



## CMO Newsletter

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## Late-Breaking Information from the EuroPCR Congress Regarding the XIENCE V® Drug-Eluting Stent

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Dear Colleagues,

At the recently held EuroPCR Congress, May 19-22 in Barcelona, Spain, first of its kind data, which is clinically relevant for your practice, was released for the XIENCE V® Drug-Eluting Stent (DES). I want to take a moment to share these data with you and to give you a brief update on the progress Abbott Vascular is making in clinical studies with regard to XIENCE V® and its second generation XIENCE PRIME (first patient was enrolled June 15, 2009); currently an investigational device.\*

Eberhard Grube, MD, Chief, Department of Cardiology and Angiology at HELIOS Heart Center in Siegburg, Germany presented for the first time the one-year follow-up data from the SPIRIT V study. In addition, he presented five-year follow-up from the SPIRIT FIRST study. Prior to this point, the SPIRIT family of studies, known as SPIRIT FIRST, II, and III, had more limited inclusion/exclusion criteria. In contrast, SPIRIT V includes patients with lesions that are “real world” reflecting the broad range of disease seen everyday in a typical catheterization laboratory. In brief, SPIRIT V is a single arm, prospectively defined study enrolling 2,700 patients with limited exclusion criteria, meaning that the XIENCE V® drug-eluting stent was used at the investigator’s discretion in most any anatomy and in most any patient population. The endpoint analyzed is MACE at one year. MACE is a composite of cardiac death, MI attributed to a target vessel, and TLR as defined by the Academic Research Consortium (ARC).

\*Caution: Investigational device. Limited by Federal (or U.S.) law to investigational use. For Important Safety Information, see the end of this newsletter.

The patient population studied in SPIRIT V is a more complex set of patients than the prior SPIRIT studies as seen in Figure 1.

