Everolimus Stent Shows Sustained Benefits

BY CHRISTINE KILGORE

FROM TRANSCATHETER CARDIOVASCULAR THERAPEUTICS 2010

WASHINGTON – The benefits seen 1 year after percutaneous coronary intervention with the everolimus-eluting Xience V stent compared with the paclitaxel-eluting Taxus stent were sustained at 2 years of follow-up in two very different types of randomized studies.

And in the case of stent thrombosis in particular, the benefits of the everolimus-eluting stent appear to have intensified at 2 years, investigators reported at the meeting.

The new 2-year findings from both the SPIRIT IV trial, a large study involving 66 U.S. sites, and the COMPARE trial, a small, single-center, "all-comers" trial in Europe, confirm the superiority of the everolimus-eluting stent in patients – except in patients with diabetes, the investigators and other discussants said.

In patients with diabetes, no significant differences in the risk of major adverse cardiac events (MACE) were observed with either stent in either trial at 1 or 2 years after PCI, a finding that led experts at the meeting to surmise that diabetic patients may fare equally well with both stents.

"We've seen this now in almost every trial" comparing these drug-eluting stents. "There is no difference in MACE rates," Dr. Gregg W. Stone of Columbia University College of Physicians and Surgeons, New York, said in a session announcing the new SPIRIT IV findings.

"In my mind, this lack of benefit [to the Xience V stent] in diabetics means without any doubt that there's a difference in the mechanistic response of diabetics versus nondiabetics … to these types of drugs," he said. Dr. Stone is principal investigator for Spirit IV and codirector of medical research and education at the Cardiovascular Research Foundation, which sponsored the TCT meeting.

The 3,687 patients in the industry-sponsored SPIRIT IV trial, including 1,185 with diabetes, were randomized in 2:1 fashion to receive either the everolimus-eluting Xience V stent (Abbott Vascular) or the first-generation paclitaxel-eluting Taxus Express stent (Boston Scientific). The patients had up to three untreated coronary artery lesions that were as long as 28 mm, in vessels with a diameter of 2.5-3.75 mm.

The lack of benefit of the Xience V stent in diabetics means there is a difference in their mechanistic response.

DR. STONE

At 2 years, treatment with Xience V resulted in a relative 30% reduction (and a 3% absolute decline) in target lesion failure compared with treatment with the Taxus stent, with target lesion failure occurring in about 6.9% and 9.9% of the patients, respectively. (The rates of this primary end point after 1 year were 4.0% and 6.9%, respectively.)

The relative reduction in target lesion failure was 39% in patients without diabetes, but in diabetic patients there was little difference between the two groups. Target lesion failure is a composite end point reflecting cardiac death, target-vessel myocardial infarction, or ischemia-driven target lesion revascularization.

Ischemia-driven target lesion revascularization, a secondary end point, occurred at a rate of 4.5% at 2 years in the Xience group, compared with 6.9% in the Taxus group, for an absolute reduction of 2.4% and a relative reduction of 34%. The rates of this secondary outcome after 1 year were 2.4% compared with 4.6%.

While there were no mortality differences, target-vessel MI also occurred at a significantly reduced rate in the Xience group at both 1 and 2 years (2.3% v. 3.5% at 2 years), said Dr. Stone.

The rates in stent thrombosis in both studies, in fact, drew significant attention at the meeting. At 2 years after intervention in SPIRIT IV, 1.2% in the Taxus group had developed definite/probable stent thrombosis according to definitions of the Academic Research Consortium (ARC), compared with 0.4% in the Xience arm.

This translates into a 64% relative risk reduction for stent thrombosis (a 0.8% absolute reduction) that occurred during each period – early (the first 30 days), late (31 days to 1 year) and very late period (over 1 year).

The 2-year reductions in stent thrombosis reported from the COMPARE trial were even more striking, discussants said at the meeting.

In this trial, 1,800 consecutive patients undergoing PCI at one center in Rotterdam, the Netherlands, were randomly assigned in 1:1 fashion to treatment with the Xience V stent or the Taxus Liberté stent, a second-generation paclitaxel-eluting stent.

(The Taxus Express stent used in SPIRIT IV is no longer commercially available, according to a spokesperson for Boston Scientific. The Taxus Liberté stent, which uses the same polymer but a different stent platform, is currently available in the United States and in Europe, he said.)

The rate of definite/probable stent thrombosis (again, by ARC definition) at 2 years in the COMPARE trial was 0.9% in the Xience V group and 3.9% in the Taxus group – higher rates than found in SPIRIT IV. Most notable, however, was a 77% reduction in very late definite/probable stent thrombosis in the Xience V arm. The rate of this outcome was 0.3% in the Xience V group and 1.5% in the Taxus Liberté group, reported Dr. Peter Smits of Maasstad Ziekenhuis.

