Chronic Aficamten Treatment Results in Sustained Favorable Cardiac Remodeling in Patients with Symptomatic Obstructive Hypertrophic Cardiomyopathy: Insights From the FOREST-HCM Trial

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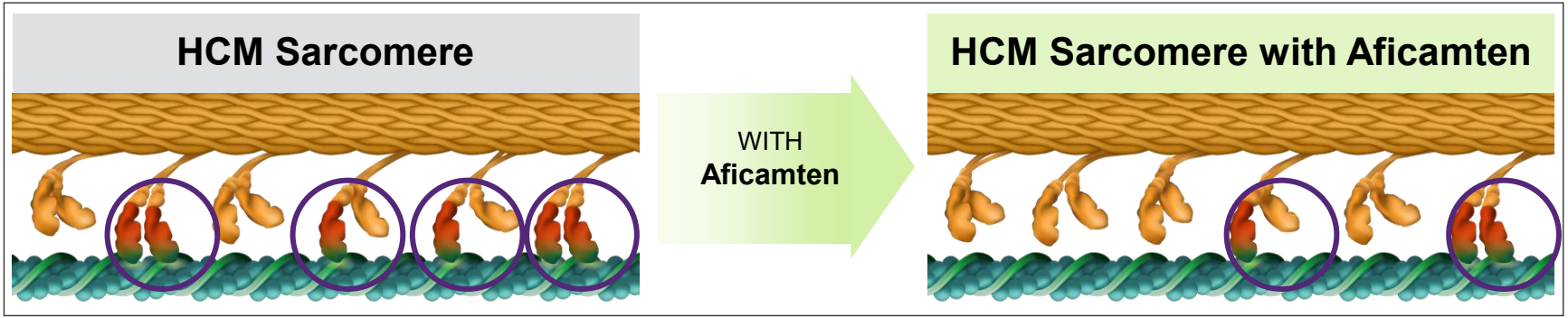
DISCLOSURES

Sheila Hegde, MD:

- Fees paid to institution for core lab services – BMS, Cytokinetics
- Advisory board – Cytokinetics

BACKGROUND

Aficamten is a next-in-class cardiac myosin inhibitor, a small-molecule selective inhibitor of the cardiac myosin ATPase, which reduces hypercontractility by reversibly binding to cardiac myosin and reducing excessive myosin-actin cross-bridges.



BACKGROUND

REDWOOD HCM

Phase 2 Study
Obstructive HCM arm
10 weeks

SEQUOIA HCM

Phase 3 Study
Obstructive HCM
24 weeks

MAPLE HCM

Phase 3 Study
Obstructive HCM
24 weeks

- ↓ LVOT Gradients
- ↓ LV Wall Thickness
- Improved LV Diastolic Function
  ↓ LAVI, ↑ e´, ↓ E/e´
- Decreased Hypercontractility
  ↓ LVEF

Research Question
Does longer-term treatment with aficamten over 48 weeks result in further cardiac remodeling?

