TAXUS
EXPRESS²

Paclitaxel-Eluting Coronary Stent System

Monorail™ and Over-The-Wire Coronary Stent Delivery System

CAUTION: Federal law restricts this product to sale by or on the order of a physician.

DIRECTIONS FOR USE

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1 TAXUS™ Express²™ Paclitaxel-Eluting Coronary Stent System

The TAXUS Express² Paclitaxel-Eluting Coronary Stent System (TAXUS Express² Stent System) is a device / drug combination product comprised of two regulated components: a device (Express² Coronary Stent System) and a drug product (a formulation of paclitaxel contained in a polymer coating). The characteristics of the TAXUS Express² Stent System are described in Table 1-1.

Table 1-1. TAXUS Express² Stent System Product Description

	TAXUS Express² Monorail Stent Delivery System	TAXUS Express² Over-The-Wire Stent Delivery System
Available Stent Lengths (mm)	8, 12, 16, 20, 24, 28, 32	8, 12, 16, 20, 24, 28, 32
Available Stent Diameters (mm)	2.50, 2.75, 3.00, 3.50	2.50, 2.75, 3.00, 3.50
Stent Material	A 316L surgical grade stainless steel Express stent	
Drug Product	A conformal coating of a polymer carrier loaded with 1 μg/mm² paclitaxel in a slow release (SR)* formulation applied to the stent with a maximum nominal drug content of 209 μg on the largest stent (3.50x32mm).	
Delivery System Working Length	140 cm	135 cm
Delivery System Y-Adapter Ports	Single access port to inflation lumen. Guidewire exit port is located approximately 25 cm from tip. Designed for guidewire ≤ 0.014".	Y-Connector (Side arm for access to balloon inflation/deflation lumen. Straight arm is continuous with shaft inner lumen). Designed for guidewire ≤ 0.014".
Stent Delivery Balloon	A compliant balloon, nominally 0.3 mm longer than the stent, with two radiopaque markers.	
Balloon Inflation Pressure	Nominal Inflation Pressure: 9 ATM; Rated Burst Inflation Pressure: 18 ATM	
Guide Catheter Inner Diameter	≥ 0.058"	≥ 0.066"
Catheter Shaft Outer Diameter	1.8F proximally, 2.7F distally (Ø up to 3.0mm, and 8-20 mm long stents with Ø > 3.0mm) 2.0F proximally, 2.7F distally (24-32mm long stents with Ø > 3.0mm)	3.2F proximally, 2.7F distally

*release rate is a function of weight/weight ration of polymer and drug, and (SR) is the formulation that was studied clinically and is used in the marketed product

1.1 Device Component Description

The device component consists of the Express stent mounted onto the Express² stent delivery system (SDS). The 2.5-3.5mm diameter 316L stainless steel stents use one design. The same stent is crimped on various size delivery catheter balloons, which are sized from 2.5 to 3.5mm. Because the identical stent component is used for the entire 2.5-3.5mm diameter range, the total drug per stent is a function of stent length, irrespective of stent diameter.

1.2 Drug Component Description

The stent component of the TAXUS Express² Paclitaxel-Eluting Coronary Stent System (referred to as the TAXUS Express Stent) is a stent with a drug / polymer coating formulation consisting of paclitaxel (the active ingredient), and Translute™ polymer carrier (the inactive ingredient).

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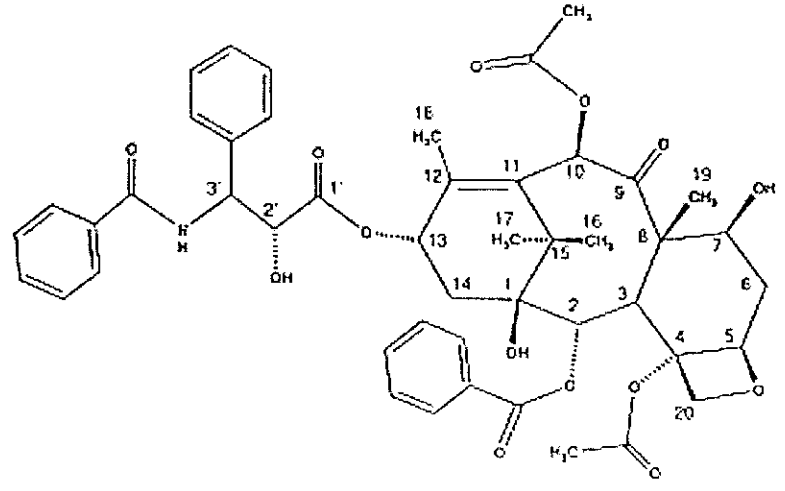
1.2.1 Paclitaxel

The active pharmaceutical ingredient in the TAXUS Express Stent is paclitaxel. It is a white powder, isolated from a spectrum of *Taxus* species and hybrids. The Chemical name of paclitaxel is: Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-,6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1*H*-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2a*R*-[2aα,4β,4aβ,6β,9α(α*R**,β*S**),11α,12α,12aα,12bα]]-.

The chemical structure of paclitaxel is shown below.

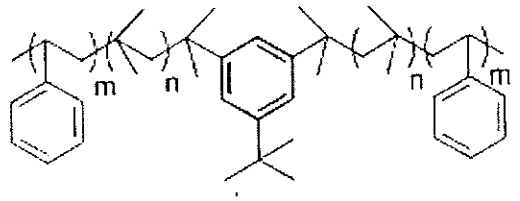
Figure 1-1. The Chemical Structure of Paclitaxel



Paclitaxel is a diterpenoid with a characteristic taxane skeleton of 20 carbon atoms, a molecular weight of 853.91 g/mol and a molecular formula of $C_{47}H_{51}NO_{14}$. It is highly lipophilic, insoluble in water, but freely soluble in methanol, ethanol, chloroform, ethyl acetate and dimethyl sulfoxide.

1.2.2 Translute™ Polymer Carrier

The only inactive ingredient in the TAXUS Express stent is SIBS [poly(styrene-b-isobutylene-b-styrene)], a tri-block copolymer (trade name: Translute™), that is composed of styrene and isobutylene units built on 1,3-di(2-methoxy-2-propyl)-5-tert-butylbenzene. It is an hydrophobic elastomeric copolymer with a molecular weight (Mn-number average molecular weight) of 80,000 to 130,000 g/mol and a polydispersity index of 1.0 to 2.0. The polymer is mixed with the drug paclitaxel and then applied to the stents. There is no primer or topcoat layer. The drug/polymer coating is adhered to the entire surface (i.e., luminal and abluminal) of the stent. The structural formula for the polymer is shown below.



m = repeating units of styrene
n = repeating units of isobutylene

1.2.3 Product Matrix and Paclitaxel Content

Table 1-2. TAXUS™ Express²™ Stent System Product Matrix and Paclitaxel Content

Product Code MR	Product Code OTW	Nominal Expanded Stent Inner Diameter (mm)	Nominal Un-expanded Stent Length (mm)	Nominal Paclitaxel Content (µg)
H7493897008250	H7493896808250	2.50	8	50
H7493897008270	H7493896808270	2.75	8	50
H7493897008300	H7493896808300	3.00	8	50
H7493897008350	H7493896808350	3.50	8	50
H7493897012250	H7493896812250	2.50	12	79
H7493897012270	H7493896812270	2.75	12	79
H7493897012300	H7493896812300	3.00	12	79
H7493897012350	H7493896812350	3.50	12	79
H7493897016250	H7493896816250	2.50	16	108
H7493897016270	H7493896816270	2.75	16	108
H7493897016300	H7493896816300	3.00	16	108
H7493897016350	H7493896816350	3.50	16	108
H7493897020250	H7493896820250	2.50	20	137
H7493897020270	H7493896820270	2.75	20	137
H7493897020300	H7493896820300	3.00	20	137
H7493897020350	H7493896820350	3.50	20	137
H7493897024250	H7493896824250	2.50	24	151
H7493897024270	H7493896824270	2.75	24	151
H7493897024300	H7493896824300	3.00	24	151
H7493897024350	H7493896824350	3.50	24	151
H7493897028270	H7493896828270	2.75	28	180
H7493897028300	H7493896828300	3.00	28	180
H7493897028350	H7493896828350	3.50	28	180
H7493897032270	H7493896832270	2.75	32	209
H7493897032300	H7493896832300	3.00	32	209
H7493897032350	H7493896832350	3.50	32	209

2 Indications

The TAXUS™ Express²™ Paclitaxel-Eluting Coronary Stent System is indicated for improving luminal diameter for the treatment of *de novo* lesions ≤ 28mm in length in native coronary arteries ≥ 2.5 to ≤ 3.75 mm in diameter.

3 Contraindications

Use of the TAXUS™ Express^{2}™ Paclitaxel-Eluting Coronary Stent System is contraindicated in patients with:

- Known hypersensitivity to paclitaxel or structurally-related compounds.
- Known hypersensitivity to the polymer or its individual components (see details in **Section 1.2.2., Translute™ Polymer Carrier,** above).

Coronary Artery Stenting is contraindicated for use in:

- Patients in whom anti-platelet and/or anticoagulant therapy is contraindicated.
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or delivery device.

4 Warnings

- To maintain sterility, the inner package should not be opened or damaged prior to use.
- The use of this product carries the risks associated with coronary artery stenting, including subacute thrombosis, vascular complications, and/or bleeding events.
- Patients with known hypersensitivity to 316L stainless steel may suffer an allergic reaction to this implant.

5 Precautions

5.1 General Precautions

- Only physicians who have received adequate training should perform implantation of the stent.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent stent blockage may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized stents is not well characterized.
- Consideration should be given to the risks and benefits of use in patients with history of severe reaction to contrast agents.
- Do not expose the delivery system to organic solvents, such as alcohol, or detergents.

5.2 Pre-and Post-Procedure Antiplatelet Regimen

In clinical trials of the TAXUS Express Stent, clopidogrel or ticlopidine was administered pre-procedure and for a period of 6 months post-procedure. Aspirin was administered concomitantly with clopidogrel or ticlopidine and then continued indefinitely to reduce the risk of thrombosis. See **Section 9, Clinical Studies**, for more specific information.

5.3 Use of Multiple Stents

The extent of the patient's exposure to drug and polymer is directly related to the number of stents implanted. Use of more than one TAXUS Express Stent has only been evaluated for bailout stenting. Use of multiple stents will result in the patient receiving larger amounts of drug and polymer than the experience reflected in the clinical studies.

When more than one stent for other than bailout stenting is required, resulting in stent to-stent contact, stent materials should be of similar composition to avoid the possibility of dissimilar metal corrosion. Potential interactions of the TAXUS Express Stent with other drug-eluting or coated stents have not been evaluated and should be avoided whenever possible.

5.4 Brachytherapy

The safety and effectiveness of the TAXUS Express Stent in patients with prior brachytherapy of the target lesion have not been established. The safety and effectiveness of use of brachytherapy to treat in-stent restenosis in a TAXUS Express Stent has not been established. Both vascular brachytherapy and the TAXUS Express Stent alter arterial remodeling. The synergy between these two treatments has not been determined.

5.5 Use in Conjunction with Other Procedures

The safety and effectiveness of using mechanical atherectomy devices (directional atherectomy catheters, rotational atherectomy catheters) or laser angioplasty catheters in conjunction with TAXUS Express Stent implantation have not been established.

5.6 Use in Special Populations

5.6.1 Pregnancy

Pregnancy "Category C". See **Drug Information – Section 6.5, Pregnancy.** There are no adequate or well-controlled studies in pregnant women or men intending to father children. Effective contraception should be initiated before implanting a TAXUS Express Stent. TAXUS Express Stents should be used in pregnant women only if the potential benefit justifies the potential risk to the embryo or fetus. Because some paclitaxel remains on the stent indefinitely, use of the TAXUS Express Stent in women who are of childbearing potential or in men intending to father children should be given careful consideration.

5.6.2 Lactation

See **Drug Information – Section 6.6, Lactation.** A decision should be made whether to discontinue nursing to implant the stent, taking into account the importance of the stent to the mother.

5.6.3 Gender

Clinical studies of the TAXUS Express Stent did not find any differences in safety and effectiveness for male and female patients.

5.6.4 Ethnicity

Clinical studies of the TAXUS Express Stent did not include sufficient numbers of patients to assess for differences in safety and effectiveness due to ethnicity, either by individual category or when grouped by Caucasian and non-Caucasian.

5.6.5 Pediatric use

The safety and effectiveness of the TAXUS Express Stent in pediatric patients have not been established.

5.6.6 Geriatric Use

Clinical studies of the TAXUS Express Stent did not find that patients age 65 years and over differed with regard to safety and effectiveness compared to younger patients.

5.7 Lesion/Vessel Characteristics

The safety and effectiveness of the TAXUS Express Stent have not been established in the following patient populations:

- Patients with unresolved vessel thrombus at the lesion site.
- Patients with coronary artery reference vessel diameters < 2.5 mm or > 3.75 mm.
- Patients with lesions located in the saphenous vein grafts, in the unprotected left main coronary artery, ostial lesions, or lesions located at a bifurcation.
- Patients with diffuse disease or poor flow distal to the identified lesions.
- Patients with tortuous vessels (>60 degrees) in the region of the obstruction or proximal to the lesion.
- Patients with a recent acute myocardial infarction where there is evidence of thrombus or poor flow.
- Patients with multiple overlapping stents.
- Patients for longer than 12 months follow-up.

5.8 Drug Interaction

Because systemic levels of paclitaxel have not been detected post-stent placement in clinical trials, possible interactions of paclitaxel with concomitantly administered medications are unlikely to be detectable. The effect of potential drug interactions on the safety and efficacy of the TAXUS Express Stent has not been formally investigated.

The metabolism of paclitaxel is catalyzed by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. In the absence of formal clinical drug interaction studies, caution should be exercised when administering paclitaxel concomitantly with known substrates or inhibitors of the cytochrome P450 isoenzymes CYP2C8 and CYP3A4.

See **Drug Information – Section 6.3, Drug Interactions.**

5.9 Magnetic Resonance Imaging (MRI)

Bench testing at field strengths of 3 Tesla (T) or less, and a maximum spatial gradient of 325 gauss/cm, showed that the TAXUS Express Stent should not migrate in this MR environment. This stent has not been evaluated to determine if it is safe in MRI systems with field strength greater than 3 T.

