

# Two-Year-Plus Follow-Up of a *Paclitaxel*-Eluting Stent in De Novo Coronary Narrowings (TAXUS I)

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Early results with polymer-based paclitaxel-eluting stents have shown significant improvements in the clinical and angiographic parameters of restenosis, as well as excellent safety outcomes. However, the duration of these beneficial effects is unknown. Therefore, the clinical outcomes of the TAXUS I study population were evaluated at 2- and 3-year follow-up. In TAXUS I, 61 patients with single, focal coronary lesions were randomly assigned to receive either a paclitaxel-eluting TAXUS stent (n = 31) or a bare metal control stent (n = 30). Low rates of composite major adverse cardiac events (MACEs) reported at 1-year follow-up (3.2% TAXUS vs 10.0% control) were maintained at 2 and 3 years, with no additional MACEs in either treatment group 1 year after implantation. The single target vessel revascularization in the TAXUS group was remote from the target lesion in contrast to 3 target lesion revascularizations in the control group. © 2005 Elsevier Inc. All rights reserved. (Am J Cardiol 2005;96:79–82)

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Restenosis continues to limit the utility of bare metal stents as a long-term treatment for patients with coronary artery disease.<sup>1</sup> Compared with bare metal stents, drug-eluting stents, using either sirolimus or paclitaxel delivered from a polymer coating, have been shown to safely reduce clinical and angiographic indexes of restenosis up to 12 months after the procedure.<sup>2–7</sup> However, the duration of anti-restenotic benefit with drug-eluting stents is unknown. Long-term follow-up is needed to determine whether these stents prevent rather than merely delay restenosis. We report 2- and 3-year clinical follow-up from the first human experience with the TAXUS polymer-based paclitaxel-eluting stent (Boston Scientific Corporation, Natick, Massachusetts).

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The TAXUS I trial is a prospective, randomized, double-blind trial comparing a polymer-based, paclitaxel-eluting stent (TAXUS NIRx) with a bare metal control stent (NIR, Boston Scientific Corporation) for the prevention of restenosis in single, focal lesions in native coronary arteries. Sixty-one patients were randomly assigned to receive either a 15-mm TAXUS (n = 31) or an uncoated control (n = 30) stent.<sup>2</sup> Stent diameters were 3.0 and 3.5 mm.

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This study was supported by Boston Scientific Corporation, Natick, Massachusetts.

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Patient eligibility criteria, device description, and study procedures have been previously reported, along with 12-month clinical follow-up and 6-month angiographic and intravascular ultrasound (IVUS) analyses.<sup>2</sup> Briefly, eligible patients had single de novo (n = 59) or restenotic (n = 2) lesions of ≤12 mm coverable by 1 study stent, ≥50% diameter stenosis, and vessel diameters from 3.0 to 3.5 mm. Exclusion criteria included a history of acute myocardial infarction, left ventricular ejection fraction <30%; stroke within the previous 6 months, serum creatinine >1.7 mg/100 ml, or contraindication to aspirin, clopidogrel, or ticlopidine.

The primary end point was the rate of composite major adverse cardiac events (MACEs), defined as cardiac death, Q-wave myocardial infarction, or clinically driven revascularization of the target vessel at 30 days after the procedure. Clinical follow-up was conducted at 1, 6, 12, 24, and 36 months after the procedure to assess rates of stent thrombosis and MACEs. For the 24-month clinical follow-up, patients were contacted by telephone to ascertain whether they had experienced stent thrombosis or any MACEs since the 12-month visit. The 36-month follow-up consisted of either a telephone interview or an office visit to determine whether stent thrombosis or MACEs had occurred since the 24-month follow-up.

Eighteen-month angiographic and IVUS follow-up conducted in a subset of patients receiving the TAXUS stent at a single study center in Germany has been reported separately.<sup>8</sup>

Baseline characteristics and procedural data are summarized using descriptive statistics for continuous variables (mean ± SD) and frequency tables or proportions for discrete variables. Differences and their 95% confidence intervals were calculated for variables collected in the 2 treat-

Table 1  
Baseline patient and lesion characteristics in the TAXUS I trial

Variable	Control (n = 30)	TAXUS (n = 31)
Men	25 (83%)	29 (94%)
Age (yrs)	64 ± 8	66 ± 7
Previous myocardial infarction	9 (30%)	8 (26%)
Hypertension	19 (63%)	20 (65%)
Hypercholesterolemia*	24 (79%)	25 (81%)
Diabetes mellitus	4 (13%)	7 (23%)
Smoking	14 (47%)	17 (57%)
Lesion length (mm)	10.7 ± 3.3	11.9 ± 4.9
Reference vessel diameter (mm)	2.99 ± 0.46	2.94 ± 0.52
Minimum luminal diameter (mm)	1.30 ± 0.43	1.23 ± 0.43
Diameter stenosis (%)	56.5 ± 12.3	57.8 ± 13.2

No statistically significant differences were found between treatment groups.

