Next-Generation DCB's

What's Next?

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HEART AND VASCULAR CENTER

Disclosures

Bard Vascular: Research Support
Biotronik: Research Support, Consultant
Cook Medical: Research Support, Speaker

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It’s hard to make predictions, especially about the future…

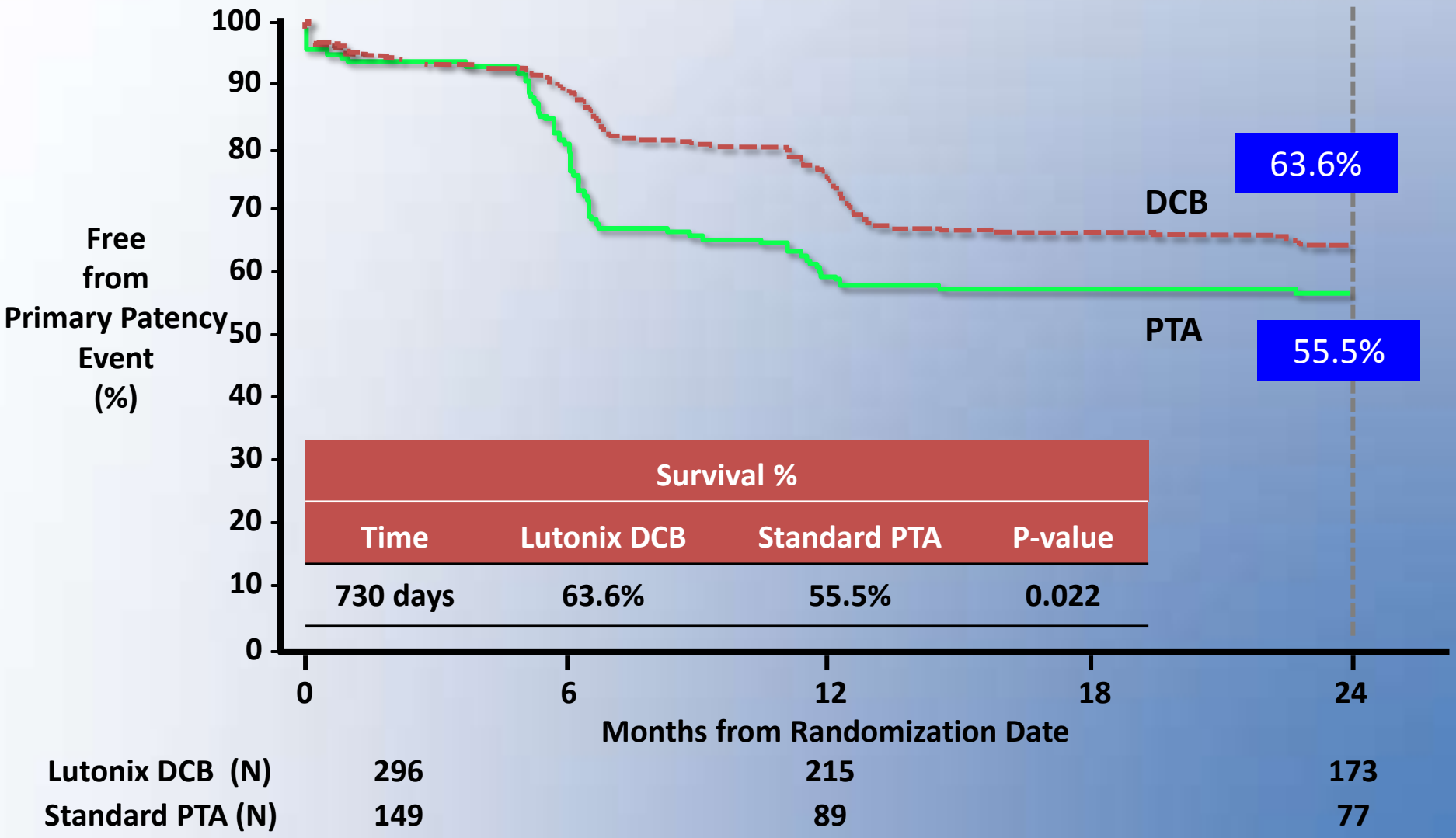
Niels Bohr, Danish physicist (source disputed)


Will We Ever Get There?

What Should A Drug-Coated Balloon Do?

