Statistical Analysis Plan

Product name	: XIENCE PRIME SV drug-eluting stents (12-303)
Study name	: Post-marketing surveillance (PMS)
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History of creation and revision

Version controlled	Time of revision	Date of preparation and revision	Preparer/reviser	Reason and details of revision
Version 1.0		2014/6/2	Narifumi Tsukamoto	New
Version 2.0	Three-Year Report (XIENCE PRIME SV) Two-Year Report (XIENCE Xpedition)	2015/6/23	Narifumi Tsukamoto	1.2 Subjects 1.3 Estimated number of registrations 1.4 Treatment of patients 2.1 Analysis population definitions Added content on XIENCE Xpedition drug-eluting stent 2.25mm 3.2 Calculation method of various items, etc. Acceptable range on the observation day was added. 4. Statistical Analysis Content Adding to the tabulation by product 4.3 Antiplatelet therapy Added definition of time point 4.4 Adverse Events Added definition of time of onset Added summaries on TVR (TLR or TVR (non-TLR)] based on ischemic findings 4.5 Appendix Form In accordance with Notification No. 1121 No. 44 of the Pharmaceutical and Food Safety Bureau, the contents were changed from Appended Form 3-1 to Appended Form 3-4.
Version 3.0	Reexamination application	2020/1/7	Narifumi Tsukamoto	Revision of the definition of the analysis population Review of tabulation

(CONTENTS)

1. Overview of Research

1.1. Purpose of investigation

This survey is a post-marketing drug use results survey (hereinafter referred to as "this survey") conducted by marketers or foreign exceptional approval holders of medical devices specified in Article 14, Paragraph 1 of the Pharmaceutical Affairs Law (Law No. 145 of 1960) and Article 14-6, Paragraph 4 of the Law (including cases where these provisions are applied mutatis mutandis in Article 19-4 of the Law). In order to ensure the safety of new medical devices, the frequency of defects and the status of defects are monitored. The objective is to collect data on efficacy and safety for reexamination.

This survey shall be conducted in compliance with the Ministerial ordinance for Standards for the Conduct of Post-marketing Surveys and Studies of Medical Devices (MHLW ordinance No. 38 of March 23, 2005, hereafter referred to as the "GPSP ordinance").

1.2. Subjects

Based on GPSP ordinance, this survey does not have specific inclusion/exclusion criteria and will enroll patients with ischemic heart disease who may be treated with XIENCE PRIME SV drug-eluting stents (approval number: 22500BZX00070000, approval date: March 7, 2013) (hereafter referred to as the device). As part of the treatment in the real-world clinical setting at each study site, patients who are treated with the device in principle and are available for 8-month angiographic follow-up and 1-year clinical follow-up will be included.

In addition to the study populations enrolled for the first time in this survey, patients who participated in the Clinical Evaluation of AVJ-09-385 Coronary Stents in Japanese Subjects in AVJ-09-385 Coronary Stent Study, which was conducted as a clinical trial in product, will also be included. The 5-year follow-up period after the procedure was conducted as a "clinical trial" until the approval date of marketing. However, the handling of this clinical trial was checked with the Pharmaceuticals and Medical Devices Agency (PMDA), and it was decided that the clinical trial should be continued as a "clinical trial results survey after the approval of marketing" and "clinical trial completion date (follow-up observation) may be the approval date of marketing," so the clinical trial should be continued as a "clinical trial results survey" after the approval of marketing.

1.3. Estimated number of registrations

This survey aims to enroll approximately 300 patients at approximately 30 institutions.

Previous studies predicted a 1-year MACE (Combined Assessment of Cardiac Death, Myocardial Infarction and Ischemic Target-Lesion Revascularization) of 15% in this survey. When 300 patients were enrolled, 1/2 of the 95% two-sided confidence interval for an MACE rate of 15% was 4.2%, corresponding to 28% of the expected MACE rate of 15%. Within this range, the efficacy and safety of

the device can be sufficiently assured in the real-world clinical setting in Japan.

A total of 62 subjects continued to participate in the clinical study described above.

1.4. Treatment of patients

The treatment plan should follow the standard of care when performing coronary interventions at each center at the discretion of the physician.

Physicians should discuss patient treatment with reference to warnings, contraindications, and PRECAUTIONS included in the updated package insert.

