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Instructions for Use Notice

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Instructions for Use

SELUTION SLR™ 014 PTCA Drug-Eluting Balloon

Sustained Limus Release Drug-Eluting PTCA Balloon Catheter

Table of Contents

1	PRODUCT DESCRIPTION	4
1.1	Catheter Description	4
1.2	Drug Coating Description	5
2	INTENDED USE / INDICATIONS FOR USE	5
3	CONTRAINDICATIONS	5
4	WARNINGS	5
5	PRECAUTIONS	6
5.1	General Precautions	6
5.2	Use in Special Populations	6
5.2.1	Pregnancy	6
5.2.2	Lactation	6
5.2.3	Sex	6
5.2.4	Race and Ethnicity	7
5.2.5	Pediatric Use	7
5.2.6	Geriatric Use	7
5.3	Lesion/Vessel Characteristics	7
6	DRUG INFORMATION	7
6.1	Mechanism of Action	7
6.2	Metabolism	7
6.3	Pharmacokinetics	7
6.4	Drug Interactions	7
6.5	Carcinogenicity, Genotoxicity, and Reproductive Toxicity	7
7	POTENTIAL ADVERSE EVENTS	8
8	HOW SUPPLIED	9
9	DIRECTIONS FOR USE	9
10	INFORMATION TO BRIEF THE PATIENT	11
11	DISCLAIMER OF WARRANTY	11
12	SELUTION4ISR CLINICAL STUDY	12
12.1	Objective	12
12.2	Study Design	12
12.3	Demographics	12
12.4	Lesion Characteristics	13
12.5	Procedural Characteristics	14
12.6	Primary Endpoint Results	16
12.7	Hypothesis-Driven Secondary Endpoint Results	17
12.8	Additional Secondary Endpoint Results	17
12.9	Serious Adverse Effects (SAEs)	19
12.10	Primary Endpoint Subgroup Analyses	20
12.11	Post-Hoc Analysis of TLF of the SELUTION SLR PTCA DEB vs Subgroups of SOC and in 1 and 2 Stent Layers	22
12.12	Imaging (Angiographic and Optical Coherence Tomography (OCT)) Sub-Study Results	23
12.13	Clinical Pharmacokinetics (PK)	23
	PRODUCT SIZE MATRIX	25

SELUTION SLR™ 014 PTCA Drug-Eluting Balloon

Sustained Limus Release Drug-Eluting PTCA Balloon Catheter

Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.
STERILE. Sterilized using E-beam radiation. Nonpyrogenic

1 PRODUCT DESCRIPTION

The **SELUTION SLR™ 014 PTCA Drug-Eluting Balloon (SELUTION SLR™ PTCA DEB)** is a rapid exchange (RX) Drug-Eluting Balloon (DEB) catheter. The **SELUTION SLR** balloon coating is a proprietary formulation composed of the drug sirolimus and various excipients. The catheter mechanically dilates the vessel lumen and improves myocardial perfusion via Percutaneous Transluminal Coronary Angioplasty (PTCA), while the drug is intended to decrease the incidence of restenosis. The **SELUTION SLR PTCA DEB** device characteristics are provided in **Table 1**.

Table 1: SELUTION SLR PTCA DEB Device Component Characteristics

Catheter Design	Rapid Exchange (RX) PTCA
Usable Catheter Length	140 cm
Nominal Pressure	6 ATM
Rated Burst Pressure (RBP)	14 ATM
Guide Catheter Compatibility (minimum size)	2.25 to 4.00 mm Diameters: 5F 4.50 mm Diameters: 6F
Guidewire Compatibility	Compatible with 0.014-inch (0.36 mm) guidewire diameter
Drug Component	Active Pharmaceutical Ingredient: Sirolimus (1.0 µg/mm ² dose density) Excipients: Poly (lactic-co-glycolic acid) or PLGA, lipid blend
Lubricious Hydrophilic Coating	Covering 18-21 cm of the distal catheter shaft, 10 ± 5 mm from the balloon proximal bond to 4 cm away from RX Port

1.1 Catheter Description

The **SELUTION SLR PTCA DEB** is a semi-compliant percutaneous transluminal coronary angioplasty (PTCA) catheter composed of an expandable balloon at the distal end and a shaft with a port at the proximal end. The catheter has a Rapid Exchange (RX) construction where the distal end has a coaxial dual lumen design. The outer lumen is used for inflation of the balloon to conform to the vessel wall, and the inner lumen permits the use of a 0.014" guidewire to facilitate advancement of the catheter. The semi-compliant balloon is designed to provide an inflatable segment of known diameter and length at recommended pressures. The balloon has two radiopaque markers that indicate the balloon working length and aid in the positioning of the balloon relative to the stenosis. The catheter tip is tapered to facilitate advancement of the catheter to the treatment area and through the stenosis. The proximal shaft consists of a stainless steel hypotube and is marked with exit markers. 18-21 cm of the distal shaft is coated with a hydrophilic coating for lubricity. **Figure 1** shows a schematic drawing of the **SELUTION SLR PTCA DEB**.

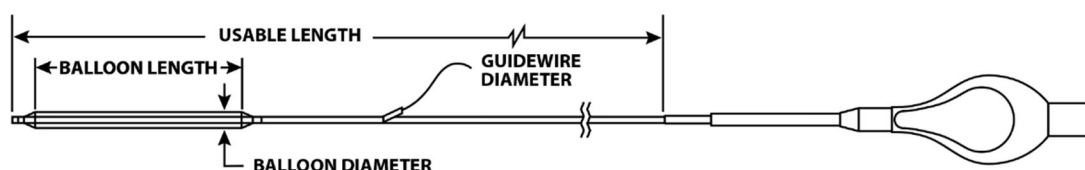


Figure 1: SELUTION SLR PTCA Drug-Eluting Balloon Catheter

The **SELUTION SLR PTCA DEB** catheter is available in a range of balloon sizes. Refer to the **PRODUCT SIZE MATRIX**. Nominal balloon diameters and lengths are printed on the strain relief that is bonded to the luer. Each device is packaged with a disposable protective sheath over the balloon and a disposable wire stylet in the distal lumen, both of which must be removed prior to use.

1.2 Drug Coating Description

The **SELUTION SLR** drug coating is applied to the surface of the angioplasty balloon and consists of the active pharmaceutical ingredient sirolimus, poly(lactic-co-glycolic acid) or PLGA, and a proprietary blend of lipid-based excipients. Sirolimus has a nominal dose density of 1.0 µg/mm². The nominal drug content per balloon size is shown in **Table 2** below.

Table 2: Nominal sirolimus content (µg) per balloon size

Balloon Diameter (mm)	Drug Content by Balloon Length (mm)			
	15	20	25	30
2.25	106	141	177	212
2.50	118	157	196	236
2.75	130	173	216	259
3.00	141	188	236	283
3.25	153	204	255	306
3.50	165	220	275	330
4.00	188	251	314	377
4.50	212	283	353	424

Sirolimus:

The drug coating on the balloon surface of the SELUTION SLR PTCA DEB is a proprietary formulation, consisting of sirolimus as the Active Pharmaceutical Ingredient (API).

The systematic (IUPAC) name of sirolimus is:

(3S,6R,7E,9R,10R,12R,14S,15E,17E,19E,21S,23S,26R,27R,34aS)-9,10,12,13,14,21,22,23,24,25,26, 27,32,33,34,34a-hexadecahydro-9,27-dihydroxy-3-[(1R)-2-[(1S,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethyl]-10,21-dimethoxy-6,8,12,14,20,26-hexamethyl-23,27-epoxy-3H-pyrido[2,1-C][1,4]-oxaazacyclohentacontine-1,5,11,28,29 (4H,6H,31H)-pentone.

Excipient Blend:

The first excipient is a biodegradable polymer poly(lactic-co-glycolic acid) or (PLGA) that is combined with sirolimus to form micro-reservoirs which regulate drug release via matrix degradation. The remaining excipient is a three-lipid system comprising a PEG-lipid, a structural phosphatidylcholine, and a cholesterol derivative, combined in a proprietary molar ratio which aims to reduce drug coating wash off in the bloodstream during insertion, tracking, and lesion crossing, optimize drug transfer to the tissue during balloon dilatation, and help adhere the microspheres to the surrounding tissue post-delivery.

2 INTENDED USE / INDICATIONS FOR USE

The **SELUTION SLR™ 014 PTCA Drug-Eluting Balloon** is intended to be used after appropriate vessel preparation in patients undergoing percutaneous coronary intervention (PCI) in coronary arteries 2.25 mm to 4.50 mm in diameter and lesions ≤ 26 mm in length for the purpose of improving myocardial perfusion when treating in-stent restenosis (ISR).

3 CONTRAINDICATIONS

The **SELUTION SLR™ 014 PTCA Drug-Eluting Balloon** is contraindicated for use in:

- Patients with known allergies or hypersensitivities to sirolimus (or analogs).
- Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy.
- The supra-aortic and cerebrovascular arteries
- Patients with unprotected native left main coronary artery disease
- Patients with coronary artery spasms in the absence of a significant stenosis
- Pregnant or breast-feeding women or women who are intending to become pregnant, or men intending to father children.

4 WARNINGS

When using this type of device, the following warnings should be observed:

- Contents are supplied STERILE using an E-beam irradiation sterilization process. DO NOT USE if the sterile barrier is damaged or opened prior to intended use.
- DO NOT USE **SELUTION SLR PTCA DEB** after the labeled "Use By" date.
- Use the recommended balloon inflation medium (50:50 mixture of contrast medium and sterile saline solution). Never use air or any gaseous medium to inflate the balloon.
- Do not advance or withdraw the catheter unless the drug-eluting balloon is fully deflated under vacuum.
- If unusual resistance is felt during manipulation, determine the cause of the resistance before proceeding. If the source of resistance cannot be determined, it is recommended to extract the entire system (as a unit) with the guide catheter.
- DO NOT EXCEED the Rated Burst Pressure (RBP) recommended for this device. Balloon rupture may occur if the RBP rating is exceeded. To prevent over-pressurization, use of a pressure-monitoring device is recommended.
- Once inflation has begun, do not move or reposition the **SELUTION SLR PTCA DEB**.
- Each **SELUTION SLR PTCA DEB** is intended for a single inflation only.

- To reduce the potential for vessel damage, the inflated diameter and length of the balloon should approximate the diameter and length of the vessel just proximal and distal to the stenosis.
- As for all PCI procedures, use in patients who are not acceptable candidates for open heart surgery requires careful consideration, including possible hemodynamic support during the procedure, as treatment of this patient population carries special risk.

