Randomized Study to Evaluate Sirolimus-Eluting Stents Implanted at Coronary Bifurcation Lesions

Antonio Colombo, MD; Jeffrey W. Moses, MD; Marie Claude Morice, MD; Josef Ludwig, MD; David R. Holmes, Jr, MD; Vassilis Spanos, MD; Yves Louvard, MD; Benny Desmedt; Carlo Di Mario, MD; Martin B. Leon, MD

Background—A sirolimus-eluting stent (Cypher, Cordis Corp) has been reported to markedly decrease restenosis in selected lesions; higher-risk lesions, including coronary bifurcations, have not been studied.

Methods and Results—This prospective study evaluated the safety and efficacy of sirolimus-eluting stents for treatment of coronary bifurcation lesions. Patients were randomly assigned to either stenting of both branches (group A) or stenting of the main branch with provisional stenting of the side branch (SB) (group B). Eighty-five patients (86 lesions) were enrolled. There was 1 case of unsuccessful delivery of any device at the bifurcation site. Given the high crossover, more lesions were treated with 2 stents (n=63) than with stent/balloon (n=22). Clinical follow-up at 6 months was completed in all patients and angiographic follow-up in 53 patients in group A (85.5%) and 21 in group B (95.4%). One patient died suddenly 4.5 months after the procedure. There were 3 cases of stent thrombosis (3.5%). The total restenosis rate at 6 months was 25.7%, and it was not significantly different between the double-stenting (28.0%) and the provisional SB-stenting (18.7%) groups. Fourteen of the restenosis cases occurred at the ostium of the SB and were focal. Target lesion revascularization was performed in 7 cases; target vessel failure occurred in 15 cases (17.6%).

Conclusions—These results are an improvement compared with historical controls using bare metal stents. Restenosis at the SB remains a problem. At this time, no statement can be made regarding the most appropriate technique to use when treating bifurcations with the Cypher stent. (Circulation. 2004;109:1244-1249.)

Key Words: stents ■ drugs ■ restenosis

Lesions at coronary bifurcations represent a challenging area in interventional cardiology. Early results using balloon angioplasty alone to treat bifurcation lesions demonstrated relatively low angiographic and clinical success rates and high restenosis.1 Although the introduction of coronary stents resulted in more predictable results and higher success rates, angiographic restenosis rates remain high, despite the use of different approaches.2–5 Specifically, the use of bare metal stents for both branches has not improved the results.5,6

The sirolimus-eluting Bx Velocity balloon-expandable stent (Cypher stent, Cordis Corp, a Johnson & Johnson Company) has been reported to remarkably reduce restenosis after implantation in selected lesions, but bifurcation lesions were excluded.7–9 This study was performed to evaluate this stent in coronary bifurcations using 2 different strategies.

Methods

The trial was conducted in 5 centers. The ethics committee at each participating institution approved the protocols, and all patients gave written informed consent.

Patient Selection

This study included male or nonpregnant female patients ≥18 years of age with a diagnosis of stable or unstable angina (Braunwald classification B and C, I–II) or silent ischemia. Additional eligibility criteria were the presence of a de novo, true coronary bifurcation lesion, defined as stenosis >50% in both the main branch (MB) and the ostium of the side branch (SB). Both branches needed to have at least TIMI I flow and a reference vessel size ≥2.5 mm and ≤3.5 mm in diameter, with a maximum treatable length ≤24 mm by visual estimation. Patients were excluded if 1 of the following was present: a myocardial infarction (MI) in the 24 hours preceding treatment, stenosis of the left main coronary artery unprotected by a graft, angiographically visible thrombus within the target lesion, left ventricular ejection fraction ≤35%, serum creatinine ≥3.0 mg/dL, or suspected intolerance to one of the study drugs.

Procedure

Randomization was performed with sealed envelopes assigning patients to 1 of 2 different treatment strategies: stenting of both branches with Cypher stents (Stent/Stent, group A) or Cypher stent implantation in the MB with balloon angioplasty (PTCA) for the SB (Stent/PTCA, group B). Crossovers to group A were allowed if balloon dilatation of the SB led to a suboptimal result.

