PROMUS Element™ Plus

MONORAIL®
OVER-THE-WIRE

Product Description

Everolimus-Eluting Platinum Chromium Coronary Stent System

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

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

1 WARNING:

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

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

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

2 DEVICE DESCRIPTION:

PROMUS Element™ Plus Everolimus-Eluting Platinum Chromium Coronary Stent System:

The PROMUS Element Plus Everolimus-Eluting Platinum Chromium Coronary Stent System is a device/drug combination product consisting of a drug/polymer-coated balloon-expandable stent, pre-mounted on a Monorail (MR) or Over-The-Wire (OTW) delivery catheter. The stent is made from a platinum chromium alloy (PtCr). The drug-polymer coating consists of a polymer, PVDF-HFP, and the active pharmaceutical ingredient, everolimus. The characteristics of the PROMUS Element Plus Stent System are described in Table 2.1.

Table 2.1. PROMUS Element Plus Stent System Product Description

	PROMUS Element Plus Monorail Stent Delivery System	**PROMUS Element Plus Over-the-Wire Stent Delivery System**
Available Stent Lengths (mm)	8, 12, 16, 20, 24, 28, 32*	
Available Stent Diameters (mm)	2.25*, 2.50, 2.75, 3.00, 3.50, 4.00	
Stent Material	Platinum Chromium Alloy (PtCr)	
Stent Strut Thickness	0.0032 inches (0.081 mm) for diameters 2.25 mm to 3.50 mm 0.0034 inches (0.086 mm) for diameter 4.00 mm	
Drug Product	A conformal coating of a polymer carrier loaded with 100 µg/cm² everolimus applied to the stent with a maximum nominal drug content of 177.3 µg on the largest stent (4.00 x 28 mm).	

Table 2.1. PROMUS Element Plus Stent System Product Description		
	PROMUS Element Plus Monorail Stent Delivery System	**PROMUS Element Plus Over-the-Wire Stent Delivery System**
Delivery System		
Effective Length	144 cm	
Delivery System Y-Adapter Ports	Single access port to inflation lumen. Guidewire exit port is located approximately 26 cm from tip. Designed for guidewire ≤0.014 inches (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 inches (0.36 mm)
Stent Delivery	A balloon, with two radiopaque balloon markers, nominally placed 0.4 mm (0.016 inches) beyond the stent at each end.	
Balloon Inflation Pressure	Nominal Inflation Pressure: • Diameters 2.25 mm, 2.50 mm, 2.75 mm, 3.00 mm, 3.50 mm, 4.00 mm: 11 atm (1117 kPa)	
	Rated Burst Inflation Pressure: • Diameters 2.25 mm – 2.75 mm: 18 atm (1827 kPa) • Diameters 3.00 mm – 4.00 mm: 16 atm (1620 kPa)	
Catheter Shaft Outer Diameter	2.3 F (≤0.80 mm) proximal and 2.7 F (≤0.95 mm) distal.	3.4F (≤1.20 mm) proximal for 2.25 to 4.00 mm sizes 2.4F (≤0.85 mm) distal for 2.25 to 2.75 mm sizes 2.7F (≤0.95 mm) distal for 3.00 to 4.00 mm sizes
Guide Catheter Minimum Inner Diameter Requirement	≥0.056 inches (1.42 mm)	≥0.066 inches (1.68 mm)
* 32 mm length is only available in 2.25 mm diameter sizes		

2.1 Device Component Description

The PROMUS Element™ stent is the everolimus-coated member of the platinum chromium (PtCr) Element™ Stent Series. The Element stent delivery system is available in four stent models, each engineered for specific diameters to provide consistent stent-to-artery ratios across the range of reference vessel diameters indicated:

- Small Vessel (SV): 2.25 mm
- Small Workhorse (SWH): 2.50, 2.75 mm
- Workhorse (WH): 3.00, 3.50 mm
- Large Vessel (LV): 4.00 mm

CONTENTS for (1) PROMUS Element Plus Over-the-Wire Stent System

• One (1) PROMUS Element Plus Over-the-Wire Stent System

CONTENTS for (1) PROMUS Element Plus Monorail Stent System

• One (1) PROMUS Element Plus Monorail Stent System

• Two (2) CLIPIT™ Coil clips

• One (1) Flushing needle with luer fitting

2.2 Drug Component Description

The stent component of the PROMUS Element Plus Stent System (referred to as the PROMUS Element stent) is a PtCr Element stent with a drug/polymer coating. The coating comprises two layers. The inner

layer consists of a polymer which is a primer for promoting adhesion of the outer layer. The outer layer consists of a polymer matrix that contains an active pharmaceutical ingredient (everolimus).

See Sections 2.2.1 and 2.2.2 for descriptions of the drug and polymers, respectively.

2.2.1 Everolimus

The active pharmaceutical ingredient in the PROMUS Element™ stent is everolimus. The everolimus chemical name is 40-O-(2-hydroxyethyl)-rapamycin and its chemical structure is provided in Figure 2.1.

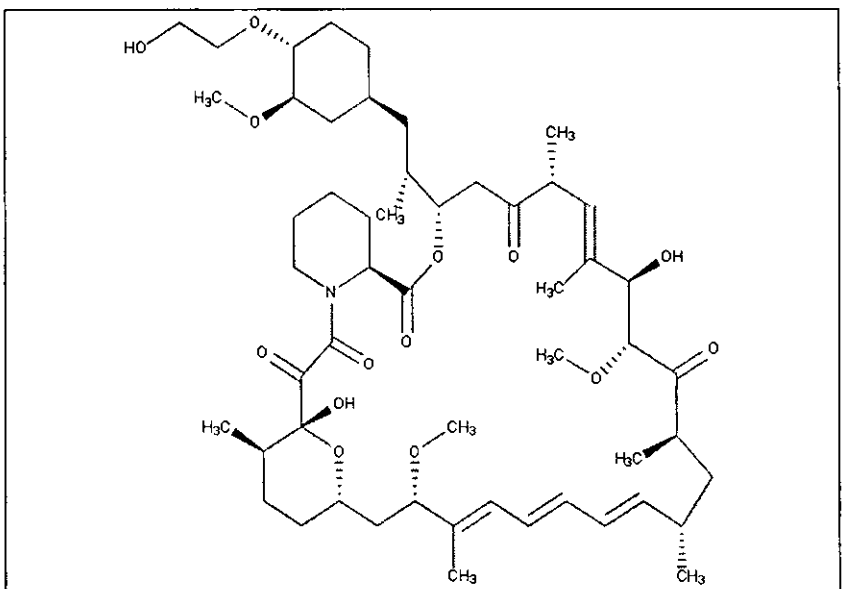

Figure 2.1. The Chemical Structure of Everolimus

2.2.2 Primer Polymer and Drug Matrix Copolymer Carrier

The PROMUS Element stent contains a primer polymer layer, PBMA, poly (n-butyl methacrylate), that functions as an adhesion promoter between the bare metal and the drug matrix layer. The chemical structure of PBMA is provided in Figure 2.2.

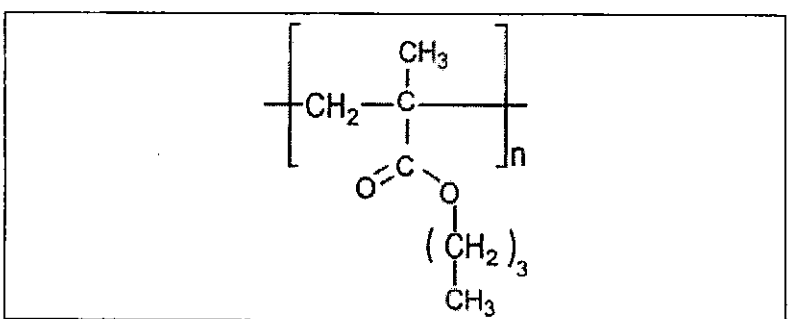

Figure 2.2. The Chemical Structure of PBMA

The drug matrix layer contains a semi-crystalline random copolymer, PVDF-HFP, poly (vinylidene fluoride-co-hexafluoropropylene), blended with everolimus. The chemical structure of PVDF-HFP is provided in Figure 2.3.

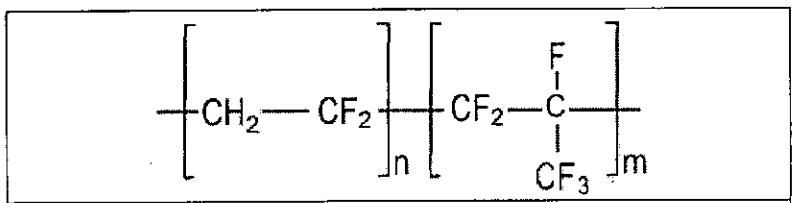

Figure 2.3. The Chemical Structure of PVDF-HFP

2.2.3 Product Matrix and Everolimus Content

Table 2.2. PROMUS Element™ Plus Stent System Product Matrix and Everolimus Content

Product Code MR	Product Code OTW	Nominal Expanded Stent Inner Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (µg)
H7493911408220	H7493911608220	2.25	8	38.2
H7493911408250	H7493911608250	2.50	8	38.9
H7493911408270	H7493911608270	2.75	8	38.9
H7493911408300	H7493911608300	3.00	8	42.0
H7493911408350	H7493911608350	3.50	8	42.0
H7493911408400	H7493911608400	4.00	8	56.1
H7493911412220	H7493911612220	2.25	12	57.3
H7493911412250	H7493911612250	2.50	12	60.6
H7493911412270	H7493911612270	2.75	12	60.6
H7493911412300	H7493911612300	3.00	12	60.1
H7493911412350	H7493911612350	3.50	12	60.1
H7493911412400	H7493911612400	4.00	12	80.4
H7493911416220	H7493911616220	2.25	16	72.7
H7493911416250	H7493911616250	2.50	16	78.0
H7493911416270	H7493911616270	2.75	16	78.0
H7493911416300	H7493911616300	3.00	16	84.3
H7493911416350	H7493911616350	3.50	16	84.3
H7493911416400	H7493911616400	4.00	16	104.6
H7493911420220	H7493911620220	2.25	20	91.8
H7493911420250	H7493911620250	2.50	20	95.4
H7493911420270	H7493911620270	2.75	20	95.4
H7493911420300	H7493911620300	3.00	20	102.4
H7493911420350	H7493911620350	3.50	20	102.4
H7493911420400	H7493911620400	4.00	20	128.8
H7493911424220	H7493911624220	2.25	24	107.2
H7493911424250	H7493911624250	2.50	24	112.7
H7493911424270	H7493911624270	2.75	24	112.7
H7493911424300	H7493911624300	3.00	24	120.5
H7493911424350	H7493911624350	3.50	24	120.5
H7493911424400	H7493911624400	4.00	24	153.0
H7493911428220	H7493911628220	2.25	28	126.3
H7493911428250	H7493911628250	2.50	28	130.1
H7493911428270	H7493911628270	2.75	28	130.1
H7493911428300	H7493911628300	3.00	28	138.6
H7493911428350	H7493911628350	3.50	28	138.6
H7493911428400	H7493911628400	4.00	28	177.3
H7493911432220	H7493911632220	2.25	32	145.5

3 INDICATIONS FOR USE:

The PROMUS Element™ Plus Everolimus-Eluting Platinum Chromium Coronary Stent System is indicated for improving luminal diameter in patients with symptomatic heart disease or documented silent ischemia due to de novo lesions in native coronary arteries ≥2.25 mm to ≤4.00 mm in diameter in lesions ≤28 mm in length.

4 CONTRAINDICATIONS:

Use of the PROMUS Element Plus Everolimus-Eluting Platinum Chromium Coronary Stent System is contraindicated in patients with known hypersensitivity to:

- 316L stainless steel or platinum
- everolimus or structurally-related compounds
- polymers or their individual components (see Section 2.2.2, Primer Polymer and Drug Matrix Copolymer Carrier)

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, visually confirm complete balloon deflation by fluoroscopy to avoid guiding catheter movement into the vessel and subsequent arterial damage.

• Stent thrombosis is a low-frequency event that current drug-eluting stent (DES) clinical trials are not adequately powered to fully characterize. Stent thrombosis is frequently associated with myocardial infarction (MI) or death. In the clinical trials analyzed to date, differences in the incidence of stent thrombosis

have not been associated with an increased risk of cardiac death, MI, or all-cause mortality. Additional data from longer-term follow-up of the PLATINUM clinical trials and analyses of stent thrombosis related to DES are expected and should be considered in making treatment decisions as data become available.

• When DES are used outside the specified Indications for Use, patient outcomes may differ from the results observed in the PLATINUM pivotal clinical trials.

• Compared to use within the specified Indications for Use, the use of DES in patients and lesions outside of the labeled indications may have an increased risk of adverse events, including stent thrombosis, stent embolization, MI or death.

• Orally-administered everolimus combined with cyclosporine is associated with increased serum cholesterol and triglyceride levels.

6.2 Pre- and Post-Procedure Antiplatelet Regimen

In the PLATINUM Clinical Program, a $P2Y_{12}$ inhibitor was administered pre-procedure and for a period of 6 months post procedure and for 12 months in patients who were not at high risk of bleeding. Aspirin was administered concomitantly with the $P2Y_{12}$ inhibitor t and then continued indefinitely to reduce the risk of thrombosis. See Section 10, Clinical Studies, for more specific information.

The optimal duration of antiplatelet therapy, specifically $P2Y_{12}$ inhibitor therapy 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 DES pivotal clinical trials may be beneficial. Provided herein are recent recommendations for post-procedural antiplatelet therapy from the 2011 ACCF/AHA/SCAI 2011 Guideline for Percutaneous Coronary Intervention (PCI); see Section 6.2.1, Oral Antiplatelet Therapy.

6.2.1 Oral Antiplatelet Therapy

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/full/j.jacc.2011.08.007v1

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, MI 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 DES and its associated recommended antiplatelet therapy is the appropriate PCI choice. Following PCI, should a surgical or dental procedure be recommended that requires suspension of antiplatelet therapy, the risks and benefits of the procedure should be weighed against the possible risk associated with premature discontinuation of antiplatelet therapy. Generally, it is recommended to postpone elective surgery for one year and among those patients for whom surgery cannot be deferred, ASA should be considered during 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 Longitudinal Stent Deformation

Crossing a newly deployed PROMUS Element™ stent with a second device, such as a balloon catheter, stent system or IVUS catheter, can lead to the second device becoming caught on the PROMUS Element stent. In this situation, if the second device is advanced or retracted, longitudinal stent deformation (i.e., longitudinal compression or elongation) of the PROMUS Element stent may occur, resulting in the need for additional treatment including repeat dilatation of the PROMUS Element, placement of a second stent, and/or surgical intervention.

Following the publication of three cases of longitudinal compression of a newly deployed DES (one of which was a PROMUS Element stent)1 Boston Scientific reviewed: (1) the PERSEUS trial (ION Stent) and PLATINUM trial (PROMUS Element Stent); and (2) all worldwide complaints received concerning ION and non-US complaints concerning PROMUS Element and Omega (bare metal stent) stent systems, all of which use the same PtCr stent platform.

Although the rate of longitudinal stent deformation is unknown, currently available information suggests that it is a rare adverse event. No cases of longitudinal stent deformation were observed in the PERSEUS trial (ION Stent) or the PLATINUM trial (PROMUS Element Stent). Based on the evaluation of the worldwide complaints concerning the Element platform, as of 31 October, 2011, there were 136 of longitudinal stent deformation events per 829,372 units sold. Of a total of 133 patients in whom longitudinal stent deformation was reported, additional stents were implanted in 76 patients, and 4 patients underwent surgery. An analysis of the complaint reports suggests that coronary artery calcification, vessel tortuosity, and stent mal-apposition in conjunction with crossing a newly deployed stent with an ancillary device may be associated with an increased risk of longitudinal stent deformation.

PROMUS Element was engineered to be a flexible, conformable stent. Characterization testing conducted by BSC indicates that some design features intended to produce these performance attributes may be associated with a reduction in longitudinal strength and contribute to the occurrence of longitudinal stent deformation. Although the majority of cases appear to occur following contact with an ancillary device, the definitive cause of longitudinal stent deformation remains uncertain.

The following procedural measures, recommended for implantation of all types of coronary stents, may reduce the risk of stent deformation:

1) Adequately prepare (predilate) the target lesion prior to stent implantation;
2) Implant the stent so that it is well-apposed to the underlying arterial wall;
3) Avoid deep seating the guide catheter;
4) Minimize wire bias where possible;
5) Use adequate inflation and deflation times for the stent device, and for any post-dilatation catheters used; typically longer times are required for longer length and/or larger diameter balloons;
6) When placing overlapped stents, place the most distal stent first;
7) If resistance is encountered when advancing an ancillary device through a stent, minimize wire bias and carefully reintroduce the ancillary device. If continued resistance to advancement is noted, cease attempts to place the ancillary device.
8) If longitudinal stent deformation occurs and requires treatment, additional balloon angioplasty or stent implantation should be considered to enhance stent apposition and provide adequate lesion treatment.

6.4 Use of Multiple Stents

In the PLATINUM Clinical Program, the protocols specified that lesions were to be treated with no more than one PROMUS Element™ stent, except in situations involving bailout stenting. The use of multiple DES will expose the patient to larger amounts of drug and polymer.

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

Potential interactions of the PROMUS Element stent with other drug-eluting or coated stents have not been evaluated and should be avoided whenever possible.

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[1] Hanratty CG, Walsh SJ. Longitudinal Compression: A "new" Complication with Modern Coronary Stent Platforms – Time to Think Beyond Deliverability? *EuroIntervention 2011 (Epub ahead of print)*

6.5 Brachytherapy

The safety and effectiveness of the PROMUS Element 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 PROMUS Element stent have not been established. Both vascular brachytherapy and the PROMUS Element stent alter arterial remodeling. The synergy between these two treatments has not been determined.

6.6 Use in Conjunction with Other Procedures

The safety and effectiveness of using mechanical atherectomy devices (directional atherectomy catheters or rotational atherectomy catheters) or laser angioplasty catheters in conjunction with PROMUS Element stent implantation have not been established.

6.7 Use in Special Populations

6.7.1 Pregnancy

Pregnancy "Category C". See Section 7.5, Pregnancy. The PROMUS Element™ stent has not been tested in pregnant women or in men intending to father children. Effects on the developing fetus have not been studied. Effective contraception should be initiated before implanting a PROMUS Element stent and continued for one year after implantation. While there is no contraindication, the risks and reproductive effects are unknown at this time.

6.7.2 Lactation

See Section 7.6, Lactation. A decision should be made whether to discontinue nursing prior to stent implantation considering the importance of the stent for the mother.

