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TAXUS® Liberté®, TAXUS® Liberté® Atom™ and TAXUS® Liberté® Long

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, 8 – 32 mm lengths), TAXUS® Liberté® Atom™ (2.25 mm, 8 – 32 mm lengths) and TAXUS Liberté Long (2.75 mm – 4.00 mm diameters, 38 mm length) 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.

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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, 38*	
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 273 µg on the largest stent (4.00 x 38 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 Diameters 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 • On balloon lengths 38 mm with diameters of 2.75 – 3.00 mm 2.0F (0.67 mm) proximal and 2.7F (0.91 mm) distal: • On balloon lengths 24-38 mm with diameters of 3.5 mm • On balloon lengths 20-38 mm with diameters of 4.0 mm	3.2F (1.08 mm) proximal, 2.7F (0.91 mm) distal

*TAXUS Liberté Long (38 mm) is available in the following diameters: 2.75, 3.00, 3.50, and 4.00 mm
**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

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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.

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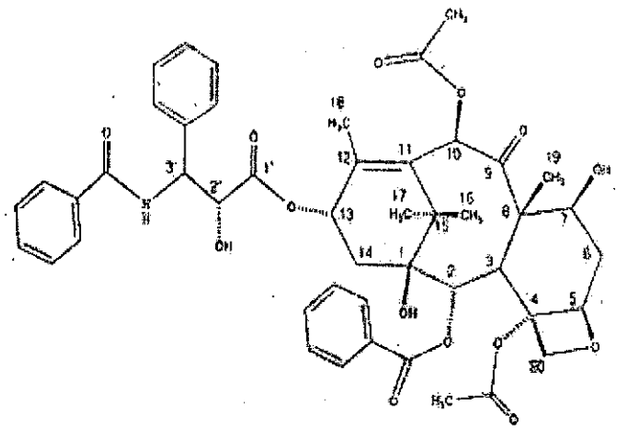
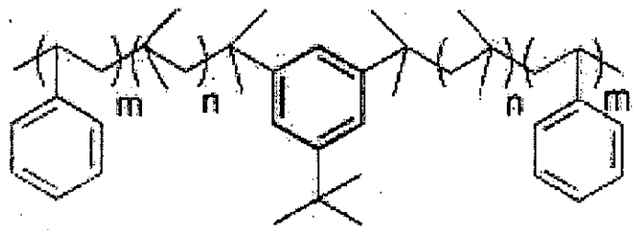


Figure 2.1. The Chemical Structure of Paclitaxel

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

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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

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H7493893638270	H7493893738270	2.75	38	266
H7493893638300	H7493893738300	3.00	38	266
H7493893638350	H7493893738350	3.50	38	266
H7493893638400	H7493893738400	4.00	38	273

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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 ≤ 34 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.

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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 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.

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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, aspirin 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.

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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.

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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 34 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.

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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.

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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

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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><th>38 mm</th></tr>
<tr><td>2.25 mm</td><td colspan="3" rowspan="6">≤ 16 Seconds</td><td colspan="2" rowspan="3">≤ 16 Seconds</td><td colspan="2">≤ 16 Seconds</td><td>N/A</td></tr>
<tr><td>2.50 mm</td><td colspan="2" rowspan="5">≤ 21 Seconds</td><td rowspan="5">≤ 30 seconds</td></tr>
<tr><td>2.75 mm</td></tr>
<tr><td>3.00 mm</td><td colspan="2" rowspan="3">≤ 21 Seconds</td></tr>
<tr><td>3.50 mm</td></tr>
<tr><td>4.00 mm</td><td colspan="2">≤ 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).

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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 46 times the dose provided by the largest TAXUS Liberté Stent coated with 273 µg paclitaxel adjusted for body surface area).

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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 46 and 251 times the dose provided by the largest TAXUS Liberté Stent coated with 273 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 46 times the dose provided by the largest TAXUS Liberté Stent coated with 273 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. This overview will include 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, as well as data from the TAXUS ATLAS Small Vessel and TAXUS ATLAS Long Lesion 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 (lesion-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.

