TAXUS® Liberté®
TAXUS® Liberté® Atom™
TAXUS® Liberté® Long

Monorail®
Over-The-Wire

Paclitaxel-Eluting Coronary Stent System

(Add RX symbol)

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 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.

STERILE - DO NOT RESTERILIZE - SINGLE USE ONLY

2 DEVICE DESCRIPTION

The TAXUS Liberté (2.50 mm - 4.00 mm diameters, 8 - 32 mm lengths), TAXUS Liberté Atom (2.25 mm diameter, 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 (VeriFLEX™ Bare Metal Coronary Stent System) and a drug product (a formulation of paclitaxel contained in a polymer coating). The characteristics of the TAXUS® Liberté® Stent System are described in Table 2.1.

Table 2.1. TAXUS Liberté Stent System Product Description

	TAXUS Liberté Monorail Stent Delivery System	TAXUS Liberté Over-the-Wire Stent Delivery System
Available Stent Lengths (mm)	8, 12, 16, 20, 24, 28, 32, 38[1]	
Available Stent Diameters (mm)	2.25, 2.50, 2.75, 3.00, 3.50, 4.00	
Stent Material	A 316L surgical grade stainless steel VeriFLEX Stent	

	TAXUS Liberté Monorail Stent Delivery System	TAXUS Liberté Over-the-Wire Stent Delivery System
Drug Product	A conformal coating of a polymer carrier loaded with 1 µg/mm2 paclitaxel in a slow release (SR)[2] 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		
Effective Length	144 cm	138 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 (≤ 0.95 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 (≤ 0.95) 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 (1.10 mm) proximal, 2.7F (0.91) distal

[1] TAXUS Liberté Long (38 mm) is available in the following diameters: 2.75, 3.00, 3.50, and 4.00 mm
[2] Release rate is a function of weight/weight ratio of polymer and drug, and (SR) is the formulation that was studied clinically and is used in the marketed product

2.1 Contents

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

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

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

2.2 Device Component Description

The TAXUS Liberté Paclitaxel-Eluting Coronary Stent System consists of a balloon expandable VeriFLEX Stent, coated with paclitaxel in a slow-release (8.8% formulation) triblock copolymer system, and pre-mounted on either the Monorail or an Over-the-Wire (OTW) delivery system. The TAXUS Liberté Stent System incorporates the identical bare VeriFLEX Stent component and a

similar delivery system to that of VeriFLEX 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.

TAXUS 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

2.3 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).

2.3.1 Paclitaxel

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

The chemical structure of paclitaxel is shown in Figure 2.1.

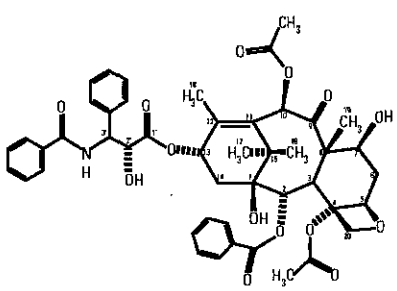
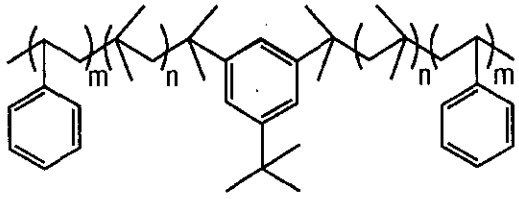


Figure 2.1. The Chemical Structure of Paclitaxel

Paclitaxel is a diterpenoid with a characteristic taxane skeleton of 20 carbon atoms, a molecular weight of 853.91 g/mol and a molecular formula of C47H51NO14. It is highly lipophilic, insoluble in water, but freely soluble in methanol, ethanol, chloroform, ethyl acetate and dimethyl sulfoxide.

2.3.2 Translute Polymer Carrier

The only inactive ingredient in the TAXUS Liberté Stent is SIBS [poly(styrene-b-isobutylene-b-styrene)], a tri-block copolymer (trade name: Translute) that is composed of styrene and isobutylene units built on 1,3-di(2-methoxy-2-propyl)-5-tert- butylbenzene. It is a hydrophobic elastomeric copolymer with a molecular weight (Mn-number average molecular weight) of 80,000 to 130,000 g/mol and a polydispersity index of 1.0 to 2.0. The polymer is mixed with the drug paclitaxel and then applied to the stents. There is no primer or topcoat layer. The drug/polymer coating is adhered to the entire surface (i.e., luminal and abluminal) of the stent. The structural formula for the polymer is shown in Figure 2.2.



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

Figure 2.2. The Chemical Structure of Translute Polymer Carrier

2.3.3 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

Product Code MR	Product Code OTW	Nominal Expanded Stent Inner Diameter (mm)	Nominal Un-expanded Stent Length (mm)	Nominal Paclitaxel Content (µg)
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
H7493893638270	H7493893738270	2.75	38	266
H7493893638300	H7493893738300	3.00	38	266
H7493893638350	H7493893738350	3.50	38	266
H7493893638400	H7493893738400	4.00	38	273

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 2.50 mm in diameter in lesions ≤ 28 mm in length;
- for the treatment of de novo lesions in native coronary arteries 2.75 mm to 4.00 mm in diameter in lesions ≤ 34 mm in length; or
- in patients undergoing primary angioplasty to treat acute ST-segment elevation myocardial infarction, true posterior myocardial infarction, or presumed new left bundle branch block with symptoms of acute myocardial infarction lasting > 20 minutes and < 12 hours in duration.

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 2.3.2, Translute Polymer Carrier for more information).

Coronary Artery Stenting is contraindicated for use in:

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

5 WARNINGS

- To maintain sterility, the inner package should not be opened or damaged prior to use.
- The use of this product carries the risks associated with coronary artery stenting, including stent thrombosis, vascular complications, and/or bleeding events.
- This product should not be used in patients who are not likely to comply with recommended antiplatelet therapy.

6 PRECAUTIONS

6.1 General Precautions

- Only physicians who have received adequate training should perform implantation of the stent.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent stent blockage may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized stents is not well characterized.
- Consideration should be given to the risks and benefits of use in patients with history of severe reaction to contrast agents.
- Do not expose the delivery system to organic solvents such as alcohol or detergents.
- Care should be taken to control the position of the guide catheter tip during stent delivery, deployment and balloon withdrawal.
- Before withdrawing the Stent Delivery System (SDS), visually confirm complete balloon deflation by fluoroscopy (See Table 6.1 System Deflation Time Specifications). Failure to do so may cause increased SDS withdrawal forces, and result in guide catheter movement into the vessel and subsequent arterial damage.
- Stent thrombosis is a low frequency event associated with the use of drug-eluting stents (DES). 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 should be considered in making treatment decisions as data become available.

- When drug-eluting stents are used outside the specified Indications for Use, patient outcomes may differ from the results observed in the pivotal clinical trials.
- Compared to use within the specified Indications for Use, the use of drug-eluting stents in patients and lesions outside of the labeled Indications, including more tortuous anatomy, may have an increased risk of adverse events, including stent thrombosis, stent embolization, myocardial infarction, or death.

6.2 Pre-and Post-Procedure Antiplatelet Regimen

In the TAXUS ATLAS Clinical Trial program specific to the TAXUS® Liberté® Stent, clopidogrel or ticlopidine was administered pre-procedure and for a period of at least 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. In the HORIZONS AMI trial, clopidogrel or ticlopidine was to be administered pre-procedure and for a period of 6 months post-procedure, and recommended for 1 year or longer. Aspirin was to be administered concomitantly with clopidogrel or ticlopidine and then continued indefinitely.

The optimal duration of antiplatelet therapy, specifically clopidogrel, after implantation of a DES 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 "2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention (PCI)", Section 6.2.1.

6.2.1 Oral Antiplatelet Therapy

For Elective PCI Procedures

Continuation of combination treatment with aspirin and a $P2Y_{12}$ inhibitor after PCI appears to reduce major adverse cardiac events. On the basis of randomized clinical trial protocols, secondary prevention measures, and expert consensus opinion, aspirin 81 mg daily should be given indefinitely after PCI. Likewise, a $P2Y_{12}$ inhibitor should be given daily for at least 12 months in patients who are not at high risk of bleeding. Full guidelines are provided at the following website:

http://content.onlinejacc.org/cgi/content/short/58/24/2550

For PCI in ST-Elevation MI (STEMI) Patients

There are ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction[1], which recommend the following:

1) A loading dose of a $P2Y_{12}$ inhibitor is recommended for STEMI patients for whom PCI is planned. Regimens should be one of the following:

a) At least 300 to 600 mg of clopidogrel should be given as early as possible before or at the time of primary or nonprimary PCI.

b) Prasugrel 60 mg should be given as soon as possible for primary PCI.

[1] Kushner F, Hand M, Smith Jr S, et al. 2009 Focused Updates: ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (Updating the 2004 Guideline and 2007 Focused Update) and ACC/AHA/SCAI Guidelines on Percutaneous Coronary Intervention (Updating the 2005 Guideline and 2007 Focused Update)/ A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2009; 54 (23): 2205

c) For STEMI patients undergoing nonprimary PCI, the following regimens are recommended:

(i) If the patient has received fibrinolytic therapy and has been given clopidogrel, clopidogrel should be continued as the thienopyridine of choice;

(ii) If the patient has received fibrinolytic therapy without a thienopyridine, a loading dose of 300 to 600 mg of clopidogrel should be given as the thienopyridine of choice;

(iii) if the patient did not receive fibrinolytic therapy, either a loading dose of 300 to 600 mg of clopidogrel should be given or, once the coronary anatomy is known and PCI is planned, a loading dose of 60 mg of prasugrel should be given promptly and no later than 1 hour after PCI.

2) The duration of $P2Y_{12}$ inhibitor therapy should be as follows:

a) In patients receiving a stent (BMS or drug-eluting [DES]) during PCI for ACS, clopidogrel 75 mg, prasugrel 10 mg daily should be given for at least 12 months;

b) If the risk of morbidity because of bleeding outweighs the anticipated benefit afforded by $P2Y_{12}$ receptor inhibitor therapy, earlier discontinuation should be considered.

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 among those patients for whom surgery canbe deferred, continuation of aspirin should be considered during the perioperative period in high risk DES patients.

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

6.3 Use of Multiple Stents

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

In the HORIZONS AMI trial, lesions > 26 mm in length were to be treated with 2 (or more as required) overlapping study stents. Table 6.1 provides clinical outcomes on patients from the HORIZONS AMI trial who were treated with multiple overlapping study stents (528 patients in the TAXUS Express arm and 124 patients in the bare metal Express arm).

Table 6.1: Clinical Outcomes in HORIZON AMI Patients with Multiple Overlapping Study Stents

	1 Year		3 Year	
	TAXUS Express (N=528)	Bare Metal Express (N=124)	TAXUS Express (N=528)	Bare Metal Express (N=124)
Death	4.2% (22)	5.0% (6)	6.8% (35)	8.4% (10)
Cardiac Death	2.9% (15)	4.1% (5)	4.1% (21)	5.1% (6)
Noncardiac Death	1.4% (7)	0.9% (1)	2.8% (14)	3.6% (4)
Reinfarction	4.5% (23)	2.5% (3)	9.1% (45)	6.2% (7)
Q-Wave	1.9% (10)	1.7% (2)	3.4% (17)	2.6% (3)

Non-Q-Wave	2.6% (13)	0.8% (1)		5.7% (28)	3.7% (4)
Death or Reinfarction	8.6% (45)	6.6% (8)		15.1% (78)	13.6% (16)
Target Vessel Revascularization	6.4% (33)	11.8 % (14)		15.7% (78)	28.5% (33)

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
See Clinical Information - Section 10, Clinical Studies. Clinical studies of the TAXUS Liberté Stent did not include formal analysis of differences in safety and effectiveness between male and female patients.

6.6.4 Ethnicity
In the TAXUS IV, TAXUS V de novo, TAXUS ATLAS Workhorse, TAXUS ATLAS Direct Stent, TAXUS ATLAS Small Vessel, and TAXUS ATLAS Long Lesion clinical trials and registries there were 2,428 pooled patients, of which 127 (5.2%) were black. The clinical trials and registries conducted with paclitaxel-eluting stents were not designed or powered to analyze for differences by race/ethnicity.

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. In the TAXUS ATLAS Workhorse, TAXUS ATLAS Small Vessel, and TAXUS ATLAS Long Lesion studies, there were

549 patients in the TAXUS Liberté group who were age 65 or older. There were 71 TAXUS Liberté patients in these three TAXUS ATLAS studies who were over 80 years of age. Nine-month clinical outcomes (primary endpoint) in these studies were generally similar between patients under 65 and over 65 years of age treated with TAXUS Liberté stents, with the exception of myocardial infarction (2.3% in those patients less than 65 years of age versus 4.4% in those 65 or older), cardiac death (0.3% in those patients less than 65 years of age versus 1.3% in those 65 or older), and total death (0.4% in those patients less than 65 years of age versus 2.0% in those 65 or older).

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 coronary disease patient populations:

- Patients not being treated for STEMI, 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 in-stent thrombosis.
- 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 in-stent restenosis.
- Patients with moderate or severe calcification in the lesion or a chronic total occlusion.
- Patients with multi-vessel disease.

6.8 Drug Interaction

Because systemic levels of paclitaxel have not been detected post-stent placement in clinical trials, possible interactions of paclitaxel with concomitantly administered medications are unlikely to be detectable. The effect of potential drug interactions on the safety and efficacy of the TAXUS Liberté Stent has not been formally investigated. The metabolism of paclitaxel is catalyzed by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. In the absence of formal clinical drug interaction studies, caution should be exercised when administering paclitaxel concomitantly with known substrates or inhibitors of the cytochrome P450 isoenzymes CYP2C8 and CYP3A4. See Drug Information – Section 7.3 Drug Interactions for more information.

6.9 Magnetic Resonance Imaging (MRI)

Through non-clinical testing, the TAXUS Liberté Stent, in single and in overlapped configurations up to 60 mm in length, has been shown to be MR Conditional (poses no known hazards under specified conditions). The conditions are as follows:

- Field strengths of 3 Tesla and 1.5 Tesla
- Static magnetic field gradient < 16 T/m (extrapolated)
- Normal operating mode (maximum whole body averaged specific absorption rate (SAR) of 2.0 W/kg) for a total active MR scan time (with RF exposure) of 15 minutes 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.

3.0 Tesla Temperature Information

Non-clinical testing of RF-induced heating was performed at 123 MHz in a 3.0 Tesla Magnetom Trio, Siemens Medical Solutions MR system, software version Numaris/4, Syngo MR A30. RF power was applied for 15 minutes and the measured conductivity of the phantom material was about 0.3 S/m. The phantom whole body averaged SAR was determined through calorimetry. The maximal in-vitro temperature rise was determined through validated calculation as 1.5°C

when the local SAR was scaled to 2 W/kg for a measured stent length of 60 mm. The calculations did not include the cooling effects due to blood flow.

1.5 Tesla Temperature Information
Non-clinical testing of RF-induced heating was performed at 64 MHz in a 1.5 Tesla Intera Philips Medical Systems, software version Release 10.6.2.0, 2006-03-10 whole body coil MR scanner. RF power was applied for 15 minutes and the measured conductivity of the phantom material was about 0.3 S/m. The phantom whole body averaged SAR was determined through calorimetry. The maximal in-vitro temperature rise was calculated as 1.2°C when the local SAR was scaled to 2 W/kg for a measured stent length of 60 mm. The calculations did not include the cooling effects due to blood flow.

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.

Image Artifact Information
The calculated image artifact extends approximately 6 mm from the perimeter of the device diameter and 5 mm beyond each end of the length of the stent when scanned in non-clinical testing using a Spin Echo sequence. With a Gradient Echo sequence the calculated image artifact extends 9 mm beyond the perimeter of the diameter and 8 mm beyond each end of the length with both sequences partially shielding the lumen in a 3 Tesla, Magnetom Trio, Siemens Medical Solutions, Software: Numaris/4, syngo MR A30; Coil: CP head for transmitting & receiving signals.

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

- For single use only. Do not resterilize or reuse this product. Note product "Use By" date (See Warning – Section 1).
- The premounted TAXUS Liberté Stent and its delivery system are designed for use as a unit. The stent is not to be removed from its delivery balloon. The stent is not designed to be crimped onto another balloon. Removing the stent from its delivery balloon may damage the stent and coating and/or lead to stent embolization.
- Special care must be taken not to handle or in any way disrupt the stent position on the delivery balloon. This is most important during catheter removal from packaging, placement over guidewire, and advancement through hemostasis valve adapter and guide catheter hub.
- Excessive manipulation or handling may cause coating damage, contamination, or dislodgment of the stent from the delivery balloon.
- Use only the appropriate balloon inflation media (see Operational Instructions – Section 14.3.3, Balloon Preparation). Do not use air or any gas medium to inflate the balloon.
- In the event the TAXUS® Liberté® Stent is not deployed, follow product returns procedures.

