

Aficamten and Right Ventricular Function in Obstructive Hypertrophic Cardiomyopathy: *Results from the SEQUOIA-HCM Trial*



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Background

- Aficamten, a next-in-class cardiac myosin inhibitor, improves exercise capacity and left-sided cardiac structure and diastolic function in patients with obstructive hypertrophic cardiomyopathy (oHCM).^{1, 2}
- The effects of aficamten on resting right ventricular (RV) function and RV–pulmonary artery (PA) coupling remain incompletely characterized.

Methods

- In the randomized, double-blind, placebo-controlled trial of aficamten in obstructive HCM (SEQUOIA-HCM), we assessed the following resting echocardiographic parameters at baseline and week 24.
- RV free wall longitudinal strain (**RVFWLS**)
- RV 4-chamber longitudinal strain (**RV4CLS**)
- **RV-right atrial (RA) gradient**
- **RVFWLS/RV-RA gradient ratio**



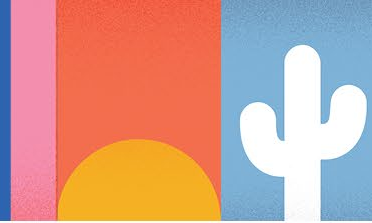
N=230

Aficamten: N=115

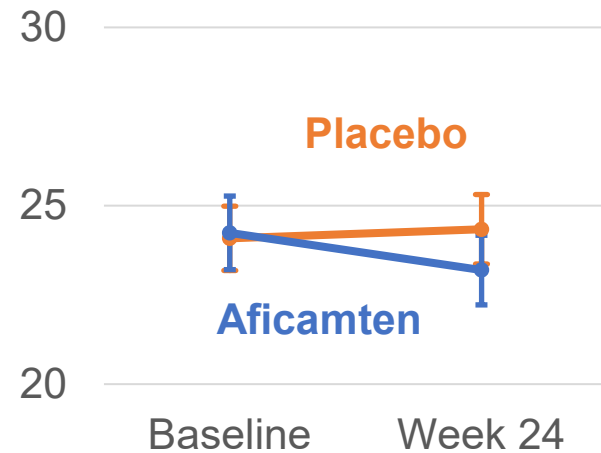
Placebo: N=115

- **Age:** 59 ± 13 years
- **Women:** 42%
- **Resting LVOT-G:** 56 ± 30 mmHg
- **Absolute RVFWLS:** $24.5 \pm 5.1\%$
(normal reference: $>20\%$)
- **Absolute RV4CLS:** $18.4 \pm 4.0\%$
(normal reference: $>17\%$)
- **RV-RA gradient:** 25.9 ± 4.1 mmHg
(normal reference: <31.4 mmHg)
- **RVFWLS/RV-RA gradient ratio:**
 1.1 ± 0.4 %/mmHg

Effect of Aficamten on Resting RV Parameters



**A. Absolute RVFWLS
(n=196)***



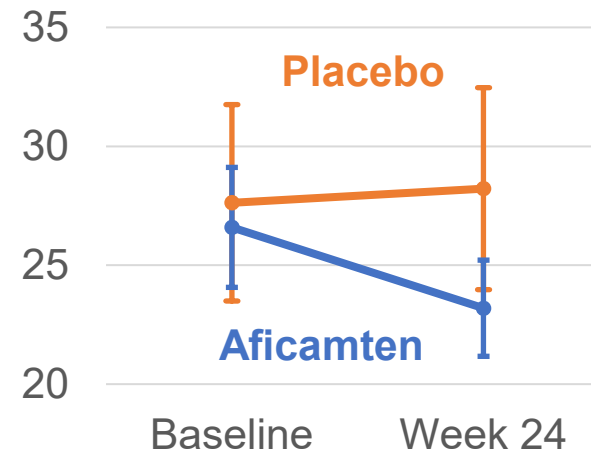
Treatment effect
-1.2 (-2.3 to -0.1) %
P=0.029

