LUTONIX® 035 Drug Coated Balloon PTA Catheter

Model 9010

Product Features: GEOALIGN® Marking System, Peel-Away Balloon Protector

INSTRUCTIONS FOR USE

CAUTION: Federal Law (USA) restricts this device to sale by or on the order of a physician.

Table of Contents

LUTONIX® 035

Drug Coated Balloon
PTA Catheter (Model 9010)

ENGLISH

Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician.

INSTRUCTIONS FOR USE

1 DEVICE DESCRIPTION

1.1 PTA Catheter Description

The LUTONIX® 035 Drug Coated Balloon PTA Catheter (LUTONIX® Catheter) consists of an over-the-wire catheter with a drug coated balloon fixed at the distal tip. The balloon is coated with a specialized formulation that includes the drug, paclitaxel. The LUTONIX® Catheter is 0.035" guidewire compatible, with a low profile, semi-compliant balloon formed to a low profile tapered tip to facilitate advancement of the catheter to and through the stenotic region of the vessel. Two radiopaque marker bands delineate the working length of the balloon and are located under the proximal and distal ends of the balloon to facilitate fluoroscopic visualization of the balloon during delivery and placement. The non-radiopaque GEOALIGN® Marking System is designated on the catheter shaft by 1 cm increment bands, see **Figure 1**. Each 10 cm increment is labeled with the distance from the distal balloon tip, see **Figure 2**. Thicker bands denote the midway point (5 cm) between the labeled distances. The GEOALIGN® Marking System is designed to be used as a location reference tool. The proximal portion of the catheter includes an inflation female luer lock hub and a guidewire female luer lock hub. Each product is packaged with a balloon protector that has been positioned over the balloon and a disposable wire lumen stylet, both of which are to be removed prior to use. **Table 1** lists the LUTONIX® Catheter characteristics. The Lutonix® Catheter is utilized in patients with stenotic lesions (see indication) who have End Stage Renal Disease (ESRD).

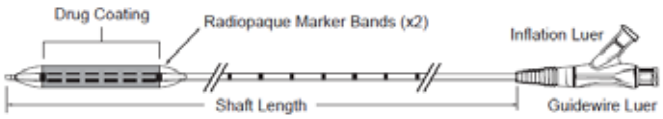


Figure 1. Lutonix® 035 Drug Coated Balloon PTA Catheter, Model 9010

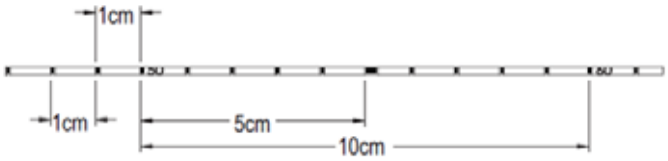


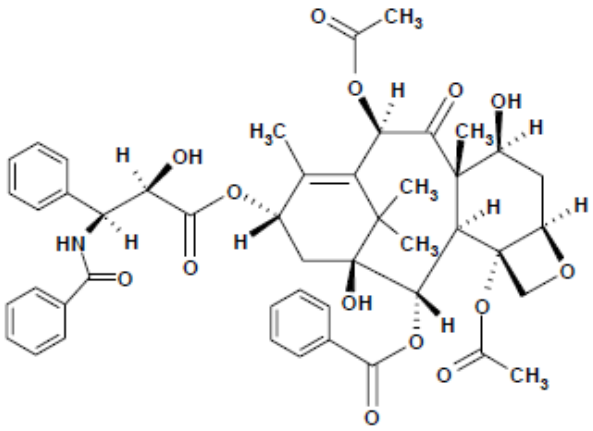
Figure 2. GEOALIGN® Marking System is non-radiopaque and designed to be utilized outside the introducer sheath

Table 1. LUTONIX® 035 Model 9010 Characteristics

LUTONIX® 035 Model 9010 Characteristics	
Model	9010
Catheter Configuration	Over-the-Wire (OTW)
Balloon Diameter	4.0, 5.0, 6.0, 7.0, 8.0, 9.0, 10.0, and 12.0 mm
Balloon Length	20, 40, 60, 80, 100 mm
Effective Catheter Length	40, 75, 100 cm
Radiopaque Marker Bands	2 placed on the catheter shaft to designate working length of the balloon
GEOALIGN® Marking System	Non-radiopaque markings located 1cm apart on the catheter shaft as a location reference tool.
Nominal Balloon Pressure	4.0, 5.0, 8.0, 9.0, 10.0, 12.0 mm: 6 atm 6.0, 7.0 mm: 7 atm
Balloon Rated Burst Pressure	Balloon Diameter ≤ 8.0 mm: 12 atm Balloon Diameter 9.0 – 10.0 mm: 11atm Balloon Diameter 12.0 mm: 10 atm
Maximum Guidewire	0.035"
Minimum Introducer Sheath	Balloon diameter 4.0 – 7.0 mm: 5F Balloon diameter 8.0 - 9.0 mm: 7F Balloon diameter 10.0 mm: 8F Balloon diameter 12.0 mm: 9F
Crossing Profile	4.0 mm diameter balloon: 5.0F (1.7 mm) 5.0 mm x 40/60/80mm lengths: 5.3F (1.8 mm) 5.0x100mm length: 5.0F (1.7 mm) 6.0 mm diameter balloon: 5.3F (1.8 mm) 7.0 mm diameter balloon: 5.5F (1.8 mm) 8.0 mm diameter balloon: 6.4F (2.1 mm) 9.0 mm diameter balloon: 6.9F (2.3 mm) 10.0 mm diameter balloon: 7.1F (2.4 mm) 12.0 mm diameter balloon: 7.5F (2.5 mm)

1.2 Drug Coating Description

The active ingredient on the LUTONIX® Catheter is paclitaxel. Paclitaxel is a white powder, manufactured by a semi-synthetic process, with the empirical formula $C_{47}H_{51}NO_{14}$ and a molecular weight of 854. It is highly lipophilic, insoluble in water, and melts at approximately 216-217°C. The chemical name for paclitaxel is 5β,20-Epoxy-1,7β-dihydroxy-9-oxotax-11-ene-2α,4,10β,13α-tetrayl 4,10-diacetate 2-benzoate 13-[(2R,3S)-3-(benzoylamino)-2-hydroxy-3-phenylpropanoate]. Paclitaxel CAS Registry number is 33069-62-4. Paclitaxel has the following chemical structure:



The drug coating is a non-polymer based formulation, consisting of paclitaxel as the active pharmaceutical ingredient with inactive ingredients, polysorbate and sorbitol, which act as the drug carrier.

The paclitaxel coating is evenly distributed across the working length of the balloon at a surface concentration of 2 µg/mm^2 see **Figure 3**. The key functional characteristic of the formulation is to allow for release of paclitaxel to the tissue of the vascular wall during inflation.

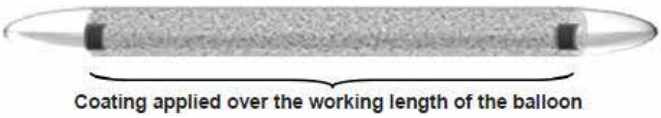


Figure 3. Uniform Drug Coating 360 Degree Distribution

Table 2 presents the balloon sizes and the nominal total quantity of paclitaxel on each balloon based on the surface concentration of 2 µg/mm^2.

Table 2. Paclitaxel Dosage per Balloon Size

Balloon Diameter (mm)	Total Dosage (mg) per Respective Balloon Length (mm)				
	20	40	60	80	100
4.0		1.0	1.5	2.0	2.5
5.0		1.3	1.9	2.5	3.1
6.0		1.5	2.3	3.0	3.8
7.0		1.8	2.6		
8.0	1.0	2.0	3.0		
9.0	1.1	2.3	3.4		
10.0	1.3	2.5	3.8		
12.0	1.5	3.0			

2 INDICATIONS FOR USE

The LUTONIX® Catheter is indicated for percutaneous transluminal angioplasty (PTA), after pre-dilatation, for treatment of stenotic lesions of dysfunctional native arteriovenous dialysis fistulae that are 4 mm to 12 mm in diameter and up to 80 mm in length.

3 CONTRAINDICATIONS

- Women who are breastfeeding, pregnant or are intending to become pregnant or men intending to father children over the next 2 years. It is unknown whether paclitaxel will be excreted in human milk and there is a potential for adverse reaction in nursing infants from paclitaxel exposure.
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system.