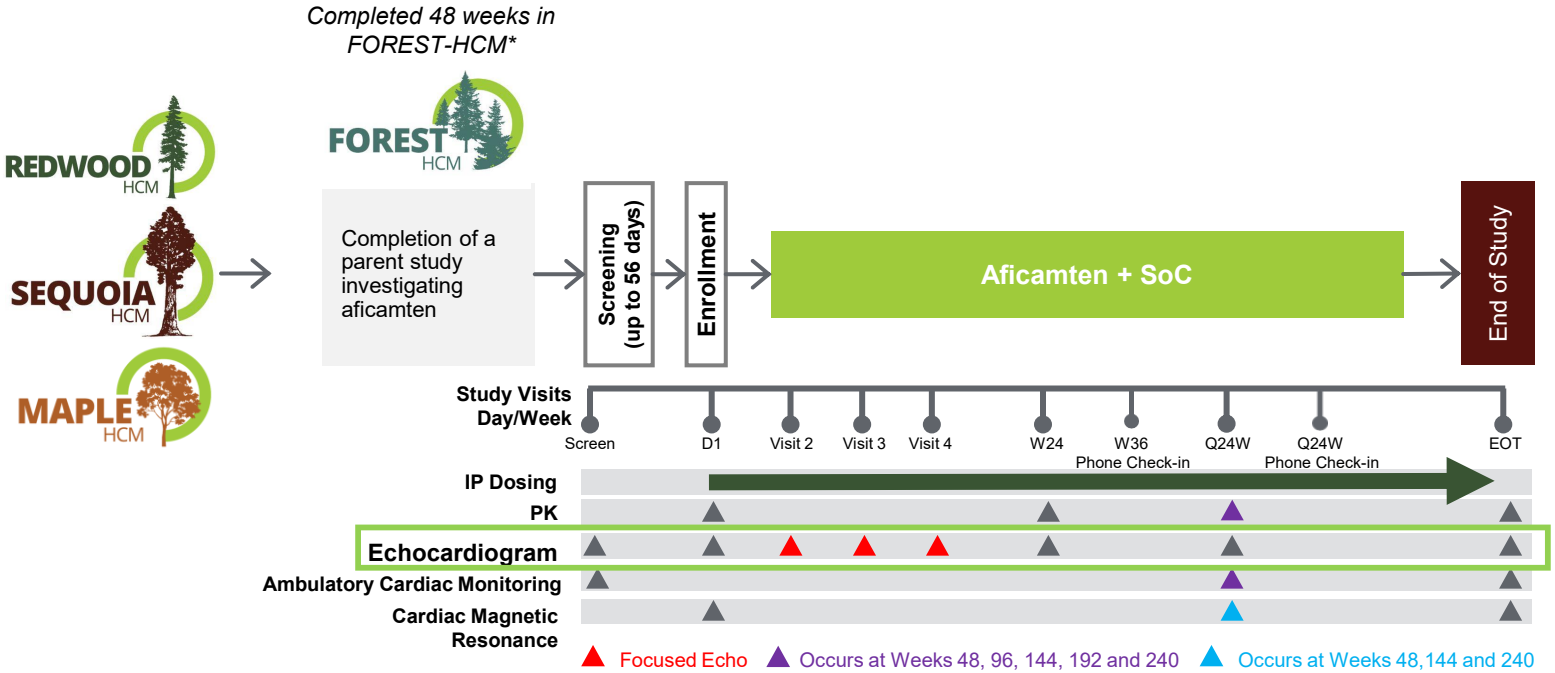
Open-label extension

FOREST HCM

Maron MS, et al. J Am Coll Cardiol. 2023 Jan 3;81(1):34-45
Maron MS, et al. *N Engl J Med* 2024;390(20):1849-61
Hegde SM, et al. J Am Coll Cardiol. 2024 Nov 5;84(19):1789-1802
Garcia-Pava P, et al. N Engl J Med. 2025 Sep 11;393(10):949-960
Hegde SM, et al. J Am Coll Cardiol. 2025 Aug 27:S0735-1097(25)07466-2

LV – left ventricle, LVOT – LV outflow tract, LAVI – left atrial volume index, LVEF – LV ejection fraction

METHODS



EOT, end of treatment; IP, investigational product; PK, pharmacokinetics; Q24W, every 24 weeks; SoC, standard of care.
*Current data includes only patients from REDWOOD-HCM and SEQUOIA-HCM. No patients from MAPLE-HCM had reached 48 weeks.

BASELINE CHARACTERISTICS

	All Patients
Age (years)	60 ± 13
Female, n (%)	77 (46)
Race, n (%)	
White	162 (96)
Black or African American	4 (2)
Asian	2 (1)
Other	1 (1)
Background HCM therapy, n (%)	
BB only	105 (62)
CCB only	18 (11)
Disopyramide only	0
Combination therapy	35 (21)
None	11 (7)
Baseline NYHA Class, n (%)	
Class I	1 (1)
Class II	101 (60)
Class III	67 (40)
Class IV	0
Medical History, n (%)	
BMI (kg/m^2)	29 ± 4
Atrial fibrillation or flutter	38 (23)
Hypertension	75 (44)
HCM Criteria, n (%)	
Positive family history of HCM	48 (28)
Known HCM-causing gene mutation	38 (23)