6.7.3 Gender

See Clinical Information – Section 10, Clinical Studies. Clinical studies of the PROMUS Element stent did not include formal analysis of differences in safety and effectiveness between male and female patients.

6.7.4 Ethnicity

See Clinical Information – Section 10, Clinical Studies. Clinical studies of the PROMUS Element stent did not include sufficient numbers of patients to assess for differences in safety and effectiveness due to ethnicity, either by individual category or when grouped by Caucasian and non-Caucasian.

6.7.5 Pediatric Use

The safety and effectiveness of the PROMUS Element stent in pediatric patients have not been established.

6.7.6 Geriatric Use

Clinical studies of the PROMUS Element stent did not have an upper age limit. Among the 862 patients treated with the PROMUS Element stent in the PLATINUM Workhorse and Small Vessel studies combined, 442 patients were age 65 or older and 43 patients were age 80 or older. A *post hoc* analysis of patients treated with the PROMUS Element stent showed no significant differences in 12-month clinical outcomes (primary endpoint of target lesion failure) between patients under age 65 and those age 65 or older with the exception of all death or MI (1.5% of patients under age 65 vs. 3.7% of patients age 65 or older) and cardiac death or MI (1.0% of patients under age 65 vs. 3.3% of patients age 65 or older).

6.8 Lesion/Vessel Characteristics

The safety and effectiveness of the PROMUS Element stent have not been established in the cerebral, carotid, or peripheral vasculature or in the following patient populations:

- Patients with vessel thrombus at the lesion site.

- Patients with coronary artery reference vessel diameters <2.25 or >4.00 mm.

• Patients with coronary artery lesions longer than 28 mm or requiring more than one PROMUS Element stent.

• Patients with lesions located in the saphenous vein grafts, in the left main coronary artery, ostial lesions, or lesions located at a bifurcation.

• Patients with diffuse disease or poor flow distal to the identified lesions.

• Patients with tortuous vessels (>60 degrees) in the region of the obstruction or proximal to the lesion.

• Patients with a recent acute myocardial infarction where there is evidence of thrombus or poor flow.

• Patients with in-stent restenosis.

• Patients with moderate or severe calcification in the lesion or a chronic total occlusion.

• Patients with 3 vessel disease

6.9 Drug Interactions

See Section 7.3, Drug Interactions. Several drugs are known to affect everolimus metabolism, and other drug interactions may also occur. Everolimus is known to be a substrate for both P4503A4 (CYP3A4) and P-glycoprotein. Everolimus absorption and subsequent elimination may be influenced by drugs that affect these pathways. Everolimus has also been shown to reduce the clearance of some prescription medications when administered orally along with cyclosporine (CsA). Formal drug interaction studies have not been performed with the PROMUS Element™ stent because of limited systemic exposure to everolimus eluted from the stent used in the PLATINUM clinical trials (see Section 7.2, Pharmacokinetics). Therefore, due consideration should be given to the potential for both systemic and local drug interactions in the vessel wall when deciding to place a PROMUS Element stent in a patient taking a drug with known interaction with everolimus, or when deciding to initiate therapy with such a drug in a patient who has recently received a PROMUS Element stent.

6.10 Immune Suppression Potential

Everolimus, the PROMUS Element stent active ingredient, is an immunosuppressive agent. Immune suppression as a result of everolimus exposure was not observed in the PLATINUM Clinical Program. However, for patients who receive several PROMUS Element stents simultaneously, it may be possible for everolimus systemic concentrations to approach immunosuppressive levels temporarily, especially in patients who also have hepatic insufficiency or who are taking drugs that inhibit CYP3A4 or P-glycoprotein. Therefore, consideration should be given to patients taking other immunosuppressive agents or who are at risk for immune suppression.

6.11 Lipid Elevation Potential

Oral everolimus use in renal transplant patients was associated with increased serum cholesterol and triglycerides that in some cases required treatment. The effect was seen with both low- and high-dose prolonged oral therapy in a dose-related manner. When used according to the indications for use, exposure to systemic everolimus concentrations from the PROMUS Element stent is expected to be significantly lower than concentrations usually obtained in transplant patients. Increased serum cholesterol and triglycerides as a result of everolimus exposure were not observed in the PLATINUM Clinical Program.

6.12 Magnetic Resonance Imaging (MRI)

The PROMUS Element stent has been shown to be MR Conditional (poses no known hazards under specified conditions) through non-clinical testing of single and overlapped configurations up to 74 mm. The conditions are as follows:

- Field strengths of 1.5 and 3 Tesla
- Static magnetic field gradient <900 gauss/cm (extrapolated)

- Normal operational mode (maximum whole body averaged specific absorption rate (SAR) of lower than 2.0 W/kg) for a total active MR scan time (with RF exposure) of 15 minutes or less

The PROMUS Element 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 on continuously stented lengths up to 74 mm. RF power was applied for 15 minutes and the measured conductivity of the phantom material was about 0.3 S/m. The phantom average SAR was calculated using calorimetry to be 2.2 W/kg. The maximal in-vitro temperature rise was calculated as 2.6°C for a measured stent length of 74 mm with the whole-body SAR scaled to 2.0 W/kg. 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 on continuously stented lengths up to 74 mm. RF power was applied for 15 minutes and the measured conductivity of the phantom material was about 0.3 S/m. The phantom average SAR was calculated using calorimetry to be 2.1 W/kg. The maximal in-vitro temperature rise was calculated as 2.6°C for a measured stent length of 39 mm with the whole-body SAR scaled to 2.0 W/kg. 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 7 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 5 mm beyond the perimeter of the diameter and 6 mm beyond each end of the length with both sequences partially shielding the lumen in a 3.0 Tesla Intera (Achieva Upgrade), Philips Medical Solutions, software version Release 2.5.3.0 2007-09-28 MR system with a transmit/receive head coil.

Medical Registration

It is recommended that patients register the conditions under which the implant can be scanned safely with the MedicAlert Foundation (www.medicalert.org) or equivalent organization.

MR Conditional

6.13 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 Section 1, Warning)

• The premounted PROMUS Element™ 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 Section 14.3.3, Balloon Preparation). Do not use air or any gas medium to inflate the balloon.

• In the event the PROMUS Element stent is not deployed, do not use the product and contact your local Boston Scientific Representative for return information.

6.14 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 Section 14.3.3, Balloon Preparation.

• If unusual resistance is felt at any time during lesion access before stent implantation, the stent delivery system and the guide catheter should be removed as a single unit (see Section 6.15, Stent Delivery 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 Section 6.15, Stent Delivery System Removal).

• Balloon pressures should be monitored during inflation. Do not exceed rated burst pressure as indicated on product label (see Section 14.5, In Vitro Information, Table 14.5.1, Typical PROMUS Element Plus Stent System Compliance). Use of pressures higher than specified on product label may result in a ruptured balloon and 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 (see Section 14.4, Post-Deployment Dilatation of Stented Segments).

• 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 generally be stented first, 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.

6.15 Stent Delivery System Removal

• If unusual resistance is felt at any time during lesion access before stent implantation, the stent delivery 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 delivery system and guide catheter as a single unit, the following steps should be executed under direct visualization using fluoroscopy:

• Following stent placement, confirm complete balloon deflation (See Table 6.1, Delivery 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 delivery system until the proximal balloon marker of the stent delivery system is just distal to the guide catheter distal tip.

• The stent delivery 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 delivery system into the guide catheter and remove the stent delivery 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 delivery system, can potentially result in stent or coating damage, stent dislodgment from the balloon, and/or damage to the delivery system.

Table 6.1. Delivery System Deflation Time Specifications (Seconds)

Balloon Length/ Diameter	8 mm	12 mm	16 mm	20 mm	24 mm	28 mm	32 mm
2.25 mm	≤16			≤16		≤16	≤16
2.50 mm							N/A
2.75 mm						≤21	N/A
3.00 mm							
3.50 mm				≤21			
4.00 mm							

6.16 Post-Procedure

• Care must be exercised when crossing a newly deployed stent with any wire, catheter or ancillary device to avoid disrupting the stent placement, apposition, geometry, and/or coating.

• In the PLATINUM Clinical Program, a $P2Y_{12}$ inhibitor was administered pre-procedure and for a period of 6 months post-procedure and for 12 months in patients who were not at high risk of bleeding. Aspirin was administered concomitantly with $P2Y_{12}$ inhibitor 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 Section 6.12, Magnetic Resonance Imaging (MRI).

7 DRUG INFORMATION:

7.1 Mechanism of Action

The mechanism by which the PROMUS Element™ stent inhibits neointimal growth as seen in pre-clinical and clinical studies has not been established. At the cellular level, everolimus inhibits growth factor-stimulated cell proliferation. At the molecular level, everolimus forms a complex with the cytoplasmic protein FKBP-12 (FK 506 Binding Protein). This complex binds to and interferes with FRAP (FKBP-12 Rapamycin Associated Protein), also known as mTOR (mammalian Target Of Rapamycin), leading to inhibition of cell metabolism, growth and proliferation by arresting the cell cycle at the late G1 stage.

7.2 Pharmacokinetics

Everolimus pharmacokinetics (PK) when eluted from the PROMUS Element stent post-implantation have been evaluated in patients from two different geographies (the United States of America [USA] and Japan) in a non-randomized sub-study of the PLATINUM clinical trial. Whole blood everolimus PK parameters determined from patients receiving the PROMUS Element stent are provided in Table 7.2.

Table 7.2. Whole Blood Everolimus Pharmacokinetic Parameters (Mean ± SD) for PLATINUM Groups with Three or More Patients Following PROMUS Element Stent Implantation

Region	USA	Japan		Combined		
Dose (µg)	102.4 µg	102.4 µg	138.6 µg	95.4 µg	102.4 µg	138.6 µg
n	3	4 [b]	3 [b]	4 [c]	7 [b]	3 [b]
t_{max}: (h)	0.66 ± 0.27	0.60 ± 0.22	0.52 ± 0.09	0.47 ± 0.03	0.62 ± 0.23	0.52 ± 0.09
C_{max}: (ng/mL)	0.58 ± 0.078	0.73 ± 0.17	0.91 ± 0.20	0.71 ± 0.09	0.67 ± 0.15	0.91 ± 0.20
AUC_{0-t}: (ng.h/mL)	4.77 ± 1.70	7.71 ± 6.97	10.87 ± 7.36	7.27 ± 4.97	6.45 ± 5.26	10.87 ± 7.36
AUC_{0-24h}: (ng.h/mL)	5.76 ± 0.85	6.42 ± 1.30	9.51 ± 0.64	6.83 ± 2.03	6.14 ± 1.10	9.51 ± 0.64
$AUC_{0-\infty}$: [a] (ng.h/mL)	NA	11.91 ± 1.39	60.74 ± 25.95	19.26 ± 11.69	12.95 ± 2.05	60.74 ± 25.95
$t_{1/2}$: [a] (h)	NA	18.77 ± 2.11	136.06 ± 62.08	34.19 ± 20.81	22.83 ± 7.20	136.06 ± 62.08
CL: [a] (L/h)	NA	8656 ± 1005	2511 ± 1073	6445 ± 3924	8044 ± 1276	2511 ± 1073

NA: Not assessable
[a]: Accurate determination not possible
[b]: n=2 for $AUC_{0-\infty}$, $t_{1/2term}$ and CL
[c]: n=3 for $AUC_{0-\infty}$, $t_{1/2term}$ and CL
t_{max} (h)= time to maximum concentration.
C_{max}= maximum observed blood concentration.
$t_{1/2}$ (h)= terminal phase half-life.
AUC_{0-t} = the area beneath the blood concentration versus time curve: time zero to the final quantifiable concentration
AUC_{0-24h} = the area beneath the blood concentration versus time curve: time zero to 24 hours post-implant
$AUC_{0-\infty}$ = the area beneath the blood concentration versus time curve: time zero to the extrapolated infinite time
CL= total blood clearance

The results show that individual whole blood concentrations of everolimus tended to increase in proportion to the total dose. Individual t_{max} values ranged from 0.42 to 1.17 hours. Individual C_{max} values ranged from 0.25 to 1.10 ng/mL. AUC_{0-24h} values ranged from 0.64 to 9.96 ng.h/mL, while AUC_{0-t} values ranged from 0.24 to 18.15 ng.h/mL. The concentration of everolimus was below the limit of quantification in all patients except for one at 72 hours. The C_{max} value never reached the minimum therapeutic value of 3.0 ng/mL necessary for effective systemic administration to prevent organ rejection. The PK parameters representing elimination $t_{½}$, AUC_{0-t}, AUC_{last}, $AUC_{0-\infty}$, and total blood clearance (CL) could also not be determined accurately due to rapid everolimus disappearance from blood. These types of results have been seen with other drug-eluting stents.

Everolimus disappearance from circulation following PROMUS Element™ stent implantation should further limit systemic exposure and adverse events associated with long-term systemic administration at therapeutic levels. Despite limited systemic exposure to everolimus, consistent local arterial delivery of everolimus from the stent has been demonstrated in pre-clinical studies.

7.3 Drug Interactions

Everolimus is extensively metabolized by the cytochrome P4503A4 (CYP3A4), in the gut wall and liver and is a substrate for the countertransporter P-glycoprotein. Therefore, absorption and subsequent elimination of everolimus may be influenced by drugs that also affect this pathway. Everolimus has also been shown to reduce the clearance of some prescription medications when it was administered orally along with a cyclosporine (CsA). Formal drug interaction studies have not been performed with the PROMUS Element stent because of limited systemic exposure to everolimus eluted from the stent (see Section 6.9, Drug Interaction and Section 7.2, Pharmacokinetics). However, consideration should be given to the potential for both systemic and local drug interactions in the vessel wall when deciding to place the PROMUS Element stent in a patient taking a drug with known interaction with everolimus.

Everolimus, when prescribed as an oral medication, may interact with the drugs/foods listed below. Medications that are strong inhibitors of CYP3A4 or PgP might reduce everolimus metabolism in vivo. Hence, co-administration of strong inhibitors of CYP3A4 or PgP may increase the blood concentrations of everolimus.

- CYP3A4 isozyme inhibitors (ketoconazole, itraconazole, voriconazole, ritonavir, erythromycin, clarithromycin, fluconazole, calcium channel blockers [verapamil and diltiazem], aprepitant, atazanavir, nefazodone, amprenavir, indinavir, nelfinavir, delavirdine, fosamprenavir, saquinavir and telithromycinInducers of CYP3A4 isozyme (rifampin, rifabutin, carbamazepine, phenobarbital, phenytoin, St. John's Wort, efavirenz, nevirapine, and dexamethasone)
- Antibiotics (ciprofloxacin, ofloxacin)
- Glucocorticoids
- HMGCoA reductase inhibitors (simvastatin, lovastatin)
- PgP inhibitors (digoxin, cyclosporine)
- Cisapride (theoretical potential interaction)
- Sildenafil (Viagra®) (theoretical potential interaction)
- Antihistaminics (terfenadine, astemizole)
- Grapefruit/grapefruit juice

Zortress®, the oral formulation of everolimus developed by Novartis Pharmaceuticals Corporation, has been evaluated in clinical trials and is approved in the United States for the prevention of organ rejection in adult kidney transplant recipients at the dose of 1.5 mg/day. Outside the U.S., Zortress® is sold under the brand name, Certican®, in more than 70 countries. Everolimus is also approved in the United States under the name of Afinitor ® for patients with advanced renal cell carcinoma (cancer), after failure of treatment with sunitinib or sorafenib, at doses of 5 to 20 mg/day when taken by mouth. The following list includes the known risks of everolimus at the oral doses listed above. The amount of drug that circulates in the bloodstream following implantation of a PROMUS Element stent is several folds lower than that obtained with oral doses (1.5 mg to 20 mg/day, see Section 7.2, Pharmacokinetics).

7.4 Carcinogenicity, Genotoxicity, and Reproductive Toxicology

The PROMUS Element stent uses the same drug and polymers (see Section 2, Device Description) as PROMUS; everolimus release, blood levels and arterial tissue concentrations are similar. Therefore, data from carcinogenicity, genotoxicity and reproductive toxicology studies of the PROMUS stent are considered to be representative of the PROMUS Element stent, and relevant data from studies of PROMUS are included below in addition to data from studies of PROMUS Element.

A 26-week carcinogenicity study was conducted to evaluate the carcinogenic potential of PROMUS (Xience V) stents following subcutaneous implantation in transgenic mice. During the course of the study, there were no abnormal clinical observations that suggested a carcinogenic effect of the test group PROMUS (Xience V) stent. The test group did not demonstrate an increased incidence of neoplastic lesions when compared to the negative control group. However, the positive control and the experimental positive control groups demonstrated notable increases in the incidence of neoplastic lesions compared to either the test or the

negative control group. Based on the results of this study, the PROMUS (Xience V) stent does not appear to be carcinogenic when implanted in transgenic mice for 26 weeks.

Genotoxicity studies were conducted on the PROMUS Element stent in both the in vivo and in vitro (mammalian cells and bacteria) systems. These studies included tests for gene mutations in bacteria (Ames assay), gene mutations and chromosomal aberrations in mammalian cells (mouse lymphoma assay), and for clastogenicity in mouse bone marrow cells (erythrocyte micronucleus assay). Based on these results the PROMUS Element stent is not genotoxic.

In addition, a reproductive toxicity (teratology) study was conducted to demonstrate that implantation of PROMUS (Xience V) stents in female Sprague-Dawley rats does not affect their fertility or reproductive capability and shows a lack of any reproductive toxicity on their offspring. There was no statistical difference between the test article PROMUS (Xience V) stent and the control system in terms of any of the evaluated parameters. The test article had no effect on litter size and caused no increase of in-utero mortality. Additionally, the PROMUS (Xience V) stent did not cause any reproductive toxicity in the offspring in this study.

7.5 Pregnancy

Pregnancy Category C: There are no adequate everolimus or PROMUS Element™ stent related studies in pregnant women. Effects of a similar stent ,(PROMUS) on prenatal and postnatal rat development were not different than the controls. When administered at oral doses of 0.1 mg/kg or above, everolimus showed effects on prenatal and postnatal rat development limited to slight body weight changes and fetal survival without any specific toxic potential.

Effective contraception should be initiated before implanting a PROMUS Element stent and continued for one year post-implantation. The PROMUS Element stent should be used in pregnant women only if the potential benefits justify the potential risks.

Safety of the PROMUS Element stent has not been evaluated in males intending to father children.

7.6 Lactation

It is not known whether everolimus is distributed in human milk. Also, everolimus pharmacokinetic and safety profiles have not been determined in infants. Consequently, mothers should be advised of potential serious adverse reactions to everolimus in nursing infants. Prior to PROMUS Element stent implantation, decisions should be made regarding whether to discontinue nursing or conduct an alternative percutaneous coronary intervention procedure.