\* Cholesterol >250 mg/dl or medically treated.

ment arms. Two-sided p values were calculated using Student's *t* test. A p value <0.05 was considered statistically significant. All statistical analyses were performed on an intention-to-treat basis using SAS version 8 (SAS Institute Inc., Cary, North Carolina).

As reported previously in our 12-month report,<sup>2</sup> the study population of 61 patients (TAXUS n = 31, control n = 30) was predominantly men (88%); mean patient age at baseline was 65 years. As listed in Table 1, baseline patient and lesion characteristics (by angiography and IVUS; Heart Core, Leiden, The Netherlands) were comparable between treatment groups, without statistically significant differences. Procedural and technical success rates were 100% in the 2 groups.

Of 61 patients enrolled in TAXUS I, 2-year clinical follow-up was obtained for 30 of 31 patients in the TAXUS group (1 patient died of lung cancer) and 30 of 30 patients in the control group. Three-year follow-up in the TAXUS group was 87% (27 of 31 patients) because of 1 patient's follow-up occurring before 1,035 days and 2 additional

noncardiac deaths, 1 caused by multiple organ failure and 1 by cancer of the liver and colon. Two patients in the control group refused follow-up at 3 years, resulting in a follow-up rate of 93%.

No stent thromboses, myocardial infarctions, or cardiac deaths occurred in either treatment group up to 3 years after implantation. No additional MACEs were reported in patients in the TAXUS and control groups from 1 to 3 years after implantation. Only 1 new event occurred in each group after 6-month follow-up. Hence, as listed in Table 2, the number of MACEs at 3 years was identical to the number at 1 year, although the rates increased slightly as a result of lower follow-up rates at 3 years. No target lesion revascularizations were performed in the TAXUS group, compared with 3 in the control group.

As shown in Figure 1, the 3 target vessel revascularizations in the control group were exclusively attributable to target lesion revascularization, whereas the single target vessel revascularization in the TAXUS group was a repeat percutaneous coronary intervention remote from the target lesion. Angiography of a typical patent TAXUS stent at 24-month follow-up is shown in Figure 2.

Eighteen-month angiographic and IVUS outcomes in the subset of patients in the TAXUS group treated at Heart Center Siegburg (Siegburg, Germany) were reported by Buellfeld et al.<sup>8</sup> In this subgroup of patients with TAXUS stents, the rate of binary restenosis remained at 0% up to 18 months. In addition, improvements in minimum luminal diameter and percentage diameter stenosis were sustained without significant change in reference vessel diameter over time. The suppression of neointimal volume was sustained without changes in vessel or luminal volume over time.

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Three-year clinical follow-up from this randomized, double-blind trial demonstrates that the polymer-controlled release of paclitaxel from a coronary stent is safe and effective, with no late deleterious effect, as evidenced by the

Table 2  
Major adverse cardiac events (MACEs) in the TAXUS I trial

Event	6 Months			1 Yr			3 Yrs		
	Control (n = 30)	TAXUS (n = 31)	p Value	Control (n = 30)	TAXUS (n = 31)	p Value	Control (n = 28*)	TAXUS (n = 27†)	p Value
Stent thrombosis	0	0	—	0	0	—	0	0	—
MACEs	2 (6.7%)	0	0.24	3 (10.0%)	1 (3.2%)	0.35	3 (10.7%)	1 (3.7%)	0.61
Cardiac death	0	0	—	0	0	—	0	0	—
Myocardial infarction	0	0	—	0	0	—	0	0	—
Target vessel revascularization	2 (6.7%)	0	0.24	3 (10.0%)	1 (3.2%)	0.35	3 (10.7%)	1 (3.7%)	0.61
Target lesion revascularization	2 (6.7%)	0	0.24	3 (10.0%)	0	0.11	3 (10.7%)	0	0.24
Target vessel revascularization, remote target lesion	0	0	—	0	1 (3.2%)	1.00	0	1 (3.7%)	0.49
Coronary bypass	0	0	—	1 (3.3%)	0	0.49	1 (3.5%)	0	1.00

Dashes indicate no information available.

\* Two patients in the control group refused follow-up at 3 years.

† In the TAXUS group, 3 patients died of noncardiac causes from 365 to 1,035 days of follow-up, and 1 patient was MACE free but had follow-up at 1,035 days.

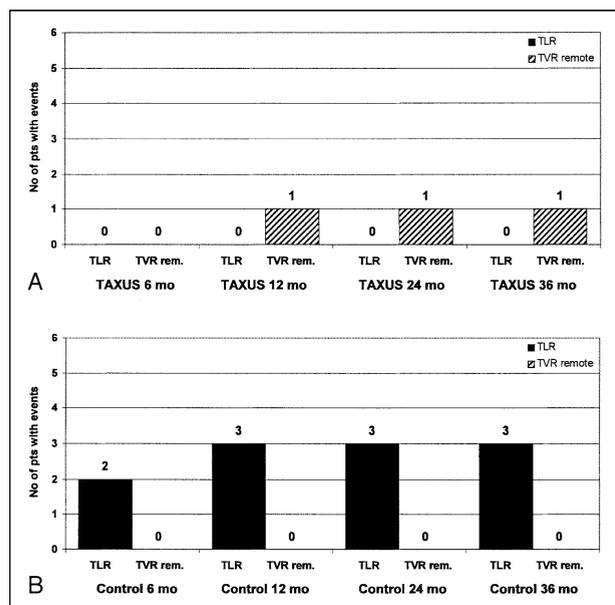


Figure 1. (A) Target vessel revascularization (TVR) in the TAXUS group exclusively attributable to interventions remote from the target lesion (B) compared with TVR in the control group exclusively attributable to target lesion revascularization (TLR; B). Rem = remote.

