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The Lutonix BTK Clinical Trial Programme: Status Update and Real World Clinical Experience

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LINC

Disclosure

Speaker name: Dierk Scheinert

I have the following potential conflicts of interest to report:

Consulting: Abbott, Angioslide, Atheromed, Biotronik, Boston Scientific, Cook Medical, Cordis, Covidien, CR Bard, Gardia Medical, Hemoteq,Intact Vascular Inc., Medtronic, Ostial Inc, TriReme Medical, Trivascular, Upstream Peripheral Technologies

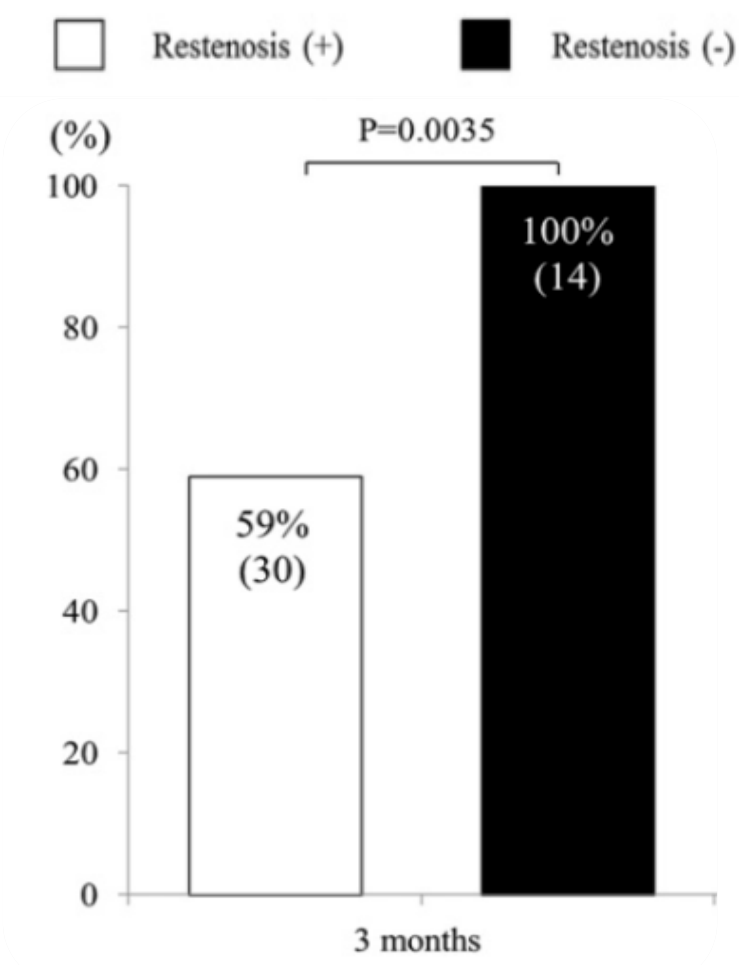
Stockholder: IDEV Technologies

POBA for CLI Treatment

- 68 CLI patients due to BTK lesions
- Lesion length: 140 ± 90 mm
- **Restenosis at 3 months: 73%**

- Restenosis delays healing

Iida O.. et al. EJVES 2012; 44:425-31



Complete ulcer healing rates

DCBs are not all the same

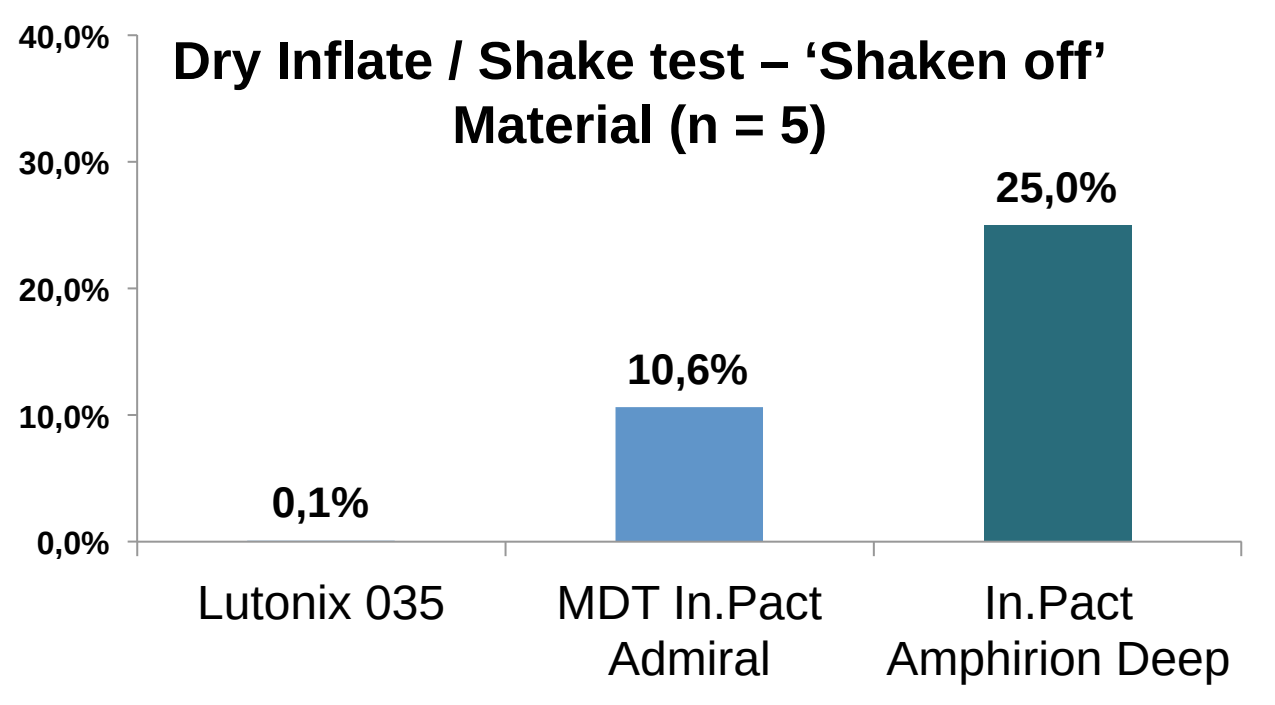
Technology of the In.Pact Deep Balloon:
first folded and then coated

