THE EFFECT OF AFICAMTEN VS METOPROLOL ON CARDIAC BIOMARKERS IN OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY

A secondary analysis from MAPLE-HCM

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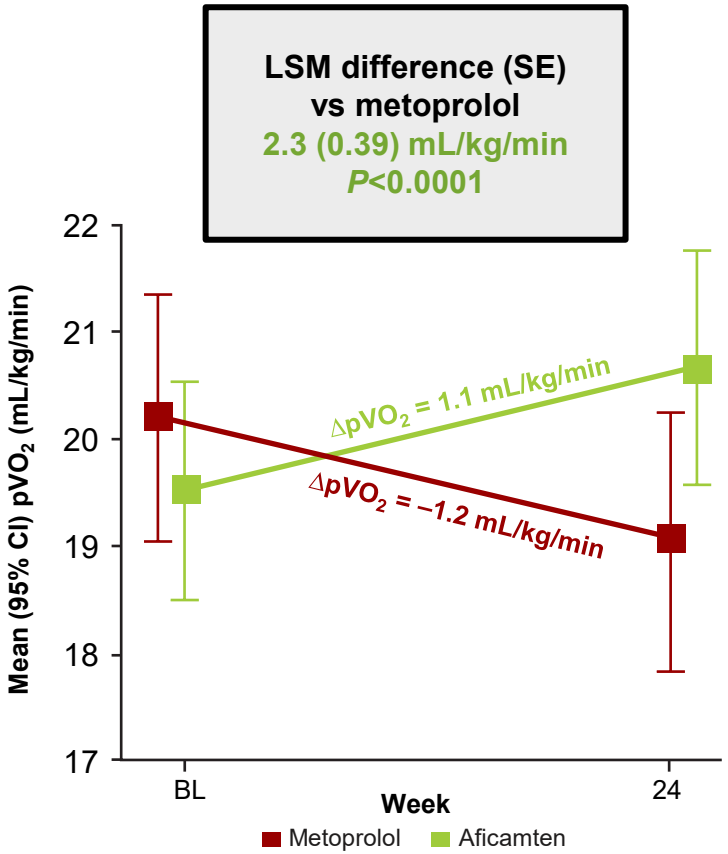
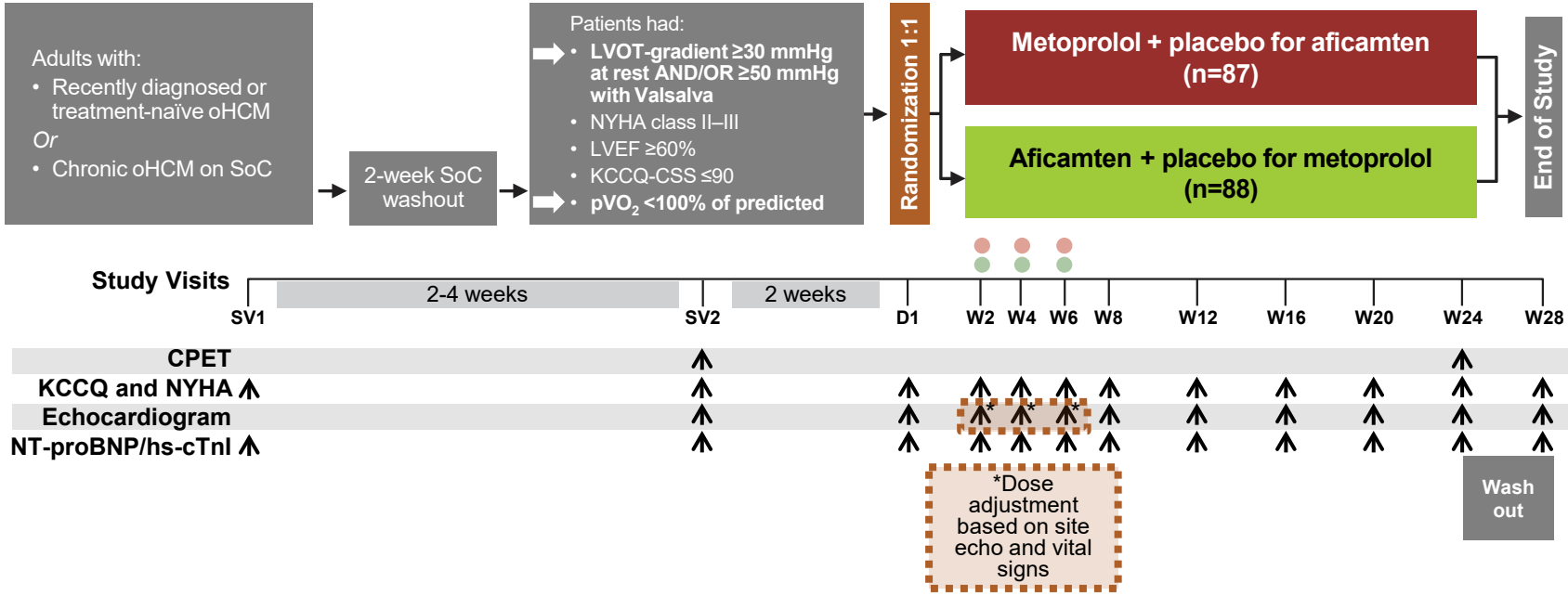
MAPLE-HCM: AFICAMTEN VS METOPROLOL IN SYMPTOMATIC OBSTRUCTIVE HCM

