Chocolate Touch® Paclitaxel Coated PTA Balloon Catheter

Instructions for Use

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"Caution: Federal law restricts this device to sale by or on the order of a physician".

1 PRODUCT NAME

Chocolate Touch® Paclitaxel Coated PTA Balloon Catheter

2 PRODUCT DESCRIPTION

Table 1. Product Components

Catheter Configuration	Over the Wire (OTW)			
Balloon Diameters and Lengths	**Diameter/Length**	**40 mm**	**80 mm**	**120 mm**
	4.0 mm	✓	✓	✓
	4.5 mm	✓	✓	✓
	5.0 mm	✓	✓	✓
	5.5 mm	✓	✓	✓
	6.0 mm	✓	✓	✓
Catheter Lengths	135 cm (4.0 diameter, all lengths) 120 cm (4.5, 5.0, 5.5, & 6.0 diameter, all lengths)			
Nominal Balloon Pressure	9 atm (4.0 mm diameter, all lengths) 8 atm (4.5, 5.0, 5.5, & 6.0 diameter, all lengths)			
Rated Burst Pressure	14 atm (4.0 diameter, all lengths) 12 atm (4.5, 5.0, 5.5, & 6.0 diameter, all lengths)			
Guidewire Compatibility	0.014 (4.0 diameter, all lengths) 0.018 (4.5, 5.0, 5.5, & 6.0 diameter, all lengths)			
Minimum Introducer Sheath	**Diameter / Length**	**40 mm**	**80 mm**	**120 mm**
	4.0 mm	5F	5F	6F
	4.5, 5.0, 5.5 mm	6F	6F	6F
	6.0 mm	6F	6F	7F
Balloon Coating	Active Pharmaceutical Ingredient (Paclitaxel) and Inactive Excipient			

2.1 Device Description

Chocolate Touch® Paclitaxel Coated PTA Balloon Catheter is an "over-the-wire" balloon dilatation catheter with a braided shaft and an atraumatic tapered tip. The product family consists of 0.014"and 0.018" systems that are compatible with 0.014"and 0.018" guidewires, respectively. Overall catheter lengths range from 120-135 cm.

The distal end of the catheter has a semi-compliant balloon that expands to known diameters (refer to compliance chart) at specific pressures. The balloon is constrained by a nitinol constraining structure (CS) which facilitates uniform inflation and fast deflation. Upon deflation, the CS is removed from the vessel along with the balloon catheter. The balloon is available in multiple sizes and contains two radiopaque markers to assist with positioning.

Catalogue Number	Description (mm)	Guidewire (in)	Catheter Length (cm)
TUAA-BBB-XXYYY OTW	Diameters (XX): 4.0, 4.5, 5.0, 5.5, 6.0 Lengths (YYY): 40, 80, 120	0.014, 0.018 (AA)	120-135 (BBB)

The 0.014" guidewire compatible catheter is 135cm in length, including 4.0mm diameter balloons of all lengths (40mm, 80mm, 120mm). The 0.018" guidewire compatible catheter is 120cm in length, including 4.5 – 6.0mm diameter balloons of all lengths (40mm, 80mm, 120mm).

The proximal end of the device is a common balloon catheter design of a braided shaft connected to a plastic hub and strain relief. The hub has two ports; the inflation port is used to inflate the balloon and the guidewire port connects to the guidewire lumen.

The Chocolate Touch® Paclitaxel Coated PTA Balloon Catheters are supplied STERILE and intended for single use (See **Figure 1**).

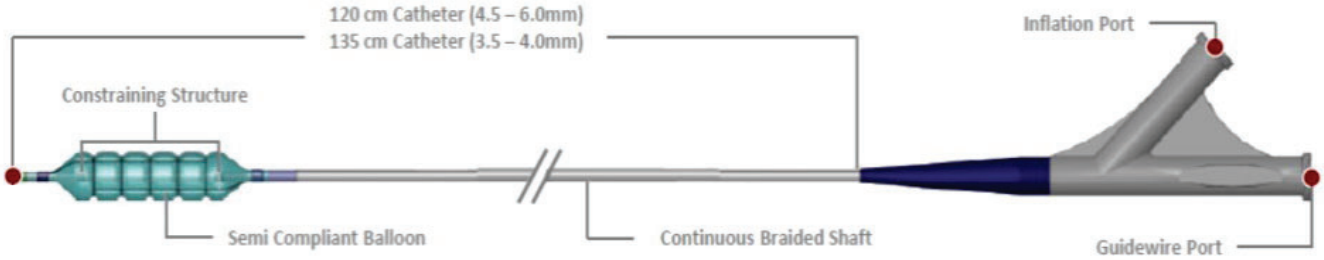


Figure 1. Schematic of Chocolate Touch®

2.2 Coating Description – Active Pharmaceutical Ingredient (API) Paclitaxel

The Chocolate Touch™ Paclitaxel Coated PTA Balloon Catheter is a peripheral angioplasty catheter having an anti-proliferative coating. The drug coating covers the distal assembly portion of the catheter. It is comprised of the active pharmaceutical ingredient, paclitaxel, and an excipient, propyl gallate.

The Paclitaxel Coated Chocolate Balloon Catheter contains paclitaxel [2α,4α,5β,7β,10β,13α)-4,10-Bis(acetyloxy)-13-{[(2R,3S)- 3-(benzoylamino)-2- hydroxy-3-phenylpropanoyl]oxy}-1,7-dihydroxy-9-oxo-5,20-epoxytax-11-en-2-yl-benzoat; CAS #33069-62-4] as the active pharmaceutical ingredient. The anti-mitotic properties of paclitaxel have been approved for the treatment of restenosis, first as a coating for drug eluting stents and more recently for paclitaxel coated balloons (DCB). The molecular mass of paclitaxel is 853.906 g/mol and has a molecular structure as shown in **Figure 2**.

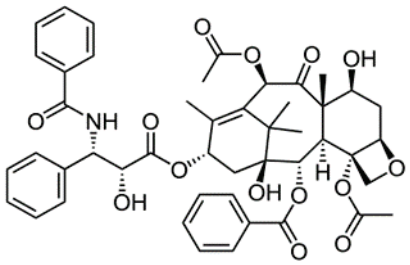


Figure 2: Molecular Structure of Paclitaxel

The total amount of paclitaxel for each balloon size is provided in **Table 2**.

Table 2. Product Matrix and Paclitaxel Content

Diameter/Length	40 mm	80 mm	120 mm
4.0 mm	1778mg	3557mg	5335mg
4.5 mm	2001mg	4002mg	6002mg
5.0 mm	2223mg	4446mg	6669mg
5.5 mm	2445mg	4891mg	7336mg
6.0 mm	2668mg	5335mg	8003mg

2.3 Coating Description – Excipient Propyl Gallate

The Chocolate Touch coating contains, propyl gallate, [3,4,5-trihydroxybenzoate]; CAS #121-79-9 as the excipient. The excipient is an inactive substance that serves to facilitate paclitaxel treatment of the Chocolate Touch device. The molecular mass of propyl gallate is 212.22 g/mol and has a molecular structure as shown in **Figure 3**.

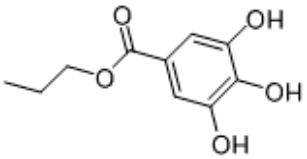


Figure 3. Molecular Structure of Propyl Gallate

3 INDICATIONS FOR USE

The Chocolate Touch® (Paclitaxel Coated PTA Balloon Catheter) is indicated for percutaneous transluminal angioplasty, after appropriate vessel preparation, of de novo or restenotic lesions up to 180 mm in length in native femoral or popliteal arteries with reference vessel diameters of 4.0 mm to 6.0 mm."

4 CONTRAINDICATIONS

- Use in the coronary arteries, renal arteries, and supra-aortic/cerebrovascular arteries
- Lesion is unable to be crossed with a guidewire.
- Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy
- Patients with known allergies or sensitivities to paclitaxel
- Pregnant or breast-feeding women or women who are intending to become pregnant, or men intending to father children.

5 WARNINGS

- **A signal for increased risk of late mortality has been identified following the use of paclitaxel-coated balloons and paclitaxel-eluting stents for femoropopliteal arterial disease beginning approximately 2-3 years post-treatment compared with the use of non-drug coated devices. There is uncertainty regarding the magnitude and mechanism for the increased late mortality risk, including the impact of repeated exposure/procedures. Physicians should discuss this late mortality signal and the benefits and risks of available treatment options with their patients. (see Section 10.4 for further information).**
- Physicians should discuss the late mortality signal and the risks and benefits of available treatment options for their specific disease or condition with their patient.
- STERILE product, for one-time use only. Re-sterilizing or re-using may compromise the structural integrity of the device and may create a risk of contamination which, in turn, may result in health risks to patients.
- The inflated diameter of the balloon should correspond to the diameter of the vessel for treatment.
- The catheter should be used under fluoroscopic guidance. Do not advance or retract the catheter unless the balloon is fully deflated under vacuum. Do not advance against resistance without first determining the cause of the resistance and taking appropriate action.
- Balloon pressure should never exceed rated burst pressure (RBP). Exceeding the RBP may result in balloon rupture.
- Use only the recommended balloon inflation medium. Never use air or any gaseous medium to inflate the balloon.
- Use Chocolate Touch® Paclitaxel Coated PTA Balloon Catheter prior to the "Use By" date specified on package.
- The Chocolate Touch® Paclitaxel Coated PTA Balloon Catheter has not been tested and should not be used for post-dilatation of stents.
- Do not use in the presence of a freshly deployed stent.

- The safety and effectiveness of implanting multiple Chocolate Touch® DCBs (Paclitaxel Coated PTA Balloon Catheter) with a total drug dosage exceeding 16,006µg of paclitaxel in a patient has not been clinically evaluated in the Chocolate Touch IDE Pivotal Study.

6 PRECAUTIONS

- Ensure the balloon size and device functionality are suitable for the intended procedure. Do not undersize.
- The device should only be used by trained physicians.
- Use appropriate anticoagulant and vasodilator therapy during and after the procedure.
- Do not pre-inflate prior to use. Prepare as directed in the Balloon Catheter Preparation section.
- If you choose to rotate the catheter, alternate the rotating direction. Do not rotate more than three (3) times in the same direction consecutively.
- Do not use the Chocolate Touch DCB for pre-dilatation or for post-dilatation.

7 USE IN SPECIAL POPULATIONS

- Pregnancy and Lactation: Do Not Use in women who are breastfeeding or pregnant
- Gender: Results of the Chocolate Touch are consistent between genders.
- Pediatric Use: The safety and effectiveness of the Chocolate Touch in pediatric patients has not been established.
- Geriatric Use: Average age of the patients enrolled in the Clinical studies of the Chocolate Touch Catheter were 69.9 ± 9.8.

8 DRUG INFORMATION

8.1 Mechanism of Action

The mechanism by which neointimal growth is inhibited by the Chocolate Touch has not been fully established. The active pharmaceutical ingredient is paclitaxel, which binds to and stabilizes microtubules during cell division inhibiting the normal mitotic process.

8.2 Drug Interactions

Formal drug interaction studies have not been conducted with the Chocolate Touch® Paclitaxel Coated PTA Balloon Catheter. Consideration for both systemic and local drug interactions should be taken for use of this device in patients taking a drug with a known drug interaction to paclitaxel.

8.3 Carcinogenicity, Genotoxicity, and Reproductive Toxicity

No long-term studies in animals have been published to evaluate the carcinogenic potential of the drug paclitaxel. Paclitaxel inhibits cell proliferation by stabilizing microtubules during cell division, and one consequence is the possible loss of chromosomes during cell division. This indirect action is consistent with positive responses in vitro and in vivo micronucleus genotoxicity assays, which detect DNA fragments. Positive results have also been reported for chromosomal aberrations in primary human lymphocytes. It is not known whether paclitaxel has a separate direct action on DNA in the generation of DNA breaks or fragments. Paclitaxel was not mutagenic in the Ames or CHO/HPRT assays for gene mutation.

There are no adequate and well-controlled studies published in pregnant women or in men intending to father children. Studies performed in rats and rabbits receiving IV paclitaxel during organogenesis revealed evidence of maternal toxicity, embryotoxicity, and fetotoxicity at dosages of 3 mg/kg/day. No teratogenicity was observed at paclitaxel doses of 1 mg/kg/day. For comparison, the maximum Chocolate Touch lesion (assuming 6.0mm, treated with 180mm length with 20mm overlap) would have 0.15mg/kg of paclitaxel assuming a 90kg person. Approximately 6-20 times lower dosages.

8.4 Pharmacokinetics

The pharmacokinetic profile of paclitaxel following treatment with the Chocolate Touch was evaluated in 15 patients receiving 4,446 µg to 13,338 µg of paclitaxel. This evaluation was conducted as a sub-study of the randomized clinical trial and is described in Summary of Clinical Investigations (Section 10). Paclitaxel systemic exposure in the treated subjects was low and cleared rapidly with a biphasic decline. The Cmax ranged from 2.5 to 15.1 ng/mL and the average AUC0-∞ was 58.9 ± 26.8 hr*ng/mL. These data indicate that treatment with the Chocolate Touch provides low systemic exposure of paclitaxel.

8.5 Potential Adverse Effects of Device on Health

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device:

- Access-site complications
- Allergic reaction to medication, paclitaxel, contrast medium or nitinol
- Amputation
- Aneurysm
- Arterial dissection or perforation
- Arterial rupture
- Arterial spasm
- Arterio-venous fistula
- Bleeding Complications
- Cardiac arrest
- Cardiac arrhythmia
- Death
- Device malfunction or failure
- Emboli (air, tissue, thrombi, material from device(s) used in the procedure)
- Emergency or non-emergency arterial bypass surgery
- Extravasation of contrast media
- Fracture of the guide wire or any component of the device that may or may not lead to device embolism, serious injury or surgical intervention
- Gastrointestinal bleed
- Hemorrhage or hematoma
- Hypotension
- Infection, local or systemic
- Inflammation
- Myocardial infarction or coronary ischemia
- Neurological deficit
- Pain or tenderness
- Peripheral limb ischemia
- Placement of a bail-out stent
- Pseudo-aneurysm
- Radiation exposure
- Reaction to contrast media / medication
- Renal insufficiency or failure
- Respiratory distress or failure
- Restenosis of treated artery or segment
- Sepsis or systemic infection
- Stroke or TIA

- Surgical repair of vascular access site
- Thrombosis
- Transfusion
- Total occlusion of the peripheral artery
- Vascular complications which may require surgical repair (conversion to open surgery)
- Worsening of peripheral arterial disease

Potential complications of balloon catheterization include, but are not limited to, the following:

- Balloon rupture
- Detachment of a component of the balloon and/or catheter system
- Failure of the balloon to perform as intended
- Failure to cross the lesion.