5 PRECAUTIONS

5.1 General Precautions

- For single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.
- Based on the results of the SELUTION4ISR study, the use of the **SELUTION SLR PTCA DEB** may be most appropriate where additional stent implantation is considered undesirable or not feasible (see **Section 12 SELUTION4ISR CLINICAL STUDY**).
- The **SELUTION SLR PTCA DEB** should only be used by physicians appropriately trained in PTCA procedures.
- Do not expose **SELUTION SLR PTCA DEB** to organic solvents such as alcohol.
- As for all PCI procedures, the need for on-site surgical backup should be considered.
- Use caution in patients who have severe reaction to contrast agents that cannot be adequately pre-medicated.
- Never advance the drug-coated balloon catheter without the guidewire extending from the tip. Do not use the **SELUTION SLR PTCA DEB** if the lesion is unable to be crossed with a guidewire.
- Significant stenosis (> 50 %) proximal to the treatment site should be pretreated.
- The **SELUTION SLR PTCA DEB** is indicated for lesions up to 26 mm. The safety and effectiveness of treating lesions longer than 26 mm has not been established.
- The treatment site should be adequately prepared (intravascular imaging guidance recommended) to achieve the maximum lumen diameter prior to treatment with the **SELUTION SLR PTCA DEB**.
- Excessive handling or contact with liquids to the drug coating should be avoided as the coating may be susceptible to premature drug release or catheter damage. Do not touch the drug-eluting balloon.
- The balloon protective sheath and disposable wire stylet must stay in place during preparation of the **SELUTION SLR PTCA DEB** and not be removed until just prior to flushing with saline and placing the device over the guidewire.
- Remove the balloon protective sheath distally and discard. If difficulty is encountered while removing the balloon protective sheath, a new **SELUTION SLR PTCA DEB** must be utilized.
- During insertion, do not over-tighten the hemostasis valve around the **SELUTION SLR PTCA DEB** shaft as lumen constriction may occur, affecting inflation/deflation of the balloon.
- Use direct fluoroscopic visualization when advancing the balloon catheter over the guidewire, positioning it in the lesion to be treated, and during balloon inflation.
- Do not use the **SELUTION SLR PTCA DEB** if the shaft has been bent or kinked.
- The safety and effectiveness of using more than one **SELUTION SLR PTCA DEB** to treat a single lesion or multiple lesions/vessels per procedure has not been established.
- Do not use a second drug-eluting balloon at the same treatment site.
- Whenever possible, the **SELUTION SLR PTCA DEB** should be the final treatment of the vessel.
- After use, the **SELUTION SLR PTCA DEB** is a biohazard. Handle and dispose of all such devices in accordance with accepted medical practice and applicable hospital, administrative, and government regulations.
- The optimal duration of dual anti-platelet therapy (DAPT) post PCI for ISR is currently unknown. The 2023 SCAI Expert Consensus has suggested that DAPT should be used for a minimum of one month post ISR PCI. While the SELUTION4ISR Study required that enrolled subjects receive a minimum of 1-month of DAPT, more than 60% of patients remained on DAPT for at least 1 year. In conjunction with this information, operators should use clinical judgment in deciding on the duration of DAPT following use of the **SELUTION SLR PTCA DEB**.

5.2 Use in Special Populations

5.2.1 Pregnancy

The **SELUTION SLR PTCA DEB** has not been tested in pregnant women or in men intending to father children. Effects on the developing fetus have not been studied. Effective contraception should be initiated prior to use of the **SELUTION SLR PTCA DEB** and continued for one year after implantation. While there is no contraindication, the risks and reproductive effects are unknown at this time. See Pregnancy section in **Section 6.5 Carcinogenicity, Genotoxicity, and Reproductive Toxicity**.

5.2.2 Lactation

A decision should be made whether to discontinue nursing prior to use of the **SELUTION SLR PTCA DEB** considering the importance of this treatment for the mother. See Lactation Section in Drug Information Section below.

5.2.3 Sex

See **Section 12 SELUTION4ISR CLINICAL STUDY**. The clinical study was not powered to study safety or effectiveness of the **SELUTION SLR PTCA DEB** in sex-specific subgroups; however, sub-group analyses were performed to explore differences in outcomes between sexes. The clinical study demonstrated that there was no difference in 12-month clinical outcomes (primary endpoint of target lesion failure) between sexes.

5.2.4 Race and Ethnicity

See **Section 12 SELUTION4ISR CLINICAL STUDY**. Race information was not collected in the clinical study and the race of patients treated with the SELUTION SLR PTCA DEB is unknown. Ethnicity information in the form of “Hispanic or Latino” and “Not Hispanic or Latino” information was collected for patients in the clinical study. The clinical study was not powered to study safety or effectiveness of the SELUTION SLR PTCA DEB in these ethnic-specific subgroups; however, sub-group analyses were performed to explore differences in outcomes between ethnicities. The clinical study demonstrated that there was no difference in 12-month clinical outcomes (primary endpoint of target lesion failure) between ethnicities.

5.2.5 Pediatric Use

The safety and effectiveness of the **SELUTION SLR PTCA DEB** in pediatric patients has not been established.

5.2.6 Geriatric Use

Clinical studies of the SELUTION SLR PTCA DEB, summarized in **Section 12 SELUTION4ISR CLINICAL STUDY**, did not have an upper age limit. Among the 197 patients treated with the SELUTION SLR PTCA DEB in the Per-Protocol (PP) analysis population of the SELUTION4ISR randomized controlled study, 42 patients were older than age 75. A sub-group analysis of patients treated with the SELUTION SLR PTCA DEB showed no difference in 12-month clinical outcomes (primary endpoint of target lesion failure) between patients age 75 or younger and those older than age 75.

5.3 Lesion/Vessel Characteristics

The safety and effectiveness of the **SELUTION SLR PTCA DEB** have not been established in the cerebral, carotid, supra-aortic, or peripheral vasculature or in the following lesions/vessel types:

- De novo coronary artery lesions
- Thrombus at the lesion site
- Lesions with reference vessel diameters <2.25 mm or >4.50 mm
- Calcified vessels
- Lesions located in the left main coronary artery
- Chronic total occlusions
- Lesions located within bypass grafts

6 DRUG INFORMATION

6.1 Mechanism of Action

Sirolimus is a macrocyclic lactone produced by the bacteria *Streptomyces hygroscopicus*. It is known that sirolimus inhibits T and B-lymphocyte activation and smooth muscle and endothelial cell proliferation in response to cytokine and growth factor stimulation. In cells, sirolimus binds to the immunophilin, FK Binding Protein-12 (FKBP-12). The sirolimus-FKBP-12 complex binds to and inhibits activity of the mechanistic Target of Rapamycin (mTOR). mTOR is a serine/threonine protein kinase that regulates cell growth, cell proliferation, cell motility, cell survival, protein synthesis, autophagy, and transcription. Inhibition of mTOR stops cell cycle progression from the G1 to the S phase.

6.2 Metabolism

Sirolimus is extensively metabolized by the hepatic CYP3A4 enzyme and is also a substrate for the P-glycoprotein (P-gp) transmembrane efflux pump found in the intestinal epithelium, liver cells, proximal tubule of the kidney and capillary endothelial cells. Clearance of sirolimus is affected by both of these pathways and displays a large inter-patient variability. The majority of metabolites, including demethyl and hydroxydemethyl sirolimus are formed via O-demethylation and hydroxylation. Sirolimus is the major component in human whole blood and contributes to more than 90% of the immunosuppressive activity. The metabolites account for less than 10% of the immunosuppressant activity of sirolimus. Biliary and fecal pathways serve as the primary routes of sirolimus elimination. The half-life of sirolimus ranges from 57 to 63 hours in the bloodstream.

6.3 Pharmacokinetics

Sirolimus Pharmacokinetics (PK) eluted from the **SELUTION SLR PTCA DEB** has been evaluated in a non-randomized sub-study of the SELUTION De Novo Trial, which included both ISR and De Novo Subjects. Whole blood sirolimus PK parameters determined from patients receiving the **SELUTION SLR PTCA DEB** are provided in **Section 12 SELUTION4ISR CLINICAL STUDY**.

6.4 Drug Interactions

Consideration should be given to the potential for drug interaction when deciding to use a **SELUTION SLR PTCA DEB** in a patient who is taking a drug that could interact with sirolimus.

The effect of drug interactions on the safety or effectiveness of the **SELUTION SLR PTCA DEB** has not been determined, however, since the **SELUTION SLR PTCA DEB** exhibits its treatment effect locally and at a low dosage, it is not expected that concomitant treatment with other drugs will affect the effectiveness or safety of the **SELUTION SLR PTCA DEB**.

There is no specific clinical data available for the interactions of sirolimus with other drugs.

6.5 Carcinogenicity, Genotoxicity, and Reproductive Toxicity

The **SELUTION SLR PTCA DEB** was assessed to be non-genotoxic (non-mutagenic and non-clastogenic) through the AMES Bacterial Mutagenicity Assay and the In-Vitro Mouse Lymphoma Assay. Genotoxicity, as well as Carcinogenicity, of the **SELUTION SLR PTCA DEB** was further assessed through chemical characterization and toxicological risk assessment and was determined to have an acceptable threshold of toxicological concern (TCC).

Studies to evaluate mutagenicity, carcinogenicity, and reproductive toxicity have been conducted on sirolimus, as included in the product monograph and summarized below:

Mutagenicity studies:

Sirolimus was not mutagenic in the in-vitro bacterial reverse mutation assay, the Chinese hamster ovary cell chromosomal aberration assay, the mouse lymphoma cell forward mutation assay, or the in-vivo mouse micronucleus assay.

Carcinogenicity studies:

Carcinogenicity studies were conducted in female mice and male and female rats. In the 86-week female mouse study at dosages of 0, 12.5, 25 and 50/6 mg/kg/day (dosage lowered from 50 to 6 mg/kg/day at week 31 due to infection secondary to immunosuppression) there was a statistically significant increase in malignant lymphoma at all dosages (approximately 86 to 357 times the maximum recommended human dose [MRHD]) compared to controls. In the 104-week rat study at dosages of 0, 0.05, 0.1, and 0.2 mg/kg/day, there was an increased incidence of testicular adenoma in the 0.1 and 0.2 mg/kg/day (approximately 1.4 to 2.9 times the MRHD) groups.

Reproductive and Developmental Toxicology:

There was no effect on fertility in female rats following the administration of sirolimus at dosages up to 0.5 mg/kg (approximately 7 times the MRHD). In male rats, there was no significant difference in fertility rate compared to controls at a dosage of 2 mg/kg (approximately 28 times the MRHD). Reductions in testicular weights and/or histological lesions (e.g., tubular atrophy and tubular giant cells) were observed in rats following dosages of 0.65 mg/kg (approximately 9 times the MRHD) and above and in a monkey study at 0.1 mg/kg (approximately 1.4 times the MRHD) and above. Sperm counts were reduced in male rats following the administration of sirolimus for 13 weeks at a dosage of 6 mg/kg (approximately 85 times the MRHD) but showed improvement by 3 months after dosing was stopped.

Based on these data, and the fact that much higher doses of sirolimus have been safely administered systemically as an immunosuppressant, the total drug load of the **SELUTION SLR PTCA DEB** would not be expected to result in adverse long term effects including genotoxicity, carcinogenicity, and reproductive toxicity.

Pregnancy:

There are no adequate sirolimus or **SELUTION SLR PTCA DEB** related studies in pregnant women. Sirolimus has been shown to be embryo/fetal toxic in rats at dosages of 0.1 mg/kg and above (approximately 17 times the maximum dose for the **SELUTION SLR PTCA DEB**). Effective contraception should be initiated before use of the **SELUTION SLR PTCA DEB** and continued for one-year post-procedure. The **SELUTION SLR PTCA DEB** should be used in pregnant women only if the potential benefits justify the potential risks. Safety of the **SELUTION SLR PTCA DEB** has not been evaluated in males intending to father children.

Lactation:

Studies in rats have shown that sirolimus is excreted in milk. It is not known whether sirolimus is distributed in human milk. Also, sirolimus pharmacokinetic and safety profiles have not been determined in infants. Consequently, mothers should be advised of potential serious adverse reactions to sirolimus in nursing infants. Prior to use of **SELUTION SLR PTCA DEB**, decisions should be made regarding whether to discontinue nursing or conduct an alternative percutaneous coronary intervention procedure.

