The 66th Annual Scientific Sessions and Expo of the American College of Cardiology (ACC) were held at the Walter E. Washington Convention Center, Washington DC, from March 17th to 19th, 2017. This meeting offered 23 Late-Breaking Clinical Trial (LBCT) presentations, 17 Featured Clinical Research presentations with and without LBCT, and 2,572 abstracts presented in oral and poster sessions by over 2,000 experts. This report presents the highlights of this meeting, including the opening showcase, several important LBCTs and some international joint symposiums.

Key Words: American College of Cardiology; Late-breaking clinical trials; Scientific sessions

Opening Showcase

After the singing of the national anthem, ACC President Richard A. Chazal, MD, FACC, welcomed the thousands of cardiovascular professionals to Washington DC to the meeting as part of the Opening Showcase session on March 17 (Figure 1C,D). He began his announcement with, “ACC.17 will ignite cardiovascular innovation. The cutting-edge science and technology you will experience over the next 3 days will pave the path of practice for the future.” Chazal thanked all those involved in making ACC.17 happen, including ACC.17 Chair Jeffrey T. Kuv, MD, FACC, and Co-Chair Andrew M. Kates, MD, FACC. Following the lead of Chazal, attendees then took a moment silence to remember ACC Past President Sylvan Lee Weinberg, MD, MACC, who Chazal noted was a superb model for an entire generation of clinical cardiologists. During the presidential address, Chazal focused on the many changes facing the cardiovascular communities, such as new educational requirements and learning styles, a transition from evidence-based medicine to personalized medicine and a changing healthcare delivery system in the United States.

One of his remarkable comments was: “How do we address all of these changes without feeling overwhelmed and frustrated? First, we should take a page out of the Washington DC playbook and accept that change is occurring regardless of what we may wish. Next, we prepare to address it. Implementing change is difficult and the transition is fraught with anxiety, but few real accomplishments are achieved without angst. Although we cannot control external events, we can control our reactions to these events. We can decide whether to emphasize the inherent challenges or the inherent opportunities presented to us. Today, in a city long accustomed to change, I challenge all of us to meet change head on.”

LBCTs

There were 23 LBCT presentations in 6 LBCT sessions (Figure 2A,B), including the joint ACC/Journal of American College of Cardiology LBCTs, joint ACC/Journal of the American Medical Association LBCTs and joint ACC/New England Journal of Medicine LBCTs. Featured Clinical Research Sessions also included 11 LBCTs, so a total of 34 LBCT presentations were provided. Among them, 16 are reported here.

FOURIER

Evolocumab is a monoclonal antibody that inhibits proprotein convertase subtilisin-kexin type 9 (PCSK9) and significantly lowers low-density lipoprotein-cholesterol (LDL-C) levels. Marc Steven Sabatine presented the results from the FOURIER trial, a randomized, double-blind,
placebo-controlled trial that involved 27,564 patients with atherosclerotic cardiovascular disease and LDL-C levels ≥70 mg/dL who were receiving statin therapy. Patients were randomly assigned to receive evolocumab (either 140 mg every 2 weeks or 420 mg monthly) or placebo group with subcutaneous injections. The primary efficacy endpoint was a composite of cardiovascular death, myocardial infarction (MI), stroke, hospitalization for unstable angina, or coronary revascularization. The key secondary efficacy endpoint was a composite of cardiovascular death, MI, or stroke. The median duration of follow-up was 2.2 years. At 48 weeks, LDL-C levels with evolocumab decreased from a median baseline value of 92 mg/dL to 30 mg/dL (P<0.001). As compared with placebo, evolocumab injection significantly reduced the risk of the primary endpoint (9.8% vs. 11.3%; hazard ratio, 0.85; 95% confidence interval [CI]; 0.79–0.92; P<0.001) and the key secondary endpoint (5.9% vs. 7.4%; hazard ratio, 0.80; 95% CI, 0.73–0.88; P<0.001).

EBBINGHAUS
Specific concerns have been raised by non-randomized data suggesting that statins may cause memory impairment. Similar questions were raised for PCSK9 inhibitors. Robert P Giugliani presented the results of the EBBINGHAUS study that enrolled 1,974 patients participating in the FOURIER trial in order to evaluate the relationship between PCSK9 inhibitor and changes in cognition. The primary endpoint was a change in spatial working memory strategy index of executive function (SWMsi). Patients were tested at baseline, weeks 24 and 48, then every 48 weeks thereafter and at the end of the study. The mean age was 63 years, 28% were women, 71% had high-intensity statin therapy, 75% had a prior MI, 20% had an ischemic stroke, and 19% had peripheral artery disease. The median follow-up was 19 months. The mean change in the primary endpoint as measured by the SWMsi was −0.29 with placebo and −0.21 with evolocumab (P for noninferiority <0.0001), suggesting the safety of evolocumab added to a statin therapy to achieve very low levels of LDL-C in terms of patient memory or cognitive functioning.

