ACC 2026

Three Days of Cutting-edge Cardiology

This year's American College of Cardiology (ACC) Scientific Session took place in New Orleans, Louisiana, USA, from March 28 to 30. Results from relevant clinical trials—many of which were published in prominent journals around the same time—were presented in a total of seven Late-Breaking Clinical Trials sessions. Here is a selection of findings that could change clinical practice in the near future.

Closure of the left atrial appendage to reduce the risk of stroke and mortality in patients with atrial fibrillation is not inferior to oral anticoagulation with direct oral anticoagulants. This was demonstrated by the prospective, multinational, randomized CHAMPION-AF clinical trial, whose results were presented during the Late-Breaking Clinical Trials I session of the ACC Congress. In non-valvular atrial fibrillation, over 90% of the thrombi causing strokes originate from the left atrial appendage. Occlusion of this structure therefore offers an alternative to permanent systemic pharmacological thromboprophylaxis.

The CHAMPION-AF trial included a total of 3,000 patients (mean age 72 years, 32% women, 85% white) with non-valvular atrial fibrillation and a moderately elevated risk of stroke (mean CHA2DS2-VASc score of 3.5) as well as a low risk of bleeding (mean HAS-BLED score of 1.3). In 1,499 participants, the left atrial appendage was occluded using the WATCHMAN FLX™ device (Boston Scientific), which was placed via a cardiac catheter. The primary endpoint was the combined rate of ischemic stroke, hemorrhagic stroke, cardiovascular death, and systemic embolism. During the conference, Dr. Saibal Kar from Los Robles Medical Center in California, USA, presented the results of the trial covering a three-year follow-up period.

During this time, 5.7% of patients in the left atrial appendage closure group and 4.8% of patients in the medication therapy group had reached the trial's primary efficacy endpoint. Thus, the CHAMPION-AF trial demonstrated the non-inferiority of the WATCHMAN-FLX™ device compared to oral anticoagulation. Furthermore, atrial appendage closure proved to be superior to long-term oral anticoagulation regarding the combined incidence of major and non-major but clinically relevant non-procedural bleeding. This primary safety endpoint occurred in 10.9% of patients in the left atrial appendage closure group against 19% of patients in the medication therapy group. However, an analysis of the individual components of this composite endpoint showed a slightly higher incidence of ischemic strokes following atrial appendage closure. Nevertheless, these events were rare, occurring in 3.2 and 2% of patients in the respective groups. Greater clarity is expected from the upcoming evaluation of the five-year data in two years. The CHAMPION-AF trial was published concurrently with the presentation in the «New England Journal of Medicine» (1).

More Evidence Supporting Aggressive LDL-Cholesterol Reduction

The PCSK9 inhibitor evolocumab reduces cardiovascular risk in patients with high-risk diabetes even in the absence of known atherosclerosis, as shown by a subgroup analysis of the VESALIUS-CV trial (Late Breaking Clinical Trials II). The VESALIUS-CV trial included 12,257 patients with a low-density lipoprotein cholesterol of 90 mg/dL (2.3 mmol/L) or higher and known atherosclerosis or diabetes who had not previously suffered a heart attack or stroke. VESALIUS-CV was the first trial to investigate the use of evolocumab in primary prevention among high-risk patients who had not previously experienced a major cardiovascular event. For the subgroup analysis now presented, data from 3,655 VESALIUS-CV participants who had diabetes but no known significant atherosclerosis were analyzed. In this population, evolocumab proved effective with respect to two composite endpoints: first, the combination of death from coronary heart disease, myocardial infarction, or ischemic stroke; and second, the combination of death from coronary heart disease, myocardial infarction, or ischemic stroke, as well as the need for revascularization. After a median follow-up of 4.8 years, the rate of both primary endpoints was reduced by 31% in the evolocumab group compared to placebo. The risk reduction was already evident after one year. The VESALIUS-CV trial was published concurrently with its presentation in «JAMA» (2).