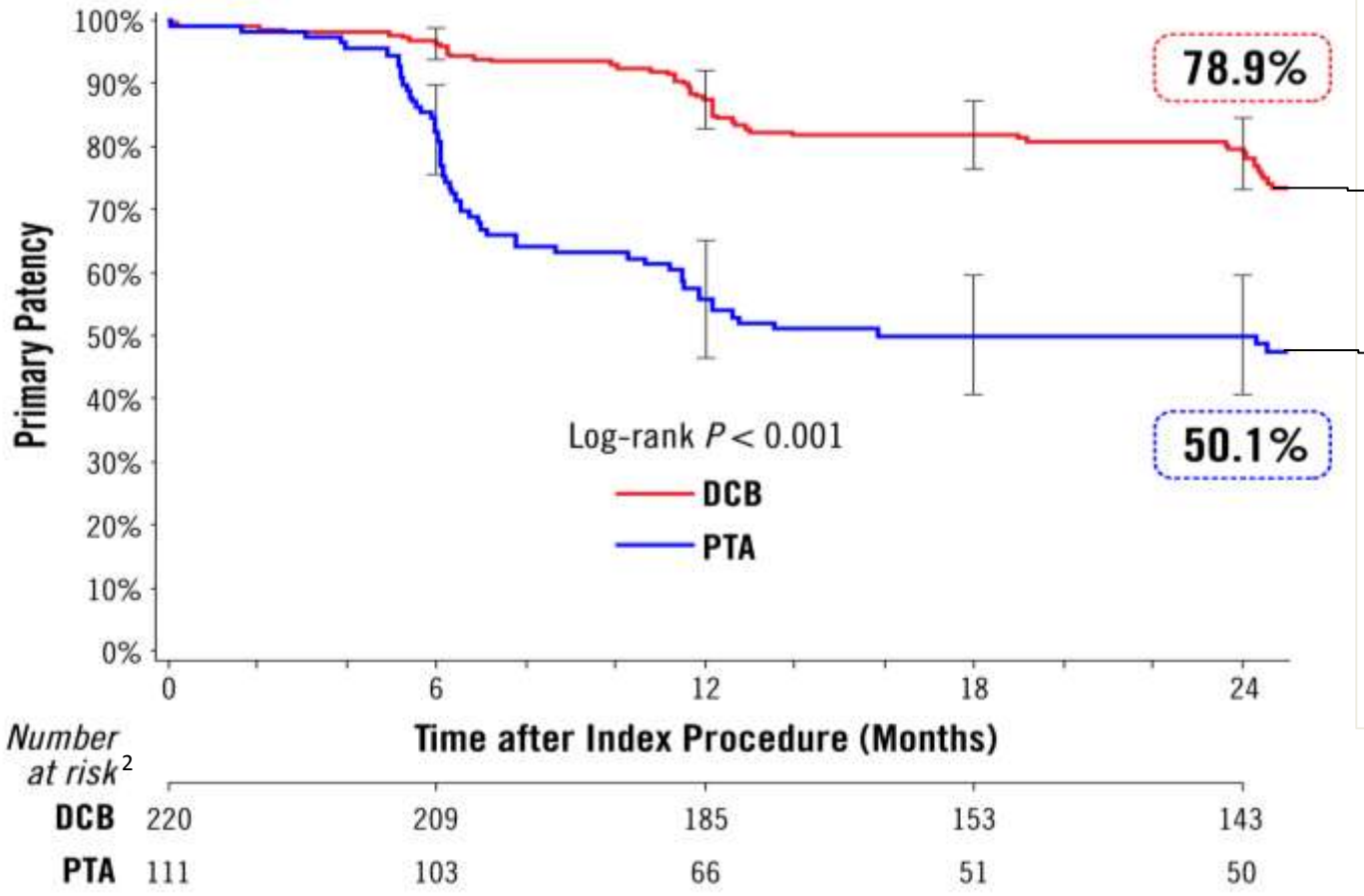
- Mimic coronary stent patency rates
- Produce durable results *in challenging patients*
- Be safe, even in patients with tissue loss
- Have multiple-vessel applicability

Lutonix Primary Patency
24 Months



Survival %			
Time	Lutonix DCB	Standard PTA	P-value
730 days	63.6%	55.5%	0.022

InPact: Primary Patency 24 Motnths



73.5%

47.4%

790 days

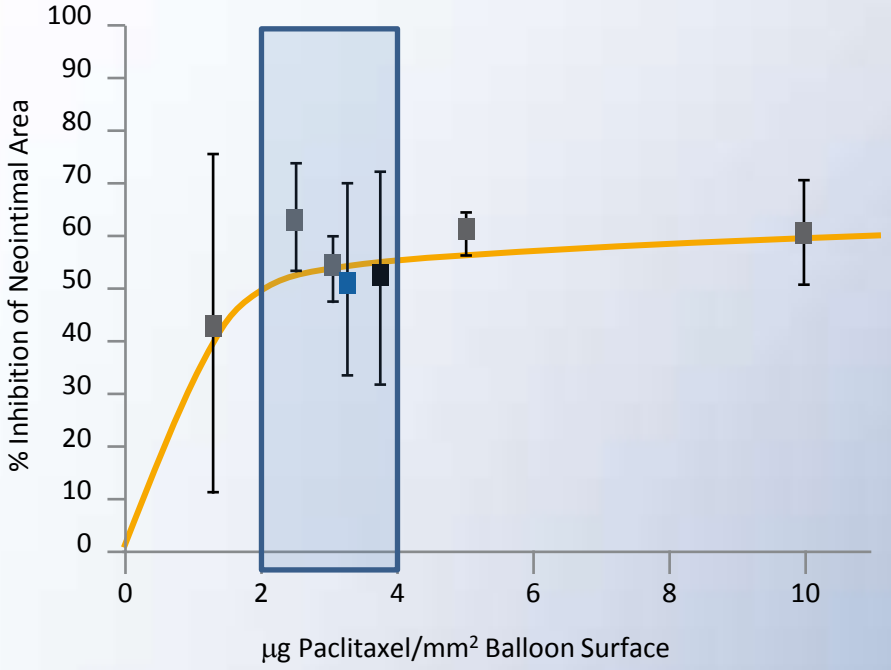
1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) or clinically-driven target lesion revascularization through 24 months (adjudicated by a Clinical Events Committee blinded to the assigned treatment)
2. Number at risk represents the number of evaluable subjects at the beginning of the 30-day window prior to each follow-up interval

Is There A Better Drug Than Paclitaxel?

- We don’t know!
- Sirolimus, everolimus
  - Good results in coronary stent trials
  - Failed in SFA stent trials
- Something better yet?

Have We Hit the Right Dose of Paclitaxel?