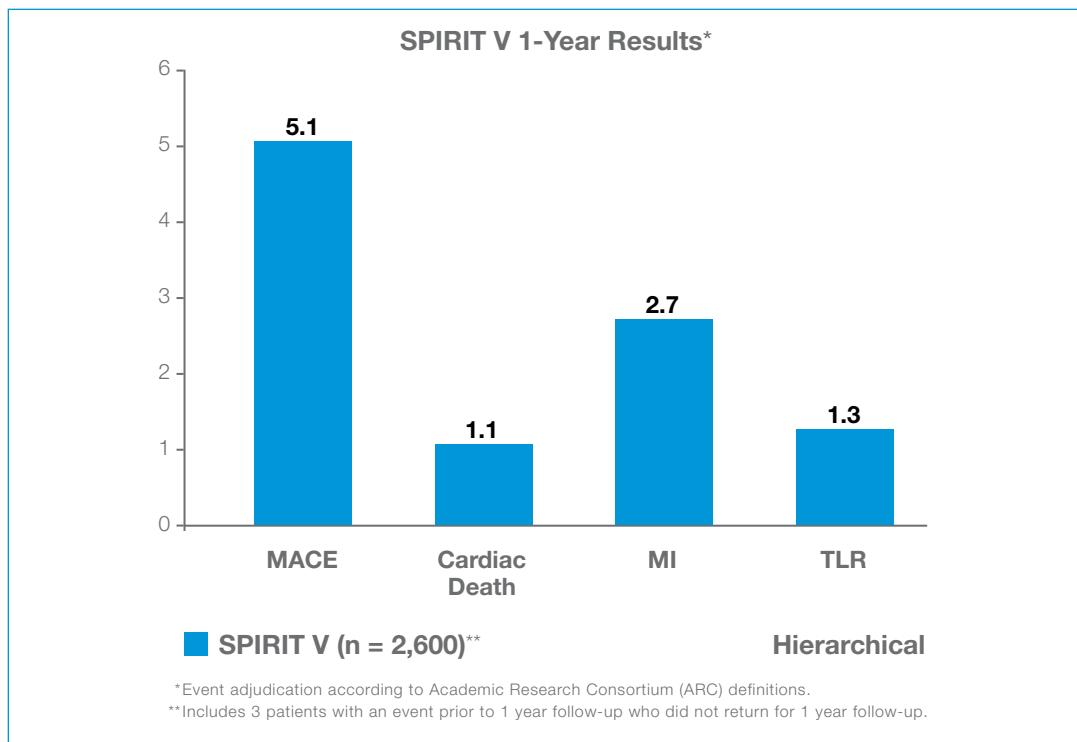
**FIGURE 1**

<b>Baseline Demographics</b>	
	N=2663
Age (yrs)	63
Male (%)	78
Current smoker (%)	24
Family history (%)	34
Diabetics (%)	30
Insulin dependent diabetic (%)	7
Hypercholesterolemia* (%)	59
Hypertension* (%)	64
Prior cardiac intervention (%)	25
Multi-vessel disease (%)	42
Prior MI (%)	31
Unstable angina	33
Braunwald Class III (%)	12
Patients with >1 target lesion (%)	29
* Requiring Medication	
<b>Baseline Lesion Characteristics**</b>	
	N <sub>L</sub> = 3645 Lesions
ACC lesion type B2 or C (%)	82
Bifurcation type C,D,F,G (%)	9
Left main (%)	1
Smaller vessels ≤ 2.75 mm (%)	35
Longer lesions ≥ 20 mm (%)	28
Calcification—moderate or severe (%)	29
Thrombus (%)	7
Eccentric (%)	53
Lesion angulation > 45° (%)	22
% Diameter stenosis (mean)	85
RVD (mean, mm)	2.97
Lesion length (mean, mm)	15.6
** Investigator Assessed	

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At one-year follow up, the hierarchical MACE rate was a low 5.1% as seen in Figure 2. This included a very low TLR rate of 1.3%.

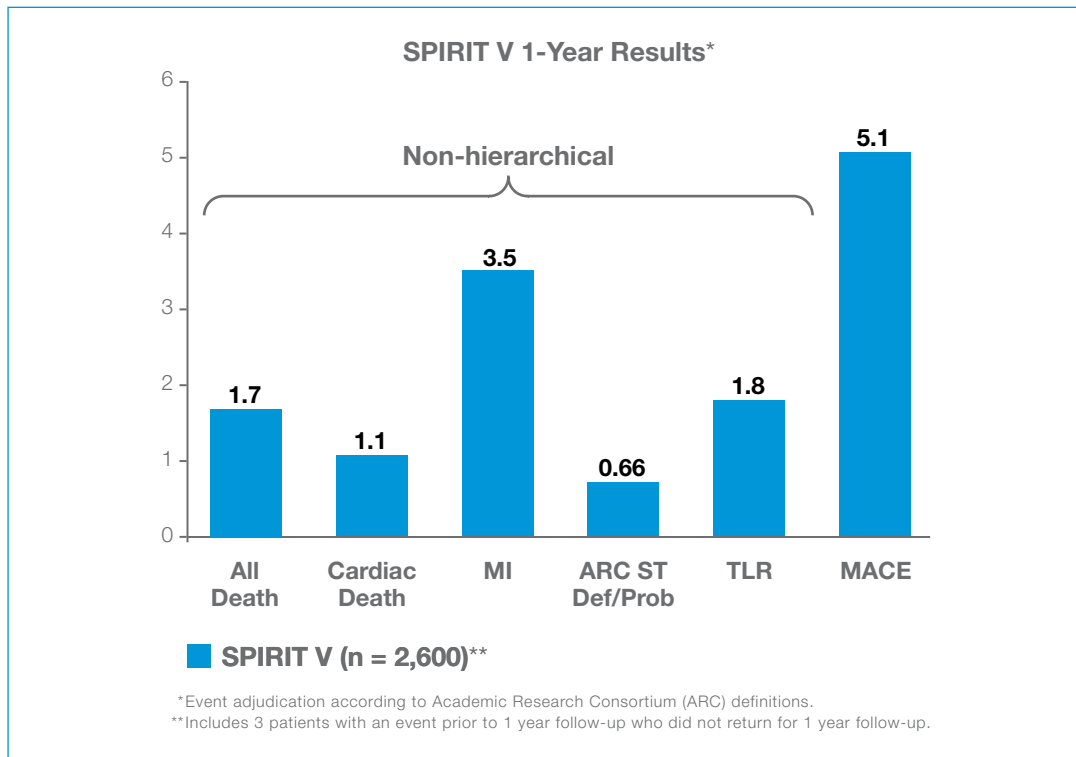
**FIGURE 2**



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In Figure 3, when assessing by a nonhierarchical analysis, which counts all events individually, the endpoints also remain very low. Most notable is the ARC-defined definite/probable stent thrombosis rate of 0.66. It should be noted that, despite being a less restrictive patient population, MI rates are consistent with the results of the more restrictive SPIRIT II and SPIRIT III randomized controlled trials.

