PLACE 2026
PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

Gli inibitori della miosina cardiaca nei pazienti con cardiomiopatia ipertrofica: dai trial al mondo reale

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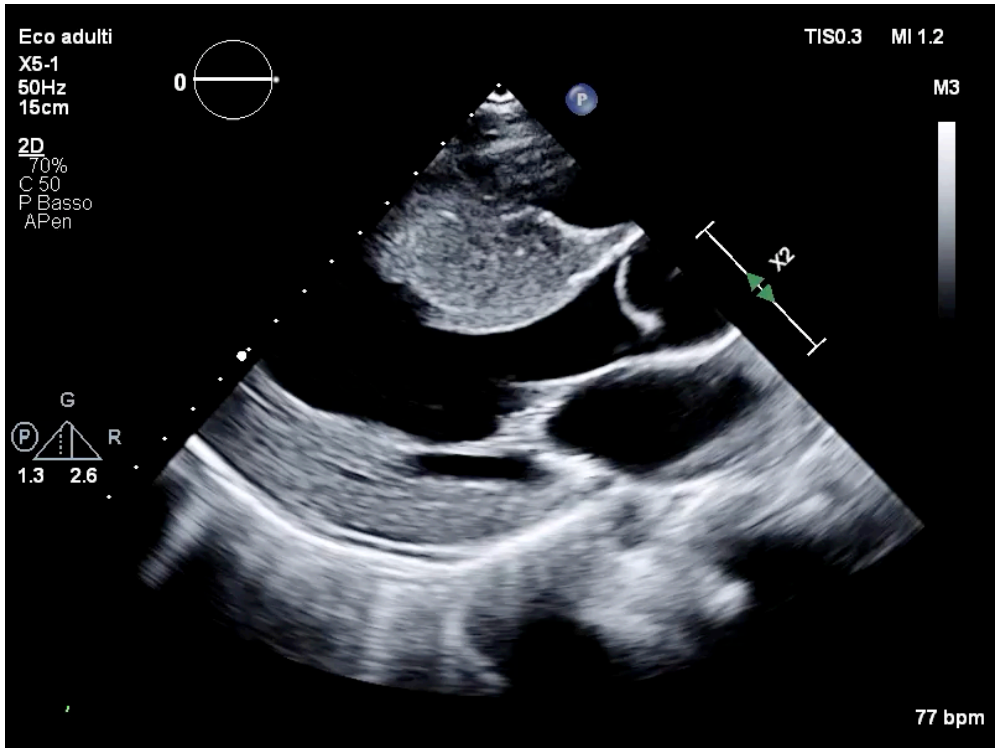
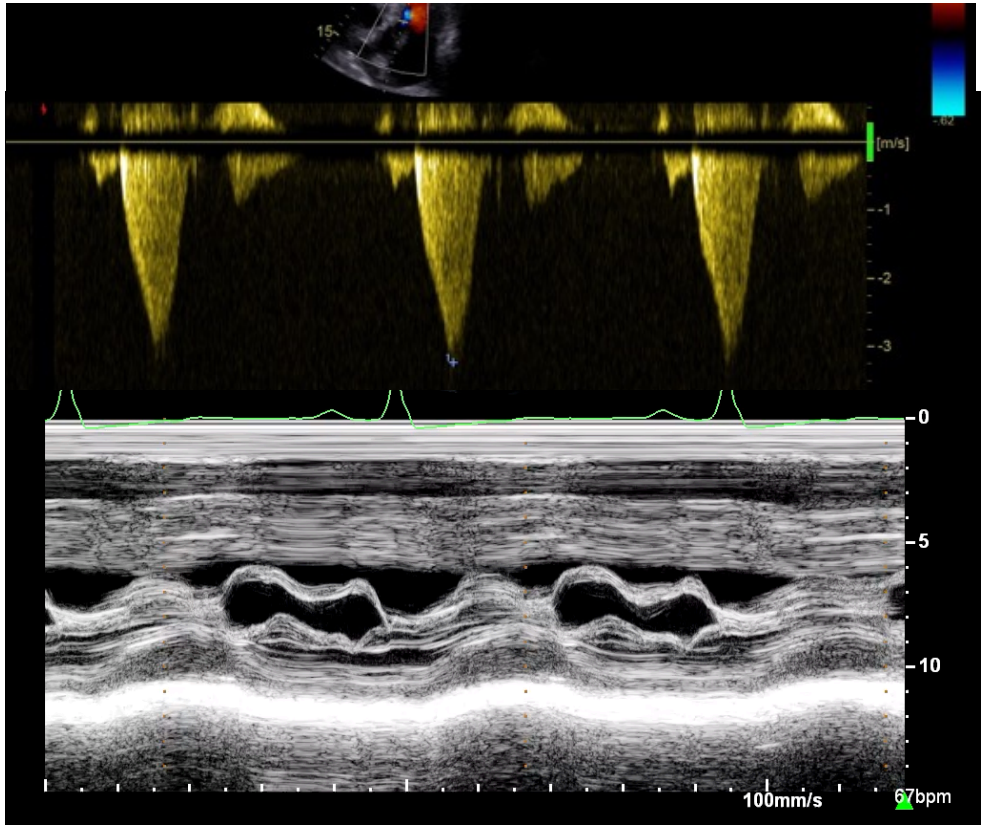
Meyer

Disclosures

Research Support: BMS, Cytokinetics, Sanofi Genzyme,
Shire Takeda, Amicus, Chiesi, Menarini International, Boston Scientific.

Advisory board: BMS, Cytokinetics, Sanofi Genzyme, Bayer, Chiesi, Shire Takeda, Amicus, Tenaya, Rocket Pharma, Edgewise, Lexeo, Lexicon.





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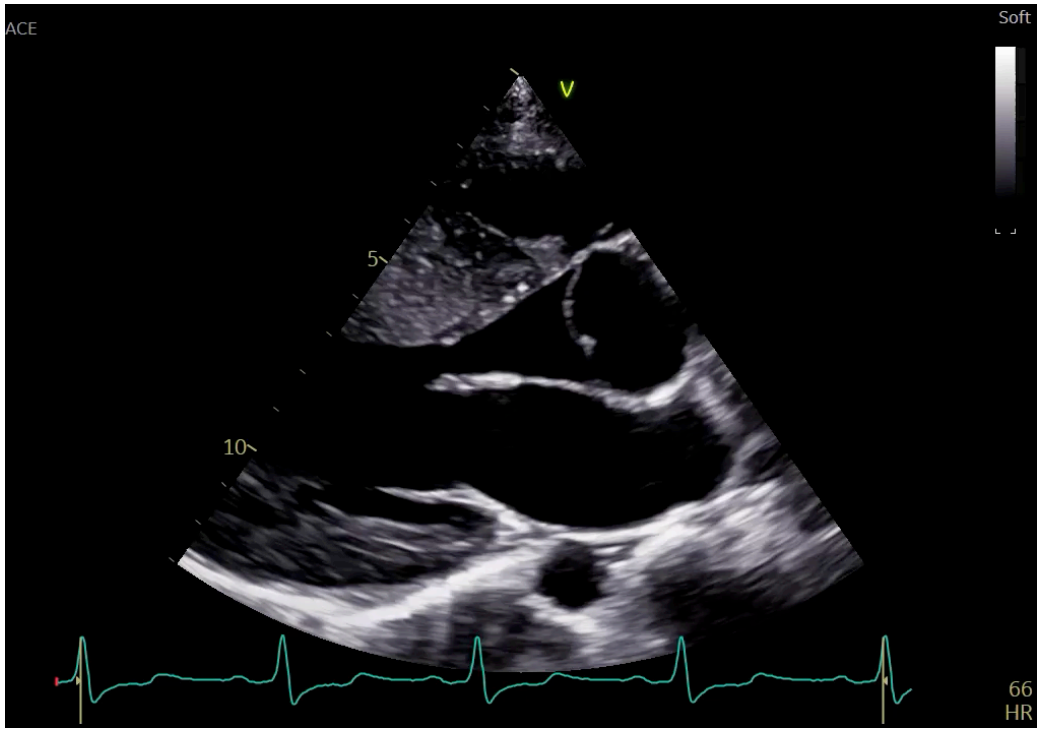
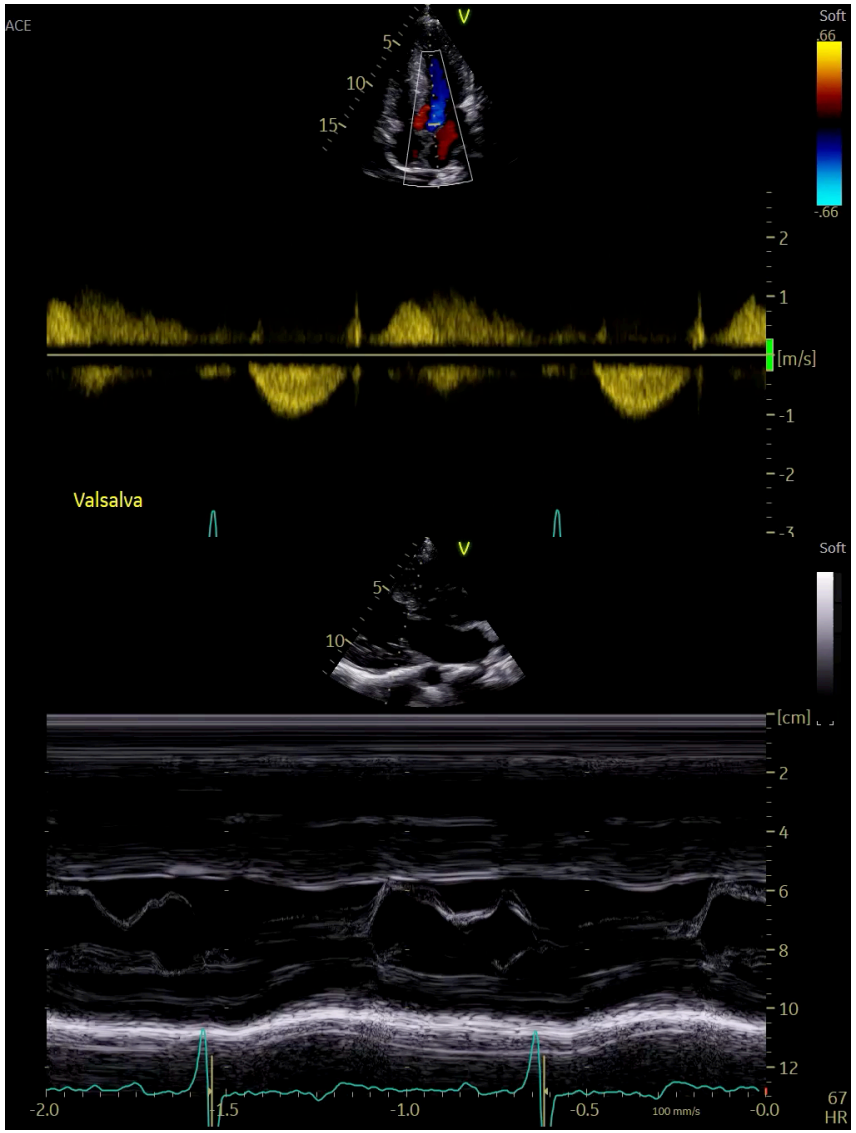
EAPC European Association of Preventive Cardiolo





