Meeting Highlights – Focus on Statins

Highlights from the
American College of Cardiology
55th Annual Meeting
Atlanta

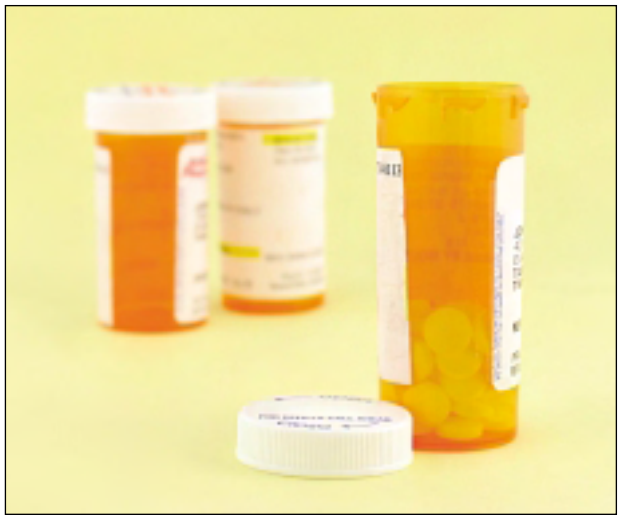
In more than 1,600 oral and poster presentations, the 55th Annual Scientific Session of the American College of Cardiology spanned the state of the art in cardiovascular medicine. In events as various as expert panels, symposia, brown-bag lunch sessions, how-to and Q&A, point-counterpoint debates, late-breaking clinical trial announcements, and original research presentations, the scope of practice was presented, discussed, challenged, and evaluated. Here are 10 key highlights from ACC 2006.

Statins May Help Reduce Post-Op Atrial Fibrillation (AF). The Atorvastatin for Reduction of Myocardial Dysrhythmia after Cardiac Surgery (ARMYDA-3) study demonstrated that statin therapy compared with placebo significantly reduced the rate of post-op AF. ARMYDA-3 was premised on the hypothesis that AF has an inflammatory etiology in the wake of cardiac surgical procedures. If so, statins might be appropriate therapy in reducing incidence of post-op AF. Compared with placebo, atorvastatin-treated patients developed post-op AF less often (35% vs. 57%). Although ARMYDA-3 was small and performed at only 1 center, its results suggest that larger clinical trials are justified to assess the role of statins in reducing post-op AF.

Comment: The placebo arm had excessive PAF incidence compared to historical controls.

Aggressive Statin Therapy Is a Survival Benefit in Acute Coronary Syndromes (ACS). A meta-analysis presented by Anthony Bavry, Cleveland Clinic, confirmed that aggressive statin therapy initiated early during ACS result in significant survival benefit as well as significant reductions of subsequent unstable angina and need for revascularization. Surveyed studies included Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE-IT), Aggrastat to Zocor (AtoZ), Myocardial Ischemia Lowering with Aggressive Cholesterol Lowering (MIRACL), Pravastatin Turkish Trial (PTT), Fluvastatin on Risk Diminishing After Acute Myocardial Infarction (FLORIDA), Lipid–Coronary Artery Disease (L-CAD), and Pravastatin Acute Coronary Treatment (PACT).

Withdraw Statins ... And Elevate CRP and LDL. The Prevention of Renal and Vascular Endstage Disease Intervention Trial (PREVEND-IT) study suggests that withdrawing long-term statin therapy leads to significant increases in CRP levels. PREVEND-IT investigators evaluated effects of pravastatin (40 mg/d) withdrawal on CRP levels in 586 subjects in the randomized, placebo, controlled study. CRP levels were measured at baseline, after 4 years of randomized treatment, and 3 months after the discontinuation of study treatment. Four years after randomization, pravastatin-treated patients had a 16% decrease in CRP levels, while placebo-treated patients had a nonsignificant 4.3% increase. LDL-C levels changed only among statin-treated patients (-27%, P<.001). Withdrawal of pravastatin therapy was associated with significant increases in both CRP and LDL-C to levels approximately equal to pretreatment levels.