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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 lesion-matched Control group derived from TAXUS IV and TAXUS V *de novo*. In order to lesion-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 (stent size-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.[2]

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 stent size-matched Control group derived from TAXUS V *de novo*. In order to identify 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 lesion-matched Control group derived from TAXUS V *de novo*. In order to lesion-match this second Control group, all TAXUS V patients randomized to the bare metal Express group with (1) a reference

[2] Reduced Risk of Restenosis in Small Vessels and Reduced Risk of Myocardial Infarction in Long Lesions with the New Thin-strut TAXUS Liberté Stent: One-year results from the TAXUS ATLAS Program. Turco MA, Ormiston JA, Popma JJ, Hall JJ, Mann T, Cannon LA, Webster MWI, Mishkel GJ, O'Shaughnessy CD, McGarry TF, Mandinov L, Dawkins KD, Baim DS. J Am Coll Cardiol Intv. 2008;1:699-709.

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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 ATLAS Long Lesion

TAXUS ATLAS Long Lesion is a multicenter, single-arm trial to evaluate the safety and efficacy of the 1 μg/mm^2 (loaded drug/stent surface area) slow-release (SR) formulation, 38 mm TAXUS Liberté stent in the treatment of long *de novo* lesions compared with the TAXUS Express Paclitaxel-Eluting Coronary Stent System (lesion-matched historic control data derived from the TAXUS IV and TAXUS V studies). A total of 150 patients at 24 clinical sites were enrolled in this study. The primary endpoint for the study was the 9-month percent diameter stenosis (%DS) of the analysis segment (as determined by QCA), adjusted for propensity score. Secondary endpoints included 9-month clinical assessments for all patients as well as additional angiographic and IVUS parameters. After the procedure, patients were treated with aspirin for at least 9 months with recommended indefinite use 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 Long Lesion was to demonstrate non-inferiority for the angiographic outcomes of %DS for the 38 mm TAXUS Liberté stent when compared to the TAXUS Express stent. Therefore, the treatment group is compared to a lesion-matched Control group derived from the TAXUS IV and V *de novo* trials. In order to lesion-match the Control group, all TAXUS IV and V patients were randomized to the TAXUS Express group with (1) a reference vessel diameter by visual estimate ≥ 2.5 mm and ≤ 4.0 mm and (2) a lesion length by visual estimate ≥ 26 mm and ≤ 34 mm. This resulted in a Control group of 145 patients.

8.4 TAXUS IV

TAXUS IV[3] 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.

8.5 TAXUS V

TAXUS V *de novo*[4] 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

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[3] 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.

[4] 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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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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Table 8.1. Comparison of TAXUS Clinical Studies

	TAXUS ATLAS Workhorse (Pivotal)	TAXUS ATLAS Small Vessel (Expansion)	TAXUS ATLAS Long Lesion (Expansion)	TAXUS IV (Pivotal)	TAXUS V *de novo* (Expansion)
Study Type	Multi-center, single-arm study	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: 295 TAXUS Liberté Long Stent: 150 TAXUS IV & V *de novo* historical control: 145	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	≥ 2.7 mm to ≤ 4.0 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	≥ 26 mm and ≤ 34 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 Liberté Long 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

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9 ADVERSE EVENTS

9.1 Observed Adverse Events

Observed adverse event experience comes from five clinical studies: TAXUS ATLAS, TAXUS ATLAS Small Vessel, TAXUS ATLAS Long Lesion, 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) and Table 9.1.3 (TAXUS ATLAS Long Lesion). Stent apposition data for TAXUS ATLAS is presented in Table 9.1.4.

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

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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 9.1.4 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 Small Vessel Major Adverse Cardiac Events (MACE) From Post-Procedure to 1-Year Follow-Up

	TAXUS Liberte Atom 2.25mm (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)

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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. TAXUS ATLAS Long Lesion Major Adverse Cardiac Events (MACE) From Post-Procedure to 1-Year Follow-Up

	TAXUS Liberte Long 38 mm (N=150)	TAXUS Express DES Control (N=145)
In-Hospital MACE	0.0% (0/150)	4.1% (6/145)
30-Day MACE, overall	0.0% (0/150)	4.9% (7/143)
9-Month MACE, overall	9.4% (14/149)	14.8% (21/142)
Cardiac Death	0.0% (0/149)	2.8% (4/142)
MI	1.3% (2/149)	6.3% (9/142)
Q-Wave MI	0.0% (0/149)	1.4% (2/142)
Non-Q-Wave MI	1.3% (2/149)	4.9% (7/142)
TVR, Overall	8.7% (13/149)	8.5% (12/142)
TLR, Overall	6.0% (9/149)	7.0% (10/142)
Non-TLR, Overall	3.4% (5/149)	1.4% (2/142)
1-Year MACE	10.9% (16/147)	16.5% (23/139)
Cardiac Death	0.0% (0/147)	3.6% (5/139)
MI	1.4% (2/147)	6.5% (9/139)
Q-Wave MI	0.0% (0/147)	1.4% (2/139)
Non-Q-Wave MI	1.4% (2/147)	5.0% (7/139)
TVR, Overall	10.2% (15/147)	10.1% (14/139)
TLR, Overall	7.5% (11/147)	8.6% (12/139)
Non-TLR, Overall	3.4% (5/147)	1.4% (2/139)
1-Year Stent Thrombosis	0.0% (0/146)	0.7% (1/135)