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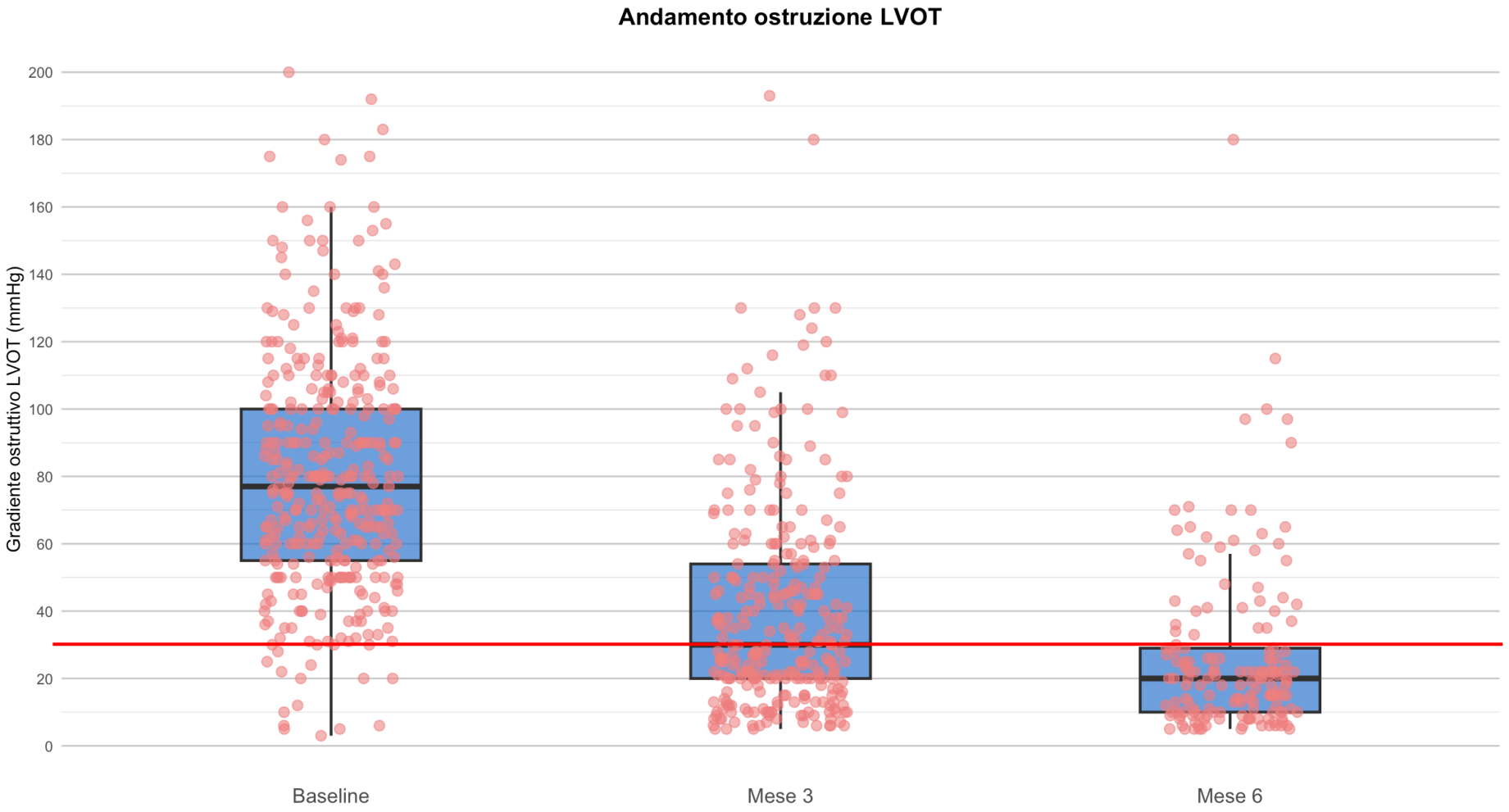
EFFICACIA DI MAVACAMTEN GRADIENTE ALL'EFFLUSSO VS



THIS OBJECT PEELS POTATOES

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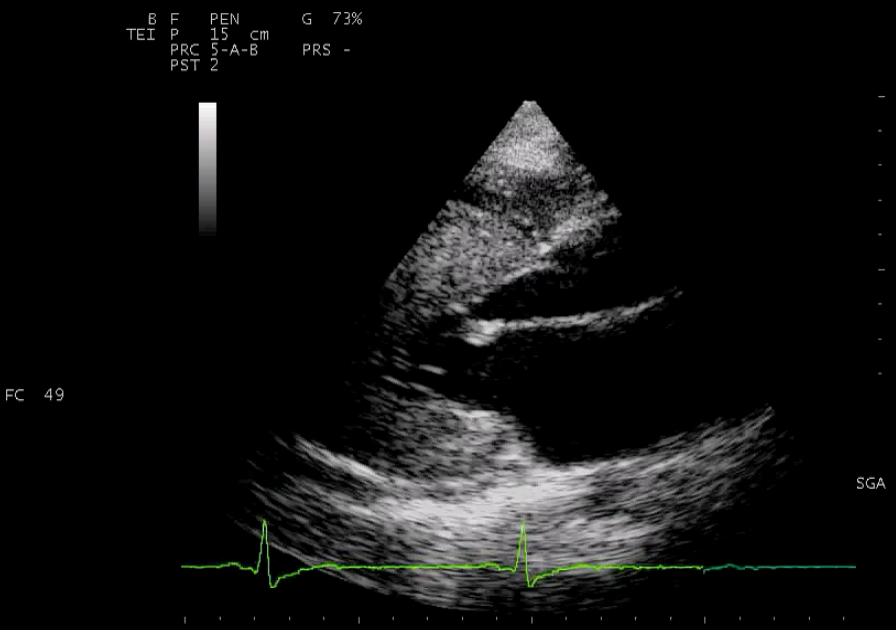
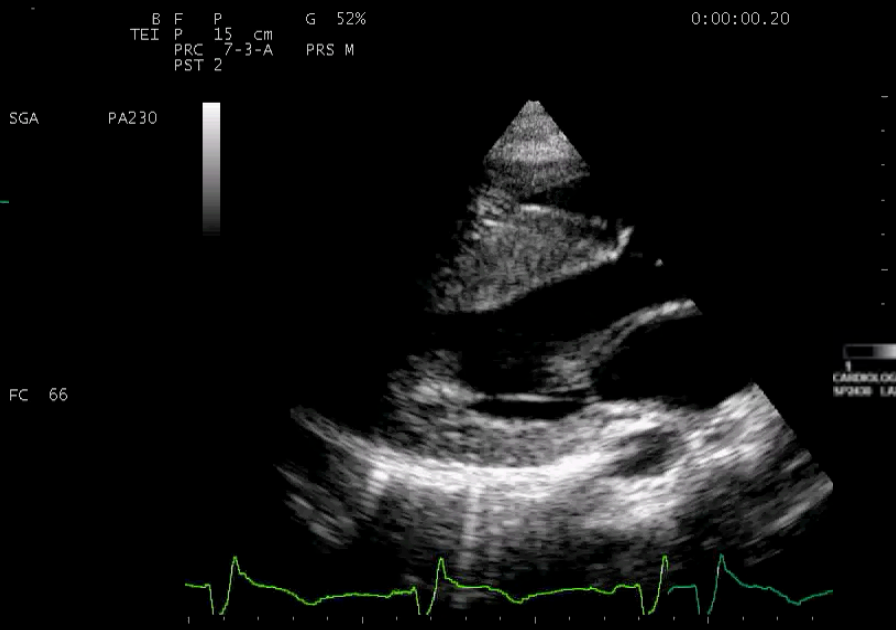
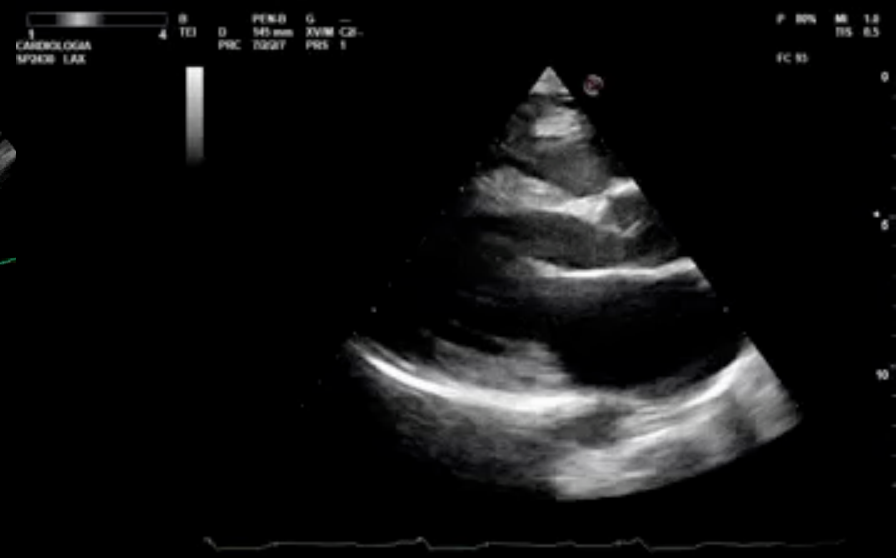
Age 22 –Pre Myectomy