With courtesy C. I. Mena

Dry Inflate / Shake Test - SFA

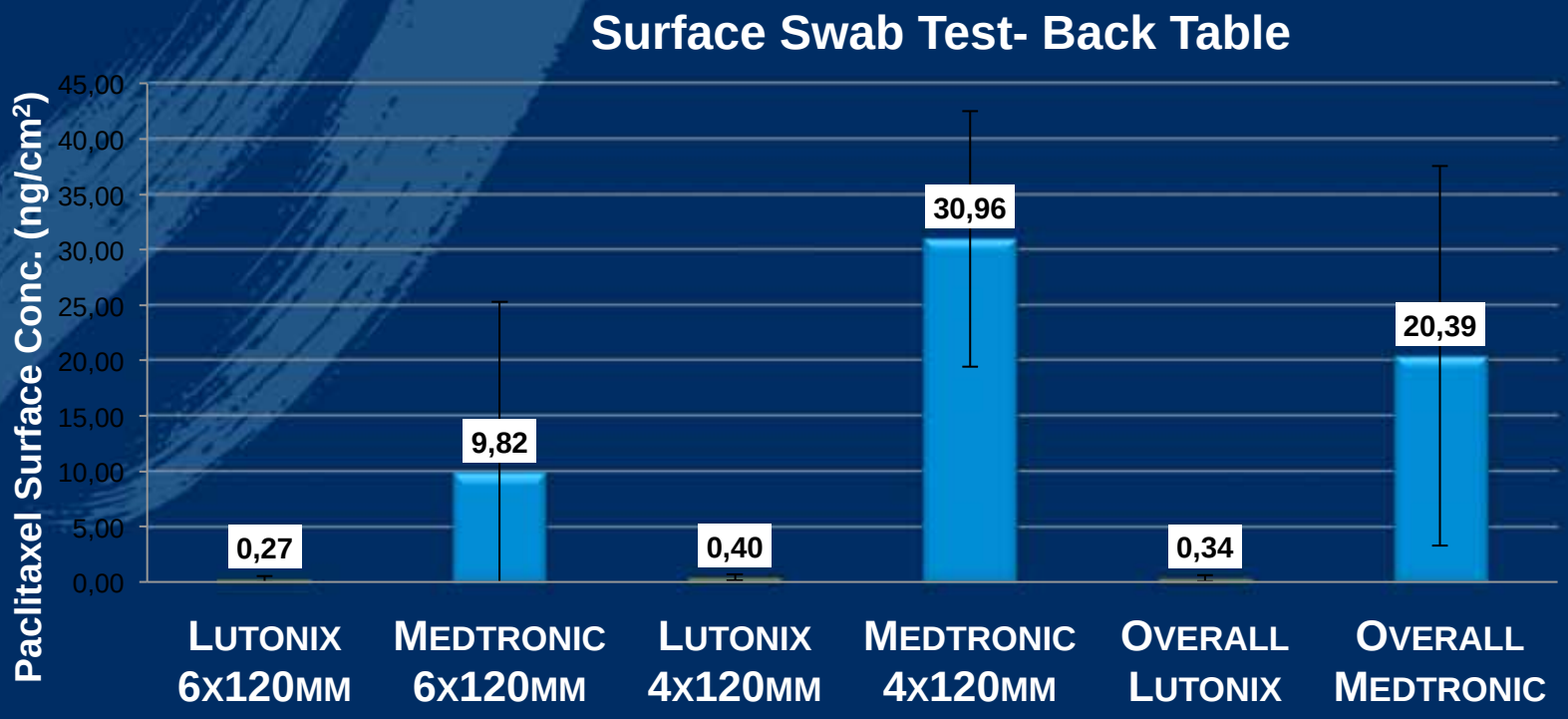
- Test Articles (n = 5 each):

  - Medtronic In.Pact Admiral 6 x 60 mm
  - Lutonix 035 Drug Coated Balloon – 6 x 60 mm
  - In.Pact Amphirion Deep 3 x 80 mm



With courtesy C. I. Mena, C.R.Bard Inc

Lutonix Coating Durability*



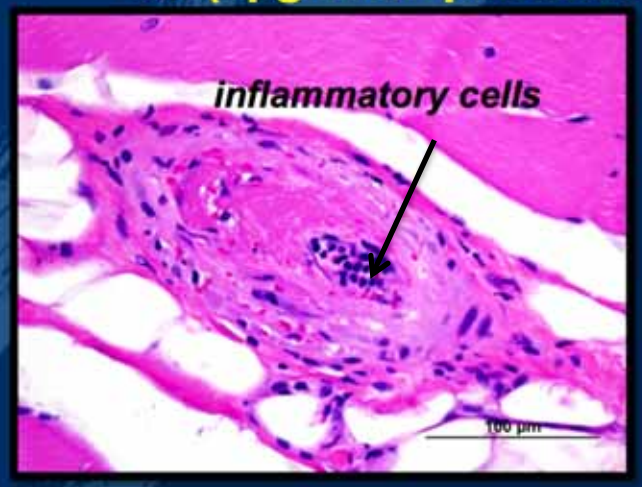
Simulated Clinical Use Test LUTONIX®

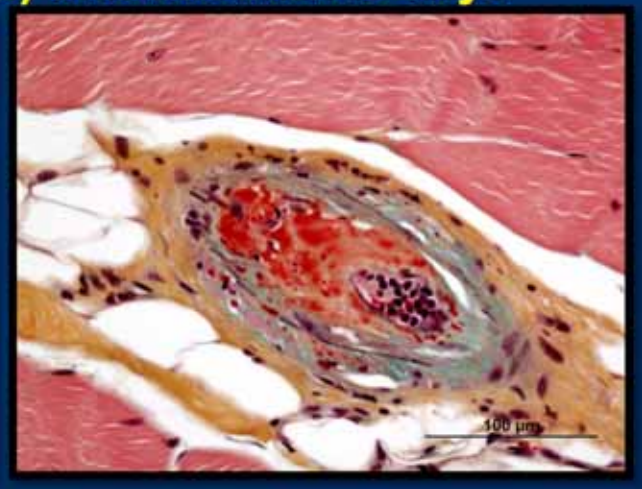
Amount of drug lost on the back table. (Drug measured- ng/mg)

Designed to minimize unnecessary drug exposure to staff and patients

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

Histologic findings of emboli/vascular changes by coronary band and skeletal muscle territories in swine peripheral artery following Lutonix drug coated balloon X3 (2µg/mm2 paclitaxel) dilatation at 90-days





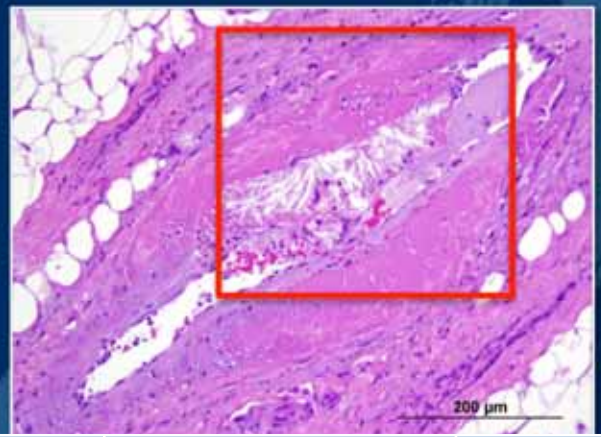
Loss of medial SMCs with replacement by proteoglycan/collagen

No.	No. of sections (Downstream muscle/coronary band)	Vascular Changes	Skeletal Muscle Necrosis/ Fibrosis	Crystalline material
1	14 (12 / 2)	1	0	0
2	14 (12 / 2)	0	0	0
3	14 (12 / 2)	4	0	0
4	14 (12 / 2)	0	0	0
Total	56	5	0	0

5 /56 (8.9 %) from DCB treatment showed findings of vascular change associated with paclitaxel and/or excipient (drug carrier).