Optimal Paclitaxel Window



Therapeutic range: 2 - 4 µg/mm²

Lutonix, Ranger 2µg/mm²

IN.PACT™ Admiral™ DCB: 3.5 µg/mm²

1. Scheller B, et al. PTX Balloon Coating, a Novel Method for Prevention and Therapy of Restenosis. *Circulation*. 2004;110:810-814. 2. Speck U, Scheller B, Abramjuk C, et al. Neointima inhibition: comparison of effectiveness of nonstent-based local drug delivery and DES in porcine coronary arteries. *Radiology*. 2006;240:411–418. 3. Cremers B, et al. Comparison of two different PTX-coated balloon catheters in the porcine coronary restenosis model. *Clin Res Cardiol*. 2009;98:325–330. 4. Cremers B, et al DEB: Very short-term exposure and overlapping. *Thromb Haemost*. 2009; 101: 201–206. 5. Rowinsky EK, Donehower RC. Paclitaxel (Taxol). *N Engl J Med*. 1995;332:1004-1014. 6. Margolis J, McDonald J, Heuser R, et al. Systemic nanoparticle PTX (nab-PTX) for ISR I (SNAPIST-I): A first-in-human safety and dose-finding study. *Clin Cardiol*. 2007;30:165-170.

Anatomy of Drug Coated Balloon

- All DCBs use Paclitaxel
- Different doses
- Different forms
  - Crystalline
  - Amorphous

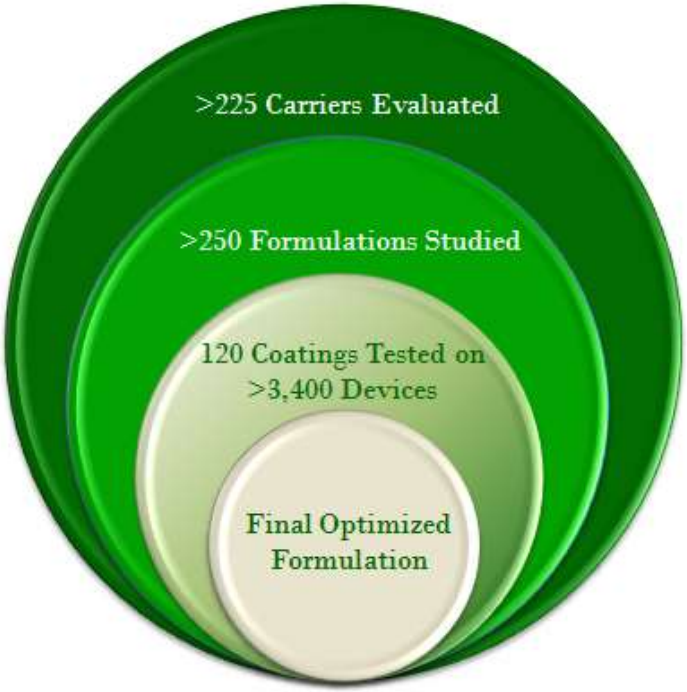
- Binds PTX to the balloon
- Differs from manufacturer to manufacturer
- Not used by all

- KEY FEATURES:

✓ Drug Uniformity
✓ Drug Retention
✓ Drug Release

Lutonix® DCB Formulation

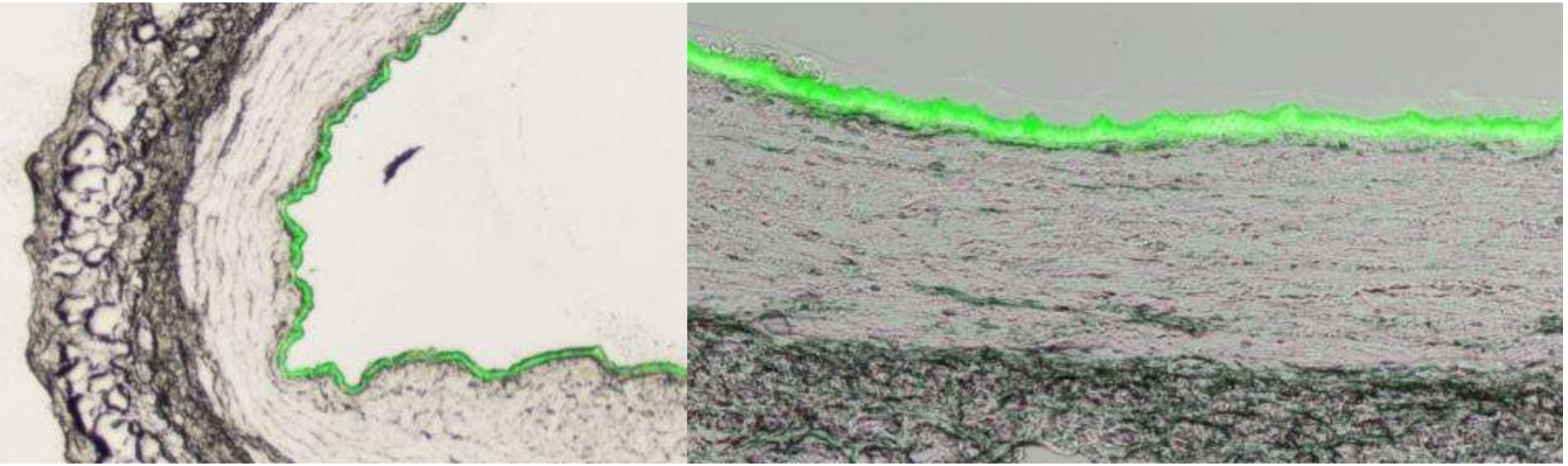
- Rigorous testing
  - 45 pre-clinical studies
  - >11,000 histology samples
- Resulted in a formulation with a dose of 2 µg/mm^2



We Want Paclitaxel in One Place…

and one place only!

In Vivo Administration of Fluorescent-Labeled PTX to Excised Porcine Arte



10% Oregon green labeled paclitaxel incorporated into Lutonix® DCB coating

Uniform Delivery in vivo at 1 hour
(Animal vessel cross section after 30 sec. inflation)

Lutonix coating uniformity allows uniform drug delivery

Preclinical animal data on file. Animal test results may not be indicative of clinical performance. Different test methods may yield different results.