Age 22 –Post Myectomy



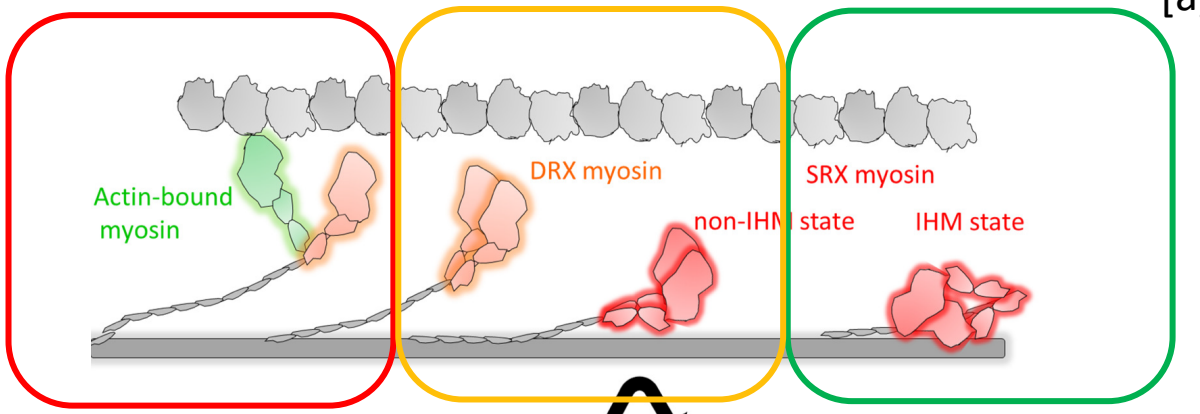
Age 34 – End-stage



Myosin States in Hypertrophic Cardiomyopathy

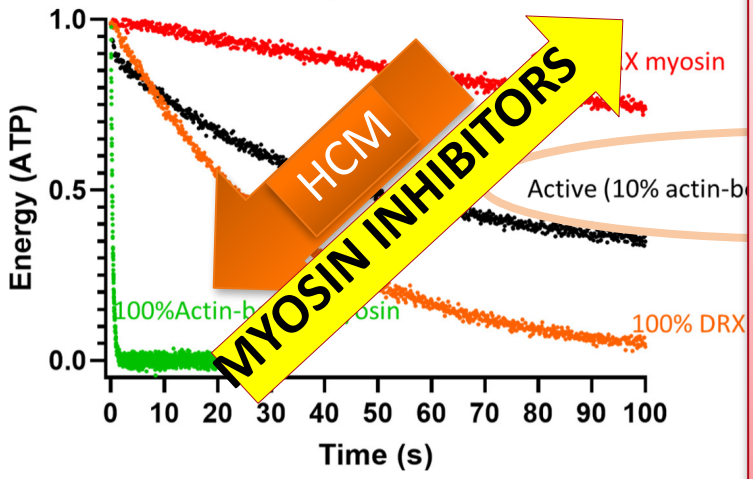
Calcium-mediated actin-myosin interaction

[a]



"A new state of cardiac myosin with very slow ATP turnover" (interacting heads motif) [b]

Energy Cycling



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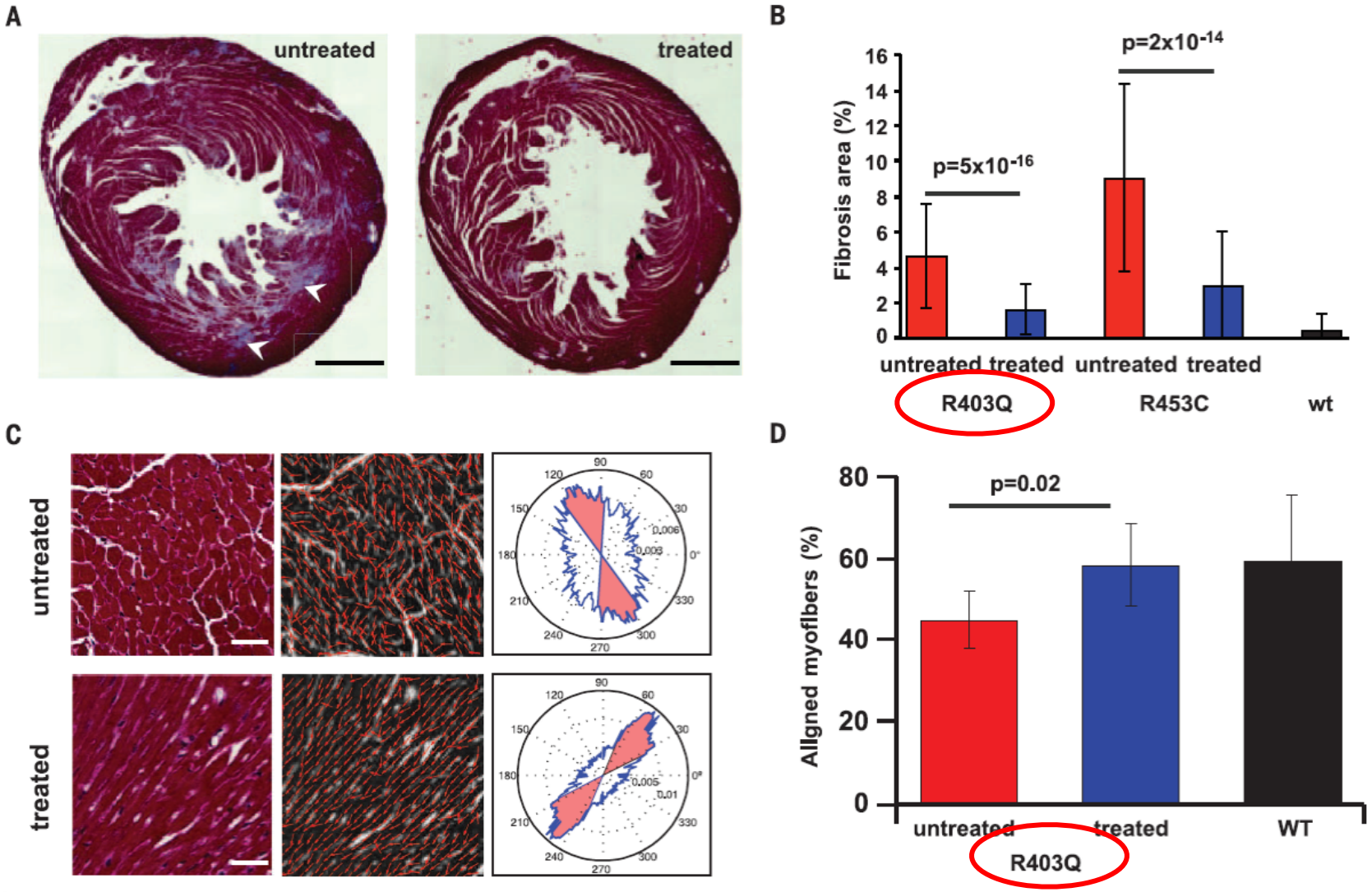
POTENTIAL FOR DISEASE MODIFICATION ?