8 OVERVIEW OF CLINICAL STUDIES

The PLATINUM Clinical Program is evaluating the PROMUS Element Everolimus-Eluting Platinum Chromium Coronary Stent System for the treatment of *de novo* atherosclerotic lesions in 5 parallel studies. The Program includes the PLATINUM Trial, which comprises a workhorse (WH) randomized controlled trial (RCT) with single-arm small vessel (SV), long lesion (LL), and pharmacokinetics (PK) sub-studies, and the PLATINUM quantitative coronary angiography (QCA) study. This overview includes a summary of the PLATINUM WH, SV, PK and QCA trial designs as well as results from each. A summary of the WH, SV, PK and QCA trial designs is presented in Table 8.1.

8.1 PLATINUM Workhorse (WH) Randomized Controlled Trial (RCT)

The PLATINUM Workhorse (WH) Trial is a prospective, randomized, controlled, single-blind, multi-center, non-inferiority trial designed to evaluate the safety and effectiveness of the PROMUS Element Everolimus-Eluting Platinum Chromium Coronary Stent System compared to the PROMUS Everolimus-Eluting Cobalt Chromium Coronary Stent System for the treatment of *de novo* coronary lesions. Patients with a maximum of 2 *de novo* lesions ≤24 mm in length (visual estimate) in native coronary arteries ≥2.50 mm to ≤4.25 mm (visual estimate) in diameter were considered for enrollment. The trial employs a 1:1 randomization to the PROMUS Element or PROMUS everolimus-eluting stents, respectively.

The primary endpoint was the rate of target lesion failure (TLF), defined as any ischemia-driven revascularization of the target lesion (TLR), myocardial infarction (MI) (Q-wave and non–Q-wave) related to

the target vessel, or cardiac death related to the target vessel, at 12 months post-index procedure. The PLATINUM WH study was designed to test the hypothesis that the rate of 12-month TLF in patients treated with the PROMUS Element stent is non-inferior to the rate of 12-month TLF in patients treated with the PROMUS stent control.

A total of 1,530 patients (768 PROMUS Element stent and 762 PROMUS stent) were randomized and enrolled at 132 sites in 17 countries in the Asia-Pacific region, Europe, Japan, and the United States. The protocol mandated antiplatelet therapy compliance in accordance with the 2007 ACC/AHA/SCAI Guidelines for PCI.[2]

The study is now considered complete with regard to the 12-month primary endpoint. Additional follow-up is ongoing to 5 years.

8.2 PLATINUM Small Vessel (SV) Sub-study

PLATINUM SV is a prospective, single-arm, multi-center sub-study of the PLATINUM Trial designed to evaluate the safety and effectiveness of the PROMUS Element Everolimus-Eluting Platinum Chromium Coronary Stent System for the treatment of *de novo* coronary lesions in small vessels. Patients with a single target lesion ≤28 mm (visual estimate) in length in a native coronary artery ≥2.25 mm to <2.50 mm (visual estimate) were considered for enrollment. The sub-study compares outcomes in patients treated with the 2.25 mm PROMUS Element stent to a performance goal based on results with the TAXUS Express small vessel stent in the TAXUS V *De Novo* Trial.

The primary endpoint was the rate of TLF at 12 months post-index procedure, compared to a performance goal based on outcomes in patients with one planned 2.25 mm TAXUS Express stent from the TAXUS V *De Novo* Trial.

A total of 94 patients were enrolled at 23 sites in Australia, Belgium, France, Japan, New Zealand, and the United States. The protocol mandated antiplatelet therapy compliance in accordance with the 2007 ACC/AHA/SCAI Guidelines for PCI.[3]

The sub-study is now considered complete with regard to the 12-month primary endpoint. Additional follow-up is ongoing to 5 years.

8.3 PLATINUM Pharmacokinetics (PK) Sub-study

PLATINUM PK is a prospective, single-arm, multi-center, observational sub-study of the PLATINUM Trial to evaluate everolimus blood levels following stent implantation in patients who undergo treatment with the PROMUS Element Everolimus-Eluting Platinum Chromium Coronary Stent System.

Patients with a maximum of 2 *de novo* lesions ≤24 mm (visual estimate) in length in native coronary arteries ≥2.50 mm to ≤4.25 mm (visual estimate) were considered for enrollment.

A total of 22 patients were enrolled at 2 sites in the United States and 3 sites in Japan. The protocol mandated antiplatelet therapy compliance in accordance with the 2007 ACC/AHA/SCAI Guidelines for PCI.[2]

Follow-up is ongoing to 5 years.

See Section 7.2, Pharmacokinetics.

[2] King SB, 3rd, Smith SC, Jr., Hirshfeld JW, Jr., et al. 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: 2007 Writing Group to Review New Evidence and Update the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention, Writing on Behalf of the 2005 Writing Committee. *Circulation* 2008;117:261-95.

8.4 PLATINUM Quantitative Coronary Angiography (QCA) Trial

PLATINUM QCA is a prospective, single-arm, multi-center, observational study designed to evaluate clinical, angiographic and IVUS outcomes in *de novo* atherosclerotic coronary lesions treated with the PROMUS Element Everolimus-Eluting Platinum Chromium Coronary Stent System. Patients with a single target lesion ≤34 mm (visual estimate) in length in a native coronary artery ≥2.25 mm and ≤4.25 mm (visual estimate) were considered for enrollment.

The primary endpoint was the 30-day composite rate of cardiac death, MI (Q-wave and non–Q-wave), target lesion revascularization (TLR), and stent thrombosis (ST). All patients were required to undergo 9-month angiography and IVUS assessments. Efficacy endpoints of in-stent late loss at 9 months (determined by QCA) in patients with workhorse target lesions (visual RVD ≥2.5 mm and ≤4.25 mm and visual lesion length ≤24 mm) and post-procedure incomplete apposition (determined by IVUS) were compared to predefined performance goals. For 9-month in-stent late loss, the performance goal was based on historical TAXUS Express stent results. For post-procedure incomplete apposition, the performance goal was based on historical PROMUS (Xience V) post-procedure incomplete apposition data from the SPIRIT III study.

A total of 100 patients were enrolled at 14 sites in Australia, Malaysia, New Zealand, and Singapore. The protocol mandated antiplatelet therapy compliance in accordance with the 2007 ACC/AHA/SCAI Guidelines for PCI.[4] The study is complete.

Table 8.1. Comparison of PLATINUM Clinical Studies

	PLATINUM			PLATINUM QCA
	Workhorse RCT	**Small Vessel**	**PK**	
Purpose	Evaluation of safety and effectiveness in workhorse lesions	Evaluation of safety and effectiveness in small vessel lesions	Evaluation of everolimus blood levels	Evaluation of angiographic and IVUS outcomes
Study Design	Prospective, randomized, controlled, multi-center, single-blind non-inferiority to PROMUS	Prospective, single arm, multicenter, comparison to performance goal	Prospective, single arm, multicenter, observational	Prospective, single arm, multicenter, observational; comparisons of 2 effectiveness endpoints to performance goals
Primary Endpoint	12M TLF	12M TLF	N/A, observational	30D composite rate (cardiac death, MI, TLR, ST)
Number of Patients (ITT)	1530 enrolled; PROMUS Element: 768 PROMUS: 762	94 PROMUS Element	22 PROMUS Element	100 PROMUS Element
Polymer	PBMA, PVDF-HFP			
Everolimus Dose Density	100 μg/cm^2			
Lesion Criteria: Vessel Diameter (by visual estimate), mm	≥2.50 to ≤4.25	≥2.25 to <2.50	≥2.50 to ≤4.25	≥2.25 to ≤4.25
Lesion Criteria: Lesion Length (by visual estimate), mm	≤24	≤28	≤24	≤34
Total Target Lesions	Up to 2	1	Up to 2	1
Stent Matrix	2.50-4.00 mm	2.25 mm	2.50-4.00 mm	2.25-4.00 mm

[4] King SB, 3rd, Smith SC, Jr., Hirshfeld JW, Jr., et al. 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: 2007 Writing Group to Review New Evidence and Update the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention, Writing on Behalf of the 2005 Writing Committee. *Circulation* 2008;117:261-95.

Table 8.1. Comparison of PLATINUM Clinical Studies				
	PLATINUM			PLATINUM QCA
	Workhorse RCT	Small Vessel	PK	
	diameter 12, 18/20[1], 28 mm length	diameter 12, 20, 28, 32 mm length	diameter 12, 20, 28 mm length	diameter 12, 20, 28, 32, 38[2] mm length
Post-Procedure Antiplatelet Therapy	A thienopyridine $P2Y_{12}$ inhibitor for at least 6 months, ideally for 12 months in patients who were not at high risk of bleeding. ASA: indefinitely			
Follow-Up	Clinical: 30 days, 6 months, 1 year, 18 months, annually 2-5 years			Clinical: 30 day, 9 month, 1 year; Angiographic: 9 month; IVUS: 9 month
[1]PROMUS available in 18 mm length; PROMUS Element available in 20 mm length. [2]2.25 mm stent not available in 38 mm length. Abbreviations: ASA=aspirin; ITT=intent-to-treat; IVUS=intravascular ultrasound; MI=myocardial infarction; PK=pharmacokinetics; PBMA=poly (n-butyl methacrylate); PVDF-HFP=poly (vinylidene fluoride-co-hexafluoropropylene); QCA=quantitative coronary angiography; RCT=randomized controlled trial; ST=stent thrombosis; TLF=target lesion failure; TLR=target lesion revascularization				

9 ADVERSE EVENTS

9.1 Observed Adverse Events

Observed adverse event experience comes from the PLATINUM Workhorse RCT, PLATINUM Small Vessel Sub-study and PLATINUM Quantitative Coronary Angiography Study. Major clinical events for these studies are shown in Table 9.1.1.

Table 9.1.1. PLATINUM Workhorse, PLATINUM Small Vessel and PLATINUM QCA Major Clinical Events From Post-Procedure to 1-Year Follow-Up				
	PLATINUM Workhorse		PLATINUM Small Vessel	PLATINUM QCA
	PROMUS Element Stent (n=768)	PROMUS Stent[1] (n=762)	PROMUS Element Stent (n=94)	PROMUS Element Stent (n=100)
In-Hospital All death, MI, TVR	0.9% (7/768)	1.2% (9/762)	0.0% (0/94)	1.0% (1/100)
All Death	0.1% (1/768)	0.0% (0/762)	0.0% (0/94)	0.0% (0/100)
Cardiac Death	0.1% (1/768)	0.0% (0/762)	0.0% (0/94)	0.0% (0/100)
Non-cardiac Death	0.0% (0/768)	0.0% (0/762)	0.0% (0/94)	0.0% (0/100)
MI	0.7% (5/768)	1.0% (8/762)	0.0% (0/94)	0.0% (0/100)
Q-Wave MI	0.0% (0/768)	0.3% (2/762)	0.0% (0/94)	0.0% (0/100)
Non-Q-Wave MI	0.7% (5/768)	0.8% (6/762)	0.0% (0/94)	0.0% (0/100)
Cardiac death or MI	0.8% (6/768)	1.0% (8/762)	0.0% (0/94)	0.0% (0/100)
TVR	0.1% (1/768)	0.7% (5/762)	0.0% (0/94)	1.0% (1/100)
TLR	0.1% (1/768)	0.7% (5/762)	0.0% (0/94)	1.0% (1/100)
Non-TLR	0.0% (0/768)	0.0% (0/762)	0.0% (0/94)	1.0% (1/100)
30-Day All death, MI, TVR	0.9% (7/766)	1.6% (12/761)	0.0% (0/94)	1.0% (1/100)
1-Year All death, MI, TVR	5.0% (37/745)	4.9% (36/732)	7.8% (7/90)	1.0% (1/100)
All Death	1.3% (10/745)	1.2% (9/732)	4.4% (4/90)	0.0% (0/100)

Table 9.1.1. PLATINUM Workhorse, PLATINUM Small Vessel and PLATINUM QCA Major Clinical Events From Post-Procedure to 1-Year Follow-Up				
Cardiac Death	0.9% (7/745)	0.7% (5/732)	3.3% (3/90)	0.0% (0/100)
Non-cardiac Death	0.4% (3/745)	0.5% (4/732)	1.1% (1/90)	0.0% (0/100)
MI	1.1% (8/745)	1.8% (13/732)	0.0% (0/90)	0.0% (0/100)
Q-Wave MI	0.1% (1/745)	0.7% (5/732)	0.0% (0/90)	0.0% (0/100)
Non-Q-Wave MI	0.9% (7/745)	1.2% (9/732)	0.0% (0/90)	0.0% (0/100)
TVR	2.7% (20/745)	2.9% (21/732)	3.3% (3/90)	1.0% (1/100)
TLR	1.9% (14/745)	1.9% (14/732)	2.2% (2/90)	1.0% (1/100)
Non-TLR	0.9% (7/745)	1.1% (8/732)	1.1% (1/90)	1.0% (1/100)
In-Hospital ARC Stent Thrombosis				
Definite or Probable	0.1% (1/768)	0.1% (1/762)	0.0% (0/94)	1.0% (1/100)
Definite	0.1% (1/768)	0.1% (1/762)	0.0% (0/94)	1.0% (1/100)
Probable	0.0% (0/768)	0.0% (0/762)	0.0% (0/94)	0.0% (0/100)
1-Year ARC Stent Thrombosis				
Definite or Probable	0.4% (3/735)	0.4% (3/725)	0.0% (0/86)	1.0% (1/100)
Definite	0.4% (3/735)	0.4% (3/725)	0.0% (0/86)	1.0% (1/100)
Probable	0.0% (0/735)	0.0% (0/725)	0.0% (0/86)	0.0% (0/100)

[1] DES Control

Numbers are % (Count/Sample Size)

Abbreviations: ARC=Academic Research Consortium; DES=drug-eluting stent; MI=myocardial infarction; QCA=Quantitative Coronary Angiography; TLR=target lesion revascularization; TVR=target vessel revascularization.

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 and ventricular tachycardia
- Arteriovenous fistula
- Bleeding
- 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, which may require transfusion
- Hypotension/hypertension
- Infection, local or systemic
- Ischemia, myocardial
- Pain, access site
- Perforation or rupture of coronary artery
- Pericardial effusion
- Pseudoaneurysm, femoral

- Renal insufficiency or failure
- Respiratory failure
- Restenosis of stented segment
- Stent embolization or migration
- Stent fracture
- Stent thrombosis/occlusion
- Stroke/cerebrovascular accident/transient ischemic attack
- Total occlusion of coronary artery
- Vessel spasm
- Vessel trauma requiring surgical repair or reintervention

Zortress®, the oral formulation of everolimus developed by Novartis Pharmaceuticals Corporation, has been evaluated in clinical trials and is approved in the United States for the prevention of organ rejection in adult kidney transplant recipients at the dose of 1.5 mg/day. Outside the U.S., Zortress® is sold under the brand name, Certican®, in more than 70 countries. Everolimus is also approved in the United States under the name of Afinitor ®for patients with advanced renal cell carcinoma (cancer), after failure of treatment with sunitinib or sorafenib, at doses of 5 to 20 mg/day when taken by mouth. The following list includes the known risks of everolimus at the oral doses listed above . The amount of drug that circulates in the bloodstream following implantation of a PROMUS Element stent is several folds lower than that obtained with oral doses (1.5 mg to 20 mg/day, see Section 7.2, Pharmacokinetics).

- Abdominal pain (including upper abdominal pain)
- Anemia
- Angioedema
- Anorexia
- Asthenia
- Constipation
- Cough
- Delayed wound healing/fluid accumulation
- Diarrhea
- Dyslipidemia (including hyperlipidemia and hypercholesterolemia)
- Dysgeusia
- Dyspepsia
- Dyspnea
- Dysuria
- Dry skin
- Edema (peripheral)
- Epistaxis
- Fatigue
- Headache
- Hematuria
- Hyperglycemia (may include new onset of diabetes)
- Hyperkalemia
- Hyperlipidemia
- Hypertension
- Hypokalemia
- Hypomagnesemia
- Hypophosphatemia
- Increased serum creatinine
- Infections and serious infections: bacterial, viral, fungal, and protozoal infections (may include herpes virus infection, polyoma virus infection which may be associated with BK virus associated nephropathy, and/or other opportunistic infections)
- Insomnia
- Interaction with strong inhibitors and inducers of CY3PA4
- Leukopenia
- Lymphoma and other malignancies (including skin cancer)
- Male infertility (azospermia and/or oligospermia)
- Mucosal inflammation (including oral ulceration and oral mucositis)
- Nausea

- Neutropenia
- Non-infectious pneumonitis
- Pain: extremity, incision site and procedural, back, chest, musculoskeletal
- Proteinuria
- Pruritus
- Pyrexia
- Rash
- Stomatitis
- Thrombocytopenia
- Thrombotic microangiopathy (TMA)/Thrombotic thrombocytopenic purpura (TTP)/Hemolytic uremic syndrome (HUS)
- Tremor
- Upper respiratory tract infection
- Urinary tract infection
- Vomiting

Live vaccines should be avoided and close contact with those that have had live vaccines should be avoided. Fetal harm can occur when administered to a pregnant woman. There may be other potential adverse events that are unforeseen at this time.

10 CLINICAL STUDIES

10.1 PLATINUM Workhorse (WH) Randomized Controlled Trial (RCT)

Primary Objective: The primary objective of the PLATINUM WH RCT was to evaluate the safety and efficacy of the PROMUS Element Everolimus-Eluting Platinum Chromium Coronary Stent System compared to the PROMUS Everolimus-Eluting Cobalt Chromium Coronary Stent System for the treatment of *de novo* atherosclerotic lesions of up to 24 mm in length (by visual estimate) in native coronary arteries of 2.50 mm to 4.25 mm in diameter (by visual estimate).

Design: PLATINUM WH is a prospective, randomized, controlled, single-blind, multi-center non-inferiority trial employing a 1:1 randomization to the PROMUS Element (test) or PROMUS (control) everolimus-eluting stent. Eligible patients were those ≥18 years old with left ventricular ejection fraction (LVEF) ≥30% and with documented stable angina pectoris, silent ischemia, or unstable angina pectoris. *De novo* target lesions in a native coronary artery with diameter stenosis ≥50% and <100% with Thrombolysis in Myocardial Infarction (TIMI) flow >1, reference vessel diameter ≥2.50 mm and ≤4.25 mm (visual estimate), and lesion length ≤24 mm (visual estimate) were eligible. Patients could have 1 or 2 target lesions treated. Patients with a single target lesion treated could also have 1 *de novo* native coronary artery lesion within a different epicardial vessel (non-target lesion) treated with a commercially-available treatment (e.g., stent, balloon angioplasty, excluding brachytherapy) during the index procedure. The non-target lesion had to be treated before the target lesion and the treatment had to be a clinical angiographic success (defined as visually assessed stenosis <50% [<30% for stents] with TIMI 3 flow without prolonged chest pain or electrocardiogram [ECG] changes consistent with MI) before the patient could be enrolled. The protocol mandated antiplatelet therapy compliance in accordance with the 2007 ACC/AHA/SCAI Guidelines for PCI.[5]

The primary endpoint was the rate of target lesion failure (TLF), defined as any ischemia-driven revascularization of the target lesion (TLR), MI (Q-wave and non–Q-wave) related to the target vessel, or cardiac death related to the target vessel, at 12 months post-index procedure. The PLATINUM WH study was designed to test the hypothesis that the rate of 12-month TLF in patients treated with the PROMUS Element stent is non-inferior to the rate of 12-month TLF in patients treated with the PROMUS stent control.