6.11 Stent Placement
Preparation

- Do not prepare or pre-inflate balloon prior to stent deployment other than as directed. Use the balloon purging technique described in Operational Instructions – Section 14.3.3 Balloon Preparation.
- If unusual resistance is felt at any time during lesion access before stent implantation, the stent system and the guide catheter should be removed as a single unit (See Precautions – Section 6.12, Stent System Removal).
- An unexpanded stent should be introduced into the coronary arteries one time only. An unexpanded stent should not be subsequently moved in and out through the distal end of the guide catheter as stent or coating damage or stent dislodgment from the balloon may occur.

Placement

- The vessel should be pre-dilated with an appropriate sized balloon. Failure to do so may increase the risk of placement difficulty and procedural complications.
- Do not expand the stent if it is not properly positioned in the vessel (see Precautions – Section 6.12, Stent System Removal).
- Balloon pressures should be monitored during inflation. Do not exceed rated burst pressure as indicated on product label (see Table 14.5.1. Typical TAXUS Liberté Stent System Compliance). Use of pressures higher than specified on product label may result in a ruptured balloon and potential intimal damage and dissection. The stent inner diameter should approximate 1.1 times the reference diameter of the vessel.
- Placement of the stent has the potential to compromise side branch patency.
- Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stented portion, and may cause acute closure of the vessel requiring additional intervention (e.g. CABG, further dilation, placement of additional stents, or other).
- When treating multiple lesions, the distal lesion should be initially stented, followed by stenting of the more proximal lesion(s). Stenting in this order alleviates the need to cross the proximal stent in placement of the distal stent and reduces the chances of dislodging the proximal stent.

6.12 Stent System Removal

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

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

- Following stent placement, confirm complete balloon deflation (See Table 6.2 System Deflation Time Specifications). If greater than usual resistance is felt during delivery system withdrawal, pay particular attention to guide catheter position. In some cases it may be necessary to pull back slightly on the guide catheter in order to prevent deep seating (unplanned advancement) of the guide catheter and subsequent vessel damage. In cases where unplanned guide catheter movement has occurred, angiographic assessment of the coronary tree should be undertaken to ensure that there is no damage to the coronary vasculature.
- Maintain guidewire placement across the lesion during the entire removal process. Carefully pull back the stent system until the proximal balloon marker of the stent system is just distal to the guide catheter distal tip.
- The stent system and the guide catheter should be pulled back until the tip of the guide catheter is just distal to the arterial sheath, allowing the guide catheter to straighten. Carefully retract the stent system into the guide catheter and remove the stent system and the guide catheter from the patient as a single unit while leaving the guidewire across the lesion.

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

Table 6.2. System Deflation Time Specifications[1]

Balloon Length/Diameter	8 mm	12 mm	16 mm	20 mm	24 mm	28 mm	32 mm	38 mm
2.25 mm	≤ 16			≤ 16		≤ 16		N/A

2.50 mm	Seconds	Seconds	Seconds	
2.75 mm			≤ 21 Seconds	≤ 30 Seconds
3.00 mm				
3.50 mm		≤ 21 Seconds		
4.00 mm				

[1]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 at least 6 months post-procedure. Aspirin was administered concomitantly with clopidogrel or ticlopidine and then continued indefinitely to reduce the risk of thrombosis. See Section 10 - Clinical Studies, for more specific information.
- If the patient requires imaging, see Precautions - Section 6.9, Magnetic Resonance Imaging (MRI).

7 DRUG INFORMATION

7.1 Mechanism of Action

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

7.2 Pharmacokinetics

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

7.3 Drug Interactions

Paclitaxel is metabolized in the liver via CYP2C8 to 6-alpha-hydroxypaclitaxel and via CYP3A4 to 3'-p-hydroxypaclitaxel and 6-alpha, 3'-p-dihydroxypaclitaxel. Paclitaxel is a substrate of P-glycoprotein. Because metabolism appears to play an important role in the elimination of paclitaxel, agents that could compete with or inhibit the CYP2C8 and CYP3A4 isoenzymes may increase paclitaxel plasma levels. Potential drug interactions may occur with any drug that affects these isoenzymes.

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

7.4 Carcinogenicity, Genotoxicity, and Reproductive Toxicology

No long-term studies in animals have been performed to evaluate the carcinogenic potential of paclitaxel. Paclitaxel interacts with microtubules; this is the major mechanism by which it inhibits

cell growth. One consequence is the loss of whole chromosomes via interactions with spindle microtubules during cell division. As such, Paclitaxel is defined as an aneugen (agent causing an alteration in chromosome number). This indirect action is consistent with positive responses in in vitro and in vivo micronucleus genotoxicity assays, which detect DNA fragments. Positive results have also been reported for chromosomal aberrations in primary human lymphocytes. It is not known whether paclitaxel has a separate direct action on DNA in the generation of DNA strand breaks or fragments. It is negative in assays for gene mutation, including salmonella and CHO/HPRT. Paclitaxel administered via IV prior to and during mating produced impairment of fertility in male and female rats at doses >1 mg/kg (approximately 36 times the dose provided by the largest TAXUS Liberté Stent coated with 273 µg paclitaxel adjusted for body surface area).

7.5 Pregnancy

Pregnancy Category C: There are no adequate and well controlled studies in pregnant women of paclitaxel or TAXUS Liberté Stents. Studies performed in rats and rabbits receiving IV paclitaxel during organogenesis revealed evidence of maternal toxicity, embryotoxicity, and fetotoxicity at dosages of 1 and 3 mg/kg, respectively (approximately 36 and 214 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 36 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, and by extension, safely and significantly reduces the need for repeat 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. The TAXUS Liberte Stent uses the same drug-polymer coating formulation as the TAXUS Express stent. Given this similarity, the HORIZONS AMI trial, which evaluated the safety and effectiveness of the TAXUS Express stent in patients with ST-elevated myocardial infarction undergoing primary stenting, is also relevant and included below. A summary of the designs of these studies is presented in Table 8.1.

8.1 TAXUS ATLAS

TAXUS ATLAS[2] was a multi-center, single-arm trial to evaluate the safety and efficacy of the 1 µg/mm2 (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 (39 sites in the US and 22 sites outside of the US) 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 analyses of angiographic and intravascular ultrasound (IVUS) parameters in a subset of patients. After the procedure, patients were treated with aspirin indefinitely and with clopidogrel or ticlopidine for at least 6 months. Follow-up through 5 years is currently available, and yearly follow-up for clinical parameters through 5 years is complete.

The objective of TAXUS ATLAS study 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[3] is a multi-center, single-arm trial to evaluate the safety and efficacy of the 1 µg/mm2 (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 (18 in the US and 5 outside of the US) 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 3 years is currently available, and yearly follow-up for clinical parameters through 5 years is ongoing.

The first objective of the TAXUS ATLAS Small Vessel study was to demonstrate non-inferiority for the angiographic outcome of %DS for the 2.25 mm TAXUS Liberté stent when compared to the TAXUS Express Stent. Therefore, the treatment group is compared to a 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,

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[2] 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.

[3] 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 Car(19diol Intv. 2008;1:699-709.

all TAXUS V patients randomized to the bare metal Express group with (1) a reference vessel diameter (RVD) by visual estimate ≤ 2.5 mm, (2) a lesion length by visual estimate ≥ 10 mm and ≤ 28 mm, and (3) receiving 1 planned 2.25 mm or 2.5 mm 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/mm2 (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 (19 in the US and 5 outside of the US) 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 3 years is currently available, and yearly follow-up for clinical parameters through 5 years is ongoing.

The objective of TAXUS ATLAS Long Lesion study 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[4] was 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 bare metal Express. 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 5 years is currently available, and yearly follow-up for clinical parameters through 5 years is complete.

8.5 TAXUS V

TAXUS V *de novo*[5] was a randomized, double-blind, controlled, expansion study of the safety and performance of the SR formulation TAXUS Express Paclitaxel-Eluting Coronary Stent in de novo lesions in small and large diameter vessels, as well as long lesions. TAXUS V *de novo* was designed to expand the data set beyond the standard-risk, de novo coronary artery lesions studied in the pivotal TAXUS IV trial. A total of 1172 patients at 66 U.S. sites were enrolled with

[4] 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.

[5] 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.

patients randomized 1:1 to the TAXUS Express Stent System or the uncoated bare metal Express 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 5 years is currently available, and yearly follow-up for clinical parameters through 5 years is complete.

8.6 HORIZONS AMI Clinical Trial

HORIZONS AMI - The HORIZONS AMI trial[6,7] is a randomized, single-blind trial in patients with ST segment elevation MI designed to compare: (1) the outcomes of anticoagulation with either unfractionated heparin plus routine GP IIb/IIIa inhibition or bivalirudin and bail-out GP IIb/IIIa inhibition, and (2) primary angioplasty with stent implantation with either a slow rate-release paclitaxel-eluting stent (TAXUS Express) or an otherwise identical uncoated bare metal stent (Express). A total of 3602 patients were consented and randomized (primary randomization) in a 1:1 fashion in the emergency room to anticoagulation with unfractionated heparin plus routine GP IIb/IIIa inhibition or bivalirudin and bail-out GP IIb/IIIa inhibition. Emergent coronary angiography with left ventriculography was performed after primary randomization, followed by triage to either percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG) surgery or medical management at physician discretion. After coronary angiography, a total of 3006 patients were triaged to PCI and randomized (secondary randomization) in a 3:1 fashion to either a TAXUS Express or an uncoated bare metal stent Express. Patients were enrolled at 123 study centers in U.S., Argentina, Europe, and Israel. The primary effectiveness endpoint of the stent randomization was ischemic target lesion revascularization at 12 months and the primary safety endpoint was the composite rate of death, reinfarction, stent thrombosis or stroke (MACE) at 12 months. Secondary endpoints included the rate of analysis segment angiographic binary restenosis at 13 months in the 1,203 patient angiographic cohort, as well as ischemic target lesion revascularization, MACE and its components at clinical follow-up through 3 years. After the procedure, patients were treated with aspirin indefinitely and with clopidogrel or ticlopidine for 6 months (1 year or longer recommended). Follow-up through 3 years is complete.

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* (Indication Expansion)	HORIZONS AMI (Indication 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	Prospective, multicenter, randomized, single-blind
Number of Patients (ITT)	Total: 871 TAXUS Liberté Stent: 871	Total: 261 TAXUS Liberté Atom™ Stent: 261	Total: 150 TAXUS Liberté Long Stent: 150 TAXUS IV & V	Total: 1314 TAXUS Express Stent: 662 Bare Metal	Total: 1156 TAXUS Express Stent: 577 Uncoated	Total: 3006 TAXUS: 2257 Control: 749

[6] Stone GW, Lansky AJ, Pocock SJ, et al. Paclitaxel-eluting stents versus bare-metal stents in acute myocardial infarction. N Engl J Med. 2009 May 7;360(19):1946-59

[7] Mehran R, Brodie B, Cox DA, et al. The Harmonizing Outcomes with RevasculariZatiON and Stents in Acute Myocardial Infarction (HORIZONS AMI) Trial: study design and rationale. Am Heart J. 2008 Jul;156(1):44-56.

	TAXUS ATLAS Workhorse (Pivotal)	TAXUS ATLAS Small Vessel (Expansion)	TAXUS ATLAS Long Lesion (Expansion)	TAXUS IV (Pivotal)	TAXUS V *de novo* (Indication Expansion)	HORIZONS AMI (Indication Expansion)
	Combined TAXUS IV & V de novo historical control: 991	TAXUS Express control: 75 Bare Metal Express control: 155	de novo historical control: 145	control: 652	Control: 579	
Dose Release Formulation	Slow Release (SR) (1 µg /mm2)					
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	≥ 2.5 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 ≤ 28 mm	≥ 10 mm and ≤ 46 mm	< 100 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	TAXUS Express Paclitaxel-Eluting Coronary Stent System
Antiplatelet Therapy	Aspirin indefinitely and clopidogrel or ticlopidine for 6 months					Aspirin indefinitely and clopidogrel or ticlopidine for 6 months (1 year or longer recommended)
Follow-Up	30 days: clinical 4 months: clinical 9 months: clinical (all), QCA and IVUS (subset) 1 – 5 years: clinical					30 days: clinical 6 months: clinical 12 month: clinical 13 month: angiographic/IVUS 2 and 3 years: clinical

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

9 ADVERSE EVENTS

9.1 Observed Adverse Events

Observed adverse event experience comes from six clinical studies: TAXUS ATLAS, TAXUS ATLAS Small Vessel, TAXUS ATLAS Long Lesion, TAXUS IV, TAXUS V *de novo*, and

HORIZONS AMI. Principal adverse events for these trials are shown in Table 9.1.1 (TAXUS ATLAS Workhorse), Table 9.1.2 (TAXUS ATLAS Small Vessel), Table 9.1.3 (TAXUS ATLAS Long Lesion) and Table 9.1.4 (HORIZONS AMI). Stent apposition data for TAXUS ATLAS Workhorse is presented in Table 9.1.5.

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

	TAXUS ATLAS Workhorse to 5 Years[1]		TAXUS IV to 5 Years[2]		TAXUS V de novo to 5 Years[3]	
	TAXUS Liberté (N=871)	TAXUS Express (N=991)	TAXUS Express (N=662)	Bare Metal Express (N=652)	TAXUS Express (N=577)	Bare Metal Express (N=579)
In-Hospital MACE[4]	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% (19/661)	2.5% (16/651)	5.1% (29/569)	3.6% (21/576)
9-Month MACE, overall	11.0% (95/862)	10.5% (102/974)	8.5% (56/655)	15.2% (98/646)	14.9% (84/562)	20.9% (119/569)
Cardiac Death	0.8% (7/862)	0.9% (9/974)	1.4% (9/655)	1.1% (7/646)	0.5% (3/562)	0.9% (5/569)
MI	3.7% (32/862)	3.9% (38/974)	3.5% (23/655)	3.7% (24/646)	5.3% (30/562)	4.6% (26/569)
Q-Wave MI	0.7% (6/862)	0.6% (6/974)	0.8% (5/655)	0.3% (2/646)	0.5% (3/562)	0.2% (1/569)
Non-Q-Wave MI	3.0% (26/862)	3.3% (32/974)	2.7% (18/655)	3.4% (22/646)	4.8% (27/562)	4.4% (25/569)
TVR, Overall	8.0% (69/862)	7.1% (69/974)	4.7% (31/655)	12.1% (78/646)	12.1% (68/562)	17.0% (97/569)
TLR, Overall	5.7% (49/862)	4.5% (44/974)	3.1% (20/655)	11.5% (74/646)	8.5% (48/562)	15.5% (88/569)
Non-TLR, Overall	3.2% (28/862)	2.7% (26/974)	1.7% (11/655)	1.1% (7/646)	5.0% (27/562)	4.2% (24/569)
1-Year MACE	12.5% (106/851)	12.3% (118/957)	10.7% (70/654)	20.3% (131/646)	18.8% (105/558)	25.9% (146/564)

	TAXUS ATLAS Workhorse to 5 Years[1]		TAXUS IV to 5 Years[2]		TAXUS V de novo to 5 Years[3]	
	TAXUS Liberté (N=871)	TAXUS Express (N=991)	TAXUS Express (N=662)	Bare Metal Express (N=652)	TAXUS Express (N=577)	Bare Metal Express (N=579)
2-Year MACE	15.6% (130/833)	16.0% (150/937)	14.8% (96/647)	25.3% (161/637)	22.1% (120/542)	29.2% (159/545)
3-Year MACE	19.0% (156/822)	20.2% (184/909)	18.6% (116/622)	28.7% (178/620)	26.4% (140/531)	31.6% (168/532)
4-Year MACE	22.5% (182/810)	23.8% (212/889)	22.2% (135/609)	31.7% (192/606)	30.1% (156/518)	33.6% (176/524)
5-Year MACE	26.2% (206/785)	27.1% (235/868)	25.2% (151/599)	35.3% (208/589)	34.5% (166/481)	38.0% (186/490)
Cardiac Death	5.1% (40/785)	4.4% (38/868)	4.5% (27/599)	4.8% (28/589)	5.6% (27/481)	3.9% (19/490)
MI	7.6% (60/785)	8.4% (73/868)	7.5% (45/599)	8.0% (47/589)	10.8% (52/481)	6.3% (31/490)
Q-Wave MI	1.8% (14/785)	1.5% (13/868)	1.5% (9/599)	1.2% (7/589)	2.1% (10/481)	0.6% (3/490)
Non-Q-Wave MI	6.0% (47/785)	7.0% (61/868)	6.2% (37/599)	7.1% (42/589)	8.7% (42/481)	5.9% (29/490)
TVR, Overall	18.9% (148/785)	20.0% (174/868)	17.5% (105/599)	29.2% (172/589)	27.9% (134/481)	32.4% (159/490)
TLR, Overall	11.0% (86/785)	11.5% (100/868)	9.3% (56/599)	21.9% (129/589)	18.9% (91/481)	25.9% (127/490)
Non-TLR, Overall	10.3% (81/785)	10.6% (92/868)	9.3% (56/599)	10.9% (64/589)	14.1% (68/481)	14.3% (70/490)
5-Year Stent Thrombosis	2.3% (17/738)	2.0% (16/807)	1.6% (9/564)	1.1% (6/548)	2.3% (10/432)	0.9% (4/446)