Lesions were excluded if they met the following criteria: the presence of a de novo, true coronary bifurcation lesion, defined as stenosis >50% in both the main branch (MB) and the ostium of the side branch (SB). Both branches needed to have at least TIMI I flow and a reference vessel size ≥2.5 mm and ≤3.5 mm in diameter, with a maximum treatable length ≤24 mm by visual estimation. Patients were excluded if 1 of the following was present: a myocardial infarction (MI) in the 24 hours preceding treatment, stenosis of the left main coronary artery unprotected by a graft, angiographically visible thrombus within the target lesion, left ventricular ejection fraction ≤35%, serum creatinine ≥3.0 mg/dL, or suspected intolerance to one of the study drugs.

Procedure

Randomization was performed with sealed envelopes assigning patients to 1 of 2 different treatment strategies: stenting of both branches with Cypher stents (Stent/Stent, group A) or Cypher stent implantation in the MB with balloon angioplasty (PTCA) for the SB (Stent/PTCA, group B). Crossovers to group A were allowed if balloon dilatation of the SB led to a suboptimal result.

Received July 11, 2003; de novo received September 24, 2003; revision received December 8, 2003; accepted December 10, 2003.

From EMO Centro Cuore Columbus, Milan, Italy (A.C., C.D.M.); Lenox Hill Hospital, New York, NY (J.W.M., M.B.L.); Institut Cardiovasculaire Paris Sud, Massy, France (M.C.M., Y.L.); University Heart Center Erlangen, Germany (J.L.); Mayo Clinic, Rochester, Minn (D.R.H.); Milan Cardiovascular Research, Milan, Italy (V.S.); and Cordis Corp, Waterloo, Brussels (B.D.).

Dr Moses has served as a consultant to and owns common stock in Johnson & Johnson.

Correspondence to Antonio Colombo, MD, Centro Cuore Columbus, Via M. Buonarroti 48, 20145 Milan, Italy. E-mail info@emocolumbus.it

© 2004 American Heart Association, Inc.

Circulation is available at http://www.circulationaha.org DOI: 10.1161/01.CIR.0000118474.71662.E3

1244
Aspirin 325 mg 12 hours before the procedure and a 300-mg loading dose of clopidogrel before the procedure were administered unless patients had already been pretreated. Percutaneous access was obtained, and intravenous heparin was administered to maintain an activated clotting time >250 seconds during the procedure. Administration of glycoprotein IIb/IIIa inhibitors was left to the operator’s discretion. Lesion predilatation and final kissing balloon inflation were recommended in all patients. In case of dissection and need for additional stenting, sirolimus-eluting stents were the first choice. With regard to the stenting technique to be used to treat the SB in the Stent/Stent group, the operators were free to use the approach that they considered the best, with the suggestion not to use the “colute” technique because of the closed stent design of the Cypher and of uncertainty related to double drug dosing.

Aspirin was continued indefinitely after the procedure. Clopidogrel 75 mg/d (alternatively, ticlopidine 250 mg BID) was continued for 3 months.

Follow-Up
Clinical patient evaluation was performed at 30 days and at 6 months. Follow-up coronary angiography was planned 6 months after the procedure unless necessary for clinical reasons at an earlier time. Angiograms performed after 4 months from the index procedure were considered as a surrogate for the 6-month follow-up angiograms.

Quantitative Coronary Angiographic Evaluation
Quantitative angiographic parameters were calculated for the target lesion before and after the procedure and at the time of angiographic follow-up using dedicated software (QCA-CMS 5.1, Medis). At follow-up, all parameters were calculated for the 5 mm proximal and distal to the stented segment as well. In-stent restenosis was defined as diameter stenosis (DS) ≥50% within the stented segment. In-segment restenosis was defined as DS ≥50% either within the stented segment or within the 5 mm proximal or distal to the stent edges. In-stent late luminal loss was defined as the difference between the minimal luminal diameter immediately after the procedure and the minimal luminal diameter at 6 months.

Intravascular Ultrasound Performance
Intravascular ultrasound (IVUS) assessment of all treated vessels was performed immediately after the procedure and at the time of follow-up angiogram. All IVUS recordings were made with an automated pullback speed of 0.5 mm/s, aiming to start at least 1 cm distal and to end at least 1 cm proximal to the stent. The main reason to perform IVUS was to document the result.