**B. Absolute RV4CLS
(n=196)***



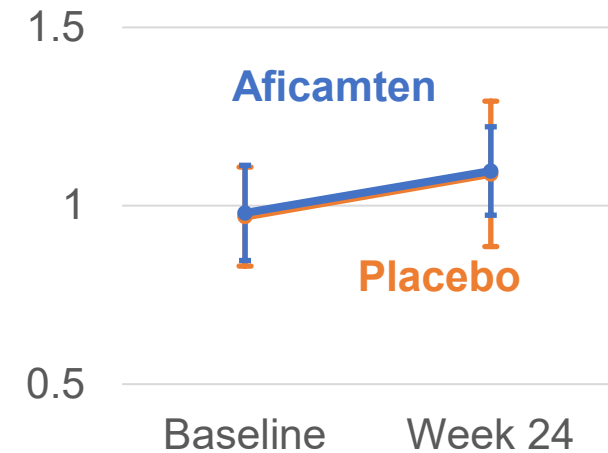
Treatment effect
-0.5 (-1.3 to +0.3) %
P=0.25

**C. RV-RA gradient
(n=74)***



Treatment effect
-4.3 (-7.2 to -1.5) mmHg
P=0.003

**D. RVFWLS/RV-RA gradient
ratio (n=48)***

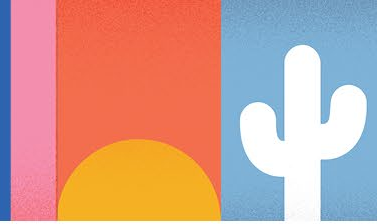


Treatment effect
+0.0 (-0.2 to +0.2)
P=0.87

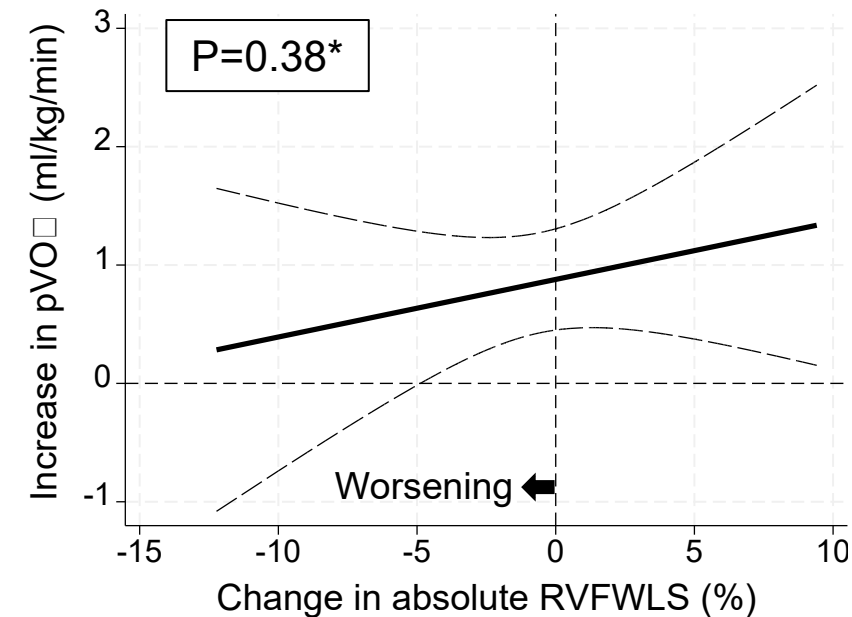
- Aficamten was associated with a modest reduction in RVFWLS compared with placebo, without significant change in RV4CLS
- Aficamten significantly reduced the RV-RA gradient, with preservation of the RVFWLS/RV-RA gradient ratio

*Number of patients with available data for both baseline and week 24.