A total of 1,530 patients (768 PROMUS Element™ stent and 762 PROMUS stent) were randomized and enrolled at 132 sites. Of the 1,530 patients included in the intent-to-treat analysis set, a total of 1,469 patients (742 PROMUS Element and 727 PROMUS) were evaluable for the 12-month primary endpoint.

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[5] King SB, 3rd, Smith SC, Jr., Hirshfeld JW, Jr., et al. 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: 2007 Writing Group to Review New Evidence and Update the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention, Writing on Behalf of the 2005 Writing Committee. *Circulation* 2008;117:261-95.

Follow-up included clinical assessments at 30 days, 6, 12 and 18 months, and 2, 3, 4 and 5 years post index procedure. After the 12-month follow-up, the study population was reduced to a pre-specified cohort (Safety Population), which consists of all patients who received a study stent (PROMUS Element stent or PROMUS stent). The study is now considered complete with regard to the 12-month primary endpoint.

Results are presented in Tables 10.1.1 to 10.1.8 and in Figures 10.1.1 to 10.1.3.

Demographics: Patients were well-matched for baseline demographics. Average age was 64.0±10.3 and 63.1±10.3 in the PROMUS Element and PROMUS stent groups, respectively. Approximately 72% of patients in the PROMUS Element stent group and 71% of patients in the PROMUS stent group were male, and 22% of patients in the PROMUS Element group and 25% in the PROMUS stent group had medically treated diabetes.

Baseline lesion characteristics: Mean reference vessel diameter (RVD) was 2.67±0.49 mm and 2.63±0.49 mm for the PROMUS Element and PROMUS stent groups, respectively. Average lesion length was 12.95±5.74 mm and 12.50±5.51 mm for the PROMUS Element and PROMUS stent groups, respectively. In both groups, diameter stenosis was approximately 72%, and over 60% of treated lesions were type B2/C.

12-Month Clinical Outcomes

Table 10.1.1. PLATINUM Workhorse 12-Month Clinical Results, Intent-to-Treat Patients

	PROMUS Element Stent (N=768)	PROMUS Stent[1] (N=762)
EFFICACY		
TVR, Overall	2.7% (20/745)	2.9% (21/732)
TLR, Overall	1.9% (14/745)	1.9% (14/732)
TLR, PCI	1.3% (10/745)	1.6% (12/732)
TLR, CABG	0.5% (4/745)	0.3% (2/732)
Non-TLR, Overall	0.9% (7/745)	1.1% (8/732)
Non-TLR, PCI	0.8% (6/745)	1.1% (8/732)
Non-TLR, CABG	0.1% (1/745)	0.0% (0/732)
SAFETY		
Total Death	1.3% (10/745)	1.2% (9/732)
Cardiac Death or MI	2.0% (15/745)	2.5% (18/732)
Cardiac Death	0.9% (7/745)	0.7% (5/732)
MI	1.1% (8/745)	1.8% (13/732)
Q-wave MI	0.1% (1/745)	0.7% (5/732)
Non-Q-wave MI	0.9% (7/745)	1.2% (9/732)
ARC Stent Thrombosis		
Definite or Probable	0.4% (3/735)	0.4% (3/725)
Definite	0.4% (3/735)	0.4% (3/725)
Probable	0.0% (0/735)	0.0% (0/725)

[1] DES Control

Numbers are % (Count/Sample Size)

This trial was not sized to determine the rate of low frequency events with a pre-specified precision.

Abbreviations: ARC=Academic Research Consortium; CABG=coronary artery bypass graft; DES=drug-eluting stent; ITT=intent-to-treat; MI=myocardial infarction; PCI=percutaneous coronary intervention; TLR=target lesion revascularization; TVR=target vessel revascularization.

Primary Endpoint (12-Month TLF): The primary endpoint was met. The PROMUS Element stent was shown to be non-inferior to the PROMUS stent with regard to the rate of 12-month TLF (Table 10.1.2).

Table 10.1.2. PLATINUM Workhorse Primary Endpoint

Per Protocol Patients[1]	PROMUS Element Stent (n=756)	PROMUS Stent[2] (n=747)	Difference	One-sided 95% Farrington-Manning Upper Confidence Bound	Non-Inferiority Margin	*P* value[3]
12-Month TLF	3.4% (25/731)	2.9% (21/714)	0.5%	2.13%	3.5%	0.0013
Intent-to-Treat Patients	**PROMUS Element Stent (n=768)**	**PROMUS Stent[2] (n=762)**	**Difference**	**One-sided 95% Farrington-Manning Upper Confidence Bound**	**Non-Inferiority Margin**	***P* value[3]**
12-Month TLF	3.5% (26/742)	3.2% (23/727)	0.3%	2.01%	3.5%	0.0009

[1] Primary analysis for assessing hypothesis of non-inferiority and study success criterion. For per protocol analyses, only PLATINUM Workhorse trial patients who had the randomly assigned study stent implanted in the target coronary artery were included.

[2] DES Control

[3] *P* values are one-sided from the Farrington-Manning test and are based on the standard normal distribution.

12-Month TLF: the proportion of patients who experience a target lesion failure (defined as any ischemia-driven revascularization of the target lesion [TLR], MI [Q-wave and non–Q-wave] related to the target vessel, or cardiac death related to the target vessel) up to 365 days post-procedure out of the population that have been followed for at least 335 days or who have experienced a TLF up to 365 days post-procedure.

Table 10.1.3. PLATINUM Workhorse Post-Procedure Angiographic Results by Lesion

Angiographic Outcomes	PROMUS Element Stent (N=853 Target Lesions, 768 Patients)	PROMUS Stent[1] (N=841 Target Lesions, 762 Patients)
MLD (mm), In-stent	2.57±0.42(846)	2.54±0.44(839)
MLD (mm), Analysis Segment	2.19±0.47(850)	2.16±0.47(840)
Acute Gain (mm), In-stent	1.81±0.43(846)	1.80±0.45(839)
Acute Gain, Analysis Segment (mm)	1.44±0.46(850)	1.42±0.47(840)
% DS, In-stent	4.27±9.09(846)	4.30±8.74(839)
% DS, Analysis Segment	18.82±8.63(850)	19.16±9.02(840)

[1] DES Control

Numbers are mean±SD (n)

Abbreviations: DES=drug-eluting stent; DS=diameter stenosis; MLD=minimum lumen diameter.

Table 10.1.4. PLATINUM Workhorse ARC Definite and Probable Stent Thrombosis

Intent-to-Treat Patients	PROMUS Element Stent (N=768)	PROMUS Stent[2] (N=762)
ARC Definite & Probable Stent Thrombosis[1]		
Cumulative through 1 year	0.4% (3/735)	0.4% (3/725)
Acute ST (≤24 hrs)	0.1% (1/768)	0.1% (1/762)
Subacute ST (>24 hrs and ≤30 days)	0.0% (0/766)	0.3% (2/762)
Late ST (>30 days and ≤12 months)	0.3% (2/764)	0.0% (0/760)

To be included in the calculation of stent thrombosis (ST) rate for a given interval, a patient either had to have a stent thrombosis during the interval (e.g. 31-365 days inclusive) or 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.

Table 10.1.4. PLATINUM Workhorse ARC Definite and Probable Stent Thrombosis

31 days).

[1] Academic Research Consortium (ARC) stent thrombosis is defined as follows.[6]

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:
   Any unexplained death within the first 30 days following stent implantation.
   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.

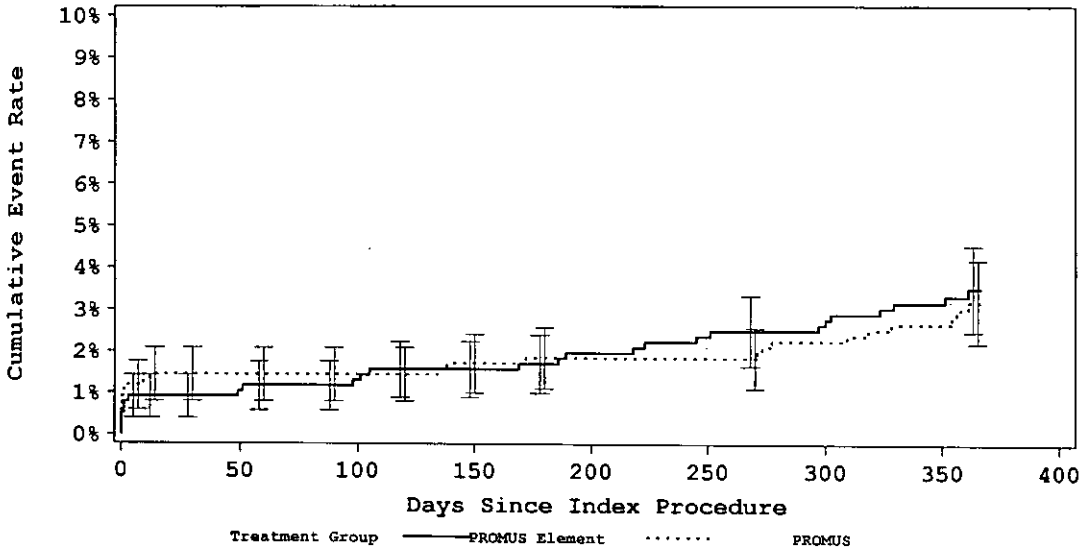
[2] DES Control

Numbers are % (Count/Sample Size).

This trial was not sized to determine the rate of low frequency events with a pre-specified precision.

Abbreviations: DES=drug-eluting stent; MI=myocardial infarction; ST=stent thrombosis

Figure 10.1.1. PLATINUM Workhorse Cumulative Rate of Target Lesion Failure to 12 Months, Intent-to-Treat, Event Rate ± 1.5 SE, All Patients (N=1530)



	Event Rate	Event Free	Log-Rank *P* value
PROMUS Element	3.5%	96.5%	0.7018
PROMUS DES Control	3.2%	96.8%	

Results in Patients with and without Diabetes: Patients with diabetes mellitus represent a high-risk group for adverse events following percutaneous coronary intervention. Tables 10.1.5 and 10.1.6 show 1-year outcomes in patients with and without medically treated diabetes (defined as treatment with oral hypoglycemic agents or insulin at enrollment). While the PLATINUM WH study randomization was stratified for diabetic status, this trial was not adequately powered to study safety or effectiveness of the PROMUS Element stent versus the PROMUS stent in patients with or without diabetes and was not designed to specifically support an indication for use in diabetic patients. These exploratory analyses show that in patients treated with the PROMUS Element stent, 1-year TLR rates were 3.7% in diabetic and 1.4% in non-diabetic patients.

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

Table 10.1.5. PLATINUM Workhorse 12-Month Clinical Results in Patients with Medically Treated Diabetes, Intent-to-Treat Patients

	PROMUS Element Stent (N=169)	PROMUS Stent[1] (N=191)
EFFICACY		
TVR, Overall	4.9% (8/163)	2.7% (5/186)
TLR, Overall	3.7% (6/163)	1.6% (3/186)
TLR, PCI	1.8% (3/163)	1.1% (2/186)
TLR, CABG	1.8% (3/163)	0.5% (1/186)
Non-TLR, Overall	1.2% (2/163)	1.1% (2/186)
Non-TLR, PCI	1.2% (2/163)	1.1% (2/186)
Non-TLR, CABG	0.0% (0/163)	0.0% (0/186)
TLF	4.3% (7/162)	2.7% (5/184)
SAFETY		
Total Death	1.2% (2/163)	1.6% (3/186)
Cardiac Death or MI	1.8% (3/163)	1.1% (2/186)
Cardiac Death	1.2% (2/163)	0.5% (1/186)
MI	0.6% (1/163)	0.5% (1/186)
Q-wave MI	0.0% (0/163)	0.0% (0/186)
Non-Q-wave MI	0.6% (1/163)	0.5% (1/186)
ARC Stent Thrombosis		
Definite or Probable	0.0% (0/160)	0.0% (0/184)
Definite	0.0% (0/160)	0.0% (0/184)
Probable	0.0% (0/160)	0.0% (0/184)

This trial was not sized to determine the rate of low frequency events with a pre-specified precision.

Numbers are % (count/sample size)

[1] DES Control

Abbreviations: ARC=Academic Research Consortium; CABG=coronary artery bypass graft; DES=drug-eluting stent; ITT=intent-to-treat; MI=myocardial infarction; PCI=percutaneous coronary intervention; TLR=target lesion revascularization; TVR=target vessel revascularization.

Table 10.1.6. PLATINUM Workhorse 12-Month Clinical Results in Patients without Medically Treated Diabetes, Intent-to-Treat Patients

	PROMUS Element Stent (N=599)	PROMUS Stent[1] (N=571)
EFFICACY		
TVR, Overall	2.1% (12/582)	2.9% (16/546)
TLR, Overall	1.4% (8/582)	2.0% (11/546)
TLR, PCI	1.2% (7/582)	1.8% (10/546)
TLR, CABG	0.2% (1/582)	0.2% (1/546)
Non-TLR, Overall	0.9% (5/582)	1.1% (6/546)
Non-TLR, PCI	0.7% (4/582)	1.1% (6/546)
Non-TLR, CABG	0.2% (1/582)	0.0% (0/546)
TLF	3.3% (19/580)	3.3% (18/543)
SAFETY		
Total Death	1.4% (8/582)	1.1% (6/546)
Cardiac Death or MI	2.1% (12/582)	2.9% (16/546)
Cardiac Death	0.9% (5/582)	0.7% (4/546)
MI	1.2% (7/582)	2.2% (12/546)
Q-wave MI	0.2% (1/582)	0.9% (5/546)
Non-Q-wave MI	1.0% (6/582)	1.5% (8/546)
ARC Stent Thrombosis		
Definite or Probable	0.5% (3/575)	0.6% (3/541)
Definite	0.5% (3/575)	0.6% (3/541)
Probable	0.0% (0/575)	0.0% (0/541)

This trial was not sized to determine the rate of low frequency events with a pre-specified precision.

Table 10.1.6. PLATINUM Workhorse 12-Month Clinical Results in Patients without Medically Treated Diabetes, Intent-to-Treat Patients		
	PROMUS Element Stent (N=599)	PROMUS Stent[1] (N=571)
Numbers are % (count/sample size) [1] DES Control Abbreviations: ARC=Academic Research Consortium; CABG=coronary artery bypass graft; DES=drug-eluting stent; ITT=intent-to-treat; MI=myocardial infarction; PCI=percutaneous coronary intervention; TLR=target lesion revascularization; TVR=target vessel revascularization.		

Results in Males and Females: PLATINUM WH data were evaluated retrospectively for possible gender-based differences in clinical outcomes, as well as for any interaction between treatment and gender. PLATINUM WH was not designed or powered to study safety or effectiveness of the PROMUS Element stent versus the PROMUS stent in gender-specific subgroups, so these analyses were performed *post hoc* and are considered hypothesis-generating.

In the PLATINUM WH ITT population, of the 768 patients randomized to PROMUS Element, 550 patients were male (71.6%) and 218 patients were female (28.4%). The proportions in the PROMUS group were similar (71.1% males, 28.9% females).

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).[7] However, it is estimated that only 36% of annual PCIs are performed in women. In PCI clinical trials, women represent only 25-35% of the enrolled populations, and there are relatively little gender-specific data. The disproportionate enrollment distribution in this trial may be partly attributable to gender differences in symptoms and pathophysiology,[8] which may lead to under-diagnosis and under-referral of female patients with CAD. 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.

In patients treated with the PROMUS Element stent, the 12-month rate of TLF was 3.4% in males and 3.8% in females. In patients treated with the PROMUS stent, the 12-month rate of TLF was 3.1% in males and 3.4% in females (Table 10.1.7.).

This *post hoc* analysis shows similar treatment effect between genders for the primary endpoint of 12-month TLF. This suggests that the overall conclusions of the trial regarding both safety and effectiveness of the PROMUS Element stent can be generalized to males and females.

Table 10.1.7. PLATINUM Workhorse Primary Endpoint Results by Gender, Intent-to-Treat, All Patients (N=1530)			
12-month TLF	PROMUS Stent (N=762)	PROMUS Element Stent (N=768)	Difference
Female (N=438)	(N=220)	(N=218)	
	3.4% (7/208)	3.8% (8/213)	0.4%
Male (N=1092)	(N=542)	(N=550)	
	3.1% (16/519)	3.4% (18/529)	0.3%

[7] 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.
[8] Shaw LJ, Bairey Merz CN, Pepine CJ, et al. Insights from the NHLBI-Sponsored Women's Ischemia Syndrome Evaluation (WISE) Study: Part I: gender differences in traditional and novel risk factors, symptom evaluation, and gender-optimized diagnostic strategies. J Am Coll Cardiol. 2006; 47(3):S4-S20.

Table 10.1.7. PLATINUM Workhorse Primary Endpoint Results by Gender, Intent-to-Treat, All Patients (N=1530)

This trial was not sized to determine the rate of low frequency events with a pre-specified precision.

Numbers are % (Count/Sample Size)

12-Month TLF is the proportion of patients who experience a target lesion failure (defined as any ischemia-driven revascularization of the target lesion [TLR], MI [Q-wave and non–Q-wave] related to the target vessel, or cardiac death related to the target vessel) up to 365 days post-procedure out of the population that have been followed for at least 335 days or who have experienced a TLF up to 365 days post-procedure.

Table 10.1.8 shows PLATINUM WH 12-month clinical results for PROMUS Element male and female patients. Outcomes were similar in male and female patients.

