J-SUPREME

A Prospective, Multicenter, Single-arm Clinical Trial of JetStream Atherectomy System for the Treatment of Japanese Patients with Symptomatic OcclUsive Atherosclerotic Lesions in the SuPeRficial FEmoral and/ or ProxiMal PoplitEal Arteries

CLINICAL INVESTIGATION PLAN

Study Reference Number: S6051

Sponsored By

Boston Scientific Japan K.K.
4-10-2, Nakano Nakano-ku
Tokyo 164-0001, Japan

Contact Information

Role	Contact
[redacted]	[redacted]
[redacted]	[redacted]
Investigational Sites	A list of investigational sites is maintained and provided as a separate attachment to the protocol.
Vendors/Labs	A list of vendors/laboratories involved in the trial is maintained by the sponsor and will be provided to investigational sites.

Original Release: February 5, 2016

Current Version: February 29, 2016

Revision History

Revision Number	Release Date	Template number and version	Section	Change	Reason for Change
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
AB	February 29, 2016	[redacted]	[redacted]	[redacted]	[redacted]
			[redacted]	[redacted]	[redacted]

2. Protocol Synopsis

<table>
<tr><td colspan="2">J-SUPREME: A Prospective, Multicenter, Single-arm Clinical Trial of Jetstream Atherectomy System for the Treatment of Japanese Patients with Symptomatic Occlusive Atherosclerotic Lesions in the Superficial Femoral and/ or Proximal Popliteal Arteries</td></tr>
<tr><td>Study Objective(s)</td><td>To evaluate the safety and effectiveness of the Boston Scientific (BSC) Jetstream Atherectomy System (Jetstream) for the treatment of Japanese patients with symptomatic occlusive atherosclerotic lesions in native superficial femoral artery (SFA) and/ or proximal popliteal arteries (PPA)</td></tr>
<tr><td>Planned Indication(s) for Use</td><td>Jetstream is intended to be used as adjunctive therapy for percutaneous intervention to remove atherosclerotic disease, debris, and thrombus from the SFA and/or PPA</td></tr>
<tr><td>Test Device</td><td>The Jetstream® Atherectomy System: A rotating, aspirating, expandable catheter system for active removal of atherosclerotic debris and thrombus in the SFA and/or PPA</td></tr>
<tr><td>Control Device</td><td>NA</td></tr>
<tr><td>Device Sizes</td><td><u>Jetstream Atherectomy System</u>
1. Jetstream Catheter
<table><tr><th>Model</th><th>Tip Diameter</th><th>Catheter Length</th><th>Min.Introducer Size</th><th>Max. Guidewire Diameter</th></tr><tr><td>SC 1.6</td><td>1.6mm</td><td>145cm</td><td rowspan="2">7Fr</td><td rowspan="4">0.014inch</td></tr><tr><td>SC 1.85</td><td>1.85mm</td><td>145cm</td></tr><tr><td>XC 2.1/3.0</td><td>2.1mm(Blade Down)
3.0mm(Blade Up)</td><td>135cm</td><td rowspan="2">7Fr</td></tr><tr><td>XC 2.4/3.4</td><td>2.4mm(Blade Down)
3.4mm(Blade Up)</td><td>120cm</td></tr></table>2. Jetstream Console</td></tr>
<tr><td>Study Design</td><td>A prospective, multicenter, single-arm trial evaluating the safety and efficacy of the Jetstream Atherectomy System in the treatment of symptomatic occlusive atherosclerotic lesions ≤150 mm in length located in the femoropopliteal arteries in subjects with symptoms classified as Rutherford categories 2-4</td></tr>
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Planned Number of Subjects	50 primary subjects will be enrolled in the J-SUPREME clinical trial. In addition, at least one roll-in subjects per site is planned, so that a total of approximately 60 subjects will be enrolled.
Planned Number of Investigational Sites / Countries	Up to 10 investigational sites in Japan may enroll subjects.
Primary Endpoint	The primary endpoint is the primary patency rate at 6 months post-procedure. Primary vessel patency, a binary endpoint, is defined as follows: - Bailout stenting or by-pass procedure during the index procedure is not needed (Procedural Success) - Duplex ultrasound (DUS) Peak Systolic Velocity Ratio (PSVR) ≤2.4 at the 6-month follow-up visit, in the absence of clinically-driven TLR and/or bypass of the target lesion and/or target limb major amputation through 6 months All Angio and DUS readings will be assessed by an independent core laboratory. Clinically-driven TLR, target lesion bypass and target limb major amputation will be adjudicated by an Independent Medical Reviewer (IMR).
Additional Endpoints	- Procedural success rate - Rate of distal emboli requiring additional treatment during the procedure or within 24 hours post-index procedure. - Reduction in lesion stenosis, that is, the difference between the percent stenosis prior to treatment with Jetstream and the percent stenosis following treatment with Jetstream (absolute mean percentage) - MAE rate at 1 month, 6 months and 12 months post-index procedure, defined as all-cause death through 1 month, and/or target limb major amputation and/or TLR through 12 months - Primary Patency and Assisted Primary Patency at 1 month, 6 months and 12 months using different PSVRs - Clinically-driven TLR and Target Vessel Revascularization (TVR) Rate at

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	each time point - Adverse Event rates at each time point - Distribution of Rutherford Class as compared to baseline at 6 months and 12 months post-index procedure - Rate of Primary and Secondary Sustained Clinical Improvement as assessed by changes in Rutherford Classification as compared to baseline at 6 months and 12 months post-index procedure - Rate of Hemodynamic Improvement as assessed by changes in Ankle-Brachial Index as compared to baseline at 1 month. 6 months and 12 months post-index procedure
[redacted]	[redacted]
Follow-up Schedule	Subjects will be evaluated at 1, 6 and 12 months post-index procedure. - Subjects who are enrolled but the Jetstream Atherectomy System is not used will be followed through the 1-month follow-up visit only. - Assessment of the primary endpoint will occur at the 6-month follow-up visit. - All follow-up visits will be conducted in the office/clinic. Planned protocol-required testing includes the following: - Angiography during the index procedure to assess procedural success and occurrence of emboli. - DUS at the 1-month, 6-months and 12-months follow-up visits to assess lesion and vessel patency
Study Duration	The trial will be considered complete (with regards to the primary endpoint) after all enrolled subjects have completed the 6 month follow-up visit, are discontinued prior to 6 month follow-up visit, have died, or the last 6 month follow-up visit window is closed. The trial will be considered complete (with regards to all follow-up) after all

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	enrolled subjects have completed the 12 month follow-up visit, are discontinued prior to 6 month follow-up visit, have died, or the last 12 month follow-up visit window is closed. It is estimated that it will take approximately 2 years to complete this trial.
[redacted]	[redacted]
Key Inclusion Criteria	1. ≥20 years of age 2. An acceptable candidate for percutaneous intervention and/or emergency surgery. 3. Willing and able to provide consent before any study specific test or procedure is performed, signs the consent form, and agrees to attend all required follow-up visits 4. Chronic, symptomatic lower limb ischemia defined as Rutherford categories 2, 3 or 4 5. Stenotic, restenotic or occlusive lesion(s) located in the native SFA and/or PPA of which meet all of the following criteria: a. Calcified lesions* with degree of stenosis ≥70% by visual angiographic assessment or occlusions, regardless of degree of calcification *Calcification needs to be in the segment 5mm proximal and 5mm distal to the stenotic lesion by visual estimate b. Guidewire must cross lesion(s) within the true lumen, without a sub-intimal course by physician's discretion based on visual estimate c. Vessel diameter ≥3.0 mm and ≤6.0 mm by visual estimate d. Total lesion length (or series of lesions) ≤150mm by visual estimate e. Target lesion located at least 3 cm above the inferior edge of the femur by visual estimate 6. Patent infrapopliteal and popliteal artery, i.e., single vessel runoff or better with at least one of three vessels patent (<50% stenosis by visual estimate) to the ankle or foot with no planned intervention
Key Exclusion	1. Target lesion must be one and decided by physician's discretion in the

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Criteria	case that eligible lesions exist in both limbs 2. Target lesion/vessel with in-stent restenosis 3. Target lesion/vessel previously treated with drug-coated balloon <12 months prior to the procedure 4. Target lesion/vessel previously treated with any stent placement, atherectomy, laser or other debulking devices prior to the procedure 5. Subjects who have undergone surgery or endovascular of the SFA/PPA in the target vessel to treat atherosclerotic disease within 3 months prior to the index procedure 6. Use of drug-coated devices, atherectomy, laser or other debulking devices other than the Jetstream System, CTO devices or cutting balloon, Angioscore or similar devices in the target limb SFA/PPA during the index procedure 7. History of major amputation in the target limb 8. Subjects who have lesions requiring treatment and planned the treatment with commercial devices in a contralateral limb within 30 days after the index procedure 9. Subjects who had lesions treated with commercial devices in a contralateral limb within 7 days prior to the index procedure (Note: If subject had treatment of contralateral limb 8 days or earlier prior to the index procedure, the procedure success needs to be confirmed by physician's discretion) 10. Life expectancy less than 24 months due to other medical co-morbid condition(s) that could limit the subject's ability to participate in the clinical trial, limit the subject's compliance with the follow-up requirements, or impact the scientific integrity of the clinical trial 11. Known hypersensitivity or contraindication to contrast dye that, in the opinion of the investigator, cannot be adequately pre-medicated 12. Known hypersensitivity/allergy to the investigational atherectomy system or protocol related therapies (e.g., nitinol, stainless steel or other stent materials, and antiplatelet or anticoagulant, thrombolytic medications) 13. Subject has a history of coagulopathy or hypercoagulable bleeding disorder 14. Subject with untreatable hemorrhagic disease or platelet count <80,000mm^3 or >600,000mm^3 as baseline assessment.

