

Highlights from ACC.17 scientific sessions

The ACC 2017 meeting was held in Washington D.C. between March 17 and 19, 2017. Although the meeting had an overall scientific impact, it was partly affected by the travel bans of colleagues from some countries. Herein, we discuss some highlights of the meeting.

The most striking aspect of ACC 2017 was the presentation of plenty of late-breaking clinical trials. The most striking among all was “FOURIER” trial in which Turkish scientists had also participated (1). Evolocumab therapy resulted in 59% further reduction of LDL cholesterol compared to standard care. The FOURIER trial shows that evolocumab, which is a fully human monoclonal antibody against PCSK9, causes a significant reduction of 15% in the primary end-points of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization; in addition, it also causes a significant reduction of 20% in some secondary end-points of cardiovascular death, myocardial infarction, or stroke. Notably, the benefit was driven by reductions in the incidence of nonfatal AMI, stroke, and coronary revascularization, but the incidence of cardiovascular (CV) death remained similar in both groups. However, it is important to note that cost issues were of concern even in the USA.

The bococizumab trial (SPIRE) was also presented in the same session (2). As we all know, bococizumab trial was halted prematurely by the sponsor company Pfizer because of the high incidence of antidrug antibodies after a median follow-up of 10 months. Pfizer decided to publish data transparently both in the meeting and also in the journal. In contrast to the overall positive result of the evolocumab trial, bococizumab did not result in a decreased rate of major cardiovascular outcomes in the predefined lower-risk group, despite an overall 56% decrease of LDL cholesterol from the baseline. Of note, in the higher-risk group, major cardiovascular events significantly decreased by 21%. Injection-site reactions were common in the bococizumab group (10.4%). Furthermore, at 1 year, 48% patients who received bococizumab had detectable antidrug antibodies after 3 months (3). This resulted in an attenuation of the decrease in LDL cholesterol levels. All these findings may be related to humanized characteristic of bococizumab, in contrast to fully human antibodies, evolocumab and alirocumab.

ACC 2017 has provided the participants the opportunity of joining the announcement of the low-awaited results of SURTAVI trial, which was simultaneously published in the New Eng-

land Journal of Medicine (NEJM) (4). Transcatheter aortic-valve replacement (TAVR) is a guideline-recommended alternative to surgery in patients with severe aortic stenosis who are at high surgical risk. However, outcomes among patients with aortic stenosis who are at intermediate surgical risk are not known. In this trial, 1660 patients with aortic stenosis and with intermediate surgical risk were randomized into TAVR and surgery groups (864 versus 796 patients consecutively). The primary end point, which was a composite of death from any cause or disabling stroke at 24 months, was noted to be 12.6% in the TAVR group and 14.0% in the surgery group (noninferiority). Of note, TAVR resulted in lower mean gradients and larger aortic-valve areas than surgery, apart from lower rates of acute kidney injury and atrial fibrillation, at a cost of higher rates of residual aortic regurgitation and pacemaker requirement. Along with this finding, ACC/AHA Valvular Heart Disease Guidelines Update was released with the following Class-IIa recommendation: “TAVR is a reasonable alternative to surgical AVR for symptomatic patients with severe AS (Stage D) and an intermediate surgical risk” (5). The same update also added a Class-IB (derived from nonrandomized studies) recommendation for mechanical prosthetic valve thrombosis as “Urgent initial treatment with either slow-infusion low-dose fibrinolytic therapy or emergency surgery is recommended for patients with a thrombosed left-sided mechanical prosthetic heart valve presenting with symptoms of valve obstruction” up on data, coming from members of Turkish Society of Cardiology (5).

Rivaroxaban or ASPIRIN for Extended Treatment of Venous Thromboembolism (EINSTEIN CHOICE) trial was also presented at ACC 2017 and simultaneously published in NEJM (6). The trial aimed to compare the efficacy and safety of once-daily rivaroxaban (doses of 20 or 10 mg) with aspirin (dose of 100 mg) for extended therapy in patients with venous thromboembolism after primary anticoagulant therapy for 6–12 months. A total of 3396 patients were randomized to rivaroxaban 20 mg (n=1121), rivaroxaban 10 mg (n=1136), and aspirin 100 mg (n=1139) groups and followed up for almost 1 year. The primary efficacy outcome was symptomatic recurrent fatal or nonfatal venous thromboembolism, which occurred in 1.5% patients with rivaroxaban 20 mg, in 1.2% patients with rivaroxaban 10 mg, and 4.4% patients with aspirin (hazard ratio for rivaroxaban 20 mg vs. aspirin, 0.34; hazard ratio for rivaroxaban 10 mg vs. aspirin, 0.26; $p<0.001$ for both comparisons). Major bleeding was 0.5% in the rivaroxaban 20

Address for correspondence: Dr. Mahmut Şahin, 19 Mayıs Üniversitesi Tıp Fakültesi
Kardiyoloji Anabilim Dalı, Samsun-Türkiye
E-mail: drmahmutsahin@gmail.com

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mg, 0.4% in the rivaroxaban 10 mg, and 0.3% in the aspirin group. In conclusion, both rivaroxaban doses were not only superior to aspirin for the primary outcome but also associated with similar rates of bleeding.

There were some important but negative trials results in the ACC 2017 as well and DECISION-CTO (Optimal Medical Therapy With or Without Stenting For Coronary Chronic Total Occlusion) was one of them (http://www.acc.org/latest-in-cardiology/clinical-trials/2017/03/17/08/40/decision-cto?w_nav=LC). It was aimed to assess the safety and efficacy of chronic total occlusion (CTO) percutaneous coronary intervention (PCI) compared with optimal medical therapy (OMT) among patients with at least one CTO. Patients were randomized to CTO-PCI + OMT (n=417) or OMT (n=398). The primary endpoint for CTO-PCI + OMT vs. OMT, major adverse cardiac events at 3 years (all-cause mortality, MI, stroke, repeat revascularization), was 20.6% vs. 19.6%. All endpoints were similar in both groups; however, the presence or absence of high ischemic burden was not thoroughly evaluated. Furthermore, low left ventricular ejection fraction was an exclusion criterion, hence, patients with ischemic heart failure had been excluded. In conclusion, routine CTO intervention seems to be an unnecessary treatment modality considering that OMT is enough to provide similar outcome.

Another negative trial that was presented at ACC 2017 was CARAT trial (CER-001 Atherosclerosis Regression Acute Coronary Syndrome Trial) which aimed to assess the efficacy of injection of a novel form of synthetic high-density lipoprotein cholesterol (HDL-C) into the arteries of patients who had recently had a myocardial infarction. CER-001 is a pre-beta high-density lipoprotein (HDL) mimetic containing sphingomyelin and dipalmitoyl phosphatidylglycerol (7). A total of 301 patients with acute coronary syndrome were randomized to 10 weekly infusions of 3-mg/kg CER-001 or placebo. Atheroma reduction was similar to standard of care according to intravascular ultrasound study; hence, the results were overall neutral.

In conclusion, ACC 2017 ended with presentation of practice-changing clinical trials along with implementation of some of them into updates of guidelines.

Mehmet Birhan Yılmaz, Mahmut Şahin¹

Department of Cardiology, Faculty of Medicine, Cumhuriyet University; Sivas-Turkey

¹Department of Cardiology, Faculty of Medicine, Ondokuz Mayıs University; Samsun-Turkey

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