This product has not been evaluated for heating in the MR environment. The effect of heating in the MR environment for overlapping stents or stents with fractured struts, or on the drug or polymer coating is not known.

MR imaging quality may be compromised if the area of interest is in the exact same area or relatively close to the position of the stent.

5.10 Stent Handling (also see Section 13, Operator's Instructions)

- For single use only. Do not resterilize or reuse this product. Note product "Use By" date. (See **Reuse Precaution Statement, Section 15.**)
- The premounted TAXUS Express Stent and its delivery system are designed for use as a unit. The stent is not to be removed from its delivery balloon. The stent is not designed to be crimped onto another balloon. Removing the stent from its delivery balloon may damage the stent and coating and/or lead to stent embolization.
- Special care must be taken not to handle or in any way disrupt the stent position on the delivery balloon. This is most important during catheter removal from packaging, placement over guidewire, and advancement through hemostasis valve adapter and guide catheter hub.
- Excessive manipulation or handling may cause coating damage, contamination, or dislodgment of the stent from the delivery balloon.
- Use only the appropriate balloon inflation media (see **Operator's Instructions – Section 13.3.2, Guidewire Flush Lumen**). Do not use air or any gas medium to inflate the balloon.
- In the event the TAXUS Express Stent is not deployed, follow product returns procedures.

5.11 Stent Placement

Preparation

- Do not prepare or pre-inflate balloon prior to stent deployment other than as directed. Use balloon purging technique described in **Operator's Instructions - Section 13, Balloon Preparation**.
- If unusual resistance is felt at any time during lesion access before stent implantation, the stent system and the guide catheter should be removed as a single unit (See **Precautions - Section 5.12, Stent System Removal**).
- An unexpanded stent should be introduced into the coronary arteries one time only. An unexpanded stent should not be subsequently moved in and out through the distal end of the guide catheter as stent or coating damage or stent dislodgment from the balloon may occur.

Placement

- The vessel should be pre-dilated with an appropriate sized balloon.
- Do not expand the stent if it is not properly positioned in the vessel (see **Precautions - Section 5.12, Stent System Removal**).
- Balloon pressures should be monitored during inflation. Do not exceed rated burst pressure as indicated on product label (see Table 14.1-1, TAXUS™ Express^{2}™ Stent System Stent and Balloon Compliance). Use of pressures higher than specified on product label may result in a ruptured balloon and potential intimal damage and dissection. The stent inner diameter should approximate 1.1 times the reference diameter of the vessel.
- Placement of the stent has the potential to compromise side branch patency.
- Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stented portion, and may cause acute closure of the vessel requiring additional intervention (e.g., CABG, further dilation, placement of additional stents, or other).
- When treating multiple lesions, the distal lesion should be initially stented, followed by stenting of the more proximal lesion(s). Stenting in this order alleviates the need to cross the proximal stent in placement of the distal stent and reduces the chances for dislodging the proximal stent.

5.12 Stent System Removal

- If unusual resistance is felt at any time during lesion access before stent implantation, the stent system and the guide catheter should be removed as a single unit.
- Do not attempt to pull an unexpanded stent back into the guide catheter, as stent or coating damage or stent dislodgment from the balloon may occur.
- Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the vascular site. Complications can include bleeding, hematoma or pseudoaneurysm.

When removing the entire stent system and guide catheter as a single unit (NOTE: The following steps should be executed under direct visualization using fluoroscopy):

- Maintain guidewire placement across the lesion during the entire removal process. Carefully pull back the stent system until the proximal balloon marker of the stent system is just distal of the guide catheter distal tip.
- The stent system and the guide catheter should be pulled back until the tip of the guide catheter is just distal to the arterial sheath, allowing the guide catheter to straighten. Carefully

retract the stent system into the guide catheter and remove the stent system and the guide catheter from the patient as a single unit while leaving the guidewire across the lesion.

Failure to follow these steps, and/or applying excessive force to the stent system can potentially result in stent or coating damage, stent dislodgment from the balloon and/or damage to the delivery system.

5.13 Post-Procedure

- Care must be exercised when crossing a newly deployed stent with an intravascular ultrasound (IVUS) catheter, a coronary guidewire, or a balloon catheter to avoid disrupting the stent placement, apposition, geometry, and/or coating.
- In clinical trials of the TAXUS Express Stent, clopidogrel or ticlopidine was administered pre-procedure and for a period of 6 months post-procedure. Aspirin was administered concomitantly with clopidogrel or ticlopidine and then continued indefinitely to reduce the risk of thrombosis. See **Section 9 – Clinical Studies**, for more specific information.
- If the patient requires imaging, see **Precautions – Section 5.9 Magnetic Resonance Imaging**.

6 Drug Information

6.1 Mechanism of Action

The mechanism (or mechanisms) by which a TAXUS Express Stent affects neointimal production as seen in clinical studies has not been established. Paclitaxel promotes the assembly of microtubules from tubulin dimers and stabilizes microtubules by preventing depolymerization. This stability results in the inhibition of the normal dynamic reorganization of the microtubule network that is essential for vital interphase and mitotic cellular functions.

6.2 Pharmacokinetics

In the clinical studies, TAXUS I, II, and III, no paclitaxel levels were detected after stent implantation using an analytical method with a lower limit of quantitation (LLOQ) of 10 ng/ml. These findings were confirmed in preclinical studies using multiple stents with total loaded doses above the clinically available stent system and an assay with an LLOQ of 0.03 ng/ml. Hence, in the absence of any systemically detectable levels, standard pharmacokinetic parameters were not estimated.

6.3 Drug Interactions

Paclitaxel is metabolized in the liver via cytochrome P450 (CYP) 2C8 to 6-alpha-hydroxypaclitaxel and via CYP 3A4 to 3'-p-hydroxypaclitaxel and 6-alpha,3'-p-dihydroxypaclitaxel. Paclitaxel is a substrate of P-glycoprotein. Because metabolism appears to play an important role in the elimination of paclitaxel, agents that could compete with or inhibit the CYP2C8 and CYP3A4

isoenzymes may increase paclitaxel plasma levels. Potential drug interactions may occur with any drug that affects these isoenzymes.

Formal drug interaction studies have not been conducted with the TAXUS Express Stent. Consideration should be given to the potential for both systemic and local drug interactions in the vessel wall when deciding to place a TAXUS Express Stent in a patient who is taking a drug with known interactions to paclitaxel or when deciding to initiate therapy with such a drug in a patient that has recently received a TAXUS Express Stent.

6.4 Carcinogenicity, Genotoxicity, and Reproductive Toxicology

No long-term studies in animals have been performed to evaluate the carcinogenic potential of paclitaxel. Paclitaxel was not mutagenic when tested in two gene mutation assays, the Ames test and the Chinese hamster ovary assay. However, paclitaxel was shown to be clastogenic in two mammalian cytogenetics assays, the *in vitro* human lymphocyte assay and the *in vivo* mouse micronucleus assay. Paclitaxel administered IV prior to and during mating produced impairment of fertility in male and female rats at doses ≥ 1 mg/kg (approximately 55 times the dose provided by the largest TAXUS Express Stent coated with 209 μg paclitaxel adjusted for body surface area).

6.5 Pregnancy

Pregnancy Category C: There are no adequate and well controlled studies in pregnant women of paclitaxel or TAXUS Express Stents. Studies performed in rats and rabbits receiving IV paclitaxel during organogenesis revealed evidence of maternal toxicity, embryotoxicity, and fetotoxicity at dosages of 1 and 3 mg/kg, respectively (approximately 55 and 300 times the dose provided by the largest TAXUS Express Stent coated with 209 μg paclitaxel adjusted for body surface area). The drug resulted in increased resorptions, and increased fetal deaths. No teratogenicity was observed in gravid rats receiving daily IV paclitaxel doses of 1 mg/kg (approximately 55 times the dose provided by the largest TAXUS Express Stent coated with 209 μg paclitaxel adjusted for body surface area).

TAXUS Express Stents should be used in pregnant women only if the potential benefit justifies the potential risk. Because some paclitaxel remains on the stent indefinitely, use of the TAXUS Express Stent in women who are of childbearing potential should be given careful consideration.

6.6 Lactation

It is not known whether paclitaxel is distributed in human milk. However, in lactating rats given radiolabeled paclitaxel, levels of radioactivity in plasma and milk were similar. Mothers should be advised of the potential for serious adverse reactions to paclitaxel in nursing infants.

Prior to implantation of a TAXUS Express Stent, a decision should be made whether to discontinue nursing or to implant the stent, taking into account the importance of the stent to the mother.

7 Overview of Clinical Studies

TAXUS IV was a randomized, double-blind, controlled pivotal U.S. study of the safety and performance of the 1 μg /mm^2 (loaded drug/stent surface area) slow rate-release formulation TAXUS™ Express™ Stent in patients with low risk, *de novo* coronary artery lesions. A total of 1,326 patients at 73 U.S. sites were enrolled with patients randomized 1:1 to the TAXUS Express Stent or the uncoated Express control stent. The primary endpoint for the study was the 9-month ischemia driven TVR rate. Secondary endpoints included 9-month clinical assessments for all patients and analysis of angiographic and intravascular ultrasound (IVUS) parameters in a subset of patients. After the procedure, patients were treated with aspirin indefinitely and with clopidogrel or ticlopidine for 6 months. Follow-up through 12 months is currently available, and yearly follow-up for clinical parameters through 5 years is ongoing.

TAXUS II was a randomized, double-blind, controlled supporting study of the safety and performance of the 1 μg/mm^2 TAXUS NIRx™ Paclitaxel-Eluting Coronary Stent System (TAXUS NIRx Stent), in which two sequential cohorts of patients with low risk, *de novo* coronary artery lesions were treated. The slow rate-release (SR) formulation was studied in Cohort I and the moderate rate-release (MR) formulation in Cohort II. A total of 536 patients in 15 countries were enrolled. Patients in each cohort were randomized (1:1) to the TAXUS NIRx Stent or the NIR™ Conformer uncoated control stent. The primary endpoint for the study was mean percent in-stent net volume obstruction at 6 months as measured by IVUS. Secondary endpoints included 6-month clinical and angiographic parameters. After the procedure, patients were treated with aspirin indefinitely and with clopidogrel or ticlopidine for 6 months. Follow-up through 12 months is currently available, and yearly follow-up for clinical parameters through 5 years is ongoing, with an additional angiographic follow-up scheduled at the 2 year time-point. For TAXUS II, results are only presented for the SR treatment group (Cohort I) and corresponding control

TAXUS I was a randomized, double-blind, controlled feasibility study comparing the 1 μg /mm^2 slow rate-release formulation of the TAXUS NIRx Stent with the NIR Conformer uncoated control stent in *de novo* lesions. IVUS guidance during the index procedure and at 6-month follow up was required. Patients received aspirin indefinitely and clopidogrel or ticlopidine for 6 months. In brief, 61 patients were enrolled by 3 centers in Germany. Baseline demographic, lesion characteristics were similar between the 2 groups. The primary endpoint was 30-Day Major Adverse Cardiac Event (MACE). Follow-up through 24 months is currently available and follow-up for clinical parameters through 5 years is ongoing.

Table 7-1. **Clinical Trial Comparison**

	TAXUS IV (Pivotal)	TAXUS II (SR) (Supportive)	TAXUS I (Feasibility)
Study Type	• prospective • multi-center randomized • double-blind	• prospective • multi-center randomized • double-blind • two sequential cohorts	• prospective • multi-center randomized • double-blind
Number of Patients	Total: 1314 TAXUS Express Stent: 662 Control: 652	Total: 267 TAXUS NIRx Stent: 131 Control: 136	Total: 61 TAXUS NIRx Stent: 31 Control: 30
Dose Release Formulation	SR (1 µg /mm^2)	SR (1 µg /mm^2)	SR (1 µg /mm^2)
Lesion Criteria	*De novo* lesions in native coronary artery ≥10mm and ≤28mm in length and vessel diameter ≥ 2.5mm to ≤ 3.75mm in diameter and coverable with 1 stent	*De novo* lesions in native coronary artery ≤ 12mm in length and vessel diameter ≥ 3.0mm to ≤ 3.5mm in diameter and coverable with 1 stent	*De novo* lesions in native coronary artery ≤ 12mm in length and vessel diameter ≥ 3.0mm to ≤ 3.5mm in diameter and coverable with 1 stent
Product Used	Express Stent on the Maverick™ Monorail Stent Delivery Balloon Catheter	NIRx Stent premounted on the Advance Monorail Stent Delivery Balloon Catheter	NIRx Stent hand-crimped on the Advance Monorail Stent Delivery Balloon Catheter
Antiplatelet Therapy	Aspirin indefinitely and clopidogrel or ticlopidine for 6 months	Aspirin indefinitely and clopidogrel or ticlopidine for 6 months	Aspirin indefinitely and clopidogrel or ticlopidine for 6 months
Follow-Up	30 days: clinical 4 months: clinical or telephone 9 month: clinical, angiographic 1 – 5 years: telephone	30 days: clinical 6 and 24 months: clinical, angiographic 1,3,4,5 years: telephone	30 days: clinical 6 and 24 months: clinical, angiographic 1,3,4,5 years: telephone

8 Adverse Events

8.1 Observed Adverse Events

Observed adverse event experience comes from three clinical studies, TAXUS IV, II and I.

Principal adverse events for these trials are shown in Table 8-1. Stent apposition was recorded for the TAXUS IV and TAXUS II trials and is presented in Table 8-2. See also **Adverse Events - Section 8.2, Potential Adverse Events**.