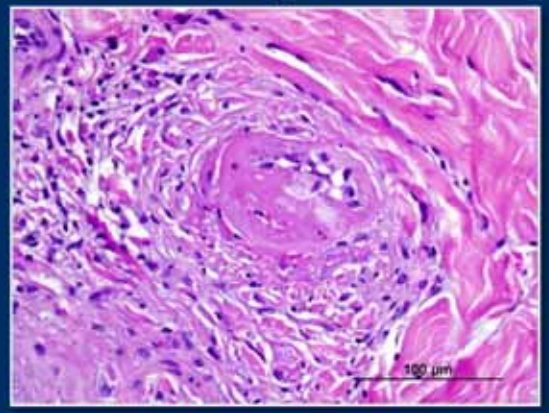
Skeletal Muscle: Gastrocnemius Muscle, Gluteus Maximus Muscle, Gracilis Muscle, Rectus Femoris Muscle, Semimembranosus Muscle, and Semitendinosus Muscle

Histologic findings of emboli/vascular changes by coronary band and skeletal muscle territories in swine peripheral artery following IN.PACT ADMIRAL DCB x3 (3.5µg/mm² paclitaxel) dilatation at 90-days

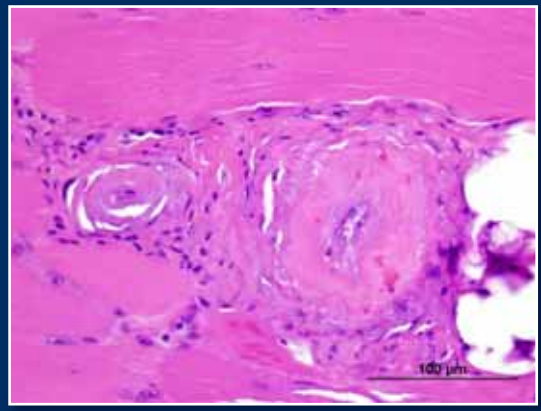


Fibrinoid Necrosis

coronary band



skeletal muscle

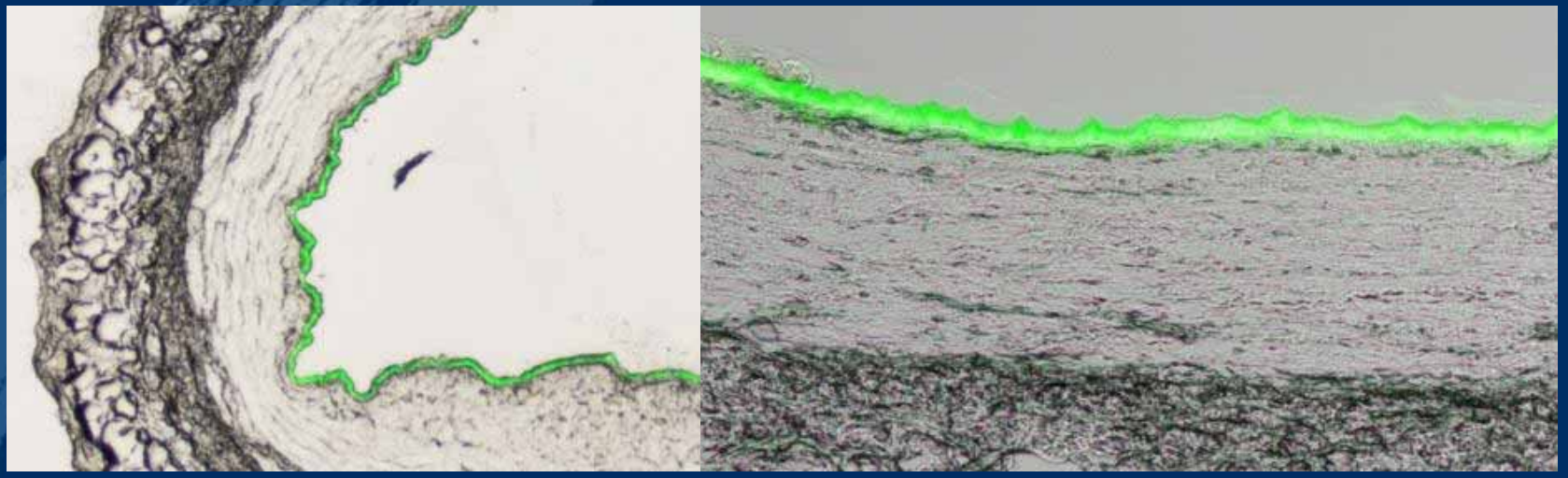


No.	No. of sections (Downstream muscle/coronary band)	Vascular Changes	Skeletal Muscle Necrosis/ Fibrosis	Crystalline material
1	13 (12 / 1)	6	0	0
2	13 (12 / 1)	5	1	0
3	13 (12 / 1)	7	2	1
4	13 (12 / 1)	8	2	1
5	13 (12 / 1)	8	3	1
6	13 (12 / 1)	4	1	1
Total	78	38	9	4

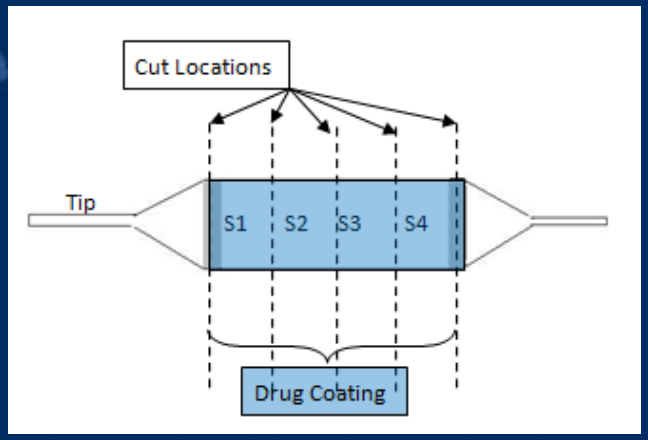
38 /78 (48.7 %) from DCB treatment showed findings of vascular change associated with paclitaxel and/or excipient (drug carrier).