Lutonix® Coating Durability

Dry Inflate "Shake" Test

	Residual Drug on DCB Balloon After Inflation/Shake	Drug Loss After DCB Inflation/Shake
LTX DCB (n=5)	**98.9% ± 1.1%**	**<0.1%***

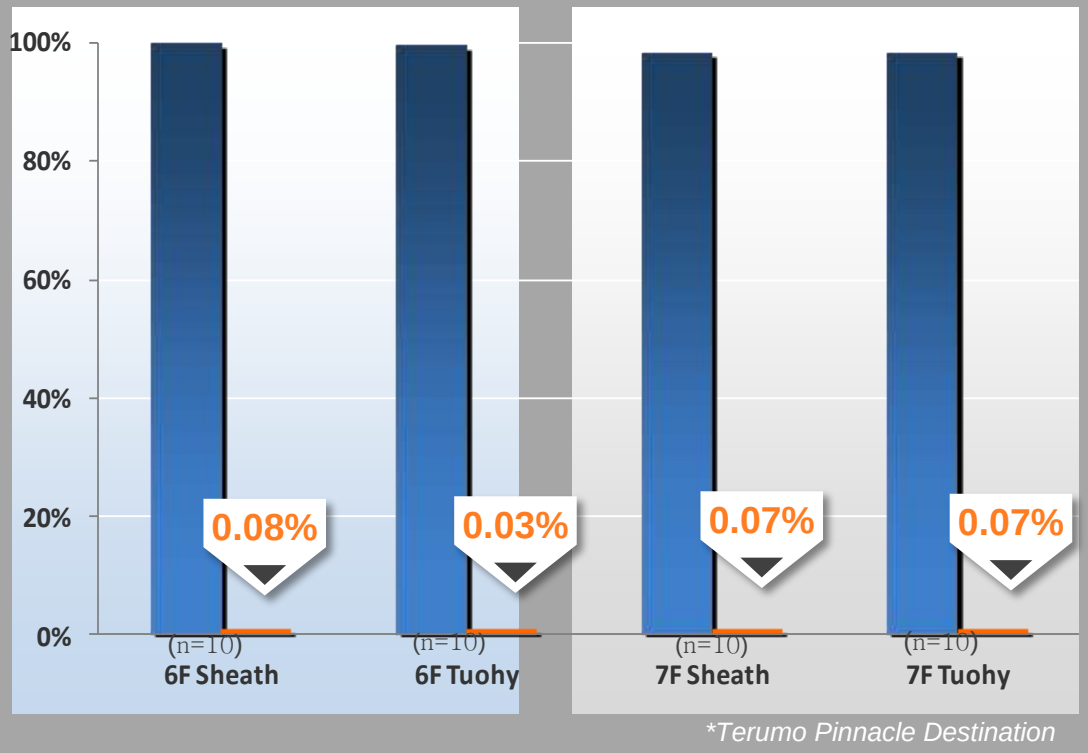
* Below limits of detection

Methods of Kelsch et al., Invest Radiol 2011; 46(4):255-63

Evidence of Durability.

*Bench test data on file. Bench results may not be indicative of clinical performance. Different test methods may yield different results.