Table 8-1. Principal Adverse Events

	TAXUS IV (SR) to 12 months		TAXUS II (SR) to 12 months		TAXUS I (SR) to 24 Months	
	TAXUS stent	Control Stent	TAXUS stent	Control Stent	TAXUS Stent	Control Stent
In-Hospital	N=662* % (n)	N=652* % (n)	N=131* % (n)	N=136* % (n)	N=31* % (n)	N=30* % (n)
MACE	2.4% (16)	2.1% (14)	1.5% (2)	4.4% (6)	0.0% (0)	0.0% (0)
Death	0.0% (0)	0.3% (2)	0.0% (0)	0.7% (1)	0.0% (0)	0.0% (0)
Myocardial Infarction	2.4% (16)	2.1% (14)	1.5% (2)	3.7% (5)	0.0% (0)	0.0% (0)
Q-wave	0.2% (1)	0.2% (1)	0.0% (0)	0.7% (1)	0.0% (0)	0.0% (0)
Non Q-wave	2.3% (15)	2.0% (13)	1.5% (2)	2.9% (4)	0.0% (0)	0.0% (0)
Target Vessel Revascularization (TVR)	0.0% (0)	0.2% (1)	0.8% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Target Lesion Revascularization (TLR)	0.0% (0)	0.2% (1)	0.8% (1)	0.0% (0)	0.0% (0)	0.0% (0)
TVR, non-target lesion	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
TVR, CABG	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
CVA	0.0% (0)	0.2% (1)	0.0% (0)	0.0% (0)	-	-
Stent Thrombosis (acute/in-hospital)	0.0% (0)	0.3% (2)	0.8% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Out-of-Hospital	N=653* % (n)	N=644* % (n)	N=129* % (n)	N=131* % (n)	N=31* % (n)	N=30* % (n)
MACE	8.4% (55)	18.3% (118)	9.3% (12)	18.3% (24)	3.2% (1)	10.0% (3)
Death	1.4% (9)	0.9% (6)	0.0% (0)	0.8% (1)	0.0% (0)	0.0% (0)
Myocardial Infarction	1.1% (7)	2.5% (16)	0.8% (1)	2.3% (3)	0.0% (0)	0.0% (0)
Q-wave	0.6% (4)	0.2% (1)	0.8% (1)	1.5% (2)	0.0% (0)	0.0% (0)
Non Q-wave	0.5%% (3)	2.3% (15)	0.0% (0)	0.8% (1)	0.0% (0)	0.0% (0)
Target Vessel Revascularization (TVR)	6.9% (45)	16.8% (108)	9.3% (12)	16.0% (21)	3.2% (1)	10.0% (3)
Target Lesion Revascularization (TLR)	4.3% (28)	14.8% (95)	3.9% (5)	13.0% (17)	0.0% (0)	10.0% (3)
TVR, non-target lesion	2.8% (18)	3.1% (20)	3.1% (4)	3.1% (4)	3.2% (1)	0.0% (0)
TVR, CABG	1.7% (11)	4.0% (26)	3.1% (4)	0.8% (1)	0.0% (0)	3.3% (1)
CVA	1.7% (11/ 654)	0.6% (4)	0.8% (1)†	0% (0/136)	-	-
Stent Thrombosis (sub-acute/<30 days)	0.3% (2)	0.3% (2)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Stent Thrombosis (late/≥31 days)	0.3% (2)	0.2% (1)	0.8% (1)	0.0% (0)	0.0% (0)	0.0% (0)

Numbers are % (Count/Sample Size). * Note: sample size is defined as N at the top of each column for In-Hospital and Out-of-Hospital measures except where noted by inclusion of a denominator

MACE: Major Adverse Cardiac Events, comprised of Cardiac Death, MI and TVR.

TVR: Target Vessel Revascularization, defined as Ischemia-driven repeat percutaneous intervention of the target vessel or bypass surgery of the target vessel. A TVR will be considered as ischemia-driven if the target vessel diameter stenosis is ≥50% by QCA and any of the following are present:

- the patient had a positive functional study corresponding to the area served by the target vessel;
- ischemic ECG changes at rest in a distribution consistent with the target vessel;
- ischemic symptoms referable to the target lesion.

Primary endpoint of TAXUS IV: 9-month TVR.

For definitions of other AEs refer to tables 9-1 and 9-2

†This event was reported by site as Serious Adverse Event (SAE) (visual field defect right eye): It was subsequently adjudicated by the Clinical Event Committee as a Transient Ischemic Attack but downgraded to the non-serious adverse event.

In the TAXUS IV trial, a pre-specified subset of patients underwent IVUS evaluation of the treated lesion immediately after treatment and as part of a scheduled angiographic evaluation at 9 months. In the TAXUS II trial, all patients underwent IVUS evaluation immediately after treatment and as part of the follow-up angiographic evaluation at 6 months. In both studies, the incomplete apposition rate post-procedure and at follow-up was comparable between patients in the TAXUS stent treatment group and the Control group. From the TAXUS IV trial, the majority of incomplete stent apposition cases that were present post-procedure had resolved, and the incidence of late acquired stent apposition was low and comparable between groups. There was no correlation of clinical adverse events or MACE events that were related to the occurrence of incomplete stent apposition. Frequencies of incomplete stent apposition are shown in Table 8-2 for both TAXUS IV and TAXUS II.

Table 8-2. Frequency of Incomplete Stent Apposition

	TAXUS IV (SR) Trial		TAXUS II (SR) Trial	
	TAXUS Stent	Control Stent	TAXUS Stent	Control Stent
Incomplete Stent Apposition Rate Post-Procedure	11.6% (13/112)	6.4% (7/109)	11.1% (14/126)	9.3% (12/129)
Incomplete Stent Apposition Rate at Follow-up	4.0% (4/99)	3.0% (3/100)	12.5% (15/120)	7.9% (10/127)
Resolved	6.4% (6/94)	5.4% (5/93)	6.8% (8/118)	4.9% (6/123)
Persistent	3.2% (3/94)	1.1% (1/93)	4.2% (5/118)	4.1% (5/123)
Late Acquired	1.1% (1/94)	2.2% (2/93)	8.5% (10/118)	4.1% (5/123)

Numbers are % (Count/Sample Size).
IA = Incomplete Apposition, BL = Baseline, FU = Follow-up.
Resolved = # patients with BL IA and without FU IA ÷ # patients evaluable at baseline and follow-up.
Persistent = # patients with BL IA and with FU IA ÷ # patients evaluable at baseline and follow-up.
Late Acquired = # patients without BL IA and with FU IA ÷ # patients evaluable at baseline and follow-up.
Incomplete Apposition variables are from assessment by IVUS core laboratory.

8.2 Potential Adverse Events

Potential adverse events (in alphabetical order) which may be associated with the use of a coronary stent in native coronary arteries include but are not limited to:

- Abrupt stent closure
- Acute myocardial infarction
- Allergic reaction to anti-coagulant and/or antithrombotic therapy, contrast medium, or stent materials
- Angina
- Aneurysm
- Arrhythmias, including ventricular fibrillation (VF) and ventricular tachycardia (VT)
- Arteriovenous fistula
- Cardiac tamponade
- Cardiogenic shock
- Death

- Dissection
- Emboli, distal (air, tissue or thrombotic emboli)
- Emergent Coronary Artery Bypass Surgery (CABG)
- Heart failure
- Hematoma
- Hemorrhage, requiring transfusion
- Hypotension/Hypertension
- Infection, including infection and/or pain at the access site
- Ischemia, myocardial
- Perforation or Rupture
- Pericardial effusion
- Pseudoaneurysm, femoral
- Renal Failure
- Respiratory Failure
- Restenosis of stented segment
- Shock/Pulmonary edema
- Spasm
- Stent embolization
- Stent thrombosis/occlusion
- Stroke/cerebrovascular accident/TIA
- Total occlusion of coronary artery
- Vessel trauma requiring surgical repair or reintervention

Potential adverse events not captured above, that may be unique to the paclitaxel drug coating:

- Allergic/immunologic reaction to drug (paclitaxel or structurally-related compounds) or the polymer stent coating (or its individual components)
- Alopecia
- Anemia
- Blood product transfusion
- Gastrointestinal symptoms
- Hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia)
- Hepatic enzyme changes
- Histologic changes in vessel wall, including inflammation, cellular damage or necrosis
- Myalgia/Arthralgia
- Peripheral neuropathy

There may be other potential adverse events that are unforeseen at this time.

9 Clinical Studies

9.1 TAXUS IV Pivotal Clinical Trial

Objective: The primary objective of this study was to demonstrate superiority of the TAXUS™ Express™ Stent as compared with a matched uncoated control stent for reduction of the target vessel revascularization rate (TVR) 9 months post index procedure.

Conclusion: In selected patients, the TAXUS Express Stent significantly reduced the rate of 9-month TVR (primary endpoint) as compared to control. This reduction was attributable to reduction in revascularization procedures [percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG)] performed on the target lesion (TLR). Quantitative coronary angiography (QCA) and IVUS analyses confirmed a significant reduction in binary restenosis rate, minimum lumen diameter (MLD), percent diameter stenosis (%DS), late loss, and % in-stent net volume obstruction. These results were achieved without increased edge stenosis and late loss at the proximal and distal edges, which were significantly lower in the TAXUS group. In addition, lower MACE rates in the TAXUS group, along with low and comparable rates of stent thrombosis, aneurysm and incomplete apposition between groups, demonstrates the safety of the TAXUS Express Stent.

Design: This was a multi-center, prospective, randomized, double-blind study in patients at 73 U.S. sites. Eligible patients were those presenting for stenting of *de novo* lesions of a single native coronary artery [reference vessel diameter (RVD) 2.5 to 3.75 mm] with a target lesion 10 to 28 mm in length and stenosis ≥50% in diameter, using visual estimates, who were candidates for PCI or CABG, and had documented angina pectoris or functional ischemia.

A total of 1314 patients were enrolled and evaluable in this study: 662 in the TAXUS group and 652 in the Control group. Patients were randomized to receive either a TAXUS Express Stent or uncoated Express™ coronary stent (bare metal control). Study randomization was sub-stratified for medically treated diabetes, reference vessel diameter, and lesion length. Multiple stenting was allowed for bailout only. After the procedure, patients were treated with aspirin indefinitely and clopidogrel or ticlopidine for 6 months.

Follow-up included 1, 4, and 9-month clinical assessments. In addition, patients agreed to annual telephone follow-up for clinical parameters through 5 years post procedure (Note: 4-month follow-up was by phone or office visit). Follow-up through 12 months (± 30 days) is currently available in 1272/1314 (96.8%) of patients.

A subset of patients were pre-assigned to have angiographic (n=732) and IVUS (n=268) follow-up at 9 months. Angiographic assessments were performed for the area of the vessel within the stent margins (in-stent) and also for the area within the stent margins, including the area immediately 5 mm proximal and distal from the stent margins (analysis segment).

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Demographics: Patients were well matched for baseline demographics with no statistically significant differences between groups. Factors evaluated included age (mean 62 years), gender (72% male), race (89.3% Caucasian, 5.0% African American, 3.1% Hispanic, 1.6% Asian, and approximately 1.0% other), diabetes (29%), prior MI (30%), hypertension (70%), hyperlipidemia (65%), ejection fraction (mean 55%), Canadian Cardiovascular Society Classification (CSS) Angina Class (26% III or IV), IIb/IIIa inhibitor use (57%), left anterior descending (LAD) (41%), left circumflex (LCX) (28%), right coronary artery (RCA) (31%), RVD (mean 2.8 mm), MLD (mean 0.93 mm), %DS (mean 66%), and lesion length (mean 13.4 mm). Smoking history (current and previous) was slightly lower in the TAXUS™ Express™ Stent arm (63.0%) than in the control arm (66.3%), and was not found to be a significant predictor of outcome in the trial.

Methods: Baseline clinical and angiographic data were collected on standardized case report forms by coordinators at the clinical sites. Angiographic and IVUS outcomes were assessed in a blinded fashion by quantitative analysis at designated core laboratories. An independent Clinical Events Committee adjudicated clinical events, and the trial was monitored by an independent Data Monitoring Committee.

Results: In selected patients, elective TAXUS Express Stent placement in native coronary artery *de novo* lesions resulted in a reduction in the incidence of TVR at 9 months compared to Control (4.7% vs. 12.1%, $p<0.0001$). Overall MACE including cardiac death, myocardial infarction (MI) and target vessel revascularization (TVR) were reduced in the TAXUS group at 9 months compared to control (8.5% vs. 15.2% , $p= 0.0002$). Stent thrombosis rates were comparable between the groups (0.6% TAXUS vs 0.8% Control, $p=0.7513$). Clinical outcomes through 12 months were consistent with the 9 month outcomes.

By follow-up angiography at 9 months, there was a significantly lower in-stent late loss (0.39 mm vs. 0.92 mm, $p<0.0001$) and analysis segment late loss (0.23 mm vs. 0.61 mm, $p<0.0001$) as compared to Control. Additionally, in-stent and analysis segment binary restenosis were significantly reduced (5.5% vs. 24.4%, $p<0.0001$, in-stent; 7.9% vs. 26.6%, $p<0.0001$, analysis segment). Percent diameter stenosis and late loss at the proximal (13.19% vs. 16.13%, $p=0.0167$; 0.15 mm vs. 0.27 mm, $p=0.0016$) and distal edges (7.60% vs. 11.83%, $p=0.0001$; 0.05 mm vs. 0.17 mm, $p=0.0007$) were significantly lower in the TAXUS as compared to the Control groups.

Examination by IVUS at 9 months showed that neointimal hyperplasia volume was significantly reduced in the TAXUS Express Stent arm (17.56 mm^3 vs. 41.48 mm^3, $p<0.0001$). The rate of incomplete stent apposition was low and comparable between the TAXUS and Control treatment arms at 9-months (4.0% vs. 3.0%, $p=0.7209$). There were no clinical events related to occurrences of incomplete stent apposition.

Forty-two (6.5 %) of the patients in the TAXUS Express Stent arm of the TAXUS IV trial received more than one stent for bailout purposes. The incidence of MACE in these patients was not different than in those patients receiving only one stent.

Table 9-1 summarizes principal safety and effectiveness results through 12 months and Figure 9-1 provides the cumulative percent of patients who are TVR-Free through 12 months.