Skeletal Muscle: Gastrocnemius Muscle, Gluteus Maximus Muscle, Gracilis Muscle, Rectus Femoris Muscle, Semimembranosus Muscle, and Semitendinosus Muscle

Ex Vivo Administration of Fluorescent-Labeled PTX to Excised Porcine Artery



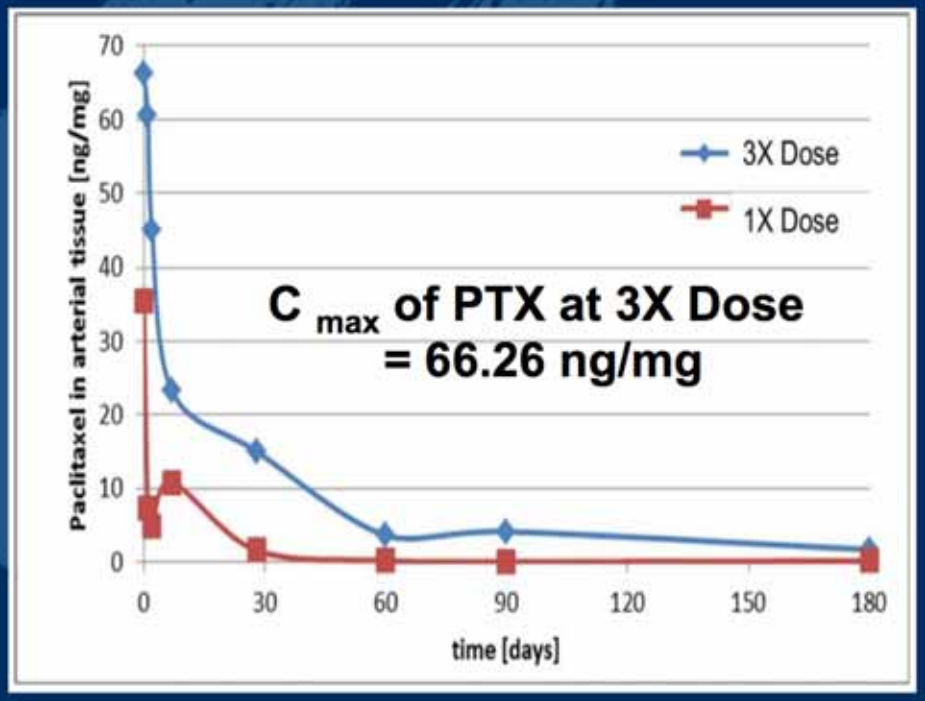
10% Oregon green labeled PTX incorporated into Lutonix DCB coating



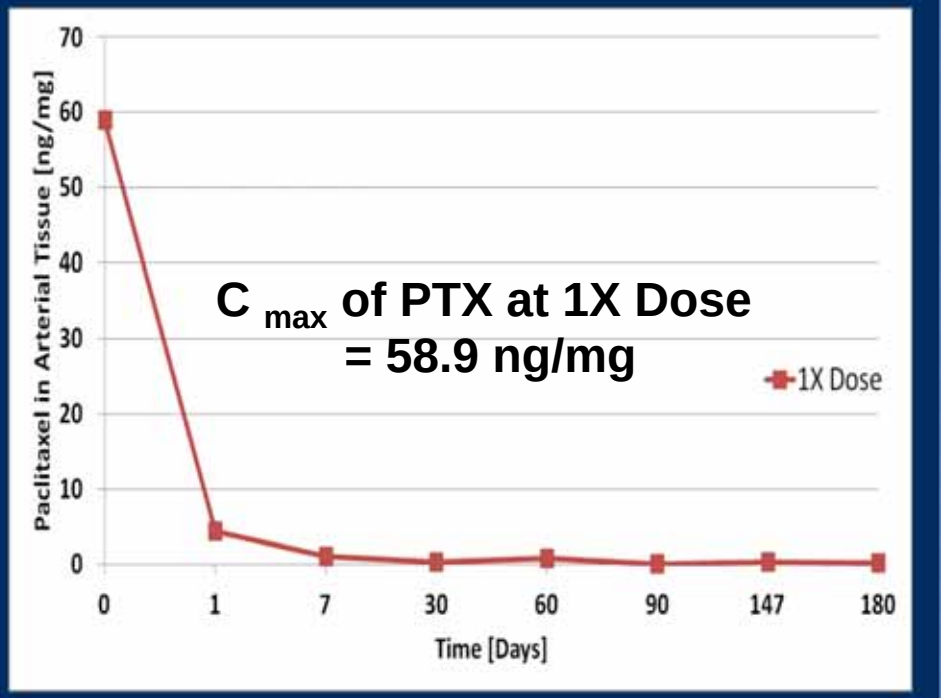
Segment-to-segment variability ± 4.0 %

Pharmacokinetics PTX in Arterial Tissue in a Porcine Model Comparison In.Pact vs. Lutonix