- Beta-blockers have been guideline-directed first-line therapy for patients with oHCM despite limited evidence.
- **MAPLE-HCM (aficamten vs metoprolol monotherapy)** demonstrated the **superiority of aficamten** over metoprolol improving[1-2]:
  - **Functional capacity (**pVO_2**)**
  - **Hemodynamics (**LVOT gradients)
  - **Health status** (KCCQ)
- This **prespecified analysis** of baseline and serial biomarker measurements (NT-proBNP, hs-cTnI) was performed to gain further insight into the treatment benefit of **monotherapy** with aficamten vs metoprolol



1. Garcia-Pavia P. *JACC: Heart Fail*. 2025;13:346-357; 2. Garcia-Pavia P. *N Engl J Med*. 2025;393:949-960.
Δ, change; hs-cTnI, high-sensitivity cardiac troponin I; KCCQ, Kansas City Cardiomyopathy Questionnaire; LSM, least square mean; LVOT, left ventricular outflow tract; N-terminal pro-B-type natriuretic peptide; oHCM, obstructive hypertrophic cardiomyopathy; pVO_2, peak oxygen volume.

MAPLE-HCM: STUDY DESIGN



CPET, Cardiopulmonary Exercise Testing; D, Day; hs-cTnI, high-sensitivity cardiac troponin I; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; oHCM, obstructive hypertrophic cardiomyopathy; pVO_2, peak oxygen volume; SoC, standard of care; W, Week.

MAPLE-HCM: KEY BASELINE CHARACTERISTICS

By Quartiles of NT-proBNP

n (%) or mean ± SD or median [IQR]	NT-proBNP Q1 [51, 198] n=44	NT-proBNP Q2 [200, 468] n=44	NT-proBNP Q3 [471, 968] n=44	NT-proBNP Q4 [980, 4659] n=43	*P* Value
Randomized to aficamten, n (%)	20 (45.5)	21 (47.7)	23 (52.3)	24 (55.8)	0.30
Hypertension, n (%)	22 (50.0)	19 (43.2)	20 (45.5)	26 (60.5)	0.33
KCCQ-OSS	64 ± 18	69 ± 15	68 ± 15	62 ± 17	0.62
Age, years (SD)	**54.2 ± 11.2**	**56.3 ± 13.0**	**58.7 ± 13.2**	**61.8 ± 14.5**	**0.004**
Female, n (%)	**12 (27.3)**	**18 (40.9)**	**15 (34.1)**	**28 (65.1)**	**0.001**
NYHA III, n (%)	**12 (27.3)**	**9 (20.5)**	**10 (22.7)**	**21 (48.8)**	**0.03**
hs-cTnI, ng/L	**7 [4, 12]**	**10 [7, 17]**	**15 [8, 26]**	**29 [13, 52]**	**<0.001**
pVO_2, mL/kg/min	**21.7 ± 5.2**	**20.3 ± 4.1**	**19.9 ± 5.0**	**17.5 ± 5.0**	**<0.001**
LVOT-Valsalva, mmHg	**59 ± 27**	**71 ± 34**	**84 ± 34**	**80 ± 30**	**<0.001**
LV max thickness, mm	**19.9 ± 2.5**	**21.1 ± 3.0**	**21.1 ± 3.7**	**21.3 ± 2.9**	**0.03**
E/e′ ratio	**14.6 ± 6.9**	**16.0 ± 5.3**	**17.5 ± 5.2**	**24.5 ± 10.0**	**<0.001**
LA volume index, mL/m^2	**32.8 ± 9.3**	**39.0 ± 13.4**	**41.0 ± 11.3**	**43.1 ± 9.2**	**<0.001**