SPIRE-1 and -2
These were trials conducted in order to examine the efficacy of bococizumab, another type of monoclonal antibody targeting PCSK9. Paul M. Ridker presented the data from the SPIRE-1 and -2 trials comprising 6 parallel, multinational lipid-lowering trials enrolling 4,300 patients with hyperlipidemia who were randomly assigned to receive 150 mg of bococizumab or placebo subcutaneously every 2 weeks. The patients were followed for up to 12 months. At 12 weeks, patients who received bococizumab had 54.2% reduction in their LDL-C levels from baseline, as compared with an increase of 1.0% in the placebo group. However, high level of antidrug antibodies developed in a substantial number of the patients in the bococizumab group, which significantly diminished the efficiency of the reduction in LDL-C levels. Furthermore, even among patients with no antidrug antibodies, there was wide variability in the reduction in LDL-C levels at both 12 and 52 weeks.
CARAT

It has been suggested by previous studies that infusion of reconstituted high-density lipoproteins (rHDL) promotes reverse cholesterol transport, vascular reactivity and, potentially, regression of coronary atherosclerosis. The effect of infusing CER-001, a pre-beta HDL mimic containing sphingomyelin and dipalmitoyl phosphatidylglycerol on coronary atheroma burden was examined by the CER-001 Atherosclerosis Regression Acute Coronary Syndrome Trial (CARAT), a phase 2, double-blind, placebo-controlled trial that randomized 301 patients with acute coronary syndrome (ACS), the results of which were presented by Stephen J. Nichols. The results showed that short-term treatment with CER-001 3 mg/kg did not produce a significant effect on the primary endpoint measured by intravascular ultrasound in patients on a background of contemporary therapy in the post ACS setting.

ORION-1

RNA interference (siRNA) targeting hepatic PCSK9 production offers the potential for sustained reductions in LDL-C with infrequent dosing. Kausik Kumar Ray showed the data from ORION-1, a phase 2 double-blind randomized controlled trial comparing 6 subcutaneous dosing regimens of inclisiran to placebo. The present analysis reported the primary endpoint of percentage reduction in LDL-C at 6 months with a single or second dose of inclisiran. A total of 501 eligible patients with atherosclerotic cardiovascular disease (ASCVD) or high ASCVD risk and in whom LDL-C was >70mg/dL or 100mg/dL, respectively, were enrolled and randomized to inclisiran or placebo injection and followed up through to 9 months. The primary endpoint of LDL-C reduction at 180 days was 27.9–41.9% with one subcutaneous injection and by 35.5–52.6% with 2 injections (P<0.001). At 240 days the reductions in PCSK9 and LDL-C remained significantly lower than baseline with all the studied doses of inclisiran.

GEMINI-ACS-1

Dual antiplatelet therapy (DAPT, aspirin+P2Y12 inhibitor) is the standard treatment for patients with ACS. The factor Xa inhibitor, rivaroxaban, significantly reduces mortality and ischemic events when added to DAPT, but is associated with increased bleeding risk. The safety of a dual pathway antithrombotic approach combining low-dose rivaroxaban (in place of aspirin) with a P2Y12 inhibitor has not been validated. Erik Magnus Ohman presented the results from GEMINI-ACS-1, a double-blind, multicenter, randomized trial performed at 371 clinical centers in 21 countries. The patients enrolled were older than 18 years with unstable angina, non-ST-segment elevation MI or ST-segment elevation MI (STEMI). Subjects were randomly assigned within 10 days after admission for the index ACS event to either aspirin or rivaroxaban. Patients received a minimum of 180 days of double-blind treatment with rivaroxaban 2.5mg twice daily or aspirin 100mg daily. The choice of clopidogrel or ticagrelor during trial conduct was not randomized and was based on investigator preference. The primary endpoint was Thrombolysis In Myocardial Infarction (TIMI) clinically significant bleeding unrelated to coronary artery bypass grafting (CABG; major, minor, or requiring medical attention) up to day 390. A total of 1,518 received aspirin and 1,519 received rivaroxaban, and 1,704 patients (56%) were in the ticagrelor and 1,333 (44%) in the clopidogrel strata. TIMI non-CABG clinically significant bleeding was similar with rivaroxaban vs. aspirin therapy.
A dual pathway antithrombotic therapy approach combining low-dose rivaroxaban with a P2Y12 inhibitor for the treatment of patients with ACS had a similar risk of clinically significant bleeding as aspirin plus a P2Y12 inhibitor.

