Changes in EQ-5D-5L with Aficamten in Obstructive Hypertrophic Cardiomyopathy: the SEQUOIA-HCM Trial

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BACKGROUND

In patients with obstructive hypertrophic cardiomyopathy (oHCM), the SEQUOIA-HCM trial demonstrated that aficamten, a next-in-class cardiac myosin inhibitor, improved exercise capacity, heart failure symptoms and hemodynamics compared with placebo.

The impact of aficamten on overall health-related quality-of-life (HRQoL) in oHCM has not been reported.

PURPOSE

To evaluate the effect of aficamten on changes in patient-reported health status using the EQ-5D-5L and the Visual Analog Scale (EQ-VAS) in patients enrolled in the SEQUOIA-HCM trial

METHODS

Study Design

- SEQUOIA-HCM (NCT05186818) is a phase 3, double-blind, placebo-controlled trial of adults with symptomatic oHCM randomized to receive aficamten (n=142) or placebo (n=140) plus standard-of-care (SoC) medical therapy
- Participants received dose escalations over 6 weeks and in total were treated for 24 weeks followed by a 4-week washout
- Participants with oHCM who were receiving SoC therapy and had LVOT-G ≥30 mmHg and Valsalva ≥50 mmHg were included in the study (Figure 1)

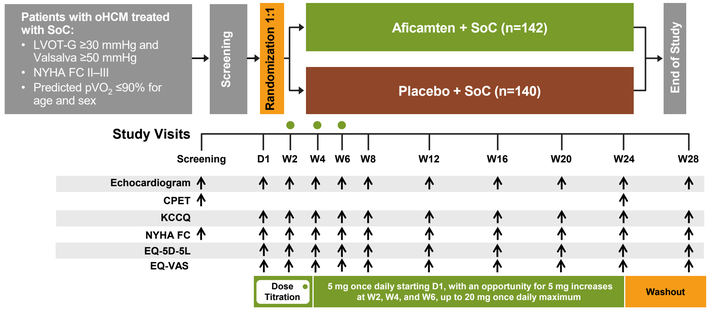
Study Outcomes

- EQ-5D-5L (scale ranges from 0 to 1) and overall QoL using a EuroQol-Visual Analog Scale (EQ-VAS; ranges from 0 to 100) were measured at baseline through week 24 with higher scores indicating better QoL
  - EQ-5D-5L comprises five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression[1]
    - Each dimension has 5 levels which are selected by the patient to indicate their health state: "no problems," "slight problems," "moderate problems," "severe problems," and "extreme problems"
    - The scores for the five dimensions are combined into a 5-digit number that describes the patient's health state
- EQ-VAS records the patient's self-reported global assessment of their health on a vertical visual analog scale (0 to 100) where 100 represents "the best health you can imagine," and 0 represents "the worst health you can imagine"[1]
- EQ-VAS is a quantitative patient-reported outcome measure of overall health that directly represents the patient's perception of their overall health

Statistical Methods

- A pre-specified analysis was conducted and included patients with EQ-5D-5L assessments at both baseline and week 24 for comparisons of changes in EQ-5D-5L index scores and EQ-VAS scores over the study period
- The effects of aficamten treatment on mean changes in EQ-5D-5L and EQ-VAS scores were estimated using linear regression (study visits) and mixed effects regression (overall treatment effect)
- Models were adjusted for baseline EQ-5D-5L score and randomization stratification variables (beta blocker use and cardiopulmonary exercise testing modality) as fixed effects

Figure 1. SEQUOIA-HCM Study Design[2]



CPET, cardiopulmonary exercise testing; D, day; EQ-5D-5L, EuroQol 5-Dimension 5-Level; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVOT-G, left outflow tract gradient; NYHA FC, New York Heart Association functional class; oHCM, obstructive HCM; SoC, standard of care; EQ-VAS, EuroQol Visual Analog Scale; W, week.

RESULTS

- Mean age (n= 282) of study participants was 59.1±12.9 years (40.8% women; 79.1% white; Table 1)
- There were no baseline differences between aficamten and placebo in any of the 5 domains of the EQ-5D-5L
- Aficamten baseline EQ-5D-5L index and EQ-VAS scores were 0.80±0.19 and 71.2±17.9, respectively (Table 2)
- Aficamten improved the EQ-5D-5L index score by 0.04 (Figure 2A; 95% CI: 0.01, 0.07; p=0.008) and the EQ-VAS by 4.5 points (Figure 2B; 95% CI: 1.7, 7.4; p=0.002) versus placebo with significant differences as early as 8 weeks after treatment initiation (p=0.005)
- After treatment withdrawal at 24 weeks, the QoL benefit for participants treated with aficamten decreased compared with placebo (Figure: EQ-5D-5L index score, p<0.001; EQ-VAS, p=0.003), with all other clinical parameters returning to baseline