Lutonix® Coating: Drug Retention



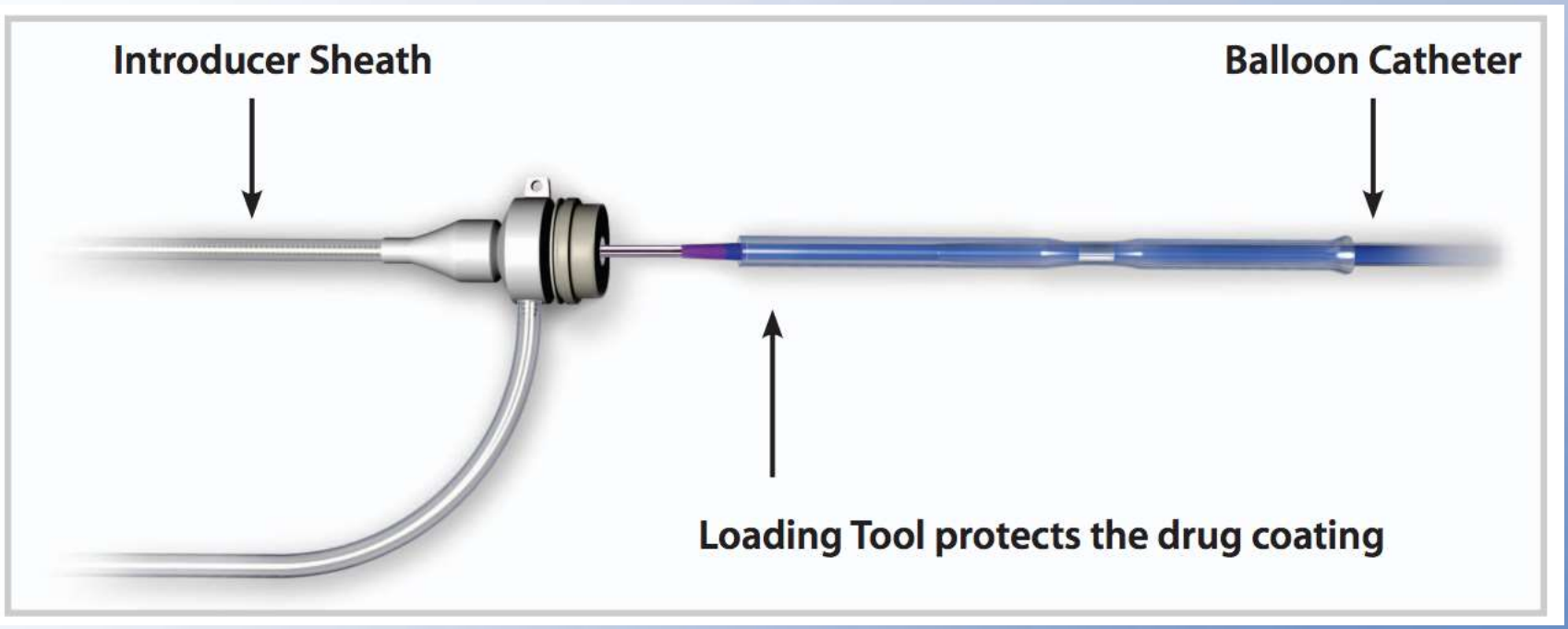
*Terumo Pinnacle Destination

Drug load preserved on balloon post-insertion through sheath valve or tuohy

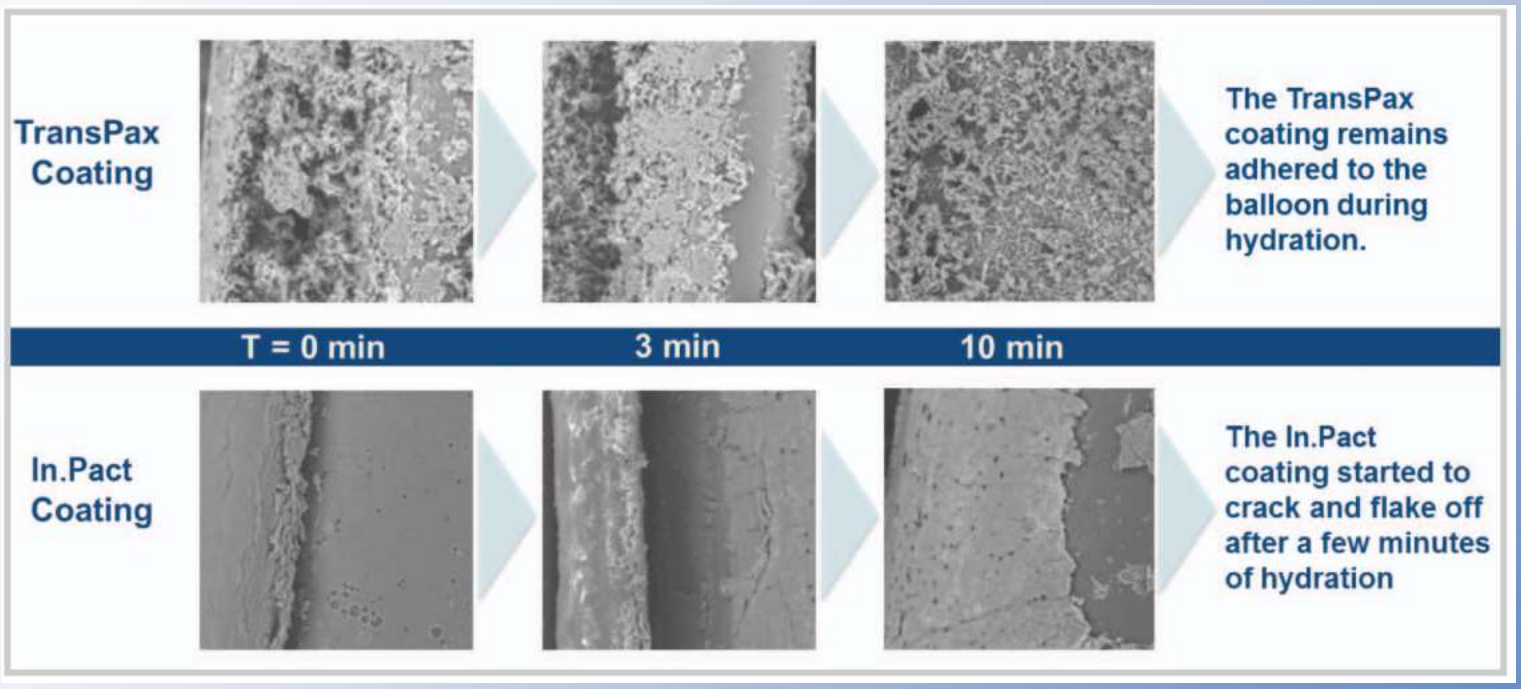
Durability of coating preserved through insertion

*Bench test data on file. Bench results may not be indicative of clinical performance. Different test methods may yield different results.

Preventing Scrape-Off



Effect of Blood Exposure



IN.PACT DEEP

Drug-Eluting Balloon Versus Standard Balloon Angioplasty for Infrapopliteal Arterial Revascularization in Critical Limb Ischemia

12-Month Results From the IN.PACT DEEP Randomized Trial

Thomas Zeller, MD,* Iris Baumgartner, MD,† Dierk Scheinert, MD,‡ Marianne Brodmann, MD,§ Marc Bosiers, MD,‖ Antonio Micari, MD, PhD,¶ Patrick Peeters, MD, PhD,# Frank Vermassen, MD, PhD,** Mario Landini, MS,†† David B. Snead, PhD,†† K. Craig Kent, MD,‡‡ Krishna J. Rocha-Singh, MD,§§ IN.PACT DEEP Trial Investigators

All lesion-specific primary and secondary endpoints showed insignificant differences between the 2 study arms.