4 WARNINGS

- Contents supplied STERILE using ethylene oxide (EO) process. Do not use if sterile barrier is damaged or opened prior to intended use.
- Do not use after the “Use by” date.
- Do not use if product damage is evident.
- The LUTONIX® Catheter is for use in one patient only; do not reuse in another patient, reprocess or resterilize. Risks of reuse in another patient, reprocessing, or resterilization include:
  - Compromising the structural integrity of the device and/or device failure which, in turn, may result in patient injury, illness or death.
  - Creating a risk of device contamination and/or 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 patient injury, illness or death.
- 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.
- Use the recommended balloon inflation medium of contrast and sterile saline (≤50% contrast). Never use air or any gaseous medium to inflate the balloon as this may cause air emboli in case of balloon burst.

This product should not be used in patients with known hypersensitivity to paclitaxel or structurally related compounds as this may cause allergic reaction (difficulty in breathing, skin rash, muscle pain).

5 PRECAUTIONS

5.1 General Precautions

- The LUTONIX® Catheter should only be used by physicians trained in peripheral vascular percutaneous interventional procedures.
- Consideration should be given to the risks and benefits of use in patients with a history of non-controllable allergies to contrast agents.
- The safety and effectiveness of the LUTONIX® Catheter have not been established for treatment in cerebral, carotid, coronary, or renal vasculature.
- The safety and effectiveness of using multiple LUTONIX® drug coated balloons that deliver greater than 7.6 mg paclitaxel in a patient has not been clinically evaluated.

5.2 Use in Conjunction with Other Procedures

The safety and effectiveness of the LUTONIX® Catheter used in conjunction with drug eluting stents or other drug coated balloons in the same procedure or following treatment has not been evaluated.

Note: Use with stent graft for bailout if needed in the same procedure following treatment with the LUTONIX® Catheter is permitted.

5.3 Device Handling Precautions

- Do not immerse the LUTONIX® Catheter in a saline bath. Replace any device where the balloon has come into contact with fluids prior to use.
- The coated balloon portion should be handled with dry sterile gloves whenever possible prior to use.
- The balloon protector and wire lumen stylet should stay in place during preparation of the LUTONIX® Catheter and not be removed until just prior to placing over guidewire.
- If difficulty is encountered while removing the balloon protector, a new LUTONIX® Catheter should be utilized. Removing the balloon protector by force can cause a kink in the catheter shaft and lumen constriction may occur, affecting inflation/deflation of the balloon.

5.4 Device Use/Procedure Precautions

- To ensure therapeutic drug delivery:
  - Never inflate the LUTONIX® Catheter prior to reaching the target lesion.
  - The LUTONIX® Catheter should be advanced to the target lesion as quickly as possible (i.e. ≤ 30 seconds) and immediately inflated to appropriate pressure to ensure full wall apposition (drug coated balloon to pre-dilatation balloon ratio of ≥ 1:1). Note: LUTONIX® Catheter has RBP range of 10 to12 atm, depending on balloon diameter. Refer to the balloon compliance chart on the product label.
  - Maintain balloon inflation for a minimum of 2 minutes. The balloon may remain inflated as long as is required by the standard of care to achieve a good angioplasty outcome.
- Vessel preparation of the target lesion, using appropriate vessel preparation method as determined by the physician to achieve residual stenosis of ≤ 30%, is required prior to the use of the LUTONIX® Catheter. The use of ultra-high pressure (≥ 25atm) balloons for pre-dilatation of the lesion is recommended. However, no difference was noted in the primary endpoint outcomes for higher pressure dilatation (≥ 25 atm) as compared to lower inflation pressures.
- Vessel preparation using only PTA for pre-dilatation was studied in the Lutonix AV study. Other methods of vessel preparation, such as atherectomy, have not been studied clinically with the LUTONIX® Catheter in dysfunctional native arteriovenous dialysis fistulae.
- After insertion, do not over-tighten the hemostatic adaptor (if used) around the LUTONIX® Catheter shaft as lumen constriction may occur, affecting inflation/deflation of the balloon.
- Always advance and retrieve the LUTONIX® Catheter under negative pressure.
- The LUTONIX® Catheter should always be manipulated under adequate visualization when in the body.

- Do not continue to use the LUTONIX® Catheter if the shaft has been bent or kinked.
- Whenever possible, the LUTONIX® Catheter should be the final treatment of the vessel; however, post-dilation is allowed with another PTA catheter or the previously-used LUTONIX® Catheter. Alternatively, placement of a stent graft for bailout is allowed, if necessary.

5.5 Pre- and Post-Procedure Antiplatelet Regimen

Medication therapy should be administered according to current medical standards. Dual antiplatelet therapy was not required for use with the LUTONIX® Catheter. See trial results for list of relevant medications, **Table 4** in **Section 10.3**.

6 USE IN SPECIAL POPULATIONS

- Pregnancy – Use in women who are breastfeeding, pregnant or intending to become pregnant or in men intending to father children over the next 2 years is contraindicated.
- Pediatric Use – The safety and effectiveness of the LUTONIX® Catheter in pediatric patients has not been established.
- Geriatric Use – Clinical studies of the LUTONIX® Catheter did not have an upper age limit. See Section 10.3 for discussion of age groups in the Lutonix AV study.

7 DRUG INFORMATION

7.1 Mechanism of Action

The LUTONIX® Catheter coating contains paclitaxel, an anti-mitotic pharmaceutical agent that specifically binds to and stabilizes microtubules. Paclitaxel has been reported in prior studies to inhibit smooth muscle cell and fibroblast proliferation and migration. Although the impact that the excipients in the Lutonix drug coating have on the mechanism of action is unknown, the fact that paclitaxel inhibits neointimal hyperplasia is well documented in the literature.

7.2 Drug Interactions

Formal drug interaction studies have not been conducted with the LUTONIX® Catheter, and therefore consideration should be given to the potential for both systemic and local drug interactions in the vessel wall when deciding to use the LUTONIX® Catheter. In the absence of formal clinical drug interaction studies, caution should be exercised when administering paclitaxel concomitantly with known substrates or inhibitors of the cytochrome P450 isoenzymes CYP2C8 and CYP3A4.

7.3 Carcinogenicity, Genotoxicity, and Reproductive Toxicology

No long-term studies in animals have been performed to evaluate the carcinogenic potential of the drug paclitaxel nor of the LUTONIX® Catheter, and there are no adequate and well-controlled studies published in pregnant women or in men intending to father children. Paclitaxel inhibits cell proliferation by interacting with microtubules, and one consequence is the loss of whole 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 strand breaks or fragments. It is negative in assays for gene mutation, including salmonella and CHO/HPRT.

Studies performed in rats and rabbits receiving IV paclitaxel during organogenesis revealed evidence of maternal toxicity, embryotoxicity, and fetotoxicity at dosages of 1 and 3 mg/kg, respectively (approximately 18 and 55 times the dose provided by the LUTONIX® Catheter coated with 3.8 mg paclitaxel (6mm x 100mm balloon) adjusted for body weight). The drug resulted in increased resorptions and increased fetal deaths. No teratogenicity was observed in gravid rats receiving daily IV paclitaxel doses of 1 mg/kg (a daily dose of approximately 18 times the dose of the LUTONIX® Catheter (6mm x 100mm), adjusted for bodyweight).

The treating physician should balance the potential medical benefits of the LUTONIX® Catheter against these genotoxic and reproductive risks.

The paclitaxel dose delivered by the largest drug coated balloon (3.8 mg) is =<1.4% of a standard chemotherapy paclitaxel dose.

The LUTONIX® Catheter coating formulation facilitates rapid paclitaxel removal from the bloodstream within 24 hours and is processed in the liver and kidneys. In a subset of patients (n=22) with varying dosage (1.3 mg – 5 mg) in the pivotal IDE study for SFA indication (LEVANT 2), all subjects had detectable serum paclitaxel immediately after the index procedure that decreased to less than 3 ng/mL within one hour. The pharmacokinetics of paclitaxel following treatment generally exhibited a bi-exponential decay; characterized by a rapid distribution phase followed by a log-linear elimination phase. Group mean (SD) values for the pharmacokinetic parameters Cmax, AUCall, and MRTlast were 5.10 (3.21) ng/mL, 8.39 (4.00) ng*h/mL, and 2.13 (1.84) h. Mean elimination half-life values were 6.88 h for evaluable subjects.

