Xience Stent Beat Taxus in 1-Year MACE Reduction

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WASHINGTON — The everolimus-eluting stent Xience V produced a clinically significant 43% reduction in major adverse cardiac events, compared with the paclitaxel-eluting Taxus at 1 year, Dr. Gregg W. Stone reported at the annual Transcatheter Cardiovascular Therapeutics conference, sponsored by the Cardiovascular Research Foundation.

That major secondary end point finding comes from Abbott Laboratory's 5-year SPIRIT III trial of 1002 patients randomized 2:1 to receive either the Xience V or the Taxus stents. This is the first time a drug-eluting stent system has shown a statistically significant improvement in event-free survival, compared with another FDA-approved drug-eluting stent in a pivotal randomized clinical trial, noted Dr. Stone of Columbia University and director of the Cardiovascular Research Foundation, New York.

The Xience V has been licensed in Europe and parts of Asia since 2006, and currently awaits approval from the Food and Drug Administration. Abbott anticipates its licensure in the first half of 2008, a company statement said.

Earlier this year at the American College of Cardiology meeting, Dr. Stone presented data showing that Xience produced a statistically significant reduction of 50%, compared with Taxus, in in-segment late loss, the primary end point of the SPIRIT III. Now, at 1 year, rates of target vessel failure (TVF) (cardiac death, MI, or ischemia-driven target vessel revascularization) were 8.3% with Xience versus 10.8% for Taxus, a 25% difference representing a nonsignificant trend in that major secondary end point.

However, the 43% difference between the two stents in major adverse cardiac events (MACE)—5.8% for Xience vs. 9.9% with Taxus—was highly significant, and, Dr. Stone believes, is more important than TVF in terms of analyzing the performance of the two stents. While the TVF includes factors such as side vessel branches and discordant lesions, the MACE outcome "is much more specific to stenting itself."

There were no differences in cardiac death (0.8% for Xience and 0.9% for Taxus) at 1 year, and MI rates—2.6% for Xience, 3.7% for Taxus—did not differ significantly. Ischemia-driven target lesion revascularization accounted for the majority of the MACE difference, with rates of 3.3% with Xience and 5.6% with Taxus, a "strong trend" difference of 41%. The 5.6% for Taxus "is a good number, but Xience was better," remarked Dr. Stone, who is a consultant for both Abbott Vascular and Taxus manufacturer Boston Scientific.

Thrombosis rates at 1 year were low in both groups, 0.8% for Xience and 0.6% for Taxus. No differences in thrombosis rates were seen when the figures were broken down according to those occurring at 30 days or sooner versus beyond 30 days.

Subgroup analyses of the 8-month late loss were consistent across most parameters, including the angiographic cohort of 501 patients, gender, single or dual vessel treated, and lesion length. One exception was by age, with the greatest reduction occurring in late loss among those aged at least 63 years, compared with those younger. "This was a significant difference. I don't know why," Dr. Stone commented.

Another somewhat surprising subgroup finding was that the Xience worked better in nondiabetics than in the diabetic population, the opposite of what has been seen in previous studies. There were, however, only 280 diabetics in SPIRIT III. "Again, you have to be cautious with subgroups," he remarked, "because the study wasn't powered to show those differences."

Indeed, the ongoing SPIRIT IV trial is designed to examine that issue. The single-blind, randomized, multicenter study will enroll 3,900 patients for the treatment of up to three de novo native coronary lesions. The primary end point is TVF at 270 days, and, like SPIRIT III, patients will be followed out to 5 years. "We'll be looking at subgroups," Dr. Stone said. ■

No Need for Pre-PCI 'Reload' in Patients Already on Clopidogrel

WASHINGTON — In patients who are on chronic clopidogrel therapy who are undergoing percutaneous coronary intervention, there is no benefit to clopidogrel loading before the procedure, Dr. Germano Di Sciascio said at a symposium sponsored by the Cardiovascular Research Foundation.

The data are the latest from the ARMYDA (Antiplatelet Therapy for Reduction of Myocardial Damage During Angioplasty) series of trials, conducted by Dr. Di Sciascio and his associates at Campus Bio-Medico University, Rome. This study, ARMYDA-4, examined the increasingly common clinical scenario of a patient who has been taking clopidogrel since undergoing a prior PCI and who now needs another procedure.

Previous data from a group in Munich had determined that further platelet inhibition could be achieved with a 600-mg pre-PCI clopidogrel "boost" in patients already on 75 mg/day of clopidogrel (Circulation 2004;110:1916-9), but that study did not show whether the effect translated to improved clinical outcomes. "The question is, Do we need to reload these patients or can we leave them alone?" said Dr. Di Sciascio, director of the department of cardiovascular sciences at the university.