Potential complications which may be associated with the use of paclitaxel include, but are not limited to:

- Allergic/immunological reaction to paclitaxel
- Alopecia
- Anemia
- Gastrointestinal symptoms (diarrhea, nausea, pain, vomiting)
- Hematologic changes in vessel wall including inflammation, cellular damage, or necrosis
- Myalgia/Arthralgia
- Myelosuppression
- Peripheral neuropathy

There may be other potential adverse events that are unforeseen at this time. For the specific adverse events that occurred in the clinical study please see **Table 12** in the Summary of Clinical Investigations **(Section 11**) below.

9 PATIENT COUNSELING INFORMATION

Physicians should consider the following when counseling patients about the Chocolate Touch:

- Discuss the risks associated with percutaneous transluminal angioplasty procedures.
- Discuss the risks associated with the Chocolate Touch.
- Discuss the risks and benefits of treatment specific to the patient
- Discuss antiplatelet therapy post-procedure and the risks or early discontinuation
- Discuss lifestyle changes for the patient in the short- and long-term

10 SUMMARY OF CLINICAL INVESTIGATIONS

10.1 The ENDURE Early Feasibility Study

10.1.1 Objective

The ENDURE study was a prospective, multi-center, single arm, first in human study designed to provide an initial evaluation of the feasibility, safety, and clinical benefits of the Chocolate Touch for the treatment of subjects with infrainguinal arterial disease.

10.1.2 Study Design

The study was planned to enroll up to 100 subjects in Europe and up to 70 subjects in New Zealand. Patients with claudication or ischemic rest pain and angiographically significant lesions (≥70% stenosis) in the superficial femoral and/or proximal popliteal (P1) artery were eligible to participate if they met all inclusion criteria and no exclusion criteria and were willing to provided written informed consent and comply with specified follow-up evaluations.

Angiographic exclusion criteria included severe calcification at the target lesion, primary target lesion within the P2 or P3 segments of the popliteal artery, previous bypass or stent at target vessel or proximal to target vessel, aneurysm in target limb, prior major amputation of target or non-target limb, lesion requiring use of a re-entry device or atherectomy, laser, or ablation procedure, or the use of a drug eluting stent, treatment with another drug coated balloon, or scoring/cutting balloon.

All subjects were treated with the Chocolate Touch device and underwent clinical follow-up at 1, 6 and 12 months, in addition to imaging follow-up: quantitative vessel angiography (QVA) at 6 months and duplex ultrasound (DUS) at 6 and 12 months.

10.1.3 Endpoints

The primary endpoint was target lesion Late Lumen Loss (LLL) at 6 months assessed by quantitative vessel angiography (QVA).

Secondary endpoints included:

- Acute success: device and technical success, bail-out stenting, occurrence and severity of target lesion dissection;
- Clinical: occurrence/severity of device related adverse events; freedom from clinically indicated TLR, major amputation free survival; and clinical improvement (based on Rutherford and ABI changes) at 1, 6 and 12 months;
- Patency: primary and secondary patency at 6 and 12 months.

The primary analysis population for all primary and secondary endpoints was the Intention to Treat (ITT) population, defined as all subjects who provided informed consent and were enrolled in the study.

10.1.4 Results

10.1.4.1 Enrollment and Follow-up

Between March 18, 2014 and June 29, 2015, a total of 67 subjects were enrolled at 4 investigational sites (one in New Zealand and 3 in Germany). Three subjects enrolled in the study were treated for two target lesions; therefore, the study included a total of 70 target lesions.

All 67 subjects enrolled in the study constituted the ITT population. At 12 months, 61 (91%) subjects had clinical follow up; two subjects were lost to follow-up and one death occurred between 6 and 12 months.

10.1.4.2 Baseline Subject and Lesion Characteristics

The baseline characteristics of the subjects enrolled in the ENDURE study were representative of the lower extremity PAD patient population with ATK lesions. The mean age was 69.2 ± 8.9 years and 61% (41/67) of patients were males. There was a high prevalence of cardiovascular risk factors, including hypertension (87% , hyperlipidemia 68%), diabetes (34% and smoking (79%). Of the 67 subjects, 20 (30% had prior coronary interventions PCI or CABG). Most patients, 62/67 93%) had Rutherford category 3. There were 2 (3%) patients with Rutherford category 4 and 3 (4.5%) patients with Rutherford category 5.

Most lesions, 65/70 (92.9% were in the SFA. The mean lesion length was 7.3 ± 3.9 cm and the average RVD was 5.2 ± 0.6 mm. Moderate or severe calcification was present in 54.3% (38/70 of cases and 33.3% (23/69 of the lesions were total occlusions. Pre-treatment average MLD was 1.2 ± 1.0 mm and %DS was 76.3 ± 19.2%.

10.1.4.3 Procedural Characteristics

On average, 1.4 ± 0.5 Chocolate Touch balloons were used per patient. A single Chocolate Touch device was used in 42 63%) cases, two in 24 (36%), and three in one case (1%). Pre-dilatation was not required for this study, but was recommended for total occlusions and pre-emptively at the discretion of the treating physician. Only 29.9% 20/67) of cases were conducted with pre-dilatation. The DCC was delivered and inflated at the target lesion in 100% of cases. No flow-limiting dissections (Type E or F) were reported after treatment with Chocolate Touch device. Post Chocolate Touch treatment was indicated in 13 cases due to residual stenosis. In one case, the DCC was unable to achieve <50% residual stenosis and bail-out stenting was performed (1/67). Other post-DCC interventions included stenting that did not meet the pre-defined bailout criteria (n=8) and PTA (n=4).

10.1.4.4 Angiographic Outcomes Post Procedure

Post procedure, mean %DS was 24.4 ± 10.4%, decreased compared with baseline 76.3 ± 19.2% and mean MLD was 3.8 ± 1.0 mm, increased compared with baseline (1.2 ± 1.0 mm). Postprocedural average acute gain was 2.6 ± 1.1 mm and blood flow was normal in all cases, 100% 69/69).

10.1.4.5 Primary Endpoints

In the ITT population, the primary endpoint of target lesion LLL at 6 months was reported in 52 subjects/54 lesions (78% of subjects [52/67]). The primary endpoint was not reported in 9 cases because the subjects refused angiography. In the ITT population, the average LLL at 6 months was 0.15 ± 0.68 mm (range: -0.31 mm to 1.92 mm). In the PP population, the primary endpoint was reported in 47 patients/47 lesions (77% of subjects [47/61]) and the average LLL was 0.14 ± 0.66 mm.

10.1.4.6 Secondary Endpoints

Acute Success

In the ITT population, the device success rate (per protocol defined as <30% residual stenosis) was 72.9% (51/70 lesions . Technical success, defined as the ability to deliver to and inflate the DCC at the intended target lesion location, was 100% (70/70 lesions). There was one case of bail-out stenting (1.4%, 1/70). No flow-limiting dissection (Type E or F) was reported after treatment with the Chocolate Touch DCC.

Major Adverse Events

Major Adverse Event (MAE) was defined post-hoc as a composite of clinically-indicated TLR, death and major amputation. At 30 days post-procedure, there were no MAE events 0% [0/67]). Major Adverse Events (MAE) through 12 months in the ITT population are presented in **Table 3**. One death occurred in the study, adjudicated by the CEC as a non-cardiovascular death that was not related to the Chocolate Touch DCC.

Table 3. ENDURE Major Adverse Events to 12 Months (ITT Population)

Secondary Endpoints **Major Adverse Events**	**DCC** **ITT population**
MAE (%, n/N)	9.7 (6/62[a])
Clinically indicated TLR	8.1 (5/62)
Death	1.6 (1/62)
Major Amputation	0 (0/62)
Freedom from Clinically Indicated TLR (%, n/N)	91.9 (57/62)
All TLR %, n/N	9.7 (6/62)[b]
Major Amputation Free Survival (%, n/N)	98.4 (61/62)
a. The denominator of 62 subjects included 61 subjects with clinical follow-up at 1 year and 1 subject who died prior to 1 year. b. One subject not clinically indicated TLR at 6 months and a clinically indicated TLR at 12 months; therefore, 7 total TLR events were reported.	

Clinical Improvement

At 1, 6 and 12 months in the ITT population, an ABI increase of ≥0.1 was achieved in 78.6%, 82.7% and 80.0% of patients, respectively. In the ITT population, clinical improvement by ≥1 Rutherford category was 90.5% at 1 month, 93.4% at 6 months and 95.1% at 12 months.

Patency

Primary and secondary patency rates at 6 and 12 months in the ITT population are presented in **Table 4**.

Table 4. Patency at 6 and 12 Months (ITT Population)

	DCC ITT Population	
	6 months	**12 months**
Primary Patency	89.3% 50/56)	80.7% 46/57)
Secondary Patency	96.4% 54/56)	89.5% 51/57)

10.2 The Chocolate Touch IDE Pivotal Study

10.2.1 Late Mortality Signal for Paclitaxel-Coated Devices

A meta-analysis of 28 randomized controlled trials published in December 2018 by Katsanos et. al. identified an increased risk of late-mortality at 2 years and beyond for paclitaxel-coated balloons and paclitaxel-eluting stents used to treat femoropopliteal arterial disease. In response to these data, FDA performed a patient-level meta-analysis of long-term follow-up data from the pivotal premarket randomized trials of paclitaxel-coated devices used to treat femoropopliteal disease using available clinical data through May 2019. The meta-analysis also showed a late mortality signal in study subjects treated with paclitaxel-coated devices compared to patients treated with uncoated devices. Specifically, in the 3 randomized trials with a total of 1090 patients and available 5-year data, the crude mortality rate was 19.8% (range 15.9% - 23.4%) in patients treated with paclitaxel-coated devices compared to 12.7% (range 11.2% - 14.0%) in subjects treated with uncoated devices. The relative risk for increased mortality at 5 years was 1.57 (95% confidence interval 1.16 – 2.13), which corresponds to a 57% relative increase in mortality in patients treated with paclitaxel-coated devices. An independent meta-analysis of similar patient-level data provided by VIVA Physicians, a vascular medicine organization, reported similar findings with a hazard ratio of HR of 1.38 (95% confidence interval 1.06 - 1.80).

The presence and magnitude of the late mortality risk should be interpreted with caution because of multiple limitations in the available data including wide confidence intervals due to a small sample size, pooling of studies of different paclitaxel-coated devices that were not intended to be combined, substantial amounts of missing study data, no clear evidence of a paclitaxel dose effect on mortality, and no identified pathophysiologic mechanism for the late deaths. Paclitaxel-coated balloons and stents improve blood flow to the legs and decrease the likelihood of repeat procedures to reopen blocked blood vessels compared to uncoated devices. The benefits of paclitaxel-coated devices (e.g., reduced reinterventions) should be considered in individual patients along with potential risks (e.g., late mortality).

For the Chocolate Touch, Kaplan Meier mortality estimates at 2 and 3 years are 3.3%, and 6.7%, respectively. For the Lutonix control device, Kaplan Meier mortality estimates at 2 and 3 years are 5.1%, and 11.1%, respectively. Additional information regarding long-term outcomes can be found in Section 10.4.

10.2.2 Study Design

TriReme performed a clinical study to establish reasonable assurance of safety and effectiveness of percutaneous transluminal angioplasty, after predilatation, of de novo and restenotic lesion in native superficial femoral and popliteal arteries with the Chocolate Touch DCB in the USA, Germany, Austria, and New Zealand under IDE # G160085. Data from this clinical study formed the basis of the PMA approval decision. A summary of the study is presented below. The Chocolate Touch Study is a prospective, randomized, multi-center, single-blind study comparing Chocolate Touch DCB to the Lutonix 035 Drug Coated PTA Catheter, (BD, Franklin Lakes, NJ) for treatment of femoropopliteal arteries in a single limb.

Patients were treated between July 26, 2017, and May 26, 2020. The database for this PMA reflected data collected through May 20, 2021, and included 333 (313 randomized and 20 Roll-In) patients randomized 1:1 to the Chocolate Touch DCB (n=152) or the control DCB device (n=161). There were 34 investigational sites (28 in the USA, 5 in Europe, and 1 in New Zealand).

10.2.2.1 Clinical Inclusion/Exclusion Criteria

Enrollment in The Chocolate Touch Study was limited to patients who met the following general and angiographic inclusion criteria:

- Minimum of 18 years of age
- Intermittent claudication or ischemic rest pain (Rutherford 2-4)
- Life Expectancy >2 years
- Patient has agreed to follow-up requirements and given informed consent
- Lesion successfully crossed with a guidewire
- Lesion in the SFA or popliteal artery defined as a lesion with a proximal origin >10mm from SFA origin (deep femoral artery) and a distal end above the knee joint (at least 3 cm above bottom of the femur – P1).
- Target Lesion ≥70% stenosis in the SFA or popliteal arteries
- Reference Vessel Diameter (RVD) between 4.0 & 6.0mm and within treatment range of Chocolate Touch to be used 1.1:1 at the Target Lesion.
- Target Lesion ≤180mm that consists of no more than two adjacent lesions ≤ 25mm apart) and is able to be completely covered with inflation of no more than two assigned balloons (with minimum of >5mm overlap to the area covered by the first balloon).
  - Note: Adjacent or tandem target lesions must be treated as a single lesion.
- Angiographic evidence of distal run-off demonstrated by at least one patent tibial vessel without evidence of significant (≥70% stenosis from origin to ankle.
- In-flow vessel without significant stenosis (≥70%) or successful treatment (≤30% residual stenosis with no complications) of a diseased vessel.
  Note: treatment of contralateral iliac is permissible.