The final decision for antiplatelet therapy will be made by the doctor, but the package insert for the device requires that subjects at low risk of bleeding receive aspirin indefinitely and thienopyridines (e.g., clopidogrel, ticlopidine) for at least 6 months. In addition, XIENCE PIME package insert states that thienopyridines will be administered for at least 12 months to subjects with XIENCE PRIME in place. Refer to the updated version of the thienopyridine package insert before starting treatment for each patient. Laboratory tests and clinical observations necessary to evaluate the adverse reactions of thienopyridines should be conducted in accordance with the package insert.

2. Definition of analysis set and abbreviations

2.1. Analysis population definitions

No	Definition name	Definition Content
1	Survey period	March 7, 2013 - December 31, 2019
2	Date of data lock (snapshot)	Data lock (snapshot) dates for annual reports are as follows 1st: September 5, 2013 2nd: September 5, 2014 3rd: September 5, 2015 4th: September 5, 2016 5th: September 5, 2017 6th: September 5, 2018 7th: September 5, 2019 Reexamination: September 5, 2019 Subjects with fixed CRFs by the time of data lock.
3	CRF-collected subjects	Subjects whose CRFs were fixed
4	Subjects who are out of the survey	The cases who were treated with out-of survey stent, among CRF-collected subjects in newly enrolled patients.
5	Subjects to be investigated	The cases excluding subjects who are out of the survey among CRF-collected subjects.
6	Non-stent implanted subjects	Among the subjects studied, the cases in which the stent to be investigated could not be placed.
7	Stenting subjects	Among the investigated subjects in newly enrolled patients, the cases who were treated with investigated stent Investigated subjects transitioning from the pre-market study.
8	Newly enrolled patients	Patients enrolled for the first time in this survey.
9	Patients transitioning from the study	Patients who participated in the Clinical Assessment of AVJ-09-385 Coronary Stenting in Japanese Subjects in AVJ-09-385 Coronary Stenting Trial.

No	Definition name	Definition Content
10	Observation status	The number of follow-up examinations will be calculated by observation time point based on the actual status of follow-up examinations at the observation time point. However, the following criteria should be followed for withdrawals. ・In the case of withdrawal due to "inability to contact" the subject shall be assessed by identifying the time point of dropout based on the scheduled date * and observing the subject up to the previous time. However, if the contact is conducted at the relevant time point before "contact is not possible" is established, the observation shall be carried out until that time. ・Other withdrawal dates will be the last follow -up date. However, "death" shall be specified based on the expected date. In addition, the time point for "other than death" should be specified after considering the range of adoption of the scheduled date. ・Even if there are no dropouts on the questionnaire, if no follow -up is performed twice at 1 year or later, it is considered dropouts, and the date of first unsupervised follow-up (expected date) is considered the final observation (e.g., if 4-year and 5-year observations are not performed, 1460 days are considered the final observation date). ※Expected date (scope of employment) 1 year: 365 days (365 ± 30 days) 2 years: 730 days (730 ± 30 days) 3 years: 1095 days (1095 ± 30 days) 4 years: 1460 days (1460 ± 30 days) 5 years: 1825 days (1825 ± 30 days)
11	Analysis set by time point	The following conditions will be added to the observation status to identify the number of patients included in the analysis at each time point: ・Cases in which death, myocardial infarction, or total revascularization occurred will be included in the analysis at all time points.

2.2. Definition of Terms

No	Term	Content
1	Dual antiplatelet therapy	Concomitant use of aspirin and thienopyridines (clopidogrel, ticlopidine)

2.3. Definition of abbreviations

No	Abbreviations	Content
1	CABG	Coronary Artery Bypass Graft Surgery (Coronary Artery Bypass Grafting)
2	CTO	Chronic total occlusion (Chronic Total Occlusion)
3	eGFR	Estimated glomerular filtration rate (Estimated Glomerular Filtration Rate)
4	LAD	Left anterior descending artery (Left Anterior Descending Artery).
5	LCX	Left circumflex artery (Left Circumflex Artery)
6	LMT	Left main coronary artery (Left Main Trunk)
7	LVEF	Left ventricular ejection fraction (Left Ventricular Ejection Fraction).
8	PCI	Coronary Angioplasty (Percutaneous Coronary Intervention)
9	POBA	Percutaneous balloon-angioplasty (Plain Old Balloon Angioplasty).
10	Q1	First quartile
11	Q3	Third quartile
12	RCA	Right coronary artery (Right Coronary Artery).
13	SVG	Saphenous vein graft (Saphenous Vein Graft).
14	TLR	Target lesion revascularization (Target Lesion Revascularization).
15	TVR	Target vessel revascularization (Target Vessel Revascularization)