hs-cTnI, high-sensitivity cardiac troponin I; IQR, interquartile range; KCCQ-OSS, Kansas City Cardiomyopathy Questionnaire-Overall Summary Score; LA, left atrial; LV, left ventricular; LVOT, left ventricular outflow tract; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; pVO_2, peak oxygen volume; Q, quartile.

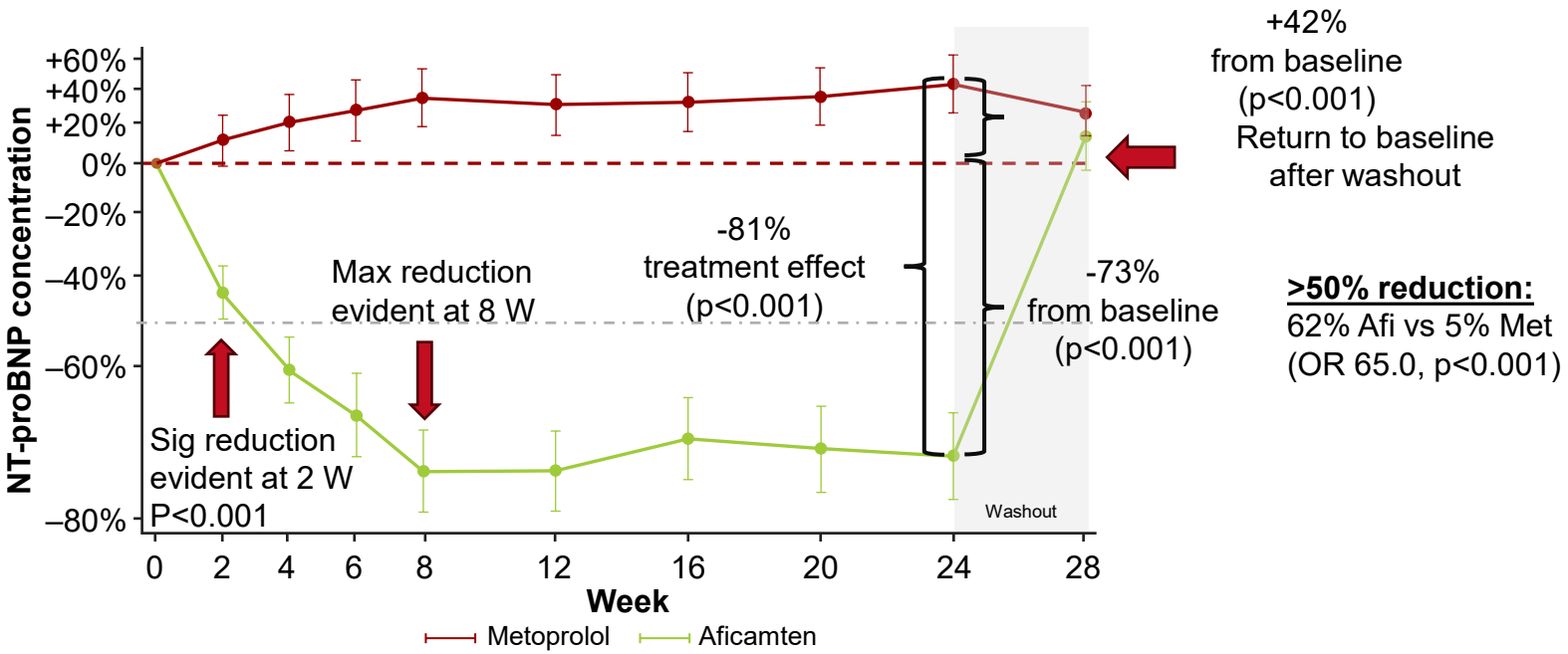
MAPLE-HCM: KEY BASELINE CHARACTERISTICS

By Quartiles of hs-cTnI

n (%) or mean ± SD or median [IQR]	hs-cTnI Q1 [2.3, 7.2] n=45	hs-cTnI Q2 [7.3, 12.8] n=43	hs-cTnI Q3 [12.9, 28.6] n=44	hs-cTnI Q4 [29.9, 663] n=43	*P* Value
Randomized to aficamten, n (%)	21 (46.7)	20 (46.5)	22 (50.0)	25 (58.1)	0.27
Age, years (SD)	56.4 ± 10.5	57.8 ± 14.6	59.1 ± 12.6	57.6 ± 15.1	0.57
Female, n (%)	22 (48.9)	20 (46.5)	16 (36.4)	15 (34.9)	0.12
KCCQ-OSS	66 ± 16	66 ± 18	63 ± 16	68 ± 17	0.80
NYHA III, n (%)	16 (35.6)	11 (25.6)	12 (27.3)	13 (30.2)	0.63
pVO_2, mL/kg/min	19.6 ± 4.4	20.6 ± 6.0	20.0 ± 5.1	19.2 ± 4.7	0.57