[1] 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.
[2] 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 5 years, the safety population is comprised of 1294 (n=651 for TAXUS Express, n=643 for Bare Metal Express).
[3] 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).
[4] MACE includes cardiac death, myocardial infarction, ischemic driven target vessel revascularization

Table 9.1.2. TAXUS ATLAS Small Vessel[1] Major Adverse Cardiac Events (MACE) From Post-Procedure to 3-Year Follow-up

	TAXUS Liberté Atom™ 2.25 mm (N=261)	TAXUS Express (N=75)	Bare Metal Express (N=155)
In-Hospital MACE[2]	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)

	TAXUS Liberté Atom™ 2.25 mm (N=261)	TAXUS Express (N=75)	Bare Metal Express (N=155)
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 M	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)
2-Year MACE	16.5% (40/243)	30.4% (21/69)	33.3% (49/147)
3-Year MACE	19.5% (45/231)	32.4% (22/68)	34.5% (49/142)
Cardiac Death	2.6% (6/231)	4.4% (3/68)	1.4% (2/142)
MI	4.3% (10/231)	4.4% (3/68)	4.2% (6/142)
Q-Wave MI	0.9% (2/231)	1.5% (1/68)	0.7% (1/142)
Non-Q-Wave MI	3.5% (8/231)	2.9% (2/68)	3.5% (5/142)
TVR, Overall	15.2% (35/231)	27.9% (19/68)	31.7% (45/142)
TLR, Overall	10.0% (23/231)	22.1% (15/68)	26.8% (38/142)
Non-TLR, Overall	8.7% (20/231)	11.8% (8/68)	10.6% (15/142)
3-Year Stent Thrombosis	1.4% (3/222)	1.5% (1/66)	1.5% (2/134)

[1] 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.
[2] MACE includes cardiac death, myocardial infarction, ischemic driven target vessel revascularization

Table 9.1.3. TAXUS ATLAS Long Lesion[1] Major Adverse Cardiac Events (MACE) From Post-Procedure to 3-Year Follow-up

	TAXUS Liberté Long 38 mm (N=150)	TAXUS Express (N=145)
In-Hospital MACE[2]	0.0% (0/150)	4.1% (6/145)
30-Day MACE, overall	0.0% (0/150)	4.9% (7/143)

	TAXUS Liberté Long 38 mm (N=150)	TAXUS Express (N=145)
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)
2-Year MACE	16.8% (24/143)	20.3% (28/138)
3-Year MACE	21.2% (29/137)	25.2% (34/135)
Cardiac Death	1.5% (2/137)	6.7% (9/135)
MI	2.9% (4/137)	10.4% (14/135)
Q-Wave MI	1.5% (2/137)	2.2% (3/135)
Non-Q-Wave MI	1.5% (2/137)	8.1% (11/135)
TVR, Overall	17.5% (24/137)	16.3% (22/135)
TLR, Overall	12.4% (17/137)	11.9% (16/135)
Non-TLR, Overall	8.8% (12/137)	4.4% (6/135)
3-Year Stent Thrombosis	0.0% (0/133)	0.8% (1/126)

[1] 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.
[2] MACE includes cardiac death, myocardial infarction, ischemic driven target vessel revascularization

Table 9.1.4 : HORIZONS AMI Major Adverse Cardiac Events (MACE) From Post-Procedure to Latest Follow-Up

	HORIZONS AMI	
	TAXUS Express (N=2257)	Bare Metal Express (N=749)
30-Day		
Net Adverse Clinical Events[1]	10.3% (232)	9.0% (67)
MACE 1[2]	4.8% (109)	4.5% (34)
MACE 2 (Safety MACE)[3]	4.5% (102)	4.3% (32)
Death	2.1% (47)	1.9% (14)
- Cardiac	2.0% (44)	1.7% (13)
- Noncardiac	0.1% (3)	0.1% (1)
Reinfarction	1.7% (37)	2.2% (16)

Table 9.1.4 : HORIZONS AMI Major Adverse Cardiac Events (MACE) From Post-Procedure to Latest Follow-Up

	HORIZONS AMI	
	TAXUS Express (N=2257)	Bare Metal Express (N=749)
- Q wave	1.2% (28)	1.6% (12)
- Non Q wave	0.4% (10)	0.5% (4)
Death or reinfarction	3.6% (80)	3.5% (26)
Ischemic TVR	2.3% (51)	2.6% (19)
Ischemic TLR	2.1% (46)	2.6% (19)
Stroke	0.5% (11)	0.5% (4)
Major bleeding (non-CABG)	7.1% (159)	5.6% (42)
TL stent thrombosis	2.3% (50)	2.7% (20)
1-Year		
Net Adverse Clinical Events[1]	15.8% (355)	16.3%(121)
MACE 1[2]	10.6% (237)	12.4% (92)
MACE 2 (Safety MACE)[3]	8.1% (181)	8.0% (59)
2-Year		
Net Adverse Clinical Events[1]	21.5% (480)	26.0% (191)
MACE 1[2]	16.8% (373)	22.2% (162)
MACE 2 (Safety MACE)[3]	11.0% (245)	11.2% (82)
3-Year		
Net Adverse Clinical Events[1]	24.5% (544)	28.0% (205)
MACE 1[2]	20.0% (441)	24.0% (175)
MACE 2 (Safety MACE)[3]	13.6% (300)	12.9% (94)
Death	5.6% (123)	6.6% (48)
- Cardiac	3.2% (71)	3.8% (28)
- Noncardiac	2.4% (52)	2.9% (20)
Reinfarction	7.0% (150)	6.6% (47)
- Q wave	3.5% (75)	2.8% (20)
- Non Q wave	4.0% (84)	3.8% (27)
Death or reinfarction	11.8% (260)	11.5% (84)
Ischemic TVR5	12.4% (265)	17.6% (125)
Ischemic TLR5	9.4% (202)	15.1% (107)
Stroke	1.6% (35)	1.4% (10)
Major bleeding (non-CABG)	8.4% (188)	7.3% (54)
TL stent thrombosis6	4.8% (103)	4.3% (31)

[1] Net Adverse Clinical Events includes MACE1 and non-CABG related major bleeding.
[2] MACE1 includes death, reinfarction, stroke, or ischemic target vessel revascularization.
[3] MACE2 includes death, reinfarction, stent thrombosis, or stroke.

Table 9.1.5. Frequency of Incomplete Stent Apposition in TAXUS ATLAS Workhorse, All Patients in the IVUS Subset at 9 Month Follow-up

Incomplete Apposition (IA)	TAXUS Liberté (N=327)	TAXUS Express (N=283)
Early (Post Procedure)	8.7% (22/254)	7.3% (14/191)
Late (9-Month)	4.3%(9/209)	10.1% (14/139)

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Paired Data		
Resolved	3.4% (6/177)	2.8% (3/108)
Persistent	2.3% (4/177)	3.7% (4/108)
Late Acquired	1.7% (3/177)	5.6% (6/108)

Resolved = # patients with baseline (BL) IA and without follow-up (FU) IA ÷ # patients evaluable at baseline and follow-up.
Persistent = # patients with BL IA and with FU IA ÷ # patients evaluable at baseline and follow-up.
Late Acquired = # patients without BL IA and with FU IA ÷ # patients evaluable at baseline and follow-up.
Incomplete Apposition variables are from assessment by IVUS core laboratory.

9.2 Potential Adverse Events

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

- Abrupt stent closure
- Acute myocardial infarction
- Allergic reaction to anti-coagulant and/or antiplatelet therapy, contrast medium, or stent materials
- Angina
- Arrhythmias, including ventricular fibrillation (VF) and ventricular tachycardia (VT)
- Arteriovenous fistula
- Cardiac tamponade
- Cardiogenic shock/Pulmonary edema
- Coronary aneurysm
- Death
- Dissection
- Emboli, distal (air, tissue or thrombotic material or material from devices(s) used in the procedure)
- Heart failure
- Hematoma
- Hemorrhage, required transfusion
- Hypotension/Hypertension
- Infection, local or systemic
- Ischemia, myocardial
- Pain, at the access site
- Perforation or Rupture of coronary artery
- Pericardial effusion
- Pseudoaneurysm, femoral
- Renal Failure
- Respiratory Failure
- Restenosis of stented segment
- Stent 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.

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 compared to the TAXUS Express Stent with respect to TVR 9 months post-index procedure.

Design: TAXUS ATLAS was a multi-center, single-arm trial in patients at 61 sites (39 in the US and 22 outside of the US). 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 were 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 consisted of all patients who received the assigned study stent at baseline (per protocol population). Follow-up through 5 years is currently available in 805/867 (92.8%) 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).

Results: The primary endpoint data (9 months) and latest available follow-up (5 year) results are presented below (Tables 10.1.1 - 10.1.6, Figure 10.1.1). The primary endpoint is defined as non-inferiority of the rate of ischemia-driven target vessel revascularization (TVR) 9 months after the index procedure for TAXUS Liberté as compared to TAXUS Express.

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, respectively. 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 the TAXUS Liberté group compared to the control group. In addition, QCA parameters of 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).

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

Table 10.1.1. TAXUS ATLAS Workhorse[1] Primary Endpoint

Per Protocol Population	TAXUS Liberté (N=867)	TAXUS Express (N=980)	Difference [Upper 1-Sided 95% CL]	P-Value[2]	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 (N=991)**	**Difference [Upper 1-Sided 95% CL]**	**P-Value[2]**	**Δ**
9-Month TVR	8.03% (69/859)	7.14% (69/967)	0.90% [2.94%]	0.0454	3.0%

[1] Refers to range of TAXUS Liberte stent diameters: 2.5-4.0 mm.
[2] *P-Values represent* unadjusted results from non-inferiority testing.

Table 10.1.2. TAXUS ATLAS Workhorse[1] Clinical Results

	9 months (ITT population)			5 year (per protocol population[2])		
	TAXUS Liberté (N=871)	TAXUS Express (N=991)	P-Value	TAXUS Liberté (N=867)	TAXUS Express (N=978)	P-Value
EFFICACY						
TVR, Overall	8.0% (69/862)	7.1% (69/974)	0.4787*	18.9% (148/785)	20.0% (174/868)	0.5410
TLR, Overall	5.7% (49/862)	4.5% (44/974)	0.2865*	11.0% (86/785)	11.5% (100/868)	0.7164
TLR, PCI	5.3% (46/862)	3.9% (38/974)	0.1472*	10.2% (80/785)	10.6% (92/868)	0.7862
TLR, CABG	0.3% (3/862)	0.6% (6/974)	0.5141*	1.0% (8/785)	1.0% (9/868)	0.9715
Non-TLR, Overall	3.2% (28/862)	2.7% (26/974)	0.4911*	10.3% (81/785)	10.6% (92/868)	0.8524
Non-TLR, PCI	2.8% (24/862)	2.1% (20/974)	0.3596*	7.8% (61/785)	7.8% (68/868)	0.9617
Non-TLR, CABG	0.5% (4/862)	0.6% (6/974)	0.7578*	2.8% (22/785)	3.1% (27/868)	0.7123

SAFETY						
Total Death	1.2% (10/863)	1.8% (18/977)	0.2570*	8.4% (67/799)	9.8% (87/884)	0.3008
Cardiac Death or MI	4.2% (36/862)	4.7% (46/974)	0.6510*	11.6% (91/785)	11.8% (102/868)	0.9200
Cardiac Death	0.8% (7/862)	0.9% (9/974)	1.0000*	5.1% (40/785)	4.4% (38/868)	0.4920
MI	3.7% (32/862)	3.9% (38/974)	0.9030*	7.6% (60/785)	8.4% (73/868)	0.5671
Q-wave MI	0.7% (6/862)	0.6% (6/974)	1.0000*	1.8% (14/785)	1.5% (13/868)	0.6472
Non-Q-wave MI	3.0% (26/862)	3.3% (32/974)	0.7901*	6.0% (47/785)	7.0% (61/868)	0.3927
Stent Thrombosis	0.8% (7/858)	0.7% (7/966)	1.0000*	2.3% (17/738)	2.0% (16/807)	0.6630

[1] Refers to range of TAXUS Liberte stent diameters: 2.5-4.0 mm.
[2] 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.

Table 10.1.3. TAXUS ATLAS Workhorse[1] Secondary Endpoints

Per Protocol Population	TAXUS Liberté (N=867)	TAXUS Express (N=980)	Bonferroni Adjusted Upper 1-Sided 95% CL[3]	P-Value[4]	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[2] (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%

[1] Refers to range of TAXUS Liberte stent diameters: 2.5-4.0 mm.
[2] Lower 1-Sided 95% CL is reported for In-Stent MLD.
[3] Bonferroni Adjusted Upper 1-sided 95% CL calculated using a 1-sided 99% CL.
[4] P-Values represent unadjusted results from non-inferiority testing.
*Variances equal: Pooled t statistic
**Variances unequal: Satterthwaite's approximate t statistic

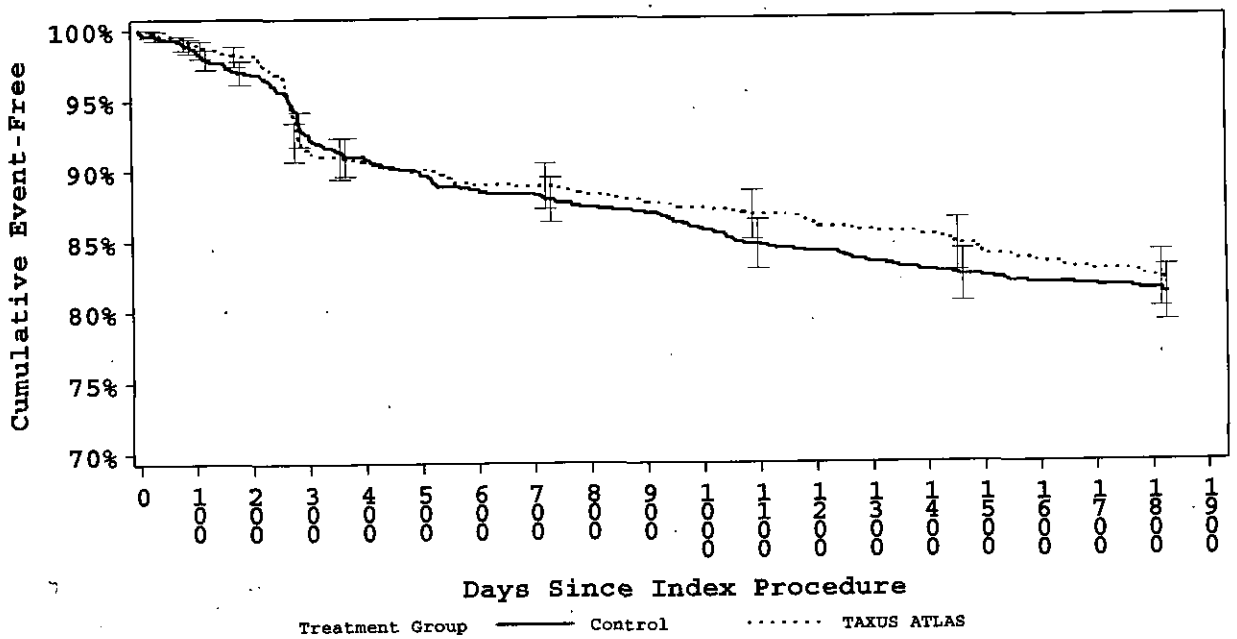

Figure 10.1.1. TAXUS ATLAS Workhorse[1] Freedom from TVR to 5 Years, Event-Free Survival ± 1.5 SE, Per Protocol Population, All Patients (N=1845)

	Event Rate	Event Free	P-Value[2]
TAXUS Liberté	17.9%	82.1%	0.5688
TAXUS Express	18.9%	81.1%	

[1] Refers to range of TAXUS Liberte stent diameters: 2.5-4.0 mm.
[2] Log-rank P-Value. P-Value is not adjusted for multiple comparisons.
P-Values are not adjusted for multiple comparisons.

