Efficacy and safety of extended treatment with aficamten in patients with symptomatic obstructive hypertrophic cardiomyopathy: Results from FOREST-HCM

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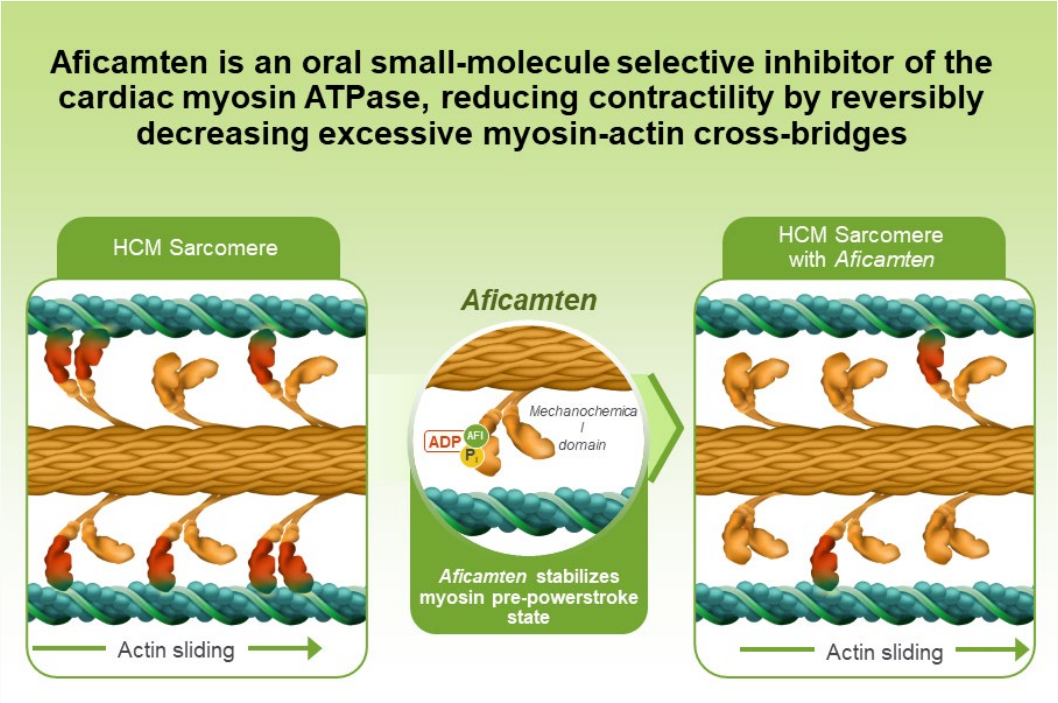
AUGUST 31, 2025

Background



Aficamten in obstructive hypertrophic cardiomyopathy (oHCM)

- Safe and effective in lowering left ventricular outflow tract gradients (LVOT-G), up to 1 year
- Improved symptom burden and exercise capacity[1-3]

1. Maron MS, et al *J Am Coll Cardiol* 2023;81(1):34-45. **2.** Maron MS, et al. *Eur Heart J* 2025 May 17:ehaf364. **3.** Saberi S, et al. *JACC Heart Fail* 2025;13(8):102496.

Purpose and Study Design

Purpose – To evaluate the long-term efficacy and tolerability of aficamten in oHCM

Population – Eligible patients completing a parent study (REDWOOD-HCM; SEQUOIA-HCM; MAPLE-HCM) were offered participation in FOREST-HCM

Titration and Monitoring* – Patients underwent echocardiographically guided titration every 2-weeks within the first 6 weeks, with aficamten dose increased in 5 mg increments to a maximum of 20 mg daily. Monitoring visits occurred every 12 weeks thereafter

Dosing decisions – Dose adjustments were made by the treating physician integrating both their clinical impression and echocardiographic measures (LVEF and LVOT-G) – mimicking real-world clinical practice

