FOREST HCM

Scientific Sessions

LONG-TERM IMPACT OF AFICAMTEN ON PATIENT-REPORTED OUTCOME MEASURES IN OBSTRUCTIVE HCM

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American Heart Association.

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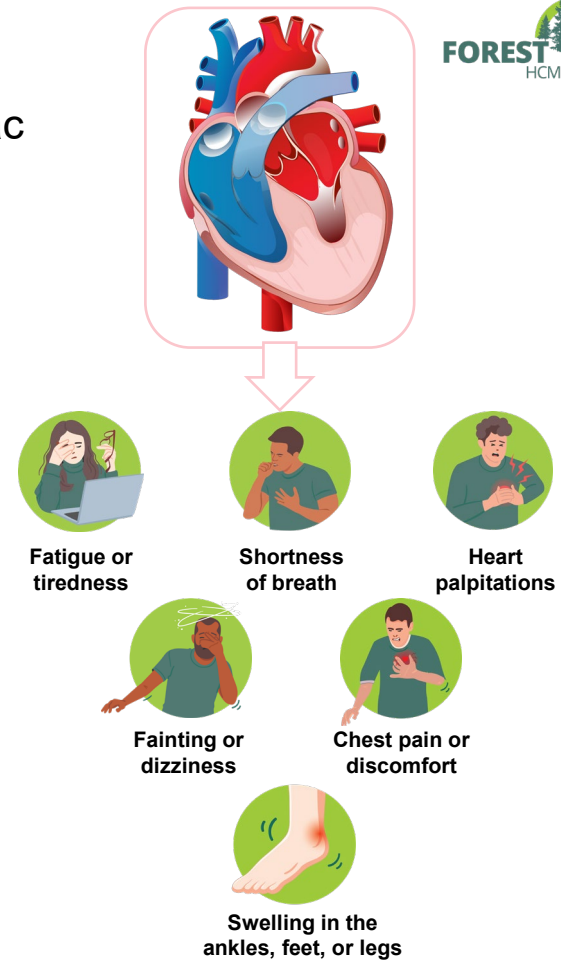
01 BACKGROUND

- Hypertrophic cardiomyopathy (HCM) is a common inherited cardiac disorder characterized by enhanced actin-myosin interactions[1,2]
  - Left ventricular (LV) hypertrophy
  - Diastolic dysfunction
  - LV outflow tract (LVOT) obstruction

- Patients with obstructive HCM (oHCM) can experience functional impairment from a wide range of symptoms[3]

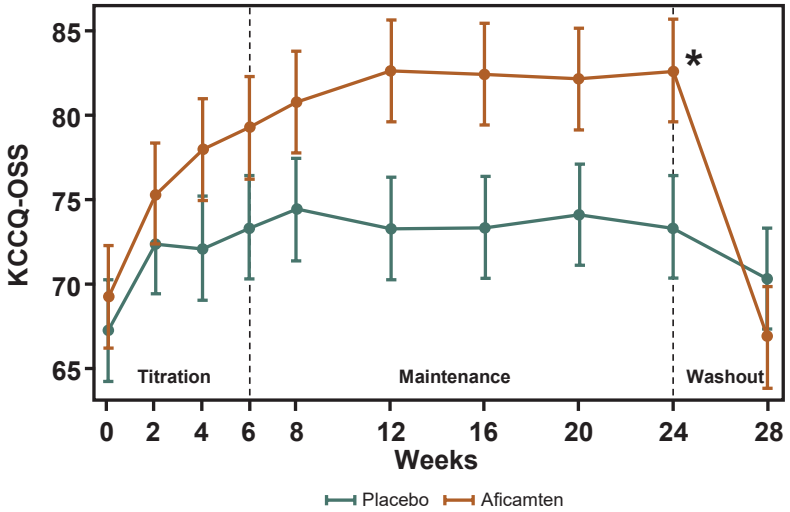
- Symptom improvement is a primary treatment objective when managing patients with oHCM



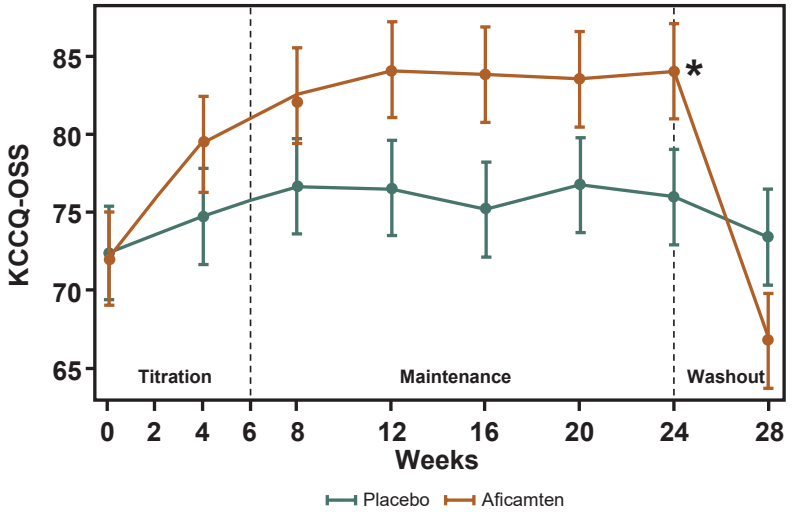
1. Marian AJ, Braunwald E. Circ Res 2017;121:749-70. 2. Maron BJ, et al. JACC 2012;60:705-15. 3.Maron BJ, et al. JACC 2022;79:390-414.