Table 10.1.4. TAXUS ATLAS Workhorse[1] 9-Month Angiographic and IVUS Results

Angiographic Outcomes[2]	TAXUS Liberté (N=543)	TAXUS Express (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[3]	**TAXUS Liberté (N=327)**	**TAXUS Express (N=283)**	**P-Value**
Neointimal Volume (mm3) (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

[1] Refers to range of TAXUS Liberte stent diameters: 2.5-4.0 *mm.*
[2] Includes all patients in the angiographic subset.
[3] 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 10.1.5. TAXUS ATLAS Workhorse[1] Stent Thrombosis

Per Protocol Population	**TAXUS Liberté (N=867)**	**TAXUS Express (N=978)**	**P-Value**
Protocol Defined Stent Thrombosis[2]			
Cumulative through 5 years	2.3% (17/738)	2.0% (16/807)	0.6630
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*
Very Late ST (>12 months to 5 years)	1.1% (9/845)	1.0% (9/939)	0.8220
ARC Definite & Probable Stent Thrombosis[3]			
Cumulative through 5 years	3.0% (22/739)	2.7% (22/808)	0.7638
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)	0.9% (8/863)	0.3% (3/972)	0.0868

Very Late ST (>12 months to 5 years)	1.4% (12/845)	1.5% (14/939)	0.9008

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).

[1] Refers to range of TAXUS Liberte stent diameters: 2.5-4.0 mm.

[2] 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.

[3] Academic Research Consortium (ARC) stent thrombosis is defined as follows[8] :

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.

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 10.1.6. TAXUS ATLAS 9 month and 5-year Clinical Results for Medically Treated Diabetic Patients

Intent to Treat Population[1]	TAXUS Liberté (N=220)	TAXUS Express (N=244)	P-Value
EFFICACY (9 month)			
TVR, Overall	12.0% (26/216)	11.8% (28/238)	1.0000

[8] 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.

TLR, Overall	8.8% (19/216)	7.6% (18/238)	0.7318
TLR, PCI	8.3% (18/216)	7.1% (17/238)	0.7254
TLR, CABG	0.5% (1/216)	0.4% (1/238)	1.0000
TVR Remote, Overall	4.6% (10/216)	4.2% (10/238)	0.8239
TVR Remote, PCI	4.2% (9/216)	2.5% (6/238)	0.4323
TVR Remote, CABG	0.5% (1/216)	1.7% (4/238)	0.3752
SAFETY (9 month)			
Total Death	1.8% (4/218)	2.5% (6/240)	0.7541
Cardiac Death or MI	4.6% (10/216)	4.2% (10/238)	0.8239
Cardiac Death	0.9% (2/216)	1.3% (3/238)	1.0000
MI	4.6% (10/216)	2.9% (7/238)	0.4591
Q-Wave MI	0.9% (2/216)	0.0% (0/238)	0.2258
Non-Q-Wave MI	3.7% (8/216)	2.9% (7/238)	0.7941
Stent Thrombosis[2]	0.9% (2/214)	0.4% (1/235)	0.6074
Per Protocol Population [a]	**TAXUS Liberté (N=220)**	**TAXUS Express (N=241)**	**P-Value**
EFFICACY (5 Year)			
TVR, Overall	24.6% (48/195)	25.5% (53/208)	0.8412
TLR, Overall	15.4% (30/195)	13.5% (28/208)	0.5826
TLR, PCI	14.9% (29/195)	13.0% (27/208)	0.5834
TLR, CABG	1.0% (2/195)	0.5% (1/208)	0.6123*
TVR Remote, Overall	12.3% (24/195)	15.4% (32/208)	0.3722
TVR Remote, PCI	9.7% (19/195)	10.1% (21/208)	0.9058
TVR Remote, CABG	3.1% (6/195)	6.3% (13/208)	0.1331
SAFETY (5 Year)			
Total Death	13.4% (27/202)	12.8% (27/211)	0.8636
Cardiac Death or MI	14.9% (29/195)	13.9% (29/208)	0.7905
Cardiac Death	7.7% (15/195)	7.7% (16/208)	1.0000
MI	9.2% (18/195)	8.7% (18/208)	0.8392
Q-Wave MI	2.1% (4/195)	0.5% (1/208)	0.2022*
Non-Q-Wave MI	7.2% (14/195)	8.2% (17/208)	0.7084

Stent Thrombosis b	3.9% (7/178)	1.1% (2/185)	0.0992*

[1] 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.
[2] Per protocol stent thrombosis.
Numbers are % (Count/Sample Size).
*P-Values are two-sided from Fisher exact test; P-Values without * are two-sided from the Chi-square test.
P-Values are not adjusted for multiple comparisons.
This trial was not adequately powered to compare the rate of low frequency events to a control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

10.2 TAXUS ATLAS *Program* Small Vessel 2.25 mm Clinical Trial

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

Design: This is 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 bare metal Express[2] 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.

A total of 261 intent-to-treat (ITT) patients were to be treated with the TAXUS Liberté 2.25 mm Stent at 23 clinical sites (18 in the US and 5 outside of the US). Angiographic follow-up at 9-months was planned in all patients participating in the study. Patients were 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]). 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 bare metal stent (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 3 years is currently available in 235/254 (92.5%) patients.

Results: The primary endpoint data (9 months) and latest available follow-up (3 year) results are presented below (Tables 10.2.1 - 10.2.4). The primary endpoint for this study is the percent diameter stenosis of the analysis segment at 9 months. The analysis segment is defined as the stented segment *plus a 5 mm shoulder* on both sides of the stented area.

Demographics: The TAXUS Express control and TAXUS ATLAS Small Vessel groups were well matched with respect to baseline patient characteristics, with no statistically significant differences in demographics, cardiac history and cardiac risk factors. In terms of comorbidities, more patients in the TAXUS Express control group had a known history of PVD (13.3%) as compared with patients in the TAXUS ATLAS Small Vessel group (5.7%, P=0.0274).

Most of the baseline angiographic lesion characteristics assessed were comparable between the 2 groups. However, patients in the TAXUS ATLAS Small Vessel group had lesions that were longer (14.53±6.89 mm) than those observed in the TAXUS Express control group (11.84±5.69 mm P=0.0025), and a greater proportion had ACC/AHA Category C lesions (34.5% versus 16.2%, respectively, P=0.0026). Lesion location demonstrated a significant difference between the groups, with more target lesions in the TAXUS ATLAS Small Vessel group being in the mid portion of the target vessels, and more lesions in the TAXUS Express control being in the proximal portion of the target vessel. Eccentric lesions were observed more frequently in the TAXUS Express control group (59.5% versus 28.7% for the TAXUS ATLAS Small Vessel group, P<0.0001).

These two study groups were not statistically significantly different with respect to the maximum diameter of stent implanted. However, on average the total length of study stents implanted was greater in the TAXUS ATLAS Small Vessel Group (21.5±0.7 mm) versus the TAXUS Express control group (19.2±0.43 mm, P=0.0104). Total stent length to lesion length ratio was lower in the TAXUS ATLAS Small Vessel Group (1.7, versus 1.9 in the TAXUS Express control group, P=0.0171, for patients with study stents only).

These differences were not expected to affect outcomes variables, as propensity score adjustments were made.

The bare metal Express control and TAXUS ATLAS Small Vessel groups were well matched with respect to most baseline patient characteristics. As compared with the bare metal Express control group, a 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 bare metal Express control group, based on the Core Lab angiographic analysis, patients in the TAXUS ATLAS Small Vessel Group had lesions with a significantly smaller RVD than those in the bare metal Express 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 significantly smaller %DS (67.26±10.91% versus 72.10±10.69%, respectively, P<0.0001). Patients in the bare metal Express control group had significantly more complex target lesions 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).

For patients with only study stents implanted, the maximum stent diameter implanted was significantly greater in the bare metal Express 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 bare metal Express control group (23.3±7.9 mm) was significantly greater than that implanted in the TAXUS ATLAS Small Vessel group (21.5±7.0 mm, P=0.0173).

These differences were not expected to affect outcomes variables, as propensity score adjustments were made.

Table 10.2.1. TAXUS ATLAS Small Vessel Primary Endpoint DES Control

Per Protocol Population	TAXUS Liberté Atom[1] (N=254)	TAXUS Express (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 (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%

[1]Atom refers to the TAXUS Liberte 2.25 mm stent
*Variances unequal: Satterthwaite's approximate t statistic.
P-Values are for non-inferiority testing, with a margin of .

Express BMS Control

Per Protocol Population	TAXUS Liberté Atom[1] (N=254)	Bare Metal Express (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)**	**Bare Metal Express (N=155)**	**Difference [Upper 1-Sided 95% CL]**	**P-Value**
Follow-up In-Segment Percent Diameter Stenosis				
Adjusted for the propensity score	31.9	45.9	-13.9 [-19.6,-8.3]	<0.0001
Unadjusted	32.09±18.38 (211) (4.07, 100.00)	45.61±23.48 (105) (7.29, 100.00)	-13.53 [-18.26, -8.80]	<0.0001

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[1]Atom refers to the TAXUS Liberte 2.25 mm stent
P-Values are for superiority testing.

Table 10.2.2 TAXUS ATLAS Small Vessel Clinical Results

	9 months (ITT population)			3 year (per protocol population[1])		
	TAXUS Liberté Atom™[2] (N=261)	TAXUS Express (N=75)	P-Value	TAXUS Liberté Atom (N=254)	TAXUS Express (N=73)	P-Value
EFFICACY						
TVR, Overall	10.1% (26/258)	17.8% (13/73)	0.0705	15.2% (35/231)	27.9% (19/68)	0.0160
TLR, Overall	5.8% (15/258)	13.7% (10/73)	0.0244	10.0% (23/231)	22.1% (15/68)	0.0084
TLR, PCI	5.8% (15/258)	12.3% (9/73)	0.0581	9.5% (22/231)	20.6% (14/68)	0.0137
TLR, CABG	0.0% (0/258)	1.4% (1/73)	0.2205*	0.4% (1/231)	1.5% (1/68)	0.4037*
Non-TLR, Overall	6.6% (17/258)	6.8% (5/73)	1.0000*	8.7% (20/231)	11.8% (8/68)	0.4396
Non-TLR, PCI	6.6% (17/258)	6.8% (5/73)	1.0000*	8.7% (20/231)	11.8% (8/68)	0.4396
Non-TLR, CABG	0.4% (1/258)	0.0% (0/73)	1.0000*	0.4% (1/231)	0.0% (0/68)	1.0000*
SAFETY						
Total Death	1.2% (3/259)	2.7% (2/73)	0.3035*	5.9% (14/236)	7.1% (5/70)	0.7780*
Cardiac Death or MI	3.5% (9/258)	5.5% (4/73)	0.4938*	6.5% (15/231)	7.4% (5/68)	0.7852*
Cardiac Death	0.8% (2/258)	2.7% (2/73)	0.2123*	2.6% (6/231)	4.4% (3/68)	0.4300*
MI	2.7% (7/258)	4.1% (3/73)	0.4643*	4.3% (10/231)	4.4% (3/68)	1.0000*
Q-wave MI	0.8% (2/258)	1.4% (1/73)	0.5277*	0.9% (2/231)	1.5% (1/68)	0.5402*
Non-Q-wave MI	1.9% (5/258)	2.7% (2/73)	0.6519*	3.5% (8/231)	2.9% (2/68)	1.0000*
Stent Thrombosis	0.4% (1/256)	1.4% (1/72)	0.3914*	1.4% (3/222)	1.5% (1/66)	1.0000*

[1]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
[2]Atom refers to the TAXUS Liberte 2.25 mm stent
* 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.

Table 10.2.3. TAXUS ATLAS Small Vessel 9-Month Angiographic Results

Angiographic Outcomes[1]	TAXUS Liberté Atom™[2] (N=261)	TAXUS Express (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

[1] Includes all patients in the angiographic subset.
[2] Atom refers to the TAXUS Liberte 2.25 mm stent
P-Values are not adjusted for multiple comparisons.

Table 10.2.4. TAXUS ATLAS Small Vessel Stent Thrombosis

Per Protocol Population	TAXUS Liberté Atom[1] (N=254)	TAXUS Express (N=73)	P-Value
Protocol Defined Stent Thrombosis			
Cumulative through 3 years	1.4% (3/222)	1.5% (1/66)	1.0000*
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*
Very Late ST (>12 months to 3 years)	0.8% (2/245)	0.0% (0/68)	1.0000*
ARC Definite & Probable Stent Thrombosis			
Cumulative through 3 years	1.4% (3/222)	1.5% (1/66)	1.0000*
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*
Very Late ST (>12 months to 3 years)	0.8% (2/245)	0.0% (0/68)	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.
[1] Atom refers to the TAXUS Liberte 2.25 mm stent
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.

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 µg/mm2 (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. A total of 150 intent-to-treat (ITT) patients were to be treated with the TAXUS Liberté 38 mm stent at a 24 clinical sites (19 in the US and 5 outside of the US). 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 planned 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 3 years is currently available in 142/150 (94.7%) patients.

Results: The primary endpoint data (9 months) and latest available follow-up (3 year) results are presented below (Tables 10.3.1 - 10.3.4). The primary endpoint for this study is the percent diameter stenosis of the analysis segment at 9 months. The analysis segment is defined as the stented segment plus a 5 mm shoulder on both sides of the stented area.

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 significantly longer for TAXUS ATLAS Long Lesion group (30.44±2.66 mm) as compared with the TAXUS Express 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 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 TAXUS Express 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).

Table 10.3.1. TAXUS ATLAS Long Lesion Primary Endpoint Intent to Treat, All Patients (N=295)

Intent-to-Treat Population	TAXUS Liberté Long (N=150)	TAXUS Express (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 10.3.2 TAXUS ATLAS Long Lesion Clinical Results

	9 months (ITT population)			3 year (per protocol population[1])		
	TAXUS Liberté Long (N=150)	TAXUS Express (N=145)	P-Value	TAXUS Liberté Long (N=150)	TAXUS Express (N=145)	P-Value
EFFICACY						
TVR, Overall	8.7% (13/149)	8.5% (12/142)	0.9335	17.5% (24/137)	16.3% (22/135)	0.7881
TLR, Overall	6.0% (9/149)	7.0% (10/142)	0.7295	12.4% (17/137)	11.9% (16/135)	0.8881
TLR, PCI	5.4% (8/149)	6.3% (9/142)	0.7246	10.9% (15/137)	11.1% (15/135)	0.9659
TLR, CABG	0.7% (1/149)	0.7% (1/142)	1.0000*	2.2% (3/137)	0.7% (1/135)	0.6223*
Non-TLR, Overall	3.4% (5/149)	1.4% (2/142)	0.4484*	8.8% (12/137)	4.4% (6/135)	0.1524
Non-TLR, PCI	2.0% (3/149)	1.4% (2/142)	1.0000*	6.6% (9/137)	4.4% (6/135)	0.4427
Non-TLR, CABG	1.3% (2/149)	0.0% (0/142)	0.4986*	2.2% (3/137)	0.0% (0/135)	0.2473*
SAFETY						
Total Death	0.7% (1/148)	2.8% (4/142)	0.2061*	5.7% (8/141)	6.7% (9/134)	0.7197
Cardiac Death or MI	1.3% (2/149)	8.5% (12/142)	0.0046	4.4% (6/137)	15.6% (21/135)	0.0021
Cardiac Death	0.0% (0/149)	2.8% (4/142)	0.0555*	1.5% (2/137)	6.7% (9/135)	0.0293
MI	1.3% (2/149)	6.3% (9/142)	0.0255	2.9% (4/137)	10.4% (14/135)	0.0135
Q-wave MI	0.0% (0/149)	1.4% (2/142)	0.2373*	1.5% (2/137)	2.2% (3/135)	0.6829*
Non-Q-wave MI	1.3% (2/149)	4.9% (7/142)	0.0969*	1.5% (2/137)	8.1% (11/135)	0.0097
Stent Thrombosis	0.0% (0/148)	0.7% (1/140)	0.4861*	0.0% (0/133)	0.8% (1/126)	0.4865*

[1] 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 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, not was it sized to determine the rate of low frequency events with a pre-specified precision.

Table 10.3.3. TAXUS ATLAS Long Lesion 9-Month Angiographic Results

Angiographic Outcomes[1]	TAXUS Liberté Long (N=150)	TAXUS Express (N=145)	P-Value
MLD (mm), In-stent			
Post-Procedure	2.60±0.40(150)	2.62±0.46(142)	0.7239

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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

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

Table 10.3.4. TAXUS ATLAS Long Lesion Stent Thrombosis

Per Protocol Population	TAXUS Liberté Long (N=150)	TAXUS Express (N=145)	P-Value
Protocol Defined Stent Thrombosis			
Cumulative through 3 years	0.0% (0/133)	0.8% (1/126)	0.4865*
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*
Very Late ST (>12 months to 3 years)	0.0% (0/146)	0.0% (0/134)	Undef
ARC Definite & Probable Stent Thrombosis			
Cumulative through 3 years	0.0% (0/133)	3.9% (5/127)	0.0267*
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)	1.4% (2/143)	0.2373*
Very Late ST (>12 months to 3 years)	0.0% (0/146)	2.2% (3/134)	0.1083*

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 (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.