*Protocol amendment 6 allows for more flexible titration visit intervals and monitoring every 6 months in selected patients

LVEF, left ventricular ejection fraction; LVOT-G, left ventricular outflow tract gradient; oHCM, obstructive hypertrophic cardiomyopathy

Results

Baseline Characteristics

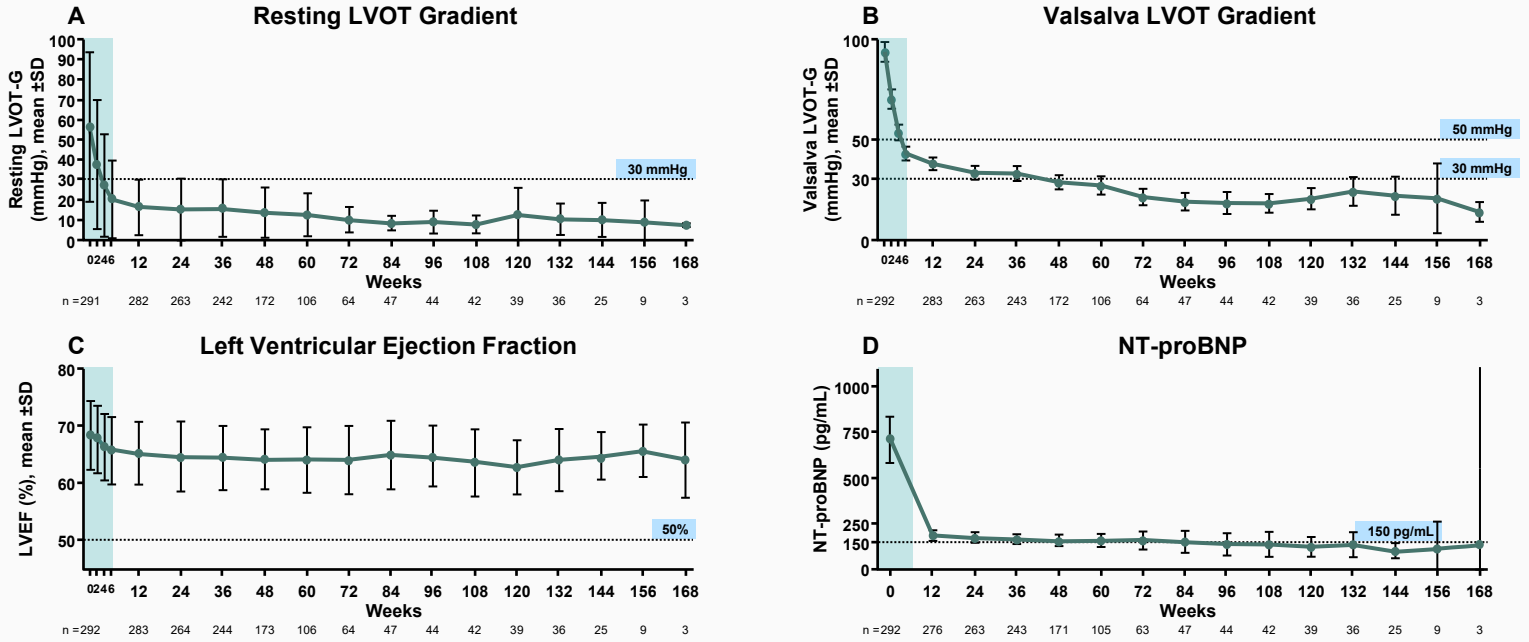
Characteristic[a]	All Patients[b] N=296
Age (years), mean ± SD	61.0 ± 12.3
Female, n (%)	131 (44.3)
White, n (%)	278 (93.9)
BMI (kg/m^2), mean ± SD	28.9 ± 4.2
Known history of HCM-causing gene variant or family history of HCM, n (%)	101 (34.1)
Background HCM therapy, n (%)	
Beta-blocker monotherapy	147 (49.7)
Non-dihydropyridine CCB monotherapy	51 (17.2)
Disopyramide	44 (14.9)
Beta-blocker + CCB	6 (2.0)
No background HCM medications, n (%)	48 (16.2)