Hypertension, n (%)	**17 (37.8)**	**19 (44.2)**	**24 (54.5)**	**27 (62.8)**	**0.01**
NT-proBNP, pg/mL	**197 [106, 443]**	**374 [200, 637]**	**656 [376, 1000]**	**863 [354, 1606]**	**<0.001**
LVOT-Valsalva, mmHg	**63 ± 36**	**71 ± 33**	**78 ± 28**	**82 ± 31**	**0.005**
LV max thickness, mm	**19.7 ± 2.5**	**20.3 ± 2.8**	**21.5 ± 2.7**	**21.9 ± 3.8**	**<0.001**
E/e′ ratio	**15.3 ± 6.7**	**17.1 ± 6.2**	**19.5 ± 10.3**	**20.6 ± 7.3**	**<0.001**
LA volume index, mL/m²	**36.0 ± 10.9**	**38.3 ± 13.4**	**40.2 ± 11.3**	**41.4 ± 10.1**	**0.02**

hs-cTnI, high-sensitivity cardiac troponin I; IQR, interquartile range; KCCQ-OSS, Kansas City Cardiomyopathy Questionnaire-Overall Summary Score; LA, left atrial; LV, left ventricular; LVOT, left ventricular outflow tract; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; pVO_2, peak oxygen volume; Q, quartile.

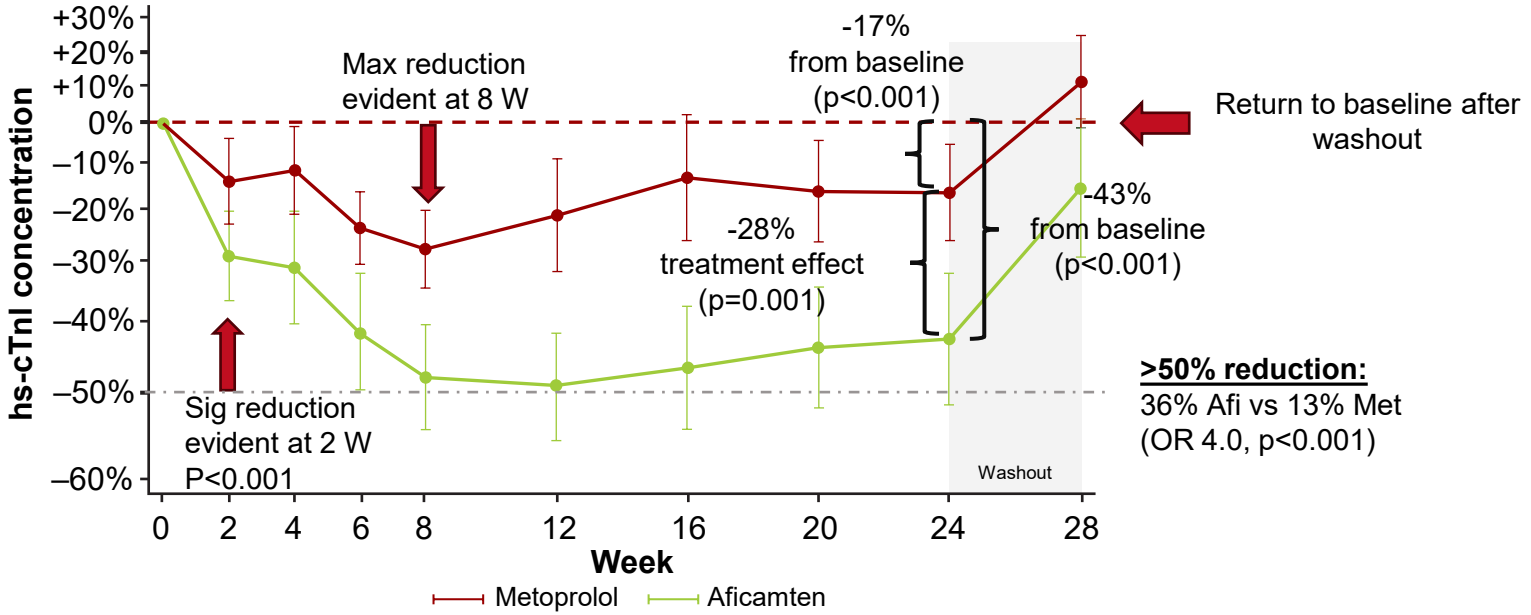
RESULTS: RELATIVE CHANGES FROM BASELINE IN THE CONCENTRATION OF NT-proBNP BY TREATMENT GROUP



