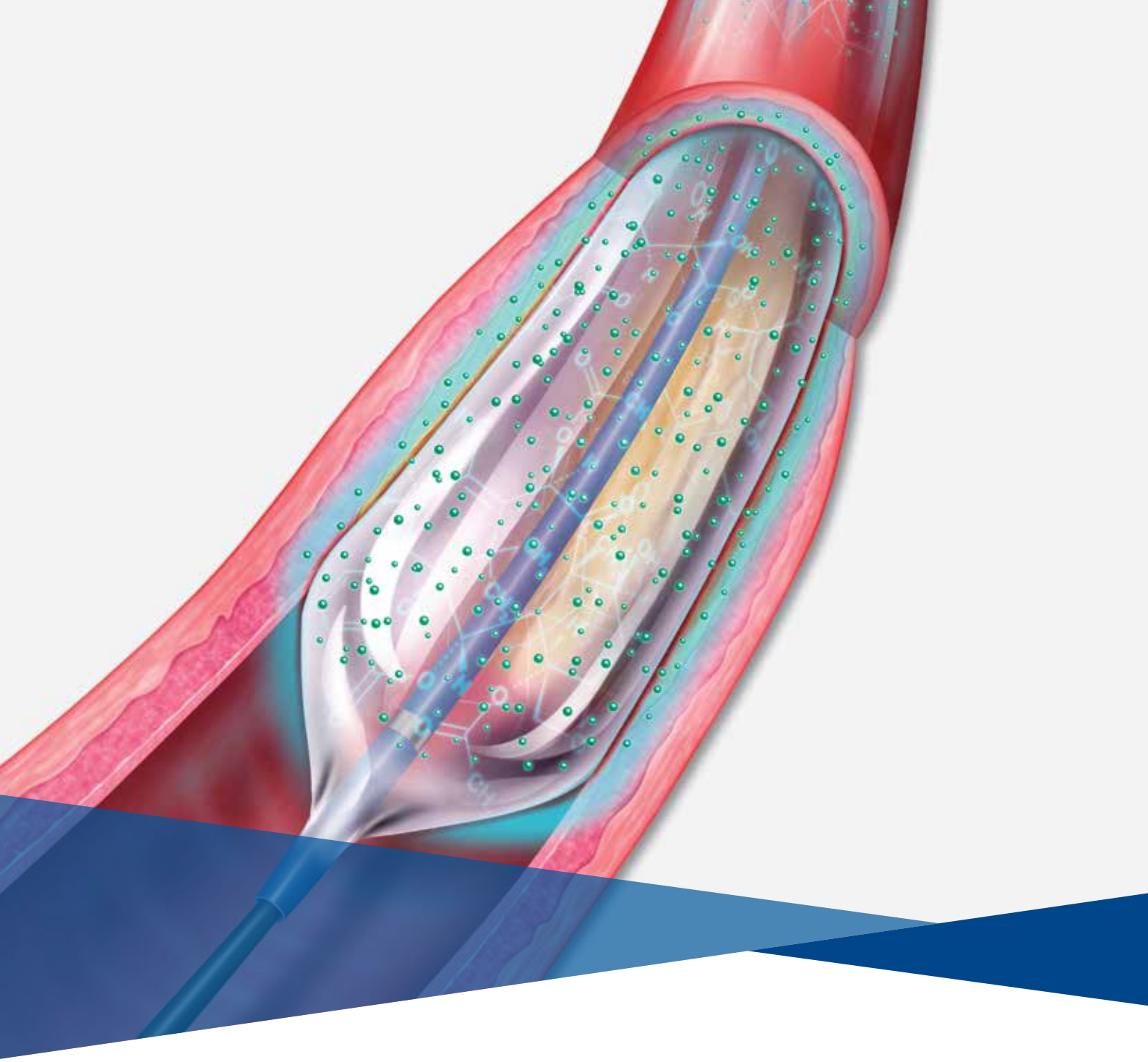


Lutonix™ 035 | 5F
Drug Coated Balloon PTA Catheter

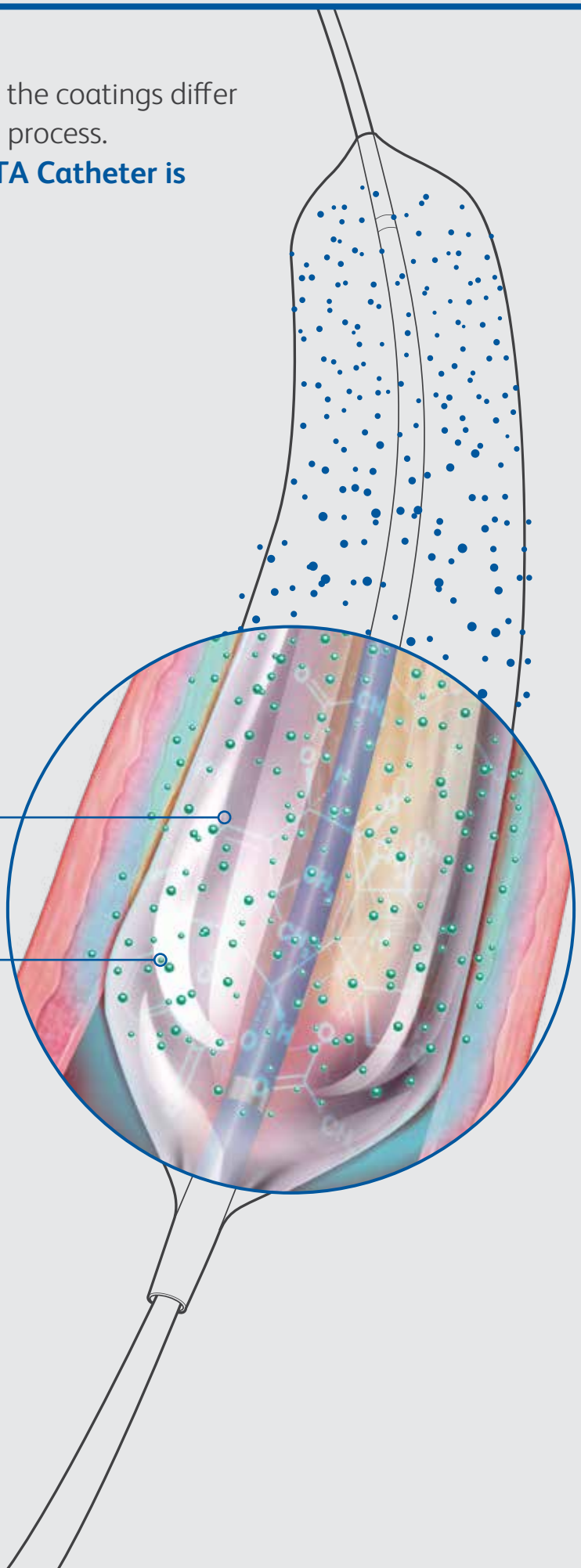
Indisputable Safety

BD

Formulation Matters

While all drug coated balloons use Paclitaxel, the coatings differ depending on the carrier and manufacturing process.
The Lutonix™ 035 Drug Coated Balloon PTA Catheter is safe for your patient.

- Coating Uniformity
- Drug Release
- Drug Retention
- **Successful DCB Formulation**



DRUG

Lutonix™ 035 DCB drug dose of Paclitaxel is 2 µg/mm²

+ CARRIER

Polysorbate and sorbitol

= COATING

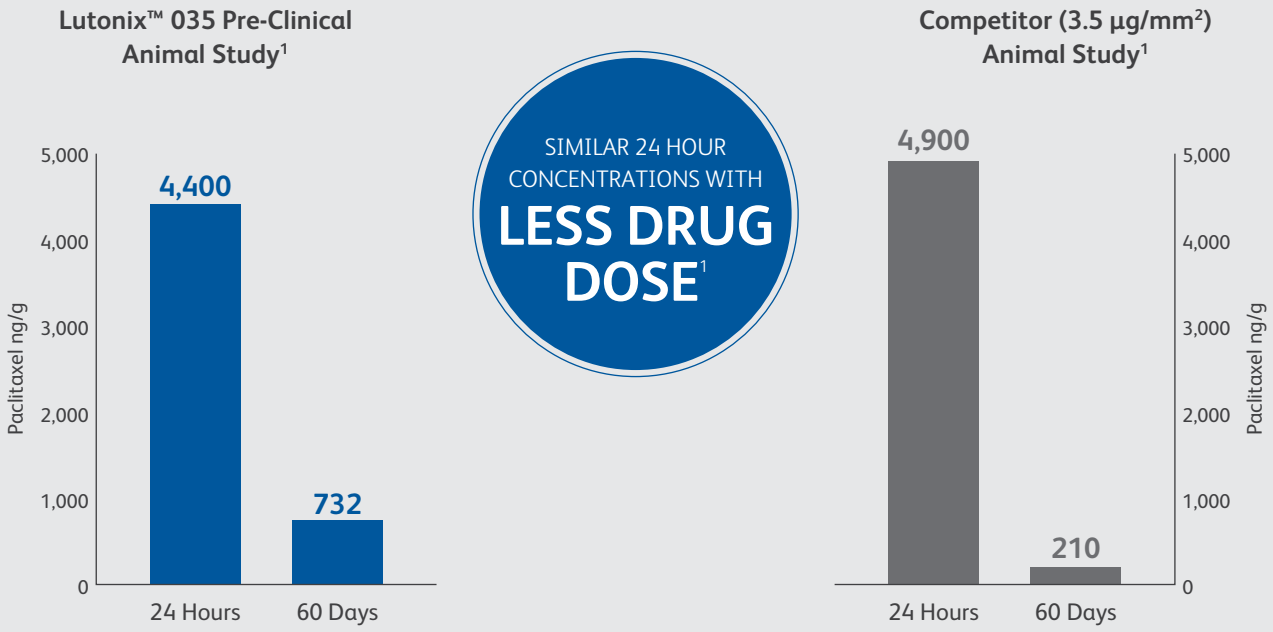
Facilitate drug retention during preparation and handling and release of therapeutic dose of the drug at the treatment site

Lutonix™ 035 | 5F

Drug Coated Balloon PTA Catheter

Lutonix™ 035 DCB offers similar Paclitaxel arterial tissue **concentration levels at 24 hours** and 60 days. Competitor has **75% more** Paclitaxel dose on the balloon.[1]

Rapid Uptake with Sustained Therapeutic Dose of Paclitaxel Arterial Tissue Concentration



	PACLITAXEL DOSE	CARRIER
Lutonix™ 035	2.0 µg/mm²	Polysorbate & sorbitol
Competitor	3.5 µg/mm²	Urea

> "It's about balancing safety, efficacy, and biological response."
>
> Dr. Renu Virmani

1 Data obtained from two data sets. Lutonix™ data from Virmani Pre-Clinical Animal Data GLP Study. Medtronic data from Medtronic own reported data, Dr. Melder, LINC presentation 2012. Bench test data on file. Bench results may not be indicative of clinical performance. Different test methods may yield different results.