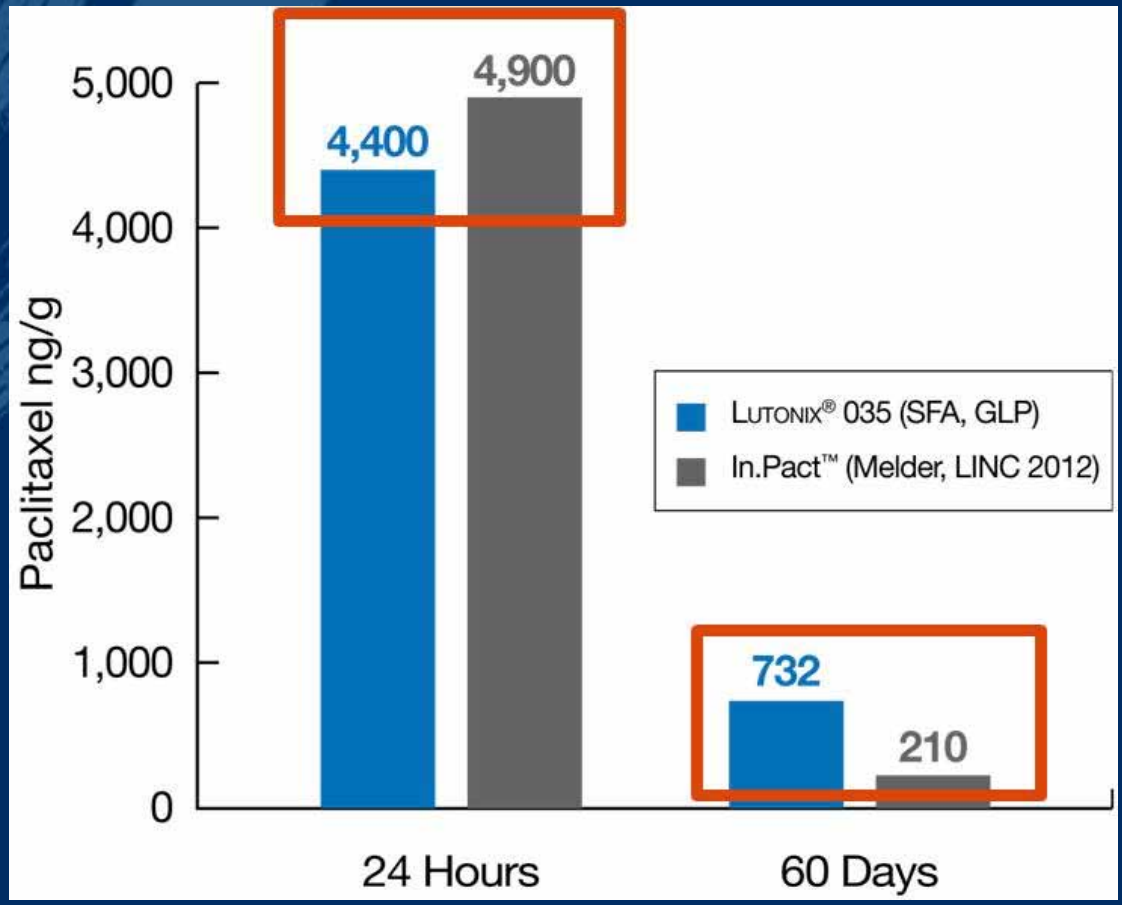
In.Pact 3 x 3µg/mm^2



Lutonix 2µg/mm^2



Does Drug Coating Matter?



**Data obtained from two data sets. Virmani preclinical animal data on file. Animal test results may not be indicative of clinical performance. Different test methods may yield different results.

German single center experience with Lutonix® DCB in BTK

presented @ LINC 2015

Sabine Steiner

Division of Interventional Angiology

University Hospital Leipzig, Germany

Study design

- Retrospective cohort study of patients undergoing below-the-knee interventions using Lutonix® drug coated balloons
- 248 patients treated, 40 lost to follow-up (16%)
- 220 limbs treated in 208 patients
- Clinical follow up:
  - Rate of death
  - BTK re-interventions and target lesion revascularization
  - Minor and major amputations

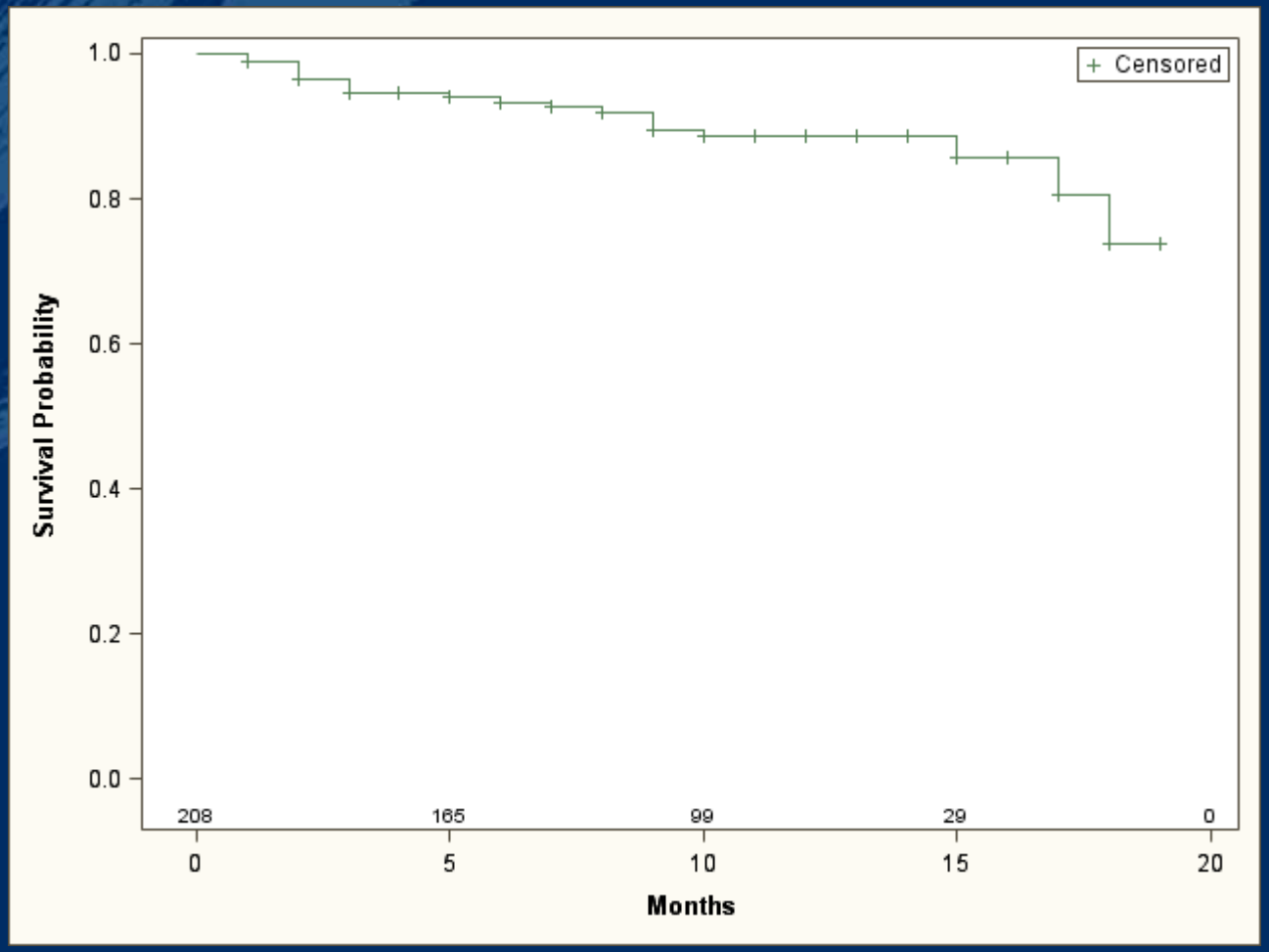
Baseline patient characteristics

	N=208
Age (years), mean± std	74.1±9.7
Female, %	33.8
Hyperlipidemia, %	77
Diabetes, %	69
Arterial Hypertension, %	95
Current/former smoking, %	45
Coronary heart disease, %	47
Cerebrovascular disease, %	8

