EXPLORER-HCM: Efficacy and Safety of Mavacamten in Adults with Symptomatic Obstructive Hypertrophic Cardiomyopathy

Purpose: This study investigated the administration of mavacamten in participants with symptomatic obstructive Hypertrophic Cardiomyopathy (oHCM).

Trial Design: N= 251, Phase III, multicenter, international (13 countries), double-blind study of the administration of mavacamten in participants with symptomatic obstructive HCM (oHCM).

Primary Endpoint: The primary endpoint is clinical response, defined as either 1) an improvement of at least 1.5 mL/kg/min in peak oxygen consumption (VO_2) accompanied by an improvement from baseline of at least one New York Heart Association (NYHA) functional class or 2) an improvement from baseline of 3.0 mL/kg/min or greater in peak VO_2 without worsening in NYHA functional class. Secondary endpoints in the Phase 3 EXPLORER-HCM trial will include the average changes from baseline in post-exercise peak LVOT gradient, NYHA functional class, and peak VO_2.

Secondary Endpoints: Included change from baseline to week 30 in: Post-exercise LVOT gradient, pVO2, Proportion of patients with ≥1 NYHA class improvement, Kansas City Cardiomyopathy Questionnaire-Clinical Summary Score (KCCQ-CSS), HCM Symptom Questionnaire Shortness of Breath (HCMSQ-SoB) subscore.

	Mavacamten (N = 123) n (%)	Placebo (N = 128) n (%)	Difference (95% CI) P value
EITHER: ≥1.5 ml/kg/min increase in PVO_2 with ≥1 NYHA class improvement **OR** ≥3.0 ml/kg/min increase in pVO_2 with no worsening of NYHA class	45 (36.6)	22 (17.2)	19.4 (8.7, 30.1) 0.0005
BOTH ≥3.0 ml/kg/min increase in pVO_2 **AND** ≥1 NYHA class improvement	25 (20.3)	10 (7.8)	12.5 (4.0, 21.0) 0.0005

Conclusion: EXPLORER-HCM trial is the largest HCM study to date, and have demonstrated efficacy of mavacamten for patients with oHCM, with both primary and all secondary endpoints met with high statistical significance. Additional studies are needed to identify optimal individual dosage and patient selection criteria. Long-term follow-up data are required.