Rosuvastatin Causes Atherosclerosis Regression

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CHICAGO — The ASTEROID trial results, showing that 2 years of high-dose rosuvastatin monotherapy resulted in significant regression of coronary atherosclerosis, were bolstered by quantitative coronary angiography assessments of the study patients, Dr. Christie M. Ballantyne reported at the annual meeting of the American College of Cardiology.

The atherosclerotic regression in response to rosuvastatin at 40 mg/day was shown both by quantitative coronary angiography (QCA) and intravascular ultrasound (IVUS). The fact that two imaging modalities measuring different parameters showed concordant improvement in atherosclerosis adds to the certainty of the findings, noted Dr. Ballantyne, professor of medicine and director of the center for cardiovascular disease prevention at Baylor College of Medicine, Houston.

"Perhaps the most important finding in this trial is that aggressive lipid-modifying therapy arrested progression or stabilized coronary stenoses during the 2 years of the study, as evidenced by the fact that 97% of patients remained stable or had regression in terms of percent diameter stenosis and 94% of patients remained stable or had regression in terms of minimum lumen diameter," he observed.

ASTEROID (a Study to Evaluate the Effect of Rosuvastatin on Intravascular Ultrasound-Derived Coronary Atheroma Burden) was a prospective, multicenter, open-label study involving 292 statin-naive coronary artery disease patients who received rosuvastatin at 40 mg/day for 2 years. For ethical reasons, it was deemed unacceptable to have a control group on no or low-dose statin therapy. However, both the IVUS measurements of atheroma volume and the determination of minimum lumen diameter and percent diameter stenosis by QCA were analyzed blindly.

Rosuvastatin reduced LDL cholesterol by 52%, from a baseline of 132 to 61 mg/dL, while raising HDL by 14.4% from a baseline of 43 to 48 mg/dL.

Mean minimum lumen diameter increased from 1.65 to 1.68 mm. Mean percent diameter stenosis decreased from 37.3% to 36.0%. The percent atheroma volume decreased by 0.98%, while the atheroma volume of the most diseased segment was reduced by a mean of 6.1 mm^3, as previously reported.

Discussant Dr. B. Greg Brown noted that rosuvastatin is a particularly effective statin at raising HDL. He added that the ASTEROID findings are consistent with his own studies, which suggest that when the sum of the percent reduction in LDL cholesterol and percent increase in HDL cholesterol achieved via therapy for dyslipidemia exceeds 60%, regression of coronary stenoses can be obtained.

"It makes an important point: that we can do best by changing both HDL and LDL," said Dr. Brown, professor of medicine at the University of Washington, Seattle. "It's encouraging," Dr. Ballantyne agreed, "but we're talking here about angiographic trials—and the real issue is event reduction."

In that regard, the recent halt of the JUPITER trial (Justification for the Use of Statins in Primary Prevention: an Intervention Trial Evaluating Rosuvastatin) because the statin was more effective than placebo at preventing cardiovascular events is exciting. It will be important to see whether the reduction in cardiovascular morbidity and mortality seen in this large multicenter double-blind trial correlated with increases HDL levels as well as LDL lowering—and with atherosclerotic regression on imaging.

He added that definitive word on the role of pharmacologic boosting of HDL cholesterol in preventing cardiovascular events is expected to come from HPS2-THRIVE (Heart Protection Study 2–Treatment of HDL to Reduce the Incidence of Vascular Events), an ongoing 20,000-patient randomized trial out of the University of Oxford (England) and the National Institutes of Health–sponsored AIM HIGH trial (Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides and Impact on Global Health Outcomes), led by Dr. Brown.

ASTEROID was funded by AstraZeneca Pharmaceuticals LP. Dr. Ballantyne has received research grants from, is on the speakers bureau for, and is a consultant to that pharmaceutical company as well as roughly a dozen others. The ASTEROID results were published online simultaneously with Dr. Ballantyne's presentation (Circulation 2008; [Epub doi:10.1161/CIRCULATIONAHA.108.773747]).