STATISTICAL ANALYSIS PLAN

Title:	A Prospective, Multi-Center, Single-Arm, Real-World Study Assessing the Clinical Use of the Bard® UltraScore™ Focused Force PTA Balloon (ULTRASCORE™ PTA Balloon Study)
Protocol No.:	BPV-16-001
Study Device:	ULTRASCORE™ Focused Force PTA Balloon
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Version & Date:	Version 2.0 – Jan 20, 2022

Approval

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1 Introduction

This document provides details of the statistical analysis plan (SAP) for the C.R. Bard, Inc. protocol BPV-16-001 (ULTRASCORE™ PTA Balloon Study). This study is being done to provide physicians with real world data on the outcomes of use of the UltraScore™ Focused Force PTA balloon, including optimal PTA results and long-term freedom from clinical target lesion revascularization (TLR), major amputation, and patency. For this study, optimal PTA results are those where ≤30% residual stenosis remains after use of the UltraScore™ Focused Force PTA balloon.

Follow-up for all treated subjects will be performed at hospital discharge, 30 days, and 6 and 12 months post-index procedure. Endpoint analysis will occur when all subjects have completed the 12 months follow up.

The statistical methods described here are based on the analyses proposed in the ULTRASCORE™ PTA Balloon Study protocol issued on June 21, 2018, Version 2.0. All data processing, summarization, and analyses will be performed using Statistical Analysis System (SAS), Version 9.4 or higher.

1.1 Changes from Protocol

No changes from the protocol.

2 Study Objective and Endpoints

2.1 Study Objective

The objective of this study is to assess the clinical use of the Bard® UltraScore™ Focused Force PTA balloon in a heterogeneous patient population in a real world, on-label clinical application.

2.2 Study Endpoints

2.2.1 Primary Endpoints

Primary endpoints are:

- Achieve optimal PTA results (≤30% residual stenosis, without major flow limiting dissection)
- Achieve technical success of use where the UltraScore™ Focused Force PTA balloon is delivered to the target lesion and inflated without movement

2.2.2 Secondary Endpoints

The following secondary endpoints will be analyzed at the index procedure or through 12 months at these time points: 30 days, 6 months, and 12 months.

After UltraScore™ Focused Force PTA balloon:

- Rate of bail-out stenting due to dissection

Through follow-up (at 30 days, and 6 and 12 months):

- Freedom from Target Lesion Revascularization (TLR)

- Freedom from major amputation (above the ankle)
- Improved clinical measures from baseline (ABI, Rutherford)
- Primary patency for ATK subjects only (as measured by DUS core lab)

3 Study Design

3.1 Overview

This study is a prospective, multi-center, single-arm, real-world study in the United States assessing the clinical use of the UltraScore™ Focused Force PTA balloon. Treated subjects will be followed for 12 months post-index procedure. A duplex ultrasound (DUS) will be done at 30 days, and 6 and 12 months post-index procedure for ATK subjects. Otherwise, there are no additional treatments or exams that are required to take place within this study. There will be minimal patient activities that will be conducted for data collection purposes for this study in addition to routine standard of care procedures.

3.2 Study Population

Male or non-pregnant female ≥ 21 years of age with an expected lifespan sufficient to allow for completion of all study procedures. Eligible subjects will have a stenotic lesion of the SFA, popliteal, or infra-popliteal arteries. ATK subjects will be those that have a lesion of the SFA or popliteal artery. BTK subjects will be those that have a lesion in the infra-popliteal arteries (posterior tibial, anterior tibial or peroneal arteries)

3.3 Sample Size Consideration

There is no formal statistical hypothesis for this study. This study will enroll up to a maximum 350 subjects at approximately 45 sites. This will allow for approximately 175 subjects in an above the knee (ATK) cohort and 175 subjects in a below the knee (BTK) cohort. No site will be allowed to enroll more than 20% of the overall number of subjects to ensure the study be reasonably well balanced. The sample size is based on potential adequacy of data to meet the study objectives; it is not based on any statistical consideration.