Patients were <u>not</u> permitted to enroll in The Chocolate Touch Study if they met any of the following general or angiographic exclusion criteria:

- Acute limb ischemia, or patient indicated for thrombolytic therapy
- Planned surgical or interventional procedures within 30 days after study procedure.
- Non-target lesion concurrent interventions involving a re-entry device, atherectomy, laser, or ablation procedures, the use of a drug eluting stent, or treatment with any other drug coated balloon.
- Myocardial infarction or stroke within 30 days prior to the procedure
- Known intolerance to required medications, contrast media that cannot be adequately premedicated, nitinol, or Paclitaxel
- Known impaired Renal Function that could have an impact on contrast tolerance with GFR ≤ 30 ml/min per 1.73 m2 and/or elevated serum creatinine >2.5mg/dL (220μmol/L) or on dialysis.
- Known bleeding disorder or uncontrolled hypercoagulable disorder
- Non-atherosclerotic lesion (e.g., vasculitis or Berger's disease)
- Female of child-bearing age who is Pregnant or intends to be pregnant during study
- Patient is enrolled in another investigational clinical study or was previously enrolled in this study
- Presence of perforation, dissection (Type D or worse) or other injury in target vessel at time of enrollment
- Severe Calcification at the target lesion (defined as angiographic evidence of dense calcification present on both sides of the vessel wall on two orthogonal views and that extends >50 continuous mm in length).
- Previous bypass graft or stent at target vessel (must be greater than 20mm from target lesion), or iliac stent that cannot permit crossing by the treatment balloon within the introducer sheath
  Note: In-stent restenosis is not allowed.

10.2.2.2 Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 30 days, 6, 12, 24 and 36 months with a telephone follow-up at 48- and 60-months post-index procedure. Please see **Table 5** below for the complete procedure and follow-up schedule.

Table 5. Procedure and Follow-Up Schedule

PROCEDURE/TEST	Baseline[1]	Procedure (Day 0)	1 Month Follow-Up Visit (30 days ± 7 days)	6 Month Follow-Up Visit (180 days ± 30 days)	12 Month Follow-Up Visit (364 days ± 30 days)	24 Month Follow-Up Visit (728 days ± 60 days)	36 Month Follow-Up Visit (1092 days ± 60 days)	48 Month Phone Call (1446 days ± 60 days)	60 Month Phone Call (1820 days ± 60 days)
Screening									
Informed Consent[2]	✓								
General Inclusion / Exclusion Criteria	✓								
Angiographic Inclusion / Exclusion Criteria		✓							
Clinical Assessments									
Medical History/ Physical Exam[3]	✓		✓	✓	✓	✓	✓		
Laboratory Assessments (creatinine or GFR)	✓								
Urine pregnancy test if female[4]	✓								
Ankle Brachial Index (ABI) / Toe Brachial Index (TBI)	✓		✓	✓	✓	✓	✓		
Rutherford Clinical Category (RCC)	✓		✓	✓	✓	✓	✓		
Adverse Events Assessment		✓	✓	✓	✓	✓	✓	✓	✓
PAD QOL	✓		✓	✓	✓	✓	✓		
WIQ	✓		✓	✓	✓	✓	✓		
Medications: Aspirin / Monotherapy[5]		✓	✓	✓	✓	✓	✓	✓	✓
Imaging									
Angiography		✓							
Duplex Ultrasound			✓	✓	✓	✓	✓		

[1] Standard of care evaluations may be done up to 30 days before the procedure. Protocol-specific exams that are non-standard of care cannot be obtained until after informed consent.
[2] Consent to be obtained within 30 days prior to enrollment.
[3] Medical History is required at baseline only. Refer to applicable Protocol section for physical exam requirements.
[4] Negative pregnancy test within 14 days of enrollment for women of childbearing potential.
[5] DAPT and aspirin are required through 30 days and then continued per physician / institutional standards of care. Aspirin therapy is to be continued indefinitely.

10.2.3 Clinical Endpoints

10.2.3.1 Primary Safety Endpoint

The primary safety endpoint assessed the occurrence of Major Adverse Events (MAEs) at 12 months defined as the composite of:

- target-limb-related death
- major amputation of the target limb and
- re-intervention of the target limb.

This primary MAE-free rate for the Chocolate Touch DCB treatment group is non-inferior to the Lutonix DCB control group. If both primary endpoints were met (non-inferior safety and effectiveness), then pre-specified hierarchical tests for superiority would be conducted. Superiority for effectiveness would be conducted prior to superiority for safety.

10.2.3.2 Primary Effectiveness Endpoint

True DCB Success at 12 months, defined as primary patency in the absence of clinically driven bail-out stenting (CD-stent), as defined below. A subject with a CD-stent failed this endpoint; subjects that did not have a CD-stent placed were assessed for primary patency for the purposes of determining True DCB Success.

a) Clinically Driven Bail-Out Stenting (CD-stent): Stents are considered clinically driven when the angiographic core lab determines that a stent was placed after DCB use during the index procedure under the following conditions that were not resolved by prolonged balloon inflation:

- Unresolved flow limiting dissection (Type E or F),

OR

- Residual lumen diameter stenosis > 50%

A subject with a CD-stent failed the True DCB success endpoint regardless of patency outcomes.

b) Primary Patency: Subjects achieved primary patency by a combination of duplex ultrasound review and no evidence of CD-TLR prior to the study required 12-month DUS as defined below:

- Duplex Ultrasound Review: A patent target lesion showed a Peak Systolic Velocity Ratio (PSVR) less than 2.4 on DUS review by the DUS core lab or
- Clinically Driven Target Lesion Revascularization (CD-TLR): any repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed that was considered clinically driven when both of the following conditions were met:
  - Worsening clinical symptoms in the target limb (based on an ankle-brachial index (ABI) decrease ≥20% or >0.15 compared to maximum early post-procedure ABI or documented increase in Rutherford by at least one class if ABI change was unattainable (independently adjudicated).
  - Angiographic core lab adjudication of the revascularization angiogram confirming that the target lesion prior to re-intervention demonstrated diameter stenosis >50%.

This primary effectiveness endpoint was designed to demonstrate that the 12-month true DCB success rate for the Chocolate Touch DCB treatment group is non-inferior to the Lutonix DCB control group. If both primary endpoints were met (non-inferior safety and effectiveness), then pre-specified hierarchical tests for superiority would be conducted. Superiority for effectiveness would be conducted prior to superiority for safety.

10.2.3.3 Secondary Endpoints

The following exploratory secondary endpoints were evaluated:

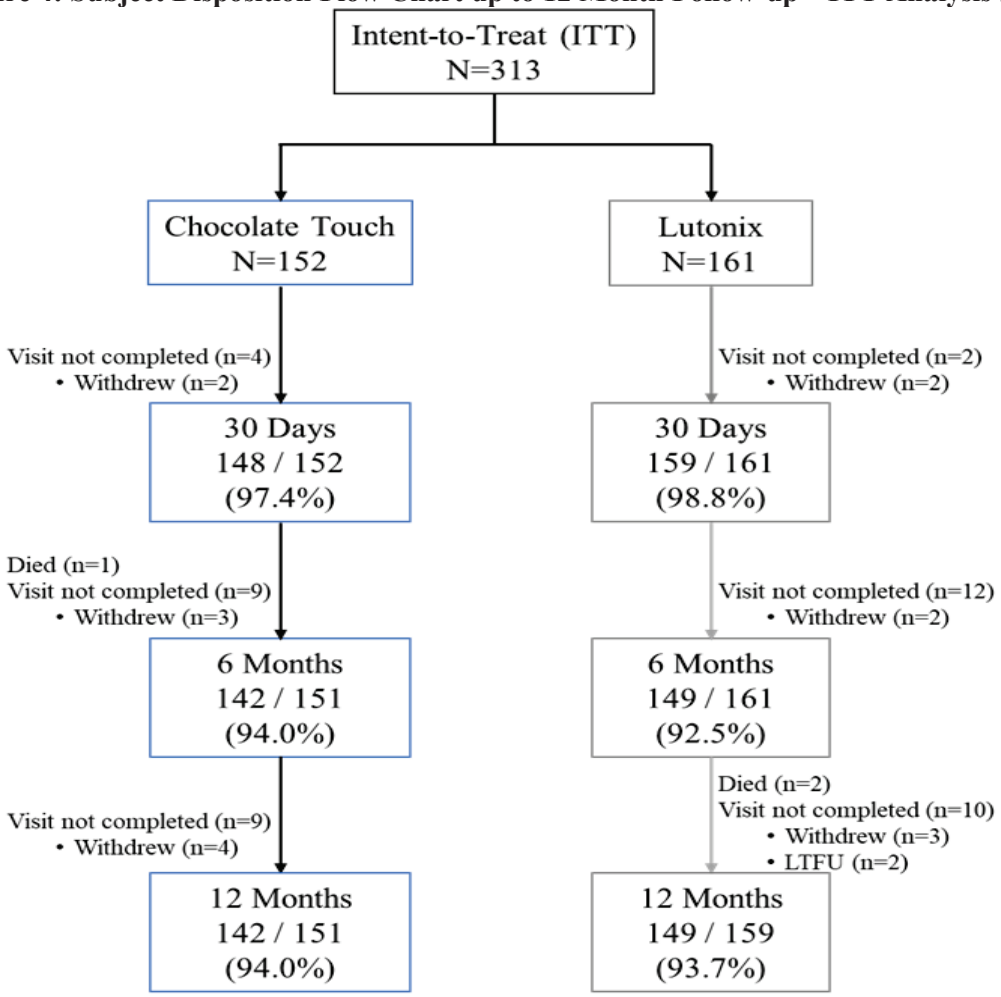
- Technical Success (acute), defined as the ability to deliver and inflate the assigned DCB at the intended target lesion.
- Device Success acute , defined as the ability to achieve an optimal PTA outcome (≤30% diameter stenosis without the occurrence of a flow-limiting dissection at the target lesion) with the assigned DCB.

- Rate of Clinically Driven Bail-out stenting (CD-stent) (acute), defined as the number of cases in which a CD-stent placement was conducted in accordance with the protocol.
- Rate of Stent Placement (acute), defined as the number of cases in which any stenting was conducted during the index procedure after DCB use.
- Length of Stented Segment (acute)
- Occurrence and severity of target lesion dissection (acute), defined as the number of cases in which dissection occurred
- Rate of Geographic Miss
- Stent-Free DCB Patency, defined as a composite endpoint that required subjects to achieve primary patency in the absence of a stent. Only subjects that did not have a stent placed were assessed for primary patency for the purposes of determining stent free patency.
- Primary Patency at 6, 12, 24, and 36 Months, defined as target lesion restenosis as determined by duplex ultrasound (PSVR < 2.4) and freedom from clinically-driven TLR
- Secondary Patency at 6, 12, 24, and 36 Months as defined by a PSVR less than 2.4 on DUS on review by the DUS Core Lab regardless of the need for TLR.
- Freedom from Clinically Driven TLR at 6, 12, 24, and 36 Months, any repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed that was clinically driven.
- Occurrence of target lesion restenosis at 6, 12, 24, and 36 Months.
- Clinical Improvement at 6, 12, 24, and 36 Months as defined by their Rutherford Classification improved by at least one category if ABI improved by at least 20% or 0.15. Results from the Walking Impairment Questionnaire (WIQ) and the Peripheral Artery Disease Specific Quality of Life (PADQOL) Questionnaire were evaluated and assessed for trends.

10.2.4 Accountability of PMA Cohort

At the time of database lock for analysis of primary endpoints, 313 patients enrolled in the PMA study, 85.3% of patients had sufficient data to assess the primary effectiveness endpoint at 1 year. Subject follow-up disposition to 12 months is provided in **Figure 4**.

Figure 4: Subject Disposition Flow Chart up to 12 Month Follow-up – ITT Analysis Set



Visit not completed = No visit reported in the database AND the visit window has closed as of the date of the database snapshot.

Primary endpoint accountability at the 12-month post-operative visit is presented in **Table 6**.

Table 6. Subject Follow-up Compliance Through 12 Months (ITT analysis set)

	Chocolate Touch	Lutonix DCB
Total Subjects	152	161
Not Assessed for primary efficacy (n, [%])	15 (9.9%)	31 (19.3%
Reason:		
Withdrew prior to 12 months	4	3
Lost to Follow-up	1	0
Missed 12-month visit	4	9
Visit outside of window	5	6
Completed visit but no DUS	1	9
Non-diagnostic DUS	0	4

10.2.5 Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a pivotal study performed in the US. Baseline demographics, medical history, and risk factors were mostly similar between the Chocolate Touch and Lutonix DCB groups. Data for the Chocolate Touch Study are summarized in **Table 7**. Minor differences

were noted for Lutonix DCB subjects who had greater prevalence of coronary artery disease (CAD) and congestive heart failure (CHF) as compared to Chocolate Touch subjects. Post hoc exploratory subgroup analyses were evaluated and it was determined that there was not a significant interaction between the primary outcomes in either of these subgroups (full details included in the Section D.3, **Table 16** and **Table 17**).

