# Outcomes 'Terrible' After Stent Thrombosis

BY BRUCE JANCIN
*Denver Bureau*

VIENNA — Urgent percutaneous coronary intervention for stent thrombosis is a situation that comes up more frequently and leads to considerably worse outcomes than generally is appreciated, Dr. Francesco Burzotta said at the annual congress of the European Society of Cardiology.

He presented the results of the Outcome of PCI for Stent Thrombosis Multicentre Study (OPTIMIST), a prospective unfunded registry of all patients who underwent PCI for stent thrombosis at 11 Rome-area hospitals during 2005 and 2006.

OPTIMIST involved 110 patients who experienced 120 stent thromboses, making this the largest-ever single series of patients with angiographically defined stent thrombosis ever reported, according to Dr. Burzotta of Catholic University of the Sacred Heart, Rome.

Stent thrombosis accounted for 3.6% of all urgent PCIs performed for ST-elevation MI at participating hospitals during the study period, so it is not a rare event. And the frequency will increase as the number of stent procedures climbs worldwide, he observed.

Clinical outcomes were disappointing, despite state-of-the-art treatment, Dr. Burzotta said. Mortality was 12% at 30 days and 16% at 6 months. The combined rate of death, myocardial infarction, stroke, or a repeat interventional procedure was 29% at 6 months.

Of the 120 stent thromboses, 62 involved drug-eluting stents (DES); the rest involved bare-metal stents (BMS). The study was not designed to assess whether the thrombosis rate was higher with DES. However, OPTIMIST did show that the clinical circumstances in which thrombosis occurs tend to be different with DES, as compared with BMS.

Stent thrombosis within 15 days after discontinuing antiplatelet therapy was nearly eightfold more frequent with DES. And thrombosis involving DES was more likely to occur late: 33 cases of stent thrombosis occurred more than 1 month post DES implantation, compared with 14 cases with BMS.

"However, once thrombosis has occurred and the patient has been directed to the cath lab, the outcome after stent thrombosis and PCI isn't significantly affected by whether it's a drug-eluting or bare-metal stent," the cardiologist said.

**'Stent thrombosis ... is a malignant disease. One out of four patients die immediately, and the other three-quarters face an in-hospital mortality of 12%.'**

Of the 110 patients, 27 underwent PCI with thrombectomy, with the choice of thrombectomy device being left to the operator. Thrombectomy was safe when performed in the high-risk setting of stent thrombosis, with no increased risk of adverse effects observed.

There was a nonsignificant trend toward higher rates of excellent TIMI-3 grade coronary blood flow in patients who underwent thrombectomy; this trend became highly significant when patients in cardiogenic shock at the time of presentation with stent thrombosis were excluded.

In a multivariate analysis, two factors were independently associated with increased 6-month mortality. Stent thrombosis occurring more than 1 year post implantation was associated with a 10-fold increased risk, while implantation of another stent during PCI for stent thrombosis conferred a 5.4-fold increased risk of mortality.

Dr. Burzotta said these findings have practical implications for interventional cardiologists: Consider keeping patients on antiplatelet therapy indefinitely after stent placement in order to reduce the risk of late thromboses, and focus on reopening the occluded artery without implanting an additional stent in an effort to prevent restenosis.

Thrombectomy during urgent PCI for stent thrombosis appears to have merit in patients without cardiogenic shock, he added.

Dr. Freek W.A. Verheugt noted in an interview that one-quarter of patients who experience stent thrombosis never make it to the catheterization laboratory because they die immediately.

"The Italian study shows that stent thrombosis—whether with a bare-metal or drug-eluting stent—is a malignant disease. One out of four patients die immediately, and the other three-quarters face an in-hospital mortality of 12%. That's terrible. We haven't seen anything like that in many years," he said.

"That's like the in-hospital mortality in the placebo arm of the lytic trials 15 years ago," continued Dr. Verheugt, professor and chairman of cardiology at University Medical Center, Nijmegen, the Netherlands. ■



# Pioglitazone May Lower Risk of MI, Stroke

BY MARY ANN MOON
*Contributing Writer*

Pioglitazone appears to lower the risk of death, myocardial infarction, and stroke in diabetes patients, just the opposite of the closely related drug rosiglitazone, according to separate meta-analyses on the two agents.

It is not yet clear why these two thiazolidinediones may have such disparate effects on cardiovascular outcomes, the investigators said.

In one meta-analysis, Dr. A. Michael Lincoff and his associates at the Cleveland Clinic used data provided by Takeda Pharma, manufacturer of Actos, to assess pioglitazone's effect on the incidence of ischemic cardiovascular complications. They pooled data on 19 randomized, double-blinded, controlled clinical trials of the drug in 16,390 diabetes patients.

The investigators found that the composite outcome of death, myocardial infarction, or stroke was 18% lower in patients who took pioglitazone than in those who received placebo or other diabetes medications.

"The magnitude and direction of this protective effect ... was homogeneous across trials of different durations ranging from 4 months to 3.5 years, across studies using a variety of control or concomitant diabetic therapies, and among trials of patients with and without established vascular disease," Dr. Lincoff and his associates said (JAMA 2007;298:1180-8).

Like rosiglitazone, pioglitazone was found to raise the rate of congestive heart failure. However, it did not increase the incidence of heart failure mortality.

"These findings suggest that the net clinical cardiovascular benefit with pioglitazone therapy is favorable, with an important reduction in irreversible ischemic events that is not attenuated by the risk of more frequent heart failure complications," Dr. Lincoff and his associates said.

**The composite outcome of death, MI, or stroke was 18% lower in patients who took pioglitazone, compared with placebo or other diabetes medications.**

In contrast, Dr. Sonal Singh of Wake Forest University, Winston-Salem, N.C., and his associates found in their meta-analysis that rosiglitazone significantly raised the risk of both myocardial infarction and heart failure.

This led them to conclude that "regulatory agencies ought to reevaluate whether rosiglitazone should be allowed to remain on the market."

The researchers pooled the results of four randomized clinical trials of at least 1 year's duration (14,291 patients) and three systematic reviews to assess rosiglitazone's effect on MI, heart failure, and cardiovascular mortality.

The drug approximately doubled the risk of heart failure, and increased the risk of MI by 42%. However, it did not affect the risk of cardiovascular death.

"We estimate that there may be more than 3.5 million current users of rosiglitazone in the United States alone," which may account for 4,000 excess MIs and 9,000 excess heart failure events among Americans each year, the researchers wrote (JAMA 2007;298:1189-95).

In August, the U.S. Food and Drug Administration announced that the labels of all thiazolidinediones will now carry a black box warning about the risk of heart failure.

"Health plans and physicians should not wait for regulatory actions. They should avoid using rosiglitazone in patients with diabetes who are at risk of cardiovascular events, especially since safer treatment alternatives are available," Dr. Singh and his associates said. ■