8 POTENTIAL ADVERSE EVENTS

Potential adverse events which may be associated with a PTA balloon dilation procedure include, but are not limited to, the following:

- Additional intervention
- Allergic reaction to drugs or contrast medium
- Aneurysm or pseudoaneurysm
- Arrhythmias
- Embolization
- Hematoma
- Hemorrhage, including bleeding at the puncture site
- Hypotension/hypertension
- Inflammation
- Loss of permanent access
- Occlusion
- Pain or tenderness
- Sepsis/infection
- Shock
- Steal Syndrome
- Stroke
- Thrombosis
- Vessel dissection, perforation, rupture, or spasm

Although systemic effects are not anticipated, refer to the Physicians' Desk Reference for more information on the potential adverse events observed with paclitaxel. Potential adverse events, not described in the above source, which may be unique to the paclitaxel drug coating include, but are not limited to, the following:

- Allergic/immunologic reaction to the drug coating (paclitaxel)
- Alopecia
- Anemia
- Blood product transfusion
- Gastrointestinal symptoms
- Hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia)
- Hepatic enzyme changes
- Histologic changes in vessel wall, including inflammation, cellular damage, or necrosis
- Myalgia/Arthralgia
- Myelosuppression
- Peripheral neuropathy

9 PATIENT COUNSELING INFORMATION

Physicians should consider the following in counseling patients about this product:

- Discuss the risks associated with a PTA procedure in the arteriovenous fistula
- Discuss the risks associated with a paclitaxel coated PTA catheter
- Discuss the risks/benefits issues for this particular patient

10 SUMMARY OF CLINICAL STUDY

The safety and effectiveness of the LUTONIX® Catheter is derived from the Lutonix AV study, a multi-center, pivotal IDE trial. Results from the Lutonix AV study through the 12 months follow-up are presented below; study is ongoing with patient follow-up planned out to 2 years.

10.1 Objective

The primary objective of the Lutonix AV study was to demonstrate superior effectiveness and non-inferior safety of the LUTONIX® Catheter, for treatment of dysfunctional AV fistulae located in the upper extremity, by direct comparison to uncoated PTA catheter.

10.2 Study Design

The study was designed as a prospective, global, multicenter, randomized, safety and effectiveness study of the LUTONIX® Catheter; 23 sites enrolled 285 subjects. After successful pre-dilatation in both treatment arms, subjects with angiographic documentation of residual stenosis ≤30% were enrolled and randomized 1:1 to LUTONIX® Catheter (TEST) or Standard PTA (CONTROL).

10.2.1 Primary Endpoints

The primary safety endpoint was defined as freedom from localized or systemic serious adverse events through 30 days that reasonably suggests the involvement of the AV access circuit. The primary safety endpoint was tested using Farrington and Manning Exact Test for non-inferiority of proportions (a one-sided test at a significance of 0.025).

- H_0: The primary safety rate p_1 in the DCB treatment group through 30 days post index procedure is inferior to that p_2 of the PTA treatment group. (i.e. $p_1 \leq p_2 - \delta$)
- H_1: The primary safety rate p_1 in the DCB treatment group through 30 days post index procedure is non-inferior to that p_2 of the PTA treatment group. (i.e. $p_1 > p_2 - \delta$)

Where $\delta = 10\%$ is the non-inferiority margin, which is the range of difference that is considered not clinically important.

The primary effectiveness endpoint was defined as Target Lesion Primary Patency (TLPP) at 6 months. The primary effectiveness endpoint was tested for superiority of the LUTONIX® Catheter compared to standard uncoated balloon (PTA), by Kaplan-Meier survival analysis to estimate the survival rate of TLPP. The test is successful if the one-sided p-value is less than 0.025 and the result is in favor of DCB.

- H_0: The (survival) rate $S_1(t)$ of subjects in the DCB treatment group with TLPP through $t \leq 6$ month post index procedure is less than or equal to that $S_2(t)$ of PTA treatment group. (i.e. $S_1(t) \leq S_2(t)$, for $t \leq 6$ months)
- H_1: The (survival) rate $S_1(t)$ of subjects in the DCB treatment group with TLPP through $t \leq 6$ month post index procedure is greater than that $S_2(t)$ of PTA treatment group. (i.e. $S_1(t) > S_2(t)$, for $t \leq 6$ months

10.3 Baseline Information

Subject demographics and medical history are provided in **Table 3** below. The average age of the 285 subjects enrolled was 62.3 ± 14 years, with the majority male (60.4%) with an average BMI of 29.3 ± 7.6 kg/m^2. While slightly over half of all subjects identified as white (55.1%), there was a considerable amount of subjects who self-reported a race other than white. Risk factors were evenly distributed between both treatment arms, the expected co-morbidities for this subject population were observed, with over half (61.8%) of the subjects diabetic and 62.8% of subjects having cardiovascular disease. Overall, baseline characteristics and comorbidities were well matched.

Table 3. Demographics

Description	LTX DCB (N=141)	Standard PTA (N=144)	Total (N=285)	P-value[1]
Age (Years), Mean (SD)	63.6 (14.46)	61.0 (13.36)	62.3 (13.95)	0.1322
Gender				0.7165
Male	87 (61.7%)	85 (59.0%)	172 (60.4%)	
Female	54 (38.3%)	59 (41.0%)	113 (39.6%)	
Ethnicity				0.3479
Hispanic Or Latino	21 (14.9%)	28 (19.4%)	49 (17.2%)	
Not Hispanic Or Latino	120 (85.1%)	116 (80.6%)	236 (82.8%)	
Race				0.7951
American Indian Or Alaska Native	5 (3.5%)	4 (2.8%)	9 (3.2%)	
Asian	3 (2.1%)	1 (0.7%)	4 (1.4%)	
Black Or African American	52 (36.9%)	56 (38.9%)	108 (37.9%)	
White	79 (56.0%)	78 (54.2%)	157 (55.1%)	
Weight (kg), Mean (SD)	84.11 (22.25)	83.70 (24.03)	83.90 (23.12)	0.6295
Height (cm), Mean (SD)	169.69 (11.13)	168.78 (10.68)	169.23 (10.89)	0.5465
BMI (kg/m^2), Mean (SD)	29.20 (7.18)	29.37 (8.02)	29.29 (7.60)	0.8016
Risk Factors	138 (97.9%)	143 (99.3%)	281 (98.6%)	0.3671
Diabetes	82 (58.2%)	94 (65.3%)	176 (61.8%)	
Type 1	3 (2.1%)	7 (4.9%)	10 (3.5%)	
Type 2	79 (56.0%)	87 (60.4%)	166 (58.2%)	
Dyslipidemia	85 (60.3%)	84 (58.3%)	169 (59.3%)	
Hypertension	133 (94.3%)	142 (98.6%)	275 (96.5%)	
Cigarette Smoking	64 (45.4%)	66 (45.8%)	130 (45.6%)	
Current	19 (13.5%)	21 (14.6%)	40 (14.0%)	
Former	45 (31.9%)	45 (31.3%)	90 (31.6%)	
Cardiovascular Disease	83 (58.9%)	96 (66.7%)	179 (62.8%)	0.1800

Description	LTX DCB (N=141)	Standard PTA (N=144)	Total (N=285)	P-value[1]
Congestive Heart Failure (CHF)	33 (23.4%)	33 (22.9%)	66 (23.2%)	
Stroke	18 (12.8%)	13 (9.0%)	31 (10.9%)	
Coronary Artery Disease (CAD)	43 (30.5%)	40 (27.8%)	83 (29.1%)	
Myocardial Infarction (MI)	16 (11.3%)	23 (16.0%)	39 (13.7%)	
Peripheral Arterial/Vascular Disease (PAD) (PVD)	14 (9.9%)	26 (18.1%)	40 (14.0%)	
Other	47 (33.3%)	41 (28.5%)	88 (30.9%)	
Other Disease	123 (87.2%)	133 (92.4%)	256 (89.8%)	0.1733
Bleeding Disorder	1 (0.7%)	1 (0.7%)	2 (0.7%)	
Cancer	33 (23.4%)	26 (18.1%)	59 (20.7%)	
Glomerulonephritis	7 (5.0%)	1 (0.7%)	8 (2.8%)	
Steal Syndrome	4 (2.8%)	2 (1.4%)	6 (2.1%)	
Allergic Reaction or Contraindication to Iodinated Contrast Media or Paclitaxel	1 (0.7%)	4 (2.8%)	5 (1.8%)	
Other	119 (84.4%)	129 (89.6%)	248 (87.0%)	

[1] P-value associated with Wilcoxon Rank sum Test comparing LTX DCB and Standard PTA group or Fisher Exact Test for categorical data.

Table 4 summarizes the medication history for the test and control groups.