Characteristic[a]	All Patients[b] N=296
Mean Duration of exposure, years (range)	1.2 (0.005-3.26)
Total person-years of exposure	352.2
NYHA functional class, n (%)	
I	10 (3.4)
II	168 (56.8)
III	118 (39.9)
KCCQ-CSS mean ± SD	70.5 ± 19.4
LVEF (%), mean ± SD	68.4 ± 5.8
Resting LVOT-G (mm Hg), mean ± SD	56.4 ± 37.3
Valsalva LVOT-G (mm Hg), mean ± SD	93.8 ± 42.5
NT-proBNP (pg/mL), median [QI, Q3]	776.5 [348.5, 1531.5]
hs-cardiac-TnI (ng/L), median [QI, Q3]	11.2 [5.8, 19.8]

[a]n (%) unless otherwise stated.
[b]Number of participants from each parent study: REDWOOD-HCM, n=45; SEQUOIA-HCM, n=222; MAPLE-HCM, n=29.
BMI, body mass index; CCB, non-dihydropyridine calcium channel blocker; HCM, hypertrophic cardiomyopathy; hs-cardiac-TnI, high-sensitivity cardiac troponin I; KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire–Clinical Summary Score; LVEF, left ventricular ejection fraction; LVOT-G, left ventricular outflow tract gradient; NT-proBNP, N-terminal pro–B-type natriuretic peptide; NYHA, New York Heart Association; Q, quartile

