TAXUS® Liberté® and TAXUS® Liberté® Atom™

PACLITAXEL-ELUTING CORONARY STENT SYSTEM

MONORAIL® AND OVER-THE-WIRE

DIRECTIONS FOR USE

Boston Scientific

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℞ ONLY

Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician.

This device is supplied in sterile condition. All materials inside the sterile barrier pouch (the delivery system and stent, as well as the carrier tube and pouch liner) are sterile. The external surface of the sterile barrier pouch, as well as the product carton, should not be considered sterile.

1 WARNING

Contents supplied STERILE using an ethylene oxide (EO) process. Do not use if sterile barrier is damaged. If damage is found, call your Boston Scientific representative.

For single patient use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.

After use, dispose of product and packaging in accordance with hospital, administrative and/or local government policy.

2 TAXUS Liberté PACLITAXEL-ELUTING CORONARY STENT SYSTEM

The TAXUS® Liberté® (2.50 mm – 4.00 mm) and TAXUS® Liberté® Atom™ (2.25 mm) Paclitaxel-Eluting Coronary Stent System (referred to from this point forward as the TAXUS Liberté Stent System) is a device/drug combination product comprised of two regulated components: a device (Liberté Coronary Stent System) and a drug product (a formulation of paclitaxel contained in a polymer coating). The characteristics of the TAXUS Liberté Stent System are described in Table 2.1.

Table 2.1. TAXUS® Liberté® Stent System Product Description

	TAXUS Liberté Monorail Stent Delivery System	TAXUS Liberté Over-the-Wire Stent Delivery System
Available Stent Lengths (mm)	8, 12, 16, 20, 24, 28, 32	
Available Stent Diameters (mm)	2.25, 2.50, 2.75, 3.00, 3.50, 4.00	
Stent Material	A 316L surgical grade stainless steel Liberté Stent	
Drug Product	A conformal coating of a polymer carrier loaded with 1 µg/mm^2 paclitaxel in a slow release (SR)* formulation applied to the stent with a maximum nominal drug content of 229 µg on the largest stent (4.00 x 32 mm).	
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 in (0.36 mm)	Y-Connector (Side arm for access to balloon inflation/deflation lumen. Straight arm is continuous with shaft inner lumen). Designed for guidewire ≤0.014 in (0.36 mm)
Stent Delivery	A balloon, nominally 0.4 mm longer than the stent, with two radiopaque markers.	
Balloon Inflation Pressure	Nominal Inflation Pressure: 9 atm (912 kPa) (Stent Diameter 2.25 mm – 2.50 mm) Nominal Inflation Pressure: 8 atm (811 kPa) (Stent Diameters 2.75 mm – 4.00 mm) Rated Burst Inflation Pressure: 18 atm (1824 kPa) (Stent Diameters 2.25 mm–4.00 mm)	
Guide Catheter Inner Diameter	≥ 0.058 in (1.47 mm)	≥ 0.066 in (1.68 mm)
Catheter Shaft Outer Diameter	1.8F (0.61 mm) proximal and 2.7F (0.91 mm) distal: • On all balloon lengths with diameters up to 3.0 mm • On balloon lengths 8-20 mm with diameters of 3.5 mm • On balloon lengths 8-16 mm with diameters of 4.0 mm 2.0F (0.67 mm) proximal and 2.7F (0.91 mm) distal: • On balloon lengths 24-32 mm with diameters of 3.5 mm • On balloon lengths 20-32 mm with diameters of 4.0 mm	3.2F (1.08 mm) proximal, 2.7F (0.91 mm) distal

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

2.1 Device Component Description

The TAXUS® Liberté® Paclitaxel-Eluting Coronary Stent System consists of a balloon expandable Liberté Stent, coated with paclitaxel in a slow-release (8.8% formulation) triblock copolymer system, and pre-mounted on either the Liberté Monorail® or an Over-the-Wire (OTW) delivery system. The TAXUS Liberté Stent System incorporates the identical bare Liberté Stent component and a similar delivery system to that of Liberté Coronary Stent System, and the identical TAXUS technology as the TAXUS® Express® Paclitaxel-Eluting Coronary Stent. The system is advanced over a guidewire through the coronary vasculature to deliver and dilate the stent at the target lesion location. Following stent deployment, the delivery balloon may be inflated with additional pressure in order to optimize the stent luminal diameter and strut apposition.

Liberté stents are manufactured from 316L stainless steel tubing. The stent design consists of a dimensionally uniform pattern of radially expandable elements that share junctions with adjacent radially expandable elements. The TAXUS Liberté Stent is available in 3 stent models each designed for specific diameters:

- Small Vessel (SV): 2.25 mm – 2.50 mm
- Workhorse (WH): 2.75 mm – 3.50 mm
- Large Vessel (LV): 4.00 mm

This Product Contains No Detectable Latex.

2.2 Drug Component Description

The stent component of the TAXUS Liberté Stent System (referred to as the TAXUS Liberté Stent) is a stent with a drug/polymer coating formulation consisting of paclitaxel (the active ingredient) and Translute™ polymer carrier (the inactive ingredient).

2.2.1 Paclitaxel

The active pharmaceutical ingredient in the TAXUS Liberté 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**,βS*),11α,12α,12aα,12bα]]-.

The chemical structure of paclitaxel is shown in Figure 2.1.

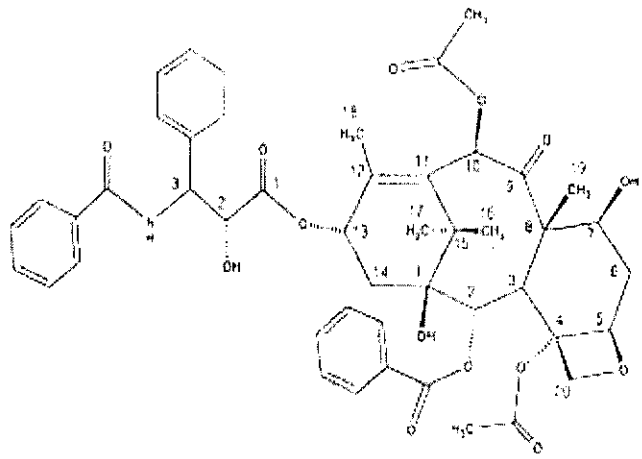
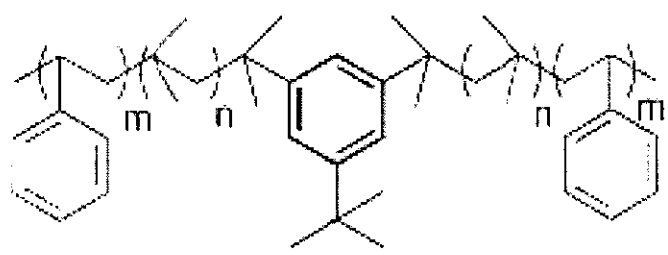


Figure 2.1. The Chemical Structure of Paclitaxel

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.

2.2.2 Translute™ Polymer Carrier

The only inactive ingredient in the TAXUS® Liberté® 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 a 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 in Figure 2.2.



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

Figure 2.2. The Chemical Structure of Translute Polymer Carrier

2.2.3 *Product Matrix and Paclitaxel Content*

Table 2.2. TAXUS® Liberté® 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)
H749389368220	H749389378220	2.25	8	38
H749389368250	H749389378250	2.50	8	38
H749389368270	H749389378270	2.75	8	55
H749389368300	H749389378300	3.00	8	55
H749389368350	H749389378350	3.50	8	55
H749389368400	H749389378400	4.00	8	61
H7493893612220	H7493893712220	2.25	12	58
H7493893612250	H7493893712250	2.50	12	58
H7493893612270	H7493893712270	2.75	12	83
H7493893612300	H7493893712300	3.00	12	83
H7493893612350	H7493893712350	3.50	12	83
H7493893612400	H7493893712400	4.00	12	88
H7493893616220	H7493893716220	2.25	16	77
H7493893616250	H7493893716250	2.50	16	77
H7493893616270	H7493893716270	2.75	16	112
H7493893616300	H7493893716300	3.00	16	112
H7493893616350	H7493893716350	3.50	16	112
H7493893616400	H7493893716400	4.00	16	114
H7493893620220	H7493893720220	2.25	20	97
H7493893620250	H7493893720250	2.50	20	97
H7493893620270	H7493893720270	2.75	20	140
H7493893620300	H7493893720300	3.00	20	140
H7493893620350	H7493893720350	3.50	20	140
H7493893620400	H7493893720400	4.00	20	141
H7493893624220	H7493893724220	2.25	24	116
H7493893624250	H7493893724250	2.50	24	116
H7493893624270	H7493893724270	2.75	24	168
H7493893624300	H7493893724300	3.00	24	168
H7493893624350	H7493893724350	3.50	24	168
H7493893624400	H7493893724400	4.00	24	176
H7493893628220	H7493893728220	2.25	28	136
H7493893628250	H7493893728250	2.50	28	136
H7493893628270	H7493893728270	2.75	28	196
H7493893628300	H7493893728300	3.00	28	196
H7493893628350	H7493893728350	3.50	28	196
H7493893628400	H7493893728400	4.00	28	203
H7493893632220	H7493893732220	2.25	32	155
H7493893632250	H7493893732250	2.50	32	155
H7493893632270	H7493893732270	2.75	32	224
H7493893632300	H7493893732300	3.00	32	224
H7493893632350	H7493893732350	3.50	32	224
H7493893632400	H7493893732400	4.00	32	229

3 INTENDED USE / INDICATIONS FOR USE

The TAXUS® Liberté® Paclitaxel-Eluting Coronary Stent System (Monorail® and Over-the-Wire Systems) is indicated for improving luminal diameter for the treatment of *de novo* lesions in native coronary arteries ≥ 2.25 mm to ≤ 4.00 mm in diameter in lesions ≤ 28 mm in length.

4 CONTRAINDICATIONS

Use of the TAXUS Liberté Paclitaxel-Eluting Coronary Stent System is contraindicated in patients with:

- Known hypersensitivity to 316L stainless steel
- Known hypersensitivity to paclitaxel or structurally-related compounds.
- Known hypersensitivity to the polymer or its individual components (see Section 2.2.2, Translute™ Polymer Carrier for more information).

Coronary Artery Stenting is contraindicated for use in:

- Patients who can not receive recommended antiplatelet and/or anticoagulant therapy (see Section 6.2 Pre- and Post-Procedure Antiplatelet Regimen for more information).
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or delivery device.

5 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 stent thrombosis, vascular complications, and/or bleeding events.
- This product should not be used in patients who are not likely to comply with recommended antiplatelet therapy.

6 PRECAUTIONS

6.1 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.
- Care should be taken to control the position of the guide catheter tip during stent delivery, deployment and balloon withdrawal.
- Before withdrawing the Stent Delivery System (SDS), visually confirm complete balloon deflation by fluoroscopy (See Table 6.1 System Deflation Time Specifications). Failure to do so may cause increased SDS withdrawal forces, and result in guide catheter movement into the vessel and subsequent arterial damage.
- Stent thrombosis is a low frequency event that current drug-eluting stent (DES) clinical trials are not adequately powered to fully characterize. Stent thrombosis is frequently associated with myocardial infarction (MI) or death. Data from the randomized clinical trials of the TAXUS ATLAS Clinical Trial Program have been evaluated and adjudicated using both the protocol definition of stent thrombosis and the definition developed by the Academic Research Consortium (ARC), and demonstrate specific patterns of stent thrombosis that vary depending on the definition used. In the TAXUS® clinical trials analyzed to date, the differences in the incidence of stent thrombosis observed with the TAXUS Stent compared to bare-metal stents have not been associated with an increased risk of cardiac death, myocardial infarction, or all-cause mortality. Additional data from longer-term follow-up in the randomized clinical trials on the TAXUS Stent and analyses of DES-related stent thrombosis are expected and should be considered in making treatment decisions as data become available.
- When drug-eluting stents are used outside the specified Indications for Use, patient outcomes may differ from the results observed in the pivotal clinical trials.
- Compared to use within the specified Indications for Use, the use of drug-eluting stents in patients and lesions outside of the labeled Indications, including more tortuous anatomy, may have an increased risk of adverse events, including stent thrombosis, stent embolization, myocardial infarction, or death.

6.2 Pre-and Post-Procedure Antiplatelet Regimen

In the TAXUS ATLAS Clinical Trial program specific to the TAXUS® Liberté® 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 10, Clinical Studies, for more specific information.

The optimal duration of antiplatelet therapy, specifically clopidogrel, is unknown and DES thrombosis may still occur despite continued therapy. Data from several studies suggest that a longer duration of antiplatelet therapy than was recommended post-procedurally in drug-eluting stent pivotal clinical trials (including TAXUS clinical trials) may be beneficial. Provided herein are recent recommendations from the ACC/AHA/SCAI 2007 Guideline for anti-thrombotic adjunctive therapies for Percutaneous Coronary Intervention (PCI), Section 6.2.1.

6.2.1 Oral Antiplatelet Therapy

Continuation of combination treatment with aspirin and clopidogrel after PCI appears to reduce rates of cardiovascular ischemic events. On the basis of randomized clinical trial protocols, aspirin 162mg to 325 mg daily should be given for at least 6 months after paclitaxel-eluting stent (PES) implantation, after which daily chronic aspirin should be continued indefinitely at a dose of 75 to 162 mg. Likewise, clopidogrel 75 mg daily should be given for at least 12 months in patients who are not at high risk of bleeding. To reduce the incidence of bleeding complications associated with dual antiplatelet therapy, lower-dose aspirin (75 to 162 mg daily) is recommended for long-term therapy. Full guidelines are provided at the following website:

http://www.acc.org/qualityandscience/clinical/statements.htm

It is very important that the patient is compliant with the post-procedural antiplatelet recommendations. Premature discontinuation of prescribed antiplatelet medication could result in a higher risk of thrombosis, myocardial infarction or death. Prior to PCI, if a surgical or dental procedure is anticipated that requires early discontinuation of antiplatelet therapy, the interventional cardiologist and patient should carefully consider whether a drug-eluting stent and its associated recommended antiplatelet therapy is the appropriate PCI choice. Following PCI, should a surgical or dental procedure be recommended that requires suspension of antiplatelet therapy, the risks and benefits of the procedure should be weighed against the possible risk associated with premature discontinuation of antiplatelet therapy. Generally, it is recommended to postpone elective surgery for one year and among those patients for whom surgery cannot be deferred. ASA should be considered during perioperative period in high risk DES patients.

Patients who require premature discontinuation of antiplatelet therapy secondary to significant active bleeding should be monitored carefully for cardiac events and, once stabilized, have their antiplatelet therapy restarted as soon as possible per the discretion of their treating physicians.

6.3 Use of Multiple Stents

In clinical trials of the TAXUS® Liberté® Stent, the protocol specified that patients were to be treated with no more than one TAXUS Liberté Stent, except in situations involving bailout stenting. The use of multiple drug-eluting stents will expose the patient to larger amounts of drug and polymer.

When more than one stent is required, resulting in stent-to-stent contact, stent materials should be of similar composition to avoid the possibility of corrosion due to the presence of dissimilar metals in a conducting medium.

Potential interactions of the TAXUS Liberté Stent with other drug-eluting or coated stents have not been evaluated and should be avoided whenever possible.

6.4 Brachytherapy

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

6.5 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 Liberté Stent implantation have not been established.

6.6 Use in Special Populations

6.6.1 Pregnancy

Pregnancy "Category C". See Drug Information – Section 7.5, Pregnancy. There are no adequate or well-controlled studies in pregnant women or men intending to father children. TAXUS Liberté 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 Liberté Stent in women who are of childbearing potential or in men intending to father children should be given careful consideration.

6.6.2 Lactation

See Drug Information – Section 7.6, Lactation. A decision should be made whether to discontinue nursing prior to implanting the stent, taking into account the importance of the stent to the mother.

6.6.3 Gender

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

6.6.4 Ethnicity

Clinical studies of the TAXUS Liberté 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.

6.6.5 Pediatric use

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

6.6.6 Geriatric Use

Clinical studies of the TAXUS Liberté Stent did not have an upper age limit.

6.7 Lesion/Vessel Characteristics

The safety and effectiveness of the TAXUS Liberté Stent have not been established in the cerebral, carotid, or peripheral vasculature or the following patient populations:

- Patients with vessel thrombus at the lesion site.
- Patients with coronary artery reference vessel diameters < 2.25 mm or > 4.00 mm.
- Patients with coronary artery lesions longer than 28 mm or requiring more than one TAXUS Liberté Stent.
- 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 in-stent restenosis.
- Patients with moderate or severe calcification in the lesion or a chronic total occlusion.
- Patients with multi-vessel disease.