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	15. Concomitant renal failure with a serum creatinine >2.0 mg/dL 16. Receiving dialysis or immunosuppressant therapy 17. History of myocardial infarction, or stroke/cerebrovascular accident (CVA) within 6 months prior to study enrollment 18. Unstable angina pectoris at the time of the enrollment 19. Pregnancy and/or breast feeding 20. Current participation in another investigational drug or device clinical study that has not completed the primary endpoint at the time of enrollment or that clinically interferes with the current study endpoints (Note: studies requiring extended follow-up for products that were investigational, but have become commercially available since then are not considered investigational studies.) 21. Septicemia at the time of enrollment 22. Presence of other hemodynamically significant outflow lesions in the target limb requiring a planned surgical intervention or endovascular procedure within 30 days after the index procedure 23. Presence of aneurysm in the target vessel 24. Acute ischemia and/or acute thrombosis of the SFA/PPA prior to the index procedure 25. Perforated vessel as evidenced by extravasation of contrast media prior to the index procedure
[redacted]	[redacted]

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[redacted]	[redacted]

3. Table of Contents

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4. Introduction

4.1. Background of development

Peripheral arterial disease (PAD) is a chronic arterial occlusive disease of the lower extremities caused by arteriosclerosis. The most common clinical symptom of PAD is intermittent claudication, and as the disease progresses, serious problems such as physical disability and significant deterioration of quality of life (QOL) can develop. For these PAD patients, various therapies have been tried including medication, exercise therapy, and surgical revascularization.[1]

As a guideline for the treatment of PAD patients, Guideline II of Diagnosis and Treatment for Arteriosclerosis Obliterans of the Lower Extremities (TASCII) was issued in 2007. Subsequently, according to the guideline, endovascular therapy (EVT) has been recommended for type A lesions in the femoropopliteal and aortoiliac arteries and also for type B lesions in principle. Accordingly, options other than conventional therapies, including percutaneous transluminal angioplasty (PTA) and stenting, have been available. In addition, Guideline on the Diagnosis and Treatment of PAD issued by the European Society of Cardiology (ESC 2011 guideline) states that EVT is the treatment of first choice for TASC type A to C lesions and that the endovascular approach as the treatment of first choice should also be considered for type D lesions. Thus, the use of EVT for PAD is increasing.

However, it is said that treatment with PTA for calcified lesions may not provide sufficient revascularization[2] and is associated with a higher risk of recurrence of stenosis or occlusions compared to other lesions.[3] Because PTA alone has limited persistence of patency, stenting after PTA is emerging as a treatment option. Inadequate stent expansion is more likely to occur in calcified lesions and there is a concern that the risk of in-stent restenosis and thrombotic events may be increased. Therefore, treatment with PTA is still considered to be a treatment option in femoropopliteal artery.

With this background, as a novel treatment for PAD, a peripheral atherectomy system to excise atheromatous tissue in severely calcified lesion has been developed and is drawing attention in PTA and stent treatment. This atherectomy system is expected to improve the procedural success rate, alone or in combination with PTA/stenting.

Jetstream Atherectomy System was approved under 510(K) for the Pathway PV System, a first-generation model, in July 2008, and later in April 2013, for the current model. Jetstream Atherectomy System was also granted a CE mark in September 2013 and is currently marketed in the United States, Europe, Austria, and other regions.

4.2. Clinical Study Summary

Summary of Pathway PVD clinical study

The pathway PVD clinical study was a prospective, multicenter, single arm study conducted using the Pathway PV System, a first-generation model of Jetstream, in which a total of 172 subjects were enrolled at 9 investigational sites in Germany, Austria, and Belgium.

The primary safety endpoints of this study was the free rate for serious adverse device effects (SADEs) and target lesion revascularization (TLR) in the 6-month post-procedure period. The primary efficacy endpoint was the procedural success rate (defined as reduction in lesion stenosis,

that is, the difference between the stenosis diameter prior to treatment with Jetstream and the stenosis diameter following treatment with Jetstream [absolute mean percentage]). Target lesions had reference vessel diameters ranging from 3–5 mm (visual estimation), total lesion lengths (alone or series of lesions) up to 10 cm for the superficial femoral and popliteal arteries as well as up to 3 cm for the tibial and fibular arteries (the superficial femoral artery), and lesions in the infrapopliteal and popliteal artery (Rutherford categories 1–5 or equivalent).

The free rate for SADEs and TLR for the 6-month post-procedure period, the primary safety endpoints of this study, was 85% and the lower limit of the 95% confidence interval was 78%, which was above 60% (the percentage pre-determined by objective performance criteria [OPC] minus a non-inferiority margin of 10%), meeting the primary endpoint.

The primary effectiveness endpoint analysis in the ITT population showed that the procedural success rate following treatment with the Pathway PV System alone was 43.5% and the lower limit of the 95% confidence interval was 40.6%, which was below 45% (the percentage pre-determined by 55% of OPC minus a non-inferiority margin of 10%), not meeting the primary endpoint. However, the procedural success rate in 116 lesions when the Pathway PV System was used in combination with an adjunctive therapy (PTA or stenting etc.) was 58.8%, which was clinically significant. The procedural success rate in the evaluable subgroup, which was defined as subjects with stenosis diameter ≥ 70% based on an assessment performed in the Angiographic Core Laboratory prior to the procedure, was 50.3%. Although this percentage was below 55% of OPC, the lower limit of the 95% confidence interval was 46.8%, within the range of the non-inferiority margin (45%), indicating that the procedural success rate using Pathway PV System in the subgroup was not inferior to OPC, meeting the primary effectiveness endpoint. In addition, the procedural success rate in 80 lesions when the Pathway PV System was used in combination with an adjunctive therapy (PTA or stenting etc.) was 66.9%. This demonstrated that the Pathway PV System can be used in combination with currently accepted treatment using PTA and stents and be of benefit to patients. The procedural success rate in the ITT population visually assessed by the investigator was 59.7% and the 95% confidence interval was 56.8%–62.6%, showing significant non-inferiority and superiority to OPC.

The TLR rate using the Pathway PV System in the 6-month post-procedure period was 8.7% (15/172 subjects). No surgical TLRs, deaths, or amputations occurred. No surgical TLRs occurred throughout the study. One event of death that was not related to the use of the Pathway PV System and two events of scheduled amputations were reported. No device malfunctions were reported.

5. Device Description

The test device is intended to be used as adjunctive therapy for percutaneous intervention to remove atherosclerotic disease, debris, and thrombus from the SFA and/or PPA.

The Jetstream Atherectomy System is a rotational atherectomy catheter system designed for use in debulking and treating vascular disease in the peripheral vasculature. The catheter includes multiple distal ports located at the catheter tip, which are designed to provide independent infusion and aspiration functions for the active removal of fluid, excised tissue and thrombus from the peripheral treatment site. The Jetstream System consists of two primary components that are packaged separately; Jetstream Atherectomy Catheter set and Jetstream Console (Figure

5.1-1).

Catheter Set

Console

Figure 5.1-1: Jetstream Atherectomy System

5.1. Jetstream Atherectomy Catheter

Jetstream Catheter set is a sterile, single use unit consisting of an electrically driven Catheter and Control Pod with detachable Activation Handle. The Catheter utilizes a differentially cutting tip and includes both aspiration and infusion capabilities. The Activation Handle provides a user interface with keypad controls for device operation. The unit, its electrical connectors, tubing, and aspirant collection bag are packaged in a single pouched tray with retention lid, and sterilized with ethylene oxide (EO). Note that the tray retention lid is not a sterile barrier.

The catheter has four types of model based on existence of expandable blade and size of catheter tip as shown in Table 5.1-1 and Figure 5.1-2. The Jetstream single cutter (SC) catheters are available in 1.6mm and 1.85mm sizes and the Jetstream expandable cutter (XC) catheters are available in 2.1mm (Blade Down)/3.0mm (Blade Up) and 2.4mm (Blade Down)/3.4mm (Blade Up). XC model has a mechanism that expandable blade is fold when blade down and expandable blade rises up (i.e. Blade Up) when MAX button in the control pod is turned on.

