PROTOCOL 12-396
XIENCE PRIME Everolimus Eluting Coronary Stent System (EECSS)
China Single-Arm Study

Version Number	Version 3.0
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Planned Number of Sites and Region(s)	Approximately 45 sites in China
Study Type	Prospective, observational, open-label, multi-center, single-arm, post-approval study
Sponsor	Abbott Cardiovascular Systems, Inc., A Subsidiary of Abbott Vascular 3200 Lakeside Drive Santa Clara, CA 95054, USA
Authorized Representative in China	Abbott Medical Devices Trading (Shanghai) Co., Ltd. 12F, Phase II IFC, No.8 Century Avenue, Pudong District

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Compliance Statement:

This study will be conducted in accordance with this Protocol, the Declaration of Helsinki and the Good Clinical Practice (GCP) guidelines of the China State Food and Drug Administration (CFDA). The most stringent requirements, guidelines or regulations must always be followed. The conduct of the study will be approved by the appropriate Ethics Committee (EC) of the respective investigational site and as specified by local regulations.

Sponsor Signatory Representative:
Approval for this protocol and any subsequent amendments shall be obtained per Abbott Vascular Standard / Detailed Operating Procedure(s).

PROTOCOL SUMMARY

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<tr><td>Study Name and Number</td><td>XIENCE PRIME China Single-Arm Study (XP China SAS): 12-396</td></tr>
<tr><td>Title</td><td>XIENCE PRIME Everolimus Eluting Coronary Stent System (EECSS) China Single-Arm Study</td></tr>
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<tr><th>Product Name</th><th>Stent Diameter (mm)</th><th>Stent Length (mm)</th></tr>
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<tr><td>Targeted number of patients to receive study device</td><td>Approximately 2000 patients will be consecutively registered from the general Chinese interventional cardiology population at approximately 45 sites in China.</td></tr>
<tr><td>Study Design</td><td>Prospective, observational, open-label, multi-center, single-arm, post-approval study</td></tr>
<tr><td>Key Endpoints</td><td>The following site reported endpoints will be assessed at 1, 2, 3, 4, and 5 years:
Composite rate of cardiac death and all myocardial infarction (MI) (Q-wave and non–Q-wave)
Composite rate of all death and all myocardial infarction (MI) (Q-wave and non–Q-wave)
Target lesion failure (TLF): the composite rate of cardiac death, target vessel MI, and ischemia-driven TLR (ID-TLR)
Target vessel failure (TVF): the composite rate of cardiac death, all MI, and ischemia-driven TVR (ID-TVR)
Stent thrombosis (definite and probable, per Academic Research Consortium [ARC] definition)
Death (cardiac, vascular, and non-cardiovascular)
All MI (Q-wave and non–Q-wave)
Revascularization (target lesion, target vessel, and non-target vessel) (PCI and CABG)</td></tr>
</table>

Patient Follow-up	Clinical follow-up will occur at 1, 2, 3, 4, and 5 years. The investigator/designee may conduct clinical follow-up(s) as hospital/office visits or telephone contacts.
Treatment Strategy	The investigator will determine the treatment strategy. Each enrolling investigator should review the most current *XIENCE PRIME Everolimus Eluting Coronary Stent System Instructions for Use (IFU)*.
Inclusion Criteria	• The patient must be at least 18 years of age at the time of signing the informed consent • The patient or his/her legally-authorized representative agrees to participate in this study by signing the Ethics Committee (EC) approved informed consent form (ICF) • Only XIENCE PRIME stent(s) is (are) implanted during the index procedure
Exclusion Criteria	No other exclusion criteria are specified for this study.
Analytical Population	The analytical population is defined as patients who received only XIENCE PRIME EECSS during the index procedure. Descriptive analyses will be provided on the analytical population and subgroups of interest. No pre-specified hypothesis tests are planned for this study.

1. INTRODUCTION

Abbott Vascular (AV) obtained marketing approval for the XIENCE PRIME Everolimus Eluting Coronary Stent System (XIENCE PRIME EECSS) in China from the China Food and Drug Administration (CFDA) on August 10th, 2011.

This prospective, observational, open-label, multi-center, single-arm, post-approval study is designed to evaluate the continued safety and effectiveness of the XIENCE PRIME EECSS in a cohort of real-world patients receiving the XIENCE PRIME EECSS during commercial use in real-world settings in China.

2. BACKGROUND INFORMATION

2.1 Background and Rationale

2.1.1 Background

Coronary Heart Disease in China
Coronary heart disease (CHD) is the second leading cause of cardiovascular death in Chinese population. CHD mortality in Chinese population is relatively low compared with that in western countries; however the burden of CHD has been increasing in recent years. About 400,000 patients died from CHD in 2004.[1] The CHD mortality rate is higher in north China compared to that in southeast China and other economically underdeveloped areas.[2,3,4]

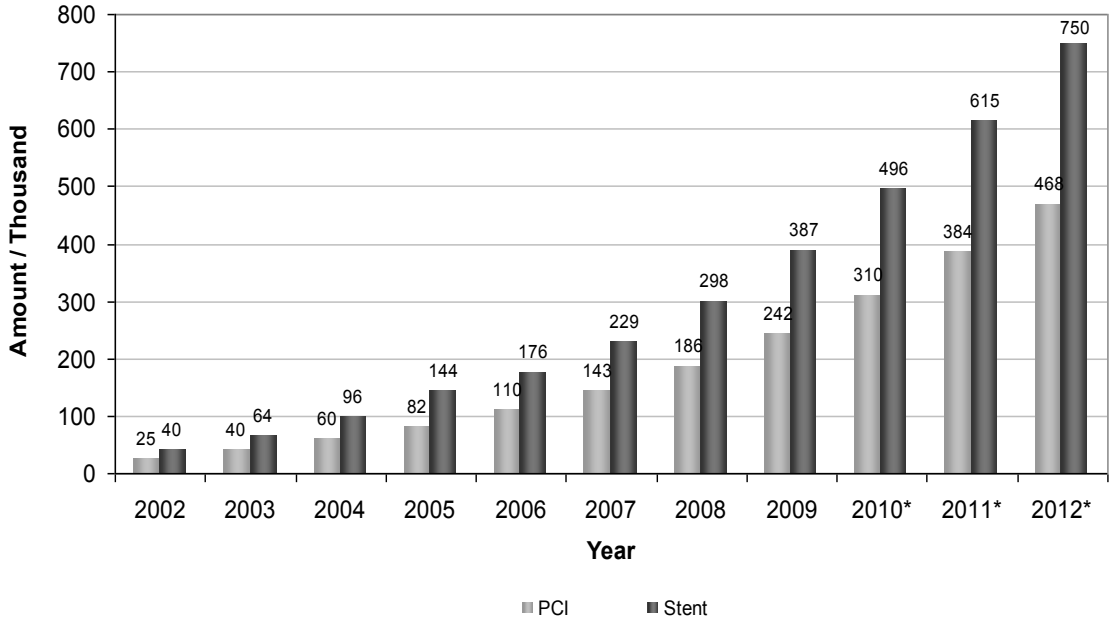
Coronary Heart Disease Risk Factors in the Chinese Population
China's emergence as a developing country has been a key contributing factor to its increase in CHD risk. By 2002 China had an estimated 540 million people with conditions such as hypertension, dyslipidemia, diabetes, and being overweight.[5] Large studies report that these listed risk factors significantly contribute to China's increase in CHD-related death. [6,7,8,9,10]

