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XIENCE Skypoint Large Vessel Post Approval Study (SPIRIT XLV PAS)
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Sponsor

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[redacted]

XIENCE Skypoint Large Vessel Post Approval Study (SPIRIT XLV PAS)

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SITE PRINCIPAL INVESTIGATOR SIGNATURE PAGE

[redacted]

NATIONAL COORDINATING CLINICAL INVESTIGATOR / STUDY PRINCIPAL INVESTIGATOR SIGNATURE PAGE

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COMPLIANCE STATEMENT:

This clinical investigation will be conducted in accordance with this Clinical Investigation Plan (CIP), the Declaration of Helsinki and the applicable regulatory requirements (US 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 54, and 21 CFR Part 11, etc., and OUS ISO 14155:2020 standard and the appropriate local legislation(s)). The most stringent requirements, guidelines or regulations must always be followed. The conduct of the clinical investigation will be approved by the Food and Drug Administration (FDA) and the appropriate Institutional Review Board (IRB) or Ethics Committee (EC) of the respective investigational site, and as specified by local regulations.

[redacted]

1.0 INTRODUCTION

The XIENCE Skypoint Large Vessel Post-Approval Study (PAS) (called "SPIRIT XLV PAS" hereafter) is a prospective, single-arm, open-label, multi-center global (United States [US] and outside of US [OUS]) clinical study to evaluate the continued safety and effectiveness of the XIENCE Skypoint Large Vessel (LV) sizes (stent diameters 4.5 mm and 5.0 mm in stent lengths of 12-33 mm) everolimus-eluting coronary stent system (EECSS) after the US market approval, in a minimum of [redacted] with a minimum of [redacted] This clinical study will be conducted in accordance with this clinical investigation plan (CIP). All investigators involved in the clinical study will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately.

1.1 Background and Rationale

1.1.1 Background

[redacted]

A post-approval study to evaluate the continued safety and effectiveness of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm was required by FDA, which is planned to be conducted following the clinical investigation plan (CIP) described in this document.

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[i] -XIENCE PRIME Everolimus Eluting Coronary Stent System (XIENCE PRIME): P110019, approved 11/1/11
-XIENCE Xpedition Everolimus Eluting Coronary Stent System (XIENCE Xpedition): P110019 / S025, approved 12/21/12
-XIENCE Alpine Everolimus Eluting Coronary Stent System (XIENCE Alpine): P110019 / S070, approved 9/3/14
-XIENCE Sierra Everolimus Eluting Coronary Stent System (XIENCE Sierra): P110019 / S094 approved 5/22/18
-XIENCE Skypoint Everolimus Eluting Coronary Stent System (XIENCE Skypoint): P110019 / S113 approved 5/13/21

[ii] - MULTI-LINK VISION® (VISION): P020047, approved 7/16/ 3 - MULTI-LINK MINI-VISION® (MINI-VISION): P020047/S003, approved 9/10/04
- Multi-Link 8® and Multi-Link 8® Long Lesion Coronary Stent System (ML8): P020047/S017, approved 6/22/10
- Multi-Link 8® Small Vessel Coronary Stent System (ML8): P020047/S022, approved 8/31/10

[redacted]

1.1.2 Rationale for Conducting this Clinical Study

The diameters of the coronary arteries have been suggested to be a potential predictor of coronary artery disease (CAD) occurrence and severity[1]. Several previous investigations have examined the influence of vessel diameter on adverse event rates over time. Both Hsieh *et al.*[2] and van der Heijden *et al.*[3] found that small vessel lesions (< 2.5 mm) had similar or higher adverse event rates than larger vessel lesions (> 3.0 mm). Although expected to be safe, the currently commercially available drug eluting stents (DES) with large diameters (4.5 mm and above) in the US and globally are limited, resulting in limited choices for physicians to treat large coronary artery lesions.

[redacted]

Prior to the market approval of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm in the US, the XIENCE Family of Stents were commercially available in sizes up to 4.0 mm in diameter, which can treat vessels up to 4.25 mm reference vessel diameter (RVD) with a maximum of 5.50 mm post dilatation expansion diameter. The new XIENCE Skypoint stent diameters 4.5 and 5.0 mm have expansion capabilities to treat vessels up to 5.25 mm RVD with an increased maximum post-dilatation expansion diameter up to 5.75 mm, compared to 5.50 mm for XIENCE Sierra, and without any modification to the stent design or manufacturing process. Owing to the similar design of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm to the other XIENCE Family of Stents, clinical evidence from previous Abbott sponsored clinical trials for the XIENCE Family of Stents relevant to large vessel treatment applies to the XIENCE Skypoint stent diameters 4.5 and 5.0 mm.

The XIENCE V USA clinical trial was a real-world post-market study of the XIENCE V stent that enrolled over 8,000 subjects, of which 5,020 were followed up through 4 years. To understand the safety and effectiveness of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm, data from the XIENCE V USA clinical trial were analyzed to evaluate the clinical results between subjects receiving larger stents to treat a target lesion RVD ≥ 4.0 mm to those receiving smaller stents to treat target lesion RVD < 4.0 mm[vi]. Overall, risk factors were similar between the ≥ 4.0 mm and < 4.0 mm groups, but the ≥ 4.0 mm group had a higher proportion of lesions located in the left main coronary artery (LMCA) (6.4% vs 1.0%) and vessel grafts (15.9% vs 4.7%) compared to the < 4.0 mm group[14]. This finding is an important characteristic as lesion location in the LMCA or graft is a known risk factor for target lesion revascularization (TLR). Additionally, no differences were observed in target lesion failure (TLF) rate through 1 year between the ≥ 4.0 mm and < 4.0 mm groups and the TLF rates remained comparable over 4 years.[ii] To further support the XIENCE V USA trial analyses, the SPIRIT IV[15,16] (a pre-approval study for XIENCE V) and SPIRIT PRIME (a pre-approval study for XIENCE PRIME) trial data were used to perform a regression analysis comparing vessel RVD to TLF and stent thrombosis (ST) event rates. The regression analysis found no significant increases in TLF or ST event rates as the size of the treated

[iii] Data on file at Abbott. The 15 million implants is based on DES data through Q1, 2020

[redacted]

vessel increases.[1] Collectively, the results demonstrate that treatment with the 4.5 and 5.0 mm diameter stents in the treatment of RVD ≤ 5.25 mm is expected to be safe and will have comparable outcomes to vessels treated with smaller stents. The clinical evidence led to the commercial approval of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm in the treatment of large coronary vessels without a pre-market study.

The SPIRIT XLV PAS is conducted to evaluate the continued safety and effectiveness of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm in a real-world setting.

2.0 CLINICAL STUDY OVERVIEW

2.1 Clinical Study Objective

To evaluate the continued safety and effectiveness of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm in stent lengths of 12-33 mm during commercial use in a real-world setting.

2.2 Device(s) Used in the Clinical Study

Commercially approved XIENCE Skypoint Everolimus Eluting Coronary Stent System (EECSS) stent diameters 4.5 and 5.0 mm.

- Stent diameters: 4.5 mm, 5.0 mm
- Stent lengths: 12, 15, 18, 23, 28 and 33 mm

2.2.1 Indication for Use/Intended Purpose

Per US Instructions For Use (IFU), the XIENCE Skypoint stent system is indicated for improving coronary artery luminal diameter in patients, including those at high risk for bleeding and those with diabetes mellitus, with symptomatic heart disease due to *de novo* native coronary artery lesions (length ≤ 32 mm) with reference vessel diameters of ≥ 2.25 mm to ≤ 5.25 mm. In addition, the XIENCE Skypoint stent system is indicated for treating *de novo* chronic total coronary occlusions. For OUS geographies, please refer to the approved country specific indication for use. The indications for XIENCE can be found in the IFU provided with the product or on the Abbott website https://vascular.eifu.abbott.

2.2.2 Description of the Device(s) Under Investigation

XIENCE Skypoint stents are composed of a L-605 cobalt chromium (CoCr) and coated with poly (n-butyl methacrylate) (PBMA) and copolymer of vinylidene fluoride and hexafluoropropylene (PVDF-HFP)/everolimus pre-mounted on a balloon catheter delivery system. The stent designs, stent size matrix, active pharmaceutical ingredient (everolimus), drug dose density, primer and drug eluting layer coating formulations, manufacturing process for incorporating the drug (drug/polymer solution compounding and solution spray coating process), sterilization process, stent contacting material and container closure system materials of XIENCE Skypoint stent diameters 4.5 and 5.0 mm are identical to those of XIENCE Sierra. The recipe parameters for drug spray passes use a narrower range of drug spray passes (60-80) compared to 40-80 for the XIENCE Family of Stents to achieve the same coating performance to the same specifications. The narrower range of drug spray passes is within the existing spray passes for the XIENCE family of stents, which doesn't impact the clinical justification presented in this section. The post-dilatation expansion diameter of the medium stent design of XIENCE Skypoint is

increased to 5.75 mm compared to 5.5 mm for the medium stent design of XIENCE Sierra to offer greater post-dilatation capability, which does not require any modification to the stent design or manufacturing process.

The XIENCE Skypoint delivery catheter uses the same deployment processes as other Abbott Rapid Exchange (RX) stent systems. All materials, including colorants, used in the XIENCE Skypoint delivery system have been used in the XIENCE family of catheters and were previously tested for biocompatibility.

The XIENCE Skypoint delivery system is based on the XIENCE Sierra delivery system. The XIENCE Skypoint balloon is similar to XIENCE Sierra as it uses the same single blow balloon methodology and material (i.e., a single layer of Pebax 72D). The XIENCE Skypoint stent diameters 4.5 and 5.0 mm balloon extrusion and tooling have been modified to facilitate the larger balloon sizes (i.e., 4.5 and 5.0 mm). The XIENCE Skypoint delivery system shaft/catheter utilizes a single-layer Pebax 72D outer member material identical to XIENCE Sierra and is manufactured using the same hot die technology as the XIENCE Sierra outer member. There is a dimensional change in the outer member between XIENCE Skypoint and XIENCE Sierra. The XIENCE Skypoint medium stent outer member has one (1) continuous diameter (single necked). The XIENCE Skypoint stent diameters 4.5 and 5.0 mm outer member has two (2) different diameters (dual necked) similar to the XIENCE Sierra outer member (dual necked). In comparison to XIENCE Skypoint medium stents and XIENCE Sierra catheter shaft design, the XIENCE Skypoint stent diameters 4.5 and 5.0 mm catheter shaft design has been modified:

- inner diameter of the outer member is increased to maintain balloon deflation performance to the same specifications as XIENCE Sierra
- outer diameter of the outer member is increased to maintain catheter tensile strength to the same specifications as XIENCE Sierra.

The dimensional change to the outer member of the delivery system shaft is not considered to impact clinical outcomes and has been assessed through non-clinical testing.

3.0 CLINICAL STUDY DESIGN

The SPIRIT XLV PAS is a prospective, single-arm, multi-center, US and OUS post-approval observational study in a [redacted] to evaluate the continued safety and effectiveness of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm in the treatment of *de novo* native coronary artery lesions.