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 target vessel revascularization rate (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 intent-to-treat (ITT) 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. 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 5 years, the safety population is comprised of 1294 patients (N=651 for TAXUS, N=643 for Control) and follow-up is available for 1230 patients (95.1%).

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).

Results: The 5-year planned follow-up is complete. The primary endpoint data (9-months) and 5-year follow-up results are presented below (Tables 10.4.1 - 10.4.3, Figure 10.4.1). The primary endpoint is defined as the rate of ischemia-driven target vessel revascularization (TVR) 9 months after the index procedure.

Table 10.4.1. TAXUS IV Clinical Results

	9 months (ITT population)			5 years (safety population[1])		
	TAXUS Express (N=662)	Bare Metal Express (N=652)	P-Value	TAXUS Express (N=651)	Bare Metal Express (N=643)	P-Value
EFFICACY						
TVR, Overall[2]	4.7% (31/662)	12.0% (78/652)	<0.0001	17.5% (105/599)	29.2% (172/589)	<0.0001
TLR, Overall	3.0% (20/662)	11.3% (74/652)	<0.0001	9.3% (56/599)	21.9% (129/589)	<0.0001
TLR, PCI	2.4% (16/662)	8.7% (57/652)	<0.0001	8.3% (50/599)	17.5% (103/589)	<0.0001
TLR, CABG	0.6% (4/662)	3.1% (20/652)	0.0008	1.0% (6/599)	5.6% (33/589)	<0.0001
Non-TLR, Overall	1.7% (11/662)	1.1% (7/652)	0.4778	9.3% (56/599)	10.9% (64/589)	0.3857
Non-TLR, PCI	1.2% (8/662)	0.8% (5/652)	0.5793	6.7% (40/599)	9.5% (56/589)	0.0736
Non-TLR, CABG	0.5% (3/662)	0.3% (2/652)	1.0000	3.2% (19/599)	2.2% (13/589)	0.3044
SAFETY						
Total Death	2.1% (14/662)	1.5% (10/652)	0.5378	10.2% (63/619)	11.4% (70/614)	0.4888
Cardiac Death or MI	4.7% (31/662)	4.3% (28/652)	0.7905	11.0% (66/599)	11.4% (67/589)	0.8454
Cardiac Death	1.4% (9/662)	1.1% (7/652)	0.8025	4.5% (27/599)	4.8% (28/589)	0.8399
MI	3.5% (23/662)	3.7% (24/652)	0.8826	7.5% (45/599)	8.0% (47/589)	0.7633
Q-wave MI	0.8% (5/662)	0.3% (2/652)	0.4520	1.5% (9/599)	1.2% (7/589)	0.6387
Non-Q-wave MI	2.7% (18/662)	3.4% (22/652)	0.5237	6.2% (37/599)	7.1% (42/589)	0.5094
Stent Thrombosis	0.6% (4/662)	0.8% (5/652)	0.7513	1.6% (9/564)	1.1% (6/548)	0.4692

[1] Patients who did not receive a study stent were not followed beyond two years.

[2] 9-month primary endpoint.

P-Values are not adjusted for multiple comparisons.

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

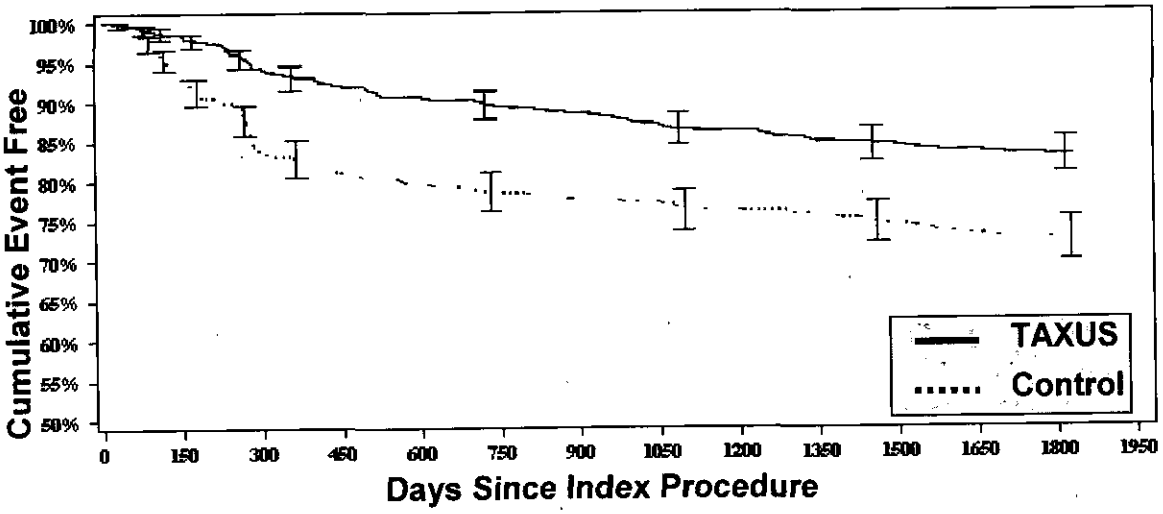

Figure 10.4.1. TAXUS IV Freedom from TVR to 5 Years, Event-Free Survival ± 1.5 SE, Safety Population, All Patients (N=1294)

	Event Rate	Event Free	P-Value*
TAXUS Express	16.9%	83.1%	<0.0001
Bare Metal Express	27.4%	72.6%	

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

Table 10.4.2. TAXUS IV 9-Month Angiographic and IVUS Results

	TAXUS Express (N=662)	Bare Metal Express (N=652)	P-Value
MLD (mm), In-stent			
Post-Procedure	2.65±0.42 (373)	2.67±0.41 (351)	0.6577
9-Month	2.26±0.58 (291)	1.75±0.65 (266)	<0.0001
MLD (mm), Analysis Segment			
Post-Procedure	2.26±0.48 (374)	2.29±0.50 (356)	0.4562
9-Month	2.03±0.55 (291)	1.68±0.61 (267)	<0.0001
% DS, In-stent			
Post-Procedure	4.21±10.84 (373)	5.16±11.41 (351)	0.2497
9-Month	17.43±17.71 (291)	37.24±19.76 (266)	<0.0001
% DS, Analysis Segment			
Post-Procedure	19.16±9.67 (374)	19.33±10.45 (356)	0.8219
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	0.23±0.44 (291)	0.61±0.57 (267)	<0.0001

	TAXUS Express (N=662)	Bare Metal Express (N=652)	P-Value
(mm)			
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)	17.35±18.20 (82)	41.48±23.02 (80)	<0.0001
% Net Volume Obstruction	12.05±12.43 (82)	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.
The QCA subgroup included 375 TAXUS and 357 Control patients; the paired lesion analysis included 292 TAXUS and 267 Control patients.
The IVUS subgroup included 133 TAXUS and 135 Control patients.
This trial was not adequately powered to compare the rate of low frequency events to a bare metal control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

Table 10.4.3. TAXUS IV Protocol Defined Stent Thrombosis[1] through 5 Years Safety Population (N=1294)

	TAXUS Express (N=662)	Bare Metal Express (N=652)	P-Value
Cumulative ST through 5 years	1.6% (9/564)	1.1% (6/548)	0.4692
Acute ST (≤24 hrs)	0.0% (0/651)	0.3% (2/643)	0.2467
Subacute ST (>24 hrs and ≤ 30 days)	0.3% (2/650)	0.5% (3/641)	0.6849
Late ST (>30 days and ≤12 months)	0.3% (2/648)	0.2% (1/639)	1.0000
Very Late ST (>12 months to 5 years)	0.8% (5/632)	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).

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

1. Clinical presentation of acute coronary syndrome with angiographic evidence of stent thrombosis:

a) Angiographic documentation of a complete occlusion (TIMI flow 0 or 1) of a previously successfully treated artery (TIMI flow 2 to 3 immediately after stent placement and diameter stenosis ≤ 30%) and/or

b) Angiographic documentation of a flow-limiting thrombus within or adjacent to a previously successfully treated lesion.

2. Acute MI of the distribution of the treated vessel.
3. Death within the first 30 days (without other obvious cause) is considered a surrogate for stent thrombosis when angiography is not available.

Numbers are % (Count/Sample Size).

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

P-Values are not adjusted for multiple comparisons.

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

10.5 TAXUS V *de novo* Expansion Clinical Trial

Objective: The primary objective of this study was to demonstrate a superior 9-month ischemia-driven target vessel revascularization (TVR) rate for the TAXUS Express Stent compared to the uncoated bare metal 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 intent-to-treat (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 of ≤2.5 mm), large diameter vessels, and long lesions. The small diameter group included a minimum of 350 patients with at least 200 of those patients receiving a 2.25 mm stent. The large diameter group included a minimum of 200 patients receiving a 4.0 mm stent. The long lesion group included a minimum of 400 patients with ≥18 mm lesion length 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.

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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 5 years is currently available in 871/1048 (83.1%) of patients eligible for 5-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).

Results: The primary endpoint data (9 months) and final follow-up (5 years) results are presented below for the overall population (Table 10.5.1 and Figure 10.5.1). Primary endpoint is defined as the rate of ischemic driven target vessel revascularization (TVR) through 9 months post index procedure.

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.

Table 10.5.1. TAXUS V de novo Clinical Results

	9 months (ITT Population)			5 years (Safety Population[1])		
	TAXUS Express (N=577)	Bare Metal Express (N=579)	P-Value	TAXUS Express (N=575)	Bare Metal Express (N=571)	P-Value
EFFICACY						
TVR, Overall[2]	12.1% (68/562)	17.0% (97/569)	0.0184	27.9% (134/481)	32.4% (159/490)	0.1192
TLR, Overall	8.5% (48/562)	15.5% (88/569)	0.0003	18.9% (91/481)	25.9% (127/490)	0.0090
TLR, PCI	7.8% (44/562)	13.7% (78/569)	0.0014	17.5% (84/481)	23.3% (114/490)	0.0249
TLR, CABG	0.7% (4/562)	1.8% (10/569)	0.1118	2.1% (10/481)	4.3% (21/490)	0.0505
Non-TLR, Overall	5.0% (28/562)	4.2% (24/569)	0.5395	14.1% (68/481)	14.3% (70/490)	0.9472
Non-TLR, PCI	4.6% (26/562)	3.2% (18/569)	0.2033	11.6% (56/481)	11.4% (56/490)	0.9169
Non-TLR, CABG	0.4% (2/562)	1.1% (6/569)	0.2874*	2.9% (14/481)	3.1% (15/490)	0.8903
SAFETY						
Total Death	1.2% (7/562)	1.4% (8/569)	0.8136	11.1% (53/479)	9.3% (45/486)	0.3532
Cardiac Death or MI	5.7% (32/562)	5.4% (31/569)	0.8570	15.4% (74/481)	9.6% (47/490)	0.0063
Cardiac Death	0.5% (3/562)	0.9% (5/569)	0.7256*	5.6% (27/481)	3.9% (19/490)	0.2030
MI	5.3% (30/562)	4.6% (26/569)	0.5513	10.8% (52/481)	6.3% (31/490)	0.0125
Q-wave MI	0.5% (3/562)	0.2% (1/569)	0.3713*	2.1% (10/481)	0.6% (3/490)	0.0468
Non-Q-wave MI	4.8% (27/562)	4.4% (25/569)	0.7417	8.7% (42/481)	5.9% (29/490)	0.0922
Stent Thrombosis	0.7% (4/560)	0.7% (4/565)	1.0000*	2.3% (10/432)	0.9% (4/446)	0.0936

[1] Patients who did not receive a study stent were not followed beyond 1 year.

[2] Primary Endpoint at 9 months

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

With the exception of the 9-month TVR P-Value, P-Values are not adjusted for multiple comparisons.

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

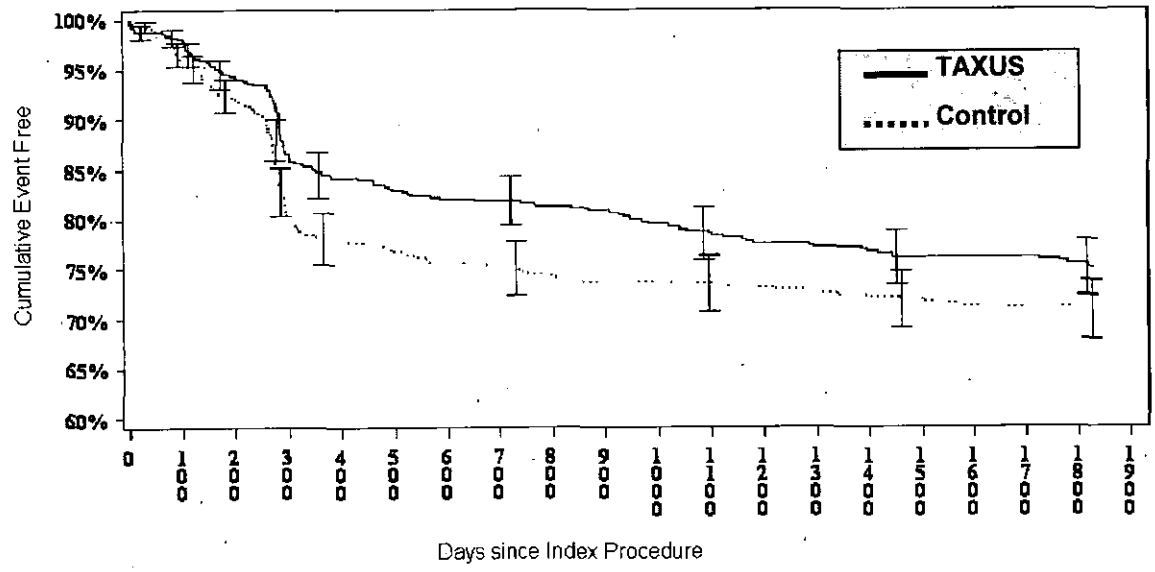

Figure 10.5.1. TAXUS V de novo Freedom from TVR to 5 Years, Event-Free Survival ± 1.5 SE, Safety Population, All Patients (N=1146)

	Event Rate	Event Free	P-Value*
TAXUS Express	24.9%	75.1%	0.0534
Bare Metal Express	29.2%	70.8%	

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

10.6 *HORIZONS AMI Clinical Trial*

Objectives: The trial had two primary objectives and was designed and powered to address both the primary and sub-study objectives.

Primary objective for the pharmacology randomization: To evaluate the use of bivalirudin in patients with ST segment elevation acute myocardial infarction (STEMI) undergoing a primary angioplasty strategy compared to unfractionated heparin plus routine use of GP IIb/IIIa inhibitors.

Primary objective for the stent randomization: To establish the safety and effectiveness of the paclitaxel-eluting TAXUS Express stent in STEMI patients by showing that compared to an otherwise identical Express BMS, the TAXUS Express results in: (1) reduced rates of ischemia-driven target lesion revascularization at 1 year; (2) a similar rate of the composite of death, reinfarction, stroke or stent thrombosis at 1 year; and (3) a lower rate of analysis segment binary angiographic restenosis at 13 months.

Design: The HORIZONS AMI trial was a prospective, dual-arm, single-blind, randomized multi-center trial that enrolled STEMI patients defined by clinical symptoms consistent with acute MI lasting greater than 20 minutes but less than 12 hours, and specific ECG criteria consisting of ST-segment elevation of ≥ 1mm in ≥ 2 contiguous leads, or presumed new LBBB, or true posterior MI with ST depression of ≥ 1mm in ≥ 2 contiguous anterior leads. A total of 3602 patients were randomized (primary randomization) in a 1:1 fashion in the emergency room to anticoagulation with unfractionated heparin plus routine GP IIb/IIIa inhibition or bivalirudin and bail-out GP IIb/IIIa inhibition.

Emergent coronary angiography with left ventriculography was performed after the primary randomization, followed by triage to either percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG) surgery or medical management at physician discretion.

After coronary angiography, a total of 3006 patients were triaged to PCI and randomized (secondary randomization) in a 3:1 fashion to either a TAXUS Express stent or an Express stent. In order to be eligible for the second randomization, patients had to have at least one acute infarct-related artery with an expectation that study stents could be delivered to all culprit lesions, Exclusion criteria included true bifurcation lesions definitely requiring stenting of the side branch vessel, lesions requiring greater than 100 mm of stent length, unprotected left main culprit lesions, and stent thrombosis lesions. The secondary randomization was stratified by the following four factors: the result from the primary randomization (to ensure equal distribution of the two arms from the primary randomization in the secondary randomization); the presence or absence of medically treated diabetes; whether any of the lesions were greater than 26 mm in length, such that overlapping stents would be used; and whether the clinical study site was within or outside of the U.S.

