Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/valor-hcm-mavacamten-alternative-surgical-septal-myectomy-or-alcohol-ablation-patients-severely-symptomatic-obstructive-hypertrophic-cardiomyopathy/14050/

Released: 04/25/2022
Valid until: 04/25/2023
Time needed to complete: 1h 25m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

VALOR-HCM: Mavacamten as An Alternative to Surgical Septal Myectomy or Alcohol Ablation in Patients With Severely Symptomatic Obstructive Hypertrophic Cardiomyopathy

Dr. Desai:
Thank you very much for the invitation. My name is Milind Desai from the Cleveland Clinic, Department of Cardiovascular Medicine and Heart and Vascular Institute. It is my privilege on behalf of my co-investigators to present the results of the VALOR-HCM trial. This is a trial which tested myosin inhibition to defer surgical myectomy or alcohol septal ablation in obstructive hypertrophic cardiomyopathy.

Hypertrophic cardiomyopathy is a primary myocardial disorder, which is characterized by a significant left ventricular hypertrophy. Prevalence is thought to be between 1:200 to 1:500, and estimated number of people in the world is about 15 to 20 million. Two-thirds of patients have obstructive hypertrophic cardiomyopathy which is due to dynamic out left ventricular outflow tract obstruction. This is also often, very often associated with symptoms. Currently, the medical therapies have not been developed specifically for hypertrophic cardiomyopathy, and, as such, septal reduction therapies, either surgical septal myectomy or alcohol ablation are recommended for patients who are intractably symptomatic despite maximal medical therapy. Although SRT improves long term survival symptoms and quality of life, optimal results require specialized care that is not widely available. As a result, there is an unmet need for noninvasive alternatives to SRT for highly symptomatic obstructive HCM patients.

Mavacamten is a targeted inhibitor of cardiac myosin that decreases the number of myosin-actin cross-bridges, and it reduces excessive contractility that is fairly characteristic in hypertrophic cardiomyopathy. This results in improved compliance and energetics, and in obstructive HCM studies have previously shown that it improves significantly left ventricular outflow tri-gradient, quality of life, as well as physical functioning.

The VALOR-HCM study was designed as a double blind placebo controlled study to last for 16 weeks, where patients were randomized to either mavacamten, starting at five milligrams dose, but could be titrated between 2.5, all the way up to 15 milligrams versus placebo. The mavacamten titration occurred using core lab measured ECHO fraction, as well as LVOT gradient at rest, and with Valsalva provocation. Patients were followed every month with ECHO, and that was predominantly what was used for titration. So the primary aim of VALOR-HCM was sought to determine if mavacamten, when added to maximal tolerated medical therapy, would allow severely symptomatic patients with obstructive HCM to improve sufficiently, such that they no longer met guideline criteria for SRT, or chose not to undergo SRT for 16 weeks.

Here is the Baseline Data and the Primary Endpoint. This was a total of 112 patients equally distributed between mavacamten and placebo group aged around 60 years. About 50% were females and 93% patients were in NYHA Class III or higher. Monotherapy with beta blocker was seen in 46%, and calcium channel blockers, almost 13%. And importantly, 32% were on combination medical therapy, and 20% were on disopyramide As would be expected, the resting in LVOT gradient were severely elevated. The primary endpoint in the current study, which was a composite of decision to proceed with SRT by week 16, or still remain guideline eligible at week 16. In the mavacamten group, only 17.9% remained eligible or met the primary endpoint. And in the placebo group, however, 76.8% remain guideline eligible. This treatment difference of 58.93 was highly significant with a P value less 0.0001.

Some secondary efficacy endpoints were tested that included resting LVOT gradient, valsalva LVOT gradient, cancer city

cardiomyopathy questionnaire NT-proBNP, as well as troponin I, and each one was significantly improved in favor of mavacamten. Additionally, what we also found was that patients had 63% patients in the mavacamten group had at least one NYHA class improvement, compared to only 21% in the placebo. Additionally, 27% patients in the mavacamten group had at least two NYHA class improvement. And all the findings were highly statistically significant.

Conclusion and Medical Relevance. In obstructive HCM patients with intractable symptoms that were referred for SRT administration of mavacamten that was titrated using ECHO, was: It safely and significantly reduced eligibility for invasive SRT procedures at 16 weeks. It showed treatment benefits for all secondary endpoints, including a reduction in LVOT gradient as significant, at least one class improvement in NYHA class, improvement in Kansas City. The summary score, as well as redux improvement in biomarkers. Hence, mavacamten may provide an alternative to SRT in severely symptomatic obstructive HCM patients, who are maximally tolerated standard HCM therapy, including disopyramide. Additional data is needed to assess the durability of improvement in SRT eligibility over long term periods. Thank you.