3.1 Clinical Study Procedures and Follow-up Schedule

A minimum of [redacted] will be registered in the SPIRIT XLV PAS. [redacted]

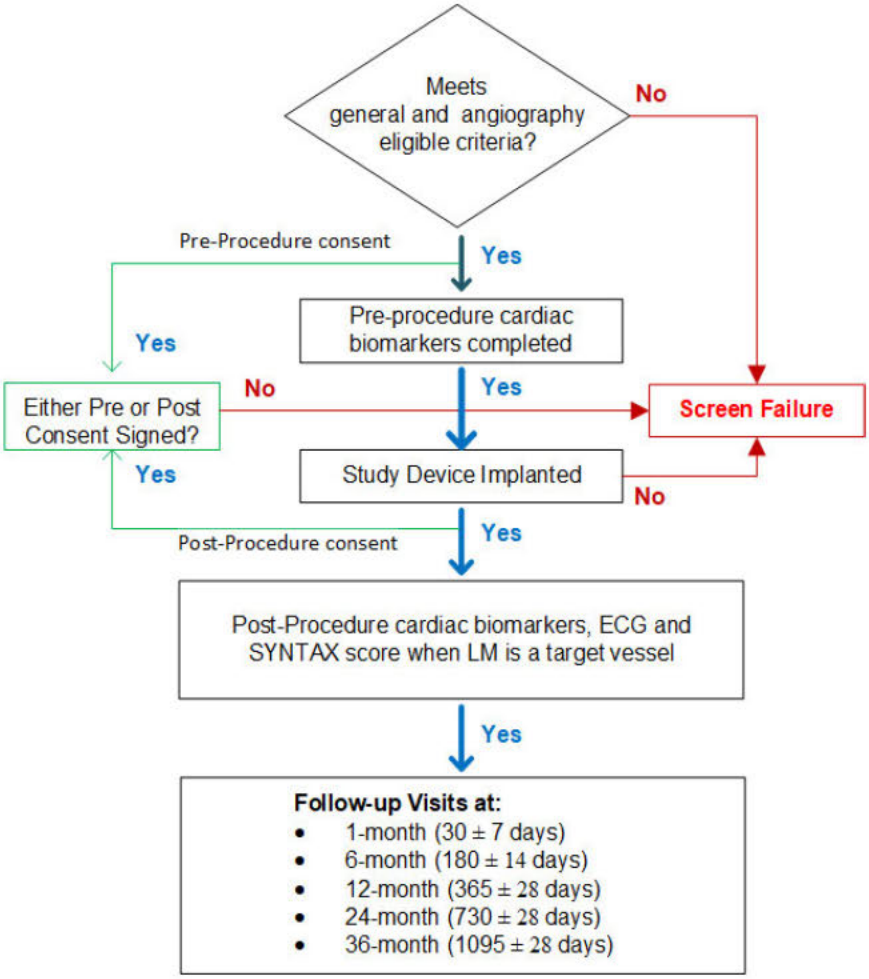
Each subject will be followed for three years. All subjects will have a follow-up visit at 30 days, 6 months, 1 year, 2 years and 3 years. All follow-ups must be conducted directly with the subject and can be either a clinic visit or a phone visit. Refer to the detailed follow-up schedule in **Section 6.4.4**.

Note: If the scheduled visit occurs outside the allowed window, it is not considered a missed visit/contact. It is a protocol deviation but will still be considered a completed visit.

[redacted]

The study procedures, data collection and follow-up requirements of this clinical study are described in Figure 1 below.

Figure 1 Clinical Study Flowchart



Note: Protocol Deviation is further explained in Section 10.6

3.2 Measures Taken to Avoid and Minimize Bias

A Clinical Events Committee (CEC) and an angiographic core laboratory will be utilized on this study to avoid and minimize bias.

3.2.1 Clinical Event Committee

A CEC will review and adjudicate all clinical endpoint events, and also determine the relationship to the investigational device XIENCE Skypoint stent diameters 4.5 and 5.0 mm. [redacted]

3.2.2 Angiographic Core Lab

The angiographic core lab will receive and review baseline images from index procedure (i.e., pre- and post-procedure) to ensure quality and readability of the images. [redacted]

[redacted]

3.3 Suspension or Early Termination of the Clinical Study

[redacted]

[redacted]

4.0 ENDPOINTS

4.1 Primary Endpoint [iv]

The descriptive primary endpoint is Target Lesion Failure (TLF) at 1 year. [iv]

- TLF is defined as the composite of cardiac death (CD), myocardial infarction (MI) related to the target vessel (TV-MI), or ischemic driven target lesion revascularization (ID-TLR).
- For the assessment of periprocedural MI, modified Academic Research Consortium (ARC) II definition[17] will be used. Cardiac troponin (cTn) will be used for the primary cardiac biomarker for MI assessment. For the assessment of spontaneous MI, the 4th universal MI definition will be used. Both MI definitions are defined in **Appendix II**.

Note: [redacted]

4.2 Secondary Endpoint

The descriptive secondary endpoints are defined as:

1. Target lesion failure ($TLF_{sp\text{-}MI}$) at 1 year [iv]

- $TLF_{sp\text{-}MI}$ is defined as the composite of CD and TV-MI, including spontaneous MI and excluding periprocedural MI and, or ID-TLR.
- cTn will be used for the cardiac biomarker for MI assessment. For the assessment of spontaneous MI, the 4th universal MI definition will be used.

2. Target Lesion Failure (TLF_{SCAI}) at 1 year [iv]

- TLF_{SCAI} is defined as the composite of CD and TV-MI, including both periprocedural MI and spontaneous MI, or ID-TLR.
- For the assessment of periprocedural MI, Society for Cardiovascular Angiography and Intervention (SCAI) definition[19] will be used, and cTn[v] will be used for the primary cardiac biomarker for MI

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iv [redacted]

v [redacted]

assessment. For the assessment of spontaneous MI, the 4th universal MI definition will be used. Both MI definitions are defined in **Appendix II.**

4.3 Other Endpoints

Clinical outcomes will be evaluated at each follow-up time point.

Composite Outcomes

[redacted]

Individual Clinical Outcomes

[redacted]

[redacted]

5.0 SUBJECT SELECTION AND WITHDRAWAL

5.1 Subject Population

This clinical study will register subjects of all genders from the general population 18 years or older. A minimum of [redacted] will be registered in the study.

Subjects in which the LMCA contains the target lesion can be treated but are not to exceed [redacted] of the study population.

5.2 Subject Recruitment/Screening and Informed Consent

5.2.1 Subject Recruitment and Screening

A member of the site's clinical study team previously trained in the CIP must evaluate subjects for the general clinical study eligibility criteria. A subject who does not satisfy all general eligibility criteria prior to informed consent is considered a screen failure and should not be registered in the clinical study. Subjects who sign informed consent, have at least one study device implanted, and are later determined to not meet the inclusion/exclusion criteria prior to discharge will be withdrawn from the study, and considered screen failures. Then, sites will ask the subjects to sign an Informed Consent form following the established Informed Consent process (described in **Section 5.2.2**) if they wish to participate in the clinical study.

5.2.2 Informed Consent

An informed consent form (ICF) must be obtained from a subject who is willing to participate in the SPIRIT XLV PAS study prior to discharge. The subject's consent has to be prior to any study-specific procedures, if not the site's SOC. These may include pre- and post-procedure cardiac biomarker collections, and SYNTAX score[20] ≤ 22 (per site assessment) if LMCA is the target vessel. The investigator or his/her authorized designee (if applicable) will conduct the informed consent process, as required by applicable regulations and the center's IRB/EC. This process will include a verbal discussion with the subject on all aspects of the clinical study relevant to the subject's decision to participate, such as details of clinical study procedures, anticipated benefits, and potential risks of clinical study participation. Sites must inform subjects about their right to withdraw from the clinical study at any time and for any reason without sanction, penalty, or loss of benefits to which the subject is otherwise entitled. Withdrawal from the clinical study will not jeopardize their future medical care or relationship with the investigator.

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the subject and will respect subject's legal rights. Financial incentives will not be given to the subjects. Subjects may be compensated for time and travel directly related to their participation in the clinical study. The site shall provide the subject with the ICF written in a language that is understandable to the subject and that has been approved by the center's IRB/EC. The subject shall have adequate time to review, ask questions, and consider participation. The Principal Investigator or his/her authorized designee will make efforts to ensure that the subject understands the information provided. If the subject agrees to participate, he/she must sign and date the ICF, along with the person obtaining the consent

[redacted]

prior to any study-specific requirements. The dated signatures can be electronic. The site will file the signed original in the subject's hospital or research charts and provide a copy to the subject. The site will follow local hospital and EC/IRB provisions for documenting electronic ICF signature.

Sites should report any failure to obtain informed consent from a subject to the Sponsor [redacted] and to the reviewing center's IRB/EC according to the IRB's/ EC's reporting requirements.

During the clinical study, if new information becomes available that can significantly affect a subject's future health and medical care, the Principal Investigator or his/her authorized designee (if applicable) will provide this information to the subject. If relevant, sites will ask the subject to confirm their continuing informed consent in writing.

For live cases at congresses, the subject must sign a specific Live Case ICF, approved by the IRB/EC. The investigator must notify the Sponsor prior to performing a live case.

5.3 Eligibility Criteria

Assessment for eligibility criteria is based on medical records of the site and an interview with a candidate subject. Subjects must meet ALL inclusion criteria to participate in the study. If ANY exclusion criteria are met, the subject is excluded from the clinical study and cannot participate in the study (screen failure).

5.3.1 Inclusion Criteria

5.3.1.1 General Inclusion Criteria

1. Subjects must be at least 18 years of age.
2. Subjects or a legally authorized representative must provide written informed consent per site requirements.
3. Subjects must have evidence of myocardial ischemia (ST-elevated MI [STEMI], Non-STEMI [NSTEMI], Unstable Angina or Stable Angina) or who have silent ischemia with evidence of ischemia, appropriate for percutaneous coronary intervention (PCI) treatment of *de novo* native coronary artery lesions[vi] with DES. Subjects with stable angina or silent ischemia must have an objective sign of ischemia as suggested by one of the following:
    - Abnormal stress or imaging stress test
    - Abnormal computed tomography-fractional flow reserve (CT-FFR)
    - Stenosis by visual estimation ≥ 70%
    - Abnormal pressure-derived indexes (such as fractional flow reserve [FFR], instantaneous wave-free ratio [iFR], diastolic hyperemia-free ratio [DFR], diastolic resting pressure ratio [DPR], or resting full-cycle ratio [RFR]).

5.3.1.2 Angiographic Inclusion Criteria

1. Subjects who have lesion(s) in a vessel with reference vessel diameter > 4.25 mm and ≤ 5.25 mm as the target lesion.

[vi] Native coronary artery is the original artery you were born with, as opposed to a bypass graft.

[redacted]

2. Subjects who receive at least one XIENCE Skypoint stent diameters 4.5 and 5.0 mm.
    a. Lesions with RVD ≤ 4.25 mm should be treated as non-target lesions during the index procedure with commercially available XIENCE family of stents.
    b. Up to three lesions (target and non-target) in two coronary vessels can be treated at the index procedure.
3. If LMCA is the intended target vessel, subjects who have unprotected LMCA disease with a SYNTAX Score[20,vii] ≤ 22.
    a. A heart team consensus approach per the site's SOC to enhance subject protection and optimal clinical practice for the left main treatment is required.

5.3.2 Exclusion Criteria

5.3.2.1 General Exclusion Criteria

1. Subjects who have contraindications to the XIENCE Skypoint stent diameters 4.5 and 5.0 mm per the instruction for use (IFU)
2. Subjects who have active symptoms and/or a positive test result of COVID-19 or other rapidly spreading novel infectious agent within the prior 2 months.
3. Subjects who are participating or planning to participate in any concurrent clinical study/investigation that may potentially impact or confound outcomes of this study.

5.3.2.2 Angiographic Exclusion Criteria:

1. Subjects who require three-vessel treatment.

5.4 Subject Enrollment and Registration

A subject is considered to be enrolled in the study from the moment the subject provides written informed consent. A subject is considered to be registered in the study when the subject provides written informed consent, has at least one XIENCE Skypoint stent diameters 4.5 and 5.0 mm implanted, and is confirmed to meet all general/angiographic eligibility criteria.

