An Open-label Extension Study of Aficamten for Chinese Patients with Symptomatic Obstructive Hypertrophic Cardiomyopathy: 48-week Results

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PURPOSE

- **Aficamten** is an oral, selective cardiac myosin inhibitor for the treatment of hypertrophic cardiomyopathy (HCM) that reduces myocardial hypercontractility, the underlying pathophysiology of the disease.
- While the Phase 3 SEQUOIA-HCM trial (NCT05186818) established the efficacy and safety of aficamten in a global population, long-term data in a Chinese population are necessary[1].
- The purpose of this study (NCT06116968) was to evaluate the **long-term (48-week) safety and efficacy** of aficamten specifically in Chinese patients with symptomatic obstructive HCM (oHCM).

METHODS

Study Population

- Chinese oHCM patients who completed 24 weeks treatment in SEQUOIA-HCM and with baseline left ventricular ejection fraction (LVEF) ≥55%.

Dosing & Titration

- Initial Phase (Weeks 0–8): Echo-guided dose titration of oral aficamten (5 mg to 20 mg daily) every two weeks.
- Maintenance Phase (Weeks 12–48): Patients monitored via echocardiography every 12 weeks to assess safety and hemodynamics.

Study Endpoints

- **Primary endpoints:** incidence of adverse events (AEs), serious adverse events (SAEs) and incidence of LVEF <50% and <40%.
- **Secondary and other endpoints:** changes from baseline to Week 48 in left ventricular outflow tract gradient (LVOT-G), New York Heart Association (NYHA) Functional Class, Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS), and N terminal pro-B-type natriuretic peptide (NT-proBNP).

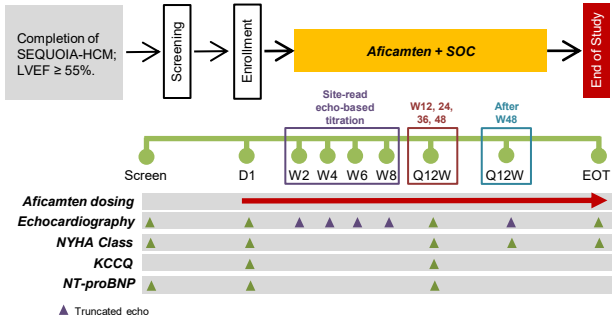
RESULTS

As of March 26, 2025, 40 patients with oHCM were enrolled and completed the Week 48 Visit. By Week 48, 87.5% of participants achieved the highest available daily doses (15 mg or 20 mg).

Baseline Characteristic	Overall (N=40)
Age, years, mean (SD)	52.7 (11.6)
Male, n (%)	28 (70.0)
BMI, kg/m², mean (SD)	26.6 (3.3)
NYHA Functional Class, n (%)	
Class I	2 (5.0)
Class II	34 (85.0)
Class III	4 (10.0)

Baseline Characteristic (Continued)	Overall (N=40)
Echocardiographic Parameters, mean (SD)	
Left Ventricular Ejection Fraction (LVEF), %	66.6 (5.3)
Resting LVOT Gradient, mmHg	70.2 (47.2)
Valsalva LVOT Gradient, mmHg	99.9 (54.0)
Background HCM therapy use, n (%)	29 (72.5)
Beta-blockers use, n (%)	21 (52.5)
Non-dihydropyridine calcium channel blockers use, n (%)	15 (37.5)

Figure 1: Study Schema



SAFETY

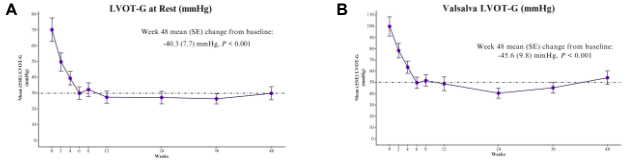
No serious AEs or severe treatment emergent AEs (TEAEs) were reported

Number (%) of Participants with the Following:	Overall (N=40)
≥ 1 TEAE	27 (67.5)
≥ 1 TESAE	0
≥ 1 TEAE leading to early withdrawal	0
≥ 1 Related TEAE	4 (10.0)
≥ 1 Moderate TEAE	8 (20.0)
≥ 1 Severe TEAE	0

TEAE = treatment-emergent adverse event; TESAE = treatment-emergent serious adverse event

Figure 2: (A) Resting and (B) Valsalva LVOT-G

At Week 48, mean LVOT-G decreased significantly from baseline by 40.3 mmHg (at rest) and 45.6 mmHg (Valsalva); both $P < 0.001$.



NYHA CLASS

NYHA improved ≥1 class in 15% patients ($P = 0.024$) from baseline to Week 48 and no worsening occurred.

NT-proBNP

Mean (SD) NT-proBNP decreased from 1579.3 (1719.3) pg/mL at baseline to 330.3 (337.0) pg/mL at Week 48. The mean (SD) percentage reduction was 59.2 (33.7) ($P < 0.001$).

Figure 3: KCCQ-CSS

The mean (SD) KCCQ-CSS improved by 8.3 (9.3) points ($P < 0.001$) from baseline.

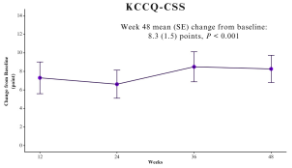
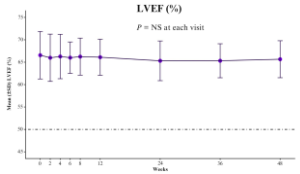


Figure 4: LVEF (%)

LVEF remained ≥50% in all patients throughout the study.



CONCLUSIONS

- **In Chinese oHCM patients aficamten was well tolerated using the same dosing strategy of individualized titration as was used globally.**
- **There were no low LVEF events or treatment discontinuations, and the majority of patients (87.5%) achieved the highest daily doses (15 or 20 mg).**
- **Significant and durable improvements were observed in hemodynamics (LVOT-G), symptom burden (NYHA Class), quality of life (KCCQ), and cardiac biomarkers (NT-proBNP).**

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Reference: 1. Maron MS, et al. *N Engl J Med*. 2024;390(20):1849-1861.