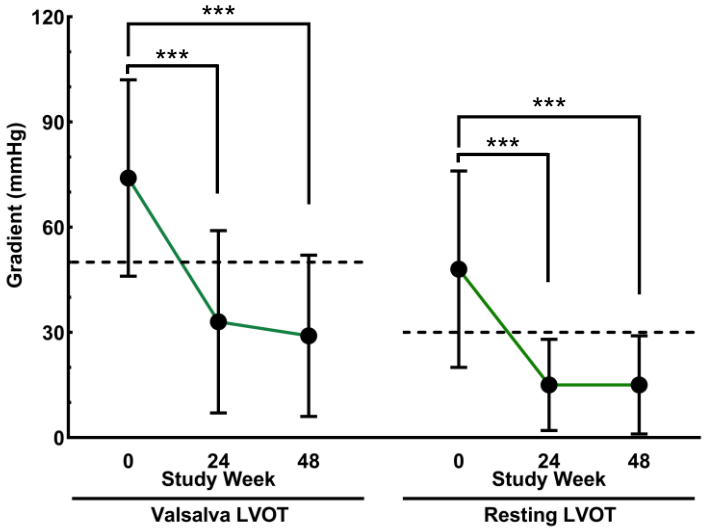
From May 2021 through August 2024, 169 patients completed 48 weeks of aficamten

- **Age**: mean age 60 ± 13 years
- **Female**: 46%
- **Race**: 96% White

Values represent mean ± SD or n (%)
BB - beta-blocker, CCB - calcium channel blocker, BMI– body mass index

RESULTS

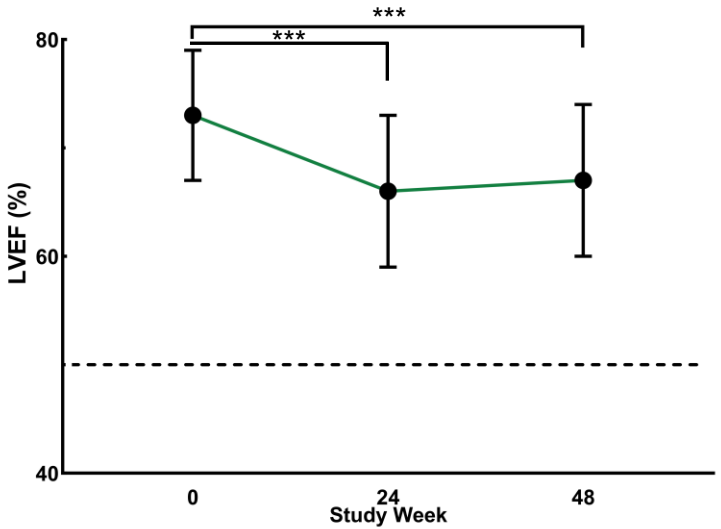
LVOT Gradients



W48 LSM Δ:
-44 mmHg (-48, -41)

W48 LSM Δ:
-33 mmHg (-35, -31)