Lutonix™ LEVANT 2 Clinical IDE Trial

Proven in a Level 1 Clinical Trial

The LEVANT 2 clinical trial was the **first U.S. IDE trial approved** by the FDA to evaluate the use of a DCB for the treatment of PAD in the SFA and popliteal arteries. **LEVANT 2 raised the bar for scientific rigor in PAD trials** and was designed to **reduce bias** in the results in order to accurately and scientifically assess and compare the long-term performance of the treatment modalities alone.

Clinical Trial Design

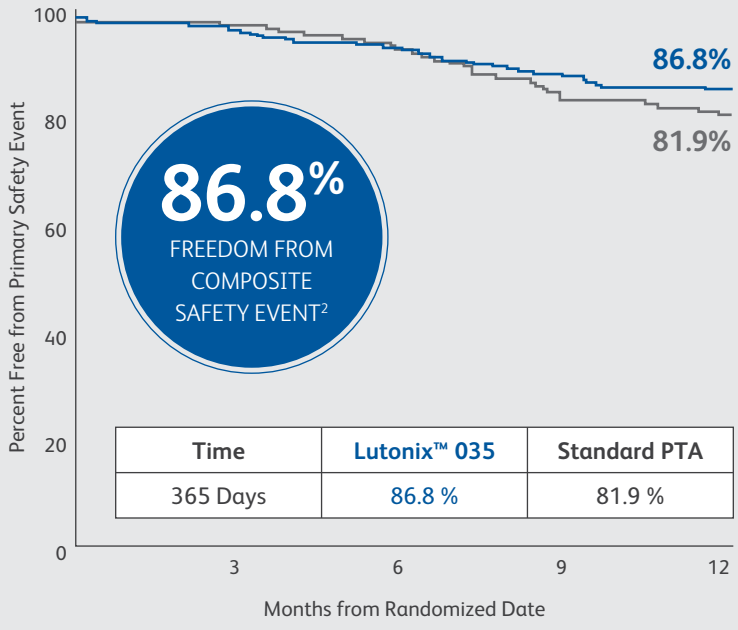
Trial Design	365 Days
Patients Enrolled	476 Patients at 54 Global Sites
Treatment Area	SFA and Popliteal (P1, P2, P3) Arteries
Inclusion Criteria	Rutherford 2-4 De Novo or Restenotic Lesions
Lesion Type	Length ≤ 150 mm Diameter 4-6 mm ≥ 70% Stenosis No In-Stent Restenosis

CHALLENGING PATIENT DEMOGRAPHIC:

- 43.4% Diabetics
- 70.6% Rutherford 3 & 4
- 59.2% Calcified Lesions
- 20.6% Total Occlusions

Established Safety Record Comparable to PTA[2]

Freedom from Composite Safety Event



Time	Lutonix™ 035	Standard PTA
365 Days	86.8 %	81.9 %

Lutonix™ 035 DCB demonstrated a safety profile that is **consistent with PTA** with **no rare adverse events** up to 24 months and no unanticipated **safety events** due to device or drug in over 1,000 patients.[2]