5.4.1 Historically Under-Represented Demographic Subgroups

The Sponsor intends to ensure adequate representation of women and other traditionally under-represented demographic subgroups in this clinical study. Some barriers to the participation of women and ethnic minorities in clinical studies have traditionally been:

- Lack of understanding of main obstacles to the participation of such subgroups in clinical research
- Inclusion/exclusion criteria potentially not needed to define the clinical study population may unintentionally exclude specific subgroups
- Under diagnosis of disease etiologies and pathophysiology leading to under referral of demographic subgroups

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[vii] SYNTAX score assessment: if LMCA is the intended target vessel. SYNTAX score I should be used based on the site's assessment using the SYNTAX score calculator: http://www.syntaxscore.org/calculator/start.htm

[redacted]

- Avoidance of specific subgroups by investigators and the Sponsor due to the perception that it takes more time and resources to recruit them
- Fear of fetal consequences (for female participants)
- Family responsibilities limiting women's ability to commit time for follow-up requirements

The Sponsor will take the following steps to ensure adequate representation of women and racial or ethnic minorities in this clinical study:

- The Sponsor will provide training to investigational site personnel to ensure adequate representation of these demographic subgroups
- The Sponsor will regularly review enrollment data to investigate whether there is under-representation of these demographic subgroups
- The Sponsor will regularly review withdrawal rates for under-represented subgroups and compare these rates with that in the overall clinical study population
- As appropriate and necessary, the Sponsor will retrain sites on the importance of recruiting and retaining subjects in the clinical study
- The Sponsor will approach sites without bias or consideration for specific demographic subgroups
- The Sponsor will have informed consent materials in alternative languages and will work with sites and IRBs/ECs on recruitment materials if needed

5.5 Subject Withdrawal and Discontinuation

Each subject meeting all general and screening eligibility criteria shall remain in the clinical study until completion of the required follow-up period; however, a subject's participation in any clinical study is voluntary, and the subject has the right to withdraw at any time without penalty or loss of benefit. Conceivable reasons for discontinuation may include, but not be limited to, the following:

- Subject death
- Subject voluntary withdrawal
- Subject lost-to follow-up as described below
- Subject's follow-up is terminated according to **Section 3.3 Suspension or Early Termination of the Clinical Study**.

Sites must notify the Sponsor of the reason(s) for subject discontinuation. Investigators must also report this to their respective IRB/EC as defined by their institution's procedure(s).

No additional follow-up is required, or recorded data from subjects once withdrawn from the clinical study, except for the status (i.e., deceased/alive).

In case of subject withdrawal of consent, the site should make attempts to schedule the subject for a final clinical study visit. At this final follow-up visit, the subject will undergo the following assessments:

- Review and report adverse events in electronic case report form (eCRF)
- Review and report protocol and concomitant medications in eCRF
- Complete subject-reported outcomes in eCRF

[redacted]

Lost-to-Follow-up

If the subject misses two consecutive scheduled follow-up time points and attempts to contact the subject detailed below are unsuccessful, then the subject is considered lost-to-follow-up. Site personnel shall make all reasonable efforts to locate and communicate with the subject (and document these efforts in the source documents), including the following, at each contact time point:

- A minimum of two telephone calls on different days over the specified follow-up windows to contact the subject should be recorded in the source documentation, including the date, time, and initials of site personnel trying to make contact.
- If these attempts are unsuccessful, the site should send a letter (certified if applicable) to the subject.

If a subject misses one or more non-consecutive follow-up contact time points, it will be considered a missed visit. The subject may then return for subsequent visits. If the subject misses two consecutive time points and the attempts mentioned above at communicating with the subject are unsuccessful, the subject will be considered lost-to-follow-up.

Note: Telephone contact with General Practitioner, non-clinical study cardiologist or relative will be considered as subject contact for the purpose of collecting vital status information. The center shall retain records of the contact.

5.6 Number of Subjects

[redacted]

5.7 Total Expected Duration of the Clinical Study

The expected duration of enrollment is [redacted] to reach a minimum of [redacted] for the SPIRIT XLV PAS. The expected duration of each subject's participation is 3 years, including the scheduled visits and data collection for this clinical study that will occur at 1 month, 6 months, 1 year, 2 years and 3 years. Subjects will be exited from the trial after their 3-year follow-up visit. Therefore, the total duration of the clinical study is expected to be [redacted] from first-patient-in (FPI) to last-patient-out (LPO), consisting of approximately [redacted] plus 3 years of follow-up.

From the time of SPIRIT XLV PAS protocol approval, the following timelines are anticipated:

- [redacted]

5.8 Clinical Report Schedule

Reports will be prepared and submitted to FDA to provide the following information:

[redacted]

- PAS Progress: The sponsor will prepare Interim PAS Status Report every [redacted] of the study and [redacted], thereafter, from the date of the PMA approval letter date, until the submission of the PAS Final Study Report.
- PAS Final Study: Submission of the final study report: [redacted] from study completion (i.e., last subject, last follow-up date)
- Enrollment Status: The Sponsor will prepare enrollment status reports per the frequency agreed with FDA.

6.0 TREATMENT AND EVALUATION OF ENDPOINTS

6.1 Pre-procedure

Subject preparation will follow standard hospital policy for interventional cardiovascular subjects. The baseline or pre-procedure assessments described below should be obtained within [redacted] prior to the index procedure, unless indicated otherwise. They will be documented in the subject medical record and on the eCRF as appropriate.

The schedule of events for this study is in **Section 6.4.4.**

6.1.1 Pre-procedure Clinical Assessments

Subject history will include but not be limited to the following demographics, risk factors, and comorbidities: age, height, weight, body mass index (BMI), gender, hypertension, hyperlipidemia, diabetes mellitus, smoking, ischemic heart disease (history of myocardial infarction, angina pectoris, previous percutaneous or surgical coronary revascularization), congestive heart failure, renal insufficiency, liver disease, cerebrovascular disease (known carotid artery disease, history of minor or major stroke or transient ischemic attack), chronic obstructive pulmonary disease (COPD), and COVID-19 test results. All information will be obtained and recorded in eCRF.

6.1.2 Pre-Procedure Laboratory Assessments

The following laboratory assessment is highly recommended to be obtained at baseline per the site's SOC:

- Baseline 12-lead ECG prior to index procedure

The following laboratory assessment is mandatory to be obtained at pre-procedure:

- At least one cTn biomarker test must be conducted for baseline within [redacted] before the index procedure[25-28]. The pre-procedure cardiac biomarker blood draw can be obtained from the arterial sheath during the procedure but prior to any angioplasty. If cTn assessments are done more than once or repeated before the index procedure, all results should be entered in the CRF. The lab results for cardiac biomarkers can be obtained post-procedure.[viii]

Other laboratory assessments are per the site's SOC.

[viii] [redacted]

6.1.3 Pre-Procedure Preparation

Subjects should be prepared according to the site's SOC for cardiology subjects undergoing PCI. The XIENCE Skypoint stent diameters 4.5 and 5.0 mm to be placed should be inspected, prepared, and implanted according to the most current IFU.

6.1.4 Pre-Procedure Medications

Pre-procedure antiplatelet/anticoagulant medications should be administrated per the site's SOC.

6.2 Index Procedure

6.2.1 Procedures Involved in the Use of the Device Under Investigation

For appropriate use of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm, refer to the latest IFU and the treatment strategy section **(section 6.2.4)** below.

6.2.2 Baseline Angiography

Baseline angiography of the target or non-target lesion(s) will be completed as per the site's SOC. Baseline (prior to pre-dilatation) angiogram must be sent to the core lab or the Sponsor.

6.2.3 Procedure Information Should be Collected

The following data should be collected (including, but not limited to):

- Stent attributes (e.g., size, diameter, overlapping, and number of stents)
- Lesion characteristics (ACC/AHA Classification Scheme of Coronary Lesions)
- All reportable AEs (refer to **section 7.3.1** Adverse Event Reporting)

6.2.4 Treatment Strategy

The treatment strategy should follow the site's SOC and latest product IFU. If not mentioned in the IFU or there is no site's SOC, Abbott recommends following measures for treating the target lesion to achieve an optimized result.

- Post dilatation with a non-compliant balloon to achieve a good stent apposition
- For unprotected left main target lesions, use intravascular imaging (either intravascular ultrasound or optical coherence tomography) when sizing the vessel and following stent implantation
- [redacted]

6.2.5 Final (Post-procedure) Angiography

In all subjects, the post-procedure target or non-target lesion(s) angiography should be performed according to the site's SOC.

Final angiographic images collected per the site's SOC, intravascular ultrasound (IVUS) or optical coherence tomography (OCT) images of the treated lesions should be sent to the Angiographic Core Lab or the Sponsor.

[redacted]

6.3 Post-Procedure

6.3.1 Post-Procedure ECG

A post-procedure ECG is required by this clinical study.

6.3.2 Post-Procedure Cardiac Biomarker Tests

[redacted]

All cardiac-related abnormal laboratory values (per assay-specific IFU) should be reported as AEs.(See **Section 7.2.1 Adverse Event Reporting**)

6.3.3 Post–procedure medication

Post-procedure antiplatelet medication should be per the site's SOC.

6.3.4 Other Chronic Concomitant Medications

Administration of concomitant medications other than any approved P2Y12 inhibitors and aspirin are not required in this protocol. Subjects may receive other medications as needed per physician's discretion.

6.4 Discharge Plan

Discharge is defined as the subject leaving the treating or referral hospital. The discharge will be performed per the site's SOC.

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ix [redacted]

All subjects registered for the clinical study will have follow-up assessments, with either a clinic visit at the investigational center or a telephone contact at the time points listed below.

6.4.1 Follow-up for All Subjects

Subjects registered in the clinical study will receive the following clinical follow-ups from the index procedure date (day 0):

- 1 month (30 ± 7 days)
- 6 months (180 ± 14 days)
- 12 months (365 ± 28 days)
- 24 months (730 ± 28 days)
- 36 months (1095 ± 28 days)

For all follow-ups, either clinic visits or phone visits are allowed. To aid in follow-up compliance, if necessary, an independent service may be utilized to provide in-home visits for clinical follow-up.

Clinical follow-up visits should be conducted by the investigator or trial personnel who have been trained to the protocol.

The following information will be collected at each of the time points:

- Any adverse events
- Antiplatelet medication
- Details of any subsequent coronary interventions (e.g., repeat PCI or coronary artery bypass graft [CABG])

Note that information obtained through indirect contact with a subject's healthcare provider or immediate family member will NOT be considered a trial visit, except when a subject passes away. Additional information for a visit, if needed but missed, may be obtained by reaching out to the subject after the visit to ensure complete data collection.

6.4.2 Additional Follow-up Visits for All Subjects

Additional subject visits, such as unscheduled visits (other than the protocol required visits considered to be related to the index procedure), may occur as clinically warranted. The following information will be collected and recorded in eCRF:

- Any adverse events
- Antiplatelet medication
- Details of any subsequent coronary interventions (e.g., repeat PCI or CABG)

If an unscheduled visit is conducted due to a suspected ischemic cardiac event, cardiac biomarkers and ECG may be performed per the site's SOC.

All efforts must be made to obtain follow-up information on subjects who have undergone procedures or have been treated for adverse events in a non-trial-related hospital(s).