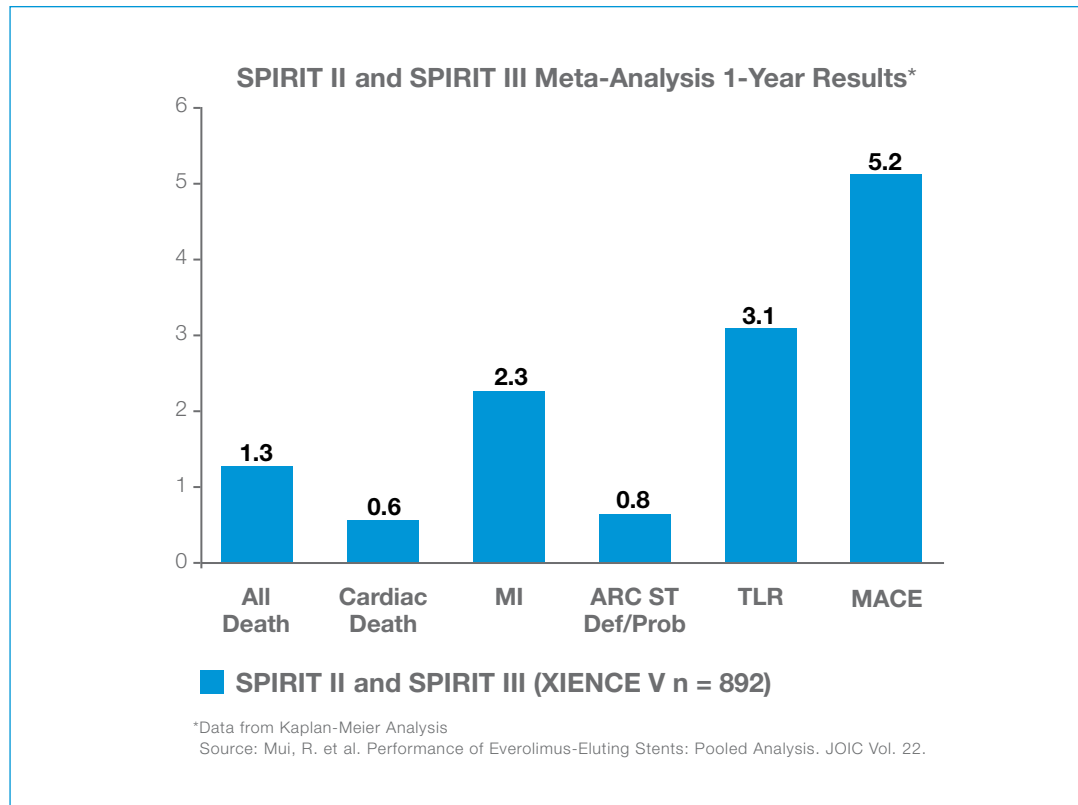
**FIGURE 3**



A very interesting finding emerges when you look at the SPIRIT V data with its less restrictive inclusion/exclusion criteria as opposed to the more restrictive inclusion/exclusion criteria of the 1,302 patients in SPIRIT II and SPIRIT III meta-analysis. One would expect to see a higher event rate in SPIRIT V because of the more complex baseline demographics. However, regardless of complexity, the two groups look more similar than different as seen in Figures 3 and 4. The TLR rates in SPIRIT V are roughly one half of the randomized controlled trial which is likely due to the contribution of the angiographic follow-up. Regardless, when examining complex lesions in a real world population, the results of one-year MACE, stent thrombosis, and TLR are consistently low with XIENCE V®.

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**FIGURE 4**



The SPIRIT body of data has now been reported on 4,000 patients with at least one year of follow-up and a maximum of five years in a limited number of patients. But the story does not stop there. I want to assure you that we, at Abbott Vascular, are not resting. We continue to study the complex anatomy that will give you answers to the everyday questions you face. Currently, we have enrolled 5,390 patients in our pre-approval studies (Figure 5). SPIRIT FIRST is the farthest along with five-year follow-up reported at EuroPCR 2009. This 60-patient, first-in-man study, comparing XIENCE V® to the Multi-Link Vision Stent, showed XIENCE V® continues to demonstrate no MACE or stent thrombosis events between one and five years with an overall MACE rate of 16.7%. SPIRIT II and SPIRIT III are each at three- and two-year follow-up, respectively, with a planned analysis out to five years. These data had updates at ACC 2009 and showed a single digit MACE rate of 7.4% in a combined analysis called the SPIRIT II and SPIRIT III meta-analysis at the two-year time period.

