Clinical trial investigating aficamten meets primary endpoint in obstructive hypertrophic cardiomyopathy

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Even though mortality and hospitalization rates have improved, the quality of life for those living with hypertrophic cardiomyopathy (HCM) can be compromised with limiting symptoms such as exertional dyspnea and decreased exercise capacity. A major cause of this in HCM patients is left ventricular outflow tract (LVOT) obstruction, which results in elevated intracardiac pressures.

A clinical trial has demonstrated that aficamten enhanced HCM patients' exercise capacity with significant improvement in peak oxygen uptake (pVO_2), improvement in limiting symptoms, and decreases in LVOT pressure gradients. The research was presented at Heart Failure 2024.

"The SEQUOIA-HCM trial demonstrated that aficamten can reliably and safely eliminate LVOT obstruction in patients with obstructive HCM using a simple and stepwise dosing regimen, and was associated with substantial improvements in clinically relevant endpoints such as exercise capacity and symptoms," said principal investigator Professor Martin Maron of the Lahey Hospital and Medical Center, Burlington, Massachusetts, US.

"HCM patients are often on multiple medications, which frequently provide suboptimal benefit, while aficamten was highly effective at providing clinical improvement as combination therapy, but also as monotherapy."

HCM occurs in approximately one in 200 to 500 individuals, with 70% of patients having obstructive disease. The condition causes the walls of

the left ventricle to become thick and stiff, which can also result in obstruction to blood flow out of the heart and increased intracardiac pressures.

Aficamten is a cardiac myosin inhibitor that was previously shown to reduce LVOT gradients in a phase 2 trial. The phase 3 SEQUOIA-HCM trial evaluated the efficacy and safety of aficamten versus placebo in adults with symptomatic obstructive HCM.

The primary endpoint was the change in pVO_2, assessed using cardiopulmonary exercise testing, from baseline to week 24. Secondary endpoints at 24 weeks included the change in KCCQ score; the proportion of patients with ≥1 class improvement in New York Heart Association (NYHA); change in Valsalva LVOT gradient; the proportion of patients with Valsalva LVOT gradient