Table 9.1.4. Frequency of Incomplete Stent Apposition in TAXUS ATLAS, All Patients in the IVUS Subset at 9 Month Follow-up

Incomplete Apposition (IA)	TAXUS® Liberte® (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.

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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 embolization 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.

DJA x00056

10 CLINICAL STUDIES

10.1 TAXUS ATLAS U.S. 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 lesion-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).

DJA x00057

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 before TAXUS ATLAS enrollment began) 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).

DJA x00058

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 drug-eluting stent control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

DJA x00059

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 DES 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.

DJA x00060

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 DES 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*

DJA x00061

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[5]:

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.

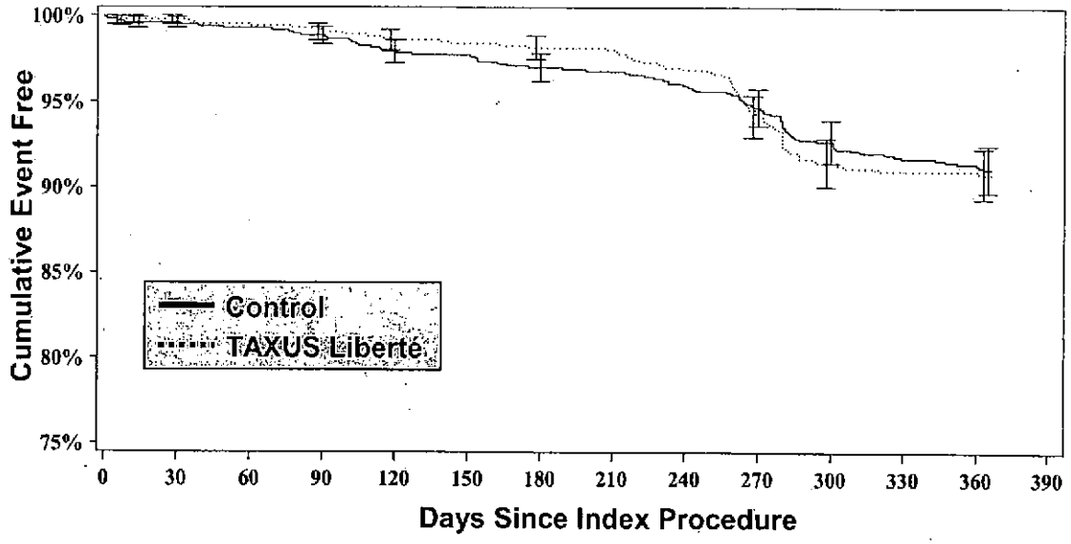
P-Values are not adjusted for multiple comparisons.

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

[5] 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.

DJA x00062

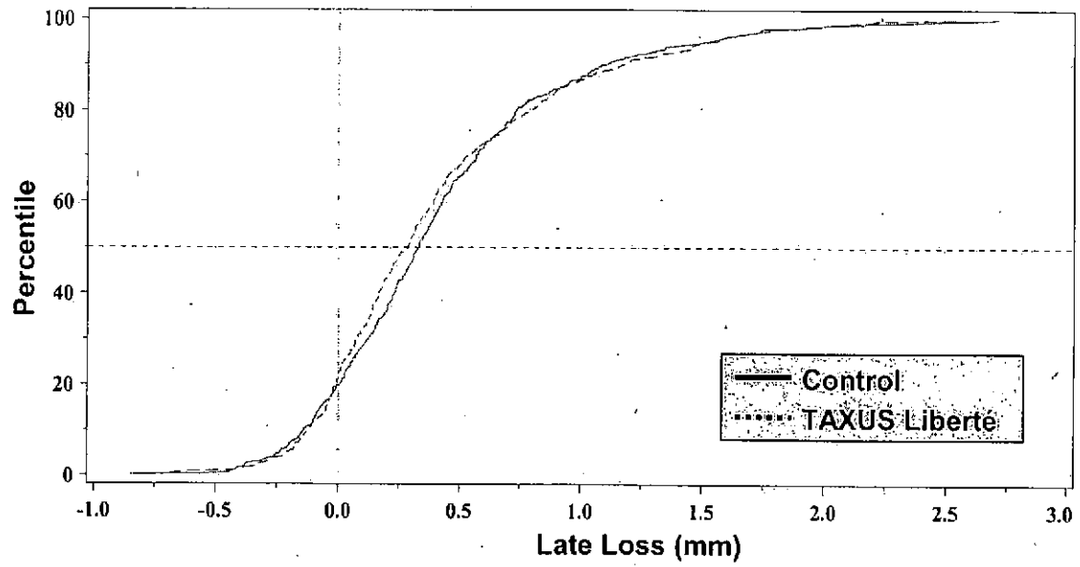
Figure 10.1.1. TAXUS ATLAS Workhorse Freedom from TVR to 1 Year, Event-Free Survival ± 1.5 SE, Per Protocol Population, All Patients (N=1845)