Clinical follow-up was performed at 30 days (± 1 week), 6 months (± 2 weeks), 1 year (± 2 weeks) and 2 years (± 1 month), and 3 years (± 1 month). Angiographic follow-up was performed at 13 months (-2 weeks, + 52 weeks) for a subset of patients (approximately the first 1500 randomized patients). Certain sites also participated in the HORIZONS IVUS substudy, where intravascular ultrasound was performed at baseline (post-procedure) and at 13 month follow-up (approximately the first 400 patients).

Results: The baseline demographics and medical history are reported in Table 10.6.1. The primary and secondary endpoints of the trial were met and are reported in Table 10.6.2 and Table 10.6.3. The clinical results of the trial are reported in Table 10.6.4. In Figure 10.6.1, the rates of ischemic TLR are illustrated for all patients and those patients who were not in the protocol-required angiographic subset. Figures 10.6.2, 10.6.3, 10.6.4, 10.6.5, and 10.6.6 provide results of major clinical outcomes to 3 years. Angiographic and IVUS results are reported in Table 10.6.7.

Table 10.6.1: HORIZONS AMI Patient Demographics and Medical History (ITT Population)

	TAXUS Express (N=2257)	Bare Metal Express (N=749)
Age (median (IQR), yrs)	59.9 (52.4, 69.4)	59.3 (51.8, 69.2)
Male	77.0% (1738/2257)	76.0% (569/749)
Diabetes mellitus	16.1% (364/2256)	15.2% (114/749)
- Insulin requiring	4.3% (98/2256)	4.1% (31/749)
Hypertension	51.2% (115/2256)	51.9% (389/749)
Hyperlipidemia	42.2% (953/2256)	41.1% (308/749)
Current smoker	46.3% (1041/2246)	51.9% (388/748)
Prior myocardial infarction	9.1% (206/2256)	10.9% (82/749)
Prior percutaneous coronary intervention	9.5% (214/2255)	7.7% (58/749)
Prior coronary artery bypass graft	2.2% (50/2256)	1.9% (14/749)
Anemia[1]	11.0% (235/2130)	7.6% (54/715)
Killip class 2-4	8.8% (199/2254)	8.0% (60/748)
Renal insufficiency[2]	15.6% (328/2102)	15.4% (107/696)
LVEF[3] <40%	14.3% (279/1948)	14.0% (91/652)

IQR = interquartile range

[1] Defined using the World Health Organization (WHO) criteria as a hematocrit value at initial presentation of <39% for men and <36% for women;

[2] Baseline calculated creatinine clearance using the Cockcroft-Gault equation <60 mL/min;

[3] Left ventricular ejection fraction, visual assessment from the baseline contrast left ventriculogram.

Table 10.6.2: HORIZONS AMI Primary Endpoints

Ischemic TLR	TAXUS Express (N=2257)	Bare Metal Express (N=749)	Difference (95% CI)	Hazard Ratio (95% CI)	P-value[1]
1 Year	4.5% (98)	7.5% (54)	-3.0% (-5.1, -0.9)	0.59 (0.43, 0.83)	0.0018
Safety MACE[2]	**TAXUS Express (N=2257)**	**Bare Metal Express (N=749)**	**Difference (95%CI)**	**Hazard Ratio (95% CI)**	**P-value[3]**
1 Year	8.1% (181)	8.0% (59)	0.1% (-2.1, 2.4)	1.02 (0.76, 1.36)	0.0075

[1] P-value for the test of superiority
[2] Safety MACE includes death, reinfarction, stroke or stent thrombosis.
[3] P-value for the test of non-inferiority

Table 10.6.3: HORIZONS AMI Secondary Endpoint

Binary Restenosis (Per Lesion)	TAXUS Express (N=2257)	Bare Metal Express (N=749)	Difference (95% CI)	Hazard Ratio (95% CI)	P-value[1]
13 Month	10.0% (108/1081)	22.9% (76/322)	-12.9% (-18.0, -7.8)	0.44 (0.33, 0.57)	<0.0001

[1] P-value for the test of superiority

Table 10.6.4: HORIZONS AMI Kaplan-Meier Estimates of Clinical Endpoints at 30 Day, 1, 2, and 3 Years (ITT Population)

	TAXUS Express (N=2257)	Bare Metal Express (N=749)
30 Day Clinical Endpoints		
Net Adverse Clinical Events[1]	10.3% (232)	9.0% (67)
MACE 1[2]	4.8% (109)	4.5% (34)
MACE 2 (Safety MACE)[3]	4.5% (102)	4.3% (32)
Death	2.1% (47)	1.9% (14)
- Cardiac	2.0% (44)	1.7% (13)
- Noncardiac	0.1% (3)	0.1% (1)
Reinfarction	1.7% (37)	2.2% (16)
- Q wave	1.2% (28)	1.6% (12)
- Non Q wave	0.4% (10)	0.5% (4)
Death or reinfarction	3.6% (80)	3.5% (26)
Ischemic TVR	2.3% (51)	2.6% (19)
Ischemic TLR	2.1% (46)	2.6% (19)
Stroke	0.5% (11)	0.5% (4)
Major bleeding (non-CABG)	7.1% (159)	5.6% (42)
Target Lesion stent thrombosis	2.3% (50)	2.7% (20)
1 Year Clinical Endpoints		
Net Adverse Clinical Events[1]	15.8% (355)	16.3%(121)
MACE 1[2]	10.6% (237)	12.4% (92)
MACE 2 (Safety MACE)[3]	8.1% (181)	8.0% (59)
Death	3.5%(78)	3.5% (26)
- Cardiac	2.4%(54)	2.7% (20)
- Noncardiac	1.1%(24)	0.8% (6)
Reinfarction	3.7%(81)	4.5% (33)
- Q wave	2.0%(45)	1.9% (14)
- Non Q wave	1.8%(39)	2.6% (19)
Death or reinfarction	6.8%(152)	7.0% (52)
Ischemic TVR	5.9% (129)	8.8% (64)
Ischemic TLR	4.6% (101)	7.4% (54)
Stroke	1.0%(23)	0.7% (5)
Major bleeding (non-CABG)	7.7% (172)	6.6% (49)
Target Lesion stent thrombosis	3.1% (69)	3.4% (25)
2 Year Clinical Endpoints		
Net Adverse Clinical Events[1]	21.5% (480)	26.0% (191)
MACE 1[2]	16.8% (373)	22.2% (162)
MACE 2 (Safety MACE)[3]	11.0% (245)	11.2% (82)
Death	4.3% (96)	5.3% (39)
- Cardiac	2.7% (60)	3.3% (24)
- Noncardiac	1.7% (36)	2.1% (15)
Reinfarction	5.7% (123)	6.0% (43)
- Q wave	3.1% (67)	2.8% (20)
- Non Q wave	3.0% (64)	3.2% (23)
Death or reinfarction	9.4% (210)	9.8% (72)
Ischemic TVR	10.9% (236)	16.7% (119)
Ischemic TLR	8.3% (180)	14.2% (101)
Stroke	1.4% (30)	1.1% (8)
Major bleeding (non-CABG)	8.0% (178)	7.0% (52)
Target Lesion stent thrombosis	4.2% (91)	4.1% (30)

Table 10.6.4: HORIZONS AMI Kaplan-Meier Estimates of Clinical Endpoints at 30 Day, 1, 2, and 3 Years (ITT Population)

	TAXUS Express (N=2257)	Bare Metal Express (N=749)
3 Year Clinical Endpoints		
Net Adverse Clinical Events[1]	24.5% (544)	28.0% (205)
MACE 1[2]	20.0% (441)	24.0% (175)
MACE 2 (Safety MACE)[3]	13.6% (300)	12.9% (94)
Death	5.6% (123)	6.6% (48)
- Cardiac	3.2% (71)	3.8% (28)
- Noncardiac	2.4% (52)	2.9% (20)
Reinfarction	7.0% (150)	6.6% (47)
- Q wave	3.5% (75)	2.8% (20)
- Non Q wave	4.0% (84)	3.8% (27)
Death or reinfarction	11.8% (260)	11.5% (84)
Ischemic TVR	12.4% (265)	17.6% (125)
Ischemic TLR	9.4% (202)	15.1% (107)
Stroke	1.6% (35)	1.4% (10)
Major bleeding (non-CABG)	8.4% (188)	7.3% (54)
Target Lesion stent thrombosis	4.8% (103)	4.3% (31)

[1] Net Adverse Clinical Events includes MACE1 and non-CABG related major bleeding.
[2] MACE1 includes death, reinfarction, stroke, or ischemic target vessel revascularization.
[3] MACE2 includes death, reinfarction, stent thrombosis, or stroke.

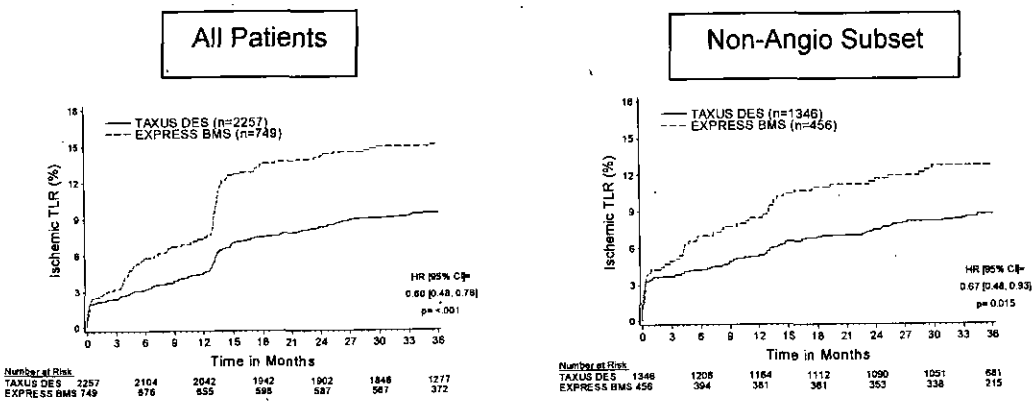

Figure 10.6.1: HORIZONS AMI Cumulative Rates of Ischemic Target Lesion Revascularization to 3 Years For All Patients and Patients Not in the Protocol Required Angiographic Subset

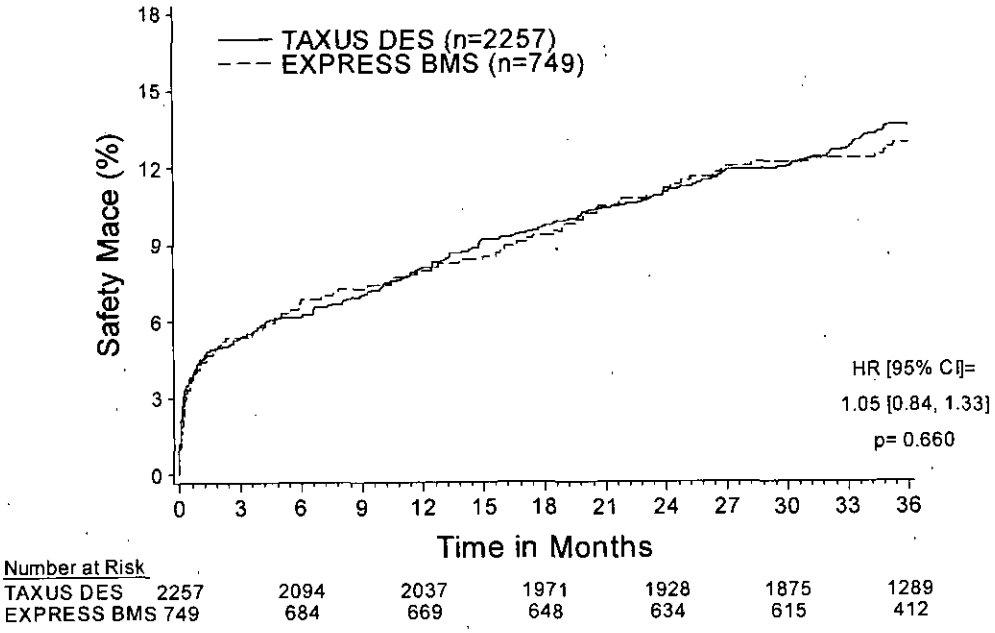

Figure 10.6.2: HORIZONS AMI Cumulative Rates of Safety MACE (Death, Reinfarction, Stent Thrombosis or Stroke) to 3 Years