Treatment with *aficamten* in patients with oHCM led to significant improvements in patient-reported outcomes in the SEQUOIA-HCM trial over 24 weeks[4]

Mean Kansas City Cardiomyopathy Questionnaire Overall Summary Scores (KCCQ-OSS)
ΔKCCQ-OSS = 7.9 (95% CI: 4.8-11.0)



Mean Seattle Angina Questionnaire Summary Scores (SAQ7-SS)
ΔSAQ7-SS = 7.8 (95% CI: 4.7-11.0)



Longer-term impact of *aficamten* on patient-reported health status has not been described.

*P<0.001 for between group difference in mean change from baseline to week 24

4. Sherrod CF, et al. JACC 2024;84(19):1773-785.

02 METHODS

FOREST-HCM

- FOREST-HCM (NCT04848506) is an ongoing, open-label extension study for eligible patients who participated in clinical trials of *aficamten*.
- Participants started on *aficamten* 5 mg daily, adjusted in 5-mg increments up to 20 mg at ≥2-week intervals according to site-read echocardiographic criteria.
- All participants with oHCM who completed ≥48 weeks of follow-up in FOREST-HCM as of August 31, 2024, were included in this study.
- Patient-reported outcome (PRO) measures were administered at Baseline and at Weeks 12, 24, 36, and 48.
- Changes in mean PRO scores from baseline through 48 weeks were tested using mixed models for repeated measures.

PATIENT-REPORTED OUTCOME MEASURES

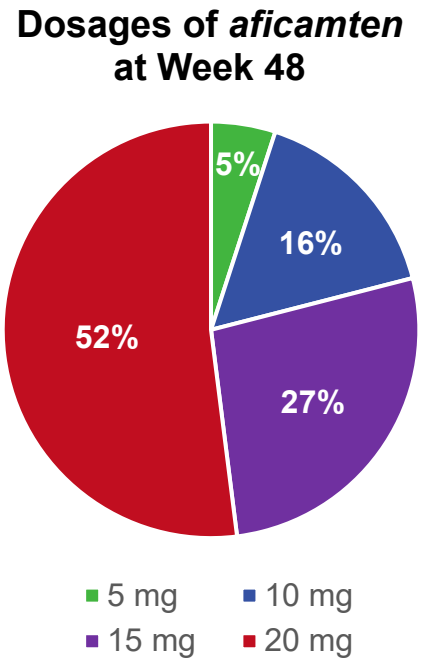
- Kansas City Cardiomyopathy Questionnaire (KCCQ)[5]
  - Developed for patients with heart failure but recently validated in HCM.[6]
- Seattle Angina Questionnaire (SAQ7)[7]
  - Developed for patients with chest pain from coronary artery disease.
- EuroQol 5-dimensional Questionnaire (EQ-5D)[8]
  - Widely used generic instrument for the measurement of health-related quality of life.
  - 2 components: EQ-5D index and Visual Analogue Scale (VAS).
- Patient Global Impression of Change (PGIC)
  - Single-item survey that asks patients “Since the start of the study, my overall status is,” with responses on a 7-point scale ranging from “Very Much Worse” to “Very Much Improved”.
- Clinician Global Impression of Improvement (CGI-I)
  - Single-item survey that uses the same 7-point scale as the PGIC.

5. Green CP, et al. JACC 2000;35:1245-55. 6. Nassif M, et al. JACC HF 2022;10:531-539. 7. Chan PS, et al. Circ Cardiovasc Qual Outcomes; 2014;7:640.
8. Herdman M, et al. Qual Life Res. 2011;20:1727-36.