**COMPARE-ACUTE**

In patients with STEMI, the use of percutaneous coronary intervention (PCI) to recanalize the infarct-related coronary artery significantly improves outcomes. However, the use of PCI in non-infarct-related coronary arteries remains controversial. Methods Pieter Smits demonstrated the data from the COMPARE-ACUTE study, which randomly assigned 885 patients with STEMI and multivessel disease who had undergone primary PCI of an infarct-related coronary artery in a 1:2 ratio to undergo complete revascularization of non-infarct-related coronary arteries guided by fractional flow reserve (FFR) or to undergo no revascularization of non-infarct-related coronary arteries. The primary endpoint was a composite of any-cause death, nonfatal MI, revascularization, and cerebrovascular events at 12 months. The primary outcome occurred in 23 patients in the complete-revascularization group and in 121 patients in the infarct-artery-only group that did not have complete revascularization, a finding that translates to 8 and 21 event points per 100 patients, respectively (hazard ratio, 0.35; 95% CI, 0.22–0.55; P=0.001). Therefore, in patients with STEMI and multivessel disease who underwent primary PCI of an infarct-related artery, the addition of FFR-guided complete revascularization of non-infarct-related arteries in the acute setting resulted in a risk of a composite cardiovascular outcome that was lower than the risk among those who were treated for the infarct-related artery only.

**DEFINE-FLAIR**

It has not been proven whether the instantaneous wave-free ratio (iFR), an alternative measure for FFR, which does not require the administration of adenosine, will offer benefits similar to those of FFR. Justin E. Davies presented the primary results of the DEFINE-FLAIR study, which randomly assigned 2,492 patients with coronary artery disease, in a 1:1 ratio, to undergo either iFR-guided or FFR-guided coronary revascularization. The primary endpoint was the 1-year risk of major adverse cardiac events, which were a composite of death from any cause, nonfatal MI, or unplanned revascularization. At 1 year, the primary endpoint had occurred in 6.8% patients in the iFR group and in 7.0% in the FFR group (difference in risk, −0.2 percentage points; 95% CI, −2.3–1.8; P=0.001 for noninferiority; hazard ratio, 0.95; 95% CI, 0.68–1.33; P=0.78). It was concluded that coronary revascularization guided by iFR was noninferior to revascularization guided by FFR with respect to the risk of major adverse cardiac events at 1 year. An additional analysis revealed that the rate of adverse procedural signs and symptoms was lower and the procedural time was shorter with iFR than with FFR.

**IFR-SWEDHEART**

Matthias Götte presented the data from IFR-SWEDHEART, an analogous to the DEFINE-FLAIR study, which evaluated whether iFR is noninferior to FFR with respect to the rate of subsequent major adverse cardiac events. They conducted a multicenter, randomized, controlled, open-label clinical trial using the Swedish Coronary Angiography and Angioplasty Registry for enrollment. A total of 2,037 participants with stable angina or ACS who had an indication for physiologically guided assessment of coronary artery stenosis were randomly assigned to undergo revascularization guided by either iFR or FFR. The primary endpoint was the rate of a composite of death from any cause, nonfatal MI, or unplanned revascularization within 12 months of the procedure. A primary endpoint event occurred in 6.7% patients in the iFR group and in 6.1% in the FFR group (difference in event rates, 0.7 percentage points; 95% CI, 1.5–1.2%); P=0.007 for noninferiority; hazard ratio, 1.12; 95% CI, 0.79–1.58; P=0.53). A significantly higher proportion of patients in the FFR group than in the iFR group complained of chest discomfort during the procedure. It was concluded that in patients with stable angina or ACS, an iFR-guided revascularization strategy was noninferior to an FFR-guided revascularization strategy in terms of the rate of major adverse cardiac events at 12 months.