3. Method of analysis

3.1. Statistical analysis environment

Statistical analysis software: SAS Institute Inc., Windows version SAS version 9 4 or later

3.2. Calculation method of various items, etc.

Items	Calculation method, etc.
Summary statistics (consecutive numbers)	Mean, standard deviation, number of specimens, median, Q1, Q3, minimum, maximum and 95% confidence interval of the mean will be calculated. Number of Samples: Displayed as an integer Mean, standard deviation, median, Q1, Q3: displayed to one order of magnitude below the data of interest Minimum and Maximum Values Shown at the Same Digit as the Data Subject
Confidence interval of the mean	Confidence intervals based on t distributions are calculated. $CI = \bar{x} \pm t_{(1-\alpha/2;n-1)} \frac{S}{\sqrt{n}}$

Items	Calculation method, etc.
Summary statistics (incidence)	Incidence rates (%), number of events (molecules), number of populations analyzed (denominators) and 95% confidence intervals of frequencies are calculated. However, cases in which the relevant variable is a missing value are also included in the population of the incidence calculation. 4.3 Population numbers for antiplatelet therapy and 4.4 adverse events are specified as follows. 4.3 Antiplatelet therapy Newly enrolled patients will be included. Pre-procedure: Case of stenting Procedure Day to Discharge Day: Stenting Cases Procedural Day ~ 8 Months Observation Day: 8 Months Analyzed by Case Time Point of Stenting Procedural Day-1 Year Observation Day: 1 Year Analyzed by Time Point of Stent Implantation Procedural Day ~ 2 Years Observation Day: 2 Years Analyzed by Time Point of Stent Implantation Procedural Day ~ 3 Years Observation Day: 3 Years Analyzed by Time Point of Stent Implantation Procedural Day ~ 4 Years Observation Day: 4 Years Analysis Population by Time Point of Stent Implantation Procedural Day ~ 5 Years Observation Day: 5 Years Analysis Population by Time Point of Stent Implantation 4.4 Adverse Events Newly enrolled patients will be included. Procedural Day + 3 Day: Stent Case Procedural Day +4 Days or Beyond to Discharge Day: Stenting Cases The day after discharge to the observation day of Month 8: 8 months for analysis by time point of stenting Observation day of 8 months to 1 year: 1 year for analysis by time point of stenting Observation day 1 to 2 years after the observation day of 1 year: 2 years for analysis by time point of stented patients Observation day of 2-year observation day to 3-year observation day: 3 years for analysis by time point of stented patients Observation day of the following day of observation in Year 3 to Year 4: 4 years for analysis by time point of stent implantation Observation day of the following day of observation in Year 4 to Year 5: 5 years for analysis by time point of stenting During hospitalization: patients with stents Until 8 months: Stent implantation Until 1 year: Stent implantation Until 2 years: Cases of stenting Until 3 years: Cases of stenting Until 4 years: Cases of stenting Until the end of the survey: patients undergoing stent placement Overall post-procedure: stenting cases

Items	Calculation method, etc.
Confidence interval for the incidence	Accurate confidence intervals based on Clopper-Pearson method will be calculated. $\pi_L = \frac{v_2}{v_2 + v_1 F_{\alpha/2}[v_1, v_2]} \quad v_1 = 2(n-x+1), v_2 = 2x$ $\pi_U = \frac{v_1 F_{\alpha/2}[v_1, v_2]}{v_2 + v_1 F_{\alpha/2}[v_1, v_2]} \quad v_1 = 2(x+1), v_2 = 2(n-x)$
Age (years)	The actual age at the date of the procedure (date of registration) is calculated from the date of birth (date is read in one day).
Body Mass Index	Calculated from weight (kg) and height (cm). Body Mass Index = Weight (kg)/ (Height (cm)/100) ^{2}
Acceptable range on the observation day	Observation day of 8 months: ±30 days 8 months after the procedure day Observation day 1 year: ±30 days after the procedure day Observation date of 2 years: ±30 days 2 years after the procedure date Observation day 3 years: ±30 days 3 years after the procedure date Observation day in Year 4: ±30 days 4 years after the procedure date Observation day in 5 years: ±30 days 5 years after the procedure date However, if it can be confirmed that there is no problem with the data quality, it should be adopted as the data at the time according to the time of the questionnaire, even if it is outside the range.