In ARMYDA-4, 464 patients on clopidogrel for longer than 10 days who had either angina or non–ST-segment elevation acute coronary syndrome were randomized to receive either a 600-mg clopidogrel reload or placebo on top of the usual 75 mg before angiography, 4-8 hours before undergoing PCI.

Of the 360 patients who proceeded to PCI—180 in each arm—about one-third in both groups were diabetic and about 40% had non-STE ACS. About 40% were receiving drug-eluting stents, reflecting European practice patterns, he noted.

The composite primary end point of death, MI, or target vessel revascularization at 30 days was nearly identical between the two groups: MI was the only one that occurred (8% with clopidogrel reload vs. 7% with placebo). There were also no significant differences in the secondary end points of postprocedural increase of markers of myocardial injury above the upper limit of normal (27% of the reload group vs. 30% of the placebo group for creatine kinase-MB; 45% vs. 46%, respectively, for troponin-I) or post-PCI peak levels of markers of myocardial injury.

Occurrence of any vascular/bleeding complications, another secondary end point, was identical between the two groups: No major bleeding occurred, and only 4% in each arm had minor bleeding, he said.

"Point of care" evaluation of platelet reactivity, the fourth secondary end point, did show significant differences at the time of drug or placebo administration (173 vs. 166 platelet reaction units for clopidogrel and placebo, respectively), but the difference was no longer significant at the time of the procedure (217 vs. 199) and was essentially the same by 2 hours and again at 6 and 24 hours.

The use of such "bedside aggregometry" is an important feature of the ARMYDA studies, Dr. Di Sciascio believes. "We think it may be important to introduce aggregometry into the cath lab. This is the value of the study, in my opinion," he said at a press briefing held during the conference.

In a critical appraisal, Dr. Dominick J. Angiolillo noted that the results of the prior trial from Munich, which showed that reloading provided greater platelet inhibition, had led many interventionalists to adopt the practice, even though there was no evidence of improved clinical outcomes. Now, ARMYDA-4 has shown that "although there is no harm with a clopidogrel reloading—as there were no differences in bleeding rates—there was also no clinical benefit," noted Dr. Angiolillo, director of cardiovascular research at the University of Florida, Jacksonville. ■

In-Lab Clopidogrel May Be a Good Alternative to Preloading

Administration of 600 mg clopidogrel "in lab" at the time of percutaneous coronary intervention may be a safe and effective alternative to "preloading" patients before they undergo angiography, Dr. Di Sciascio said at the annual Transcatheter Cardiovascular Therapeutics conference.

That conclusion came from ARMYDA-5, conducted by Dr. Di Sciascio and his associates at Campus Bio-Medico University, Rome. ARMYDA-5 aimed to resolve a clinical conundrum: "Preloading" prior to angiography could increase the patient's risk for bleeding later during PCI, but "in-lab" loading at the time of the procedure might not provide adequate platelet inhibition.

"The in-lab strategy may obviate the need of preloading before knowing the patients' anatomy," said Dr. Di Sciascio.

In all, 438 clopidogrel-naive patients with either angina or non–ST-segment elevation acute coronary syndrome were randomized to receive 600 mg clopidogrel given either 4-8 hours prior to angiography (preload) or at the time of PCI (in lab). Following exclusion of about 20% of the patients for medical reasons, 174 in the preload group and 176 in the in-lab group proceeded to undergo PCI.

There were no significant differences in the 30-day primary composite end point of death, or target vessel revascularization. Only MI occurred (in 8% of the preload and 11% of the in-lab group). There were also no significant differences in the secondary end points of postprocedural markers of myocardial injury above the upper limit of normal, or in postprocedural peak levels of those markers.

The occurrence of bleeding—another secondary end point—also did not differ between preload and in-lab groups. Only minor bleeding occurred (in 4% of the preload and in 5% of the in-lab patients), Dr. Di Sciascio reported.

Point-of-care aggregometry measurements of platelet reactivity did differ significantly between the two groups at the time of PCI and again at 2 hours post procedure, but were no longer significantly different at 6 and 24 hours.

In a critical appraisal, Dr. Daniel I. Simon called ARMYDA-5 "a very important study that has a number of strengths." But its biggest weakness was a lack of adequate statistical power. An example of a better-powered study is ISAR-REACT-2, which compared abciximab before PCI with placebo in more than 2,000 patients and yielded event rates similar to those of ARMYDA-5, said Dr. Simon, chief of the division of cardiovascular medicine at Case Western Reserve University, Cleveland.