Table 10.1.8. PLATINUM Workhorse 12-Month Clinical Endpoints by Gender, Intent-to-Treat, PROMUS Element Male and Female Patients (N=768)

	PROMUS Element Stent Male Patients (N=550)	PROMUS Element Stent Female Patients (N=218)
EFFICACY		
TVR, Overall	2.8% (15/532)	2.3% (5/213)
TLR, Overall	1.7% (9/532)	2.3% (5/213)
TLR, PCI	1.3% (7/532)	1.4% (3/213)
TLR, CABG	0.4% (2/532)	0.9% (2/213)
Non-TLR, Overall	1.3% (7/532)	0.0% (0/213)
Non-TLR, PCI	1.1% (6/532)	0.0% (0/213)
Non-TLR, CABG	0.2% (1/532)	0.0% (0/213)
TLF	3.4% (18/529)	3.8% (8/213)
SAFETY		
Total Death	1.7% (9/532)	0.5% (1/213)
Cardiac Death or MI	2.3% (12/532)	1.4% (3/213)
Cardiac Death	1.1% (6/532)	0.5% (1/213)
MI	1.1% (6/532)	0.9% (2/213)
Q-wave MI	0.2% (1/532)	0.0% (0/213)
Non-Q-wave MI	0.9% (5/532)	0.9% (2/213)
ARC Stent Thrombosis		
Definite or Probable	0.6% (3/524)	0.0% (0/211)
Definite	0.6% (3/524)	0.0% (0/211)
Probable	0.0% (0/524)	0.0% (0/211)

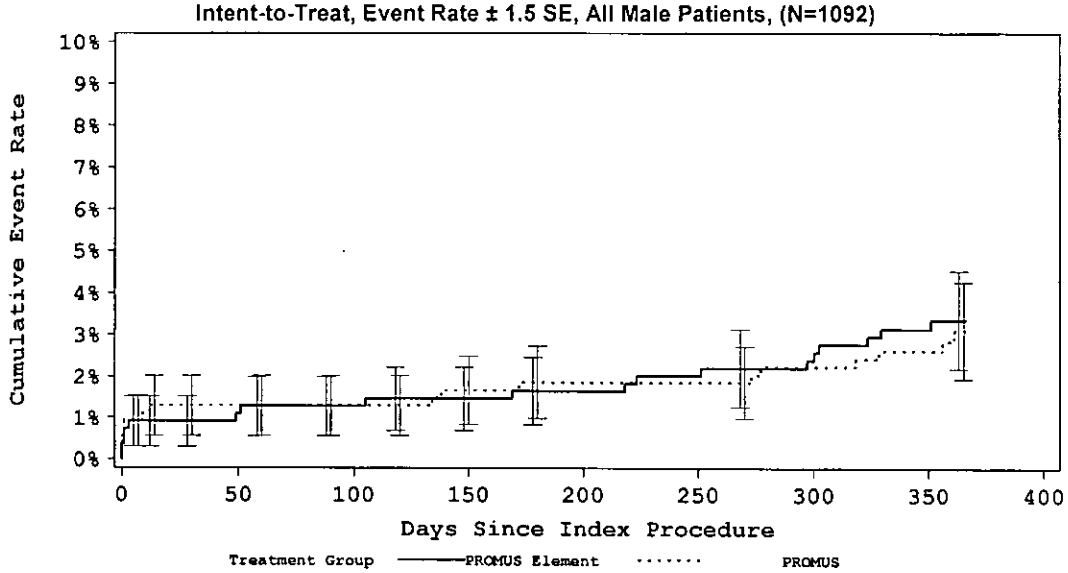
This trial was not sized to determine the rate of low frequency events with a pre-specified precision.

Numbers are % (Count/Sample Size)

Abbreviations: ARC=Academic Research Consortium; CABG=coronary artery bypass grafting; MI=myocardial infarction; PCI=percutaneous coronary intervention; TLF=target lesion failure; TLR=target lesion revascularization; TVR=target vessel revascularization.

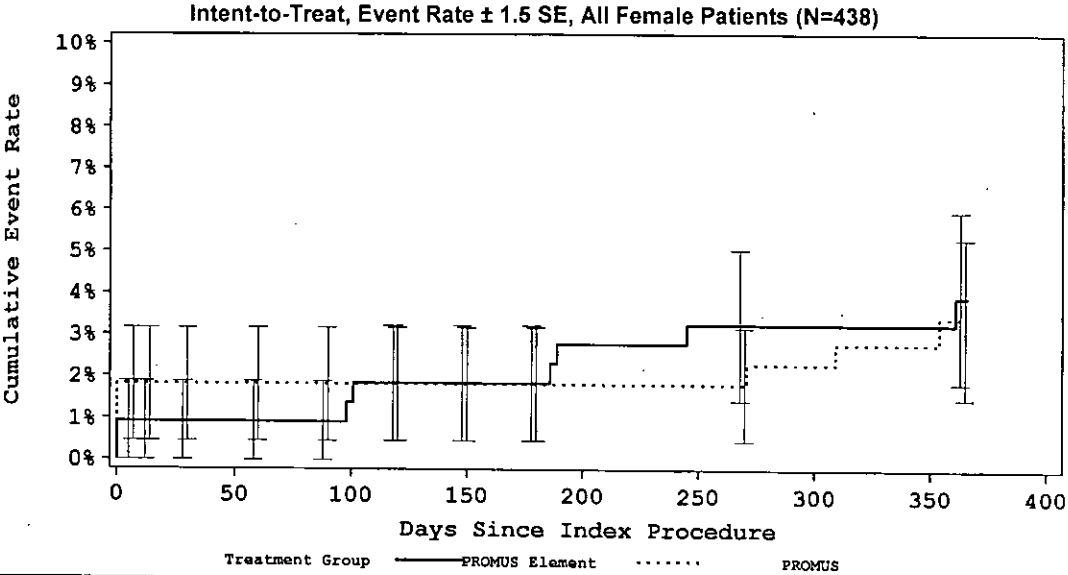
Figures 10.1.2 and 10.1.3 show the cumulative rate of TLF through 12-months for males and females, respectively. This *post hoc* analysis shows that there were similar TLF rates for PROMUS Element and PROMUS groups for males and females at all follow-up time-points (30 days, 6 months, and 12 months).

Figure 10.1.2. PLATINUM Workhorse Cumulative Rate of Target Lesion Failure to 12 Months, Intent-to-Treat, Event Rate ± 1.5 SE, All Male Patients, (N=1092)



	Event Rate	Event Free
PROMUS Element	3.4%	96.6%
PROMUS DES Control	3.1%	96.9%

Figure 10.1.3. PLATINUM Workhorse Cumulative Rate of Target Lesion Failure to 12 Months, Intent-to-Treat, Event Rate ± 1.5 SE, All Female Patients (N=438)



	Event Rate	Event Free
PROMUS Element	3.9%	96.1%
PROMUS DES Control	3.4%	96.6%

10.2 PLATINUM Small Vessel (SV) Sub-study

Primary Objective: The primary objective of the PLATINUM SV sub-study was to evaluate the safety and efficacy of the PROMUS Element Everolimus-Eluting Platinum Chromium Coronary Stent System for the treatment of *de novo* atherosclerotic lesions of ≤28 mm in length in native coronary arteries with visual RVD of ≥2.25 mm to <2.50 mm in diameter.

Design: PLATINUM SV is a prospective, single-arm, multi-center sub-study of the PLATINUM Trial. The sub-study compares outcomes in patients treated with the 2.25 mm PROMUS Element stent to a performance goal based on TAXUS Express small vessel stent results from the TAXUS V *De Novo* Trial. Eligible patients were those ≥18 years old with left ventricular ejection fraction (LVEF) ≥30% and with documented stable angina pectoris, silent ischemia, or unstable angina pectoris. *De novo* target lesions in a native coronary artery with diameter stenosis ≥50% and <100% with Thrombolysis in Myocardial Infarction (TIMI) flow >1, reference vessel diameter ≥2.25 mm to <2.50 mm (visual estimate), and lesion length ≤28 mm (visual estimate) were eligible. Patients had a single target lesion and could also have 1 *de novo* native coronary artery lesion within a different epicardial vessel (non-target lesion) treated with a commercial treatment (e.g., stent, balloon angioplasty, excluding brachytherapy) during the index procedure. The non-target lesion had to be treated before the target lesion and the treatment had to be a clinical angiographic success (defined as visually assessed stenosis <50% [<30% for stents] with TIMI 3 flow without prolonged chest pain or ECG changes consistent with myocardial infarction [MI]) before the patient could be enrolled. The protocol mandated antiplatelet therapy compliance in accordance with the 2007 ACC/AHA/SCAI Guidelines for PCI.[9]

The primary endpoint was the rate of target lesion failure (TLF), defined as any ischemia-driven revascularization of the target lesion (TLR), MI (Q-wave and non–Q-wave) related to the target vessel, or cardiac death related to the target vessel, at 12 months post-index procedure, compared to a performance goal based on outcomes in patients with 2.25 mm TAXUS Express stents from the TAXUS V *De Novo* Trial.[10]

A total of 94 patients were enrolled at 23 sites. Of the 94 patients included in the intent-to-treat analysis set, a total of 89 patients were evaluable for the 12-month primary endpoint.

Follow-up included clinical assessments at 30 days, 6, 12 and 18 months, and 2, 3, 4 and 5 years post index procedure. After the 12-month follow-up, the study population was reduced to a pre-specified cohort (Safety Population), which consists of all patients who received a study stent. The study is now considered complete with regard to the 12-month primary endpoint.

Results are presented in Tables 10.2.1 to 10.2.6.

Demographics: Average age was 64.3±11.0. Approximately 72% of patients were male, and 43% of patients had medically treated diabetes.

Baseline lesion characteristics: Mean reference vessel diameter (RVD) was 2.04±0.26 mm. Average lesion length was 14.15±7.03 mm. Diameter stenosis was approximately 75%, and approximately 69% of treated lesions were type B2/C.

12-Month Clinical Outcomes

Table 10.2.1. PLATINUM Small Vessel 12-Month Clinical Results, Intent-to-Treat, All Patients

	PROMUS Element Stent (N=94)
EFFICACY	
TVR, Overall	3.3% (3/90)
TLR, Overall	2.2% (2/90)
TLR, PCI	2.2% (2/90)
TLR, CABG	0.0% (0/90)
Non-TLR, Overall	1.1% (1/90)

[9] King SB, 3rd, Smith SC, Jr., Hirshfeld JW, Jr., et al. 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: 2007 Writing Group to Review New Evidence and Update the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention, Writing on Behalf of the 2005 Writing Committee. *Circulation* 2008;117:261-95.

[10] 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.

Table 10.2.1. PLATINUM Small Vessel 12-Month Clinical Results, Intent-to-Treat, All Patients	
Non-TLR, PCI	1.1% (1/90)
Non-TLR, CABG	0.0% (0/90)
SAFETY	
Total Death	4.4% (4/90)
Cardiac Death or MI	3.3% (3/90)
Cardiac Death	3.3% (3/90)
MI	0.0% (0/90)
Q-wave MI	0.0% (0/90)
Non-Q-wave MI	0.0% (0/90)
ARC Stent Thrombosis	
Definite or Probable	0.0% (0/86)
Definite	0.0% (0/86)
Probable	0.0% (0/86)
This trial was not sized to determine the rate of low frequency events with a pre-specified precision. Numbers are % (count/sample size) Abbreviations: ARC=Academic Research Consortium; CABG=coronary artery bypass graft; ITT=intent-to-treat; MI=myocardial infarction; PCI=percutaneous coronary intervention; TLR=target lesion revascularization; TVR=target vessel revascularization.	

Primary Endpoint (12-Month TLF): The primary endpoint was met. The rate of 12-Month TLF was shown to be significantly less than the performance goal.

Table 10.2.2. PLATINUM Small Vessel Primary Endpoint					
Per Protocol Patients[1]	**PROMUS Element Stent (n=89)**	**[95% CI]**	**One-sided 95% Clopper-Pearson Upper Confidence Bound**	**Performance Goal**	***P* value[2]**
12-Month TLF	2.4% (2/84)	[0.3%, 8.3%]	7.31%	21.1%	<0.0001
Intent-to-Treat Patients	**PROMUS Element Stent (n=94)**	**[95% CI]**	**One-sided 95% Clopper-Pearson Upper Confidence Bound**	**Performance Goal**	***P* value[2]**
12-Month TLF	5.6% (5/89)	[1.8%, 12.6%]	11.45%	21.1%	<0.0001
[1] Primary analysis for comparing to the performance goal and study success criterion. [2] *P* values are one-sided from the exact binomial test. 12-Month TLF: the proportion of patients who experience a target lesion failure (defined as any ischemia-driven revascularization of the target lesion [TLR], MI [Q-wave and non–Q-wave] related to the target vessel, or cardiac death related to the target vessel) up to 365 days post-procedure out of the population that have been followed for at least 335 days or who have experienced a TLF up to 365 days post-procedure.					

Table 10.2.3. PLATINUM Small Vessel Post-Procedure Angiographic Results	
Angiographic Outcomes	**PROMUS Element Stent (N=94 Patients)**
MLD (mm), In-stent	1.98±0.19(91)
MLD (mm), Analysis Segment	1.64±0.32(94)
Acute Gain (mm), In-stent	1.47±0.27(91)
Acute Gain, Analysis Segment (mm)	1.13±0.35(94)
% DS, In-stent	3.95±10.95(91)
% DS, Analysis Segment	21.29±10.17(94)

Table 10.2.3. PLATINUM Small Vessel Post-Procedure Angiographic Results
Abbreviations: DS=diameter stenosis; MLD=minimum lumen diameter. Numbers are mean±SD (n)

Table 10.2.4. PLATINUM Small Vessel ARC Definite and Probable Stent Thrombosis	
Intent-to-Treat Patients	**PROMUS Element Stent (N=94)**
ARC Definite & Probable Stent Thrombosis[1]	
Cumulative through 1 year	0.0% (0/86)
Acute ST (≤24 hrs)	0.0% (0/94)
Subacute ST(>24 hrs and ≤30 days)	0.0% (0/94)
Late ST (>30 days and ≤12 months)	0.0% (0/94)

To be included in the calculation of stent thrombosis (ST) 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] Academic Research Consortium (ARC) stent thrombosis is defined as follows.[11]

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:
   Any unexplained death within the first 30 days following stent implantation.
   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.

Numbers are % (Count/Sample Size).

This trial was not sized to determine the rate of low frequency events with a pre-specified precision.

Abbreviations: MI=myocardial infarction; ST=stent thrombosis

Results in Males and Females: PLATINUM SV data were evaluated retrospectively for possible gender-based differences in clinical outcomes. PLATINUM SV was not designed or powered to study safety or effectiveness of the PROMUS Element stent in gender-specific subgroups, so these analyses were performed *post hoc* and are considered hypothesis generating.

In the PLATINUM SV ITT population, of the 94 patients enrolled, 68 patients were male (72.3%) and 26 patients were female (27.7%). In patients treated with the PROMUS Element stent, the 12-Month rate of TLF was 7.9% in males and 0% in females (Table 10.2.5). Given the small number of patients enrolled, no conclusions can be drawn from these data.

Table 10.2.5. PLATINUM Small Vessel Primary Endpoint Results by Gender, Intent-to-Treat, All Patients (N=94)			
	PROMUS Element Stent Male Patients (N=68)	**PROMUS Element Stent Female Patients (N=26)**	**Difference**
12-Month TLF	7.9% (5/63)	0.0% (0/26)	7.9%

This trial was not sized to determine the rate of low frequency events with a pre-specified precision.

Numbers are % (Count/Sample Size)

12-Month TLF is the proportion of patients who experience a target lesion failure (defined as any ischemia-driven revascularization of the target lesion [TLR], MI [Q-wave and non–Q-wave] related to the target vessel, or cardiac death related to the target vessel) up to 365 days post-procedure out of the population that have been followed for at least 335 days or who have experienced a TLF up to 365 days post-procedure.

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

Table 10.2.6 shows PLATINUM SV 12-month clinical results for male and female patients. There were no events through 12 months in the small population of female patients. Given the small number of patients enrolled, no conclusions can be drawn from these data.

Table 10.2.6. PLATINUM Small Vessel 12-Month Clinical Endpoints by Gender, Intent-to-Treat, PROMUS Element Male and Female Patients (N=94)

	PROMUS Element Stent Male Patients (N=68)	PROMUS Element Stent Female Patients (N=26)
EFFICACY		
TVR, Overall	4.7% (3/64)	0.0% (0/26)
TLR, Overall	3.1% (2/64)	0.0% (0/26)
TLR, PCI	3.1% (2/64)	0.0% (0/26)
TLR, CABG	0.0% (0/64)	0.0% (0/26)
Non-TLR, Overall	1.6% (1/64)	0.0% (0/26)
Non-TLR, PCI	1.6% (1/64)	0.0% (0/26)
Non-TLR, CABG	0.0% (0/64)	0.0% (0/26)
TLF	7.9% (5/63)	0.0% (0/26)
SAFETY		
Total Death	6.3% (4/64)	0.0% (0/26)
Cardiac Death or MI	4.7% (3/64)	0.0% (0/26)
Cardiac Death	4.7% (3/64)	0.0% (0/26)
MI	0.0% (0/64)	0.0% (0/26)
Q-wave MI	0.0% (0/64)	0.0% (0/26)
Non-Q-wave MI	0.0% (0/64)	0.0% (0/26)
ARC Stent Thrombosis		
Definite or Probable	0.0% (0/60)	0.0% (0/26)
Definite	0.0% (0/60)	0.0% (0/26)
Probable	0.0% (0/60)	0.0% (0/26)

This trial was not sized to determine the rate of low frequency events with a pre-specified precision.

Numbers are % (Count/Sample Size)

Abbreviations: ARC=Academic Research Consortium; CABG=coronary artery bypass grafting; MI=myocardial infarction; PCI=percutaneous coronary intervention; TLF=target lesion failure; TLR=target lesion revascularization; TVR=target vessel revascularization.

10.3 PLATINUM Quantitative Coronary Angiography (QCA) Trial

Primary Objective: The primary objective of the PLATINUM QCA Trial was to evaluate the clinical, angiographic, and IVUS outcomes of the PROMUS Element Everolimus-Eluting Platinum Chromium Coronary Stent System for the treatment of *de novo* atherosclerotic lesions of up to 34 mm in length (by visual estimate) in native coronary arteries of 2.25 mm to 4.25 mm in diameter (by visual estimate).

Design: PLATINUM QCA is a prospective, single-arm, multi-center, observational trial. Eligible patients were those ≥18 years old with left ventricular ejection fraction (LVEF) ≥30% and with documented stable angina pectoris, silent ischemia, or unstable angina pectoris. *De novo* target lesions in a native coronary artery with diameter stenosis ≥50% and <100% with Thrombolysis in Myocardial Infarction (TIMI) flow >1, reference vessel diameter ≥2.25 mm to ≤4.25 mm (visual estimate), and lesion length ≤34 mm (visual estimate) were eligible. Patients had a single target lesion treated and could also have 1 *de novo* native coronary artery lesion within a different epicardial vessel (non-target lesion) treated with a commercial treatment (e.g., stent, balloon angioplasty, excluding brachytherapy) during the index procedure. The non-target lesion had to be treated before the target lesion and the treatment had to be a clinical angiographic success (defined as visually assessed stenosis <50% [<30% for stents] with TIMI 3 flow without prolonged chest pain or ECG changes consistent with myocardial infarction [MI]) before the patient could be enrolled.