Study End Points
The primary study end point was binary in-segment restenosis of both the MB and SB (stented or not stented) evaluated at the follow-up angiogram. Because this study was designed to assess the performance of the device, we analyzed the results according to the actual treatment received and not by the intention to treat.

Angiographic success was defined as achievement of <50% residual stenosis by any percutaneous method. Procedural success was defined as angiographic success without the occurrence of death, Q-wave MI, or repeat revascularization of the target lesion during hospital stay. Target lesion revascularization (TLR) and target vessel revascularization (TVR) were defined as repeat revascularization driven by symptoms or laboratory testing and a stenosis ≥50% within the treated vessel on follow-up angiography. Target vessel failure (TVF) was defined as presence of cardiac death, Q-wave or non-Q-wave MI, or TVR.

Stent thrombosis was defined as any of the following: angiographic demonstration of stent closure or intrastent thrombus, unexplained sudden death, or MI occurring within 30 days of stent implantation and without concomitant documentation of a patent stent.

Statistical Analysis
This study was a pilot evaluation of the Cypher stent in lesions without any previous experience with this device in these lesions. For this reason, no definite sample size could be formally calculated to establish a powered analysis to compare the 2 techniques. The Steering Committee felt that an initial evaluation performed on 86 lesions could be adequate to provide valuable information to be used to plan future studies.

Comparisons for continuous variables were performed with Student’s t test and nonparametric Mann-Whitney U test. Analyses of discrete variables were performed with Fisher’s exact test and χ² test, with implementation of Yates correction when applicable. The occurrence of adverse events during the follow-up period was analyzed by the Kaplan-Meier method. The differences between event-free survival curves were compared by the log-rank test. Because of the high crossover rate from the Stent/PTCA to the Stent/Stent groups, the analysis was performed according to the actual treatment instituted.

Results
Between June 2001 and April 2002, 85 patients with 86 bifurcation lesions were enrolled in the study and assigned to either double stenting (group A, n=43) or Stent/PTCA (group B, n=43). Sixty-one cases involved the left anterior descending/diagonal bifurcation, 15 the left circumflex/obtuse marginal, and 5 the distal right coronary artery/posterior descending right coronary artery; there were also 2 bifurcations of a diagonal branch and a small SB, 2 right coronary artery/right ventricular branches, and 1 bifurcation of the left anterior descending coronary artery with a large septal branch. There were 22 patients who crossed over from group B to group A (51.2%) and 2 patients who crossed over from group A to

<table>
<thead>
<tr>
<th>TABLE 1. Patient Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Diabetics</td>
</tr>
<tr>
<td>Multivessel disease</td>
</tr>
<tr>
<td>Unstable angina</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
</tr>
</tbody>
</table>

Values are n (%) or mean±SD.

<table>
<thead>
<tr>
<th>TABLE 2. Procedural Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>MB</td>
</tr>
<tr>
<td>Balloon size, mm</td>
</tr>
<tr>
<td>Balloon/artery ratio</td>
</tr>
<tr>
<td>Maximal inflation pressure, atm</td>
</tr>
<tr>
<td>SB</td>
</tr>
<tr>
<td>Balloon size, mm</td>
</tr>
<tr>
<td>Balloon/artery ratio</td>
</tr>
<tr>
<td>Maximal inflation pressure, atm</td>
</tr>
<tr>
<td>Kissing balloon inflation</td>
</tr>
<tr>
<td>Use of IIb/IIIa inhibitors</td>
</tr>
</tbody>
</table>

Values are n (%) or mean±SD.
TABLE 3. Serial Intrastent QCA Measurements for the MB

<table>
<thead>
<tr>
<th>Parameters Measured</th>
<th>Stent/Stent</th>
<th>Stent/PTCA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre (n=63)</td>
<td>Post (n=63)</td>
</tr>
<tr>
<td>RVD, mm</td>
<td>2.6±0.4</td>
<td>3.0±0.4</td>
</tr>
<tr>
<td>MLD, mm</td>
<td>0.99±0.35</td>
<td>2.66±0.40</td>
</tr>
<tr>
<td>DS, %</td>
<td>61.7±12.5</td>
<td>11.5±7.7</td>
</tr>
<tr>
<td>Length, mm</td>
<td>10.8±4.8</td>
<td>...</td>
</tr>
</tbody>
</table>

Pre indicates preprocedure; post, postprocedure; FU, at follow-up; and RVD, reference vessel diameter.