Drug-Eluting Stent Use in China
China experienced a rapid growth of percutaneous coronary intervention (PCI) between 2002 and 2012 (Figure 1).[11] An article in BMC Public Health[12] projects that absolute numbers of CHD events and deaths will increase dramatically in China over 2010–2029, due to a growing and aging population alone. The authors went on to predict 7.8 million excess CHD events (a 69% increase) and 3.4 million excess CHD deaths (a 64% increase) in the decade 2020–2029 compared with 2000–2009. Additionally, a recent economic analysis[13] reported that the Chinese market for coronary stent devices reached $323.1 million in 2011. By 2016, it is expected to reach $678.4 million, a projected compound annual growth rate (CAGR) of 16.0% between 2011 and 2016. The majority of these early PCI procedures used balloon angioplasty.[14] Coronary stenting was not

introduced in China until 1992, and subsequently Drug Eluting Stents (DES) followed in 2002.[15]

China's increased DES utilization has precipitated the need for the collection of CFDA mandated long-term, real-world safety and efficacy data. To address these surveillance needs, several studies are being conducted in China using the XIENCE V, ENDEAVOR, CYPHER, FIREBIRD, and TAXUS DES. The EXCEL sirolimus-eluting biodegradable stent is also being studied.[16,17,18]

Figure 1: Number of PCI procedures and coronary stents from 2002 to 2012 in China [11] (* estimates)



Clinical Studies of the XIENCE V and XIENCE Prime EECSS

XIENCE V EECSS has demonstrated outstanding clinical outcomes in both pre-marketing and post-marketing studies.[19] It is important to note that the XIENCE V EECSS has also been previously evaluated in native Chinese populations, including 63 patients from mainland China in the SPIRIT V single-arm study and 50 patients from the SPIRIT Women single-arm study.[20] Additionally, Abbott Vascular completed enrollment for two clinical studies (XIENCE V China Randomized, Controlled Trial [RCT] and XIENCE V single-arm study [SAS]) in China, 2011. These two studies are designed to evaluate the long-term safety and effectiveness of XIENCE V in real-world clinical settings in China, with approximately 500 patients enrolled in XIENCE V China RCT and 2500 patients enrolled in the XIENCE V SAS. In the SPIRIT V single-arm study, the primary endpoint (the adjudicated composite rate of all death, myocardial infarction [MI], and target vessel revascularization [TVR] at 30 days) was a composite of safety and effectiveness. The study's primary endpoint rate in overall patient population (2663

patients) was 2.6% compared to 0.0% in the China sites. Additionally, for these 63 patients no stent thrombosis (ST) was reported and clinical device and procedural successes were 100%.[21] The positive results from these Chinese patients thus suggest the safety and effectiveness of the XIENCE V EECSS in the Chinese population.

The XIENCE PRIME EECSS, the next generation DES from the XIENCE V EECSS, has showed similar and consistent safety and effectiveness profile. The safety and effectiveness of the XIENCE PRIME was demonstrated in the SPIRIT PRIME study by meeting its primary endpoint of target lesion failure at 1 year when compared to pre-specified performance goal derived from trials with XIENCE V. [22]

2.1.2 Rationale to Conduct this Clinical Study

This is a CFDA-mandated study aiming to assess the continued safety and effectiveness of XIENCE PRIME EECSS in real-world settings in China. Furthermore, this study will add to the group of DES studies currently being conducted in China and provide additional region-specific information.

2.2 Summary of Study Device

2.2.1 Name of the Study Device

The Clinical Study Device to be used is the XIENCE PRIME Everolimus Eluting Coronary Stent System, manufactured by Abbott Vascular, Santa Clara, USA.

The XIENCE PRIME EECSS is composed of 2 regulated components: the base device (MULTI-LINK VISION Coronary Stent System (CSS) or MULTI-LINK MINI VISION CSS) and the drug (everolimus, [contained in a polymer coating]). The MULTI-LINK VISION® stents are manufactured from medical grade L-605 cobalt chromium (CoCr) alloy. Refer to the most recent Instructions for Use (IFU) for descriptions, indications for use, contraindications, system preparation, precautions, and warnings.

The stent diameters and stent lengths are as follows:

Clinical Study Device: XIENCE PRIME EECSS

Product Name	Stent Diameter (mm)	Stent Length (mm)
XIENCE PRIME	2.5, 2.75, 3.0, 3.5, 4.0	8, 12, 15, 18, 23, 28
XIENCE PRIME SV (Small Vessel)	2.25	8, 12, 15, 18, 23, 28
XIENCE PRIME LL (Long Lesion)	2.5, 2.75, 3.0, 3.5, 4.0	33, 38

3. STUDY OBJECTIVE

The study is to evaluate the continued safety and effectiveness of the XIENCE PRIME EECSS in a cohort of real-world patients receiving the XIENCE PRIME EECSS during commercial use in China.

4. CLINICAL STUDY FLOW AND FOLLOW-UP SCHEDULE

Clinical follow-ups will occur at 1, 2, 3, 4, and 5 years. See APPENDIX III: for detailed flow chart. The Investigator/designee may conduct follow-ups as hospital/office visits (preferable) or telephone contacts. If follow-ups have to be conducted by telephone, the Investigator/designee should contact the study patient. If efforts to reach the patient by telephone are unsuccessful or the patient wishes to continue his/her participation but is not immediately available by telephone, a relative may be contacted.

If the patient or his/her relative cannot be reached after 3 telephone attempts on different days at different times, it is then recommended to send a registered letter requesting the patient to follow up.

4.1 Number of Patients to Be Registered

Approximately 2000 patients at approximately 45 sites across China will be consecutively registered in this study. Only patients who agree to participate by signing the informed consent form (ICF) and who will have or have received only XIENCE PRIME stents during the index procedure are eligible to be registered.

4.2 Early Termination of the Clinical Study

No statistical rule for early study termination is defined. However, Abbott Vascular may discontinue the study in part or in total at any time with written notice to the Investigators.

If a study is terminated early, AV will provide a written statement describing why this will occur and notify the CFDA if applicable. In the case of early study termination, the Investigators are responsible for notifying the Ethics Committee (EC) and their patients. All applicable clinical study documents will be maintained under the same retention policy as detailed in section 12.3 Record Retention.

4.3 Termination of Study Site Participation

AV reserves the right to terminate study site participation and remove appropriate study materials at any time. Specific instances that may lead to such termination include, but are not limited to:

- Unsatisfactory patient enrollment
- Failure to comply with protocol
- Failure to comply with applicable CFDA guidelines
- Inaccurate and/or incomplete data recording on a recurrent basis

The Investigator may also discontinue study participation with suitable written notice to AV.

5. KEY ENDPOINTS

The following key site reported endpoints will be assessed at 1, 2, 3, 4, and 5 years:

- Composite rate of cardiac death and all myocardial infarction (MI) (Q-wave and non–Q-wave)
- Composite rate of all death and all myocardial infarction (MI) (Q-wave and non–Q-wave)
- Target lesion failure (TLF): the composite rate of cardiac death, target vessel MI (TV-MI), and ischemia-driven target lesion revascularization (ID-TLR)
- Target vessel failure (TVF): the composite rate of cardiac death, all MI, and ischemia-driven target vessel revascularization (ID-TVR)
- Stent thrombosis (definite and probable, per Academic Research Consortium[ARC] definition)
- Death (cardiac, vascular, and non-cardiovascular)
- All MI (including Q-wave and non–Q-wave)
- Revascularization (target lesion, target vessel, and non-target vessel) (PCI and Coronary Artery Bypass Graft [CABG])

The clinical endpoints described above are direct measurement of safety and effectiveness of coronary stent implantation. These endpoints are widely used in stenting randomized control studies and registries and accepted by cardiac intervention medical communities.

6. PATIENT SELECTION AND WITHDRAWAL

6.1 Patient Screening and Informed Consent

6.1.1 Patient Screening

Patients admitted for PCI, and who will have or have had only XIENCE PRIME EECSS implanted, should be invited to participate in the study. Once informed consent is obtained, patient's data is to be entered into the electronic Case Report Form (eCRF) screening log.

