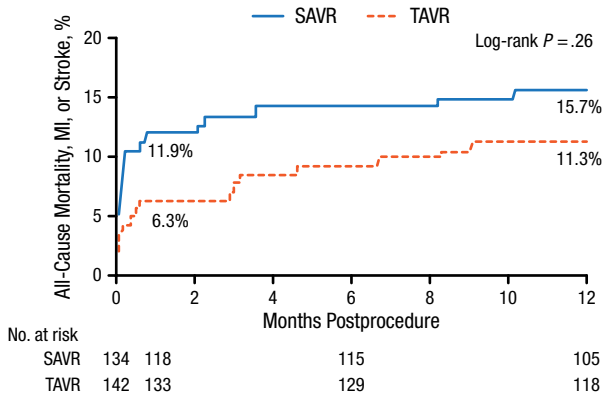
280 patients (mean age 79 years; 53% men) with low-risk severe aortic valve stenosis (mean STS score 3%) who were expected to live >1 year to TAVR (n=145) or SAVR (n=135). The primary outcome was a composite of death from any cause, stroke, or MI at 1 year. Secondary outcomes included safety and efficacy and echocardiographic outcomes. Baseline characteristics and comorbidities were not significantly different in the 2 groups.

In intention-to-treat analysis, the composite rate of death from any cause, stroke, or MI at 1 year was 13.1% for TAVR vs 16.3% for SAVR (P=.43). In as-treated analysis, rates for the primary end point also failed to reach statistical significance (Figure 1).

Figure 1. Death From Any Cause, Stroke, or Myocardial Infarction at 1 Year in As-Treated Population



MI, myocardial infarction; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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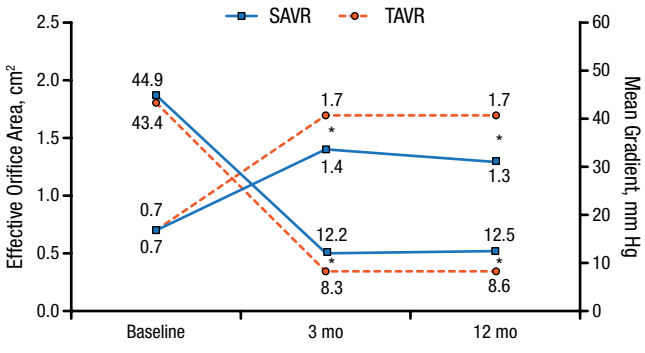
Figure 2. Aortic Valve Performance



SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

*P<.001.

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The only secondary outcomes to achieve statistical significance at 1 year were rates of atrial fibrillation (TAVR, 21.2% [n=142]; SAVR, 59.4% [n=134]; P<.001) and pacemaker implantation (TAVR, 38%; SAVR, 2.4%; P<.001). Among surviving patients at 1 year, 67.4% in the TAVR group (n=132) were NYHA class I compared with 81.7% in the SAVR group (n=120). A statistically significant difference (P<.001) favoring TAVR was seen for aortic valve performance (Figure 2). Rates of moderate-to-severe aortic valve regurgitation were 15.7% for TAVR vs 0.9% for SAVR at 1 year.

In summary, the NOTION trial failed to demonstrate that TAVR was superior to SAVR for the primary outcome of the composite rate of death from any cause, stroke, or MI after 1 year in patients with low-risk severe AS. Dr Thyregod concluded that long-term durability and morbidity data were required in lower-risk patients.

Ezetimibe Plus Simvastatin More Beneficial Than Simvastatin Alone in Reducing Recurrent Cardiovascular Events: A Secondary Analysis From IMPROVE-IT

Written by Maria Vinall

According to results of a secondary analysis of the IMPROVE-IT study presented by Sabina A. Murphy, MPH, Brigham and Women's Hospital, Boston, Massachusetts, USA, adding ezetimibe to simvastatin therapy significantly improved clinical outcomes beyond a first event compared with simvastatin alone. This analysis also confirmed the importance of continuing intensive combination lipid-lowering therapy after a first cardiovascular (CV) event.

Ezetimibe is a nonstatin lipid-lowering therapy that reduces cholesterol absorption in the intestine. When added to a statin, achievement of low-density lipoprotein cholesterol (LDL-C) levels <70 mg/dL or <100 mg/dL was approximately 20% higher compared with a statin alone [Morrone D et al. *Atherosclerosis.* 2012]. IMPROVE-IT [NCT00202878] was a phase 3, multicenter, randomized, double-blind, active-control trial that evaluated whether ezetimibe added to simvastatin improved CV outcomes compared with simvastatin therapy alone.

IMPROVE-IT included 18 144 moderate- to high-risk patients stabilized after acute coronary syndromes (≤10 days) receiving standard medical and interventional therapy. Patients with a LDL-C level between 50 and 125 mg/dL (or 50 to 100 mg/dL if they had been taking prior lipid-lowering therapy) were randomized in

a 1:1 ratio to once-daily doses of either ezetimibe/simvastatin (10/40 mg) or simvastatin monotherapy (40 mg) and followed for 2.5 years or until at least 5250 patients experienced a primary end point event.