Low rates of thrombosis **0.4%** at 12 months*, **similar to PTA.**

* 1/285

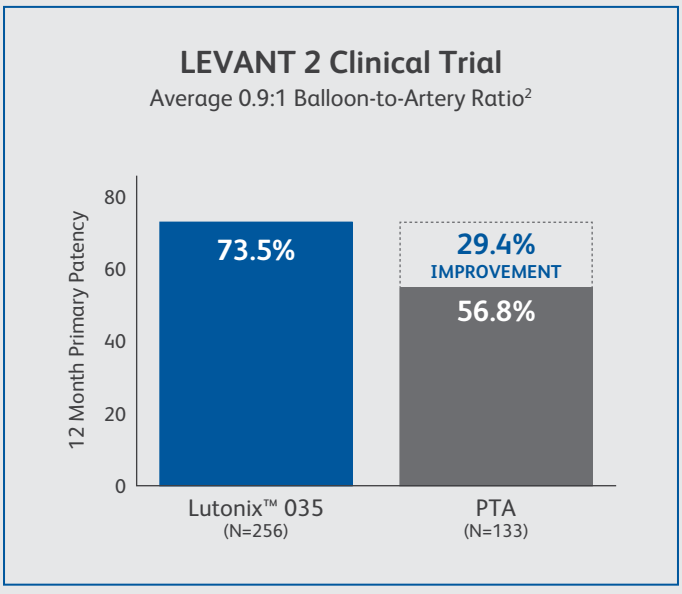
Sustained Improvement at 12 Months

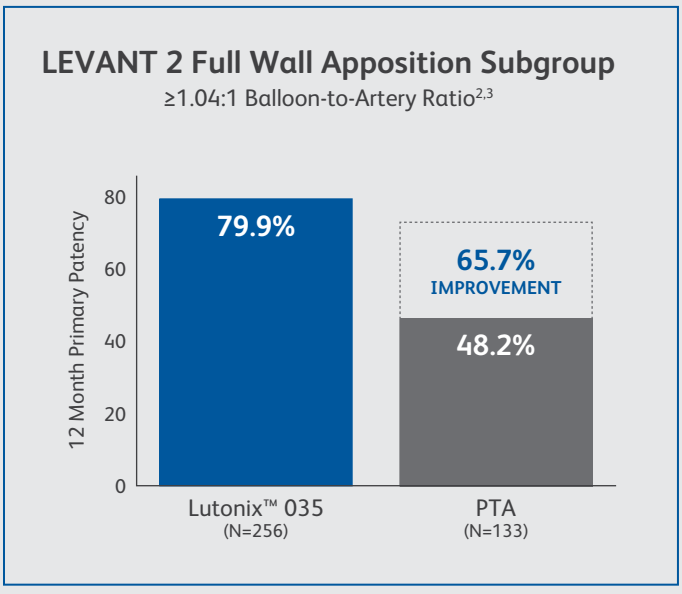
Patients treated with a DCB reported **less pain and the ability to walk further** at 12 months compared to patients treated with PTA alone.[1] **9 out of 10** patients treated with Lutonix™ 035 DCB did not require reintervention within one year.

88.2%
RUTHERFORD SUSTAINED IMPROVEMENT[2]

29.4% Improved Primary Patency over PTA at 12 Months[2]

- Lutonix™ 035 DCB demonstrated a statistically significant superior primary patency rate at 12 months compared to PTA[2] (By Kaplan-Meier analyses, p=0.001)
- A port-hoc subgroup analysis suggests that **full wall apposition** of the Lutonix™ 035 DCB **positively impacted primary patency** results at 12 months[2,3]





Lutonix™ Procedural Techniques For Optimal Drug Delivery[4]

- Transit time to lesion < 30 sec.
- Balloon Sizing of ≥ 1:1 (full wall apposition)
- Final residual stenosis < 20%
- Balloon inflation time ≥ 120 sec.
- Balloon pressure > 7 atm

1 Patients self-reported pain and walking distance in a questionnaire at 12 months in LEVANT 2. N=397 (DCB = 264, PTA =133). Patients were blinded to their original treatment modality.

2 LEVANT 2 clinical trial data on file. N=476. At 12 months, treatment with Lutonix™ 035 resulted in a primary patency rate of 73.5% versus 56.8% with PTA alone (p=0.001). Primary patency defined as absence of binary restenosis defined by DUS PSVR >2.5 and freedom from Target Lesion Revascularization (TLR). At 12 months, treatment with Lutonix™ 035 resulted in a freedom from composite safety event rate of 86.8% versus 81.9% with PTA alone. Primary safety defined as composite of freedom from all-cause Perioperative death and freedom at 1 year in the index limb from Amputation (ATK or BTK), Reintervention, and Index-limb related death. Percentages reported are derived from Kaplan-Meier analyses (not pre-specified).

3 A post-hoc subgroup analysis suggests the full wall apposition of the Lutonix™ 035 Drug Coated Balloon (minimum 1.04:1 balloon-to-artery ratio of the treatment device) showed increased primary patency of 79.9%. At 12 months, treatment with Lutonix™ 035 resulted in a freedom from primary safety event rate of 85.8% (balloon-to-artery ration <1). Primary safety defined as composite of freedom from all- cause perioperative death and freedom at 1 year in the index limb from Amputation (ATK or BTK). Reintervention, and Index-limb relate death. Numbers reported are Kaplan-Meier analyses, not pre-specified. Warning: Do Not Exceed Rated Burst Pressure.

4 The data presented herein are observational only. Further confirmatory clinical evidence is required to support the conclusion that the combination of any of these procedural techniques would yield an improved primary patency result beyond the 12-month primary patency rate of 73.5% demonstrated in LEVANT 2.

Lutonix™ Global SFA Real-World Registry

The primary objective of the Global SFA Real-World Registry was to demonstrate safety and assess the clinical use and outcomes of the Lutonix™ DCB in a heterogeneous patient population in real world clinical practice.

Registry Statistics

Patients	691
Sites/Countries	38/10

Selected Demographics

Diabetes (n/N)	39.5 % (273/691)
Rutherford Category	
Grade 2	20.6 % (142/689)
Grade 3	66.9 % (461/689)
Grade 4	7.4 % (51/689)
Grade 5 & 6	1.6 % (11/689)

Angiographic Data

Target Lesion Length (mm) mean ± SD (n)	101.2 ± 84.2 (685)
Calcification (n/N)	50.2 % (238/474)
Total Occlusion (n/N)	31.2 % (214/686)

Most Distal Lesion Location (n/N)

SFA	70.0 % (483/690)
Proximal Popliteal	16.8 % (116/690)
Mild Popliteal	10.1 % (10/690)
Distal Popliteal	3.0 % (21/690)

Primary Endpoints

Freedom from TLR[1]	
at 12 Months	**94.1 %**
at 24 Months	**90.3 %**
30 Day Safety[2]	**99.4 %**

90.3%
FREEDOM FROM TLR
AT 24 MONTHS[1]

1 Primary efficacy endpoint is defined as freedom from TLR at 12 months. Total of 648 subjects were evaluable for the primary efficacy endpoint analysis. The 12 month TLR Free rate by subject counts at 12 months was 93.4%. The Kaplan-Meier estimates TLR-Free survival was 94.1% at 12 months and 90.3% at 24 months. TLR-Free survival by lesion location was 94.7% (n=483) for SFA, 92.9% (n=86) for popliteal, and 92.3% (n=121) for patients with lesions in both SFA and popliteal.