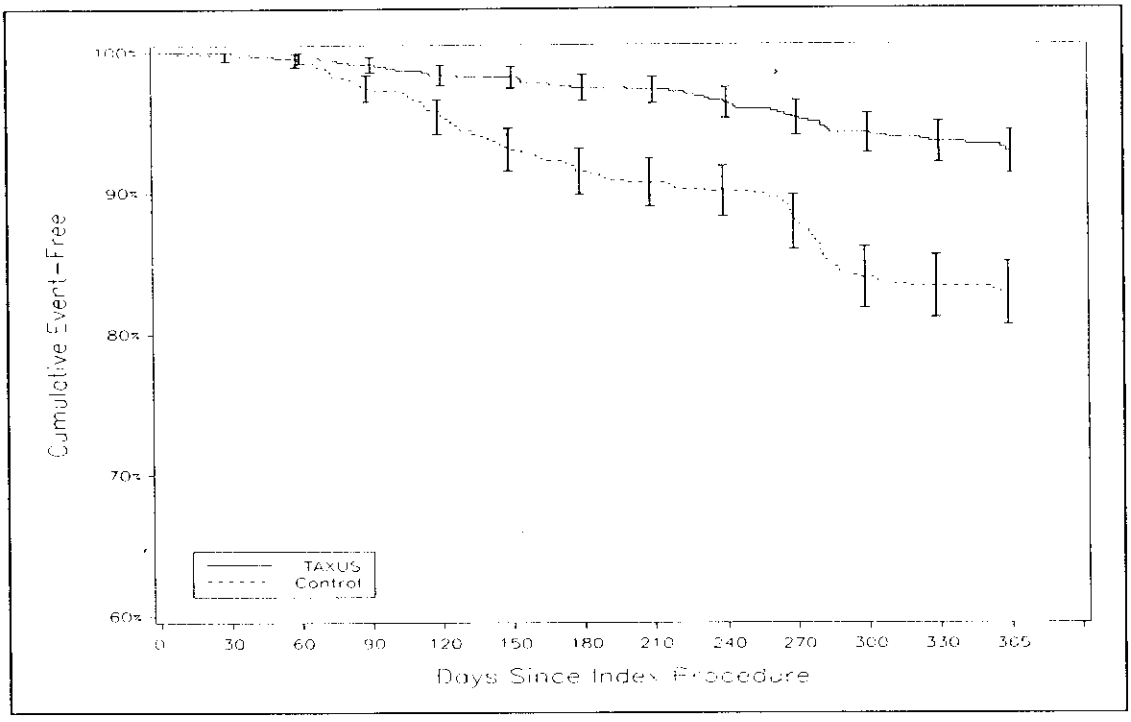
Table 9-1.TAXUS IV Principal Safety and Effectiveness Results through 12 months

	TAXUS (N=662)	Control (N=652)	Difference [95% CI]	P
Effectiveness Measures				
Clinical Procedural Success	97.3% (643/661)	97.4% (635/652)	-0.1% [-1.9%, 1.6%]	1.0000
Technical Success	97.9% (648/ 661)	98.2% (640/ 652)	;0.3% [-1.8%, 1.2%]	0.8436
9 Month Results				
[2]Target Vessel Revascularization	4.7% (31/655)	12.1% (78/ 645)	-7.4% [-10.4%, -4.4%]	<0.0001
In-stent restenosis	5.5% (16/ 291)	24.4% (65/ 266)	-18.9% [-24.7%,-13.1%]	<0.0001
Analysis segment restenosis	7.9% (23/ 291)	26.6% (71/ 267)	-18.7% [-24.8%,-12.5%]	<0.0001
MLD (mm), In-stent				
Post-Procedure	2.65 +/- 0.42 (373)	2.67 +/- 0.41 (351)	-0.01 [-0.07,0.05]	0.6577
9-Month	2.26 +/- 0.58 (291)	1.75 +/- 0.65 (266)	0.51 [0.41,0.61]	<0.0001
MLD (mm), Analysis Segment				
Post Procedure	2.26 +/- 0.48 (374)	2.29 +/- 0.50 (356)	-0.03 [-0.10,0.04]	0.4526
9-Month	2.03 +/- 0.55 (291)	1.68 +/- 0.61 (267)	0.35 [0.26, 0.45]	<0.0001
% DS, In-stent				
Post Procedure	4.21 +/- 10.84 (373)	5.16 +/- 11.41 (351)	-0.95 [-2.57, 0.67]	0.2497
9-Month	17.43 +/-17.71 (291)	37.24 +/- 19.76 (266)	-19.82 [-22.93,16.70]	<0.0001
% DS, Analysis Segment				
Post Procedure	19.16 +/- 9.67 (374)	19.33 +/- 10.45 (356)	-0.17 [-1.63, 1.29]	0.8219
9-Month	26.29 +/- 15.45 (291)	39.79 +/- 18.45 (267)	-13.50 [-16.31,-10.68]	<0.0001
Late Loss, In-stent (mm)	0.39 +/- 0.50 (291)	0.92 +/- 0.58 (266)	-0.53 [-0.62, -0.44]	<0.0001
Late Loss, Analysis Segment (mm)	0.23 +/- 0.44 (291)	0.61 +/- 0.57 (267)	-0.38 [-0.47, -0.30]	<0.0001
% Net Volume Obstruction	12.20 +/- 12.44 (81)	29.40 +/- 14.05 (80)	-17.19 [-21.29,-13.10]	<0.0001
Minimum Lumen Area	5.14 +/- 2.19 (81)	4.15 +/- 1.64 (80)	0.99 [0.39, 1.59]	0.0014
Neointimal Volume	17.56 +/- 18.21 (81)	41.48 +/- 23.02 (80)	-23.92 [-30.33,-17.51]	<0.0001
Clinical Endpoints to 9 months				
[†]TVR-Free	95.25%	87.89%	7.36% [4.35%, 10.37%]	<0.0001
[†]TLR-Free	96.93%	88.51%	8.42% [5.62%, 11.22%]	<0.0001
[†]TVF-Free	92.40%	85.48%	6.92% [3.54%, 10.30%]	0.0001
[†]MACE-Free	91.51%	84.88%	6.63% [3.14%, 10.12%]	0.0003
Clinical Endpoints to 12 months				
[†]TVR-Free	92.87%	82.88%	9.99% [6.41%, 13.57%]	<0.0001
[†]TLR-Free	95.58%	84.89%	10.69% [7.46%, 13.92%]	<0.0001
[†]TVF-Free	90.03%	80.57%	9.46% [5.61%, 13.31%]	<0.0001
[†]MACE-Free	89.15%	79.97%	9.18% [5.26%, 13.10%]	<0.0001
[2]Safety Measures				
In-hospital MACE	2.4% (16/662)	2.1% (14/ 652)	0.3% [-1.3%, 1.9%]	0.854
MACE to 9 months	8.5% (56/ 655)	15.2% (98/ 645)	-6.6% [-10.1%, -3.1%	0.0002
MACE to 12 months	10.7% (70/ 653)	20.0% (129/ 644)	-9.3% [-13.2%, -5.4%]	<0.0001
TVR to 9 months (Primary Endpoint)	4.7% (31/ 655)	12.1% (78/ 645)	-7.4% [-10.4%, -4.4%]	<0.0001
TVR to 12 months	6.9% (45/ 653)	16.9% (109/ 644)	-10.0% [-13.5%, -6.5%]	<0.0001
TVF to 9-months	7.6% (50/655)	14.6% (94/645)	-6.9% [-10.3%, -3.5%]	0.0001
TVF to 12-months	9.7% (64/ 653)	19.2% (125/ 644)	-9.6% [-13.4%, -5.8%]	<0.0001
Stent Thrombosis to 30 days	0.3% (2/ 662)	0.6% (4/ 652)	-0.3% [-1.0%, 0.4%]	0.4487
Stent Thrombosis to 9 months	0.6% (4/ 655)	0.8% (5/ 645)	-0.2% [-1.1%, 0.7%]	0.7513
Stent Thrombosis to 12 months	0.6% (4/ 653)	0.8% (5/ 644)	-0.2% [-1.1%, 0.7%]	0.7515
CVA to 12 months	1.7% (11/ 654)	0.8% (5/ 644)	0.9% [-0.3%, 2.1%]	0.2075
Serious Bleeding Events to 12 months	2.8% (18/654)	1.9% (12/644)	0.9% [-0.7%, 2.5%]	0.3564
Serious Vascular Events to 12 months	1.8% (12/653)	1.9% (12/644)	-0.0% [-1.5%, 1.4%]	1.0000
Platelet Disorders to 12 months	0.6% (4/653)	0.8% (5/644)	-0.2% [-1.1%, 0.7%]	0.7515
Hematological Dyscrasia to 12 months	1.5% (10/654)	0.8% (5/644)	0.7% [-0.4%, 1.9%]	0.2991

Numbers are % (Count/Sample Size) or Mean±SD (N) (Min, Max). CI = Confidence Interval.
Difference = TAXUS SR – Control.

SE of Difference: = $\text{sqrt}(p_1q_1/n_1+p_2q_2/n_2)$ for proportions, = $\text{sqrt}[\{(1/n_1 + 1/n_2)\{(n_1-1)s_1^2 + (n_2-1)s_2^2\}/(N-2)]$ for continuous variables.
95% CI of Difference = Diff±1.96·SE. 95%
P-values are two-sided and from Student's t test for continuous variables and Fisher's exact test for discrete variables.
Undef = Undefined.
Primary endpoint is 9-month TVR.
Clinical Procedural Success: using the assigned study stent to achieve an in-target-lesion diameter stenosis <30% in the average of 2 near-orthogonal projections, as visually assessed by the physician, without the occurrence of in-hospital MACE.
Technical success: successful delivery and deployment of the study stent to the target lesion, without balloon rupture, embolization, or use of a device outside the treatment strategy.
MLD = Minimum Lumen Diameter
WHO-defined non-Q-wave MI – Elevation of post-procedure CK levels to >2 times normal with elevated CKMB in the absence of new pathological Q-waves.
Stent thrombosis:
Clinical presentation of acute coronary syndrome with angiographic evidence of stent thrombosis
Angiographic documentation of a complete occlusion (TIMI flow 0 or 1) of a previously successfully treated artery (TIMI flow 2 to 3 immediately after stent placement and DS ≤30%), and/or angiographic documentation of a flow limiting thrombus within or adjacent to a previously successfully treated lesion
Acute MI of the distribution of the treated vessel
Death within first 30 days (without other obvious cause) was considered a surrogate for stent thrombosis when angiography was not available
CVA – Sudden onset of vertigo, numbness, aphasia, or dysarthria due to vascular lesions of the brain such as hemorrhage, embolism, thrombosis, or rupturing aneurysm, that persisted >24 hours.
9-Month MACE: the proportion of patients who experience a MACE up to the 9-month follow-up. MACE includes cardiac death, myocardial infarction (MI) including WHO defined Q- and non-Q-wave MI, and target vessel revascularization (TVR).
30-Day MACE: binary MACE rate to 30 days post-procedure.
9-Month Restenosis: the proportion of patients who demonstrate ≥50% diameter stenosis of the target lesion by Quantitative Coronary Analysis (QCA) performed at the Angiographic Core Laboratory at the 9-month follow-up.
Serious Bleeding Complications included: hemorrhage (gastric ulcer, mediastinal, rectal, upper GI, and GI not specified), hematuria, hemoptysis, and hemothorax. Serious Vascular Complications included: hematoma (catheter site and not specified), hemorrhage (catheter site and retroperitoneal), arterial injury, and vascular pseudoaneurysm. Platelet disorders included thrombocytopenia. Hematologic dyscrasia included: anemia, and pancytopenia.
The following survival estimates are by Kaplan-Meier Methods with standard error estimates by Greenwood formula:
†TLR-Free– No target lesion revascularization.
†TVR-Free – No target vessel revascularization.
†TVF-Free – No cardiac death, Q-wave or WHO-defined non Q-wave MI, or target vessel revascularization.
†MACE-Free – No death, Q-wave or WHO-defined non Q-wave MI, or target vessel revascularization.
[2] For each parameter in the safety measures, the denominator is the number of patients randomized to each treatment arm (excluding de-registered patients) who had sufficient follow up (at least 240 days for 9 month visit and at least 330 days for 12 month visit) plus any patients who had an event prior to the milestone visit.

Figure 9-1.TAXUS IV Freedom From TVR to 1 Year (Event-Free Survival ± 1.5 SE)



Time After Initial Procedure

TAXUS	0	7	14	30	60	90	120	150	180	270	365
Entered	662	662	660	660	660	656	652	646	641	633	615
Censored	0	2	0	0	1	1	1	4	3	4	330
Events	0	0	0	0	3	3	5	1	5	14	14
At Risk	662	661	660	660	659.5	655.5	651.5	644	639.5	631	450
Events/Month	0.0	0.0	0.0	0.0	3.0	3.0	5.0	1.0	5.0	4.7	4.4
Event Free	100.0%	100.0%	100.0%	100.0%	99.5%	99.1%	98.3%	98.2%	97.4%	95.2%	92.9%
Std Error	0.00%	0.00%	0.00%	0.00%	0.26%	0.37%	0.50%	0.52%	0.62%	0.83%	1.04%

Control	0	7	14	30	60	90	120	150	180	270	365
Entered	652	652	650	650	648	646	631	616	597	586	562
Censored	0	1	0	1	0	2	2	4	1	1	274
Events	0	1	0	1	2	13	13	15	10	23	31
At Risk	652	651.5	650	649.5	646	645	630	614	596.5	585.5	425
Events/Month	0.0	4.3	0.0	1.9	2.0	13.0	13.0	15.0	10.0	7.7	9.8
Event Free	100.0%	99.8%	99.8%	99.7%	99.4%	97.4%	95.4%	93.0%	91.5%	87.9%	82.9%
Std Error	0.00%	0.15%	0.15%	0.22%	0.31%	0.63%	0.82%	1.00%	1.10%	1.29%	1.50%

Tests Between Groups, To 365 Days

Test	Chi-Square	Degrees of Freedom	p-Value
Log-Rank	31.5258	1	<0.0001
Wilcoxon	32.3772	1	<0.0001

Patients event-free at 366 days or later are censored at 366 days.
Intervals are end inclusive, e.g. interval 90 is defined as 31-90 days, inclusive.
Event-free and standard error estimates are for interval end. Standard errors by Greenwood formula.
"at risk" is the number of patients who "entered" an interval minus (the number of patients "censored" during the interval divided by 2).
"censored" is the number of patients whose last follow-up occurred during that interval and did not have a TVR, e.g., a patient who did not have a TVR and whose last follow-up was on Day 178 would be censored in the 151-180 interval (180 column).