Table 7. Baseline Demographics and Medical History

Parameter	Chocolate Touch	Lutonix DCB	P-value[1]
Age	70.0 ± 9.7 (152)	68.8 ± 9.3 (161)	0.2573
	[43.0, 91.0]	[47.0, 89.0]	
Gender			
Male	87 / 152 (57.2%	93 / 161 (57.8%	1.0000
Female	65 / 152 (42.8%	68 / 161 (42.2%	1.0000
Race			
African American / Black	9 / 152 (5.9%)	12 / 161 (7.5%	0.6554
Alaska Native	0 / 152 (0.0%)	0 / 161 (0.0%)	
American Indian	0 / 152 (0.0%)	0 / 161 (0.0%)	
Asian	1 / 152 (0.7%)	2 / 161 (1.2%)	1.0000
Caucasian / White	139 / 152 (91.4%	146 / 161 (90.7%	0.8454
Native Hawaiian / Pacific Islander	0 / 152 (0.0%)	0 / 161 (0.0%)	
Unknown	0 / 152 (0.0%)	0 / 161 (0.0%)	
Other	3 / 152 (2.0%)	1 / 161 (0.6%)	0.3587
Refuse to disclose	0 / 152 (0.0%)	0 / 161 (0.0%)	
Ethnicity			
Hispanic or Latino	8 / 138 (5.8%)	8 / 147 (5.4%)	1.0000
Not Hispanic or Latino	67 / 138 (48.6%	75 / 147 (51.0%	0.7227
Unknown	36 / 138 (26.1%	33 / 147 (22.4%	0.4919
Refuse to disclose	27 / 138 (19.6%	31 / 147 (21.1%	0.7704
BMI	27.5 ± 4.7 (149)	27.2 ± 4.9 (159)	0.2020
	[10.5, 49.6]	[16.8, 52.4]	
BMI >=30	38 / 149 (25.5%	33 / 159 (20.8%	0.3455
History of Smoking			
Current	51 / 152 (33.6%	54 / 161 (33.5%	1.0000
Past	72 / 152 (47.4%	70 / 161 (43.5%	0.4979
Never	29 / 152 (19.1%	37 / 161 (23.0%	0.4094
Hypertension requiring treatment	137 / 152 (90.1%	139 / 161 (86.3%	0.3815
Hyperlipidemia requiring treatment	131 / 152 (86.2%	139 / 161 (86.3%	1.0000
Aortic Disease	13 / 152 (8.6%	12 / 161 (7.5%	0.8355
Carotid Disease	37 / 152 (24.3%	25 / 161 (15.5%	0.0647
Coronary Artery Disease	48 / 152 (31.6%	75 / 161 (46.6%	0.0077
Congestive heart failure	9 / 152 (5.9%)	20 / 161 (12.4%	0.0527
NYHA Class			
I	2 / 9 (22.2%)	4 / 20 (20.0%)	1.0000
II	1 / 9 (11.1%)	4 / 20 (20.0%)	1.0000
III	2 / 9 (22.2%)	2 / 20 (10.0%)	0.5680
IV	0 / 9 (0.0%)	0 / 20 (0.0%)	
Missing/Unknown	4 / 9 (44.4%)	10 / 20 (50.0%	1.0000
COPD	18 / 152 (11.8%	23 / 161 (14.3%	0.6157
Coronary Percutaneous Intervention	34 / 151 (22.5%	48 / 161 (29.8%	0.1581
Coronary Artery Bypass Surgery	17 / 152 (11.2%	21 / 161 (13.0%	0.7296
Deep vein Thrombosis	5 / 152 (3.3%)	11 / 161 (6.8%	0.2013

Parameter	Chocolate Touch	Lutonix DCB	P-value[1]
Renal Insufficiency History	18 / 152 (11.8%	13 / 161 (8.1%	0.3441
Cerebrovascular event	12 / 152 (7.9%	22 / 161 (13.7%	0.1063
Transient Ischemic Attack (TIA)	6 / 152 (3.9%)	11 / 161 (6.8%	0.3223
Cerebrovascular Accident (CVA) or Stroke	7 / 152 (4.6%)	13 / 161 (8.1%	0.2516
Diabetes mellitus	66 / 152 (43.4%	53 / 161 (32.9%	0.0627
Insulin Dependent	21 / 152 (13.8%	21 / 161 (13.0%	0.8695
Non-Insulin Dependent	45 / 152 (29.6%	32 / 161 (19.9%	0.0497
Baseline Rutherford			
2	27 / 152 (17.8%	23 / 160 (14.4%	0.4431
3	117 / 152 (77.0%	128 / 160 (80.0%	0.5817
4	8 / 152 (5.3%)	9 / 160 (5.6%)	1.0000
Baseline ABI	0.71 ± 0.16 (150)	0.75 ± 0.22 (154)	0.1866
	[0.20, 1.17]	[0.21, 1.70]	
Interventions with paclitaxel coated devices prior to this Procedure?	32 / 141 (22.7%	34 / 147 (23.1%	1.0000

1 Categorical variables compared using Fisher's Exact test. Continuous variables compared using the Wilcoxon Rank Sum Test.

Baseline lesion characteristics were similar between the Chocolate Touch and Lutonix DCB groups. The total lesion length treated was similar between treatment groups (Chocolate Touch 87.1 mm, Lutonix DCB 86.3 mm; p=0.8255). Reference vessel diameter was the same for both groups (5.4 mm; p=0.7294). The baseline lesion characteristics are summarized in **Table 8**. A significant difference was noted in the use of DCB as the final treatment, with the Chocolate Touch being the final treatment 67.8% of the time vs the Lutonix DCB being the final treatment 79.5% of the time (p=0.0208). This may be associated with appeared to be mostly dictated by the site reported assessment of residual diameter stenosis (>30%) post DCB, which was present in 17.8% of Chocolate Touch subjects and 10.6% Lutonix DCB subjects.

Table 8. Baseline Lesion Characteristics

Parameter	Chocolate Touch	Lutonix DCB	P-value[1]
Lesion Location			
Proximal Segment			
Iliac	0 / 152 (0.0%)	0 / 161 (0.0%)	
Common Femoral	0 / 152 (0.0%)	0 / 161 (0.0%)	
SFA	137 / 152 (90.1%	150 / 161 (93.2%	0.4135
Popliteal	15 / 152 (9.9%	10 / 161 (6.2%	0.2977
Anterior Tibial	0 / 152 (0.0%)	0 / 161 (0.0%)	
Tibial-Peroneal trunk	0 / 152 (0.0%)	0 / 161 (0.0%)	
Posterior Tibial	0 / 152 (0.0%)	0 / 161 (0.0%)	
Peroneal	0 / 152 (0.0%)	0 / 161 (0.0%)	
Distal Segment			
Iliac	0 / 152 (0.0%)	0 / 161 (0.0%)	
Common Femoral	0 / 152 (0.0%)	0 / 161 (0.0%)	
SFA	115 / 152 (75.7%	132 / 161 (82.0%	0.2120
Popliteal	37 / 152 (24.3%	29 / 161 (18.0%	0.2120
Anterior Tibial	0 / 152 (0.0%)	0 / 161 (0.0%)	
Tibial-Peroneal trunk	0 / 152 (0.0%)	0 / 161 (0.0%)	
Posterior Tibial	0 / 152 (0.0%)	0 / 161 (0.0%)	
Peroneal	0 / 152 (0.0%)	0 / 161 (0.0%)	
Reference Vessel Diameter (RVD) (visual estimate) – Proximal, mm	5.4 ± 0.6 (152)	5.4 ± 0.6 (160)	0.7294
	[3.6, 6.0]	[4.0, 6.1]	
Reference Vessel Diameter (RVD) (visual estimate) – Distal, mm	5.4 ± 0.6 (151)	5.4 ± 0.6 (160)	0.9868

Parameter	Chocolate Touch	Lutonix DCB	P-value[1]
	[3.6, 6.0]	[4.0, 6.0]	
Worst % Diameter Stenosis (visual estimate), %	90.4 ± 8.6 (152)	89.4 ± 9.2 (161)	0.3636
	[70.0, 100.0]	[70.0, 100.0]	
Total Lesion Length, mm	87.1 ± 48.3 (152)	86.3 ± 50.4 (161)	0.8255
	[5.0, 180.0]	[10.0, 180.0]	
Tandem Lesion	5 / 152 (3.3%)	6 / 161 (3.7%)	1.0000
If yes, distance between lesions, mm	11.5 ± 6.0 (4)	17.3 ± 4.6 (3)	0.1384
	[6.0, 20.0]	[12.0, 20.0]	
Lesion(s) Type			
DeNovo Lesion	139 / 152 (91.4%	150 / 161 (93.2%	0.6722
Restenotic Lesion	13 / 152 (8.6%	11 / 161 (6.8%	0.6722
Lesion Calcification			
None	46 / 143 (32.2%	44 / 150 (29.3%	0.6145
Mild	49 / 143 (34.3%	56 / 150 (37.3%	0.6267
Moderate	48 / 143 (33.6%	50 / 150 (33.3%	1.0000
Severe	0 / 143 (0.0%)	0 / 150 (0.0%)	
DCB TREATMENT			
Diameter Stenosis (after pre-dilatation), %[2]	30.2 ± 15.2 (121)	28.5 ± 17.3 (129)	0.2019
	[0.0, 90.0]	[0.0, 80.0]	
Number of DCB used at Target Lesion			
0	0 / 152 (0.0%)	0 / 161 (0.0%)	
1	106 / 152 (69.7%	113 / 161 (70.2%	1.0000
2	45 / 152 (29.6%	45 / 161 (28.0%	0.8030
>2	1 / 152 (0.7%)	3 / 161 (1.9%)	0.6232
POST DCB ASSESSMENT			
Total DCB Treated Length, mm	108.1 ± 46.9 (150)	112.9 ± 49.9 (159)	0.4297
	[20.0, 230.0]	[20.0, 240.0]	
DCB(s) covered the pre-treated target lesion length	152 / 152 (100.0%)	159 / 161 (98.8%	0.4988
Residual % Diameter Stenosis[2]	16.3 ± 17.8 (152)	13.8 ± 16.6 (161)	0.1627
	[0.0, 100.0]	[0.0, 95.0]	
Final outcome Post-DCB treatment			
Successful (< 30% DS)	99 / 152 (65.1%	117 / 161 (72.7%	0.1786
Dissection	31 / 152 (20.4%	35 / 161 (21.7%	0.7834
Residual Diameter Stenosis	27 / 152 (17.8%	17 / 161 (10.6%	0.0747
Distal embolization	1 / 152 (0.7%)	1 / 161 (0.6%)	1.0000
Pseudoaneurysm	0 / 152 (0.0%)	0 / 161 (0.0%)	
Perforation	0 / 152 (0.0%)	1 / 161 (0.6%)	1.0000
Thrombus	1 / 152 (0.7%)	2 / 161 (1.2%)	1.0000
Other	5 / 152 (3.3%)	3 / 161 (1.9%)	0.4912
Dissection Type			
Type A	9 / 31 (29.0%)	11 / 35 (31.4%	1.0000
Type B	7 / 31 (22.6%)	11 / 35 (31.4%	0.5807
Type C	8 / 31 (25.8%)	5 / 35 (14.3%)	0.3536
Type D	6 / 31 (19.4%)	6 / 35 (17.1%)	1.0000
Type E	1 / 31 (3.2%)	2 / 35 (5.7%)	1.0000
Type F	0 / 31 (0.0%)	0 / 35 (0.0%)	
Type Unknown	0 / 31 (0.0%)	0 / 35 (0.0%)	
DCB = final treatment	103 / 152 (67.8%	128 / 161 (79.5%	0.0208

1 Categorical variables compared using Fisher's Exact test. Continuous variables compared using the Wilcoxon Rank Sum Test.

2 Diameter stenosis was site reported

10.2.6 Safety and Effectiveness Results

10.2.6.1 Safety Results

The analysis of safety was based on the ITT cohort of 293 patients/procedures (144 Chocolate Touch and 149 Lutonix DCB) available for 12-month evaluation. The primary safety endpoint was defined as freedom from major adverse events (MAEs) within 12 months of the study procedure. Major adverse events were defined as a composite of target limb related death, amputation of the target limb, and re-intervention of the target limb. Freedom from MAE at 12 months occurred in 88.9% (128/144) of subjects in the Chocolate Touch group and 84.6% 126/149) of subjects in the Lutonix DCB group (difference, 4.3% [95% CI, -3.4%, 12.1%]) in the primary ITT analysis set as presented in **Table 9**. Therefore, non-inferiority of Chocolate Touch to Lutonix DCB (based on a 10% absolute non-inferiority margin) was met ($P_{non\text{-}inferiority}$=0.0001). The superiority criterion for Chocolate Touch to the Lutonix DCB was not met for the primary safety endpoint ($P_{superiority}$=0.2738).

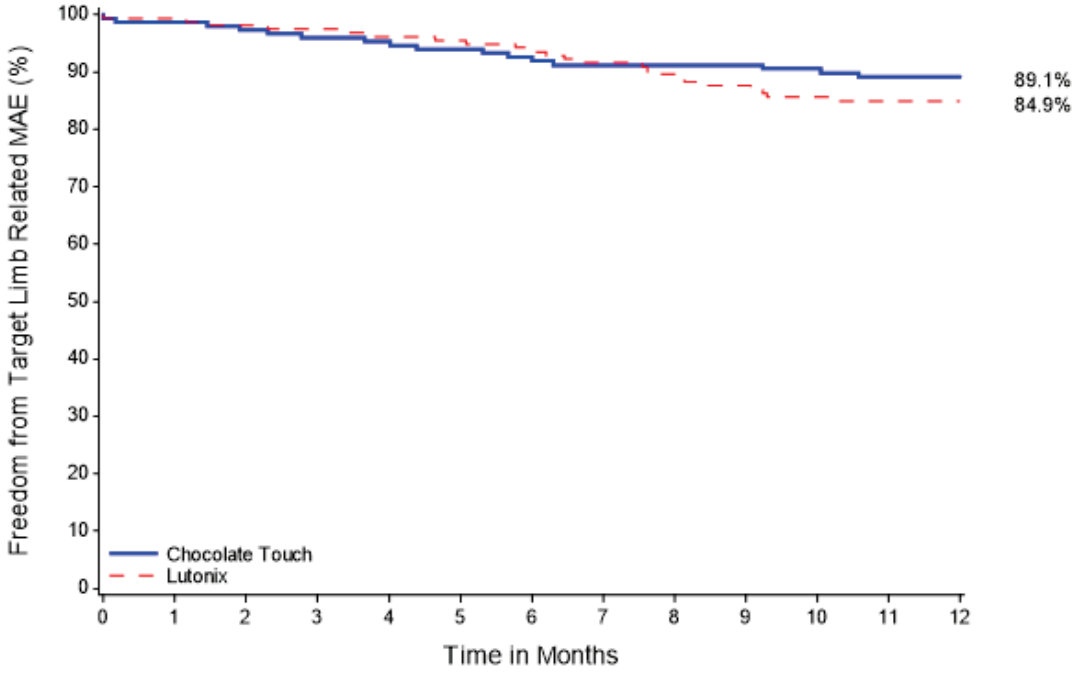
Table 9. Primary Safety Endpoint, Freedom from MAE at 12 months as adjudicated by the CEC – ITT

	#/#(%) (95% CI)[1]					
Event	**Chocolate Touch**	**Lutonix DCB**	**Total**	**Difference (95% CI)[2]**	**Non-Inferiority P-Value[2]**	**Superiority P-Value[2]**
Freedom from MAE	128 / 144 (88.9%)	126 / 149 (84.6%)	254 / 293 (86.7%)	4.3% (-3.4%, 12.1%	0.0001	0.2738
	(82.6%, 93.5%	(77.7%, 90.0%	(82.3%, 90.4%			
Target Limb Related Death	1 / 144 (0.7%)	0 / 149 (0.0%)	1 / 293 (0.3%)	0.7% (-0.7%, 2.1%		
	(0.0%, 3.8%)	(0.0%, 2.4%)	(0.0%, 1.9%)			
Major Amputation of the Target Limb	0 / 143 (0.0%)	0 / 149 (0.0%)	0 / 292 (0.0%)	-		
	(0.0%, 2.5%)	(0.0%, 2.4%)	(0.0%, 1.3%)			
Re-Intervention of the Target Limb	15 / 143 (10.5%)	23 / 149 (15.4%	38 / 292 (13.0%)	-4.9% (-12.6%, 2.7%		
	(6.0%, 16.7%)	(10.0%, 22.3%	(9.4%, 17.4%)			

NOTE: Subjects are counted only once within each category.
Denominators include all subjects who have the indicated event or who have adequate follow-up at 12 Months.
[1] Exact 95% confidence intervals.
[2] P-value from the Z-test for the difference in proportion with un-pooled variance. Non-inferiority P-value tested versus the absolute non-inferiority margin of 10%.
Confidence interval from the corresponding normal approximation.