Table 1. Baseline Characteristics

	Aficamten n=142	Placebo n=140
Age, y	59.2 ± 12.6	59.0 ± 13.4
Female sex, n (%)	56 (39.4)	59 (42.1)
Race, n (%)		
White	108 (76.1)	115 (82.1)
Geographic region, n (%)		
North America	49 (34.5)	45 (32.1)
China	24 (16.9)	22 (15.7)
Europe and Israel	69 (48.6)	73 (52.1)
Medical history, n (%)		
Hypertension	75 (52.8)	70 (50.0)
Paroxysmal atrial fibrillation	21 (14.8)	20 (14.3)
Permanent atrial fibrillation	2 (1.4)	1 (0.7)
CPET		
pVO_2 (mL/kg/min)	18.5 (4.5)	18.6 (4.5)
Percent of predicted pVO_2 (%)	58 (13)	57 (12)
Background HCM therapy, n (%)		
Beta-blocker	86 (60.6)	87 (62.1)
Calcium channel blocker	45 (31.7)	36 (25.7)
Disopyramide	16 (11.3)	20 (14.3)
None	19 (13.4)	22 (15.7)
KCCQ-CSS	76 ± 18	74 ± 18
SAQ7	72.0 ± 21.0	72.4 ± 18.3
NYHA FC, n (%)		
II	108 (76.1)	106 (75.7)
III/IV	34 (23.9)	34 (24.3)
Median NT-proBNP (IQR), pg/mL	818 (377–1630)	692 (335–1795)
Median hs-cTnI (IQR), ng/L	12.9 (7.6–33.6)	11.5 (7.7–25.0)
Echocardiographic parameters		
Valsalva LVOT-G, mmHg	82.9 ± 32	83.3 ± 33
Resting LVOT-G, mmHg	54.8 ± 27	55.3 ± 32
LVEF, %	74.8 ± 5.5	74.8 ± 6.3
Maximal LV wall thickness, mm	20.7 ± 3.0	21.0 ± 3.0

Values are the mean ± SD unless otherwise indicated.

CPET, cardiopulmonary exercise testing; HCM, hypertrophic cardiomyopathy; hs-cTnI, high-sensitivity troponin I; IQR, interquartile range; KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire-Clinical Summary Score; LV, left ventricle; LVEF, left-ventricular ejection fraction; LVOT-G, left ventricular outflow tract gradient; NT-proBNP, N-terminal pro-B type natriuretic peptide; NYHA FC,New York Heart Association functional class; pVO_2, peak oxygen uptake; SAQ7, Seattle Angina Questionnaire 7.

Table 2: Baseline Scores

	Aficamten n=142	Placebo n=140
EQ-5D-5L index score, Mean (±SD)	0.80±0.19	0.78±0.20
EQ-VAS, Mean (±SD)	71.2±17.9	68.9±18.6

EQ-5D-5L, EuroQol 5 Dimension 5 Level; EQ-VAS, EuroQol Visual Analog Scale

Figure 2A: Change in EQ-5D-5L Index Score Over Time – by Treatment

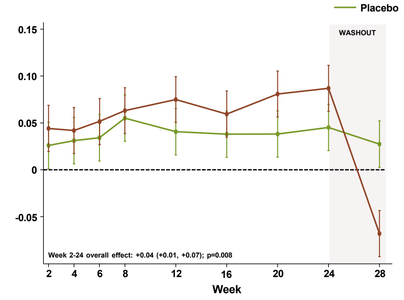
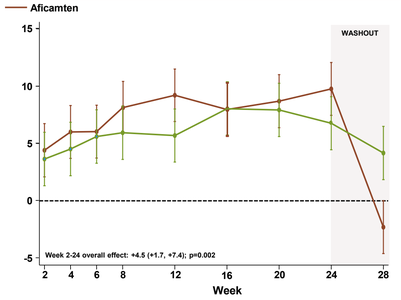


Figure 2B: Change in EQ-VAS Score Over Time – by Treatment



EQ-5D-5L, EuroQol 5 Dimension 5 Level; EQ-VAS, EuroQol Visual Analog Scale

CONCLUSIONS

- **Participants treated with aficamten had an early, sustained, and significant improvement in their overall HRQoL compared with those taking placebo**
- **Withdrawal of aficamten at 24 weeks was associated with the loss of treatment benefit**

These data support a role of aficamten in improving HRQoL among patients with oHCM, as measured using EQ-5D-5L

References

1.Herdman M, et al. *Qual Life Res* 2011;20(10):1727-1736.
2.Coats CJ, et al. *J Am Coll Cardiol* HF 2024;12:199-215.

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