DCB below the knee: ongoing trials and perspectives

Lawrence A. Garcia, MD
Chief, Section Interventional Cardiology
and Vascular Interventions
Director, Vascular Medicine
St. Elizabeth's Medical Center
Tufts University School of Medicine
Boston, MA

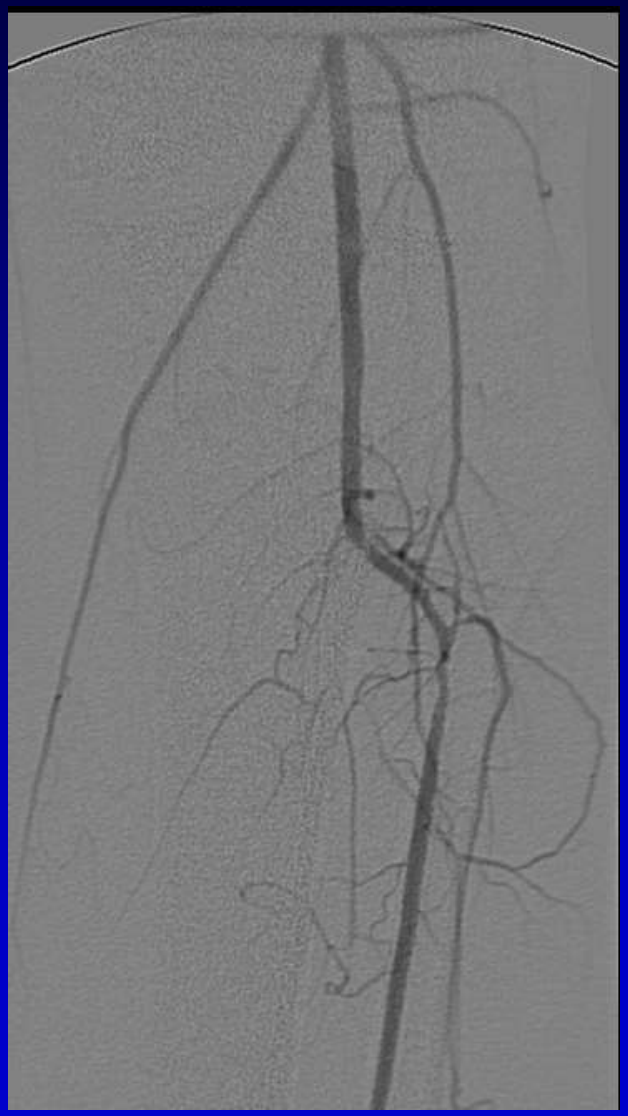
Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support	• iDev, Covidien/Medtronic
• Consulting Fees/Honoraria	• Covidien/Medtronic, Boston Scientific, Angiosculpt/Spectranetics
• Major Stock Shareholder/Equity	• Arsenal, Primacea, TissueGen, CV Ingenuity, Scion Cardiovascular, Spirox, Essential Medical
• Royalty Income	• None
• Ownership/Founder	• None
• Intellectual Property Rights	• None
• Other Financial Benefit	• None

Infra-popliteal revascularization

- Short vessel
  - popliteal
- Long vessels
  - tibials
- Generally angled proximally and distally
- Usually calcified
- Total occlusions
- Generally critical limb
  - Outcomes based on AFS