The protocol mandated antiplatelet therapy compliance in accordance with the 2007 ACC/AHA/SCAI Guidelines for PCI.[12]

The primary endpoint was the 30-day composite rate of cardiac death, MI (Q-wave and non-Q-wave), target lesion revascularization (TLR), and stent thrombosis (ST). No formal statistical testing was performed for the primary endpoint in this single arm observational trial. All patients were required to undergo 9-month angiography and IVUS assessments. Efficacy endpoints of in-stent late loss at 9 months (determined by QCA) in patients with workhorse target lesions (visual RVD ≥2.5 mm and ≤4.25 mm and visual lesion length ≤24 mm) and post-procedure incomplete apposition (determined by IVUS) were compared to predefined performance goals. For 9-month in-stent late loss, the performance goal was based on historical TAXUS Express stent results. For post-procedure incomplete apposition, the performance goal was based on historical PROMUS (Xience V) post-procedure incomplete apposition data from the SPIRIT III study. No adjustments were made for multiple comparisons.

A total of 100 patients were enrolled at 14 sites. Of the 100 patients included in the intent-to-treat analysis set, all were evaluable for the 30-day primary endpoint, 88 underwent angiography at 9 months post procedure, and 83 underwent IVUS at 9 months post-procedure.

Follow-up included clinical assessments at 30 days, 9 months and 12 months post index procedure, and angiographic and IVUS assessments at 9 months post procedure. Angiographic assessments were performed for the area of the vessel within the stent margins (in-stent) and the areas immediately 5 mm proximal and distal from the stent margins (analysis segment). The study is now complete.

Results are presented in Tables 10.3.1 to 10.3.8.

Demographics: Average age was 61.8±9.9. 77% of patients were male, and 19% of patients had medically treated diabetes.

Baseline lesion characteristics: Reference vessel diameter was 2.72±0.53 mm with baseline lesion length 15.40±7.03 mm. Percent diameter stenosis was 74.09±10.93 and 67% of treated lesions were type B2/C.

12-Month Clinical Outcomes

Table 10.3.1. PLATINUM QCA 12-Month Clinical Results, Intent-to-Treat, All Patients

	PROMUS Element Stent (N=100)
EFFICACY	
TVR, Overall	1.0% (1/100)
TLR, Overall	1.0% (1/100)
TLR, PCI	1.0% (1/100)
TLR, CABG	0.0% (0/100)
Non-TLR, Overall	1.0% (1/100)
Non-TLR, PCI	1.0% (1/100)
Non-TLR, CABG	0.0% (0/100)
SAFETY	
Total Death	0.0% (0/100)
Cardiac Death or MI	0.0% (0/100)
Cardiac Death	0.0% (0/100)
MI	0.0% (0/100)
Q-wave MI	0.0% (0/100)
Non-Q-wave MI	0.0% (0/100)
ARC Stent Thrombosis	
Definite or Probable	1.0% (1/100)

[12] King SB, 3rd, Smith SC, Jr., Hirshfeld JW, Jr., et al. 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: 2007 Writing Group to Review New Evidence and Update the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention, Writing on Behalf of the 2005 Writing Committee. *Circulation* 2008;117:261-95.

Table 10.3.1. PLATINUM QCA 12-Month Clinical Results, Intent-to-Treat, All Patients	
	PROMUS Element Stent (N=100)
Definite	1.0% (1/100)
Probable	0.0% (0/100)
This trial was not sized to determine the rate of low frequency events with a pre-specified precision.	
Numbers are % (count/sample size)	
Abbreviations: ARC=Academic Research Consortium; CABG=coronary artery bypass graft; DES=drug-eluting stent; ITT=intent-to-treat; MI=myocardial infarction; PCI=percutaneous coronary intervention; TLR=target lesion revascularization; TVR=target vessel revascularization.	

Primary Endpoint: 30-day composite rate of cardiac death, MI, TLR, and ARC definite/probable ST was 1.0% (1/100).

Table 10.3.2. PLATINUM QCA Primary Endpoint	
Per Protocol Patients	**PROMUS Element Stent (N=100)**
Cardiac Death, MI, TLR, ARC Stent Thrombosis (definite and probable) through 30 days	1.0% (1/100)
Cardiac Death	0.0% (0/100)
MI	0.0% (0/100)
Q-wave MI	0.0% (0/100)
Non-Q-wave MI	0.0% (0/100)
TLR	1.0% (1/100)
ARC ST (definite and probable)	1.0% (1/100)
Intent-to-Treat Patients	**PROMUS Element Stent (N=100)**
Cardiac Death, MI, TLR, ARC Stent Thrombosis (definite and probable) through 30 days	1.0% (1/100)
Cardiac Death	0.0% (0/100)
MI	0.0% (0/100)
Q-wave MI	0.0% (0/100)
Non-Q-wave MI	0.0% (0/100)
TLR	1.0% (1/100)
ARC ST (definite and probable)	1.0% (1/100)
Numbers are % (count/sample size)	
Abbreviations: ARC=Academic Research Consortium; MI=myocardial infarction; ST=stent thrombosis; TLR=target lesion revascularization	

Efficacy Endpoint (9-month In-stent Late Loss by QCA): In-stent late loss of 0.17±0.25 mm (n=73) in workhorse lesions (visual RVD ≥2.5 mm and ≤4.25 mm and visual lesion length ≤24 mm) was significantly less than the performance goal of 0.44 mm (P<0.0001) at 9 months. No adjustments to p-values were made for multiple comparisons.

Table 10.3.3. PLATINUM QCA Efficacy Endpoint: 9-Month In-stent Late Loss					
Per-protocol Workhorse Patients	**PROMUS Element Stent (N=85)**	**[95% CI]**	**One-sided 95% upper confidence bound**	**Performance Goal**	***P* value[1]**
9-Month In-Stent Late Loss, mm	0.17±0.25 (73) (-0.41, 0.87)	[0.12, 0.23]	0.22	0.44	<0.0001

Table 10.3.3. PLATINUM QCA Efficacy Endpoint: 9-Month In-stent Late Loss					
Intent-to-treat Workhorse Patients	**PROMUS Element Stent (N=85)**	**[95% CI]**	**One-sided 95% upper confidence bound**	**Performance Goal**	***P* value[1]**
9-Month In-Stent Late Loss, mm	0.17±0.25 (73) (-0.41, 0.87)	[0.12, 0.23]	0.22	0.44	<0.0001
[1] *P* value is from the Student t-test.					

Efficacy Endpoint (Post-procedure Incomplete Apposition by IVUS): Post-procedure incomplete apposition rate of 5.7% (5/88) was significantly less than the performance goal of 34.4% (*P*<0.0001). No adjustments to p-values were made for multiple comparisons.

Table 10.3.4. PLATINUM QCA Efficacy Endpoint: Post-procedure Incomplete Apposition					
Per-protocol Patients	**PROMUS Element Stent (N=100)**	**[95% CI]**	**One-sided 95% Clopper-Pearson upper confidence bound**	**Performance Goal**	***P* value[1]**
Post-procedure Incomplete Apposition	5.7% (5/88)	[1.9%, 12.8%]	11.6%	34.4%	<0.0001
Intent-to-treat Patients	**PROMUS Element Stent (N=100)**	**[95% CI]**	**One-sided 95% Clopper-Pearson upper confidence bound**	**Performance Goal**	***P* value[1]**
Post-procedure Incomplete Apposition	5.7% (5/88)	[1.9%, 12.8%]	11.6%	34.4%	<0.0001
[1] *P* value is from the exact binomial test.					

Table 10.3.5. PLATINUM QCA Angiographic and IVUS Results	
Angiographic Outcomes[1]	**PROMUS Element Stent (N=100)**
MLD (mm), In-stent	
Post-Procedure	2.64±0.46(88)
9-Month	2.44±0.49(88)
MLD (mm), Analysis Segment	
Post-Procedure	2.27±0.52(88)
9-Month	2.20±0.49(88)
Acute Gain (mm), In-stent	1.93±0.47(88)
Acute Gain, Analysis Segment (mm)	1.56±0.51(88)
% DS, In-stent	
Post-Procedure	3.58±7.98(88)
9-Month	10.00±11.59(88)
% DS, Analysis Segment	
Post-Procedure	17.99±7.88(88)
9-Month	19.66±8.95(88)
Late Loss, In-stent (mm) [2]	0.20±0.28(88)
Late Loss, Analysis Segment (mm)	0.07±0.27(88)
Binary Restenosis	
In-stent Restenosis	1.1% (1/88)
Analysis segment restenosis	1.1% (1/88)
IVUS Outcomes	
Neointimal Volume (mm^3) (9 months)	12.73±11.74(73)
% In-stent Net Volume Obstruction (9 months)	7.24±6.22(73)

Table 10.3.5. PLATINUM QCA Angiographic and IVUS Results	
Angiographic Outcomes[1]	**PROMUS Element Stent (N=100)**
Incomplete Apposition	
Late (9 months)	0.0% (0/69)
Late Acquired	0.0% (0/69)

[1] Includes all patients with paired lesion data.

[2] Secondary endpoint of in-stent late loss (0.17±0.25 mm) is based on patients with workhorse lesions (n=73). Table 10.3.5 includes all patients with QCA at 9 months (n=88).

Numbers are % (Count/Sample Size) or mean±SD (n)

Table 10.3.6. PLATINUM QCA ARC Definite and Probable Stent Thrombosis	
Intent-to-Treat Patients	**PROMUS Element Stent (N=100)**
ARC Definite & Probable Stent Thrombosis [1]	
Cumulative through 1 year	1.0% (1/100)
Acute ST (≤24 hrs)	1.0% (1/100)
Subacute ST (>24 hrs and ≤30 days)	0.0% (0/100)
Late ST (>30 days and ≤12 months)	0.0% (0/100)

To be included in the calculation of stent thrombosis (ST) 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] Academic Research Consortium (ARC) stent thrombosis is defined as follows.[13]

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:
   Any unexplained death within the first 30 days following stent implantation.
   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.

Numbers are % (Count/Sample Size).

This trial was not sized to determine the rate of low frequency events with a pre-specified precision.

Results in Males and Females: PLATINUM QCA data were evaluated retrospectively for possible gender-based differences in clinical outcomes. PLATINUM QCA was not designed or powered to study safety or effectiveness of the PROMUS Element stent in gender-specific subgroups, so these analyses were performed *post hoc* and are considered hypothesis generating.

In the PLATINUM QCA ITT population, of the 100 patients enrolled, 77 patients were male (77.0%) and 23 patients were female (23.0%). In patients treated with the PROMUS Element stent, the 12-Month rate of TLF was 0% in males and 4.3% in females (Table 10.3.7). Given the small number of patients enrolled, no conclusions can be drawn from these data.

Table 10.3.7. PLATINUM QCA 12-Month Target Lesion Failure Results by Gender, Intent-to-Treat, PROMUS Element Male and Female Patients (N=100)		
	PROMUS Element Stent Male Patients (N=77 Patients, 67 WH Patients)	**PROMUS Element Stent Female Patients (N=23 Patients, 18 WH Patients)**

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

Table 10.3.7. PLATINUM QCA 12-Month Target Lesion Failure Results by Gender, Intent-to-Treat, PROMUS Element Male and Female Patients (N=100)		
	PROMUS Element Stent Male Patients (N=77 Patients, 67 WH Patients)	**PROMUS Element Stent Female Patients (N=23 Patients, 18 WH Patients)**
12-Month TLF	0.0% (0/77)	4.3% (1/23)
This trial was not sized to determine the rate of low frequency events with a pre-specified precision. Numbers are % (Count/Sample Size) TLF is the proportion of patients who experience a target lesion failure (defined as any ischemia-driven revascularization of the target lesion [TLR], MI [Q-wave and non–Q-wave] related to the target vessel, or cardiac death related to the target vessel) up to 365 days post-procedure out of the population that have been followed for at least 335 days or who have experienced a TLF up to 365 days post-procedure.		

Table 10.3.8 shows PLATINUM QCA primary endpoint and efficacy endpoints for males and females. There were no events through 12 months in the small population of male patients. Given the small number of patients enrolled, no conclusions can be drawn from these data.

Table 10.3.8. PLATINUM QCA Primary and Efficacy Endpoint Results by Gender, Intent-to-Treat, PROMUS Element Male and Female Patients (N=100)		
	PROMUS Element Stent Male Patients (N=77 Patients, 67 WH Patients)	**PROMUS Element Stent Female Patients (N=23 Patients, 18 WH Patients)**
Primary Endpoint		
Cardiac Death, MI, TLR, ARC ST (definite and probable) through 30 days	0.0% (0/77)	4.3% (1/23)
Efficacy Endpoints		
Peri-procedural Incomplete Apposition	7.5% (5/67)	0.0% (0/21)
9-Month In-stent Late Loss (WH Patients)	0.20±0.24(60) (-0.26,0.87)	0.03±0.25(13) (-0.41,0.55)
This trial was not sized to determine the rate of low frequency events with a pre-specified precision. Numbers are % (Count/Sample Size) Abbreviations: ARC=Academic Research Consortium; MI=myocardial infarction; QCA=quantitative coronary angiography; ST=stent thrombosis; TLF=target lesion failure; TLR=target lesion revascularization; WH=workhorse		

11 INDIVIDUALIZATION OF TREATMENT:

See Section 6.7, Use in Special Populations and Section 6.8, Lesion/Vessel Characteristics.

The risks and benefits should be carefully considered for each patient before use of the PROMUS Element™ Plus Stent System. Patient selection factors to be assessed should include a judgment regarding risk of prolonged antiplatelet therapy. On the basis of randomized clinical trial protocols, a $P2Y_{12}$ inhibitor should be given for at least 6 months after everolimus-eluting stent (EES) implantation and ideally up to 12 months. 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 whom antiplatelet 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 an everolimus-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 patient materials are available for this product:

• A Patient Information Guide (included in the package and available on-line) which includes both product information and a stent implant card.

• An Angioplasty and Stent Education Guide (available on-line 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.

HANDLING and STORAGE: Keep dry and protect from light. Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).
Store product in outer carton.

DO NOT REMOVE FROM FOIL POUCH UNTIL READY FOR USE.
THE FOIL POUCH IS NOT A STERILE BARRIER.
Do not store devices where they are directly exposed to organic solvents or ionizing radiation.
The foil pouch contains Argon (Ar) as a storage medium.

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

Check foil pouch for "Use By" date. Do not use the product after the "Use By" date. Carefully inspect the foil pouch and the sterile package before opening. If the integrity of the foil pouch or 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 Delivery System, if the proximal shaft (hypotube) has been bent or kinked, do not continue to use the catheter.

14.2 Materials Required (not included in Stent Delivery System package)

Quantity	Material
1	Appropriate guide catheter (see Table 2.1, PROMUS Element™ Plus Stent System Product Description)
2-3	20 ml (cc) syringe
1000 u/500 cc	Normal heparinized sterile saline
1	≤0.014 in (0.36 mm) guidewire
1	Rotating hemostatic valve
1	Diluted contrast medium 1:1 with normal heparinized

	sterile 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. Open the outer box to reveal the foil pouch and carefully inspect the foil pouch for damage.

2. Carefully open the foil pouch by tearing along the tear strip as indicated on the foil pouch to access the sterile barrier package containing the stent delivery system.

3. Carefully inspect the sterile barrier package for damage.

4. Carefully peel open the sterile barrier using aseptic techniques and extract the stent delivery system.

5. Carefully remove the stent delivery system from its protective tubing for preparation of the delivery system. When using a Monorail system, do not bend or kink proximal shaft during removal.

6. 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.

Note: If unusual resistance is felt during product mandrel and stent protector removal, do not use the product and replace with another.

7. Examine the device for any damage. If it is suspected that the sterility or performance of the device has been compromised, the device should not be used.

8. A Monorail Catheter may be coiled once and secured using the CLIPIT® Coil Clips 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 CLIPIT Coil Clip.

14.3.2 Guidewire Lumen Flush

Step Action

1. (Over-The-Wire only) Flush the stent delivery system guidewire lumen with normal heparinized saline through the straight arm of the Y connector manifold.

2. (Monorail system only) Flush the stent delivery system guidewire lumen with normal heparinized saline using the flushing needle supplied for the Monorail delivery 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 proximal shaft when connecting to inflation device/syringe.

4. With tip down, orient stent delivery system vertically.

5. Open stopcock to stent delivery system; pull negative for 15 seconds; release to neutral for contrast fill.

6. Close stopcock to stent delivery 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 delivery 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 delivery system.

4. Backload stent delivery 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 delivery system into the hub of the guide catheter. When using a Monorail® stent delivery system be sure to keep the proximal shaft straight. Ensure guide catheter stability before advancing the stent delivery 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 delivery system and guide catheter as a single unit.

7. Advance the stent delivery 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 – Section 6.15, Stent Delivery 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 delivery system and the guide catheter should be removed as a single unit. (See also Precautions – Section 6.15, Stent Delivery System Removal). Once the stent delivery system has been removed do not re-use.

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 11 atm (1117 kPa). 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 (1827 kPa) for the 2.25 mm – 2.75 mm diameter stents and 16 atm (1620 kPa) for the 3.00 mm - 4.00 mm diameter stent sizes (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 delivery system balloon, or another high-pressure, 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 (refer to product labeling and/or Table 14.5.1 for balloon compliance chart). Deflate the balloon (see Table 6.1, Delivery System Deflation Time Specifications).

7. If more than one PROMUS Element 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 PROMUS Element 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 CLIPIT® Coil Clip (see 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 tabulated below.

Nominal Stent Diameter (ID)	Dilatation Limits (ID)
2.25 mm	2.75 mm
2.50 mm – 2.75 mm	3.50 mm
3.00 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. The stent may be expanded using a low profile and high pressure balloon catheter. If this is required, the stented segment should be recrossed 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.

Note: In line with Section 6.16, Post-Procedure: Care must be exercised when crossing a newly deployed stent with any wire, catheter or ancillary device to avoid disrupting the stent placement, apposition, geometry, and/or coating.

