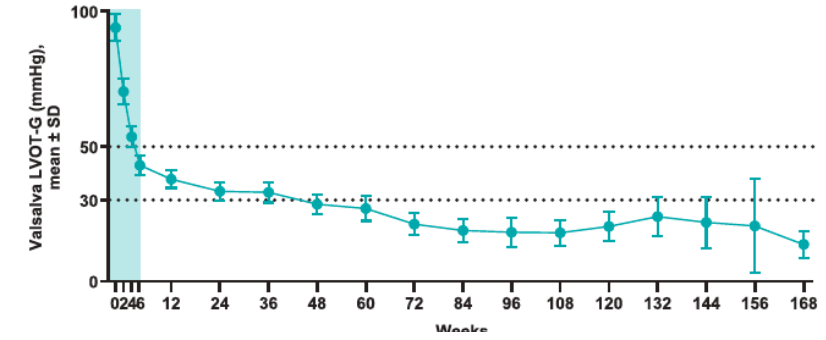
Median (IQR) NT-proBNP



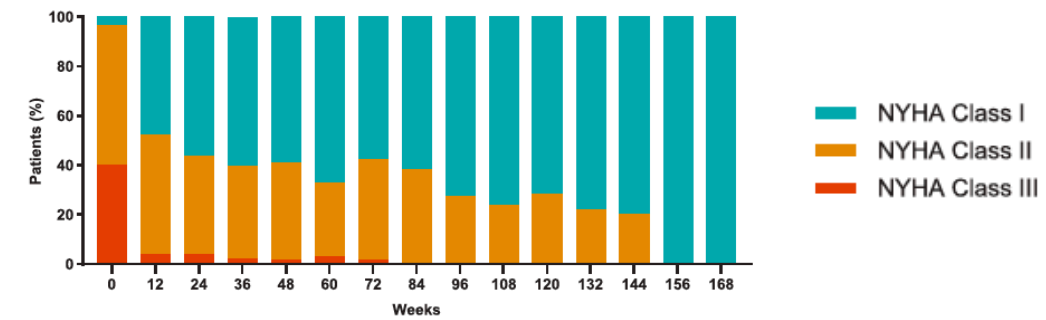
Long-term effect of Cardiac MI In oHCM

Aficacamten

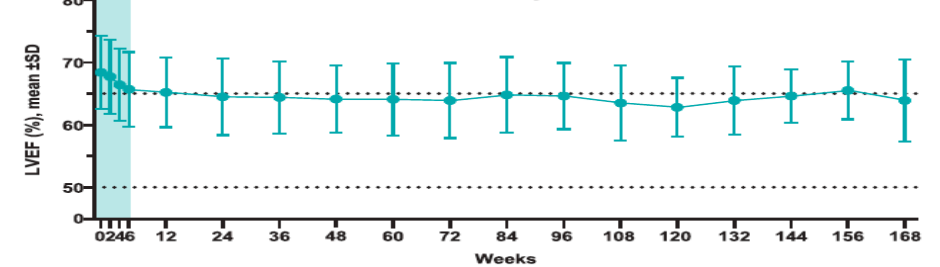
Valsalva LVOT Gradient



NYHA Class



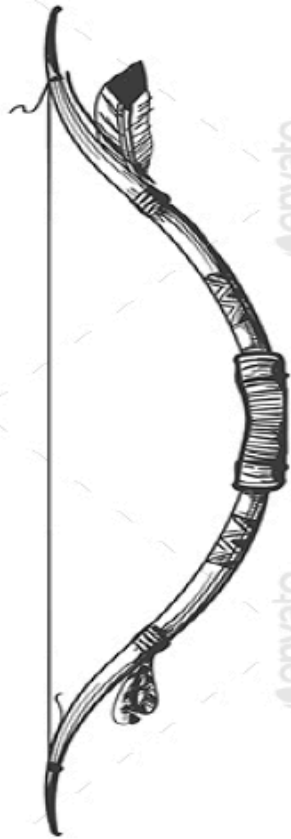
Left Ventricular Ejection Fraction



- No treatment interruptions due to LVEF <50%
- 2.9 LVEF <50% events per 100 patient-years
- No LVEF <40%
- Low incidence of new-onset atrial fibrillation -2 per 100 patient-years

Eur Heart J 2024; 45: 5071–5083

Eur Heart J 2026; 00:1–12



Beta-Blockers

Verapamil

Disopyramide

DDD-Pacing

Myectomy

Alcohol Septal Ablation

Myosin Inhibitors