Lutonix AV Clinical Trial

Long Term Effects of LUTONIX® 035 DCB Catheter
18 month Interim Results

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LU/9010//1017/0054a

Conflicts of Interest

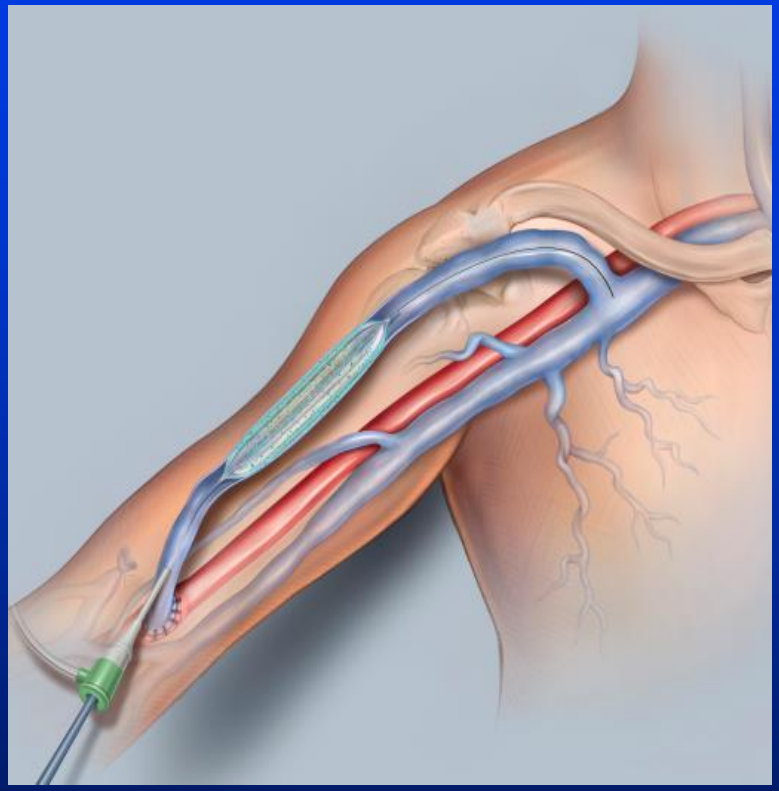
- Paid consultant for the following companies:
  - Bard Peripheral Vascular
  - LUTONIX
  - WL Gore
  - B Braun
  - Teleflex
  - Medcomp
  - Cook
- Royalties
  - Cook
  - Teleflex
- PI, Lutonix AV Trial and Lutonix AV PAS

Disclosures/Disclaimers

- The speaker's presentation today is on behalf of C. R. Bard/LUTONIX, Inc. The physician has been compensated by Lutonix for the time and effort to present this information.
- Please consult Bard product labels and inserts relevant to your geography for indications, contraindications, hazards, warnings, cautions, and instructions for use.
- The opinions and clinical experiences presented herein are for informational and educational purposes only. The results presented may not be predictive for all studies and patients. Results may vary depending on a variety of experimental and clinical parameters. Individual results may vary depending on a variety of patient specific attributes.

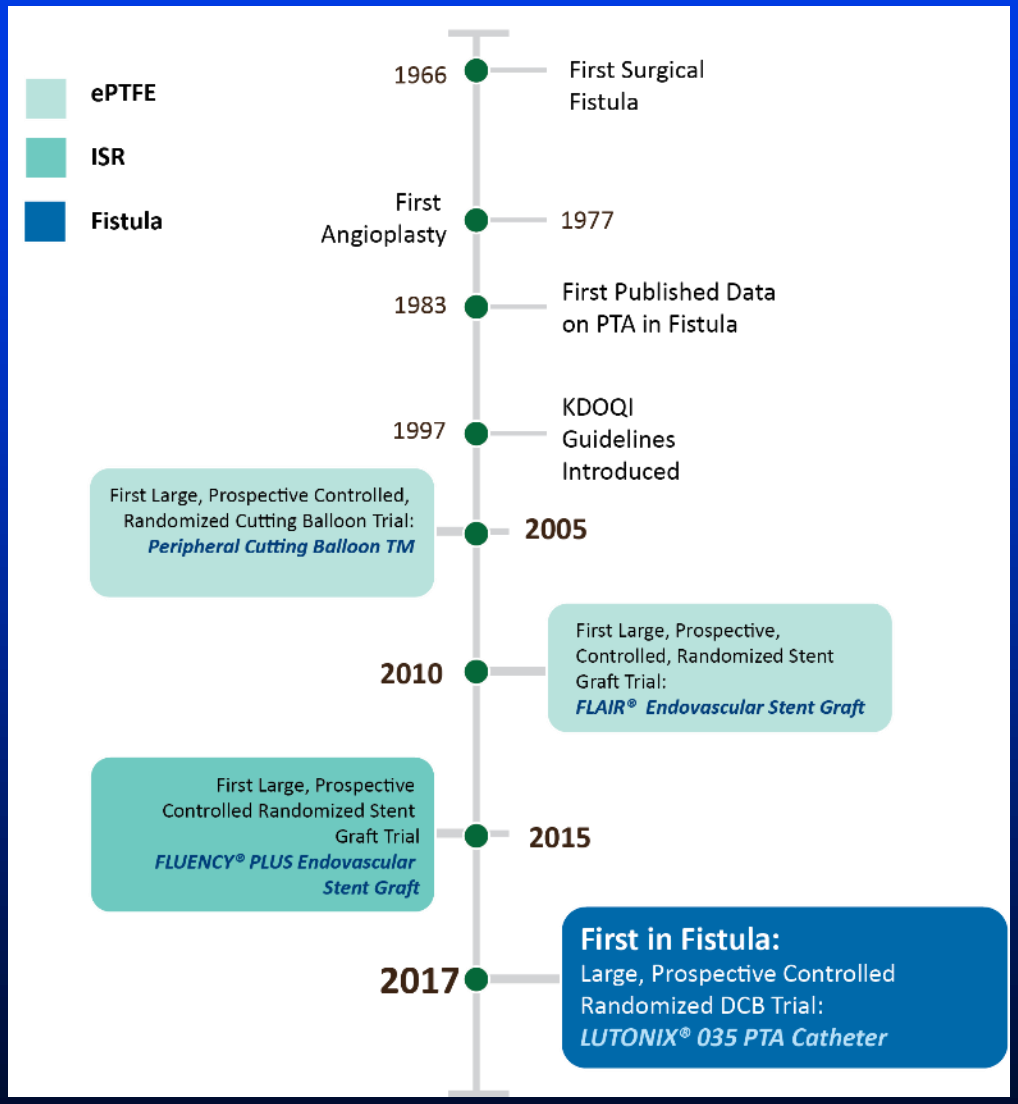
Agenda

- Fistula history and dysfunction
- LUTONIX® 035 DCB Catheter AV IDE Trial
  - Trial design
  - Primary efficacy/safety endpoint
  - 18 month IDE interim results
- Summary