6.1.2 Informed Consent

The Investigator or designee, who has been trained on the protocol, will explain the nature and scope of the study and answer questions for the patients. A patient who is considered as part of a vulnerable population may not be registered in the study, except for members of the armed forces. However, special protection must be given to these patients. When obtaining Informed Consent from these patients, the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. When obtaining the consent, provision of a copy to the patient, along with the date and time must be documented in the patient's medical records. All patients or their legally-authorized representatives and the investigator/designee must personally sign and date the EC-approved ICF.

It is strongly recommended that patients (or legally authorized patients' representatives if applicable) sign, date and time the Ethics Committee (EC) approved ICF prior to the index procedures. In the event that the signed ICF cannot be obtained prior to the procedure, it must be obtained no later than the time of hospital discharge and no later than 7 days post index procedure if hospital stay is prolonged due to any reasons. Sites must also abide by their respective EC ICF requirements, including signature timelines, if site requirements are more stringent.

For patients signing the ICF post procedure, data for the study is to be collected retrospectively and can only be entered into eCRF after the ICF is obtained. Finally, at the time of signing the ICF, patients must be assessed and deemed capable of signing.

Failure to obtain a signed ICF will render the patient ineligible for the study. The signed and dated ICF is to be maintained in the patient's medical records and a copy given to the patient or his/her legally-authorized representative. The ICF will include language that satisfies the CFDA requirements and accounts for any applicable regulations.

For any live cases at congresses the patient needs to sign a specific Live Case ICF approved by the IRB/EC. The investigator must notify AV prior to performing a live case.

6.2 Eligibility Criteria

Assessment for general eligibility criteria is based on medical records of the site and interview with a candidate patient. If some of the clinical and laboratory tests are not included in site standard tests, they must be done but after written informed consent obtained. Patients must meet ALL of the inclusion criteria to be considered for the clinical evaluation. If ANY of the exclusion criteria are met, the patient is excluded from the clinical evaluation and cannot be registered.

6.2.1 Inclusion Criteria

- The patient must be at least 18 years of age at the time of signing the informed consent.
- The patient or his/her legally-authorized representative signs the EC-approved ICF.
- Only XIENCE PRIME stent(s) is (are) implanted during the index procedure.

6.2.2 Exclusion Criteria

No other exclusion criteria are specified for this study.

6.3 Point of Registration

The enrollment service must be called after both of the following conditions have been met:

1. A patient or patient's legally-authorized representative has provided an EC approved, signed and dated ICF.
2. Only XIENCE PRIME stent(s) is/are implanted in the coronary vasculature during the index procedure.

6.4 Patient Deregistration

This study will consecutively register all consenting patients who have met these eligibility criteria. If a registered patient didn't receive a XIENCE PRIME stent (s) during the index procedure, this patient is to be de-registered.

A de-registered patient will not undergo the protocol follow-up regimen or follow-up by the study team. De-registered patients may be replaced until the total number of required

patients for the study is reached (refer to section 4.1 Number of Patients to Be Registered).

6.5 Patient Discontinuation

Each registered patient should remain in the clinical study until the required follow-up periods are complete. The patient has the right to withdraw from the study at any time without penalty or loss of benefit. Possible reasons for patient discontinuation may include, but are not limited to:

- Patient death
- Patient voluntary withdrawal
- Patient withdrawn by Investigator
- Patient lost to follow-up
- Study is terminated (refer to section 4.2 Early Termination of the Clinical Study)

The Investigator may terminate the patient's participation without regard to the patient's consent if the Investigator believes the termination is medically necessary. Patient participation in a clinical study is voluntary and the patient may discontinue participation (refuse all subsequent testing/follow-up) at any time without loss of benefits or receiving any penalty.

However, if a patient withdraws from the study due to problems related to the study device safety or performance, the investigator shall ask for the patient's permission to follow his/her status/condition outside of the clinical investigation

Lost to-follow-up:

If the patient misses two consecutive scheduled follow-up time points, and the attempts to contact the patient or patient's healthcare provider or relative detailed below are unsuccessful, then the patient is considered lost to-follow-up.

- A minimum of three telephone calls to contact the patient should be recorded in the source documentation, including date, time, and initials of site personnel trying to make contact;
- If these attempts are unsuccessful, a certified letter should be sent to the patient.

6.6 Study Completion

A Study Completion form must be completed when:

- the patient is considered lost to follow-up (refer to section 6.5 Patient Discontinuation) or
- the patient withdraws from the Clinical Study or
- the investigator withdraws the patient from the Clinical Study or
- the patient has died or
- upon Clinical Study completion (5 year follow-up time point has been reached)

AV must be notified of the reason for patient discontinuation. The site will provide this information on the eCRF. Investigators must also report this to their EC as defined by their institution's procedure. Discontinued patients will not be replaced.

7. TREATMENT AND EVALUATION OF SAFETY AND EFFICACY

Patients should be prepared according to the healthcare facility's standard of care for interventional cardiology patients. The schedule of events for this study is located in section APPENDIX IV: SCHEDULE OF EVENTS. The Investigator will determine the treatment strategy.

Each enrolling investigator should review the most current XIENCE PRIME EECSS IFU, appropriate Chinese PCI guidelines[23], and/or the American College of Cardiology (ACC)/American Heart Association (AHA)/Society for Cardiovascular Angiography and Interventions (SCAI) 2005/2007 guidelines for PCI.[24]

7.1 Baseline

7.1.1 Baseline Laboratory Assessments

Baseline laboratory data may be collected up to 4 weeks prior to the index procedure as appropriate. If multiple assessments are performed within 4 weeks prior to the index procedure, the most recent assessment value, or clinical significant findings should be included with the baseline laboratory information. In the event that the laboratory data (excluding cardiac biomarkers and electrocardiogram) is not available within the baseline window, it is strongly suggested that it be collected after the index procedure or before hospital discharge, but no later than 7 days post index procedure. Refer to Appendix IV: SCHEDULE OF EVENTS for specific collection time frames.

If available, the following baseline laboratory assessments should be collected:

- Lipid profile (low-density lipoprotein, high-density lipoprotein, triglycerides, and total cholesterol)
- Serum insulin, serum creatinine, serum fasting glucose, and glycated hemoglobin (HbA1c)

- For female subjects of childbearing potential, a urine pregnancy test should be performed according to hospital standard of care.

7.1.2 Patient History

If available, the following medical history data should be collected at baseline (including, but not limited to):

- Demographics, including age and gender
- Cardiac history including Canadian Cardiovascular Society and Braunwald classifications of angina[25] Acute Coronary Syndrome, prior MI, and previous CABG and PCI
- Physical measurements, including weight, height, and current left ventricular ejection fraction
- Other risk factors, including stroke, diabetes mellitus, hypertension, dyslipidemia, renal insufficiency, anemia, tobacco use, and family history of premature coronary artery disease (CAD)

Any baseline medical history data that is not collected within 4 weeks prior to the index procedure may be obtained up to 7 days post procedure and will still be considered baseline data (refer to APPENDIX IV: SCHEDULE OF EVENTS for specific data collection time periods).

7.2 Pre-procedure

Patients should be prepared according to the healthcare facility's standard of care for cardiology patients undergoing PCI. The XIENCE PRIME stent(s) to be placed should be inspected, prepared, and implanted according to the most current IFU.