Freedom from Primary Safety Endpoint through 12 months is presented in **Figure 5.**

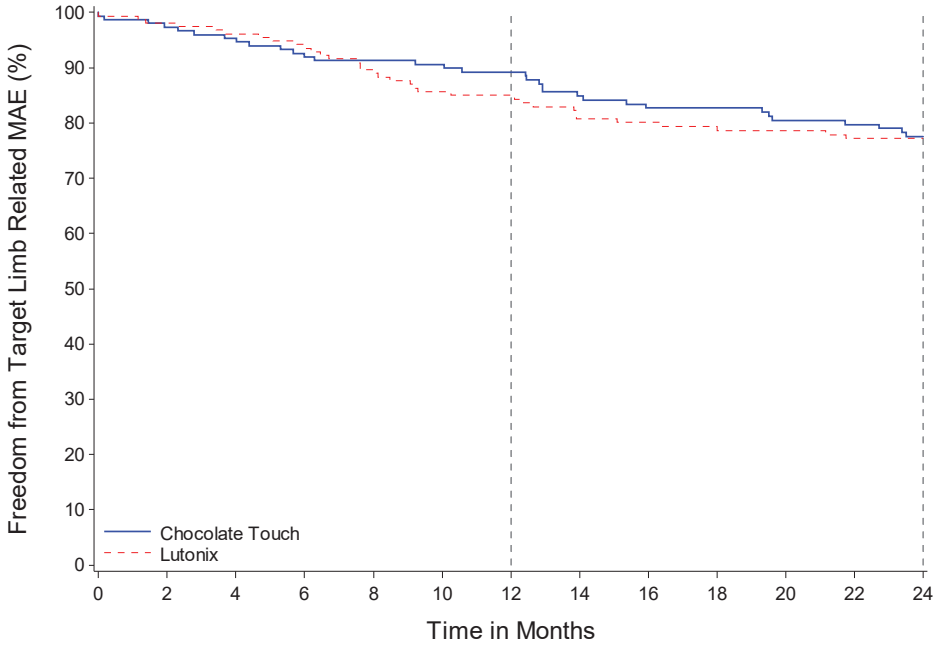
Figure 5. Kaplan-Meier Curve for Freedom from Target Limb Related MAE - ITT Analysis Set



Months Since Index Procedure	0	1	6	12	Logrank P-value
Chocolate Touch					0.3174
Survival (95% CI)	100.0% (100.0%,100.0%)	98.7% (96.9%,100.0%)	92.6% (88.4%,96.8%)	89.1% (84.1%,94.2%)	
Number with Event	0	2	11	16	
Number Remaining at Risk	152	148	136	97	
Lutonix DCB					
Survival (95% CI)	100.0% (100.0%,100.0%)	99.4% (98.2%,100.0%)	94.2% (90.5%,97.9%)	84.9% (79.2%,90.6%)	
Number with Event	0	1	9	23	
Number Remaining at Risk	161	155	145	108	

[1]The p-value should be interpreted with caution because a hypothesis test for the survival endpoint was not pre-specified and was not adjusted for multiplicity.

Kaplan-Meier Curve for Freedom from Target Limb Related MAE at 24mo* - ITT Analysis Set



***NOTE: 24month data provided in this graph is an interim analysis and should be interpreted with caution. Data at 24mo is not complete or fully adjudicated at this time.**

Months Since Index Procedure	0	1	6	12	24
Chocolate Touch					
Survival (95% CI)	100.0% (100.0%,100.0%	98.7% (96.9%,100.0%)	92.6% (88.4%,96.8%	89.2% (84.2%,94.2%)	77.5% (70.6%,84.4%)
Number with Event	0	2	11	16	32
Number Remaining at Risk	152	148	137	127	92
Lutonix					
Survival (95% CI)	100.0% (100.0%,100.0%	99.4% (98.2%,100.0%)	94.2% (90.5%,97.9%	85.0% (79.4%,90.7%)	77.2% (70.4%,83.9%)
Number with Event	0	1	9	23	34
Number Remaining at Risk	161	155	145	124	95

10.2.6.2 Adverse events that occurred in the PMA clinical study

Site-reported serious adverse events (SAEs) through 12 months are shown in **Table 10**. A SAE was defined as an event, which leads to death due to any cause, life-threatening condition, persistent or significant disability/incapacity, requires in-patient hospitalization or prolonged hospitalization, intervention to prevent permanent impairment of body function or permanent damage to body structure, and congenital abnormality. As presented below, the rate of serious adverse event was low and comparable between groups. No unanticipated adverse device effects occurred.

Table 10. Treatment Emergent Serious Adverse Events Through 12 Months – ITT Analysis Set

	Adverse Events					
	Chocolate Touch		Lutonix DCB		Total	
Adverse Event Code	**#**	**#(%) Patients**	**#**	**#(%) Patients**	**#**	**#(%) Patients**
Total	111	73 / 152 (48.0%	141	73 / 161 (45.3%	252	146 / 313 (46.6%
Angiographic / Procedural Events (A)	4	4 / 152 (2.6%)	6	6 / 161 (3.7%)	10	10 / 313 (3.2%
A1: Access site complication requiring surgery or transfusion	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
A2: Arterial occlusion or thrombus at puncture site	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
A3: Arterial perforation or rupture (vessel)	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
A6: Embolization, distal	3	3 / 152 (2.0%)	0	0 / 161 (0.0%)	3	3 / 313 (1.0%)

	Adverse Events					
	Chocolate Touch		Lutonix DCB		Total	
Adverse Event Code	**#**	**#(%) Patients**	**#**	**#(%) Patients**	**#**	**#(%) Patients**
A7: Groin hematoma _5cm, with or without surgical repair	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
A8: Hematoma at access site	1	1 / 152 (0.7%)	1	1 / 161 (0.6%)	2	2 / 313 (0.6%)
A9: Perforation / Extravasation of contrast media	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
A10: Thrombosis	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
A11: Thromboembolic episodes	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
A12: Vessel spasm or recoil	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
Cardiac I	23	19 / 152 (12.5%	12	10 / 161 (6.2%	35	29 / 313 (9.3%
C1: Angina	6	4 / 152 (2.6%)	1	1 / 161 (0.6%)	7	5 / 313 (1.6%)
C2: Atrial Fibrillation	3	3 / 152 (2.0%)	4	2 / 161 (1.2%)	7	5 / 313 (1.6%)
C3: Cardiac arrest	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
C4: Cardiac arrhythmia	1	1 / 152 (0.7%)	2	2 / 161 (1.2%)	3	3 / 313 (1.0%)
C5: Cardiogenic shock	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
C6: Congestive Heart Failure	1	1 / 152 (0.7%)	1	1 / 161 (0.6%)	2	2 / 313 (0.6%)
C7: Coronary artery disease	7	7 / 152 (4.6%)	2	2 / 161 (1.2%)	9	9 / 313 (2.9%)
C8: Hypertension	1	1 / 152 (0.7%)	0	0 / 161 (0.0%)	1	1 / 313 (0.3%)
C9: Hypotension	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
C10: Myocardial infarction	3	3 / 152 (2.0%)	1	1 / 161 (0.6%)	4	4 / 313 (1.3%)
C11: Myocardial ischemia	1	1 / 152 (0.7%)	0	0 / 161 (0.0%)	1	1 / 313 (0.3%)
C12 Ventricular fibrillation	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
C13: Ventricular tachycardia	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
Hematological (H)	4	4 / 152 (2.6%)	2	2 / 161 (1.2%)	6	6 / 313 (1.9%)
H1: Anemia	1	1 / 152 (0.7%)	1	1 / 161 (0.6%)	2	2 / 313 (0.6%)
H2: Bacteremia	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
H3: Bleeding, from anticoagulant or antiplatelet meds	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
H4: Disseminated intravascular coagulation	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
H5: Hemorrhage, with or without transfusion	1	1 / 152 (0.7%)	0	0 / 161 (0.0%)	1	1 / 313 (0.3%)
H6: Septicemia or sepsis	2	2 / 152 (1.3%)	0	0 / 161 (0.0%)	2	2 / 313 (0.6%)
Neurological (N)	1	1 / 152 (0.7%)	1	1 / 161 (0.6%)	2	2 / 313 (0.6%)
N1: Cerebrovascular Accident (CVA, stroke)	1	1 / 152 (0.7%)	0	0 / 161 (0.0%)	1	1 / 313 (0.3%)
N2: Seizure	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
N3: Transient Ischemic Attack (TIA)	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
Pulmonary (P)	2	2 / 152 (1.3%)	3	2 / 161 (1.2%)	5	4 / 313 (1.3%)
P1: Chronic Obstructive Pulmonary Disease (COPD	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
P2: Pneumonia	2	2 / 152 (1.3%)	2	1 / 161 (0.6%)	4	3 / 313 (1.0%)
P3: Pulmonary edema	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
P4: Pulmonary embolism	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
P5: Respiratory arrest	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
P6: Respirator distress	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
P7: Respiratory failure	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
Renal I	1	1 / 152 (0.7%)	2	2 / 161 (1.2%)	3	3 / 313 (1.0%)
R1: Renal failure	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
R2: Renal insufficiency	1	1 / 152 (0.7%)	2	2 / 161 (1.2%)	3	3 / 313 (1.0%)

	Adverse Events					
	Chocolate Touch		Lutonix DCB		Total	
Adverse Event Code	**#**	**#(%) Patients**	**#**	**#(%) Patients**	**#**	**#(%) Patients**
Vascular / Peripheral Vascular (V)	35	28 / 152 (18.4%	82	45 / 161 (28.0%	117	73 / 313 (23.3%
V1: Abrupt occlusion	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
V2: Amputation, major (above or at the ankle)	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
V3: Amputation, minor (below the ankle)	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
V4: Aneurysm	0	0 / 152 (0.0%)	3	3 / 161 (1.9%)	3	3 / 313 (1.0%)
V5: Arterial stenosis (non-target – lesion or vessel; not restenosis)	7	7 / 152 (4.6%)	18	13 / 161 (8.1%	25	20 / 313 (6.4%
V6: Arteriovenous fistula	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
V7: Claudication, recurrent or worsening	1	1 / 152 (0.7%)	7	7 / 161 (4.3%)	8	8 / 313 (2.6%)
V8: Ischemic ulcer	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
V9: Necrosis	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
V10: Peripheral ischemia (lower extremity)	0	0 / 152 (0.0%)	2	2 / 161 (1.2%)	2	2 / 313 (0.6%)
V11: Pseudoaneurysm	2	2 / 152 (1.3%)	1	1 / 161 (0.6%)	3	3 / 313 (1.0%)
V12: Restenosis of the non-target vessel (target or non-target limb)	9	7 / 152 (4.6%)	15	9 / 161 (5.6%)	24	16 / 313 (5.1%
V13: Restenosis of the target lesion (treated segment)	10	9 / 152 (5.9%)	20	19 / 161 (11.8%	30	28 / 313 (8.9%
V14: Restenosis of the target vessel (treated vessel)	4	4 / 152 (2.6%)	10	9 / 161 (5.6%)	14	13 / 313 (4.2%
V15: Thrombophlebitis	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
V16: Total occlusion of a peripheral artery	2	2 / 152 (1.3%)	4	4 / 161 (2.5%)	6	6 / 313 (1.9%)
Other (O)	41	35 / 152 (23.0%	33	25 / 161 (15.5%	74	60 / 313 (19.2%
O1: Allergic reaction (medication, contrast media, device, etc.)	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
O2: Fever (>38.3oC / 101oF)	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
O3: Gastrointestinal bleeding	0	0 / 152 (0.0%)	1	1 / 161 (0.6%)	1	1 / 313 (0.3%)
O4: Headache related to anesthesia (>24 hrs after procedure)	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)
O5: Infected peripheral wound	2	1 / 152 (0.7%)	1	1 / 161 (0.6%)	3	2 / 313 (0.6%)
O6: Infection	1	1 / 152 (0.7%)	1	1 / 161 (0.6%)	2	2 / 313 (0.6%)
O7: Pain	2	2 / 152 (1.3%)	1	1 / 161 (0.6%)	3	3 / 313 (1.0%)
O8: Urinary tract infection (UTI)	1	1 / 152 (0.7%)	1	1 / 161 (0.6%)	2	2 / 313 (0.6%)
O9: Other	35	31 / 152 (20.4%	26	19 / 161 (11.8%	61	50 / 313 (16.0%
Other NOT SPECIFIED	0	0 / 152 (0.0%)	0	0 / 161 (0.0%)	0	0 / 313 (0.0%)

10.2.6.3 Effectiveness Results

The analysis of effectiveness was based on the 267 (137 Chocolate Touch and 130 Lutonix DCB) evaluable patients at the 12-month time point. The primary effectiveness endpoint of the Chocolate Touch study was True DCB Success at 12 months, defined as primary patency in the absence of clinically driven bail-out stenting. Specifically, primary patency was defined as absence of target lesion restenosis (as assessed by duplex ultrasound review based on Peak Systolic Velocity Ratio (PSVR) <2.4) and freedom from clinically driven target lesion revascularization (CD-TLR) through 12 months. In the primary ITT analysis set, 85.3% of all subjects had sufficient data to assess True DCB Success at 12 months missing data included 9.9% Chocolate Touch subjects vs. 19.3% Lutonix DCB subjects . This rate is consistent with the assumed 15% loss to follow-up for the primary effectiveness endpoint that was assumed when determining the required sample size. Key effectiveness outcomes are presented in **Table 11**. The Kaplan Meier Curve for True DCB Success through 12 months is presented in **Figure 6**. As shown in the data below, the Chocolate Touch met its primary endpoint of non-inferiority compared to the Lutonix DCB. Given that non-inferiority of the effectiveness endpoint was met, a pre-specified superiority analysis for effectiveness of Chocolate Touch to Lutonix DCB was conducted and met (Superiority=0.0386). The imbalance in missing data between treatment groups may add uncertainty to the superiority results. The results of a

tipping point analysis demonstrate that there may be uncertainty to the robustness of the superiority result. The primary endpoint of True DCB success at 12mo was statistically superior , but this was not maintained at the later 24-month time point.