P=NS for all comparisons (between Stent/Stent and Stent/PTCA groups).

Procedural Characteristics

When the results are evaluated according to the actual treatment implemented, lesion angiographic success was attained in 59 cases in the Stent/Stent group (93.6%) and 17 cases in Stent/PTCA group (77.3%) and procedural success in 58 (92.2%) and 17 (77.3%) cases, respectively. All cases without angiographic success were because of residual stenosis ≥50% in the SB.

The T-stenting technique was used in all but 3 cases of stent implantation in both branches; there were 1 case of V and 2 cases of Y stenting. Modified T stenting was used in 40 cases (63.5%), with simultaneous insertion and sequential delivery of the 2 stents in 36 cases (57.1%). Maximal inflation pressure was higher for the SB in the Stent/Stent group than the stent/PTCA group (13.3±3.6 atm versus 9.1±2.7 atm, P<0.001). There were no other significant differences in the procedural characteristics between the 2 groups (Table 2).

Quantitative Angiographic Analysis

Angiographic follow-up was performed for 53 patients in the Stent/Stent and 21 patients in the Stent/PTCA group (84.1% and 95.4% of patients, respectively, P=0.27). Serial quantitative coronary angiographic measurements for MB and SB are reported in Tables 3 and 4. The mean reference vessel diameter was 2.6 mm for the MB and 2.1 mm for the SB at baseline. SBs treated with PTCA had higher minimal lumen diameter (MLD) and lower DS at baseline compared with SBs treated with stent (P=0.02, Table 4). Postprocedural MLD was higher and DS was lower in the SBs treated with stenting; these differences disappeared at 6 months (Table 4). In-stent late luminal loss for the MB was 0.28±0.47 mm in the Stent/Stent and 0.14±0.25 mm in the Stent/PTCA group (P=0.19). Late luminal loss in the SB was 0.50±0.61 mm in the double-stenting and 0.37±0.48 mm in the Stent/PTCA group (P=0.41).

Angiographic Restenosis

There were 14 cases of focal restenosis at the ostium of the SB, 11 in the double-stenting, and 3 in the Stent/PTCA group and 1 case with total occlusion distal to the stent implanted in the SB. There were also 4 cases of in-segment restenosis in the MB (6.1%): 1 inside the stent, 2 proximal, and 1 distal to the stent. The total in-segment restenosis rate per lesion (in-segment restenosis of either the SB or the MB or both) was 25.7% (17 of 66 cases with angiographic success and angiographic follow-up). Fourteen of these cases were observed in the Stent/Stent (28%) and 3 in the Stent/PTCA group (18.7%, P=0.53). A typical example of restenosis at the ostium of an SB is shown in Figure 1.

IVUS Insights in the Restenosis Cases

In the 4 cases of restenosis in the MB, only 1 was intrastent. This was the case of an underexpanded stent, without evidence of development of neointimal hyperplasia inside the stent during IVUS interrogation. At the tightest point, corresponding to the site of angiographic restenosis (51.6% by...
quantitative coronary angiography), the stent cross-sectional area was equivalent to the lumen cross-sectional area (3.2 mm², Figure 2).

In the 11 cases of SB restenosis initially treated with stent placement, advancement of an IVUS catheter at follow-up has been performed in 4. Three of these examinations were suggestive of incomplete coverage of the ostium by the stent struts. In all cases, there was evidence of focal neointimal hyperplasia development at the ostium extending inside the proximal edge of the SB stent.

**Adverse Events**

Clinical follow-up was completed for all patients at a mean time of 6.4 months. One patient died suddenly 4.5 months after the procedure. There were 3 cases of stent thrombosis (3.5%), occurring 1, 3, and 32 days after the procedure and affecting the SB in 2 of them and both branches in the other one. All 3 patients with thrombotic events and the patient with sudden death had stenting performed on both branches. In the first case, a diagonal branch occluded, resulting in non-Q-wave MI; no further action was taken. In the other 2 cases, a repeat procedure was performed (TLR). Angina, class I–III according to the Canadian Cardiovascular Society Classification of Angina, was present in 17 patients in the Stent/Stent (27.4%) and 3 patients in the Stent/PTCA (13.6%, P=0.25) group. There were 7 cases of TLR (8.2%) and 15 cases of TVF (17.6%) for the entire patient group. All cases of vessel revascularization during follow-up were performed in the presence of ischemic symptoms or signs. Major adverse cardiac events in hospital and at 6 months are presented in Table 5. The event-free survival curves for both treatment groups are shown in Figure 3.