Bard Owned Image: Illustration by Mike Austin

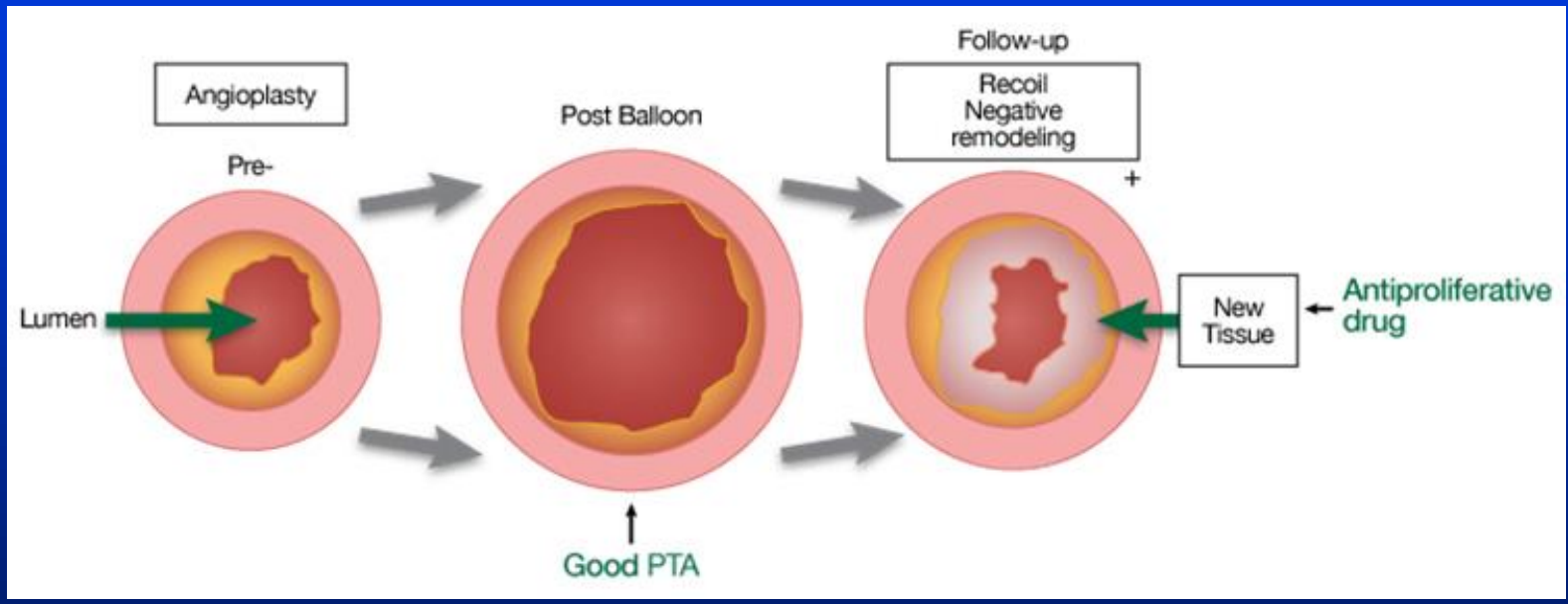
History of Therapeutic Interventions for Hemodialysis Access



51 Years

Successful DCB Treatment

Mechanical (vessel recoil and negative remodeling) and biological response (smooth muscle cell proliferation) due to injury during PTA leads to stenosis



- Paclitaxel inhibits cell proliferation
- Good PTA needed to mechanically produce a large lumen
- Vessel overstretch is impacted by balloon dilation
  - Overstretch = Balloon diameter/reference vessel diameter

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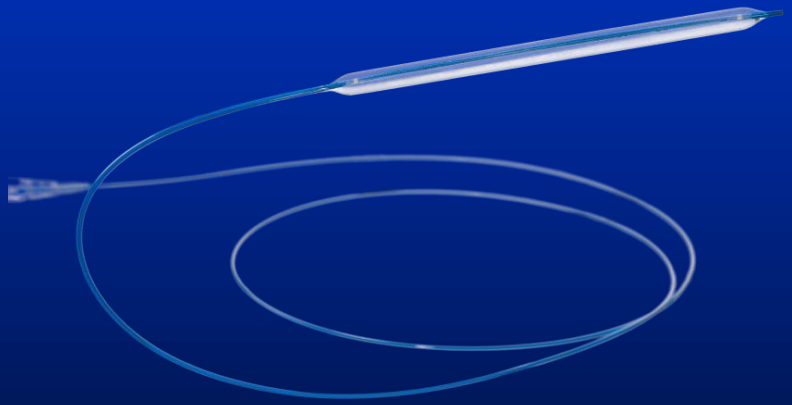
Trial Design



Lutonix AV IDE Clinical Trial

Study Design	Prospective, Global, Multicenter, Randomized, Safety and Effectiveness
Objective	To assess the safety and effectiveness of the LUTONIX® 035 AV Drug Coated Balloon PTA Catheter in the treatment of dysfunctional AV fistulae
Number of patients/sites	285 randomized subjects at 23 clinical sites
Primary Effectiveness Endpoint	Target Lesion Primary Patency (TLPP) - 6 months
Primary Safety Endpoint	Freedom from any serious adverse event(s) involving the AV access circuit through 30 days
Follow Up	1, 3, 6, 9, 12, 18, 24 month visits
Status	First Subject: June 2015 Enrollment Completion: March 2016

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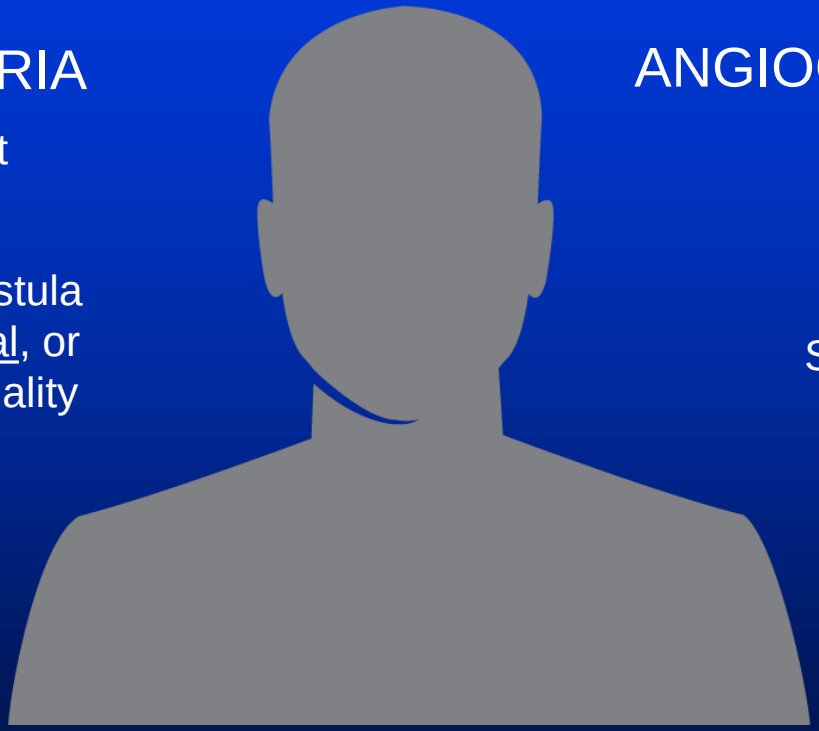
Key Inclusion Criteria

CLINICAL CRITERIA

Male or non-pregnant female ≥21 years old

Upper extremity AV Fistula w/clinical, physiological, or hemodynamic abnormality

Fistula created ≥30 days
- 1+ hemodialysis session
- 2 needles
- Catheter removed ≥ 30 days



ANGIOGRAPHIC CRITERIA

Length ≤10 cm

≥50% stenosis

Successful pre-dilation

Diameter 4-12 mm

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Key Exclusion Criteria

CLINICAL CRITERIA

- Lower extremity access
- Central veins
- Thrombosed access

ANGIOGRAPHIC CRITERIA

- >2 lesions in circuit
- Secondary non-target lesions that cannot be successfully treated
- Central veins as a secondary lesion, which is clinically significant
- Bare or covered stent in target or secondary non-target lesions