4. Statistical Analysis Content

4.1. SUMMARY OF SURVEY AND CASE STRUCTURE

- Analysis set: Cases collected by questionnaire

4.1.1. Number of patients at each center

The number of patients collected by questionnaire, the number of patients not covered by the survey, the number of patients surveyed, the number of patients not stented, and the number of patients stented will be tabulated. In addition, the corresponding case number is indicated for cases not covered by the survey and cases not covered by the stent.

Figure 1. Case structure

- Analysis set: Cases collected by questionnaire

4.1.2. Number of patients at each center

The number of patients collected by institution, the number of patients surveyed, and the number of stented patients will be tabulated.

Table 1. Number of patients by center

- Analysis set: Cases collected by questionnaire

4.1.3. Observation status

Follow-up by booklet and the number of patients included in the analysis by time point will be tabulated.

Table 2. Conduct of follow-up examinations

- Subjects for analysis: Subjects for investigation

4.1.4. Status at the end of the survey

The status at the end of the survey is tabulated.

Table 3. Status at the end of the survey

- Analysis set: Stent implantation cases

4.1.5. Ischemic findings at enrollment

For ischemic findings at the time of enrollment specified below, the proportion and confidence interval of relevant cases will be calculated.

Table 4. Ischemic findings at enrollment

- Analysis set: Stent implantation cases (newly enrolled patients)

Items: [ ] indicating Breakdown

No	Item name
1	Acute myocardial infarction [ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction]

No	Item name
2	Unstable Angina [Branwald Classification: Class I to Class III].
3	Stable angina pectoris [CCS Angina Classification: Class I to Class IV].
4	Silent ischemia
5	Old myocardial infarction (no evidence of ischemia)
6	Coronary stenosis (no evidence of ischemia)

4.1.6. Basic demographic information

Summary statistics of the basic demographic information specified below or proportions and confidence intervals of relevant cases will be calculated.

Table 5. Basic demographic information

- Analysis set: Stent implantation cases (newly enrolled patients)

Items * calculate summary statistics

No	Item name
1*	Age (years)
2	Age 75 years or older
3	Sex at birth (male, female)
4*	Height (cm)
5*	Body weight (kg)
6*	Body Mass Index (kg/ m^2)
7	Body Mass Index: Less than 18.5kg/m^2 Body Mass Index: 18.5kg/m^2 or more, less than 25kg/m^2 Body Mass Index: 25kg/m^2 or more, less than 30kg/m^2 Body Mass Index: 30kg/m^2 or more, less than 35kg/m^2 Body Mass Index: 35kg/m^2 or more, less than 40kg/m^2 Body Mass Index: 40kg/m^2 or higher

4.1.7. Risk Factors and History

The proportion and confidence interval of relevant cases will be calculated for the risk factors and medical history specified below.

Table 6 Risk Factors and History

- Analysis set: Stent implantation cases (newly enrolled patients)

Items [ ] indicating Breakdown

No	Item name
1	LVEF < 30%
2	History of myocardial infarction
3	History of CABG
4	History of PCI
5	Family History of Juvenile Coronary Artery Disease
6	Current smoking or cessation within the past month
7	Hypertension [requiring pharmacotherapy, not requiring pharmacotherapy]
8	Dyslipidemia [requiring pharmacotherapy, not requiring pharmacotherapy]
9	Renal failure (kidney disease) History [intradialytic, end-stage renal failure (eGFR < 30 mL/min/1.73m^2), chronic kidney disease (eGFR < 60 mL/min/1.73m^2)]
10	History of stroke
11	History of serious bleeding

No	Item name
12	History of unstable arrhythmia
13	Anticoagulant therapy

4.1.8. History of diabetes

The percentage and confidence interval of relevant cases will be calculated for the history of diabetes mellitus specified below.

Table 7. History of diabetes mellitus

- Analysis set: Stent implantation cases (newly enrolled patients)

Items [ ] indicating Breakdown

No	Item name
1	History of diabetes mellitus [type 1 diabetes mellitus, type 2 diabetes mellitus]
2	History of diabetes mellitus requiring pharmacotherapy [insulin therapy, oral antidiabetic drug treatment]

4.2. Lesions and Techniques

4.2.1. Information on treated lesions

Summary statistics or percentages and confidence intervals of relevant cases will be calculated for the information on the treated lesions specified below.