7.2.1 Pre-procedure Laboratory Assessment

If available, the following pre-procedural assessments should be collected within 72 hours prior to the procedure:

- Creatine kinase (CK), creatine kinase myocardial-band isoenzyme (CK-MB), and/or troponin I/T (the most recent assessment)
- Electrocardiogram (ECG)

7.3 Index Procedure

7.3.1 Procedural Information to be Recorded

If available, the following data should be collected (including, but not limited to):

- Stent use attributes (eg, size, diameter, overlapping, and number of stents)
- Lesion characteristics (ACC/AHA Classification Scheme of Coronary Lesions)
- All reportable adverse events (AEs) (refer to section 8.3 Adverse Event Reporting)

7.3.2 Bailout Stenting or Alternative Procedures

If bailout stenting is needed during the index procedure and the patient wants to continue to be registered in the study, the bail-out stent(s) **must** be XIENCE PRIME stents.

For patients who will have planned staged procedures scheduled at the index procedure, it is recommended that the physician treat these patients with only the XIENCE PRIME EECSS. If these planned staged procedure patients receive stents other than XIENCE PRIME stents during their follow-up procedure(s), they will still remain in the study.

7.4 Post-procedure

7.4.1 Post-procedure Information to be Recorded

If available, the following data should be collected post procedure/on discharge:

- All reportable AEs (refer to list in section 8.3 Adverse Event Reporting):

7.4.2 Post-procedure Laboratory Assessment

If available, the following post-procedure cardiac biomarkers and ECG should be collected between 12 hours post procedure and the time of hospital discharge. For those patients with prolonged hospital stays, it is recommended that the assessment be conducted no later than 72 hours post procedure.

- CK, CK-MB, and/or troponin I/T
- Electrocardiogram (ECG)

7.5 Clinical Follow-up for All Patients (Hospital/Office Visit or Telephone Contact)

Clinical follow-up will occur as either hospital/office visits (preferable) or telephone contacts at the following time points:

Follow-up time point	Time window (± days)	Type of Visit
1 year	60	Hospital/office visit or telephone contact

2 years	60	Hospital/office visit or telephone contact
3 years	60	Hospital/office visit or telephone contact
4 years	60	Hospital/office visit or telephone contact
5 years	60	Hospital/office visit or telephone contact

When possible, all contacts should be directly with the patient. If the patient cannot be reached, follow-up visit information may be collected from the patient's relative. Data involving the following events should be collected at the specified time points:

- All reportable AEs (refer to list in section 8.3 Adverse Event Reporting)
- Dual antiplatelet therapy (aspirin, thienopyridine)

7.6 Additional Follow-up Visits for All Patients

If a patient completes a hospital/office visit independent of this protocol and outside of the protocol-recommended follow-up time points for an AE-driven visit, all efforts must be made to obtain follow-up information on patients who have undergone procedures or have been treated for reportable AEs in a non–study-related health care facility.
The following data should be collected at any additional follow up visits:

- All reportable AEs (refer to list in section 8.3 Adverse Event Reporting)
- Dual antiplatelet therapy (aspirin, thienopyridine)

8. ADVERSE EVENTS

8.1 Definitions

To comply with worldwide standards and guidelines on clinical trial adverse event reporting (ISO14155, MEDDEV2.7/3, US 21 CFR 812), AV has developed the below definitions to be used and adhered to by the investigators. The exact definitions as referenced in these standards and guidelines are included in APPENDIX II: DEFINITIONS.

8.1.1 Adverse Event

An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.

NOTE 1: This definition includes events related to the investigational medical device or the comparator.
NOTE 2: This definition includes events related to the procedures involved.
NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices.

An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

8.1.2 Serious Adverse Event

If the AE meets any of the criteria below, it is regarded as serious adverse event (SAE).

a) Led to a death
b) Led to a serious deterioration in health that either:
1) Resulted in a life-threatening illness or injury, or
2) Resulted in a permanent impairment of a body structure or a body function, or
3) Required in-patient hospitalization or prolongation of existing hospitalization, or
4) Resulted in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
c) Led to fetal distress, fetal death or a congenital abnormality or birth defect
d) An important medical event that may not result in death, be life-threatening, or require hospitalization but may be considered serious when based upon appropriate medical judgment, may jeopardize the subject and/or may require intervention to prevent one of the outcomes listed in this definition

NOTE 1: This includes device deficiencies that might have led to a SAE if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate. These are handled under the SAE reporting system.

NOTE 2: A planned hospitalization for pre-existing condition, or a procedure required by the Clinical Investigation Plan, without a serious deterioration in health, is not considered to be a serious adverse event.

8.1.3 Device Deficiency

All device deficiencies should be reported to Abbott Vascular customer service at (800) 227-9902 in the USA or (951) 914-4669 outside the USA. Device deficiencies should be reported to the IRB/EC per the investigative site's local requirements.

8.2 Device Relationship

Determination of whether there is a reasonable possibility that an investigational product or device caused or contributed to an AE is to be **determined by the Investigator** and recorded on the appropriate CRF form. Determination should be based on assessment of temporal relationships, biologic plausibility, association (or lack of association) with underlying disease and presence (or absence) of a more-likely cause.

8.3 Adverse Event Reporting

8.3.1 Adverse Event Monitoring

During each clinical follow-up, the Investigator/designee will determine and report all of the following AEs to AV:

- All events resulting in death
- Stent Thrombosis (ST)
- Myocardial Infarction (MI)
- All coronary revascularizations
- Major bleeding complications (to be reported per the Global Use of Strategies to Open Occluded Coronary Arteries [GUSTO] classification, severe and moderate bleeding combined)
- All device-related AEs, including events in which device relationship is unknown
- All cardiac AEs which meet one or more of the criteria of a serious AE (SAE) (Refer to section 8.1.2 Serious Adverse Event)

The Investigator will monitor the occurrence of AEs for each subject during the course of the clinical trial/investigation and report as required by this protocol. AEs need to be collected at the time point of on the appropriate AE eCRF form. A fax form will be made available to allow the investigator to report SAEs in the event the eCRF is not available. This does not replace the EDC reporting system. All information must still be entered in the EDC system once the system is back to normal function.

Unchanged, chronic, non-worsening or pre-existing conditions are not AEs and should not be recorded on the AE eCRF page.

8.3.2 Serious Adverse Event and device deficiency/product experience reporting to Sponsor and IRB/EC

The investigator should report all SAEs to the Sponsor and IRB/MEC as soon as possible but no later than outlined below.

Study sites	Reporting timelines
	SAEs must be reported no later than 3 calendar days from the site becoming aware of the event or as per the investigative site's local requirements if the requirement is more stringent than those outlined.

The date the site staff became aware that the event met the criteria of a serious adverse event must be recorded in the source document.

Serious adverse events that do not occur in the study subject but occur in the user or other persons should not be entered in the EDC system, however need to be reported on the fax notification form titled SAE Notification Form.

The Investigator will further report the event to the local IRB/EC according to the institution's IRB/EC reporting requirements.

8.4 Safety Monitoring

Every effort will be made to conduct an unbiased review of patient safety information and ensure patient safety. Qualified safety personnel designated by AV will review the safety data throughout enrollment and follow-up periods.

9. STATISTICAL ANALYSIS

9.1 Statistical Overview

This prospective, open-label, multi-center, observational, single-arm post-approval study is designed to evaluate the continued safety and effectiveness of the XIENCE PRIME EECSS in a cohort of real-world patients receiving the XIENCE PRIME EECSS during commercial use. Approximately 2000 patients will be consecutively registered at up to 45 sites in China. No pre-specified hypothesis tests are planned for this study. Only descriptive analyses will be performed.

9.2 Analysis Populations

The analytical population is defined as patients who received only XIENCE PRIME EECSS during the index procedure.

9.3 Sample Size Calculations and Assumptions

Approximately 2000 patients will be consecutively registered into the study from the general Chinese interventional cardiology population. The sample size of 2000 is based on CFDA's requirements for post approval studies, but not based on statistical hypothesis testing.