14.5 In Vitro Information

Table 14.5.1. Typical PROMUS Element™ Plus Stent System Compliance

Pressure Atm (kPa)		2.25 mm Stent I.D.(mm)	2.50 mm Stent I.D.(mm)	2.75 mm Stent I.D. (mm)	3.00 mm Stent I.D. (mm)	3.50 mm Stent I.D. (mm)	4.00 mm Stent I.D. (mm)
8.0 (814)			2.29	2.50	2.72	3.24	3.72
9.0 (910)		2.13	2.37	2.58	2.81	3.34	3.81
10.0 (1014)		2.19	2.43	2.65	2.88	3.43	3.89
11.0 (1117)	Nominal	2.24	2.50	2.72	2.95	3.51	3.96
12.0 (1213)		2.29	2.55	2.78	3.01	3.58	4.02
13.0 (1317)		2.34	2.60	2.84	3.06	3.63	4.08
14.0 (1420)		2.38	2.65	2.89	3.10	3.68	4.13
15.0 (1517)		2.42	2.68	2.93	3.14	3.73	4.17
16.0 (1620)*		2.45	2.72	2.96	3.17	3.77	4.21
17.0 (1724)		2.47	2.75	2.99	3.20	3.81	4.25
18.0 (1827)*		2.50	2.77	3.03	3.24	3.85	4.30
19.0 (1924)		2.52	2.80	3.06	3.28	3.91	4.36
20.0 (2027)		2.55	2.83	3.09	3.32	3.97	4.43
21.0 (2130)		2.57	2.87	3.13			
22.0 (2227)		2.60	2.90	3.17			

* RATED BURST PRESSURE. DO NOT EXCEED.

Note: The Stent I.D. values listed are actual average stent inner diameters at the specific balloon inflation pressures obtained during in vitro testing at 37°C. Balloon pressure must not exceed rated burst pressure of 18 atm (1827 kPa) for the 2.25 mm – 2.75 mm diameter stents and 16 atm (1620 kPa) for the 3.00 mm - 4.00 mm diameter stent sizes.

15 WARRANTY STATEMENT:

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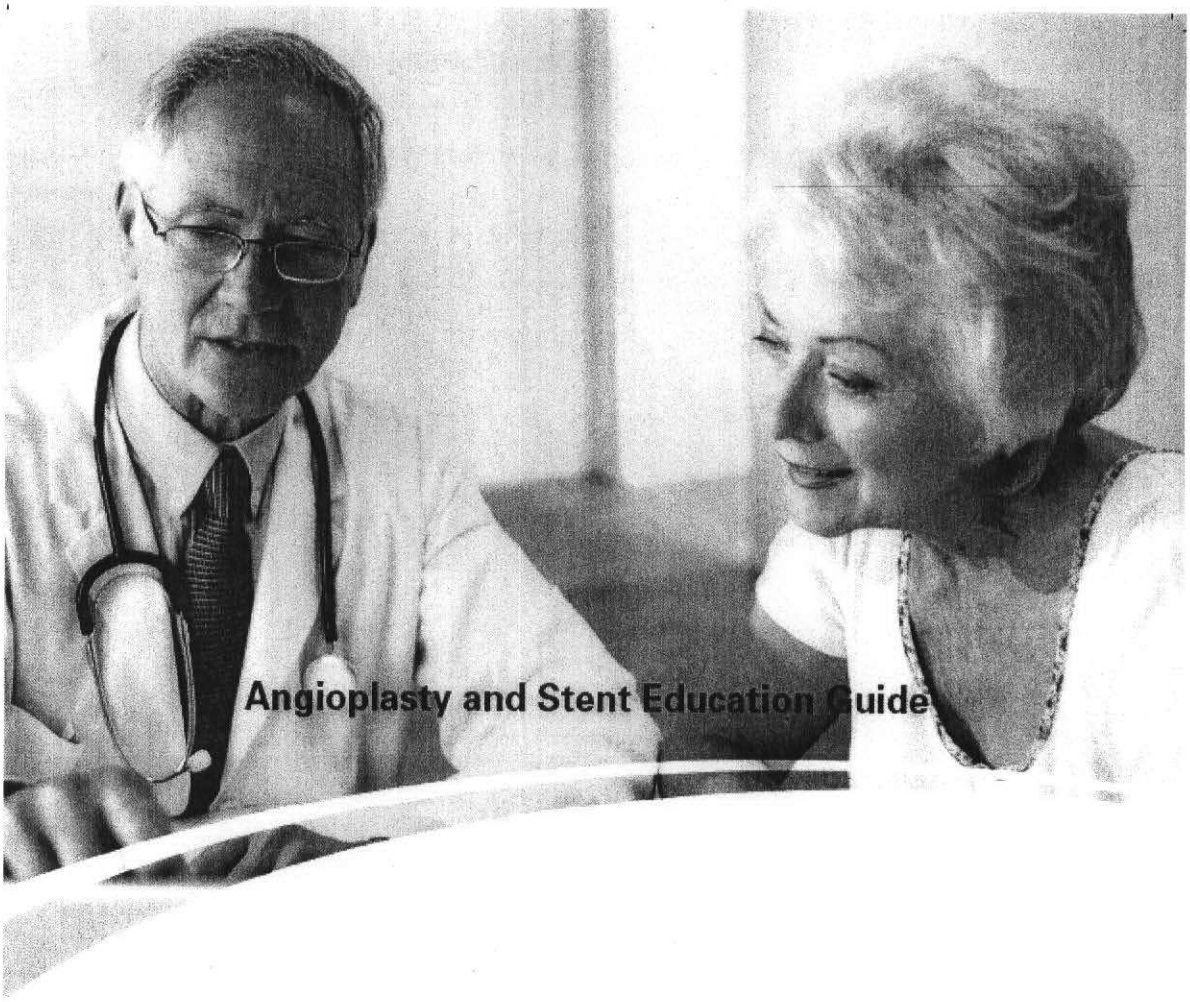

Angioplasty and Stent Education Guide

Boston Scientific

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Treating coronary artery disease

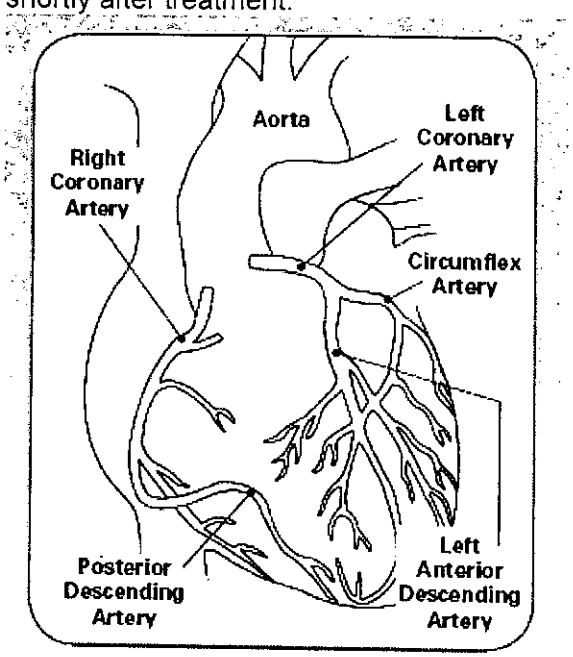
Your doctor may want you to have a *stent* placed in your coronary artery. This is to help treat a blockage in your artery that is caused by *coronary artery disease*. This guide explains the *stent* procedure and what you can expect from start to finish. A glossary at the end of this guide defines common medical terms related to this procedure.

You will also learn steps you can take to live a healthier life with *coronary artery disease*.

What is coronary artery disease?

Coronary Artery Disease (CAD) is the narrowing of the arteries in the heart. This narrowing can also be called stenosis. It is usually caused by a build up of fat or calcium deposits called *plaque*. Over time, this *plaque* can build to a total blockage of the artery. This process is called *atherosclerosis*.

When the heart doesn't receive enough blood flow due to blockage in the artery, it may cause mild to severe chest pain or pressure. This pain or pressure can also spread to the arms or jaw. If the artery is completely blocked, it can result in a heart attack. Anyone who experiences symptoms like those described above should promptly call 911. More than 13 million Americans suffer from CAD each year. However, the treatment of CAD has changed in recent years, and many CAD patients are able to return to a normal lifestyle shortly after treatment.



Who is at risk?

If you have a history of high cholesterol, diabetes, smoking, high blood pressure, being overweight or a family history of CAD, you have an increased chance of developing blockage in your *coronary arteries*. As you get older, you have a greater chance of developing CAD. In addition, women who have reached menopause have a greater chance of developing CAD.

How do I know if I have Coronary Artery Disease?
There are a number of tests that your doctor can perform to help determine if you have CAD. A test that measures the electrical activity in your heart is called an *electrocardiogram (ECG or EKG)*. A *stress test* can be done to evaluate the electrical activity in your heart while you are exercising. These tests may show your doctor if part of your heart has been damaged or is not receiving enough blood. To directly determine if your arteries may be blocked or narrowed, your doctor may schedule a procedure with a cardiologist. This procedure is called a *coronary angiogram* and is performed in a Cardiac Catheterization Lab. During the *coronary angiogram*, dye is injected into your *coronary arteries*. By doing this procedure, the cardiologist can see your *coronary arteries* on an X-ray screen and can make a decision of how best to treat you.

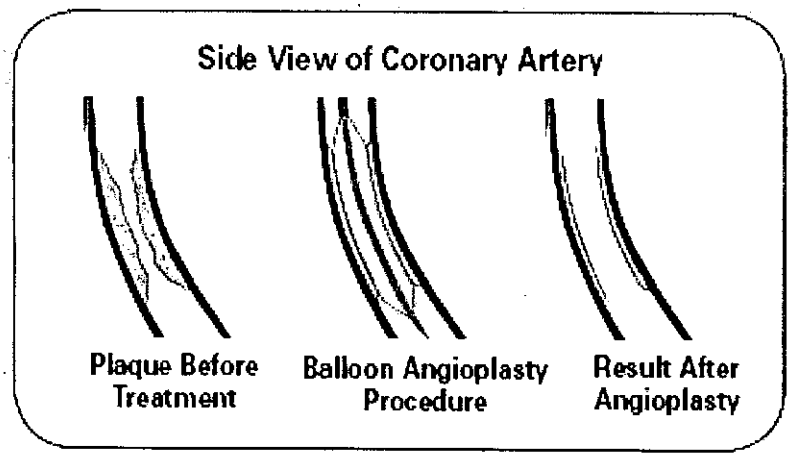
Coronary artery disease treatment options

There are many different treatment options for treating *coronary artery disease*. The options focus on increasing blood flow to the heart, along with changes to your every day lifestyle, including diet, physical activity and medications. The type of treatment your doctor recommends for you depends on your symptoms and how much damage has been done to your heart.

Treatment Options for *Coronary Artery Disease* may include:
1. Medications
2. *Balloon angioplasty*
3. Coronary artery stenting
4. *Coronary artery bypass graft surgery (CABG)*

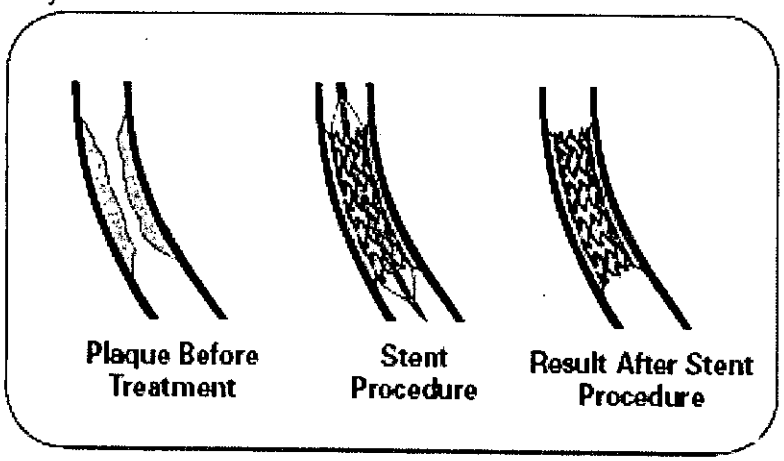
1. Medications
Nitroglycerin may be given to relieve chest discomfort due to coronary blockages. It does not treat the blockage itself. Your cardiologist may also prescribe a number of other medications (aspirin, beta-blockers, cholesterol medications, etc.) to thin your blood and to help prevent blockage of the arteries.

2. Angioplasty
A procedure known as *angioplasty* can also treat artery narrowing. A thin tube known as a guide *catheter* is inserted into the artery at the groin or wrist. A small balloon located at the end of a second *catheter* is moved through the guide *catheter* to the site of the narrowing. The balloon is then inflated to reduce the blockage. The balloon is deflated and removed after the *angioplasty* is done. The patient remains awake while the cardiologist performs the procedure. The procedure may end here or you could have a bare-metal or drug-eluting *stent* implanted to help keep the artery open.



3. Coronary artery stenting

During this procedure a small mesh tube is implanted into the artery to widen the artery and restore adequate blood flow to the heart. This mesh tube is called a *stent*. Once the *stent* is placed into the coronary artery, it is expanded with the inflation of a balloon *catheter*. The *stent* is left in the artery to keep it open and help prevent further narrowing of the coronary artery.



4. Coronary artery bypass graft surgery (CABG)

This surgery is also called a heart bypass or open heart surgery. Your surgeon will need to take a short length of artery from your inner chest wall and/or a vein from your leg and surgically attach it above and below the blocked area of the heart artery.

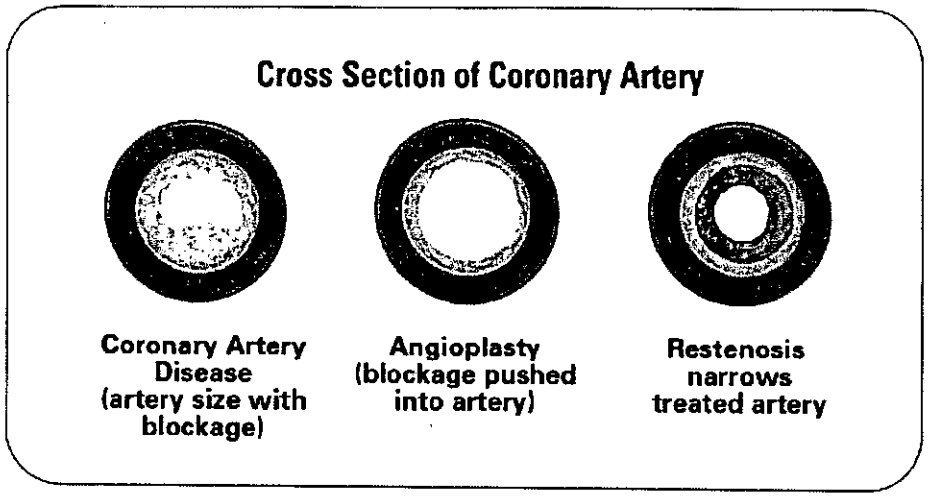
What are coronary artery stents?

Coronary artery *stents* are small mesh tubes that can help to reduce blockage of a coronary artery. The *stent* is implanted into an artery and expanded to fit the size, shape and bend of the coronary artery. The *stent* props the artery open and helps to prevent the blockage from returning. Once the *stent* is in place, the *stent* will remain in your artery. Over time, the artery wall will heal around the *stent* as it continues to support the artery.

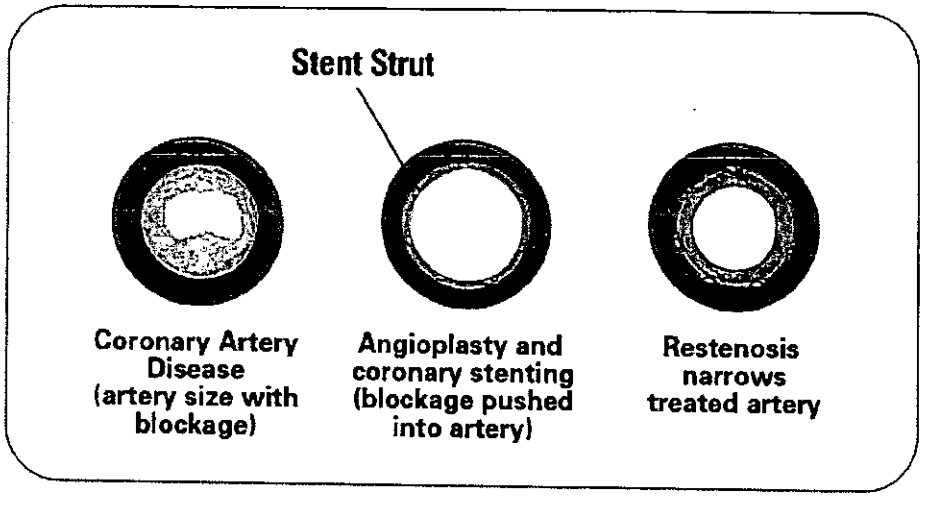
Why are stents used?

Many patients who undergo *balloon angioplasty* treatment will experience a re-narrowing of the artery. This re-narrowing is called *restenosis*. This re-narrowing of the coronary artery can happen more often following a *balloon angioplasty* procedure than for patients who receive a *stent*. The re-narrowing can be caused by a combination of factors including the blockage reforming or new tissue growth within the treated area.

Coronary artery with *angioplasty*



Coronary artery with stenting



What are the different types of coronary stents?

There are two kinds of *stents*, bare-metal and drug-coated. Bare-metal *stents* provide support to help keep the artery open after *angioplasty*. A drug-coated *stent* is a bare-metal *stent* with a special drug coating added to help reduce the chance of the artery becoming blocked again. The drug is released from the *stent* over the period of time during which re-blockage is most likely to occur. *Stents* are designed to be very flexible, allowing them to fit the shape of your artery.

Boston Scientific offers bare-metal and drug-eluting *stents*. Depending upon your specific needs, your doctor may choose to place a bare metal, drug-eluting or some combination of these *stents*. There are differences between the two *stent* types (such as the need for longer-term dual antiplatelet therapy with drug-eluting *stents*) that you should discuss with your doctor. Please refer to the PROMUS Element Plus Everolimus-Eluting Platinum Chromium Coronary Stent System Patient Information Guide for more details about the *stent*.

How does the drug coating and polymer work on a drug-eluting stent?

Polymer Coating
The *stent* is coated with a polymer which was developed specifically for drug-eluting *stents*. The polymer carries and protects the drug before and during the procedure. Once the *stent* is implanted, it helps control drug release into the coronary arterial wall. This controlled release contributes to even and consistent distribution of the drug in the wall of the artery.

Drug Release
The drug-eluting *stent* is coated with a drug and polymer and has been designed to allow for a consistent and controlled release of the drug from the *stent* surface into the artery walls. Both the amount of drug and release rate have been determined so that healing can occur while allowing the processes leading to restenosis to be minimized, thus reducing the need for additional treatment in the stented area.