Lower Triglycerides Are Associated with Higher HDL-C. "Lower-is-better" might also apply to triglycerides with regard to resulting effect on HDL-C, according to Michael Miller, MD, University of Maryland Medical Center. While an inverse association between triglycerides and HDL-C is well documented, the impact on raising HDL-C by lowering triglycerides had not been well established. Dr. Miller and colleagues analyzed 159 patients with CHD or CHD risk factors who made multiple clinic visits (n=1201) between 1991 and 2005. Mean HDL-C levels within each National Cholesterol Education Program triglyceride category (desirable, borderline-high, high, very high, etc.) demonstrated higher HDL-C at successively lower triglyceride levels. These data offer the possibility that lower triglycerides may be advantageous as part of an overall program of risk reduction.

Better Outcomes Seen with Rosuvastatin in Hispanic-Americans. Ramon Lloret, MD, Cardiovascular Center of South Florida, presented the first-ever data on statin therapy in a Hispanic-American population. The Study Assessing Rosuvastatin in Hispanic Population (STARSHIP) was a prospective, randomized, controlled trial comparing lipid-lowering therapy in 696 Hispanic-American patients (50% male) with hypercholesterolemia and moderate to high CHD risk. Participants were randomized to 1 of 4 open-label treatments for 6 weeks: rosuvastatin 10 or 20 mg, or atorvastatin 10 or 20 mg. After 6 weeks of therapy, rosuvastatin 10 and 20 mg had greater efficacy than either dose of atorvastatin in reducing LDL-C, non–HDL-C, and total cholesterol. Of patients on rosuvastatin 10 mg, 78% reached National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) LDL-C targets, compared with 60% of patients on atorvastatin 10 mg. In encouraging other studies in ethnic and racial populations, Dr. Lloret noted that STARSHIP helps to further understanding of disease as well as assess therapeutic strategies in special populations who may have been previously underrepresented in clinical trials—and speaks to a continuing divide in access to care experienced by special populations.

Metabolic Syndrome (MetS) Is Still On the Rise. The Brigham & Women's Hospital in Boston, MA, along with TNS Healthcare in the U.K. released data indicating that the prevalence of metabolic syndrome (MetS) has increased by nearly 50% over the past 6 years in both the U.S. and Europe. The rise in MetS is despite decreases in incidence of hypertension, hypertriglyceridemia, and low HDL-C. Utilizing information from CardioMonitor (an international sample of patients with cardiovascular disease including more than 5000 patients annually in the U.S. and over 15,000 patients each year in Europe), rates of hypertriglyceridemia and hypertension both decreased over the last 6 years, as statin use increased, from 37% to 52%. But MetS increased (20% to 24%), a phenomenon apparently driven by sharply rising rates of obesity (30% to 48%) and impaired glucose tolerance (18% to 27%).

MetS On the Rise—But Not Solely Due to Obesity. Data from the EUROPA trial suggests that obesity, in and of itself, is not an independent predictor of CV death in patients with CVD. More than 8,000 study participants were categorized as dysmetabolic if they had either DM or MetS, but not based on BMI. They were followed over 4.2 years. Dysmetabolic status but not being overweight or obese increased the risk of CV death among EUROPA participants. Compared with normal-weight individuals without dysmetabolic features, the relative risk of CV death associated with obesity and dysmetabolic status was 2.4 , overweight and dysmetabolic status 3.0, and normal weight and dysmetabolic status 4.1. Overweight or obese individuals without diabetes or metabolic syndrome did not appear to be at increased risk of CV death, confirming the specific importance of DM and MetS—even in normal weight individuals—as key factors in CV risk.

No Added Anti-Inflammatory Benefit of Statin plus Fibrate in Diabetics with Mixed Dyslipidemia. The Diabetes and Combined Lipid Therapy Regimen (DIACOR) study found no specific anti-inflammatory benefit in combining statins and fibrates in diabetics with mixed dyslipidemias beyond the already-known benefits of each agent alone. DIACOR randomized 300 patients with type 2 DM, no CHD history, and mixed dyslipidemia to receive either simvastatin 20 mg, fenofibrate 160 mg, or a combination of the two. At 12 weeks, high-sensitivity C-reactive protein (hs-CRP) in the overall study population was significantly reduced from baseline—but that effect was no different among the three study arms. The overall effect, however, was greatest among patients with baseline hs-CRP levels above 2 mg/L.