Table 11. Primary Effectiveness Endpoint, True DCB Success at 12 Months – ITT

	#/#(%) (95% CI)[1]					
Event	**Chocolate Touch**	**Lutonix**		**Difference (95% CI)[2]**	**Non-Inferiority P-Value[2]**	**Superiority P-Value[2]**
	108 / 137 (78.8%) 71.0%, 85.3%)	88 / 130 (67.7%) 58.9%, 75.6%)	196 / 267 (73.4%) 67.7%,78.6%)	11.1% (0.6%, 21.7%)	<.0001	0.0386
	0 / 152 (0.0% 0.0%, 2.4%)	0 / 161 (0.0% 0.0%, 2.3%)	0 / 313 (0.0% 0.0%, 1.2%)	-		
Patency	108 / 137 (78.8%) (71.0%,85.4%)	88 / 130 (67.7%) (58.9%,75.6%)	196 / 267 (73.4%) (67.7%,78.6%)	11.1% (0.6%, 21.7%)		

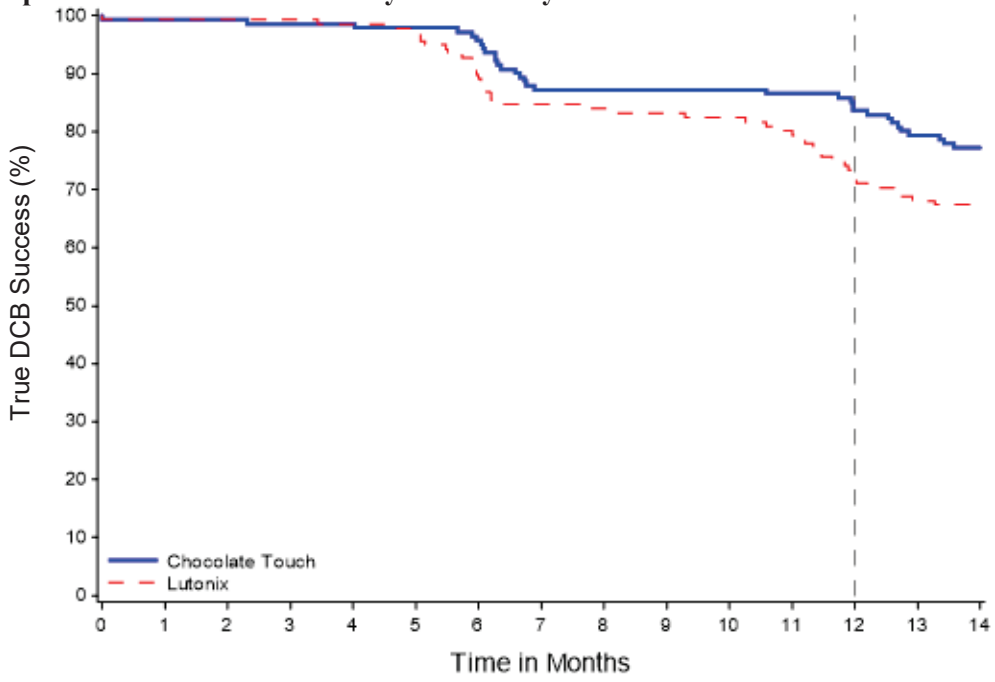
NOTE: Success is defined as completion of the 12 month visit at day 334 or greater with a patent DUS finding and no occurrence of a clinically driven target lesion revascularization prior to the 12 month visit and no placement of CD-stent during the index procedure. A patent DUS finding at a subsequent visit can be imputed for a missing DUS at the 12 month visit given no intervening target lesion revascularization.

1 Exact 95% confidence intervals.

2 P-value from the Z-test for the difference in proportion with un-pooled variance. Non-inferiority P-value tested versus the absolute non-inferiority margin of 10%.

Confidence interval from the corresponding normal approximation.

Figure 6. Kaplan-Meier Curve for Patency - ITT Analysis Set



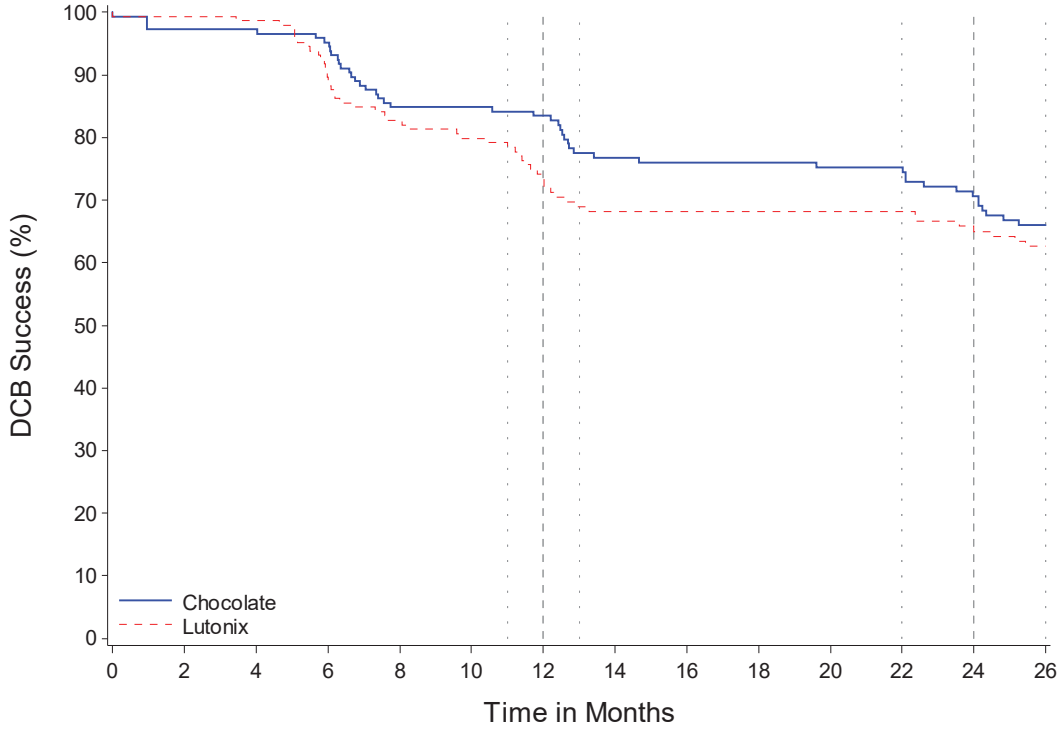
Months Since Index Procedur	0	1	6	12	13	Logrank P-value
Chocolate Touch						0.0429
Survival (95% CI)	100.0% (100.0%,100.0%)	99.3% (97.9%,100.0%)	96.4% (93.3%,99.5%)	83.3% (77.1%,89.5%)	78.9% (72.1%,85.7%)	
Number with Event	0	1	5	23	29	
Number Remaining at Risk	140	139	134	113	107	
Lutonix						

Months Since Index Procedur	0	1	6	12	13	Logrank P-value
Survival (95% CI)	100.0% (100.0%,100.0%)	99.3% (97.9%,100.0%)	91.3% (86.6%,96.0%)	73.0% (65.4%,80.5%)	68.3% (60.3%,76.2%)	
Number with Event	0	1	12	36	42	
Number Remaining at Risk	139	138	123	94	88	

NOTE: Subjects with an assessment of patent within the 12- month analysis window, are censored at the end of the window (month 13 otherwise subjects are censored at their last known patency assessment. Days to loss of patency are calculated as the time to earliest loss c patency for subjects not patent at 12 months via DUS, or as the time to CDTLR, whichever comes first.

[1]The p-value should be interpreted with caution because a hypothesis test for the survival endpoint was not pre-specified and was not adjuste for multiplicity.

Kaplan-Meier Curve for True DCB Success at 24mo *- ITT Analysis Set



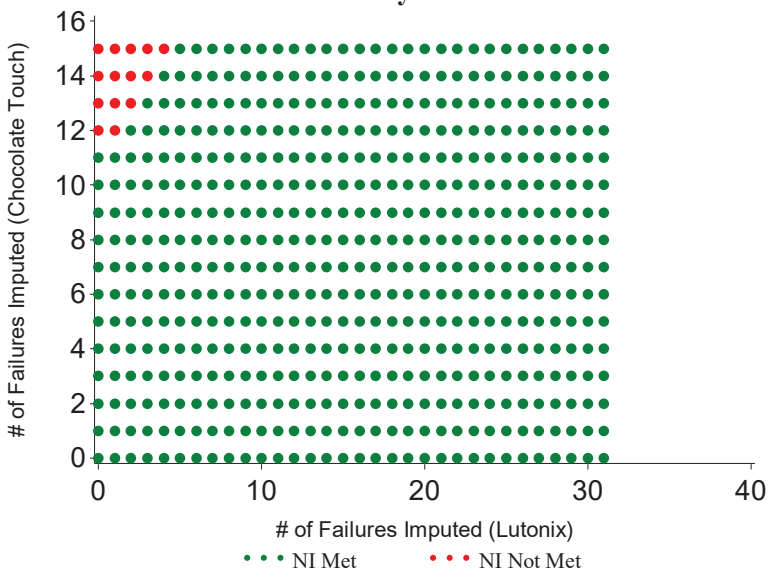
<u>*NOTE: 24month data provided in this graph is an interim analysis and should be interpreted with caution. Data at 24mo is not complete or fully adjudicated at this time.</u>

Months Since Index Procedure	0	1	6	12	13	24	26
Chocolate Touch							
Survival (95% CI)	100.0% (100.0%,100.0%)	97.3% (94.7%,99.9%)	95.2% (91.8%,98.7%)	83.4% (77.4%,89.5%)	77.5% (70.6%,84.4%)	70.6% (63.0%,78.2%)	66.0% (58.0%,73.9%)
Number with Event	0	4	7	24	32	41	47
Number Remaining at Risk	149	143	138	115	102	92	75
Lutonix							
Survival (95% CI)	100.0% (100.0%,100.0%)	99.3% (98.0%,100.0%)	91.1% (86.5%,95.7%)	73.5% (66.2%,80.7%)	69.0% (61.4%,76.6%)	65.0% (57.1%,73.0%)	62.6% (54.5%,70.7%)
Number with Event	0	1	13	38	44	49	52
Number Remaining at Risk	151	148	132	100	89	81	71

NOTE: Subjects with an assessment of patent within the analysis window, are censored at the end of the window, otherwise subjects are censored at their last known patency assessment. Days to loss of patency are calculated as the time to earliest loss of patency for subjects not patent via DUS, or as the time to CDTLR, whichever comes first.
Dotted lines represent visit windows.

The impact of missing data is evaluated in the sensitivity analyses presented in **Figure 7** for non-inferiority and **Figure 8** for superiority. Tipping point analyses were conducted for the primary effectiveness endpoint in the ITT analysis set to determine at what point of imputation of missing data the significance is lost. The tipping point analysis for the non-inferiority test demonstrated that it is unlikely that missing data would change the non-inferiority result for the primary effectiveness endpoint. At least 80% of subjects with missing data in the Chocolate Touch group would have to be imputed as failures and 100% of subjects with missing data in the Lutonix DCB group imputed as successes. The tipping point analysis for the superiority test is less likely. If all missing outcomes from both groups are imputed as successes, superiority would not continue to be met. Of the 512 possible combinations of imputations in **Figure 8**, 302 59%) of imputation scenarios result in superiority continuing to be met, and 210 (41%) result in superiority not continuing to be met.

Figure 7. True DCB Success at 12 Months, Tipping Point Analysis for Non-Inferiority – ITT Analysis Set



	Chocolate Touch			Lutonix			
Variable Description	**# Missing**	**# Failures Imputed**	**# Successes Imputed**	**# Missing**	**# Failures Imputed**	**# Successes Imputed**	**Non-inferiority Met**
Best Case	15	0	15	31	31	0	Yes
TIPPING POINT	15	12	3	31	0	31	No
Worst Case	15	15	0	31	0	31	No

[1] Tipping point analysis conducts all possible combinations of imputation between best and worst case to determine at what point of imputation significance is lost. Green dots denotes values where the endpoint is met while red dots indicated points where the endpoint the statistical is not met.
[2] Best case analysis imputes success for all Chocolate Touch subjects with missing data and all Lutonix subjects as failures and is the upper bound of the tipping point.
[3] Worst case analysis imputes failures for all Chocolate Touch subjects with missing data and successes for all Lutonix subjects with missing data and is the lower bound of tipping point.