Table 4. Medication History

Time point	Medication	LTX DCB (N=141)	Standard PTA (N=144)	Total (N=285)
Pre-Procedure (Within 72hrs)	Aspirin	61 (43.3%)	56 (38.9%)	117 (41.1%)
	Clopidogrel	17 (12.1%)	13 (9.0%)	30 (10.5%)
	Heparin	1 (0.7%)	3 (2.1%)	4 (1.4%)
	Other Antiplatelet / Antithrombotic / Anticoagulant	18 (12.8%)	14(9.7%)	32 (11.2%)
Post Discharge To 30 Day Visit	Aspirin	54 (38.3%)	55 (38.2%)	109 (38.2%)
	Clopidogrel	15 (10.6%)	12 (8.3%)	27 (9.5%)
	Heparin	6 (4.3%)	4 (2.8%)	10 (3.5%)
	Other Antiplatelet / Antithrombotic / Anticoagulant	18 (12.8%)	14 (9.7 %)	32 (11.2%)
Post 30 Day Visit To 3 Month Visit	Aspirin	57 (40.4%)	55 (38.2%)	112 (39.3%)
	Clopidogrel	18 (12.8%)	11 (7.6%)	29 (10.2%)
	Heparin	1 (0.7%)	6 (4.2%)	7 (2.5%)
	Other Antiplatelet / Antithrombotic / Anticoagulant	17 (12.0%)	16 (11.1%)	33 (11.6%)
Post 3 Month Visit To 6 Month Visit	Aspirin	60 (42.6%)	54 (37.5%)	114 (40.0%)
	Clopidogrel	20 (14.2%)	11 (7.6%)	31 (10.9%)
	Heparin	8 (5.7%)	10 (6.9%)	18 (6.3%)
	Other Antiplatelet / Antithrombotic / Anticoagulant	18 (12.8%)	21 (14.6%)	39 (13.7%)

Baseline angiographic data for the test and control groups were similar with respect to access age, target limb, and access site, see **Table 5.**

Table 5. Baseline Angiographic Data

Description	LTX DCB (N=141)	Standard PTA (N=144)	Total (N=285)
Target Index Limb			
Right Arm	47/141 (33.3%)	34/143 (23.8%)	81/284 (28.5%)
Left Arm	94/141 (66.7%)	109/143 (76.2%)	203/284 (71.5%)
Access Site			
Across Antecubital Fossa	7/141 (5.0%)	7/143 (4.9%)	14/284 (4.9%)
Forearm	47/141 (33.3%)	31/143 (21.7%)	78/284 (27.5%)
Upper Arm	87/141 (61.7%)	105/143 (73.4%)	192/284 (67.6%)
Target Lesion Location			
Anastomotic	6/139 (4.3%)	5/142 (3.5%)	11/281 (3.9%)
Cephalic Arch	26/139 (18.7%)	32/142 (22.5%)	58/281 (20.6%)
In Cannulation Zone	6/139 (4.3%)	14/142 (9.9%)	20/281 (7.1%)
Inflow	47/139 (33.8%)	42/142 (29.6%)	89/281 (31.7%)
Outflow	34/139 (24.5%)	32/142 (22.5%)	66/281 (23.5%)
Swing Point	20/139 (14.4%)	17/142 (12.0%)	37/281 (13.2%)
Tandem Lesion less than or equal to 2cm apart			
Yes	4/141 (2.8%)	10/143 (7.0%)	14/284 (4.9%)

Description	LTX DCB (N=141)	Standard PTA (N=144)	Total (N=285)
No	137/141 (97.2%)	133/143 (93.0%)	270/284 (95.1%)
Lesion Fully Effaced			
Yes	121/141 (85.8%)	126/143 (88.1%)	247/284 (87.0%)
No	10/141 (7.1%)	8/143 (5.6%)	18/284 (6.3%)
Unable To Assess	10/141 (7.1%)	9/143 (6.3%)	19/284 (6.7%)
Lesion Length (mm)			
N	141	143	284
Mean (SD)	28.4 (15.09)	29.5 (18.69)	28.9 (16.98)
Median	26.9	25.6	26.1
Min – Max	6.1 – 83.1	4.6 – 93.2	4.6 – 93.2

Table 6 summarizes the study devices used for the test and control groups.

Table 6. Summary of Study Device

Description	LTX DCB (N=141)	Standard PTA (N=144)	Total (N=285)
Maximum Pressure of Pre-Dilatation Balloon Inflation (atm)			
N	140	143	283
Mean (SD)	21.3 (7.98)	21.7 (8.33)	21.5 (8.15)
Median	20.0	20.0	20.0
Min – Max	8 – 40	6 – 40	6 – 40
Max Inflation Pressure ≥25atm Difference (95% CI)	–	–	84/285 (29.5%)
Number of Study Device			
1	128/141 (90.8%)	143/144 (99.3%)	271/285 (95.1%)
2	13/141 (9.2%)	1/144 (0.7%)	14/285 (4.9%)
Balloon Diameter (mm)			
N	154	145	299
Mean (SD)	8.31 (1.79)	8.12 (1.79)	8.22 (1.79)
Median	8.00	8.00	8.00
Min – Max	4.0 – 12.0	5.0 – 12.0	4.0 – 12.0
Balloon Length (mm)			
N	154	145	299
Mean (SD)	51.2 (12.10)	45.7 (12.41)	48.5 (12.53)
Median	60.0	40.0	40.0
Min – Max	40 – 100	40 – 100	40 – 100
Transit Time (sec)			
N	152	142	294
Mean (SD)	18.1 (32.16)	19.1 (38.57)	18.6 (35.35)
Median	11.0	10.0	10.0
Min – Max	0 – 320	1 – 420	0 – 420
Device Inserted into Subject			
Yes	151/154 (98.1%)	145/145 (100.0%)	296/299 (99.0%)
Device Used to Treat Target Lesion			
Yes	150/154 (97.4%)	145/145 (100.0%)	295/299 (98.7%)
If No, Reason			
User Error	4/4 (100.0%)	0	4/4 (100.0%)
Number of Inflations per Device			
1	151/151 (100.0%)	122/145 (84.1%)	273/296 (92.2%)
2	0	20/145 (13.8%)	20/296 (6.8%)
3	0	3/145 (2.1%)	3/296 (1.0%)
Type of Catheter use for Treatment[1]			
Conventional (RBP < 15 atm), n/N (%)	150/150 (100%)	83/144 (57.6%)	233/294 (79.4%)
High Pressure/Fiber (RBP ≥ 15 atm), n/N (%)	0/150 (0%)	61/144 (42.4%)	61/144 (20.7%)
Maximum Pressure of Balloon Inflation (atm)[2]			
N	150	167	318
Mean (SD)	9.7 (2.13)	12.1 (4.96)	11.0 (4.11)
Median	10.0	11.0	10.0
Min – Max	4 – 14	3 – 35	3 – 35
Max Inflation Pressure ≤12atm, n/N(%)	139/140 (99.3%)	95/143 (66.4%)	234/283 (82.7%)
Max Inflation Pressure >12atm, n/N(%)	1/140 (0.7%)	48/143 (33.6%)	49/283 (17.3%)
Total Duration of Inflation (sec)			

Description	LTX DCB (N=141)	Standard PTA (N=144)	Total (N=285)
N	1501	170	321
Mean (SD)	115.1 (33.78)	89.7 (40.88)	101.4 (39.75)
Median	120.0	120.0	120.0
Min – Max	30 – 180	5 – 240	5 – 240
Operator able to Deliver to the Intended Treatment Site, Inflate and Retrieve the Device			
Yes	151/151 (100.0%)	171/171 (100.0%)	322/322 (100.0%)
Final %DS [Core Lab][3]			
N	141	143	284
Mean (SD)	16.6 (11.02)	17.0 (10.27)	16.8 (10.64)
Median	16.6	16.5	16.6
Min – Max	-27.5 – 47.4	-16.0 – 44.2	-27.5 – 47.4

[1] Maximum RBP rating for LUTONIX® Catheter is 12 atm.
[2] Occurrence of balloon burst are excluded from the analysis.
[3] Final residual stenosis is the last value of stenosis post deployment, post dilation, or after other treatment modalities.