Table 5.1-1: Jetstream Specifications

Model	Tip Diameter	Catheter Length	Minimun Introducer Size	Maximum Guidewire Diameter
SC 1.6	1.6 mm	145cm	7Fr	0.014inch
SC 1.85	1.85mm	145cm		
XC 2.1/3.0	2.1mm (Blade Down) 3.0mm (Blade Up)	135cm	7Fr	
XC 2.4/3.4	2.4mm (Blade Down) 3.4mm (Blade Up)	120cm		

Figure 5.1-2: Jetstream Catheter Tip

5.2. Jetstream Console

A reusable PV Console consists of two (2) peristaltic pumps for aspiration and infusion, power supply, system controller, keypad interface, and LED indicators for device operational status. The PV Console mounts on a standard IV stand and remains outside the sterile field during the procedure (Figure 5.1-1).

5.3. Device Labeling of investigational device

The Directions for Use (DFU) for the Jestream Atherectomy System will be included in the Manual of Operations. The Jetstream catheter and control pod set is labeled on the back and side of the outer carton, and on the inside sterile pouch. The Jetstream Console is labeled on the product box. Packaging will include peelable, self-adhesive labels for each unit shipped. The labeling will include the following information in Japanese or in English.

In Japanese:

- Identification number
- Sponsor name and address
- Storage condition
- Exclusively for Clinical Investigations

In English:

- Lot number
- Serial number

- Jetstream Catheter model (diameter in mm)
- Expiration (use by) date

6. Study Objectives

The objective of the J-SUPREME clinical trial is to evaluate the safety and effectiveness of the Boston Scientific (BSC) Jetstream Atherectomy System (Jetstream) for the treatment of Japanese patients with symptomatic occlusive atherosclerotic lesions in native superficial femoral artery (SFA) and/ or proximal popliteal arteries (PPA).

7. Study Endpoints

7.1. Primary Endpoint

The primary endpoint is the primary patency rate at 6 months post-procedure. Primary vessel patency, a binary endpoint, is defined as follows:

- Bailout stenting or surgical procedure during the index procedure is not needed (Procedural Success)
- Duplex ultrasound (DUS) Peak Systolic Velocity Ratio (PSVR) ≤ 2.4 at the 6-month follow-up visit, in the absence of clinically-driven TLR and/or bypass of the target lesion and/or target limb major amputation through 6 months

7.2. Additional Endpoint

Additional endpoints that will be evaluated, but are not necessarily powered to make statistically based conclusions are as follows:

- Procedural success rate
- Rate of distal emboli requiring additional treatment during the procedure or within 24 hours post-index procedure.
- Reduction in lesion stenosis, that is, the difference between the percent stenosis prior to treatment with Jetstream and the percent stenosis following treatment with Jetstream (absolute mean percentage)
- MAE rate at 1 month, 6 months and 12 months post-index procedure, defined as all-cause death through 1 month, and/or target limb major amputation and/or TLR through 12 months
- Primary Patency and Assisted Primary Patency at 1 month, 6 months and 12 months using different PSVRs
- Clinically-driven TLR and Target Vessel Revascularization (TVR) Rate at each time point
- Adverse Event rates at each time point
- Distribution of Rutherford Class as compared to baseline at 6 months and 12 months post-index procedure

- Rate of Primary and Secondary Sustained Clinical Improvement as assessed by changes in Rutherford Classification as compared to baseline at 6 months and 12 months post-index procedure
- Rate of Hemodynamic Improvement as assessed by changes in Ankle-Brachial Index as compared to baseline at 1 month. 6 months and 12 months post-index procedure

8. Study Design

The J-SUPREME clinical trial is a prospective, multicenter, single-arm clinical trial of Jetstream Atherectomy System for the treatment of Japanese patients with symptomatic occlusive atherosclerotic lesions in the superficial femoral and/or proximal popliteal arteries.

8.1. Scale and Duration

50 primary subjects will be enrolled in the J-SUPREME clinical trial. In addition, at least one roll-in subject per site is planned, so that a total of approximately 60 subjects will be enrolled.

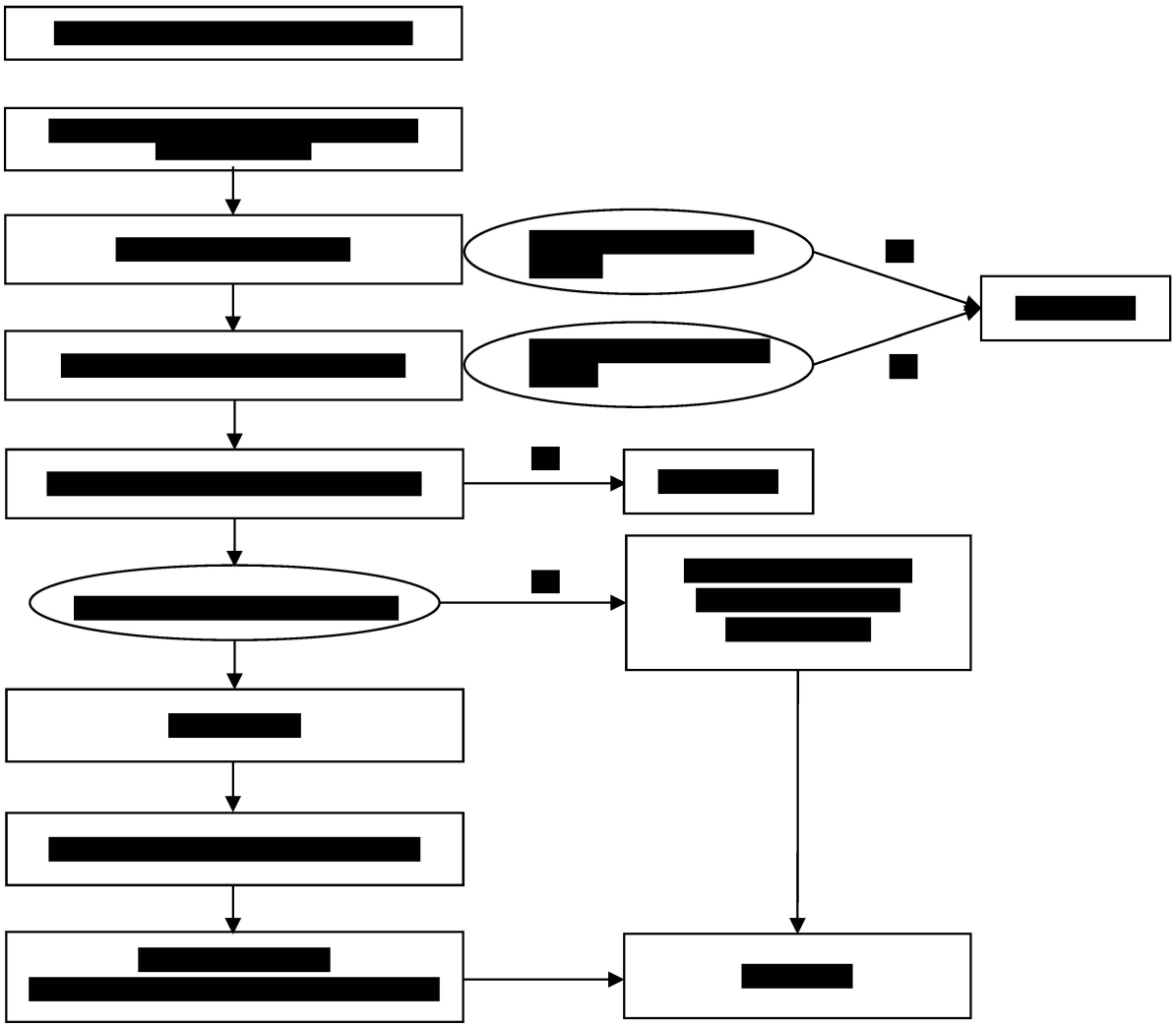
The enrollment period is expected to last approximately 10 months.

The trial will be considered complete (with regards to the primary endpoint) after all enrolled subjects have completed the 6 month follow-up visit, are discontinued prior to 6 month follow-up visit, have died, or the last 6 month follow-up visit window is closed.

The trial will be considered complete (with regards to all follow-up) after all enrolled subjects have completed the 12 month follow-up visit, are discontinued prior to 12 month follow-up visit, have died, or the last 12 month follow-up visit window is closed.

It is estimated that it will take approximately 2 years to complete this trial.

[redacted]



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8.4. Justification for the Study Design

Pathway PV system which is the first generation model of Jetstream received 510(K) approval in July 2008, and then, the current generation model (Jetstream) in April, 2013. Also, it received CE Mark certification in September 2013.

Jetstream is now commercially available in the U.S., EU, Australia or other foreign areas except for Japan and its' effectiveness and safety have been confirmed.

J-SUPREME clinical trial is to intent to be conducted in Japan to evaluate the safety and effectiveness of Jetstream for the treatment of Japanese patients, which is a single arm clinical trial compared to the Performance Goal, because patients with lesions need to be treated with atherectomy device that sufficient revascularization cannot be expected from the PTA alone, can be a study population. [redacted]

Also, this trial defines at least one roll-in subject per site.

During the trial, ongoing dynamic data safety monitoring will be performed throughout the trial to minimize subject risk. All enrolled subjects receiving the study device will be followed for 1 year post index procedure.