Green et al, Science, 2016

PK/PD Parameters	Mavacamten	Aficamten
CYP metabolism	CYP2C19/3A4/2C9	CYP2D6
	PM most common in Asian populations	PM/IM common in Asian, Caucasian, and African American populations
CYP induction potential	Pre-clinical and clinical studies demonstrating induction of CYP3A4	Pre-clinical data published indicating no CYP induction liability
Half-life	6 to 9 days (slow/poor CYP2C19 metabolizer ~23 days)	75 to 85 hours (3 to 3.5 days) in normal metabolizer ~110 hours (~4.5 days) in CYP2D6-PM*
Time to steady state	21 – 35 days	10 – 12 days
PK Variability	High including CYP2C19 poor metabolizers	Medium including potentially CYP2D6 PM
Therapeutic Window		Shallow concentration response-unknown on impact

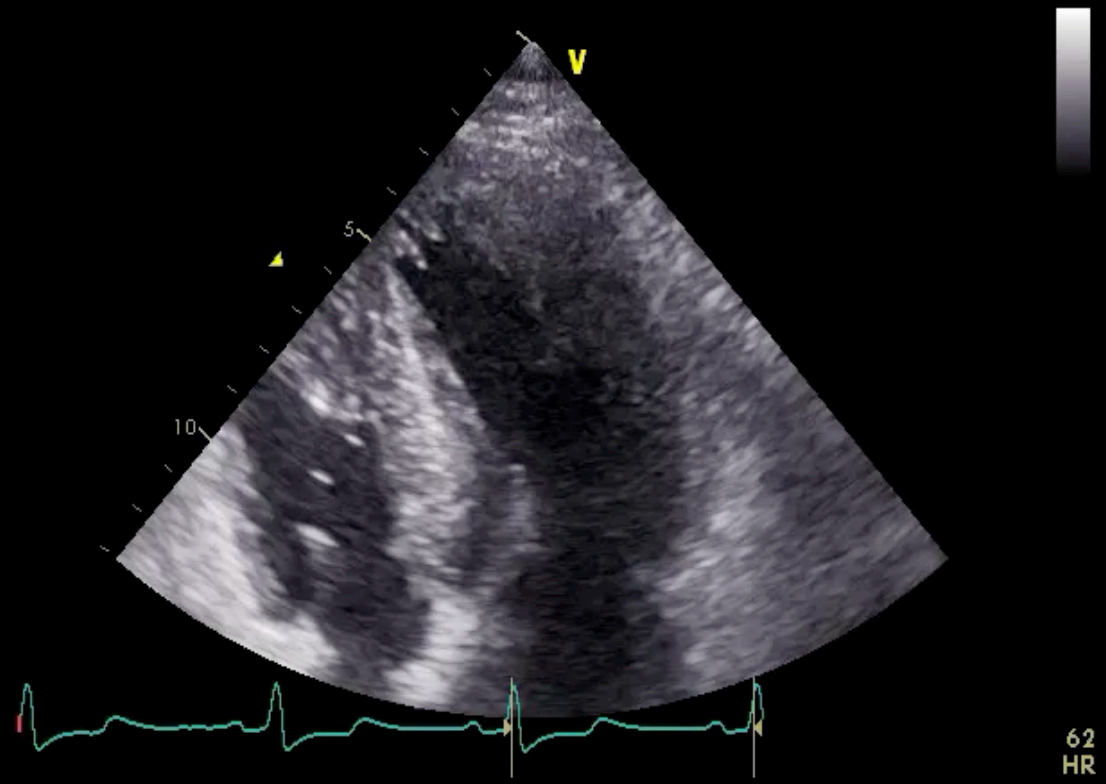
Malik FI, et al. *J Am Coll Cardiol Basic Trans Science*. 2022;7(8):763-775. Chuang C, et al. *J Med Chem*. 2021. e-pub ahead of print. BMS, data on file.

Change from baseline	EXPLORER-HCM (N = 251) at Week 30			SEQUOIA-HCM (N=282) at week 24		
	CAMZYOS (n = 123)	Placebo (n = 128)	Treatment difference (95% CI)	Aficamten (n=142)	Placebo (n=140)	Treatment difference (95% CI)
CPET parameters						
Mean (SD) change in pVO_2, mL/kg/min	1.4 (3.1)	-0.1 (3.0)	1.4 (0.6, 2.1) P = 0.0006	1.8 (1.2-2.3)	0 (-0.5-0.5)	1.7 (1.0, 2.4) *P* = 0.001
Obstruction parameters						
Mean (SD) change in Valsalva LVOT gradient, mmHg	-49 (34)	-12 (31)	−37	-47.6 (-54-41)	1.8 (-4-8)	-50 (-57,-44) *P* < 0.001
Proportion of Valsalva LVOT gradient <30 mmHg	Post-exercise LVOT peak gradient <30 mm Hg			9.3%	3.6%	45.7 %(36.9-54.5) *P* < 0.001
	64/113 (57%)	8/114 (7%)	49,6 (39,3-59,9)			
Symptoms and biomarker						
n (%) of patients with ≥1 improvement in NYHA Class	80 (65%)	40 (31%)	34% (22-45) *P* < 0.0001	83 (58.5%)	34 (24.3%)	34.2% (23.4-45) *P* < 0.001
Mean (SD) change in KCCQ-23-CSS	13.6 (14.4)	4.2 (13.7)	9.1 (5.5 - 12.7) *P* < 0.0001	12 (9-14)	5 (3-7)	7 (5-10) *P* < 0.001

Olivotto et al Lancet 2020, Maron et al N Engl J Med 2024

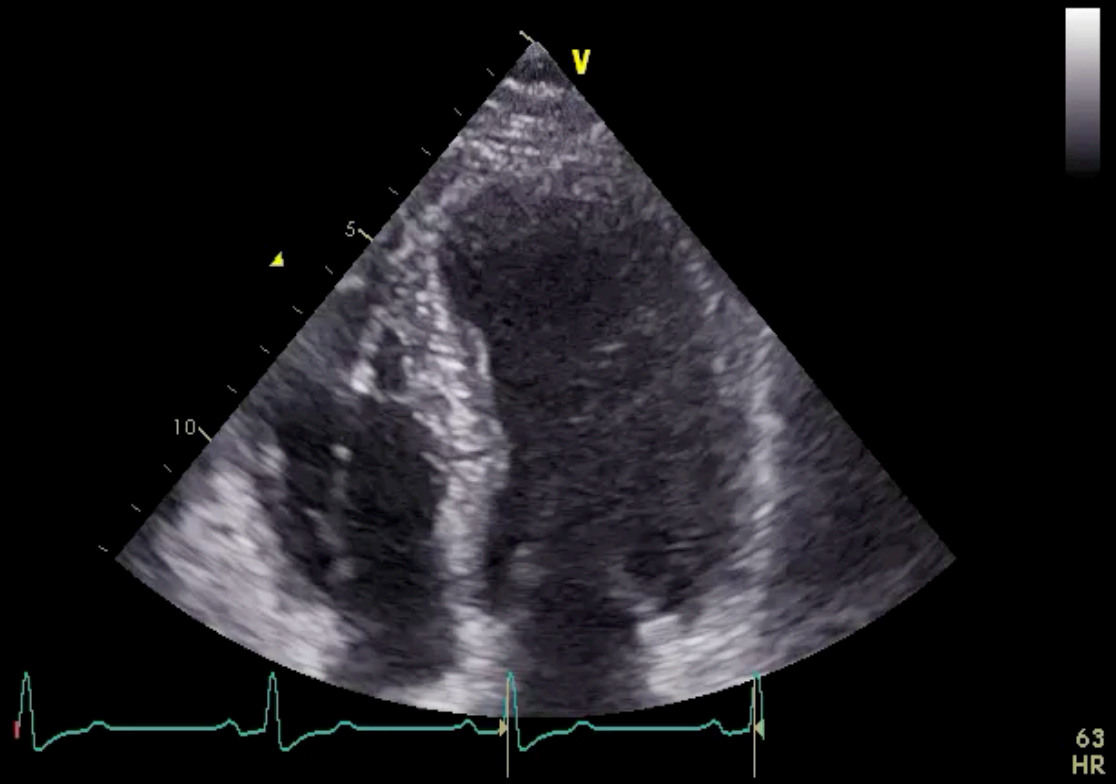
Before mavacamten

EF = 75 %



3 years on mavacamten

EF = 65 %



Effect of Aficamten on Cardiac Structure and Function in Obstructive Hypertrophic Cardiomyopathy

SEQUOIA-HCM CMR Substudy

Ahmad Masri, MD, MS,[a] Rhanderson N. Cardoso, MD,[b] Theodore P. Abraham, MD,[c] Brian L. Claggett, PhD,[b] Caroline J. Coats, MBBS, PhD,[d] Sheila M. Hegde, MD, MPH,[e] Ian J. Kulac, MS,[b] Matthew M.Y. Lee, MBChB, PhD,[d] Martin S. Maron, MD,[f] Bela Merkely, MD, PhD, DSc,[g] Michelle Michels, MD, PhD,[h] Iacopo Olivotto, MD,[i] Artur Oreziak, MD,[j] Daniel L. Jacoby, MD,[k] Stephen B. Heitner, MD,[k] Stuart Kupfer, MD,[k] Fady I. Malik, MD, PhD,[k] Lisa Meng, PhD,[k] Scott D. Solomon, MD,[e] Amy Wohltman, ME,[k] Raymond Y. Kwong, MD, MPH,[b] Christopher M. Kramer, MD,[l] the SEQUOIA-HCM Investigators

