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CONTACT: Andrew Crosby
(901) 575-0010
acrosby@crosbyvolmer.com
Amy Murphy
(202) 375-6476
amurphy@acc.org
ACC.08 Newsroom
(312) 949-3450

**SPECIFIC BLOOD GLUCOSE LOWERING STRATEGY PREVENTED THE
PROGRESSION OF CORONARY ATHEROSCLEROSIS IN DIABETIC
PATIENTS**

New Study Demonstrates Relationship for First Time

Chicago, IL – Heart disease is the leading cause of death in diabetics, responsible for more than 75 percent of mortality in these patients. While management of blood glucose levels (glycemic control) is one of the principal treatment goals of diabetes therapy, it has been difficult to demonstrate a favorable effect of glycemic control on arterial complications, such as buildup of plaque. Previously, no diabetes therapy regimen has shown the ability to reduce the progression of coronary atherosclerosis, or build-up of plaque, within the arterial walls. For that reason, there has been little evidence to support a preference for one class of anti-diabetic medication over another as a means to reduce atherosclerotic disease.

According to the PERISCOPE trial (Pioglitazone Effect on Regression of Intravascular Sonographic Coronary Obstruction Prospective Evaluation), presented today at the American College of Cardiology's 57th Annual Scientific Session, one of two approaches to diabetes management proved more effective at slowing the progression of atherosclerosis in patients with type 2 diabetes, the most common form of diabetes in adults. ACC.08 is the premier cardiovascular medical meeting, bringing together cardiologists and cardiovascular specialists to further breakthroughs in cardiovascular medicine.

PERISCOPE compared the effects of two widely used yet distinctively different classes of oral glucose-lowering agents on the rate of progression of coronary atherosclerosis in diabetic patients, measured using intravascular ultrasound. Patients were randomly assigned to receive a **thiazolidinediones (TZD)**, **pioglitazone (Actos™)**, a relatively new type of drug that reduces blood glucose by increasing insulin sensitivity *or* a **sulfonylureas, glimepiride (Amaryl™)**, that lowers blood glucose by acting as an insulin secretagogue (stimulates insulin release by the pancreas). The principal finding

was an absence of progression of coronary plaque buildup with pioglitazone (-0.16%) compared with highly significant progression with glimepiride (+0.73%). The *p* value for progression with glimepiride was $p < 0.001$. The between groups *p* value was $p = 0.002$.

There were also major differences between the two treatments in biochemical effects including marked differences in levels of HDL cholesterol, triglycerides and C-reactive protein. Other important endpoints included changes in glycohemoglobin levels, insulin levels, other lipid parameters and blood pressure – all more favorable for patients treated with pioglitazone. There were adverse effects in both treatment groups with more patients assigned to glimepiride experiencing episodes of low blood sugar or angina and more patients assigned to pioglitazone experiencing edema and fractures.

This prospective, randomized, multicenter, double-blind trial treated 543 patients with coronary disease and type 2 diabetes for 18 months at 97 academic and community hospitals in North and South America. Patients underwent intravascular ultrasonography (IVUS) to measure the amount of plaque volume on the arterial wall at study entry. Patients were randomized to receive glimepiride, 1-to-4 mg, or pioglitazone, 15-to-45 mg, for 18 months and titrated to maximum dosage, if tolerated. After 18 months, a second IVUS examination was performed to determine the amount of change in coronary plaque volume. The primary endpoint was the rate of progression of coronary plaque as measured by IVUS.

“Atherosclerosis can be particularly aggressive in patients with diabetes, which is currently increasing at an alarming rate in the developed and developing world,” said Steven Nissen, M.D., Chairman, Department of Cardiovascular Medicine, Cleveland Clinic and lead author. “By defining the optimal strategy for managing coronary heart disease in this patient population, this study has major implications for how we will treat diabetics with coronary disease in the future.”

The study will be simultaneously published in the *Journal of the American Medical Association (JAMA)* and will appear in the April 2 print edition and will be released online at the time of presentation.

Dr. Nissen will present The PERISCOPE Trial (Pioglitazone Effect on Regression of Intravascular Sonographic Coronary Obstruction Prospective Evaluation) in the Late-Breaking Clinical Trials II session on Monday, March 31, 2008 at 11:00 a.m. in North Hall B1.

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The American College of Cardiology (www.acc.org) represents the majority of board certified cardiovascular physicians in the United States. Its mission is to advocate for quality cardiovascular care through education, research, promotion, development and application of standards and guidelines – and to influence health care policy. ACC.08 is the largest cardiovascular meeting, bringing together cardiologists and cardiovascular specialists to share the newest discoveries in the treatment and prevention, while helping the ACC achieve its mission to address and improve issues in cardiovascular medicine.