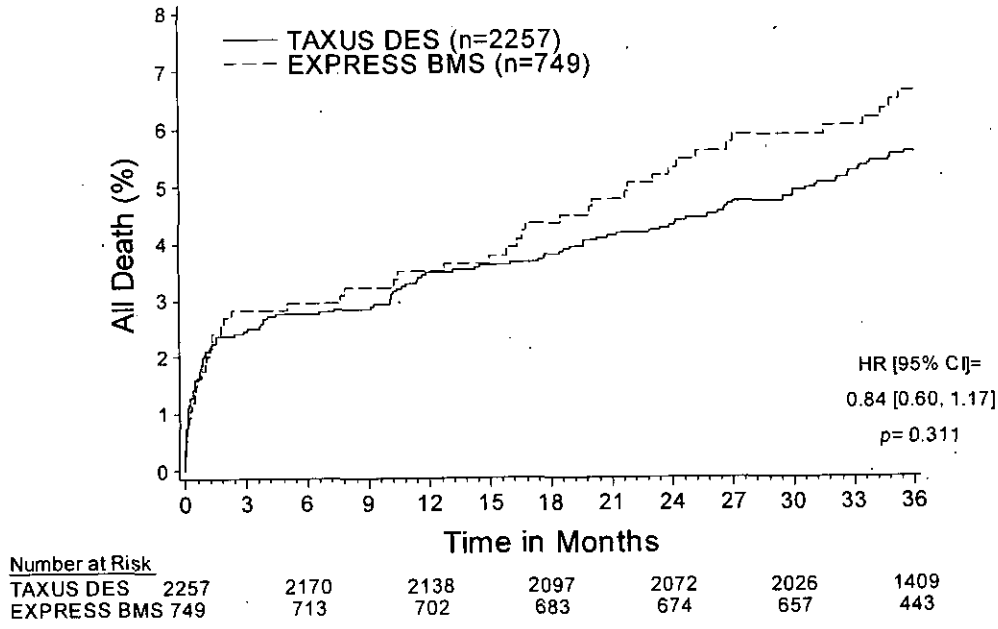

Figure 10.6.3: HORIZONS AMI Cumulative Rates of All Death to 3 Years

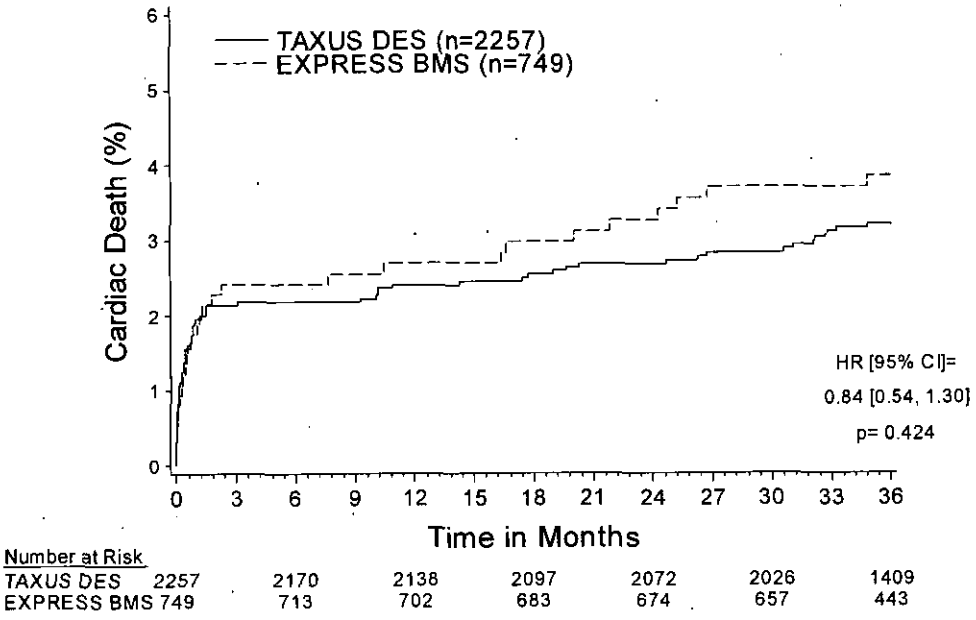

Figure 10.6.4: HORIZONS AMI Cumulative Rates of Cardiac Death to 3 Years

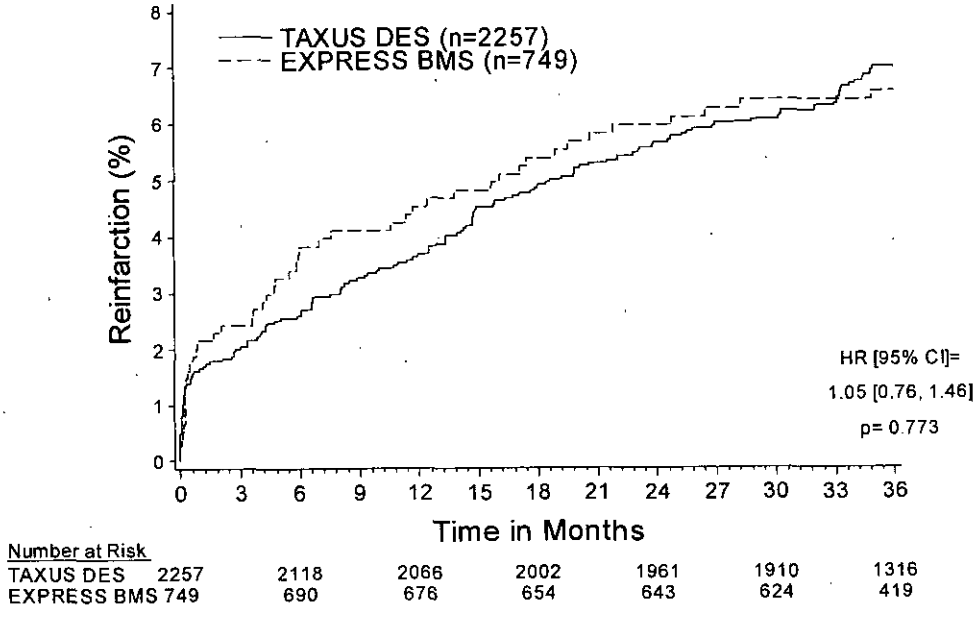

Figure 10.6.5: HORIZONS AMI Cumulative Rates of Reinfarction to 3 Years

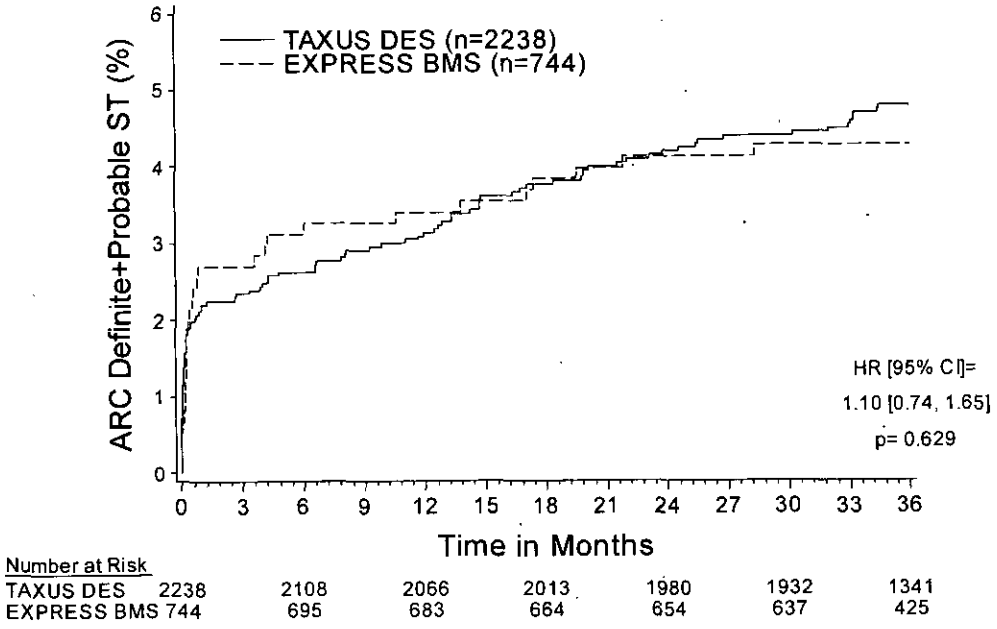

Figure 10.6.6: HORIZONS AMI Cumulative Rates of Target Lesion Definite and Probable Stent Thrombosis to 3 Years

Table 10.6.5 HORIZONS AMI 13 Month Angiographic and IVUS Results)

QCA	TAXUS Express (N=910 Patients / 1081 Lesions)	Bare Metal Express (N=293 Patients / 332 lesions)
Follow-up MLD in-stent (mm)	2.36 ± 0.75 (1062)	1.98 ± 0.82 (328)
Follow-up MLD in-segment (mm)	2.09 ± 0.68 (1062)	1.84 ± 0.76 (328)
Follow-up %DS in-stent	18.7 ± 22.8 (1062)	32.6 ± 24.9 (328)
Follow-up %DS in-segment	28.8 ± 19.6 (1062)	37.4 ± 22.0 (328)
Late Loss in-stent (mm)	0.41 ± 0.64 (1062)	0.82 ± 0.70 (328)
Late Loss in-segment (mm)	0.30 ± 0.56 (1062)	0.59 ± 0.64 (328)
Binary restenosis, in-stent	8.2% (87/1062)	21.0% (69/328)
Binary restenosis, in-segment	9.6% (102/1062)	23.2% (76/328)
IVUS	**TAXUS Express (N=196 pts / 219 lesions)**	**Bare Metal Express (N=62 pts / 67 lesions)**
Neointimal Volume (mm^3)	19.4 ± 21.6 (191)	37.4 ± 30.0 (65)
Percent net volume obstruction (%)	7.9 ± 7.4 (191)	19.8 ± 15.8 (65)
Incomplete Apposition (late)	58.3% (95/163)	33.3% (12/36)
Incomplete Apposition (late-acquired)	42.9% (70/163)	19.4% (7/36)

QCA = quantitative coronary angiography, RVD = reference vessel diameter, MLD = minimal lumen diameter, %DS = percent diameter stenosis, IQR = interquartile range, SD = standard deviation
Follow-up QCA results on stented lesions only (per lesion)

Results in Males and Females: The HORIZONS AMI trial data were retrospectively evaluated for possible sex-based differences in baseline characteristics and clinical outcomes, as well as for any interaction between treatment and sex/gender. The HORIZONS AMI trial was not designed or powered to study safety or effectiveness in sex-specific subgroups, so these analyses were performed *post hoc* and are considered hypothesis generating.

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In the HORIZONS AMI population, of patients randomized to TAXUS Express DES 1738/2257 (77%) subjects were male and 519/2257 (23%) subjects were female. The proportions in the Express BMS group were similar (76% male, 24% female). According to the Nationwide Inpatient Sample (a large database of inpatient admissions from 1988 to 2004), men had almost 2 times the age-adjusted STEMI rate as women (men 62.4%, women 37.6%)[9]. The gender proportions enrolled in this trial are similar to other trials in the STEMI population[10,11].

In subjects treated with TAXUS Express DES, 12-month TLR rates were 6.8% in females and 3.9% in males and Safety MACE rates were 10.1% in females and 7.5% in males. In subjects treated with Express BMS, 12-month TLR rates were 12.1% in females and 6.0% in males and Safety MACE rates were 12.3% in females and 6.6% in males (Table 10.6.6). Primary and secondary endpoint outcomes data stratified by gender are shown in tables 10.6.6 and 10.6.7. HORIZONS AMI clinical results at 30 Days, 1 Year, 2 Year and 3 Year in male and female patients are reported in Table 10.6.8. Within the female group, cardiac death was numerically higher through 30 days in those treated with TAXUS Express versus bare metal Express, but the numerical difference between groups narrowed over time. Other trials of interventional treatment for AMI have shown female sex to be associated with higher mortality rates compared to men,[12,13] but differences appear to be largely explained by baseline risk factors such as BSA and angiographic disease severity. Rates of reinfarction and stent thrombosis in females were numerically lower in TAXUS Express DES versus bare metal Express at 30 days and through 3 years. Formal interaction testing revealed no difference (at a significance level of p=0.15) between males and females in treatment effect at any time point, suggesting the conclusions of the overall study can be generalized for males and females.

Table 10.6.6: HORIZONS AMI Primary Endpoints by Gender

1 Year Ischemic TLR	TAXUS Express (N=2257)	Bare Metal Express (N=749)
Male (N=2307)	(N=1738)	(N=569)
	3.9% (66)	6.0% (33)
Female (N=699)	(N=519)	(N=180)
	6.8% (34)	12.1% (21)
Safety MACE[1]	**TAXUS Express (N=2257)**	**Bare Metal Express (N=749)**
Male (N=2307)	(N=1738)	(N=569)
	7.5% (129)	6.6% (37)
Female (N=699)	(N=519)	(N=180)
	10.1% (52)	12.3% (22)

[1] Safety MACE includes death, reinfarction, stroke or stent thrombosis

Table 10.6.7: HORIZONS AMI Secondary Endpoint by Gender

Binary Restenosis at 13 Months (Per Lesion)	TAXUS Express (N=2257)	Bare Metal Express (N=749)

[9] Movahed M, Ramaraj R, Hashemzadeh, M, et. al. Rate of Acute ST-Elevation Myocardial Infarction in the United States from 1988 to 2004 (from the Nationwide Inpatient Sample), Am J Cardiol. 2009;104:5-8.
[10] GUSTO Investigators, An International Randomized Trial Comparing Four Thrombolytic Strategies for Acute Myocardial Infarction, N Engl J Med; 1993; 329, 673-82.
[11] Lansky AJ, Pietras C, Costa RA, et. al. Gender Differences in Outcomes After Primary Angioplasty Versus Primary Stenting With and Without Abciximab for Acute Myocardial Infarction: Results of the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) Trial; Circulation; 2005: 111:1611-18.
[12] Lansky AJ, Pietras C, Costa RA, et. al. Gender Differences in Outcomes After Primary Angioplasty Versus Primary Stenting With and Without Abciximab for Acute Myocardial Infarction: Results of the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) Trial; *Circulation*; 2005: 111:1611-18.
[13] Berger JS, Elliott L, Gallup, et al. Sex Differences in Mortality Following Acute Coronary Syndrome; *JAMA*. 2009;302(8):874-882

Male (N=2307)	(N=1738)	(N=569)
	9.6% (83/863)	22.6% (55/243)
Female (N=699)	(N=519)	(N=180)
	11.5% (25/218)	23.6% (21/89)

Table 10.6.8: HORIZONS AMI Clinical Endpoints, All TAXUS Express Male and Female Patients at 30 Day, 1 Year, 2 Year and 3 Year (Stent ITT Population)

Endpoint	TAXUS Express Male Patients (N=1738)	TAXUS Express Female Patients (N=519)	Bare Metal Express Male Patients (N=569)	Bare Metal Express Female Patients (N=180)
30 Day				
Net Adverse Clinical Events[1]	8.6% (149)	16.2% (84)	7.2% (41)	16.1% (29)
MACE 1[2]	4.1% (71)	7.4% (38)	3.5% (20)	7.8% (14)
MACE 2 (Safety MACE)[3]	3.9% (68)	6.6% (34)	3.2% (18)	7.8% (14)
Death	1.5% (26)	4.1% (21)	1.6% (9)	2.8% (5)
- Cardiac	1.4% (24)	3.9% (20)	1.6% (9)	2.2% (4)
- Noncardiac	0.1% (2)	0.2% (1)	0.0% (0)	0.6% (1)
Reinfarction	1.6% (27)	2.0% (10)	1.6% (9)	3.9% (7)
- Q wave	1.2% (21)	1.4% (7)	1.2% (7)	2.8% (5)
- Non Q wave	0.4% (7)	0.6% (3)	0.4% (2)	1.1% (2)
Death or reinfarction	2.9% (51)	5.6% (29)	2.8% (16)	5.6% (10)
Ischemic TVR	2.0% (35)	3.5% (18)	2.1% (12)	3.9% (7)
Ischemic TLR	1.8% (32)	3.1% (16)	2.1% (12)	3.9% (7)
Stroke	0.6% (10)	0.2% (1)	0.2% (1)	1.7% (3)
Major bleeding (non-CABG)	6.1% (105)	10.7% (55)	4.6% (26)	10.6% (19)
Target Lesion stent thrombosis	2.0% (35)	2.8% (14)	2.1% (12)	4.5% (8)
1 Year				
Net Adverse Clinical Events[1]	13.3% (231)	23.7% (122)	13.7% (77)	24.5% (44)
MACE 1[2]	9.3% (161)	14.8% (76)	10.4% (58)	19.0% (34)
MACE 2 (Safety MACE)[3]	7.5% (129)	10.1% (52)	6.6% (37)	12.3% (22)
Death	2.9% (50)	5.4% (28)	2.8% (16)	5.6% (10)
- Cardiac	1.8% (32)	4.3% (22)	2.3% (13)	3.9% (7)
- Noncardiac	1.1% (18)	1.2% (6)	0.5% (3)	1.8% (3)
Reinfarction	3.6% (62)	3.8% (19)	3.8% (21)	6.8% (12)
- Q wave	2.1% (36)	1.8% (9)	1.6% (9)	2.8% (5)
- Non Q wave	1.7% (28)	2.2% (11)	2.2% (12)	4.0% (7)
Death or reinfarction	6.2% (108)	8.6% (44)	6.0% (34)	10.0% (18)
Ischemic TVR	5.0% (85)	8.9% (44)	7.2% (40)	13.8% (24)
Ischemic TLR	3.9% (66)	6.8% (34)	6.0% (33)	12.1% (21)
Stroke	0.9% (16)	1.4% (7)	0.4% (2)	1.7% (3)
Major bleeding (non-CABG)	6.4% (110)	12.0% (61)	5.0% (28)	11.7% (21)
Target Lesion stent thrombosis	3.1% (52)	3.4% (17)	2.9% (16)	5.1% (9)
2 Year				
Net Adverse Clinical	19.4% (333)	28.7% (147)	24.5% (135)	30.7% (55)

Events[1]				
MACE 1[2]	15.9% (271)	20.0% (102)	21.4% (117)	24.7 (44)
MACE 2 (Safety MACE)[3]	10.5% (179)	12.9% (58)	10.5% (58)	13.4% (24)
Death	3.7% (63)	6.5% (33)	5.1% (28)	6.2% (11)
- Cardiac	2.2% (38)	4.3% (22)	2.9% (16)	4.5% (8)
- Noncardiac	1.5% (25)	2.3% (11)	2.3% (12)	1.8% (3)
Reinfarction	5.8% (96)	5.5% (27)	5.3% (29)	8.0% (14)
- Q wave	3.3% (55)	2.4% (12)	2.6% (14)	2.4% (6)
- Non Q wave	2.8% (46)	3.7% (18)	2.8% (15)	4.6% (8)
Death or reinfarction	9.0% (153)	11.2% (57)	9.4% (52)	11.2% (20)
Ischemic TVR	10.4% (173)	12.9% (63)	16.0% (86)	18.5% (32)
Ischemic TLR	7.7% (128)	10.2% (50)	13.6% (73)	16.2% (28)
Stroke	1.3% (22)	1.6% (8)	1.0% (5)	1.7% (3)
Major bleeding (non-CABG)	6.5% (113)	12.4% (63)	5.4% (30)	12.3% (22)
Target Lesion stent thrombosis	4.1% (69)	4.2% (21)	3.6% (20)	5.7% (10)
3 Year				
Net Adverse Clinical Events[1]	22.3% (381)	31.9% (163)	26.7% (148)	31.9% (57)
MACE 1[2]	18.9% (321)	23.7% (120)	23.4% (129)	25.9% (46)
MACE 2 (Safety MACE)[3]	12.9% (220)	15.8% (80)	12.5% (69)	14.0% (25)
Death	5.0% (85)	7.5% (38)	6.4% (35)	7.4% (13)
- Cardiac	2.8% (47)	4.7% (24)	3.6% (20)	4.5% (8)
- Noncardiac	2.3% (38)	2.9% (14)	2.8% (15)	3.0% (5)
Reinfarction	6.9% (115)	7.2% (35)	6.1% (33)	8.0% (14)
- Q wave	3.7% (62)	2.6% (13)	2.6% (14)	3.4% (6)
- Non Q wave	3.6% (59)	5.3% (25)	3.6% (19)	4.6% (8)
Death or reinfarction	11.2% (190)	13.8% (70)	11.4% (63)	11.8% (21)
Ischemic TVR	11.7% (194)	14.6% (71)	17.1% (92)	19.2% (33)
Ischemic TLR	8.7% (145)	11.7% (57)	14.5% (78)	16.9% (29)
Stroke	1.6% (26)	1.9% (9)	1.3% (7)	1.7% (3)
Major bleeding (non-CABG)	7.0% (120)	13.4% (68)	5.7% (32)	12.3% (22)
Target Lesion stent thrombosis	4.6% (77)	5.3% (26)	3.8% (21)	5.7% (10)

[1] Net Adverse Clinical Events includes MACE1 and non-CABG related major bleeding.
[2] MACE1 includes death, reinfarction, stroke, or ischemic target vessel revascularization.
[3] MACE2 includes death, reinfarction, stent thrombosis, or stroke.