Zeller, T. J Am Coll Cardiol 2014;64:1568-76

IN.PACT DEEP

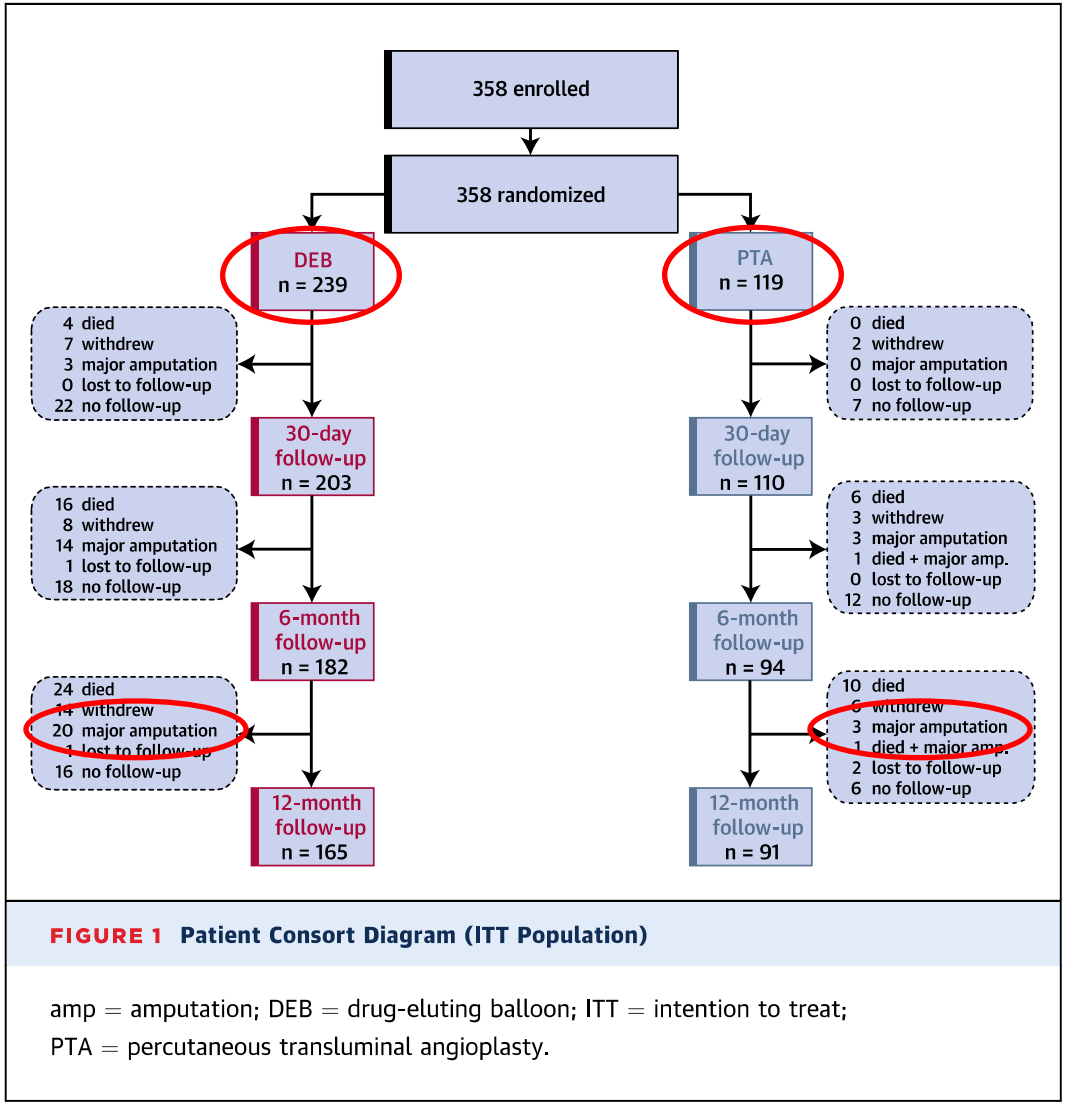


FIGURE 1 Patient Consort Diagram (ITT Population)

amp = amputation; DEB = drug-eluting balloon; ITT = intention to treat; PTA = percutaneous transluminal angioplasty.