2 The primary safety endpoint is defined as Freedom at 30 days from TVR, major index limb amputation, and device- and procedure-related death (VIVA safety endpoint). Please refer to the Lutonix™ 035 IFU for complete data sets and more detailed Lutonix™ 035 DCB clinical information, including with regard to the Lutonix™ DCB Global SFA Registry and the LEVANT 2 global, prospective, randomized, pivotal study.

In-Stent Restenosis (ISR) Subgroup

Angiographic Data

Target Lesion Length (mm) mean ± SD (n)	154.4 ± 97.1 (89)
Calcification (n/N)	37.7 % (26/69)
Total Occlusion (n/N)	28.1 % (25/89)

ISR Subgroup Results

Freedom from TLR	
at 12 Months	**90.7 %**
at 24 Months	**84.6 %**

84.6%
FREEDOM FROM TLR
AT 24 MONTHS

Long Lesion (LL) Subgroup

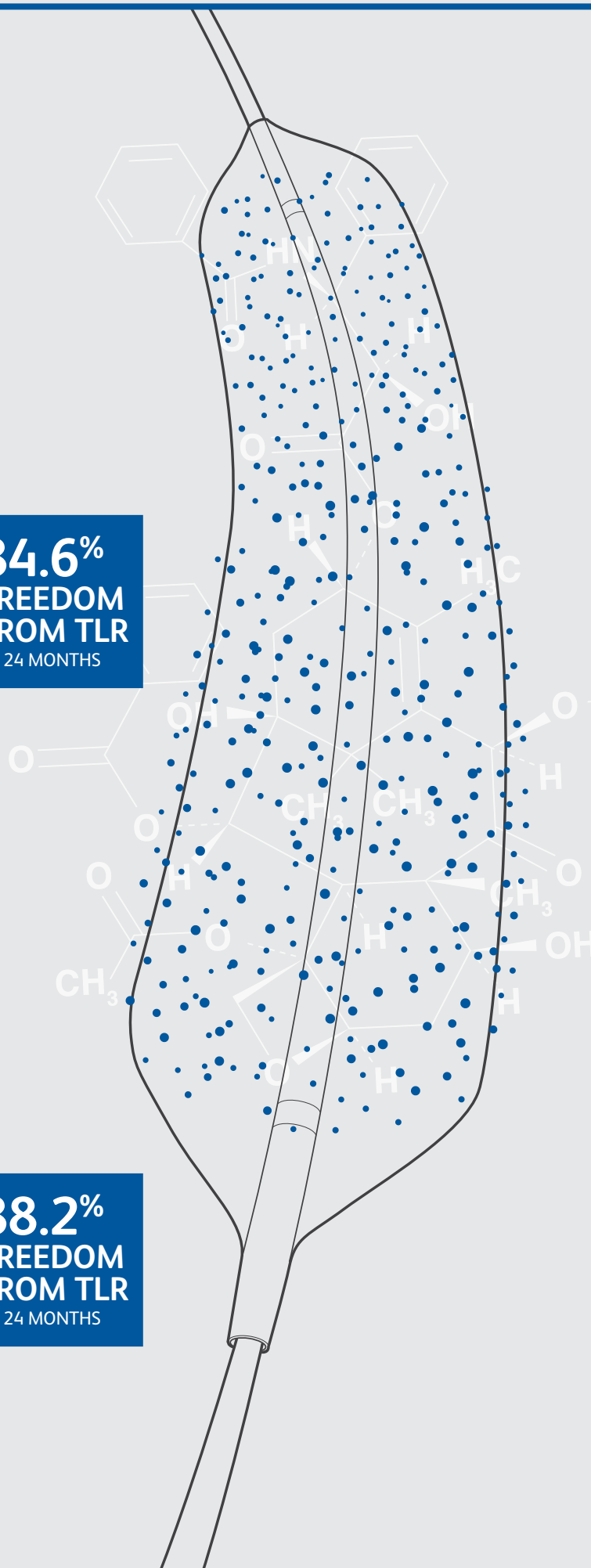
Angiographic Data

Target Lesion Length (mm) mean ± SD (n)	212.3 ± 65.3 (140)
Calcification (n/N)	57.5 % (46/80)
Total Occlusion (n/N)	42.1 % (59/140)

