The efficacy and safety of evolocumab were assessed in 1896 patients with primary hypercholesterolemia and mixed dyslipidemia (LDL-C ≥80 mg/dL) who were also taking a high- or moderate-intensity statin. Patients were eligible for the study if they had a central laboratory fasting LDL-C at screening of ≥150 mg/dL (4.0 mmol/L; no statin at screening), ≥100 mg/dL (2.6 mmol/L; nonintensive statin at screening), or ≥80 mg/dL (2.1 mmol/L; intensive statin at screening). The primary objective of this study was to evaluate the efficacy (vs placebo) of 12 weeks of subcutaneous (SC) evolocumab administered every 2 weeks or every month when used in combination with a daily statin with or without ezetimibe on percent change from baseline in LDL-C.

Patients were initially randomized to high (atorvastatin 80 mg or rosuvastatin 40 mg) or moderate (atorvastatin 10 mg, rosuvastatin 5 mg, or simvastatin 40 mg) intensity statin therapy. Following a 4-week stabilization period, patients randomized to atorvastatin 10 or 80 mg were then randomized to 1 of 6 treatment groups: SC evolocumab 140 mg Q2W and oral placebo QD; SC evolocumab (420 mg) QM and oral placebo QD; SC placebo Q2W and oral placebo QD; SC placebo QM and oral placebo QD; SC placebo Q2W and ezetimibe 10 mg QD; or SC placebo QM and ezetimibe 10 mg QD. Patients randomized to rosuvastatin or simvastatin were then randomized to 1 of 4 treatment groups: evolocumab Q2W, evolocumab QM, SC placebo Q2W, or SC placebo QM.

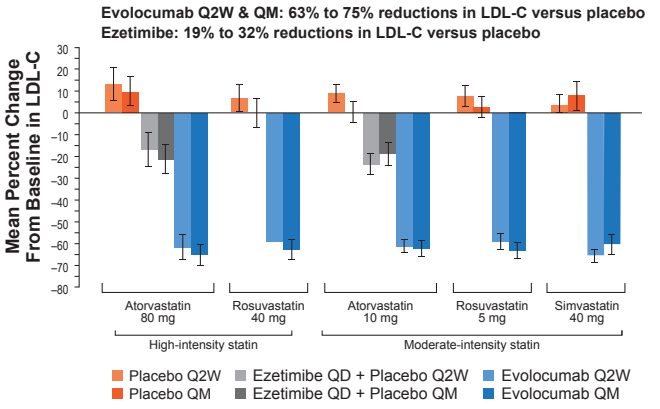
Overall, 1896 patients were randomized, mean patient age was 60 years, ~20% had coronary artery disease, ~10% had peripheral arterial disease or cerebrovascular disease, and ~16% had type 2 diabetes. Their mean baseline LDL-C was ~110 mg/dL (2.85 mmol/L). When combined with either a high- or moderate-intensity statin, evolocumab-treated groups showed highly significant reductions in LDL-C versus placebo of 63% to 75% (Figure 1). Compared with placebo, ezetimibe when combined with atorvastatin reduced levels of LDL-C by 19% to 32%. An LDL-C level <70 mg/dL was achieved by 86% to 94% of evolocumab recipients on a moderate-intensity statin and 93% to 95% on a high-intensity statins.

Adding evolocumab to moderate-intensity statin regimens reduced LDL-C levels to a mean of 38 to 45 mg/dL (0.98 to 1.16 mmol/L), and to 35 to 38 mg/dL (0.09 to 0.98 mmol/L) with high-intensity statin regimens.

Compared with placebo, evolocumab also significantly reduced levels of non-high-density lipoprotein cholesterol by 58% to 65%, apolipoprotein B by 51% to 59%, and lipoprotein (a) by 21% to 36%.

There were no notable differences in safety and tolerability in evolocumab-, placebo-, and ezetimibe-treated patients.

Figure 1. LDL-C Response at Mean of Weeks 10 and 12



LDL-C=low-density lipoprotein cholesterol.

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Higher Rate of Device Success With Balloon-Expandable Transcatheter Aortic Valve (CHOICE)

Written by **Wayne Kuznar**

In the first head-to-head randomized comparison of two devices used for transcatheter aortic valve replacement (TAVR) in high-risk patients with severe aortic stenosis (AS), a balloon-expandable transcatheter valve was found to have a higher rate of device success than a self-expanding valve.

Data from the Comparison of Transcatheter Heart Valves in High Risk Patients With Severe Aortic Stenosis: Medtronic CoreValve Versus Edwards SAPIEN XT trial [CHOICE; Abdel-Wahab M et al. *JAMA* 2014], were presented by Mohamed Abdel-Wahab, MD, Academic Teaching Hospital of the Universities of Kiel and Hamburg, Bad Segeberg, Germany.

The primary objective of CHOICE was to compare the procedural success of the two valves in patients with symptomatic severe AS who were at high surgical risk or deemed inoperable. Procedural success was defined as successful vascular access, deployment of the device, retrieval of the delivery system, correct position of the device, intended performance of the heart valve without moderate or severe regurgitation, and only one valve implanted in the proper anatomical location. The combined safety endpoint was a composite of all-cause mortality, major stroke, life-threatening or disabling bleeding, acute kidney injury Stage 3 (including renal replacement therapy), periprocedural myocardial infarction, major vascular complications and repeat procedure for valve-related dysfunction.