9. Subject Selection

9.1. Study Population and Eligibility

Clinical and angiographic inclusion and exclusion criteria are included in Table9.2-1 and Table 9.3-1, respectively. Prior to enrollment, a subject must meet all of the clinical and angiographic inclusion criteria and none of the clinical and angiographic exclusion criteria.

9.2. Inclusion Criteria

Subjects who meet all of the following criteria (see Table 9.2-1) may be given consideration for inclusion in this clinical investigation, provided no exclusion criterion (see Section 9.3) is met.

Table 9.2-1: Inclusion Criteria

Inclusion Criteria	1. ≥20 years of age 2. An acceptable candidate for percutaneous intervention and/or emergency surgery. 3. Willing and able to provide consent before any study specific test or procedure is performed, signs the consent form, and agrees to attend all required follow-up visits 4. Chronic, symptomatic lower limb ischemia defined as Rutherford categories 2, 3 or 4 5. Stenotic, restenotic or occlusive lesion(s) located in the native SFA and/or PPA of which meet all of the following criteria: a. Calcified lesions* with degree of stenosis ≥70% by visual angiographic assessment or occlusions, regardless of degree of calcification. *Calcification needs to be in the segment 5mm proximal and 5mm distal to the stenotic lesion by visual estimate. b. Guidewire must cross lesion(s) within the true lumen, without a sub-intimal course by physician's discretion based on visual estimate c. Vessel diameter ≥3.0 mm and ≤6.0 mm by visual estimate d. Total lesion length (or series of lesions) ≤150mm by visual estimate e. Target lesion located at least 3 cm above the inferior edge of the femur by visual estimate 6. Patent infrapopliteal and popliteal artery, i.e., single vessel runoff or better with at least one of three vessels patent (<50% stenosis by visual estimate) to the ankle or foot with no planned intervention

[redacted]

9.3. Exclusion Criteria

Subjects who meet any one of the following criteria (Table 9.3-1) will be excluded from this clinical study.

Table 9.3-1: Exclusion Criteria

Exclusion Criteria	1. Target lesion must be one and decided by physician's discretion in the case that eligible lesions exist in both limbs 2. Target lesion/vessel with in-stent restenosis 3. Target lesion/vessel previously treated with drug-coated balloon <12 months prior to the procedure 4. Target lesion/vessel previously treated with any stent placement, atherectomy, laser or other debulking devices prior to the procedure 5. Subjects who have undergone surgery or endovascular of the SFA/PPA in the target vessel to treat atherosclerotic disease within 3 months prior to the index procedure 6. Use of drug-coated devices, atherectomy, laser or other debulking devices other than the Jetstream System, CTO devices or cutting balloon, Angioscore or similar devices in the target limb SFA/PPA during the index procedure 7. History of major amputation in the target limb 8. Subjects who have lesions requiring treatment and planned the treatment with commercial devices in a contralateral limb within 30 days after the index procedure 9. Subjects who had lesions treated with commercial devices in a contralateral limb within 7 days prior to the index procedure (Note: If subject had treatment of contralateral limb 8 days or earlier prior to the index procedure, the procedure success needs to be confirmed by physician's discretion) 10. Life expectancy less than 24 months due to other medical co-morbid condition(s) that could limit the subject's ability to participate in the clinical trial, limit the subject's compliance with the follow-up requirements, or impact the scientific integrity of the clinical trial 11. Known hypersensitivity or contraindication to contrast dye that, in the opinion of the investigator, cannot be adequately pre-medicated 12. Known hypersensitivity/allergy to the investigational atherectomy system or protocol related therapies (e.g., nitinol, stainless steel or other stent materials, and antiplatelet or anticoagulant, thrombolytic medications) 13. Subject has a history of coagulopathy or hypercoagulable bleeding disorder 14. Subject with untreatable hemorrhagic disease or platelet count <80,000mm^3 or >600,000mm^3 as baseline assessment. 15. Concomitant renal failure with a serum creatinine >2.0 mg/dL

	16. Receiving dialysis or immunosuppressant therapy 17. History of myocardial infarction, or stroke/cerebrovascular accident (CVA) within 6 months prior to study enrollment 18. Unstable angina pectoris at the time of the enrollment 19. Pregnancy and/or breast feeding 20. Current participation in another investigational drug or device clinical study that has not completed the primary endpoint at the time of enrollment or that clinically interferes with the current study endpoints (Note: studies requiring extended follow-up for products that were investigational, but have become commercially available since then are not considered investigational studies.) 21. Septicemia at the time of enrollment 22. Presence of other hemodynamically significant outflow lesions in the target limb requiring a planned surgical intervention or endovascular procedure within 30 days after the index procedure 23. Presence of aneurysm in the target vessel 24. Acute ischemia and/or acute thrombosis of the SFA/PPA prior to the index procedure 25. Perforated vessel as evidenced by extravasation of contrast media prior to the index procedure

[redacted]

10. Subject Accountability

10.1. Point of Enrollment

Once the subject has signed the IRB-approved study ICF, and has met all clinical inclusion and no clinical exclusion criteria, the subject will be considered eligible to be enrolled in the trial. If the subject is found to meet exclusion criteria during the angiographic eligibility assessment, the subject will be considered a screen failure and should not be enrolled or receive an investigational device, nor should the subject be followed post-procedure per protocol.

[redacted]

10.2. Withdrawal

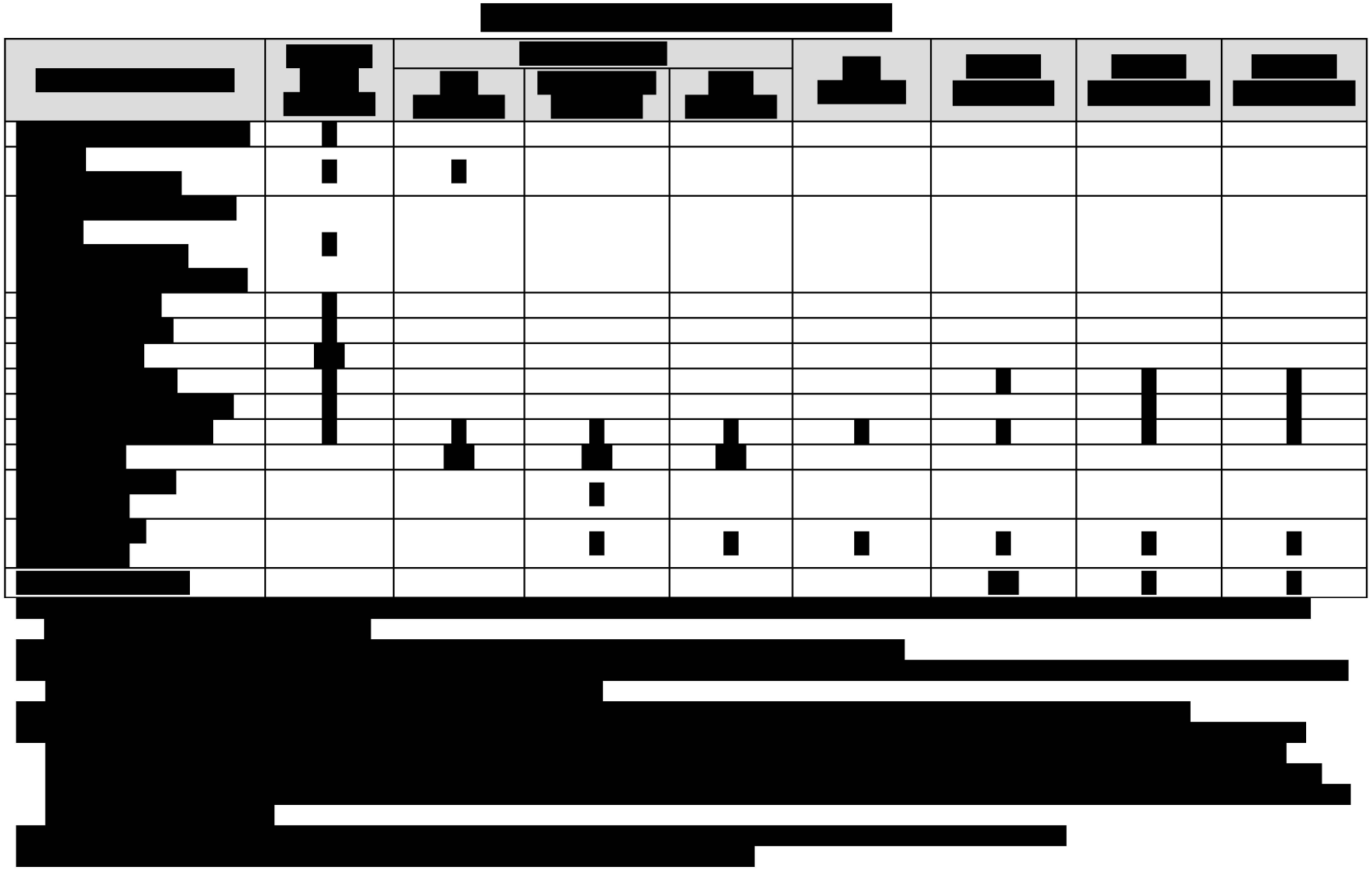
All subjects enrolled in the clinical study (including those withdrawn from the clinical study or lost to follow-up) shall be accounted for and documented.