8.8%

3.6%

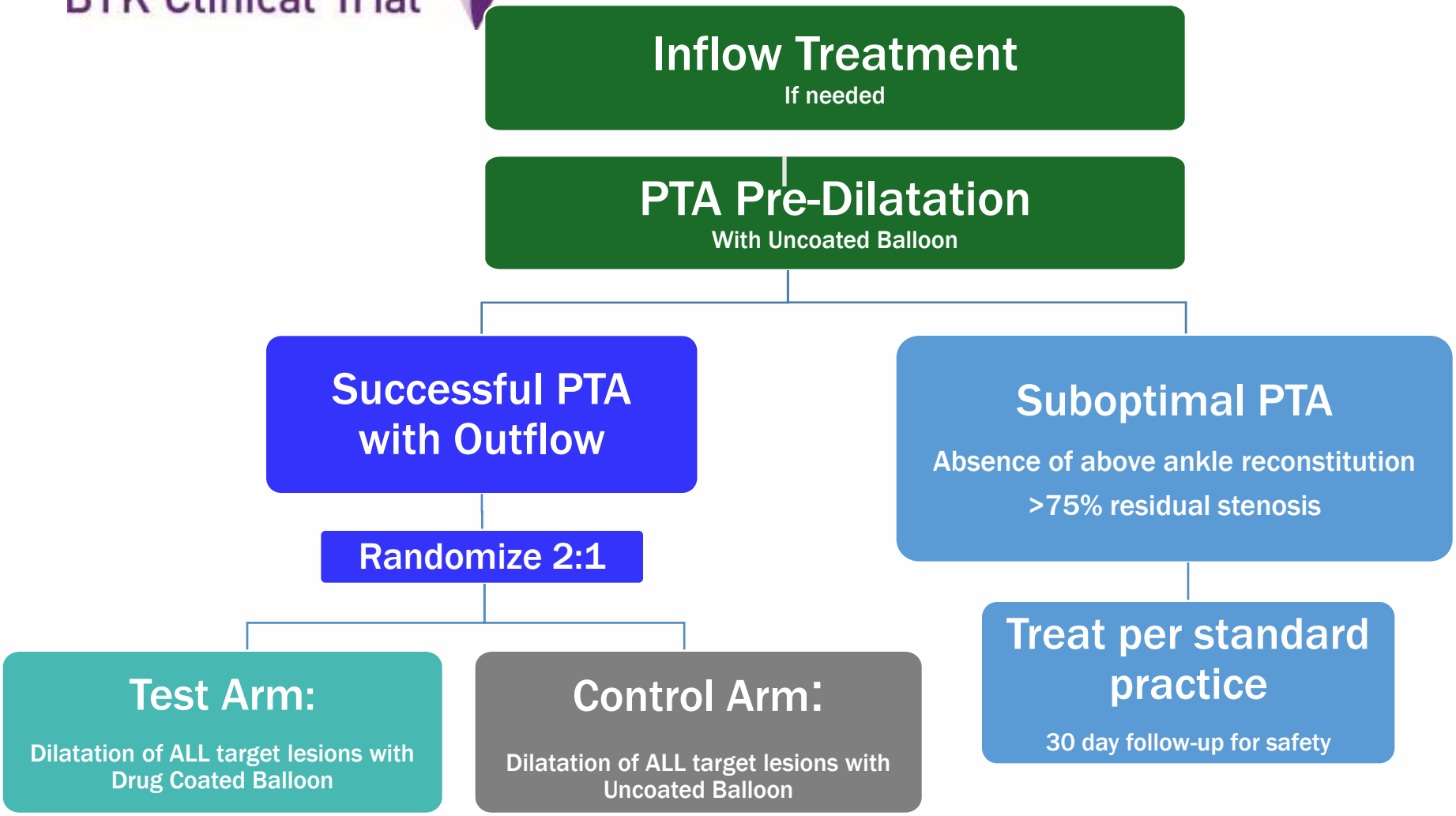
Zeller, T. J Am Coll Cardiol 2014;64:1568-76

IN.PACT DEEP

- Conflicting results compared to single-center BTK trials (and expectations)
- Followed by pulling IN.PACT Amphirion from the market
- Left questions about role of BTK DCB

LUTONIX
BTK Clinical Trial

Study Flowchart



Caution – Investigational Device, Limited by Federal (USA) Law to Investigational Use

LUTONIX
BTK Clinical Trial

Primary Endpoints

SAFETY

Freedom from Major Adverse Limb Events & All-Cause Death at **30 DAYS**

★ Amputation (above ankle)

★ Major re-intervention

- New bypass graft
- Jump/Interposition graft revision
- Thrombectomy/Thrombolysis

EFFICACY

Composite of Limb Salvage and Primary Patency at **12 Months**

Defined as freedom from the composite of above ankle amputation, target vessel occlusion, and clinically-driven target lesion re-intervention. ★

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LUTONIX
BTK Clinical Trial

Patient Eligibility

Inclusion Criteria

- Rutherford 4-5
- Life expectancy ≥ 1 year
- Significant stenosis (≥70%)
- A patent inflow artery
- Target vessel(s) diameter between 2 and 4 mm
- Target vessel(s) reconstitute(s) at or above the ankle

Exclusion Criteria

- Prior or planned major amputation
- GFR ≤ 30 ml/min per 1.73m^2
- Acute limb ischemia
- In-stent restenosis of target lesion

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LUTONIX
BTK Clinical Trial

BTK Trial Design

Protocol Features

- Permits treatment of two tibial arteries
- Combined lesion length of up to 32 cm
- Retrograde wire access permitted, but not retrograde intervention

Caution – Investigational Device, Limited by Federal (USA) Law to Investigational Use