10.4 Methods

Patients presenting with a stenosed venous AV fistula in the arm, confirmed by angiography, were enrolled in the study. After the target lesion size and stenosis were confirmed by angiography, pre-dilatation of the target vessel was performed per standard treatment. After successful pre-dilatation in both treatment arms, subjects with documented angiographic residual stenosis ≤ 30% were enrolled and randomized 1:1 for subsequent treatment with LUTONIX® Catheter (Test) or standard PTA (Control). Subjects that were randomized and had an adjunct procedure were followed for the entire duration of the study. Any adjunct procedures were done according to standard of care and were captured on the electronic case report form. Standard off-line Quantitative Vascular Angiography (QVA) procedures were followed for analysis of baseline and un-scheduled angiograms by an independent blinded angiographic core laboratory.

All deaths, events leading to AV access circuit re-interventions, device related adverse events and SAEs involving the access circuit were adjudicated by an independent (blinded) Clinical Events Committee (CEC).

The Modified Intent-To-Treat (mITT) population, which consists of enrolled, randomized, and treated subjects was pre-specified as the primary analysis population. Since all subjects were treated with the assigned devices, the modified Intent to Treat (mITT) is the same as the ITT population. All analyses including the primary analyses are based on the mITT population.

10.5 Results

A total of 285 patients (141 LUTONIX® Catheter and 144 Control PTA) were enrolled and randomized from 23 clinical sites. Balloon sizes for the LUTONIX® Catheter ranged from 4 – 12 mm in diameter and 20 – 100mm in length.

Primary Endpoint Analysis

The primary safety endpoint was defined as freedom from localized or systemic serious adverse events through 30 days that reasonably suggests the involvement of the AV access circuit. Results for the primary safety endpoint for the Lutonix AV study are summarized in **Table 7**. Based on the mITT population, 94.9% of the patients in the test group were free from primary safety event, compared to 95.8% in the control group. Based on the rate difference (95% confidence interval) greater than 10%, non-inferiority margin, the objective of the primary safety endpoint was met.

Table 7. Primary Safety Endpoint

Primary Safety Endpoint	Lutonix DCB (N=141) n/N (%)	Standard PTA (N=144) n/N (%)	Difference (95% CI) [1]	P-value[1]
Free from primary safety event	130/137 (94.9%)	138/144 (95.8%)	-0.9% (-7.1% , 5.2%)	0.0019

[1] 95% CI of the difference and the one sided p-value were calculated using non-inferiority Farrington and Manning Test, with 10% as non-inferiority margin

The primary effectiveness endpoint was Target Lesion Primary Patency (TLPP) by Kaplan Meier survival analysis at 180 days. Target Lesion Primary Patency was defined as freedom from clinically-driven reintervention of the target lesion or access thrombosis. Results for primary effectiveness endpoint for the Lutonix AV study are shown in **Table 8**. Based on the Kaplan Meier survival analysis of TLPP at 180 days, effectiveness was 71.4% for test group and 63.0% for the control group. The primary effectiveness endpoint for superiority of DCB compared to PTA was not met with p = 0.0562, see **Table 8**.

Table 8. Primary Effectiveness Endpoint

Description	LTX DCB (N=141)	Standard PTA (N=144)	Difference % (95% CI)	P-value
Number of Events, n (%)	37 (26.2%)	52 (36.1%)		
Number Censored, n (%)	104 (73.8%)	92 (63.9%)		
Discontinued Early	16 (11.3%)	7 (4.9%)		
No Event	88 (62.4%)	85 (59.0%)		
180 Day Event Free Rate	71.4%	63.0%	8.4% (-2.8%, 19.6%)	0.0562

Subgroup Analysis

Gender
There were no significant differences observed in primary endpoints between men and women, see table below.

Table 9. Primary Endpoint Analysis by Gender

Primary Analysis	Gender	LTX DCB (N=141)	Standard PTA (N=144)	Difference	P-value[1]
Primary Safety	Male	80/84 (95.2%)	82/85 (96.5%)	-1.2%	0.874
	Female	50/53 (94.3%)	56/59 (94.9%)	-0.6%	
Primary Efficacy	Male	57/75 (76.0%)	56/83 (67.5%)	8.5%	0.878
	Female	32/51 (62.7%)	32/57 (56.1%)	6.6%	

[1] P-value was type 3 test of the interaction where a logistic regression model was fitted including fixed effect for treatment group, site and the interaction of treatment group and site.

Secondary Endpoint Analysis

Primary safety endpoint was analyzed through the 12 months results by Kaplan Meier and is shown in **Figure 4** and **Table 10**. As shown, the clinical safety of LUTONIX® Catheter is sustained through the 12 month time point.

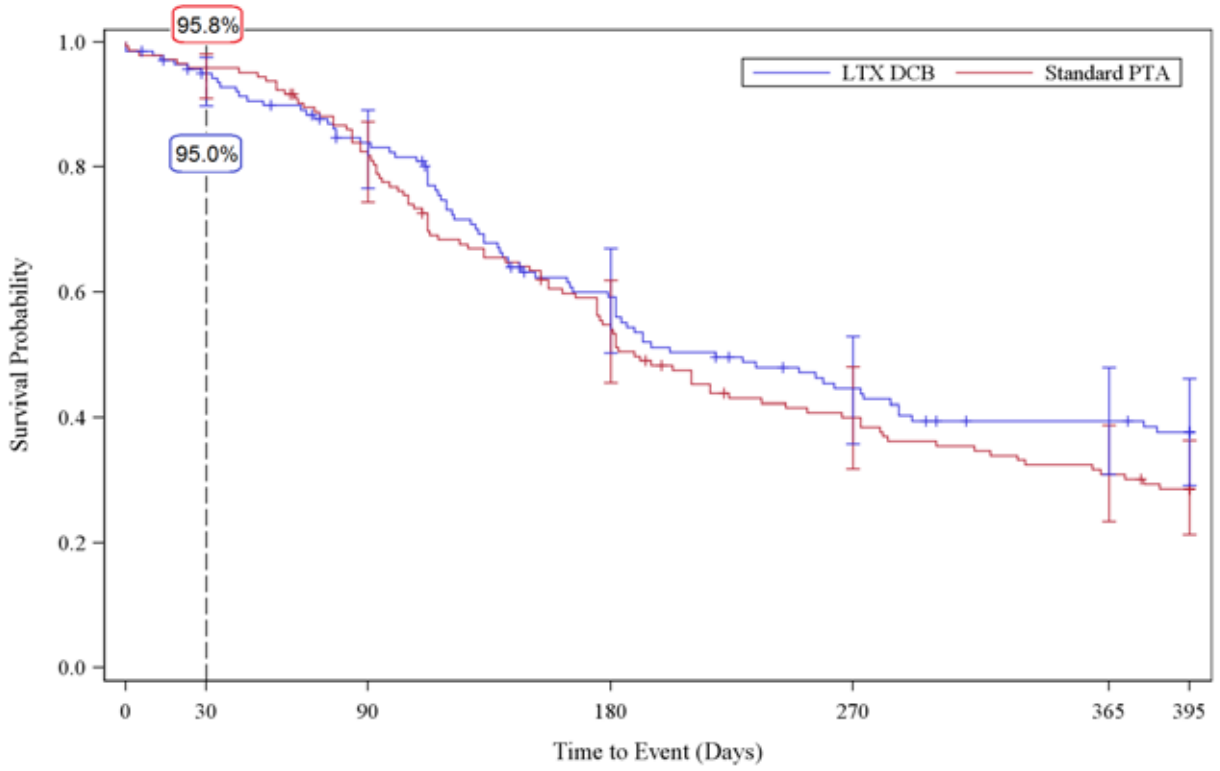


Figure 4. Kaplan-Meier analysis of Primary Safety through 12 months

Table 10. Freedom from Primary Safety Endpoint by Kaplan-Meier (ITT)

Description	LTX DCB (N=141)	Standard PTA (N=144)	Difference % (95% CI)
Number of Events, n (%)	80 (56.7%)	99 (68.8%)	
Number Censored, n (%)	61 (43.3%)	45 (31.3%)	
Discontinued Early	20 (14.2%)	8 (5.6%)	
No Event	41 (29.1%)	37 (25.7%)	
Time to Event (days, Median)	219.0	189.0	30.0
30 Day Event Free	95.0%	95.8%	-0.8% (-5.7%, 4.0%)
3 Month Event Free	83.9%	81.8%	2.1% (-6.7%, 10.9%)
6 Month Event Free	59.2%	54.0%	5.1% (-6.6%, 16.9%)

Description	LTX DCB (N=141)	Standard PTA (N=144)	Difference % (95% CI)
9 Month Event Free	44.5%	40.0%	4.5% (-7.4%, 16.4%)
12 Month Event Free	39.5%	31.0%	8.5% (-3.0%, 20.1%)

95% CI of the rate and the rate difference at each time point were calculated based on normal approximation and were not adjusted for multiplicity.