absence of target lesion revascularizations through 3 years of follow-up. Supportive evidence was also provided by angiographic evidence of 0% binary restenosis at 18-month follow-up in a subset of TAXUS-treated patients with scheduled angiographic long-term follow-up, as reported by Buellesfeld et al.<sup>8</sup> The 18-month angiographic and IVUS analyses in these patients also showed that the gains in minimum luminal diameter and minimum luminal area were sustained over time, as were reductions in percentage diameter stenosis and the suppression of neointimal volume.

The safety of this polymer-based paclitaxel-eluting stent is shown by the absence of stent thrombosis, myocardial infarctions, and cardiac deaths and by a low rate of MACEs that remained unchanged from 1 to 3 years after implantation. These results are excellent compared with late clinical follow-up from the larger trials of bare metal stents in which MACEs rates increased from 6-month to 1- to 3-year end points.<sup>9,10</sup>

Beneficial short-term results of any new therapy under evaluation do not always translate to lasting efficacy, and the issue of the "late catch-up" phenomenon is an important one given the recent unfavorable experience with vascular brachytherapy. Longer term results of trials have suggested that vascular brachytherapy delays rather than prevents restenosis. The 5-year follow-up data of the Scripps Coronary Radiation to Inhibit Proliferation Post-Stenting trial<sup>11</sup> showed the target lesion revascularization rate in the brachytherapy arm gradually increasing over the years (11.5% at 6 months, 15.4% at 3 years, and 23.1% at 5 years), despite the continuing significant difference compared with the control group. In addition, the 5-year results of the Gamma-1 study<sup>12</sup> also showed that there was no

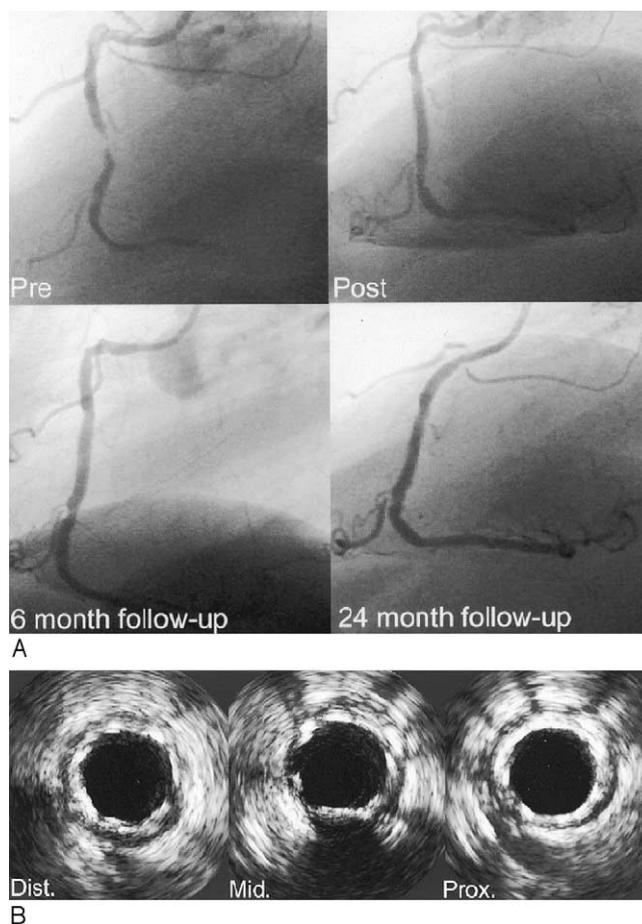


Figure 2. (A) Patent TAXUS stent up to 2 years after implantation. (B) Corresponding IVUS results at 24-month follow-up: examples of proximal (prox.), middle (mid.), and distal (dist.) stent segment without evidence of significant neointimal ingrowth.

longer any significant difference in the MACE or target lesion revascularization rates between the irradiated and control groups after 5 years.

In contrast to these late catch-up phenomena, our findings demonstrate sustained efficacy and safety up to 3 years after implantation of the polymer-based paclitaxel-eluting TAXUS stent. Annual follow-up through 5 years in all pivotal TAXUS trials will provide further valuable insights into the long-term benefit of this stent design.

**Acknowledgment:** We thank Laurie LaRusso, MS (Boston Scientific Corporation), for her assistance in writing this report.

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