3.4 Study Procedure

All subjects will undergo a clinical evaluation at screening (prior to index procedure); after consent is voluntarily obtained, study subjects will be treated with the UltraScore™ Focused Force PTA balloon per the site's standard of care and adhering to the IFU. Examinations, evaluations, procedural preparation, angiography, treatment and hospital discharge procedures will be conducted per the study site's standard of care.

Investigators are able to treat One (1) lesion per patient in this study. If a subject has multiple eligible lesions, the investigator may use his or her medical judgment as to which becomes the study target lesion. Standard of care treatment of non-target lesions is allowed.

Subjects with treated ATK lesions will undergo clinical evaluations with a Duplex Ultrasound (DUS) performed at 30 days, 6 and 12 months post-index procedure.

Subjects with treated BTK lesions will undergo clinical evaluations performed at 30 days, and 6 and 12 months post-index procedure. DUS is not required for subjects with a treated BTK lesion for this study.

Lesions that cross from ATK to BTK may not be treated as the study target lesion. Diffuse lesions will be considered separate lesions if there is 2 cm of healthy tissue between lesions.

Angiographic imaging of the target lesion is captured at Baseline cine-run, Pre-UltraScore™ adjunctive treatment cine-run (if performed), UltraScore™ balloon inflation(s), Post UltraScore™ balloon inflation(s) cine run, and Post UltraScore™ adjunctive treatment cine-run (if performed). Angiographic imaging is also done at Re-Intervention visit. Major flow limiting dissections are collected and reporting is restricted to grades D, E, and F per the National Heart, Lung, and Blood Institute (NHLBI).

Adjunctive treatment of the target lesion before or after use of the UltraScore™ balloon as part of standard care procedures is allowed. Bail out stenting and stenting of non-study lesions is acceptable at any time.

Collection and reporting of AEs/SAEs will be limited to those events that are device and/or procedure related and reporting will begin immediately following subject enrollment, during the index procedure.

If an angiographically acceptable result cannot be obtained after two inflations of the UltraScore™ balloon (>30% residual stenosis), the subject should be considered a treatment failure.

An overview of the study visit schedules is shown in Table 1, which summarizes the schedule for subject treatment and evaluation.

Table 1: Follow-up Schedule and Testing Requirements for Enrolled Subjects

	Screening / Index Procedure / Discharge	30 Days (±7 days)	6 Months (±30 days)	12 Months (±30 days)
Informed Consent	✓			
Demographics / Medical History	✓			
Physical Examination (Clinical Assessments)	✓			
Rutherford (Category and Grade)	✓	✓	✓	✓
Resting ABI (Treated Limb only)	✓	✓	✓	✓
Anticoagulation/Anti-platelets	✓	✓	✓	✓
Eligibility Criteria	✓			
Angiographic Image Collection	✓			
Duplex Ultrasound§		✓	✓	✓
TLR Assessment*		✓	✓	✓
Adverse Event Assessment	✓	✓	✓	✓

§ATK subjects only
*Collect angiographic images for TLR/TVR

4 Analysis Set

Enrolled: All subjects who have signed the Informed Consent Form (ICF) and the UltraScore™ balloon was introduced into the subject.

Intent-to-Treat (ITT): All enrolled subjects who have signed the ICF and were treated with the study device.

There is no formal statistical hypothesis for this study. Baseline characteristics, demographics, primary endpoints, secondary endpoints, other analyses and subgroup analyses will be based on the ITT population.

5 Statistical Analysis of the Primary Endpoints

The proportion of subjects with optimal PTA results and technical success will be reported with frequency counts, percentages and 95% confidence intervals (CI) for the percentages from exact binomial test.