EXCEL trial

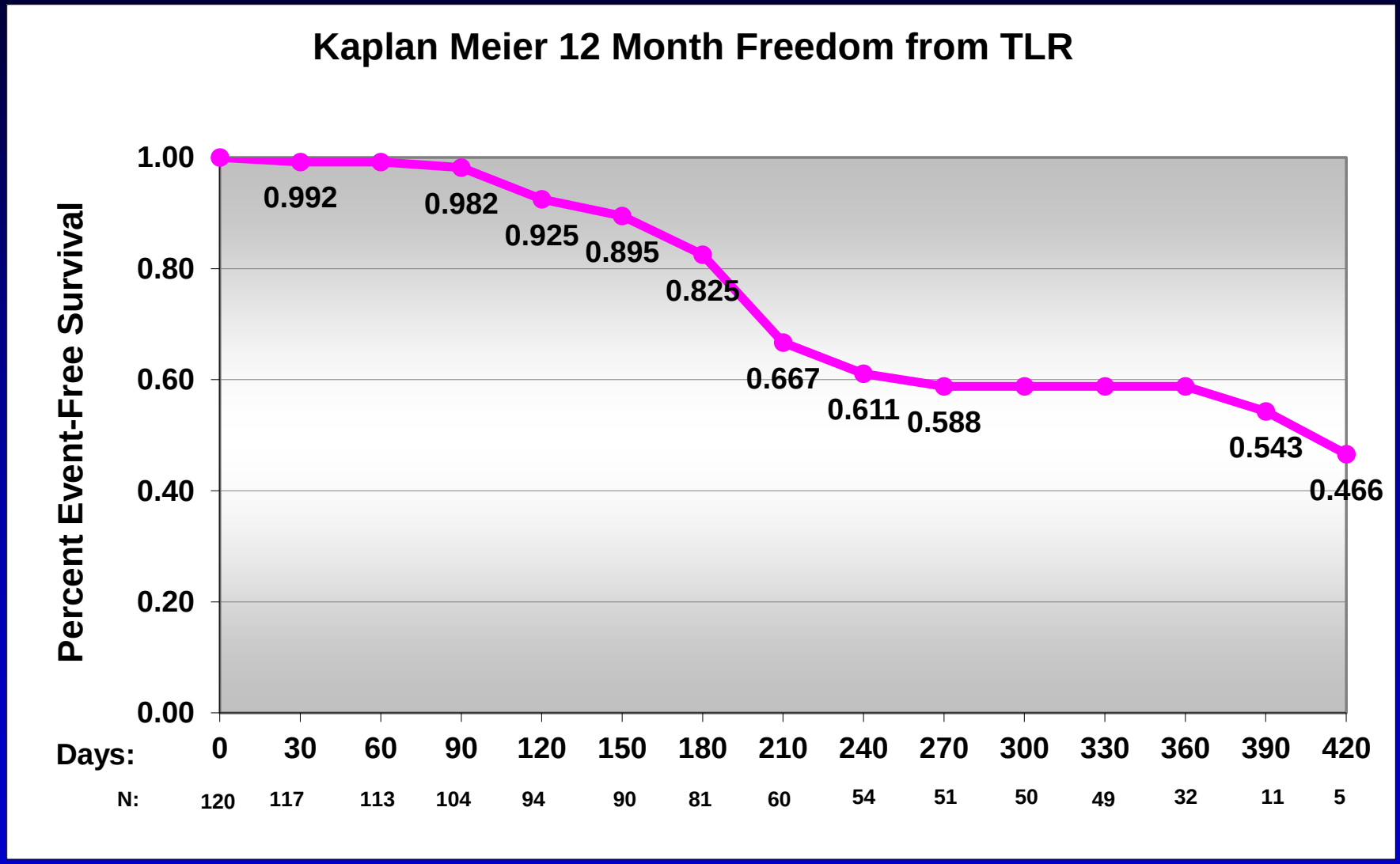
- Patients/limbs 120/140
- Lesion lengths 4-15cm
- Popliteal/infra-popliteal lesions
- Rutherford Category 4 (max of 60), 5 and 6
  - Non-pulsatile PPG
  - 0, 1 or 2 Pulse Volume Recording
  - $TcPO_2$ <30 mmHg or ankle pressure < 40mmHg

EXCELL: Core Lab Lesion Baseline Characteristics

Lesion Characteristics	N=140 Lesions/N=120 Patients
Lesion Length, cm	
Overall	4.7 ± 4.2
Stenosis ≤ 99% (95 lesions)	3.6 ± 3.5
Occlusions (42 lesions)	7.1 ± 4.5
Lesions / Patient	1.2 ± 0.4
RVD	2.8 ± 0.7
Pre – stenosis, % (in-lesion)	81.1 ± 16.5
Pre – MLD, mm (in-lesion)	0.5 ± 0.5
Post – stenosis, % (in-stent)	12.3 ± 13.2
Post – MLD, mm (in-stent)	2.4 ± 0.6