Figure 8. True DCB Success at 12 Months, Tipping Point Analysis for Superiority – ITT Analysis Set

	Chocolate Touch			Lutonix			
Variable Description	**# Missing**	**# Failures Imputed**	**# Successes Imputed**	**# Missing**	**# Failures Imputed**	**# Successes Imputed**	**Superiority Met**
Best Case	15	0	15	31	31	0	Yes
TIPPING POINT	15	0	15	31	0	31	No
Worst Case	15	15	0	31	0	31	No

[1] Tipping point analysis conducts all possible combinations of imputation between best and worst case to determine at what point of imputation significance is lost. Green dots denotes values where the endpoint is met while red dots indicated points where the endpoint the statistical is not met.
[2] Best case analysis imputes success for all Chocolate Heart subjects with missing data and all Lutonix subjects as failures and is the upper bound of the tipping point.
[3] Worst case analysis imputes failures for all Chocolate Heart subjects with missing data and successes for all Lutonix ubjects with missing data and is the lower bound of tipping point.

10.2.6.4 Secondary Endpoint Results

A summary of Angiographic Core Lab (ACL)-reported acute secondary endpoints in the primary ITT analysis is presented in **Table 12**. There were no significant differences between treatment groups. Technical and device success in the Chocolate Touch group were 98.0% and 86.0%, respectively, and in the Lutonix DCB group were 99.4% and 85.3%. There were no CD-stents implanted in either treatment group. The rates of any stent placement were similar between treatment groups (7.9% Chocolate Touch vs. 9.4% Lutonix DCB) and the length of stented segment showed numerical differences but were not statistically different (54.3 ± 19.0 mm Chocolate Touch vs. 85.7 ± 53.3 mm Lutonix DCB).

Table 12. Acute Secondary Endpoints by Angiographic Core Lab Review - ITT Analysis Set

	#/#(%) (95% CI) or mean ± SD (n) [min,max] (95% CI)			
Parameter	**Chocolate Touch**	**Lutonix DCB**	**Total**	**Difference[1]**
Technical Success	149 / 152 (98.0%) 94.3%, 99.6%)	160 / 161 (99.4%) 96.6%, 100.0%)	309 / 313 (98.7%) 96.8%, 99.7%)	-1.4% (-3.9%,1.2%)
Device Success	129 / 150 (86.0%) 79.4%, 91.1%)	133 / 156 (85.3%) 78.7%, 90.4%)	262 / 306 (85.6%) 81.2%, 89.4%)	0.7% (-7.1%,8.6%)
CD-Stent[2]	0 / 152 (0.0%) 0.0%, 2.4%)	0 / 161 (0.0%) 0.0%, 2.3%)	0 / 313 (0.0%) 0.0%, 1.2%)	-

Parameter	#/#(%) (95% CI) or mean ± SD (n) [min,max] (95% CI)			
	Chocolate Touch	Lutonix DCB	Total	Difference[1]
Any Stent Placement	12 / 152 (7.9%) 4.1%, 13.4%	15 / 160 (9.4%) 5.3%, 15.0%	27 / 312 (8.7%) 5.8%, 12.3%	-1.5% (-7.7%,4.7%)
Length of Stented Segment	54.3 ± 19.0 (12) [17.9, 91.3] (42.2,66.3)	85.7 ± 53.3 (15) [30.5, 217.0] (56.1,115.2)	71.7 ± 44.0 (27) [17.9, 217.0] (54.3,89.1)	
Ratio of Stented Segment to Lesion Length	0.99 ± 0.63 (12) [0.35, 2.29] (0.59,1.39)	0.98 ± 0.49 (15) [0.21, 1.97] (0.71,1.26)	0.99 ± 0.55 (27) [0.21, 2.29] (0.77,1.20)	
Any Target Lesion Dissection	84 / 152 (55.3% 47.0%, 63.3%)	76 / 159 (47.8% 39.8%, 55.9%)	160 / 311 (51.4%) 45.7%, 57.1%)	7.5% (-3.6%,18.5%)
Dissection Type E or F	0 / 152 (0.0%) 0.0%, 2.4%)	0 / 159 (0.0%) 0.0%, 2.3%)	0 / 311 (0.0%) 0.0%, 1.2%)	-
Geographic Miss	11 / 126 (8.7%) 4.4%, 15.1%	7 / 131 (5.3%) 2.2%, 10.7%	18 / 257 (7.0%) 4.2%, 10.8%	3.4% (-2.9%,9.6%)

[1] Not adjusted for multiplicity

[2] Adjudicated by the Clinical Events Committee

A summary of DUS-reported secondary endpoints in the primary ITT analysis set at 6- and 12-month follow-up is presented in **Table 13**. True DCB Success at 6 months was similar between treatment groups 85.5% Chocolate Touch vs. 79.9% Lutonix DCB). At 6- and 12-month months, there were no significant differences between treatment groups with respect to primary patency, stent-free patency, and secondary patency. Secondary patency rates at 12-month follow-up were similar between groups (83.3% Chocolate Touch vs. 75.6% Lutonix DCB).

Table 13. Secondary Endpoints, by DUS Core Lab Review – ITT Analysis Set

Parameter	#/#(%) (95% CI)			
	Chocolate Touch	Lutonix DCB	Total	Difference
True DCB success				
6 Months	112 / 131 (85.5%) 78.3%, 91.0%)	107 / 134 (79.9% 72.1%, 86.3%)	219 / 265 (82.6%) 77.5%, 87.0%)	5.6% (-3.4%,14.7%)
12 Months*	108/137 (78.8% (71.0%, 85.3%	88/130 (67.7% (58.9%, 75.6%	196/267 (73.4% (67.7%, 78.6%	11.1% (0.6%, 21.7%)
Primary Patency				
6 Months	112 / 131 (85.5%) 78.3%, 91.0%)	107 / 134 (79.9% 72.1%, 86.3%)	219 / 265 (82.6%) 77.5%, 87.0%)	5.6% (-3.4%,14.7%)
12 Months	108/137 (78.8% (71.0%, 85.3%	88/130 (67.7% (58.9%, 75.6%	196/267 (73.4% (67.7%, 78.6%	11.1% (0.6%, 21.7%)
StentFree Patency				
6 Months	103 / 121 (85.1%) 77.5%, 90.9%)	95 / 120 (79.2% 70.8%, 86.0%)	198 / 241 (82.2%) 76.7%, 86.8%)	6.0% (-3.7%,15.6%)
12 Months	98 / 129 (76.0% 67.7%, 83.1%)	79 / 120 (65.8% 56.6%, 74.2%)	177 / 249 (71.1%) 65.0%, 76.6%)	10.1% (-1.1%,21.4%)
Secondary Patency				
6 Months	114 / 129 (88.4%) 81.5%, 93.3%)	110 / 134 (82.1% 74.5%, 88.2%)	224 / 263 (85.2%) 80.3%, 89.2%)	6.3% (-2.2%,14.8%)

	#/#(%) (95% CI)			
Parameter	**Chocolate Touch**	**Lutonix DCB**	**Total**	**Difference**
12 Months	115 / 138 (83.3%) 76.0%, 89.1%)	99 / 131 (75.6% 67.3%, 82.7%)	214 / 269 (79.6%) 74.2%, 84.2%)	7.8% (-1.9%,17.4%)

*This is the primary efficacy endpoint.

10.2.7 Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes: gender, geography (OUS/US), diabetes, baseline Rutherford category, pre-dilatation method, calcification, lesion length, treatment location, and vascular location. Subgroup analyses in the primary ITT analysis set for the primary safety endpoint are presented in **Table 14** and for the primary efficacy endpoint **Table 15**.

For the safety endpoint, there were no significant treatment interactions (evaluated at a p-value of 0.15) in pre-specified subgroup analyses: male vs female (P=0.1545); US vs. OUS (P=0.3544); diabetes vs. no diabetes (P=0.9634); baseline Rutherford Classification, ≤3 vs. >3 (P=0.4923); predilatation method, atherectomy vs. standard balloon angioplasty (P=0.8195); calcification, minimal/none vs. moderate/severe (P=0.1546); treatment location, hospital vs. outpatient (P=0.9648); or target lesion location, SFA vs. popliteal (P=0.9736). A significant treatment interaction was observed in a subgroup analysis according to lesion length, ≤10 cm vs. >10 cm P=0.0484). The rates of freedom from MAE were higher for lesion length ≤10 cm with Chocolate Touch compared with Lutonix DCB: 90.0% vs.73.1%, P=0.0408. These results demonstrate that the relative safety profile of Chocolate Touch was consistent across pre-specified subgroups, with a potential safety benefit in subjects with lesion length ≤10 cm.

Table 14. Additional Subgroup Analyses: Primary Safety Endpoint of Freedom from MAE at 12 Months

	#/#(%)				
Subgroup	**Chocolate Touch**	**Lutonix DCB**	**Difference (95% CI)**	**P-Value[1]**	**Interaction P-Value[2]**
Gender					0.1545
Male	75 / 84 (89.3%	78 / 86 (90.7%	-1.4% (-10.4%,7.6%)	0.8029	
Female	53 / 60 (88.3%	48 / 63 (76.2%	12.1% (-1.1%,25.4%)	0.1007	
Geography					0.3544
US	43 / 48 (89.6%	43 / 54 (79.6%	10.0% -3.8%,23.7%)	0.1861	
OUS	85 / 96 (88.5%	83 / 95 (87.4%	1.2% -8.1%, 10.4%	0.8277	
Diabetes					0.3544
Diabetes	55 / 62 (88.7%	42 / 50 (84.0%	4.7% -8.1%, 17.6%	0.5795	
No Diabetes	73 / 82 (89.0%	84 / 99 (84.8%	4.2% -5.6%, 14.0%	0.5107	
Baseline Rutherford					0.9634
<=3	122 / 136 (89.7%	121 / 140 (86.4%	3.3% -4.4%, 10.9%	0.4602	
>3	6 / 8 (75.0%)	4 / 8 (50.0%)	25.0% -20.8%, 70.8%)	0.6084	
Predilatation					0.4923
Atherectomy	16 / 19 (84.2%	12 / 16 (75.0%	9.2% -17.6%, 36.0%)	0.6772	
Standard balloon angioplasty	112 / 125 (89.6%	114 / 133 (85.7%	3.9% -4.1%, 11.9%	0.4502	
Calcification					0.8195
Minimal/None	81 / 89 (91.0%	73 / 92 (79.3%	11.7% 1.5%, 21.8%	0.0363	
Moderate/Severe	42 / 47 (89.4%	42 / 46 (91.3%	-1.9% (-13.9%, 10.1%	1.0000	
Lesion Length					0.1546
<=10 cm	45 / 50 (90.0%	38 / 52 (73.1%	16.9% 2.3%, 31.6%	0.0408	
>10 cm	83 / 94 (88.3%	88 / 97 (90.7%	-2.4% (-11.1%, 6.3%)	0.6415	
Treatment Location					0.0484

	#/#(%)				
Subgroup	**Chocolate Touch**	**Lutonix DCB**	**Difference (95% CI)**	**P-Value[1]**	**Interaction P-Value[2]**
Hospital Based Procedure	124 / 138 (89.9%	120 / 139 (86.3%	3.5% -4.1%, 11.1%	0.4587	
Outpatient Based Lab	4 / 6 (66.7%)	6 / 10 (60.0%)	6.7% -41.8%, 55.1%)	1.0000	
Location					0.9648
SFA	115 / 129 (89.1%	117 / 140 (83.6%	5.6% -2.6%, 13.7%	0.2165	
Popliteal	13 / 15 (86.7%	9 / 9 (100.0%)	-13.3% (-30.5%, 3.9%	0.5109	

1 Fisher's Exact test for the difference in proportion within subgroup.
2 P-value from the fixed effects logistic regression model treatment by subgroup interaction term. Heterogeneity testing at p-value<0.15 was prespecified for Gender and Geography.

For the efficacy endpoint, there were no significant treatment interactions (evaluated at a p value of 0.15) in pre-specified subgroup analyses: male vs female (P=0.8874); US vs OUS (P=0.6560); diabetes vs. no diabetes (P=0.5826); baseline Rutherford Classification, ≤3 vs. >3 (P=0.9386); predilatation method, atherectomy vs. standard balloon angioplasty (P=0.3342); calcification, minimal/none vs. moderate/severe P=0.2296); lesion length, ≤10 cm vs. >10 cm P=0.4555 ; treatment location, hospital vs. outpatient (P=0.9761); target lesion location, SFA vs. popliteal (P=0.9696). These results demonstrate that the effectiveness of the Chocolate Touch was consistent across all pre-specified subgroups.

Table 15. Additional Subgroup Analyses: Primary Efficacy Endpoint of True DCB Success at 12 Months

	#/#(%)				
Subgroup	**Chocolate Touch**	**Lutonix DCB**	**Difference (95% CI)**	**P-Value[1]**	**Interaction P-Value[2]**
Gender					0.8874
Male	66 / 81 (81.5%	52 / 72 (72.2%	9.3% (-4.1%, 22.6%	0.1836	
Female	42 / 56 (75.0%	36 / 58 (62.1%	12.9% -3.9%,29.8%)	0.1613	
Geography					0.6560
US	31 / 42 (73.8%	26 / 45 (57.8%	16.0% -3.6%,35.7%)	0.1753	
OUS	77 / 95 (81.1%	62 / 85 (72.9%	8.1% -4.2%, 20.4%	0.2161	
Diabetes					0.5826
Diabetes	44 / 57 (77.2%	26 / 43 (60.5%	16.7% -1.5%, 35.0%)	0.0816	
No Diabetes	64 / 80 (80.0%	62 / 87 (71.3%	8.7% -4.2%, 21.7%	0.2114	
Baseline Rutherford					0.9386
<=3	103 / 131 (78.6%	82 / 122 (67.2%	11.4% 0.5%, 22.3%	0.0473	
>3	5 / 6 (83.3%)	5 / 7 (71.4%)	11.9% -32.9%, 56.7%)	1.0000	
Predilatation					0.3342
Atherectomy	15 / 17 (88.2%	9 / 14 (64.3%)	23.9% -5.5%, 53.4%)	0.1975	
Standard balloon angioplasty	93 / 120 (77.5%	79 / 116 (68.1%	9.4% -1.9%, 20.7%	0.1100	
Calcification					0.2296
Minimal/None	68 / 84 (81.0%	50 / 81 (61.7%	19.2% 5.7%, 32.7%	0.0093	
Moderate/Severe	34 / 45 (75.6%	27 / 38 (71.1%	4.5% -14.6%, 23.6%)	0.8034	
Lesion Length					0.4555
<=10 cm	36 / 47 (76.6%	25 / 43 (58.1%	18.5% (-0.6%, 37.5%)	0.0736	
>10 cm	72 / 90 (80.0%	63 / 87 (72.4%	7.6% -4.9%, 20.1%	0.2896	
Treatment Location					0.9761
Hospital Based Procedure	103 / 132 (78.0%	80 / 120 (66.7%	11.4% 0.4%, 22.4%	0.0484	

	#/#(%)				
Subgroup	**Chocolate Touch**	**Lutonix DCB**	**Difference (95% CI)**	**P-Value[1]**	**Interaction P-Value[2]**
Outpatient Based Lab	5 / 5 (100.0%)	8 / 10 (80.0%)	20.0% -4.8%, 44.8%)	0.5238	
Location					0.9696
SFA	97 / 124 (78.2%	81 / 123 (65.9%	12.4% 1.3%, 23.5%	0.0339	
Popliteal	11 / 13 (84.6%	7 / 7 (100.0%)	-15.4% (-35.0%, 4.2%	0.5211	

1 Fisher's Exact test for the difference in proportion within subgroup.
2 P-value from the fixed effects logistic regression model treatment by subgroup interaction term. Heterogeneity testing at p-value<0.15 was prespecified for Gender and Geography.