9.2 TAXUS II (SR) Supporting Clinical Trial

Objective: The primary objective of this study was to evaluate the safety and effectiveness of the TAXUS™ NIRx™ Paclitaxel-Eluting Coronary Stent System (1 $\mu g/mm^2$ SR formulation) compared with a matched uncoated control stent.

Conclusion: In selected patients, use of the SR formulation of the TAXUS NIRx (SR) Stent significantly reduced the percent of in-stent net volume obstruction as determined by IVUS at 6 months. There were significant improvements in overall MACE rates as well as reintervention procedures required in the target lesion. No substantial differences were observed as compared to the uncoated control group with respect to safety assessments.

Design: This was a prospective, double-blind trial conducted at 38 sites in 15 countries. Eligible patients had documented angina pectoris and a single *de novo* lesion in a native coronary artery measuring ≤ 12 mm in length with a visual RVD ≥ 3.0 mm and ≤ 3.5 mm.

A total of 267 patients were enrolled and evaluable in this study: 131 TAXUS group and 136 in the Control group. Patients were randomized to receive either a TAXUS NIRx™ (SR) Stent or uncoated NIR coronary stent (bare metal control). After the procedure, patients were treated with aspirin indefinitely and clopidogrel or ticlopidine for 6 months.

Follow-up included 1, 6, and 12 month clinical assessments. In addition, patients agreed to annual telephone follow-up for MACE clinical parameters through 5 years post procedure. Follow-up through 12 months (± 30 days) is currently available for 264/267 (98.8%) of patients.

All patients were required to have angiographic and IVUS follow-up at 6 and 24 months. Angiographic assessments were performed for the area of the vessel within the stent margins (in-stent) and also for the area within the stent margins, including the area immediately 5 mm proximal and distal from the stent margins (analysis segment).

Demographics: There were no clinically significant differences between groups with respect to baseline demographics or clinical characteristics. Factors evaluated included age (mean 61 years), gender (74.5% male), diabetes (13.5%), prior MI (38.5%), hypertension (65%), LAD (42%), LCX (19%), RCA (39%), RVD (mean 2.7 mm), MLD (mean 1.0 mm), %DS (mean ~63%), current smoking (21.4%), IIb/IIIa use (12%) and lesion length (mean 10.5 mm). Demographic data regarding hyperlipidemia, ethnicity and ejection fraction were not monitored in this study. A statistically significantly higher CCS Class was noted in the uncoated control group as compared to the TAXUS group (P=0.0104). This was due to a

difference in CCS Class II (42.7% TAXUS vs. 27.9% Control) and CSS Class III (7.6% TAXUS vs. 19.9% Control). CCS Class I, and CCS Class IV were comparable between treatment groups. The difference in CCS class was not found to be a significant predictor of outcome in the trial.

Methods: Baseline clinical and angiographic data were collected on standardized case report forms by coordinators at the clinical sites. Angiographic and IVUS outcomes were assessed in a blinded fashion by quantitative analysis at designated core laboratories. An independent Clinical Events Committee adjudicated clinical events, and the trial was monitored by an independent Data Monitoring Committee.

Results: In selected patients, 6-month percent in-stent net volume obstruction (primary endpoint) as determined by IVUS was statistically significantly lower in the TAXUS™ NIRx™ (SR) Stent treatment group as compared with the uncoated control group (7.85% versus 23.17%, $p<0.0001$).

In-stent restenosis, for the TAXUS NIRx (SR) Stent treatment group was 2.3% as compared to 17.9% for the uncoated control group ($p<0.0001$). Analysis segment restenosis, was 5.5% for the TAXUS NIRx (SR) Stent group as compared to 20.1% for the uncoated control group ($p=0.0004$). At the 6-month time-point, statistically significant improvements were also observed in late loss, MLD, and %DS for the TAXUS NIRx (SR) Stent group as compared to the uncoated control group.

Lower rates for MACE were observed in the TAXUS NIRx (SR) Stent group as compared with the uncoated control group at 6-months follow-up (8.5% versus 19.5%, $p=0.0125$), and 12-month follow-up (10.9% versus 22.0%, $p=0.0191$) (Table 9-2). MACE-free survival was improved in the TAXUS group as compared with the uncoated control group at both 6 and 12 months.

Table 9-2 summarizes the principle safety and effectiveness results of the TAXUS II (SR) trial through 12 months. Figure 9-2 provides the cumulative percent of patients who are TVR-Free through 12 months.

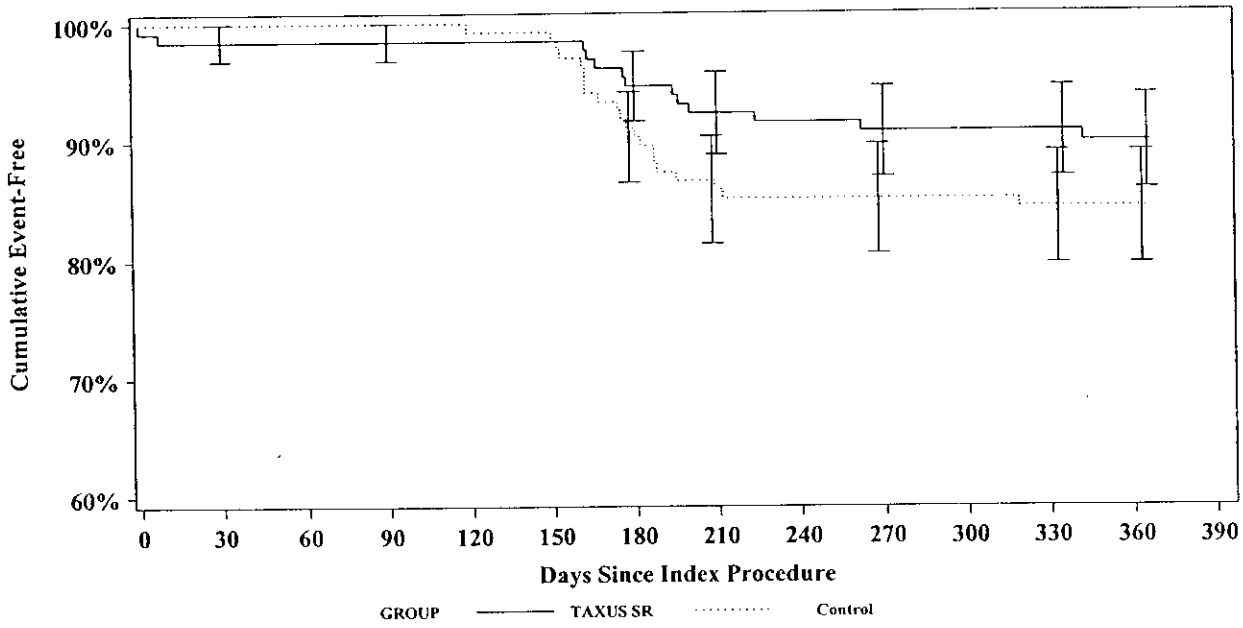
Table 9-2. TAXUS II (SR) Principal Safety and Effectiveness Results through 12 months

	TAXUS II (SR) (N=131)	Control (N=136)	Difference [95% CI]	P Value
Effectiveness Measures				
Clinical Procedural Success	95.4% (125/131)	93.4% (127/136)	2.0% [-3.5%, 7.5%]	0.5976
Technical Success	97.7% (128/131)	98.5% (134/136)	-0.8% [-4.1%, 2.4%]	0.6794
6-Month % Net Volume Obstruction	7.85±9.87 (118)	23.17±18.19 (125)	-15.32 [-19.03, -11.61]	<0.0001
6-month In-stent restenosis	2.3% (3/128)	17.9% (24/134)	-15.6% [-22.6%, -8.6%]	<0.0001
6-month Analysis segment restenosis	5.5% (7/128)	20.1% (27/134)	-14.7% [-22.5%, -6.8%]	0.0004
MLD (mm), Stented Segment				
Post-Procedure	2.53±0.29 (128)	2.58±0.37 (135)	-0.05 [-0.13, 0.03]	0.2132
6-Month	2.23±0.47 (128)	1.79±0.54 (134)	0.44 [0.32, 0.56]	<0.0001
MLD (mm), Analysis Segment				
Post Procedure	2.15±0.37 (128)	2.23±0.43 (135)	-0.08 [-0.17, 0.02]	0.1202
6-Month	2.01±0.46 (128)	1.70±0.49 (134)	0.31 [0.20, 0.43]	<0.0001
% DS, Stented Segment				
Post Procedure	10.90±6.52 (128)	10.20±5.94 (135)	0.70 [-0.81, 2.20]	0.3659
6-Month	19.53±12.71 (128)	31.77±17.11 (134)	-12.25 [-15.91, -8.59]	<0.0001
% DS, Analysis Segment				
Post Procedure	23.07±9.27 (128)	21.24±8.41 (135)	1.83 [-0.31, 3.97]	0.0943
6-Month	26.79±12.78 (128)	35.11±15.09 (134)	-8.32 [-11.71, -4.93]	<0.0001
6-Month Late Loss (mm), Stented Segment	0.31±0.38 (127)	0.79±0.45 (134)	-0.48 [-0.58, -0.38]	<0.0001
TLR Free to 12 months	95.4%	87.5%	7.9% [1.3%, 14.5%]	0.0279
TVR Free to 12 months	90.1%	84.6%	5.5% [-2.4%, 13.5%]	0.2013
MACE free to 12 months	89.3%	78.7%	10.6% [2.0%, 19.3%]	0.0201
[1]**Safety Measures**				
In-Hospital MACE	1.5% (2/131)	4.4% (6/136)	-2.9% [-6.9%, 1.2%]	0.2823
MACE to 30 days	2.3% (3/131)	4.4% (6/136)	-2.1% [-6.4%, 2.2%]	0.5010
MACE to 6 months	8.5% (11/130)	19.5% (26/133)	-11.1% [-19.4%, -2.8%]	0.0125
MACE to 12 months	10.9% (14/129)	22.0% (29/132)	-11.1% [-20.0%, -2.2%]	0.0191
Stent Thrombosis to 1 day	0.8% (1/131)	0.0% (0/136)	0.8% [-3.8%, 7.4%]	0.4906
Stent Thrombosis to 6 months	0.8% (1/130)	0.0% (0/133)	0.8% [-3.9%, 7.4%]	0.4906
Stent Thrombosis to 12 months	1.6% (2/129)	0.0% (0/132)	1.5% [-3.4%, 9.0%]	0.2398
Serious Bleeding Events to 12 months	3.9% (5/129)	6.0% (8/133)	-2.1% [-7.4%, 3.1%]	0.5718
Serious Vascular Events to 12 months	3.1% (4/129)	0.8% (1/132)	2.3% [-1.0%, 5.7%]	0.2098

Numbers are % (Count/Sample Size) or Mean±SD (N) (Min, Max). CI = Confidence Interval.
Difference = TAXUS SR stent – Control.
SE of Difference: = $\text{sqrt}(p_1q_1/n_1+p_2q_2/n_2)$ for proportions, = $\text{sqrt}[(1/n_1 + 1/n_2)\{(n_1-1)s_1^2 + (n_2-1)s_2^2\}/(N-2)]$ for continuous variables.
95% CI of Difference = Diff±1.96·SE. 95% for all measures except stent thrombosis where exact confidence intervals were calculated due to one group having a rate of zero
P-values are two-sided and from Student's t test for continuous variables and Fisher's exact test for discrete variables.
Primary endpoint is 6-Month Percent Stented Segment Net Volume Obstruction, determined by IVUS.
Event/success rates are number of patients with the outcome ÷ the number of patients evaluable for the outcome.
Clinical Procedural Success: using the assigned study device to achieve an in-target-lesion diameter stenosis <30% in the average of 2 near-orthogonal projections, as visually assessed by the physician, without the occurrence of in-hospital MACE.

6-Month MACE: the proportion of patients who experience a MACE up to the 6-month follow-up. MACE includes cardiac death, myocardial infarction (MI) including Q- and non-Q-wave MI, and target vessel revascularization (TVR).
30-Day MACE: binary MACE rate to 30 days post-procedure.
12-Month MACE: binary MACE rate to 365 days post-procedure.
6-Month Restenosis: the proportion of patients who demonstrate ≥50% diameter stenosis of the target lesion by Quantitative Coronary Analysis (QCA) performed at the Angiographic Core Laboratory at the 6-month follow-up.
[1] For each parameter in the safety measures, the denominator is the number of patients randomized to each treatment arm who had sufficient follow up (at least 150 days for 6 month visit and at least 335 days for 12 month visit) plus any patients who had an event prior to the milestone visit.

Figure 9-2. TAXUS II (SR) Freedom From TVR to 1 Year (Event-Free Survival ± 1.5 SE)



Time After Initial Procedure

TAXUS SR	0	14	30	90	180	210	270	335	365
Entered	131	130	129	129	129	124	120	118	113
Censored	0	0	0	0	0	1	0	5	69
Events	1	1	0	0	5	3	2	0	1
At Risk	131	130	129	129	129	123.5	120	115.5	78.5
Events/Month	30.0	2.1	0.0	0.0	1.7	3.0	1.0	0.0	1.0
Event Free	99.2%	98.5%	98.5%	98.5%	94.7%	92.3%	90.8%	90.8%	89.9%
Std Error	0.8%	1.1%	1.1%	1.1%	2.0%	2.3%	2.5%	2.5%	2.7%

Control	0	14	30	90	180	210	270	335	365
Entered	136	136	135	135	135	122	115	114	107
Censored	0	1	0	0	0	1	0	6	54
Events	0	0	0	0	13	6	1	1	0
At Risk	136	135.5	135	135	135	121.5	115	111	80
Events/Month	0.0	0.0	0.0	0.0	4.3	6.0	0.5	0.5	0.0
Event Free	100%	100%	100%	100%	90.4%	85.9%	85.2%	84.4%	84.4%
Std Error	0.0%	0.0%	0.0%	0.0%	2.5%	3.0%	3.1%	3.1%	3.1%

Tests Between Groups, To 365 Days

Test	Chi-Square	Degrees of Freedom	p-Value
Log-Rank	1.945	1	0.163
Wilcoxon	2.093	1	0.148

Patients event-free at 366 days or later are censored at 366 days.
Intervals are end inclusive, e.g. interval 90 is defined as 31-90 days, inclusive.