6.8 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 Liberté 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 7.3 Drug Interactions for more information.

6.9 Magnetic Resonance Imaging (MRI)

Through non-clinical testing, the TAXUS® Liberté® Stent has been shown to be MR Conditional (poses no known hazards under specified conditions). The conditions are as follows:

- Field strengths of 3 Tesla or less.
- A maximum whole body averaged specific absorption rate (SAR) of 2.0 W/kg or less for a total active MR scan time (with RF exposure) of 15 minutes or less.
- Maximum Spatial Field Gradient of 70 mT/cm or less.
- A rate of change of magnetic field (dB/dt) of 60 T/s or less.

The TAXUS Liberté Stent should not migrate in this MRI environment. MR imaging within these conditions may be performed immediately following the implantation of the stent. This stent has not been evaluated to determine if it is MR Conditional beyond these conditions.

Boston Scientific conducted tests using both single stents and overlapped stents. The maximum temperature rise was less than 2.0 degrees Celsius in all cases. The effect of heating in an MRI environment for stents with simulated fractures has been tested and found to be similar to single stents. In vivo, local SAR depends on MR field strength and may be different than the estimated whole body averaged SAR, due to body composition, stent position within the imaging field, and scanner used, thereby affecting the actual temperature rise.

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

*6.10 **Stent Handling*** (also see Section 14, Operational Instructions)

- For single use only. Do not resterilize or reuse this product. Note product "Use By" date. (See Warning – Section 1)
- The premounted TAXUS Liberté 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 Operational Instructions – Section 14.3.3, Balloon Preparation). Do not use air or any gas medium to inflate the balloon.
- In the event the TAXUS Liberté Stent is not deployed, follow product returns procedures.

6.11 Stent Placement

Preparation

- Do not prepare or pre-inflate balloon prior to stent deployment other than as directed. Use the balloon purging technique described in Operational Instructions – Section 14.3.3 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 6.12, 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. Failure to do so may increase the risk of placement difficulty and procedural complications.
- Do not expand the stent if it is not properly positioned in the vessel (see Precautions – Section 6.12, Stent System Removal).
- Balloon pressures should be monitored during inflation. Do not exceed rated burst pressure as indicated on product label (see Table 14.5.1. Typical TAXUS® Liberté® Stent System 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 of dislodging the proximal stent.

6.12 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):

- Following stent placement, confirm complete balloon deflation (See Table 6.1 System Deflation Time Specifications). If greater than usual resistance is felt during delivery system withdrawal, pay particular attention to guide catheter position. In some cases it may be necessary to pull back slightly on the guide catheter in order to prevent deep seating (unplanned advancement) of the guide catheter and subsequent vessel damage. In cases where unplanned guide catheter movement has occurred, angiographic

assessment of the coronary tree should be undertaken to ensure that there is no damage to the coronary vasculature.

- 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 to 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.

Table 6.1. System Deflation Time Specifications*

<table>
<tr><th>Balloon Length / Diameter</th><th>8 mm</th><th>12 mm</th><th>16 mm</th><th>20 mm</th><th>24 mm</th><th>28 mm</th><th>32 mm</th></tr>
<tr><td>2.25 mm</td><td colspan="3" rowspan="4">≤ 16 Seconds</td><td colspan="2" rowspan="2">≤ 16 Seconds</td><td colspan="2">≤ 16 Seconds</td></tr>
<tr><td>2.50 mm</td><td colspan="2" rowspan="3">≤ 21 Seconds</td></tr>
<tr><td>2.75 mm</td><td colspan="2" rowspan="2">≤ 21 Seconds</td></tr>
<tr><td>3.00 mm</td><td colspan="2" rowspan="2">≤ 21 Seconds</td></tr>
<tr><td>3.50 mm</td><td colspan="2" rowspan="2">≤ 21 Seconds</td></tr>
<tr><td>4.00 mm</td><td colspan="3">≤ 21 Seconds</td></tr>
</table>

*All product tested during Design Verification met 95/95 confidence/conformance levels.

6.13 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 the clinical trial (TAXUS ATLAS) for the TAXUS® Liberté® 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 10 - Clinical Studies, for more specific information.
- If the patient requires imaging, see Precautions - Section 6.9, Magnetic Resonance Imaging (MRI).

7 DRUG INFORMATION

7.1 Mechanism of Action

The mechanism (or mechanisms) by which a TAXUS® Liberté® Stent affects neointimal production as seen in clinical studies has not been fully 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.

7.2 Pharmacokinetics

In the clinical studies TAXUS I, II, and III, no paclitaxel levels were detected after stent implantation using a bioanalytical method with a lower limit of quantitation (LLOQ) of 10 ng/ml. These findings were further 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 systemic levels, standard pharmacokinetic parameters were not estimated.

7.3 Drug Interactions

Paclitaxel is metabolized in the liver via CYP2C8 to 6-alpha-hydroxypaclitaxel and via CYP3A4 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 Liberté 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 Liberté 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 Liberté Stent.

7.4 Carcinogenicity, Genotoxicity, and Reproductive Toxicology

No long-term studies in animals have been performed to evaluate the carcinogenic potential of paclitaxel. Paclitaxel interacts with microtubules; this is the major mechanism by which it inhibits cell growth. One consequence is the loss of whole chromosomes via interactions with spindle microtubules during cell division. As such, Paclitaxel is defined as an aneugen (agent causing an alteration in chromosome number). This indirect action is consistent with positive responses in in vitro and in vivo micronucleus genotoxicity assays, which detect DNA fragments. Positive results have also been reported for chromosomal aberrations in primary human lymphocytes. It is not known whether paclitaxel has a separate direct action on DNA in the generation of DNA strand breaks or fragments. It is negative in assays for gene mutation, including salmonella and CHO/HPRT. Paclitaxel administered via 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 Liberté Stent coated with 229 µg paclitaxel adjusted for body surface area).

7.5 Pregnancy

Pregnancy Category C: There are no adequate and well controlled studies in pregnant women of paclitaxel or TAXUS® Liberté® 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 Liberté Stent coated with 229 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 Liberté Stent coated with 229 µg paclitaxel adjusted for body surface area). TAXUS Liberté 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 Liberté Stent in women who are of childbearing potential should be given careful consideration.

7.6 Lactation

It is not known whether paclitaxel is distributed in human milk. However, in lactating rats given radio labeled 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 Liberté 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.

8 OVERVIEW OF CLINICAL STUDIES

The TAXUS® Liberté® Clinical Trial Program consists of a series of single-arm, historically-controlled, multicenter trials designed to assess the risk/benefit profile of the polymer-controlled, paclitaxel-eluting TAXUS Liberté Stent. The specific goal of the TAXUS Liberté Clinical Trial Program is to demonstrate that the TAXUS Liberté Stent performs as well as the TAXUS® Express® Stent to safely and significantly reduce the need for revascularization compared to bare metal stents within defined target lesions. The TAXUS Liberté Clinical Trial Program was specifically designed to start with relatively simple lesions, and progress to increasingly more complex lesions, patient populations and procedures. This overview will focus on data generated with the pivotal TAXUS ATLAS trial comparing the TAXUS Liberté Stent to a historical control population of TAXUS Express patients treated in the TAXUS IV and TAXUS V *de novo* clinical trials. A summary of the designs of these studies is presented in Table 8.1.

8.1 TAXUS ATLAS

TAXUS ATLAS[1] is a multi-center, single-arm trial to evaluate the safety and efficacy of the 1 µg/mm^2 (loaded drug/stent surface area) slow-release (SR) formulation TAXUS Liberté Stent in the treatment of *de novo* coronary lesions compared with the TAXUS Express Stent (case-matched historic control data derived from the TAXUS IV and TAXUS V *de novo* studies). A total of 871 patients at 61 clinical sites were enrolled in this study. The primary endpoint for the study was the 9-month ischemia driven target vessel revascularization (TVR) rate. Secondary endpoints included 9-month clinical assessments for all patients and analysis of

[1] Turco MA, Ormiston JA, Popma JJ, et al. Polymer-based, paclitaxel-eluting TAXUS Liberté stent in *de novo* lesions: The pivotal TAXUS ATLAS trial. J Am Coll Cardiol. 2007;49(16):1676-1683.

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 at least 6 months. Follow-up through 1 year is currently available, and yearly follow-up for clinical parameters through 5 years is ongoing.

The objective of TAXUS ATLAS was to demonstrate non-inferiority of clinical and angiographic outcomes for the TAXUS® Liberté® Stent when compared to the TAXUS® Express® Stent. Therefore, the treatment group is compared to a case-matched Control group derived from TAXUS IV and TAXUS V *de novo*. In order to case-match the Control group, all TAXUS IV and V patients randomized to the TAXUS Express group with (1) a reference vessel diameter (RVD) by visual estimate ≥ 2.5 mm and ≤ 4.0 mm, (2) a lesion length by visual estimate ≥ 10 mm and ≤ 28 mm, and (3) receiving 1 planned study stent were included. This resulted in inclusion of all 662 patients randomized into the TAXUS Express treatment arm of TAXUS IV and 329 out of 577 patients randomized into the TAXUS Express treatment arm of TAXUS V *de novo*.

8.2 TAXUS ATLAS Small Vessel

TAXUS ATLAS Small Vessel is a multi-center, single-arm trial to evaluate the safety and efficacy of the 1 μg/mm^2 (loaded drug/stent surface area) slow-release (SR) formulation, 2.25 mm TAXUS Liberté Stent in the treatment of *de novo* coronary lesions in small vessels with a reference vessel diameter of 2.25 mm (2.2 -2.5 mm by visual estimate) compared with the TAXUS Express Stent (case-matched historic control data derived from the TAXUS V *de novo* study). A total of 261 patients at 23 clinical sites were enrolled in this study. The primary endpoint for the study was the percent diameter stenosis (%DS) of the analysis segment at 9 months, as determined by QCA. Secondary endpoints included 9-month clinical assessments for all patients as well as additional angiographic parameters. After the procedure, patients were treated with aspirin indefinitely and with clopidogrel or ticlopidine for at least 6 months. Follow-up through 1 year is currently available, and yearly follow-up for clinical parameters through 5 years is ongoing.

The first objective of the TAXUS ATLAS Small Vessel study was to demonstrate non-inferiority for the angiographic outcome of %DS for the 2.25 mm TAXUS Liberté stent when compared to the TAXUS Express Stent. Therefore, the treatment group is compared to a case-matched Control group derived from TAXUS V *de novo*. In order to case-match this first Control group, all TAXUS V patients randomized to the TAXUS Express group with (1) a reference vessel diameter (RVD) by visual estimate ≤ 2.5 mm, (2) a lesion length by visual estimate ≥ 10 mm and ≤ 28 mm, and (3) receiving 1 planned 2.25 mm study stent were included. This resulted in inclusion of 75 out of 577 patients randomized into the TAXUS Express treatment arm of TAXUS V *de novo*.

The second objective of the TAXUS ATLAS Small Vessel study was to demonstrate superiority for the angiographic outcome of %DS for the 2.25 mm TAXUS Liberté stent when compared to the bare metal Express stent. Therefore, the treatment group is compared to a case-matched Control group derived from TAXUS V *de novo*. In order to case-match this second Control group, all TAXUS V patients randomized to the bare metal Express group with (1) a reference vessel diameter (RVD) by visual estimate ≤ 2.5 mm, (2) a lesion length by visual estimate ≥ 10 mm and ≤ 28 mm, and (3) receiving 1 planned 2.25 mm or 2.5mm study stent were included. This resulted in inclusion of 155 out of 579 patients randomized into the bare metal Express treatment arm of TAXUS V *de novo*.

8.3 TAXUS IV

TAXUS IV[2] is a randomized, double-blind, controlled pivotal Phase III U.S. study of the safety and performance of the SR formulation TAXUS Express Paclitaxel-Eluting Coronary Stent System 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 IVUS parameters in a subset of patients. After the procedure, patients were treated with aspirin indefinitely and with clopidogrel or ticlopidine for at least 6 months. Follow-up through 4 years is currently available, and yearly follow-up for clinical parameters through 5 years is ongoing.

8.4 TAXUS V

TAXUS V *de novo*[3] is a randomized, double-blind, controlled, expansion study of the safety and performance of the SR formulation TAXUS Express Paclitaxel-Eluting Coronary Stent in *de novo* lesions in small and large diameter vessels, as well as long lesions. TAXUS V *de novo* was designed to expand the data set beyond the standard-risk, *de novo* coronary artery lesions studied in the pivotal TAXUS IV trial. A total of 1172 patients at 66 U.S. sites were enrolled with patients randomized 1:1 to the TAXUS Express Stent System or the uncoated Express Control Stent. The primary end point was the incidence rate of ischemia-driven TVR through 9 months post-index procedure. Secondary end points included the cumulative major adverse cardiac event (MACE) rate at follow-up and detailed quantitative coronary analysis (QCA) and IVUS analysis in pre-specified subgroups at 9 months. After the procedure, patients were treated with aspirin indefinitely and with clopidogrel or ticlopidine for at least 6 months. Follow-up through 2 years is currently available, and yearly follow-up for clinical parameters through 5 years is ongoing.

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[2] Stone GW, Ellis SG, Cox DA, et al. One-year clinical results with the slow-release, polymer-based, paclitaxel-eluting TAXUS stent: the TAXUS-IV trial. *Circulation.* 2004;109(16):1942-1947.
Stone GW, Ellis SG, Cox DA, et al. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med.* 2004;350(3):221-231.

[3] Stone GW, Ellis SG, Cannon L, et al. Comparison of a polymer-based paclitaxel-eluting stent with a bare metal stent in patients with complex coronary artery disease: A randomized controlled trial. JAMA. 2005;294(10):1215-1223.

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Table 8.1. Comparison of TAXUS Clinical Studies

	TAXUS ATLAS Program TAXUS® Liberté® Workhorse	**TAXUS ATLAS Program TAXUS® Liberté® Atom™ Small Vessel (SV) 2.25 mm**	**TAXUS IV (Pivotal)**	**TAXUS V *de novo* (Expansion)**
Study Type	Multi-center, single-arm study	Multi-center, single-arm study	Prospective, multicenter, randomized, double-blind	Prospective, multicenter, randomized, double-blind
Number of Patients (ITT)	Total: 871 TAXUS Liberté Stent: 871 Combined TAXUS IV & V *de novo* historical control: 991	Total: 261 TAXUS Liberté Atom Stent: 261 DES Control Group: 75 BMS Control Group: 155	Total: 1314 TAXUS® Express® Stent: 662 Uncoated Control: 652	Total: 1156 TAXUS® Express® Stent: 577 Uncoated Control: 579
Dose Release Formulation	Slow Release (SR) (1 µg /mm^2)			
Lesion Criteria: Vessel Diameter (by visual estimate)	≥ 2.5 mm to ≤ 4.0 mm	2.20 mm to 2.50 mm	≥ 2.5 mm to ≤ 3.75 mm	≥ 2.25 mm to ≤ 4.0 mm
Lesion Criteria: Lesion Length (by visual estimate)	≥ 10 mm and ≤ 28 mm	≥ 10 mm and ≤ 28 mm	≥ 10 mm and ≤ 28mm	≥ 10 mm and ≤ 46 mm
Product Used	TAXUS Liberté Paclitaxel-Eluting Coronary Stent System	TAXUS Liberté Atom Paclitaxel-Eluting Coronary Stent System	TAXUS Express Paclitaxel-Eluting Coronary Stent System	TAXUS Express Paclitaxel-Eluting Coronary Stent System
Antiplatelet Therapy	Aspirin indefinitely and clopidogrel or ticlopidine for 6 months			
Follow-Up	30 days: clinical 4 months: clinical 9 months: clinical (all), QCA and IVUS (subset) 1 – 5 years: clinical			

Abbreviations: ITT=intent-to-treat; IVUS=intravascular ultrasound; QCA=quantitative coronary angiography

9 ADVERSE EVENTS

9.1 Observed Adverse Events

Observed adverse event experience comes from four clinical studies: TAXUS ATLAS, TAXUS ATLAS Small Vessel, TAXUS IV and TAXUS V *de novo*. Principal adverse events for these trials are shown in Table 9.1.1 and Table 9.1.2 (TAXUS ATLAS Small Vessel). Stent apposition data for TAXUS ATLAS is presented in Table 9.1.3.