Marked decrease in NT-proBNP with aficamten; modest increase with metoprolol

Afi, aficamten; Met, metoprolol; NT-proBNP, N-terminal pro-B-type natriuretic peptide; OR, odds ratio; W, Week.

RESULTS: RELATIVE CHANGES FROM BASELINE IN THE CONCENTRATION OF hs-cTnI BY TREATMENT GROUP



>50% reduction:
36% Afi vs 13% Met
(OR 4.0, p<0.001)

hs-cTnI decreased to significantly greater extent with Afi

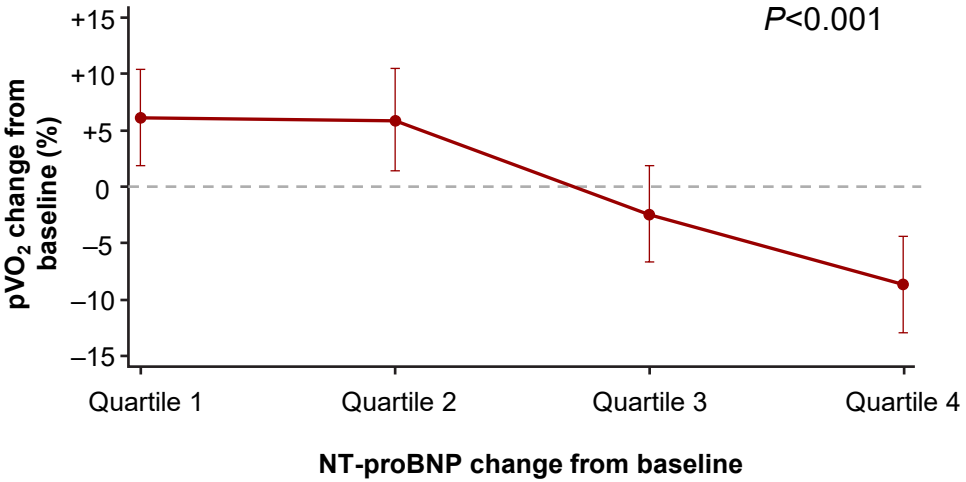
Afi, aficamten; hs-cTnI, high-sensitivity cardiac troponin I; Met, metoprolol; OR, odds ratio; W, Week.

