



INNOVATION IN INTERVENTION

American College of Cardiology in co-sponsorship with SCAI

EMBARGOED FOR RELEASE
Monday, March 26, 2:30 PM CDT

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STUDIES HIGHLIGHT "REAL WORLD" USE, SAFETY OF DRUG-ELUTING STENTS

*Whether Patients Stick With Anti-Clotting Medications—And Are Naturally Responsive To Them—
May Be Key Factors In Preventing Dangerous Complications*

NEW ORLEANS, La (March 26, 2007) — Research presented today at the American College of Cardiology's *Innovation in Intervention: i2 Summit 2007* in New Orleans, La, paints a picture of the "real world" use of drug-eluting stents and offers new insight into the connection between blood clotting, or thrombosis, in the stent—a dangerous complication—and adherence and responsiveness to anti-clotting medication. *Innovation in Intervention: i2 Summit* is an annual meeting for practicing cardiovascular interventionalists sponsored by the American College of Cardiology in partnership with the Society for Cardiovascular Angiography and Interventions.

Long-Term Safety of Drug-Eluting Stents in Off-Label Use: Results of the MATRIX Registry (Presentation Number: 2414-6)

A large community-based registry is offering a wealth of information on the "real world" effectiveness and risks associated with long-term use of drug-eluting stents to treat a wide variety of patients with coronary artery disease—most of whom do not fit the strict profile used in clinical trials leading to device approval by the Food and Drug Administration.

"Complex patients come with complex lesions," said Dr. George Dangas, program director of interventional cardiology at Columbia University Medical Center, New York City. "The only way to test drug-

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2 – 2 – 2 "Real World" Use of Stents

eluting stents as physicians really use them is to include an unselected population, just as you would find in the community."

So far, the MATRIX Registry has enrolled more than 1,500 patients treated with the Cypher stent (Cordis, Johnson & Johnson), which slowly releases a coating of sirolimus into the artery wall to prevent overgrowth of scar tissue and renarrowing of the artery. Some 34 percent of patients in the registry have diabetes, 33 percent have a history of heart attack, and well over half have previously had a catheter-based intervention or bypass surgery to treat clogged coronary arteries. Approximately 80 percent of patients would not have qualified to participate in early device-approval clinical trials. Treatment of such patients with drug-eluting stents is considered "off label," but is both common in clinical practice and legal.

At one year, total mortality among patients enrolled in the MATRIX registry was 1.7 percent. Cardiac mortality was 0.8 percent. The rate of heart attack was 3.1 percent, and 7.3 percent of patients required catheter-based or surgical intervention to reopen the treated artery.

The registry is also shedding light on the importance of long-term anti-clotting medication in preventing a worrisome complication associated with drug-eluting stents: development of blood clots that block the stent long after implantation, or late stent thrombosis. Patients in the MATRIX registry were counseled to continue using clopidogrel (trade name, Plavix) for one year to prevent dangerous blood clots, though some found it difficult to do so. "We found that about one-third of patients were *not* taking Plavix at one year," Dr. Dangas said.

As a result, Dr. Dangas and colleagues have had the opportunity to analyze the relationship between discontinuation of anticlotting medication and the risk of late stent thrombosis—although the MATRIX study was not designed with the necessary statistical power to make a definitive statement about this complication, Dr. Dangas said.

Overall, 0.4 percent of patients developed stent thrombosis at one year, and another 0.3 percent of patients developed probable stent thrombosis. The combined rate of major adverse cardiac events (MACE) was 10.7 percent. Dr. Dangas will report results from specific subgroups of patients in New Orleans, as well as two-year clinical outcomes. The researchers are considering extending follow-up to five years in order to better assess long-term clinical outcomes.

Dr. Dangas will present results from the MATRIX Registry at a Late Breaking Clinical Trials session on Monday, March 26, at 2:15 p.m.

Low Responsiveness to Clopidogrel and Sirolimus- or Paclitaxel-Eluting Stent Thrombosis (RE-CLOSE) Trial

(Presentation Number: 2414-7)

Patients who do not respond to medication that inhibits the function of blood platelets face three times the risk of developing dangerous blood clots, or thrombosis, inside a drug-eluting stent when compared to patients who are responsive to the drug's effects. These findings suggest that faithful adherence to antiplatelet therapy with clopidogrel may not offer enough protection against late stent thrombosis.

"In most cases, inadequate platelet inhibition plays a key role in precipitating thrombosis," said Dr. David Antoniucci, head of cardiology at Careggi Hospital, Florence, Italy. "The RECLOSE trial is the first prospective clinical trial that has shown an increased risk of thrombosis in drug-eluting stents in patients who are nonresponders to clopidogrel."

The RECLOSE study recruited 804 patients who had had successful implantation of a drug-eluting stent and were taking antiplatelet medications as prescribed. After the patients were given a large dose of clopidogrel (600 mg), researchers took blood samples and tested whether the medication was effective in blocking platelet activity. To do this, they shined a light through the blood samples before and after adding a chemical that makes untreated platelets clump together. If 70 percent or more of the platelets clumped together despite the large clopidogrel dose, the patient was considered a nonresponder.

All patients then received double antiplatelet therapy with 325 mg aspirin and 75 mg clopidogrel for six months. During that time, Dr. Antoniucci and colleagues found that 8.6 percent of nonresponders experienced late stent thrombosis, as compared to 2.3 percent responders. After taking into account a variety of factors that might have influenced the results, the researchers found that a lack of response to clopidogrel tripled the risk of late stent thrombosis.

Dr. Antoniucci said that testing for clopidogrel responsiveness before stenting might have an important influence on the treatment plan. "Nonresponders might need alternative antiplatelet drugs or different dosages, or perhaps they should be treated with bare-metal stents or offered the opportunity for coronary bypass surgery," he said.

Dr. Antoniucci will present this study on Monday, March 26, at 2:30 p.m.

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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.07 and the i2 Summit 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.