7 POTENTIAL ADVERSE EVENTS

Potential adverse events, which may be associated with a PTCA procedure, include, but are not limited to:

- Additional interventions, including surgical intervention
- Allergic reaction (e.g. to contrast medium, medications, or device components)
- Arrhythmias
- Bleeding (including Hemorrhage or Hematoma possibly requiring transfusion or additional intervention)
- Chest Pain (anginal)
- Death
- Embolism
- Fever
- Hypertension
- Hypotension
- Infection/Sepsis
- Inflammation
- Myocardial infarction/ ischemia
- Organ insufficiency/failure
- Pain or tenderness at the vascular access site
- Pericardial effusion/cardiac tamponade
- Renal failure
- Shock
- Stroke or transient ischemic attack (TIA)
- Vessel injury (dissection, perforation, rupture, arteriovenous fistula, aneurysm or pseudoaneurysm)
- Vessel occlusion (spasm, abrupt closure/recoil, slow flow/no reflow, thrombosis, restenosis)

Potential adverse events related to the oral administration of the active pharmaceutical ingredient (sirolimus) include, but are not limited to:

- Abnormal liver function tests
- Anemia
- Arthralgias
- Diarrhea
- Hypercholesterolemia
- Hypersensitivity, including anaphylactic/anaphylactoid type reactions
- Hypertriglyceridemia
- Hypokalemia
- Infection
- Interstitial lung disease
- Leukopenia
- Lymphoma and other malignancies
- Thrombocytopenia

The potential adverse events listed above are related to systemic orally-administered sirolimus at higher doses than what would be delivered by the application of one **SELUTION SLR PTCA DEB** locally to the vessel wall.

8 HOW SUPPLIED

Sterile:

The **SELUTION SLR PTCA DEB** is supplied sterile and for single use only. It is sterilized by E-beam irradiation. If left unopened and stored properly, the device will remain stable through the labelled Use By Date. Do not use if the packaging is damaged.

Storage:

The **SELUTION SLR PTCA DEB** should be stored in its original packaging in a dry, dark, cool place between 15-25°C(59-77°F). Do not store near radiation or ultraviolet sources.

Contents:

The unit carton is the protective packaging for the device. It contains a sealed foil pouch. The sealed foil pouch is the sterile barrier system and contains one (1) **SELUTION SLR PTCA DEB** stored inside a catheter dispenser coil, a card containing balloon compliance information and an oxygen absorber and desiccant.

9 DIRECTIONS FOR USE

Prior to angioplasty, carefully examine all equipment and materials to be used during the procedure. Carefully examine the product to verify that neither the **SELUTION SLR PTCA DEB** nor sterile packaging have been damaged.

Caution: Care should be taken when handling the device to avoid damage to the folded balloon. Excessive handling or contact with liquids to the drug coating should be avoided as the coating may be susceptible to premature drug release or catheter damage. Do not touch the drug coating on the balloon.

The following materials may be required for use with the **SELUTION SLR PTCA DEB**:

- 0.014-inch (0.36 mm) guidewire
- Torque device
- Guiding Catheter (5F, 6F)
- Hemostasis valve
- Contrast medium
- Sterile saline solution
- Inflation device with pressure-monitoring (e.g. manometer)
- Luer lock syringe for purging
- Stopcock (for purging)

1. Inflation Device Preparation

- a. Prepare the inflation device according to the manufacturer's instructions.
- b. Purge the inflation device of air.

2. SELUTION SLR PTCA DEB Catheter Selection

- a. The chosen nominal balloon size should be equal to the reference vessel diameter. The balloon should extend at least 2 mm beyond the lesion both proximally and distally. If multiple **SELUTION SLR PTCA DEBs** are required to complete the treatment of a lesion, the devices used should be minimally sized and angiographically positioned so that the balloon marker bands of consecutively placed devices overlap by at least 1 mm. The use of a radiopaque ruler is recommended to ensure appropriate placement of the **SELUTION SLR PTCA DEB**.
 - **Caution:** The **SELUTION SLR PTCA DEB** is indicated for lesions up to 26 mm. The safety and effectiveness of treating lesions longer than 26 mm has not been established.
- b. Vessel preparation is required prior to use of the **SELUTION SLR PTCA DEB** to achieve optimal results.
 - **Caution:** The treatment site should be adequately prepared (intravascular imaging guidance recommended) to achieve the maximum lumen diameter prior to treatment with the **SELUTION SLR PTCA DEB**.

3. SELUTION SLR PTCA DEB Preparation

- a. Carefully remove the **SELUTION SLR PTCA DEB** from the packaging and verify it is not damaged.
 - **Warning:** Contents are supplied STERILE using an E-beam irradiation sterilization process. DO NOT USE if the sterile barrier is damaged or opened prior to intended use.
 - **Warning:** DO NOT USE **SELUTION SLR PTCA DEB** after the labeled "Use By" date.
 - **Caution:** Do not use the **SELUTION SLR PTCA DEB** if the shaft has been bent or kinked.

- b. Purge the **SELUTION SLR PTCA DEB** of air prior to use. Keep the balloon protective sheath in place during the purging procedure. Begin by pointing the distal tip of the **SELUTION SLR PTCA DEB** downward while holding it vertically. Connect a stopcock and luer lock syringe partially filled with the saline-contrast mixture to the inflation port of the **SELUTION SLR PTCA DEB** luer. Apply negative pressure until air is completely evacuated and release the plunger. Repeat this operation until migration of air bubbles towards the syringe stops. Close the stopcock while vacuum is being applied to the device.
 - **Warning:** Use the recommended balloon inflation medium (50:50 mixture of contrast medium and sterile saline solution). Never use air or any gaseous medium to inflate the balloon.
 - **Caution:** The balloon protective sheath and disposable wire stylet must stay in place during preparation of the **SELUTION SLR PTCA DEB** and not be removed until just prior to flushing with saline and placing the device over the guidewire.
 - c. While the device is under vacuum, remove the stylet and the balloon protective sheath and discard. Do not use the balloon protective sheath as an introduction aid or rewiring tool.
 - **Caution:** Remove the balloon protective sheath distally and discard. If difficulty is encountered while removing the balloon protective sheath, a new **SELUTION SLR PTCA DEB** must be utilized.
 - d. Flush the guidewire lumen thoroughly with sterile heparinized saline solution from the distal tip utilizing a flushing needle, until fluid exits the Rx port of the **SELUTION SLR PTCA DEB**.
4. Inflation Device Connection
- a. To remove any air lodged in the distal luer fitting of the inflation device, purge approximately 1 ml (cc) of diluted contrast medium.
 - **Warning:** Use the recommended balloon inflation medium (50:50 mixture of contrast medium and sterile saline solution). Never use air or any gaseous medium to inflate the balloon.
 - **Caution:** Use caution in patients who have severe reaction to contrast agents that cannot be adequately pre-medicated.
 - b. With the stopcock in the closed position, disconnect the syringe used in preparation, slightly applying positive pressure. A meniscus of contrast medium will appear in the inflation port of the **SELUTION SLR PTCA DEB** luer when the syringe is removed. Verify a meniscus of contrast medium is evident in both the inflation port of the **SELUTION SLR PTCA DEB** luer and the inflation device's connection. Securely couple the inflation device to the inflation port of the **SELUTION SLR PTCA DEB** luer.
5. Use of the **SELUTION SLR PTCA DEB**
- a. Use a guide catheter to facilitate entry. Refer to the **SELUTION SLR PTCA DEB** labeling for information on the appropriate guide catheter size.
 - b. Insert a guidewire through the guide catheter according to the manufacturer's instructions or standard practice. Advance the guidewire through the guide catheter past the lesion location.
 - c. If needed, attach a torque device to the guidewire to advance to the desired vessel under fluoroscopy. Advance across the stenosis then remove the torque device once it is positioned.
 - d. Load the distal tip of the **SELUTION SLR PTCA DEB** onto the guidewire.
 - **Caution:** Never advance the drug-eluting balloon catheter without the guidewire extending from the tip. Do not use the **SELUTION SLR PTCA DEB** if the lesion is unable to be crossed with a guidewire.
 - e. Open the hemostasis valve to allow for easy passage of the balloon and to prevent damage to the balloon coating. With the balloon fully deflated, advance the **SELUTION SLR PTCA DEB** through the guiding catheter. To avoid kinking, advance the **SELUTION SLR PTCA DEB** slowly, in small increments, until the proximal end of the guidewire emerges from the catheter. Close the hemostasis valve only as much as needed to prevent blood return while permitting easy movement of the **SELUTION SLR PTCA DEB**. If the **SELUTION SLR PTCA DEB** encounters resistance, do not advance it through the hemostasis valve.
 - **Warning:** Do not advance or withdraw the catheter unless the drug-eluting balloon is fully deflated under vacuum.
 - **Warning:** If unusual resistance is felt during manipulation, determine the cause of the resistance before proceeding. If the source of resistance cannot be determined, it is recommended to extract the entire system (as a unit) with the guide catheter.
 - **Note:** Do not inflate the **SELUTION SLR PTCA DEB** prior to reaching the target lesion.
 - **Note:** Maintain tight luer connections and always advance and retrieve the **SELUTION SLR PTCA DEB** under negative pressure.
 - **Caution:** During insertion, do not over-tighten the hemostasis valve around the **SELUTION SLR PTCA DEB** shaft as lumen constriction may occur, affecting inflation/deflation of the balloon.
 - f. Under fluoroscopy, use the balloon's radiopaque markers to position the balloon within the lesion to be dilated; then inflate the balloon to the reference vessel diameter using the appropriate pressure (refer to the balloon compliance chart included in the device packaging).
 - **Warning:** DO NOT EXCEED the Rated Burst Pressure (RBP) recommended for this device. Balloon rupture may occur if the RBP rating is exceeded. To prevent over-pressurization, use of a pressure-monitoring device is recommended.
 - **Warning:** Once inflation has begun, do not move or reposition the **SELUTION SLR PTCA DEB**.

- g. Maintain balloon inflation for a minimum of 30 seconds and to an optimal target of 1 minute as tolerated.
 - **Warning:** Each **SELUTION SLR PTCA DEB** catheter is intended for a single inflation only. Do not reinflate the **SELUTION SLR PTCA DEB** catheter.
 - **Note:** Ensure that there is full contact between the inflated balloon and lesion across the entire length of the treated area.
 - **Note:** If treating a long lesion (longer than the maximum balloon length available), each individual segment should be treated only once with the **SELUTION SLR PTCA DEB** and overlap by at least 1mm
 - **Caution:** Whenever possible, the **SELUTION SLR PTCA DEB** should be the final treatment of the vessel.
 - h. Open the hemostasis valve and apply negative pressure to fully deflate the **SELUTION SLR PTCA DEB**. Prior to removal, confirm that the balloon is fully deflated under fluoroscopy.
 - **Note:** The balloon deflation time has been established as ≤ 30 seconds based on in vitro bench testing results.
 - i. Perform angiography to confirm vessel patency and ensure the drug-eluting balloon is fully deflated.
 - j. Ensure hemostasis valve is open and withdraw the **SELUTION SLR PTCA DEB** from the body under negative pressure.
 - **Note:** If bailout is required, a commercially available drug-eluting stent may be used.
 - k. Remove all equipment from the body and close the access site per standard clinical practice.
 - **Caution:** After use, the **SELUTION SLR PTCA DEB** is a biohazard. Handle and dispose of all such devices in accordance with accepted medical practice and applicable hospital, administrative, and government regulations.
6. Pre and Postprocedural Antiplatelet Regimen
 - a. Administer antiplatelet and anticoagulant therapy before and during the procedure per the hospital's standard of care for PTCA procedures.
 - b. The optimal duration of dual anti-platelet therapy (DAPT) post PCI for ISR is currently unknown. Published expert consensus opinion as recorded in the 2023 SCAI Expert Consensus Statement has suggested that DAPT should be used for a minimum of one month post ISR PCI. While the SELUTION4ISR trial required that enrolled subjects receive a minimum of 1-month of DAPT followed by antiplatelet monotherapy for the duration of the study, more than 60 % of enrolled patients remained on DAPT for at least 1 year. In conjunction with this information, operators should use clinical judgment in deciding on the duration of DAPT following use of **SELUTION SLR PTCA DEB**.
 7. Post procedure
 - Any serious incident that occurs in relation to this device should be reported to the manufacturer and relevant local regulatory authority.