Table 9.1.1. TAXUS ATLAS, TAXUS IV, and TAXUS V *de novo* Major Adverse Cardiac Events (MACE) From Post-Procedure to Latest Follow-Up

	TAXUS ATLAS Workhorse to 1 Year*		TAXUS IV to 4 Years**		TAXUS V *de novo* to 2 Years†	
	TAXUS® Liberté®	TAXUS® Express® DES Control	TAXUS Express	Express BMS Control	TAXUS Express	Express BMS Control
In-Hospital MACE	2.4% (21/871)	2.6% (26/991)	2.4% (16/662)	2.1% (14/652)	4.0% (23/577)	3.1% (18/579)
30-Day MACE, overall	2.8% (24/870)	3.3% (33/987)	2.9% (19/662)	2.5% (16/652)	5.1% (29/569)	3.6% (21/576)
9-Month MACE, overall	11.0% (95/862)	10.5% (102/974)	8.5% (56/662)	15.0% (98/652)	15.0% (84/560)	21.2% (120/567)
Cardiac Death	0.8% (7/862)	0.9% (9/974)	1.4% (9/662)	1.1% (7/652)	0.5% (3/560)	0.9% (5/567)
MI	3.7% (32/862)	3.9% (38/974)	3.5% (23/662)	3.7% (24/652)	5.4% (30/560)	4.6% (26/567)
Q-Wave MI	0.7% (6/862)	0.6% (6/974)	0.8% (5/662)	0.3% (2/652)	0.5% (3/560)	0.2% (1/567)
Non-Q-Wave MI	3.0% (26/862)	3.3% (32/974)	2.7% (18/662)	3.4% (22/652)	4.8% (27/560)	4.4% (25/567)
TVR, Overall	8.0% (69/862)	7.1% (69/974)	4.7% (31/662)	12.0% (78/652)	12.1% (68/560)	17.3% (98/567)
TLR, Overall	5.7% (49/862)	4.5% (44/974)	3.0% (20/662)	11.3% (74/652)	8.6% (48/560)	15.7% (89/567)
Non-TLR, Overall	3.2% (28/862)	2.7% (26/974)	1.7% (11/662)	1.1% (7/652)	4.8% (27/560)	4.2% (24/567)
1-Year MACE	12.5% (106/851)	12.3% (118/957)	10.6% (70/662)	19.8% (129/652)	18.9% (105/556)	25.9% (146/563)
2-Year MACE	NA	NA	14.7% (95/645)	25.2% (161/640)	22.1% (120/542)	29.2% (159/544)
3-Year MACE	NA	NA	18.9% (116/614)	29.0% (178/613)	NA	NA
4-Year MACE	NA	NA	22.1% (133/601)	31.5% (190/604)	NA	NA
Cardiac Death	NA	NA	3.0% (18/601)	4.0% (24/604)	NA	NA
MI	NA	NA	7.2% (43/601)	7.1% (43/604)	NA	NA
Q-Wave MI	NA	NA	1.3% (8/601)	1.0% (6/604)	NA	NA
Non-Q-Wave MI	NA	NA	6.0% (36/601)	6.5% (39/604)	NA	NA
TVR, Overall	NA	NA	16.0% (96/601)	26.0% (157/604)	NA	NA
TLR, Overall	NA	NA	7.8% (47/601)	20.2% (122/604)	NA	NA
Non-TLR, Overall	NA	NA	9.0% (54/601)	9.3% (56/604)	NA	NA

4-Year Stent Thrombosis	NA	NA	1.6% (9/579)	1.1% (6/569)	NA	NA

* After 9 months, the TAXUS ATLAS study population was reduced to a pre-specified cohort (per protocol population), which consists of all patients who received a study stent at baseline.
** After 2 years the TAXUS IV study population was reduced to a pre-specified cohort, which consists of all patients who received a study stent at baseline (Safety Population). At 4 years, the safety population is comprised of 1290 (n=649 for TAXUS, n=641 for Control).
† After 1 year the TAXUS V *de novo* study population was reduced to a pre-specified cohort, which consists of all patients who received a study stent at baseline (Safety population).
NA= Not Applicable; variable and/or time point not calculated.

In TAXUS ATLAS, a pre-specified subset of patients underwent IVUS evaluation of the treated lesion immediately after treatment and as a part of a scheduled angiographic evaluation at 9 months. Table 9.1.3 presents incomplete apposition rates by treatment group for the IVUS subset (n=610), based on core lab identification of one or more struts not apposed to the vessel wall, with evidence of speckling indicative of blood flow. There were no statistically significant differences between treatment groups with respect to percent of patients with incomplete apposition post-procedure (*P*=0.7260). However, the rate of late incomplete apposition at 9-month follow-up was significantly lower in the TAXUS® Liberté® group than in the TAXUS® Express® Control group (p=0.0461). Paired IVUS analysis for both post-procedure and 9 months was available for 285 patients. In this patient group, the rates were comparable between TAXUS ATLAS and Control with regard to resolved (present post-procedure, absent at 9 months), persistent (present post-procedure and at 9 months), or late-acquired (absent post-procedure, present at 9 months) incomplete apposition.

Table 9.1.2. TAXUS ATLAS Clinical Program TAXUS® Liberté® Atom™ Small Vessel 2.25 mm Major Adverse Cardiac Events (MACE) From Post-Procedure to Latest Follow-Up

	TAXUS ATLAS TAXUS Liberté Small Vessel (SV) 2.25 mm to 1 Year		
	TAXUS Liberté Atom 2.25 mm (N=261)	**TAXUS Express DES Control (N=75)**	**Express BMS Control (N=155)**
In-Hospital MACE	1.9% (5/261)	2.7% (2/75)	1.9% (3/155)
30-Day MACE, overall	1.9% (5/261)	4.1% (3/74)	2.6% (4/154)
9-Month MACE, overall	12.8% (33/258)	20.5% (15/73)	21.6% (33/153)
Cardiac Death	0.8% (2/258)	2.7% (2/73)	0.7% (1/153)
MI	2.7% (7/258)	4.1% (3/73)	2.6% (4/153)
Q-Wave MI	0.8% (2/258)	1.4% (1/73)	0.0% (0/153)
Non-Q-Wave MI	1.9% (5/258)	2.7% (2/73)	2.6% (4/153)
TVR, Overall	10.1% (26/258)	17.8% (13/73)	19.6% (30/153)
TLR, Overall	5.8% (15/258)	13.7% (10/73)	17.6% (27/153)
Non-TLR, Overall	6.6% (17/258)	6.8% (5/73)	5.9% (9/153)
1-Year MACE	13.4% (33/247)	26.8% (19/71)	28.4% (42/148)
Cardiac Death	1.2% (3/247)	4.2% (3/71)	0.7% (1/148)
MI	2.4% (6/247)	4.2% (3/71)	2.7% (4/148)
Q-Wave MI	0.8% (2/247)	1.4% (1/71)	0.0% (0/148)
Non-Q-Wave MI	1.6% (4/247)	2.8% (2/71)	2.7% (4/148)
TVR, Overall	10.5% (26/247)	22.5% (16/71)	26.4% (39/148)
TLR, Overall	6.1% (15/247)	16.9% (12/71)	22.3% (33/148)
Non-TLR, Overall	6.9% (17/247)	8.5% (6/71)	8.8% (13/148)
1-Year Stent Thrombosis	0.4% (1/243)	1.5% (1/67)	1.4% (2/146)

Table 9.1.3. Frequency of Incomplete Stent Apposition in TAXUS ATLAS, All Patients in the IVUS Subset at 9 Month Follow-up

Incomplete Apposition (IA)	TAXUS® Liberté® (N=327)	TAXUS Express® DES Control (N=283)
Early (Post-Procedure)	8.7% (22/254)	7.3% (14/191)
Late (9-Month)	4.3%(9/209)	10.1% (14/139)
Paired Data		
Resolved	3.4% (6/177)	2.8% (3/108)
Persistent	2.3% (4/177)	3.7% (4/108)
Late Acquired	1.7% (3/177)	5.6% (6/108)

Resolved = # patients with baseline (BL) IA and without follow-up (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.

9.2 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 antiplatelet therapy, contrast medium, or stent materials
- Angina
- Arrhythmias, including ventricular fibrillation (VF) and ventricular tachycardia (VT)
- Arteriovenous fistula
- Cardiac tamponade
- Cardiogenic shock/Pulmonary edema
- Coronary aneurysm
- Death
- Dissection
- Emboli, distal (air, tissue or thrombotic material or material from devices(s) used in the procedure)
- Heart failure
- Hematoma
- Hemorrhage, required transfusion
- Hypotension/Hypertension
- Infection, local or systemic
- Ischemia, myocardial
- Pain, at the access site
- Perforation or Rupture of coronary artery
- Pericardial effusion
- Pseudoaneurysm, femoral
- Renal Failure
- Respiratory Failure
- Restenosis of stented segment
- Stent emobolization or migration
- Stent thrombosis/occlusion
- Stroke/cerebrovascular accident /TIA
- Total occlusion of coronary artery
- Vessel spasm
- 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.

10 CLINICAL STUDIES

10.1 TAXUS ATLAS Pivotal Clinical Trial

Primary Objective: The primary objective of this study was to demonstrate non-inferiority of the TAXUS® Liberté® Stent as compared to the TAXUS® Express® Stent with respect to TVR 9 months post-index procedure.

Design: TAXUS ATLAS is a multi-center, single-arm trial in patients at 61 sites. Eligible patients were those presenting for stenting of *de novo* lesions of a single native coronary artery (RVD of 2.5 to 4.0 mm) with a target lesion of 10 to 28 mm in length and stenosis ≥ 50% in diameter (visual estimates) who are candidates for percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG), and had documented angina pectoris or functional ischemia.

A total of 871 intent-to-treat (ITT) patients were enrolled and evaluable in this study. The Control group (991 total ITT patients) was comprised of case-matched, historic data derived from the TAXUS IV and TAXUS V *de novo* studies. Multiple stenting was allowed for bail-out only. After the procedure, patients who received the assigned study stent (protocol population) were treated with aspirin indefinitely and clopidogrel or ticlopidine for at least 6 months.

Follow-up included clinical assessments at 1, 4, and 9 months. In addition, patients agreed to annual telephone follow-up for clinical parameters through 5 years post-procedure. After the 9-month follow-up, the study population was reduced to a pre-specified cohort, which consists of all patients who received the assigned study stent at baseline (per protocol population). Follow-up through 1 year is currently available in 856/867 (98.7%) patients.

A subset of patients was pre-assigned to have angiographic (N=543) and IVUS (N=327) follow-up at 9 months. Angiographic assessments were performed for the area of the vessel within the stent margins (in-stent) and the areas immediately 5 mm proximal and distal from the stent margins (analysis segment).

The primary endpoint data (9 months) and latest available follow-up (1 year) results are presented below (Tables 10.1.1 - 10.1.7, Figure 10.1.1 and Figure 10.1.2).

Demographics: Patients were well-matched for baseline demographics. QCA analysis of the baseline lesion characteristics showed well-matched RVD (mean 2.75±0.50 mm versus 2.79±0.49 mm, p=0.1274) between TAXUS® Liberté® and the Control group. However, minimum lumen diameter (MLD) was smaller (mean 0.85±0.36 mm versus 0.92±0.34 mm, p<0.0001), percent diameter stenosis was greater (mean 69.13±11.83 % versus 66.76±10.80 %, p<0.0001), and lesion length was longer (mean 14.76±6.61 mm versus 13.60±6.11 mm, p<0.0001) for TAXUS Liberté group compared to the Control group. In addition, QCA parameters assessing baseline lesion complexity (bend, tortuosity, calcification, and presence of branch vessel disease) were significantly higher for TAXUS Liberté, resulting in a significantly higher proportion of lesions with ACC/AHA Type B2 or C lesion complexity (75.5% for TAXUS Liberté versus 61.2% for Control, p<0.0001). In the presence of rigid matching criteria, these differences indicate a change in clinical practice patterns from the TAXUS Express Control (enrolled 2 to 3 years ago) to the TAXUS Liberté treatment group.

Despite the higher lesion complexity, stent placement in the TAXUS Liberté group was accomplished with shorter procedure times (47.8±25.5 minutes versus 53.0±49.5 minutes, p=0.0052) and a lower incidence of geographic miss during the stent placement (5.6% versus 9.2%, p=0.0036).

Table 10.1.1. TAXUS ATLAS Workhorse Clinical Results

	9 months (ITT population)			1 year (per protocol population**)		
	TAXUS® Liberté® (N=871)	TAXUS® Express® DES Control (N=991)	P-Value	TAXUS Liberté (N=867)	TAXUS Express DES Control (N=978)	P-Value
EFFICACY						
TVR, Overall	8.0% (69/862)	7.1% (69/974)	0.4787*	9.2% (78/851)	8.9% (85/957)	0.8334
TLR, Overall	5.7% (49/862)	4.5% (44/974)	0.2865*	6.1% (52/851)	5.5% (53/957)	0.6035
TLR, PCI	5.3% (46/862)	3.9% (38/974)	0.1472*	5.9% (50/851)	5.0% (48/957)	0.4203
TLR, CABG	0.3% (3/862)	0.6% (6/974)	0.5141*	0.2% (2/851)	0.5% (5/957)	0.4579*
Non-TLR, Overall	3.2% (28/862)	2.7% (26/974)	0.4911*	4.2% (36/851)	3.8% (36/957)	0.6111
Non-TLR, PCI	2.8% (24/862)	2.1% (20/974)	0.3596*	3.5% (30/851)	2.8% (27/957)	0.3925
Non-TLR, CABG	0.5% (4/862)	0.6% (6/974)	0.7578*	0.8% (7/851)	0.9% (9/957)	0.7894
SAFETY						
Total Death	1.2% (10/863)	1.8% (18/977)	0.2570*	1.3% (11/854)	2.3% (22/961)	0.1110
Cardiac Death or MI	4.2% (36/862)	4.7% (46/974)	0.6510*	4.5% (38/851)	4.7% (45/957)	0.8102
Cardiac Death	0.8% (7/862)	0.9% (9/974)	1.0000*	0.8% (7/851)	1.0% (10/957)	0.6248
MI	3.7% (32/862)	3.9% (38/974)	0.9030*	4.0% (34/851)	3.9% (37/957)	0.8879
Q-wave MI	0.7% (6/862)	0.6% (6/974)	1.0000*	0.7% (6/851)	0.6% (6/957)	0.8383
Non-Q-wave MI	3.0% (26/862)	3.3% (32/974)	0.7901*	3.3% (28/851)	3.2% (31/957)	0.9515
Stent Thrombosis	0.8% (7/858)	0.7% (7/966)	1.0000*	0.9% (8/846)	0.7% (7/947)	0.6318

**After 9 months, the TAXUS ATLAS Workhorse study population was reduced to a pre-specified cohort (per protocol population), which consists of all patients who received a study stent at baseline.

* P-Values are two-sided from Fisher's exact test; P-Values without * are two-sided from the Chi-square test.

P-Values are not adjusted for multiple comparisons.

This trial was not adequately powered to compare the rate of low frequency events to a bare metal control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

Table 10.1.2. TAXUS ATLAS Workhorse Primary Endpoint

Per Protocol Population	TAXUS® Liberté® (N=867)	TAXUS® Express® DES Control (N=980)	Difference [Upper 1-Sided 95% CI]	P-Value[a]	Δ
9-Month TVR	7.95% (68/855)	7.01% (67/956)	0.94% [2.98%]	0.0487	3.0%
Intent-to-Treat Population	**TAXUS Liberté (N=871)**	**TAXUS Express Control (N=991)**	**Difference [Upper 1-Sided 95% CI]**	**P-Value[a]**	**Δ**
9-Month TVR	8.03% (69/859)	7.14% (69/967)	0.90% [2.94%]	0.0454	3.0%

[a] P-Values represent unadjusted results from non-inferiority testing.