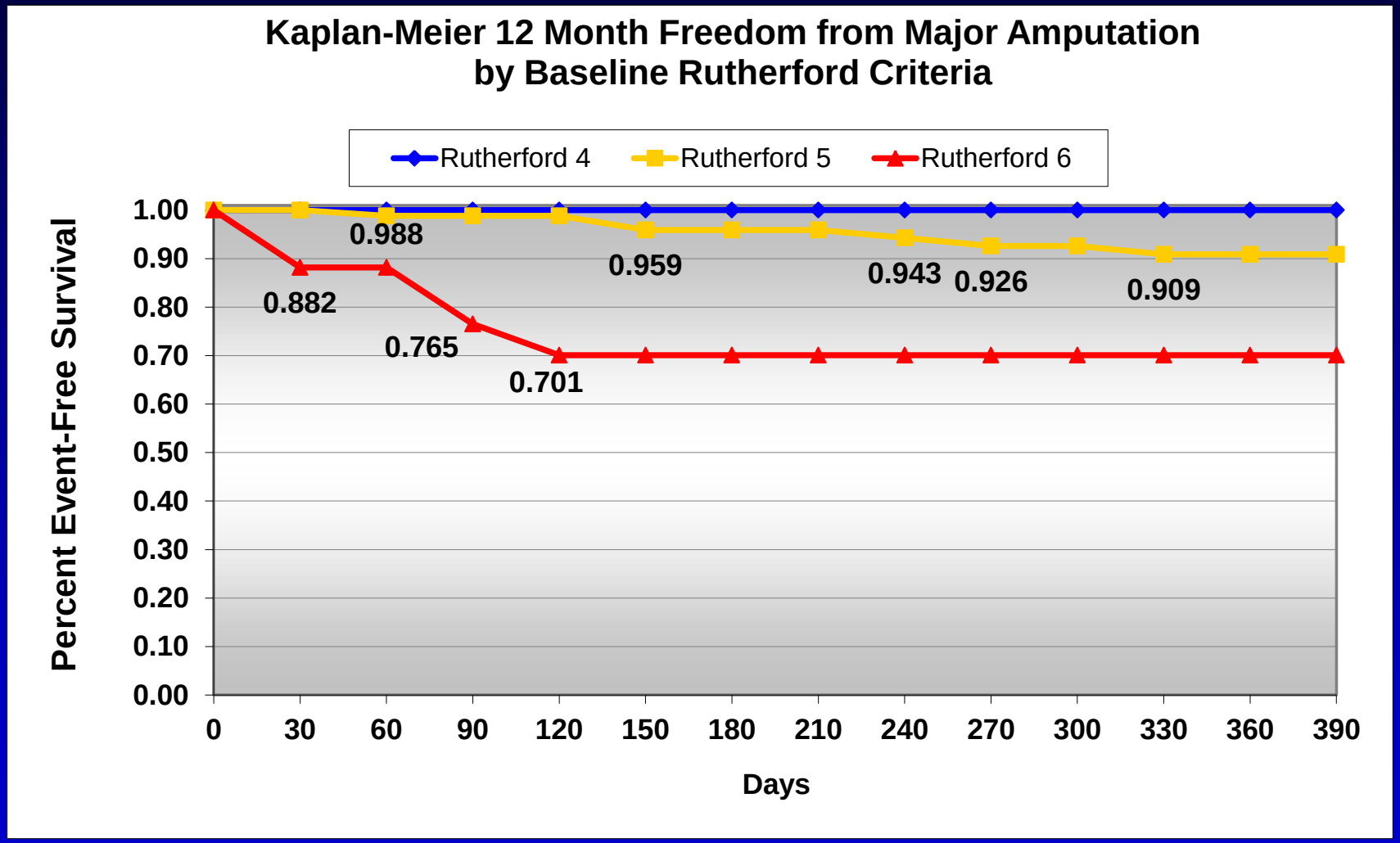
Values indicate mean ± SD of the lesion characteristic.

