Adiponectin Gene Variant Predicts Cardiovascular Risk

BY BRUCE JANCIN
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BARCELONA — A variant of the adiponectin gene may have a future as a novel predictor of cardiovascular risk, Dr. Stefan Aczel reported at a joint meeting of the European Society of Cardiology and the World Heart Federation.

The G alleles of the –11377 promoter polymorphism of the adiponectin gene proved strongly predictive of increased risk of cardiovascular events independent of all standard risk factors in a prospective study involving 402 men with coronary artery disease (CAD) followed for 4 years, according to Dr. Aczel of the Academic Teaching Hospital at Feldkirch (Austria).

Serum adiponectin has been inversely associated with cardiovascular risk in some studies, but not in others. The inconsistency probably results from the fact that adiponectin levels can fluctuate widely depending upon the presence of illness, obesity, and other factors. Dr. Aczel and his coworkers decided to study promotor polymorphisms of the adiponectin gene as a potential risk predictor because the genotype—unlike serum adiponectin—remains constant, he explained in an interview.

The adiponectin gene has three different promotor variants identifiable by polymerase chain reaction (PCR): CC, GC, and GG. In the prospective study involving 402 consecutive men with CAD referred for angiography, the prevalence of the –11377 CC variant was 56.5%. The GC variant was present in 37.1%, and the GG variant occurred in 6.5%. Coronary stenosis of at least a 50% was present at baseline in 64% of men with the CC variant, in 73% with the GC, and in 89% with GG.

In all, 24% of subjects experienced one or more vascular events during follow-up. After adjustment for diabetes, lipids, age, smoking status, and other standard cardiovascular risk factors, the presence of a G-containing allele was an independent risk factor for future vascular events. Men with the GC genotype were 1.6-fold more likely to experience an event than were those with the CC genotype. Men who were GG were at an adjusted 2.4-fold increased risk.

Dr. Aczel and coworkers are interested in developing a commercial test for the G alleles. First, however, they want to confirm the associated risk in other populations, including women. They are also studying whether other gene variants associated with adiponectin—at least 13 are known—confer increased risk and might further boost risk prediction. ■

Ezetimibe/Simvastatin Lowered LDL Better Than Rosuvastatin Alone

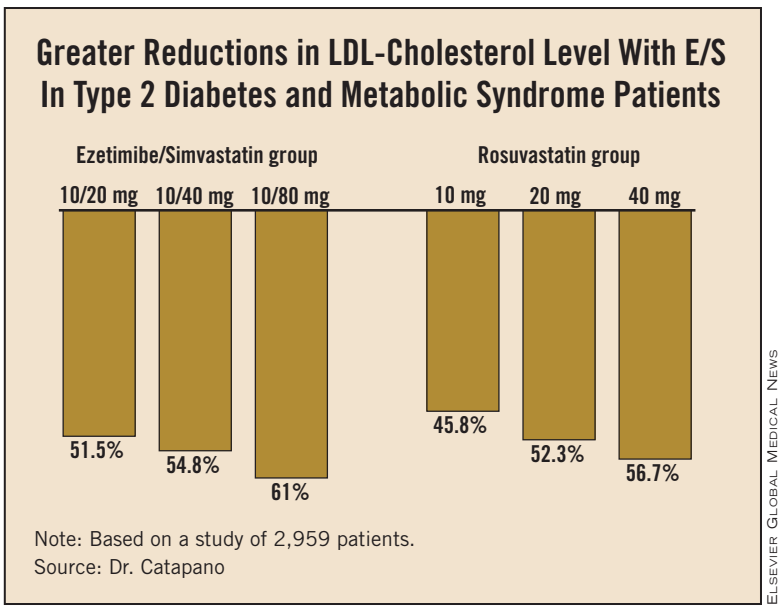
BY MIRIAM E. TUCKER
Senior Writer

COPENHAGEN — A combination of ezetimibe and simvastatin provides additional lipid-modifying benefits compared with rosuvastatin monotherapy among patients with type 2 diabetes or with metabolic syndrome without diabetes, Dr. Alberico L. Catapano reported at the annual meeting of the European Association for the Study of Diabetes.

"Overall, ezetimibe/simvastatin, a single-tablet, dual-cholesterol inhibitor [Vytorin, Merck], offers an effective and well-tolerated lipid-modifying option for the treatment of hypercholesterolemia in patients with type 2 diabetes and metabolic syndrome," said Dr. Catapano, of the department of pharmacological sciences at the University of Milan.