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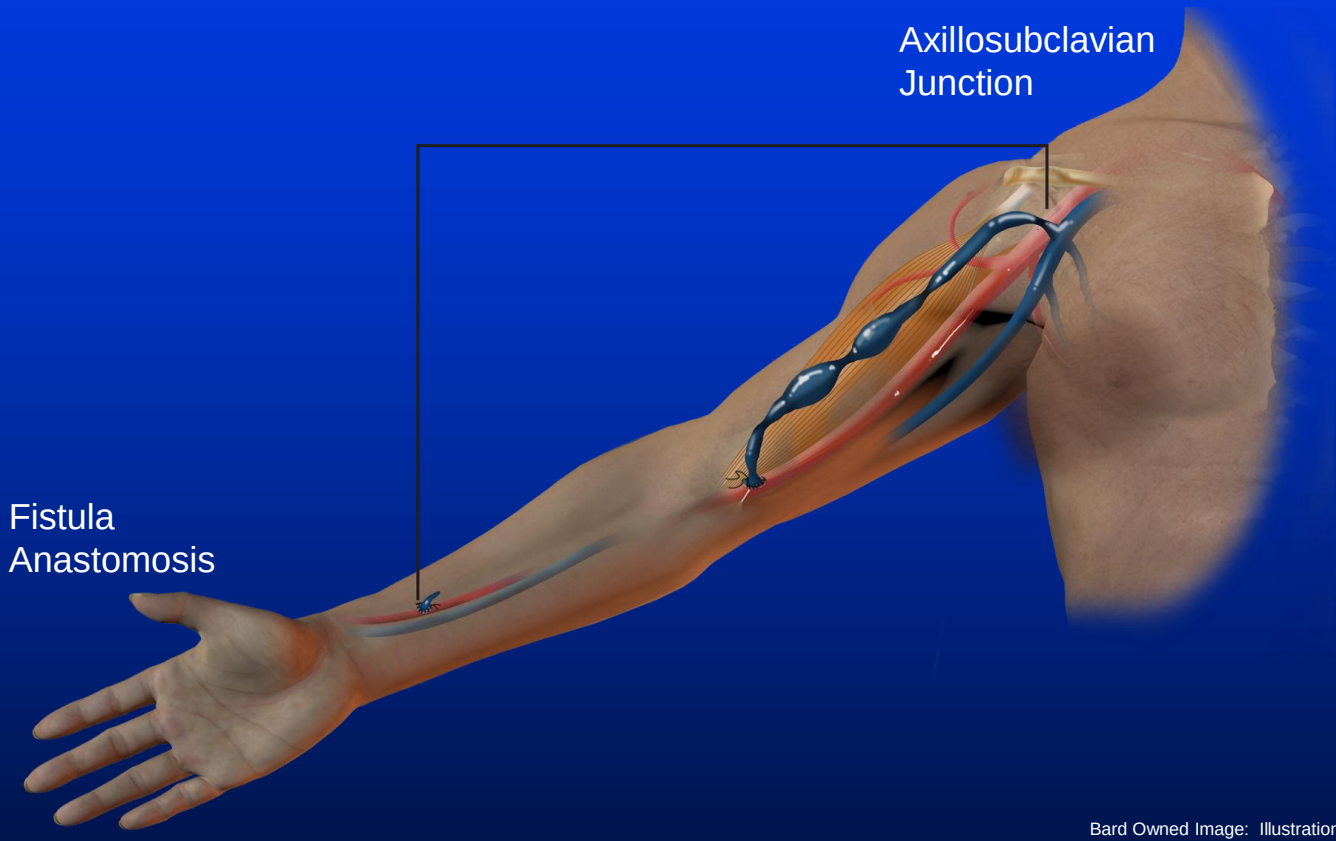
Key Inclusion Criteria



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Study Device Offering

- 4-12 mm diameters
- 0.035” guidewire compatible, nylon, semi-compliant balloon
- Over the wire, co-axial shaft, 75 cm

Diameter (mm)	Balloon lengths (mm)	Nominal (atm)	RBP (atm)	Sheath Profile
4	40 - 100	6	12	5F
5	40 - 100	6	12	5F
6	40 - 100	6	12	6F
7	40 - 60	6	12	7F
8	40 - 60	6	12	7F
9	40 - 60	6	11	7F
10	40 - 60	6	11	8F
12	40	6	10	10F

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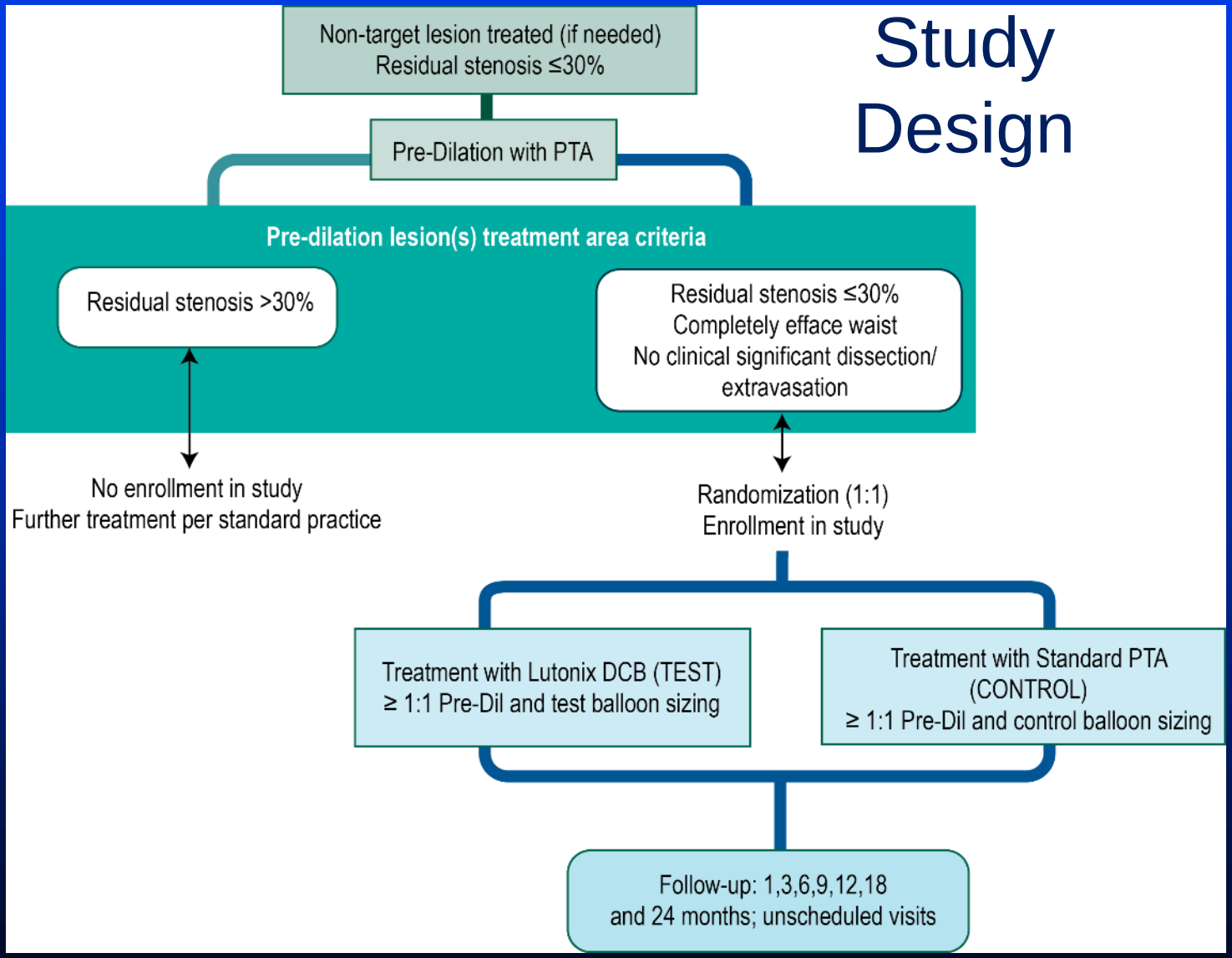

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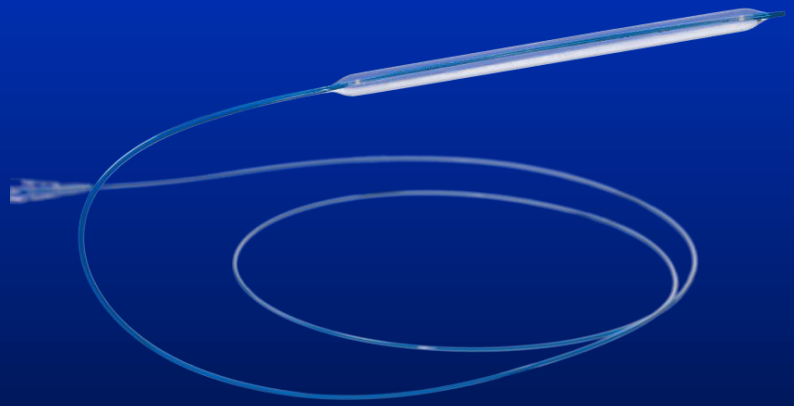
Demographic Data



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Demographics

Baseline Characteristics

Variable	LUTONIX® 035 DCB (N=141)	Control (N=144)
Age	63.6	61.0
Male, n (%)	61.7%	59.0%
Hypertension, n (%)	94.3%	98.6%
Diabetes mellitus, n (%)	58.2%	65.3%
Dyslipidemia, n (%)	60.3%	58.3%
Current smoking, n (%)	13.5%	14.6%
Peripheral arterial disease, n (%)	9.9%	18.1%
Coronary heart disease, n (%)	30.5%	27.8%