Table 10.1.3. TAXUS ATLAS Workhorse Secondary Endpoints

Per Protocol Population	TAXUS Liberté (N=867)	TAXUS Express DES Control (N=980)	Bonferroni Adjusted Upper 1-Sided 95% CI[b]	P-Value[c]	Δ
In-Stent Percent Diameter Stenosis	21.04±21.40 (448) (-21.01, 100.00)	18.80±19.44 (486) (-23.34, 100.00)	2.24 [5.35]	0.0006**	6.6%
In-Stent Binary Restenosis	11.38% (51/448)	8.64% (42/486)	2.74% [7.32%]	0.0354	6.3%
In-Stent MLD[a] (mm)	2.19±0.71 (448) (0.00, 4.23)	2.28±0.66 (486) (0.00, 4.08)	-0.09 [-0.19]	0.0316*	-0.17 mm
In-Stent Late Loss (mm)	0.41±0.54 (446) (-0.77, 2.55)	0.42±0.54 (484) (-0.85, 2.71)	-0.01 [0.07]	<0.0001*	0.18 mm
% In-Stent Net Volume Obstruction	13.92±11.30 (209) (-8.77, 50.96)	12.26±13.73 (139) (-27.01, 53.96)	1.66 [4.80]	0.0021**	5.7%

*Variances equal: Pooled t statistic
**Variances unequal: Satterthwaite's approximate t statistic
[a] Lower 1-Sided 95% CI is reported for In-Stent MLD.
[b] Bonferroni Adjusted Upper 1-sided 95% CI calculated using a 1-sided 99% CI.
[c] P-Values represent unadjusted results from non-inferiority testing.

Table 10.1.4. TAXUS ATLAS Workhorse Procedural Results

Procedural Outcomes	TAXUS Liberté (N=871)	TAXUS Express DES Control (N=991)	P-Value
Procedure Time	47.8±25.5 (870)	53.0±49.5 (991)	0.0052
Geographic Miss	5.6% (49/869)	9.2% (91/985)	0.0036

P-Values are not adjusted for multiple comparisons.

Table 10.1.5. TAXUS ATLAS Workhorse 9-Month Angiographic and IVUS Results

Angiographic Outcomes [a]	TAXUS® Liberté® (N=543)	TAXUS® Express® DES Control (N=704)	P-Value
MLD (mm), In-stent			
Post-Procedure	2.60±0.46 (446)	2.70±0.45 (484)	0.0006
9-Month	2.19±0.71 (448)	2.28±0.66 (486)	0.0541
MLD (mm), Analysis Segment			
Post-Procedure	2.22±0.51 (447)	2.28±0.50 (484)	0.0615
9-Month	1.97±0.67 (449)	2.01±0.61 (486)	0.3132
% DS, In-stent			
Post-Procedure	7.30±8.87 (446)	4.43±10.29 (484)	<0.0001
9-Month	21.04±21.40 (448)	18.80±19.44 (486)	0.0934
% DS, Analysis Segment			
Post-Procedure	21.30±9.47 (447)	19.77±9.97 (484)	0.0169
9-Month	29.15±19.06 (449)	28.47±17.24 (486)	0.5688
Late Loss, In-stent (mm)	0.41±0.54 (446)	0.42±0.54 (484)	0.6872
Late Loss, Analysis Segment (mm)	0.25±0.50 (447)	0.27±0.46 (484)	0.5889
Binary Restenosis			
In-stent restenosis	11.4% (51/448)	8.6% (42/486)	0.1893
Analysis segment restenosis	14.3% (64/449)	12.1% (59/486)	0.3836
IVUS Outcomes [b]	**TAXUS Liberté (N=327)**	**TAXUS Express Control (N=283)**	**P-Value**
Neointimal Volume (mm^3) (9 months)	24.9±24.1 (209)	21.6±25.0 (140)	0.2089
% Net Volume Obstruction (9 months)	13.9±11.3 (209)	12.3±13.7 (139)	0.2197
Incomplete Apposition			
Late (9 months)	4.3% (9/209)	10.1% (14/139)	0.0461
Late Acquired	1.7% (3/177)	5.6% (6/108)	0.0871

[a] Includes all patients in the angiographic subset.
[b] Includes all patients in the IVUS subset.
P-Values are not adjusted for multiple comparisons.
This trial was not adequately powered to compare the rate of low frequency events to a drug-eluting stent control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

Table 10.1.6. TAXUS ATLAS Workhorse Stent Thrombosis

Per Protocol Population	TAXUS Liberté (N=867)	TAXUS Express DES Control (N=978)	P-Value
Protocol Defined Stent Thrombosis [a]			
Cumulative through 1 year	0.9% (8/846)	0.7% (7/947)	0.6318
Acute ST (≤24 hrs)	0.0% (0/867)	0.2% (2/978)	0.5015*
Subacute ST (>24 hrs and ≤30 days)	0.2% (2/865)	0.3% (3/976)	1.0000*
Late ST (>30 days and ≤12 months)	0.7% (6/863)	0.2% (2/972)	0.1583*
ARC Definite & Probable Stent Thrombosis [b]			
Cumulative through 1 year	1.2% (10/846)	0.8% (8/947)	0.4745
Acute ST (≤24 hrs)	0.0% (0/867)	0.2% (2/978)	0.5015*

Table 10.1.6. TAXUS ATLAS Workhorse Stent Thrombosis

Subacute ST (>24 hrs and ≤30 days)	0.2% (2/865)	0.3% (3/976)	1.0000*
Late ST (>30 days and ≤12 months)	0.9% (8/863)	0.3% (3/972)	0.0868

To be included in the calculation of stent thrombosis rate for a given interval, a patient either had to have a stent thrombosis during the interval (e.g. 31-365 days inclusive) or they had to be stent thrombosis-free during the interval with last follow-up on or after the first day of the given interval (e.g. 31 days).

[a] Per protocol, stent thrombosis is defined as the occurrence of any of the following:

1. Clinical presentation of acute coronary syndrome with angiographic evidence of stent thrombosis:
   a) 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 diameter stenosis ≤30%) and/or
   b) Angiographic documentation of a flow-limiting thrombus within or adjacent to a previously successfully treated lesion.
2. Acute MI of the distribution of the treated vessel.
3. Death within the first 30 days (without other obvious cause) is considered a surrogate for stent thrombosis when angiography is not available.

[b] Academic Research Consortium (ARC) stent thrombosis is defined as follows[4]:

1. Definite ST is considered to have occurred after intracoronary stenting by either angiographic or pathologic confirmation of stent thrombosis.
2. Probable ST is considered to have occurred after intracoronary stenting in the following cases:
   a) Any unexplained death within the first 30 days following stent implantation.
   b) Irrespective of the time after the index procedure, any MI which is related to documented acute ischemia in the territory of the implanted stent without angiographic confirmation of ST and in the absence of any other obvious cause.

After 9 months, the TAXUS ATLAS study population was reduced to a pre-specified cohort (per protocol population), which consists of all patients who received a study stent at baseline. Patients who did not receive a study stent were not followed beyond 9 months.

Numbers are % (Count/Sample Size).

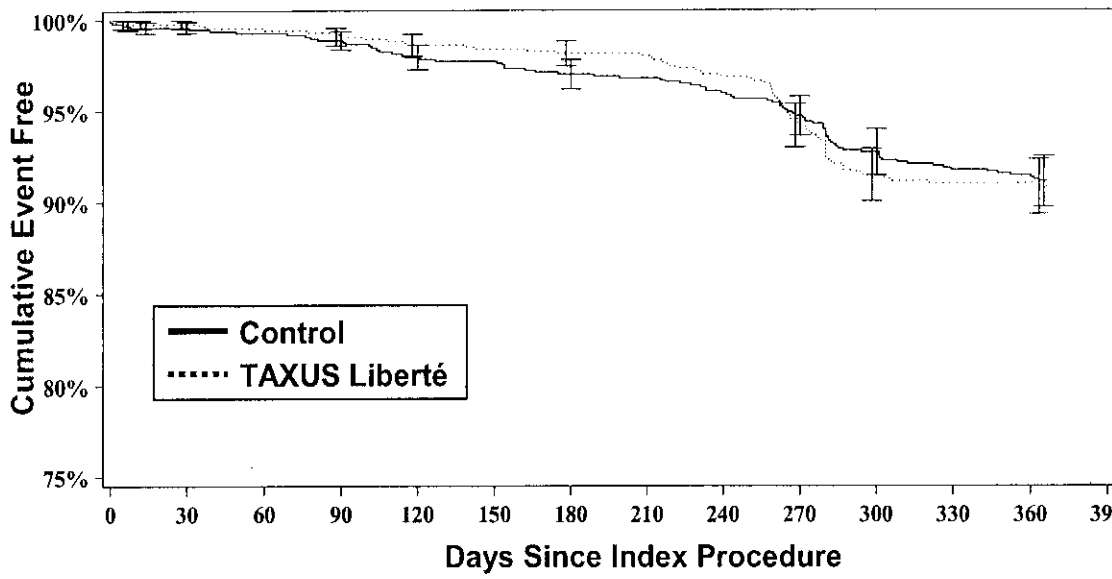
*P-Values are two-sided from Fisher's exact test; P-Values without * are two-sided from the Chi-square test.

P-Values are not adjusted for multiple comparisons.

This trial was not adequately powered to compare the rate of low frequency events to a bare metal control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

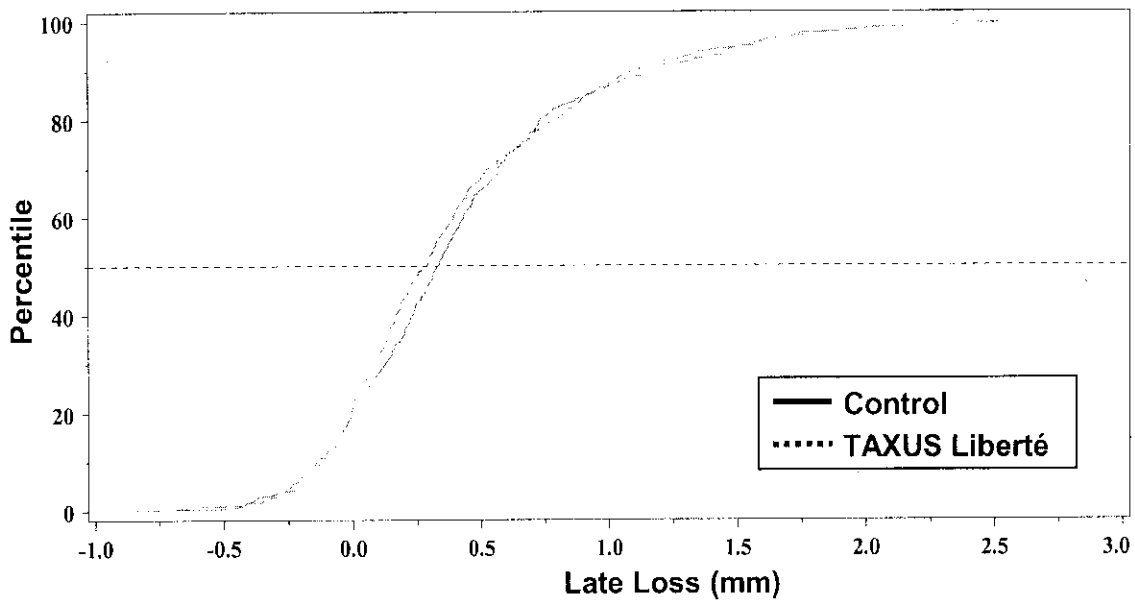
[4] Cutlip DE, Windecker S, Mehran R, et al. Clinical End Points in Coronary Stent Trials: A Case for Standardized Definitions. *Circulation.* 2007;115(17):2344-2351.

Figure 10.1.1. TAXUS ATLAS Workhorse Freedom from TVR to 1 Year, Event-Free Survival ± 1.5 SE, Per Protocol Population, All Patients (N=1845)



	Event Rate	Event Free	P-Value*
TAXUS® Liberté®	9.2%	90.8%	0.8092
TAXUS® Express® DES Control	8.9%	91.1%	

Figure 10.1.2. TAXUS ATLAS Workhorse Cumulative Frequency Distribution of In-Stent Late Loss by QCA, Intent-to-Treat, All Angiographic Subset Patients (N=1247)



	TAXUS® Liberté® (N=543)	TAXUS® Express® Control (N=704)
N	446	484
Median	0.29	0.33
Minimum	-0.77	-0.85
Maximum	2.55	2.71
Mean	0.41	0.42
SD	0.54	0.54
COV	133.09%	126.64%
Diff (95% CI)	-0.01 [-0.08, 0.06]	

COV = coefficient of variation.
MLD = Minimum Lumen Diameter
Late Loss = Final MLD – 9-Month MLD

Diabetic Patients in TAXUS ATLAS Workhorse: Patients with diabetes mellitus represent a high-risk group for adverse events following percutaneous coronary intervention. The TAXUS ATLAS clinical trial did not stratify for diabetic status, and this trial was not adequately powered to study safety and effectiveness of TAXUS® Liberté® versus TAXUS® Express® in patients with diabetes. Diabetics were further defined as medically treated (all patients treated with oral medication and/or insulin) for diabetes mellitus.

The TAXUS ATLAS clinical trial was not designed to specifically support an approval for use in diabetic patients. The following table includes patient level data from the TAXUS ATLAS clinical trial in diabetic patients.

Table 10.1.7. TAXUS ATLAS 1-year Clinical Results for Medically Treated Diabetic Patients

Per Protocol Population [a]	TAXUS® Liberté® (N=220)	TAXUS® Express® DES Control (N=241)	P-Value
EFFICACY			
TVR, Overall	13.5% (29/215)	12.9% (30/233)	0.8480
TLR, Overall	9.3% (20/215)	8.2% (19/233)	0.6668
TLR, PCI	8.8% (19/215)	7.7% (18/233)	0.6693
TLR, CABG	0.5% (1/215)	0.4% (1/233)	1.0000*
TVR Remote, Overall	6.0% (13/215)	5.2% (12/233)	0.6797
TVR Remote, PCI	4.7% (10/215)	3.0% (7/233)	0.3621
TVR Remote, CABG	1.4% (3/215)	2.1% (5/233)	0.7259*
SAFETY			
Total Death	2.3% (5/218)	3.0% (7/235)	0.6500
Cardiac Death or MI	5.1% (11/215)	4.3% (10/233)	0.6800
Cardiac Death	0.9% (2/215)	1.7% (4/233)	0.6869*
MI	5.1% (11/215)	3.0% (7/233)	0.2554
Q-Wave MI	0.9% (2/215)	0.0% (0/233)	0.2298*
Non-Q-Wave MI	4.2% (9/215)	3.0% (7/233)	0.5007
Stent Thrombosis [b]	1.4% (3/213)	0.4% (1/229)	0.3561*

[a] After 9 months, the TAXUS ATLAS study population was reduced to a pre-specified cohort (per protocol population), which consists of all patients who received a study stent at baseline. Patients who did not receive a study stent were not followed beyond 9 months.
[b] Per protocol stent thrombosis.
Numbers are % (Count/Sample Size).
*P-Values are two-sided from Fisher exact test; P-Values without * are two-sided from the Chi-square test.
P-Values are not adjusted for multiple comparisons.
This trial was not adequately powered to compare the rate of low frequency events to a control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

10.2 TAXUS ATLAS Program Small Vessel 2.25 mm Clinical Trial

Primary Objective: The primary objective of this study was to evaluate the safety and effectiveness of the 2.25 mm TAXUS® Liberté® Paclitaxel-Eluting Coronary Stent System for treatment of *de novo* coronary artery lesions in small vessels with a reference vessel diameter (RVD) of 2.25 mm (2.2 – 2.5 mm [visual estimate]).

Design: This was a multicenter, single-arm trial to evaluate the safety and efficacy of the TAXUS® Liberté® Atom™ 2.25 mm stent in the treatment of *de novo* lesions in small coronary vessels compared with the Express$^{2™}$ BMS and TAXUS® Express$^{2™}$ Paclitaxel-Eluting Coronary Stent System (size-matched cohorts derived from the TAXUS V study). Treatment was open label._
Two-hundred-sixty patients were to be treated with the TAXUS Liberté 2.25 mm Stent at a maximum of 25 clinical sites. Angiographic follow-up at 9-months was to be completed in all patients participating in the study. Patients are to have annual follow-up until 5 years post-index procedure.

This multicenter, single-arm study was carried out in patients who presented for stenting of *de novo* lesions in small coronary vessels with an RVD of 2.25 mm (2.2–2.5 mm [visual estimate]). Diabetics were also included in the study as they are at the highest risk for restenosis post-coronary stenting[5]. There were 2 historical controls:

- Control 1: TAXUS® Express$^{2™}$ Paclitaxel-Eluting Coronary Stent System (control data derived from a TAXUS V *de novo* lesion and stent size-matched cohort randomized to receive a single, planned 2.25 mm DES)
- Control 2: Express$^{2™}$ Coronary Stent System (control data derived from a TAXUS V *de novo* lesion size-matched cohort randomized to receive a 2.25 mm or 2.5 mm BMS)

Follow-up included clinical assessments at 1, 4, and 9 months. In addition, patients agreed to annual telephone follow-up for clinical parameters through 5 years post-procedure. After the 9-month follow-up, the study population was reduced to a pre-specified cohort, which consists of all patients who received the assigned study stent at baseline (per protocol population). Follow-up through 1 year is currently available in 249/254 (98.0%) patients.