Table 8-1 Information on treated lesions (main branches for bifurcation lesions)

- Analysis set: Stent implantation cases (newly enrolled patients)

Items * calculate summary statistics

No	Item name
1*	Number of target lesions per patient
2	Number of target lesions per patient 1 lesion
3	Target number of lesions per patient 2 lesions
4	Target number of lesions per patient 3 lesions
5	Number of target lesions per patient ≧4 lesions
6	Lesion type new lesion
7	Lesion-type stent restenosis
8	Restenosis other than lesion-type stent treatment
9	Lesion type, etc.

Table 8-2 Location of target lesions (branches, main branches)

- Analysis set: Stent implantation cases (newly enrolled patients)

Items [ ] indicating Breakdown

No	Item name
1	Autologous coronary artery [LMT [protected, unprotected], RCA, LAD, LCX]
2	SVG
3	Arterial graft

Table 8-3. AHA segments (branches, main branches) of target lesions

- Analysis set: Stent implantation cases (newly enrolled patients)

Items

No	Item name
1	AHA-1 - AHA-15

Table 8-4. Presence of complex lesions

- Analysis set: Stent implantation cases (newly enrolled patients)

Items

No	Item name
1	Complex lesion bifurcation lesion
2	Complex lesion ST-elevation myocardial infarction culprit lesion
3	Complex lesion chronic total occlusion (CTO) lesions.
4	Complex lesion entrance lesion (less than 3mm from the aortic inlet or LAD/ LCX bifurcation)
5	Complex lesion hypermineralization
6	Thrombi within complex lesion-treated vessels
7	Complex lesion or proximal flexion >90 degrees
8	Complex lesion or excessive tortuosity of the proximal segment
9	Complex lesions, etc.

4.2.2. Treatment Lesion Stenosis Evaluation (All Lesions, Evaluated by Institution)

Summary statistics for preprocedural lesion length (mm) are calculated. Also, summary statistics for pre-procedure vessel diameter (mm) and %DS will be calculated by product.

Table 9. Target lesion stenosis assessment (all lesions, assessed by center)

- Analysis set: Stent implantation cases (newly enrolled patients)

4.2.3. Procedural Information-General Information

Summary statistics or percentages and confidence intervals of relevant cases will be calculated by product for procedural information specified below.

TABLE 10 PROCEDURES INFORMATION-GENERAL INFORMATION

- Analysis set: Stent implantation cases (newly enrolled patients)

Items * calculate summary statistics

No	Item name
1	Access site femoral artery
2	Access site radial artery
3	Access site brachial artery
4	Access site, etc.
5*	Number of care lesions per patient
6*	Number of target lesions per patient
7*	Number of lesions treated with XP_SV only Mean, standard deviation and sample size only calculated
8*	Mean number of lesions treated with XP_SV combined with other stents,

No	Item name
	standard deviation and sample size only calculated
9*	Number of non-target lesions Mean, standard deviation and sample size only calculated
10*	Total number of stents placed per patient
11*	Total length of stent placed per patient (mm)
12*	Time (min) required for the procedure

4.2.4. Treatment of the treated lesion

Summary statistics or percentages and confidence intervals will be calculated by product for treatment of the treatment lesion specified below.

TABLE 11-1 TREATMENT OF TARGET LESIONS

- Analysis set: Stent implantation cases (newly enrolled patients)

Items * calculate summary statistics

No	Item name
1	Thrombus aspiration
2	Direct stent only
3	Direct stent + posterior dilatation
4	Pretreatment + stenting
5	Conditioning + stenting + posterior dilatation
6	Pretreatment direct stent (no pretreatment)
7	Pre-dilatation with pre-lesion treatment POBA
8	Lesion conditioning rotablator
9	Pre-dilatation with a pre-lesion conditioning cutting balloon
10	Pre-dilatation with a prelesion conditioning scoring balloon
11	Pretreatment of lesions, etc.
12	Post dilatation
13*	Maximum balloon diameter (mm)
14*	Maximum diastolic pressure (atm)

Table 11-2 Number of stents placed in target lesions

- Analysis set: Stent implantation cases (newly enrolled patients)

Items * calculate summary statistics

No	Item name
1*	Number of stents with target lesions (per lesion)
2*	Number of indwelling XP_SV Mean, standard deviation and sample size only calculated
3	XP_SV number placed 1 stent
4	Placed XP_SV number 2 stents
5	Implanted XP_SV number 3 stents
6*	Number of other stents placed Mean, standard deviation and sample size only calculated
7	Number of other stents placed 0 stents
8	No. of other stents placed 1 stent
9	Number of other stents placed 2 stents
10	Bailout stent
11*	Total length of stent placed (mm per lesion)

4.2.5. Bifurcation lesion information

The proportion and confidence interval of relevant cases will be calculated by product for the branching lesion information specified below.