Interventional characteristics

	N=220
No. of devices used, mean± std	2.3±1.1
Cumulative length of devices (mm), mean± std	242±122
Treatment of inflow lesions, %	48
Femoropopliteal, %	29
Popliteal, %	19
Rutherford stage before intervention, %	
Stage 3	38.7
Stage 4	12.3
Stage 5	46.4
Stage 6	2.7

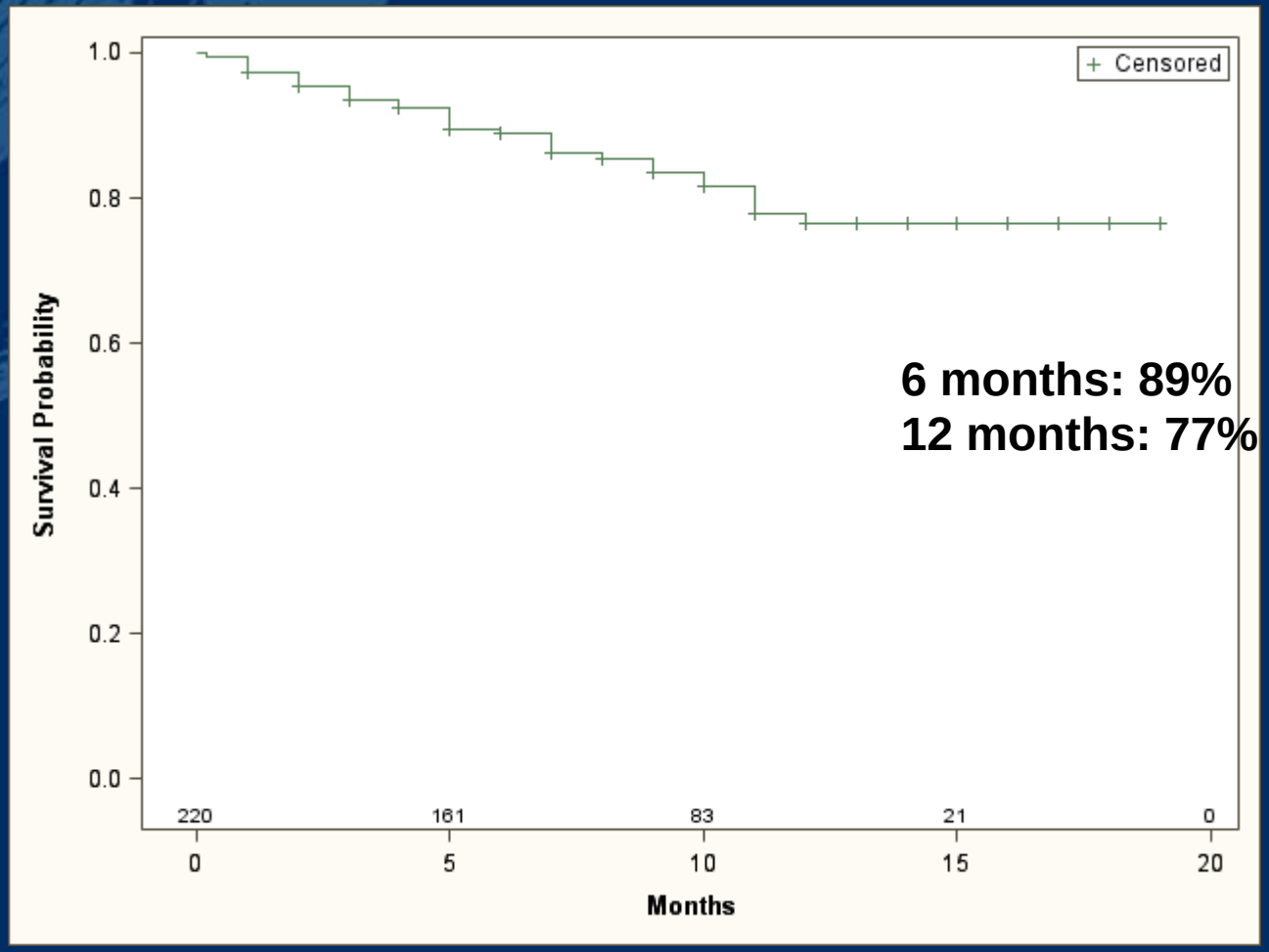
All cause death



Follow up II – Re-interventions

	N=220
BTK re-intervention (including pre-planned secondary interventions), %	22.7
Time to 1st re-intervention (months), mean± std	7.6±4.8
Target lesion revascularization, %	15.9
Time to 1st target lesion revascularization (months), mean± std	8.1± 4.7