This difference is especially notable because the vast majority of patients were no longer taking dual antiplatelet therapy at 2 years, said Dr. Smits, principal investigator of COMPARE. In contrast, more than 70% of patients in each arm of the SPIRIT IV trial remained on dual antiplatelet therapy at 2 years.

Unlike the SPIRIT design, the COMPARE trial was designed to be an "all-comer, real-world study" without exclusions for complex patients. At 2 years, the superiority of the Xience V stent for the primary end point – a composite of all mortality, nonfatal MI, and target vessel revascularization (MACE) – was maintained, with larger absolute differences between the stents than at 12 months.

At 1 year, this primary end point had occurred in 6.2% and 9.1% in the Xience V and Taxus groups, respectively, for an absolute difference of 2.9%. At 2 years, these rates rose to 9.0% and 13.7%, for an absolute difference of 4.7%. There were similar reductions in secondary end points. As in SPIRIT IV, there were no benefits of the Xience V stent for diabetic patients.

Both studies are still ongoing and will conclude with 5-year analyses. ■

VITALS

Major Finding: At 2 years, treatment with the everolimus-eluting Xience V stent rather than the paclitaxel-eluting Taxus stent resulted in a 30% relative reduction in target lesion failure, a 34% relative reduction in ischemia-driven target lesion revascularization, and a 64% relative reduction in stent thrombosis. Between 1 and 2 years in the COMPARE trial, there was a 77% reduction in very late definite or probable stent thrombosis in favor of Xience V.

Data Source: SPIRIT IV: a randomized prospective study of 3,687 patients treated at 66 U.S. medical centers. COMPARE: a randomized single-center trial of 1,800 patients.

Disclosures: The SPIRIT IV trial is sponsored by Abbott Vascular; the COMPARE trial is funded by Abbott Vascular and Boston Scientific. Dr. Stone disclosed that he sits on the advisory boards for, and receives honoraria from, Abbott Vascular and Boston Scientific. Dr. Smits disclosed that he received a speaking fee from Abbott Vascular and that his cardiology department has received unrestricted research grants from Abbott Vascular and Boston Scientific.

Stent Thrombosis Occurs More Often in Black Patients

BY HEIDI SPLETE

FROM CIRCULATION

Black patients who received drug-eluting stents were significantly more likely to develop stent thrombosis compared with nonblack patients, based on data from more than 7,000 adults.

To determine the incidence of early, late, and very late stent thrombosis (ST) in black patients compared with nonblack patients, Dr. Sara D. Collins and her colleagues at the Washington (D.C.) Hospital Center reviewed data from 7,236 adults who underwent percutaneous coronary intervention at a single hospital from April 2003 through December 2008.

The study group included 1,594 black patients and 5,642 nonblack patients (Circulation 2010 Aug. 30 [doi:10.1161/CIRCULATIONAHA.109.907998]).

For all patients, the incidence of early ST at 30 days was 0.83%. The cumulative incidence of late ST was 0.24% per year between 30 days and 1 year, which rose to 0.36% per year between 1 and 2 years.

The rates of ST were more than twice as high in blacks vs. nonblacks across all time points. At 30 days, the rate of ST in blacks vs. nonblacks was 1.71% vs. 0.59%. At 1 year, 2 years, and 3 years, the ST rates in blacks were 2.25%, 2.78%, and 3.67%, respectively. In nonblacks, the ST rates were 0.79%, 1.09%, and 1.25%, respectively.

In a multivariate analysis, black race was the strongest significant independent predictor of ST more than 30 days after PCI, and it was a significant predictor of early ST at 30 days.

"Black race is an independent predictor of ST even when accounting for potential confounders such as socioeconomic status and comorbidities," the researchers said.

Black patients were more likely than nonblack patients to be taking clopidogrel at the time of the ST (88% vs. 78%), but the difference was not significant.

In a univariate analysis, black patients were significantly more likely than nonblack patients to have a history of hypertension, chronic renal insufficiency, diabetes, and heart failure. Black patients were significantly younger than nonblack patients (average age, 63 years vs. 65 years), and the median household income was significantly lower for black patients, the researchers noted.

The results support data from previous studies suggesting that black patients are more likely to experience ST, but this study is the first to control for variables typically associated with racial disparities in health care, the investigators noted.

"Because our analysis adjusts for traditional variables associated with racial disparities in health care, further mechanisms such as genetic polymorphisms and responsiveness to antiplatelet therapy must be pursued," they said. ■