Benefits of a Lower Low-density Lipoprotein Cholesterol (LDL-C) Target

The results of the Ez-PAVE trial (Late Breaking Clinical Trials II) point in a similar direction. This trial was the first to compare LDL-C targets of 55 mg/dL (1.4 mmol/L) with 70 mg/dL (1.8 mmol/L) in a randomized head-to-head design. The trial, conducted at 17 centers in South Korea, enrolled approximately 3,000 patients with atherosclerotic cardiovascular disease and randomized them to treatment aimed at one of the two LDL-C targets. Statins, ezetimibe, and PCSK9 inhibitors were used in accordance with Korean guidelines. The respective treatment decisions were made by the treating physicians in consultation with the patients. The trial demonstrated a significant benefit for the lower LDL-C target with regard to the combined primary endpoint of cardiovascular death, non-fatal myocardial infarction, revascularize-

tion, or hospitalization for unstable angina pectoris. Within three years, this endpoint occurred in 6.6% of patients treated to an LDL-C target of 55 mg/dL (1.4 mmol/L) — compared to 9.7% of patients with an LDL-C target of 70 mg/dL (1.8 mmol/L), corresponding to a 33% risk reduction in favor of the more aggressive treatment. The main driver of this benefit was a reduction in nonfatal myocardial infarctions and revascularizations in the more aggressively treated group. The combined endpoint of cardiovascular death, myocardial infarction, and stroke also occurred significantly less frequently in the group with the lower LDL-C target (2.3 vs. 3.6%). Ez-PAVE was published concurrently with its presentation in the «New England Journal of Medicine» (3).

Total Occlusion: Angioplasty Reduces Chest Pain and Improves Quality of Life

Percutaneous angioplasty of a completely blocked coronary artery is time-consuming and can be technically challenging; however, initial results from the ORBITA-CTO trial (Late Breaking Clinicals Trial III) show that it pays off. In the first randomized, placebo-controlled study of its kind, angioplasty and stent implantation were compared with a sham procedure in a cohort of patients with chronic total occlusion of a coronary artery. The results showed statistically significant reductions in chest pain and improvements in quality of life following the procedure. The primary endpoint of the trial was an angina score based on the number of daily episodes of chest pain, which along with the antianginal medications taken, was documented using a smartphone app. Secondary endpoints included quality of life and a clinician-assessed evaluation of angina severity. The analysis demonstrated a significant superiority of the intervention over the sham procedure. Patients who underwent percutaneous coronary intervention had more than a fourfold increased chance of symptom improvement (odds ratio: 4.38 [Credible Interval (CrI): 1.57–12.69]). Over the 24-week observation period, patients in the intervention group had 30.6 more angina-free days than patients in the sham group (CrI: 11.1– 50.7). The publication coincided with the presentation in the «Journal of the American College of Cardiology» (4).

Mavacamten Also Effective in Adolescent Patients

Hypertrophic cardiomyopathy (HCM) is defined as left ventricular hypertrophy that cannot be explained by cardiac, systemic, or metabolic causes. The hypertrophy results from sarcomere dysfunction characterized by hypercontractility and impaired relaxation. A distinction is made between obstructive HCM (OHCM) and non-obstructive HCM, with OHCM defined by a pressure gradient in the left ventricular outflow tract (LVOT) of at least 30 mmHg. Between 50 and 70% of all patients with HCM suffer from OHCM, which can not only cause symptoms but can also lead to heart failure and death. The myosin inhibitor mavacamten was approved as the first causal medication for the management of OHCM in adult patients. However, there is no approved therapy for pediatric HCM, which has a prevalence of 3–9 per 100,000 children and a poorer prognosis than the HCM occurring later in life.

In the SCOUT-HCM trial (Late Breaking Clinicals Trial IV), mavacamten was investigated in a pediatric population with OHCM. The trial enrolled 44 patients aged 12 to 17 years at centers in North America, Europe, and Australia. All participants exhibited symptoms of heart failure that limited their activities, LVOT gradients of more than 50 mmHg, and a normal left ventricular ejection fraction (above 60%). They were randomized in a 1:1 ratio to receive either mavacamten or placebo over 28 weeks. The primary endpoint was the change in LVOT gradient during the Valsalva maneuver. In the mavacamten group, the LVOT gradient decreased by an average of 48.5 mmHg, compared to a decrease of 0.5 mmHg in the placebo group. Benefits of mavacamten were also demonstrated by the secondary endpoints. The LVOT gradient at rest, maximum left ventricular wall thickness, myocardial oxygen consumption, and symptoms such as fatigue and shortness of breath improved under the treatment with mavacamten, whereas relevant biomarkers such as troponin and NT-proBNP decreased significantly. The SCOUT-HCM trial was published concurrently with its presentation in the «New England Journal of Medicine» (5).