Freedom from TLR



Limb Salvage

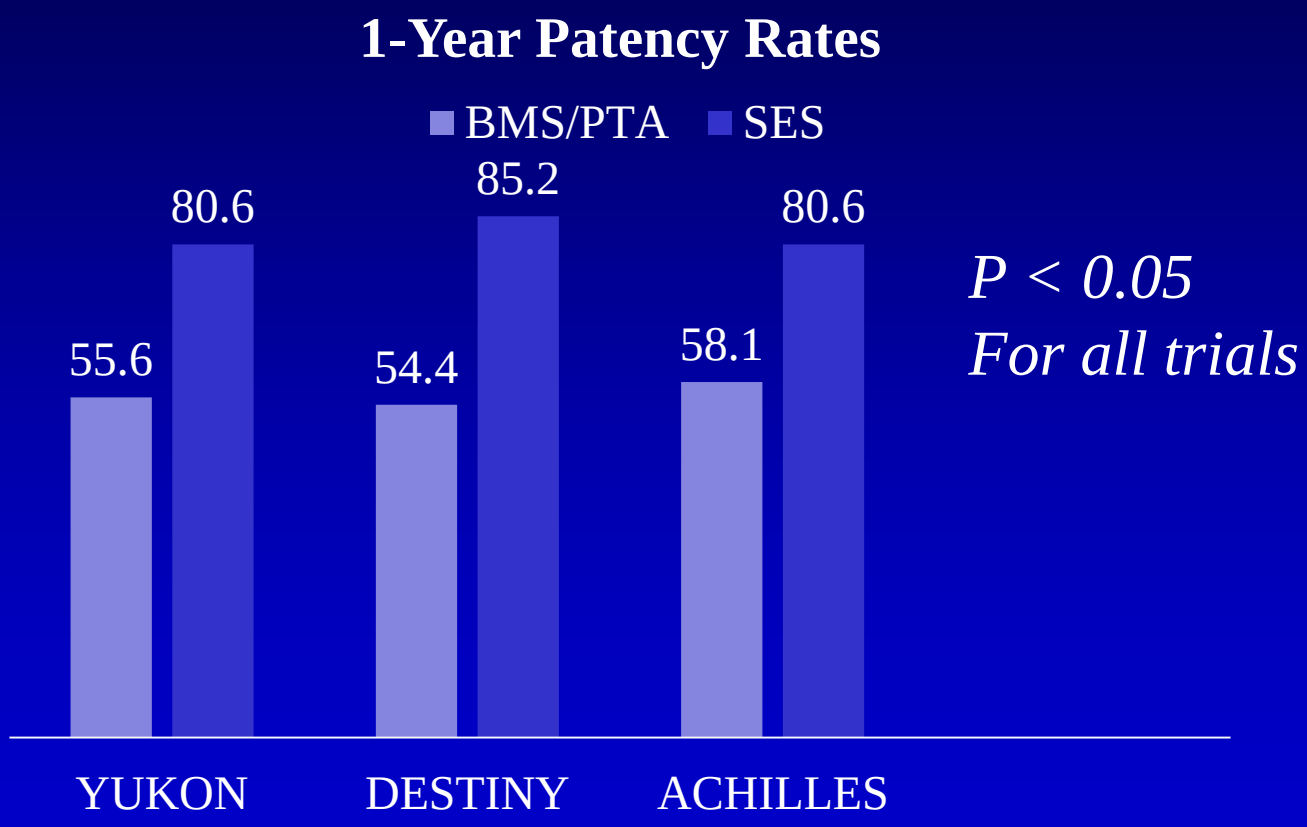
By Baseline Rutherford Criteria



CURRENTLY PRESENTED OR PUBLISHED TRIALS ON DES IN BTK LESIONS

- YUKON-BTK—LL 27mm
  - Sirolimus eluting polymer free vs. bare metal stent (Yukon),Translumina. PI: T. Zeller
- DESTINY—LL 15-19 mm
  - Everolimus eluting stent (Xience V) vs. bare metal stent (Multilink vision), Abbott Vascular. PI: M. Bosiers
- ACHILLES
  - Sirolimus stent with polymer coating (Cypher select) vs. POBA, Cordis. PI: D. Scheinert

