MEETING HIGHLIGHTS

American College of Cardiology, 58th Annual Scientific Session

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Investigations into the use and effects of statins again played a major role in this year’s meeting of the American College of Cardiology, as reflected by their inclusion in four of the five trials reviewed in this article. Two of the trials suggest extending statin target populations. The sessions, which took place from March 29 to 31, in Orlando, Florida, attracted 25,000 attendees (15,000 cardiac specialists), down by 4,000 from last year, attesting to the weak economy’s effects.

Trial Data Suggest Wider, More Intensive Statin Use

DYSIS (Dyslipidemia International Study)

• Anselm K. Gitt, MD, Vice Director, Institut für Herzinfarktforschung, Ludwigshafen, University of Heidelberg, Germany

DYSIS, a study that evaluated more than 22,000 outpatients in Europe and Canada who were consecutively treated for dyslipidemia, found that most of these patients were not reaching lipid targets despite statin therapy. DYSIS was conducted at 2,987 centers, and most patients (73.6%) were treated by primary care physicians.

All patients were 45 years of age or older and were receiving a statin. Documented fasting lipid profiles were developed after they had been receiving statins for at least three months.

Dr. Gitt reported that the investigators examined the prevalence of persistent lipid abnormalities according to Adult Treatment Panel III (ATP III) risk profile criteria. Patients included those with coronary heart disease (CHD) or its risk equivalent, those with two or more risk factors, or those with no risk factors or one risk factor. Most of the patients (70%) were in the highest-risk group (n = 15,365); 19% had two or more risk factors; and 11% had zero to one risk factor. Most patients (47.7%) were receiving simvastatin (Zocor, Merck) or atorvastatin (Lipitor, Pfizer) (28%). Non-statin lipid therapies, such as ezetimibe (Zetia, Merck/Schering), fibrates, nicotinic acid, and bile-acid sequestrants, were given to 13.5% of patients.

ATP III definitions of low-density lipoprotein-cholesterol (LDL-C) for those not at goal for the three risk groups (in descending order of risk) are 100 mg/dL or higher, 130 mg/dL, or 160 mg/dL for LDL-C levels. For all groups, low levels of high-density lipoprotein-cholesterol (HDL-C) were defined as below 40 and 50 mg/dL for men and women, respectively. Elevated triglycerides were defined as 150 mg/dL or greater.

For the 19,196 patients with total lipid profiles, LDL-C targets had not been reached by 43.3% of those in the highest-risk category, by 35.7% of those with two or more risk factors, and by 16.7% of those with no risk factors or one risk factor (Table 1).

JUPITER (Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin)

• Robert J. Glynn, PhD, ScD, Biostatistician, Brigham and Women’s Hospital, and Associate Professor of Medicine, Harvard Medical School, Boston, Mass.
• Harvey D. White, MB, ChB, DSc, Director, Coronary Care and Cardiovascular Research, Green Lane Cardiac Service, Auckland City Hospital, Auckland, New Zealand
• Paul Ridker, Director, Center for Cardiovascular Disease Prevention, Brigham and Women’s Hospital, Boston, Mass.

An analysis of venous thromboembolism (VTE) in JUPITER showed the benefits of rosvastatin (Crestor, AstraZeneca) to be independent of the statin’s effect on arterial events and to be as great as that effect. In the study’s primary analysis, the primary endpoint of myocardial infarction (MI), stroke, unstable angina/vascularization, and cardiovascular death was reduced by 44% with rosvastatin therapy compared with placebo (P < 0.00001). The number needed to treat (NNT) to prevent one adverse event was 25. JUPITER included 17,802 patients (men 50 years of age or older, women 60 years of age or older) with no prior cardiovascular disease (CVD) or diabetes, and with LDL-C levels below 130 mg/dL and high-sensitivity C-reactive protein (hsCRP) levels of 2 mg/L or higher.

Dr. Glynn noted that both venous and arterial thromboses are common, serious age-related events that often occur to-
The primary combined outcome occurred at 96 hours in 9.3% of those in the early-strategy group and in 10% receiving the delayed provisional strategy; this amounted to a non-significant reduction of 8% (P = 0.23). Reductions in individual components were also nonsignificant. The difference in the primary endpoint at 30 days (12.5% early, 13.8% delayed, 11% reduction; P = 0.065) showed a favorable trend for eptifibatide but was not significant. At 30 days, the death or recurrent MI rate for the early-strategy group was 11.2% compared with 12.3% for the delayed provisional group (P = 0.079).

Bleeding, however, occurred at significantly higher rates in the early-strategy group, with 118 patients experiencing TIMI major bleeding, compared with 83 patients in the delayed provisional group (P = 0.015). Investigators reported a 7.6% vs. 5.1% rate of moderate or severe bleeding (P < 0.001) in the early-treatment group compared with the delayed provisional group.

Red blood cell transfusions were required in 8.6% of patients in the study group compared with 6.7% of patients in the delayed provisional group (P = 0.001).

Dr. Newby concluded that EARLY ACS results did not support a strategy of early, routine eptifibatide use in this population; however, in an ACC press conference, she added:

It may be possible, looking at this balance of bleeding and risk, to identify groups with higher risk for ischemic events and low bleeding risk who are potentially highly likely to benefit from early routine eptifibatide use. We have some hints that high-risk patients who are troponin-positive might be a target group.

Analyses that may identify such subgroups are ongoing.