9.4 Statistical Analyses

For binary variables such as ST, Death and MI, results will be summarized with patient counts, percentages, and exact 95% Clopper-Pearson confidence intervals. [26] For continuous variables such as age, results will be summarized with the numbers of observations, means, standard deviations, and 95% confidence intervals for the means. These calculations will be done under the assumption that the data are approximately normal in distribution. For time-to-event variables, such as time to TLF, survival curves may be constructed using Kaplan-Meier estimates, and log rank test results for subgroup analysis will be displayed for descriptive purposes only.

9.4.1 Key Endpoint Analysis

Rates and confidence intervals will be summarized descriptively for the following key site reported endpoints at 1, 2, 3, 4, and 5 years:

- Composite rate of cardiac death and all myocardial infarction (MI) (Q-wave and non–Q-wave)
- Composite rate of all death and all myocardial infarction (MI) (Q-wave and non–Q-wave)
- Target lesion failure (TLF): the composite rate of cardiac death, target vessel MI (TV-MI), and ischemia-driven target lesion revascularization (ID-TLR)
- Target vessel failure (TVF): the composite rate of cardiac death, all MI, and ischemia-driven target vessel revascularization (ID-TVR)
- Stent thrombosis (definite and probable, per Academic Research Consortium[ARC] definition)
- Death (cardiac, vascular, and non-cardiovascular)
- All MI (including Q-wave and non–Q-wave)
- Revascularization (target lesion, target vessel, and non-target vessel) (PCI and Coronary Artery Bypass Graft [CABG])

9.4.2 Additional Analyses

Descriptive analyses will be provided for patient demographics, medical histories, and co-morbidities.

Logistic regression analyses may be used to screen a wide range of parameters for their association with some endpoints. Each patient will serve as their own control. Correlation analyses will be conducted for several parameters including, but not limited to, late stent thrombosis incidence.

9.4.3 Subgroup Analysis

Subgroup analyses for diabetic, non-diabetic, single-vessel and dual-vessel patients, etc. will be performed descriptively. Results that will be presented are baseline demographics, lesion characteristics as well as clinical outcomes. In addition, for future regulatory submissions, data may be evaluated to allow data pooling etc.

9.4.4 Procedures for Accounting for Missing, Unused or Spurious Data

All analyses will be based on available data with missing data excluded. Any unused or spurious data will be noted as appropriate in report.

10. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The Investigator/designee or institution will permit direct access to source data and documents for clinical study-related monitoring, audits, EC review, and regulatory inspections.

Patients providing informed consent agree to allow AV/designee access and copying rights to pertinent medical record information. As part of informed consent, the Investigator/designee will obtain permission for AV representatives or regulatory authorities to review, in confidence, any records identifying patients in this clinical study. AV will not otherwise release any personal information (refer to section 13.2 Confidentiality).

11. QUALITY CONTROL AND QUALITY ASSURANCE

11.1 Selection of Clinical Sites and Investigators

AV will select investigators who are qualified physicians with experience in interventional cardiovascular procedures and are qualified to perform clinical research. Sites will be selected using a combination of Investigator qualifications and site assessment criteria.

11.2 Protocol and Informed Consent Approval

- The Principal investigator must agree with the content of the protocol prior to taking part in the study.
- Approval of the protocol, informed consent forms, and other documents associated with the study must be obtained from the IRB/EC.
- The investigators are required to keep the IRB/EC informed of the study progress on a regular basis until termination of the study.

11.3 Protocol Amendments

AV/designee will provide AV-approved protocol amendments to Investigators when the protocol is amended. The Principal Investigator will be responsible for notifying the EC and/or obtaining documented EC approval of any protocol amendments prior to amendment implementation. Documentation of necessary EC approvals must be provided to AV.

11.4 Training

AV/designee will be responsible for providing training to the Investigator and appropriate clinical site personnel. All Investigators/study personnel that are trained must sign a training log upon completion of the training. Investigators are responsible for assuring that their designated study staff is fully trained to this protocol, its procedures and any subsequent amendments to the protocol.

AV's monitors/designees will be appropriately trained to the protocol, eCRFs, and other relevant study procedures and process. Training will be conducted and recorded in accordance with relevant standard procedures.

11.5 Monitoring

AV/designee will monitor the study over its duration according to the pre-specified monitoring plan which will include the planned extent of source data verification.

11.6 Deviations from Protocol

It is the Investigator's responsibility to ensure that there are no deviations from the protocol **without prior notification and approval of AV** and that all actions are in full compliance with all established procedures of the EC or equivalent committee. The Investigator will not deviate from the protocol for any reason without prior written approval from AV except in cases of medical emergencies, when the deviation is necessary to protect the life or physical well-being of the subject or eliminate an apparent immediate hazard to the subject. In that event, the Investigator will notify AV immediately by phone or in writing. All deviations must be reported to AV. In subject-specific deviations from the protocol, a Protocol Deviation Case Report Form will be completed. The occurrence of protocol deviations will be monitored by AV for evaluation of Investigator compliance to the protocol and regulatory requirements, and dealt with according to written procedures. Investigators will inform their EC or equivalent committee of all Protocol Deviations in accordance with their specific EC or equivalent committee reporting policies and procedures.

In the event that an Investigator does not comply with the Clinical Trial Agreement or protocol, the Investigator will be notified of the site's non-compliance.

In the event of repeated non-compliance, as determined by AV, an AV's monitor or company representative will attempt to secure compliance by one or more of the following (and not limited to):

- Visiting the Investigator
- Telephoning the Investigator
- Corresponding with the Investigator

Repeated non-compliance with the signed agreement, the protocol or any other conditions of the study may result in further escalation in accordance with AV's written procedures including securing compliance or, at the sole discretion of AV, terminating the Investigator's participation in the study.

11.7 Compliance Assessments

AV/designee may conduct periodic compliance assessments at various study sites. AV/designee may request access to all study records including source documentation for inspection and duplication during a compliance assessment. The Investigator and Research Coordinator must be available to respond to reasonable requests and queries made during the compliance assessment process.

11.8 Publications Committee

The Publication Committee is composed of Principle Investigators, KOLs (as needed) and representatives from AV Clinical Research. This team will oversee and determine presentation and/or publication aspects of the study. The committee will also review and approve all external study-related data and publication requests. This committee will follow AV's applicable policies and standard operating procedures.

12. DATA HANDLING AND RECORD KEEPING

AV/designee will perform all data management activities including documentation of the systems and procedures to be used. All eCRF data collection will be performed through a secure web portal and all authorized personnel with access to the electronic data capture (EDC) system must use an electronic signature access method to enter, review or correct data. Passwords and electronic signatures will be strictly confidential.

All eCRF data will be downloaded from the EDC system and reformatted into a data structure acceptable to AV. The data will be subject to consistency and validation checks within the EDC system and will be subject to supplemental validation following download. At the conclusion of the study, completed eCRF images with the date-and-time stamped electronic audit trail indicating the user, the data entered, and any reason for change (if applicable) will be archived at the Investigator's site and a backup copy archived with AV.

The Investigator will maintain complete and accurate documentation including but not limited to medical records, clinical trial progress records, laboratory reports, eCRF, signed ICF, device accountability records, correspondence with the EC and clinical trial monitor/AV, AE reports, and information regarding subject discontinuation or completion of the clinical trial.