YUKON, DESTINY & ACHILLES Trials (n=515)
Primary Patency



P < 0.05
For all trials

Rastan et al. EHJ 2011
Scheinert et al. LINC 2011
Bosiers et al. JVS 2011

INPACT DEEP

- Prospective, Multicenter, Randomized
- Independent Data Safety Monitoring Board (DSMB) [1]
- Independent Clinical Event Committee (CEC) [1]
- Independent Angiographic Corelab [2]
- Independent Wound Corelab [2]
- Wound Measurement through Electronic Reader [3]
- External Monitoring, 100% Source Data Verification [1]

1. *Third-party safety monitoring, Clinical Event Committe and external data monitoring services provided by Genae Associates (Antwerp, Belgium)*
2. *Angiographic and Wound Corelab: SynvaCor (Springfield IL, US)*
3. *Electronic wound capturing through Sylouette Mobile (Aranz Medical, Auckland, New Zealand)*

Primary IN.PACT DEEP Outcomes

Primary Efficacy	DEB	PTA	*p*
12-month LLL (mm) [1]	0.61 ± 0.78	0.62 ± 0.78	*0.950*
12-month CD-TLR [2]	9.2% (18/196)	13.1% (14/107)	*0.291*

Primary Safety	DEB	PTA	*p*
6-month Death Major Amputation or CD TLR	17.7% (41/232)	15.8% (18/114)	*0.021* (non-inferiority) *0.662 (superiority)*

1. *Angio Cohort, Corelab adjudicated. Angiogaphic Imaging 12-month FU compliance = 70.9% (DEB) vs. 71.4% (PTA)*
2. *Clinically driven TLR of the target lesion in the (major) amputation free surviving subjects at 12 months. "Clinically driven TLR" defined as any TLR of the target lesion associated with: a) deterioration of RC and / or b) Increase in size of pre-existing wounds and / or c) occurrence of a new wound(s), with b) and c) adjudicated by the Wound Healing Core lab*

Angio Cohort Outcomes

12-month Outcomes [1]	DEB	PTA	*p*
Mean Lesion Length (mm±SD)	59.1 ± 41.7	79.7 ± 74.6	*0.060*
Binary (50%) Rest. Rate (%)	41.0% (25/61)	35.5% (11/31)	*0.609*
Occlusion Rate (%)	11.5% (7/61)	16.1% (5/31)	*0.531*
Longitudinal Restenosis (%) [2]	62.7 ± 56.2	93.2 ± 60.8	*0.167*
Revalidated Lumen Loss [3]	**DEB**	**PTA**	***p***
12-month LLL (mm, mean ± SD)	0.51 ± 0.66	0.60 ± 0.97	*0.654*

1. *Angio Cohort, Corelab adjudicated. Angiogaphic Imaging 12-month FU compliance = 70.9% (DEB) vs. 71.4% (PTA)*
2. *Mean % of stenosis length vs. treated lesion length± SD (Angiographic Cohort, ITT)*
3. *As evaluated by additional angiographic core laboratory (Beth Israel Deconess Medical Center, Boston, MA) to confirm earlier analysis*