Table 12. Branch lesion information

- Analysis set: Stent implantation cases (newly enrolled patients)

Items

No	Item name
1	Branched-lesion True
2	Branched-lesion False
3	Divergent lesion type unknown
4	Detailed retention below

4.2.6. Method of treating bifurcation lesions

For the method of treating bifurcation lesions, the proportion and confidence intervals of relevant cases will be calculated by bifurcation lesion type and product.

TABLE 13-1 METHODS OF TREATMENT OF FUNCTION LESIONS (FUNCTION LESIONS TYPE-True)

TABLE 13-2 METHODS OF TREATMENT OF FUNCTION LESIONS (FUNCTION LESIONS TYPE-False)

Table 13-3. Treatment of bifurcation lesions (bifurcation lesion type-all types)

- Analysis set: Stent implantation cases (newly enrolled patients)

Items

No	Item name
1	Provisional Stent [stenting in main branches only, Provisional T, Provisional Culottes]
2	Elective Stent [Classic T、Modified T、Crush、Culottes、Kissing Stent]
3	Kissing balloon

4.2.7. Use of stents

The XP_SV stents used will be summarized by diameter and length. Cross-tabulation of stent length × stent diameter is also performed.

Table 14. Number of stents used by size

Table 14-1. Breakdown of indwelling stents by size

- Analysis set: Stent implantation cases (newly enrolled patients)

Items

No	Item name
1	Diameter of the stent 2.25mm

No	Item name
2	Length of the stent 8 mm、12 mm、15 mm、18 mm、23 mm、28 mm、33 mm、38 mm

4.2.8. Success rate

Success rates and confidence intervals will be calculated by product for per-device placement (XP_SV only), per-lesion procedure and per-patient XP_SV placement.

No	Items	Analysis set
1	Successful placement per device (XP_SV only)	Number of devices used by the study population cases
2	Successful procedure for each lesion	Number of lesions in the subject cases (only those for which lesion information is collected)
3	Successful XP_SV placement per patient	Number of subjects surveyed

Table 15. Success rate

- Analysis set: Surveyed patients (newly enrolled patients)

4.2.9. Hospitalization information

Summary statistics will be calculated for length of stay (days) after the procedure date. In addition, the proportion and confidence interval of relevant patients will be calculated by product for prolongation of hospital stay due to serious adverse events.

Table 16. Hospitalization information

- Analysis set: Stent implantation cases (newly enrolled patients)

4.3. Antiplatelet therapy

4.3.1. Antiplatelet therapy

For antiplatelet therapy, the proportion and confidence interval of the relevant cases will be calculated by product for each observation time point.

No	Time of observation
1	Before the procedure
2	Procedure Day to Discharge Day
3	Procedural date-8 months observation day
4	Procedural date-Observation date of Year 1
5	Procedural date-Observation date for 2 years
6	Procedural date-3 Years Observation Day
7	Procedural date-Observation date, Year 4
8	Procedural date-5 Years Observation Day

Table 17. Antiplatelet therapy (by observation time point)

- Analysis set: Stent implantation cases (newly enrolled patients)

Items

No	Item name
1	Dual antiplatelet therapy [aspirin + clopidogrel, aspirin + ticlopidine]
2	Aspirin, clopidogrel, ticlopidine, cilostazol, and others

4.4. Adverse Events

4.4.1. Adverse events (composite endpoint)

For adverse events (composite endpoint), incidence rates will be calculated by product for each time of onset.

