Sirolimus-Eluting Stents Edge Past Paclitaxel Stents

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ORLANDO, FLA. — Three more salvos were fired in the battle of competing drug-eluting coronary stents. When the smoke cleared and findings from the new head-to-head trials were reported at the annual meeting of the American College of Cardiology, the sirolimus-eluting stent, Cypher, had edged the paclitaxel stent, Taxus, in two studies, with the third and largest trial ending in a draw.

With the results from at least four head-to-head studies now reported (results from the fourth were reported in January), the sirolimus-eluting stent has shown some consistent advantages.

The biggest difference between the two types of stents was seen in a study with 1,012 patients who were randomized to treatment with either sirolimus- or paclitaxel-eluting stents at two Swiss university hospitals. The study, named SIRTAX, was completely funded by the hospitals and received no industry sponsorship, said Stephan Windecker, M.D., a cardiologist at the University Hospital in Bern.

The study randomized all comers who required coronary stenting. Slightly more than half of the patients had acute coronary syndrome, almost a quarter had triple-vessel disease, and about 20% had diabetes. About 8% had ostial lesions, another 8% had lesions at bifurcations, 35% had calcified lesions, 37% had lesions of moderate or excessive tortuosity, and 2% of lesions were in saphenous vein grafts.

All patients were treated with 75 mg clopidogrel daily for a year following stenting, and all received 100 mg aspirin daily indefinitely.

The study's primary end point was the combined incidence of cardiac death, myocardial infarction, or ischemia-driven target lesion revascularization (TLR) within 9 months of treatment. The rate of this end point was 6.2% in the 503 patients who received sirolimus-eluting stents and 10.8% in the 509 who received paclitaxel-eluting stents, a statistically significant difference.

This outcome was driven largely by the difference in the need for TLR: 4.8% in patients who received sirolimus-eluting stents and 8.3% in those who got paclitaxel-eluting stents, also a statistically significant difference. All of the secondary end points also favored the sirolimus-eluting stent, although some of these were not statistically significant.

The advantage in the primary, combined end point for the sirolimus-eluting stents was especially dramatic in patients with diabetes. In this subgroup, sirolimus-eluting stents were associated with a better than threefold reduction in events, compared with the paclitaxel-eluting stents. The advantage was half as large in patients without diabetes. The two groups had identical rates of stent thrombosis.

An even larger, higher-profile trial failed to show a clear advantage for either type of stent. The highly anticipated prospective randomized multicenter head-to-head comparison of the two stents, named REALITY, was done at 90 centers in Europe, Asia, South America, and Mexico (but not in the United States), enrolled 1,353 patients, and was sponsored by Cordis, the company that makes and markets the sirolimus-eluting coronary stent.

This study involved a more highly selected group of patients, excluding those with ostial lesions, recent MIs, total occlusions, and certain other high-risk conditions. But 28% of patients had diabetes. After stenting, all patients received 100 mg of aspirin indefinitely. Daily treatment with a thienopyridine (clopidogrel or ticlopidine) was used for at least 2 months in all patients who received sirolimus-eluting stents and for at least 6 months in all patients who got paclitaxel-eluting stents.

The study's primary end point was the rate of in-lesion binary restenosis at 8 months after stenting, as measured by angiography. This rate was 9.6% in the sirolimus-eluting stents and 11.1% in the paclitaxel-eluting stents, a difference that was not statistically significant, reported Marie-Claude Morice, M.D., a cardiologist at the Cardiovascular Institute in Paris.

Other important clinical end points also failed to show a statistically significant difference between the two stent types. The combined rate of major coronary end points—cardiac death, MI, and TLR, was 9.2% in the patients who received sirolimus-eluting stents and 10.6% in those who received paclitaxel-eluting stents. The difference in the revascularization rate only was even tighter: 5.0% in the sirolimus-eluting stent group and 5.4% in

those who got paclitaxel-eluting stents.

The only major differences between stent types in this study were in late in-stent lumen loss after 8 months, and in the rate of stent thrombosis during the first 30 days of treatment. Late loss averaged 0.1 mm with the sirolimus stents and 0.3 mm with the paclitaxel stents. Stent thrombosis occurred in 0.4% of patients who received sirolimus stents and in 1.8% of those who received paclitaxel stents. But the rate of stent thrombosis was not a prespecified end point for this study and a difference between the two stent types for this measure was unexpected. As a result, the clinical significance of this finding was unclear, Dr. Morice said.

The third set of study results presented at the meeting came from a single-center study with a total of 250 patients, all of whom had diabetes. Like the larger Swiss trial, this study, called ISAR-DIABETES, had no commercial funding and was sponsored solely by the German Heart Center in Munich.

This study had fewer exclusion criteria than the REALITY study. Exclusions were limited to patients with acute MI, left-main disease, in-stent restenosis, or an allergy to one of the study drugs.

The study's primary end point was the rate of in-segment, late lumen loss at 6-8 months after stenting, as measured by angiography. The average amount of late loss was 0.43 mm in patients who received sirolimus stents and 0.67 mm in those who got paclitaxel stents, a difference that was statistically significant, reported Adnan Kastrati, M.D., professor of cardiology at the German Heart Center.

Patients who received sirolimus stents also had significantly less angiographic restenosis than did those who got paclitaxel stents, 6.9% vs. 16.5%, respectively. But there were no statistically significant differences in clinical end points, including clinical restenosis and the rates of death and MI at 9 months after stenting.

Although the results from this third study showed differences only for angiographic end points, Dr. Kastrati said that he was convinced by the outcome. "The results will push us to select sirolimus-eluting stents for patients with diabetes," he said.

In January, results were reported from a fourth study by Dr. Kastrati and associates that compared the two stent types, in 200 patients with in-stent restenosis. In that study, patients who received sirolimus-eluting stents had significantly less clinical restenosis compared with the patients who received paclitaxel-eluting stents (JAMA 2005;293:165-71). ■