TNT (Treating to New Targets)

Nanette K. Wenger, MD, Professor of Medicine (Cardiology), Emory University School of Medicine, Atlanta, Ga.

In older patients who have survived cardiovascular events, higher-dose atorvastatin (Lipitor) (80 mg) reduces the risk of future cardiovascular events compared with the 10-mg dose, according to Dr. Wenger, TNT lead investigator. Prior research in TNT had indicated that intensive lipid lowering with atorvastatin 80 mg significantly decreased the incidence of cardiovascular disease (CVD) compared with 10 mg in patients 65 years of age or older with stable coronary heart disease. The TNT analysis, however, was limited to the time to first events. Because patients often have a series of cardiovascular events, Dr. Wenger and her colleagues conducted a post hoc analysis to evaluate the trial period after first cardiovascular events to determine potential benefits of the higher statin dose over time.

In TNT, 3,809 subjects 65 years of age and older were randomly assigned to receive atorvastatin at a dose of either 10 or 80 mg daily. The patients were observed for a median of 4.9 years. The time-to-event analysis estimated treatment hazard ratios for the first through fifth cardiovascular events. Included events encompassed CHD, death, nonfatal MI, resuscitated cardiac arrest, a revascularization procedure, a procedure-related MI or documented angina, cerebrovascular events (fatal or nonfatal stroke, transient ischemic attack), peripheral artery disease, or hospitalization with a primary diagnosis of
congestive heart failure.

During the study period, 1,130 stable patients with CHD, 65 years of age or older, experienced a first event. The most commonly experienced endpoint as a first event was angina in 171 patients receiving 80 mg and in 180 patients receiving 10 mg. Overall, coronary revascularization was the most common event, with 300 patients in the 80-mg group and 437 patients in the 10-mg group.

The relative risk of a first cardiovascular event was reduced significantly by 22% (P < 0.0001) in the higher-dose group, compared with the lower-dose group. The benefit was found for the second through fifth events, although the difference between treatments at the fifth event was no longer statistically significant, presumably because of the small number of events.

Dr. Wenger concluded: “Treatment with atorvastatin 80 mg continued to reduce the risk of any cardiovascular event over time compared with atorvastatin 10 mg among patients 65 years or older.”

The data further showed that the benefits of long-term intensive statin therapy were maintained after multiple cardiovascular events in this population.

Dr. Wenger commented, “These data demonstrate the significant benefits of maintaining long-term, high-dose statin therapy among patients in this age group.”

**TIPS (The Indian PolyCap Study)**

Salim Yusuf, MD, DPhil, Director, Population Health Research Institute, and Professor, Department of Medicine, McMaster University, Hamilton, Ontario, Canada

A “polypill” containing blood pressure (BP)–lowering agents, a statin, and aspirin has the potential to reduce CVD rates by half, according to results of TIPS. Noting that CVD is a global problem and that average levels of risk factors are likely to be abnormal in all individuals in most urban settings, Dr. Yusuf said that theoretically, a polypill that could be given to all individuals 50 years of age and older might be able to reduce CVD by more than 80%.

TIPS was launched to determine whether a polypill (Polycap, Cadila) could significantly reduce LDL-C levels, BP, and platelet aggregability. Polycap is composed of three BP-lowering drugs, including low doses of thiazide (12.5 mg/day), atenolol (50 mg/day), ramipril (5 mg/day); simvastatin (20 mg/day); and aspirin (100 mg/day). The TIPS investigators also wanted to learn whether the polypill could perform as well as its components and whether it would be superior in reducing BP compared with only one or two BP-lowering agents with simvastatin and aspirin.

Conducted at 50 centers in India, TIPS included 2,053 subjects 45 to 80 years of age with at least one cardiovascular risk factor: stable type-2 diabetes, hypertension, current smoking, elevated lipids, or a waist-to-hip ratio of more than 0.85 for women and above 0.9 for men. The mean age of these patients was 54.

During 12 weeks of treatment, 400 of the study participants took the polypill; the rest of the subjects were divided into eight groups of 200 each who received either individual components of the polypill or combinations of them. Three groups of 200 patients received only aspirin, simvastatin, or a thiazide, respectively; three groups received two of the three BP medications, and another received all three BP medications. The last group received all three medications combined with aspirin.

Dr. Yusuf reported that the mean change in systolic BP in subjects receiving the Polycap was −7.4 mm Hg, compared with −2.2, mm Hg, −4.7 mm Hg, and −6.9 mm Hg for one to three BP-lowering drugs, respectively. Although LDL-C reductions with the polypill arms were significantly greater than in the non-statin arms, simvastatin alone reduced LDL-C levels by 27.7% compared with 23.3% with the polypill.

Reductions in urinary thromboxane B₂ (a measure of platelet aggregability), when compared with baseline values, were similar for aspirin alone and for the polypill (P < 0.001). The polypill, Dr. Yusuf said, was well tolerated.

The TIPS estimate of Polycap’s CHD/stroke risk reductions in those with average risk factor levels, combining known reductions from LDL-C, BP, and platelet function, was 62% for CHD and 48% for stroke.

Dr. Yusuf concluded that for patients with average risk factors and no CVD, the polypill would be similarly to the added effects of each of its three BP-lowering components. Aspirin does not interfere with BP-lowering effects. The polypill, he said, had the potential to reduce CVD risk by about half, but this needs to be confirmed in future studies.

Cadila Pharmaceuticals of India played no role in data collection, analysis, or interpretation, Dr. Yusuf said.