ISR Subgroup Results

Freedom from TLR	
at 12 Months	**93.2 %**
at 24 Months	**88.2 %**

88.2%
FREEDOM FROM TLR
AT 24 MONTHS



Lutonix™ BTK Global IDE Trial

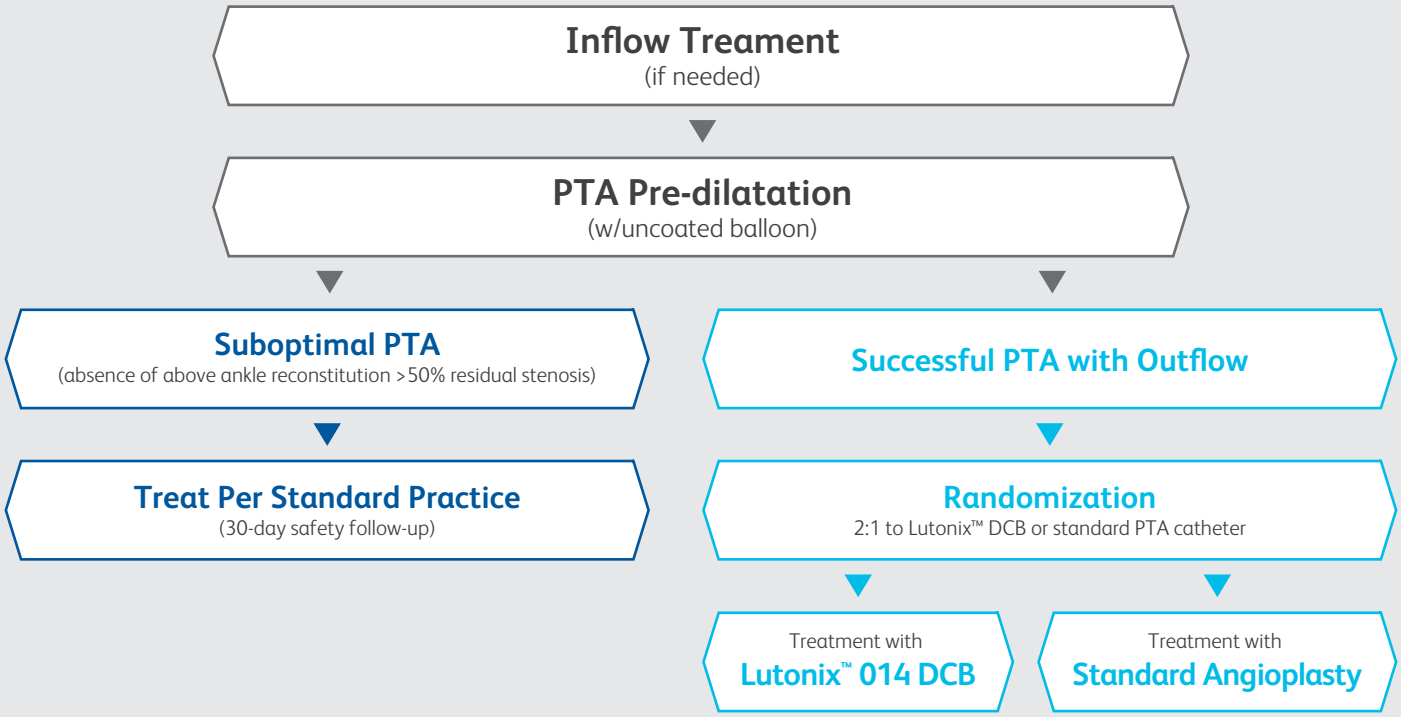
A Prospective, Multicenter, Single Blind, Randomized, Controlled Trial Comparing the Lutonix™ Drug Coated Balloon vs. Standard Balloon Angioplasty for Treatment of **Below-the-Knee (BTK) Arteries.**

- Primary safety endpoint:
  No difference between DCB and PTA (p=<0.0001) at 30 days
- No difference in All Cause Death at 6 Months
- Primary efficacy by Kaplan meier estimate at 6 month: DCB - 85.3% / PTA - 70.7% (△14.6%, p=<0.001)

Lutonix™ BTK Global IDE Trial Design

Trial Design	Prospective, Multicenter, Randomized, Single Blind
Number of Patients/Sites	442 randomized subjects at 51 clinical sites in 8 countries (US/EU / Japan / Canada)
Key Inclusion Criteria	Target vessel(s) reconstitute(s) at or above the ankle
Lesion Type	≥70% stenosis, diameter 2-4mm
Primary Safety Endpoint	Freedom from Major Adverse Limb Events (MALE) & All-Cause Perioperative Death (POD) - 30 Days
Primary Effectiveness Endpoint	Composite of Limb Salvage and Primary Patency - 6 Months
Follow Up	1, 6, 12, 24, 36 Months

