Clinical Trial Lancet. 2021 Jun 26;397(10293):2467-2475. doi: 10.1016/S0140-6736(21)00763-7.
Epub 2021 May 15.

Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): health status analysis of a randomised, double-blind, placebo-controlled, phase 3 trial

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PMID: 34004177 DOI: 10.1016/S0140-6736(21)00763-7

Abstract

Background: Improving symptoms is a primary treatment goal in patients with obstructive hypertrophic cardiomyopathy. Currently available pharmacological options for hypertrophic cardiomyopathy are not disease-specific and are often inadequate or poorly tolerated. We aimed to assess the effect of mavacamten, a first-in-class cardiac myosin inhibitor, on patients' health status-ie, symptoms, physical and social function, and quality of life.

Methods: We did a health status analysis of EXPLORER-HCM, a phase 3, double-blind, randomised, placebo-controlled trial. The study took place at 68 clinical cardiovascular centres in 13 countries. Adult patients (≥18 years) with symptomatic obstructive hypertrophic cardiomyopathy (gradient ≥50 mm Hg and New York Heart Association class II-III) were randomly assigned (1:1) to mavacamten or placebo for 30 weeks, followed by an 8-week washout period. Both patients and staff were masked to study treatment. The primary outcome for this secondary analysis was the Kansas City Cardiomyopathy Questionnaire (KCCQ), a well validated disease-specific measure of patients' health status. It was administered at baseline and weeks 6, 12, 18, 30 (end of treatment), and 38 (end of study). Changes from baseline to week 30 in KCCQ overall summary (OS) score and all subscales were analysed using mixed model repeated measures. This study is registered with ClinicalTrials.gov, NCT03470545.

Findings: Between May 30, 2018, and July 12, 2019, 429 adults were assessed for eligibility, of whom 251 (59%) were enrolled and randomly assigned. Of 123 patients randomly assigned to mavacamten, 92 (75%) completed the KCCQ at baseline and week 30 and of the 128 patients randomly assigned to placebo 88 (69%) completed the KCCQ at baseline and week 30. At 30 weeks, the change in KCCQ-OS score was greater with mavacamten than placebo (mean score 14·9 [SD 15·8] vs 5·4 [13·7]; difference +9·1 [95% CI 5·5-12·8]; p<0·0001), with similar benefits across all KCCQ subscales. The proportion of patients with a very large change (KCCQ-OS ≥20 points) was 36% (33 of 92) in the mavacamten group versus 15% (13 of 88) in the placebo group, with an estimated absolute difference of 21% (95% CI 8·8-

33·4) and number needed to treat of five (95% CI 3–11). These gains returned to baseline after treatment was stopped.

Interpretation: Mavacamten markedly improved the health status of patients with symptomatic obstructive hypertrophic cardiomyopathy compared with placebo, with a low number needed to treat for marked improvement. Given that the primary goals of treatment are to improve symptoms, physical and social function, and quality of life, mavacamten represents a new potential strategy for achieving these goals.

Funding: MyoKardia, a Bristol Myers Squibb company.

Comment in

Quality first in obstructive hypertrophic cardiomyopathy.

Prasad SB, Atherton JJ.

Lancet. 2021 Jun 26;397(10293):2440-2441. doi: 10.1016/S0140-6736(21)00898-9. Epub 2021 May 15.

PMID: 34004178 No abstract available.

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