10 INFORMATION TO BRIEF THE PATIENT

Physicians should consider the following points when counseling patients on the use of the **SELUTION SLR PTCA DEB**:

- Discuss the risks and benefits including potential adverse events associated with the **SELUTION SLR PTCA DEB** and PTCA procedures.
- Discuss patient allergies, in particular, the risks for patients who may be allergic to sirolimus, PLGA or contrast medium.
- Discuss the planned anti-platelet therapy duration and risks and benefits of the anti-platelet therapy including risk of thrombosis if patient prematurely discontinues the use.
- Discuss post-procedure instructions, including any follow up appointments, lifestyle modifications, medications and home care or rehabilitation guidance.
- Advise the patient that additional information may be available on the Cordis Labeling website (www.cordislabeling.com).

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12 SELUTION4ISR CLINICAL STUDY

12.1 Objective

The objective of the SELUTION4ISR Study was to demonstrate the safety and effectiveness of the **SELUTION SLR PTCA DEB** for treatment of bare-metal or drug-eluting in-stent restenosis (ISR).

12.2 Study Design

The SELUTION4ISR Study is a prospective, multi-center, randomized, single blind, controlled, noninferiority clinical trial that enrolled 418 randomized subjects (including 60 subjects in an angiographic and optical coherence tomography [OCT] sub-study) at 48 sites in the United States (US), Canada, Brazil, and Europe (EU). A minimum of 50% of the subjects were planned to be enrolled in the US.

Subjects with previous bare-metal stent (BMS) or Drug Eluting Stent (DES) and qualifying evidence for ISR were screened per the protocol inclusion and exclusion criteria. Eligible subjects were randomized 1:1 to treatment with either the **SELUTION SLR PTCA DEB** or Standard of Care (SOC) to include contemporary DES (zotarolimus-eluting stents [ZES] and everolimus-eluting stents [EES] only) or Balloon Angioplasty (BA). A maximum of 20% of patients randomized to the SOC arm were treated with BA.

The primary safety and effectiveness endpoint is target lesion failure (TLF) at 12 months post-index procedure for **SELUTION SLR PTCA DEB** versus SOC. TLF is a composite endpoint including all cardiac death, target vessel myocardial infarction (MI), or clinically driven target lesion revascularization (TLR). MI includes spontaneous (Type 1) MI using the 4th Universal Definition of Myocardial Infarction (UDMI) and peri-procedural MI using the Society for Cardiac Angiography and Intervention (SCAI) definition. The primary analysis population was the per-protocol (PP) analysis population. Select results are also presented for the intention-to-treat (ITT) analysis population. Two additional analysis populations (modified PP and modified ITT) were pre-specified to evaluate the effect of missing biomarker data. The results of these analysis populations confirmed the results of the primary analysis and are not included herein.

The study protocol defined a single hypothesis-driven secondary endpoint to be evaluated if the primary endpoint was met, which was incidence of TLF at 12 months among the cohort of subjects with one previous layer of stent, comparing the **SELUTION SLR PTCA DEB** arm to the DES cohort of the SOC arm. Other secondary endpoints include clinical, performance, and imaging endpoints. Subjects are planned to be followed through 5 years post-index procedure, with clinical follow-up at 1 month, 6 months, 12 months, and annually thereafter through 5 years.

A separate 12-20 subject cohort was evaluated for clinical pharmacokinetics (PK).

12.3 Demographics

Table 3 presents demographic and baseline clinical characteristics for the PP analysis set. The mean age of patients was 69 years and 22% of patients were female. The **SELUTION SLR PTCA DEB** and SOC treatment groups were well-balanced with no significant differences in baseline characteristics except for the prevalence of peripheral vascular disease, which was significantly higher in the **SELUTION SLR PTCA DEB** group compared with the SOC group (19.80% vs. 11.40%; p=0.026).

Table 3: Subject Demographics, Medical History, and Baseline Characteristics (PP)

Patient Characteristic	SELUTION SLR PTCA DEB (N=197)	SOC (N=193)	Total (N=390)	P-value ¹ (SELUTION SLR PTCA DEB vs SOC)
Age (years)				
Mean ± SD (N)	68.17 ± 9.03 (197)	69.55 ± 9.01 (193)	68.85 ± 9.04 (390)	0.130
Age (years)				0.194
>75	21.32% (42/197)	27.46% (53/193)	24.36% (95/390)	
≤ 75	78.68% (155/197)	72.54% (140/193)	75.64% (295/390)	
Female Sex	18.27% (36/197)	25.91% (50/193)	22.05% (86/390)	0.087
Ethnicity				0.064
Hispanic or Latino	4.57% (9/197)	7.77% (15/193)	6.15% (24/390)	
Non-Hispanic or non-Latino	69.54% (137/197)	75.13% (145/193)	72.31% (282/390)	
Did not provide response	25.89% (51/197)	17.10% (33/193)	21.54% (84/390)	
Body Mass Index				
Mean ± SD (N)	28.82 ± 5.49 (196)	29.43 ± 5.51 (193)	29.12 ± 5.50 (389)	0.270
History of Prior MI	47.72% (94/197)	48.19% (93/193)	47.95% (187/390)	1.000
History of STEMI	21.83% (43/197)	19.17% (37/193)	20.51% (80/390)	0.455
History of Stroke or TIA	9.64% (19/197)	6.22% (12/193)	7.95% (31/390)	0.262
Smoking Habits				0.896
Never Smoked	41.62% (82/197)	44.04% (85/193)	42.82% (167/390)	
Ex-Smoker	42.13% (83/197)	41.45% (80/193)	41.79% (163/390)	
Current Smoker	15.23% (30/197)	13.99% (27/193)	14.62% (57/390)	
Former drug use	3.55% (7/197)	2.59% (5/193)	3.08% (12/390)	0.758
Renal Insufficiency	16.75% (33/197)	11.40% (22/193)	14.10% (55/390)	0.147
Undergoing Dialysis	0.51% (1/197)	1.04% (2/193)	0.77% (3/390)	0.620
Hypertension	92.89% (183/197)	93.26% (180/193)	93.08% (363/390)	1.000

Patient Characteristic	SELUTION SLR PTCA DEB (N=197)	SOC (N=193)	Total (N=390)	P-value ¹ (SELUTION SLR PTCA DEB vs SOC)
Hyperlipidemia	90.86% (179/197)	88.60% (171/193)	89.74% (350/390)	0.507
Diabetes	43.15% (85/197)	42.49% (82/193)	42.82% (167/390)	0.919
Peripheral Vascular Disease	19.80% (39/197)	11.40% (22/193)	15.64% (61/390)	0.026
History of PCI	100% (197/197)	100.0% (193/193)	100% (390/390)	1.000
History of CABG	22.34% (44/197)	20.73% (40/193)	21.54% (84/390)	0.713
History of Drug Eluting Stent (DES)	90.86% (179/197)	95.85% (185/193)	93.33% (364/390)	0.066
History of Drug Coated Balloon (DCB)	2.54% (5/197)	3.63% (7/193)	3.08% (12/390)	0.573
History of Bare Metal Stent (BMS)	19.29% (38/197)	12.95% (25/193)	16.15% (63/390)	0.099
Angina Status				0.978
Stable Angina	62.44% (123/197)	61.66% (119/193)	62.05% (242/390)	
Unstable Angina	30.46% (60/197)	30.05% (58/193)	30.26% (118/390)	
Silent Ischemia	4.06% (8/197)	5.18% (10/193)	4.62% (18/390)	
No Angina	3.05% (6/197)	3.11% (6/193)	3.08% (12/390)	
CCS classification				0.241
I	15.23% (30/197)	18.65% (36/193)	16.92% (66/390)	
II	35.03% (69/197)	26.42% (51/193)	30.77% (120/390)	
III	34.01% (67/197)	39.38% (76/193)	36.67% (143/390)	
IV	8.63% (17/197)	6.74% (13/193)	7.69% (30/390)	
ACS ²	34.52% (68/197)	32.12% (62/193)	33.33% (130/390)	0.668
Baseline Cardiac Enzymes				
CK Out of Normal Range	1.02% (2/197)	0.00% (0/193)	0.51% (2/390)	0.538
CKMB Out of Normal Range	2.54% (5/197)	1.55% (3/193)	2.05% (8/390)	0.486
Troponin T Out of Normal Range	2.03% (4/197)	1.55% (3/193)	1.79% (7/390)	0.702
Troponin I Out of Normal Range	2.03% (4/197)	1.04% (2/193)	1.54% (6/390)	1.000
Baseline Creatinine Out of Normal Range	2.03% (4/197)	3.11% (6/193)	2.56% (10/390)	0.539

1. P-value calculated using ANOVA for continuous variables and Fisher's exact test for categorical variables.
2. ACS is defined as: Subjects with unstable angina or any elevated cardiac enzymes at baseline (any pre-procedure CK, CKMB, or Troponin out of normal range).

12.4 Lesion Characteristics

Table 4 presents the lesion characteristics as assessed by the angiographic core laboratory. The most frequent vessel treated was the left anterior descending artery (LAD), which was treated in 39.49% (154/390) of subjects. Only 1.28% (5/390) of lesions treated were severely calcified. The overall mean lesion length was 12.15 mm (12.38 mm in the **SELUTION SLR PTCA DEB** group and 11.91 mm in the SOC group). There were also differences in post-study device reference vessel diameter, minimal lumen diameter, and diameter stenosis between the **SELUTION SLR PTCA DEB** group and the SOC group.