Event-free and standard error estimates are for interval end. Standard errors by Greenwood formula.
"at risk" is the number of patients who "entered" an interval minus (the number of patients "censored" during the interval divided by 2).
"censored" is the number of patients whose last follow-up occurred during that interval and did not have a TVR, e.g., a patient who did not have a TVR and whose last follow-up was on Day 178 would be censored in the 151-180 interval (180 column).

9.3 TAXUS I Feasibility Clinical Trial

Objective: The primary objective of this study was to evaluate the safety at 30 days (MACE) of the TAXUS™ NIRx™ Paclitaxel-Eluting Coronary Stent System (1 μg /mm^2 SR formulation), as compared with a matched uncoated control stent. Secondary objectives included QCA and IVUS evaluation at 6 months.

Conclusion: In selected patients, use of the TAXUS NIRx (SR) Stent provided favorable MACE, QCA, and IVUS results through 24 months of follow-up.

Design: This was a multi-center, prospective, randomized, double-blind study. Eligible patients were those presenting for stenting of *de novo* or restenotic lesions of a native coronary artery (RVD 3.0 to 3.5 mm) with a target lesion ≤12 mm in length and stenosis between 50% and 99% in diameter, using visual estimates, who were candidates for PCI and CABG, and had documented angina pectoris or functional ischemia.

A total of 61 patients were enrolled and evaluable in this study: 31 in the TAXUS group and 30 in the Control group. Patients were randomized to receive either a paclitaxel-eluting TAXUS NIRx (SR) Stent or an uncoated NIRx coronary stent (bare metal control). After the procedure, patients were treated with aspirin indefinitely and clopidogrel or ticlopidine for 6 months.

Follow-up included 1, 6, 9, 12 months, and 2 year clinical assessments. In addition, patients agreed to annual telephone follow-up for clinical parameters through 5 years post-procedure. Clinical follow-up is available through 2 years.

Angiography and IVUS were performed at the 6-month follow-up visit for all patients.

Demographics: Patients were well matched for baseline demographics with no statistically significant differences between groups ($p>0.05$). Factors evaluated included age (mean 65 years), gender (89% male), diabetes (18%), prior MI (28%), hypertension (61%), hyperlipidemia (74%), smoking history (49%), LAD (41%), LCX (29.5%), RCA (29.5%), RVD (mean 2.97 mm), MLD (mean 1.27 mm), %DS (mean 57%), and lesion length (mean 11.28 mm). Demographic data regarding hyperlipidemia, smoking history, IIb IIIa use, ethnicity and ejection fraction were not monitored in this study. There were more patients with CSS Class II in the TAXUS group (61.3% TAXUS vs. 33.3% Control) and more patients with CSS Class III and IV in the control group (25.8% TAXUS vs. 36.6% Control) though none of the differences were statistically significant. The difference in CCS class was not found to be a significant predictor of outcome in the trial.

Methods: Baseline clinical and angiographic data were collected on standardized case report forms by coordinators at the clinical sites. Angiographic and IVUS outcomes were assessed in

a blinded fashion by quantitative analysis at designated core laboratories. An independent Clinical Events Committee adjudicated clinical events.

Results: The primary endpoint, the 30-day MACE rate, was zero in both groups. The cumulative MACE rate in the TAXUS group at 12 months was 3% (1/31) and in the Control group was 10% (3/30). No additional MACE events were reported in either the TAXUS NIRx (SR) Stent treatment group or control group at two years.

In-stent improvements were noted in MLD, late lumen loss and loss index.

Table 9-3 summarizes the principle safety and effectiveness results of the TAXUS I trial through 2 years.

Table 9-3. TAXUS I Principal Safety and Effectiveness Results Through 2 Years

Safety Measures and Other Clinical Events	TAXUS NIRx™ (SR) N=31	NIR™ Control N=30	*p-value*
MACE (30-day)	0% (0/31)	0% (0/30)	NA
Cardiac Death	0% (0/31)	0% (0/30)	NA
Q-Wave MI	0% (0/31)	0% (0/30)	NA
TVR (CABG and/or PCI)	0% (0/31)	0% (0/30)	NA
MACE (12-Month)	3% (1/31)	10% (3/30)	0.612
Cardiac Death	0% (0/31)	0% (0/30)	NA
Q-Wave MI	0% (0/31)	0% (0/30)	NA
TVR (CABG and/or PCI)	3% (1/31)	10% (3/30)	0.612
MACE (2-Year)	3% (1/31)	10% (3/30)	0.612
Cardiac Death	0% (0/31)	0% (0/30)	NA
Q-Wave MI	0% (0/31)	0% (0/30)	NA
TVR (CABG and/or PCI)	3% (1/31)	10% (3/30)	0.612
Stent Thrombosis to 2 years	0% (0/31)	0% (0/31)	NA
QCA In-Stent Lesion Characteristics			
Pre-procedure			
RVD, mm	2.99±0.46 (31)	2.94±0.52 (29)	0.699
MLD, mm	1.30±0.43 (31)	1.23±0.43 (29)	0.558
%DS	56.51±12.26 (31)	57.82±13.24 (29)	0.692
Lesion length, mm	10.70±3.27 (31)	11.89±4.93 (29)	0.272
Post-procedure			
MLD, mm			0.414
%DS	6.12±9.49 (31)	2.95±0.34 (31)	0.096
6-Month follow-up			
RVD, mm	3.02±0.47 (30)	3.01±0.53 (29)	0.899
MLD, mm	2.60±0.49 (30)	2.19±0.65 (29)	0.008
%DS	13.56±11.77 (30)	27.23±16.69 (29)	<0.001
Restenosis Rate ≥50%	0% (0/30)	10% (3/29)	0.112
Late lumen loss, mm	0.36±0.48 (30)	0.71±0.47 (26)	0.009
Loss index	0.22±0.29 (30)	0.45±0.29 (26)	0.004

Numbers are % (Count/Sample Size) or Mean±SD (N).
P-values are two-sided and from Student's t test for continuous variables and Fisher's exact test for discrete variables.
Primary endpoint is 30-day MACE.
Event/success rates are number of patients with the outcome ÷ the number of patients evaluable for the outcome.

MLD = Minimum Lumen Diameter
RVD = Reference Vessel Diameter
% DS = Percent diameter stenosis
MACE includes cardiac death, myocardial infarction (MI) including Q- and non-Q-wave MI, and target vessel revascularization (TVR).binary MACE rate to 30 days post-procedure
MACE (30-day): the proportion of patients who experience a MACE up 30 days post-procedure
MACE (6-Months): the proportion of patients who experience a MACE up to 6 months post-procedure
MACE (12-month): the proportion of patients who experience a MACE up to 12 months post-procedure
MACE (2-year): the proportion of patients who experience a MACE up to 2 years post-procedure.
Restenosis rate: the proportion of patients who demonstrate ≥50% diameter stenosis of the target lesion by Quantitative Coronary Analysis (QCA) performed at the Angiographic Core Laboratory at the 6-month follow-up.

10 Individualization of Treatment

See also **Precautions - Section 5.6, Use in Special Populations** and **Section 5.6.1, Lesion/Vessel Characteristics.**

The risks and benefits should be carefully considered for each patient before use of the TAXUS™ Express^{2}™ Stent System. Patient selection factors to be assessed should include a judgment regarding risk of prolonged anticoagulation. On the basis of the clinical trial results, administration of clopidogrel or ticlopidine is recommended pre-procedure and for a period of 6 months post procedure. Aspirin should be administered concomitantly with clopidogrel or ticlopidine and then continued indefinitely. Stenting is generally avoided in those patients at heightened risk of bleeding (e.g., those patients with recently active gastritis or peptic ulcer disease) in which anticoagulation therapy would be contraindicated.

Premorbid conditions that increase the risk of poor initial results or the risks of emergency referral for bypass surgery (diabetes mellitus, renal failure, and severe obesity) should be reviewed.

11 Patient Counseling Information

Physicians should consider the following in counseling patients about this product:

- Discuss the risks associated with stent placement.
- Discuss the risks associated with a paclitaxel-eluting stent.
- Discuss the risks/benefits issues for this particular patient.
- Discuss alteration to current lifestyle immediately following the procedure and over the long term.

The following information is included in the package (or on-line) for physicians to provide to their patients.

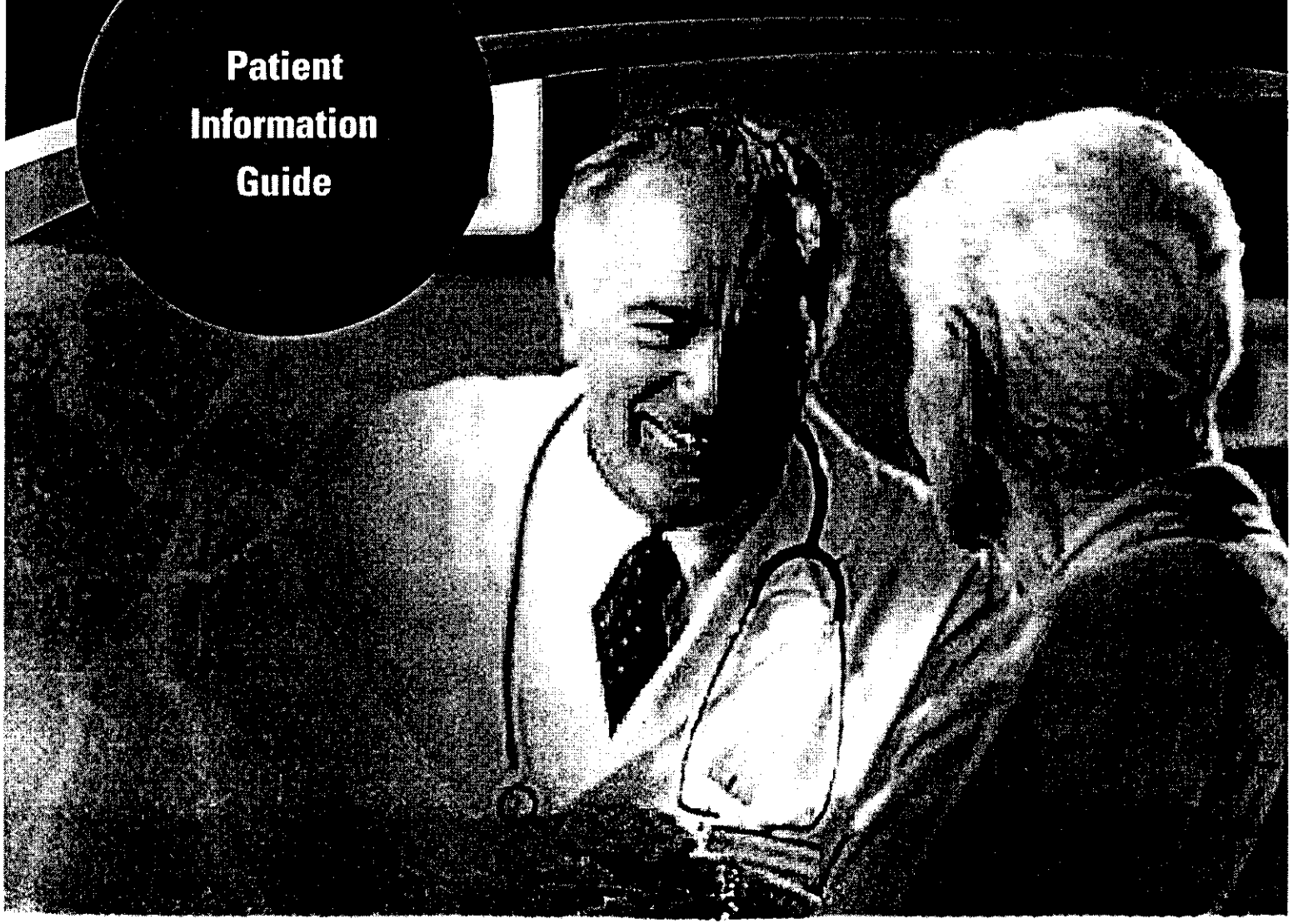
- A Patient Information Guide which includes information on coronary artery disease, the implant procedure and the TAXUS Express^{2} Stent System.
- A Patient Implant Card that includes both patient information and stent implant information.

TAXUS™ Express²™

Paclitaxel-Eluting Coronary Stent System

Boston Scientific

Patient Information Guide



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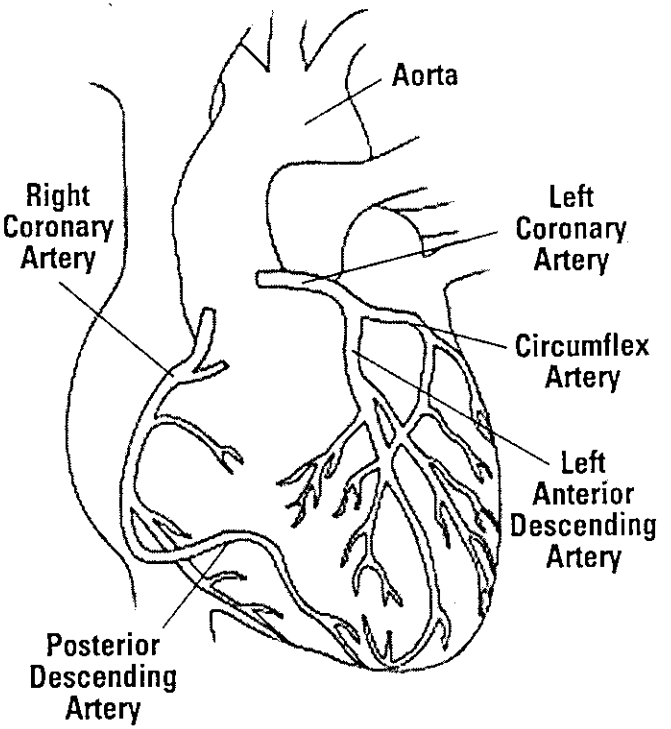
Coronary Artery Disease

Coronary Artery Disease (CAD) is usually caused by *atherosclerosis,* and affects the *coronary arteries* that surround the heart. These coronary arteries supply blood with oxygen and other nutrients to the heart muscle to make it function properly. CAD occurs when the inner walls of the coronary arteries thicken due to a buildup of cholesterol, fatty deposits, calcium, and other elements. This material is known as *plaque.* As plaque develops, the vessel narrows. When the vessel narrows (for example with physical exertion or mental stress), blood flow through the vessel is reduced so less oxygen and other nutrients reach the heart muscle. This reduced blood flow may cause mild to severe chest pains or chest pressure. This pain or pressure can also spread to the arms or jaw, a condition known as *angina pectoris.* Complete obstruction (no blood flow) of a coronary artery can result in a heart attack *(myocardial infarction).*



Anyone who experiences symptoms of angina pectoris or myocardial infarction should promptly seek medical care.