JACC VOL. 84, NO. 19, 2024

NOVEMBER 5, 2024:1806-1817

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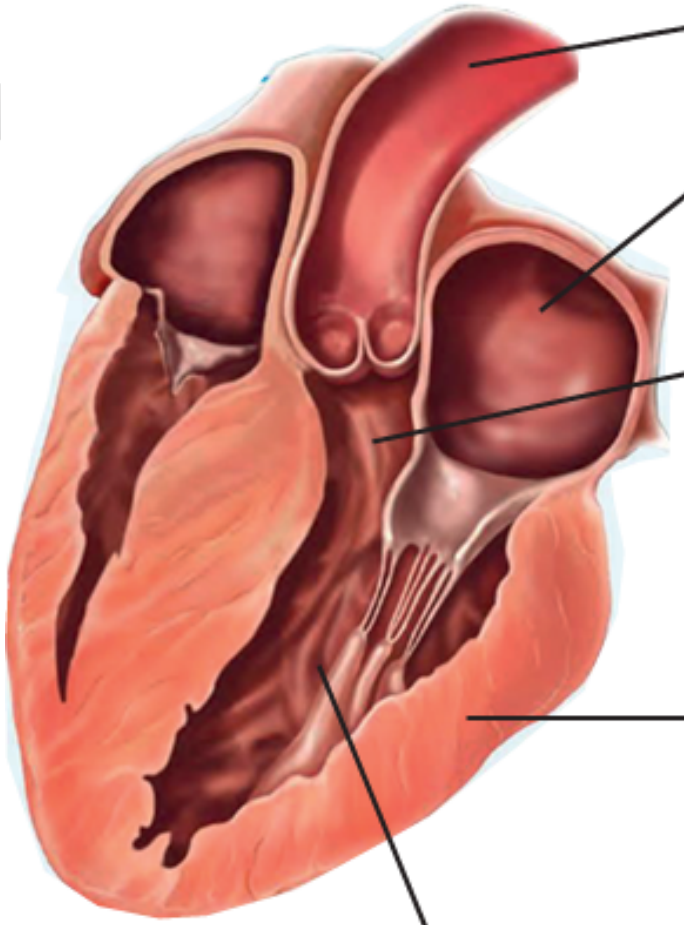
Placebo-Corrected Changes From Baseline to Week 24 in Patients Receiving Aficamten

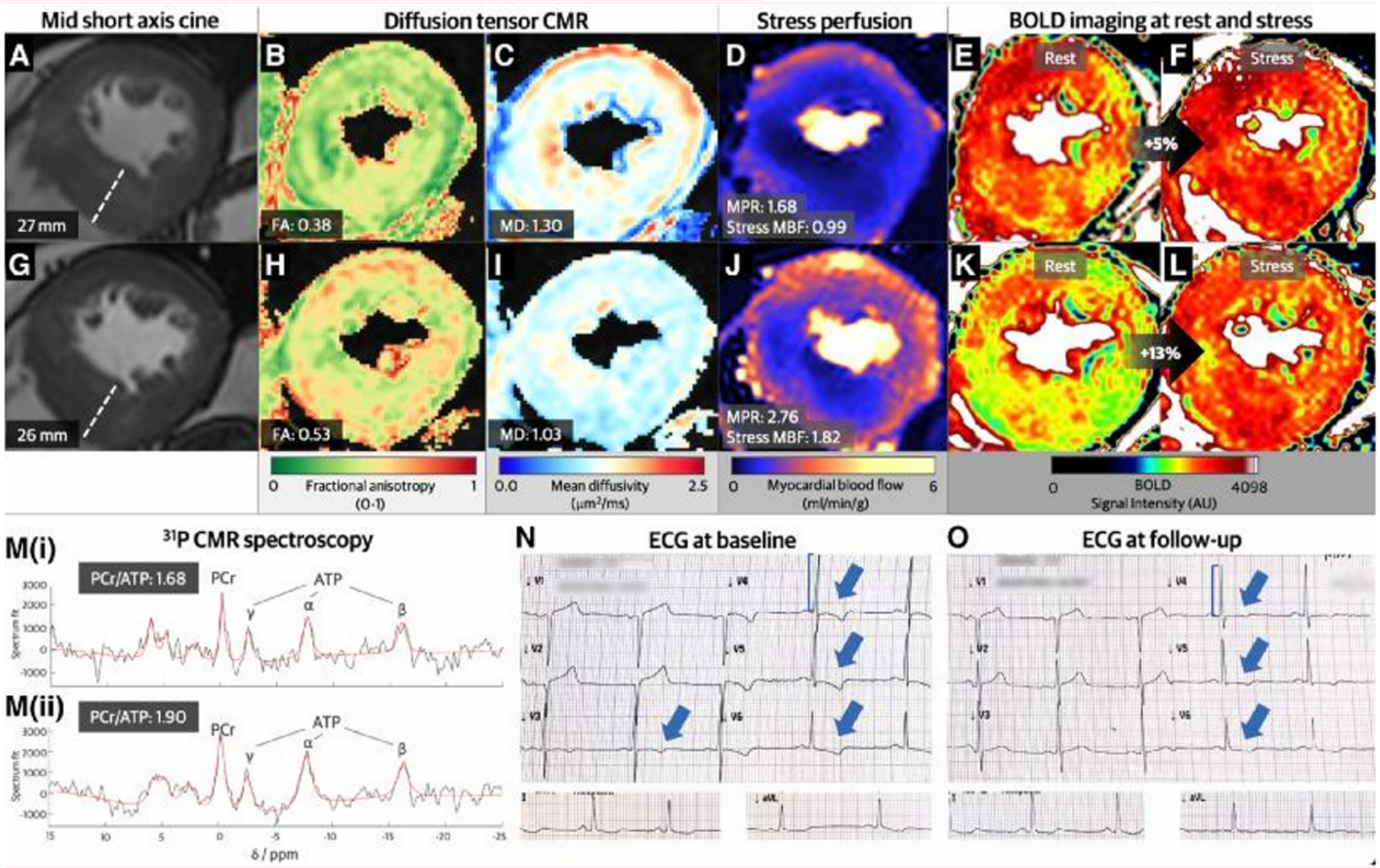


- ↓ NT-proBNP −85%
- ↓ Left atrial volume index −13 mL/m^2
- ↓ Resting LVOT-G −38 mm Hg
- ↓ Valsalva LVOT-G − 47 mm Hg
- ↓ LV mass index −15 g/m^2
- ↓ LV wall thickness −2.1 mm
- ↓ Native T1 relaxation time − 37 ms
- ↔ LV replacement fibrosis (LGE mass) −0.7 g
- ↔ LV extracellular volume fraction 0.7%
- ↔ LV chamber volume

Multiparametric cardiovascular magnetic resonance evaluation of myocardial perfusion, oxygenation, and energetics in hypertrophic cardiomyopathy following cardiac myosin inhibitor therapy

Lucy E.M. Finnigan *†, **Niklas Beyhoff** †, **Zakariye Ashkir**, **Hugh Watkins**, **Stefan Neubauer**, **and Betty Raman** *

https://doi.org/10.1093/ehjci/jeae297
Online publish-ahead-of-print 28 November 2024



3500-IT-2500042

Scientific Sessions

IMPACT OF MAVACAMTEN ON THE RATES OF HOSPITALIZATION AND EMERGENCY ROOM (ER) VISITS IN PATIENTS WITH OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY (HCM) IN THE UNITED STATES

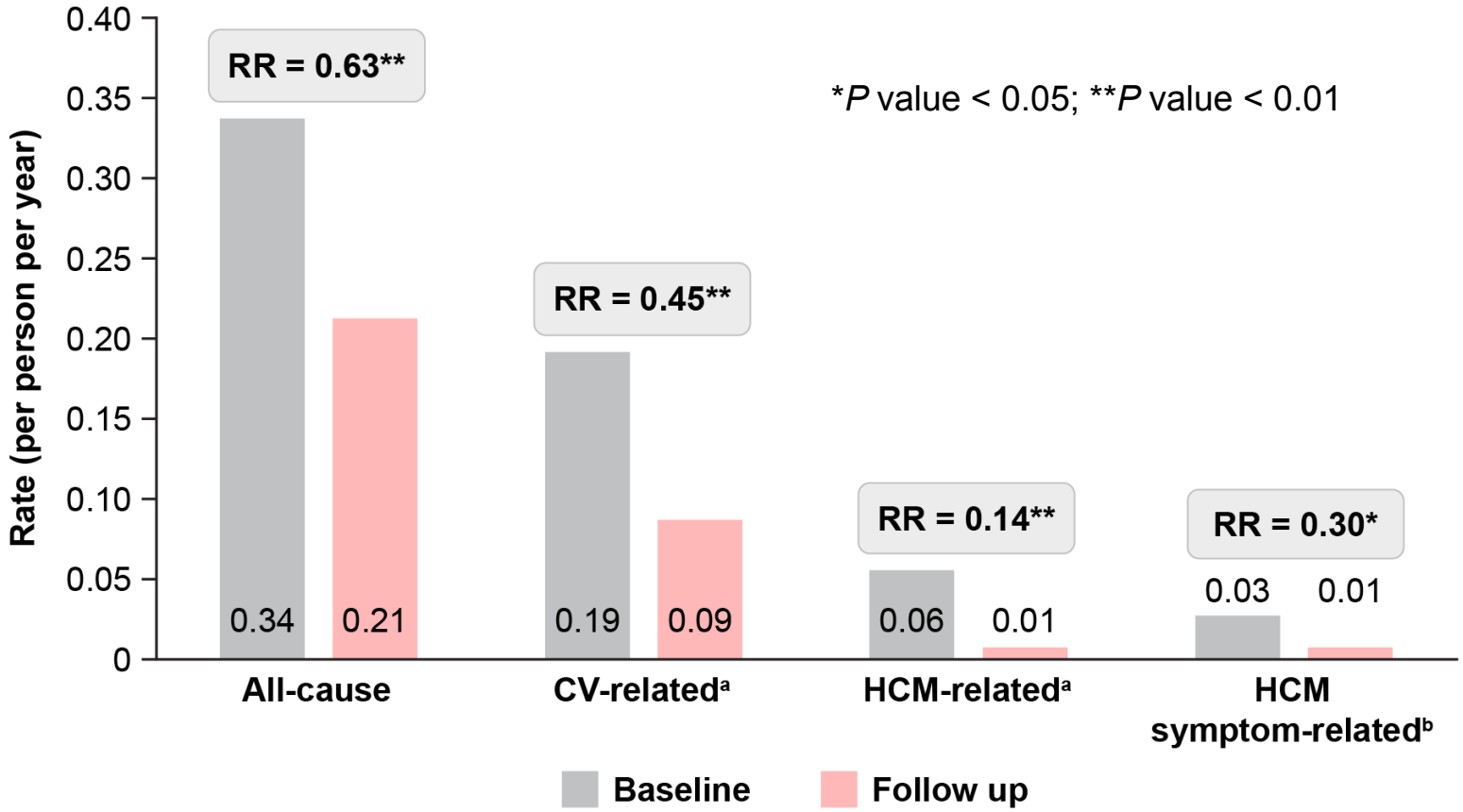
Anjali Owens[1], Weihua Gao[2], Ervant J. Maksabedian Hernandez[2], Anandkumar Dubey[2], Warren Stevens[3], Matthew Davis[3], Patricia Schuler[2], Manish Pandya[2], Xu Han[2]