Next in line is SPIRIT IV. This will be the largest prospectively defined head to head DES study, comparing XIENCE V® to TAXUS Express, with a clinical only endpoint and no angiographic follow-up. These data are anticipated to be reported at TCT 2009 in September. We have initiated a 500 patient study to look at our 2nd generation DES - XIENCE PRIME.\* With modifications to the stent and delivery system this product is expected to deliver a 38 mm DES similarly to an 18 mm DES. XIENCE PRIME will have an expanded size matrix including SV for small vessels and LL for long lesions. With the addition of XIENCE PRIME to the SPIRIT studies almost 6,000 patients will be looked at over a five year period in pre-approval studies.

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**FIGURE 5**



## Investment in Clinical Programs: Worldwide DES Clinical Trial

Pre-approval		
Trial Name	# of Enrolling Sites	# of Patients
SPIRIT FIRST	9	60
SPIRIT II	28	300
SPIRIT III	65	1,002
SPIRIT III Japan	12	88
SPIRIT IV	58	3,690
SPIRIT Small Vessel	50	250
SPIRIT PRIME	75	500

Post-market		
Trial Name	# of Enrolling Sites	# of Patients
SPIRIT V	102	2,663
SPIRIT Women	100	2,000
XIENCE V USA	250	5,065
XIENCE V India	19	1,000
XIENCE V China	TBD	~2,450
XIENCE V Japan	TBD	~1,900
XIENCE V EXCEED	110	2,508
DAPT	TBD	~3,000

To answer the more challenging day-to-day questions, we have a very extensive postmarket approval program aimed at looking at the population of real world complex patient subsets. The very first glimpse of these 21,000 patients was discussed above in SPIRIT V. In addition to SPIRIT V, other studies include:

- XIENCE V® SPIRIT WOMEN, the world's first drug-eluting stent trial to study only women patients, at centers in Europe, Asia Pacific, Canada and Latin America
- XIENCE V® USA, a postmarket approval study in the United States
- XIENCE V® India, a postmarket approval study in India
- XIENCE V® China, a postmarket approval study in China
- XIENCE V® Japan, a postmarket approval study in Japan
- XIENCE V® EXCEED, a postmarket approval study in the United States
- DAPT, a postmarket approval study in the United States looking at durations of dual antiplatelet therapy of 12 months vs. 30 months

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I want you to feel confident in the Abbott Vascular clinical trials program. We are working very hard to find the answers to the questions that you face everyday as you treat patients with complex coronary artery disease. As we obtain answers, we will continue to disseminate the information to you as quickly as possible.

Sincerely,

Chuck Simonton, MD, FACC  
Chief Medical Officer and  
Divisional Vice President, Medical Science Group  
Abbott Vascular

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## **R<sub>x</sub>** The XIENCE™ V Everolimus Eluting Coronary Stent on the MULTI-LINK MINI-VISION® or MULTI-LINK VISION® Delivery System

### INDICATIONS

The XIENCE V Everolimus Eluting Coronary Stent System (XIENCE V stent) is indicated for improving coronary luminal diameter in patients with symptomatic heart disease due to *de novo* native coronary artery lesions (length ≤ 28 mm) with reference vessel diameters of 2.5 mm to 4.25 mm.

### CONTRAINDICATIONS

The XIENCE V stent is contraindicated for use in patients:

- Who cannot receive antiplatelet and/or anti-coagulant therapy
- With lesions that prevent complete angioplasty balloon inflation or proper placement of the stent or stent delivery system
- With hypersensitivity or contraindication to everolimus or structurally-related compounds, cobalt, chromium, nickel, tungsten, acrylic, and fluoropolymers.

### WARNINGS

- Ensure that the inner package sterile barrier has not been opened or damaged prior to use.
- Judicious patient selection is necessary because device use has been associated with stent thrombosis, vascular complications, and/or bleeding events.
- This product should not be used in patients who are not likely to comply with the recommended antiplatelet therapy.

### PRECAUTIONS

- Stent implantation should only be performed by physicians who have received appropriate training.
- Stent placement should be performed at hospitals where emergency coronary artery bypass graft surgery is accessible.
- Subsequent restenosis may require repeat dilatation of the arterial segment containing the stent. Long-term outcomes following

repeat dilatation of the stent is presently unknown.