6.4.3 Unscheduled Angiography

There is no required angiographic follow-up for this clinical study. However, angiograms for all unscheduled revascularizations must be sent to the Angiographic Core Lab. The angiographic core laboratory will determine the type of revascularization (i.e., TLR, TVR or non-TVR), ST, or necessary assessments.

6.4.4 Schedule of Events

PROCEDURE/TEST	Baseline/pre-procedure (within 3-months prior to index procedure)	Procedure	Post-Procedure	1-month (30±7d) Clinic visit or phone contact[1]	6-month (180 ±14d) Clinic visit or phone contact[1]	12-month (365 ± 28d) Clinic visit or phone contact[1]	24-month (730 ± 28d) Clinic visit or phone contact[1]	36-month (1095 ± 28d) Clinic visit or phone contact[1]	Unscheduled visits
Subject Medical/Clinical History	✓								
Subject Informed Consent	✓		✓						
General Inclusion/Exclusion Criteria	✓								
ECG	✓[2]		✓[2]						
Angiographic Inclusion/Exclusion Criteria including SYNTAX score if LMCA is treated		✓							
Coronary Angiogram		✓							✓
cTn biomarker measurement(s)	✓[3]		✓[4]						
Stent and Procedure Information		✓							
Post-procedure Antiplatelet Medications			✓	✓	✓	✓	✓	✓	✓
Adverse Events		✓	✓	✓	✓	✓	✓	✓	✓

[1] For all follow-up visits, either clinic visits or phone visits are allowed. To aid in follow-up compliance, if necessary, an independent service may be utilized to provide in-home visits for clinical follow-up.

[2] Pre-procedure ECG is highly recommended, post-procedure ECG is mandatary.

[3] [redacted]

[4] [redacted]

T [redacted]

[redacted]

7.0 ADVERSE EVENTS

To comply with worldwide standards and guidelines on clinical study AE reporting, the Sponsor has adopted uniform and worldwide applicable standard definitions and reporting timelines to be used and adhered to by the investigators.

7.1 Definition

7.1.1 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, in the context of a clinical investigation, whether or not related to the investigational medical device.

As part of ISO14155 Section 3.2, the AE definition has the following notes:

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 the use of investigational medical devices or comparators.

7.1.2 Serious Adverse Event

Serious Adverse Event (SAE) is an AE that led to any of the following:

a) death,

b) serious deterioration in the health of the subject, that resulted in any of the following:

   1. life-threatening illness or injury,
   2. permanent impairment of a body structure or a body function,
   3. hospitalization or prolongation of patient hospitalization,
   4. medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
   5. chronic disease

c) fetal distress, fetal death or a congenital physical or mental impairment or birth defect.

Note: A planned hospitalization for pre-existing condition, or a procedure required by the CIP, without a serious deterioration in health, is not considered to be a SAE.

7.1.3 Device Deficiency/Device Malfunction

Device deficiency is defined as 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. This includes the failure of the device to meet its performance specifications or otherwise perform as intended. Note: Performance specifications include all claims made in the labeling of the device.

[redacted]

Note 1: The definition includes device deficiencies related to investigational medical device or the comparator.
Note 2: Cyber-security incidents related to the investigational product, shall be reported as device deficiencies

A device malfunction is the failure of a device to meet its performance specifications or otherwise perform as intended, when used in accordance with the instructions for use or CIP.

7.2 Adverse Event and Device Deficiency/Device Malfunction Reporting

7.2.1 Adverse Event Reporting

General AE Reporting

Safety surveillance and reporting start as soon as the subject is registered in the clinical study. Safety surveillance and reporting will continue until the last follow-up visit has been performed, the subject is deceased, the subject concludes participation in the clinical study, or the subject withdraws from the clinical study. For the purposes of this clinical study, the following events will be reported to the Sponsor on a CRF: device- and procedure-related AEs, SAEs, cardiovascular-related AEs, deaths and device deficiency data. Additional information with regard to an AE should be updated within the appropriate CRF. AEs will not be collected for screen failure subjects. If the subject gets consented after the index procedure, reporting will be collected from the index procedure, and the AE awareness date should be entered the same as the post-procedure consent date.

Unchanged, chronic, non-worsening or pre-existing conditions are not AEs and should not be reported. The Sponsor will provide an offline form to allow the investigator to report SAEs if the entry cannot be made in the electronic data capture (EDC). This does not replace the EDC reporting system. Sites must still enter all information in the EDC system as soon as feasible.

[redacted]

Non-cardiac related abnormal laboratory values will not be considered AEs unless:

1. the investigator determined that the value is clinically significant,
2. the abnormal lab value required intervention, or
3. the abnormal lab value required subject withdrawal from the clinical study.

SAE Reporting

The investigator must report all SAEs to the Sponsor as soon as possible but no later than outlined below.

[redacted]

Clinical Site	Reporting timelines
All Sites	Sites must report SAEs to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined.

Sites must record the date the site staff became aware that the event met the criteria of an SAE in the source document. The investigator will report the SAE to the local IRB/EC according to the institution's IRB/EC reporting requirements.

7.2.2 Device Deficiency/Malfunctions Reporting

Sites should report all device deficiencies/malfunctions on the appropriate CRF form.

The investigator must report all device deficiencies/malfunctions to the Sponsor as soon as possible but no later than outlined below.

Clinical Sites	Reporting timelines
All Sites	Sites must report device deficiencies/malfunctions to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined.

Sites must report device deficiencies/malfunctions to the IRB/EC per the investigative site's local requirements.

Sites should return the device, if not implanted or not remaining in the subject, to the Sponsor.

7.2.3 Adverse Event Reporting to Country Regulatory Authorities by the Sponsor

The Sponsor will report SAEs and reportable device deficiencies/malfunctions to the country regulatory authority per local requirements.

Note: Reportable device deficiencies include device deficiencies that might have led to an 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.

7.3 Device Relationship

Determination of whether there is a reasonable possibility that an investigational product or device under investigation 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 the assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility and patient condition (pre-existing condition).

8.0 STATISTICAL CONSIDERATIONS

The following section describes the statistical methods for the clinical study.

[redacted]

8.1 Analysis Populations

[redacted]

8.2 Statistical Analyses

[redacted]

8.3 Timing of Analysis

[redacted]

8.4 Subgroup Analysis

[redacted]

8.5 Procedures for Accounting for Missing Data

[redacted]

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x [redacted]

8.6 Deviations from Statistical Plan

[redacted]

9.0 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

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

Subjects providing informed consent are agreeing to allow clinical study monitors or regulatory authorities, including foreign countries, to review in confidence any records identifying the subjects in this clinical study. This information may be shared with regulatory agencies; however, the Sponsor undertakes not to otherwise release the subject's personal and private information.

10.0 QUALITY CONTROL AND QUALITY ASSURANCE

10.1 Selection of Clinical Sites and Investigators

The Sponsor will select investigators qualified by training and experience to participate in the clinical study. Sites will be selected based upon review of a recent site assessment, if applicable, and the qualifications of the investigators who will participate in the clinical study.

10.2 Site Principal Investigator Responsibilities

The role of the Site Principal Investigator is to implement, oversee the management of the day-to-day conduct of the clinical study as well as ensure data integrity and the rights, safety and well-being of the subjects involved in the clinical study. The Principal Investigator shall support monitoring and reporting to IRB/EC and local competent authorities as necessary, throughout the conduct of the clinical study. The Principal Investigator is responsible for ensuring adequate training and qualification of the investigation site team and for maintaining oversight of their activities. The Principal Investigator may delegate tasks to members of the investigation site team but retains responsibility for the clinical study. This also applies when activities are outsourced to an external organization by the Principal Investigator in which case he/she shall exercise oversight to ensure the integrity of all tasks performed and any data generated by this external organization.

10.3 CIP Amendments

The Sponsor will provide approved CIP amendments to the Investigators prior to implementing the amendment. The Principal Investigator is responsible for notifying the IRB/EC or equivalent committee of the CIP amendment (administrative changes) or obtaining IRB's/EC's approval of the CIP amendment (changes in subject care or safety), according to the instructions provided by the Sponsor with the CIP amendment.

The Sponsor will submit the CIP Amendment to regulatory bodies per applicable regulation and await regulatory approval before implementing the CIP amendment.

[redacted]

Sites must document in writing acknowledgement/approval of the CIP amendment by the IRB/EC prior to implementation of the CIP amendment. Sites must also provide copies of this documentation to the Sponsor.

10.4 Training

10.4.1 Site Training

All Investigators and clinical study personnel are required to attend Sponsor training sessions, which may be conducted at an Investigator's meeting, a site initiation visit, or other appropriate training sessions. Over-the-phone or self-training may take place as required. Training of Investigators and clinical study personnel will include, but is not limited to, the CIP requirements, electronic CRF completion, and clinical study personnel responsibilities. All Investigators and clinical study personnel that are trained must sign a training log (or an equivalent) upon completion of the training. Prior to signing the training log, Investigators and clinical study personnel must not perform any CIP-related activities that are not considered the site's SOC.

10.5 Monitoring

The Sponsor and/or designee will monitor the clinical study over its duration according to the CIP-specific monitoring plan which will include the planned extent of source data verification.

Prior to initiating any procedure, the Sponsor monitor (or delegate) will ensure that the following criteria are met:

- The investigator understands and accepts the obligation to conduct the clinical study according to the CIP and applicable regulations and has signed the Investigator Agreement
- The Investigator and his/her staff should have sufficient time and facilities to conduct the clinical study and should have access to an adequate number of appropriate subjects to conduct the clinical study.
- Sites must have source documentation (including original medical records) to substantiate proper informed consent procedures, adherence to CIP procedures, adequate reporting and follow-up of adverse events, accuracy of data collected on case report forms, and device information.
- The Investigator/site will permit access to such records and will maintain a monitoring visit sign-in log at the site. The Investigator will agree to dedicate an adequate amount of time to the monitoring process. The Investigator and/or research coordinator will be available for monitoring visits. It is expected that the Investigator will provide the monitor with a suitable working environment for review of clinical study-related documents.

10.6 Deviations from CIP

The Investigator should not deviate from the CIP for any reason except in cases of medical emergencies when the deviation is necessary to protect the rights, safety, and well-being of the subject, or to eliminate an apparent immediate hazard to the subject. In that event, the Investigator will notify the Sponsor immediately by phone or in writing.

The Sponsor will not grant any waivers for CIP deviations. Sites must report all deviations to the Sponsor using the Deviation CRF. The Sponsor will monitor the occurrence of CIP deviations for evaluation of investigator compliance to the CIP and regulatory requirements and handle according to written procedures. Investigators will determine the cause of deviations, implement corrective actions and inform their IRB/EC or equivalent committee of CIP deviations in accordance with their specific IRB/EC or equivalent committee reporting policies and procedures.

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

- Visiting the investigator and/or delegate
- Telephoning the investigator and/or delegate
- Corresponding with the investigator and/or delegate

Repeated non-compliance with the signed agreement, the CIP, or any other conditions of the clinical study may result in further escalation in accordance with the Sponsor's written procedures, including securing compliance or, at its sole discretion, the Sponsor may terminate the investigator's participation in the clinical study.

The following categories of protocol deviations will be considered as major:

- Informed Consent not obtained
- Eligibility criteria not met
- SAE reporting deviation

The following categories of protocol deviations will be considered as minor:

- Data outside time window
- Missed visit

10.7 Quality Assurance Audit

A Sponsor representative or designee may request access to all clinical study records, including source documentation, for inspection during a Quality Assurance audit.