**DECISION CTO**

In patients with coronary chronic total occlusion (CTO), it has not been established whether optimal medical treatment (OMT) is a reasonable initial treatment strategy as compared with PCI. Seung-Jung Park presented the results from DECISION CTO, a multicenter, randomized noninferiority trial at 19 cardiac centers in Asia, in which 798 patients with coronary CTO were randomly assigned to either OMT or PCI (387 patients randomly assigned to the OMT group and 411 randomly assigned to the PCI group). The primary endpoint was a composite of death, MI, stroke, or any repeat revascularization at 3 years after randomization. After 3 years, the primary endpoint had occurred in 19.8% of the patients in the OMT group and in 21.4% of the patients in the PCI group (P=0.007 for noninferiority). It could be concluded that in patients with coronary CTO, OMT as an initial strategy was shown to be noninferior to drug-eluting stent-based PCI with respect to the primary endpoint of the composite of death, MI, stroke or any revascularization at 3 years.

**SURTAVI**

Transcatheter aortic valve replacement (TAVR) is now a widely-recognized alternative to surgery in patients with severe aortic stenosis (AS) at high surgical risk. However, comparative outcomes among patients with AS who are at intermediate surgical risk are less well known. Michael J. Reardon presented the data from the SURTAVI trials regarding the clinical outcomes in intermediate-risk patients with severe asymptomatic AS in a randomized trial comparing TAVR by the use of a self-expanding prosthesis (CoreValve or EVOLUT R system) with surgical AVR (SAVR). The primary endpoint was a composite of any-cause death or disabling stroke at 24 months in patients undergoing attempted AVR. Next, they examined the noninferiority of TAVR as compared with SAVR. A total of 1,746 patients underwent randomization at 87 centers, and among them 1,660 underwent attempted TAVR or the surgical procedure. The age of the patients was 79.8±6.2 years (mean±SD), and all were at intermediate risk for surgery (Society of Thoracic Surgeons Predicted Risk of Mortality, 4.5±1.6%). At 24 months, the estimated incidence of the primary endpoint was 12.6% in the TAVR group and 14.0% in the SAVR group (95% CI, 5.2–2.3%; posterior probability of noninferiority, >0.999). Surgery was associated with higher frequency of acute kidney injury, atrial fibrillation, and
transfusion requirements, while TAVR had higher rates of residual aortic regurgitation and need for pacemaker implantation. TAVR resulted in lower mean pressure gradients and larger aortic valve area than surgery. It was concluded that TAVR is a noninferior alternative to surgery in patients with severe AS at intermediate surgical risk, although there was a different pattern of adverse events in each procedure.

**TAVR for Bicuspid vs. Tricuspid Aortic Valve Stenosis**

TAVR in patients with bicuspid AS is being increasingly considered. From the Bicuspid AS TAVR multicenter registry, Sung-Han Yoon presented the procedural and clinical outcomes in patients with bicuspid vs. tricuspid AS. Outcomes of 561 patients with bicuspid AS and 4,546 patients with tricuspid AS were compared after propensity-score matching assembling 546 pairs of patients with similar baseline characteristics. Compared with the patients with tricuspid AS, patients with bicuspid AS had more frequent conversion to surgery (2.0% vs. 0.2%; P=0.006) and significantly lower device success rate (85.3% vs. 91.4%; P=0.002). In the group who received early generation devices, bicuspid AS had more frequent aortic root injury (4.5% vs. 0.0%; P=0.015). In the group who had new generation devices, however, procedural results were comparable across different prostheses. The cumulative all-cause mortality rates at 2 years were not significantly different between bicuspid and tricuspid AS (17.2% vs. 19.4%; P=0.28).

**Cerebral Embolic Protection Devices During SAVR**

Periprocedural ischemic neurological injury is prevalent (=65%) after surgical aortic valve replacement (SAVR). Michael Mack showed the results of a study that validated the safety and effectiveness of 2 cerebral embolic protection devices in reducing ischemic CNS injury. A total of 383 patients were randomly assigned to those who underwent SAVR with 2 different embolic protection devices (Cardiogard, Embol-X) or a shared standard cannula control. The primary endpoint was freedom from clinical or radiographic CNS infarcts at 7 days post-op. However, the use of these devices was not associated with an improvement in freedom from infarcts.

**LEVO-CTS**

Levosimendan is an inotropic agent that was previously shown in small studies to treat low cardiac output syndrome after cardiac surgery. John H. Alexander presented the data from the LEVO-CTS trial, a multicenter, randomized, placebo-controlled, phase 3 trial that evaluated the efficacy and safety of levosimendan in patients with a left ventricular ejection fraction ≥35% who were undergoing cardiac surgery with the use of cardiopulmonary bypass. Patients were randomly assigned to receive either intravenous levosimendan (at a dose of 0.2 µg/kg/min, followed by a dose of 0.1 µg/kg/min for 23 h) or placebo, with the infusion starting before surgery. However, prophylactic levosimendan did not result in a rate of the short-term composite endpoint that was lower than the rate with placebo among the patients enrolled.