03 RESULTS

BASELINE CHARACTERISTICS AND DOSING

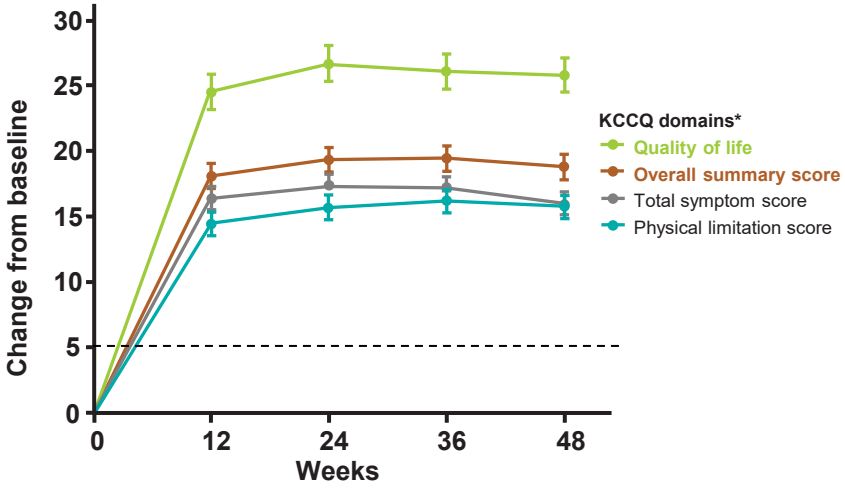
Baseline characteristics*	n=172
Age (year)	60 ± 13
Female	78 (45)
Prior AF	37 (22)
NYHA functional class	
I	1 (1)
II	103 (60)
III	68 (39)
IV	0
LVOT gradient at rest, mmHg	58 ± 38
LVOT gradient with Valsalva, mmHg	93 ± 40
LVEF %	68 ± 6
Patient-reported outcomes	
KCCQ-OSS	65.9 ± 20.3
KCCQ-QLS	52.1 ± 23.9
SAQ7-SS	69.7 ± 21.7
SAQ7-QLS	59.8 ± 29.6
EQ-5D-5L VAS	68.3 ± 18.1



[a] Data are expressed as number (percentage) or mean ± standard deviation.
AF, atrial fibrillation; EQ-5D-5L, EuroQol Five-Dimensional Questionnaire; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; NYHA, New York Heart Association; OSS, overall summary score; QLS, quality of life score; SAQ, Seattle Angina Questionnaire 7-item; SS, summary score; VAS, visual analog scale.

KCCQ RESPONSE OVER TIME

Improvements seen across all domains in KCCQ, as early as 12 weeks and sustained through 48 weeks.



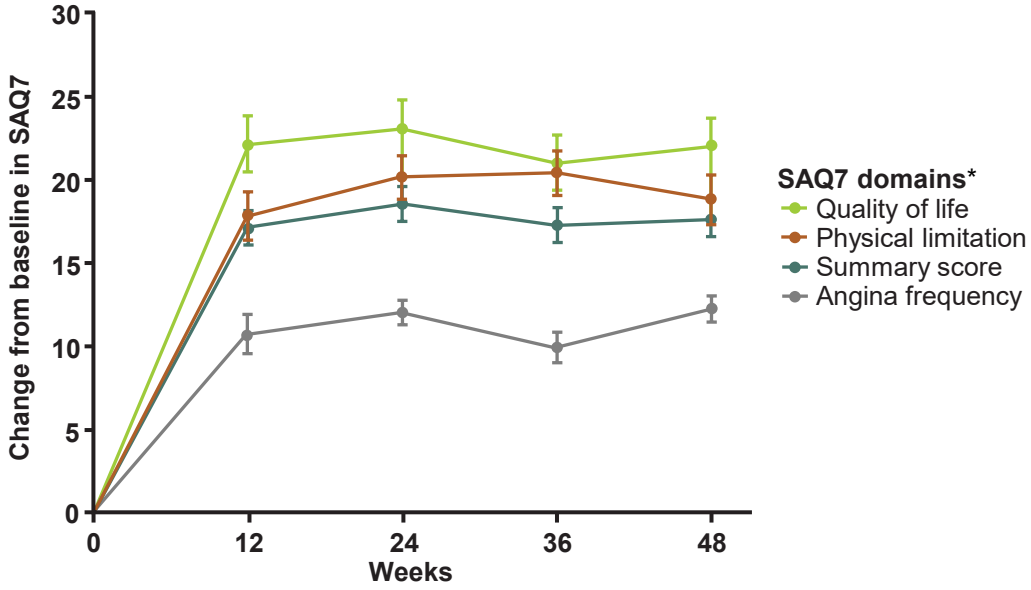
*P<0.001 for change from baseline to Week 48 in all domains.

Minimally clinically important difference = 5 point change

KCCQ, Kansas City Cardiomyopathy Questionnaire.

SAQ7

Improvements seen across all domains in SAQ7 as early as 12 weeks and sustained through 48 weeks.