5.1 To Achieve Optimal PTA Results (≤30% residual stenosis, without major flow limiting dissection)

The residual stenosis (Interpolated %DS) and major flow limiting dissection (Dissection) will be used from the Angio Core Lab CRF page (Image Findings-After UltraScore™ Balloon QVA). If Angio Core Lab data is missing use the site data (site reported residual stenosis after inflations (%) from the Study Device CRF page and flow limiting dissection (D to F) from the Procedure Overview CRF page).

An optimal PTA result will be analyzed by subject as a binary endpoint based on the following definition:

Not Evaluable: Subject has missing data for the residual stenosis and major flow limiting dissection; or it has success for one component and one component is missing.

Failure: Subject has a failure event if residual stenosis after 2 inflations (%): is > 30% or if there is a major flow limiting dissection (D to F) as recorded from angio core lab. If angio data is missing use site data.

Success: Subject has a no failure event in both the components and is evaluable.

The two-sided 95% CI will be provided for ATK, BTK and All UltraScore™ subjects based on the binomial proportion for the ITT population.

5.2 To Achieve Technical Success of Use where the UltraScore™ Focused Force PTA Balloon is Delivered to the Target Lesion and Inflated Without Movement

A technical success of device recorded from the Study Device Details CRF page will be analyzed by device and not by subject, as a binary endpoint based on the following definition:

Not Evaluable: Device has missing data for the question "Was the Device Delivered to the Target Lesion and Inflated without Movement?"

Failure: Device has a failure event if the device was not delivered to the target lesion and not inflated without movement (i.e. failure event if "Was the Device Delivered to the Target Lesion and Inflated without Movement?" = No). If one device has several inflations and at least one of them is a failure, then the device is considered as failure.

Success: Device has a no failure event and is evaluable.

The two-sided 95% CI will be provided for ATK, BTK and All UltraScore™ subjects based on the binomial proportion for the ITT population.

6 Statistical Analysis of Secondary Endpoints

6.1 After UltraScore™ Focused Force PTA balloon: Rate of Bail-Out Stenting due to Dissection

After UltraScore™ Focused Force PTA balloon, rate of bail-out stenting due to dissection will be reported with frequency counts, percentages and 95% CIs for the percentages from exact binomial test. Bail-out stenting due to dissection after UltraScore™ Focused Force PTA balloon reported from the Procedure Overview CRF page will be used. It will be analyzed by subject as a binary endpoint based on the following definition:

Evaluable: All ITT subjects.

Failure: Subject has a failure event if they have flow limiting dissection after UltraScore™ use time point with bail-out stenting. Also, subject with flow limiting dissection at Index procedure with bail-out stenting are failures.

Success: Subject does not have a flow limiting dissection or subject has a flow limiting dissection after UltraScore™ use time point with no bail-out stenting. Subject has a no failure event and is evaluable.

The two-sided 95% CI will be provided for ATK, BTK and All UltraScore™ subjects based on the binomial proportion for the ITT population.

6.2 Freedom from TLR

Target lesion information will be obtained from 'Core Lab Analysis – Angio Re-Intervention Analysis' CRF page. If for some reason the Angio data is missing, but there was TLR reported by site then Site Re-Intervention data will be used from 'Target Vessel Re-Intervention' CRF page. Freedom from TLR will be analyzed by subject at 30 days, 6 months, and 12 months visit.

Evaluable subjects: To be included in the denominator at a particular visit, the subject should have been followed-up beyond the beginning of the lower end of the respective visit window (23 days for 30 days, 150 days for 6 months, and 335 days for the 12 months) or the subject should have had a TLR event before the upper limit of visit window (37 days for 30 days, 210 days for 6 months, and 395 days for the 12 months).

The TLR (Re-intervention date) is based on the following definition:

TLR duration = (Date of TLR - Date of Index Procedure).

Failure: Subject has a failure event if Target Lesion Re-Intervention occurred before the upper limit of the respective visit window (Core Lab Angio CRF page). If TLR was reported by site but was missing in the Core lab page, then use Target Lesion Revascularization occurred before the upper limit of the visit window (Site Re-Intervention CRF page) as failure.