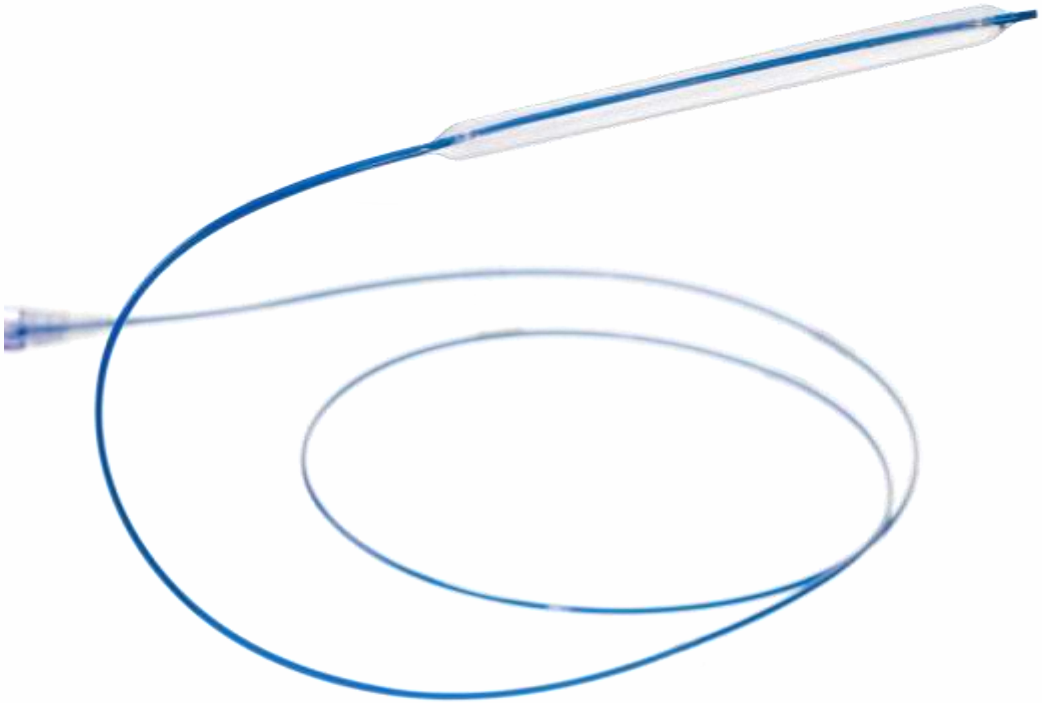
LUTONIX
BTK Clinical Trial

Safety Review

- 8 Data Monitoring Committee meetings so far
- 273 randomized patients:
  - 184 have completed 6 month follow-up
  - 134 have completed 12 month follow-up
- Only 11 major amputations (3% of enrolled pts) recorded
- **Only approved and ongoing BTK trial in the US**

Caution – Investigational Device, Limited by Federal (USA) Law to Investigational Use

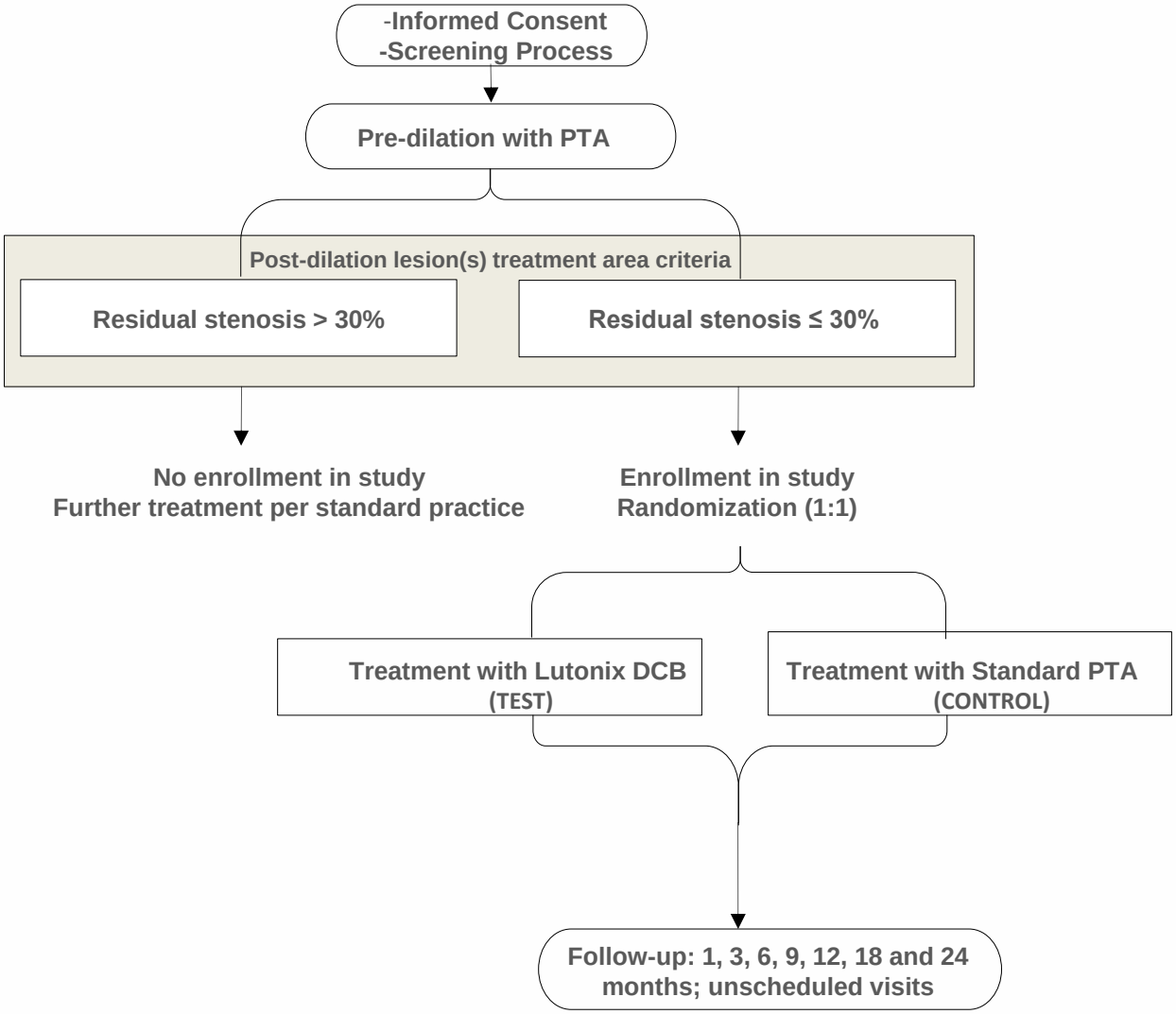
Lutonix AV Clinical Trial Design



Lutonix AV IDE Clinical Trial

Number of patients/sites	284 randomized subjects at up to 35 clinical sites
Primary Effectiveness Endpoint	Target Lesion Primary Patency (TLPP) - 6 months
Follow Up	1, 3, 6, 9, 12, 18, 24 month visits
Status	First Patient: June 2015 Enrollment Completion: 9/2016

Study Design



Summary

- Drug-coated balloons have become standard of care for many patients with SFA disease
- Still room for improvement
- They hold promise for other challenging vascular beds:
  - BTK
  - Dialysis access

Paclitaxel Remains in Vessel Wall