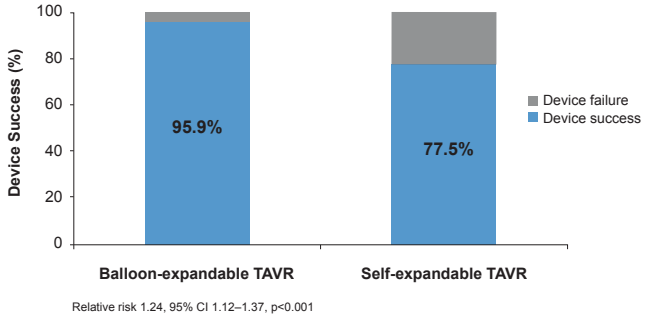
In five centers in Germany, 241 patients at high risk of surgical aortic valve replacement with suitable transfemoral vascular access were randomized to either the balloon-expanding valve (n=121) or the self-expanding valve group (n=120). Device size selection was based on manufacturers' sizing charts, 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

discontinuation of therapy [Zhang H et al. *Ann Intern Med* 2013; Mancini GB et al *Can J Cardiol* 2011]. Reduced adherence to, and discontinuation of, statins adversely affect survival in both the primary and secondary prevention settings [Chowdhury R et al. *Eur Heart J* 2013; Perreault S et al. *Eur J Clin Pharmacol* 2009; Rasmussen JN et al. *JAMA* 2007]. Further therapeutic efforts are therefore needed to lower low-density lipoprotein cholesterol (LDL-C) in this setting. Evolocumab, a fully human monoclonal antibody that binds proprotein convertase subtilisin/kexin type 9 (PCSK9), reduced levels of low-density lipoprotein cholesterol (LDL-C) to a greater extent than ezetimibe in hypercholesterolemic patients who could not tolerate effective doses of statins.

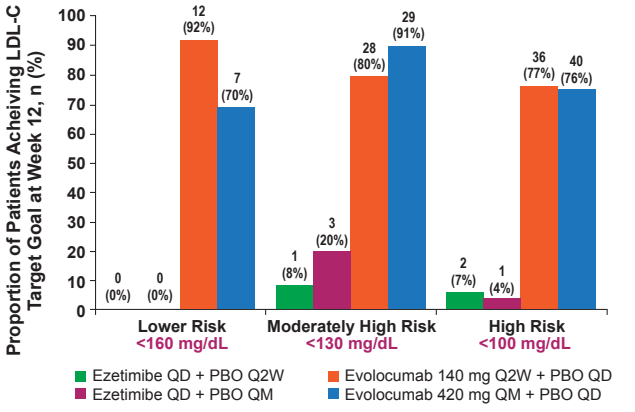
Erik Stroes, MD, Academic Medical Center, Amsterdam, The Netherlands, presented the results from a double-blind multicenter Phase 3 Goal Achievement After Utilizing an Anti-PCSK9 Antibody in Statin-Intolerant Subjects 2 study [GAUSS-2; Stroes E et al. *J Am Coll Cardiol* 2014] in which 307 patients with hypercholesterolemia who were statin intolerant were randomized on a 2:2:1:1 basis to evolocumab, 140 mg Q2W or 420 mg QM plus daily oral placebo, or subcutaneous placebo (Q2W or QM) plus 100 mg/day of oral ezetimibe. The study was designed to build on the Phase 2 experience with evolocumab, which demonstrated potent LDL-C lowering in hypercholesterolemic patients intolerant to at least one statin [Sullivan D et al. *JAMA* 2012].

Participants qualified for the study if they were unable to tolerate effective doses of ≥2 statins because of myalgia, myopathy, myositis, or rhabdomyolysis that resolved with statin discontinuation [Stroes E et al. *J Am Coll Cardiol* 2014]. Their mean LDL-C at baseline was ~195 mg/dL. The coprimary endpoints were the mean percent change from baseline in LDL-C at Week 12 and the mean at Weeks 10 and 12.

Mean age of patients ranged from 60 to 63 years in the four treatment groups. More than 90% were white and the distribution between males and females was fairly equal. About 60% of patients qualified as high risk under the National Cholesterol Education Program risk category system. An additional 15% were classified as moderate risk. More than half of the patients were intolerant to at least three statins. Seventy eight percent to 88% had myalgia as their worst muscle-related side effect to statins.

Compared with ezetimibe, patients randomized to evolocumab Q2W had a 37% reduction in LDL-C at a mean of 10 and 12 weeks, and a 38% reduction at 12 weeks. Patients randomized to monthly evolocumab had a 39% reduction in LDL-C at a mean of 10 and 12 weeks and a 38% reduction at 12 weeks as compared with ezetimibe ($p<0.001$ for all comparisons). Compared with baseline, the mean reductions in LDL-C at 12 weeks were 56% with Q2W evolocumab and 53% with monthly dosing. Of evolocumab-treated patients at high risk, >75% achieved LDL-C <100 mg/dL compared with <10% of ezetimibe-treated patients (Figure 1).

Figure 1. LDL-C Goal Achievement at Week 12



LDL-C=low-density lipoprotein cholesterol.

Reproduced from Stroes E et al. Anti-PCSK9 Antibody Effectively Lowers Cholesterol in Patients with Statin Intolerance: The GAUSS-2 Randomized, Placebo-controlled Phase 3 Clinical Trial of Evolocumab. *J Am Coll Cardiol* 2014 doi: 10.1016/j.jacc.2014.03.019. With permission from Elsevier.

Both dosing frequencies of evolocumab also significantly reduced levels of apolipoprotein B and lipoprotein (a) and increased levels of high-density lipoprotein cholesterol (HDL-C) and apolipoprotein A-I.

The rate of adverse events was generally balanced across treatment groups. The most common adverse events (>5% in evolocumab combined group) were headache (8% with evolocumab vs 9% with ezetimibe), myalgia (8% vs 18%), pain in extremity (7% vs 1%), and muscle spasms (6% vs 4%).

Dr. Stroes noted that the robust LDL-C lowering and good tolerability suggests that evolocumab is a promising therapy for high-risk hypercholesterolemic patients.

Dual PPAR Agonist Fails to Improve CV Outcomes After ACS (AleCardio)

Written by **Wayne Kuznar**

A dual agonist of peroxisome proliferator-activated receptors (PPARs) did not reduce adverse cardiovascular (CV) outcomes in patients with type 2 diabetes mellitus (T2DM) Findings from the Phase 3, multinational, AleCardio study [Lincoff AM et al. *JAMA* 2014] were announced by A. Michael Lincoff, MD, Cleveland Clinic, Cleveland, Ohio, USA.

Aleglitazar is a PPAR agonist with balanced affinity for the PPAR-α and PPAR-γ subtypes. The primary effect of agonists of PPAR-α is to improve the plasma lipid profile, and the primary effect of agonists of PPAR-γ is to improve insulin sensitivity. A dual PPAR agonist, therefore, was