In Transcatheter Aortic Valve Implantation (TAVI): Coronary PCI Can Be Postponed

Approximately 50% of all patients with severe aortic valve stenosis also suffer from significant coronary artery disease (CAD). If valve replacement is performed via open-heart surgery, bypass surgery is performed at the same time to address the CAD (6). With the use of TAVI in increasingly broader populations, the situation has changed fundamentally. In the presence of CAD, percutaneous coronary intervention (PCI) was routinely performed prior to TAVI. Since TAVI is primarily indicated for older and sicker patients, who would be more severely burdened by the additional procedure, the question arose as to whether this coronary intervention is actually always necessary in the presence of CAD. This question was investigated in the multicenter, randomized PRO-TAVI trial (Late Breaking Clinicals Trial IV). The trial included 466 TAVI candidates with an average age of 81 years, severe aortic valve stenosis, and significant CAD. These patients either routinely underwent PCI prior to TAVI, or the procedure was deferred and performed only if a clinical need arose at a later date. The primary endpoint was a composite of all-cause mortality, myocardial infarction, stroke, or major bleeding within one year of the procedure. This endpoint occurred in 25.8% of patients in the PCI group and in 24.1% in the group with deferred PCI, thus proving deferring PCI prior to TAVI as non-inferior. An analysis of the individual components of the primary endpoint showed a significant advantage of deferred PCI with regard to major bleeding (14.8 vs. 6.2%). Ischemic events occurred numerically, but not significantly, more frequently when PCI was not performed prior to TAVI. The publication of PRO-TAVI coincided with its presentation in «The Lancet» (7).

Digoxin for Rheumatic Heart Disease and Beta-blockers after Myocardial Infarction

A trial from India (Late Breaking Clinical Trials VI) provides important information, particularly for countries with a low gross national product: Digoxin reduces the risk of death or worsening heart failure in patients with rheumatic heart disease. This finding is especially relevant since digoxin has frequently been used for this indication, but without evidence to support it. The trial, conducted at twelve centers, included 1,769 patients (72% women) with symptomatic rheumatic heart disease. The trial was conducted according to the all-comer principle; therefore, exclusion occurred only in cases of contraindication. After a median treatment duration of 2.1 years with digoxin or placebo, the combined endpoint of death, new-onset heart failure, or worsening heart failure occurred significantly more frequently (by 18%) in the placebo group. The driver behind this result was the new onset or worsening of heart failure; mortality did not differ between the groups. This trial was first presented during the ACC Congress (8).

Discontinuing Beta-blockers

The SMART-DECISION trial (Late Breaking Clinical Trials VI) showed that beta-blockers can be safely discontinued one year after a heart attack, provided there is no heart failure. The study included 2,540 patients at 26 centers in South Korea who had taken beta-blockers for at least one year following a myocardial infarction and had not experienced any further cardiovascular events. Exclusion criteria included a history of heart failure and atrial fibrillation. Trial patients were randomized in a 1:1 ratio to either discontinue their beta-blockers or continue taking them. After a median follow-up of 3.5 years, the primary endpoint, a composite of all-cause mortality, recurrent myocardial infarction, and hospitalization for heart failure, occurred in 7.2% of patients who had discontinued beta-blockers and 8.8% of patients who continued taking beta-blockers, demonstrating non-inferiority for discontinuation. This conclusion also applied to a number of secondary endpoints, including the individual components of the primary endpoint, new-onset atrial fibrillation, adverse changes in left ventricular function, deterioration in quality of life, and serious adverse events. SMART-DECISION was published concurrently with its presentation in the «New England Journal of Medicine» (9).