If an investigator is contacted by a Regulatory Agency in relation to this clinical study, the Investigator will notify Sponsor immediately. The Investigator and Research Coordinator must be available to respond to reasonable requests and audit queries made during the audit process. The Investigator must provide the Sponsor with copies of all correspondence that may affect the review of the current clinical study (e.g., Form FDA 483, Inspectional Observations, Warning Letters, Inspection Reports, etc.). The Sponsor may provide any needed assistance in responding to regulatory audits.

10.8 Sponsor Auditing

1. The Sponsor shall prepare an audit plan as well as the operating procedures for the related duties and conduct audits in accordance with the audit plan and the operating procedures.

[redacted]

2. Individuals engaged in auditing (hereinafter referred to as "auditor") shall be different than those in charge of medical device development or monitoring.
3. The auditor shall prepare an audit report documenting the matters confirmed in the audit to certify and verify that the audit has been conducted and submit them to the Sponsor.

10.9 Committees

10.9.1 Clinical Events Committee (CEC)

The CEC is an independent adjudication body comprised of qualified physicians who are not participants in the clinical study. The CEC will review and adjudicate pre-specified events reported by investigators or identified by Safety personnel for the clinical study as defined in the CEC charter and according to definitions provided in this CIP.

11.0 DATA HANDLING AND RECORD KEEPING

Sponsor and/or its affiliates will maintain documentation of the systems and procedures used in data collection for the duration of the clinical study.

CRF data collection will be performed through a secure web portal and only authorized personnel will access the EDC system using a unique username and password to enter, review or correct data. Passwords and electronic signatures will be strictly confidential.

The data will be subjected to consistency and validation checks within the EDC system and supplemental review by the Sponsor.

At the end of the clinical study, completed CRF 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 provided to the investigational sites, if requested.

For the duration of the clinical study, the Investigator will maintain complete and accurate documentation including, but not limited to, medical records, clinical study progress records, laboratory reports, CRFs, signed ICFs, device accountability records (if applicable), correspondence with the IRB/EC and clinical study monitor/the Sponsor, adverse event reports, and information regarding subject discontinuation or completion of the clinical study.

11.1 Protection of Personally Identifiable Information

The Sponsor respects and protects personally identifiable information collected or maintained for this clinical study.

The Sponsor implements technical and physical access controls to ensure that Personal Information is accessible only to and processed only on a 'need to know' basis, including periodic review of access rights, and revocation of access when an individual's employment is terminated or the individual transitions to a role that does not require access to Personal Information, and appropriate restrictions on physical access to premises, facilities, equipment, and records containing Personal Information.

[redacted]

The Sponsor requires the investigational sites to enter only pseudonymous Personal Information (key-coded) necessary to conduct the clinical study, such as the patient's medical condition, treatment, dates of treatment, etc., into the Sponsor's data management systems. The Sponsor discloses as part of the clinical study informed consent process that some Sponsor representatives still may see Personal Information at the participating sites for technical support of the participating physicians on the device implant or procedures, monitoring and quality control purposes. All parties will observe confidentiality of Personal Information always throughout the clinical study. All reports and data publications will preserve the privacy of each subject and confidentiality of his/her information.

The Sponsor data management systems and processes were designed, developed, and tested according to industry standards to appropriately safeguard Confidential Information (including any Personal Information) against unauthorized access and/or interference by third parties, intrusion, theft, destruction, loss or alteration. Clinical study data are encrypted in transit and at rest.

The Sponsor maintains a Privacy Incident procedure that complies in all respects with Applicable Law and industry best practices.

11.2 Data Management Plan

[redacted]

11.3 Source Documentation

Regulations and GCP require the Investigator to maintain information in the subject's original medical records that corroborates data collected on the CRFs. To comply with these regulatory requirements/GCP, sites should include the following information in the subject record at a minimum and if applicable to the clinical study:

- Medical history/physical condition of the subject before involvement in the clinical study sufficient to verify CIP entry criteria
- Dated and signed notes on the day of entry into the clinical study referencing the Sponsor, CIP number, subject ID number, and a statement that informed consent was obtained
- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- AEs 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 assessment of device relationship for SAEs.
- Notes regarding CIP-required and prescription medications taken during the clinical study (including start and stop dates)
- Subject's condition upon completion of or withdrawal from the clinical study
- Any other data required to substantiate data entered into the CRF
- Patient reported outcome measures may be completed using CRF worksheets. This serves as source documentation.

[redacted]

11.4 Case Report Form Completion

Site research personnel trained on the CIP and CRF completion will perform the primary data collection clearly and accurately based on source-documented hospital and/or clinic chart reviews. The investigator will ensure accuracy, completeness, legibility, and timeliness of the data reported to the Sponsor on the CRFs and in all required reports.

Sites will collect data on all subjects registered into the clinical study.

Only authorized site personnel will be permitted to enter the CRF data through the EDC system deployed by the Sponsor. The Sponsor will use an electronic audit trail to track any subsequent changes of the entered data.

11.5 Record Retention

The Sponsor and Investigator/Site will archive and retain all documents pertaining to the clinical study as per the applicable regulatory record retention requirements. The Investigator must obtain permission from Sponsor in writing before destroying or transferring control of any clinical study records.

12.0 ETHICAL CONSIDERATION

12.1 Institutional Review Board/Medical Ethics Committee Review and Approval

The Principal Investigator at each investigational site will obtain IRB/EC approval for the CIP and ICF/other written information provided to the patient prior to consenting and enrolling subjects in this clinical study. The site must receive the approval letter prior to the start of this clinical study and provide a copy to the Sponsor.

Sites will submit any amendments to the CIP as well as associated ICF changes to the IRB/EC and written approval obtained prior to implementation, according to each institution's IRB/EC requirements.

No changes will be made to the CIP or ICF or other written information provided to the patient without appropriate approvals, including IRB/EC, the Sponsor, and the regulatory agencies (if applicable).

Until the clinical study is completed, the Investigator will advise his/her IRB/EC of the progress of this clinical study, per IRB/EC requirements. Written approval must be obtained from the IRB/EC yearly to continue the clinical study, or according to each institution's IRB/EC requirements.

Sites will not perform any investigative procedures, other than those defined in this CIP, on the enrolled subjects without the written agreement of the IRB/EC and the Sponsor.

13.0 CLINICAL STUDY CONCLUSION

The clinical study will be concluded when:

- All sites are closed AND
- The final report has been provided to investigators or the Sponsor has provided formal documentation of clinical study closure.

[redacted]

14.0 PUBLICATION POLICY

The data and results from the clinical study are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during the clinical study. The Investigators will not use this clinical study-related data without the written consent of the Sponsor for any purpose other than for clinical study completion or for generation of publication materials, as referenced in the Clinical Trial Agreement. Single-center results are not allowed to be published or presented before the multi-center results. The Sponsor must review and approve any proposals for publications or presentations by the investigators in a timely manner in compliance with the Sponsor's publication policy set forth in the Clinical Trial Agreement.

The Sponsor will be responsible for determining whether to register the clinical study on www.clinicaltrials.gov or any other clinical trials, in accordance with the International Committee of Medical Journal Editors guidelines, or any other applicable guidelines. In the event the Sponsor determines that the clinical study should be registered, the Sponsor shall be responsible for any such registration and results posting as required by the ClinicalTrials.gov website. Institution and/or Principal Investigator(s) shall not take any action to register the clinical study.

15.0 RISK ANALYSIS

15.1 Anticipated Clinical Benefits

Inheriting the anti-thrombotic characteristics of the XIENCE Family of Stents owing to its unique design, the XIENCE Skypoint is a new iteration of the XIENCE family of Stents, which includes XIENCE V®, XIENCE PRIME®, XIENCE XPEDITION®, XIENCE ALPINE, XIENCE Sierra. Over 15 million XIENCE Family of Stents have been implanted into patients with CAD.[iii,3] The XIENCE Family of Stents have been the subject of extensive clinical studies for the treatment of patients with CAD. A robust clinical program of Abbott-sponsored clinical investigations assesses the safety and effectiveness of the XIENCE Family of Stents, which encompasses over 125,000 patients across multiple geographies.[iii, 4-14] Altogether, the safety and effectiveness of the XIENCE Family of Stents have been well established.

Prior to the market approval of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm in the US, the XIENCE Family of Stents were commercially available in sizes up to 4.0 mm in diameter, which can expand to 4.25 mm RVD with a maximum of 5.5 mm post dilation expansion diameter. Without any modification to the stent design or manufacturing process, the XIENCE Skypoint stent diameters 4.5 and 5.0 mm have expansion capabilities to treat vessels up to 5.25 mm RVD with an increased maximum post-dilatation expansion diameter up to 5.75 mm, compared to 5.5 mm for XIENCE Sierra. Owing to the similarity of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm to the other XIENCE Family of Stents in stent design, clinical evidence from previous Abbott sponsored clinical trials for the XIENCE Family of Stents relevant to large vessel treatment are applicable and supported the safety and effectiveness of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm for market approval in treatment of large coronary vessels without a pre-market trial.

The intended clinical benefits of treatment with the XIENCE Skypoint in coronary indications are:

- Improved outcomes with revascularization versus medical treatment
- Improved outcomes with new-generation DES vs other PCI devices

- No increased ischemic risk, and decreased risk of major bleeding (Bleeding Academic Research Consortium [BARC] 3-5) with shorter dual antiplatelet therapy (DAPT) for high bleeding risk (HBR) population
- Noninferiority of PCI versus coronary artery bypass graft (CABG) in composite of death, MI, and stroke up to 3 years for LMCA lesions[xi]

15.2 Foreseeable Adverse Events and Anticipated Adverse Device Effects

Risks associated with stenting using the XIENCE Skypoint stent diameters 4.5 and 5.0 mm, together with their likely incidence, are described in the IFU and **Appendix III**.

15.3 Residual Risks Associated with the Device Under Investigation, as Identified in the Risk Management Report / Risk Analysis Report

Based upon bench testing and prior Abbott sponsored clinical study data, all risks have been identified and mitigated as far as possible through application of appropriate controls and inspections and determined to be within acceptable levels.

Residual risks are likewise disclosed in the IFU in the form of clear instructions of what actions to take or to avoid, to avoid a hazardous situation of harm from occurring (contra-indications, warnings, and precautions). The anticipated AEs disclosed in the IFU (and CIP Appendix III provide further information to enable the user, and potentially the subject, to make an informed decision that weighs the residual risk against the benefit of using the device.

15.4 Risks Associated with Participation in this Clinical Study

The risks associated with participating in this clinical study are listed in the product IFU.

15.5 Steps Taken to Control or Mitigate Risks

In-depth recommendations, special precautions and instructions regarding subject selection, device handling, device placement and system removal are included in the IFU.

Risks associated with the use of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm during this clinical study are minimized through device design, investigator selection and training, pre-specified subject eligibility requirements, and study monitoring to ensure adherence to the protocol.

These risk management aspects are detailed below:

Device Design: the design of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm includes many features aimed at minimizing potential risks. The major safety features of the device are described below:

[xi] [redacted]

- The stent size matrix includes large stent diameters enable better size matching between target vessel and implant.
- The drug everolimus and drug dose density are the same as the predecessor.
- The XIENCE Skypoint stent diameters 4.5 and 5.0 mm is constructed from well-characterized, biocompatible materials that have undergone extensive testing.

Investigator Selection and Training: It is also stated in the IFU that the devices can only be used by physicians who have received appropriate training on how to use the device. This statement is interpreted to mean that the physician users are expected to be aware of the known and foreseeable safety risks associated with the use of the devices including the surgical and/or non-surgical treatment of these conditions.