Table 4: Angiographic Core Lab Reported Lesion Characteristics (PP)

Measure	SELUTION SLR PTCA DEB (N=197)	SOC (N=193)	All Subjects (N=390)	P-value ¹ (SELUTION SLR PTCA DEB vs SOC)
Vessel Location ²				0.303
RCA	34.52% (68/197)	33.68% (65/193)	34.10% (133/390)	
LAD	39.59% (78/197)	39.38% (76/193)	39.49% (154/390)	
LCX	25.38% (50/197)	23.32% (45/193)	24.36% (95/390)	
Left Main	0.51% (1/197)	3.11% (6/193)	1.79% (7/390)	
Pre-Procedure TIMI Flow				0.212
0	0.00% (0/197)	1.04% (2/193)	0.51% (2/390)	
1	0.00% (0/197)	0.52% (1/193)	0.26% (1/390)	
2	4.06% (8/197)	2.07% (4/193)	3.08% (12/390)	
3	94.92% (187/197)	94.82% (183/193)	94.87% (370/390)	
4	0.00% (0/197)	0.00% (0/193)	0.00% (0/390)	
Severe Calcification	0.00% (0/197)	2.59% (5/193)	1.28% (5/390)	0.020
Vessel Angulation				0.188

Measure	SELUTION SLR PTCA DEB (N=197)	SOC (N=193)	All Subjects (N=390)	P-value ¹ (SELUTION SLR PTCA DEB vs SOC)
None or Mild (< 45 degrees)	84.77% (167/197)	88.60% (171/193)	86.67% (338/390)	
Moderate (≥ 45 - < 90 degrees)	14.21% (28/197)	9.84% (19/193)	12.05% (47/390)	
Severe (≥ 90 degrees)	0.51% (1/197)	0.00% (0/193)	0.26% (1/390)	
Vessel Tortuosity				1.000
None or Mild	98.48% (194/197)	99.48% (192/193)	98.97% (386/390)	
Moderate	0.51% (1/197)	0.00% (0/193)	0.26% (1/390)	
Excessive	0.00% (0/197)	0.00% (0/193)	0.00% (0/390)	
Bifurcation Lesion	37.56% (74/197)	35.75% (69/193)	36.67% (143/390)	0.753
Eccentric	55.33% (109/197)	60.10% (116/193)	57.69% (225/390)	0.352
Thrombus	0.51% (1/197)	0.00% (0/193)	0.26% (1/390)	1.000
Length, mm				
Mean ± SD (N)	12.38 ± 6.00 (196)	11.91 ± 5.65 (190)	12.15 ± 5.83 (386)	0.423
Length, mm				0.724
Length ≤ 26 mm	96.95% (191/197)	96.89% (187/193)	96.92% (378/390)	
Length > 26 mm	2.54% (5/197)	1.55% (3/193)	2.05% (8/390)	
Length, mm - additional categories				0.797
Length < 10 mm	44.16% (87/197)	46.63% (90/193)	45.38% (177/390)	
Length 10 - 20 mm	43.65% (86/197)	39.90% (77/193)	41.79% (163/390)	
Length > 20 mm	11.68% (23/197)	11.92% (23/193)	11.79% (46/390)	
RVD, mm				0.831
RVD ≤ 2.75 mm	67.01% (132/197)	65.80% (127/193)	66.15% (258/390)	
RVD > 2.75 mm	32.99% (65/197)	34.20% (66/193)	33.59% (131/390)	
Pre-Procedure Reference Vessel Diameter (mm) - Treated Segment Interpolated				
Mean ± SD (N)	2.50 ± 0.48 (106)	2.63 ± 0.50 (101)	2.57 ± 0.50 (207)	0.063
Pre-Procedure Minimal Lumen Diameter (mm) - Treated Segment				
Mean ± SD (N)	0.89 ± 0.35 (108)	0.91 ± 0.37 (102)	0.90 ± 0.36 (210)	0.726
Pre-Procedure Percent Diameter Stenosis (%)				
Mean ± SD (N)	64.62 ± 11.95 (106)	65.13 ± 11.66 (101)	64.87 ± 11.78 (207)	0.755
Post-Study Device Reference Vessel Diameter (mm) - Treated Segment Interpolated				
Mean ± SD (N)	2.68 ± 0.44 (169)	2.79 ± 0.57 (135)	2.73 ± 0.50 (304)	0.049
Post-Study Device Minimal Lumen Diameter (mm) - Treated Segment				
Mean ± SD (N)	2.22 ± 0.43 (172)	2.47 ± 0.52 (135)	2.33 ± 0.49 (307)	<0.001
Post-Study Device Percent Diameter Stenosis (%)				
Mean ± SD (N)	16.99 ± 9.59 (169)	12.05 ± 7.96 (135)	14.80 ± 9.22 (304)	<0.001
1. P-value calculated using ANOVA for continuous variables and Fisher's exact test for categorical variables.				
2. Vessel location is assigned based on Core Lab Segment CASS #.				

Procedural Characteristics

Table 5 presents the procedural characteristics for the PP analysis set. The treatment groups were well-balanced in procedural characteristics. Significant differences were seen in procedure time, heparin administered, study device length, study device inflation pressure, study device inflation time, and prevalence and reason of post-dilatation that was performed.

The average **SELUTION SLR PTCA DEB** device length (mean=21.62 mm) was significantly longer than the SOC device length (mean=19.30 mm, p<0.001). Mean device diameters were similar between groups. The average inflation pressure was 10.24 atm in the **SELUTION SLR PTCA DEB** group compared to 16.09 atm in the SOC group (p<0.001). The mean inflation time was 69.24 seconds for the **SELUTION SLR PTCA DEB** group and 22.94 seconds for the SOC group (p<0.001). Post-dilatation was performed for 1.52% of **SELUTION SLR PTCA DEB** subjects and 48.19% of SOC subjects. Bailout stenting was needed in 1.52% of **SELUTION SLR PTCA DEB** subjects and 0.52% of SOC subjects, all due to persistent dissection ≥ NHLBI grade C.

Table 5: Procedural Characteristics (PP)

Characteristic	SELUTION SLR PTCA DEB (N=197)	SOC (N=193)	Total (N=390)	P-value ¹ (SELUTION SLR PTCA DEB vs SOC)
Non-target lesion(s) treated	10.66% (21/197)	11.40% (22/193)	11.03% (43/390)	0.869
Number of existing stent layers				0.903
1	77.66% (153/197)	78.24% (151/193)	77.95% (304/390)	
2	22.34% (44/197)	21.76% (42/193)	22.05% (86/390)	
Time of procedure (mins)				
Mean ± SD (N)	53.99 ± 23.78 (197)	60.15 ± 31.38 (193)	57.04 ± 27.94 (390)	0.029
Heparin administered (IU)	90.86% (179/197)	88.60% (171/193)	89.74% (350/390)	0.507
Mean ± SD (N)	7852.29 ± 3670.28 (179)	8925.15 ± 5453.28 (171)	8376.46 ± 4652.38 (350)	0.030
ACT monitoring performed	67.01% (132/197)	65.28% (126/193)	66.15% (258/390)	1.000
ACT levels stay within the suggested range	94.70% (125/132)	94.44% (119/126)	94.57% (244/258)	1.000
Pre-dilatation				
Pre-treatment device ²				0.431
PTCA	87.31% (172/197)	83.94% (162/193)	85.64% (334/390)	
Cutting Balloon	28.43% (56/197)	35.75% (69/193)	32.05% (125/390)	
Scoring Balloon	15.74% (31/197)	17.10% (33/193)	16.41% (64/390)	
Dilation balloon diameter (mm) ³				
Mean ± SD (N)	3.13 ± 0.56 (197)	3.09 ± 0.67 (193)	3.11 ± 0.61 (390)	0.569
Dilation balloon length (mm) ³				
Mean ± SD (N)	13.77 ± 4.76 (195)	13.28 ± 4.11 (190)	13.53 ± 4.45 (385)	0.278
Inflation pressure (atm) ⁴				
Mean ± SD (N)	18.94 ± 6.46 (193)	19.36 ± 8.58 (188)	19.14 ± 7.57 (381)	0.589
Inflation time (s) ⁵				
Mean ± SD (N)	73.87 ± 78.21 (191)	68.76 ± 73.52 (186)	71.35 ± 75.87 (377)	0.514
Treatment				
Number of study devices used				
1	90.36% (178/197)	N/A	N/A	
2	8.12% (16/197)	N/A	N/A	
3	1.02% (2/197)	N/A	N/A	
Number of control stents used				
1	N/A	90.91% (140/154)	N/A	
2	N/A	8.44% (13/154)	N/A	
3	N/A	0.65% (1/154)	N/A	
Number of control balloons used				
1	N/A	84.62% (33/39)	N/A	
2	N/A	10.26% (4/39)	N/A	
3	N/A	2.56% (1/39)	N/A	
4	N/A	2.56% (1/39)	N/A	
Device diameter (mm) ⁶				
Mean ± SD (N)	3.26 ± 0.45 (197)	3.26 ± 0.56 (193)	3.26 ± 0.51 (390)	0.998
Device length (mm) ⁶				
Mean ± SD (N)	21.62 ± 6.05 (197)	19.30 ± 7.49 (193)	20.47 ± 6.89 (390)	<0.001
Inflation pressure (atm) ⁷				

Characteristic	SELUTION SLR PTCA DEB (N=197)	SOC (N=193)	Total (N=390)	P-value ¹ (SELUTION SLR PTCA DEB vs SOC)
Mean ± SD (N)	10.24 ± 3.68 (197)	16.09 ± 5.58 (191)	13.12 ± 5.54 (388)	<0.001
Inflation time (s) ⁸				
Mean ± SD (N)	69.24 ± 28.10 (197)	22.94 ± 19.83 (190)	46.51 ± 33.62 (387)	<0.001
Post-Treatment				
Post-dilatation performed after stenting or initial balloon treatment for SELUTION SLR DEB	1.52% (3/197)	48.19% (93/193)	24.62% (96/390)	<0.001
Number of post-dilatation devices used				
Mean ± SD (N)	1.33 ± 0.58 (3)	1.25 ± 0.60 (83)	1.26 ± 0.60 (86)	0.820
Reason for post-dilatation				0.033
Dissection	0.51% (1/197)	0.00% (0/193)	0.26% (1/390)	
Recoil	0.00% (0/197)	6.22% (12/193)	3.08% (12/390)	
Other	1.02% (2/197)	41.45% (80/193)	21.03% (82/390)	
Bailout stenting occurred	1.52% (3/197)	0.52% (1/193)	1.03% (4/390)	0.623
Residual stenosis > 50%	0.00% (0/197)	0.00% (0/193)	0.00% (0/390)	
Persistent dissection ≥ NHLBI grade C	1.52% (3/197)	0.52% (1/193)	1.03% (4/390)	
Other	0.00% (0/197)	0.00% (0/193)	0.00% (0/390)	
1. P-value calculated using ANOVA for continuous variables and Fisher's exact test for categorical variables. 2. A subject may have had more than one type of pre-treatment device used, so subgroups may sum to more than total. 3. If multiple pre-dilatation balloons were present in the dataset, the final entry was used to summarize dilation balloon diameter and length. 4. If multiple pre-dilatation balloons were present in the dataset, the maximum inflation pressure (atm) was used. 5. If multiple pre-dilatation balloons were present in the dataset, the inflation times were summed to present total inflation time. 6. If multiple treatment devices were present in the dataset, the final entry was used to summarize device diameter and length. 7. If multiple treatment devices were present in the dataset, the maximum inflation pressure (atm) was used. 8. If multiple treatment devices were present in the dataset, the inflation times were summed to present total inflation time.				

12.5 Primary Endpoint Results

Table 6 presents the primary endpoint results of Target Lesion Failure (TLF) at 12 months. 16.24% (32/197) subjects treated with **SELUTION SLR PTCA DEB** and 14.51% (28/193) of the SOC treated subjects in the PP population experienced TLF by 1 year. The difference between the two groups was 1.71% with a corresponding 95% Bayesian credible interval of (-5.49%, 8.87%). The upper bound 95% of the credible interval was below the predefined non-inferiority margin of 10%. Therefore, the primary endpoint was met, as shown by the posterior probability of noninferiority of 98.80%, which was above the defined success threshold of 97.5%. **Figure 2** depicts the Kaplan-Meier Survival Plot for Time to TLF (PP).