No	Time of onset
1	Procedural day + 3 days from procedure date
2	Procedural Day + Day 4 or later to discharge date
3	Observation day of the day after discharge to Month 8
4	Observation day of Month 8 to Observation day of Year 1
5	Observation day of 1 year to the following day of 2 years
6	Observation day of the following day of Year 2 to Observation day of Year 3
7	Observation day of Year 3 to Year 4
8	Observation day following the observation day of Year 4 to the observation day of Year 5
9	During hospitalization
10	Up to 8 months
11	Until one year
12	Until 2 years
13	Up to 3 years
14	Up to 4 years
15	Until the end of the survey
16	Entire post-procedure

Table 18. Adverse events (composite endpoint, by time of onset)

- Analysis set: Stent implantation cases (newly enrolled patients)

Items [ ] indicating Breakdown

No	Item name
1	Target Lesion Failure [TLR Based on Cardiac Death, Myocardial Infarction Associated with Target Vessels, and Ischemic Findings].
2	Death + myocardial infarction + revascularization [death, myocardial infarction, revascularization]
3	Target vessel failure [cardiac death, myocardial infarction, TLR based on ischemic findings, TVR (non-TLR) based on ischemic findings, TVR (TLR or TVR (non-TLR)) based on ischemic findings].
4	Major adverse cardiac events (cardiac death, total myocardial infarction, TLR based on ischemic findings)
5	Death or myocardial infarction
6	Cardiac death or myocardial infarction
7	Myocardial infarction related to cardiac death or target vessel

Determination of myocardial infarction is based on the WHO (SPIRIT III) definitions

4.4.2. Adverse Events (by Event)

For adverse events (by event), the incidence rate will be calculated by product for each time of onset.

Table 19. Adverse events (by event and time of onset)

- Analysis set: Stent implantation cases (newly enrolled patients)

Items [ ] indicating Breakdown

No	Item name
1	Death [cardiac death, death attributable to non-coronary vessels, death not attributable to cardiovascular causes]
2	Myocardial infarction [ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction, Q-wave myocardial infarction, non-Q-wave myocardial infarction]
3	TLR [TLR based on ischemic findings [CABG, PCI], TLR not based on ischemic findings [CABG, PCI].
4	TVR (non-TLR) [TVR (non-TLR) [CABG, PCI) based on ischemic findings, TVR (non-TLR) [CABG, PCI) not based on ischemic findings].
5	TVR (TLR or TVR (non-TLR)) [TVR based on ischemic findings (TLR or TVR (non-TLR)) [CABG, PCI)], TVR not based on ischemic findings (TLR or TVR (non-TLR)) [CABG, PCI)].
6	Non-TVR [CABG、PCI]
7	Total revascularization [revascularization based on ischemic findings [CABG, PCI], revascularization not based on ischemic findings [CABG, PCI].
8	Bleeding

Determination of myocardial infarction is based on the WHO (SPIRIT III) definitions

4.4.3. Adverse events (stent thrombosis)

For adverse events (stent thrombosis), the incidence rate is calculated.

Table 20. Adverse events (stent thrombosis)

- Analysis set: Stent implantation cases (newly enrolled patients)

4.4.4. Adverse events (survival time analysis)

Cumulative incidence is plotted by Kaplan-Meier for the AEs defined below, with the first occurrence as an event and non-occurrence as censored. In addition, the sample size, cumulative incidence, and 95% confidence interval of the cumulative incidence will be calculated for the at-risk population at 240, 365, 730, 1095, 1460, 1825 days, and the entire period.

Figure 21. Adverse events (by survival time analysis event)

- Analysis set: Stent implantation cases (newly enrolled patients)

No	Items	Definitions
1	Event	Death, TLR based on ischemic findings, first occurrence of stent thrombosis as event Use non-event cases as truncation examples
2	Survival time	Event example: Event date-Procedure date + 1 Censored: last contact date or withdrawal date-procedure date + 1

4.5. Appendix Form

4.5.1. List of occurrence of malfunctions and infectious diseases

Prepare a list of the occurrence of malfunctions and infectious diseases.

List of Incidence of Failure/Infectious Diseases (Annual Report: Form 3 Re-Examination: Form 2)

- Analysis set: Stent implantation cases

Line

No	Item name	Definition Content
1	Number of facilities surveyed	Use the same site as a single institution
2	Number of subjects surveyed	Tabulate the number of patients surveyed
3	Number of patients with malfunctions	If more than one malfunction etc. occurs in the same patient, the data will be summarized as 1 subject.
4	Number of incidents of failure, etc.	Aggregate the number of incidents of failure, etc.
5	Incidence of failure	= number of cases with malfunctions, etc. ♂ × 100 number of cases to be investigated.
6	Event name	Aggregate using MedDRA coding

4.5.2. List of Incidence of Failures and Infectious Diseases by Patient Background

The number of patients, the number of patients with malfunctions and infections, and the incidence of malfunctions and infections will be calculated according to patient characteristics.