- Risks and benefits should be considered in patients with severe contrast agent allergies.
- Care should be taken to control the guiding catheter tip during stent delivery, deployment and balloon withdrawal. Use fluoroscopy to avoid 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.
- When DES are used outside the specified Indications for Use, patient outcomes may differ from the results observed in the XIENCE V SPIRIT family of trials.
- Compared to use within the specified Indications for Use, the use of DES in patients and lesions outside of the labeled indications, including more tortuous anatomy, may have an increased risk of adverse events, including stent thrombosis, stent embolization, MI, or death.
- Orally administered everolimus combined with cyclosporine is associated with increased serum cholesterol and triglycerides levels.
- A patient's exposure to drug and polymer is proportional to the number of and total length of implanted stents. See *Instructions for Use* for current data on multiple stent implantation.
- Safety and effectiveness of the XIENCE V stent have not been established for subject populations with the following clinical settings:
  - Patients with prior target lesion or in-stent restenosis related brachytherapy, patients in whom mechanical atherectomy devices or laser angioplasty devices are used simultaneously, women who are pregnant or lactating, men intending to father children, pediatric patients, unresolved vessel thrombus at the lesion site, coronary artery reference vessel diameters < 2.5 mm or > 4.25 mm or lesion lengths > 28 mm, lesions located

in saphenous vein grafts, unprotected left main coronary artery, ostial lesions, chronic total occlusions, lesions located at a bifurcation or previously stented lesions, diffuse disease or poor flow (TIMI < 1) distal to the identified lesions, excessive tortuosity proximal to or within the lesion, recent acute myocardial infarction (AMI) or evidence of thrombus in target vessel, moderate or severe lesion calcification, multivessel disease, in-stent restenosis, and patients with longer than 24 months follow-up

- Everolimus has been shown to reduce the clearance of some prescription medications when it was administered orally along with cyclosporine (CsA). Formal drug interaction studies have not been performed with the XIENCE V stent because of limited systemic exposure to everolimus eluted from XIENCE V.
- Everolimus is an immunosuppressive agent. Consideration should be given to patients taking other immunosuppressive agents or who are at risk for immune suppression.
- Oral everolimus use in renal transplant patients was associated with increased serum cholesterol and triglycerides that in some cases required treatment.
- Non-clinical testing has demonstrated that the XIENCE V stent, in single and in overlapped configurations up to 68 mm in length, is MR Conditional. It can be scanned safely under the conditions in the *Instructions for Use*.
- The XIENCE V stent should be handled, placed, implanted, and removed according to the *Instructions for Use*.

## POTENTIAL ADVERSE EVENTS

Adverse events (in alphabetical order) which may be associated with coronary stent use in native coronary arteries include but are not limited to:

- Abrupt closure, Access site pain, hematoma, or hemorrhage, Acute myocardial infarction, Allergic reaction or hypersensitivity to contrast agent or cobalt, chromium, nickel, tungsten, acrylic and fluoropolymers; and drug reactions to antiplatelet drugs or contrast agent, Aneurysm, Arterial perforation and injury

to the coronary artery, Arterial rupture, Arteriovenous fistula, Arrhythmias, atrial and ventricular, Bleeding complications, which may require transfusion, Cardiac tamponade, Coronary artery spasm, Coronary or stent embolism, Coronary or stent thrombosis, Death, Dissection of the coronary artery, Distal emboli (air, tissue or thrombotic), Emergent or non-emergent coronary artery bypass graft surgery, Fever, Hypotension and / or hypertension, Infection and pain at insertion site, Injury to the coronary artery, Ischemia (myocardial), Myocardial infarction (MI), Nausea and vomiting, Palpitations, Peripheral ischemia (due to vascular injury), Pseudoaneurysm, Renal Failure, Restenosis of the stented segment of the artery, Shock/pulmonary edema, Stroke / cerebrovascular accident (CVA), Total occlusion of coronary artery, Unstable or stable angina pectoris, Vascular complications including at the entry site which may require vessel repair, Vessel dissection

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

- Abdominal pain, Acne, Anemia, Coagulopathy, Diarrhea, Edema, Hemolysis, Hypercholesterolemia, Hyperlipidemia, Hypertension, Hypertriglyceridemia, Hypogonadism male, Infections: wound infection, urinary tract infection, pneumonia, pyelonephritis, sepsis and other viral, bacterial and fungal infections, Leukopenia, Liver function test abnormality, Lymphocele, Myalgia, Nausea, Pain, Rash, Renal tubular necrosis, Surgical wound complication, Thrombocytopenia, Venous thromboembolism, Vomiting

Prior to use, please reference the *Instructions for Use* at [www.abbotvascular.com/ifu](http://www.abbotvascular.com/ifu) for more information on indications, contraindications, warnings, precautions, and adverse events.