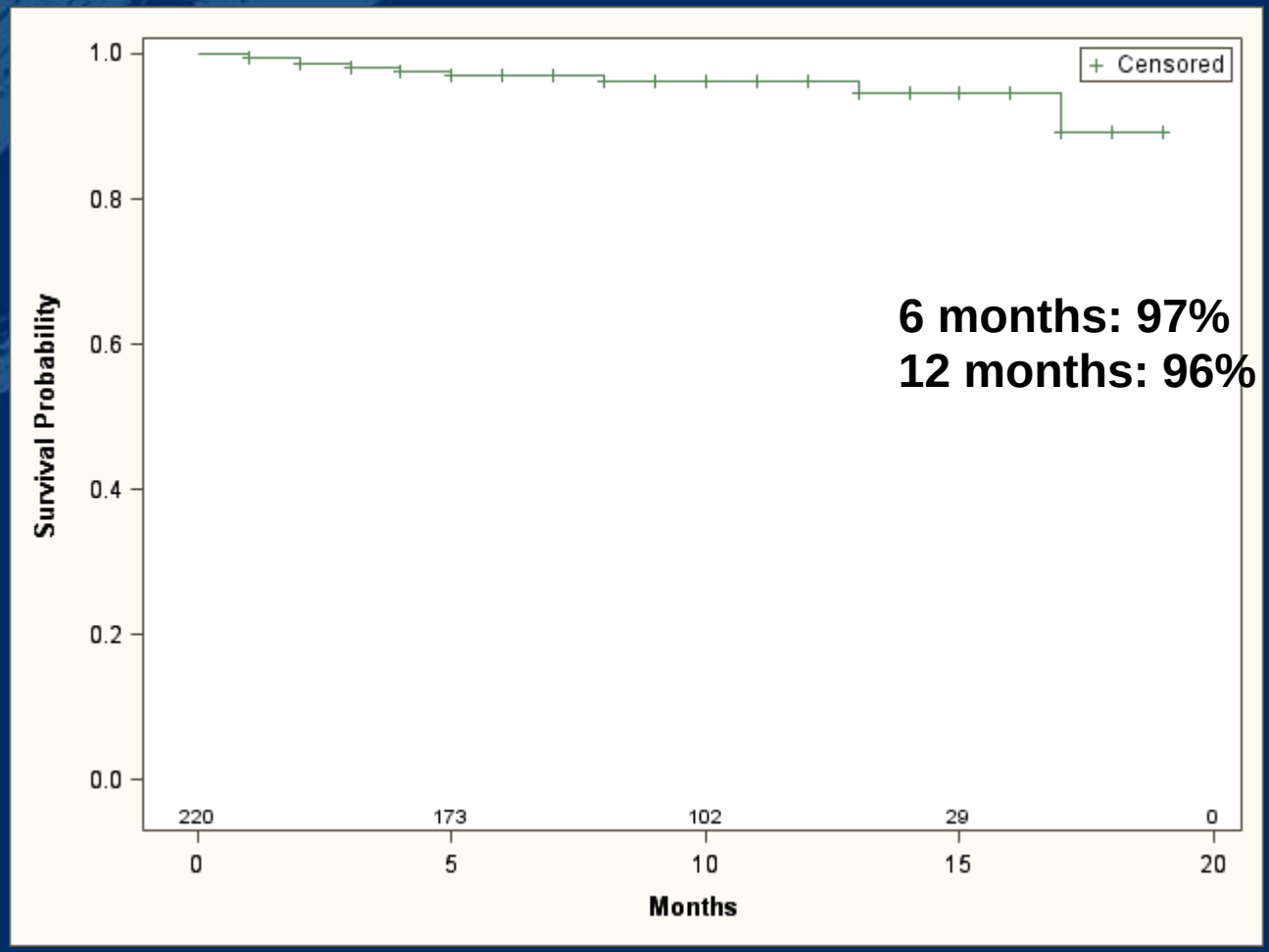
Freedom from target lesion revascularization



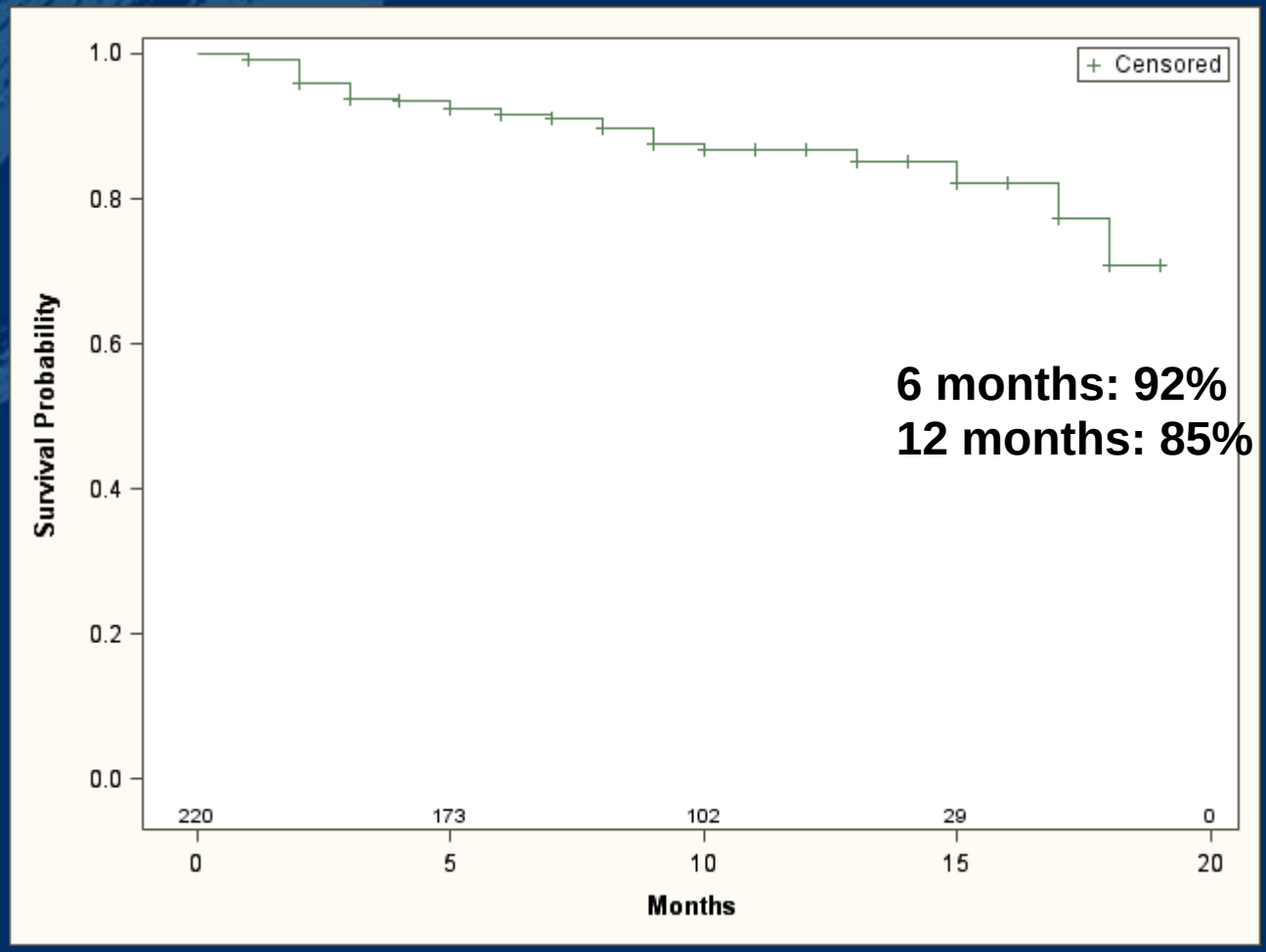
Follow up III – Amputations

- In total, 39 amputations were performed in 31 limbs (31 patients)
- From these 39 amputations were
  - 17 pre-planned minor amputations
  - 13 un-planned minor amputations
  - 9 major amputations
- All major amputations were performed in CLI patients (6.6% of the CLI cohort)
  - 6 patients with baseline Rutherford stage 5
  - 3 patients with baseline Rutherford stage 6

Freedom from major amputations



Freedom from death or major amputation



Summary

- Real world data of patients undergoing below the knee interventions using Lutonix® DCB
- Clinical follow-up indicates re-assuring effectiveness and safety profile