12.1 Source Documentation

Regulations and Good Clinical Practice (GCP) require that the Investigator maintain information in the subject's medical records that corroborate data collected on the Case Report Forms. In order to comply with these regulatory requirements/GCP, the following information should be included in the subject's record, at a minimum, and if applicable to the study:

- Medical history/physical condition of the subject before involvement in the study sufficient to verify protocol entry criteria
- Dated and signed notes on the day of entry into the study referencing AV, protocol number, subject ID number and treatment assigned, and a statement that Informed Consent was obtained

- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- Adverse Events reported and their resolution including supporting documents such as discharge summaries, catheterization laboratory reports, ECGs, and lab results including documentation of site awareness of SAEs and of Investigator's device relationship assessment of SAEs.
- Study-required laboratory reports and 12-lead ECGs, signed and dated for review and annotated for clinical significance of out of range results.
- Notes regarding protocol-required and prescription medications taken during the study (including start and stop dates)
- Subject's condition upon completion of or withdrawal from the study
- Any other data required to substantiate data entered into the eCRF

12.2 Electronic Case Report Form Completion

Primary data collection based on source-documented hospital and/or clinic chart reviews will be performed clearly and accurately by site personnel trained on the protocol and eCRF completion. eCRF data will be collected for all patients that are registered into the study. AV or designee will provide clinical monitoring as specified in **Section 11.5 Monitoring**.

12.3 Record Retention

The Investigator must maintain all study records for a minimum of 10 years following study completion or as otherwise instructed by AV. AV will maintain copies of correspondence, data, adverse device effects, and other relevant clinical study records. The Investigator must obtain permission from AV in writing before destroying or transferring control of any clinical study records.

13. ETHICAL CONSIDERATION

13.1 Ethics Committee Review

EC approval for study required documents will be obtained by the Investigator prior to study participation. No changes may be made to study required documents without appropriate approval from the EC, AV, and/or the regulatory agencies. Any protocol amendments and/or associated informed consent changes will be submitted to the EC as needed, with written approval required prior to implementation.

13.2 Confidentiality

To ensure compliance with the CFDA and any applicable private information protection laws, confidentiality of protected health information shall be maintained by all parties throughout the study. All data should be secured against unauthorized access. Study patients will be assigned a unique coded identifier on his/her eCRF and other study records sent to AV.

13.3 Submitting Reports to Competent Authority

AV will prepare and submit interim reports to the CFDA according to the CFDA's appropriate guidelines. Annual clinical updates will be distributed to Investigators. Reports may also be distributed to other regulatory bodies.

14. PUBLICATION POLICY

Study-derived data are the sole property of AV. Investigators will not use study-related data without written consent from AV for any purpose other than study completion, as stated in the study site agreement.

The presentation and/or publication of individual site results must not precede those from multiple centers. In order to publish multicenter results, investigators are required to obtain the approval of AV's Publication Committee.

Presentation and/or publication materials must be received at least 60 days prior to any deadlines. AV will review all materials for compliance and alignment with AV's scientific publication policy and presentation and publication strategy. Any exceptions must be approved by the Publication Committee.

AV will control and maintain responsibility for international study registration and results posting, as appropriate.

APPENDIX I: ABBREVIATIONS AND ACRONYMS

Acronym/ Abbreviation	Term
ACC	American College of Cardiology
AE	Adverse Event
AHA	American Heart Association
ARC	Academic Research Consortium
AV	Abbott Vascular
CABG	Coronary Artery Bypass Graft
CAD	Coronary Artery Disease
CAGR	Compound Annual Growth Rate
CFDA	China Food and Drug Administration
CHD	Coronary Heart Disease
CK	Creatine Kinase
CK-MB	Creatine Kinase Myocardial-Band Isoenzyme
CoCr	Cobalt Chromium
CSS	Coronary Stent System
CVD	Cardiovascular Disease
DES	Drug-eluting Stent
DD	Device Deficiency
DS	Diameter Stenosis
EC	Ethics Committee
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EECSS	Everolimus Eluting Coronary Stent System
FFR	Function Flow Reserve
GCP	Good Clinical Practice
GUSTO	Global Use of Strategies to Open Occluded Coronary Arteries
HbA_{1c}	Hemoglobin A_{1c} (glycated hemoglobin)
ICF	Informed Consent Form
ID	Ischemia-Driven
IFU	Instructions for Use
IRB	Institutional Review Board
KOL	Key Opinion Leader
LAD	Left Anterior Descending Artery
LBBB	Left Bundle Branch Block
LCX	Left Circumflex Artery
MI	Myocardial Infarction
PAS	Post-Approval Study
PCI	Percutaneous Coronary Intervention
RCA	Right Coronary Artery
SAE	Serious Adverse Event
SAS	Single-arm Study
SC	Study Completion
SCAI	Society for Cardiovascular Angiography and Interventions
ST	Stent Thrombosis

Acronym/ Abbreviation	Term
TIMI	Thrombosis in Myocardial Infarction flow
TLF	Target Lesion Failure
TLR	Target Lesion Revascularization
TVF	Target Vessel Failure
TVR	Target Vessel Revascularization
ULN	Upper Limit of Normal
URL	Upper Reference Limit
USFDA	United States Food and Drug Administration
WHO	World Health Organization

APPENDIX II: DEFINITIONS

ACC/AHA Classification Scheme of Coronary Lesions: Lesion-Specific Characteristics

Type A Lesions (High Success, >85%; Low Risk)	
• Discrete (< 10 mm length)	• Little or no calcification
• Concentric	• Less than totally occlusive
• Readily accessible	• Not ostial in location
• Nonangulated segment, < 45°	• No major branch involvement
• Smooth contour	• Absence of thrombus
Type B Lesions* (Moderate Success, 60-85%; Moderate risk)	
• Tubular (10-20 mm length)	• Moderate-to-heavy calcification
• Eccentric	• Total occlusions < 3 mo old
• Moderate tortuosity of proximal segment	• Ostial in location
• Moderately angulated segment, > 45°, < 90°	• Bifurcation lesions requiring double guide wires
• Irregular contour	• Some thrombus present
* Type B1 lesions: One adverse characteristic * Type B2 lesions: ≥ two adverse characteristics	
Type C Lesions (Low Success, <60%; High Risk)	
• Diffuse (> 2 cm length)	• Total occlusions > 3 mo old
• Excessive tortuosity of proximal segment	• Inability to protect major side branches
• Extremely angulated segments > 90°	• Degenerated vein grafts with friable lesions

Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.

Angina

Braunwald Classification of Unstable Angina[25]

I. New onset of severe or accelerated angina: Patients with new onset (< 2 months in duration) exertional angina pectoris that is severe or frequent (> 3 episodes/day) or patients with chronic stable angina who develop accelerated angina (that is, angina distinctly more frequent, severe, longer in duration, or precipitated by distinctly less exertion than previously) but who have not experienced pain at rest during the preceding 2 months.

II. Angina at rest, subacute: Patients with 1 or more episodes of angina at rest during the preceding month but not within the preceding 48 hours.

III. Angina at rest, acute: Patients with 1 or more episodes of angina at rest within the preceding 48 hours.

Canadian Cardiovascular Society Classification of Stable Angina

I. Ordinary physical activity does not cause angina, such as walking or climbing stairs. Angina occurs with strenuous, rapid or prolonged exertion at work or recreation.

II. Slight limitation of ordinary activity. Angina occurs on walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, or in cold, in wind, under emotional stress or only during the few hours after awakening. Angina occurs on walking more than two blocks on the level and climbing more than one flight of ordinary stairs at a normal pace and in normal condition.

III. Marked limitation of ordinary physical activity. Angina occurs on walking one to two blocks on the level and climbing one flight of stairs in normal conditions and at a normal pace.

IV. Inability to carry on any physical activity without discomfort – angina symptoms may be present at rest.

Bail-out stent

Bailout stenting may be performed in cases of one of the following during the index procedure:

- Dissection
- Occlusive complication as evidenced by a decrease in target vessel flow
- Chest pain or ischemic ECG changes that do not respond to treatment
- Unplanned additional stent required to fully cover the target lesion (caused by geographic miss or under estimation of lesion length)

Bifurcation Lesion

A lesion located at both the main vessel and a side branch of that main vessel.