The primary endpoint data (9 months) and latest available follow-up (1 year) results are presented below (Tables 10.2.1 - 10.2.5).

[5] Elezi, S., A. Kastrati, J. Pache, A. Wehinger, M. Hadamitzky, J. Dirschinger, F.J. Neumann and A. Schomig, Diabetes mellitus and the clinical and angiographic outcome after coronary stent placement. J Am Coll Cardiol, 1998. 32(7): p. 1866-73.

Demographics: The groups were well matched with respect to most baseline patient characteristics. As compared with the BMS Control Group, a statistically significantly larger proportion of patients in the TAXUS ATLAS Small Vessel Group were with CCS Class 1 angina (4.5% versus 10.0%, respectively, *P*=0.0469), however, patients with clinically more significant angina class 2, 3 or 4 were similarly distributed between the 2 groups.

Several statistically significant differences between study groups were noted. Although inclusion criteria for RVD were identical in the TAXUS ATLAS Small Vessel study and for the TAXUS V patients included in the BMS Control group, based on the angiographic analysis at the Core Lab, patients in the TAXUS ATLAS Small Vessel Group had lesions with a statistically significantly smaller RVD than those in the BMS Control Group (2.02±0.30 mm versus 2.20±0.34 mm, respectively, *P*<0.0001). Patients in the TAXUS ATLAS Small Vessel Group had a statistically significantly smaller %DS (67.26±10.91% versus 72.10±10.69%, respectively, *P*<0.0001). Patients with a BMS had statistically significantly more complex target lesions as compared with the TAXUS ATLAS Small Vessel Group (59.4% were eccentric lesions versus 28.7% for patients in the TAXUS ATLAS Small Vessel Group, *P*<0.0001, and 79.4% were classified as B2/C as compared with 69.0% in the TAXUS ATLAS Small Vessel Group, p=0.0213). These differences were not expected to affect outcomes variables, as propensity score adjustments were made.

For patients with only study stents implanted, maximum diameter implanted was statistically significantly greater in the BMS Control Group (2.39±0.17 mm) versus the TAXUS ATLAS Small Vessel Group (2.25±0.00 mm, *P*<0.0001), as expected due to the differences in protocol design. The total length implanted in patients in the BMS Control Group (23.3±7.9 mm) was statistically significantly greater than that implanted in the TAXUS ATLAS Small Vessel Group (21.5±7.0 mm, *P*=0.0173).

Table 10.2.1 TAXUS ATLAS Small Vessel Clinical Results

	9 months (ITT population)			1 year (per protocol population**)		
	TAXUS® Liberté® Atom™ 2.25 mm (N=261)	TAXUS® Express® DES Control (N=75)	P-Value	TAXUS® Liberté® Atom™ 2.25 mm (N=254)	TAXUS® Express® DES Control (N=73)	P-Value
EFFICACY						
TVR, Overall	10.1% (26/258)	17.8% (13/73)	0.0705	10.5% (26/247)	22.5% (16/71)	0.0084
TLR, Overall	5.8% (15/258)	13.7% (10/73)	0.0244	6.1% (15/247)	16.9% (12/71)	0.0039
TLR, PCI	5.8% (15/258)	12.3% (9/73)	0.0581	6.1% (15/247)	15.5% (11/71)	0.0107
TLR, CABG	0.0% (0/258)	1.4% (1/73)	0.2205*	0.0% (0/247)	1.4% (1/71)	0.2233*
Non-TLR, Overall	6.6% (17/258)	6.8% (5/73)	1.0000*	6.9% (17/247)	8.5% (6/71)	0.6530
Non-TLR, PCI	6.6% (17/258)	6.8% (5/73)	1.0000*	6.9% (17/247)	8.5% (6/71)	0.6530
Non-TLR, CABG	0.4% (1/258)	0.0% (0/73)	1.0000*	0.4% (1/247)	0.0% (0/71)	1.0000*
SAFETY						
Total Death	1.2% (3/259)	2.7% (2/73)	0.3035*	2.8% (7/249)	4.3% (3/69)	0.4569*
Cardiac Death or MI	3.5% (9/258)	5.5% (4/73)	0.4938*	3.6% (9/247)	7.0% (5/71)	0.3204*
Cardiac Death	0.8% (2/258)	2.7% (2/73)	0.2123*	1.2% (3/247)	4.2% (3/71)	0.1275*
MI	2.7% (7/258)	4.1% (3/73)	0.4643*	2.4% (6/247)	4.2% (3/71)	0.4234*
Q-wave MI	0.8% (2/258)	1.4% (1/73)	0.5277*	0.8% (2/247)	1.4% (1/71)	0.5327*
Non-Q-wave MI	1.9% (5/258)	2.7% (2/73)	0.6519*	1.6% (4/247)	2.8% (2/71)	0.6187*
Stent Thrombosis	0.4% (1/256)	1.4% (1/72)	0.3914*	0.4% (1/243)	1.5% (1/67)	0.3861*

* P-Values are two-sided from Fisher's exact test; P-Values without * are two-sided from the Chi-square test.

**After 9 months, the TAXUS ATLAS Workhorse study population was reduced to a pre-specified cohort (per protocol population), which consists of all patients who received a study stent at baseline

P-Values are not adjusted for multiple comparisons.

Table 10.2.2. TAXUS ATLAS Small Vessel Primary Endpoint

DES Control

Per Protocol Population	TAXUS Liberté® Atom™ (N=254)	TAXUS® Express® DES Control (N=73)	Difference [Upper 1-Sided 95% CL]	P-Value	Δ
Follow-up In-Segment Percent Diameter Stenosis					
Adjusted for the propensity score	32.2	39.6	-7.3 [-0.8]	<0.0001	10.00%
Unadjusted	31.70±18.23 (207) (4.07, 100.00)	37.69±23.32 (54) (5.36, 100.00)	-5.99 [-1.10]	<0.0001*	10.00%
Intent-to-Treat Population	**TAXUS Liberté Atom (N=261)**	**TAXUS Express DES Control (N=75)**	**Difference [Upper 1-Sided 95% CL]**	**P-Value**	**Δ**
Follow-up In-Segment Percent Diameter Stenosis					
Adjusted for the propensity score	32.4	40.1	-7.7 [-1.1]	<0.0001	10.00%
Unadjusted	32.09±18.38 (211) (4.07, 100.00)	38.36±23.64 (55) (5.36, 100.00)	-6.27 [-1.38]	<0.0001*	10.00%

*Variances unequal: Satterthwaite's approximate t statistic.

P-Values are for non-inferiority testing, with a margin of Δ.

BMS Control

Per Protocol Population	TAXUS Liberté® Atom™ (N=254)	Express® BMS Control (N=152)	Difference [95% CI]	P-Value
Follow-up In-Segment Percent Diameter Stenosis				
Adjusted for the propensity score	31.9	45.3	-13.4 [-18.7,-8.0]	<0.0001
Unadjusted	31.70±18.23 (207) (4.07, 100.00)	45.61±23.48 (105) (7.29, 100.00)	-13.91 [-18.64, -9.18]	<0.0001
Intent-to-Treat Population	**TAXUS Liberté Atom (N=261)**	**Express BMS Control (N=155)**	**Difference [Upper 1-Sided 95% CL]**	**P-Value**
Follow-up In-Segment Percent Diameter Stenosis				
Adjusted for the propensity score	31.9	45.9	-13.9 [-19.6,-8.3]	<0.0001

Unadjusted	32.09±18.38 (211) (4.07, 100.00)	45.61±23.48 (105) (7.29, 100.00)	-13.53 [-18.26, -8.80]	<0.0001

P-Values are for superiority testing,

Table 10.2.3. TAXUS ATLAS Small Vessel Procedural Results

Procedural Outcomes	TAXUS Liberté® Atom™ (N=254)	TAXUS® Express® DES Control (N=75)	P-Value
Procedure Time	43.7±24.8(258)	53.2±33.1(75)	0.0074

P-Values are not adjusted for multiple comparisons.

Table 10.2.4. TAXUS ATLAS Small Vessel 9-Month Angiographic Results

Angiographic Outcomes [a]	TAXUS Liberté Atom (N=261)	TAXUS Express DES Control (N=75)	P-Value
MLD (mm), In-stent			
Post-Procedure	1.87±0.25(208)	1.91±0.26(54)	0.2325
9-Month	1.59±0.48(207)	1.47±0.60(54)	0.1365
MLD (mm), Analysis Segment			
Post-Procedure	1.57±0.31(212)	1.59±0.32(55)	0.6414
9-Month	1.41±0.45(211)	1.26±0.51(55)	0.0323
% DS, In-stent			
Post-Procedure	8.72±11.26(208)	6.50±9.56(54)	0.1865
9-Month	23.35±20.89(207)	27.73±28.12(54)	0.2051
% DS, Analysis Segment			
Post-Procedure	23.72±9.51(212)	23.02±10.72(55)	0.6365
9-Month	32.09±18.38(211)	38.36±23.64(55)	0.0351
Late Loss, In-stent (mm)	0.28±0.45(207)	0.44±0.61(54)	0.0297
Late Loss, Analysis Segment (mm)	0.16±0.40(211)	0.33±0.52(55)	0.0085
Binary Restenosis			
In-stent restenosis	13.0% (27/207)	25.9% (14/54)	0.0205
Analysis segment restenosis	18.5% (39/211)	32.7% (18/55)	0.0219

[a] Includes all patients in the angiographic subset.

P-Values are not adjusted for multiple comparisons.

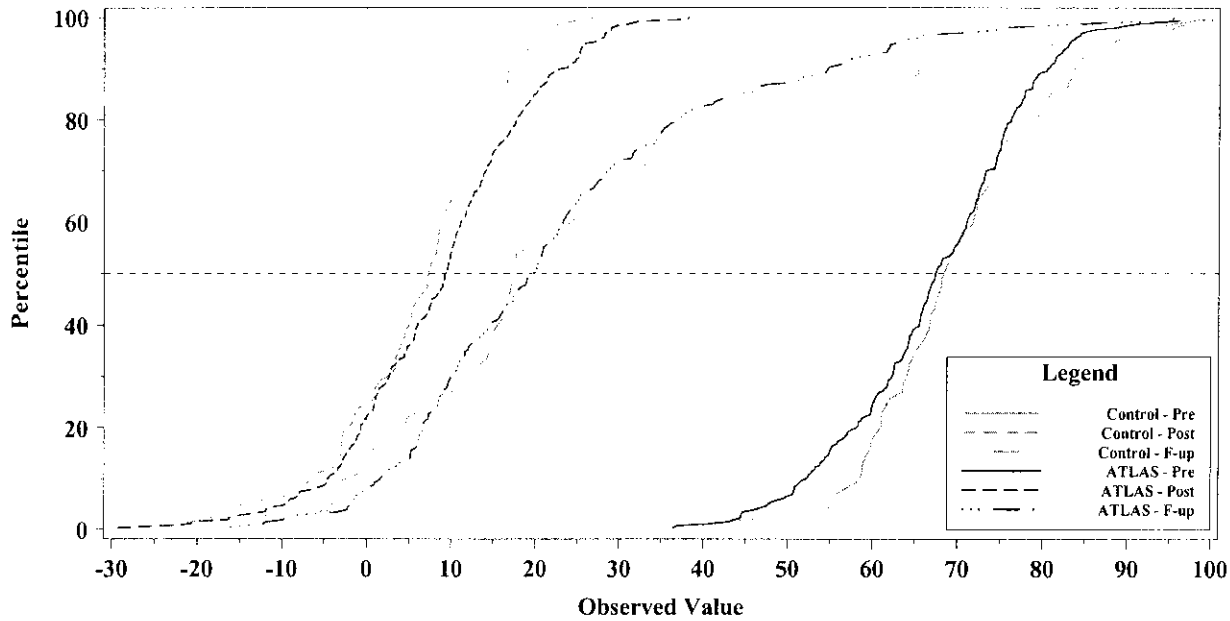
This trial was not adequately powered to compare the rate of low frequency events to a drug-eluting stent control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

Table 10.2.5. TAXUS ATLAS Small Vessel Stent Thrombosis

Per Protocol Population	TAXUS® Liberté® Atom™	TAXUS® Express® DES Control	P-Value
Protocol Defined Stent Thrombosis			
Cumulative through 1 year	0.4% (1/243)	1.5% (1/67)	0.3861*
Acute ST (≤24 hrs)	0.0% (0/254)	1.4% (1/73)	0.2232*
Subacute ST (>24 hrs and ≤30 days)	0.0% (0/253)	0.0% (0/72)	Undef
Late ST (>30 days and ≤12 months)	0.4% (1/253)	0.0% (0/72)	1.0000*
ARC Definite & Probable Stent Thrombosis			
Cumulative through 1 year	0.4% (1/243)	1.5% (1/67)	0.3861*
Acute ST (≤24 hrs)	0.0% (0/254)	0.0% (0/73)	Undef
Subacute ST (>24 hrs and ≤30 days)	0.0% (0/254)	1.4% (1/72)	0.2209*
Late ST (>30 days and ≤12 months)	0.4% (1/253)	0.0% (0/72)	1.0000*

* P value determined by Fisher exact test.
P-Values are not adjusted for multiple comparisons.
This trial was not adequately powered to compare the rate of low frequency events to a control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

Figure 10.2.1 Cumulative Frequency Distribution of In-Stent Percent Diameter Stenosis by QCA, Intent-to-Treat, All Patients (N=336)



	Post-Procedure		Follow-Up		Pre-Procedure	
	TAXUS® Liberté® Atom™ (N=261)	TAXUS® Express® DES Control (N=75)	TAXUS Liberté Atom (N=261)	TAXUS Express DES Control (N=75)	TAXUS Liberté Atom (N=261)	TAXUS Express DES Control (N=75)
N	255	72	207	54	261	74
Median	9.43	7.41	20.04	17.40	67.45	68.56
Minimum	-29.41	-21.17	-16.12	-18.31	36.49	41.29
Maximum	38.19	26.90	100.00	100.00	95.37	100.00
Mean	8.64	6.36	23.35	27.73	67.26	69.97
SD	11.10	9.60	20.89	28.12	10.91	10.59
COV	128.51%	150.91%	89.47%	101.43%	16.22%	15.14%
Diff (95% CI)	2.28 [-0.55, 5.10]		-4.38 [-11.14, 2.38]		-2.71 [-5.51, 0.08]	

COV = coefficient of variation.
Post-Procedure and Follow-up measurements are in-stent measurements.

10.3 TAXUS IV Pivotal Clinical Trial

Primary Objective: To demonstrate superiority of the TAXUS® Express® Stent compared to a matched, uncoated control stent for reduction of the TVR rate at 9 months post-index procedure.

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 in a single native coronary artery (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, and 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 an uncoated Express® 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 clinical assessments at 1, 4, and 9 months. In addition, patients agreed to annual telephone follow-up for clinical parameters through 5 years post-procedure. Follow-up through 2 years is available in 1238/1314 (94.2%) of patients. After the 2-year follow-up, the TAXUS IV study population was reduced to a pre-specified cohort, which consists of all patients who received a study stent at baseline (Safety Population). At 4 years, the safety population is comprised of 1290 (N=649 for TAXUS, N=641 for Control) and follow-up is available for 1230 patients (95.4%).

A subset of patients was 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 for the area within the stent margins, plus the area immediately 5 mm proximal and distal from the stent margins (analysis segment).

The primary endpoint data (9 months) and latest available follow-up (48 months) results are presented below (Table 10.3.1, Table 10.3.2, and Figure 10.3.1), as well as stent thrombosis data through 48 months (Table 10.3.3).