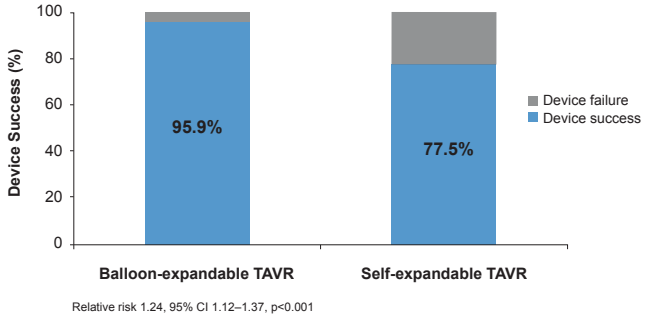
In five centers in Germany, 241 patients at high risk of surgical aortic valve replacement with suitable transfemoral vascular access were randomized to either the balloon-expanding valve (n=121) or the self-expanding valve group (n=120). Device size selection was based on manufacturers' sizing charts, but the study's steering committee strongly recommended sizing to be based on 3D imaging. All procedures were performed by experienced operators in centers with an established multidisciplinary TAVR program.

Following implantation, aortic insufficiency (AI) was assessed using angiography, transthoracic echocardiography, and invasive hemodynamic measurements. Valve function at follow-up was evaluated using transthoracic echocardiography and cardiac magnetic resonance imaging. Assessment of postprocedural AI utilized core laboratory angiography.

The average age of patients in the study was 80 years. Comorbidities, severity of AS and mean annulus diameter (measured with either transesophageal echocardiography or multislice computed tomography) were similar between the two groups. The most common valve size in the balloon-expandable arm was 26 mm and 29 mm in the self-expandable arm.

The occurrence of postprocedural AI on angiography (either any degree or greater than mild) was significantly less (p<0.001) in the balloon-expandable group. Patients in the balloon-expandable group underwent fewer procedures to reduce AI following valve implantation. Device success occurred in 95.9% of patients treated with the balloon-expandable device compared with 77.5% of patients in the self-expanding-device group (RR, 1.24; 95% CI, 1.12 to 1.37; p<0.001; Figure 1). This difference in device success in favor of the balloon-expandable device was attributed to the lower rate of moderate or severe AI in this group compared with the group treated with the self-expandable device (4.1% vs 18.3%; p<0.001), and the less frequent implantation of more than one valve (0.8% vs 5.8%; p=0.03).

Figure 1. Primary Endpoint



TAVR=transcatheter aortic valve replacement.

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Clinical outcomes, including all-cause mortality and cardiovascular mortality at 30 days, were not significantly different between the groups (Table 1). The combined safety endpoint occurred in 18.2% in the balloon-expandable group and 23.1% in the self-expandable group. There was a numerical excess of stroke that did not reach statistical significance in the patients treated with balloon expandable valve (n=7) as compared with the patients treated with self-expandable valves (n=3). There were five rehospitalizations for heart failure in the self-expandable group and none in the balloon-expandable group. Patients in the balloon-expandable group required fewer new permanent pacemakers (17.3% vs 37.6%; p=0.001).

Table 1. Clinical Outcomes at 30 Days

	Balloon-expandable (n=121)	Self-expandable (n=117)	p Value
Death			
From any cause	5/121 (4.1%)	6/117 (5.1%)	0.77
From CV causes	5/121 (4.1%)	5/117 (4.3%)	0.99
Stroke	7/121 (5.8%)	3/117 (2.6%)	0.33
Major	3/121 (2.5%)	3/117 (2.6%)	0.99
Minor	4/121 (3.3%)	0/117 (0.0%)	0.12
Myocardial infarction	1/121 (0.8%)	0/117 (0.0%)	0.99
Bleeding			
Life threatening	10/121 (8.3%)	14/117 (12.0%)	0.35
Major	23/121 (19.0%)	17/117 (14.5%)	0.36
Minor	11/121 (9.1%)	9/117 (7.7%)	0.70
Major or minor	34/121 (28.1%)	26/117 (22.2%)	0.30
Vascular complications			
All	17/121 (14.0%)	15/117 (12.8%)	0.78
Major	12/121 (9.9%)	13/117 (11.1%)	0.76
Minor	5/121 (4.1%)	2/117 (1.7%)	0.28
Pacemaker Implantation	19/110 (17.3%)	38/101 (37.6%)	0.001

CV=cardiovascular

This investigator-initiated comparative effectiveness trial provides near-term outcomes in a head-to-head comparison of these alternative TAVR devices in experienced operator centers. Studies with larger samples sizes and longer follow-up are warranted to further evaluate the relative efficacy and safety of these TAVR platforms.

PCSK9 Inhibitor Slashes LDL-C in Statin-Intolerant Patients (GAUSS-2)

Written by Wayne Kuznar

Approximately 10% to 20% of patients treated with statins experience side effects, primarily musculoskeletal side effects, which diminish compliance or cause