Table 6: Primary Endpoint – TLF at 12 Months (PP)

Endpoint	SELUTION SLR PTCA DEB (N=197)	SOC (N=193)	Difference [95% Credible Interval]	Posterior Probability of Non-inferiority ¹
TLF at 12 Months (365 Days)	16.24% (32/197)	14.51% (28/193)	1.71% [-5.49%, 8.87%]	98.80%
Cardiac Death	2.03% (4/197)	1.55% (3/193)		
Target Vessel MI ²	7.61% (15/197)	5.18% (10/193)		
Clinically driven TLR	12.69% (25/197)	12.44% (24/193)		
¹ Posterior probability > 97.5% required to meet non-inferiority. Non-inferiority margin is 10%. ² Target vessel MI includes spontaneous (Type 1) MI using the 4th Universal Definition of Myocardial Infarction (UDMI) and periprocedural MIS using the Society for Cardiac Angiography and Intervention (SCAI) definition.				

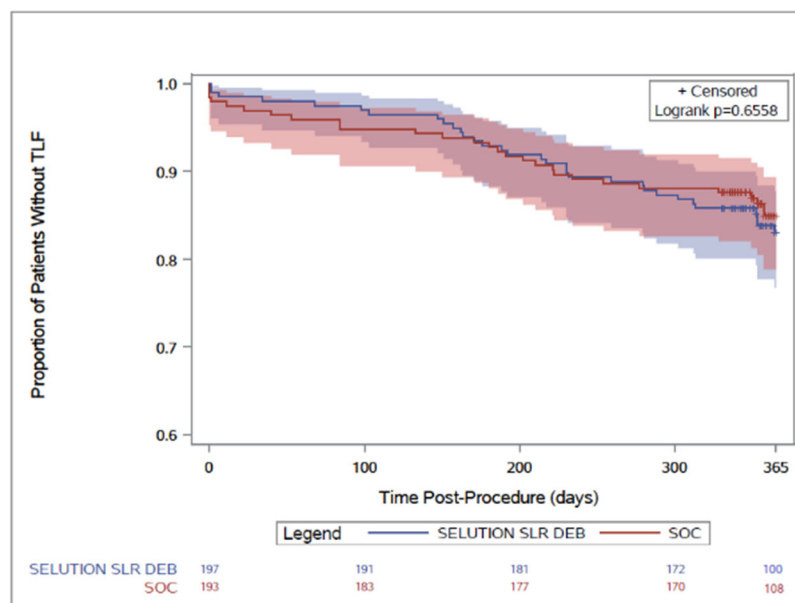


Figure 2: Kaplan-Meier Survival Plot for Time to TLF (PP)

Similar outcomes were observed in the ITT population, with rates of 15.24% (32/210) subjects treated with **SELUTION SLR PTCA DEB** and 13.46% (28/208) of the SOC treated subjects in the ITT population experienced TLF by 1 year. The difference between the two groups was 1.80% with a corresponding 95% Bayesian credible interval of (-4.88%, 8.46%). The posterior probability of noninferiority was 99.18%.

12.6 Hypothesis-Driven Secondary Endpoint Results

The study protocol defined a single hypothesis-driven secondary endpoint, which was incidence of TLF at 12 months among the cohort of subjects with one previous layer of stent, comparing the **SELUTION SLR PTCA DEB** arm to the DES cohort of the SOC arm. Similar to the primary endpoint, the PP population was defined as the primary analysis cohort and analogous Bayesian methods were used. In the **SELUTION SLR PTCA DEB** group, 14.19% (22/155) of subjects with 1 previous stent layer experienced TLF within 12 months, compared to 6.52% (9/138) of DES subjects in the SOC control group. The difference between the two groups was 7.53% (95% CI: 0.59%, 14.59%). The hypothesis-driven secondary endpoint was not met, as indicated by the posterior probability of non-inferiority of 76.07%, which was below the predefined success threshold of 95%. Similar results were seen in the ITT analysis population.

12.7 Additional Secondary Endpoint Results

The key additional secondary endpoint results for this study are presented by timepoint in **Table 7**.

Table 7: Secondary Clinical Endpoints by Timepoint (PP)

Secondary Endpoints	SELUTION SLR PTCA DEB (N=197)	SOC (N=193)	All Subjects (N=390)
Pre-Discharge			
Any death, any MI, or any repeat revascularization	3.05% (6/197)	1.55% (3/193)	2.31% (9/390)
All-cause mortality	0.00% (0/197)	0.00% (0/193)	0.00% (0/390)
Cardiovascular mortality	0.00% (0/197)	0.00% (0/193)	0.00% (0/390)
MI (UDMI, ARC2)	1.02% (2/197)	1.04% (2/193)	1.03% (4/390)
MI (UDMI, SCAI)	1.52% (3/197)	1.04% (2/193)	1.28% (5/390)
Target vessel MI (TV MI)	1.52% (3/197)	1.04% (2/193)	1.28% (5/390)
Non-target vessel MI (NTVMI)	0.00% (0/197)	0.00% (0/193)	0.00% (0/390)
Clinically driven TLR (CD TLR)	0.00% (0/197)	0.52% (1/193)	0.26% (1/390)
All TLR	0.00% (0/197)	0.52% (1/193)	0.26% (1/390)
Clinically driven TVR	0.51% (1/197)	0.52% (1/193)	0.51% (2/390)
All TVR	0.51% (1/197)	0.52% (1/193)	0.51% (2/390)
Non-TVTR	0.51% (1/197)	0.00% (0/193)	0.26% (1/390)
TLF ¹	1.52% (3/197)	1.04% (2/193)	1.28% (5/390)
Target Vessel Failure ²	2.03% (4/197)	1.04% (2/193)	1.54% (6/390)
BARC type 2-5 bleeding ³	2.03% (4/197)	2.59% (5/193)	2.31% (9/390)
Net adverse clinical event ⁴	4.06% (8/197)	4.15% (8/193)	4.10% (16/390)

Secondary Endpoints	SOLUTION SLR PTCA DEB (N=197)	SOC (N=193)	All Subjects (N=390)
Any death, any MI, or any repeat revascularization	3.05% (6/197)	1.55% (3/193)	2.31% (9/390)
1-Month Follow-up			
Any death, any MI, or any repeat revascularization	5.58% (11/197)	5.18% (10/193)	5.38% (21/390)
All-cause mortality	0.00% (0/197)	0.00% (0/193)	0.00% (0/390)
Cardiovascular mortality	0.00% (0/197)	0.00% (0/193)	0.00% (0/390)
MI (UDMI, ARC2)	2.54% (5/197)	2.59% (5/193)	2.56% (10/390)
MI (UDMI, SCAI)	2.54% (5/197)	2.59% (5/193)	2.56% (10/390)
Target vessel MI (TV MI)	1.52% (3/197)	2.59% (5/193)	2.05% (8/390)
Non-target vessel MI (NTVMI)	0.51% (1/197)	0.00% (0/193)	0.26% (1/390)
Clinically driven TLR (CD TLR)	0.51% (1/197)	1.04% (2/193)	0.77% (3/390)
All TLR	0.51% (1/197)	1.04% (2/193)	0.77% (3/390)
Clinically driven TVR	1.02% (2/197)	1.55% (3/193)	1.28% (5/390)
All TVR	1.02% (2/197)	1.55% (3/193)	1.28% (5/390)
Non-TV R	2.54% (5/197)	1.04% (2/193)	1.79% (7/390)
TLF ¹	1.52% (3/197)	3.11% (6/193)	2.31% (9/390)
Target Vessel Failure ²	2.03% (4/197)	3.63% (7/193)	2.82% (11/390)
BARC type 2-5 bleeding ³	2.03% (4/197)	3.63% (7/193)	2.82% (11/390)
Net adverse clinical event ⁴	5.08% (10/197)	7.25% (14/193)	6.15% (24/390)
6-Month Follow-up			
Any death, any MI, or any repeat revascularization	13.20% (26/197)	12.44% (24/193)	12.82% (50/390)
All-cause mortality	0.51% (1/197)	0.00% (0/193)	0.26% (1/390)
Cardiovascular mortality	0.51% (1/197)	0.00% (0/193)	0.26% (1/390)
MI (UDMI, ARC2)	6.09% (12/197)	4.66% (9/193)	5.38% (21/390)
MI (UDMI, SCAI)	6.09% (12/197)	4.66% (9/193)	5.38% (21/390)
Target vessel MI (TV MI)	5.58% (11/197)	3.63% (7/193)	4.62% (18/390)
Non-target vessel MI (NTVMI)	1.02% (2/197)	1.04% (2/193)	1.03% (4/390)
Clinically driven TLR (CD TLR)	5.08% (10/197)	5.18% (10/193)	5.13% (20/390)
All TLR	6.09% (12/197)	5.18% (10/193)	5.64% (22/390)
Clinically driven TVR	7.11% (14/197)	5.70% (11/193)	6.41% (25/390)
All TVR	7.61% (15/197)	5.70% (11/193)	6.67% (26/390)
Non-TV R	5.58% (11/197)	4.66% (9/193)	5.13% (20/390)
TLF ¹	7.61% (15/197)	7.25% (14/193)	7.44% (29/390)
Target Vessel Failure ²	9.14% (18/197)	7.77% (15/193)	8.46% (33/390)
BARC type 2-5 bleeding ³	5.08% (10/197)	5.70% (11/193)	5.38% (21/390)
Net adverse clinical event ⁴	12.18% (24/197)	11.92% (23/193)	12.05% (47/390)
1-Year Follow-up			
Any death, any MI, or any repeat revascularization	22.84% (45/197)	22.28% (43/193)	22.56% (88/390)
All-cause mortality	2.54% (5/197)	1.55% (3/193)	2.05% (8/390)
Cardiovascular mortality	2.03% (4/197)	1.55% (3/193)	1.79% (7/390)
MI (UDMI, ARC2)	8.12% (16/197)	6.74% (13/193)	7.44% (29/390)
MI (UDMI, SCAI)	8.12% (16/197)	6.74% (13/193)	7.44% (29/390)
Target vessel MI (TV MI)	7.61% (15/197)	5.18% (10/193)	6.41% (25/390)
Non-target vessel MI (NTVMI)	1.52% (3/197)	1.55% (3/193)	1.54% (6/390)
Clinically driven TLR (CD TLR)	12.69% (25/197)	12.44% (24/193)	12.56% (49/390)
All TLR	13.71% (27/197)	13.47% (26/193)	13.59% (53/390)
Clinically driven TVR	15.74% (31/197)	13.47% (26/193)	14.62% (57/390)

Secondary Endpoints	SOLUTION SLR PTCA DEB (N=197)	SOC (N=193)	All Subjects (N=390)
All TVR	16.75% (33/197)	14.51% (28/193)	15.64% (61/390)
Non-TVR	7.11% (14/197)	6.74% (13/193)	6.92% (27/390)
TLF ¹	16.24% (32/197)	14.51% (28/193)	15.38% (60/390)
Target Vessel Failure ²	18.78% (37/197)	15.54% (30/193)	17.18% (67/390)
BARC type 2-5 bleeding ³	7.61% (15/197)	9.33% (18/193)	8.46% (33/390)
Net adverse clinical event ⁴	19.80% (39/197)	18.65% (36/193)	19.23% (75/390)
1. TLF is defined as all cardiac death, target vessel MI (TV MI; spontaneous or peri-procedural) or clinically driven TLR. 2. Target vessel failure (TVF), defined as cardiovascular death, target vessel MI (TV MI; spontaneous or peri-procedural) and any clinically driven TVR. 3. Bleeding according to Bleeding Academic Research Consortium (BARC) classification 2-5. 4. Net adverse clinical events defined as death, MI (spontaneous or peri-procedural), TVR, stent/target lesion stent thrombosis, or bleeding (BARC types 2-5).			