[1]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, US; [2]Bristol Myers Squibb, Princeton, NJ, US; [3]Medicus Economics, Milton, MA, US

American Heart Association.

#AHA25

MAVACAMTEN WAS ASSOCIATED WITH STATISTICALLY SIGNIFICANT REDUCTIONS IN HOSPITALIZATION RATES



*P value < 0.05; **P value < 0.01

Baseline (mean ± SD): 9.9 ± 3.6 months; Follow-up (mean ± SD): 8.6 ± 6.6 months

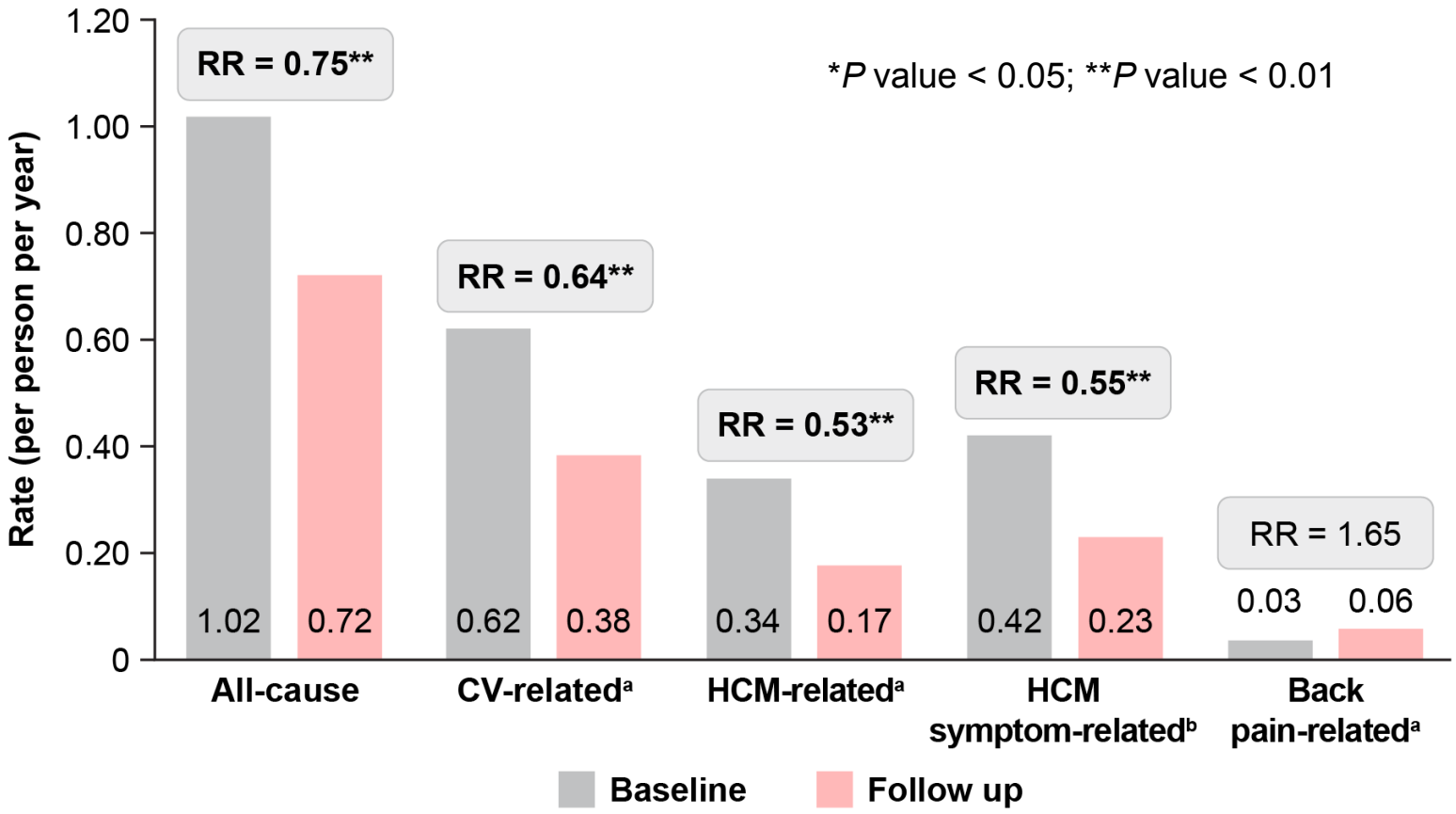
Following mavacamten initiation among the 554 patients, hospitalization rates decreased by:

- 37% for all-cause[c]
- 55% for CV-related
- 86% for HCM-related
- 70% for HCM symptom-related

[a]CV-related, HCM-related, and back pain-related hospitalizations were identified by the presence of a diagnosis of any CV disease, HCM, or back pain in the primary position on a claim. [b]HCM symptom-related hospitalizations were identified by the presence of a diagnosis of any key HCM symptoms (including fatigue, chest pain/angina, syncope, dyspnea, and palpitations) in the primary position on a claim. [c]RR for back pain could not be estimated due to insufficient number of events.

CV, cardiovascular; HCM, hypertrophic cardiomyopathy; RR, rate ratio; SD, standard deviation

MAVACAMTEN WAS ALSO ASSOCIATED WITH STATISTICALLY SIGNIFICANT REDUCTIONS IN ER VISIT RATES



Baseline (mean ± SD): 9.9 ± 3.6 months; Follow-up (mean ± SD): 8.6 ± 6.6 months

Following mavacamten initiation among the 554 patients, ER visit rates decreased by:

- 25% for all-cause
- 36% for CV-related
- 47% for HCM-related
- 45% for HCM symptom-related

[a]CV-related, HCM-related, and back pain-related ER visits were identified by the presence of a diagnosis of any CV disease, HCM, or back pain on a claim.
[b]HCM symptom-related ER visits were identified by the presence of a diagnosis of any key HCM symptoms (including fatigue, chest pain/angina, syncope, dyspnea, and palpitations) on a claim.

CV, cardiovascular; ER, emergency room; HCM, hypertrophic cardiomyopathy; RR, rate ratio; SD, standard deviation

TRIALS (MAVA+AFI)

Prov. Gradient reduction 50 mmhg

>60% improve at least 1 NYHA class

Improved QOL

50% drop in NTProBNP

Satisfactory safety profile (AFI>MAVA)

Initial evidence of favorable cardiac remodeling

REAL WORLD (MAVA)

- 9/10 patients improve significantly
- Substantial LVOT gradient reduction
- Improved QOL
- Satisfactory safety profile (lower doses utilized)
- Initial evidence of favorable cardiac remodeling
- Cautious titration compared to trials
- Older, NYHA 2 patients?

ORIGINAL ARTICLE

Mavacamten in Symptomatic Nonobstructive Hypertrophic Cardiomyopathy

M.Y. Desai,[1,2] A.T. Owens,[3] T. Abraham,[4] I. Olivotto,[5] P. Garcia-Pavia,[6] R.D. Lopes,[7] P. Elliott,[8] F. Fernandes,[9] N. Verheyen,[10] L. Maier,[11] B. Meder,[12] O. Azevedo,[13] H. Kitaoka,[14] K. Wolski,[2] Q. Wang,[2] W. Jaber,[2] L. Mitchell,[2] J. Myers,[15] T. Rano,[16] Z. Gong,[16] Y. Zhong,[16] S. Carter-Bonanza,[16] V. Florea,[16] R. Aronson,[16] and S.E. Nissen,[2] for the ODYSSEY-HCM Investigators*

Figure 1. Panel A. Peak Oxygen Uptake (pVO2)