In a post-hoc analysis of data from a multicenter, double-blind, randomized, parallel-group, 6-week study sponsored by Merck & Co., 375 patients with type 2 diabetes, 840 with metabolic syndrome but without diabetes, 1,722 with neither condition, and 22 who could not be placed in a category because of missing data were randomized to one of six treatment groups: ezetimibe/simvastatin (E/S) in doses of 10 mg/20 mg (respectively), 10 mg/40 mg, or 10 mg/80 mg; or rosuvastatin (Crestor, AstraZeneca) in doses of 10, 20, or 40 mg. All had hypercholesterolemia, defined as an LDL-cholesterol level of 145-249 mg/dL with triglycerides at or below 350 mg/dL.

Among the whole cohort of 2,959 patients, significant reductions in LDL cholesterol from baseline were seen among the E/S group at the usual starting, next highest, and maximum dosing levels. (See chart.)



Across all doses, the difference in LDL-cholesterol reduction between E/S and rosuvastatin was significant for the whole cohort (55.8% vs. 51.6%). Consistent with that, LDL-cholesterol lowering was also greater with E/S among the patients with type 2 diabetes (58.5% vs. 54.2%), nondiabetics with metabolic syndrome (55% vs. 51.8%), and those with neither (55.6% vs. 51%), Dr. Catapano reported.

Overall, 95.3% of the E/S group, compared with 92.1% of the rosuvastatin group, attained the recommended LDL goals of less than 100 mg/dL for the diabetics, 130 mg/dL for the nondiabetics with metabolic syndrome, or 160 mg/dL for the group with neither. A total of 88.2% of the E/S patients versus 81.9% of the rosuvastatin patients achieved an LDL-cholesterol level of less than 100 mg/dL, whereas 45.3% vs. 29.5% reached an LDL-cholesterol level of less than 70 mg/dL. All of these differences were significant, he said.

Reductions in total cholesterol, non-HDL cholesterol, apolipoprotein B, and triglycerides were also significantly greater with E/S, whereas there were no significant differences between the two treatments in HDL cholesterol, or high-sensitivity C-reactive protein.

Both drugs were well tolerated in all patient groups, with similar rates of drug-related adverse events (8.1% with E/S vs. 7.4% with rosuvastatin) and discontinuations because of adverse events (2.2% for both drugs). Proteinuria was higher at baseline in the rosuvastatin group and among those with diabetes, Dr. Catapano noted. ■

In CAD, Mild Renal Impairment Increases Cardiac Event Risk

BY MITCHEL L. ZOLER
Philadelphia Bureau

BARCELONA — Mild renal impairment can have a substantial effect on the rate of death or myocardial infarction in patients with coronary artery disease, according to a review of more than 5,000 patients.

"Renal insufficiency is usually defined as a glomerular filtration rate [GFR] of less than 60 mL/min 1.73 per m^2, but these results show that patients with mild renal impairment [defined as a GFR of 61-80 mL/min 1.73 per m^2] have an increased risk of death, cardiac death, or myocardial infarction," Ron T. van Domburg, Ph.D., and his associates said in a poster presented at a joint meeting of the European Society of Cardiology and the World Heart Federation.

"Many physicians only care about renal function if a patient's serum creatinine is more than 2 mg/dL. For non-nephrologists it's a new concept that mild renal dysfunction" can have a significant effect on outcomes, said Dr. Don Poldermans, a professor in the department of anesthesiology at Erasmus University Medical Center in Rotterdam, the Netherlands, and a coauthor of the poster.

The study reviewed 5,041 patients who were seen at Erasmus Medical Center with known or suspected coronary artery disease during 1993-2004. None of these patients was on dialysis. Their follow-up ranged from 6 months to 12 years with an average of 6 years.

Renal function was normal (GFR greater than 80) in 41%, mildly impaired in 28%, moderately impaired (GFR 41-60) in 19%, and severely impaired (GFR 40) in 12%.

The researchers then determined the rate of all-cause death, cardiac death, and nonfatal MI in each subgroup, and calculated the risk for each end point faced by each group relative to patients with normal renal function and adjusted for baseline demographic and clinical differences.

The results showed a substantial and statistically significant increased risk for all three adverse outcomes that tracked with the extent of renal impairment (see chart), reported Dr. van Domburg, a researcher in the Thoraxcenter at Erasmus University Medical Center.

The implication is that all patients with known or suspected coronary artery disease and any degree of impaired renal function should undergo close surveillance and intensive medical therapy, including treatment with a statin, an ACE inhibitor, and a β-blocker, the authors concluded. ■