Table 10.3.1. TAXUS IV Clinical Results

	9 months (ITT population)			4 years (safety population*)		
	TAXUS Express (N=662)	**Express BMS Control (N=652)**	**P-Value**	**TAXUS Express (N=649)**	**Express BMS Control (N=641)**	**P-Value**
EFFICACY						
TVR, Overall[§]	4.7% (31/ 662)	12.0% (78/ 652)	<0.0001	16.0% (96/601)	26.0% (157/604)	<0.0001
TLR, Overall	3.0% (20/662)	11.3% (74/652)	<0.0001	7.8% (47/601)	20.2% (122/604)	<0.0001
TLR, PCI	2.4% (16/662)	8.7% (57/652)	<0.0001	7.0% (42/601)	15.9% (96/604)	<0.0001
TLR, CABG	0.6% (4/662)	3.1% (20/652)	0.0008	0.8% (5/601)	5.5% (33/604)	<0.0001
Non-TLR, Overall	1.7% (11/662)	1.1% (7/652)	0.4778	9.0% (54/601)	9.3% (56/604)	0.8629
Non-TLR, PCI	1.2% (8/662)	0.8% (5/652)	0.5793	6.5% (39/601)	7.8% (47/604)	0.3836
Non-TLR, CABG	0.5% (3/662)	0.3% (2/652)	1.0000	2.7% (16/601)	2.2% (13/604)	0.5636
SAFETY						
Total Death	2.1% (14/662)	1.5% (10/652)	0.5378	7.3% (45/618)	8.4% (52/617)	0.4540
Cardiac Death or MI	4.7% (31/662)	4.3% (28/652)	0.7905	9.3% (56/601)	9.9% (60/604)	0.7170
Cardiac Death	1.4% (9/662)	1.1% (7/652)	0.8025	3.0% (18/601)	4.0% (24/604)	0.3545
MI	3.5% (23/662)	3.7% (24/652)	0.8826	7.2% (43/601)	7.1% (43/604)	0.9809
Q-wave MI	0.8% (5/662)	0.3% (2/652)	0.4520	1.3% (8/601)	1.0% (6/604)	0.5844
Non-Q-wave MI	2.7% (18/662)	3.4% (22/652)	0.5237	6.0% (36/601)	6.5% (39/604)	0.7373
Stent Thrombosis	0.6% (4/662)	0.8% (5/652)	0.7513	1.6% (9/579)	1.1% (6/569)	0.4558

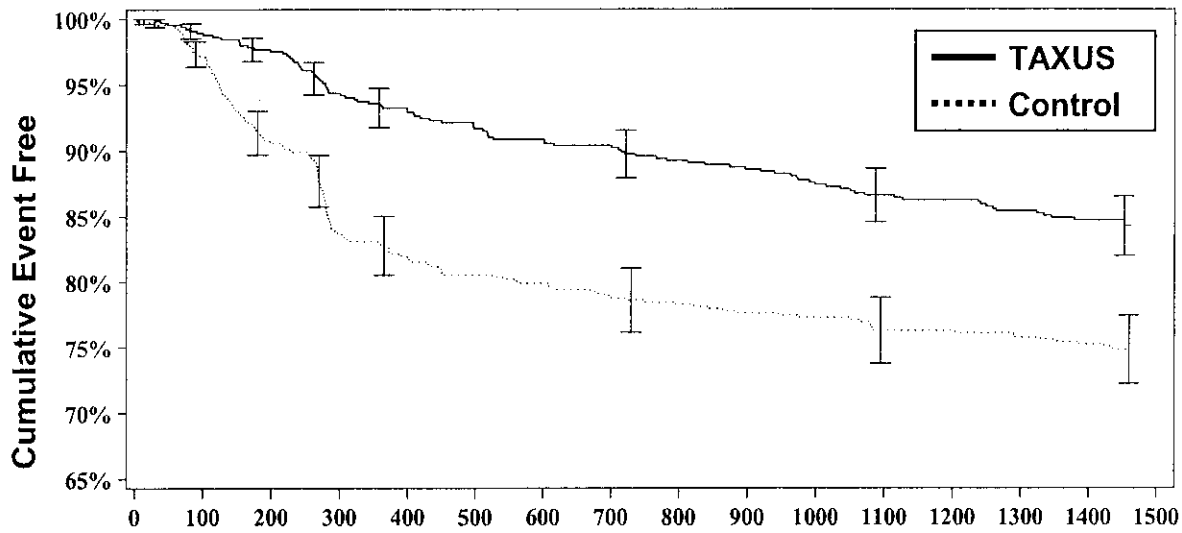
[§] 9-month primary endpoint.

* Patients who did not receive a study stent were not followed beyond two years.

P-Values are not adjusted for multiple comparisons.

This trial was not adequately powered to compare the rate of low frequency events to a bare metal control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

Figure 10.3.1. TAXUS IV Freedom from TVR to 4 Years, Event-Free Survival ± 1.5 SE, Safety Population, All Patients (N=1290)



	Event Rate	Event Free	P-Value*
TAXUS Express	15.7%	84.3%	<0.0001
Express BMS Control	25.2%	74.8%	

* Log-rank P-Value. P-Value is not adjusted for multiple comparisons.

Table 10.3.2. TAXUS IV 9- Month Angiographic and IVUS Results

	TAXUS Express (N=662)	Express BMS Control (N=652)	P-Value
MLD (mm), In-stent			
Post-Procedure	2.65±0.42 (372)	2.67±0.41 (350)	0.6338
9-Month	2.26±0.58 (291)	1.75±0.65 (266)	<0.0001
MLD (mm), Analysis Segment			
Post-Procedure	2.26±0.48 (373)	2.29±0.50 (355)	0.4617
9-Month	2.03±0.55 (291)	1.68±0.61 (267)	<0.0001
% DS, In-stent			
Post-Procedure	4.22±10.85 (372)	5.14±11.42 (350)	0.2695
9-Month	17.43±17.71 (291)	37.24±19.76 (266)	<0.0001
% DS, Analysis Segment			
Post-Procedure	19.14±9.67 (373)	19.31±10.47 (355)	0.8136
9-Month	26.29±15.45 (291)	39.79±18.45 (267)	<0.0001
Late Loss, In-stent (mm)	0.39±0.50 (291)	0.92±0.58 (266)	<0.0001
Late Loss, Analysis Segment (mm)	0.23±0.44 (291)	0.61±0.57 (267)	<0.0001
Binary Restenosis			
In-stent restenosis	5.5% (16/ 291)	24.4% (65/ 266)	<0.0001
Analysis segment restenosis	7.9% (23/ 291)	26.6% (71/ 267)	<0.0001
IVUS			
Neointimal Volume (mm^3)	17.56±18.21 (81)	41.48±23.02 (80)	<0.0001
% Net Volume Obstruction	12.20±12.44 (81)	29.40±14.05 (80)	<0.0001
Incomplete Apposition			
Late (9 months)	4.0% (4/99)	3.0% (3/100)	0.7209
Late Acquired	1.1% (1/94)	2.2% (2/93)	0.6210

P-Values are not adjusted for multiple comparisons.
This trial was not adequately powered to compare the rate of low frequency events to a bare metal control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

Table 10.3.3. TAXUS IV Protocol Defined Stent Thrombosis* through 4 Years Safety Population

	TAXUS Express	Express BMS Control	P-Value
Cumulative ST through 4 years	1.6% (9/579)	1.1% (6/569)	0.4558
Acute ST (≤24 hrs)	0.0% (0/660)	0.3% (2/650)	0.2467
Subacute ST (>24 hrs and ≤ 30days)	0.3% (2/660)	0.5% (3/649)	0.6849
Late ST (>30 days and ≤12 months)	0.3% (2/658)	0.2% (1/647)	1.0000
Very Late ST (>12 months to 4 years)	0.8% (5/630)	0.2% (1/625)	0.2177

To be included in the calculation of stent thrombosis rate for a given interval, a patient either had to have a stent thrombosis during the interval (e.g. 31-365 days inclusive) or they had to be stent thrombosis-free during the interval with last follow-up on or after the first day of the given interval (e.g. 31 days).

*Per protocol, stent thrombosis is defined as the occurrence of any of the following:

1. Clinical presentation of acute coronary syndrome with angiographic evidence of stent thrombosis:
   a) 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 diameter stenosis ≤ 30%) and/or
   b) Angiographic documentation of a flow-limiting thrombus within or adjacent to a previously successfully treated lesion.
2. Acute MI of the distribution of the treated vessel.
3. Death within the first 30 days (without other obvious cause) is considered a surrogate for stent thrombosis when angiography is not available.

Numbers are % (Count/Sample Size).

Patients who did not receive a study stent were not followed beyond two years

P-Values are not adjusted for multiple comparisons.

This trial was not adequately powered to compare the rate of low frequency events to a bare metal control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

10.4 TAXUS V de novo Expansion Clinical Trial

Objective: The primary objective of this study was to demonstrate a superior 9-month ischemia-driven TVR rate for the TAXUS® Express® Stent compared to the uncoated Express Stent in long lesion lengths, small and large vessel diameters and with multiple overlapping stents in the treatment of *de novo* coronary artery lesions.

Design: This was a multicenter, prospective, randomized, double-blind study in patients at 66 U.S. sites. Eligible patients were those presenting for stenting of *de novo* lesions of a single, native coronary artery (RVD ≥ 2.25 and ≤ 4.00 mm) with a target lesion 10 to 46 mm in length, stenosis ≥ 50% (visual estimate), candidates for PCI or CABG, and had documented angina pectoris or functional ischemia.

A total of 1156 ITT patients were enrolled and evaluable in this study: 577 in the TAXUS group and 579 in the Control group. Patients were randomized to receive either a TAXUS Express Stent or uncoated Express Stent (bare metal control). Study randomization was sub-stratified for target lesion length (< 18 mm vs. ≥ 18 mm), the presence or absence of medically treated diabetes, and clinical site. Enrollment targeted high-risk sub-populations including patients with small diameter vessels (RVD ≤ 2.5 mm n ≥ 350 with at least 200 2.25 mm stent patients), large diameter vessels (4.00 mm diameter stent; n ≥ 200), and long lesions (≥ 18 mm lesion length n ≥ 400 with at least 300 patients with lesion lengths > 26 mm [overlapping stents]). Post-procedure patients were treated with aspirin (recommended indefinitely, mandatory for 9 months) and clopidogrel or ticlopidine for 6 months.

Follow-up included clinical assessments at 1, 4, and 9 months. In addition, patients agreed to annual telephone follow-up for clinical parameters through 5 years post-procedure. After the 1-year follow-up, the TAXUS V *de novo* study population was reduced to a pre-specified cohort, which consists of all patients who received an assigned study stent at baseline (Safety Population). Follow-up through 2 years is currently available in 1052/1108 (94.9%) of patients eligible for 2-year follow-up.

All patients were to have angiographic follow-up at 9 months and a subset of patients were to receive IVUS at 9 months (N=300). Angiographic assessments were performed for the area of the vessel within the stent margins (in-stent) and for the area within the stent margins, plus the area immediately 5 mm proximal and distal from the stent margins (analysis segment).

The TAXUS ATLAS trial utilized data from the TAXUS V *de novo* trial as part of the case-matched historical control. Specifically, control patients were identified based on lesion characteristics to match those of the TAXUS ATLAS clinical trial. From the 577 patients in the TAXUS group of TAXUS V *de novo*, 108 patients were excluded who has RVD less than 2.5 mm, 90 patients were excluded who had lesions greater than 28 mm in length, and 50 patients were excluded who had planned use of more than one study stent. This resulted in a total of 329 patients used from the TAXUS V *de novo* study as part of the case-matched historical control. These patients, along with all 662 patients from the TAXUS arm of the TAXUS IV trial constituted the entire TAXUS Express control population (N=991) for the TAXUS ATLAS trial.

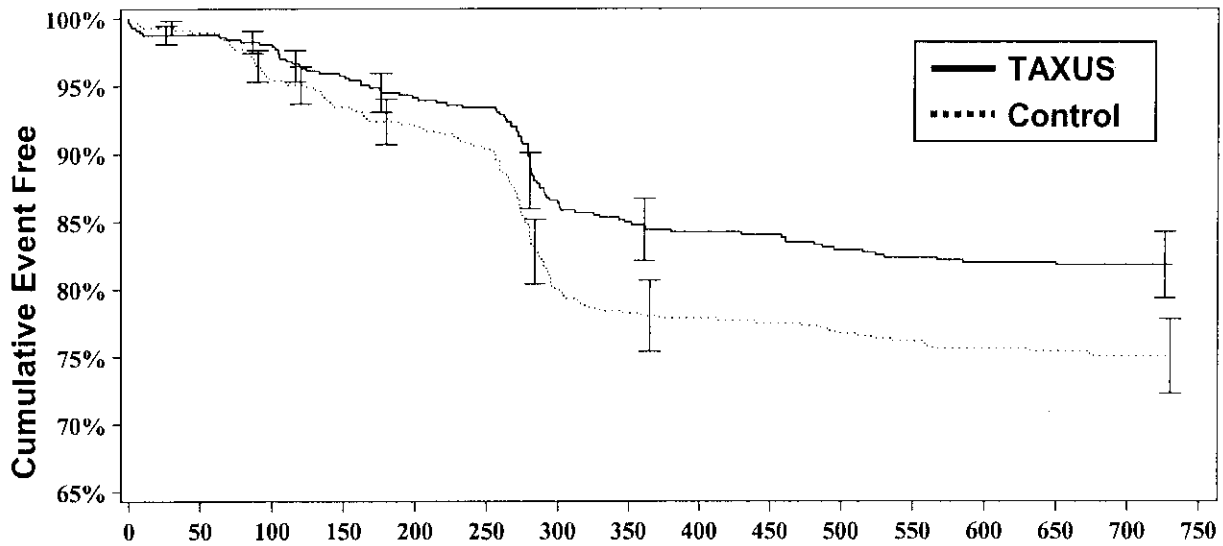
The primary endpoint data (9 months) and latest available follow-up (2 years) results are presented below for the overall population (Table 10.4.1 and Figure 10.4.1).

Table 10.4.1. TAXUS V *de novo* Clinical Results

	9 months (ITT Population)			2 years (Safety Population**)		
	TAXUS Express (N=577)	Express BMS Control (N=579)	P-Value	TAXUS Express (N=575)	Express BMS Control (N=571)	P-Value
EFFICACY						
TVR, Overall[§]	12.1% (68/560)	17.3% (98/567)	0.0184*	18.6% (101/542)	25.4% (138/544)	0.0074
TLR, Overall	8.6% (48/560)	15.7% (89/567)	0.0003*	13.3% (72/542)	21.5% (117/544)	0.0004
TLR, PCI	7.9% (44/560)	13.9% (79/567)	0.0011*	12.5% (68/542)	19.5% (106/544)	0.0018
TLR, CABG	0.7% (4/560)	1.8% (10/567)	0.1770*	0.7% (4/542)	2.4% (13/544)	0.0283
Non-TLR, Overall	4.8% (27/560)	4.2% (24/567)	0.6691*	7.9% (43/542)	8.6% (47/544)	0.6730
Non-TLR, PCI	4.5% (25/560)	3.2% (18/567)	0.2793*	7.2% (39/542)	6.8% (37/544)	0.7991
Non-TLR, CABG	0.4% (2/560)	1.1% (6/567)	0.2874*	0.9% (5/542)	1.8% (10/544)	0.1961
SAFETY						
Total Death	1.3% (7/559)	1.4% (8/566)	1.0000*	3.3% (18/541)	3.8% (21/548)	0.6539
Cardiac Death or MI	5.7% (32/560)	5.5% (32/567)	0.8973*	7.2% (39/542))	6.1% (33/544)	0.4545
Cardiac Death	0.5% (3/560)	0.9% (5/567)	0.7256*	1.7% (9/542)	1.5% (8/544)	0.8010
MI	5.4% (30/560)	4.6% (26/567)	0.5853*	5.9% (32/542)	4.8% (26/544)	0.4098
Q-wave MI	0.5% (3/560)	0.2% (1/567)	0.3712*	0.6% (3/542)	0.4% (2/544)	0.6863*
Non-Q-wave MI	4.8% (27/557)	4.4% (25/562)	0.7777*	5.4% (29/542)	4.4% (24/544)	0.4728
Stent Thrombosis	0.7% (4/557)	0.7% (4/562)	1.0000*	0.8% (4/529)	0.8% (4/530)	1.0000*

** Patients who did not receive a study stent were not followed beyond 1 year.
* P-Values are two-sided from Fisher's exact test; P-Values without * are two-sided from the Chi-square test.
[§] Primary Endpoint at 9 months.
With the exception of the 9-month TVR P-Value, P-Values are not adjusted for multiple comparisons.
This trial was not adequately powered to compare the rate of low frequency events to a bare metal control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

Figure 10.4.1. TAXUS V *de novo* Freedom from TVR to 2 Years, Event-Free Survival ± 1.5 SE, Safety Population, All Patients (N=1146)



	Event Rate	Event Free	P-Value*
TAXUS Express	18.2%	81.8%	0.0053
Express BMS Control	24.9%	75.1%	

* Log-rank P-Value – not adjusted for multiple comparisons.