While trial withdrawal is discouraged, subjects may choose to withdraw from the trial at any time, with or without reason and without prejudice to further treatment. Withdrawn subjects will not undergo any additional trial follow-up, nor will they be replaced (the justified sample size considers an estimated allowance for attrition). The reason for withdrawal will be recorded (if given) in all cases of withdrawal. The Investigator may discontinue a subject from participation in the trial if the Investigator feels that the subject can no longer fully comply with the requirements of the trial or if any of the trial procedures are deemed potentially harmful to the subject. Data that have already been collected on withdrawn subjects will be retained and used for analysis but no new data will be collected after withdrawal.

[redacted]

11. Study Methods

[redacted]



11.2. Study Candidate Screening

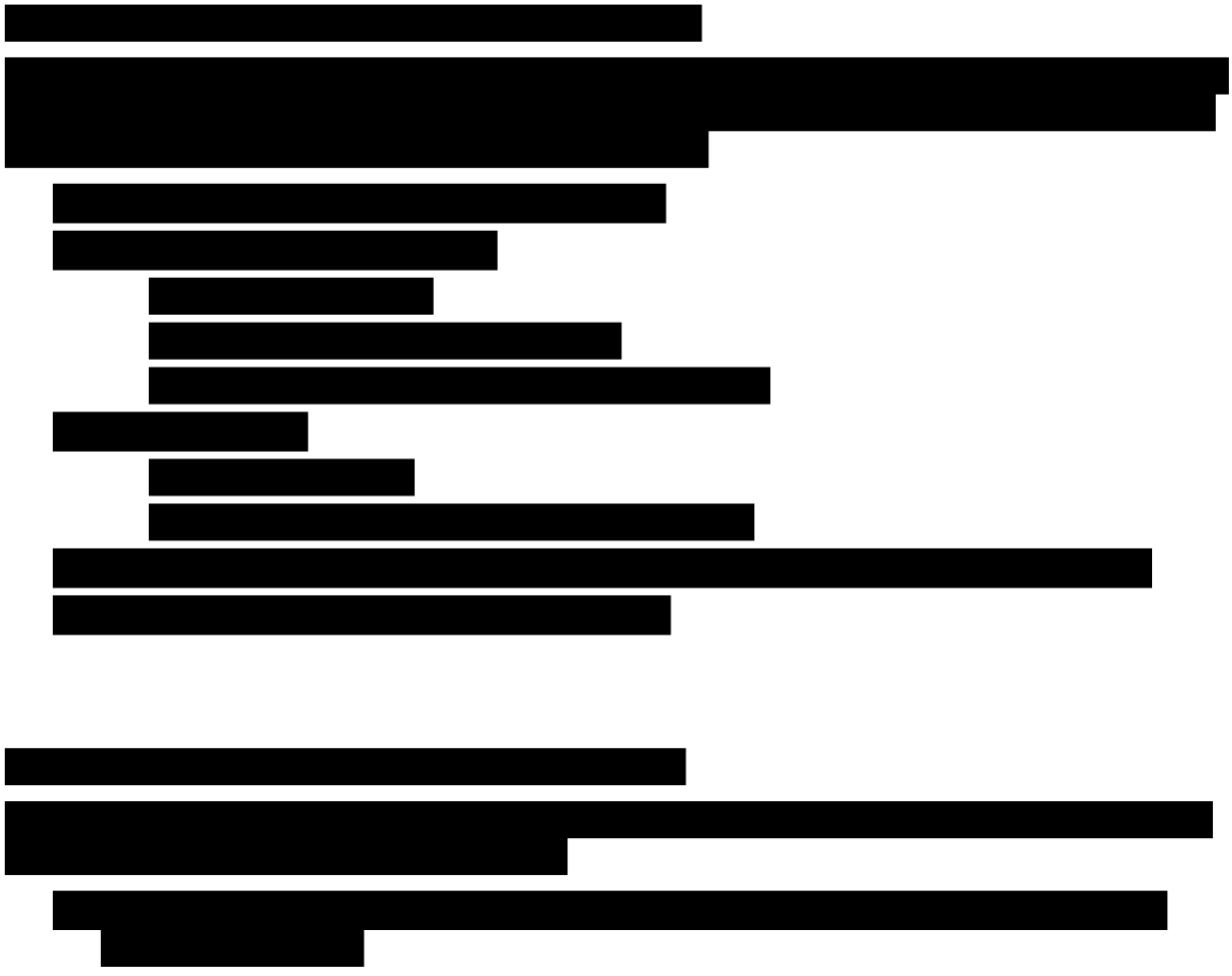
A Screening Log will be maintained by each investigational site to document selected information about subjects who fail to meet the J-SUPREME clinical trial eligibility criteria, including the reason for screen failure.

11.3. Informed Consent

Before any study specific tests or procedures are performed, subjects who meet the clinical eligibility criteria will be asked to sign the IRB-approved study ICF. Subjects must be given ample time to review the ICF and have questions answered before signing.

Study personnel should explain to the subject that even if the subject agrees to participate in the trial and signs the ICF, catheterization may demonstrate that the subject is not a suitable candidate for the trial.

Refer to section 10.1 for definition of point of enrollment.



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Jetstream

The DFU for the Jetstream System is provided in the Manual of Operations. Prior to use of the device, the treating physician must carefully read and be familiar with the entire DFU. The Jetstream DFU must be followed for performing the device.

Anticoagulant therapy should be consistent with the hospital standard of practice during the procedure.

[redacted]

It is important that trial site personnel review the trial requirements with the subject to maximize compliance with the follow-up schedule and required medication regimen as per standard local practice. It is also important that trial site personnel instruct subjects to return for follow-up assessments according to the data collection schedule in Table 11.1-1. Study staff should establish a date for the follow-up visit with the subject and if possible, schedule the visit at the time of hospital discharge.

[redacted]

11.12. Follow-up

All enrolled subjects who receive a treatment of Jetstream system will be evaluated prior to discharge from the index procedure and at 1 month, 6 months and 12 months after the index procedure.

[redacted]

Subjects requiring reintervention should be treated according to the Investigator's discretion and standard of care. These subjects should receive an approved, commercially available treatment (if appropriate).

Note: Follow-up angiograms and ultrasounds will not be required for any subject who underwent by-pass surgery of the target lesion during the 12 month follow-up timeframe.

[redacted]

Requirements of each follow-up evaluation are described below.

[redacted]

[redacted]

12. Statistical Considerations

This section describes statistical approaches to the roll-in subjects and the main cohorts of study. More details will be described in a separate statistical analysis plan.

12.1. Primary Endpoints

Data from roll-in subjects (each site will perform at least one roll-in case) will be summarized separately from the population for primary subjects. Roll-in subjects will not be included in the endpoint analyses below.

[redacted]

12.2. General Statistical Methods

12.2.1. Analysis Sets

The primary endpoints and additional endpoint / measurements will be analyzed on an Intent-To-Treat (ITT) and a Per-Protocol (PP) basis. All subjects who sign the written informed consent form (ICF) (see Section 21.) and are enrolled in the trial (see Section 10.1 for point of enrollment) will be included in the ITT analysis population, regardless of whether the test device is activated. For PP analysis, only subjects who are activated with the test device will be included in the analysis population. In this trial, those subjects enrolled after roll-in phase will be analyzed for endpoints.

[redacted]

12.2.2. Control of Systematic Error/Bias

All subjects who have met the inclusion/exclusion criteria and signed the ICF will be eligible for enrollment in the study. [redacted]

To control for inter-observer variability, data from independent core laboratories (see Section 13.3) / an Independent Medical Reviewer (IMR) (see Section 22.2) will be used for analysis. These include a core lab to assess Angio and DUS readings, and IMR events using standard procedures

[redacted]

[redacted]

12.3.2. Interim Analyses

No formal interim analyses are planned.

[redacted]

12.3.4. Justification of Pooling

Not applicable.

[redacted]

12.3.6. Other Analyses

Handling of dropouts and missing data will depend on their frequency and the nature of the outcome measure. Sensitivity analyses (e.g., tipping-point analysis) will be performed to assess the impact of subjects with inadequate follow-up (i.e., missing data) on the primary endpoint and to assess the robustness of the conclusion of the primary analysis. Statistical models that account for censored data will be employed in appropriate circumstances (e.g., for time-to-event outcomes). Suspected invalid data will be queried and corrected in the database prior to statistical analysis. Additional information may be found in the Statistical Analysis Plan.

12.3.7. Changes to Planned Analyses

Any changes to the planned statistical analyses described above made prior to performing the analyses will be documented in an amended Statistical Analysis Plan approved prior to performing the analyses. Changes from the planned statistical methods after performing the analyses will be documented in the clinical study report along with a reason for the deviation.

13. Data Management

13.1. Data Collection, Processing, and Review

Subject data will be recorded in a limited access secure electronic data capture (EDC) system.