**EINSTEIN-CHOICE**

In patients without reversible risk factors, the risk of recurrent venous thromboembolism (VTE) is approximately 10%/year if anticoagulation therapy is stopped. In addition, such patients are at increased risk for MI, stroke, and vascular death. However, concerns about bleeding often lead to a reluctance to continue anticoagulation beyond 6–12 months. In order to reduce the risk of bleeding with extended treatment, lower-dose anticoagulant therapy or aspirin have been used, but never tested head-to-head. Jeffrey Weitz presented the data of the EINSTEIN-CHOICE trial, a randomized, double-blind, phase 3 study that assigned 3,396 patients with VTE to receive either once-daily rivaroxaban (at doses of 20 mg or 10 mg) or 100 mg of aspirin. All the study patients had completed 6–12 months of anticoagulation therapy and were in need of continued anticoagulation. Study drugs were administered for up to 12 months. The primary efficacy outcome was symptomatic recurrent fatal or nonfatal VTE, and the principal safety outcome was major bleeding. A total of 3,365 patients were included in the intention-to-treat analyses (median treatment duration, 351 days). The primary efficacy outcome occurred in 1.5% of the patients receiving 20 mg of rivaroxaban and in 1.2% receiving 10 mg of rivaroxaban, as compared with 4.4% receiving aspirin (hazard ratio for 20 mg of rivaroxaban vs. aspirin, 0.34; 95% CI 0.20–0.59; hazard ratio for 10 mg of rivaroxaban vs. aspirin, 0.26; 95% CI 0.14–0.47; P<0.001 for both comparisons). Rates of major bleeding were 0.3% in the group receiving 20 mg of rivaroxaban, 0.4% in the group receiving 10 mg of rivaroxaban, and 0.3% in the aspirin group. The incidence of adverse events was similar in all 3 groups. They concluded that the risk of a recurrent event was significantly lower with rivaroxaban at either a dose of 20 mg or of 10 mg than with aspirin, with no significant increase in bleeding.

**SPAIN**

The SPAIN study was a prospective double-blind randomized placebo-controlled study to evaluate the utility of a physiological pacing algorithm known as closed loop stimulation (DDD-CLS) in patients with cardioinhibitory refractory reflex vasovagal syncope. Patients were randomized into 2 arms: Group A with active DDD-CLS pacing for 12 months following by placebo DDI mode pacing during the second year, and group B with placebo DDI mode during 12 months followed by DDD-CLS pacing during the second year. Gonzalo Baron Esquivias showed from the examination of 54 patients that events occurred in 8.7% of patients during DDD-CLS and in 45.65% in patients during DDI. Hazard ratio was 6.72 (95% CI 2.29–19.76), and odds ratio was 0.11 (95% CI 0.034–0.368), P<0.0001.

**International Symposium**

Among the thousands of oral or abstract presentations (Figure 2C.D), more than 25 international programs with representation by 38 international societies were offered. In this meeting, the Joint Symposium of the Japanese Circulation Society and the American College of Cardiology was held on March 19, 2017, chaired by Athena Poppas and Atsushi Hirayama, entitled “Cutting Edge Innovations in Cardiovascular Imaging”. In this symposium, Atsushi Hirayama talked on “State of the Art: Non-Obstructive Angioscopy”, and Takafumi Hiro on “Future Technology of Intravascular Ultrasound and Optical Imaging” on behalf of the Japanese Circulation Society, while Izhak Kronzon spoke on “Fusion Imaging to Guide Transcatheter Repair of Structural Heart Disorders”, and Kyle W. Klarich
on “Cardiac Amyloid - Imaging for Diagnosis in ATTR” on behalf of the ACC. At ACC.17, the joint symposium of the Japanese College of Cardiology, Saudi Heart Association, and American College of Cardiology was also held on March 18, featuring “Diabetes, Hyperlipidemia, and Coronary Artery Disease, Prevention and Treatment”.

Closing Remarks
This year, the number of Japanese participants was relatively small because of complete overlap of ACC.17 and the Annual Session of the Japanese Circulation Society held in Kanazawa. This author sure hopes that this report is informative for all cardiologists, especially those who could not participate in ACC.17.

Disclosure
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References