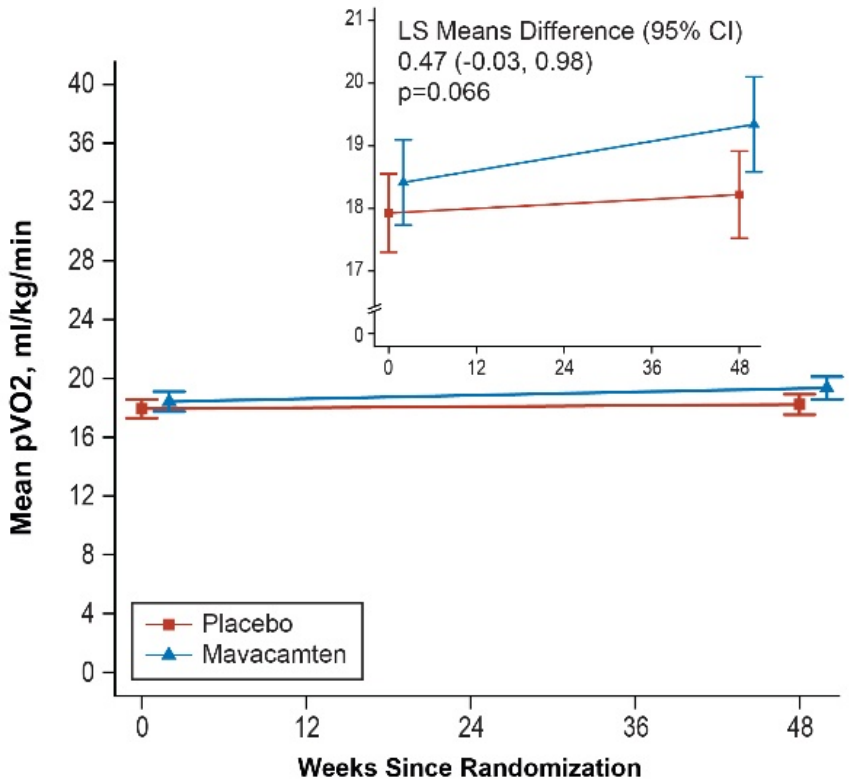
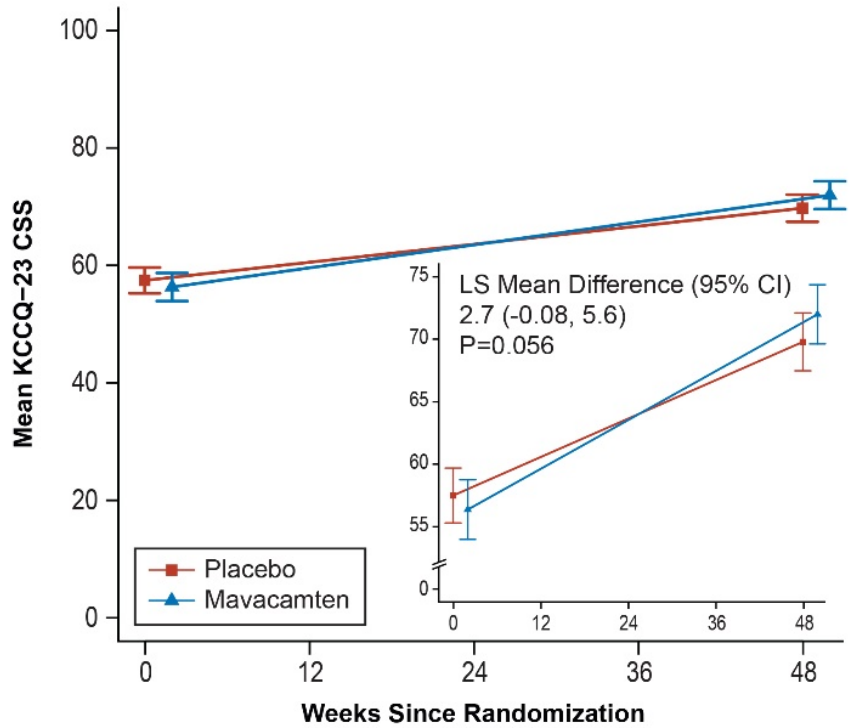


Figure 1. Panel B. KCCQ-23 Clinical Summary Score

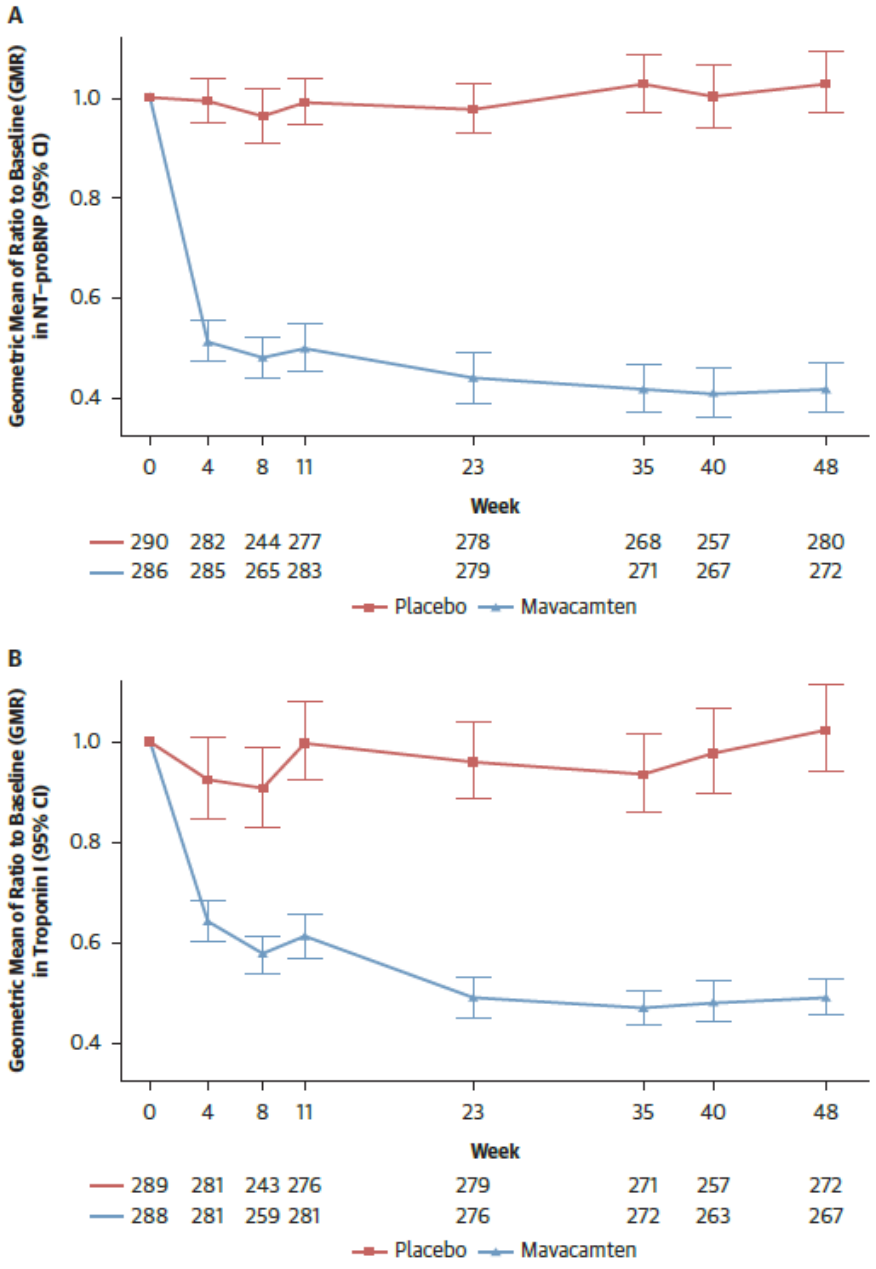


Effects of Mavacamten on Cardiac Biomarkers in Nonobstructive Hypertrophic Cardiomyopathy

Insights From the ODYSSEY-HCM Trial

Milind Y. Desai, MD, MBA,[a,b] Iacopo Olivotto, MD,[c] Theodore Abraham, MD,[d] Steven E. Nissen, MD,[b] Pablo Garcia-Pavia, MD, PhD,[e] Renato D. Lopes, MD, PhD,[f] Perry M. Elliott, MD,[g] Fabio Fernandes, MD, PhD,[h] Edileide de Barros Correia, MD,[i] Roberto Barriales-Villa, MD, PhD,[j] Esther Zorio, PhD,[k,l] Michael Arad, MD,[m] Sung-Hee Shin, MD,[n] Nicolas Verheyen, MD,[o] Benjamin Meder, MD,[p] Olga Azevedo, MD, PhD,[q] Hiroaki Kitaoka, MD,[r] Kathy Wolski, MPH,[b] Qiuqing Wang, MS,[b] Bharat Suryawanshi, MS,[s] Zhaoqing Wang, MS,[s] Victoria Florea, MD,[s] Ron Aronson, MD,[s] Anjali T. Owens, MD,[t] the ODYSSEY-HCM Investigators