Results

Effect of Aficamten on Clinical HCM Characteristics

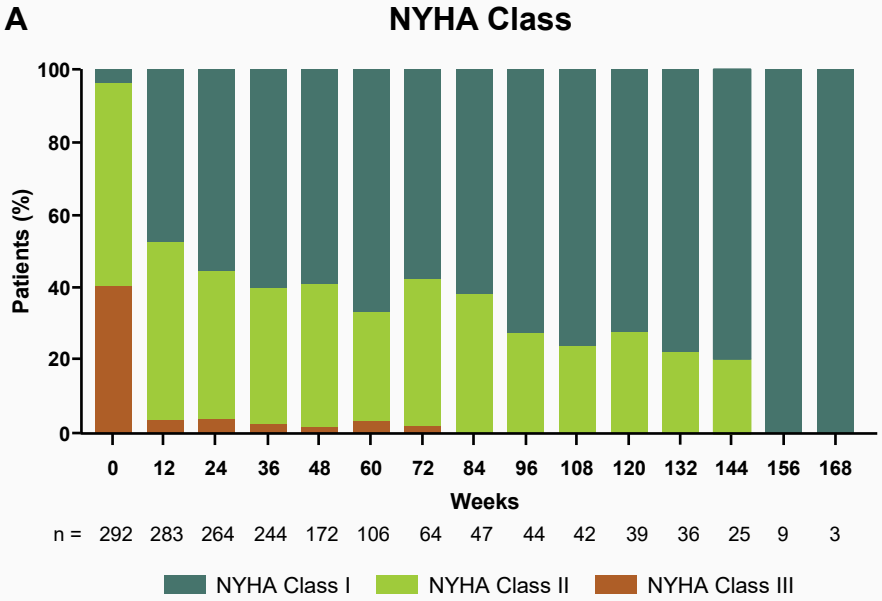


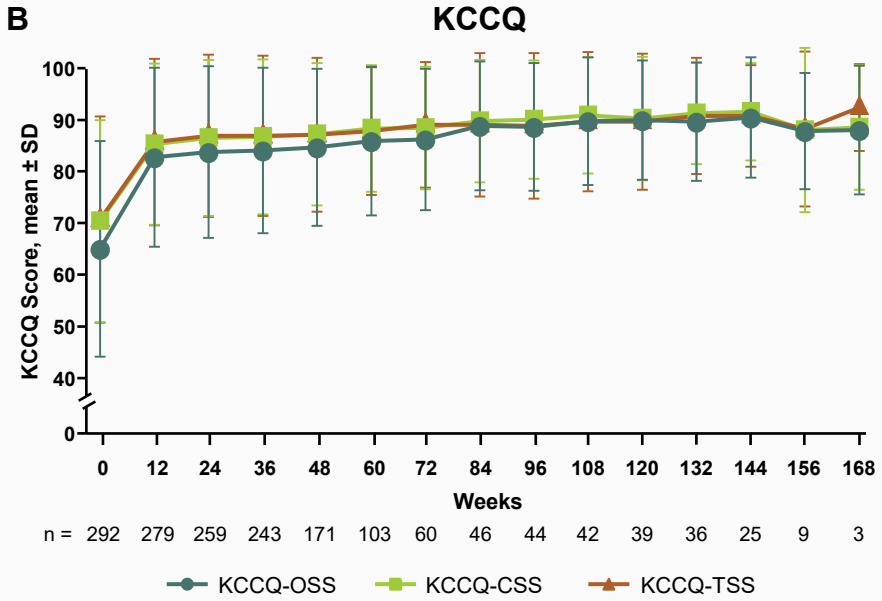
Shaded area represents the titration phase.

HCM, hypertrophic cardiomyopathy; LVEF, left ventricular ejection fraction; LVOT-G, left ventricular outflow tract gradient; NT-proBNP, N-terminal pro–B-type natriuretic peptide.

Results

Effect of Aficamten on Clinical HCM Characteristics





HCM, hypertrophic cardiomyopathy; KCCQ-CSS/OSS/TSS, Kansas City Cardiomyopathy Questionnaire–clinical summary score/overall summary score/total summary score; NYHA, New York Heart Association

Results

Safety and Tolerability of Aficamten

	Patients, n (%)	Patients with Event per 100 person-years
LVEF <50%	10 (3.4)	2.9
LVEF <50% associated with reported adverse event	3 (1.0) → *table*	0.9
Any atrial fibrillation	17 (5.7)	5.1
New-onset atrial fibrillation	7 (2.4)	2.0
Recurrent atrial fibrillation	10 (3.4)	2.9
Ventricular arrhythmias requiring treatment	1 (0.3)	0.3
Appropriate ICD discharge	1 (0.3)	0.3
Heart failure leading to hospitalization	1[a] (0.3)	0.3

Age, y	Sex	Study Week of LVEF <50%	AFI dose at low EF, mg/d	Site-Read LVEF%	Core-Read LVEF%	NYHA FC	Reported Adverse Event	Next visit LVEF%
45	M	8	15	47	53	II	EtOH Afib	60.2
77	F	12	15	49	55	III	Dyspnea	42
75	F	6	10	45	55	III	Dyspnea	52

[a]Acute on chronic diastolic heart failure exacerbation

AFI, aficamten; EtOH, ethanol; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; NYHA FC, New York Heart Association Functional Class

Conclusions

- Extended treatment (comprising >352 patient-years of follow up) with aficamten in patients with symptomatic oHCM was associated with early, substantial, and sustained improvements in LVOT-G and symptom burden
- Dosing in the FOREST-HCM protocol mimics real-world clinical practice, including site-read echocardiograms and integration of clinical judgment in dose titration
- Extended treatment with aficamten was shown to be safe and well tolerated over a mean follow-up of ~62 weeks
  - Low incidence of LVEF <50% and none associated with treatment interruptions
  - No occurrences of LVEF <40%
  - Very low incidence of heart failure hospitalization (1), and none associated with systolic dysfunction
  - Low incidence of new-onset atrial fibrillation – consistent with background risk
  - No deaths

LVEF, left ventricular ejection fraction; LVOT-G, left ventricular outflow tract gradient; oHCM, obstructive hypertrophic cardiomyopathy