Selected Demographics



Selected Demographics

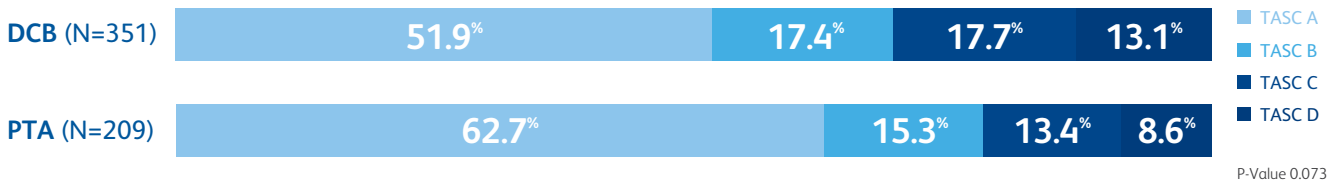
	DCB (N=287)	PTA (N=155)	P-Value
Age, Mean ± SD (n)	72.9 ± 9.65 (287)	72.9 ± 9.62 (155)	0.9586
Gender, % (n/N)			
Male	70.4 % (202/287)	67.1 % (104/155)	0.5173
Female	29.6 % (85/287)	32.9 % (51/155)	
History of Risk Factors, % (n/N)	**99.3 % (285/287)**	**100.0 % (155/155)**	
Diabetes	71.1 % (204/287)	68.4 % (106/155)	
Dyslipidemia	78.4 % (225/287)	74.8 % (116/155)	0.5436
Hypertension	92.0 % (264/287)	95.5 % (148/155)	
Cigarette Smoking	59.2 % (170/287)	57.4 % (89/155)	
Subject has Undergone Previous Peripheral Vascular Interventions	53.7 % (154 / 287)	54.2 % (84/155)	0.921

Baseline Rutherford Category

Lutonix™ BTK Global IDE Trial

Lesion Characteristics

	DCB (N=351)	**PTA** (N=209)
Vessel Locations, % (n/N)		
Popliteal	10.2 % (33/322)	9.3% (17/183)
Tibioperoneal Trunk	28.0 % (90/322)	31.1% (57/183)
Anterior Tibial	41.0 % (132/322)	35.5% (65/183)
Posterial Tibial	24.2 % (78/322)	27.3% (50/183)
Peroneal	23.6 % (76/322)	24.6% (45/183)
Mean Target Lesion Length, mm (n/N)	111.8 ± 92.6 mm (349/352)	94.7 ± 85.4 mm (206/213)
Severe Calcification, % (n/N)	15.1% (53/352)	13.2% (28/212)
CTO, % (n/N)	36.1% (137/380)	33.3% (75/225)

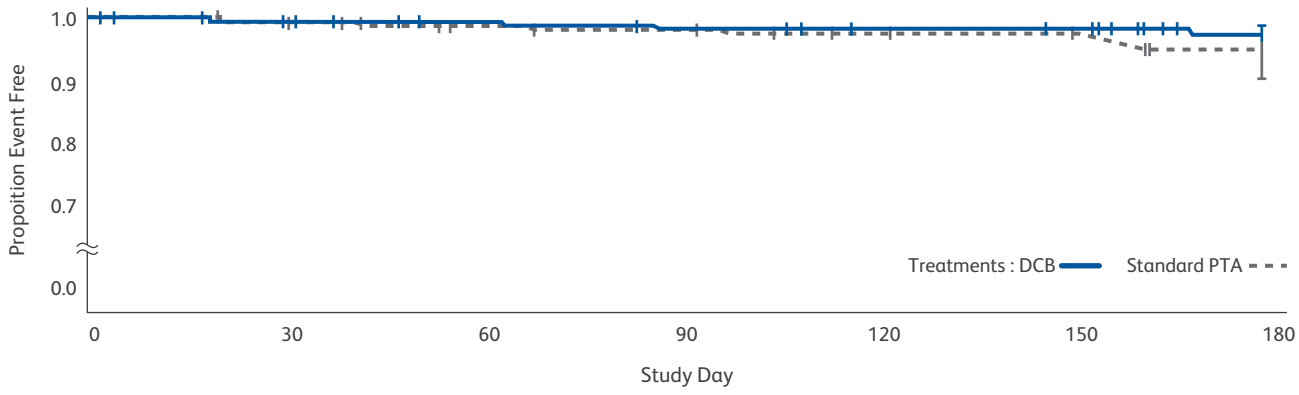


Primary Safety Endpoint (30-Day Safety*)

No difference in primary safety by KM estimate at 6 months (DCB – 97.8%, PTA – 95.3%, p=0.096)

	DCB (N=287), % (n/N)	**PTA** (N=155), % (n/N)	**Difference in Response**,% (95% CI)	**P-Value**
Free from Primary Safety Event at 30 Days * Freedom at 30 days from TVR, major index limb amputation, and device and all cause death	99.3% (283/285)	99.4% (154/155)	-0.1% (-3.9%, 3.8%)	<.0001

Primary Safety Endpoints (Kaplan-Meier 30-Day Safety)