Target Lesion Primary Patency (TLPP) was analyzed through 12 months by Kaplan Meier and is shown in **Figure 5** and **Table 11**. As shown, the increase in TLPP for the LUTONIX® Catheter is sustained through the 12 month time point.

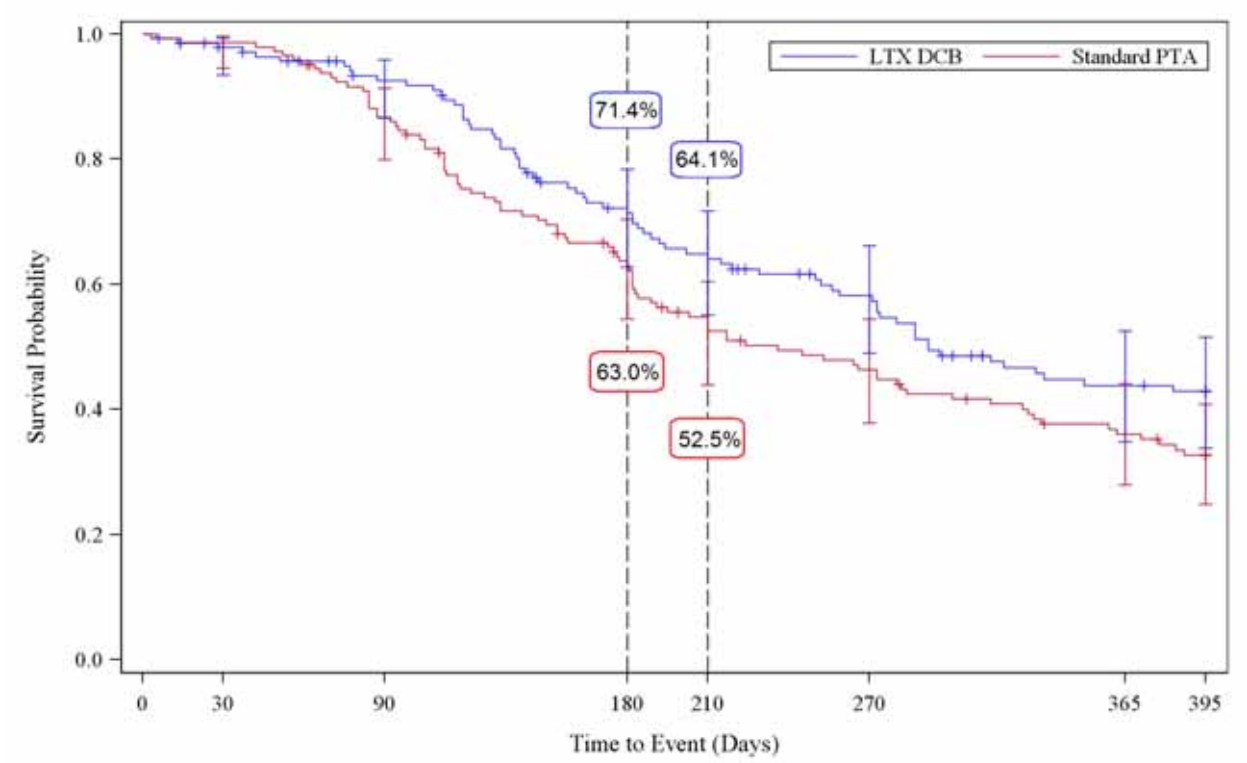


Figure 5. Kaplan-Meier analysis of TLPP through 12 months

Table 11. Kaplan Meier Analysis of TLPP through 12 months

Description	LTX DCB (N=141)	Standard PTA (N=144)	Difference % (95% CI)
Number of Events, n (%)	70 (49.6%)	91 (63.2%)	
Number Censored, n (%)	71 (50.4%)	53 (36.8%)	
Discontinued Early	27 (19.1%)	14 (9.7%)	
No Event	44 (31.2%)	39 (27.1%)	
Time to Event (days, Median)	292.0	236.0	56.0
180 Day Event Free Rate	71.4%	63.0%	8.4% (-2.8%, 19.6%)
210 Day Event Free Rate	64.1%	52.5%	11.6% (-0.2%, 23.4%)
270 Day Event Free Rate	58.2%	46.4%	11.8% (-0.3%, 23.9%)
300 Day Event Free Rate	48.6%	42.5%	6.1% (-6.0%, 18.3%)
365 Day Event Free Rate	43.8%	36.0%	7.8% (-4.3%, 19.9%)
395 Day Event Free Rate	42.9%	32.7%	10.2% (-1.9%, 22.2%)

95% CI rate difference at each time point were calculated based on normal approximation using Greenwood formula variance estimators and were not adjusted for multiplicity.

Table 12 summarizes the results for access circuit primary patency (ACPP).

Table 12. Kaplan Meier Analysis, ACPP through 12 months

Description	LTX DCB (N=141)	Standard PTA (N=144)	Difference % (95% CI)
Number of Events, n (%)	79 (56.0%)	95 (66.0%)	
Number Censored, n (%)	62 (44.0%)	49 (34.0%)	
Discontinued Early	23 (16.3%)	11 (7.6%)	
No Event	39 (27.7%)	38 (2.64%)	
Time to Event (days, median)	229.0	210.0	19.0
6 Month (180 Day) Event Free Rate	62.2%	58.1%	4.2% (-7.5%, 15.9%)
9 Month (270 Day) Event Free Rate	46.5%	42.5%	4.0% (-8.1%, 16.0%)
12 Month (365 Day) Event Free Rate	36.8%	30.8%	6.1% (-5.6, 17.7)

95% CI of the rate and rate difference at each time point were calculated based on normal approximation using Greenwood formula variance estimators without adjustment for multiplicity.

Table 13 summarizes the results for Abandonment of Permanent Access in Index extremity through 12 months.

Table 13. Abandonment of Permanent Access in Index extremity through 12 months

Time Point	LTX DCB (N=141)	Standard PTA (N=144)	Difference (95% CI)[1]
6 Month (180 Day)	4 (2.8%)	1 (0.7%)	2.1% (-0.9%, 5.2%)
9 Month (270 Day)	10 (7.1%)	4 (2.8%)	4.3% (-0.7%, 9.3%)
12 Month (365 Day) [2]	11 (7.8%)	6 (4.2%)	3.6% (-1.9%, 9.1%)

[1] 95% CI of the rate difference was estimated using Wald asymptotic method without adjustment for multiplicity.
[2] Reasons for abandonment at 12 months: DCB (7 – transplant, 2 – aneurysm, 2- stenosis), PTA (4 – transplant, 1 – peritoneal dialysis, 1 – thrombosis)

Table 14 summarizes the number of re-interventions required to maintain target lesion patency through 12 months.

Table 14. Number of Re-interventions Required to Maintain Target Lesion Patency through 12 months

Time Point	LTX DCB (N=141)	Standard PTA (N=144)	% Reduction
3 Month – Interventions (Subjects)	11 (n=10)	19 (n=19)	42.1% (8/19)
6 Month – Interventions (Subjects)	44 (n=37)	64 (n=52)	31.3% (20/64)
9 Month – Interventions (Subjects)	76 (n=53)	103 (n=74)	26.2% (27/103)
12 Month – Interventions (Subjects)	115 (n=69)	138 (n=87)	16.7% (23/138)

Deaths

The total number of deaths that have been reported through 12 months is shown in **Table 15**. None of the deaths were related to the test device or the procedure. The death rate observed in the Lutonix AV study for both study arms is consistent with the 22.5% yearly rate reported in the literature[1].

Table 15. Number of Deaths at 12 Months

Description	LTX DCB (N=141) (n/N %)	Standard PTA (N=144) (n/N %)
Number of Deaths through Day 365	18 (12.8%)	14 (9.7%)

Serious Adverse Events

Summary of the serious adverse events (**Table 16**) through 12 months that have been CEC adjudicated to date are summarized in the tables below. There was no significant difference in the SAE rates between the LUTONIX® Catheter and control PTA. No device-related thrombotic events or downstream embolic events were observed with the use of LUTONIX® Catheter. A serious adverse event is defined as an event that led to death; is life threatening; requires inpatient hospitalization or prolongation of existing hospitalization (> 24 hours); persistent or significant disability/incapacity; requires intervention to prevent permanent impairments or damage.