Success: Subject has no failure event and is an evaluable subject as defined above.

Kaplan-Meier Analysis:

In addition to the analyses that are proportion-based, survival analysis will be performed (Kaplan-Meier estimate of survival function). Freedom from TLR at 30 days, 6 months, and 12 months: the time to first event will be the time from index-procedure to the first occurrence

of the first failure event, all subjects who have succeeded the TLR endpoint will be censored at Day 395 if not discontinued (discontinued subjects will be censored at discontinuation day), and all the subjects with missing TLR endpoint will be censored at the last available study day.

Binary outcome and Kaplan-Meier analyses for ATK, BTK and All UltraScore™ subjects will be provided for the ITT population.

6.3 Freedom from Major Amputation (Above the Ankle)

Freedom from major amputation of target limb (above the ankle) will be reported at 30 days, 6 months, and 12 months using data from 'Target Limb Amputation' CRF page.

Evaluable subjects: To be included in the denominator at a particular visit, the subject should have been followed-up beyond the beginning of the lower end of the respective visit window (23 days for 30 days, 150 days for 6 months, and 335 days for the 12 months) or the subject should have had a major amputation of target limb (above the ankle) event before the upper limit of visit window (37 days for 30 days, 210 days for 6 months, and 395 days for the 12 months).

The freedom from major amputation is based on the following definition:

Major amputation duration = (Date of Amputation - Date of Index Procedure).

Failure: Subject has a failure event if Major amputation of target limb is above the ankle which includes Below knee or Through Knee or Above Knee.

Success: Subject has no failure event and is an evaluable subject as defined above.

Kaplan-Meier Analysis:

In addition to the analyses that are proportion-based, survival analysis will be performed (Kaplan-Meier estimate of survival function). Freedom from major amputation at 30 days, 6 months, and 12 months: the time to first event will be the time from index-procedure to the first occurrence of the first failure event, all subjects who have succeeded the major amputation endpoint will be censored at Day 395 if not discontinued (discontinued subjects will be censored at discontinuation day), and all the subjects with missing major amputation endpoint will be censored at the last available study day.

Binary outcome and Kaplan-Meier analyses for ATK, BTK and All UltraScore™ subjects will be provided for the ITT population.

6.4 Improved Clinical Measures from Baseline (ABI, Rutherford)

ABI:

Resting ABI measurements of the target limb will be summarized at 30 days, 6 months, and 12 months. Absolute values and change from baseline value will be summarized at each visit by subject. Absolute values and change from baseline values will be reported as continuous variable including N, mean, standard deviation, median, minimum and maximum.

Analyses for ATK, BTK and All UltraScore™ subjects will be provided for the ITT population.

Rutherford:

Rutherford classification of the target limb will be summarized at 30 days, 6 months, and 12 months. Proportion of subjects on each category will be summarized at each visit by subject. A shift table from baseline will be presented with categories as improved, same and worsened.

Analyses for ATK, BTK and All UltraScore™ subjects will be provided for the ITT population.

6.5 Primary Patency for ATK subjects only (as measured by DUS Core Lab)

Primary patency of the target lesion for ATK subjects will be reported through 12 months at 30 days, 6 months, and 12 months using Target Lesion DUS Stenosis category (recorded from the 'Core Lab Analysis – DUS Image Findings' CRF page). Primary patency for ATK subjects will be analyzed by subject.

Evaluable subjects: To be included in the denominator at a particular visit, the subject should have had a valid stenosis category result (patent, 50-99%, or occluded) in the DUS for the visit (23 - 37 days for 30 days, 150 - 210 days for 6 months, and 335 - 395 days for the 12 months), or the last DUS result prior to the respective visit indicates failure, or the subject should have had a TLR event before the upper limit of visit window (37 days for 30 days, 210 days for 6 months, and 395 days for the 12 months).

