ACC.18

644
JACC March 20, 2018
Volume 71, Issue 11

Heart Failure and Cardiomyopathies

REDUCTION IN LEFT VENTRICULAR OUTFLOW TRACT GRADIENT WITH MAVACAMTEN (MYK-461) IN SYMPTOMATIC OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY PATIENTS (PIONEER-HCM)

Oral Contributions
Room 312 A
Sunday, March 11, 2018, 8:51 a.m.-9:01 a.m.

Session Title: Highlighted Original Research: Heart Failure and Cardiomyopathies and the Year in Review
Abstract Category: 13. Heart Failure and Cardiomyopathies: Clinical
Presentation Number: 901-10

Authors: *Daniel Jacoby, Steven Lester, Anjali Owens, Andrew Wang, Don Young, Radhika Tripuraneni, Marc Semigran, Stephen Heitner, MyoKardia, Inc., South San Francisco, CA, USA*

Background: In obstructive hypertrophic cardiomyopathy (oHCM) LV hypertrophy, reduced compliance, and hyperdynamic function result in dyspnea, fatigue, and limited exercise capacity. Mavacamten is an oral, allosteric modulator of cardiac myosin that targets an underlying biomechanical abnormality in HCM and was found to reduce LV hypercontractility in a phase 1 study of HCM patients.

Methods: PIONEER-HCM (NCT02842242) is a phase 2 open-label trial to assess safety and efficacy of mavacamten in symptomatic oHCM. In Cohort A, patients received 10 or 15 mg of mavacamten per day, were eligible for dose adjustment at week 4 (based on LVEF), and continued drug to week 12. Patients then underwent a 4-week washout.

Results: 10 of 11 patients (mean age, 56 yrs; 64% NYHA II; 36% III) completed the treatment phase in Cohort A. Mavacamten significantly reduced post-exercise peak LV outflow tract (LVOT) gradient (primary endpoint; p=0.002) and improved other parameters (Table) at week 12 compared to baseline. Resting LVOT gradient was <30 mmHg by week 2 in 9/10 patients. Mavacamten was generally well tolerated. One patient had a serious adverse event (AE) and withdrew from the study. All other AEs were deemed mild to moderate, and most were unrelated to study drug.

Conclusion: These results illustrate the ability of mavacamten to reduce LVOT obstruction and improve symptoms for oHCM patients. The Cohort A results from Pioneer-HCM suggest that mavacamten may present an alternative approach to treating oHCM patients.

Cohort A Results

Parameter	Baseline n=11 mean ±SD	Week 12 n=10 mean ±SD	Change n=10 mean ±SD	Wilcoxon Signed Rank p-value
Post-exercise peak LVOT gradient*, mmHg	125 ± 60.0	19 ± 12.9	−112 ± 63.8	0.002
Resting LVOT gradient, mmHg	68 ± 34.4	14 ± 24.6	-55 ± 41.8	0.006
Resting LVEF, %	70 ± 7.0	54 ± 12.4	-16 ± 14.1	0.008
Peak VO_2, mL/kg/min	20.7 ± 7.44	24.6 ± 8.78	+3.5 ± 3.25	0.004
Dyspnea numerical rating	4.9 ± 1.6	1.7 ±1.8	-3.1 ± 1.4	0.002

*Primary efficacy endpoint.