- Only physicians who are skilled in the manipulation of catheter-based technology in the vasculature and heart and have a good understanding of the risks associated with these manipulations, will be selected as investigators for this trial.
- Emergency surgical back-up should be available as per the institution's standard procedures.
- The Sponsor will be available to provide technical support to answer questions regarding the function of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm.
- Pre-specified subject eligibility requirements - as stated in **Section 5.3** of the protocol.

Ensuring strict adherence to the clinical study protocol

The clinical study will be carefully monitored by the Sponsor monitor (or designee) to ensure adherence to the CIP. AEs and device deficiencies will be reported to Abbott/designee and will be monitored internally for safety surveillance purposes.

15.6 Risk to Benefit Rationale

The XIENCE Skypoint stent diameters 4.5 and 5.0 mm were approved for commercial use in the US. The foreseeable rates of the anticipated AEs associated with the procedure and implantation of XIENCE Skypoint stent diameters 4.5 and 5.0 mm are listed in the IFU and in **Appendix III**. The clinical benefit that may be expected from treatment of coronary lesions with large diameter with the XIENCE Skypoint stent diameters 4.5 and 5.0 mm outweighs the possible risks that subjects may experience when participating in this trial.

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APPENDIX I: ABBREVIATIONS AND ACRONYMS

Acronym or Abbreviation	Complete Phrase or Definition
%DS	percent diameter stenosis
ACC/AHA	American College of Cardiology/American Heart Association
AE	adverse event
AMI	acute myocardial infarction
ARC	Academic Research Consortium
BMI	body mass index
CABG	coronary artery bypass graft
CAD	coronary artery disease
CD	cardiac death
CEC	clinical events committee
CIP	clinical investigation plan
COPD	chronic obstructive pulmonary disease
COVID-19	coronavirus disease 2019
CK-MB	creatine kinase myocardial-band isoenzyme
CT-FFR	computed tomography-fractional flow reserve
cTn	cardiac troponin
DAPT	dual antiplatelet therapy
DD	device deficiency
DES	drug-eluting stent
DFR	diastolic hyperemia-free ratio
DM	device malfunction
DPR	diastolic pressure ratio
ECG	electrocardiogram
eCRF	electronic case report form
EDC	electronic data capture
EECS	everolimus eluting coronary stent
EECSS	everolimus eluting coronary stent system
FAS	full analysis set
FDA	The Food and Drug Administration
FPI	first-patient-in

Acronym or Abbreviation	Complete Phrase or Definition
GCP	good clinical practice
HBR	high bleeding risk
ICF	informed consent form
IFU	instructions for use
iFR	instantaneous wave-free ratio
ID	ischemic driven
IRB	institutional review board
IVUS	intravascular ultrasound
LMCA	left main coronary artery
LPO	last-patient-out
mg	milligram
MI	myocardial infarction
mm	millimeter
NSTEMI	non-ST-Elevation MI
NQMI	non-Q wave myocardial infarction
OCT	optical coherence tomography
OUS	outside of United States
PBMA	poly (n-butyl methacrylate)
PCI	percutaneous coronary intervention
PVDF-HFP	polymer of vinylidene fluoride and hexafluoropropylene
QCA	quantitative coronary angiography
QMI	Q wave myocardial infarction
RFR	resting full-cycle ratio
RVD	reference vessel diameter
RX	rapid exchange
SAE	serious adverse event
SOC	standard of care
ST	stent thrombosis
STEMI	ST-elevation MI
TBD	to be determined
TIMI	thrombolysis in myocardial infarction

Acronym or Abbreviation	Complete Phrase or Definition
TLF	target lesion failure
TLR	target lesion revascularization
TVF	target vessel failure
TVR	target vessel revascularization
ULN	upper limits of normal (per site standard)
URL	upper reference limit (per assay IFU)
US	United States

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)
- Concentric
- Readily accessible
- Nonangulated segment, < 45°
- Smooth contour
- Little or no calcification
- Less than totally occlusive
- Not ostial in location
- No major branch involvement
- Absence of thrombus

Type B Lesions* (Moderate Success, 60-85%; Moderate risk)

- Tubular (10-20 mm length)
- Eccentric
- Moderate tortuosity of proximal segment
- Moderately angulated segment, > 45°, < 90°
- Irregular contour
- Moderate-to-heavy calcification
- Total occlusions < 3 months old
- Ostial in location
- Bifurcation lesions requiring double guide wires
- 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)
- Excessive tortuosity of proximal segment
- Extremely angulated segments > 90°
- Total occlusions > 3 months old
- Inability to protect major side branches
- Degenerated vein grafts with friable lesions

DEATH (Per ARC Circulation 2007; 115: 2344-2351)

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

Cardiac death:

[redacted]

Any death due to proximate cardiac cause (e.g. MI, low-output failure, fatal arrhythmia), unwitnessed death and death of unknown cause, all procedure related deaths including those related to concomitant treatment.

Vascular death:
Death due to non-coronary vascular causes such as cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular cause.

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.

MYOCARDIAL INFARCTION [MI]

1. Periprocedure MI

Periprocedural MI – Modified ARC-2 Definition[xii]
Periprocedural myocardial infarction occurring within 48 hours after all percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) procedures:[20]

Absolute rise (from baseline to within 48 hours of procedure) in cardiac troponin of ≥35x the 99th percentile upper reference limits (URL) (or ≥35x upper limits of Normal [ULN] if URL is not available) or in the absence of cardiac troponin, rise in CK-MB to ≥ 5x the 99th percentile URL (or ≥5x ULN if URL is not available). Note, cardiac troponin assessments are preferentially used if available; otherwise CK-MB may be used.

In addition, 1 (or more) of the following measures of myocardial ischemia must be present post-procedure:

- New significant Q waves (≥40 ms in duration and ≥1 mm deep in voltage in ≥2 contiguous leads) or equivalent
- Persistent flow-limiting angiographic complications in a major epicardial vessel or branch ≥ 1.5 mm in diameter present at the end of the PCI procedure (or during angiography performed to evaluate a post-CABG complication) as assessed at the angiographic core laboratory
- New substantial loss of viable myocardium on serial imaging

These assessments apply to patients: a) with baseline CK-MB or cardiac troponin levels ≤1x the 99th percentile URL (or ≤1x ULN if URL is not available); b) in whom the baseline biomarker is >1x the 99th percentile URL (or >1x ULN if URL is not available) and stable or falling; and c) with a single elevated baseline draw who have a chronic coronary syndrome (CCS). In the latter two groups (patients in whom the baseline is elevated and stable or falling and CCS patients with a single elevated baseline draw), the post-procedural troponin (or CK-MB) must rise above the most recent baseline by an increment of the values above (i.e. for troponin ≥35x the 99th percentile URL or ≥35x ULN if URL is not available) or in the absence of cardiac troponin, for CK-MB ≥5x the 99th percentile URL (or ≥5x ULN if URL is not available).

[xii] Garcia-Garcia HM, McFadden EP, Farb A, et al. Standardized End Point Definitions for Coronary Intervention Trials: The Academic Research Consortium-2 Consensus Document. *Eur Heart J.* 2018;39(23):2192-2207.

[redacted]

These assessments do not apply to patients: a) in whom baseline CK-MB or troponin levels are elevated and rising; and b) with a single elevated baseline level who presented with a NSTEMI or STEMI in whom it is uncertain whether the peak has been reached. In such patients periprocedural MI will only be adjudicated if the troponin (or CK-MB) biomarker increases from the prior measure by the increments thresholds specified above, and at least 2 of the 3 above criteria for myocardial ischemia are present.

Periprocedural MI per SCAI definition[19] J Am Coll Cardiol. 2013; 62(17):1563-70):

defined as the occurrence within 48 hours after either PCI or CABG of either:

- CK-MB above 10 x URL (*determined on a single measurement), OR
- CK-MB above 5 x URL (*determined on a single measurement), PLUS
    - new pathological Q waves in at least 2 contiguous leads or new persistent non-rate related LBBB

In the absence of CK-MB measurements and a normal baseline cardiac troponin (cTn), peri-procedural MI can also be defined as a cTn (I or T) level measured within 48 hours of the PCI rises to ≥70 x the local laboratory URL, or ≥35 x URL with new pathologic Q-waves in ≥2 contiguous leads, or new persistent LBBB.

2. Spontaneous MI

All MIs which are not peri-procedural are considered spontaneous MIs. Spontaneous myocardial infarctions are usually related to atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with resulting intraluminal thrombus in one or more of the coronary arteries leading to decreased myocardial blood flow or distal platelet emboli with ensuing myocyte necrosis. However, spontaneous MIs can also be due to an imbalance between supply and demand, or due to stent thrombosis, graft occlusion or other causes. Most patients with spontaneous MI have underlying severe CAD but on occasion non-obstructive or no CAD. Spontaneous MIs usually occur beyond 48 hours post-procedure but can occasionally occur within 48 hours of a revascularization procedure if the cause is clearly distinct from the index procedure (e.g. a stent thrombosis at 24 hours). Spontaneous MIs are defined and subclassified according to types 1, 2, 3, 4b and 4c according to the 4th Universal Definition of MI classification[xiii] (below).

Spontaneous Myocardial Infarction: Fourth Universal Definition

Type 1: MI caused by atherothrombotic coronary artery disease (CAD) and usually precipitated by atherosclerotic plaque disruption (rupture or erosion) is designated as a Type 1 MI. Type 1 MI is characterized by detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL and with at least one of the following:

[xiii] Thygesen K, Alpert JS, Jaffe AS, et al. Fourth Universal Definition of Myocardial Infarction (2018). *J Am Coll Cardiol.* 2018;72(18):2231-2264.

[redacted]

- Symptoms of acute myocardial ischaemia;
- New ischaemic ECG changes;
- Development of pathological Q waves;
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology;
- Identification of a coronary thrombus by angiography including intracoronary imaging or by autopsy[xiv]

Type 2: Myocardial infarction secondary to an ischemic imbalance.
The pathophysiological mechanism leading to ischaemic myocardial injury in the context of a mismatch between oxygen supply and demand has been classified as type 2 MI. Type 2 MI is characterized by detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL, and evidence of an imbalance between myocardial oxygen supply and demand unrelated to coronary thrombosis, requiring at least one of the following:

- Symptoms of acute myocardial ischaemia;
- New ischaemic ECG changes;
- Development of pathological Q waves;
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology;

Type 3: Myocardial infarction resulting in death when biomarker values are unavailable. Patients are designated as having Type 3 MI who suffer cardiac death, with symptoms suggestive of myocardial ischaemia accompanied by presumed new ischaemic ECG changes or ventricular fibrillation, but die before blood samples for biomarkers can be obtained, or before increases in cardiac biomarkers can be identified, or MI is detected by autopsy examination.

Type 4b: Myocardial infarction related to stent thrombosis associated with percutaneous coronary intervention (PCI).
Myocardial infarction associated with stent thrombosis is designated as Type 4b MI, detected by angiography or autopsy using the same criteria utilized for Type 1 MI.

Type 4c: Myocardial infarction related to restenosis associated with percutaneous coronary intervention (PCI).
This PCI-related MI type is designated as Type 4c MI, defined as focal or diffuse restenosis, or a complex lesion associated with a rise and/or fall of cTn values above the 99th percentile URL applying, the same criteria utilized for Type 1 MI.

3. **Myocardial infarctions** will also be adjudicated based on the following classification:

- **Q wave MI**

[xiv] Post-mortem demonstration of an atherothrombus in the artery supplying the infarcted myocardium, or a macroscopically large circumscribed area of necrosis with or without intramyocardial haemorrhage, meets the type 1 MI criteria regardless of cTn values.