12.8 Serious Adverse Effects (SAEs)

Serious Adverse Effects (SAEs) that were reported by sites and coded using MedDRA preferred terms are presented in **Table 8**.

Table 8: Serious Adverse Events Through 1 Year with Event Rate ≥0.95% (ITT)

SAE to 365 Days	SOLUTION SLR PTCA DEB (N=210)	SOC (N=208)	All Subjects (N=418)
Any SAE	37.14% (78/210)	43.75% (91/208)	40.43% (169/418)
Cardiac disorders	21.90% (46/210)	24.04% (50/208)	22.97% (96/418)
Angina pectoris	5.71% (12/210)	8.17% (17/208)	6.94% (29/418)
Acute myocardial infarction	7.14% (15/210)	5.29% (11/208)	6.22% (26/418)
Angina unstable	3.81% (8/210)	1.92% (4/208)	2.87% (12/418)
Atrial fibrillation	3.81% (8/210)	1.44% (3/208)	2.63% (11/418)
Cardiac failure congestive	1.90% (4/210)	1.44% (3/208)	1.67% (7/418)
Arteriosclerosis coronary artery	0.95% (2/210)	2.40% (5/208)	1.67% (7/418)
Cardiac failure	1.90% (4/210)	0.48% (1/208)	1.20% (5/418)
Coronary artery disease	0.95% (2/210)	1.92% (4/208)	1.44% (6/418)
Ventricular tachycardia	0.00% (0/210)	2.40% (5/208)	1.20% (5/418)
Myocardial infarction	0.95% (2/210)	0.96% (2/208)	0.96% (4/418)
Cardiac arrest	0.48% (1/210)	0.96% (2/208)	0.72% (3/418)
Cardiac failure acute	0.95% (2/210)	0.48% (1/208)	0.72% (3/418)
Coronary artery dissection	0.95% (2/210)	0.48% (1/208)	0.72% (3/418)
Coronary artery stenosis	0.95% (2/210)	0.48% (1/208)	0.72% (3/418)
Aortic valve stenosis	0.00% (0/210)	0.96% (2/208)	0.48% (2/418)
Atrial flutter	0.00% (0/210)	0.96% (2/208)	0.48% (2/418)
Atrioventricular block complete	0.00% (0/210)	0.96% (2/208)	0.48% (2/418)
Bradycardia	0.95% (2/210)	0.00% (0/208)	0.48% (2/418)
Cardiac failure chronic	0.95% (2/210)	0.00% (0/208)	0.48% (2/418)
Myocardial ischaemia	0.95% (2/210)	0.00% (0/208)	0.48% (2/418)
Respiratory, thoracic and mediastinal disorders	6.19% (13/210)	4.33% (9/208)	5.26% (22/418)
Respiratory failure	2.38% (5/210)	0.48% (1/208)	1.44% (6/418)
Chronic obstructive pulmonary disease	0.95% (2/210)	0.48% (1/208)	0.72% (3/418)
Dyspnoea	1.90% (4/210)	0.00% (0/208)	0.96% (4/418)
Acute respiratory failure	0.00% (0/210)	1.44% (3/208)	0.72% (3/418)
Infections and infestations	4.29% (9/210)	4.81% (10/208)	4.55% (19/418)
Urinary tract infection	0.95% (2/210)	1.44% (3/208)	1.20% (5/418)
Pneumonia	0.95% (2/210)	0.48% (1/208)	0.72% (3/418)
Septic shock	0.48% (1/210)	0.96% (2/208)	0.72% (3/418)
Injury, poisoning and procedural	5.24% (11/210)	7.21% (15/208)	6.22% (26/418)

SAE to 365 Days	SELUTION SLR PTCA DEB (N=210)	SOC (N=208)	All Subjects (N=418)
complications			
Coronary artery restenosis	0.48% (1/210)	1.44% (3/208)	0.96% (4/418)
Vascular access site haematoma	0.95% (2/210)	0.48% (1/208)	0.72% (3/418)
Vascular access site haemorrhage	0.48% (1/210)	0.96% (2/208)	0.72% (3/418)
Femur fracture	0.00% (0/210)	0.96% (2/208)	0.48% (2/418)
General disorders and administration site conditions	6.19% (13/210)	5.29% (11/208)	5.74% (24/418)
Chest pain	1.43% (3/210)	3.37% (7/208)	2.39% (10/418)
Vascular stent stenosis	2.38% (5/210)	1.44% (3/208)	1.91% (8/418)
Non-cardiac chest pain	0.95% (2/210)	0.00% (0/208)	0.48% (2/418)
Nervous system disorders	4.29% (9/210)	5.29% (11/208)	4.78% (20/418)
Syncope	0.48% (1/210)	1.92% (4/208)	1.20% (5/418)
Cerebrovascular accident	1.90% (4/210)	0.00% (0/208)	0.96% (4/418)
Gastrointestinal disorders	3.33% (7/210)	4.81% (10/208)	4.07% (17/418)
Small intestinal obstruction	0.48% (1/210)	1.92% (4/208)	1.20% (5/418)
Rectal hemorrhage	0.95% (2/210)	0.96% (2/208)	0.96% (4/418)
Gastrointestinal hemorrhage	0.00% (0/210)	0.96% (2/208)	0.48% (2/418)
Renal and urinary disorders	3.33% (7/210)	3.85% (8/208)	3.59% (15/418)
Acute kidney injury	1.43% (3/210)	1.92% (4/208)	1.67% (7/418)
Nephrolithiasis	0.48% (1/210)	0.96% (2/208)	0.72% (3/418)
Vascular disorders	4.76% (10/210)	3.37% (7/208)	4.07% (17/418)
Hypotension	1.43% (3/210)	0.48% (1/208)	0.96% (4/418)
Aortic stenosis	0.95% (2/210)	0.00% (0/208)	0.48% (2/418)
Orthostatic hypotension	0.95% (2/210)	0.00% (0/208)	0.48% (2/418)
Investigations	2.38% (5/210)	0.96% (2/208)	1.67% (7/418)
Troponin increased	0.95% (2/210)	0.48% (1/208)	0.72% (3/418)
Metabolism and nutrition disorders	2.38% (5/210)	0.96% (2/208)	1.67% (7/418)
Diabetic ketoacidosis	0.95% (2/210)	0.00% (0/208)	0.48% (2/418)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1.43% (3/210)	1.92% (4/208)	1.67% (7/418)
Blood and lymphatic system disorders	1.43% (3/210)	0.48% (1/208)	0.96% (4/418)
Anemia	1.43% (3/210)	0.00% (0/208)	0.72% (3/418)
Surgical and medical procedures	2.38% (5/210)	0.48% (1/208)	1.44% (6/418)
Arterial revascularization	0.95% (2/210)	0.00% (0/208)	0.48% (2/418)
Musculoskeletal and connective tissue disorders	1.43% (3/210)	0.96% (2/208)	1.20% (5/418)
Skin and subcutaneous tissue disorders	0.95% (2/210)	0.48% (1/208)	0.72% (3/418)
Eye disorders	0.48% (1/210)	0.96% (2/208)	0.72% (3/418)
Cataract	0.00% (0/210)	0.96% (2/208)	0.48% (2/418)
Psychiatric disorders	0.95% (2/210)	0.00% (0/208)	0.48% (2/418)

Only events with a rate $\geq 0.95\%$ in either arm are included and listed by preferred term; thus, the sum of events that are included in each category may not equal the total.

12.9 Primary Endpoint Subgroup Analyses

With the exception of the hypothesis-driven secondary endpoint examining TLF at 12 months post-index procedure for **SELUTION SLR PTCA DEB** versus DES among subjects with one previous layer of stent the SELUTION4ISR Study was not designed or powered to study safety or effectiveness of the **SELUTION SLR PTCA DEB** versus SOC in subgroups, so these analyses are considered hypothesis-generating. The primary endpoint results for pre-specified and post-hoc subgroups are included in

Table 9. Subgroup analyses of the primary endpoint demonstrated no significant interactions with treatment effect. The forest plot for the sub-group analyses is included in **Figure 3**.

Table 9: Primary Endpoint Subgroup Analyses (PP)

Subgroup	SOLUTION SLR PTCA DEB (N=197)	SOC (N=193)	Difference [95% Credible Interval]	Posterior Probability of Non-inferiority	P-value for Interaction ¹
Stent Layers					0.167
1	14.19% (22/155)	10.19% (16/157)	3.96% [-3.12%,11.38%]	94.65%	
2	23.81% (10/42)	33.33% (12/36)	-9.38% [-28.60%,10.13%]	97.48%	
BMS ISR					0.878
Yes	10.53% (4/38)	8.00% (2/25)	1.47% [-14.80%,16.36%]	86.68%	
No	17.72% (28/158)	15.57% (26/167)	2.13% [-5.94%,10.18%]	97.22%	
DES ISR					0.359
Yes	16.85% (30/178)	15.14% (28/185)	1.76% [-5.78%,9.23%]	98.35%	
No	11.11% (2/18)	0.00% (0/8)	5.12% [-21.0%,27.63%]	65.74%	
Diabetes					0.492
Yes	25.88% (22/85)	20.73% (17/82)	5.04% [-7.67%,17.54%]	78.25%	
No	8.93% (10/112)	9.91% (11/111)	-0.94% [-8.94%,6.90%]	99.70%	
RVD					0.341
> 2.75mm	16.92% (11/65)	10.61% (7/66)	6.07% [-5.47%,18.02%]	74.94%	
≤ 2.75mm	15.91% (21/132)	16.54% (21/127)	-0.68% [-9.80%,8.15%]	98.95%	
Lesion Length					0.433
> 26mm	20.00% (1/5)	0.00% (0/3)	8.70% [-39.30%,52.23%]	51.58%	
≤ 26mm	16.15% (31/192)	14.74% (28/190)	1.44% [-5.82%,8.59%]	98.90%	
Lesion Length, Updated Categories²					0.474
< 10mm	16.09% (14/87)	18.68% (17/91)	-2.52% [-13.70%,8.33%]	98.60%	
10-20mm	16.09% (14/87)	11.39% (9/79)	4.40% [-6.13%,14.92%]	84.84%	
> 20mm	17.39% (4/23)	8.7% (2/23)	8.02% [-11.50%,28.19%]	58.83%	
Lesion Type					0.528
Focal	16.44% (12/73)	17.11% (13/76)	-0.63% [-12.60%,11.42%]	95.99%	
Diffuse	8.77% (5/57)	14.00% (7/50)	-5.15% [-17.90%,6.86%]	99.29%	
ISR					0.668
< 1 year	21.67% (13/60)	20.63% (13/63)	1.03% [-13.20%,15.46%]	88.76%	
≥ 1 year	14.05% (17/121)	10.66% (13/122)	3.31% [-4.82%,11.58%]	94.39%	
Covid-19					N/A
Yes	N/A	0.00% (0/1)	N/A	N/A	
No	20.59% (7/34)	11.54% (3/26)	7.86% [-11.00%,26.04%]	59.09%	
Age³					0.513
≤ 75 years	16.13% (25/155)	12.86% (18/140)	3.14% [-4.85%,11.23%]	95.07%	
> 75 years	16.67% (7/42)	18.87% (10/53)	-1.83% [-17.17%,14.01%]	93.05%	
Sex³					0.891
Male	16.15% (26/161)	14.69% (21/143)	1.43% [-6.68%,9.49%]	98.09%	
Female	16.67% (6/36)	14.00% (7/50)	3.00% [-12.10%,19.37%]	81.26%	
Ethnicity³					0.441
Hispanic or Latino	0.00% (0/9)	13.33% (2/15)	-8.71% [-32.90%,16.41%]	93.59%	
Not Hispanic or Latino	19.71% (27/137)	15.86% (23/145)	3.87% [-4.96%,12.83%]	91.00%	
1. Interaction was assessed using the Breslow-Day test. 2. The pre-specified subgroups analyses for lesion length included grouping for ≤26 mm and >26 mm. Additional size groupings were included as a post-hoc analysis to better evaluate the effect of lesion length on the primary endpoint outcomes. 3. Age, sex, and ethnicity were not pre-specified subgroup analyses but were included to fully evaluate the impact of these important subgroups on the primary endpoint outcomes.					