**Discussion**

The most important findings in this study are as follows: (1) use of the Cypher stent in bifurcation lesions leads to a low restenosis rate in the MB, (2) angioplasty at the ostium of the SB frequently results in high residual stenosis leading to implantation of an additional stent, (3) follow-up restenosis rates on the SB are relatively high when an additional Cypher stent is implanted, and (4) the 3.5% risk of stent thrombosis reported in this study is higher than previous experiences with the Cypher stent used in less complex lesions.

The low incidence of restenosis observed in the MB is offset by the 19% TVF and the 4.7% incidence of thrombosis and sudden death (4/85) in the Stent/Stent group. When we examine the group of patients treated with stenting only in the MB, the absence of any thrombotic event or death and the 13.6% TVF may lead us to assume that this strategy may be superior to double stenting. We would like to caution about
this interpretation, which suffers from the fact that the group of patients who ultimately received only a stent in the MB may represent the ones with more favorable lesions, whereas the Stent/Stent group was ultimately penalized by the crossovers.

The 51.2% (22/43) crossover rate is very high but represents what was thought to be necessary to obtain an acceptable angiographic result. This statement is further supported by the fact that despite liberal usage of double stenting, the group of patients treated with Stent/PTCA had a final angiographic success of only 77.3%. A more stringent crossover policy would unacceptably lower the rate of angiographic success.

Comparison With Historical Controls

Restenosis and event rates have been relatively high after treatment of bifurcation lesions with bare metal stents. The data available are from studies without planned angiographic follow-up. Event rates of 26.8% have been reported for the Stent/PTCA group and 47.7% for the double-stenting group in a series of 131 bifurcation lesions treated in 1 center. An in-hospital complication rate of 13% with double stenting versus 0% with Stent/PTCA was reported from another study in 92 patients that used bare metal stents. The angiographic restenosis rates per lesion were 48.1% (Stent/PTCA) and 61.6% (Stent/Stent); the respective restenosis rates for the MB were 33.3% and 38.5% and for the SB 33.3% and 51.3% (Stent/PTCA and Stent/Stent groups, respectively). The event rates at 6-month follow-up were 38% (Stent/PTCA) and 51% (Stent/Stent).

Restenosis in the Study

One point to be considered is the reference vessel size of the arteries treated in this study. The mean value of 2.6 mm for the MB and 2.1 mm for the SB clearly indicate that in addition to being a study of bifurcation lesions, this experience also evaluated Cypher stenting in quite small vessels when evaluated by angiography.

The in-segment restenosis rates for the MB (6.1%) are similar to the results reported from the SIRIUS trial (a US multicenter, randomized, double-blind study of the sirolimus-eluting stents in de novo native coronary lesions). It is also important to consider that the late loss in the MB was 2 times greater when double stenting was applied than with single stenting. It is possible that the tissue growth that occurred in cases of restenosis on the SB contributed to this result. We

<table>
<thead>
<tr>
<th></th>
<th>In-Hospital</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0 (0)</td>
<td>1 (1.6)</td>
<td>0</td>
</tr>
<tr>
<td>Q-wave MI</td>
<td>0 (0)</td>
<td>1 (4.5)</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Non-Q-wave MI</td>
<td>6 (9.5)</td>
<td>1 (4.5)</td>
<td>6 (9.5)</td>
</tr>
<tr>
<td>MB restenosis*</td>
<td>...</td>
<td>...</td>
<td>3/53 (5.7)</td>
</tr>
<tr>
<td>SB restenosis*</td>
<td>...</td>
<td>...</td>
<td>12/55 (21.8)</td>
</tr>
<tr>
<td>Re-PTCA, TLR</td>
<td>1 (1.6)</td>
<td>0</td>
<td>6 (9.5)</td>
</tr>
<tr>
<td>Bypass</td>
<td>0 (0)</td>
<td>0</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Re-PTCA, TVR</td>
<td>0</td>
<td>1 (4.3)</td>
<td>7 (11.1)</td>
</tr>
<tr>
<td>TVF</td>
<td>6 (9.5)</td>
<td>2 (9.1)</td>
<td>12 (19.0)</td>
</tr>
</tbody>
</table>

Values are n (%).