[redacted]

Development of new, pathological Q wave on the ECG (≥ 0.04 seconds in duration and ≥ 1 mm in depth) in ≥ 2 contiguous precordial leads or ≥ 2 adjacent limb leads)

- **Non-Q wave MI**

  Those MIs which are not Q-wave MI.

All Myocardial infarctions will be adjudicated by CEC by different definitions mentioned above, and also be adjudicated as to their relation to the target vessel

All infarcts that cannot be clearly attributed to a vessel other than the target vessel will be considered related to the target vessel.

STENT THROMBOSIS (Per ARC Circulation 2007; 115: 2344-2351)

- **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.
† Including "primary" as well as "secondary" late stent thrombosis; "secondary" late stent thrombosis is a stent thrombosis after a target segment revascularization.

- **Categories (Definite, Probable, and Possible):**

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)
- Non-occlusive thrombosis
  - Intracoronary thrombus is defined as a (spheric, ovoid, or irregular) non-calcified 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).

Pathological confirmation of stent thrombosis

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

* 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.

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.

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 trial follow-up.

REVASCULARIZATION (Per ARC Circulation 2007; 115: 2344-2351)

Target Lesion Revascularization (TLR)

TLR 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 ischemic driven [ID] or not ischemic driven by the investigator prior to repeat angiography. The target lesion is defined as the treated segment from 5 mm proximal to the stent and to 5 mm distal to the stent.

Target Vessel Revascularization (TVR)

TVR 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)**

[redacted]

A revascularization is considered ischemic driven if angiography at follow-up shows a percent diameter stenosis ≥ 50% and if one of the following occurs:

- A positive history of recurrent angina pectoris, presumably related to the target vessel;
- Objective signs of ischemia at rest (ECG changes) or during exercise test (or equivalent), presumably related to the target vessel;
- Abnormal results of any invasive functional diagnostic test (e.g., Doppler flow velocity reserve, fractional flow reserve);
- A TLR/TVR with a diameter stenosis ≥70% in the absence of the above mentioned ischemic signs or symptoms.

TARGET LESION FAILURE (TLF)
TLF is defined as a composite of all cardiac death, myocardial infarction attributed to target vessel or clinically-indicated TLR.

TARGET VESSEL FAILURE (TVF)
TVF is defined as a composite of cardiac death, MI attributed to target vessel, clinically-indicated TLR, or clinically-indicated TVR, non-TLR.

COVID-19 Relatedness Definitions
The COVID-19 relatedness to an adverse event, is adjudicated by the CEC committee into 3 categories: likely related, possibly related, or not likely related, based on the COVID-19 relatedness definitions that are described on the CEC charter. Please refer to the CEC charter for the COVID-19 relatedness definitions.

IN-STENT

Within the margins of the stent.

Minimal Lumen Diameter (MLD)

Minimum lumen diameter is defined as the shortest diameter through the center point of the lumen. Data are collected from two projections.

PERCENT DIAMETER STENOSIS (%DS)

The value calculated as 100 * (1 - MLD/RVD) using the mean values from two orthogonal views (when possible) by QCA.

REFERENCE VESSEL DIAMETER (RVD)

Reference vessel diameter based on QCA is derived from either the user-defined method using average diameter of proximal and distal healthy segments or the interpolated method.

RESTENOSIS

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

[redacted]

TIMI (THROMBOSIS IN MYOCARDIAL INFARCTION) FLOW GRADES

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: RISKS OF FORSEEABLE ADVERSE EVENTS

Imaging Catheter, PCI, and Contrast Media

Below are the possible risks that may occur with use of XIENCE Skypoint stent diameters 4.5 - 5.0 mm. These risks are not specific to the XIENCE Skypoint stent diameters 4.5 – 5.0 mm and may happen with any stent for heart vessels:

- Allergic reactions or hypersensitivity to rubber, contrast agent, anesthesia, device materials (cobalt, chromium, tungsten, nickel, methacrylic polymer, and fluoropolymer), and drug reactions to everolimus, anticoagulation, or antiplatelet drugs
- Vascular complications in arteries used to access the coronary artery which may require blood transfusion or surgical artery repair, including:
    - Complications at the groin or arm access site
    - Bleeding
    - Formation of an abnormal connection between an artery and the vein next to it
    - Leaking of blood from an artery to the surrounding tissue (usually as a result of a puncture to the artery)
    - Weakness in wall of artery (causing possible serious bleeding complications)
    - Partial or complete tear of the wall of the artery
    - Vessel puncture or rupture
    - Movement of air, tissue, plaque, blood clot, or device material (stent or catheter parts) downstream in the arteries resulting in blockage in blood flow
    - Nerve damage caused by compression of the nerves, injury to the nerve, or interruption of blood supply to the nerves
    - Decreased blood supply to the arms and / or legs which may cause cramping or pain
- Complications at the heart arteries which may require additional treatment or surgery, including:
    - Complete blockage of the coronary artery, which may require a repeat procedure or emergency surgery to reopen the coronary artery
    - Formation of an abnormal connection between a heart artery and the vein next to it
    - Leaking of blood from a heart artery to the surrounding tissue (usually as a result of a puncture to the artery)
    - Weakness in wall of the heart artery (causing possible serious bleeding complications)
    - Partial or complete tear of the wall of the artery supplying the heart muscle
    - Puncture or rupture of the wall of the artery supplying the heart muscle
    - Movement of air, tissue, plaque, blood clot, or device material (stent or catheter parts) that partially or completely blocks the heart artery and / or implanted stent
    - Development of blood clots partially or completely blocking blood flow within the artery and / or the implanted stent
    - Narrowing or re-narrowing of the treated heart artery
- Complications in the sac around the heart which may require additional treatment, including:
    - Rapid accumulation of blood in the sac around the heart resulting in compression of the heart so it cannot pump out blood to the rest of the body which may require additional treatment or emergency surgery
    - An abnormal accumulation of blood around the heart
    - Inflammation of the tissue around the heart (causing possible chest pain)

- Irregular heartbeats (caused by abnormal electrical activity in the heart from the upper or lower heart chambers)
  - Rapid, irregular beating of the heart's upper chambers. Blood may pool and clot inside the heart, increasing the risk for heart attack and stroke.
  - Rapid, irregular beating of the heart's lower chambers.
- Decreased blood and / or oxygen supply to part of the heart muscle which may cause:
  - Decreased blood supply to heart muscles
  - Heart attack (permanent damage of an area of the heart tissue, due to interruption in the blood flow to the heart muscle)
  - Temporary spasm of the heart arteries
  - Chest pain (which may radiate to jaw or arm) or discomfort caused by inadequate supply of blood to the heart)
- Stroke or temporary stroke symptoms as a result of decreased oxygen to the brain causing blurred vision, dizziness, faintness, and numbness
- Abnormal organ function in very ill patients including:
  - Stoppage of the heart
  - Heart function failure (potentially leading to the development of fluid in the lungs and severe breathing difficulty)
  - Lung function failure (potentially leading to severe breathing difficulty)
  - Kidney failure
  - Shock (a life-threatening condition in which blood pressure is too low to maintain adequate-blood flow to your organs)
- Bleeding
- Blood count abnormalities
- Low or high blood pressure
- Infection
- Nausea and vomiting
- Feeling of the heart beating rapidly (palpitations), dizziness, or fainting
- Chest pain
- Fever
- Pain
- Death

Magnetic resonance imaging (MRI): If a subject requires a magnetic resonance imaging (MRI) scan, tell the doctor or MRI technician that the subject has a stent implant. Non-clinical testing has demonstrated that the XIENCE Skypoint stent, in single and in overlapped configurations up to 91 mm in length, is MR Conditional. A patient with this device can be safely scanned in an MR system under the following conditions:
Static magnetic field of 1.5 and 3 Tesla

- Maximum gradient slew rate capability of 200 T/m/s
- Maximum spatial field gradient of 3000 gauss/cm (30 T/m)

[redacted]

- Maximum MR system reported whole-body-averaged Specific Absorption Rate (SAR) of 2.0 W/kg (normal operating mode).

Under the scan conditions defined above, the XIENCE Skypoint stents are expected to produce a maximum temperature rise of less than 4.8°C after 15 minutes of continuous scanning. In non-clinical testing, the image artifact caused by the device extends approximately 5 mm from the XIENCE Skypoint stent when imaged with a gradient echo or spin echo pulse sequence and a 3 Tesla MRI system.

The XIENCE Skypoint stent should not migrate in this MRI environment. Non-clinical testing at field strengths greater than 3 Tesla has not been performed to evaluate stent migration or heating. MRI at 1.5 or 3 Tesla may be performed immediately following the implantation of the

XIENCE Skypoint stent. There may be other risks or discomforts to a subject that are not known at this time. If important information is learned during the course of this clinical study, the site will be notified by the Sponsor. The Study Doctor from the site will discuss with a subject important new information that is learned during the course of this study that may affect a subject's condition or willingness to continue to take part in this clinical study.

If a subject is a woman who is able to become pregnant, it is expected that the subject will use an effective method of birth control to prevent exposing a fetus to a potentially dangerous agent with unknown risk. If a subject is pregnant or currently breast feeding, she should not participate in this study.

The rates of foreseeable adverse events are:

Anticipated Adverse Events			**Frequency Rate Ranges**				
Category	**Subcategory**	**Layman terminology**	**Very common: ≥10%**	**Common: ≥ 1.0% to < 10%**	**Uncommon: ≥ 0.1% to < 1.0%**	**Rare: ≥ 0.01% to < 0.1 %**	**Very Rare : < 0.01 %**
Allergic reaction or hypersensitivity to latex, contrast agent anesthesia, device materials, and drug reactions to everolimus, anticoagulation, or antiplatelet drugs.		Allergic reactions or hypersensitivity to rubber, contrast agent, anesthesia, device materials (cobalt, chromium, tungsten, nickel, methacrylic polymer, and fluoropolymer), and drug reactions to everolimus, anticoagulation, or antiplatelet drugs			X		

[redacted]

Vascular access complications which may require transfusion or vessel repair, including:	**Catheter site reactions**		Vascular complications in arteries used to access the coronary artery which may require blood transfusion or surgical artery repair, including:	Complications at the groin or arm access site		X			
	Bleeding (ecchymosis, oozing, hematoma, hemorrhage, retroperitoneal hemorrhage)			Bleeding		X			
	Arteriovenous fistula, pseudoaneurysm, aneurysm, dissection, perforation / rupture	**Arteriovenous fistula**		Formation of an abnormal connection between an artery and the vein next to it				X	
		Pseudoaneurysm		Leaking of blood from an artery to the surrounding tissue (usually as a result of a puncture to the artery)			X		
		Aneurysm		Weakness in wall of artery (causing possible serious bleeding complications)			X		
		Dissection		Partial or complete tear of the wall of the artery					
		Perforation/rupture		Vessel puncture or rupture				X	

	Embolism (air, tissue, plaque, thrombotic material or device)		Movement of air, tissue, plaque, blood clot, or device material (stent or catheter parts) downstream in the arteries resulting in blockage in blood flow			X		
	Peripheral nerve injury		Nerve damage caused by compression of the nerves, injury to the nerve, or interruption of blood supply to the nerves			X	X	
	Peripheral ischemia		Decreased blood supply to the arms and / or legs which may cause cramping or pain			X		
Coronary artery complications which may require additional	**Total occlusion or abrupt closure**	Complications at the heart arteries which may require	Complete blockage of the coronary artery, which			X		