*Note:

a) If a subject misses the respective visit or does not have valid DUS result for the respective visit, yet the DUS result in the next visit is patent and the subject has no TLR by the next visit date, then the subject is evaluable and will be counted as success.

b) If a subject misses the respective visit or does not have valid DUS result for the respective visit, and the last DUS result prior to the respective visit indicates failure, and there is no DUS result on subsequent visits to indicate patency, then the subject is evaluable and will be counted as failure.

c) If a subject misses the respective visit or does not have valid DUS result for the respective visit, has no TLR prior to the respective visit, and does not meet the conditions specified in a) and b) above, then the subject is not evaluable.

Primary patency for ATK subjects is based on the following definition:

Primary patency of the target lesion duration = (The earlier date of (Date of Imaging DUS/TLR date) - Date of Index Procedure)

Failure: Subject has a failure event if the stenosis category for Target Lesion as adjudicated by Core Lab DUS is occluded or 50-99%, or TLR has occurred before the upper limit of visit window (as per section 6.2), or as indicated in the *Note section b) above.

Success: Subject has no failure event and is an evaluable subject as defined above, or as defined in *Note section a).

Kaplan-Meier:

In addition to the analyses that are proportion-based, survival analysis will be performed (Kaplan-Meier estimate of survival function). Primary patency of the target lesion for ATK subjects at 30 days, 6 months, and 12 months, the time to first event will be the time from index-procedure to the first occurrence of the first failure event, all subjects who have succeeded the primary patency endpoint will be censored at Day 395 if not discontinued (discontinued subjects will be censored at discontinuation day), and all the subjects with missing primary patency endpoint will be censored at the last available study day.

Binary outcome and Kaplan-Meier analyses for ATK subjects will be provided for the ITT population.

6.6 Restenosis for ATK Subjects Late for More Than 30 Days at 12-Month Visit due to COVID-19 (as measured by DUS Core Lab)

Restenosis of the target lesion for ATK subjects late for more than 30 days at 12-month visit due to covid-19 will be reported using Target Lesion DUS Stenosis category (recorded from the 'Core Lab Analysis – DUS Image Findings' CRF page) by subject.

Evaluable subjects: To be included in the denominator, the subject should have been late for more than 30 days at the 12-month visit (more than 395 days since index procedure) due to COVID-19 (identified via Protocol Deviation and Study Visit CRFs) and had a valid stenosis category result (patent, 50-99%, or occluded) in the DUS for the visit.

Restenosis: Subject has restenosis if the stenosis category for Target Lesion as adjudicated by Core Lab DUS is occluded or 50-99%.

7 Statistical Analysis of Subgroup Analyses

7.1 Primary and Secondary Endpoints for Above the Knee (ATK) and Below the Knee (BTK) subjects

The primary and secondary endpoints will be presented descriptively for ATK and BTK subjects. The endpoints and statistical methods will be similar to section 5 and section 6.

7.2 Primary and Secondary Endpoints for Different Adjunctive Treatments

The two primary endpoints will be analyzed for different adjunctive treatments ('Prior to UltraScore™ Use', 'After UltraScore™ Use' and both combined) for ATK, BTK and All UltraScore™ subjects. The secondary endpoints (TLR, Major Amputation and Primary Patency) will be analyzed for different adjunctive treatments ('After UltraScore™ Use') for ATK, BTK and All UltraScore™ subjects. The endpoints and statistical methods will be similar to section 5 and section 6.

7.3 Additional Analysis - Assessment of Primary Endpoint by Site

7.3.1 Assessment of Primary Endpoint by Site

The primary endpoints across sites will be reported for ATK, BTK and All UltraScore™ subjects separately.

7.3.2 Assessment of Secondary Endpoints for subjects with DCB used at baseline

Freedom from TLR and major amputation will be separately reported for ATK, BTK and All UltraScore™ subjects with DCB used at baseline either before or after ultrascore.

Primary patency will be reported for ATK subjects with DCB used at baseline either before or after ultrascore.