The clinical database will reside on a production server hosted by EDC System. All changes made to the clinical data will be captured in an electronic audit trail and available for review by Boston Scientific Japan K.K. (BSJ) or its representative. The associated RAVE software and database have been designed to meet regulatory compliance for deployment as part of a validated system compliant with laws and regulations applicable to the conduct of clinical studies pertaining to the use of electronic records and signatures. Database backups are performed regularly.

The Investigator provides his/her electronic signature on the appropriate electronic case report forms (eCRFs) in compliance with local regulations. Changes to data previously submitted to the sponsor require a new electronic signature by the Investigator acknowledging and approving the changes.

Visual and/or electronic data review will be performed to identify possible data discrepancies. Manual and/or automatic queries will be created in the EDC system and will be issued to the site for appropriate response. Site staff will be responsible for resolving all queries in the database.

13.2. Data Retention

The Principal Investigator or his/her desginee and Investigational site will maintain all essential trial documents and source documents, in original format, that support the data collected on study patients in compliance with GCP guidelines. Documents must be retained for at least 3 years after the last approval of marketing application or the formal discontinuation of the clinical investigation of the device, whichever is longer.

When these documents no longer need to be maintained, it is BSJ's responsibility to inform the Investigator and Site. The Investigator and Site will take measures to ensure that these essential documents are not accidentally damaged or destroyed. If for any reason the Investigator and Site withdraw responsibility for maintaining these essential documents, custody must be transferred to an individual who will assume responsibility. BSJ must receive written notification of this custodial change.

BSJ must maintain necessary essential documents for 5 years from the date of the marketing application approval (or during the period of user-results evaluation, if applicable and if longer than 5 years) or until 3 years have elapsed since the formal discontinuation of the clinical investigation of the device, whichever is longer.

[redacted]

14. Amendments

If a protocol revision is necessary which affects the rights, safety or welfare of the subject or scientific integrity of the data, an amendment is required. Appropriate IRB approvals of the revised protocol must be obtained prior to implementation.

15. Deviations

An Investigator must not make any changes or deviate from this protocol, except to protect the life and physical well-being of a subject in an emergency. An investigator shall notify the sponsor and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency, and those deviations which affect the scientific integrity of the clinical investigation. Such notice shall be given as soon as possible, but no later than 5 working days after the emergency occurred.

All deviations from the investigational plan, with the reason for the deviation and the date of occurrence, must be documented and reported to the sponsor using EDC.

Deviations will be reviewed and evaluated on an ongoing basis and, as necessary, appropriate corrective and preventive actions (including notification, site re-training, or site discontinuation/termination) will be put into place by the sponsor.

16. Device/Equipment Accountability

The investigational devices/equipment shall be securely maintained, controlled, and used only in this clinical study.

BSJ shall keep records to document the physical location of all Jetstream investigational devices from shipment of investigational devices to the investigation sites until return or disposal.

The Principal Investigator or an authorized designee shall keep records documenting the receipt, use, return and disposal of the Jetstream investigational devices, which shall include the following:

- Date of receipt
- Identification of each investigational device (Lot number or unique code)
- Expiry date, as applicable
- Date of use
- Subject identification
- Date on which the investigational device was returned, if applicable
- Date of return (and number) of unused, expired, or malfunctioning investigational devices, if applicable.

Once the Investigator and Site are notified by BSJ that subject enrollment is complete, all unused test devices and/or accessories must be returned to BSJ.

17. Compliance

17.1. Statement of Compliance

The J-SUPREME clinical trial will be conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and that are consistent with Good Clinical Practices (GCP), Order for Enforcement of the Pharmaceutical and Medical Device Law, regulatory requirements and this protocol. The study shall not begin until the required approval from the IRB and/or favorable opinion from regulatory authority has been obtained, if appropriate. Any additional requirements imposed by the IRB or regulatory authority shall be followed, if appropriate

17.2. Investigator Responsibilities

The Principal Investigator of an investigational site is responsible for ensuring that the study is conducted in accordance with the Clinical Study Agreement, the clinical investigational plan, GCP, ethical principles that have their origins in the Declaration of Helsinki, any conditions of approval imposed by the reviewing IRB, and Pharmaceutical Affairs Law, Regulatory authority, whichever affords the greater protection to the subject.

The Principal Investigator's responsibilities include, but are not limited to, the following.

- Prior to beginning the study, confirm the Clinical Study Agreement and Protocol Signature page documenting his/her agreement to conduct the study in accordance with the protocol.
- The investigator(s) should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial.
- The investigator should be aware of, and should comply with, GCP.
- The investigator should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Kiki-gaiyosho, in the product information, and in other information sources provided by the sponsor.
- The investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authority(ies).
- The investigator should have sufficient time to properly conduct and complete the trial within the agreed trial period.
- The investigator should be able to demonstrate (e.g., based on retrospective data) a potential for recruiting the required number of suitable subjects within the agreed recruitment period.
- The investigator should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.
- Ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- Record, report, and assess (seriousness and relationship to the device/procedure) every adverse event as applicable per protocol and observed device deficiency.

- Report to sponsor, per the protocol requirements, all SAEs and device deficiencies that could have led to a SADE and potential/USADE.
- Report to the IRB and regulatory authorities any SAEs and device deficiencies that could have led to a SADE and potential/USADE., if required by the national regulations or this protocol or by the IRB, and supply BSJ with any additional requested information related to the safety reporting of a particular event.
- Inform the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required.
- Provide the subject with well-defined procedures for possible emergency situations related to the clinical study.
- Ensure that clinical medical records are clearly marked to indicate that the subject is enrolled in this clinical study.
- Make all reasonable efforts to ascertain the reason(s) for a subject's premature withdrawal from clinical investigation while fully respecting the subject's rights.

17.2.1. Delegation of Responsibility

When specific tasks are delegated by an investigator, including but not limited to conducting the informed consent process, the Principal Investigator is responsible for providing appropriate training and adequate supervision of those to whom tasks are delegated. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

17.3. Institutional Review Board

The written IRB approval of the protocol and Informed Consent Form, must be received by the sponsor before recruitment of subjects into the study and shipment of investigational products (test device and/ or accessory).

Annual IRB approval and renewals will be obtained throughout the duration of the study as required by IRB requirements. Copies of the Investigator's reports and/ or the IRB continuance of approval must be provided to the Sponsor.

17.4. Sponsor Responsibilities

The clinical trial organization in Japan, including investigational sites in Japan, is provided as an attachment to the protocol.

All information and data sent to BSJ and its authorized designee concerning subjects or their participation in this study will be considered confidential by BSJ. Only authorized BSJ personnel, representatives, or designees will have access to these confidential records. Authorized regulatory personnel have the right to inspect and copy all records pertinent to this study. Study data collected during this study may be used by BSJ for the purposes of this study, publication, and to support future research and/or other business purposes. Data used in the analysis and reporting of this study will not be identified by specific subject name.

Note: BSJ may utilize a contract research organization (CRO) or other contractors to act as its representative for carrying out designated tasks. Responsibilities for these entities are defined in the applicable contracts or agreements. Contact information for the CROs is provided as an attachment to the protocol or in the study Manual of Operations (MOP).

BSJ will keep subjects' identifiable health information confidential in accordance with all applicable Regulatory authority. BSJ may use subjects' health information to conduct this research, as well as for additional purposes, such as overseeing and improving the performance of its device, new medical research and proposals for developing new medical products or procedures, and other business purposes. Information received during the study will not be used to market to subjects; subject names will not be placed on any mailing lists or sold to anyone for marketing purposes.

17.5. Reimbursement and Compensation

Subject Reimbursement: Travel and other expenses incurred by subjects as a result of participation in the study will be reimbursed in accordance with pertinent Regulations and per the investigational sites.

Compensation for Subject's Health Injury: BSJ will stipulate an insurance policy to cover potential health injury for study subjects. If any study related health injury occurs and a site is held responsible for its compensation, BSJ will assume the responsibility, except in the case those damages are incurred due to intentional misconduct or negligence at the site.

18. Monitoring

Monitoring will be performed during the study according to the monitoring plan to assess continued compliance with the protocol and applicable regulations. In addition, the clinical research monitor verifies that study records are adequately maintained, that data are reported in a satisfactory manner with respect to timeliness, adequacy, and accuracy, and that the Investigator continues to have sufficient staff and facilities to conduct the study safely and effectively.

For the J-SUPREME trial, source documents include, at a minimum but are not limited to, the ICF; patient medical records, including nursing records and catheterization laboratory records; diagnostic imaging records; laboratory results; reports of SAEs; and device accountability logs. Data documented in the eCRF relevant to device deficiencies, relationship of AE to study device(s), index procedure, antiplatelet medication; and the anticipated assessment of ADEs, may be considered source data for the study.

The Investigator/institution guarantees direct access to original source documents by BSJ personnel, CRO or other contractors, and appropriate regulatory authorities. In the event that the original medical records cannot be obtained for a subject that is seen by a non-study physician at a non-study institution, all reasonable attempts must be made to obtain photocopies of the original source documents for review. Photocopies of original source documents related to IMR events that are adjudicated by the IMR (from either the study site or a non-study institution, if applicable) must also be made available for submission to the sponsor Safety Group.

