Cypher Beat Brachytherapy For In-Stent Restenosis

Target-vessel failure at 9 months was significantly lower with the sirolimus-eluting stent than with brachytherapy.

BY MITCHEL L. ZOLER
Philadelphia Bureau

DALLAS — Treatment of coronary artery in-stent restenosis with sirolimus-eluting stents cut the rate of target-vessel failure by more than 40%, compared with brachytherapy, in a study with 384 patients.

As of now, brachytherapy is the only treatment approved by the Food and Drug Administration for treating in-stent restenosis, Dr. David R. Holmes Jr. said at the annual scientific sessions of the American Heart Association. But in practice, brachytherapy has been largely abandoned, whereas drug-eluting stents have become widely used for many coronary-stenting applications.

At 9 months after treatment, the rate of the study's primary end point—target-vessel failure defined as death, myocardial infarction, or the need for target-vessel revascularization—was 12% in 259 patients who received a sirolimus-eluting stent (Cypher), compared with 22% in 125 patients treated with brachytherapy, a statistically significant difference, reported Dr. Holmes, professor of medicine at the Mayo Medical School in Rochester, Minn.

The study was sponsored by Cordis Corp., a division of Johnson & Johnson, which markets the sirolimus-eluting coronary stent. Dr. Holmes has not reported any financial relationships with Cordis or Johnson & Johnson.

The study enrolled patients during February 2003–July 2004 at 26 centers in the United States. The patients had in-stent restenosis in a native coronary artery that was 15-40 mm long and 2.5-3.5 mm in diameter. They were randomized in a 2:1 fashion, with more patients treated with sirolimus-eluting stents.

Several secondary end points were also measured. The rate of binary angiographic restenosis at 6 months after treatment was 20% in the sirolimus-eluting stent group and 30% in the brachytherapy group; the difference just missed statistical significance.

Other secondary measures that were significantly different between the two study groups included the rate of target-lesion revascularization after 9 months (9% with the sirolimus-eluting stent compared with 19% with brachytherapy), and the rate of target-vessel revascularization (11% in the stent group compared with 22% in the brachytherapy group). The average diameter stenosis in the analysis segment of the treated coronary artery 6 months after treatment was 32% in the sirolimus-eluting stent group and 41% in the brachytherapy group.

The advantages of the sirolimus-eluting stent over brachytherapy were seen regardless of whether patients had diabetes and regardless of gender. The benefit from the sirolimus-eluting stent compared with brachytherapy was greatest in medium-sized coronary arteries, compared with smaller benefits when the arteries were narrower or wider. ■

Dedicated Stent for Bifurcated Lesions Cuts Late Loss Rates

BY ALICIA AULT
Contributing Writer

WASHINGTON — A stent dedicated to difficult-to-treat bifurcated lesions appears to significantly reduce restenosis and in-stent late loss, according to results presented at a symposium sponsored by the Cardiovascular Research Foundation.

Dr. Eberhard Grube, chief of cardiology and angiology at the Siegburg (Germany) Heart Center, reported on the 6-month results of Axxess Plus, a registry designed to evaluate the safety and efficacy of the Axxess Plus stent in de novo coronary bifurcation lesions and to determine the best treatment strategy in branch vessels.

Axxess Plus is made from a self-expanding nickel-titanium (nitinol) alloy, which is coated with a bioabsorbable polylactic acid polymer that elutes biolimus A9, a sirolimus analogue. The device is manufactured by Devax Inc. (Irvine, Calif).

So far, the registry has enrolled 139 patients from 13 centers in the United States and abroad. Dr. Grube, principal investigator in the trial, reported on the first 125 patients. Data from Axxess Plus will be used to support applications for regulatory approval in Europe and the United States, according to Devax.

About 15%-20% of the 2.5 million percutaneous coronary interventions worldwide involve lesions at a bifurcation, but treating such lesions is extremely difficult, said Dr. Grube.

With Axxess Plus, the stent is implanted with the appropriate shape to treat the bifurcation, then more stents can be added as needed to cover the lesion, said Dr. Grube.

The registry accepts patients with any and all bifurcations. The primary end point is in-stent late loss at 6 months. With angiographic follow-up on 93% of the patients with Axxess Plus stents, the late loss was 0.11 mm, plus or minus 0.62 mm, compared with 0.46 mm, plus or minus 0.51 mm, for the control group of patients who had previously received an Axxess bare metal stent, a statistically significant difference.

Just over 5% of patients had binary restenosis in the parent vessel, as measured by qualitative coronary angiography, said Dr. Grube.