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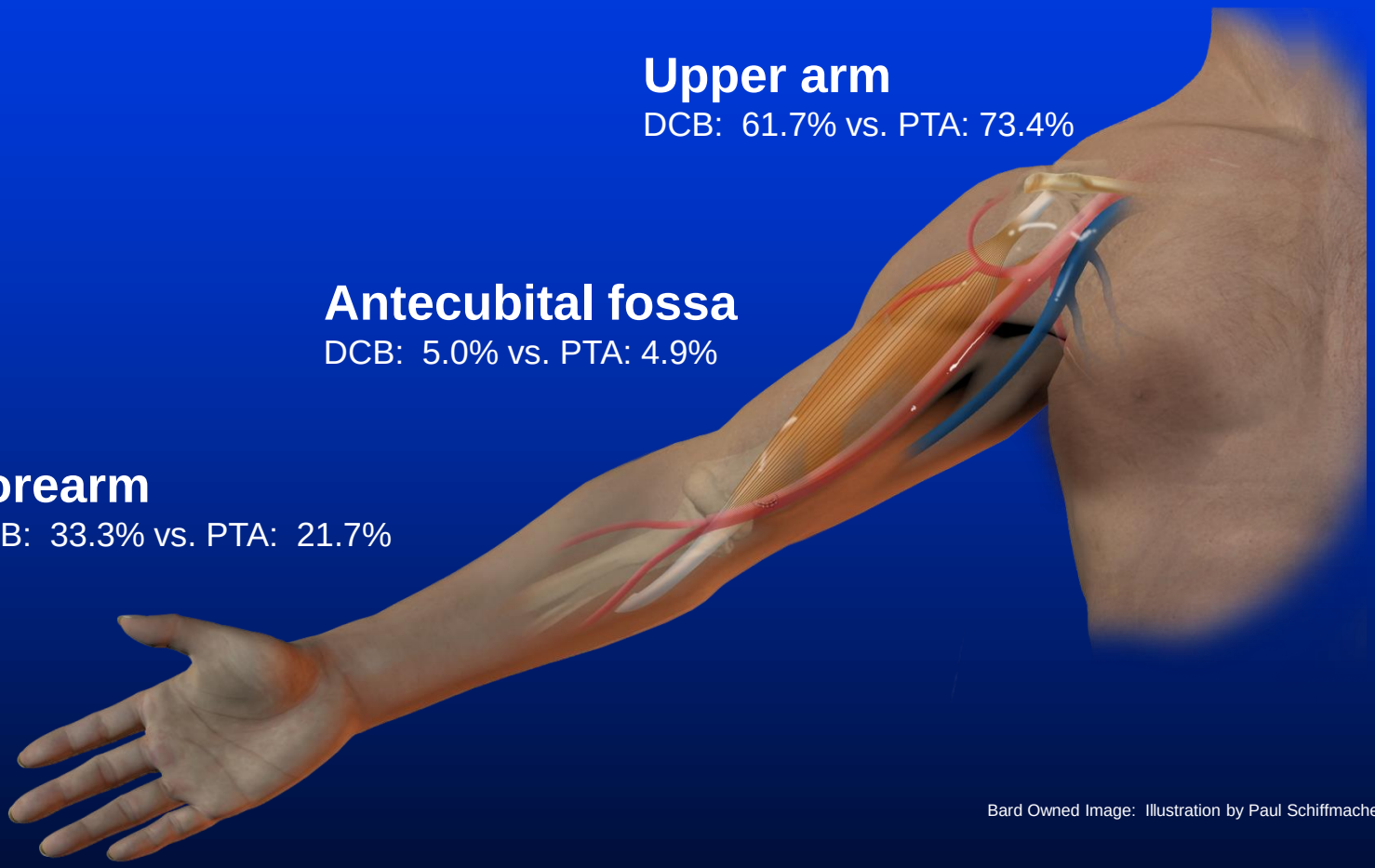
Fistula Locations

Upper arm
DCB: 61.7% vs. PTA: 73.4%

Antecubital fossa
DCB: 5.0% vs. PTA: 4.9%

Forearm
DCB: 33.3% vs. PTA: 21.7%



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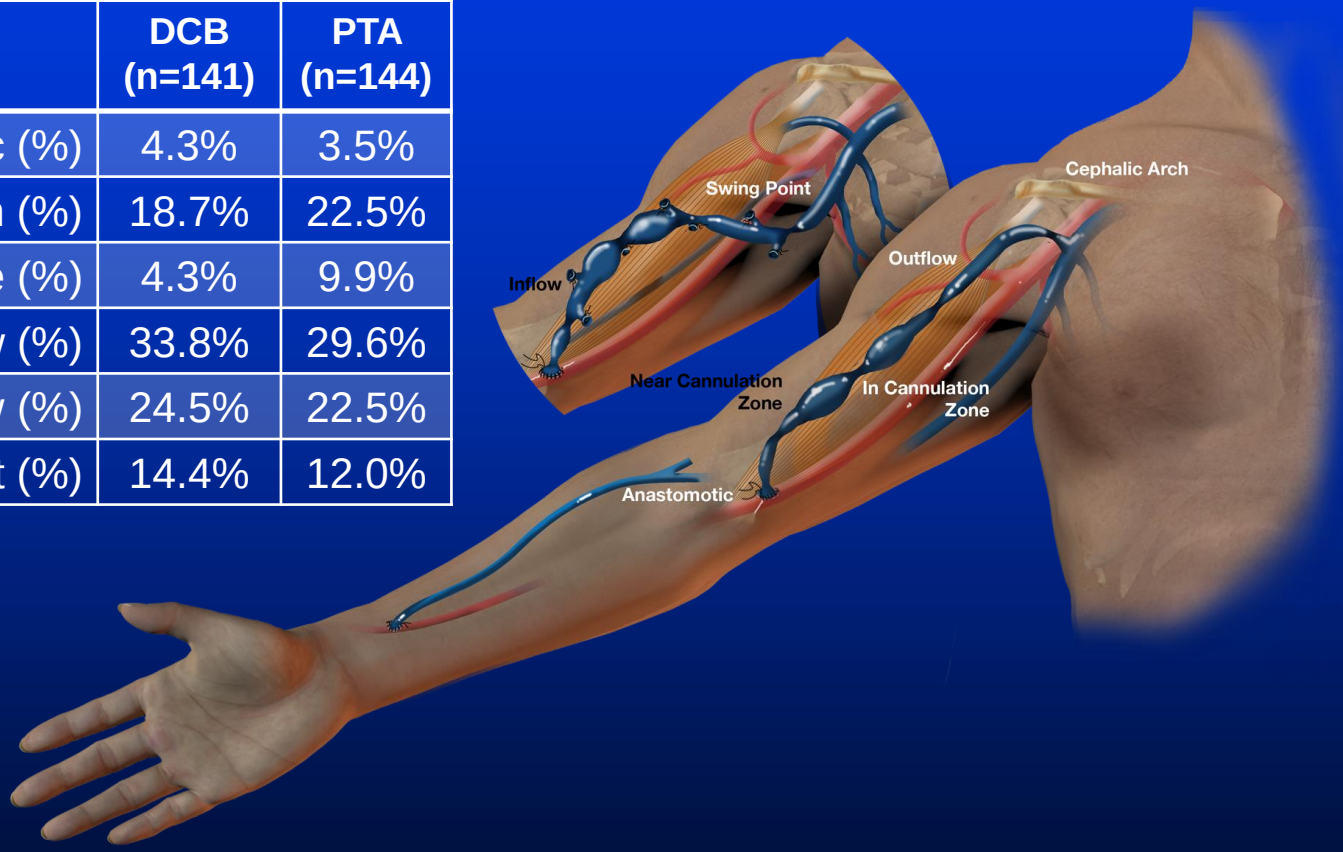
Target Lesion Locations

	DCB (n=141)	PTA (n=144)
Anastomotic (%)	4.3%	3.5%
Cephalic arch (%)	18.7%	22.5%
Cannulation zone (%)	4.3%	9.9%
Inflow (%)	33.8%	29.6%
Outflow (%)	24.5%	22.5%
Swing point (%)	14.4%	12.0%



