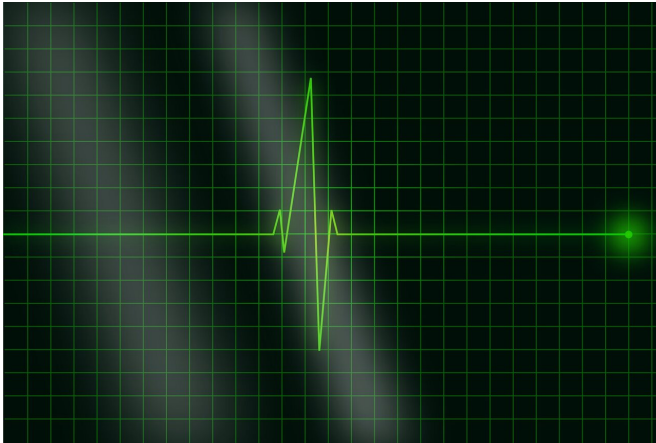


Valsartan trial reveals cardiac improvements for patients with early-stage genetic heart condition

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An randomized, clinical trial of 178 patients with sarcomeric hypertrophic cardiomyopathy found evidence that patients who received the angiotensin II receptor blocker valsartan had improved cardiac structure, function and remodeling over a two-year period

Hypertrophic cardiomyopathy (HCM) is the most common genetic heart disease, affecting between 1 in 500 to 1 in 1,000 people in the general population. Patients with HCM are at increased risk of atrial fibrillation, heart failure and sudden cardiac death. With advancements in genetic testing, patients can be identified early, but there are currently no therapies approved to prevent the disease from progressing. The Valsartan for Attenuating Disease Evolution in Early Sarcomeric Hypertrophic Cardiomyopathy (VANISH) trial tested the angiotensin II receptor blocker (ARB) valsartan—a widely available drug used to treat high blood pressure and heart failure—for diminishing disease progression in individuals with

early stage HCM. In a late-breaking clinical trial presentation at ESC Congress 2021, Carolyn Ho, MD, of Brigham and Women's Hospital's Division of Cardiovascular Medicine, presented the positive findings from the trial.

"Valsartan improved cardiac structure/function and remodeling in patients with early stage sarcomeric HCM, suggesting that this strategy may help prevent disease progression among those who have received a genetic diagnosis of HCM," said Ho. "This trial builds upon decades of work to identify the genetics and elucidate the disease mechanism of HCM and takes a key step toward translating seminal lab studies and fundamental discoveries into developing new treatment strategies for patients."

HCM is a genetic disorder of the heart muscle and an important cause of nonviolent sudden death in young adults. More than a decade ago, Brigham and Harvard Medical School researchers Christine E. Seidman, MD, and Jonathan G. Seidman, PhD, determined that HCM is caused by mutations in one of eight genes that encode the protein components of the sarcomere and coordinate the contraction and relaxation of the heart muscle. First-degree relatives (parents, siblings, and children) of people with HCM have a 50 percent chance of inheriting a disease-causing mutation and developing HCM.

Previous clinical trials of ARBs have not found a clinical benefit for their use in adult patients with established HCM. But the VANISH trial set out to test an ARB in patients with asymptomatic or mildly symptomatic overt disease who carried sarcomeric HCM mutations. These younger patients with earlier and more modest disease expression were hypothesized to be more likely to respond to disease-modifying therapy. Patients were enrolled

from 17 sites in four countries. A total of 178 patients were randomized to receive valsartan (320 mg daily in adults; 80-160 mg daily in children) or placebo for two years. The mean age of participants was 20-30 years younger than prior studies.

Rather than evaluating traditional, long-term clinical outcomes, such as mortality and major adverse cardiac events, investigators evaluated nine different metrics that captured cardiac function, structure and remodeling. The primary composite outcome included changes in left ventricular wall thickness, mass and volume; left atrial volumes; tissue Doppler diastolic and systolic velocities; and serum levels of high-sensitivity troponin T and N-terminal pro-B-type natriuretic protein.

"We know that disease progression takes place over a long period of time, which means it may take 10 to 20 years to see adverse clinical outcomes," said Ho. "We wanted to see if intervening early could change disease biology. The benefit we saw in the metrics we examined may indicate that we successfully altered biology. This may have the potential to prevent or slow the course of disease progression."

Compared to placebo, valsartan improved the primary composite outcome. The largest effects of valsartan were on tissue Doppler diastolic velocity, LV end diastolic volume, and NTproBNP levels. These measures were stable or improved over the course of two years for patients randomized to valsartan; among patients randomized to placebo, these measures worsened.

"Our results suggest that valsartan may not only stabilize disease progression but may also promote improvement," said Ho.

Valsartan treatment was safe and well-tolerated with no excess of adverse events.

"Imagine inheriting a gene that causes your heart to become enlarged over time and may cause heart failure or sudden cardiac death," said Kristin Burns, MD, a study coauthor and chief of the Heart Development and Structural Diseases branch within the Division of Cardiovascular Sciences at

the National Heart, Lung, and Blood Institute. "Now, imagine being able to take treatment that is already widely available and potentially mitigates progression of disease if taken early, before the [heart](#) becomes too thick. The findings from this study suggest that this may be an option for children and young adults with hypertrophic cardiomyopathy. We look forward to following this research in larger trials that study the immediate and long-term impacts of this type of targeted treatment."

Ho notes several limitations to the study, including that the biologic metrics measured in the study may not correlate with clinical outcomes.

"Patients should speak with their providers to think about the results of this trial in the context of their care," said Ho. "This will be a personal decision for patients and their providers, but we are excited to find evidence that a drug that is easily accessible, safe and well-tolerated has the potential to change disease evolution in early HCM."

More information: ESC Congress: digital-congress.escardio.org/...nce-in-heart-failure

Provided by Brigham and Women's Hospital

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