No Benefit Found from Lowered Homocysteine. While earlier studies have associated lower levels of homocysteine with lower rates of CHD and stroke, data from the Heart Outcomes Prevention Evaluation (HOPE) 2 trial failed to demonstrate any effect from B-vitamin and folic-acid supplementation (which lower homocysteine levels), in preventing CV events. HOPE 2 was a randomized, double-blind trial that randomly assigned 5,522 patients aged 55 years older with histories of vascular disease (coronary, cerebrovascular, or peripheral arterial disease), or with diabetes and at least 1 additional risk factor, to daily treatment with one of three study arms: a combination of

2.5 mg folic acid + 50 mg vitamin B6, 1 mg vitamin B12, or placebo. Study participants were recruited from countries with mandatory fortification of food with folate, such as the United States and Canada, comprising about 70% of the study population. The rest came from countries (Brazil, western Europe, Slovakia) without mandatory folate fortification. Participants were followed for 5 years. Homocysteine levels did, in fact, decrease in the active-treatment group—but active treatment did not reduce the risk of major CV events in patients with established vascular disease, nor did it significantly decrease risk of death from CV causes. There were also no differences in outcomes in any subgroup analyses, including those from countries with or without folate supplementation or those with higher or lower baseline homocysteine levels.

LDL-C Levels: Still Far from Goal. Data culled from CardioMonitor, the Brigham & Women's Hospital, Boston, MA, and TNS Healthcare, U.K. indicate that LDL-C levels remained significantly above goal in highest-risk patients in 2004. This conclusion was based on a sample of 4,676 patients with CVD from 250 primary care physicians and 50 cardiologists. Extrapolation of that data to the entire U.S. population suggests that approximately 67 million individuals have CVD or CAD risk factors, with 35 million of those exhibiting overt disease. Of some 26 million individuals with 2 or more risk factors, 24% had LDL-C levels >130 mg/dL despite 33% of that group on statins. We are very clearly far short of treatment goals recommended by NCEP, ACC, AHA, or ESC. More aggressive disease recognition, treatment, and public education remain vital.

International Chair/Committee on Cardiometabolic Risk Announced

To highlight the growing worldwide problem of cardiovascular disease and diabetes and to promote research and education on prevention, assessment and optimal management of patients at elevated cardiometabolic risk, the Université Laval, Quebec City, Canada announced the launch of the first international and multidisciplinary chair on cardiometabolic risk.

Dr. Jean-Pierre Després, University Laval professor and Director of research in cardiology at Laval Hospital Research Center, is the Chair's scientific director: "The mission of the Chair is to highlight the growing problem we call cardiometabolic risk. The Chair will provide a platform for integrated research into cardiometabolic risk to define a set of risk factors and markers that will allow physicians to develop strategies to better assess and manage this risk."

Cardiometabolic risk describes the overall risk of developing cardiovascular disease and type 2 diabetes; combining classical risk factors such as smoking, high cholesterol, and hypertension with a more recently identified set of factors closely related to a specific form of fat accumulation: abdominal obesity. When simultaneously present in a patient, these cardiometabolic risk factors are strongly predictive of cardiovascular disease and type 2 diabetes.

Cardiovascular disease (CVD) is a leading cause of death, responsible for an estimated 17 million deaths each year. This number is expected to rise to 24 million by 2030. Although remarkable progress has been made in the management of CVD, it remains, along with type 2 diabetes, a critical public health issue worldwide. Through various educational activities, scientific projects and professional meetings, the Chair will offer a unique forum for everyone interested in fighting those diseases. The Chair will hold two key meetings every year in which leading researchers, clinicians, scientific associations, and health policy makers will be invited to discuss the underlying causes of cardiometabolic risk and to develop goals for improving patient care.

In addition to Dr. Després, the Chair's board of experts includes multidisciplinary scientists Bryan Brewer (Washington Hospital Center), Peter Libby (Harvard Medical School), Philip Barter (The Heart Research Institute, Sydney), and Jean-Claude Coubard (Fournier, Paris) as Executive Director.