11 INDIVIDUALIZATION OF TREATMENT

See also Precautions - Section 6.6, Use in Special Populations and Section 6.7, Lesion/Vessel Characteristics.

The risks and benefits should be carefully considered for each patient before use of the TAXUS® Liberté® Stent System. Patient selection factors to be assessed should include a judgment regarding risk of prolonged anticoagulation therapy. 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.

12 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 Liberté Stent System.
- A Patient Implant Card that includes both patient information and stent implant information.

13 HOW SUPPLIED

STERILE: This product is sterilized with ethylene oxide gas. It is intended for single use only. Do not resterilize. Non-pyrogenic. Do not use if package is opened or damaged.

CONTENTS for (1) TAXUS Liberté Over-the-Wire Stent System:

- One (1) TAXUS Liberté Over-the-Wire Stent System

CONTENTS for (1) TAXUS® Liberté® Monorail® Stent System:

- One (1) TAXUS Liberté Monorail Stent System
- Two (2) CLIPIT® hypotube clips
- One (1) Flushing needle with luer fitting

HANDLING and STORAGE: Protect from light. Do not remove from carton until ready for use. Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

DISPOSAL INSTRUCTIONS: After use, dispose of product and packaging in accordance with hospital, administrative and/or local government policy.

14 OPERATIONAL INSTRUCTIONS

14.1 Inspection Prior to Use

Carefully inspect the sterile package before opening. Do not use after the "Use By" date. If the integrity of the sterile package has been compromised prior to the product "Use By" date (e.g. damage of the package), contact your local Boston Scientific representative for return information. Do not use if any defects are noted.

NOTE: At any time during use of the Monorail Stent System, if the stainless steel proximal shaft has been bent or kinked, do not continue to use the catheter.

14.2 Materials Required (not included in Stent System package)

Quantity	Material
1	Appropriate guide catheter (see Table 2.1, TAXUS Liberté Stent System Product Description)
2-3	20 ml (cc) syringe
1,000u / 500cc	Normal heparinized saline
1	≤ 0.014 in (0.36 mm) guidewire
1	Rotating hemostatic valve
	Diluted contrast medium 1:1 with normal heparinized saline
1	Inflation device
1	Torque device
1	Pre-deployment dilation catheter
1	Three-way stopcock
1	Appropriate arterial sheath

14.3 Preparation

14.3.1 Packaging Removal

Step Action

1. Carefully remove the delivery system from its protective tubing for preparation of the delivery system. When using a Monorail® system, do not bend or kink hypotube during removal.
2. Remove the product mandrel and stent protector by grasping the catheter just proximal to the stent (at the proximal balloon bond site), and with the other hand, grasp the stent protector and gently remove distally. If unusual resistance is felt during product mandrel and stent protector removal, do not use this product and replace with another. Follow product returns procedure for the unused device.
3. A Monorail Catheter may be coiled once and secured using the coil clip (CLIPIT®) provided in the catheter package. Only the proximal shaft should be inserted into the CLIPIT device; the clip is not intended for the distal end of the catheter.

NOTE: Care should be taken not to kink or bend the shaft upon application or removal of the coil clip.

14.3.2 Guidewire Lumen Flush

Step Action

1. (Over-the-Wire only) Flush stent system guidewire lumen with normal heparinized saline through the back port of the manifold.
2. (Monorail system only) Flush stent system guidewire lumen with normal heparinized saline using the flushing needle supplied for the Monorail system at the distal end.
3. Verify that the stent is positioned between the proximal and distal balloon markers. Check for bends, kinks and other damage. Do not use if any defects are noted.

NOTE: Avoid manipulation of the stent during flushing of the guidewire lumen, as this may disrupt the placement of the stent on the balloon.

14.3.3 Balloon Preparation

Step Action

1. Stent contact with any fluid is not recommended, as there is a possibility of initiating drug release. However, if it is absolutely necessary to flush the stent with saline, contact time should be limited (1 minute maximum).
2. Prepare inflation device/syringe with diluted contrast medium.
3. Attach inflation device/syringe to stopcock; attach to inflation port. Do not bend the hypotube when connecting to inflation device/syringe.
4. With tip down, orient stent system vertically.
5. Open stopcock to stent system; pull negative for 15 seconds; release to neutral for contrast fill.
6. Close stopcock to stent system; purge inflation device/syringe of all air.
7. Repeat steps 4 through 6 until all air is expelled. If bubbles persist, do not use product.
8. If a syringe was used, attach a prepared inflation device to stopcock.
9. Open stopcock to stent system.
10. Leave on neutral.

14.3.4 Delivery Procedure

Step Action

1. Prepare the vascular access site according to standard PTCA practice.
2. Predilate the lesion/vessel with appropriate diameter balloon.
3. Maintain neutral pressure on inflation device attached to stent system.
4. Backload stent system onto proximal portion of guidewire while maintaining guidewire position across target lesion.
5. Fully open rotating hemostatic valve to allow for easy passage of the stent and prevent damage to the stent.
6. Carefully advance the stent system into the hub of the guide catheter. When using a Monorail® system be sure to keep the hypotube straight. Ensure guide catheter stability before advancing the stent system into the coronary artery.

NOTE: If unusual resistance is felt before the stent exits the guide catheter, do not force passage. Resistance may indicate a problem, and use of excessive force may result in stent damage or stent dislodgment from the balloon. Maintain guidewire placement across the lesion, and remove the stent system and guide catheter as a single unit.

7. Advance the stent system over the guidewire to target lesion under direct fluoroscopic visualization. Utilize the proximal and distal radiopaque balloon markers as a reference point. If the position of the stent is not optimal, it should be carefully repositioned or removed (See also Precautions - 6.12 Stent System Removal). The inside edges of the marker bands indicate both the stent edges and balloon shoulders. Expansion of the stent should not be undertaken if the stent is not properly positioned in the target lesion segment of the vessel.

NOTE: 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 also Precautions - 6.12 Stent System Removal).

8. Sufficiently tighten the rotating hemostatic valve. The stent is now ready to be deployed.

14.3.5 Deployment Procedure

Step Action

1. Inflate the delivery system expanding the stent to a minimum pressure of 9 atm (912 kPa) for the 2.25 mm - 2.50 mm stents and 8 atm (811 kPa) for the 2.75 – 4.00 mm stents sizes (nominal pressure). Higher pressure may be necessary to optimize stent apposition to the arterial wall. Accepted practice generally targets an initial deployment pressure that would achieve a stent inner diameter of about 1.1 times the reference vessel diameter (see Table 14.5.1). Balloon pressure must not exceed rated burst pressure of 18 atm (1824 kPa). (see Table 14.5.1).
2. Maintain inflation pressure for 15-30 seconds for full expansion of the stent.
3. Deflate balloon by pulling negative pressure on inflation device until balloon is fully deflated, see Table 6.1 System Deflation Time Specifications.
4. Confirm stent position and deployment using standard angiographic techniques. For optimal results, the entire stenosed arterial segment should be covered by the stent. Fluoroscopic visualization during stent expansion should be used in order to properly judge the optimum expanded stent diameter as compared to the proximal and distal

coronary artery diameter(s). Optimal expansion requires that the stent be in full contact with the artery wall. Stent wall contact should be verified through routine angiography or intravascular ultrasound (IVUS).

5. If stent sizing/apposition requires optimization, readvance the stent system balloon, or another high-pressure, non-compliant balloon catheter of the appropriate size, to the stented area using standard angioplasty techniques.
6. Inflate the balloon to the desired pressure while observing under fluoroscopy. Deflate the balloon (refer to product labeling and/or Table 14.5.1 for proper stent inflation pressure).
7. If more than one TAXUS® Liberté® Stent is needed to cover the lesion and balloon treated area, it is suggested that, to avoid the potential for gap restenosis, the stents be adequately overlapped. To ensure that there are no gaps between stents, the balloon marker bands of the second TAXUS Liberté Stent should be positioned inside of the deployed stent prior to expansion.
8. Reconfirm stent position and angiographic result. Repeat inflations until optimal stent deployment is achieved.

14.3.6 Removal Procedure

Step Action

1. Ensure balloon is fully deflated before delivery system withdrawal.
2. Fully open rotating hemostatic valve.
3. While maintaining guidewire position and negative pressure on inflation device, withdraw delivery system.
4. Monorail catheters may be coiled once and secured using the coil clip (CLIPIT®) (see Operational Instructions - Section 14.3.1, Packaging Removal).
5. Repeat angiography to assess the stented area. If an adequate expansion has not been obtained, exchange back to the original stent delivery catheter or exchange to another balloon catheter of appropriate balloon diameter to achieve proper stent apposition to the vessel wall.

14.4 Post-Deployment Dilatation of Stented Segments

Precaution: Do not dilate the stent beyond the limits noted below.

Nominal Stent Diameter (ID)	Dilatation Limits (ID)
2.25 mm – 2.50 mm	3.00 mm
2.75 mm – 3.50 mm	4.25 mm
4.00 mm	5.75 mm

All efforts should be taken to assure that the stent is not under dilated. If the deployed stent size is still inadequate with respect to vessel diameter, or if full contact with the vessel wall is not achieved, a larger balloon may be used to expand the stent further. The stent may be further expanded using a low profile, high pressure, and non-compliant balloon catheter. If this is required, the stented segment should be re-crossed carefully with a prolapsed guidewire to avoid dislodging the stent. The balloon should be centered within the stent and should not extend outside of the stented region.

14.5 In Vitro Information

Table 14.5.1. Typical TAXUS® Liberté® Stent System Compliance

Pressure atm (kPa)		2.25 mm Stent I.D. (mm)	2.50 mm Stent I.D. (mm)	2.75 mm Stent I.D. (mm)	3.00 mm Stent I.D. (mm)	3.50 mm Stent I.D. (mm)	4.00 mm Stent I.D. (mm)
8.0 (811)	Nominal	NA	NA	2.76	2.97	3.43	3.95
9.0 (912)		2.19	2.44	2.81	3.02	3.49	4.03
10.0 (1013)		2.24	2.49	2.87	3.08	3.56	4.11
11.0 (1115)		2.29	2.55	2.93	3.14	3.63	4.18
12.0 (1216)		2.32	2.59	2.98	3.19	3.68	4.24
13.0 (1317)		2.36	2.64	3.02	3.23	3.73	4.29
14.0 (1419)		2.39	2.67	3.06	3.27	3.78	4.34
15.0 (1520)		2.42	2.70	3.09	3.31	3.81	4.38
16.0 (1621)		2.44	2.74	3.12	3.34	3.85	4.42
17.0 (1723)		2.47	2.76	3.14	3.37	3.88	4.46
18.0* (1824)		2.49	2.79	3.17	3.39	3.92	4.50

* RATED BURST PRESSURE. DO NOT EXCEED.

Note: The Stent I.D. values listed are actual average stent inner diameters at the specific balloon inflation pressures obtained during in vitro testing at 37 °C

15 WARRANTY

Boston Scientific Corporation (BSC) warrants that reasonable care has been used in the design and manufacture of this instrument. **This warranty is in lieu of and excludes all other warranties not expressly set forth herein, whether express or implied by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability or fitness for a particular purpose.** Handling, storage, cleaning and sterilization of this instrument as well as other factors relating to the patient, diagnosis, treatment, surgical procedures and other matters beyond BSC's control directly affect the instrument and the results obtained from its use. BSC's obligation under this warranty is limited to the repair or replacement of this instrument and BSC shall not be liable for any incidental or consequential loss, damage or expense directly or indirectly arising from the use of this instrument. BSC neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this instrument. **BSC assumes no liability with respect to instruments reused, reprocessed or resterilized and makes no warranties, express or implied, including but not limited to merchantability or fitness for a particular purpose, with respect to such instruments.**

Australian Sponsor Address:
Boston Scientific (Australia) Pty Ltd
PO Box 332
BOTANY
NSW 1455
Australia
Free Phone 1800 676 133
Free Fax 1800 836 666

EC REP EU Authorized Representative

Boston Scientific International S.A.
55 avenue des Champs Pierreux
TSA 51101
92729 NANTERRE CEDEX
FRANCE

Legal Manufacturer

Boston Scientific Corporation
One Boston Scientific Place
Natick, MA 01760-1537
USA
USA Customer Service 888-272-1001

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ANGIOTECH

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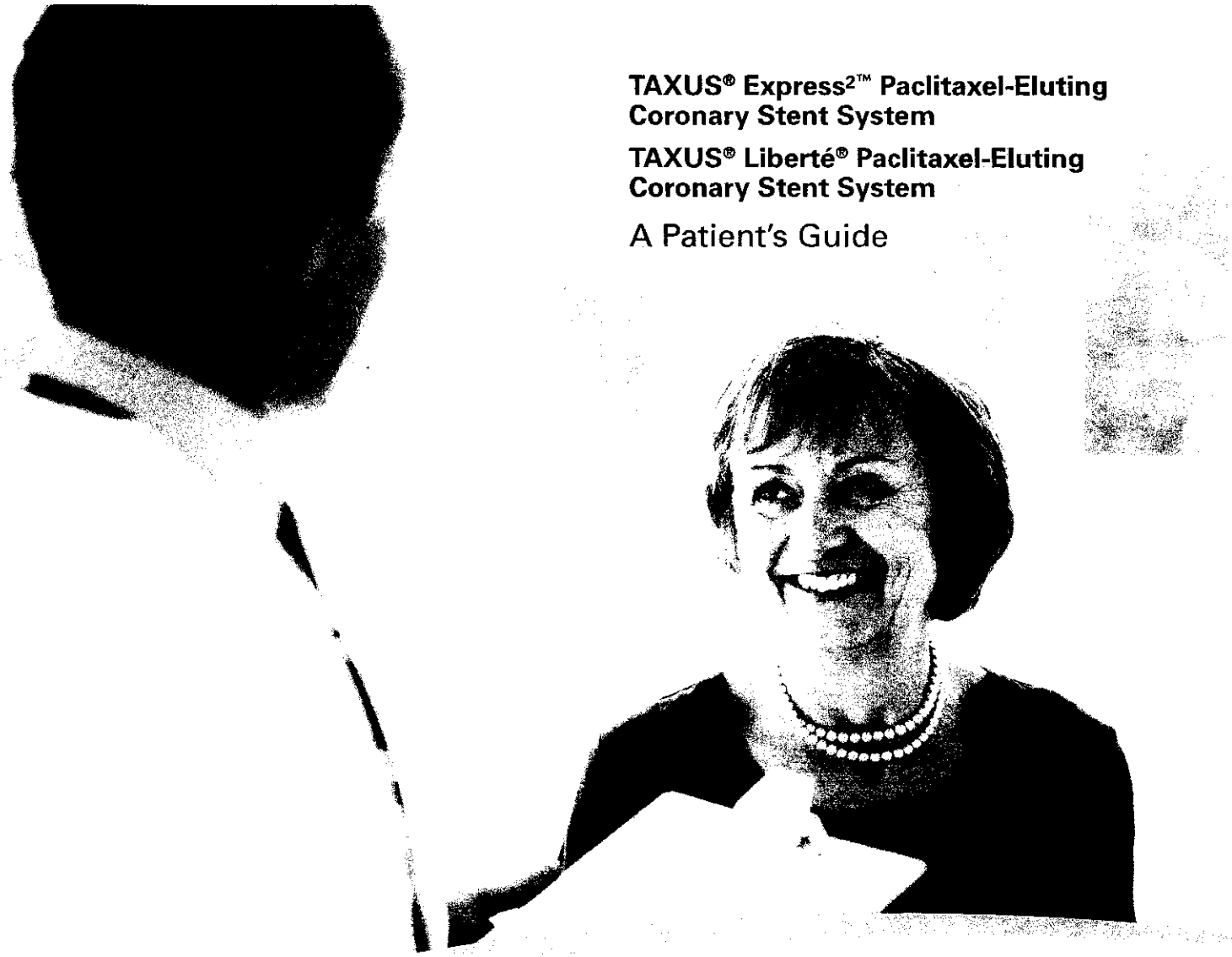

