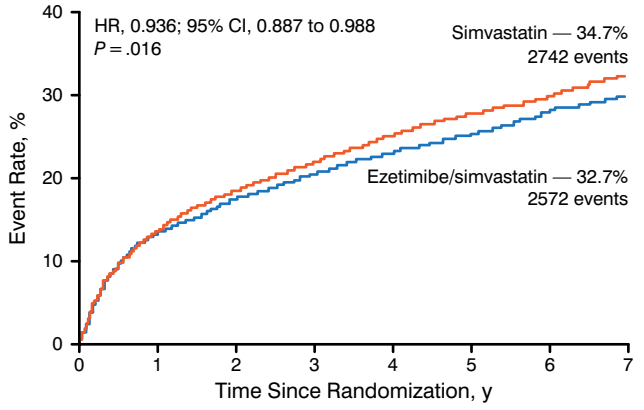
were excluded if they were undergoing CABG, their current statin therapy had potency > simvastatin 40 mg, their creatinine clearance was < 30 mL/min, or they had active liver disease.

The primary end point of the IMPROVE-IT trial was a composite score of CV death, MI, hospital admission for UA, coronary revascularization, or stroke [Blazing MA et al. *Am Heart J.* 2014]. Secondary end points included individual CV end points, as well as various composite scores. At baseline, the mean age was 64 years, 24.5% of patients were female, 27% had DM and 35.5% were on prior lipid-lowering therapy. In addition, the mean LDL-C level at the time of the ACS event was 95 mg/dL.

Treatment with ezetimibe plus simvastatin resulted in a greater decrease in mean LDL-C levels beginning at week 1 after randomization and remained steady up to 96 months. A significantly higher number of patients in the simvastatin monotherapy arm experienced the primary end point (34.7%) compared with patients in the ezetimibe plus simvastatin arm (34.7% vs 32.7%; HR, 0.936; 95% CI, 0.887 to 0.988; $P = .016$) with a number needed to treat (NNT) of 50 (Figure 1). Similarly, significantly fewer patients reached the composite of CV death, nonfatal MI, or nonfatal stroke in the ezetimibe plus simvastatin arm (20.4%) compared with the simvastatin arm (20.4% vs 22.2%; HR, 0.90; 95% CI, 0.84 to 0.97; $P = .003$) with an NNT of 56. In addition, fewer patients experienced the individual end points of MI and ischemic stroke in the combination therapy arm compared with simvastatin monotherapy.

Similar rates of adverse events occurred among both arms, such as elevated liver enzymes, cholecystectomy, gallbladder-related events, rhabdomyolysis, myopathy, and cancer.

Figure 1. Primary End Point of the IMPROVE-IT Trial



IMPROVE-IT, Improved Reduction of Outcomes: Vytorin (Ezetimibe/Simvastatin) Efficacy International Trial.

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In conclusion, Dr Cannon stated that data from the IMPROVE-IT trial suggest that the addition of a nonstatin, LDL-C–lowering agent provides an additional clinical benefit beyond statin monotherapy. In addition, he commented that the results support the LDL hypothesis that lowering LDL-C can reduce the risk of CV events.

Losartan Lacks Benefit in Inherited HCM

Written by Emma Hitt Nichols, PhD

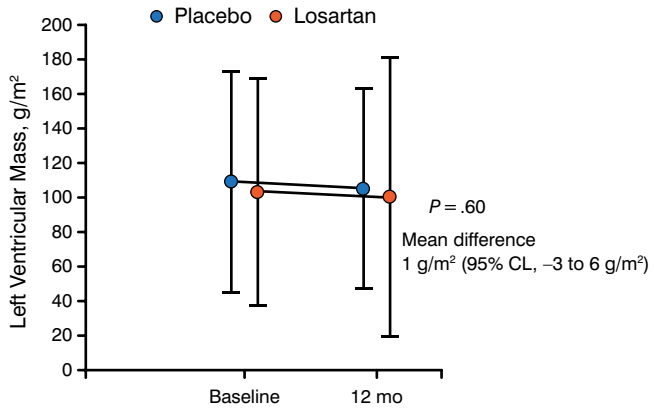
Losartan treatment in patients with hypertrophic cardiomyopathy (HCM) did not alter left ventricular mass from baseline over 12 months compared with placebo. Anna Axelsson, MD, The Heart Center, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark, presented data from the Inhibition of the Renin Angiotensin System With Losartan in Patients With Hypertrophic Cardiomyopathy [INHERIT; NCT01447654] trial.

HCM has a prevalence of 1 in every 500 individuals, making it the most frequently inherited cardiomyopathy, and it results in the fibrosis and hypertrophy of the left ventricle [Green JJ et al. *JACC Cardiovasc Imaging.* 2012]. Data from in vivo studies performed in animal models and humans indicate that angiotensin receptor blockers (ARBs) may have a benefit on diastolic function, left ventricular mass, exercise capacity, and myocardial fibrosis [Shimada YJ et al. *JACC Heart Fail.* 2013; Penicka M et al. *J Mol Diagn.* 2009; Araujo AQ et al. *Am J Cardiol.* 2005]. The purpose of the INHERIT trial was to evaluate the effect of the ARB losartan on morphology and function of the left ventricle in patients with HCM.