List of Incidence of Failures and Infectious Diseases by Patient Background

- Analysis set: Stent implantation cases (newly enrolled patients)

Patient characteristics: [ ] indicating Breakdown

No	Item name
1	Acute myocardial infarction (yes/no) [ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction]
2	Unstable angina pectoris (with or without) [Blanwald classification: Class I to Class III]
3	Stable angina pectoris (with or without) [CCS angina classification: Class I-IV]
4	Asymptomatic ischemia (with or without)
5	Old myocardial infarction (no evidence of ischemia) (yes/no)
6	Coronary artery stenosis (no evidence of ischemia) (yes/no)
7	Age (<75 years, ≧75 years)
8	Sex at birth (male, female)
9	Height (< 160cm, > 160cm, < 170cm, > 170cm)
10	Body weight (< 60kg, ≧ 60kg, < 70kg, and ≧70kg)
11	Body Mass Index (less than 18.5kg/m^2, greater than 18.5kg/m^2, less than 25kg/m^2, greater than 25kg/m^2, less than 30kg/m^2, greater than or equal to 30kg/m^2, less than 35kg/m^2, greater than or equal to 35kg/m^2, less than or equal to 40kg/m^2, greater than or equal to 40kg/m^2)
12	LVEF < 30% (< 30, > 30)
13	History of myocardial infarction (yes/no)
14	History of CABG (with or without)
15	Past PCI (Yes, No)

No	Item name
16	Family history of juvenile coronary artery disease (yes/no)
17	If you are currently smoking or quit smoking within the past month (yes/no).
18	Hypertension (yes/no) [requiring pharmacotherapy, not requiring pharmacotherapy]
19	Dyslipidemia (yes/no) [requiring pharmacotherapy, not requiring pharmacotherapy]
20	Renal failure (Kidney disease) History (yes/no) [On dialysis, end-stage renal failure (eGFR < 30 mL/min/1.73m^2), chronic kidney disease (eGFR < 60 mL/min/1.73m^2)]
21	History of stroke (yes/no)
22	History of serious bleeding (with or without)
23	History of unstable arrhythmia (present or absent)
24	Anticoagulant therapy (continuous administration, no continued administration)
25	History of diabetes mellitus (with or without) [Type 1 diabetes mellitus, Type 2 diabetes mellitus]
26	History of diabetes mellitus requiring medical care (with or without) [insulin therapy, oral antidiabetic drug therapy]

4.5.3. Listing of Incidence of Serious Adverse Events

Prepare a list of serious adverse events.

Listing of Incidence of Serious Adverse Events (Form 3-2)

- Analysis set: Stent implantation cases

Line

No	Item name	Definition Content
1	Number of facilities surveyed	Use the same site as a single institution
2	Number of subjects surveyed	Tabulate the number of patients surveyed
3	Number of patients with adverse events	If more than one serious adverse event occurs in the same patient, it will be summarized as one subject.
4	The number of incidences of the adverse events	The number of serious adverse events is summarized.
5	Incidence of adverse events	= number of subjects with serious adverse events ♂ × 100 number of subjects surveyed
6	Event name	Aggregate using MedDRA coding

4.6. Quantitative coronary angiography (QCA).

4.6.1. QCA results before the procedure, immediately after the procedure, and at follow-up.

Summary statistics will be calculated for each observation period based on QCA results.

Table Q1 QCA results before the procedure, immediately after the procedure, and at follow-up

- Analysis set: Stent implantation cases (newly enrolled patients)

Items

No	Item name
1	Lesion length (mm)

No	Item name
2	Minimum lumen diameter (mm)
3	Reference vessel diameter (mm)
4	Diameter stenosis (%)

4.6.2. Acute-phase diameter gain and late-phase diameter loss

Summary statistics will be calculated for each stent, proximal, distal, and segment with respect to the acquired lumen diameter in the acute phase and the loss diameter in the distant phase.

Table Q2 Acute phase diameter gain and late phase diameter loss

- Analysis set: Stent implantation cases (newly enrolled patients)

Items

No	Item name
1	Acute Gain (mm)
2	Late Loss (mm)
3	Net Gain

4.7.Listing of Case Summaries Subjects Subject to Drug Use Results Survey

4.7.1. Listing of Case Summaries Subjects Subject to Drug Use Results Survey

Prepare a case summary list for drug use-results surveys.

Listing of Case Summaries Subjects Subject to Drug Use Results Survey

- Analysis set: Cases collected by questionnaire

End of document