Table 16. Summary of Serious Adverse Events through 12 months

Body System/ Preferred Term	LTX DCB (N=141)	Standard PTA (N=144)
Any Serious Adverse Events	196	201

[1] 225 per 1000 patient years: https://www.usrds.org/2016/view/v1_03.aspx

Body System/ Preferred Term	LTX DCB (N=141)	Standard PTA (N=144)
Any Subjects with at least One Serious Adverse Event	94 (66.7%)	104 (72.2%)
Cardiac disorders	7 (5.0%)	6 (4.2%)
Acute coronary syndrome	1 (0.7%)	0
Cardiac arrest	3 (2.1%)	3 (2.1%)
Cardiogenic shock	0	1 (0.7%)
Mitral valve incompetence	1 (0.7%)	0
Myocardial infarction	0	2 (1.4%)
Pulseless electrical activity	1 (0.7%)	0
Ventricular tachycardia	1 (0.7%)	0
Gastrointestinal disorders	1 (0.7%)	0
Ischemic colitis	1 (0.7%)	0
General disorders and administration site conditions	2 (1.4%)	1 (0.7%)
Cardiac death	1 (0.7%)	0
Death	1 (0.7%)	1 (0.7%)
Infections and infestations	2 (1.4%)	1 (0.7%)
Pneumonia	1 (0.7%)	1 (0.7%)
Septic shock	1 (0.7%)	0
Injury, poisoning and procedural complications	79 (56.0%)	96 (66.7%)
Arteriovenous fistula aneurysm	3 (2.1%)	3 (2.1%)
Arteriovenous fistula occlusion	0	1 (0.7%)
Arteriovenous fistula site complication	76 (53.9%)	90 (62.5%)
Arteriovenous fistula site hemorrhage	1 (0.7%)	0
Arteriovenous fistula thrombosis	6 (4.3%)	10 (6.9%)
Vascular graft thrombosis	1 (0.7%)	0
Metabolism and nutrition disorders	1 (0.7%)	3 (2.1%)
Diabetic complication	0	1 (0.7%)
Hyperkalemia	1 (0.7%)	1 (0.7%)
Hypervolemia	0	1 (0.7%)
Nervous system disorders	1 (0.7%)	0
Cerebrovascular accident	1 (0.7%)	0
Renal and urinary disorders	3 (2.1%)	1 (0.7%)
Renal failure chronic	3 (2.1%)	1 (0.7%)
Respiratory, thoracic and mediastinal disorders	1 (0.7%)	1 (0.7%)
Acute respiratory failure	0	1 (0.7%)
Respiratory failure	1 (0.7%)	0
Skin and subcutaneous tissue disorders	1 (0.7%)	0
Skin ulcer	1 (0.7%)	0
Skin ulcer hemorrhage	1 (0.7%)	0
Vascular disorders	3 (2.1%)	4 (2.8%)
Arteriosclerosis	0	1 (0.7%)
Deep vein thrombosis	0	1 (0.7%)
Hypertension	0	1 (0.7%)
Steal syndrome	2 (1.4%)	0
Thrombosis	0	1 (0.7%)
Venous occlusion	1 (0.7%)	0

11 HOW SUPPLIED

- **Sterile:** This device is sterilized with ethylene oxide gas. Do not use if package is opened or damaged. For one use only. Do not resterilize.
- The LUTONIX® Catheter has a protective sheath placed over the balloon, is stored within a standard dispensing hoop, and is sterilized within a dual chamber pouch. The dual chamber pouch contains both a catheter compartment and desiccant compartment. The compartments are separated by a sterile barrier. The desiccant compartment contains packets used to help control package environment and should not be opened.
- **Contents**: One (1) LUTONIX® Catheter.
- **Storage:** Store in a dry, dark place. Store at 15-30°C (59-86°F). Do not store near radiation or ultra-violet light sources.

12 DIRECTIONS FOR USE

12.1 Equipment

In addition to the LUTONIX® Catheter, the following standard materials may also be required:

- 0.035″ Guidewire
- Introducer sheath
- Pre-dilatation balloon catheter(s)
- Contrast medium
- Sterile saline
- Inflation device with manometer
- Luer lock syringe for purging

12.2 Inspection Prior to Use

Prior to angioplasty, carefully examine all equipment to be used during the procedure, including the dilation catheter, to verify proper function. Verify that the catheter and sterile packaging have not been damaged in shipment.

Warning: Contents supplied STERILE using ethylene oxide (EO) process. Do not use if sterile barrier is damaged or opened prior to intended use.

12.3 Use of Multiple LUTONIX® Catheters

If multiple LUTONIX® Catheters are required to complete treatment of a lesion, the sequentially used LUTONIX® Catheter should be minimally sized and positioned so that the radiopaque marker bands of consecutively placed balloons overlap as necessary to cover the lesion and margins of the pre-dilatation/injury segment. The LUTONIX® Catheter should extend a minimum of 5 mm proximally and distally from the lesion and injury segment. Care should be taken not to extend the entire injury segment(s) unnecessarily, see **Figure 6.** The use of a radiopaque ruler or the GEOALIGN® marking system is recommended to ensure appropriate placement of the LUTONIX® Catheter.

Precaution: The safety and effectiveness of using multiple LUTONIX® drug coated balloons that deliver greater than 7.6 mg paclitaxel in a patient has not been clinically evaluated.

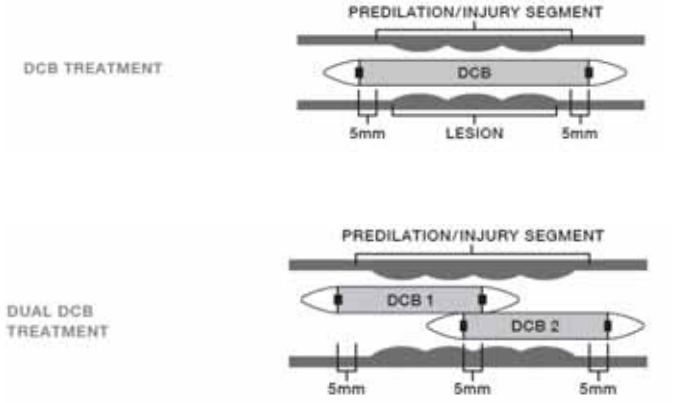


Figure 6. Balloon placement

12.4 Target Lesion Vessel Preparation

Vessel preparation of the target lesion, using appropriate vessel preparation method as determined by the physician to achieve residual stenosis of ≤ 30%, is required prior to the use of the LUTONIX® Catheter. Vessel preparation using pre-dilatation with a standard (non fiber) or ultra high pressure (fiber) balloon angioplasty were the only methods studied in the clinical trial. The use of ultra high pressure (≥ 25 atm) for pre-dilatation of the lesion is recommended. However, no difference was noted in the primary endpoint outcomes for higher pressure dilatation (≥ 25 atm) as compared to lower inflation pressures. The DCB is sized to extend 5mm beyond the pre-dilatation balloon on each side to fully cover the area of expansion.

Optional: If using the GEOALIGN® Marking System, take note of the band visible in relation to the introducer sheath, see Figure 7 below.

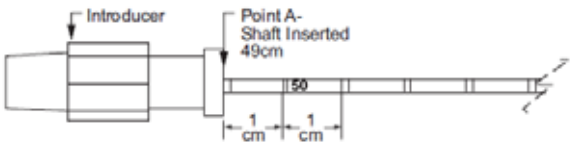


Figure 7. GEOALIGN® Marking System number in relation to introducer sheath (example)

12.5 LUTONIX® 035 DCB Catheter Preparation

1. Verify the balloon size is suitable for the procedure and the selected accessories are compatible with the catheter as labeled. The LUTONIX® Catheter should be sized to ensure full wall apposition (drug coated balloon to pre-dilatation balloon ratio of ≥ 1:1). See **Figure 8**.
2. Remove device from packaging.
3. Prepare the inflation device/syringe with diluted contrast medium.

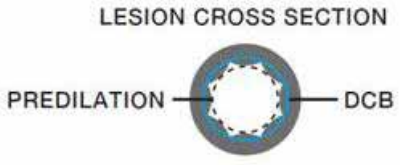


Figure 8. Pre-dilatation and DCB Sizing

Warning: Use the recommended balloon inflation medium of contrast and sterile saline (≤50% contrast). Never use air or any gaseous medium to inflate the balloon.