Over 13 million Americans suffer from CAD each year. However, treatment options for CAD have substantially improved in recent years, and many CAD patients are now able to return to a normal lifestyle shortly after treatment.

Who Is at Risk?

People with a history of high cholesterol, diabetes, smoking, high blood pressure, being overweight and a family history of CAD have an increased risk of developing atherosclerosis in the coronary arteries. Increasing age adds to the risk of CAD. In addition, menopausal status may play a role in women.

Diagnosis of Coronary Artery Disease

Doctors may use various tests to diagnose CAD. An *electrocardiogram (EGG or EKG)* measures your heart's electrical activity and may show whether parts of your heart muscle have been damaged by a heart attack due to CAD. A *stress test* records your heart's electrical activity while you are exercising and may tell your doctor whether part of your heart muscle is damaged. A *coronary angiogram* is a procedure performed by a cardiologist in a Cardiac Catheterization Lab. This procedure is done by injecting a contrast dye into the coronary arteries so that the vessels can be seen on an x-ray screen. The angiogram will show if any blockages and/or artery narrowing has occurred. This will help your doctor decide how to treat you.

Treatment of Coronary Artery Disease

CAD may be managed through a combination of changes in lifestyle and physical activity, diet, and medical treatment. The therapy your doctor recommends will depend on the condition and severity of the disease. Nitroglycerin is often given to relieve chest discomfort due to blockages, but does not treat the blockage itself. Medical treatments of the blockage may include medications, *angioplasty,* with or without *stent* placement, or *coronary artery bypass graft surgery (CABG).*

Notes

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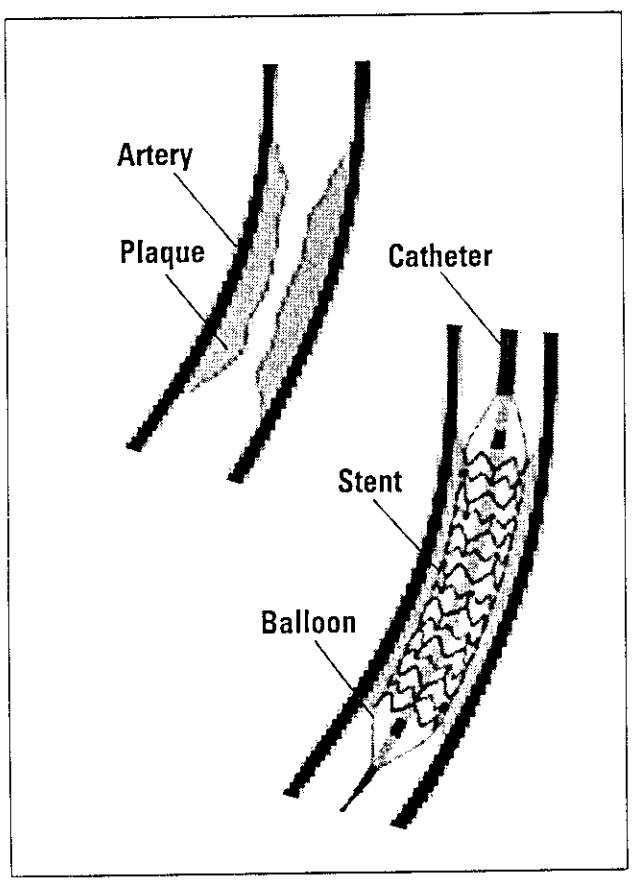
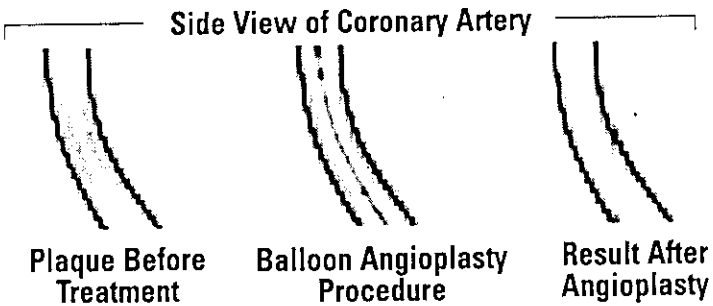
Angioplasty

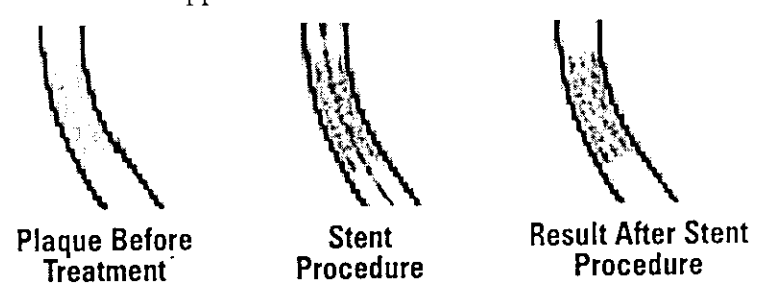
Angioplasty is a minimally invasive treatment of the coronary arteries performed in the hospital to open blocked arteries, also known as percutaneous transluminal coronary angioplasty (PTCA). A thin tube known as a *catheter* is inserted through the groin or wrist and is then threaded through a major blood vessel to the site of the blockage. A small balloon, located on the tip of the catheter, is then expanded to reduce the blockage. PTCA can be performed with a balloon alone, or can involve the placement of a coronary stent.





Coronary Artery Stents

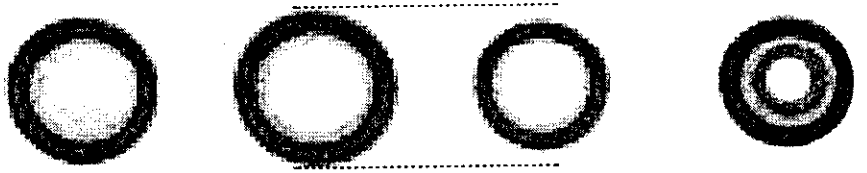
Coronary artery stents are devices that can help to reduce the risk of recurrent blockage or narrowing following an angioplasty procedure. Stents are small expandable metal tubular structures (lattice) that are implanted into a vessel and expanded to fit the size, shape, and bend of the vessel wall, propping it open to help prevent further blockages. Once in place, the stent will remain in your artery. Over time, the artery wall will heal around the stent as it continues to support the vessel.



Restenosis

Many patients who undergo *balloon angioplasty* treatment will experience a renarrowing of the artery, or *restenosis*, in the area that was being treated. The rate of restenosis is between 30 and 50 percent for angioplasty patients who do not receive a stent within the first six months after their initial procedure. The renarrowing can be caused by a combination of factors including vessel recoil and formation of tissue ingrowth in the treated area.

Cross-Section of Coronary Artery



Coronary Artery Disease (Initial Artery Size with Typical Plaque)

After Expansion by Balloon Angioplasty—Plaque Pushed Back. Artery Wall Stretches

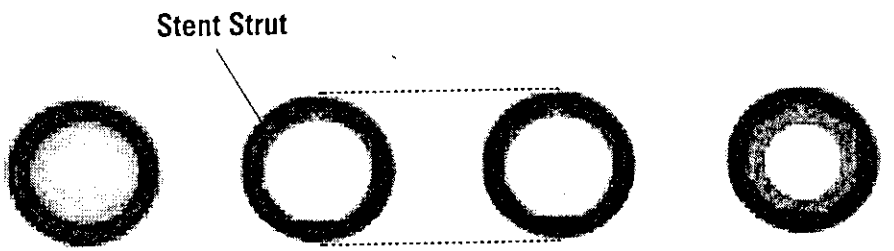
Vessel Recoil (Stretched Vessel Naturally Returns to Initial Size)

Restenosis Narrows Treated Vessel Over Time (Initial Artery Size Plus Tissue Ingrowth)

Notes

Notes

Although coronary artery stents have proven to reduce the occurrence of restenosis compared to balloon angioplasty, restenosis still occurs in approximately 10 to 30 percent of patients who receive bare metal stents. Unlike restenosis after balloon angioplasty, restenosis in a stent (*in-stent restenosis*) is not typically associated with *vessel recoil*. Instead, in-stent restenosis primarily results from increased tissue ingrowth.



Coronary Artery Disease (Initial Artery Size with Typical Plaque)

After Expansion by Balloon Angioplasty with Stent Plaque Pushed Back. Artery Wall Stretches

Stent Prevents Stretched Vessel from Recoiling to Initial Size

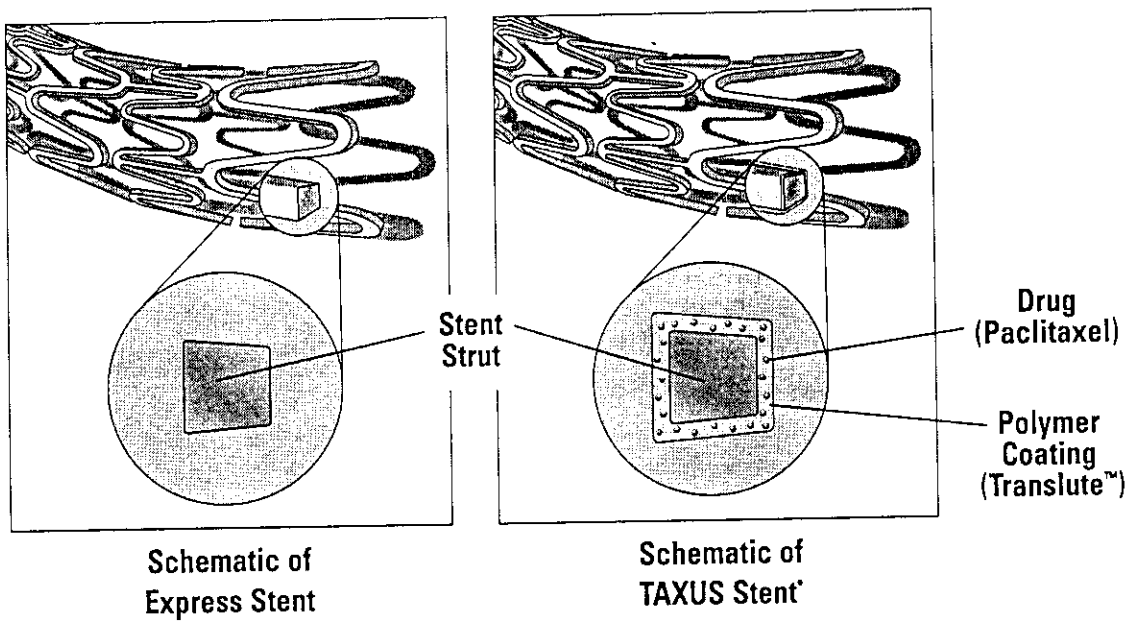
Restenosis Narrows Treated Vessel Over Time (Initial Artery Size Plus Tissue Ingrowth)

Your Drug-Eluting Stent, the TAXUS™ Express²™ Paclitaxel-Eluting Coronary Stent System

Drug-Eluting Stents

A drug-eluting stent is a bare metal stent that has been coated with a drug and a polymer. Drug-eluting stents are designed to deliver a drug locally to reduce tissue ingrowth.

Cross Section of a coated stent to point out how coating conforms to the surface of the bare metal stent



**Note: A green color is used to show coating but actual coating is clear*

The Express Stent Platform for the TAXUS Express Stent (i.e. TAXUS Stent)

The Express stent, the small steel tube upon which the drug/polymer coating is applied, has been used extensively as a bare metal stent and is very flexible, allowing it to conform to the natural curves of your artery.

The Polymer Coating on the TAXUS Stent

The stent is coated with a proprietary polymer (a chemical compound) called Translute™, which was developed specifically for the TAXUS Stent. The Translute polymer is also known as SIBS [poly(styrene-b-isobutylene-b-styrene)]. The polymer carries and protects the drug before and during the procedure. Then, once the stent is implanted in the coronary artery, it helps control drug release into the arterial wall. This contributes to even and consistent distribution of the drug from the stent.

Notes

The Drug that is Released from the TAXUS Stent

The TAXUS stent was designed by coating the Express stent with the drug paclitaxel, and the polymer. The paclitaxel/polymer coating has been designed to allow for a consistent and controlled release of the drug from the stent surface into the artery walls, to minimize release into the blood stream. Both the amount of drug and release rate have been determined so that healing can occur while allowing the processes leading to restenosis to be minimized, thus reducing the need for additional treatment in the stented area.

The TAXUS stent uses a very small but effective dose of paclitaxel, which is released slowly over the time period when restenosis is most likely to occur. Some paclitaxel will remain on the stent, with no additional measurable amount being released into the body.

NOTE: Paclitaxel is also available in injection form, known by the trade name Taxol®, and is also available in generic formulations. Let your doctor know if you are currently using this drug.

When should the TAXUS Stent NOT be Used? (Contraindicated)

- If you have an allergy to the drug paclitaxel or structurally related drugs, or to the SIBS polymer.
- If you cannot take aspirin or blood-thinning medications (also called antiplatelets or anticoagulants).
- If the physician decides that the blockage will not allow complete inflation of the angioplasty balloon or proper placement of the stent.