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10.7 Sex-Specific Information from Pooled Analysis

In the United States, an estimated 17,600,000 adults age 20 and older (9.1% of men and 7.0% of women) suffer from coronary artery disease (CAD)[14]. Once diagnosed and treated, poorer revascularization outcomes have been reported in women due to smaller coronary arteries and increased prevalence of baseline comorbidities including advanced age, diabetes, hypertension, and peripheral vascular disease compared with men[15,16].

To evaluate for sex-specific differences in long-term outcomes after percutaneous coronary intervention with the paclitaxel-eluting coronary stent, Boston Scientific conducted a retrospective pooled analysis of patients enrolled in five randomized trials (TAXUS I, II SR, IV, V *de novo*, and TAXUS ATLAS Workhorse), and two 'real world' registries (ARRIVE 1 and 2). Of the 2,271 patients pooled from the randomized trials, 665 (29.3%) were women. The proportion of women included in these studies is similar to that reported in literature.[15,17,]

Despite significantly more adverse baseline risk factors in women (which was also observed in the TAXUS stent program, see Table 10.7.1), recent randomized trials of drug-eluting stents have demonstrated comparable safety and effectiveness outcomes in men and women[18,19]. As shown in Table 10.7.2 and Figure 10.7.1, clinical event rates were generally similar between men and women. Information on bleeding is not available, as these data were not collected in the randomized trials. Overall, the influence of gender on long-term drug-eluting stent outcomes has not been fully elucidated.[19]

The clinical trials and registries conducted with paclitaxel-eluting stents were not designed or powered to specifically analyze for differences by sex/gender.

Table 10.7.1: Baseline Clinical and Lesion Characteristics for Patients Receiving PES[1] in Randomized Trials

Variable	Women (N=665)	Men (N=1606)	P value
Age, (yr)	64.9±11.1 (665)	61.4±10.7 (1606)	<0.001
Weight (lbs)	171.3±37.1 (397)	200.8±38.4 (970)	<0.001
Cardiac History			
Stable Angina	55.1% (365/663)	57.8% (929/1606)	0.22
Unstable Angina	37.4% (248/663)	31.5% (496/1577)	0.006
Silent Ischemia	10.1% (67/665)	12.5% (201/1602)	0.10
Congestive Heart Failure	7.7% (51/664)	3.9% (63/1605)	<0.001
Previous Myocardial Infarction	25.8% (171/663)	31.8% (501/1577)	0.005
Previous Percutaneous Coronary Intervention	28.0% (174/622)	33.8% (500/1481)	0.01
Previous Coronary Artery Bypass Graft	5.9% (39/663)	9.3% (146/1577)	0.008
Cardiac Risk Factors			
Current Smoking	20.8% (138/665)	23.5% (378/1606)	0.15

[14] Lloyd-Jones D, Adams RJ, Brown TM, et al. Heart Disease and Stroke Statistics—2010 Update. A Report From the American Heart Association. Circulation. 2010;121(7):e46-e215.
[15] Berenguer A, Mainar V, Bordes P, Valencia J, Gomez S, Lozano T.. Incidence and predictors of restenosis after sirolimus-eluting stent implantation in high-risk patients. Am.Heart J 2005;150:536-42.
[16] Seth A, Serruys PW, Lansky A, et al. A pooled gender based analysis comparing the Xience V everolimus-eluting stent and the TAXUS paclitaxel-eluting stent in male and female patients with coronary artery disease, results of the SPIRIT II and SPIRIT III studies: two-year analysis. EuroIntervention 2010;5:788-27.
[17] Women and Heart Disease Fact Sheet, Women's Heart Foundation, www.womensheart.org
[18] Lansky AJ, Costa RA, Mooney M, et al. Gender-based outcomes after paclitaxel-eluting stent implantation in patients with coronary artery disease. J am Coll Cardiol 2005;45;1180-5.
[19]Mikhail GW, Gerber RT, Cox DA, et al. Influence of Gender on Long-Term Outcomes after Percutaneous Coronary Intervention with the Paclitaxel-Eluting Coronary Stent: Results of the 'TAXUS Woman' Analysis. J Am Coll Cardiol Intv, 2010;3:1250-9.).

Table 10.7.1: Baseline Clinical and Lesion Characteristics for Patients Receiving PES[1] in Randomized Trials

Variable	Women (N=665)	Men (N=1606)	P value
Diabetes, Medically Treated	33.5% (223/665)	21.9% (352/1606)	<0.001
Hypertension	78.0% (519/665)	69.5% (1116/1606)	<0.001
Hyperlipidemia	71.7% (477/665)	72.8% (1166/1602)	0.61
History of Coronary Artery Disease	62.0% (372/600)	52.6% (762/1450)	<0.001
Comorbid Conditions			
Peripheral Vascular Disease	10.2% (63/ 615)	7.6% (112/1475)	0.046
Previous Transient Ischemic Attack	3.7% (7/187)	2.9% (14/475)	0.60
Previous Cerebrovascular Accident	6.0% (27/453)	3.8% (41/1080)	0.06
Renal Disease	5.1% (23/ 453)	3.9% (42/1080)	0.29
Lesion Characteristics (by QCA)			
Reference Vessel Diameter (mm)	2.63± 0.46 (659)	2.79± 0.52 (1597)	<0.001
Minimum Lumen Diameter (mm)	0.87± 0.35 (658)	0.89±0.35 (1569)	0.24
Diameter Stenosis (%)	67.09± 11.54 (658)	67.98±11.14 (1569)	0.09
Lesion Length (mm)	14.65±7.31 (659)	14.72±7.31 (1592)	0.84
Left Anterior Descending Vessel Location	39.0% (259/664)	41.2% (661/1603)	0.33
Bend > 45 degrees	23.8% (148/622)	22.2% (328/1476)	0.43
Tortuosity	11.9% (74/622)	10.5% (155/1475)	0.35
Modified ACC/AHA Lesion Type			
A	8.0% (50/622)	7.1% (105/1478)	0.45
B1	22.5% (140/622)	24.4% (361/1478)	0.35
B2	41.6% (259/622)	38.6% (571/1478)	0.20
C	27.8% (173/622)	29.8% (441/1478)	0.35
B2/C	69.5% (432/622)	68.5% (1012/1478)	0.66

[1] PES = paclitaxel-eluting stent The TAXUS NIRx stent was utilized in the TAXUS I and TAXUS II trials, the TAXUS Express stent was utilized in the TAXUS IV and TAXUS V *de novo* trials, and the TAXUS Liberté stent was utilized in the TAXUS ATLAS Workhorse trial.

Numbers are % (count/sample size) or mean ± standard deviation (n). *P* values for continuous variables were calculated by the Student *t*-test and for categorical variables were calculated by the Chi-square test. Abbreviations: ACC=American College of Cardiology; AHA=American Heart Association; PES= paclitaxel-eluting stent; QCA=quantitative coronary angiography.

Table 10.7.2: *Clinical Outcomes* at 5 Years for Patients Receiving PES in Randomized Trials

Variable	Male (N=1606)	Female (N= 665)
TVR, Overall	19.8% (291/1470)	20.8% (124/595)
TLR, Overall	11.9% (175/1470)	12.4% (74/595)
TLR, PCI	10.5% (155/1470)	11.8% (70/595)
TLR, CABG	1.6% (23/1470)	1.0% (6/595)
Non-TLR	10.2% (150/1470)	11.4% (68/595)
Non-TLR, PCI	7.8% (114/1470)	8.7% (52/595)
Non-TLR, CABG	2.8% (41/1470)	3.0% (18/595)
Total Death	9.1% (134/1470)	10.4% (62/595)
Cardiac Death or MI	11.3% (166/1470)	12.3% (73/595)
Cardiac Death	4.6% (68/1470)	5.0% (30/595)
MI	7.4% (109/1470)	8.7% (52/595)
Q-wave MI	1.8% (27/1470)	1.2% (7/595)
Non-Q-wave MI	5.8% (85/1470)	7.6% (45/595)

Table 10.7.2: Clinical Outcomes at 5 Years for Patients Receiving PES in Randomized Trials		
Variable	Male (N=1606)	Female (N= 665)
ARC Stent Thrombosis Definite or Probable	2.9% (40/1360)	2.0% (11/541)
Definite	2.1% (29/1360)	1.1% (6/541)
Probable	1.0% (13/1360)	0.9% (5/541)

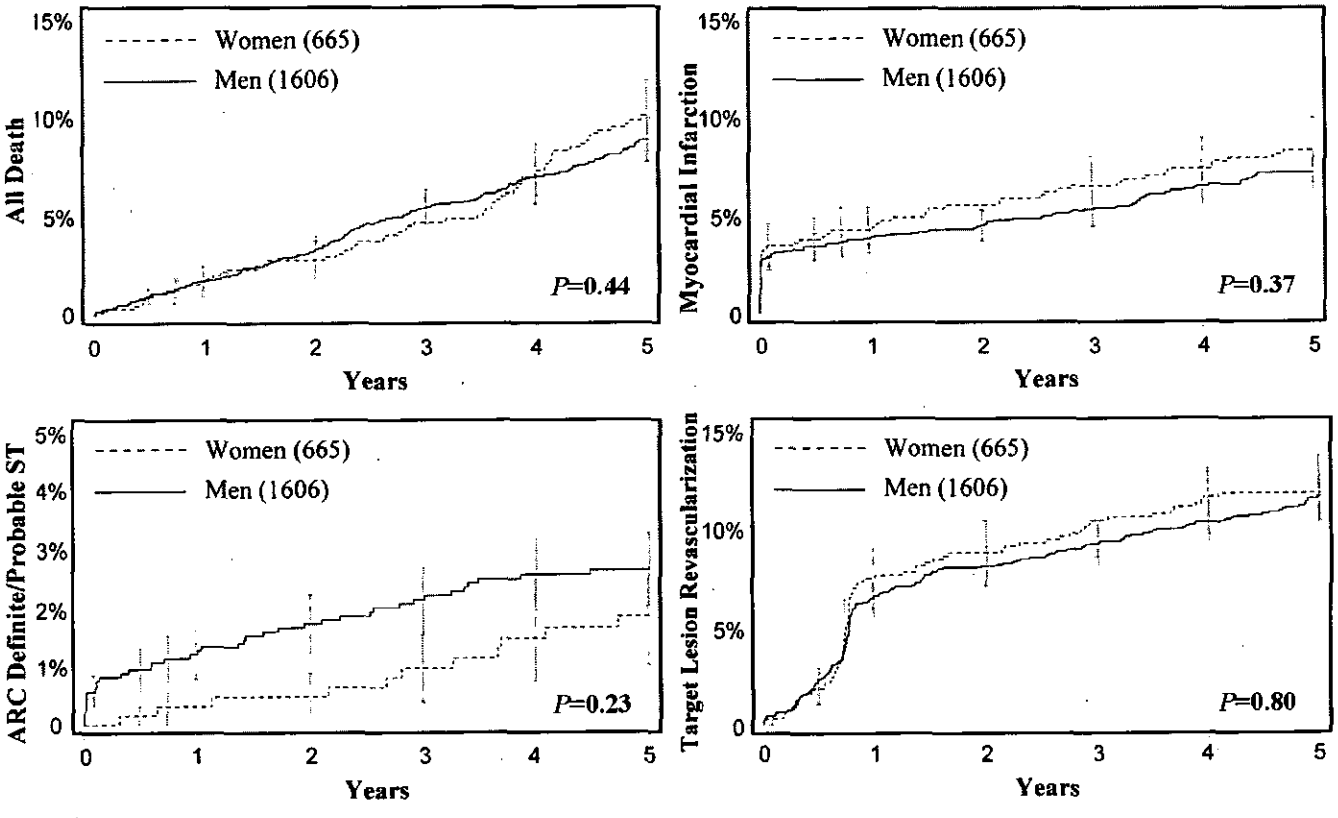

Figure 10.7.1: Kaplan-Meier Estimates of 5-year Cumulative Rates of Clinical Outcomes for Women versus Men for Patients Receiving Paclitaxel-eluting Stents in the Randomized Trials

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 antiplatelet therapy. For Elective PCI Procedures, based on randomized clinical trial protocols, a $P2Y_{12}$ inhibitor should be given for at least 6 months after paclitaxel-eluting stent (PES) implantation and ideally up to 12 months in patients who are not at high risk of bleeding. For PCI in ST-elevated MI Patients, a $P2Y_{12}$ inhibitor should be given for at least 12 months; however if the risk of morbidity because of bleeding outweighs the anticipated benefit afforded by $P2Y_{12}$ inhibitor therapy, earlier discontinuation should be considered. Aspirin should be administered concomitantly with the $P2Y_{12}$ inhibitor 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.
- An angioplasty and stent education guide (available online or by request) which includes information on coronary artery disease, the implant procedure, and frequently asked questions.

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.
- Do not use if labeling is incomplete or illegible.

See **section 14.2 Materials Required** for additional equipment required for the safe use of the product.

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

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

14 OPERATIONAL INSTRUCTIONS

14.1 Inspection Prior to Use

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

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

14.2 Materials Required (not included in Stent System package)

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

1	Torque device
1	Pre-deployment dilation catheter
1	Three-way stopcock
1	Appropriate arterial sheath

14.3 Preparation

14.3.1 Packaging Removal

Step Action

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

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

14.3.2 Guidewire Lumen Flush

Step Action

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

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

14.3.3 Balloon Preparation

Step Action

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

14.3.4 Delivery Procedure

Step Action

1. Prepare the vascular access site according to standard PTCA practice.
2. Predilate the lesion/vessel with appropriate diameter balloon.

3. Maintain neutral pressure on inflation device attached to stent system.
4. Backload stent system onto proximal portion of guidewire while maintaining guidewire position across target lesion.
5. Fully open rotating hemostatic valve to allow for easy passage of the stent and prevent damage to the stent.
6. Carefully advance the stent system into the hub of the guide catheter. When using a Monorail system be sure to keep the hypotube straight. Ensure guide catheter stability before advancing the stent system into the coronary artery.

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

---

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

Note: If unusual resistance is felt at any time during lesion access before stent implantation, the stent system and the guide catheter should be removed as a single unit. (See also Precautions - 6.12 Stent System Removal).

---

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

14.3.5 Deployment Procedure

Step Action

1. Inflate the delivery system expanding the stent to a minimum pressure of 9 atm (912 kPa) for the 2.25 mm - 2.50 mm stents and 8 atm (811 kPa) for the 2.75 mm – 4.00 mm stents sizes (nominal pressure). Higher pressure may be necessary to optimize stent apposition to the arterial wall. Accepted practice generally targets an initial deployment pressure that would achieve a stent inner diameter of about 1.1 times the reference vessel diameter (see Table 14.5.1). Balloon pressure must not exceed rated burst pressure of 18 atm (1824 kPa). (see Table 14.5.1).
2. Maintain inflation pressure for 15-30 seconds for full expansion of the stent.
3. Deflate balloon by pulling negative pressure on inflation device until balloon is fully deflated, see Table 6.1 System Deflation Time Specifications.
4. Confirm stent position and deployment using standard angiographic techniques. For optimal results, the entire stenosed arterial segment should be covered by the stent. Fluoroscopic visualization during stent expansion should be used in order to properly judge the optimum expanded stent diameter as compared to the proximal and distal coronary artery diameter(s). Optimal expansion requires that the stent be in full contact with the artery wall. Stent wall contact should be verified through routine angiography or intravascular ultrasound (IVUS).
5. If stent sizing/apposition requires optimization, readvance the stent system balloon, or another high-pressure, non-compliant balloon catheter of the appropriate size, to the stented area using standard angioplasty techniques.
6. Inflate the balloon to the desired pressure while observing under fluoroscopy. Deflate the balloon (refer to product labeling and/or Table 14.5.1 for proper stent inflation pressure).
7. If more than one TAXUS® Liberté® Stent is needed to cover the lesion and balloon treated area, it is suggested that, to avoid the potential for gap restenosis, the stents be adequately overlapped. To ensure that there are no gaps between stents, the balloon marker bands of the second TAXUS Liberté Stent should be positioned inside of the deployed stent prior to expansion.

8. Reconfirm stent position and angiographic result. Repeat inflations until optimal stent deployment is achieved.

14.3.6 Removal Procedure

Step Action

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

14.4 Post-Deployment Dilatation of Stented Segments

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

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

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

14.5 In Vitro Information

Table 14.5.1. Typical TAXUS Liberté Stent System Compliance

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

■ Nominal Pressure
■ RATED BURST PRESSURE. DO NOT EXCEED.
Note: The Stent Diameter values listed are actual average stent diameters at the specific balloon inflation pressures obtained during in vitro testing at 37°C.

15 WARRANTY

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

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