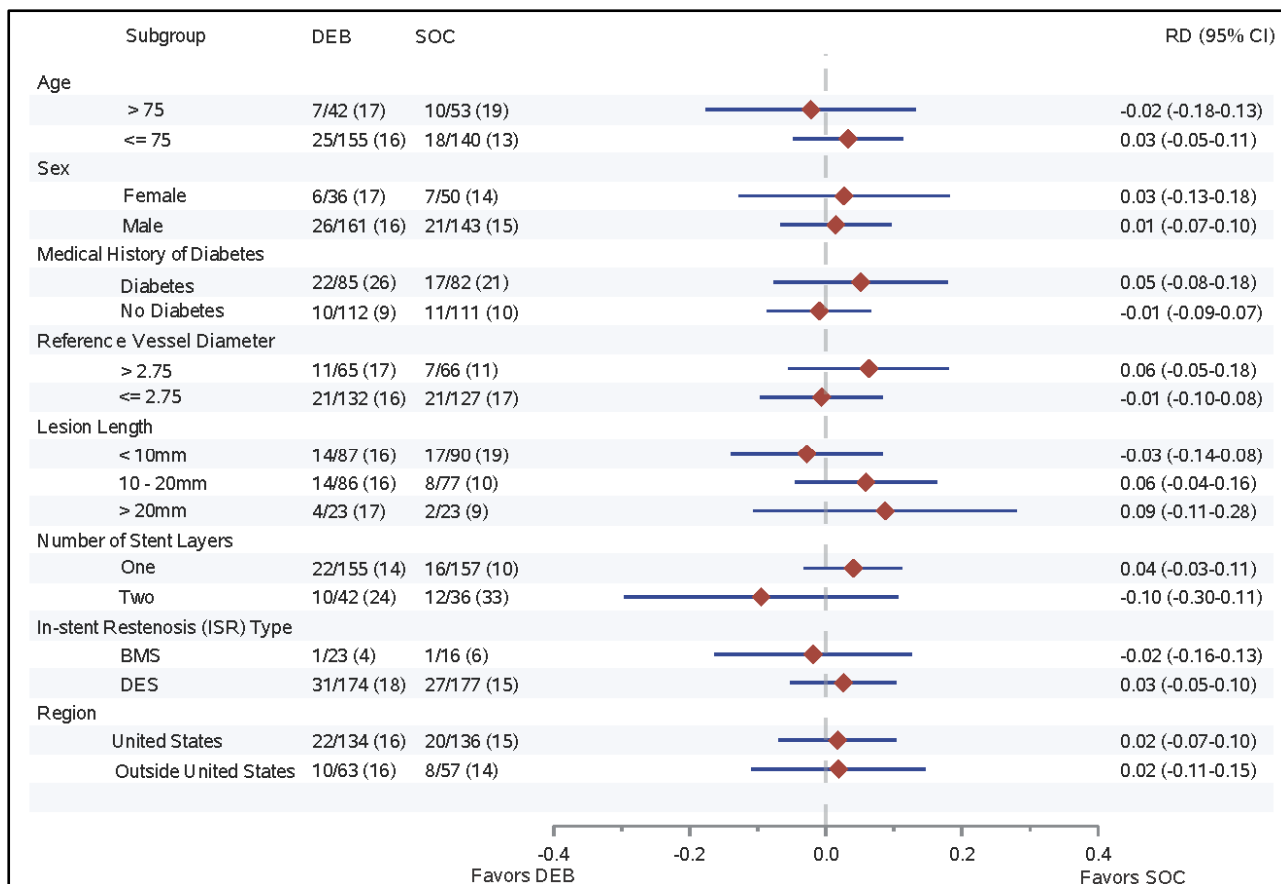


Figure 3: Forest Plot for Primary Endpoint Subgroup Analyses (PP)

12.10 Post-Hoc Analysis of TLF of the SELUTION SLR PTCA DEB vs Subgroups of SOC and in 1 and 2 Stent Layers

The SELUTION4ISR Study was designed to study the safety and effectiveness of the **SELUTION SLR PTCA DEB** versus SOC, a combination of DES and POBA. The study was also designed to include a powered secondary endpoint to study the **SELUTION SLR PTCA DEB** vs DES among subjects with one previous layer of stent. It was not designed or powered to study safety or effectiveness of the **SELUTION SLR PTCA DEB** versus the subgroups of the SOC arm in 2 stent layers. However, a post-hoc analysis was conducted in order to provide insight into how the **SELUTION SLR PTCA DEB** performed compared to both DES and BA in 1 and 2 stent layers, as shown in **Table 10**. The choice between repeat stenting and drug-coated balloon therapy should be based on physician judgement considering lesion characteristics and patient-specific factors.

Table 10: 12-Month TLF in SELUTION SLR PTCA DEB, SOC, BA, and DES in 1- and 2-layer ISR

Endpoint	SELUTION SLR PTCA DEB	SOC	SOC: BA	SOC: DES
One-Layer ISR				
TLF at 12 Months	14.19% (22/155)	10.19% (16/157)	36.84% (7/19)	6.52% (9/138)
Cardiac Death	1.94% (3/155)	1.27% (2/157)	0.00% (0/19)	1.45% (2/138)
Target Vessel MI ¹	7.74% (12/155)	3.82% (6/157)	15.79% (3/19)	2.17% (3/138)
CD-TLR	9.68% (15/155)	7.64% (12/157)	26.32% (5/19)	5.07% (7/138)
Two-Layer ISR				
TLF at 12 Months	23.81% (10/42)	33.33% (12/36)	50.00% (10/20)	12.5% (2/16)
Cardiac Death	2.38% (1/42)	2.78% (1/36)	0.00% (0/20)	6.25% (1/16)
Target Vessel MI ¹	7.14% (3/42)	11.11% (4/36)	10.00% (2/20)	12.5% (2/16)
CD-TLR	23.81% (10/42)	33.33% (12/36)	50.00% (10/20)	12.5% (2/16)

¹Target vessel MI includes spontaneous (Type 1) MI using the 4th Universal Definition of Myocardial Infarction (UDMI) and peri-procedural MI using the Society for Cardiac Angiography and Intervention (SCAI) definition.

12.11 Imaging (Angiographic and Optical Coherence Tomography (OCT)) Sub-Study Results

The trial enrolled 60 of the randomized subjects in an angiographic and optical coherence tomography (OCT) sub-study. Subjects in the imaging sub-study had to meet the same inclusion and exclusion criteria as the main study subjects. The baseline and lesion characteristics of this sub-study were similar to the full study population. At 12-month follow-up, several secondary endpoints were assessed by angiography, including binary angiographic restenosis, in-stent and in-segment percent diameter stenosis, in-stent and in-segment LLL, and in-stent and in-segment MLD. OCT was utilized to evaluate neointimal hyperplasia, neo-atherosclerosis, and stent underexpansion. No significant differences were observed between groups, as reported in **Table 11**.

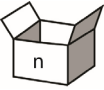
Table 11: Secondary Imaging Endpoints at 12 Months - Angiographic and OCT Sub-study

Secondary Endpoints	SELUTION SLR PTCA DEB (N=36)	SOC (N=24)	All Subjects (N=60)
Treated segment percent diameter stenosis (at 12m)			
Mean +/- SD (N)	37.06 +/- 23.52 (32)	27.69 +/- 18.26 (16)	33.94 +/- 22.16 (48)
Binary angiographic restenosis (at 12m) % (n/N)	31.25% (10/32)	18.75% (3/16)	27.08% (13/48)
Treated segment late lumen loss (LLL) (at 12m)			
Mean +/- SD (N)	0.59 +/- 0.57 (32)	0.46 +/- 0.53 (16)	0.55 +/- 0.55 (48)
Treated segment minimum lumen diameter (MLD) (at 12m)			
Mean +/- SD (N)	1.60 +/- 0.65 (32)	1.71 +/- 0.87 (18)	1.64 +/- 0.73 (50)
OCT study assessments			
Neointimal hyperplasia	57.69% (15/26)	61.54% (8/13)	58.97% (23/39)
Neoatherosclerosis	26.92% (7/26)	7.69% (1/13)	20.51% (8/39)
Underexpansion	15.38% (4/26)	23.08% (3/13)	17.95% (7/39)

12.12 Clinical Pharmacokinetics (PK)

The pharmacokinetic (PK) profile of sirolimus following treatment with the **SELUTION SLR PTCA DEB** was evaluated in 17 patients receiving 118-400 µg of sirolimus. Mean whole blood concentration (mean C_{max} 1.81 ng/mL) peaked immediately post-procedure (median T_{max}: 0.007 days; 10 minutes) and decreased steadily over time with only 6 of the 17 subjects having quantifiable concentrations at 1.0 days post-administration and no subjects having quantifiable levels beyond 3 days post-administration. These data indicate that treatment with the **SELUTION SLR PTCA DEB** provides low systemic exposure to sirolimus which clears rapidly.

Explanation of symbols on package labeling:

	Manufacturer
	Use-by date
	Catalogue number
	Lot number
	Consult instructions for use or consult electronic instructions for use
	Caution: Federal (USA) law restricts this device to sale by or on the order of a physician
	Keep away from sunlight
	Keep dry
	Do not use if package is damaged and Consult instructions for use
	Non-pyrogenic
	Do not re-sterilize
	Do not re-use
	n units per box
	Date of manufacture
	Temperature limit

	Sterilized using irradiation
	Single sterile barrier system; Sterilized using irradiation
	Balloon Pressure
	Rapid Exchange
	Rate Burst Pressure
	Nominal Pressure
	Balloon Length
	Balloon Diameter
	Sirolimus Dose Density
	Unique Device identifier
	Contains a medicinal substance
	Country of manufacture
	Guidewire Compatibility
	Guide Catheter Compatibility

PRODUCT SIZE MATRIX

Balloon Diameter (mm)	Balloon Length (mm)			
	15	20	25	30
2.25	SCB14U-225015D	SCB14U-225020D	SCB14U-225025D	SCB14U-225030D
2.50	SCB14U-250015D	SCB14U-250020D	SCB14U-250025D	SCB14U-250030D
2.75	SCB14U-275015D	SCB14U-275020D	SCB14U-275025D	SCB14U-275030D
3.00	SCB14U-300015D	SCB14U-300020D	SCB14U-300025D	SCB14U-300030D
3.25	SCB14U-325015D	SCB14U-325020D	SCB14U-325025D	SCB14U-325030D
3.50	SCB14U-350015D	SCB14U-350020D	SCB14U-350025D	SCB14U-350030D
4.00	SCB14U-400015D	SCB14U-400020D	SCB14U-400025D	SCB14U-400030D
4.50	SCB14U-450015D	SCB14U-450020D	SCB14U-450025D	SCB14U-450030D



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