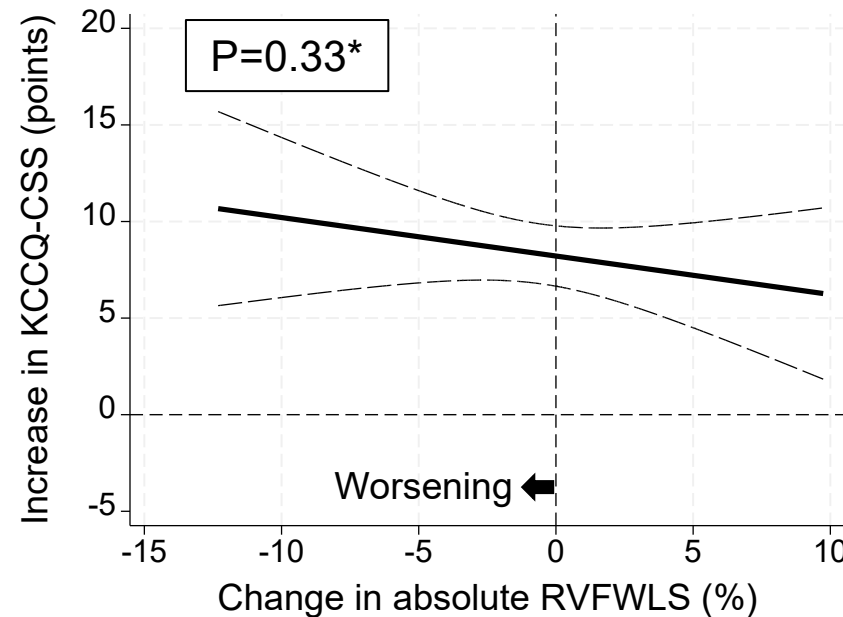
Association of RV Strain with Clinical Parameters



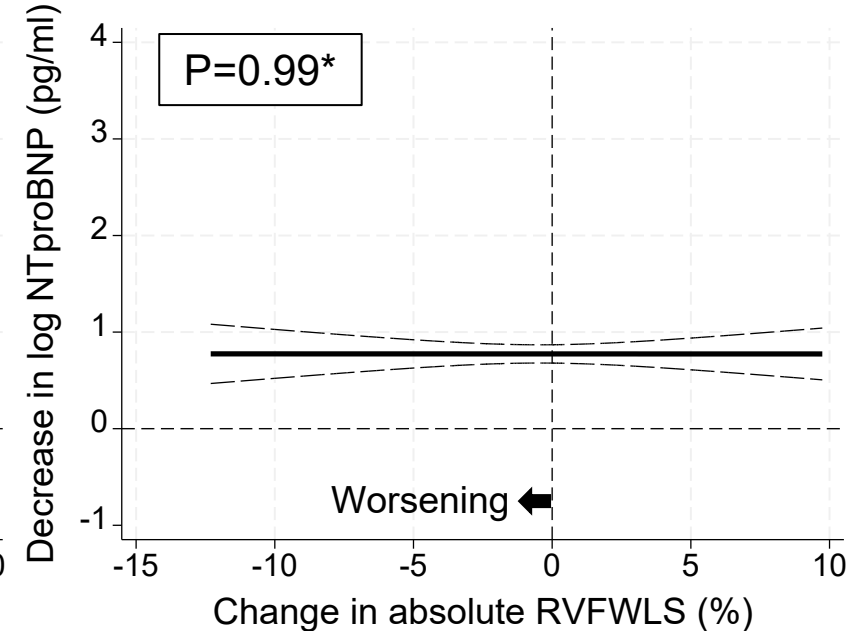
A. Peak VO₂



B. KCCQ-CSS



C. NT-proBNP



*Linear regression model, adjusting for baseline values and randomized treatment.

➤ **Changes in RVFWLS from baseline to week 24 were not associated with changes in peak oxygen uptake, Kansas City Cardiomyopathy Questionnaire Clinical Summary Scores, or NT-proBNP levels.**

Limitations

- Exploratory, post hoc RV strain analysis.
- Missing data for RV parameters with potential influence on the results, although missingness was balanced between treatment groups.
- Unknown impact of physical activity on these metrics.

Conclusions

- In patients with oHCM, aficamten was associated with a mild reduction in RVFWLS, yet it remained within the normal range, alongside a significant reduction in RV-RA gradient, with preservation of RV–PA coupling
- Changes in RV strain were not associated with clinical measures
- These data provide reassurance regarding RV performance with aficamten treatment in oHCM