Long-term Safety and Effectiveness of Mavacamten in Symptomatic Obstructive Hypertrophic Cardiomyopathy Patients, PIONEER-Open Label Extension Study (PIONEER-OLE)

Stephen B. Heitner, MD, 1 Daniel Jacoby, MD, 2 Steven Lester, MD, 3 Andrew Wang, MD, 4 Liang Fang, PhD, 5 Amy J. Sehnert, MD 5

1Knight Cardiovascular Institute, Oregon Health & Sciences University, Portland, OR, USA; 2Yale University School of Medicine, New Haven, CT, USA; 3Mayo Clinic Arizona, Phoenix, AZ, USA; 4Duke University Medical Center, Durham, NC, USA; 5MyoKardia, Inc., South San Francisco, CA, USA

INTRODUCTION

- Obstructive hypertrophic cardiomyopathy (HCM) comprises left ventricular (LV) hypertrophy, LV outflow tract obstruction (LVOTO), and impaired myocardial relaxation.
- Disease pathogenesis is associated with sarcomere gene mutations resulting in hypercontractility, reduced ventricular compliance, and inefficient energy utilization.
- Symptom management is with either medications (β-blockers, calcium channel blockers, or diospyrosin) or septal reduction procedures (septal myectomy or alcohol septal ablation).
- Mavacamten is a first-in-class selective allosteric modulator of cardiac myosin that reversibly attenuates cardiac contractility—thus addressing the primary pathophysiologic mechanism of HCM—and is proposed to have clinical effects (Figure 1).

OBJECTIVE

- We report interim results from the first 24 weeks of the 2-year PIONEER-OLE study, which is an ongoing open-label extension study to examine the long-term safety and effectiveness of mavacamten using individualized dosing.

METHODS

- PIONEER-OLE (NCT02446160) is a 2-year trial for patients who completed PIONEER-HCM (NCT02842242) (Figure 2).
- PIONEER-OLE (NCT03496168) is a 2-year label extension study to examine the long-term safety and effectiveness of mavacamten in patients with symptomatic HCM, which was initiated to examine the long-term safety and effectiveness of mavacamten in this patient population.

Figure 1. Mavacamten Mechanism of Action

Mavacamten targets proteins in the sarcomere to normalize cardiac contractility and restore the appropriate number of sarcomere cross bridges.

Figure 2. PIONEER-OLE Study Design

COMPLETED PIONEER-HCM

ONGOING PIONEER-OLE

CONCLUSIONS

- Despite management with current therapies such as β-blockers, patients enrolled in PIONEER-OLE with similar levels of obstruction and hypercontractility after completing PIONEER-HCM 6-18 months prior.
- After 24 months of treatment patients demonstrated a significant reduction in LVOT peak instantaneous gradient, surrogate measures of left ventricular filling pressures, and improvement in clinical status.
- There were significant reductions in LVOT gradient and levels of NT-proBNP, as well as in E\textsubscript{\text{LV}} and LA volume.
- Eight out of 10 evaluable patients reported significant improvements in NYHA Class at Week 24 (per-protocol evaluable timepoint).

Figure 4. Change in NYHA Class at Week 24

- Eight out of 10 patients reported significant improvements in NYHA Class at Week 24 (per-protocol evaluable timepoint) (Figure 4).

REFERENCES


DISCLOSURES

SB Heitner, S. Lester, A. Wang, Consultant/Advisory Board MyoKardia, A. Jacoby, Consultant/Advisory Board MyoKardia, A. Sehnert, Employee, MyoKardia.

MyoKardia, Inc. funded the study. Editorial support was provided by NorthStar, San Francisco, CA, USA, and funded by MyoKardia.

Copy of this poster submitted through CircA Response (CR). Copies of this poster may be made for personal use only and may not be reproduced without prior permission from MyoKardia, Inc. and the authors of the poster.