Risks of treatment options

You should not have a drug-eluting *stent* placed in your coronary artery if you have any of the following conditions:

- You are allergic to the drug or related drugs
- You are allergic to the polymer
- You are allergic to stainless steel or platinum chromium
- You are unable to take medicines that make your blood take longer to clot (also called anticoagulants)
- You are unable to take medicines that make your blood cells slippery and make it more difficult for your blood to clot (also called antiplatelets)
- You have a blockage that will not allow proper placement of the *stent*
- You are allergic to the dye used during the procedure (also called contrast agent)

- Your doctor decides that you are not able to have the required medication prior to *stent* placement

Your doctor and the medical staff will monitor you during and after the procedure for complications. If a complication does occur, your doctor will decide what type of treatment you may need.

The placement of *stents* in arteries is done to treat blockages and to try to prevent re-narrowing.

As with any *stent* procedure, there is a chance that complications may occur, including, but not limited to, the following:

- Air bubbles, tissue or clots which can block the artery (emboli)
- Allergic reaction to the contrast dye (which could cause kidney failure)
- Allergic reaction to the drug
- Allergic reaction to the metal used to make the *stent* (stainless steel or platinum chromium)
- Allergic reaction to the polymer
- Aneurysm
- Arterial trauma which could require surgical repair or reintervention
- Bleeding (which may require a blood transfusion)
- Bruising at the access site
- Bruising which occurs on a blood vessel (pseudo-aneurysm)
- Chest pain or discomfort
- Collection of blood in the lining of the heart
- Coronary spasm
- Death
- Emergency bypass surgery
- Heart attack
- High or low blood pressure
- Inadequate supply of blood to the heart
- Infection and/or pain at the access site
- Injury or tearing of artery
- Irregular heartbeat (arrhythmia)
- Movement of the *stent* to an unintended location
- Plugging of the *stent* with blood clots
- Re-narrowing of the treated artery (*restenosis*)
- Shock/pulmonary edema
- Side effects due to contrast dye, heparin or other medications
- Stroke or other neurological problems
- Total blockage (occlusion) of the artery
- Unnatural connection between vein and artery (arterio-venous fistula)
- Worsening of heart and lung function

There is a chance that complications may occur relating to the drug everolimus (based on studies of patients who used the drug for a prolonged period of time) or the polymer which include:

- Abdominal pain
- Abnormal laboratory tests which may include:
  - Increased levels of creatinine in the blood (which reflect reduced kidney function)
  - Increased or decreased levels of potassium in the blood
  - Decreased levels of magnesium or phosphorous in the blood
  - Increased sugar (glucose) levels in the blood (possible new-onset diabetes)
  - Increased cholesterol levels in the blood
  - Increased levels of fats and triglycerides in the blood
- Back pain
- Blood in the urine
- Constipation
- Cough
- Decrease or changes in sense of taste
- Decreased red blood cell, white blood cell, or platelet cell counts (platelet cells help the blood clot)
- Decrease or loss of sperm count in men
- Delayed wound healing/fluid accumulation (may include surgical wounds)
- Diarrhea
- Dry or itchy skin
- Fatigue
- Fever
- Headache
- Increased blood pressure
- Indigestion
- Infections: increased risks of bacterial, viral, fungal, or protozoal infections (may include herpes virus infections, BK virus infection, polyoma virus infection, opportunistic infections, or a combination of the above)
- Inflammation of the lining of the digestive system and mucous membranes
- Inflammation of the lung (not due to infections)
- Infection of the lungs and upper airways
- Insomnia
- Interactions with medications that are influenced by the CYP3A4 metabolic pathway (consult your doctor for more information)
- Loss of appetite
- Lymphoma and other malignancies (may include skin cancers)
- Mouth ulcers or sores
- Nosebleeds
- Nausea
- Pain in the arms, chest, legs, incision site or related to the procedure
- Pain or difficulty with urination
- Presence of protein in the urine
- Rash
- Reactive swelling, usually in the face
- Shortness of breath, and lung or breathing problems
- Swelling in the body (usually in the legs) caused by water retention

- Tremor
- Urinary tract infection
- Vomiting
- Weakness

Live vaccines and close contact with people that have received them should also be avoided. There is also potential harm to a fetus for pregnant women.

When used with cyclosporine medication, there may be an increased risk of the following:

- Blood clots in the small blood vessels
- Bleeding that appears as purple patches or spots on the skin
- Blood clotting in the smallest blood vessels of the body that may affect the kidneys

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

Before your coronary artery stenting procedure

Before your coronary artery stenting procedure:

- Tell your doctor about any medications you are taking.
- Let your doctor know about any allergies you have. It is important he or she knows about allergies to contrast dye, iodine, cobalt, chromium, nickel, titanium, stainless steel; platinum or plastics.
- Tell your doctor if you cannot take aspirin or blood-thinning medicines. These medications are usually prescribed before and after your procedure.
- Make sure you understand the possible risks and benefits of your coronary *stent* procedure.

Below is a typical checklist. Your doctor may ask you to go through this before your procedure:

- Do not eat or drink anything after midnight on the night before your procedure.
- Follow the instructions you receive from your doctor and nurses.
- Take all your medications with you.
- You may be given a sedative to relax you before starting your *stent* procedure. The sedative can make you sleepy.

During a typical coronary artery stenting procedure

1. You will be taken to an area of the hospital called the Cardiac Catheterization Laboratory. While in the cath lab, you may be given a sedative that will make you feel sleepy during the procedure.

2. A small puncture is made in your arm or groin. A needle is used to gain access to your artery and a guide *catheter* and guide wire are fed through the artery and moved up into the coronary artery. All of this is done using X-rays for a guide.

3. The diseased artery may first need to be enlarged to make room for the *stent.* To do this, the doctor places a small, deflated balloon over the guide wire and through the *catheter* to the blocked area of the coronary artery. When the balloon is in the correct position, it is inflated. This pushes the *plaque* buildup aside and reopens the artery to restore blood flow.

4. The balloon is deflated and removed, and a small metal mesh tube called a *stent* is advanced into the same blocked area of the artery and expanded against the artery wall to fit the shape of your artery. Your doctor may choose to expand the *stent* by using another balloon. This is to make sure the *stent* is in better contact with the artery.

5. If your doctor places a drug-eluting *stent* into your artery, a drug will be released from the *stent* slowly over a period of time.

6. After the *stent* is implanted, the *catheter* and wire are removed and the puncture site is closed. The *stent* remains in place permanently and is designed to help keep the artery open and prevent future narrowing of the coronary artery.

After a typical coronary artery stenting procedure

- You may feel sleepy from the sedative given to you. This will wear off over the next few hours.
- You will be taken to a unit where nurses and doctors can monitor you.
- You will be asked to stay in bed for several hours. You will be asked to keep your arm or leg straight so the entry site can heal.
- You may need to stay in the hospital before you can go home.
- You should follow your doctor's recommendations and let them know if you are experiencing any of the following:
  - Chest pain
  - Shortness of breath
  - Sudden weakness or paralysis of the face, arm or leg
  - Pain, bleeding or infection at the entry site in your arm or leg
  - Any other unexplained symptoms
- You can return to normal activities gradually. Check with you doctor about physical activities.
- You should not stop taking your medications unless you are asked to stop by the doctor who implanted your *stent*.
- You should keep all of your follow-up appointments, including blood testing.
- You should carry your Stent Implant Card.
- You should always show your dentist or medical doctor your Stent Implant Card.

Medications

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

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

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

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

Follow-Up Examinations
You will need to see the cardiologist who implanted your *stent* for routine follow-up examinations. During these visits, your doctor will monitor your progress and evaluate your medications, the clinical status of your *coronary artery disease*, and how the *stent* is working for you.

Frequently Asked Questions

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

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

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

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

Can I undergo *MRI* or scanner testing with a *stent*?
MRI safety testing has shown that the coronary *stent* is MR Conditional and that a patient with a coronary *stent* may safely undergo an *MRI* scan under certain conditions listed on the Stent Implant Card. Prior to undergoing an *MRI* scan, inform your doctor or MR technologist that you have a coronary *stent* and show them your Stent Implant Card.

Can I play sports?
Your doctor will tell you what sports you can play and when you can start them.

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

Glossary

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

Angioplasty
A minimally invasive treatment to open blocked *coronary arteries*. Also known as *percutaneous transluminal coronary angioplasty (PTCA)*.

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

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

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

Coronary Angiogram
A test in which contrast dye is injected into the *coronary arteries* allowing the doctor to see the arteries on an X-ray machine.

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

Coronary Artery Bypass Graft Surgery (CABG)
Open heart or bypass surgery. A section of an artery or vein from your chest or leg is harvested and surgically attached to a coronary artery below the blocked area of the heart.

Coronary Artery Disease (CAD)
Disease affecting the *coronary arteries* that surround the heart and supply blood to the heart muscle.

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

In-Stent Restenosis
Recurrent blockage or narrowing of a previously stented area in an artery.

Lumen
The inner channel of an artery.

Magnetic Resonance Imaging (MRI)
A non-invasive way to take pictures of the body. MRI uses powerful magnets and radio waves, unlike x-rays and computed tomographic (CT) scans which use radiation.

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

Percutaneous Transluminal Coronary Angioplasty (PTCA)
See *Angioplasty*.

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

Restenosis
Recurrent blockage or re-narrowing of a previously treated artery.

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

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

[Back Panel]

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

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To order product or for more information, contact customer service at 1.888.272.1001.

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Prior to use, please see the complete "Directions for Use" and "Instructions for Use" at www.bostonscientific.com/PROMUSelement for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events and Operator's Instructions.

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PROMUS Element™ Plus Everolimus-Eluting Platinum Chromium Coronary Stent System
Patient Information Guide

You have recently had a PROMUS Element drug-coated stent implanted in the coronary arteries of your heart. The following information is important for you to know, including the possible risks associated with having a stent implant along with medication recommendations and questions you may have about your stent.

PROMUS Element Drug-Eluting Stent

The PROMUS Element stent is a bare-metal stent with a special drug coating added to help reduce the chance of the artery becoming blocked again. The drug is released from the stent over the period of time during which re-blockage is most likely to occur. The stent was designed to be very flexible, to increase its ability to reach the site of your heart artery blockage.

The PROMUS Element stent is delivered to the artery using the PROMUS Element Plus balloon delivery catheter. Together the PROMUS Element stent and the PROMUS Element Plus balloon delivery catheter make up the PROMUS Element Plus Stent System.

Polymer Coating

The stent is coated with a polymer which was developed specifically for drug-eluting stents. The polymer carries and protects the drug before and during the procedure. Once the stent is implanted, it helps control drug release into the coronary arterial wall. This contributes to even and consistent distribution of the drug from the stent.

Drug Release

The PROMUS Element drug-eluting stent is coated with a drug and polymer and has been designed to allow for a consistent and controlled release of the drug from the stent surface into the artery walls. Both the amount of drug and release rate have been selected so that healing can occur while minimizing the processes leading to restenosis (recurrent blockage of the artery), thus reducing the need for additional treatment in the stented area.

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 and ventricular tachycardia
- Arteriovenous fistula
- Bleeding
- Cardiac tamponade
- Cardiogenic shock/pulmonary edema
- Coronary aneurysm

- Death
- Dissection
- Emboli, distal (air, tissue or thrombotic material or material from device(s) used in the procedure)
- Heart failure
- Hematoma
- Hemorrhage, which may require transfusion
- Hypotension/hypertension
- Infection, local or systemic
- Ischemia, myocardial
- Pain, access site
- Perforation or rupture of coronary artery
- Pericardial effusion
- Pseudoaneurysm, femoral
- Renal insufficiency or failure
- Respiratory failure
- Restenosis of stented segment
- Stent embolization or migration
- Stent fracture
- Stent thrombosis/occlusion
- Stroke/cerebrovascular accident/transient ischemic attack
- Total occlusion of coronary artery
- Vessel spasm
- Vessel trauma requiring surgical repair or reintervention

Adverse events associated with daily oral administration of everolimus to organ transplant patients include but are not limited to:

- Abdominal pain
- Abnormal laboratory tests which may include:
  - Increased levels of creatinine in the blood (which reflect reduced kidney function)
  - Increased or decreased levels of potassium in the blood
  - Decreased levels of magnesium or phosphorous in the blood
  - Increased sugar (glucose) levels in the blood (possible new-onset diabetes)
  - Increased cholesterol levels in the blood
  - Increased levels of fats and triglycerides in the blood
- Back pain
- Blood in the urine
- Constipation
- Cough
- Decrease or changes in sense of taste
- Decreased red blood cell, white blood cell, or platelet cell counts (platelet cells help the blood clot)
- Decrease or loss of sperm count in men
- Delayed wound healing/fluid accumulation (may include surgical wounds)
- Diarrhea
- Dry or itchy skin
- Fatigue
- Fever

- Headache
- Increased blood pressure
- Indigestion
- Infections: increased risks of bacterial, viral, fungal, or protozoal infections (may include herpes virus infections, BK virus infection, polyoma virus infection, opportunistic infections, or a combination of the above)
- Inflammation of the lining of the digestive system and mucous membranes
- Inflammation of the lung (not due to infections)
- Infection of the lungs and upper airways
- Insomnia
- Interactions with medications that are influenced by the CYP3A4 metabolic pathway (consult your doctor for more information)
- Loss of appetite
- Lymphoma and other malignancies (may include skin cancers)
- Mouth ulcers or sores
- Nosebleeds
- Nausea
- Pain in the arms, chest, legs, incision site or related to the procedure
- Pain or difficulty with urination
- Presence of protein in the urine
- Rash
- Reactive swelling, usually in the face
- Shortness of breath, and lung or breathing problems
- Swelling in the body (usually in the legs) caused by water retention
- Tremor
- Urinary tract infection
- Vomiting
- Weakness

Live vaccines and close contact with people that have received them should also be avoided. There is also potential harm to a fetus for pregnant women.

When used with cyclosporine medication, there may be an increased risk of the following:

- Blood clots in the small blood vessels
- Bleeding that appears as purple patches or spots on the skin
- Blood clotting in the smallest blood vessels of the body that may affect the kidneys

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

Clinical Data Summary

The safety and effectiveness of the PROMUS Element stent were compared to the PROMUS stent in the PLATINUM Workhorse clinical trial that included 1530 patients with a planned five-year clinical follow-up. The study results showed that patients who received a PROMUS Element stent had a similar incidence of bypass surgery or repeat angioplasty in the lesion where the stent was placed, when compared to patients who received a PROMUS stent (1.9% in both the PROMUS Element and PROMUS groups at

12 months). The combined occurrence of death, heart attack, bypass surgery and repeat angioplasty, was 5.0% (PROMUS Element) vs. 4.9% (PROMUS) at 12 months.

Full study results are provided in the PROMUS Element Plus Everolimus-Eluting Platinum Chromium Coronary Stent System Directions for Use, which can be found on www.bostonscientific.com/PROMUSelement.

MEDICATIONS

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

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

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

AFTER THE PROCEDURE

After the stent is implanted, you will rest in a cardiology ward for a short period where you can be monitored closely as you begin to recover. It may be one or more days before you are discharged from the hospital.

Activity

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

FREQUENTLY ASKED QUESTIONS

Can the stent move or rust?

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

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

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

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

Can I undergo MRI or scanner testing with a stent?
MRI safety testing has shown that the PROMUS Element stent is MR Conditional and that a patient with a PROMUS Element stent may safely undergo an MRI scan under certain conditions listed on the Stent Implant Card. Prior to undergoing an MRI scan, inform your doctor or MR technologist that you have a PROMUS Element stent.

Can I play sports?
Your doctor will tell you what sports you can play and when you can start them.

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

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

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

Indications, contraindications, warnings and instructions for use can be found in the labeling supplied with each product. CAUTION: Federal (U.S.A.) law and governing law outside the U.S.A. restricts these products to sale by or on the order of a physician. PROMUS Element Plus Everolimus-Eluting Platinum Chromium Coronary Stent System is a product of Boston Scientific Corporation.

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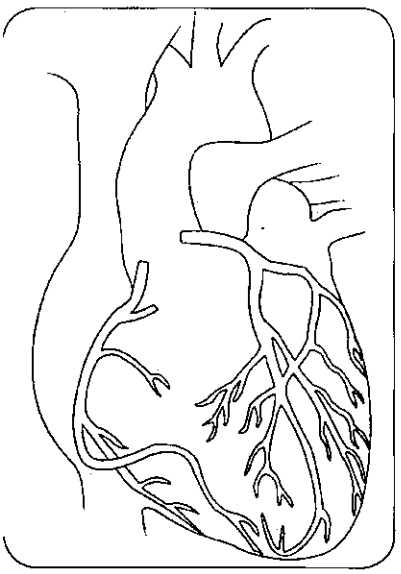

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[Stent Implant Card – front side]

PROMUS Element™ Plus Everolimus-Eluting Platinum Chromium Coronary Stent System

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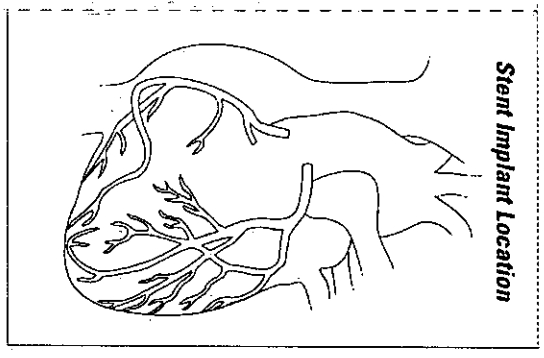

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[Stent Implant Card – back side]

PROMUS Element™ Plus Everolimus-Eluting Platinum Chromium Coronary Stent System

If you require a magnetic resonance imaging (MRI) scan, tell your doctor or MRI technician technologist that you have a stent implant. Test results indicate that the PROMUS Element stent is MR Conditional. Patients with single or overlapped PROMUS Element stents up to 74 mm in total length can undergo MRI scans safely under the following conditions:

- Field strengths of 1.5 Tesla and 3 Tesla
- Static magnetic field gradient <900 gauss/cm (extrapolated)
- Normal operating mode (maximum whole body averaged specific absorption rate (SAR) of lower than 2.0 W/kg) for a total active MR scan time (with RF exposure) of 15 minutes or less

The stent(s) should not migrate in this MRI environment and MRI may be performed immediately following the implantation of a PROMUS Element stent(s). Prior to undergoing an MRI scan, inform your doctor that you have a PROMUS Element stent. MR image quality will be compromised if the area of interest is in the same area or relatively close to the position of the stent. Please contact 1.888.272.1001 for more information about MR image artifact.

PLEASE CARRY YOUR CARD AT ALL TIMES

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

Stent Identification Information

Patient Name	Patient Phone Number
Implanting Physician's Name	Stent Material
Physician's Phone Number	Date of Implant
Product Name	Product Name
Product Lot Number	Product Lot Number
Stent Location	Stent Location

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