Secondary endpoints and evaluable subjects are as defined in section 6.2, 6.3 and 6.5, respectively, with an additional requirement that the subjects have had DCB at index procedure.

7.3.3 Assessment of death for subjects with DCB used at baseline either before or after ultrascore

Freedom from death will be reported at 30 days, 6 months, and 12 months using data from 'Subject Disposition' CRF page.

Evaluable subjects: To be included in the denominator at a particular visit, the subject should have had DCB as adjunctive treatment either before or after Ultrascore and been followed-up beyond the beginning of the lower end of the respective visit window (23 days for 30 days, 150 days for 6 months, and 335 days for the 12 months) or the subject should have had died before the upper limit of visit window (37 days for 30 days, 210 days for 6 months, and 395 days for the 12 months).

Death duration = (Date of Death - Date of Index Procedure).

8 Statistical Analyses of Adverse Events and Device Deficiencies

8.1 Adverse Events (AEs)

Collection of AEs will be limited to those that are associated with a localized or systemic clinical manifestation that reasonably suggests the involvement of the UltraScore™ device and/or procedure. Adverse Events (AEs) experienced by the subject will be collected from the time point of enrollment until the subject's end of study participation. Event occurred prior to enrollment will be documented as medical history. All adverse events occurring in this study will be classified in accordance with the adverse event signs or symptoms and will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). AEs will be summarized by system organ class and preferred term.

The number and percentage of subjects with at least one AE, total number of AEs, AEs by relationship to the device/procedure, and AEs by severity of the event will be summarized by ATK, BTK and All UltraScore™ subjects using site-reported data. A summary of SAE will be provided. A listing of all AEs, as well as of the SAEs, will be provided.

8.2 Device Deficiencies

A device deficiency has occurred if a study device used in the study procedure failed to meet its performance specifications whether due to mechanical failure, malfunction, or defect.

Device deficiencies also include errors and inadequate labeling. Device failures, malfunctions or defects will be tabulated by the failure code for ATK, BTK and All UltraScore™ subjects.

9 Statistical Analyses of Baseline Examination, Other Analyses and Reporting Requirements

9.1 Demographics, Medical History, Risk Factors and Previous Target lesion Interventions

Demographics and background disease characteristics will be summarized with descriptive statistics for ATK, BTK and All UltraScore™ subjects using the ITT analysis set. Summary statistics for categorical variables will include frequency counts and percentages and for continuous variables will include mean, standard deviation, minimum, median, and maximum.

Demographics and baseline characteristics variables will include:

- Age at screening (year)
- Sex (Male, Female)
- Race (American Indian or Alaskan Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White and Other)
- Baseline Weight
- Baseline Height
- Baseline Body mass index (BMI) calculated from weight and height.
- Medical history, including antiplatelet/anticoagulation medications, risk factors, cardiac disease, renal disease, other disease, sub terms and Previous Target Lesion Interventions will be summarized.
- Rutherford Classification
- Ankle Brachial Index (ABI) for treated limb only

9.2 Relevant Medication

Relevant medications will include anti-platelet, anti-coagulant and cardiovascular related medications administered during the study follow up period. Each Medication will be summarized by interval for ATK, BTK and All UltraScore™ subjects.

9.3 Target Lesion Characteristics (e.g. location, type)

Target lesion characteristics at baseline Lesion Type, De Novo, TASC category, Lesion Location, Degree of Calcification, Lesion Length (mm), Reference Vessel Diameter (RVD) (mm) and Baseline Stenosis (%) will be reported for ATK, BTK and All UltraScore™ subjects. Summary statistics for categorical variables will include frequency counts and percentages; and for continuous variables will include mean, standard deviation, minimum, median, and maximum.

