BACKGROUND

- Hypertrophic cardiomyopathy (HCM) is a disease affecting the cardiac sarcomere, resulting in myocardial hypertrophy and cardiac hypertrophy.
- Patients with obstructive HCM (oHCM) have left ventricular outflow tract (LVOT) obstruction that occurs during systole and is the primary driver for the development of heart failure symptoms.
- Beta-blockers are commonly favored for treatment of symmetrical oHCM based on guidelines provided by ESC and ACC/AHA.

Although beta-blockers have been shown to reduce symptom burden and improve hemodynamics, there are no controlled data on the long-term effects of beta-blockers on cardiac structure and function. Moreover, they do not improve exercise capacity and can be associated with poor tolerability. Furthermore, there are no data on the long-term effects on cardiac structure and function.

Aficamten is a next-in-class cardiac myosin inhibitor (CMI) that selectively and reversibly stabilizes the myosin head into the actin filament, resulting in decreased contractility (actomyosin ATPase activity thereby preventing myosin from entering the rigor state).

Aficamten was safe and well tolerated in healthy participants in a Phase 1 study. In addition, the safety and tolerability in participants with symptomatic oHCM was generally well tolerated in healthy participants in a Phase 2 study.

The Phase 2b MAPLE-HCM study demonstrated that treatment with aficamten for 10 weeks was generally well tolerated in participants with symptomatic oHCM. There were also notable improvements in LVOT gradient (reducing and stabilizing), NYHA functional class (PCI), and clinical biomarkers (hs-cTnl and hs-CRP).

Aficamten is an investigational agent that is not approved by any regulatory agency, including the FDA, at the time of publication. The safety and efficacy of aficamten have not been established in any population. It is allowed for titration as early as 2 weeks.

Aficamten was generally well tolerated in healthy participants in a Phase 2 study. There were also notable improvements in LVOT gradient (reducing and stabilizing), NYHA functional class (PCI), and clinical biomarkers (hs-cTnl and hs-CRP).

OBJECTIVES

- To evaluate the effect of a head-to-head comparison to evaluate the safety and efficacy of aficamten.

- Prespecified primary end points: randomized with symmetric oHCM and treatment status: randomization.

- Secondary objectives: to evaluate the effect of aficamten compared with metoprolol on exercise capacity.

- Secondary objectives: to evaluate the effect of aficamten compared with metoprolol on exercise capacity and symptom status.

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