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

DJA x00063

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® Liberte® (N=543)	TAXUS® Express® DES 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

DJA x00064

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.

DJA x00065

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 and lesion-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[6]. 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).

[6] 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.

DJA x00066

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).

DJA x00067

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 Small Vessel 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.

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.

DJA x00068

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

DJA x00069

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.

DJA x00070

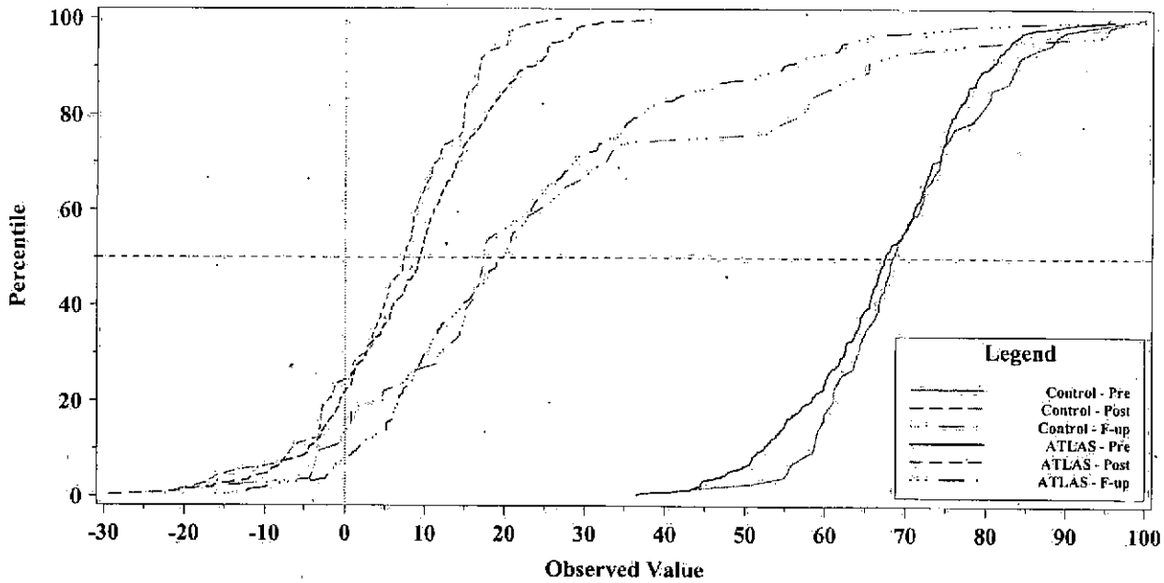
Table 10.2.5. TAXUS ATLAS Small Vessel Stent Thrombosis

Per Protocol Population	TAXUS® Liberté® Atom™	TAXUS® Express® DES Control	P-Value
Protocol Defined Stent Thrombosis [a]			
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 [b]			
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*

See definitions provided with Table 10.1.6.
After 9 months, the TAXUS ATLAS Small Vessel 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 drug-eluting stent control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

DJA x00071

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.

DJA x00072

10.3 TAXUS ATLAS Program Long Lesion 38 mm Clinical Trial

Primary Objective: The primary objective of this study was to evaluate the safety and effectiveness of the 38 mm TAXUS Liberté Paclitaxel-Eluting Coronary Stent System with 1 $\mu g/mm^2$ (loaded drug/stent surface area) of paclitaxel incorporated into a slow-release formulation of a triblock copolymer carrier system for treatment of long *de novo* coronary artery lesions (cumulative length ≥26 mm and ≤34 mm).