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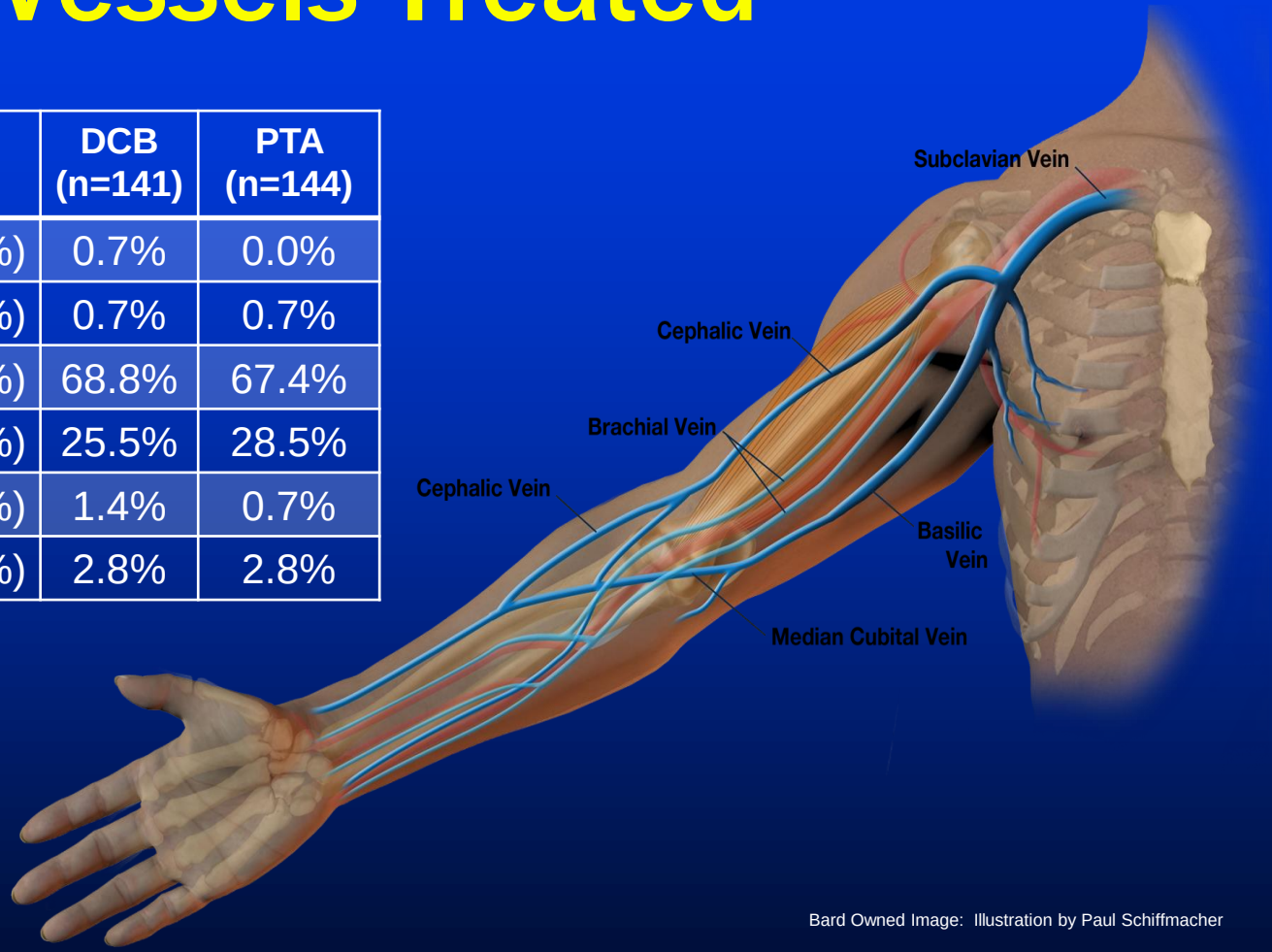
Vessels Treated

	DCB (n=141)	PTA (n=144)
Subclavian vein (%)	0.7%	0.0%
Brachial vein (%)	0.7%	0.7%
Cephalic vein (%)	68.8%	67.4%
Basilic vein (%)	25.5%	28.5%
Median cubital vein (%)	1.4%	0.7%
Other (%)	2.8%	2.8%



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Lesion Characteristics

	DCB (N=141)	PTA (N=144)
Restenotic (%)	69.5%	72.9%
Tandem (%)	2.8%	7.0%
Mean target lesion length, mm (±SD)	28.4 ± 15.09	29.5 ± 18.69

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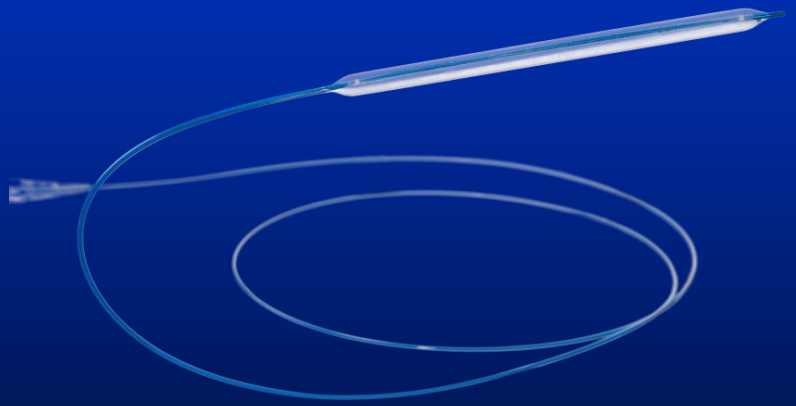
18 Month Interim Results



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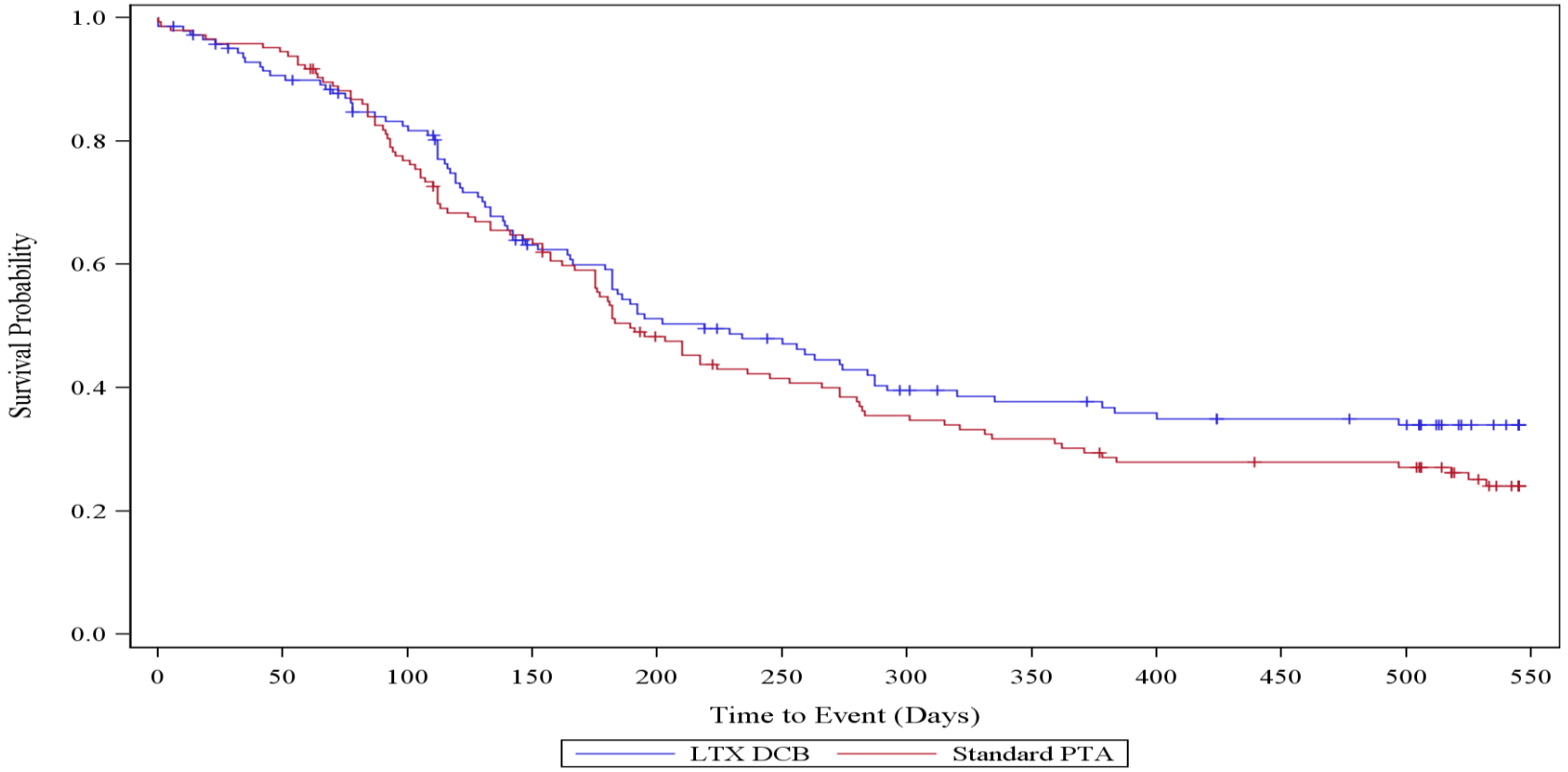
Safety- Interim 18 Months