The study may also be subject to a quality assurance audit by BSJ, CRO or other contractors, as well as inspection by appropriate regulatory authorities. It is important that the Investigator and relevant study personnel are available during on-site monitoring visits or audits and that sufficient time is devoted to the process.

19.2. Risks associated with Participation in the Clinical Study

There may be additional risks linked to the procedure, and follow-up testing which are unforeseen at this time. All testing planned for the follow-up period is standard of care.

19.3. Possible Interactions with Concomitant Medical Treatments

Antiplatelet therapy is required during at least the first 6 months consistent with current local requirements of the investigational site. Refer to the local package insert for further information on drug interactions and side effects associated with antithrombotic/antiplatelet medications.

19.4. Risk Minimization Actions

Additional risks may exist. Risks can be minimized through compliance with this protocol, performing procedures in the appropriate hospital environment, adherence to subject selection criteria, close monitoring of the subject's physiologic status during research procedures and/or follow-ups and by promptly supplying BSJ with all pertinent information required by this protocol.

19.5. Anticipated Benefits

Potential anticipated benefits include the improvement of procedural success of atherosclerotic SFA/PPA lesions with improvement in the symptoms of disease. However, the Jetstream system is an investigational device and these potential benefits may or may not actually be present.

19.6. Risk to Benefit Rationale

The Jetstream system is expected to be suitable for its intended purpose. There are no unacceptable residual risks/intolerable risks and all applicable risks have been addressed through the provision of appropriate Directions for Use (DFU) and Kiki-Gaiyosho. Evaluation of the risks and benefits that are expected to be associated with the use of the Jetstream system demonstrate that when used under the conditions intended, the benefits associated with the use of the Jetstream system should outweigh the risks in Japan.

20. Safety Reporting

20.1. Reportable Events by investigational site to Boston Scientific

It is the responsibility of the investigator to assess and report to BSJ any event which occurs in any of following categories:

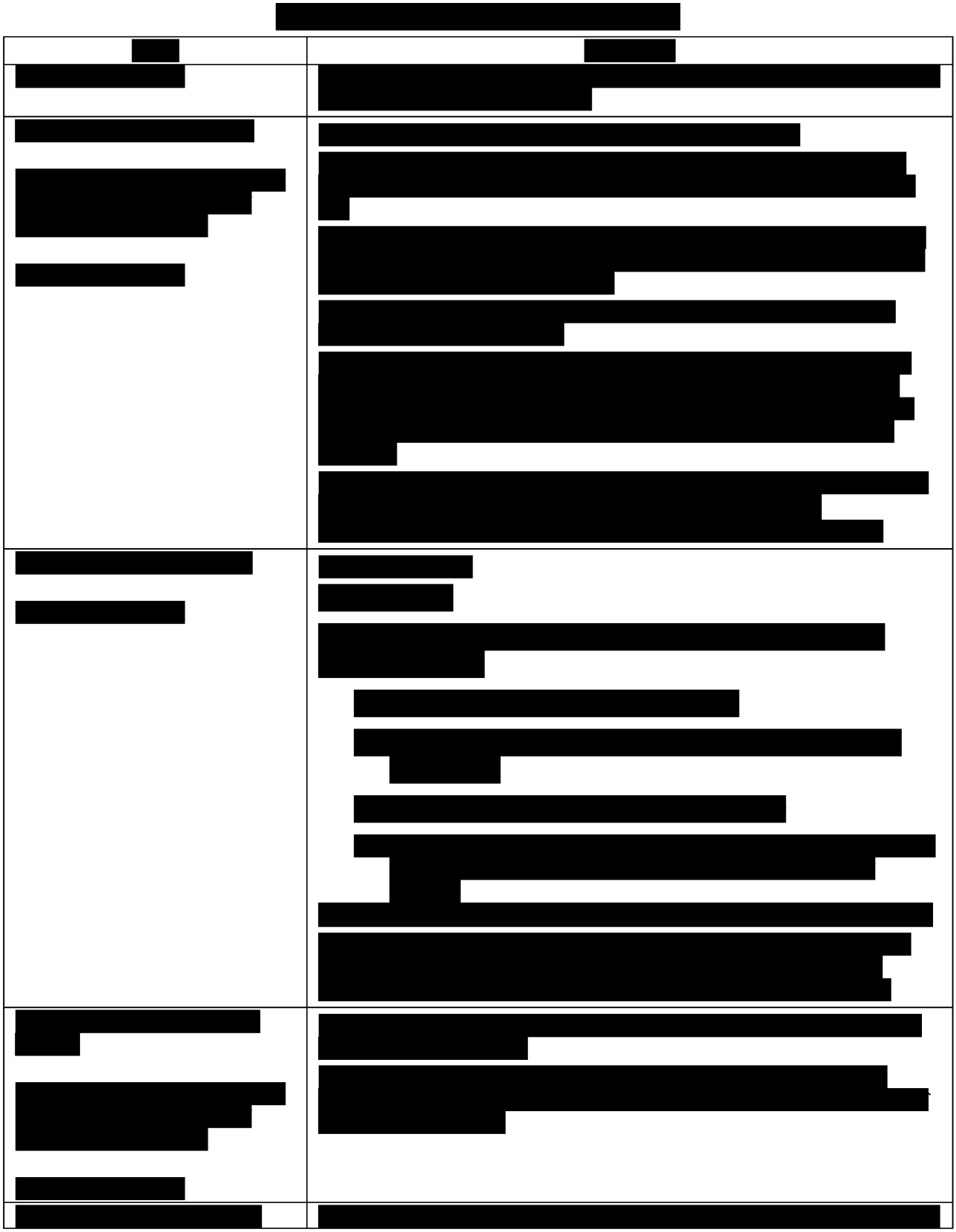
- All Serious Adverse Events
- All Investigational Device Deficiencies
- Unanticipated Serious Adverse Device Effects
- New findings/updates in relation to already reported events

When possible, the medical diagnosis should be reported as the Event Term instead of individual symptoms.

If it is unclear whether or not an event fits one of the above categories, or if the event cannot be isolated from the device or procedure, it should be submitted as an adverse event and/or device deficiency.

Any AE event required by the protocol, experienced by the study subject after informed consent and once considered enrolled in the study (as defined in study subject classification section), whether during or subsequent to the procedure, must be recorded in the eCRF.

Refer to Section 19 for the known risks associated with the study.



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20.5. Boston Scientific Device Deficiencies

All investigational device deficiencies (including but not limited to failures, malfunctions, use errors, product nonconformities, and inadequacy in the information supplied by the

manufacturer) will be documented and reported to BSC. If possible, the device(s) should be returned to BSC for analysis. Instructions for returning the investigational device(s) will be provided in the Manual of Operations. If it is not possible to return the device, the investigator should document why the device was not returned and the final disposition of the device. Device failures and malfunctions should also be documented in the subject's medical record.

Device deficiencies (including but not limited to failures, malfunctions, and product nonconformities) are not to be reported as adverse events. However, if there is an adverse event that results from a device failure or malfunction, would be recorded as an adverse event on the appropriate eCRF.

Any Investigational Device Deficiency that might have led to a SAE if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate is considered a reportable event.

20.6. Reporting to Regulatory Authorities / IRBs / Investigators

BSJ will report to regulatory agency and notify all PIs and head of the investigational sites if any significant safety information was received. Additionally, information which implies possible influence to patient's safety and the conduct of the study will also notified to all PIs and the head of the investigational sites.

21. Informed Consent

Subject participation in this clinical study is voluntary. Informed Consent is required from each subject. The Investigator is responsible for ensuring that Informed Consent is obtained prior to the use of any investigational devices, study-required procedures and/or testing, or data collection.

The obtaining and documentation of Informed Consent must be in accordance with the ethical principles that have their origins in the Declaration of Helsinki and that are consistent with Good Clinical Practices (GCP), Pharmaceutical Affairs Law, regulatory authority and this protocol. The ICF must be accepted by BSJ or its delegate (e.g. CRO), and approved by the site's IRB, or central IRB, if applicable.

Boston Scientific Japan K.K. will provide a study-specific template of the ICF to investigators participating in this study. The ICF template may be modified to meet the requirements of the investigative site's IRB. Any modification requires acceptance from BSJ prior to use of the form. The ICF must be in a language understandable to the subject and if needed. Privacy language shall be included in the body of the form or as a separate form as applicable.

The process of obtaining Informed Consent shall at a minimum include the following steps, as well as any other steps required by applicable laws, rules, regulations and guidelines:

- be conducted by the Principal Investigator or designee authorized to conduct the process,
- include a description of all aspects of the clinical study that are relevant to the subject's decision to participate throughout the clinical study,
- avoid any coercion of or undue influence of subjects to participate,

- not waive or appear to waive subject's legal rights,
- use native language that is non-technical and understandable to the subject,
- provide ample time for the subject to consider participation and ask questions if necessary,
- ensure important new information is provided to new and existing subjects throughout the clinical study.