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. ★

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

LUTONIX
BTK Clinical Trial

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

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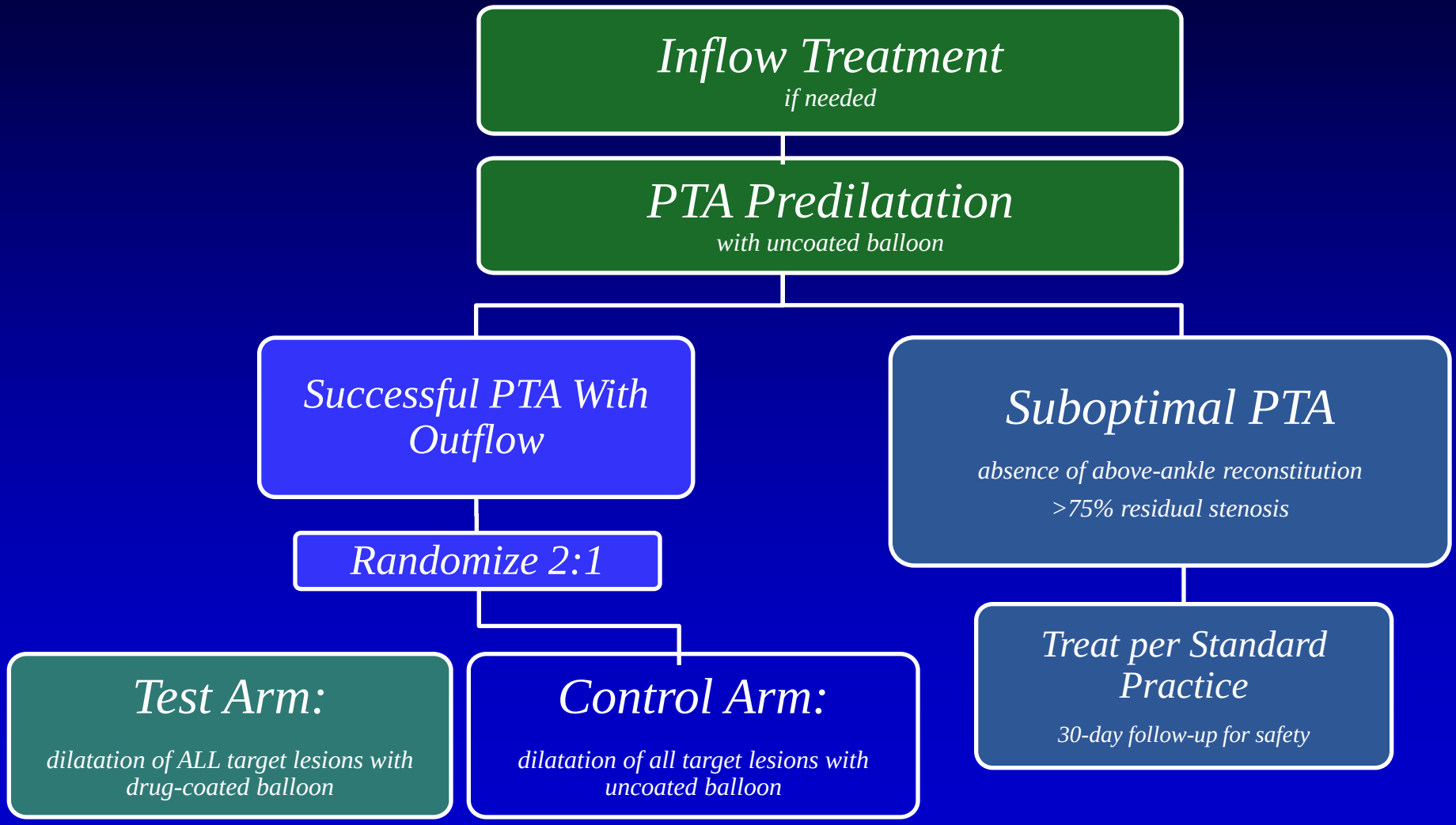
LEVANT BTK


Inflow Treatment
if needed
PTA Predilatation
with uncoated balloon
Successful PTA With Outflow
Suboptimal PTA
absence of above-ankle reconstitution
>75% residual stenosis
Randomize 2:1
Treat per Standard Practice
30-day follow-up for safety
Test Arm:
dilatation of ALL target lesions with drug-coated balloon
Control Arm:
dilatation of all target lesions with uncoated balloon

LUTONIX
BTK Clinical Trial

Safety Review

- *5 Data Monitoring Committee meetings so far*
- *165 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*

Perspectives

- All interventions afford AFS
- BMS primary patency poor
- Focal DES excellent primary patency compared with BMS
- DCB (IN-Pact DEEP)failed in largest trial for below knee use
  - Principal studies using DCB still may be appealing but given the data?
  - Several issues with balloon and drug coating
- LUTONIX BTK awaiting outcomes
- Current review of data supports revascularization for infra-popliteal disease though DCB currently not proven