*In-segment restenosis: calculated for all lesions with angiographic follow-up.

P=NS for all comparisons.

Figure 3. Kaplan-Meier survival estimates free of TVF at 6 months according to treatment.
should also consider that the late loss in the Stent/PTCA group is calculated on only 21 lesions.

Regarding the cases of restenosis occurring at the SB, it is intriguing to notice that most of these restenoses occurred at the ostium of the SB, a location that can easily be left without strut coverage with the techniques used in this study. The angiographic and IVUS data so far available are not sufficient or conclusive to fully support this hypothesis.

The low rate of TLR (7 of 17 cases with restenosis) reflects the small clinical importance of many cases of restenosis that occurred in SBs with a small reference size.

**Stenting Technique**

The current practice of stenting only the MB is supported by lack of effective alternate solutions. It may be reasonable to assume that the low success by the angiographic core laboratory may not be clinically important when dealing with small SBs. This concept is different when dealing with bifurcations with a large SB, for which an angiographic success may become clinically relevant. On the basis of the results of this study, we can state that a discrentional strategy of SB stenting seems advisable.

When it is necessary to stent the SB and given the potential contribution of incomplete coverage of the ostium of the SB in restenosis development, a technique capable of ensuring full coverage of the ostium is needed whenever the 2-stent approach is used. The “culotte” technique could provide an answer, but it was not used in this study. The T-stenting and modified T-stenting techniques cannot guarantee full ostium coverage, especially in cases with a narrow bifurcation angle. New techniques for double stenting, like the recently described modified T-stenting technique with “crushing,”11 may overcome this limitation and hold promise for future deployment of sirolimus-eluting stents to coronary bifurcations.

**Thrombotic Events**

The occurrence of 3.5% of thrombotic events, increasing to 4.6% if we include the patient with sudden death and up to 6.3% if we consider only the Stent/Stent group in which these events occurred, is of concern. All 3 episodes of thrombosis occurred in patients taking double antiplatelet therapy, including the patient with sudden death, who did not discontinue clopidogrel therapy as prescribed by the protocol. In regard to this issue, it is appropriate to point out that in the 2 cases of early thrombosis at day 1 and day 3, there was a clear suboptimal angiographic result with a dissection distal to the SB stent. The 2 patients who developed early stent thrombosis were not treated with IIb/IIIa inhibitors. Overall, we should consider that careful attention to achieve an optimal result and possibly a more liberal usage of IIb/IIIa inhibitors (used only in 41.2% of patients) could have lowered the incidence of the early events.12

**Study Limitations**

The major limitation of this study is the high crossover rate occurring from the single-stent to the double-stent group. This was primarily because of the absence of a strict policy to guide crossover. This decision was left to the operator, who evaluated whether the results obtained with 1 stent could be considered acceptable or not.

In addition, there was not a completely uniform approach with regard to the stenting technique. The lack of an arm of patients treated with bare metal stents constitutes another limitation.

**Conclusions**

The use of sirolimus-eluting stents in coronary bifurcations appears feasible and relatively safe. Results obtained in this preliminary study constitute an improvement compared with historical controls using any other approach, including bare metal stents. However, restenosis at the SB remains a problem to be solved, and additional efforts need to be addressed to reduce the risk of thrombosis, as reported in this study. At this time, no statement can be made regarding the most appropriate technique or approach to use when treating bifurcations with the Cypher stent.

**Acknowledgment**

This study was supported by a grant from Cordis, a Johnson & Johnson company.

**References**


Randomized Study to Evaluate Sirolimus-Eluting Stents Implanted at Coronary Bifurcation Lesions
Antonio Colombo, Jeffrey W. Moses, Marie Claude Morice, Josef Ludwig, David R. Holmes, Jr, Vassilis Spanos, Yves Louvard, Benny Desmedt, Carlo Di Mario and Martin B. Leon

Circulation. 2004;109:1244-1249; originally published online February 23, 2004; doi: 10.1161/01.CIR.0000118474.71662.E3
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/109/10/1244

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/