The primary end point of the first occurrence of CV death, nonfatal myocardial infarction (MI), rehospitalization for unstable angina (UA), coronary revascularization (occurring ≥30 days after randomization), or stroke occurred in significantly more patients in the simvastatin monotherapy arm vs combination therapy arm (34.7% vs 32.7%; HR, 0.94; 95% CI, 0.89 to 0.99; $P=.016$). The number needed to treat was 50.

The occurrence of a first event for each of the 3 prespecified secondary end points was also significantly higher with simvastatin monotherapy vs combination therapy. All-cause death/MI/UA/coronary revascularization/stroke occurred in 40.3% vs 38.7%, respectively ($P=.034$). Coronary heart disease (CHD) death/MI/urgent coronary revascularization occurred in 18.9% vs 17.5% ($P=.016$). CV death/MI/UA/any revascularization/stroke occurred in 36.2% vs 34.5% ($P=.035$). Significance was driven by fewer MIs, strokes, and urgent revascularization events.

The present analysis determined the number of first and recurrent events recorded during the mean 6-year follow-up, with the hypothesis that the number of total events would be reduced with combination therapy vs simvastatin monotherapy. There were 5314 first primary end point events and 4231 additional primary end point events, the majority of which were revascularization for both first and recurrent events. Overall, there were significantly fewer total primary end point events with combination therapy (RR, 0.91; 95% CI, 0.85 to 0.97; $P=.007$; Figure 1). These results were reflected in a reduction in additional primary end point events (RR, 0.88; 95% CI, 0.79 to 0.98; Figure 1).

Figure 1. Fewer Total (First and Recurrent) Primary End Point Events With Combination Therapy

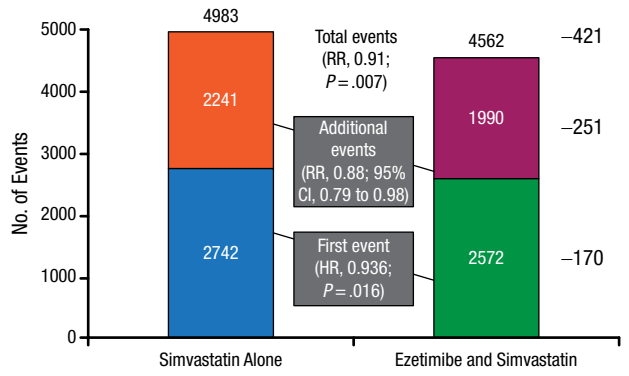

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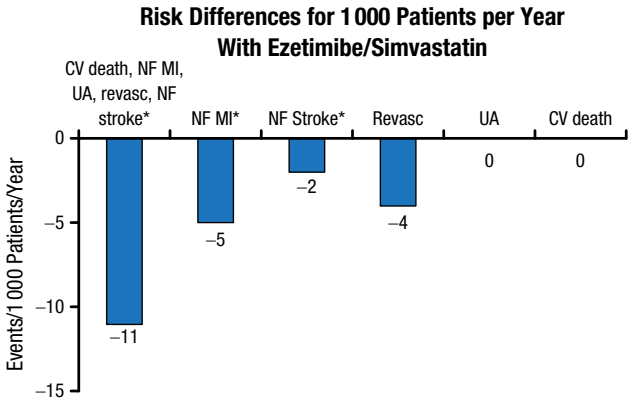
Figure 2. Risk Differences for Total Primary End Point Events



CV, cardiovascular; MI, myocardial infarction; NF, nonfatal; Revasc, revascularization; UA, unstable angina.
*$P<.05$; others not significant.
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There were fewer total secondary end point events with combination therapy as well, including fewer CHD deaths, MIs, and urgent revascularization events (RR, 0.85; 95% CI, 0.76 to 0.94; $P=.002$), fewer all-cause death/MI/UA/coronary revascularization/stroke (RR, 0.92; 95% CI, 0.87 to 0.98; $P=.009$), and fewer CV death/MI/UA/any revascularization/stroke (RR, 0.93; 95% CI, 0.87 to 0.99; $P=.02$).

Sensitivity analysis using the Wei, Lin, and Weissfeld model for the occurrence of primary end point events favored combination therapy (model average HR, 0.93; 95% CI, 0.89 to 0.99; $P=.01$). The absolute risk difference for total primary end point events, nonfatal MI, and nonfatal stroke also favored ezetimibe/simvastatin therapy ($P<.05$; Figure 2).

This is the first trial demonstrating clinical benefit when adding a nonstatin lipid-lowering agent to statin therapy. By treating patients with a daily combination of ezetimibe/simvastatin rather than simvastatin alone, more than twice the number of recurrent adverse CV events was prevented compared with first events.

LEGACY: Sustained Weight Loss Improves Heart Rhythm Control in 5-Year Trial

Written by Francesca Coltrera

Steady, sustained weight loss can help control atrial fibrillation (AF) in overweight patients, even freeing some from the need for medications or surgical ablation. Rajeev K. Pathak, MBBS, University of Adelaide