Primary Endpoint: Non-inferior to PTA



[1]95% CI of the rate and the rate difference at each time point were calculated based on normal approximation and one-sided p-value is from test for non-inferiority, with 10% as non-inferiority margin.

Data shown are interim, site reported and subject to change

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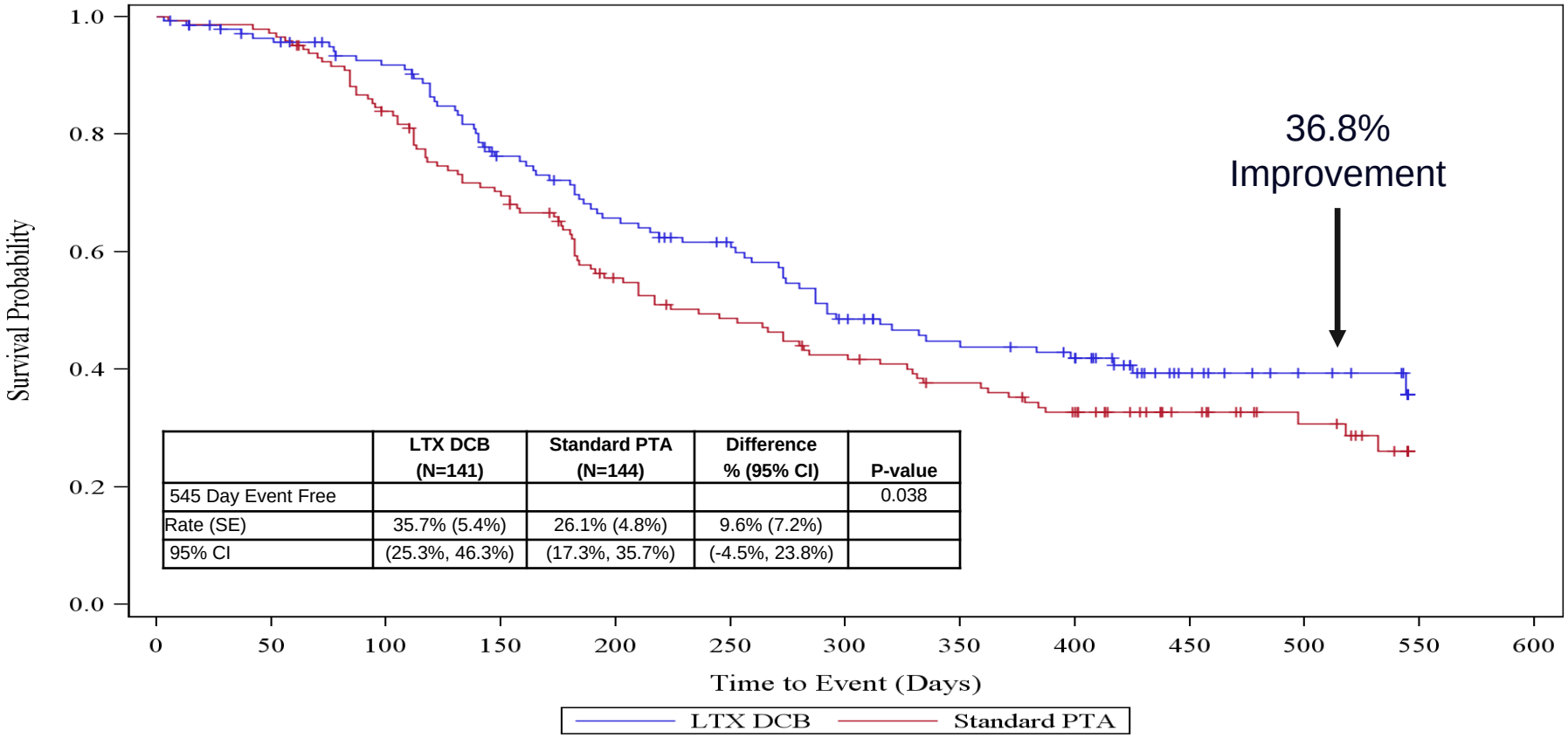
TLPP-Interim 18 months



	LTX DCB (N=141)	Standard PTA (N=144)	Difference % (95% CI)	P-value
545 Day Event Free				0.038
Rate (SE)	35.7% (5.4%)	26.1% (4.8%)	9.6% (7.2%)	
95% CI	(25.3%, 46.3%)	(17.3%, 35.7%)	(-4.5%, 23.8%)	

Target Lesion Primary Patency (TLPP) ends with a clinically driven re-intervention of the target lesion or access thrombosis.
95% CI of the rate and rate difference at each time point were calculated based on normal approximation using Greenwood formula variance estimators. Log-Rank Test was used to compare the two treatment curves between Day 0-550 and one-sided p-value was provided.

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Number of Interventions Required to Maintain TLP

	LTX DCB (n=141)	Standard PTA (n=144)	P-value*	% Fewer Interventions than PTA
Number of interventions, 180 days	44	64	0.068	31.3% Fewer
Number of interventions, 210 days	58	86	0.022	32.6% Fewer