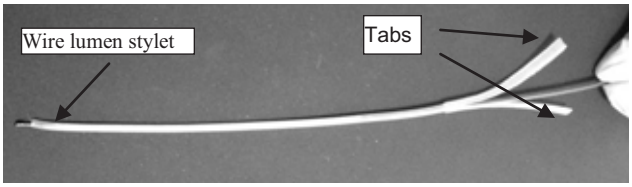
4. Prior to use, the air in the balloon catheter should be removed. To facilitate purging, select a syringe or inflation device with a 10 mL or larger capacity and fill approximately half of it with the recommended contrast medium.

5. Connect a stopcock to the balloon inflation female Luer hub on the dilation catheter.
6. Connect the syringe to the stopcock.
7. Hold the syringe with the nozzle pointing downward, open the stopcock and aspirate for approximately 15 seconds. Release the plunger.

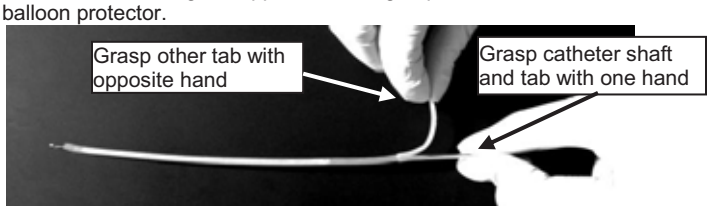
Repeat as needed until bubbles no longer appear during aspiration (negative pressure). Once completed, evacuate all air from the barrel of the syringe/inflation device and close the stopcock. This maintains vacuum during insertion and tracking.

12.6 Use of the LUTONIX® Catheter

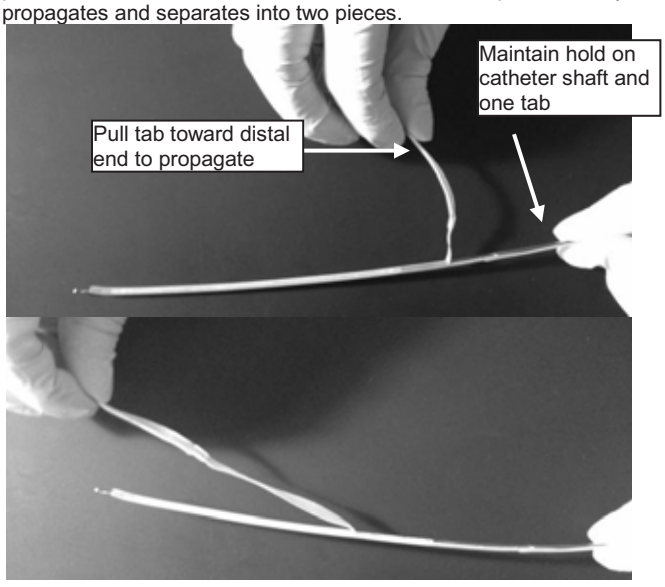
1. Perform the following steps to remove the balloon protector. Shown below is a catheter and balloon protector when removed from the catheter hoop.

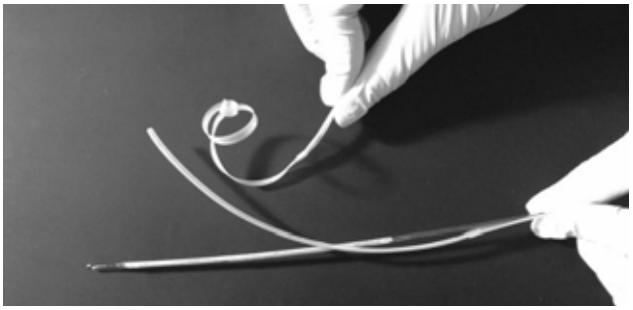


Step 1- Leaving the wire lumen stylet in place; use one hand to grasp both a single tab of the balloon protector and the catheter shaft as shown. Caution should be taken to not kink or crush the catheter shaft. Using the opposite hand, grasp the other tab of the balloon protector.

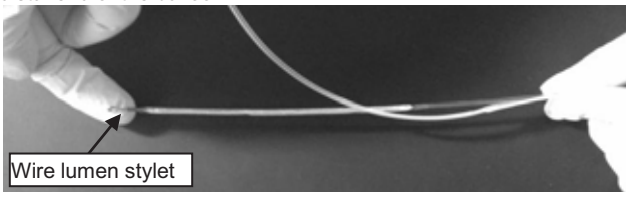


Step 2- With the hand holding the balloon protector tab only; gently pull the balloon protector tab toward the distal end of the balloon. Continue to pull the tab and hold the other balloon protector tab with the catheter shaft until the balloon protector fully propagates and separates into two pieces.

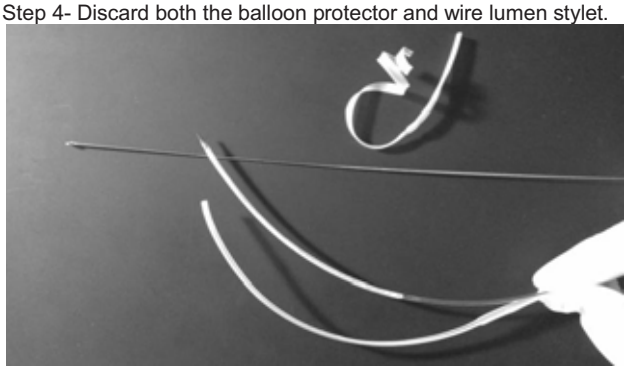




Step 3- Maintaining the grasp on the catheter shaft with one hand; use the opposite hand to remove the wire lumen stylet. Do this by gently pulling the hoop of the wire lumen stylet protruding from the distal end of the balloon.



Step 4- Discard both the balloon protector and wire lumen stylet.



2. With the catheter tip oriented down/vertically, flush the wire lumen.
3. Backload the distal tip of the dilation catheter onto the guidewire.
4. While the balloon is still fully deflated and under negative pressure, slowly advance the LUTONIX® Catheter through the introducer sheath and over the wire to the site of inflation. During catheter advancement, inspect the catheter shaft for damage.
5. To ensure therapeutic drug delivery, the LUTONIX ® Catheter should be advanced to the target site in the shortest possible time (i.e., ≤30 seconds) and immediately inflated to appropriate pressure to ensure full wall apposition (drug coated balloon to pre-dilatation balloon ratio of ≥ 1:1). If the time to deployment of the LUTONIX® Catheter exceeds 3 minutes, the catheter requires replacement with a new unit.
6. Position the balloon relative to the lesion/pre-dilatation segment, ensuring coverage of at least 5mm proximally and distally beyond the margins of the lesion and the pre-dilatation segment, and immediately inflate to appropriate pressure to achieve full wall apposition (drug coated balloon to pre-dilatation balloon ratio of ≥ 1:1). Refer to Compliance Chart included on product label. The use of a radiopaque ruler and/or the GEOALIGN® marking system is recommended to ensure appropriate placement of the LUTONIX® Catheter.

   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.

7. Maintain balloon inflation for a minimum of 2 minutes. The balloon may remain inflated as long as is required by the standard of care to achieve a good angioplasty outcome.
8. Apply negative pressure to fully deflate the LUTONIX® Catheter. Prior to removal, confirm that the balloon is fully deflated under adequate visualization.
9. Withdraw the LUTONIX® Catheter from the sheath under negative pressure. Maintain the guidewire across the stenosis.
10. Confirm dilation of the lesion using adequate visualization.
11. Best outcomes are obtained when the final % diameter stenosis is 0 – 20%. To achieve the suggested % diameter stenosis, if needed, post-dilation is allowed with another PTA catheter or used LUTONIX® Catheter.
12. After confirming that a satisfactory dilation was achieved, remove all equipment from the body and close access site per standard clinical practice.
13. After use, this product may be a potential biohazard. Handle and dispose of in accordance with acceptable medical practices and applicable laws and regulations.

13 DISCLAIMER OF WARRANTY

LUTONIX, INC. 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 LUTONIX'S SOLE DISCRETION, OR REFUNDING YOUR NET PRICE PAID. WEAR AND TEAR FROM NORMAL USE OR DEFECTS RESULTING FROM MISUSE OF THIS PRODUCT IS NOT COVERED BY THIS LIMITED WARRANTY.
TO THE EXTENT ALLOWABLE BY APPLICABLE LAW, 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 LUTONIX BE LIABLE TO YOU FOR ANY INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES RESULTING FROM YOUR HANDLING OR USE OF THIS PRODUCT.

Manufacturer
Lutonix, Inc.
9409 Science Center Drive
New Hope, MN 55428 USA
www.bardpv.com

BARD