Lutonix BTK Trial Summary

PRIMARY ENDPOINTS	Safety at 30 days Limb salvage & primary patency at 12 months
NUMBER OF PATIENTS/SITES	480 patients at 55 global sites
FOLLOW-UP	**Clinical:** 1, 6, 12, 24, and 36 Months **Duplex Ultrasound (DUS):** 0–30 days, 6,12, 24, & 36 months **Angiography in subset of patients:** 12 months **Telephone:** 48 and 60 Months
NATIONAL PRINCIPAL INVESTIGATORS	**Patrick Geraghty:** Washington University, St. Louis, MO **Jihad Mustapha:** Metro Health Hospital, Wyoming, MI **Marianne Brodmann:** Medical University Graz, Austria
SPONSOR	Lutonix Inc., Minneapolis, MN

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

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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Patient Eligibility

Inclusion Criteria

- Male or non-pregnant female ≥18 years of age
- 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

- Pregnant or planning on becoming pregnant
- History of stroke within 3 months
- History of MI, thrombolysis or angina within 30 days of enrollment
- Prior or planned major amputation
- GFR ≤ 30 ml/min per 1.73m^2
- Acute limb ischemia
- In-stent restenosis of target lesion

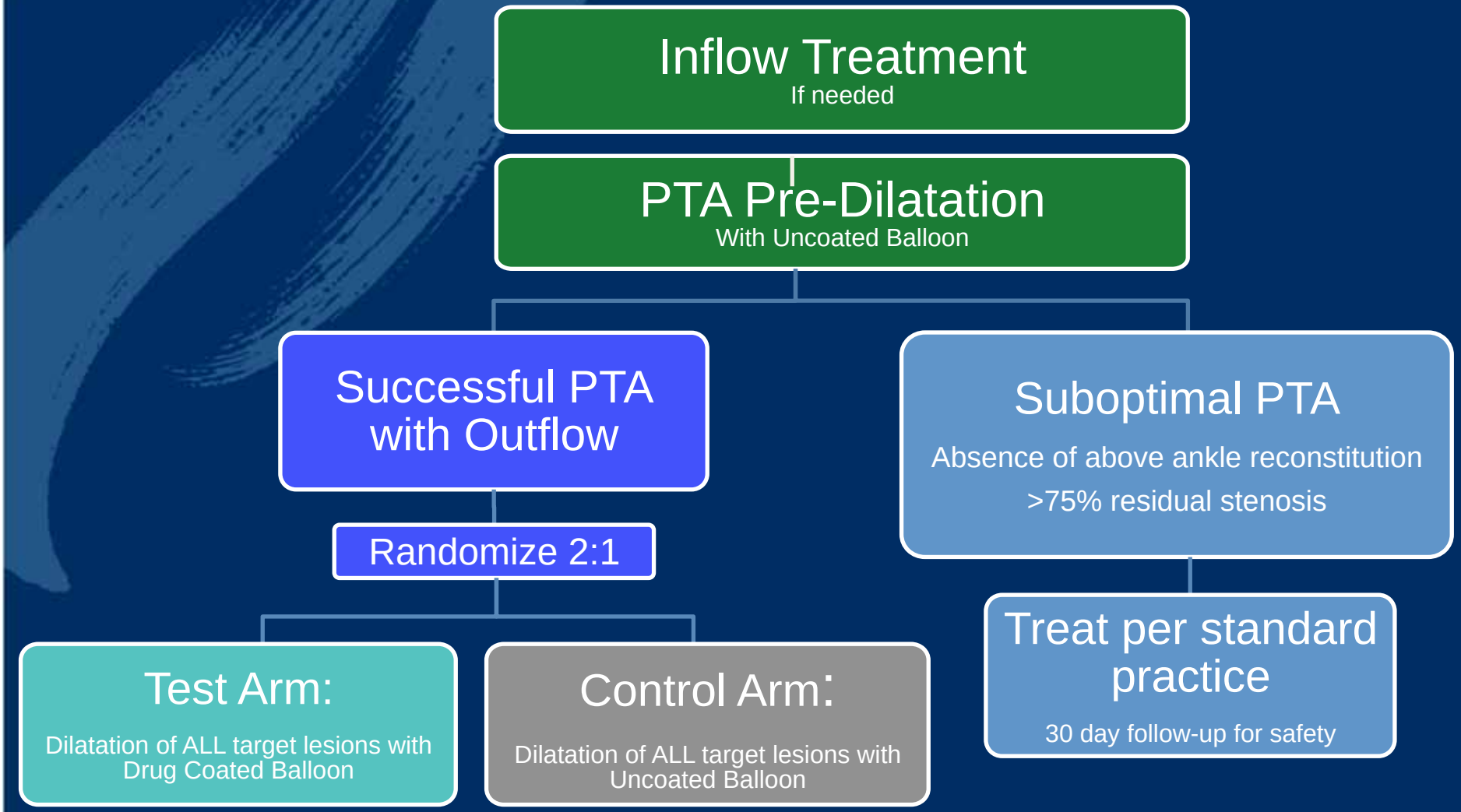
BTK Trial Design

Protocol Features

- Randomized 2:1 versus POBA
- Permits treatment of two tibial arteries (two flow pathways)
- Combined lesion length of up to 32 cm treatable (36 cm balloon length allowed)
- Retrograde wire access permitted, but not retrograde intervention
- Balloon lengths of up to 12 cm
- First U.S. use of tibial patency assessment via duplex ultrasound (VasCore)
- Angiographic assessment of normal-risk subset at one year (Synvacor)
- Broad range of secondary endpoints including QOL instruments

LUTONIX
BTK Clinical Trial

Study Flowchart



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LUTONIX
BTK Clinical Trial

DMC Monitoring

What is the Data Monitoring Committee?

- Unbiased panel of leading experts in peripheral vascular disease, cardiovascular medicine and biostatistics not associated with Lutonix or the trial

- During the enrollment phase of the trial, DMC reviews accumulating safety data to monitor for incidence of serious vascular events that would warrant termination of the trial

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BTK Clinical Trial

Safety Review

- 5 Data Monitoring Committee meetings so far
- 172 randomized patients:
  - 95 have completed 6 month follow-up
  - 39 have completed 12 month follow-up
- Only 5 major amputations (3% of enrolled pts) recorded
- **Only approved and ongoing BTK trial in the US**

Summary

- There is still an unmet need for improved durability in the BTK area
- Drug-delivery via balloon-based solutions may still be the most realistic approach
- The Lutonix clinical trial programme is proceeding well – data can be expected in 2016 time frame.

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