Coronary Artery Bypass Graft (CABG) Surgery

Acute CABG surgery is defined as immediate transfer from the catheterization laboratory to the operative room for emergent bypass surgery during the initial treatment phase. Coronary artery bypass graft surgery during follow-up is only considered as a target vessel revascularization and major adverse coronary event if coronary angiography indicates a diameter of stenosis >50% of the stented coronary segment associated with one of the following conditions:

- A positive history of recurrent angina pectoris presumably related to the target vessel
- Objective signs of ischemia (exercise test or equivalent) presumably related to the target vessel
- Abnormal results of any invasive functional diagnostic test (eg, Doppler flow velocity reserve, fractional flow reserve)

Death

Death is defined by the Academic Research Consortium[27] as follows:

All deaths are considered cardiac unless an unequivocal noncardiac cause can be established. Specifically, any unexpected death even in patients with coexisting potentially fatal noncardiac disease (eg, cancer, infection) should be classified as cardiac.

- **Cardiac death**

  Any death due to proximate cardiac cause (eg, myocardial infarction, low-output failure, fatal arrhythmia), unwitnessed death and death of unknown cause, and all procedure-related deaths, including those related to concomitant treatment, will be classified as cardiac death.

- **Vascular death**

  Death caused by noncoronary vascular causes, such as cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular diseases.

- **Non-cardiovascular death**

  Any death not covered by the above definitions, such as death caused by infection, malignancy, sepsis, pulmonary causes, accident, suicide, or trauma.

Deregistration

Refers to patients who, after having previously been registered are removed from the study population. De-registered patients are no longer associated with the study. They do not receive the study device, do not take part in study-required follow-up and are not part of the Intent-to-Treat population.

Device deficiency

A device deficiency (DD) is an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labeling.

Epicardial Vessels

- Left anterior descending artery (LAD) with septal and diagonal branches
- Left circumflex artery (LCX) with obtuse marginal and/or ramus intermedius branches
- Right coronary artery (RCA) and any of its branches

Legally-Authorized Representative

An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective patient to the patient's participation in the procedure(s) involved in the research.

Myocardial Infarction (MI) by World Health Organization (WHO)

- **Q wave MI**

  Development of new, pathological Q wave on the ECG

- **Non-Q wave MI**

  Elevation of CK levels to ≥ **two** times the upper limit of normal (ULN) with elevated CK-MB in the absence of new pathological Q waves

Percutaneous Coronary Intervention (PCI)

Refers to all interventional cardiology procedures used to treat coronary artery disease.

Primary Investigator

A physician-specialist who is responsible for overseeing study conduct at all sites, protocol compliance, and relevant regulations

Principal Investigator

A physician responsible for conducting the study at each investigational site

Restenosis

Re-narrowing of the artery following the removal or reduction of a previous narrowing

Revascularization

Revascularization is defined as follows:

- **Target Lesion Revascularization (TLR)**

  Target lesion revascularization is defined as any repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed for restenosis or other complication of the target lesion. All TLR should be classified prospectively as ischemia-driven (ID) or not ischemia-driven by the investigator prior to repeat angiography. An independent angiographic core laboratory should verify that the severity of percent diameter stenosis meets requirements for ischemia-driven and will overrule in cases where investigator reports are not in agreement if applicable. The target lesion is defined as the treated segment from 5 mm proximal to the scaffold/stent and to 5 mm distal to the scaffold/stent.

- **Target Vessel Revascularization (TVR)**

  Target vessel revascularization is defined as any repeat percutaneous intervention or surgical bypass of any segment of the target vessel. The target vessel is defined as the entire major coronary vessel proximal and distal to the target lesion, which includes upstream and downstream branches and the target lesion itself.

- **Non Target Lesion Revascularization (non-TLR)**

  Any revascularization in the target vessel for a lesion other than the target lesion is considered a non-TLR.

- **Non Target Vessel Revascularization (non-TVR)**

  Revascularization of the vessel identified and treated as the non-target vessel at the time of the index procedure.

- **Ischemic-Driven (ID) Revascularization (TLR/TVR)**

  A revascularization is considered ischemic driven if associated with any of the following:

a) Positive functional ischemia study including positive functional flow reserve (FFR)

b) Ischemic symptoms and angiographic diameter stenosis ≥ 50% by core laboratory QCA
c) Angiographic diameter stenosis ≥ 70% by core laboratory QCA without angina or positive functional study

Serious Adverse Event (SAE)

If the AE meets any of the criteria below, it is regarded as serious adverse event (SAE).

a) Led to a death,
b) Led to a serious deterioration in health that either:
    1) Resulted in a life-threatening illness or injury, or
    2) Resulted in a permanent impairment of a body structure or a body function, or
    3) Required in-patient hospitalization or prolongation of existing hospitalization, or
    4) Resulted in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
c) Led to fetal distress, fetal death or a congenital abnormality or birth defect.
d) An important medical event that may not result in death, be life-threatening, or require hospitalization but may be considered serious when, based upon appropriate medical judgment, may jeopardize the subject and/or may require intervention to prevent one of the outcomes listed in this definition.

Stent Thrombosis

Stent thrombosis is defined by the Academic Research Consortium[27] as follows:

Stent thrombosis should be reported as a cumulative value at the different time points and with the different separate time points. Time 0 is defined as the time point after the guiding catheter has been removed and the patient left the catheterization laboratory.

Timing

Acute stent thrombosis*	0-24 hours post stent implantation
Subacute stent thrombosis*	> 24 hours-30 days post stent implantation
Late stent thrombosis†	> 30 days-1 year post stent implantation
Very late stent thrombosis†	> 1 year post stent implantation

* Acute/subacute can also be replaced by early stent thrombosis. Early stent thrombosis (0-30 days) – this definition is currently used in the community.
† Including "primary" as well as "secondary" late stent thrombosis; "secondary" late stent thrombosis is a stent thrombosis after a target segment revascularization.

Stent Thrombosis Categories: a) Definite b) Probable, and c) Possible

a) Definite stent thrombosis

Definite stent thrombosis is considered to have occurred by either angiographic or pathologic confirmation.

Angiographic confirmation of stent thrombosis*

The presence of a thrombus† that originates in the stent or in the segment 5 mm proximal or distal to the stent and presence of at least 1 of the following criteria within a 48-hour time window:

- Acute onset of ischemic symptoms at rest
- New ischemic ECG changes that suggest acute ischemia
- Typical rise and fall in cardiac biomarkers (refer to definition of spontaneous MI)
- Nonocclusive thrombus
  -Intracoronary thrombus is defined as a (spheric, ovoid, or irregular) noncalcified filling defect or lucency surrounded by contrast material (on 3 sides or within a coronary stenosis) seen in multiple projections, or persistence of contrast material within the lumen, or a visible embolization of intraluminal material downstream.
- Occlusive thrombus
  -TIMI 0 or TIMI 1 intrastent or proximal to a stent up to the most adjacent proximal side branch or main branch (if originates from the side branch).

*The incidental angiographic documentation of stent occlusion in the absence of clinical signs or symptoms is not considered a confirmed stent thrombosis (silent occlusion).

†Intracoronary thrombus.

Pathological confirmation of stent thrombosis

Evidence of recent thrombus within the stent determined at autopsy or via examination of tissue retrieved following thrombectomy.

b) Probable stent thrombosis

Clinical definition of probable stent thrombosis is considered to have occurred after intracoronary stenting in the following cases:

- Any unexplained death within the first 30 days‡
- Irrespective of the time after the index procedure, any MI that is related to documented acute ischemia in the territory of the implanted stent without angiographic confirmation of stent thrombosis and in the absence of any other obvious cause

‡ For studies with ST-elevation MI population, one may consider the exclusion of unexplained death within 30 days as evidence of probable stent thrombosis.

c) Possible stent thrombosis

Clinical definition of possible stent thrombosis is considered to have occurred with any unexplained death from 30 days after intracoronary stenting until end of study follow-up.