Design: TAXUS ATLAS Long Lesion is a multicenter, single-arm trial to evaluate the safety and efficacy of the TAXUS Liberté 38 mm stent in the treatment of long *de novo* lesions compared with the TAXUS Express® Paclitaxel-Eluting Coronary Stent System (lesion-matched historic control data derived from the TAXUS IV and TAXUS V studies). Treatment was open label. One-hundred-fifty patients were treated with the TAXUS Liberté 38 mm stent at a maximum of 25 clinical sites. Eligible patients were those presenting for stenting of *de novo* lesions of a single native coronary artery (RVD of 2.7 to 4.0 mm) with a cumulative target lesion of 26 to 34 mm in length and stenosis ≥ 50% in diameter (visual estimates) who were candidates for percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG), and had documented angina pectoris or functional ischemia. Multiple stenting with the TAXUS Liberté stent was allowed for bail-out only. After the procedure, patients who received the assigned study stent (protocol population) were treated with aspirin for at least 9 months (but recommended indefinitely) and clopidogrel or ticlopidine for at least 6 months.

Angiographic follow-up at 9 months was completed in all patients inclusive of an intravascular ultrasound (IVUS) analysis in 50 patients at qualified sites participating in the IVUS substudy. Patients were randomly allocated to the IVUS subset at participating sites through the Interactive Voice Response System (IVRS). 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 146/150 (97.3%) patients.

The primary endpoint data (9 months) and latest available follow-up (1 year) results are presented below (Tables 10.3.1 - 10.3.5, Figure 10.3.1).

Demographics: Baseline characteristics were comparable between the 2 groups with few statistically significant differences in demographics, cardiac history, and cardiac risk factors. Lesion length by visual estimation was statistically significantly longer for TAXUS ATLAS Long Lesion group (30.44±2.66 mm) as compared with the Control group (28.19±1.79 mm, $P<0.0001$). QCA analysis of the baseline lesion characteristics were comparable between the 2 groups; however, patients in the TAXUS ATLAS Long Lesion group had lesions that were statistically significantly longer (28.08±8.31 mm, versus 21.64±7.28 mm, respectively, $P<0.0001$), had a greater degree of bend (40.21±25.51° versus 32.19±20.99°, respectively, $P=0.0037$), and calcification was reported more often (48.0% versus 29.6%, respectively, $P=0.0013$) than those observed in the Control group. Patients in the TAXUS ATLAS Long Lesion group also had a significantly greater proportion of more complex ACC/AHA Category C lesions (83.3% versus 65.5%, respectively, $P=0.0005$).

DJA x00073

Table 10.3.1 TAXUS ATLAS Long Lesion Clinical Results

	9 months (ITT population)			1 year (per protocol population**)		
	TAXUS® Liberté® Long (N=150)	TAXUS® Express® DES Control (N=145)	P-Value	TAXUS® Liberté® Long (N=150)	TAXUS® Express® DES Control (N=145)	P-Value
EFFICACY						
TVR, Overall	8.7% (13/149)	8.5% (12/142)	0.9335	10.2% (15/147)	10.1% (14/139)	0.9705
TLR, Overall	6.0% (9/149)	7.0% (10/142)	0.7295	7.5% (11/147)	8.6% (12/139)	0.7207
TLR, PCI	5.4% (8/149)	6.3% (9/142)	0.7246	6.1% (9/147)	7.9% (11/139)	0.5527
TLR, CABG	0.7% (1/149)	0.7% (1/142)	1.0000*	1.4% (2/147)	0.7% (1/139)	1.0000*
Non-TLR, Overall	3.4% (5/149)	1.4% (2/142)	0.4484*	3.4% (5/147)	1.4% (2/139)	0.4486*
Non-TLR, PCI	2.0% (3/149)	1.4% (2/142)	1.0000*	2.0% (3/147)	1.4% (2/139)	1.0000*
Non-TLR, CABG	1.3% (2/149)	0.0% (0/142)	0.4986*	1.4% (2/147)	0.0% (0/139)	0.4986*
SAFETY						
Total Death	0.7% (1/148)	2.8% (4/142)	0.2061*	0.7% (1/147)	3.6% (5/139)	0.1120*
Cardiac Death or MI	1.3% (2/149)	8.5% (12/142)	0.0046	1.4% (2/147)	9.4% (13/139)	0.0024
Cardiac Death	0.0% (0/149)	2.8% (4/142)	0.0555*	0.0% (0/147)	3.6% (5/139)	0.0261*
MI	1.3% (2/149)	6.3% (9/142)	0.0255	1.4% (2/147)	6.5% (9/139)	0.0246
Q-wave MI	0.0% (0/149)	1.4% (2/142)	0.2373*	0.0% (0/147)	1.4% (2/139)	0.2353*
Non-Q-wave MI	1.3% (2/149)	4.9% (7/142)	0.0969*	1.4% (2/147)	5.0% (7/139)	0.0957*
Stent Thrombosis	0.0% (0/148)	0.7% (1/140)	0.4861*	0.0% (0/146)	0.7% (1/135)	0.4804*