[redacted]

intervention, including:			additional treatment or surgery, including:	may require a repeat procedure or emergency surgery to reopen the coronary artery					
	Arteriovenous fistula, pseudoaneurysm, aneurysm, dissection, perforation / rupture	**Arteriovenous fistula**		Formation of an abnormal connection between a heart artery and the vein next to it					X
		Pseudoaneurysm		Leaking of blood from a heart artery to the surrounding tissue (usually as a result of a puncture to the artery)					Not reported
		Aneurysm		Weakness in wall of the heart artery (causing possible serious bleeding complications)					Not reported
		Dissection		Partial or complete tear of the wall		X			

				of the artery supplying the heart muscle						
		Perforation/rupture		Puncture or rupture of the wall of the artery supplying the heart muscle			X			
	Tissue prolapse/plaque shift			Consider covered under layman term for restenosis based on FDA input			X			
	Embolism (air, tissue, plaque, thrombotic material, or device)			Movement of air, tissue, plaque, blood clot, or device material (stent or catheter parts) that partially or completely blocks the heart artery and / or implanted stent			X			
	Coronary or stent thrombosis (acute, subacute, late, very late)	Thrombosis in device		Development of blood clots partially or			X			
		Coronary artery				X (cumula				

		thrombosis, stent thrombosis (acute, subacute, late, very late v)		completely blocking blood flow within the artery and / or the implanted stent		tive 4 and 5 year rate based on XIENCE V USA and ABSORB III/ Japan)			
	Stenosis or restenosis			Narrowing or re-narrowing of the treated heart artery	X (4-year follow-up; includes non-target lesion/ vessel revascularization)	X			
Pericardial complications which may require additional intervention, including:	**Cardiac tamponade**		Complications in the sac around the heart which may require additional treatment, including:	Rapid accumulation of blood in the sac around the heart resulting in compression of the heart so it cannot pump out blood to the rest of the body which may require additional treatment or emergency surgery				X	
	Pericardial effusion			An abnormal accumulation of blood			X		

			around the heart					
	Pericarditis		Inflammation of the tissue around the heart (causing possible chest pain)				X	
Cardiac arrhythmias (including conduction disorders, atrial and ventricular arrhythmias)		Irregular heartbeats (caused by abnormal electrical activity in the heart from the upper or lower heart chambers)	NA			X		
Cardiac ischemic conditions (including myocardial ischemia, myocardial infarction (including acute), coronary artery spasm, and unstable or stable angina pectoris)	**Myocardial Ischemia**	Decreased blood and / or oxygen supply to part of the heart muscle which may cause:	Decreased blood supply to heart muscles			X		
	Myocardial Infarction		Heart attack (permanent damage of an area of the heart tissue, due to interruption in the blood flow to the heart muscle)	X (4 -year cumulative rate per ARC definition for overall population including on-lable, near-on label subjects and others)				
	Coronary Artery Spasm		Temporary spasm of the			X		

				heart arteries					
	Unstable or stable angina pectoris			Chest pain (which may radiate to jaw or arm) or discomfort caused by inadequate supply of blood to the heart)		X			
Stroke/Cerebrovascular accident (CVA) and Transient Ischemic Attack (TIA)	**Stroke/CVA**		Stroke or temporary stroke symptoms as a result of decreased oxygen to the brain causing blurred vision, dizziness, faintness, and numbness				X		
	TIA							X	
System organ failures	**Cardio-respiratory arrest**		Abnormal organ function in very ill patients including:	Stoppage of the heart				X	
	Cardiac failure			Heart function failure (potentially leading to the development of fluid in the lungs and severe breathing difficulty)			X		
	Cardiopulmonary failure (including pulmonary edema)			Lung function failure (potentially leading to severe breathing difficulty)			X		
	Renal insufficiency / failure			Kidney failure			X		

[redacted]

	Shock		Shock (a life-threatening condition in which blood pressure is too low to maintain adequate -blood flow to your organs)				X	
Bleeding		Bleeding			X (based on 1 year rate of Major bleeding by TIMI in XIENCE V, non-HBR population; also 4 year cumulative rate from XIENCE V USA LTF cohort)			
Blood cell disorders (including Heparin Induced Thrombocytopenia (HIT)		Blood count abnormalities				X		
Hypotension		Low blood pressure				X		
Hypertension		High blood pressure				X		
Infection		Infection				X		
Nausea and vomiting		Nausea and vomiting				X		
	Palpitations	Feeling of the heart beating rapidly				X		

Palpitations, dizziness, and syncope	**Dizziness**	(palpitations), dizziness, or fainting			X		
	Syncope				X		
Chest pain		Chest pain		X			
Fever		Fever				X	
Pain		Pain		X			
Death		Death		X (Cardiac death thru 4 and 5 years, XIENCE V USA and (ABSORB Japan – XIENCE arm respectively)			

APPENDIX IV: LABELS

[redacted]

APPENDIX V: CASE REPORT FORM

[redacted]

APPENDIX VI: INFORMED CONSENT FORM

[redacted]

APPENDIX VII: MONITORING PLAN

[redacted]

APPENDIX VIII: EXCEPTIONS FROM ISO 14155 COMPLIANCE

[redacted]

APPENDIX IX: REVISION HISTORY

[redacted]

APPENDIX X: CIP SUMMARY

Title	XIENCE Skypoint Large Vessel Post Approval Study (SPIRIT XLV PAS)
Study Device	Commercially approved XIENCE Skypoint Large Vessel Everolimus Eluting Coronary Stent System (EECSS) stent diameters 4.5 and 5.0 mm. • Stent diameters: 4.5 mm, 5.0 mm • Stent lengths: 12, 15, 18, 23, 28 and 33 mm
Study Design	A prospective, single arm, multi-center, US and OUS post-approval observational study
Objective	To evaluate the continued safety and effectiveness of the XIENCE Skypoint stent diameters 4.5 and 5.0 mm in stent lengths of 12-33 mm during commercial use in a real-world setting
Number of subjects	[redacted]
Number of Sites	[redacted]
Inclusion Criteria	General Inclusion Criteria 1. Subjects must be at least 18 years of age. 2. Subjects or a legally authorized representative must provide written informed consent per site requirements. 3. Subjects must have evidence of myocardial ischemia (ST-elevated MI [STEMI], Non-STEMI [NSTEMI], Unstable Angina or Stable Angina) or who have silent ischemia with evidence of ischemia, appropriate for percutaneous coronary intervention (PCI) treatment of *de novo* native coronary artery lesions[xv] with DES. Subjects with stable angina or silent ischemia must have an objective sign of ischemia as suggested by one of the following: o Abnormal stress or imaging stress test o Abnormal computed tomography-fractional flow reserve (CT-FFR) o Stenosis by visual estimation ≥ 70%

[xv] Native coronary artery is the original artery you were born with, as opposed to a bypass graft.

[redacted]

	○ Abnormal pressure-derived indexes (such as fractional flow reserve [FFR], instantaneous wave-free ratio [iFR], diastolic hyperemia-free ratio [DFR], diastolic resting pressure ratio [DPR], or resting full-cycle ratio [RFR]). Angiographic Inclusion Criteria 1. Subjects who have lesion(s) in a vessel with reference vessel diameter > 4.25 mm and ≤ 5.25 mm as the target lesion. 2. Subjects who receive at least one XIENCE Skypoint stent diameters 4.5 and 5.0 mm. a. Lesions with RVD ≤ 4.25 mm should be treated as non-target lesions during the index procedure with commercially available XIENCE family of stents. b. Up to three lesions (target and non-target) in two coronary vessels can be treated at the index procedure. 3. If LMCA is the intended target vessel, subjects who have unprotected LMCA disease with a SYNTAX Score[20,xvi] ≤ 22. a. A heart team consensus approach per the site's SOC to enhance subject protection and optimal clinical practice for the left main treatment is required.
Exclusion Criteria	General Exclusion Criteria 1. Subjects who have contraindications to the XIENCE Skypoint stent diameters 4.5 and 5.0 mm per the instruction for use (IFU) 2. Subjects who have active symptoms and/or a positive test result of COVID-19 or other rapidly spreading novel infectious agent within the prior 2 months. 3. Subjects who are participating or planning to participate in any concurrent clinical study/investigation that may potentially impact or confound outcomes of this study. Angiographic Exclusion Criteria: 1. Subjects who require three-vessel treatment.

[xvi] SYNTAX score assessment: if LMCA is the intended target vessel. SYNTAX score I should be used based on the site's assessment using the SYNTAX score calculator: http://www.syntaxscore.org/calculator/start.htm

[redacted]

Follow-up	• At 1, 6 months, 1, 2 and 3 years, Office visits are strongly recommended for all follow-ups. Phone visits are only allowed if otherwise the subject will be missing the visits.
Primary Endpoint	Target Lesion Failure (TLF) at 1 year[iv] • TLF is defined as the composite of cardiac death (CD), myocardial infarction (MI) related to the target vessel (TV-MI), or ischemic driven target lesion revascularization (ID-TLR). • For the assessment of periprocedural MI, modified Academic Research Consortium (ARC) II definition will be used. cTn will be used for the primary cardiac biomarker for MI assessment. For the assessment of spontaneous MI, the 4th universal MI definition will be used. Both MI definitions are defined in **Appendix II**. [redacted]
Secondary Endpoint	The descriptive secondary endpoints are defined as: 1. Target lesion failure ($TLF_{sp\text{-}MI}$) at 1 year[iv] • $TLF_{sp\text{-}MI}$ is defined as the composite of CD, and TV-MI, including spontaneous MI and excluding periprocedural MI and, or ID-TLR cTn will be used for the primary cardiac biomarker for MI assessment. For the assessment of spontaneous MI, the 4th universal MI definition will be used. Note that the study will allow CKMB on sites (Site Number:US0879) that (1) are already participating in CIP-Rev A; (2) do not have cTn as the site's SOC. 2. Target Lesion Failure (TLF_{SCAI}) at 1 year[iv] • TLF_{SCAI} is defined as the composite of CD, and TV-MI, including both periprocedural MI and spontaneous MI, or ID-TLR • For the assessment of periprocedural MI, Society for Cardiovascular Angiography and Intervention (SCAI) definition will be used, and cTn will be used for the primary cardiac biomarker for MI assessment. For the assessment of spontaneous MI, the 4th universal MI definition will be used. Both MI definitions are defined in **Appendix II**
Other Endpoints	Clinical Outcomes will be evaluated at each follow-up time point. **Composite Outcomes** • [redacted]

[redacted]

	[redacted]
Treatment Strategy	The sites can treat patients per their standard practice. However, Abbott recommends following measures for the treatment of the target lesion to achieve an optimized result. • Post dilatation with a non-compliant balloon to achieve a good stent apposition • For unprotected left main target lesions, use an intravascular imaging (either intravascular ultrasound or optical coherence tomography) when sizing the vessel and following stent implantation • [redacted]
Antiplatelet Medications	**Peri-procedure Medications:** • Per the site's SOC. **Post-procedure Medications:** • Per the site's SOC.
Analysis	• [redacted] •

[redacted]

Analysis population	[redacted]
Adverse Event Reporting	Safety surveillance and reporting start as soon as the subject is registered in the clinical study. Safety surveillance and reporting will continue until the last follow-up visit has been performed, the subject is deceased, the subject concludes participation in the clinical study, or the subject withdraws from the clinical study. For the purposes of this clinical study, the following events will be reported to the Sponsor on a CRF: device- and procedure-related AEs, SAEs, cardiovascular-related AEs, deaths, and device deficiency data. Additional information with regard to an AE should be updated within the appropriate CRF. AEs will not be collected for screen failure subjects. If the subject gets consented after the index procedure, reporting will be collected from the index procedure, and the AE awareness date should be entered as the post-procedure consent date. All cardiac-related abnormal laboratory values (per assay-specific IFU) should be reported as AEs.