Target Lesion

A lesion to be treated during the index procedure

Target Vessel

The entire epicardial vessel containing the treated lesion

Thrombosis in Myocardial Infarction (TIMI) Flow Grades

Thrombosis in Myocardial Infarction flow grades are defined by the following:

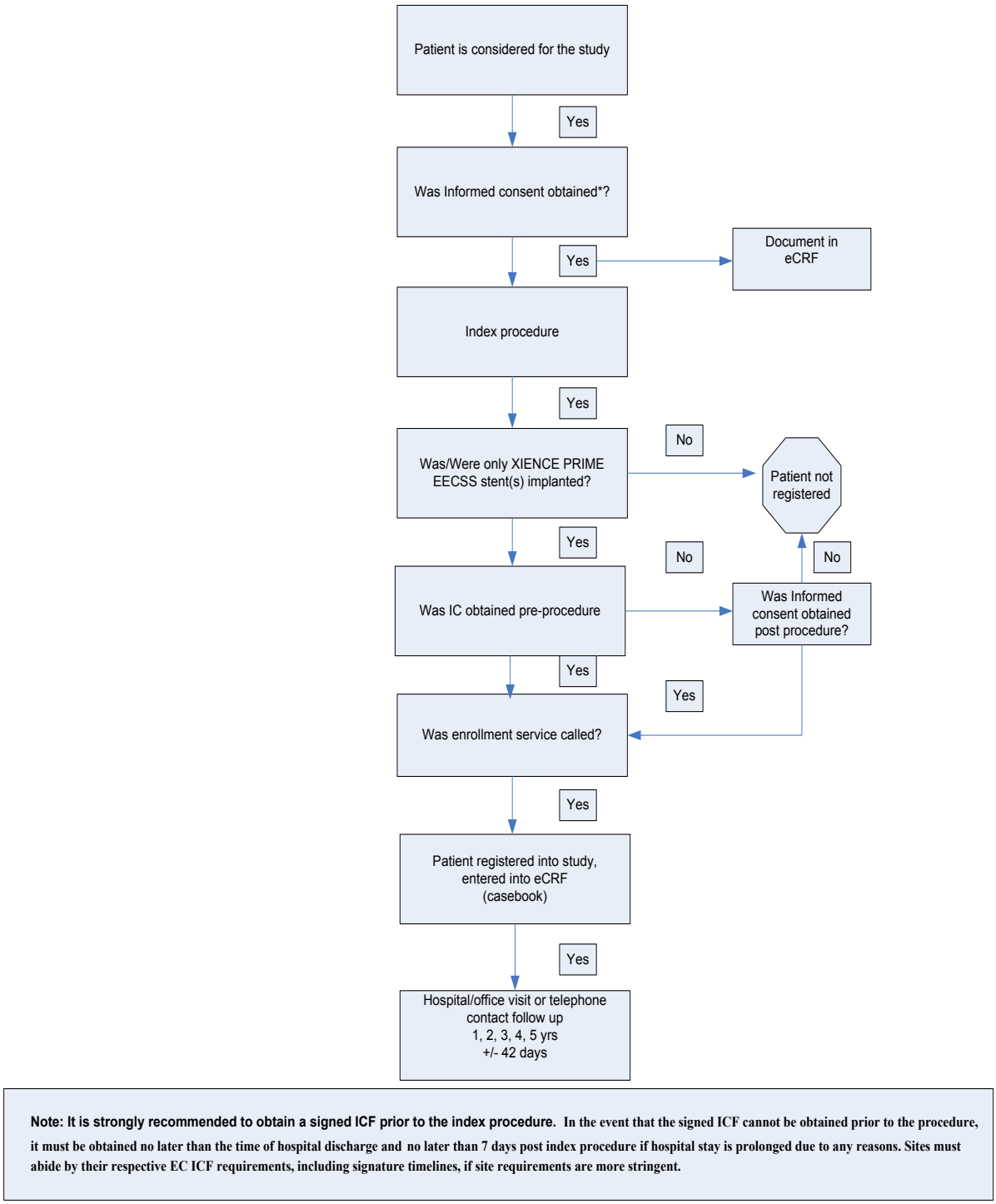
0. No contrast flow through the stenosis.

1. A small amount of contrast flows through the stenosis but fails to fully opacify the artery beyond.

2. Contrast material flows through the stenosis to opacify the terminal artery segment. However, contrast enters the terminal segment perceptibly more slowly than more proximal segments. Alternatively, contrast material clears from a segment distal to a stenosis noticeably more slowly than from a comparable segment not preceded by a significant stenosis.

3. Anterograde flow into the terminal coronary artery segment through a stenosis is as prompt as anterograde flow into a comparable segment proximal to the stenosis. Contrast material clears as rapidly from the distal segment as from an uninvolved, more proximal segment.

APPENDIX III: STUDY FLOW



Note: It is strongly recommended to obtain a signed ICF prior to the index procedure. In the event that the signed ICF cannot be obtained prior to the procedure, it must be obtained no later than the time of hospital discharge and no later than 7 days post index procedure if hospital stay is prolonged due to any reasons. Sites must abide by their respective EC ICF requirements, including signature timelines, if site requirements are more stringent.

APPENDIX IV: SCHEDULE OF EVENTS

	Baseline	Index Procedure	Post Procedure	1 year (± 60 days) hospital/office visit or phone contact	2 years (± 60 days) hospital/office visit or phone contact	3 years (± 60 d) hospital/office visit or phone contact	4 years (± 60 days) hospital/office visit or phone contact	5 years (± 60 days) hospital/office visit or phone contact	Unscheduled visit
Patient Medical/Clinical History (refer to 7.1 Baseline)	✓[1]								
Patient ICF (Inclusion/Exclusion Criteria)	✓[2]								
Lipid Profile, Serum Insulin, Serum Glucose, Serum Creatinine, HbA_{1c}, Urine pregnancy test	✓[1,3]								
CK, CK-MB, and/or Troponin I/T	✓[4]		✓[5]						
ECG	✓[4]		✓						
Stent Attributes		✓							
Lesion Characteristics (ACC/AHA/SCAI Classification Scheme of Coronary Lesions)		✓							
Dual Antiplatelet Therapy (loading dose)		✓							
Dual Antiplatelet Therapy (post-procedure maintenance dose)			✓	✓	✓	✓	✓	✓	✓
Reportable AE(s) (refer to 8.3 Adverse Event Reporting)		✓	✓	✓	✓	✓	✓	✓	✓

1. May be collected up to 4 weeks prior to the index procedure. If multiple assessments are performed within 4 weeks prior to the index procedure, it is recommended that the most recent assessment value be included with the baseline information. Data that is not collected during the baseline time window may be obtained up to 7 days post procedure and will still be considered baseline data.
2. It is strongly recommended to obtain a signed ICF prior to the index procedure. In the event that the signed ICF cannot be obtained prior to the procedure, it must be obtained no later than the time of hospital discharge and no later than 7 days post index procedure if hospital stay is prolonged due to any reasons. Sites must abide by their respective EC ICF requirements, including signature timelines, if site requirements are more stringent.
3. In the event that this information was not available within the baseline window, it is strongly recommended that it be collected immediately after, but no later than 7 days post index procedure.
4. If available, these preprocedural laboratory assessments should be collected within 72 hours prior to the procedure (refer to 7.1 Baseline).
5. If available, postprocedural cardiac biomarkers and ECG should be collected between 12 hours post procedure and the time of hospital discharge. For those patients with a prolonged hospital stay, it is recommended that the assessment be conducted no later than 72 hours post procedure.

APPENDIX V: REFERENCES

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