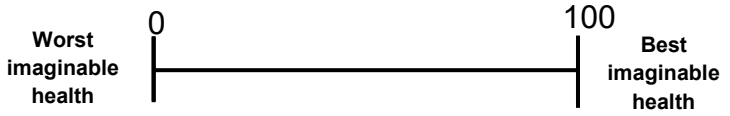


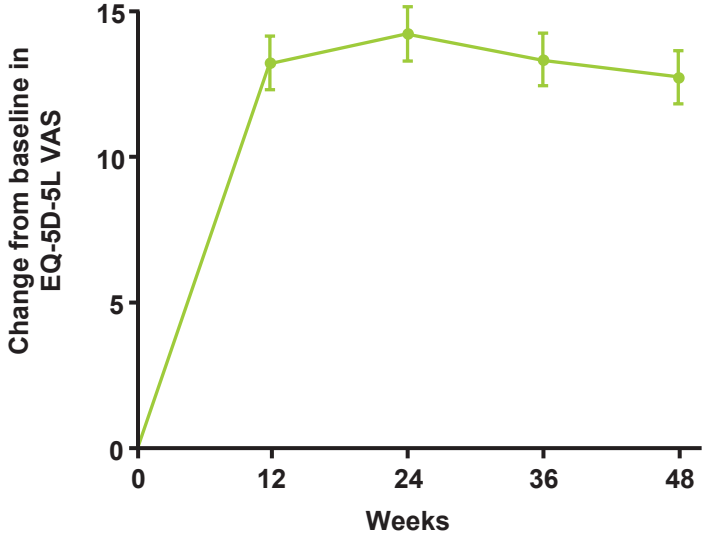
Minimally clinically important difference = 5 point change

***P<0.001 for change from baseline to week 48 in all domains**

SAQ7, Seattle Angina Questionnaire 7-item.

EQ-VAS





P<0.001 for change from baseline to Week 48 for EQ-VAS.

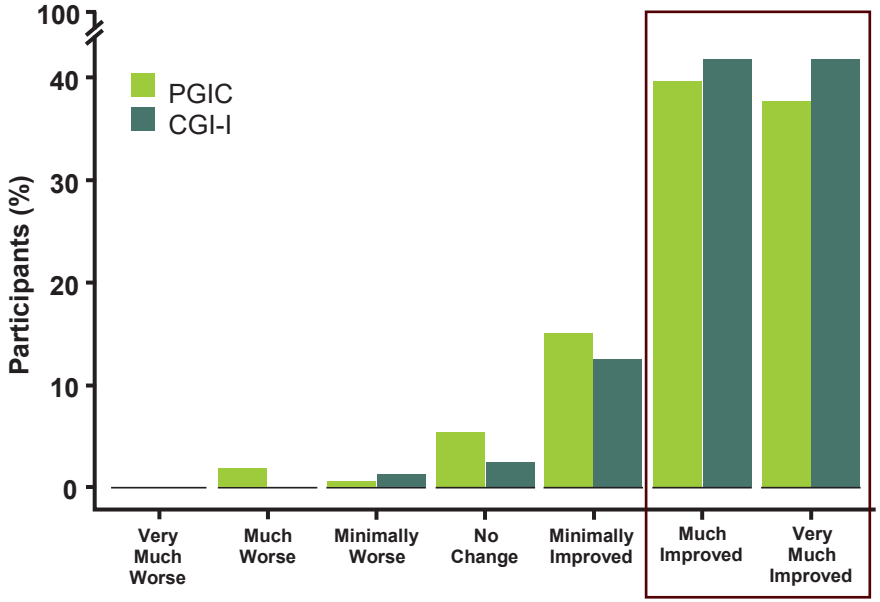
EQ-5D-5L INDEX

- Improvements noted across all 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.
- Most notably, at baseline, 47.7% of participants reported no anxiety or depression, whereas at 48 weeks this increased to 64.1% of participants.

EQ-5D-5L, EuroQol Five-Dimensional Questionnaire; VAS, visual analog scale.

PGIC AND CGI-I

At week 48, 77% of participants reported feeling either “Much Improved” or “Very Much Improved” based on the PGIC. 84% of treating clinicians reported their patients were either “Much Improved” or “Very Much Improved” based on the CGI-I.



CGI-I, clinician global impression of improvement; PGIC, patient global impression of change.

04 DISCUSSION

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LIMITATIONS

- Open label design
- Despite use of multiple PROs, not all domains of patient experience may have been fully captured.

CONCLUSION

- Treatment with *aficamten* in patients with oHCM was associated with significant and sustained improvements in multiple PROs over 48 weeks, particularly in quality of life.
- These findings extend the results of SEQUOIA-HCM by demonstrating meaningful and durable health status improvement beyond 6 months.

Aficamten treatment led to meaningful and sustained improvements in oHCM patient health status across all symptom domains

THANK YOU

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