* 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 Long Lesion 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.

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.

DJA x00074

Table 10.3.2. TAXUS ATLAS Long Lesion Primary Endpoint Intent to Treat, All Patients (N=295)

Intent-to-Treat Population	TAXUS Liberté Long (N=150)	TAXUS Express DES Control (N=145)	Difference [Upper 1-Sided 95% CL]	P-Value	Δ
Follow-up In-Segment Percent Diameter Stenosis					
Adjusted for the propensity score	31.43	35.55	-4.12 [0.41]	<0.0001	6.89
Unadjusted	31.65±17.24 (126) (8.34, 100.00)	32.57±19.28 (91) (2.54, 100.00)	-0.93 [3.19]	0.0010*	6.89

*Variances equal: Pooled t statistic.
P-Values are for non-inferiority testing, with a margin of Δ.
The Per Protocol population was identical to the Intent-to-Treat population, therefore the Primary Endpoint analyses are the same.

Table 10.3.3. TAXUS ATLAS Long Lesion Procedural Results

Procedural Outcomes	TAXUS Liberté® Long (N=150)	TAXUS® Express® DES Control (N=145)	P-Value
Procedure Time	52.56±32.38 (149)	52.40±23.96 (145)	0.9608, 0.3854*
No Non-Target Lesion Treatment	43.02±19.54 (103)	49.39±23.30 (114)	0.0313

* Wilcoxon Rank Sum Two-Sample Test.
P-Values are not adjusted for multiple comparisons.

DJA x00075

Table 10.3.4. TAXUS ATLAS Long Lesion 9-Month Angiographic Results

Angiographic Outcomes [a]	TAXUS Liberté Long (N=150)	TAXUS Express DES Control (N=145)	P-Value
MLD (mm), In-stent			
Post-Procedure	2.60±0.40(150)	2.62±0.46(142)	0.7239
9-Month	2.13±0.65(126)	2.11±0.70(91)	0.8445
MLD (mm), Analysis Segment			
Post-Procedure	2.26±0.47(150)	2.23±0.52(142)	0.6469
9-Month	1.94±0.60(126)	1.88±0.65(91)	0.5160
% DS, In-stent			
Post-Procedure	8.53±9.33(150)	6.52±10.69(142)	0.0884
9-Month	24.64±19.69(126)	23.57±23.04(91)	0.7143
% DS, Analysis Segment			
Post-Procedure	21.29±8.90(150)	21.03±9.79(142)	0.8079
9-Month	31.65±17.24(126)	32.57±19.28(91)	0.7108
Late Loss, In-stent (mm)	0.49±0.55(126)	0.51±0.62(91)	0.8724
Late Loss, Analysis Segment (mm)	0.34±0.52(126)	0.36±0.58(91)	0.7756
Binary Restenosis			
In-stent restenosis	11.9% (15/126)	13.2% (12/91)	0.7777
Analysis segment restenosis	14.3% (18/126)	18.7% (17/91)	0.3850

[a] Includes all patients in the angiographic subset.
P-Values are not adjusted for multiple comparisons.