J Am Coll Cardiol 2025



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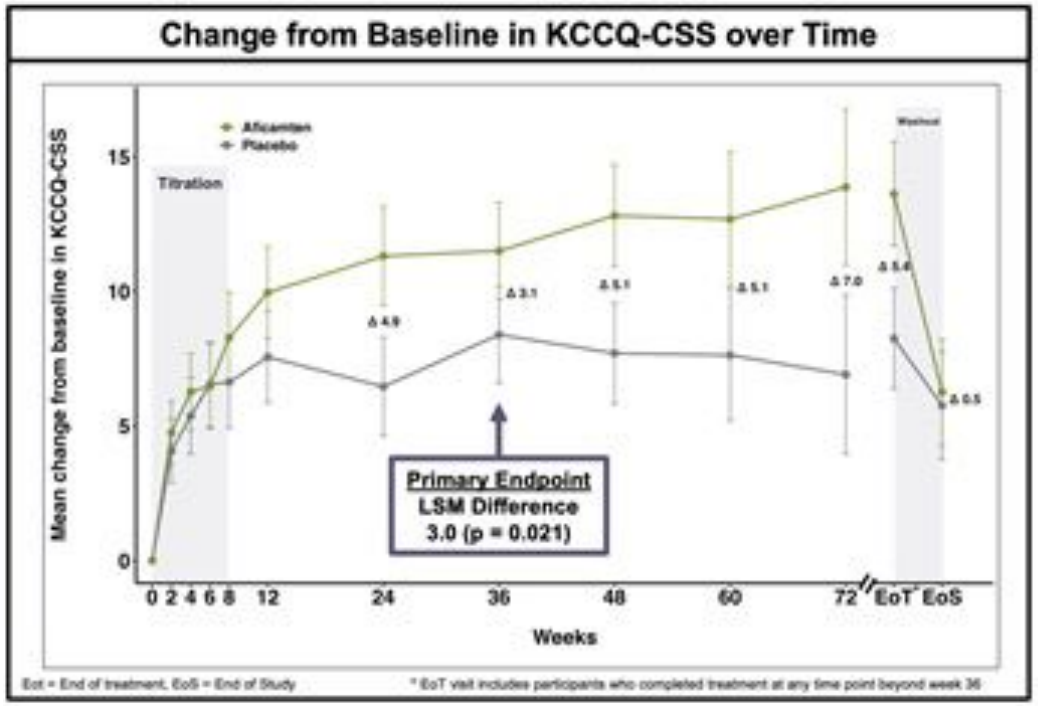
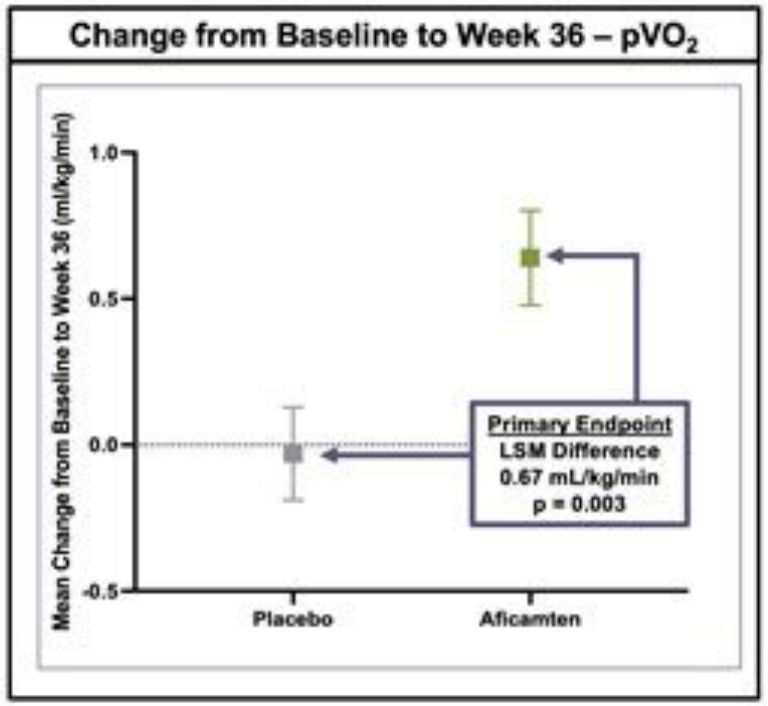
Cytokinetics Announces Positive Topline Results from ACACIA-HCM, the Pivotal Phase 3 Clinical Trial of Aficamten in Patients with Non-Obstructive Hypertrophic Cardiomyopathy

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

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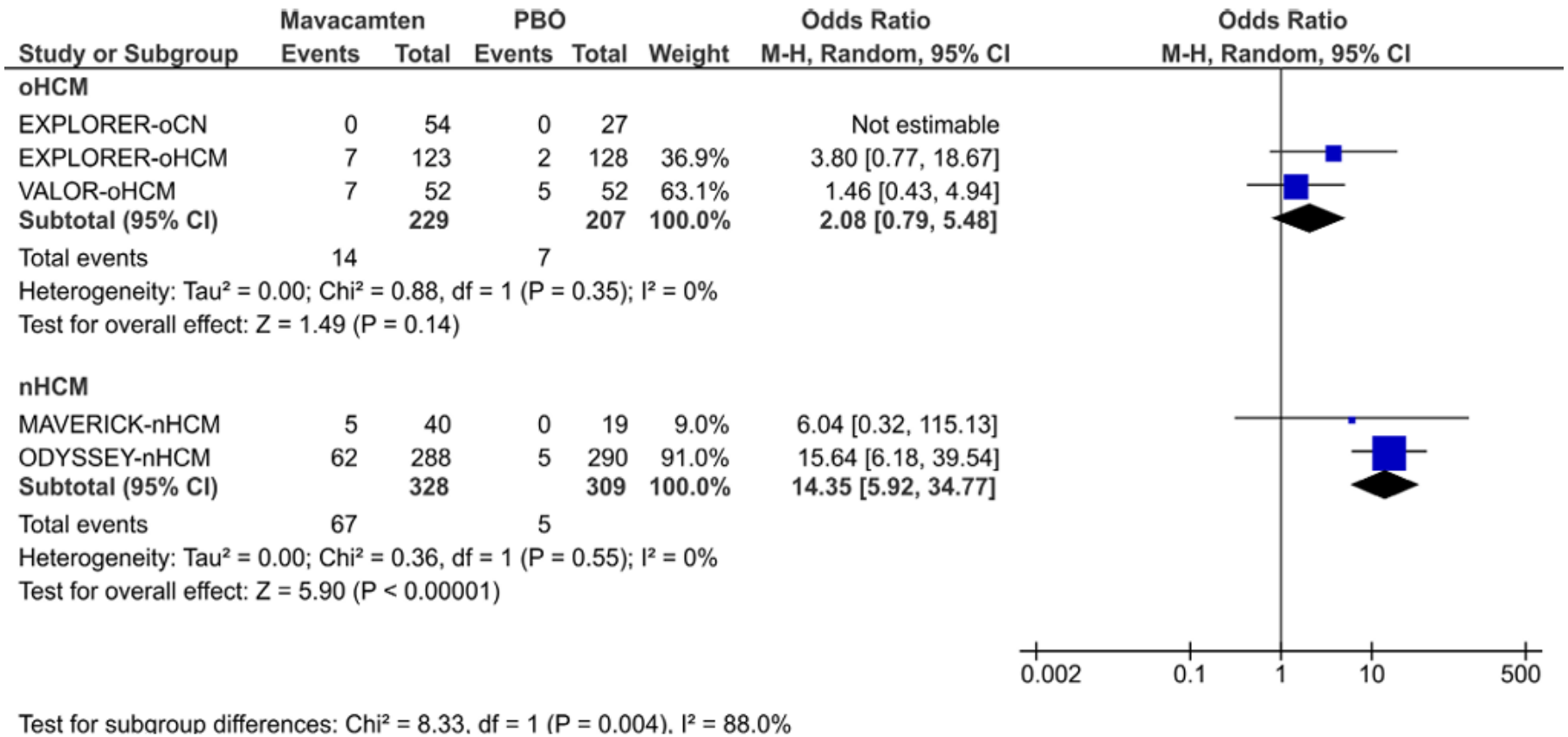
Safety and efficacy of mavacamten in obstructive versus non-obstructive hypertrophic cardiomyopathy: a meta-analysis of randomised controlled trials

Figure 2 Risk of LVEF decline <50%. Pooled ORs stratified by phenotypes. HCM, hypertrophic cardiomyopathy; LVEF, left ventricular ejection fraction; nHCM, non-obstructive HCM; oHCM, obstructive HCM; PBO, placebo.

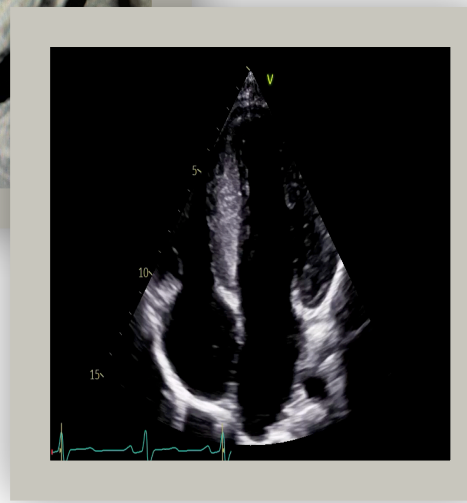


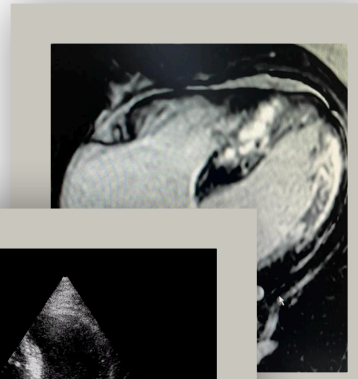
Alazzam AY, et al. Heart 2026

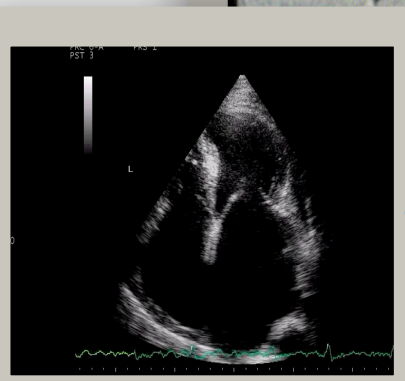
L’Inconoscibile Empireo

Il Prodigio

La Conquista







La Terra dei Rimpianti