*Two-sided P-value

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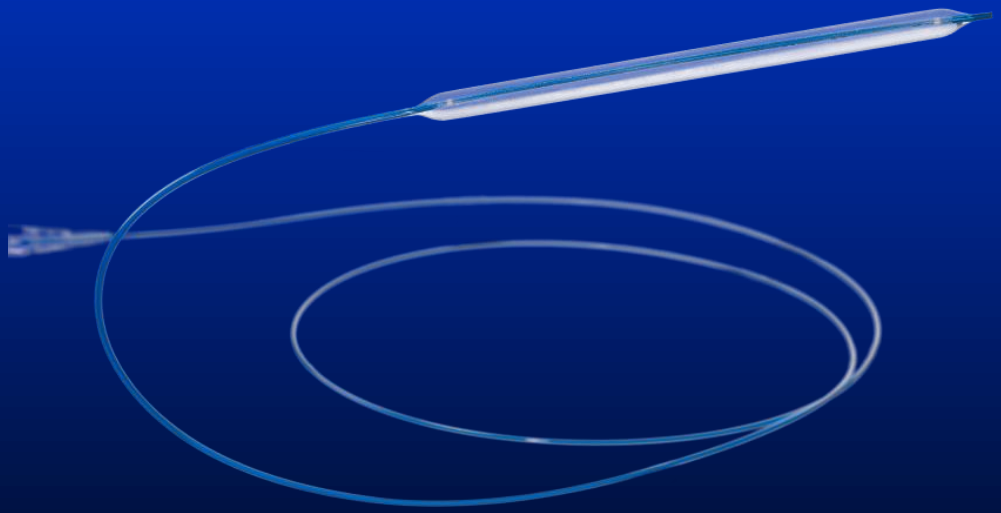
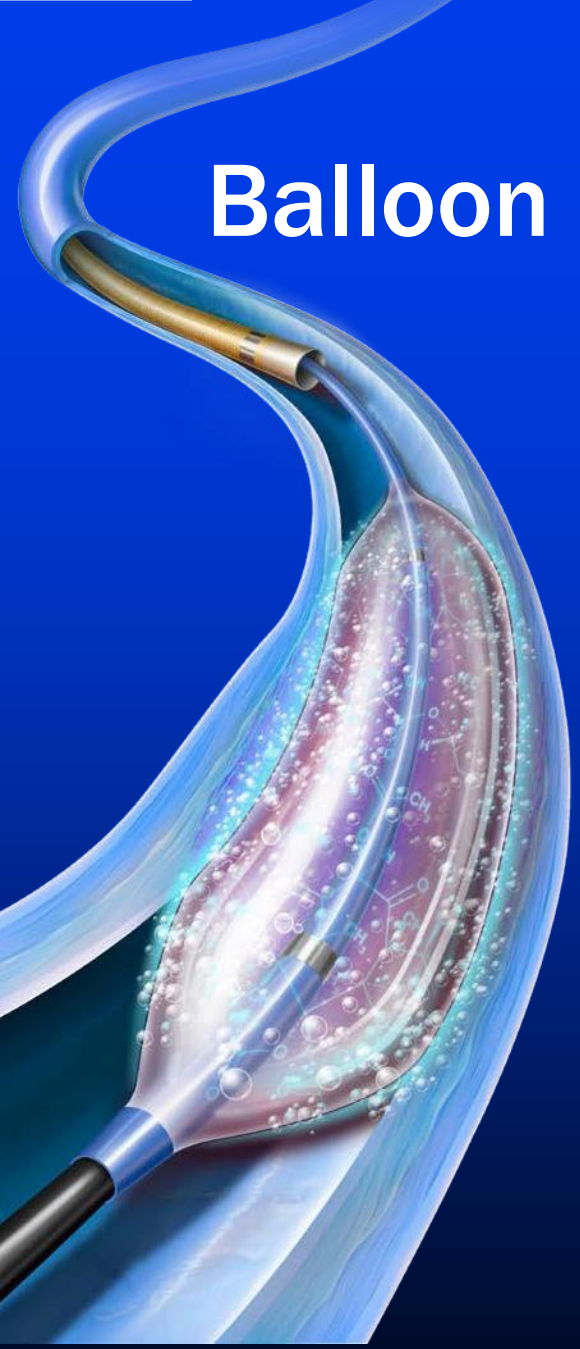
Recommended
Clinical Trial Procedure Techniques





Balloon Preparation Considerations IFU Handling

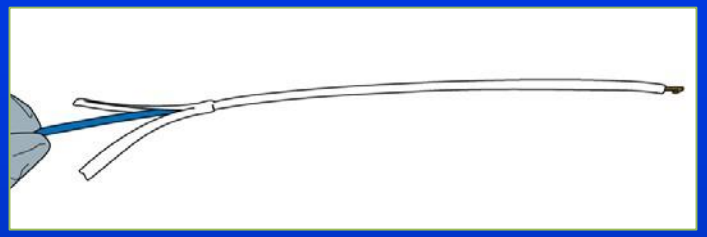
- Coated balloon portion should be handled with dry sterile gloves when possible prior to use
- When flushing, point balloon tip down to prevent backflow on balloon/coating
- Always advance and retrieve under negative pressure

LUTONIX® 035 DCB Peel Away Balloon Protector Removal

Carefully adhere to the following instructions to properly remove the balloon guard from the LUTONIX ® 035 DCB

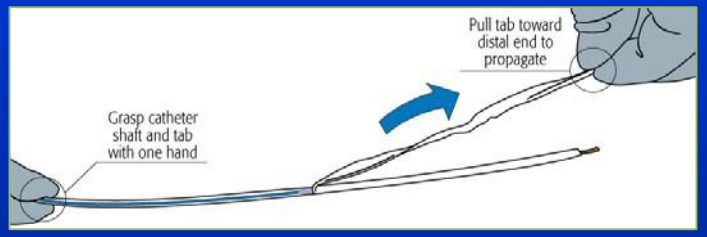
Step 1:

Use negative pressure, and keep the stylet in place.



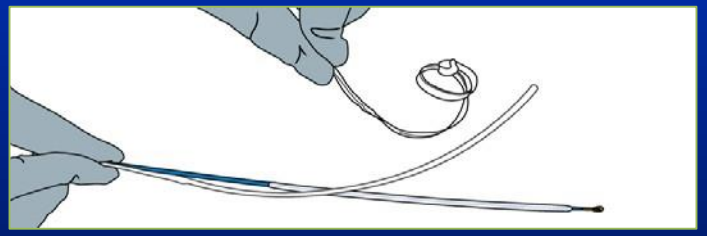
Step 2:

Gently pull the balloon protector tab toward the distal end of the balloon.



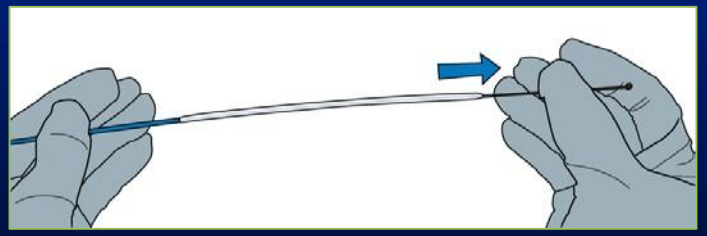
Step 3:

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 4:

Maintaining the grasp on the catheter shaft with one hand, and use the opposite hand to remove the wire lumen stylet.



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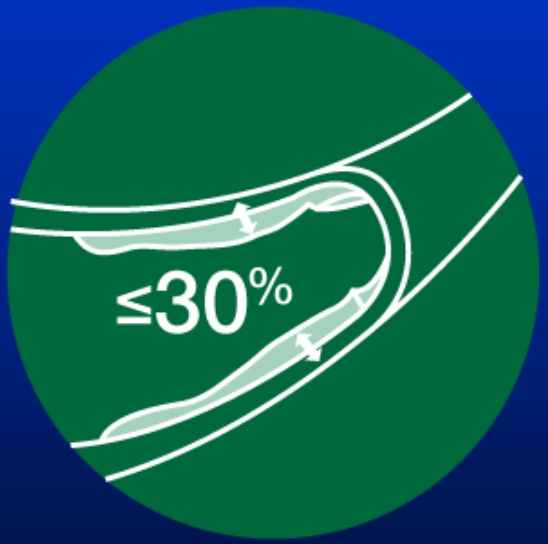
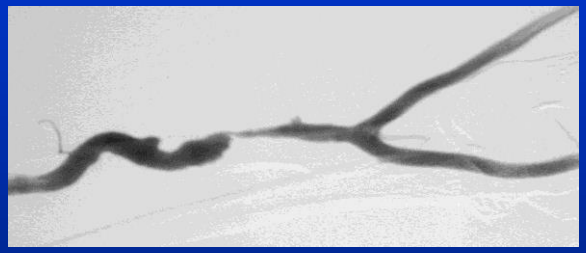
Successful Pre-Dilation

Optimal pre-dilation results of <30% residual stenosis and full balloon effacement





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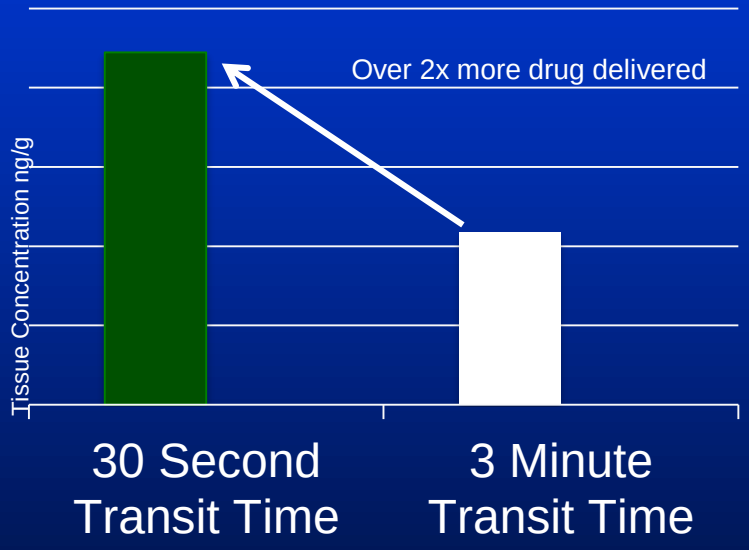
≤ 30 Second DCB Transit Time

Shorter transit time = more drug delivered to vessel*

Paclitaxel tissue concentration 1 hour after treatment in the swine arterial model



*Preclinical test data on file. Preclinical results may not be indicative of clinical performance.