The ICF shall always be signed and personally dated by the subject to sign the ICF under the applicable laws, rules, regulations and guidelines and by the investigator and/or an authorized designee responsible for conducting the informed consent process. If a legal representative signs, the subject shall be asked to provide informed consent for continued participation as soon as his/her medical condition allows. The original signed ICF will be retained by the site and a copy of the signed and dated document and any other written information must be given to the person signing the form. Informed Consent signature can be replaced by printed name and seals of appropriate individuals.

If new information becomes available that can significantly affect a subject's future health and medical care, that information shall be provided to the affected subject(s) in written form via a revised ICF or, in some situations, enrolled subjects may be requested to sign and date an addendum to the ICF. In addition to new significant information during the course of a study, other situations may necessitate revision of the ICF, such as if there are amendments to the applicable laws, protocol, a change in Principal Investigator, administrative changes, or following annual review by the IRB. The new version of the ICF must be approved by the IRB. Acceptance by Boston Scientific Japan K.K. is required if changes to the revised ICF are requested by the site's IRB. The IRB will determine the subject population to be re-consented.

Study personnel should explain to the subject that even if the subject agrees to participate in the trial and signs the ICF, catheterization may demonstrate that the subject is not a suitable candidate for the trial. A Screening Log will be maintained by the investigational site to document select information about candidates who fail to meet the trial eligibility criteria, including, but not limited to, the reason for screen failure.

22. Committees

22.1. Executive Committee

An Executive Committee composed of BSC/BSJ Clinical Management and selected Coordinating Principal Investigator(s) will be convened. This committee will be responsible for the overall conduct of the study which will include protocol development, study progress, subject safety, overall data quality and integrity, and timely dissemination of study results through appropriate scientific sessions and publications. As appropriate the Executive Committee may request participation of J-SUPREME clinical trial Investigators on the committee.

[redacted]

23. Suspension or Termination

23.1. Premature Termination of the Study

Boston Scientific Japan K.K. reserves the right to terminate or discontinue the study at any stage but intends to exercise this right only for valid scientific or administrative reasons and reasons related to protection of subjects. Investigators, associated IRBs, and regulatory authorities, as applicable, will be notified in writing in the event of study termination or discontinuation.

23.1.1. Criteria for Premature Termination of the Study

Possible reasons for premature study termination include, but are not limited to, the following.

- The occurrence of unanticipated adverse device effects that present a significant or unreasonable risk to subjects enrolled in the study.
- An enrollment rate far below expectation that prejudices the conclusion of the study.
- A decision on the part of Boston Scientific Japan K.K. to suspend or discontinue development of the device.

23.2. Termination of Study Participation by the Investigator or Withdrawal of IRB Approval

Any investigator or IRBs in the J-SUPREME clinical trial may discontinue participation in the study or withdrawal approval of the study, respectively, with suitable written notice to BSJ. Investigators, associated IRBs, and regulatory authorities, as applicable, will be notified in writing in the event of these occurrences.

24. Publication Policy

BSJ requires disclosure of its involvement as a sponsor or financial supporter in any publication or presentation relating to a BSJ study or its results. BSJ will submit study results for publication (regardless of study outcome) in a timely manner. Boston Scientific Corporation follows authorship principals as set forth in the Uniform Requirements of the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org). In order to ensure the public disclosure of study results in a timely manner, while maintaining an unbiased presentation of study

outcomes, BSC personnel may assist authors and investigators in publication preparation provided the following guidelines are followed.

- All authorship and contributorship requirements as described above must be followed.
- BSJ involvement in the publication preparation and the BSC Publication Policy should be discussed with the Coordinating Principal Investigator(s) at the onset of the project.
- The First and Senior authors are the primary drivers of decisions regarding publication content, review, approval, and submission.

[redacted]

26. Abbreviations and Definitions

26.1. Abbreviations

Abbreviations are shown in Table 26.1-1.

Table 26.1-1: Abbreviations

Abbreviation	Terminology
ABI	Ankle Brachial Index
ADE	Adverse Device Effect
AE	Adverse Event
BSC	Boston Scientific Corporation
BSJ	Boston Scientific Japan K.K.
CE	Conformité Européenne (meaning European Conformity)
CIN	Contrast-Induced Nephropathy
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organization

Table 26.1-1: Abbreviations

Abbreviation	Terminology
CVA	Cerebrovascular Accident
DFU	Directions for Use
DUS	Duplex Ultrasound
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EVT	Endovascular Therapy
GCP	Good Clinical Practice
HCP	Health Care Professional
ICF	Informed Consent Form
ICMJE	International Committee of Medical Journal Editors
ICH	International Conference on Harmonisation
IMR	Independent Medical Reviewer
ITT	Intent to Treat
IRB	Institutional Review Board
IVUS	Intravascular Ultrasound
MAE	Major Adverse Event
OPC	Objective Performance Criteria
PAO	Peripheral arterial disease
PG	Performance Goal
PMDA	Pharmaceutical Medical Device Agency
PPA	Proximal Popliteal Artery
PSVR	Peak Systolic Velocity Ratio
PTA	Percutaneous Transluminal Angioplasty

Table 26.1-1: Abbreviations

Abbreviation	Terminology
QA	Quantitative Angiography
QOL	Quality of Life
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SC	Single Cutter
SFA	Superficial Femoral Artery
TASC	Transatlantic Inter-Societal Concensus
TBI	Tibial Brachial Index
TLR	Target Lesion Revascularization
TVR	Target Vessel Revascularization
USADE	Unanticipated Serious Adverse Device Effect
UPN	Universal Product Number
XC	Expandable Cutter

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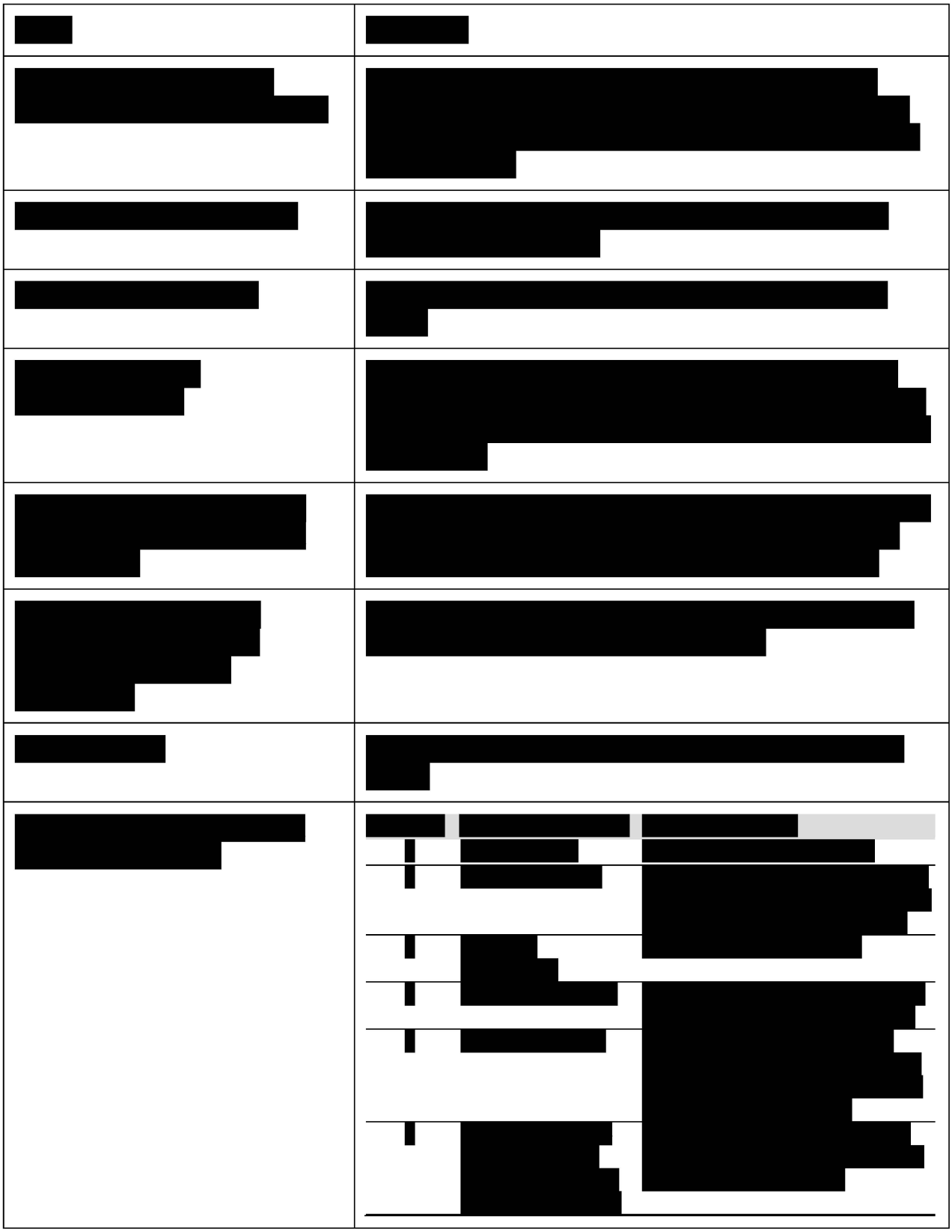

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