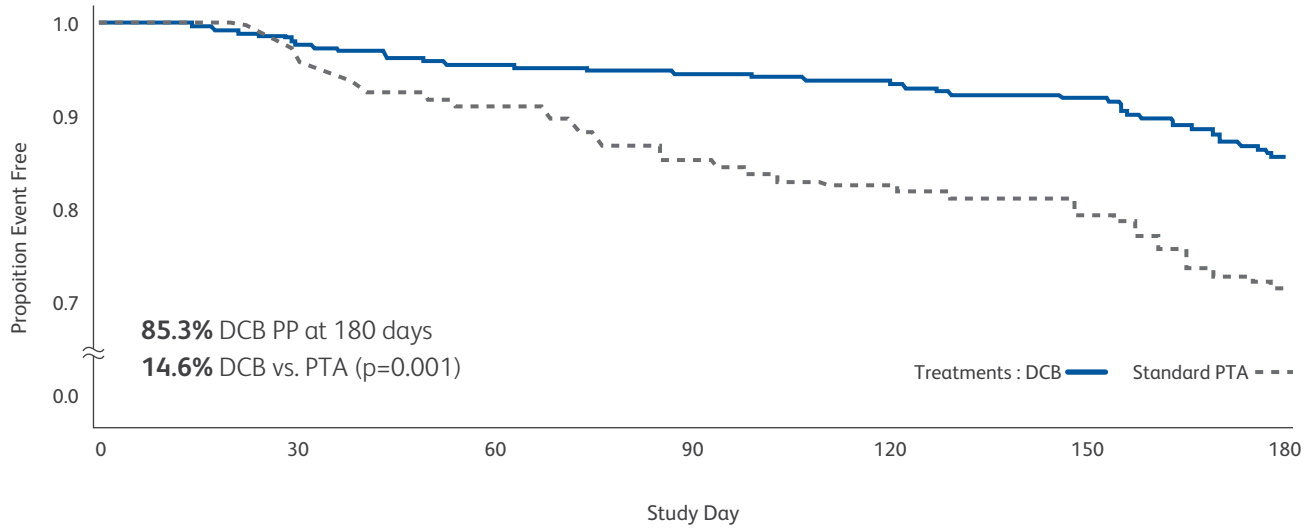


1 Kaplan-Meier estimate of proportion of subjects without a key safety event at the visit day
2 Subjects ongoing without an event at the visit day
3 95% CI for difference and p-value for one-sided test that DCB response is less than or equal to Standard PTA response obtained from Kaplan-Meier estimates and standard error estimates from Greenwood's method

Primary Efficacy Endpoint

	DCB (N=287), % (n/N)	**PTA** (N=155), % (n/N)	**Difference in Response**,% (95% CI)	**P-Value**
Free from Primary Efficacy Failure at 6 Months * Freedom at 6 months from major index limb amputation, target lesion occlusion and CD-TLR	73.7% (196/266)	63.5% (87/137)	10.2% (-0.2%, 18.7%)	0.0273

Primary Endpoints (Kaplan-Meier 6 Month Efficacy)



			Count Information at Visit Day			**Survival Difference**	
Group	**Time Point**	**Survival %[1]**	**Cumulative Subjects with Events**	**Cumulative Subjects Censored**	**Subjects Left[2]**	**Difference (95% CI)[3]**	**P-value[3]**
DCB	Day 1 Day 30 Day 180	100.0 % 97.7 % 85.3 %	0 7 41	24 24 51	299 292 231	2.0% (-1.4, 5.8%) 14.6% (5.6, 23.9%)	0.137<.0014
PTA	Day 1 Day 30 Day 180	100.0 % 95.6 % 70.7 %	0 7 42	21 24 45	163 153 97		

1 Kaplan-Meier estimate of proportion of subjects without a key safety event at the visit day
2 Subjects ongoing without an event at the visit day
3 95% CI for difference and p-value for one-sided test that DCB response is less than or equal to Standard PTA response obtained from Kaplan-Meier estimates and standard error estimates from Greenwood's method

Lutonix™ 035 Drug Coated Balloon PTA Catheter

Indications for Use:
The Lutonix™ 035 Drug Coated Balloon PTA catheter is indicated for percutaneous transluminal angioplasty, after appropriate vessel preparation, of de novo, restenotic, or in-stent restenotic lesions up to 300 mm in length in native superficial femoral or popliteal arteries with reference vessel diameters of 4-7 mm.

Contraindications: The Lutonix™ Catheter is contraindicated for use in:
1) Patients who cannot receive recommended anti-platelet and/or anticoagulant therapy.
2) Women who are breastfeeding, pregnant or are intending to become pregnant or men intending to father children. 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. 3) Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system.

Warnings:
1) Contents supplied STERILE using ethylene oxide (EO) process. Do not use if sterile barrier is damaged or opened prior to intended use.
2) Do not use if product damage is evident.
3) 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.
4) 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.
5) Use the recommended balloon inflation medium of contrast and sterile saline (≤50% contrast). Never use air or any gaseous medium to inflate the balloon.
6) This product should not be used in patients with known hypersensitivity to Paclitaxel or structurally related compounds.
7) The safety and effectiveness of the Lutonix™ Catheter have not been established for treatment in cerebral, carotid, coronary, or renal vasculature.
8) The safety and effectiveness of using more than four Lutonix™ drug coated balloons (i.e., a maximum drug coating quantity of approximately 15.1 mg Paclitaxel) in a patient has not been clinically evaluated.

Precautions: General Precautions:
1) The Lutonix™ Catheter should only be used by physicians trained in percutaneous interventional procedures.
2) Consideration should be given to the risks and benefits of use in patients with a history of non-controllable allergies to contrast agents.

Potential Adverse Events:
Potential adverse events which may be associated with a peripheral balloon dilatation procedure include: Additional intervention · Allergic reaction to drugs, excipients, or contrast medium · Amputation/loss of limb · Aneurysm or pseudoaneurysm · Arrhythmias · Embolization · Hematoma · Hemorrhage, including bleeding at the puncture site · Hypotension/ hypertension · Inflammation · Occlusion · Pain or tenderness · Pneumothorax or hemothorax · Sepsis/infection · Shock · 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: 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

Please consult product labels and instructions for use for all indications, contraindications, Hazards and warnings and precautions.

벡톤디킨슨코리아(주)
서울특별시 강남구 테헤란로 142, 16층

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