TAXUS® Express2™ Paclitaxel-Eluting Coronary Stent System

TAXUS® Liberté® Paclitaxel-Eluting Coronary Stent System

A Patient's Guide

Boston Scientific

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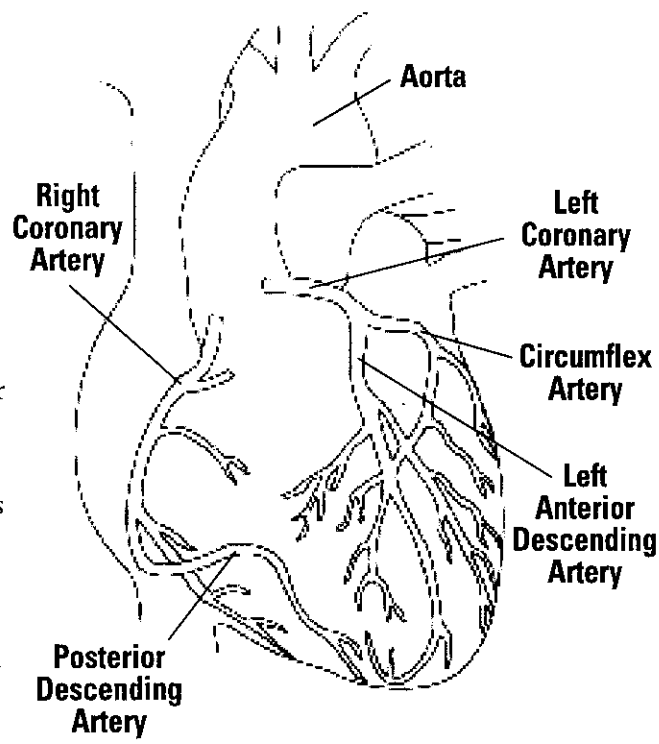
Coronary Artery Disease

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 artery narrows. When the artery narrows (for example with physical exertion or mental stress), blood flow through the artery is reduced so less oxygen and other nutrients reach the heart muscle. This reduced blood flow may cause mild to severe chest pain 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

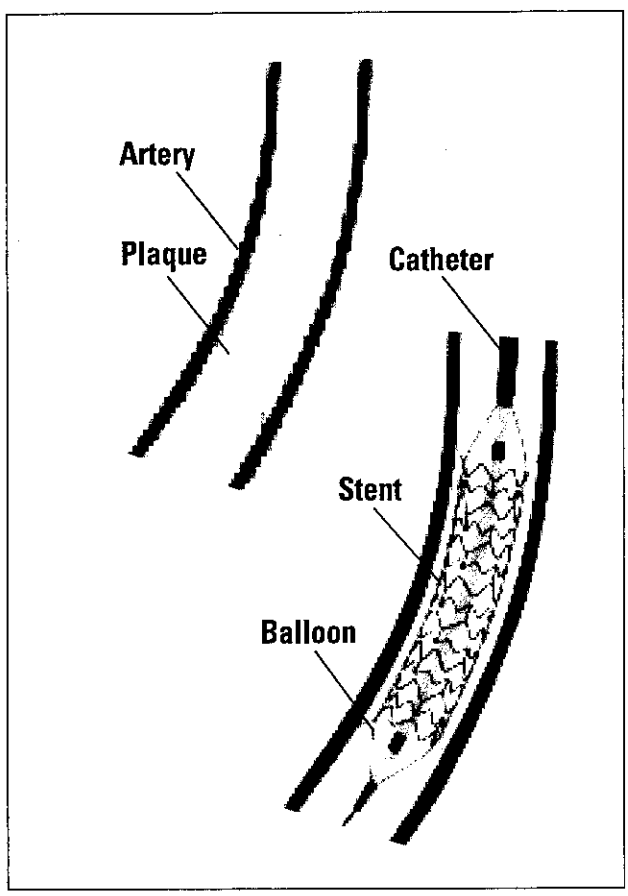
Doctors may use various tests to diagnose CAD. An *electrocardiogram (ECG or EKG)* measures your heart's electrical activity and may show whether parts of your heart muscle have been damaged by a heart attack due to CAD. A *stress test* records your heart's electrical activity while you are exercising 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 arteries 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.

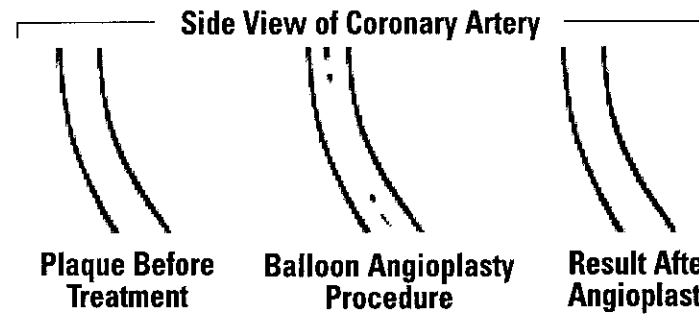
Treatment of Coronary Artery Disease

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).*

Angioplasty

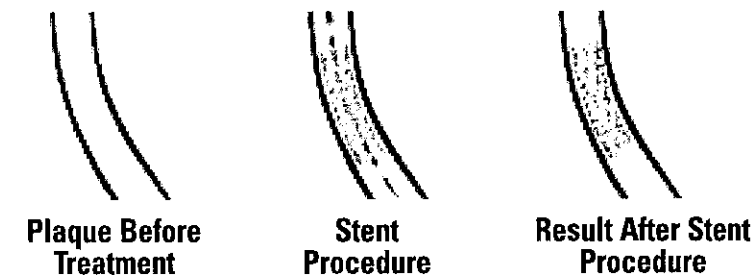
Angioplasty is a minimally invasive treatment of the coronary arteries performed in the hospital to open blocked arteries, also known as percutaneous transluminal coronary angioplasty (PTCA). A thin tube known as a *catheter* is inserted through the groin or wrist and is then threaded through a major artery 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

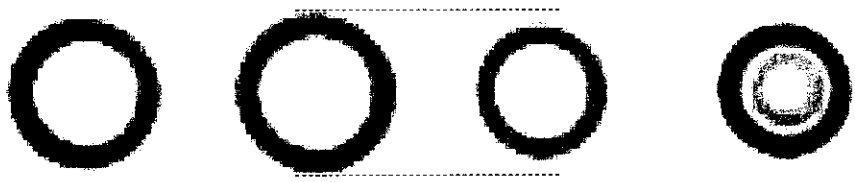
Coronary artery stents are devices that can help to reduce the risk of recurrent blockage or narrowing following an angioplasty procedure. Stents are small expandable metal tubular structures (lattice) that are implanted into an artery and expanded to fit the size, shape and bend of the arterial wall, 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 artery.



Restenosis

Many patients who undergo *balloon angioplasty* treatment will experience a re-narrowing of the artery, or *restenosis*, in the area that was treated. The rate of restenosis within the first six months after the angioplasty procedure is between 30 and 50 percent for angioplasty patients who do not receive a stent. The re-narrowing 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



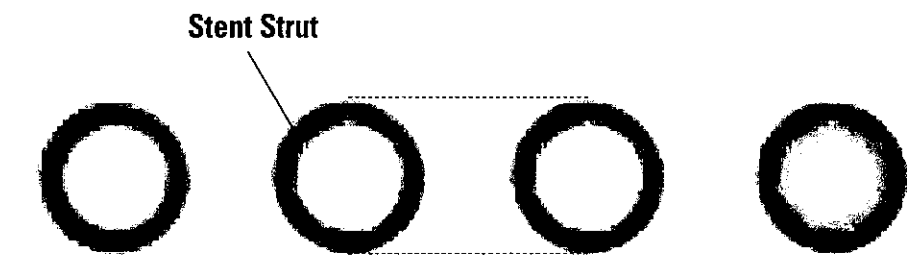
Coronary Artery Disease (Initial Artery Size with Typical Plaque)

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)

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

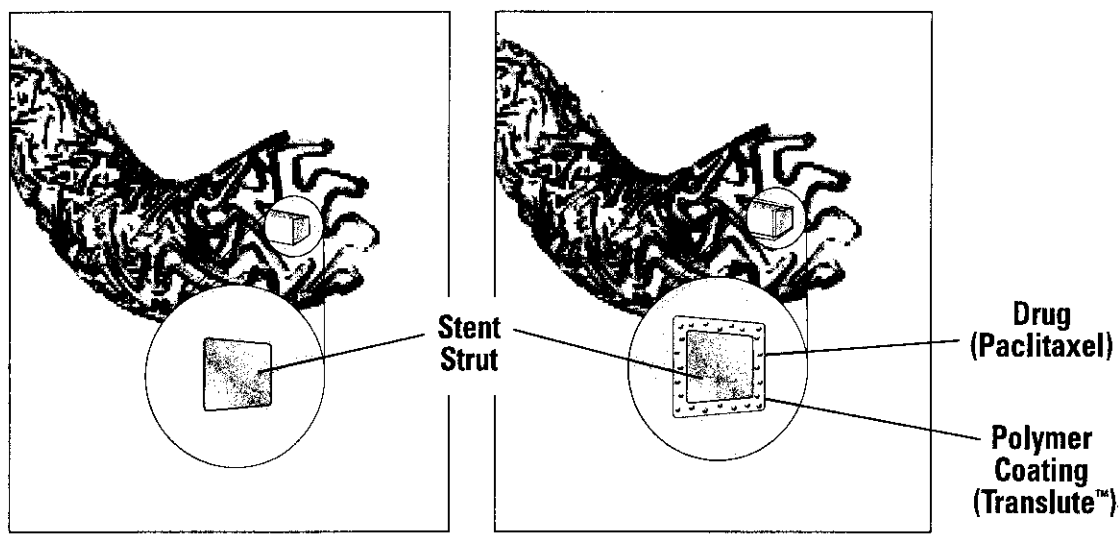
Restenosis Narrows Treated Vessel Over Time (Initial Artery Size Plus Tissue Ingrowth)

Your Drug-Eluting Stent, the TAXUS® Paclitaxel-Eluting Coronary Stent Systems

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



Schematic of Bare Metal Stent*

Schematic of TAXUS Stent*

Note: A green color is used to show coating but actual coating is clear.
**Liberté® stent design shown*

TAXUS Paclitaxel-Eluting Coronary Stent Systems:

TAXUS® Express²™ Paclitaxel-Eluting Coronary Stent System
TAXUS® Liberté® Paclitaxel-Eluting Coronary Stent System

Boston Scientific offers two stent platforms or designs: the TAXUS Express® Stent and the TAXUS Liberté Stent. The information in this guide generally applies to both stent platforms. Depending upon your specific needs, your physician may have chosen to place either the TAXUS Express Stent or TAXUS Liberté Stent. Both stents are designed to be very flexible, allowing them 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.

The Drug That Is Released from the TAXUS Stent

The TAXUS Stent is coated 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 bloodstream. 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, the SIBS polymer or stainless steel.
- 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.

- If you have an allergy to the dye (also called contrast agent) used during the procedure and the physician decides that pre-medication prior to stent placement is not possible.

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 at the access site
- 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 heartbeat (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

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® Express® Stent was compared to the Express Stent (an uncoated stent) in the TAXUS IV clinical trial that included 1,314 patients with a planned five-year clinical follow-up. The study results showed that patients who received a TAXUS Express Stent had a significantly lower incidence of bypass surgery or repeat angioplasty in the artery where the stent was placed, when compared to patients who received an uncoated Express Stent (4.7% vs. 12% at 9 months, 16% vs. 26% at four years). The combined occurrence of Major Adverse Cardiac Events, which is comprised of death, heart attacks, bypass surgery and repeat angioplasty, was 8.5% vs. 15% at 9 months and 22.1% vs. 31.5% at four years.

The safety and effectiveness of the TAXUS® Liberté® Stent was compared to case-matched historical control data for the TAXUS Express Stent, in the TAXUS ATLAS clinical study that included 871 patients with a planned five-year clinical follow-up. The study results showed that patients who received a TAXUS Liberté Stent had a similar incidence of bypass surgery or repeat angioplasty in the artery where the stent was placed, when compared to patients who received a TAXUS Express Stent (8.0% vs. 7.1% at 9 months). The combined occurrence of Major Adverse Cardiac Events, which is comprised of death, heart attacks, bypass surgery and repeat angioplasty, was 11% vs. 10.5% at 9 months.

Full study results are provided in the device's Directions for Use which can be found on www.bostonscientific.com.

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.

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 lie 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 artery.

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.

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 cardiologist may prescribe a number of medications to thin the blood and prevent blood clots from forming and adhering to the surface of the stent. These medications will include aspirin and blood thinning drugs such as clopidogrel (Plavix®) or ticlopidine (Ticlid®). It is extremely important to follow your medication regimen. **If you stop taking these medications before being instructed to do so by your cardiologist, the chances of blood clot formation on the stent, subsequent heart attack or even death are increased.**

If you plan to have any type of surgery or dental work which may require you to stop taking these medications prematurely, you and your cardiologist should discuss whether or not placement of a drug-eluting stent is the right treatment choice for you.

If surgery or dental work which would require you to stop taking these medications prematurely is recommended after you've received the stent, you and your doctors should carefully consider the risks and benefits of this additional surgery versus the possible risks from early discontinuation of these medications.

If you do require premature discontinuation of these medications because of significant bleeding, then your cardiologist will be carefully monitoring you for possible complications. Once your condition has stabilized, your cardiologist will possibly put you back on these medications.

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 coronary artery disease, 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, immediately inform your cardiologist or the center where the procedure was performed.

Can I undergo MRI or scanner testing with a stent?
MRI safety testing has shown that the stent should not migrate in the MRI environment typically used in a clinical setting (≤3T), and that MRI may be performed immediately following stent implantation. Testing also demonstrated that stent heating due to the MRI is less than 1 degree Celsius and should not affect performance of the implanted stent or the drug coating. Please refer to the TAXUS® Express®or TAXUS® Liberté® Stent Directions for Use for additional information.

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 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, jaw or back pain, shortness of breath, nausea, vomiting).

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

Angioplasty A minimally invasive treatment to open blocked coronary arteries. 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 artery.

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 arteries 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®

Paclitaxel-Eluting Coronary Stent System

Boston Scientific

Boston Scientific Corporation
One Boston Scientific Place
Natick, MA 01760-1537
1.888.272.1001
www.bostonscientific.com

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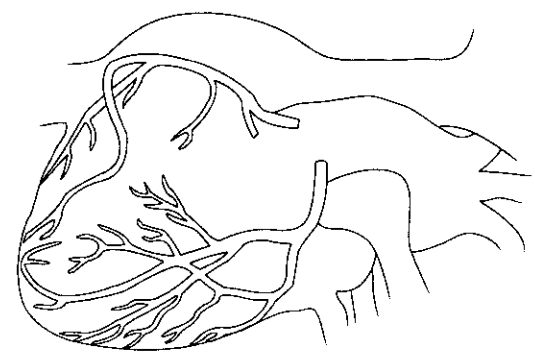

Stent Implant Location

105

TAXUS® 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.

Your cardiologist has prescribed a number of medications to thin the blood and prevent blood clots after your implant. It is extremely important to follow the medication regimen as prescribed by your cardiologist. Before considering any surgery or dental work which would require you to stop taking these medicines early, you and your doctors should consider the risks from premature discontinuation of these medications. **For questions regarding your Coronary Stent System or other procedures (e.g., MRI), please contact your implanting cardiologist.**

Stent Identification Information

Product Code

Product Lot Number

Stent Location

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Product Lot Number

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Product Code

Product Lot Number

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Stent Location

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

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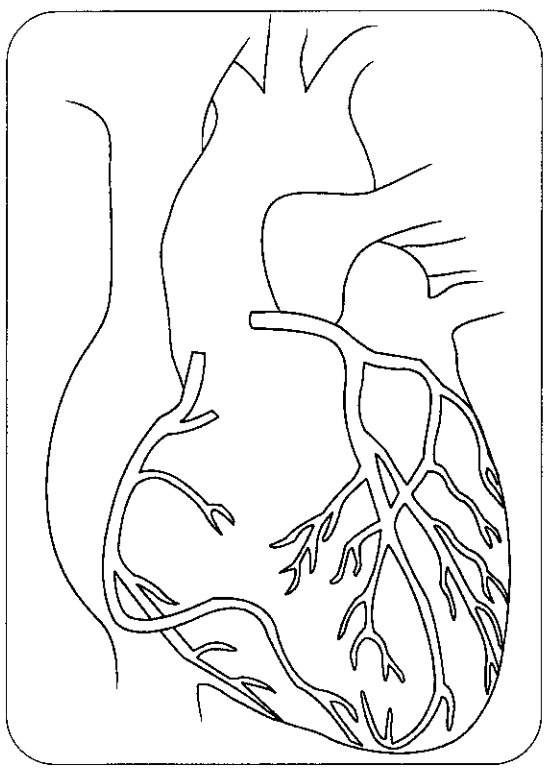

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Boston Scientific Corporation
One Boston Scientific Place
Natick, MA 01760-1537
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