In the single-center, double-blind, phase 2 INHERIT trial, 133 adult patients with HCM were randomly assigned to receive losartan 100 mg/d or placebo for 12 months. All patients were in sinus rhythm upon inclusion into the study. Patients were excluded if they had a left ventricular ejection fraction < 50%, significant valvular disease, blood pressure > 140/90 mm Hg, an estimated glomerular filtration rate < 30 mL/min per 1.73 m^2, were currently taking an ARB or angiotensin-converting enzyme inhibitor, or had septal reduction treatment within 6 months. At baseline, the mean age was 52 years and 36% of participants were women. In the study, 64%, 30%, and 6% of patients were classified as having NYHA functional class I, II, and II, respectively. In addition, 43% of patients were identified as having a disease-causing genetic mutation.

The primary end point was change in left ventricular mass as determined by magnetic resonance imaging or computed tomography imaging. Secondary end points

Figure 1. Effect of Losartan on Left Ventricular Mass in Patients With Hypertrophic Cardiomyopathy



95% CL, 95% confidence limit.

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included changes in left ventricular maximal wall thickness, outflow tract gradient, and fibrosis, as well as changes in diastolic function, exercise tolerance, and symptoms of HCM. In the study, 93% of patients were compliant with study medication as determined by pill count.

There was no significant difference in change in left ventricular mass from baseline among patients who received losartan or placebo at 12 months ($P = .60$). Similarly, there was no significant difference in change in maximal ventricular wall thickness, echocardiographic findings such as outflow gradient. In addition, a subgroup analysis demonstrated that there was no benefit with losartan treatment based on age, presence of a genetic mutation causing HCM, left ventricular outflow tract obstruction, maximal wall thickness, or history of myectomy or alcohol septal ablation.

The rate of adverse events (AEs) was similar among the losartan and placebo arms. AEs included sudden cardiac death, angioedema, hyperkalemia, renal impairment, worsening of NYHA functional class, and left ventricular outflow tract gradient. Seven patients discontinued therapy; unspecified symptoms led to discontinuation by 2 patients in the losartan arm and 1 patient in the placebo arm, 1 patient in the losartan arm discontinued treatment because of deterioration of renal function, angioedema caused 1 patient in the losartan arm to discontinue therapy, and 2 patients in the losartan arm were referred for septal reduction therapy and excluded from follow-up. In addition, 2 patients in the placebo arm died from sudden cardiac death.

In conclusion, Dr Axelsson stated that the results from the INHERIT trial indicate that losartan does not provide a benefit for left ventricular mass in patients with HCM; however, losartan treatment was safe and may be used, albeit with caution, for other indications in this population such as for treatment of hypertension.

CABG Plus Valve Repair Provides No Benefit in MR Over CABG Alone

Written by Emma Hitt Nichols, PhD

Coronary artery bypass grafting (CABG) plus mitral valve repair resulted in similar changes in left ventricular reverse modeling and rate of death in patients with multivessel coronary disease and moderate ischemic mitral regurgitation (MR) but was associated with higher rates of serious adverse events (SAEs) when compared to CABG alone. Robert E. Michler, MD, Montefiore-Einstein Heart Center, New York, New York, USA, presented data from the Surgical Interventions for Moderate Ischemic Mitral Regurgitation study [Smith PK et al. *N Engl J Med.* 2014].

About 50% of MR cases are associated with ischemia, 10% of which are moderate in severity. Importantly, ischemic MR is associated with an increased risk of morbidity and mortality [Go AS et al. *Circulation.* 2014]. Surgical treatment options for MR include CABG, with or without mitral valve replacement. The purpose of this study was to determine whether valve repair for moderate ischemic MR at the time of CABG was superior to CABG alone.

In this phase 2 trial, 301 patients with moderate ischemic MR were randomly assigned to undergo CABG alone or CABG plus mitral valve repair with an undersized ring and were followed for 12 months. At baseline, 68% of patients were men; 47% had diabetes mellitus; and the mean age was 64.5 years. The primary end point was the degree of reverse modeling in the left ventricle according to changes in left ventricular end systolic volume index. Secondary end points included major adverse cardiac and cerebrovascular events (MACCEs), mortality, residual MR, hospitalization, quality of life, and other SAEs.

There was no significant difference in change in left ventricular end systolic volume index in patients who underwent CABG alone or CABG with mitral valve repair at 12 months ($P = .61$). In addition, the mortality rate was similar between arms, with 30-day mortality occurring in 2.7% and 1.3% of patients who underwent CABG or CABG plus valve repair, respectively ($P = .68$), and with 12-month mortality occurring in 7.3% and 6.7%, respectively ($P = .81$). Similarly, the rate of MACCEs was similar between arms at 12 months. Patients who had CABG plus valve repair experienced a greater reduction in severity of MR when compared with patients who had CABG alone.