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Heart Failure and Cardiomyopathies

THE EFFECT OF MAVACAMTEN ON CARDIOPULMONARY EXERCISE TESTING PERFORMANCE OF PATIENTS WITH OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY IN EXPLORER-HCM

Moderated Poster Contributions
Heart Failure and Cardiomyopathies Moderated Poster Theater 2_Hall C
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Authors: *Matthew Thomas Wheeler, Iacopo Olivotto, Perry M. Elliott, Sara Saberi, Anjali Tiku Owens, Mathew S. Maurer, Ahmad Masri, Amy Sehnert, Jay Edelberg, Wanying Li, Victoria Florea, Rajeev Malhotra, Andrew Wang, Artur Oreziak, Daniel Jacoby, Jonathan N. Myers, Bristol Myers Squibb, Brisbane, CA, USA*

Background: Mavacamten, a cardiac myosin inhibitor, improved peak VO_2 in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM) in the EXPLORER-HCM study. The mechanism for mavacamten-related improvements in exercise physiology was further assessed by cardiopulmonary exercise testing (CPET).

Methods: Peak exercise values for VE/VCO_2, measured metabolic equivalents (METs), circulatory power, respiratory exchange ratio and exercise time, as well as VE/VCO_2 slope and ventilatory power CPET parameters were assessed with a standardized treadmill or bicycle ergometer at baseline and week 30 in 251 patients with symptomatic obstructive HCM.

Results: Patients were randomized to mavacamten (n = 123) or placebo (n = 128). There were significant improvements with mavacamten vs placebo in peak VE/VCO_2 (least square [LS] mean difference: -2.2 [$p < 0.0001$]), peak METs (0.4 [$p = 0.0006$]), peak circulatory power (372.9 mL/kg/min x mm Hg [$p = 0.0010$]) and peak exercise time (0.7 min [$p = 0.0153$]) (Table). There was a statistically significant improvement in VE/VCO_2 slope ($p < 0.0001$) and increase in ventilatory power ($p = 0.0002$) favoring mavacamten vs placebo.

Conclusion: Mavacamten improved a range of CPET parameters beyond peak VO_2, including peak-independent parameters, indicating consistent and broad benefits on maximal exercise capacity as well as on submaximal exertional tolerance.

Table. Change in CPET parameters from baseline to week 30.

Parameters	Mavacamten		Placebo		LS mean difference (95% CI): mavacamten–placebo	*p* value
	Baseline	Change at wk 30	Baseline	Change at wk 30		
Peak VE/VCO_2	35.4 (5.2)	-1.9 (3.7)	34.2 (5.5)	0.5 (3.8)	-2.2 (-3.05, -1.26)	<0.0001
Peak METs	5.4 (1.4)	0.4 (0.9)	5.7 (1.4)	-0.02 (0.86)	0.4 (0.17, 0.60)	0.0006
Peak circulatory power, mL/kg/min x mm Hg	3087.1 (1165.2)	414.1 (972.0)	3284.8 (1173.3)	-17.9 (869.1)	372.9 (153.12, 592.61)	0.0010
Peak exercise time, min	10.1 (4.0)	0.8 (2.4)	10.5 (4.2)	0.1 (2.0)	0.7 (0.13, 1.24)	0.0153
Peak RER	1.1 (0.1)	0.0 (0.1)	1.1 (0.1)	-0.001 (0.089)	0.02 (-0.003, 0.040)	0.0885
VE/VCO_2 slope	33.6 (6.2)	-2.4 (4.6)	33.4 (6.2)	0.4 (4.1)	-2.6 (-3.58, -1.52)	<0.0001
Ventilatory power, mm Hg	4.9 (1.4)	0.7 (1.4)	5.2 (1.5)	-0.03 (1.23)	0.6 (0.29, 0.90)	0.0002

Data presented are mean (SD). CI = confidence interval; LS = least square; METs = metabolism equivalents; RER = respiratory exchange ratio. The LS means (95% CI) and the p-values are based on ANCOVA (analysis of covariance).