Table 10.3.5. TAXUS ATLAS Long Lesion Stent Thrombosis

Per Protocol Population	TAXUS® Liberté® Long	TAXUS® Express® DES Control	P-Value
Protocol Defined Stent Thrombosis [a]			
Cumulative through 1 year	0.0% (0/146)	0.7% (1/135)	0.4804*
Acute ST (≤24 hrs)	0.0% (0/150)	0.0% (0/145)	Undef
Subacute ST (>24 hrs and ≤30 days)	0.0% (0/150)	0.0% (0/143)	Undef
Late ST (>30 days and ≤12 months)	0.0% (0/150)	0.7% (1/143)	0.4881*
ARC Definite & Probable Stent Thrombosis [b]			
Cumulative through 1 year	0.0% (0/146)	0.7% (1/135)	0.4804*
Acute ST (≤24 hrs)	0.0% (0/150)	0.0% (0/145)	Undef
Subacute ST (>24 hrs and ≤30 days)	0.0% (0/150)	0.0% (0/144)	Undef
Late ST (>30 days and ≤12 months)	0.0% (0/150)	0.7% (1/143)	0.4881*

See definitions provided with Table 10.1.6.
After 9 months, the TAXUS ATLAS Long Lesion study population was reduced to a pre-specified cohort

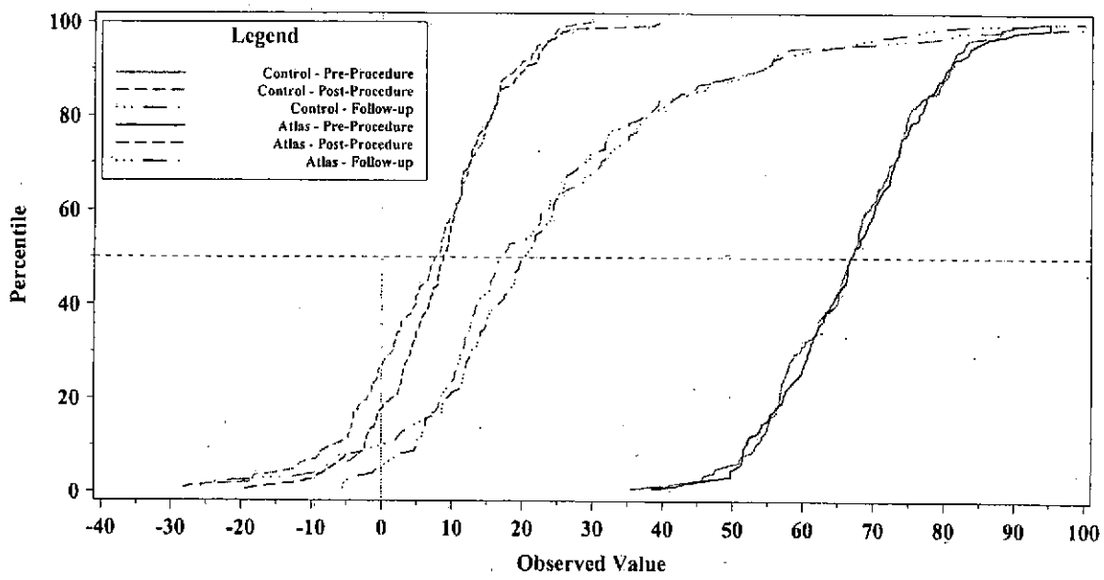
DJA x00076

Table 10.3.5. TAXUS ATLAS Long Lesion Stent Thrombosis

(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 drug-eluting stent control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

DJA x00077

Figure 10.3.1 TAXUS ATLAS Long Lesion Cumulative Frequency Distribution of In-Stent Percent Diameter Stenosis by QCA, Intent-to-Treat, All Patients (N=295)



	Post-Procedure		Follow-Up		Pre-Procedure	
	TAXUS Liberté Long (N=150)	TAXUS Express DES Control (N=145)	TAXUS Liberté Long (N=150)	TAXUS Express DES Control (N=145)	TAXUS Liberté Long (N=150)	TAXUS Express DES Control (N=145)
N	150	142	126	91	150	142
Mean	8.53	6.52	24.64	23.57	67.04	66.46
SD	9.33	10.69	19.69	23.04	11.01	10.88
Diff (95% CI)	2.00 [-0.29, 4.30]		1.07 [-4.64, 6.77]		0.58 [-1.94, 3.09]	

Post-Procedure and Follow-up measurements are in-stent measurements.

DJA x00078

10.4 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 10.4.1, Table 10.4.2, and Figure 10.4.1), as well as stent thrombosis data through 48 months (Table 10.4.3).

DJA x00079

Table 10.4.1. 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.

