Electrocardiographic Changes and Associations with Echocardiographic Changes in Patients with Symptomatic Obstructive Hypertrophic Cardiomyopathy: Insights from the SEQUOIA-HCM Trial

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BACKGROUND

- The electrocardiograms of patients with obstructive hypertrophic cardiomyopathy (oHCM) have characteristic abnormalities.
- Although aficamten has been shown to benefit patients with oHCM, the electrocardiogram (ECG) features and ECG-echocardiographic associations are not well described.

METHODS

- SEQUOIA-HCM (NCT05186818) was a randomized, placebo-controlled clinical trial testing aficamten in participants with oHCM.
- Qualitative ECG assessment for ST segment (ST) changes and the presence of left ventricular hypertrophy strain pattern (LVHsp) was performed. QT interval was corrected using the Bazett formula.
- Multivariable linear regression was used to assess the placebo-corrected treatment differences in echo measures according to LVHsp at baseline. All analyses were adjusted for baseline parameter, beta-blockers use at baseline, and exercise mode.

RESULTS

- Among the 282 participants of the SEQUOIA-HCM trial, ST changes and LVHsp were the most prevalent ECG features at baseline (64% and 52%, respectively).
- After 24 weeks, aficamten decreased the presence of any ST changes (adjusted OR 0.23; 95% CI 0.11, 0.46; p<0.001; **Figure 1**), ECG LVHsp (adjusted OR 0.15; 95% CI 0.06, 0.41; p<0.001; **Figure 2**), and reduced QTc interval (adjusted mean difference: -5.9 ms (95% CI -10.1, -1.6 ms), p<0.01; **Figure 3**).
- The effect of aficamten on lowering LV outflow tract (LVOT) gradients at rest did not differ by presence of LVHsp at baseline (+LVHsp: -44.4 [95% CI -52.5, -36.2], p<0.01; - LVHsp: -35 [95% CI -44.7, -26.1], p<0.01; $P_{interaction}$ = 0.13).

FIGURE 1

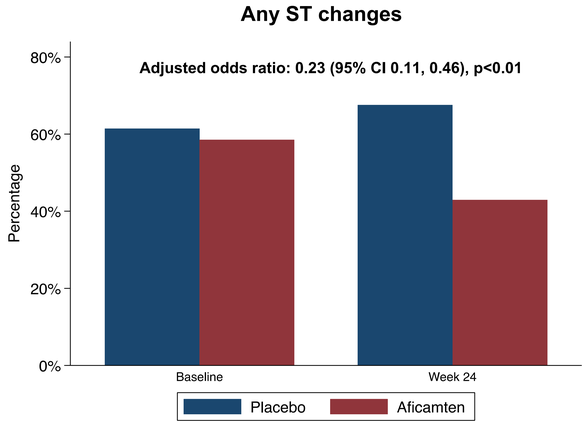


FIGURE 2

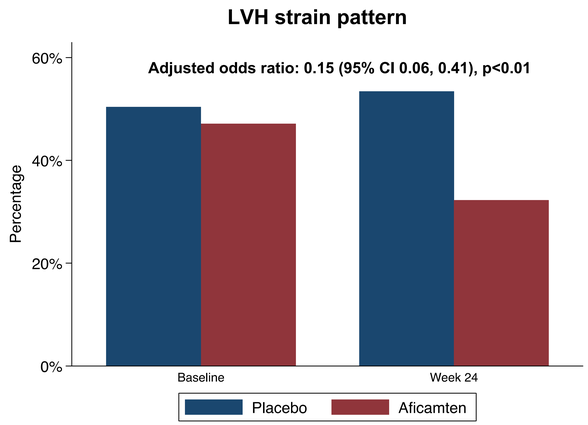
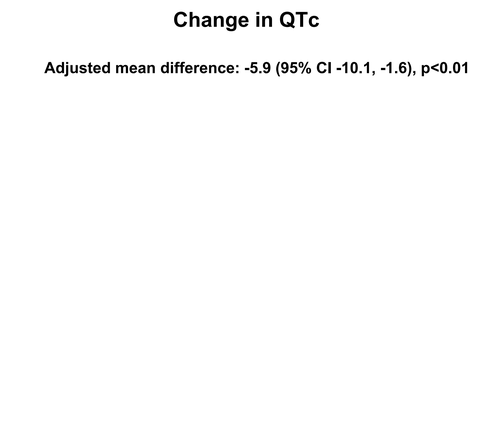


FIGURE 3



CONCLUSIONS

Aficamten treatment compared to placebo in SEQUOIA-HCM led to improvements in ST changes and LVH strain, and shortening of the QTc interval.

The benefits of aficamten on cardiac structure and function appear to be consistent in participants with and without LVH strain pattern.

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TABLE 1 - Echo parameters according to LVH strain pattern

	Baseline		Week 24	
Characteristic	LVH strain pattern (n=133)	No LVH strain pattern (n=123)	LVH strain pattern (N=99)	No LVH strain pattern (n=151)
LVOT gradient, rest, mmHg	61.5 ± 30.0	47.8 ± 27.4	48.4 ± 35.6	33.4 ± 30.1
LVOT gradient, Valsalva, mmHg	88.9 ± 30.7	76.4 ± 33.2	69.6 ± 40.1	53.9 ± 37.8
Max wall thickness, mm	21.2 ± 3.0	20.4 ± 3.0	20.5 ± 2.7	19.2 ± 3.2
LV ejection fraction, %	75.3 ± 5.2	74.6 ± 6.0	71.1 ± 6.3	70.4 ± 7.8
LV mass index, g/m²	141.2 ± 35.2	120.4 ± 29.4	147.3 ± 39.3	121.7 ± 30.9
Left atrial volume index, mL/m²	40.5 ± 13.5	39.5 ± 12.4	39.4 ± 10.2	39.2 ± 12.3
Lateral E/e'	16.8 ± 8.3	14.1 ± 6.3	16.0 ± 9.6	12.8 ± 5.9
Septal E/e'	21.8 ± 9.7	17.9 ± 6.8	19.7 ± 9.3	16.8 ± 6.1

TABLE 2 – Treatment effects according to LVH strain pattern

	Treatment effect LVH strain pattern		Treatment effect No LVH strain pattern		$P_{interaction}$
Characteristic	Difference	P value	Difference	P value	
LVOT gradient, rest, mmHg	-44.4 (-52.5; -36.2)	<0.01	-35 (-44.7; -26.1)	<0.01	0.13
LVOT gradient, Valsalva, mmHg	-57.1 (-66.8; -47.4)	<0.01	-44.2 (-54.8; -33.5)	<0.01	0.072
Max wall thickness, mm	-1.5 (-2.3; -0.7)	<0.01	-1.2 (-2.2; -0.2)	0.08	0.29
LV ejection fraction, %	-4.8 (-6.9; -2.8)	<0.01	-5.0 (-7.5; -2.5)	<0.01	0.83
LV mass index, g/m²	-11.8 (-20.9; -2.6)	0.01	-11.3 (-19.8; -2.8)	0.01	0.88
Left atrial volume index, mL/m²	-4.5 (-6.7; -2.3)	<0.01	-3.0 (-5.6; -0.4)	0.02	0.39
Lateral E/e'	-5.0 (-6.7; -3.3)	<0.01	-2.6 (-4.1; -1.2)	<0.01	0.018
Septal E/e'	-4.6 (-6.5; -2.6)	<0.01	-2.5 -3.9; -1.2)	<0.01	0.094

DISCLOSURE INFORMATION

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