Post Hoc Analysis: Tirzepatide Superior to Dulaglutide

During the Featured Clinical Research II session, a post hoc analysis of the SURPASS-CVOT was presented, showing that the dual incretin mimetic tirzepatide was superior to the GLP-1 mimetic dulaglutide with respect to a six-component cardiorenal endpoint. In the SURPASS-CVOT trial, tirzepatide had been shown to be non-inferior to dulaglutide with respect to a composite endpoint of cardiovascular death, myocardial infarction, and stroke (10). For the current analysis, this endpoint was expanded to include coronary revascularization, hospitalization for heart failure, and renal events.

After a median follow-up of 47.4 months, the six-component endpoint occurred in 1,591 (24.2%) patients treated with tirzepatide and 1,824 (27.7%) patients treated with dulaglutide, corresponding to a significant 15% risk reduction (hazard ratio [HR]: 0.85; 95% confidence interval [CI]: 0.80–0.91; $p < 0.001$). All individual endpoint components also occurred less frequently within the tirzepatide group. Sensitivity analyses for a narrower, five-component endpoint (excluding the renal endpoint) showed a similar HR of 0.86 (95% CI: 0.80–0.93) and a four-component endpoint analysis (excluding renal or heart failure endpoints) a HR of 0.86 (95% CI: 0.80–0.93). Gastrointestinal adverse events were more common with tirzepatide (42.5%) than with dulaglutide (35.9%). Other adverse events occurred with similar frequency. The analysis was published in «JAMA Cardiology» (11).

Platelet Inhibition after DAPT: Positive Data for Clopidogrel

During the Featured Clinical Research III session, 10-year data from the HOST-EXAM study (Harmonizing Optimal Strategy for Treatment of Coronary Artery Stenosis-Extended Antiplatelet Monotherapy) was presented. HOST-EXAM was initiated to enable a direct comparison between acetylsalicylic acid (ASA) and clopidogrel in thrombosis prophylaxis following the implantation of a drug-eluting coronary stent. Current recommendations from professional societies call for dual antiplatelet therapy (DAPT) for six to twelve months following stent implantation, typically using ASA and a P2Y12 inhibitor such as ticagrelor, prasugrel, or clopidogrel. Subsequently, antiplatelet therapy with either ASA or clopidogrel as monotherapy is recommended. The HOST-EXAM study compared these two strategies, with patients randomized to receive either aspirin or clopidogrel after the end of DAPT. The primary endpoint was a composite of all-cause mortality, non-fatal myocardial infarction (MI), stent thrombosis (ST), stroke, hospitalization due to acute coronary syndrome (ACS), and major bleeding events. Secondary endpoints included the thrombotic composite endpoint, consisting of cardiovascular death, non-fatal myocardial infarction, ischemic stroke, ACS-related readmission, and the bleeding endpoint (BARC type 2 or higher). The primary analysis at two years showed significant benefits for clopidogrel (12). This result was confirmed in a further analysis with 5.8 years of follow-up (13).

The analysis of the ten-year data now presented further demonstrates that clopidogrel remains the superior option compared to ASA. The primary composite endpoint occurred less frequently in the clopidogrel group (24.6 vs. 27.4% for clopidogrel vs. ASA; hazard ratio [HR]: 0.877; 95% confidence interval [CI]: 0.790–0.973; $p = 0.014$). The thrombotic endpoint also occurred less frequently in the clopidogrel group than in the ASA group (12.7 vs. 15.2%; HR: 0.821; 95% CI: 0.712–0.947; $p = 0.007$). Also noteworthy

are the bleeding results, which show that clopidogrel is the safer option. Bleeding events occurred in 7.8 vs. 10.0% of patients (HR: 0.774; 95% CI: 0.646–0.926; log-rank p = 0.005). The results were even more pronounced in the per-protocol analysis, which showed risk reductions for the thrombosis endpoint of 31% (HR: 0.69; 95% CI: 0.60–0.81; p < 0.0001) and for the bleeding endpoint by 27% (HR: 0.73; 95% CI: 0.59–0.89; p = 0.00025). The results were published in «The Lancet». □

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