As noted in the demographics and baseline parameters section 10.2.5, minor differences were noted for Lutonix DCB subjects who had greater prevalence of coronary artery disease (CAD) and congestive heart failure (CHF) as compared to Chocolate Touch DCB subjects. Post-hoc, exploratory subgroup analyses were evaluated and it was determined that there was not a significant interaction between the primary outcomes in either of these subgroups (**Table 16** and **Table 17**).

Table 16. Exploratory Subgroup Analyses: Primary Effectiveness Endpoint of True DCB Success at 12 Months

	#/#%()				
Subgroup	**Chocolate Touch DCB**	**Lutonix DCB**	**Difference (95% CI)**	**P-Value[1]**	**Interaction P-Value[2]**
CAD					0.5077
CAD	29 / 40 (72.5%	33 / 58 (56.9%	15.6% (-3.2%, 34.4%	0.1386	
No CAD	79 / 97 (81.4%	55 / 72 (76.4%	5.1% (-7.4%, 17.5%	0.4476	
CHF					0.2463
CHF	5 / 7 (71.4%	10 / 12 (83.3%	-11.9% (-51.5%, 27.6%	0.6027	
No CHF	103 / 130 (79.2%	78 / 118 (66.1%	13.1% (2.1%, 24.2%	0.0224	

[1] Fisher's Exact test for the difference in proportion within subgroup.
[2] P-value from the fixed effects logistic regression model treatment by subgroup interaction term.

Table 17. Exploratory Subgroup Analyses: Primary Safety Endpoint of Freedom from MAE at 12 months

	#/#(%)				
Subgroup	**Chocolate Touch DCB**	**Lutonix DCB**	**Difference (95% CI)**	**P-Value[1]**	**Interaction P-Value[2]**
CAD					0.0938
CAD	40 / 44 (90.9%	52 / 67 (77.6%	13.3% (0.2%, 26.4%	0.0775	
No CAD	88 / 100 (88.0%	74 / 82 (90.2%	-2.2% (-11.3%, 6.8%	0.8124	
CHF					0.8872
CHF	8 / 9 (88.9%	14 / 17 (82.4%	6.5% (-20.8%, 33.9%)	1.0000	
No CHF	120 / 135 (88.9%	112 / 132 (84.8%	4.0% (-4.1%, 12.1%	0.3676	

[1] Fisher's Exact test for the difference in proportion within subgroup.
[2] P-value from the fixed effects logistic regression model treatment by subgroup interaction term.

10.3 Pharmacokinetic Sub-study

A pharmacokinetic subgroup analysis within The Chocolate Touch Study was performed to characterize plasma paclitaxel levels following Chocolate Touch use and calculate the PK parameters in a representative patient cohort. The results from this sub-study help to clearly define the pharmacokinetic profile of paclitaxel delivery in human plasma following treatment with Chocolate Touch. Fifteen (15) subjects were enrolled at two (2) sites in Austria and New Zealand. Blood was sampled at baseline (before treatment), 30min, 1hr, 2hr, 4hr, 8hr, 24hr, and 7days post-treatment. This resulted in bioanalysis of 119 samples, evaluated in multiple runs.

Based on individual data points from the 15 patient PK Cohort, **Table 18** summarizes the pharmacokinetic parameters including maximum concentration (Cmax), time to maximum concentration (Tmax), area under the curve (AUC0-24h) and terminal elimination half-life (T1/2) that were calculated using the IV bolus model. Values are the mean of data for all patients. The mean, standard deviation, and the coefficient of variation are reported.

Table 18. PK Parameter Summary – PK value for 15 Subjects

	C_{max} (ng/mL)	T_{max} (hr)	AUC_{∞} (hr*ng/ml)	$T_{1/2}$ (hr)	CL (L/hr)	Vz (L)
Mean	8.21	0.53	58.9	32.0	168	6250
St. Dev	4.13	0.13	26.8	18.9	71.2	2190
% CV	50.4%	24.2%	45.5%	59.1%	42.4%	35.1%

10.4 3-Year safety endpoint was designed to demonstrate that the 12-month Analysis

An analysis was conducted to characterize the long-term mortality profile of the Chocolate Touch device, relative to other FDA-approved paclitaxel-coated devices, by comparison with the active comparator arm of the Chocolate Touch IDE trial which utilized a commercially available paclitaxel-coated balloon, as well as publicly available data on other commercially available paclitaxel-coated devices.

As of the data freeze date, 140 of the 171 Chocolate Touch subjects had been on study for at least 3 years. **Table 19** displays the counts of death in each year of follow up for the IIT population.

Table 19. Counts of Death for Annual Follow-Up Periods

	IIT Chocolate Touch (N=152)	**IIT Lutonix DCB (N=161)**
1 Year	1	2
2 Years	4	6
3 Years	4	7

Table 20 displays Kaplan-Meier estimates in tabular form for the AT population of the IDE Study. The estimated event rates are numerically lower at 1, 2, and 3 years in the Chocolate Touch arm, but confidence intervals overlap at these points, and the survival curves are not significantly different over the 3 years of follow- up (p=0.113, logrank test).

Table 20. Kaplan-Meier Event Rate Estimates (AT population)

	Chocolate Touch (N=171)		**Lutonix DCB (N=160)**	
	Rate	**95% CI**	**Rate**	**95% CI**
1 Year	0.006	(0.001,0.041)	0.013	(0.003,0.049)
2 Years	0.029	(0.012,0.069)	0.052	(0.026,0.101)
3 Years	0.059	(0.031,0.110)	0.111	(0.068,0.179)
Logrank p	0.113			

The Kaplan-Meier mortality estimates are provided in tabular form for the ITT analysis set (**Table 21**). The estimated event rates are numerically lower in the Chocolate Touch arm for all years (1, 2, and 3 years). The trial was not adequately powered to detect differences in mortality alone. Survival curves are not significantly different over the 3 years of follow-up (p=0.220, logrank test).

Table 21. Kaplan-Meier Event Rate Estimates - ITT Analysis Set

	Chocolate Touch (N=152)		Lutonix DCB (N=161)	
	Rate	**95% CI**	**Rate**	**95% CI**
1 Year	0.007	(0.001,0.046)	0.012	(0.003,0.049)
2 Years	0.033	(0.014,0.077)	0.051	(0.026,0.100)
3 Years	0.067	(0.035,0.126)	0.111	(0.068,0.178)
Logrank p	0.220			

A Bayesian Piecewise Exponential (PWE) survival model fit to the mortality data indicates a 0.999 predictive probability that the 3-year mortality rate in subjects treated with the Chocolate Touch device will be statistically less than the prespecified performance goal of 0.132 when all study subjects (including 171 total Chocolate Touch subjects) have had the opportunity to reach the 3-year follow-up milestone (**Table 22**).

Table 22. Main Predictive Analysis Result

Predictive Probability that [P($Rate_{3yr}$ < 0.132 | data)] exceeds 0.95	0.999

The Bayesian Piecewise Exponential (PWE) survival analysis demonstrated a 0.999 posterior probability that the 3-year mortality rate in subjects treated with the Chocolate Touch device is less than the prespecified performance goal of 0.132 (based on the observed mortality rates of paclitaxel-treated subjects from a patient-level meta-analysis of US IDE randomized controlled trials of paclitaxel coated devices, using the most complete publicly available data set).

Separately, a Bayesian predictive analysis resulted in a 0.999 predictive probability that the 3-year mortality rate in subjects treated with the Chocolate Touch device will be statistically less than the prespecified performance goal of 0.132 when all study subjects (including 171 total Chocolate Touch subjects) have had the opportunity to reach the 3-year follow-up milestone. The Bayesian predictive analysis demonstrated that the 3-year mortality rate of the Chocolate Touch device is comparable to that of other FDA-approved paclitaxel-coated devices.

11 HOW SUPPLIED

Sterile: Sterilized with ethylene oxide gas. Non-pyrogenic. Do not use if the package is open or damaged.
Contents: Each package contains one (1) Chocolate Touch® Paclitaxel Coated PTA Balloon Catheter.
Product Shelf Life: 24 months
Storage: Store in a dry, cool place. Do not expose to organic solvents (e.g., alcohol), ionizing radiation or ultraviolet light.

12 INSTRUCTIONS FOR USE

Note: *Do not expose the catheter to organic solvents (e.g., alcohol).*

1. Carefully remove the product from the sterile packaging. Examine carefully for defects. Examine the catheter for bends, kinks or other damage. Do not use any defective device. Do not use if the integrity of the package has been compromised or the sterile barrier is damaged.
2. Remove the protective balloon cover and stylet, discard.
3. Attach a stopcock and a 20ml syringe half filled with contrast medium to the balloon port.
4. Point the syringe nozzle downward and aspirate until all air is removed from the balloon.
5. Turn the stopcock off and maintain the vacuum in the balloon for 15-20 seconds.
6. Disconnect the syringe from the stopcock.

7. Flush the guidewire lumen with heparinized saline thoroughly.

12.1 CATHETER INSERTION AND DILATATION

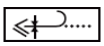
Note: *Use an appropriately sized introducer sheath as indicated on the label. Make sure to select the appropriate compatible system with the guidewire used. DO NOT use 0.018" guidewire with the 0.014" system or vice versa.*

1. Lesion prep may include atherectomy and PTA or PTA balloon only. Distal embolic protection is recommended, but at the discretion of the investigator.
2. Pre-dilatation with an uncoated PTA balloon that is undersized by ≥1mm to the RVD is required before use of the assigned DCB.
3. Backload the distal tip of the Chocolate Touch® catheter onto the guidewire which has been placed through the lesion. **Note:** *To avoid kinking, advance catheter slowly.*
4. Advance the catheter over the guidewire. If hemostatic valve is used, open the hemostatic valve to allow insertion.
5. Advance the Chocolate Touch® catheter to the lesion under fluoroscopic guidance. Use the radiopaque marker(s) at the balloon for positioning.
6. **Do not advance against resistance**. When resistance is felt while crossing the lesion, slightly pull back the catheter, turn the hub no more than 180 degrees and try to advance again. If resistance persists, DO NOT force passage.
7. Inflate the balloon to desired diameter per compliance chart to perform PTA per standard procedure. The diameter of the balloon should correspond to the diameter of the vessel for treatment with a balloon to artery ratio of 1.1:1.
8. The Chocolate Touch® balloon must be inflated to at least nominal pressure. Maintain balloon inflation for a minimum of 2 minutes. The balloon may be inflated as long as required to achieve optimal angioplasty outcome.
9. Fully deflate the balloon by applying negative pressure.
10. Maintain negative pressure, withdraw the deflated balloon catheter.
11. Confirm results by angiography.
12. Complete any additional interventions as clinically indicated (e.g. stent placement).

13 DISCLAIMER OF WARRANTY

TRIREME MEDICAL WARRANTS TO THE FIRST PURCHASER OF THIS PRODUCT, THAT THIS PRODUCT WILL BE FREE FROM DEFECTS IN MATERIALS AND WORKMANSHIP FOR A PERIOD OF ONE YEAR FROM THE DATE OF FIRST PURCHASE AND LIABILITY UNDER THIS LIMITED PRODUCT WARRANTY WILL BE LIMITED, TO REPAIR OR REPLACEMENT OF THE DEFECTIVE PRODUCT, IN TRIREME MEDICAL'S SOLE DISCRETION, OR REFUNDING YOUR NET PRICE PAID. WEAR AND TEAR FROM NORMAL USE OR DEFECTS RESULTING FROM MISUSE OR ANY USE OUTSIDE OF THE LABELED INTENDE USE OF THIS PRODUCT IS NOT COVERED BY THIS LIMITED WARRANTY. THIS LIMITED PRODUCT WARRANTY IS IN LIEU OF ALL OTHER WARRANTIES, WHETHER EXPRESS OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. IN NO EVENT WILL TRIREME MEDICAL BE LIABLE TO YOU FOR ANY INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES RESULTING FROM YOUR HANDLING OR USE OF THIS PRODUCT.

EXPLANATIONS OF SYMBOLS USED IN LABELING

	Consult Instruction for Use	SHEATH	Recommended sheath size
	Do not resterilize		Maximum guidewire diameter
	Do not re-use	NP	Nominal pressure
	Do not use if package is damaged	RBP	Rated burst pressure
REF	Catalog Number	Non-Pyrogenic	Non-pyrogenic

LOT	Batch code	STERILE EO	Sterilized using ethylene oxide gas
	Use-by date		Manufacturer
	Keep dry		Temperature limit: 0° to 30° C
	Keep away from sunlight		

EC REP

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COMPANY INFORMATION

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