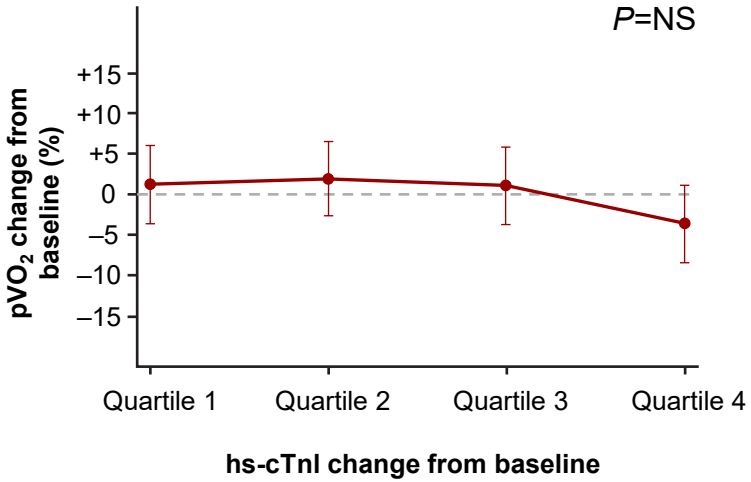
RESULTS: CHANGES IN EFFICACY METRICS STRATIFIED BY QUARTILES OF NT-proBNP CHANGE AT 24 WEEKS

	Change in NT-proBNP Q1	Change in NT-proBNP Q2	Change in NT-proBNP Q3	Change in NT-proBNP Q4	*P* Value
	n=44	n=43	n=43	n=43	
NT-proBNP ratio	0.13	0.46	1.07	2.32	
NT-proBNP, baseline (pg/mL)	784 [470, 1292]	304 [163, 665]	412 [72, 837]	322 [155, 637]	<0.001
Randomized to aficamten, N (%)	44 (100.0%)	31 (72.1%)	10 (23.3%)	2 (4.7%)	<0.001
hs-cTnI ratio	0.41	0.70	0.89	0.89	<0.001
pVO_2 change (ml/kg/min)	1.1 ± 2.8	0.9 ± 2.8	–0.4 ± 2.2	–1.8 ± 2.1	<0.001
VE/VCO_2 change	–3.3 ± 4.1	–1.8 ± 6.5	0.0 ± 4.0	–0.2 ± 3.3	0.003
KCCQ-CSS change	16.8 ± 14.5	14.4 ± 16.0	9.1 ± 15.7	8.7 ± 16.5	0.04
Rest LVOT-G change, mmHg	–39.0 ± 29.4	–22.8 ± 24.1	1.7 ± 32.4	2.6 ± 28.8	<0.001
Valsalva LVOT-G change, mmHg	–50.7 ± 34.5	–31.7 ± 35.3	–1.0 ± 35.5	–4.7 ± 32.4	<0.001

hs-cTnI, high-sensitivity cardiac troponin I; KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire-Clinical Summary Score; LVOT-G, left ventricular outflow tract gradient; NT-proBNP, N-terminal pro-B-type natriuretic peptide; pVO_2, peak oxygen volume; Q, quartile; VCO_2, carbon dioxide output; VE, minute ventilation.

RESULTS: CHANGE FROM BASELINE IN NT-proBNP or hs-cTnI VS CHANGES IN PEAK VO_2 FROM BASELINE





Improvements in NT-proBNP, but not hs-cTnI, are associated with improved pVO_2

hs-cTnI, high-sensitivity cardiac troponin I; NT-proBNP, N-terminal pro-B-type natriuretic peptide; pVO_2, peak oxygen volume.

CONCLUSIONS

- As monotherapy for oHCM, aficamten led to statistically significant reductions in NT-proBNP and hs-cTnI compared with metoprolol monotherapy.
- Reductions in NT-proBNP and hs-cTnI were associated with clinically meaningful improvements in efficacy markers.
- These results provide mechanistic insights regarding the benefit of aficamten monotherapy over metoprolol monotherapy.
  - Aficamten improved ventricular wall stress, decreased myocyte injury and decreased filing pressures.
  - Metoprolol may *increase* wall stress while decreasing myocyte injury to a lesser extent than aficamten.

hs-cTnI, high-sensitivity cardiac troponin I; NT-proBNP, N-terminal pro-B-type natriuretic peptide; oHCM, obstructive hypertrophic cardiomyopathy.

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Steering Committee Members: Pablo Garcia-Pavia (Co-PI), Michael Fifer (Co-PI), Edileide Correra de Barros, Ozlem Bilen, Melissa Burroughs, Juan Pablo Costabel, Anne Dybro, Perry Elliott, Neal Lakdawala, Amy Mann, Ajith Nair, Michael Nassif, Steen Poulsen, Patricia Reant, Christian Schulze, Andrew Wang

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- Investigators and study site staff
- Data Monitoring Committee members

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THANK YOU

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