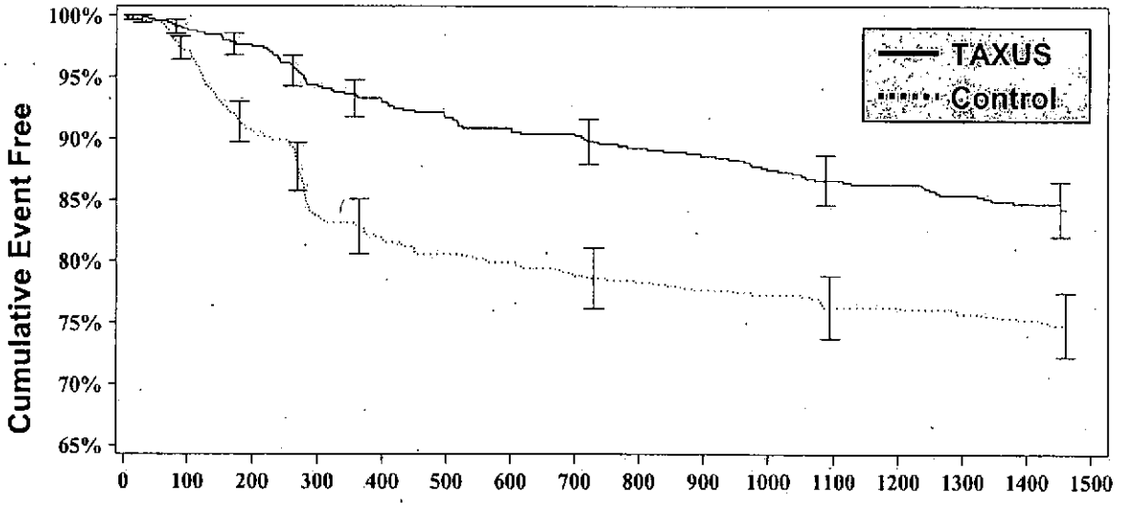
* Patients who did not receive a study stent were not followed beyond two years.

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.

DJA x00080

Figure 10.4.1. 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.

DJA x00081

Table 10.4.2. 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.

DJA x00082

Table 10.4.3. 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.

DJA x00083

10.5 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 lesion-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 had an 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 lesion-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 10.5.1 and Figure 10.5.1).

DJA x00084

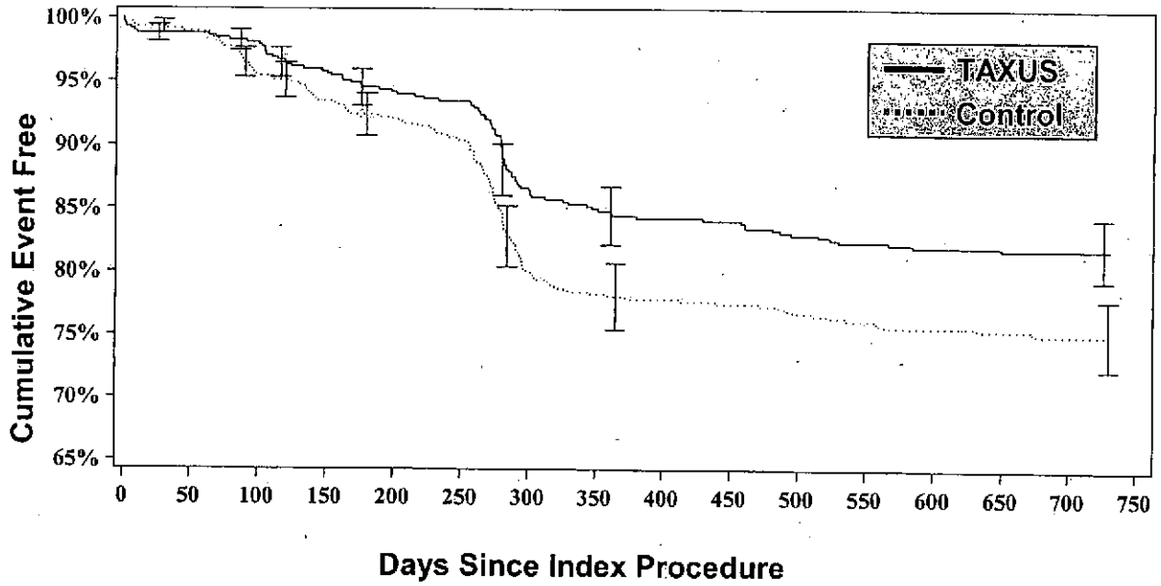
Table 10.5.1. TAXUS V *de novo* Clinical Results

	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.

DJA x00085

Figure 10.5.1. 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.

DJA x00086

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

DJA x00087

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