9.4 Procedure Details (e.g. duration, inflation times, inflation pressures, number of inflations to efface/dilate the target lesion)

Procedure details duration, inflation times, inflation pressure and number of inflations to efface/dilate the target lesion will be reported for ATK, BTK and All UltraScore™ subjects. Summary statistics for categorical variables will include frequency counts and percentages; and for continuous variables will include mean, standard deviation, minimum, median, and maximum.

9.5 Adjunctive Therapies Before and After UltraScore Use

Adjunctive therapies before and after UltraScore™ use Treatment, Reason for Procedure and Residual Stenosis (%) will be reported for ATK, BTK and All UltraScore™ subjects. Summary statistics for categorical variables will include frequency counts and percentages; and for continuous variables will include mean, standard deviation, minimum, median, and maximum.

9.6 Follow-up Period

The duration of follow-up period after Index procedure during the study will be reported for ATK, BTK and All UltraScore™ subjects and calculated as:

(Date of the last study visit – Date of the index procedure).

9.7 Subjects Dispositions

The summary of the number of subjects enrolled, intent to treat (ITT), completed the study, and discontinued from the study by reason of discontinuation will be provided. Screen failures will be summarized for each inclusion/exclusion criteria that were not met for ATK, BTK and All UltraScore™ subjects.

9.8 Protocol Deviations

The number of subjects with protocol deviations will be summarized with descriptive statistics by nature of the deviation. Protocol deviations will be listed with date of occurrence and the nature of deviation. This summary will be reported for ATK, BTK and All UltraScore™ subjects based on the ITT population.

10 IVUS Sub-Study

IVUS is a standard of care imaging modality with no additional risks to patients undergoing catheterization and percutaneous transluminal angioplasty (PTA), with or without additional adjunctive therapies for the treatment of peripheral arterial disease (PAD). The protocol addendum number BPV-16-001a provides guidance for an IVUS sub-study for select sites participating in study protocol BPV-16-001 Version 1.0 (May 2, 2017). The statistical methods described here are based on the analyses proposed in the ULTRASCORE™ PTA Balloon Study protocol issued on June 21, 2018, Version 2.0.

A maximum of 50 subjects will participate in this sub-study at up to 77 clinical sites. Analysis of study endpoints for the sub-study population will occur once all sub-study subjects have completed the 30 day follow-up visit. Only ATK subjects are enrolled in the IVUS sub-study.

10.1 Provisions

- Subjects must consent to participate in the UltraScore™ study before signing consent to participate in the IVUS sub-study.
- Subjects may consent to participate in the UltraScore™ study and decline participation in the IVUS sub-study.
- There are no additional inclusion/exclusion criteria for participation.
- Index procedure angiography will still be completed as specified in the UltraScore™ study protocol.
- Index procedure IVUS imaging will be uploaded along with index procedure angiography, as described in the UltraScore™ study protocol, for each subject consenting to participate in the IVUS sub-study.
- Pre- (diagnostic) and post- (post-UltraScore™ inflation) treatment, along with final run (post-adjunctive therapy) IVUS images are required. Imaging of the target lesion should include distal and proximal healthy tissue for reference.

10.2 Endpoints

The primary analysis endpoint for the IVUS sub-study is the same as that found in the UltraScore™ study.

- Achieve optimal PTA results (≤30% residual stenosis, without major flow limiting dissection).

Additionally, sub-study IVUS imaging will be analyzed to describe the following:

- Target lesion characteristics (e.g. location, type, calcification)
- Dissection characteristics
- Luminal gain (i.e. lumen diameter changes from baseline)

All secondary endpoints described in the UltraScore™ study protocol will be analyzed through 30 days for this sub-study.

11 SAP Revision History

Version Number	Rationale for Change	Section or Page Affected	Description of Change
1.0	Original SAP		

2.0	Amendment	Section 6.5 Section 6.6 Section 7	Revised definition of evaluable, success and failure. Added description of analysis of restenosis in subjects late for more than 30 days at 12-month visit due to COVID-19. Added section 7.2 & 7.3 to include additional analysis of secondary endpoints and death for subjects with DCB used at baseline