What are the Risks & Potential Benefits of Treatment with the TAXUS Stent?

Potential adverse events, which may be associated with the implantation of a coronary stent, include:

- air, tissue, or clots which can block the vessel (emboli)
- allergic reaction to the contrast dye (which could include kidney failure)
- allergic reaction to the metal used to make the stent (stainless steel)
- aneurysm
- bleeding that would require a blood transfusion
- bruising which resides on a blood vessel (pseudo-aneurysm)
- chest pain or discomfort
- collection of blood in the lining of the heart
- coronary spasms
- death
- emergency bypass surgery
- heart attack
- high or low blood pressure
- inadequate supply of blood to the heart
- infection and/or pain at the access site
- injury or tearing of blood vessel
- irregular heart beat (arrhythmia)
- movement of the stent as it is sliding from the balloon into the blood vessel (embolization)
- plugging of the stent with blood clots
- renewed formation of a narrowing in the treated vessel (restenosis)
- side effects due to contrast dye or heparin
- shock/pulmonary edema
- stroke or other neurological events
- total occlusion of the vessel
- unnatural connection between vein and artery (arterio-venous fistula)
- vessel trauma requiring surgical repair or reintervention
- worsening of heart and lung function

Notes

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Potential adverse events related to the drug paclitaxel (based on studies of patients who used the drug for a prolonged period of time) or the polymer include:

- abnormal liver values
- allergic or immunologic reaction to the drug (paclitaxel)
- allergic reaction to the polymer [Translute: poly(styrene-b-isobutylene-b-styrene)] or polymers with similar chemical structures
- anemia
- blood transfusion
- changes in blood profile (decrease of white and red blood cells and platelets)
- changes of the tissue in the vessel wall including inflammation, cell injury, and cell death
- disturbances of the gastrointestinal (GI) tract and stomach
- loss of hair
- muscle pain/joint pain
- nerve disease in arms and legs

There may be other potential adverse events that are unforeseen at this time.

Exposure to paclitaxel and the polymer coating is directly related to the number of implanted stents. Use of more than one TAXUS Stent has not been adequately evaluated. Use of multiple stents will result in your exposure to a larger amount of paclitaxel and polymer coating than experienced in the clinical studies.

There is no clinical experience on the performance of the TAXUS Stent before or after use of *brachytherapy,* or when used with other types of coated or drug-eluting stents.

The safety and effectiveness of the TAXUS Stent was compared to the Express Stent (an uncoated stent) in the TAXUS IV trial that included 1,314 patients. All patients were followed for 1 year. The study results showed that patients who received a TAXUS Stent had a significantly lower incidence of repeat procedures in the vessel where the stent was placed, when compared to the uncoated Express stent, (6.9% for TAXUS Stent, 16.9% for Express Stent). The combined occurrence of Major Adverse Cardiac Events which is comprised of death, heart attacks, bypass surgery, and repeat angioplasty was 10.7% for TAXUS Stent patients and 20% for Express Stent patients.

The study showed the risks associated with the TAXUS Stent are equivalent to the risks associated with the uncoated Express Stent.

Long term risks and benefits (i.e., greater than one year) associated with the TAXUS Stent are currently unknown.

Alternative Practices and Procedures

Treatment of patients with coronary artery disease including in-stent restenosis may include exercise, diet, drug therapy, percutaneous coronary interventions (such as angioplasty, bare metal stents, coated stents, and other drug eluting stents), and coronary artery bypass surgery.

Notes

Notes

The Angioplasty Procedure

Preparation for the Procedure

Your doctor will instruct you on how to prepare for the angioplasty procedure and stent implantation procedure prior to being admitted to the hospital. Your doctor may ask you to take aspirin and other prescribed medications for several days before the procedure. This is done to "thin" the blood to prevent blood clots from forming during the procedure. It is important to tell your doctor if you cannot take aspirin or have a history of bleeding problems. Your doctor also needs to know if you are taking any other medications, have drug allergies, or are allergic to any metals or plastics.

Angioplasty and Stent Placement Procedure

Your angioplasty procedure will be performed in a specially equipped area of the hospital called the Cardiac Catheterization Laboratory. You will have to lay flat on your back during the procedure and you will remain awake, allowing you to follow your cardiologist's instructions (e.g., "breathe deeply"). Your groin or arm will be shaved and cleaned with antiseptic and you will be given a local anesthetic to numb the area.

Your cardiologist will place an *introducer sheath* either in your groin or in your arm to gain access to the artery. The sheath enables the cardiologist to slide a small guiding catheter up to the entrance of the coronary artery. Through the guiding catheter, a contrast dye will be injected that helps the doctor see the coronary arteries on the x-ray machine. A finer guide wire is then advanced through the guiding catheter to the stenosis, or blockage, in the diseased artery. This provides the "railway track" which carries all the equipment necessary for the procedure.

Using the guiding catheter, a balloon catheter is then positioned precisely in the clogged area of the coronary artery. Once in place, the balloon is inflated, compressing the plaque buildup and widening the artery. At this time you may experience some chest pain. Although this is normal, let your doctor know if you are experiencing any pain.

After the artery has been widened, your doctor will then pass the stent, mounted on a delivery catheter, into the coronary artery where the balloon was inflated. Your doctor will again inflate the balloon to expand the stent and deliver it to the inner wall of the artery. The stent will expand to shape itself to the size and contours of your vessel.

Your doctor may choose to expand the stent further by using another balloon. If required, the balloon catheter is inserted inside the stent and then inflated to help the stent make better contact with the artery wall. This part of the procedure is called *post-dilatation.* Post-dilatation is done to enable full contact of the stent to the artery wall. Once in place, the TAXUS stent will remain as a permanent implant in your artery. The TAXUS stent uses a very small but effective dose of paclitaxel, which is released slowly over the time period when restenosis is most likely to occur. Some paclitaxel will remain in the stent, with no additional measurable amount being released into the body.

POST-TREATMENT

After the Procedure

After the stent is implanted, you will be moved to a cardiology ward for a short period where you can be monitored closely as you begin to recover. On average, your hospital stay may last one to three days before you are discharged.

Notes

Notes

Activity

- Follow your doctor's guidelines.
- Return to normal activities gradually, pacing your return to activity as you feel better. Check with your doctor about strenuous activities.
- Let your doctor know about any changes in lifestyle you make during your recovery period.
- Report side effects from medications immediately. These may include headaches, nausea, vomiting, or rash.
- Do not stop taking your medications unless you are asked to stop by the doctor who implanted your stent.
- Keep all follow-up appointments, including laboratory blood testing.
- Carry your Patient Information Card (provided in the back of this booklet) at all times. If you receive dental or medical care or report to an emergency room/center, show your Patient Identification Card.

Medications

Your doctor may prescribe a number of medications to thin the blood and prevent blood clots from forming and adhering to the surface of the stent. You will be asked to take a small daily dose of aspirin indefinitely. In addition, your treatment regimen will include either clopidogrel or ticlopidine for a period of 6 months in combination with aspirin. It is extremely important to follow your medication regimen.

Follow-Up Examinations

You will need to see the doctor who implanted your stent for routine follow-up examinations. During these visits, your doctor will monitor your progress and evaluate your medications, the clinical status of your CAD, and how the stent is working for you.

FREQUENTLY ASKED QUESTIONS

Can the stent move or rust?
Once positioned by your physician, the stent does not move on its own. It is manufactured so it will not rust.

Can I walk through metal detectors with a stent?
Yes, without any fear of setting them off.

How soon can I go back to work?
The majority of people return to work within a few days following the procedure.

What if I still get pains?
If you experience pain, inform your cardiologist or the center where the procedure was performed immediately.

Can I undergo MRI or scanner testing with a stent?
Your stent should not move during an MRI scan, but it is unknown whether an MRI scan will heat your stent, and possibly change how the drug is released from the stent. Prior to undergoing these examinations, inform your doctor that you have a drug-eluting stent.

Can I play sports?
Yes, but be cautious! Your doctor will tell you what sports you can play and when you can start them.

What should I change in my diet?
Your doctor may prescribe a low-fat, low-cholesterol diet to help reduce the levels of fat in your blood and reduce your risk.

Does paclitaxel have any drug interactions that I should be concerned about?
Formal drug interaction studies with paclitaxel after use of a TAXUS Express Stent have not been conducted. Since some paclitaxel will remain on the stent, interactions at the location of the stent itself affecting the performance of the drug cannot be ruled out. Be sure to discuss with your doctor any drugs you are taking or planning to take.

What if I have taken paclitaxel before for cancer treatment and had a reaction to it?
Be sure to let your doctor know if you have had a previous allergic reaction to paclitaxel.

GLOSSARY

Angina Pectoris Symptoms experienced when the heart muscle is not receiving adequate oxygen (may include chest, arm or back pain, shortness of breath, nausea, vomiting).

Angiogram X-ray of the heart using contrast dye injection.

Angioplasty A minimally invasive treatment of the coronary arteries, to open blocked arterial vessels. Also known as percutaneous transluminal coronary angioplasty (PTCA).

Atherosclerosis A disease in which the flow of blood to the heart is restricted with plaque deposits and, therefore, less oxygen and other nutrients reach the heart muscle. This may lead to chest pain (angina pectoris) or to a heart attack (myocardial infarction).

Balloon Angioplasty Opening the blocked artery by using a balloon catheter that is inflated inside the vessel.

Brachytherapy The use of a locally delivered dose of radiation to control the process of restenosis.

Catheter A small, thin plastic tube used to provide access to parts of the body, such as the coronary arteries.

Coronary Angiogram A test in which contrast dye is injected into the coronary arteries and allows the doctor to see the vessels on an x-ray machine.

Coronary Arteries The arteries that surround the heart and supply blood containing oxygen and nutrients to the heart muscle.

Coronary Artery Bypass Graft Surgery (CABG) Open heart or bypass surgery.

Coronary Artery Disease (CAD) Disease affecting the coronary arteries that surround the heart and supply blood to the heart muscle. CAD occurs when the lumen of the coronary arteries becomes narrowed with plaque deposits (a buildup of cholesterol and other fats, calcium and elements carried in the blood).

Electrocardiogram (ECG/EKG) A test that records changes in the electrical activity of the heart. May show whether parts of the heart muscle have been damaged due to insufficient oxygen flow to the heart.

In-Stent Restenosis Recurrent blockage or narrowing of a previously stented vessel.

Introducer Sheath A tube that is inserted into the body to provide an access point and allow the insertion of other instruments into the artery.

Lumen The inner channel of a vessel.

Myocardial Infarction Permanent damage to the heart tissue and muscle due to the interruption of the blood supply to the area. Commonly referred to as a heart attack.

Percutaneous Transluminal Coronary Angioplasty (PTCA) See Angioplasty.

Plaque Accumulation or buildup of cholesterol, fatty deposits, calcium and collagen in a coronary vessel that leads to blockages in the blood vessel.

Post-Dilatation After the stent has been expanded, another balloon catheter may be inserted inside the stent and inflated to size the stent more precisely to the wall.

Restenosis Recurrent blockage or narrowing of a previously treated vessel.

Stent An expandable metal tubular structure (lattice) that supports the vessel wall and maintains blood flow through the opened vessel.

Stress Test A test that records the heart's electrical activity while the patient exercises. May show whether parts of the heart muscle have been damaged due to insufficient oxygen flow to the heart.

Vessel Recoil When an artery is stretched during an angioplasty procedure, the elastic properties of the coronary vessel wall may cause the vessel to "shrink back" after the procedure.

TAXUS™ Express²™ Paclitaxel-Eluting Coronary Stent System

Patient Name

Patient Phone Number

Implanting Physician's Name

Stent Material

Physician's Phone Number

Date of Implant

PLEASE CARRY YOUR CARD AT ALL TIMES.

Before you have a Magnetic Resonance Imaging (MRI) scan, or for questions regarding your Coronary Stent System or procedure, please contact the implanting physician.

Stent Identification Information

Product Code

Product Lot Number

Stent Location

Product Code

Product Lot Number

Stent Location

Product Code

Product Lot Number

Stent Location

Product Code

Product Lot Number

Stent Location

4b

TAXUS™ Express²™

Paclitaxel-Eluting Coronary Stent System

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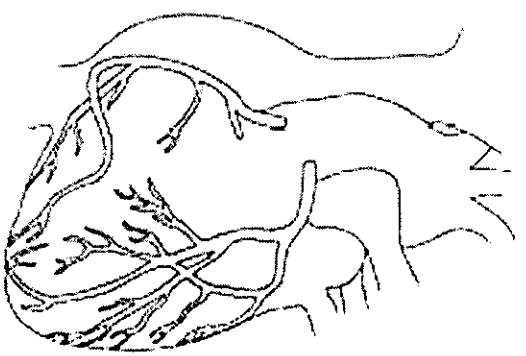
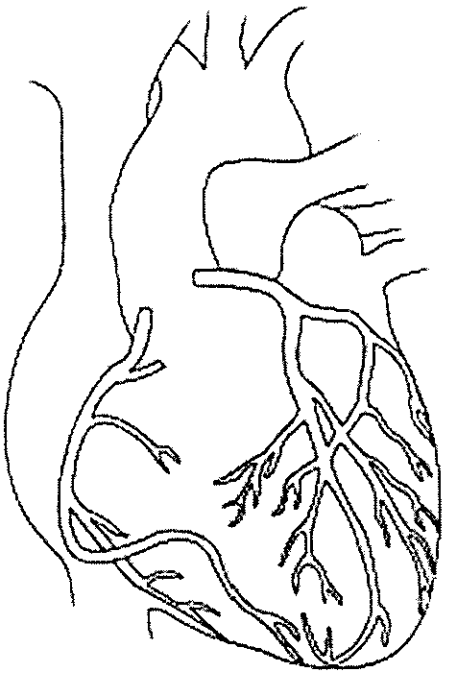


Stent Implant Location



Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each product. CAUTION: Federal (USA) law and governing law outside the U.S.A. restricts these products to sale by or on the order of a physician. TAXUS™ Express²™ Stent is a product of Boston Scientific Corporation.

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