Patients with side branch involvement received no treatment, percutaneous transcatheter coronary angioplasty (PTCA), or a stent. The choice of procedure was left to the investigator's discretion, Dr. Grube said.

Across those three groups, the mean late loss was 0.24 mm for the 26 patients who received no treatment, 0.19 mm for the PTCA group (40 patients), and 0.21 mm for the stent group (70 patients).

The in-segment restenosis rate was 12% for the no treatment group, 25% for the PTCA group, and 7.9% for the Axxess Plus group. "The lesion success with PTCA was clearly lower than leaving it alone or using a stent," noted Dr. Grube. ■

Neurologic Complications of Carotid Stenting Are Unavoidable

BY KAREN M. DENTE, M.D.
Contributing Writer

NEW YORK — Although carotid angioplasty and stenting have emerged as treatment alternative to carotid artery stenosis, there are still unavoidable complications associated with the procedures.

Both embolization and hypotension during the carotid angioplasty and stenting (CAS) have been linked to neurologic injury, and the current standard remains carotid endarterectomy (CEA), said Dr. Peter H. Lin at the Veith symposium on vascular medicine sponsored by Montefiore Medical Center.

Stroke after CAS is assumed to be embolic. "Disruption of atherosclerotic plaque is a disadvantage with carotid stenting. There are eight times more embolizations seen with CAS than with CEA," said Dr. Lin of Baylor College of Medicine, Houston. "Neurologic deficit remains the most feared of all procedure-related complications."

Dr. Lin and colleagues conducted a study showing the significance of carotid plaque echomorphology in assessing the embolization risk during CAS. Results from a total of 234 CAS procedures performed in 213 patients with a mean stenosis of 85% showed that the incidence of embolization was increased with hypoechoic plaque. The researchers concluded that that neuroprotective devices should be used in such procedures.

At the session, Dr. Klaus D. Mathias agreed that embolic injury to the brain is the main problem associated with carotid stenting procedures. "Clinically silent embolic showers occur frequently during CAS. Any phase of stenting can produce emboli, which is not good for the brain. There is 3-5 times more embolic material released to the brain with unprotected carotid stenting than with surgery," said Dr. Mathias of the department of radiology at Klinikum Dortmund (Germany).

According to Dr. Mathias, filter protection is the preferred embolic protective device. A 60% reduction in complications from 3.5% to 1.5% has been reported in previous studies of neuroprotective filters. "The German PROCAS registry showed a 30%-60% reduction in neurologic events with protective filters, but we are still missing prospective trials," said Dr. Mathias.

Another feared periprocedural complication leading to neurologic injury is hypotension. "Hemodynamic changes are common events during CAS and CEA, occurring in up to 30% of patients," said Marc van Sambeek, Ph.D., head of the section of vascular surgery at University Hospital, Rotterdam (the Netherlands).

Hypotension, if sufficiently severe, may cause watershed infarction. Lesser degrees of hypotension may render an otherwise inconsequential microembolic shower very relevant if washout is impaired washout, and also lead to a reduction in adequate collateral blood flow to an ischemic territory in the brain.

Hemodynamic instability is well recognized in patients after endarterectomy, where postoperative hypertension has been known to be associated with stroke or death, and studies suggest that CEA is also associated with hypotension. CAS is being investigated as a promising alternative, but despite favorable results from initial series, hemodynamic instability may complicate this procedure," said Dr. Sambeek.

Hemodynamic instability can be caused by the triggering of baroreceptors of the carotid sinus, as well as the release of catecholamines. "Hemodynamic instability is greater during CAS than in CEA," said Dr. Sambeek. "Complications are clearly related to hypotension and bradycardia during the procedure."

In a study presented at the meeting, Dr. Sambeek and colleagues evaluated the patterns of adrenaline and noradrenaline release in CAS, compared with CEA. They found that patterns of catecholamine release were significantly different in patients undergoing CAS and CEA with much higher and more variable surges occurring in CEA patients.

"CAS should be performed with cerebral protection using filter devices," said Dr. Ron Fairman, chief of the division of vascular surgery at the Hospital of the University of Pennsylvania, Philadelphia, when asked to comment on this article."In our own series, we have experienced occasional hypotension requiring continuous pharmacologic support for 24-36 hours following CAS. Other troubling phenomenon include troponin "leaks" in association with hypotension, as well as symptoms of cerebral reperfusion which seem to occur with greater frequency than following CEA. Physicians should anticipate these events and be prepared to intervene in order to prevent cardiac and cerebral compromise" he concluded. ■