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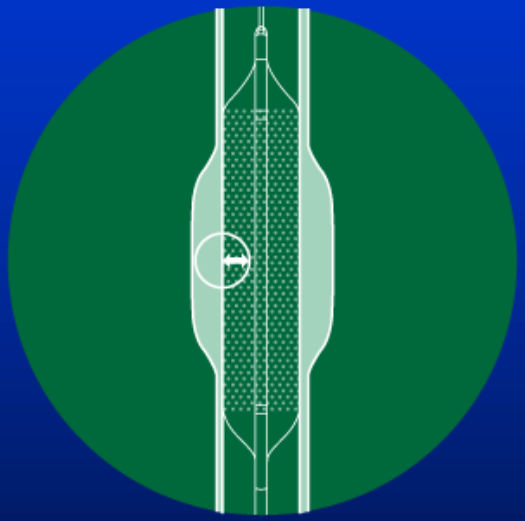
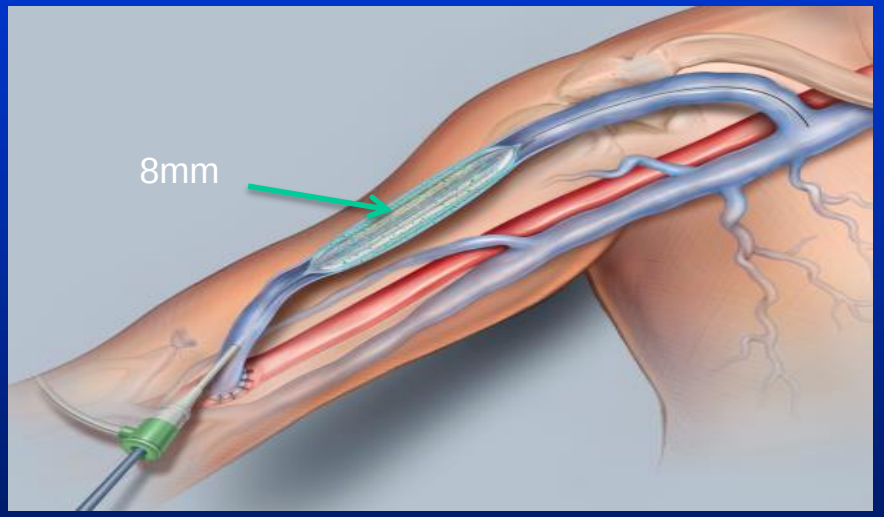
Maximize DCB-to-Wall Contact

DCB must be the same diameter as the pre-dilation balloon, ensuring full wall apposition of the balloon





Example:
Pre-Dilation 8mm, DCB ≥8mm

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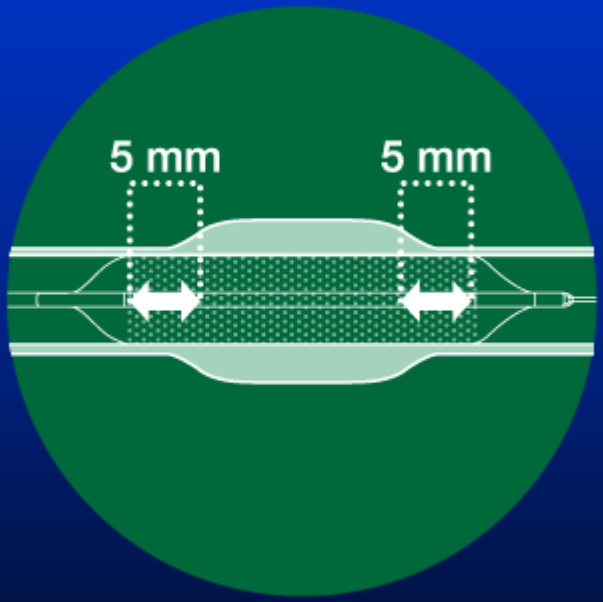
DCB Longer than Pre-Dilation

The DCB must extend ~5mm beyond the pre-dilation balloon length



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Semi-Compliant Balloon: ≥ Nominal Pressure

Higher inflation pressures have the potential to maximize DCB-to-wall contact

Atm	4mm	5mm	6mm	7mm	8mm	9mm	10mm	12mm
4	3.9	4.8	5.7	6.6	7.7	8.6	9.7	11.6
5	3.9	4.9	5.8	6.7	7.9	8.8	9.9	11.9
6	4.0	5.0	5.9	6.9	8.1	9.0	10.1	12.1
7	4.1	5.0	6.0	7.0	8.2	9.2	10.3	12.2
8	4.1	5.1	6.1	7.1	8.3	9.3	10.4	12.4
9	4.1	5.2	6.2	7.2	8.4	9.4	10.5	12.6
10	4.2	5.2	6.2	7.3	8.5	9.5	10.7	12.8
11	4.2	5.3	6.3	7.3	8.6	9.7	10.8	
12	4.3	5.3	6.3	7.4	8.7			

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.

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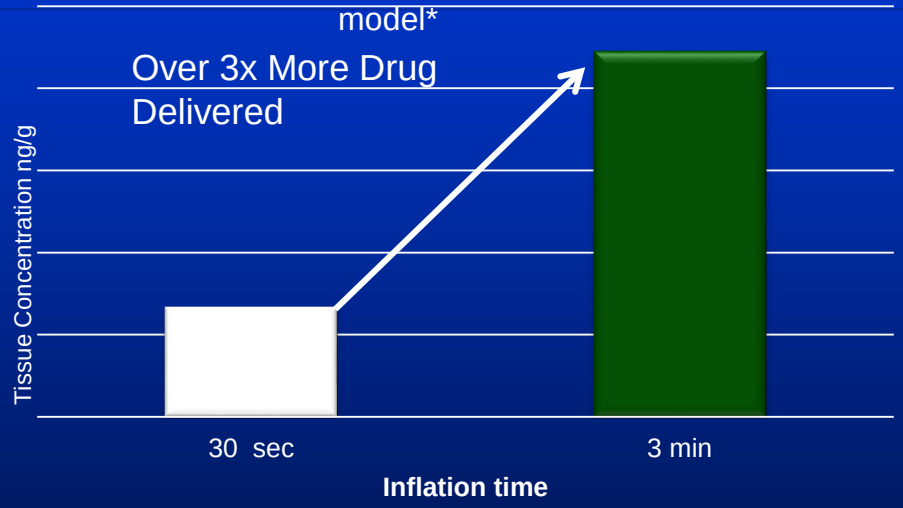
Longer Inflation Times

Minimum of 30 seconds
Preferably 2+ minutes at nominal or greater pressure

Paclitaxel tissue concentration 1 hour after treatment in the swine arterial model*



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Lutonix AV IDE Clinical Trial

Summary

- First and only DCB with 18 month Level 1 data in AV fistulae
- Safety outcomes are non-inferior to PTA
- 71.4% target lesion primary patency (TLPP) at 6 months
- 31.3% fewer number of interventions required to maintain TLP at 6 months
- Sustained effectiveness benefit
  - –36.8% improvement in primary patency over PTA at 18 months

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Data shown are interim, site reported and subject to change

Merci

INDICATIONS FOR USE

The Lutonix® 035 Drug Coated Balloon Catheter is intended for Percutaneous Transluminal Angioplasty (PTA) in the peripheral vasculature and for the treatment of obstructive lesions and decreasing the incidence of restenosis.

In addition, the Lutonix® 035 Drug Coated Balloon Catheter is intended for PTA of native dialysis fistulae or synthetic grafts, opening narrowing and immature fistulae, to improve blood flow, and decreasing the incidence of restenosis.

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.

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:

o Compromising the structural integrity of the device and/or

device failure which, in turn, may result in patient injury, illness or death.

o 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).