LV Ejection Fraction

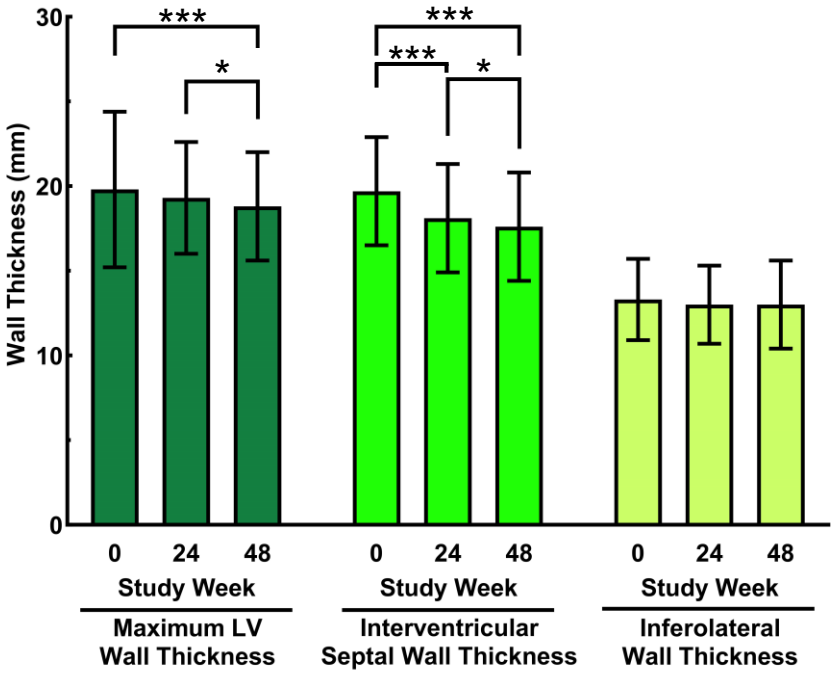


W48 LSM Δ:
-7% (-7, -5)

*** p<0.0001

RESULTS

LV Wall Thickness



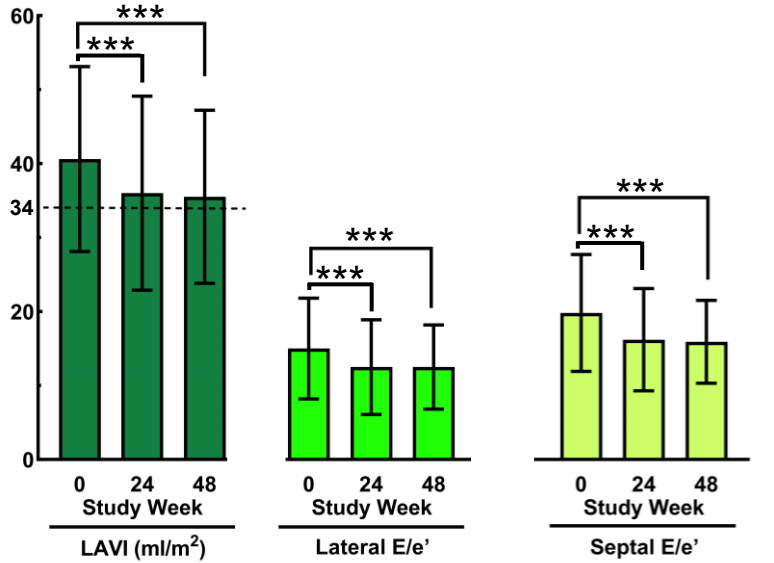
Maximum LV Wall Thickness	Interventricular Septal Wall Thickness	Inferolateral Wall Thickness
W48 LSM Δ: -1 mm (-2, -1)	W48 LSM Δ: -2 mm (-3, -2)	W48 LSM Δ: -0.3 mm (-0.7, 0.1)

* p<0.05, *** p<0.0001

LV – left ventricle, W48 – week 48, LSM – least square mean, Δ - change

RESULTS

LV Diastolic Function



W48 LSM Δ:	W48 LSM Δ:	W48 LSM Δ:
-5 ml/m² (-6, -4)	-2 (-3, -2)	-4 (-5, -3)

A 50% reduction of NT-proBNP was associated with †:

- ↓ **LAVI (ml/m²):** -1.6 (-2.6, -0.6), p=0.002
- ↓ **Lateral E/e':** -1.1 (-1.6, -0.5), p=0.0001
- ↓ **Septal E/e':** -1.1 (-1.6, -0.6), p<0.0001

*** p<0.0001

LAVI – left atrial volume index, W48 – week 48, LSM – least square mean, Δ - change
†Values represent beta coefficient (95%CI) from a linear aggression model adjusted for baseline echo value and baseline NT-proBNP

CONCLUSION

- Treatment with aficamten for 48 weeks in patients with obstructive HCM resulted in significant improvement in important measures of cardiac structure and function
- Improvement in cardiac structure and function appeared sustained over extended exposure in measures of LVOT gradients and diastolic function while there was evidence of progressive changes in wall thickness
- There were no meaningful adverse effects on LV systolic function
- These findings extend the findings from SEQUOIA-HCM and MAPLE-HCM in supporting the potential remodeling benefit of aficamten in chronic treatment of symptomatic oHCM

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THANK YOU

Scientific Sessions

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