DCB real world registries an Update

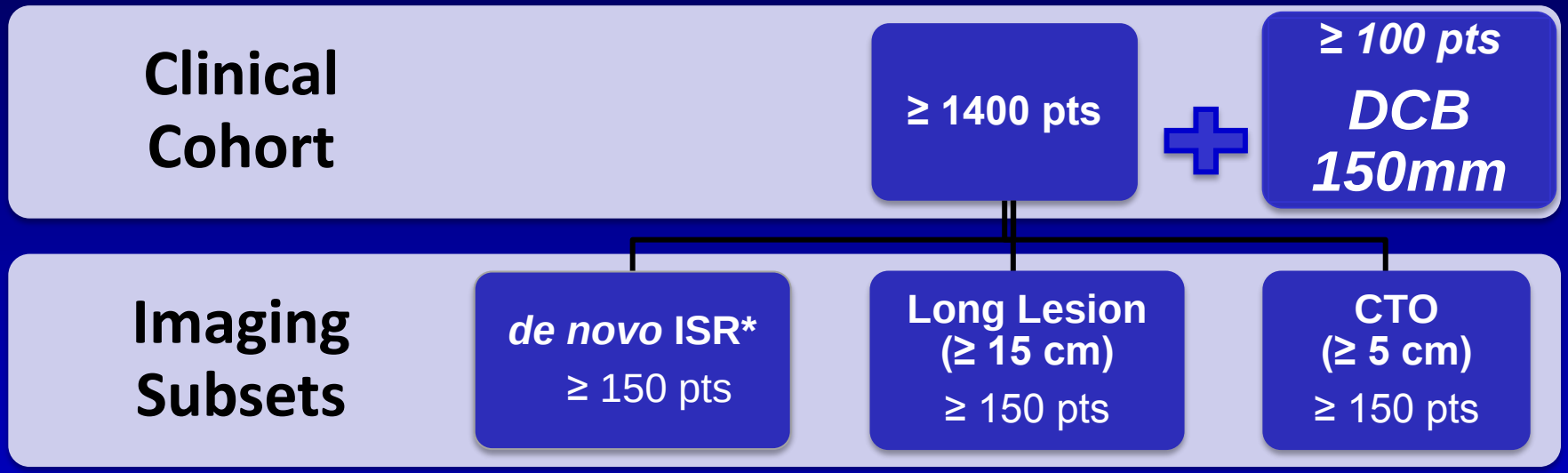
Lawrence A. Garcia, MD
Chief, Section Interventional Cardiology
and Vascular Interventions
Director, Vascular Medicine
St. Elizabeth's Medical Center
Tufts University School of Medicine
Boston, MA

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	• Abbott, Covidien/Medtronic
• Consulting (non-compensated)	• Covidien/Medtronic, Boston Scientific, Abbott
• Major Stock Shareholder/Equity	• Arsenal, Primacea, TissueGen, CV Ingenuity, Spirox, Scion Cardiovascular, Syntervention, Essential Medical
• Royalty Income	• None
• Ownership/Founder	• Innovation Vascular Partners, Consulting
• Intellectual Property Rights	• None
• Other Financial Benefit	• None

IN.PACT Global Study Patient Cohorts



1538 patients enrolled

**ISR is not an approved indication in the US*

IN.PACT Global Study
*Primary Endpoints**

Safety

- ***Composite***
  - *30-day freedom from device- and procedure-related mortality*
  - *12-month freedom from major target limb amputation and clinically-driven TVR*

Efficacy

- ***Imaging Cohort: 12-Month Primary Patency***
  - *Freedom from clinically-driven TLR and freedom from restenosis as determined by DUS PSVR ≤ 2.4.*

IN.PACT Global Long Lesion Imaging Cohort: Lesion/Procedural Characteristics

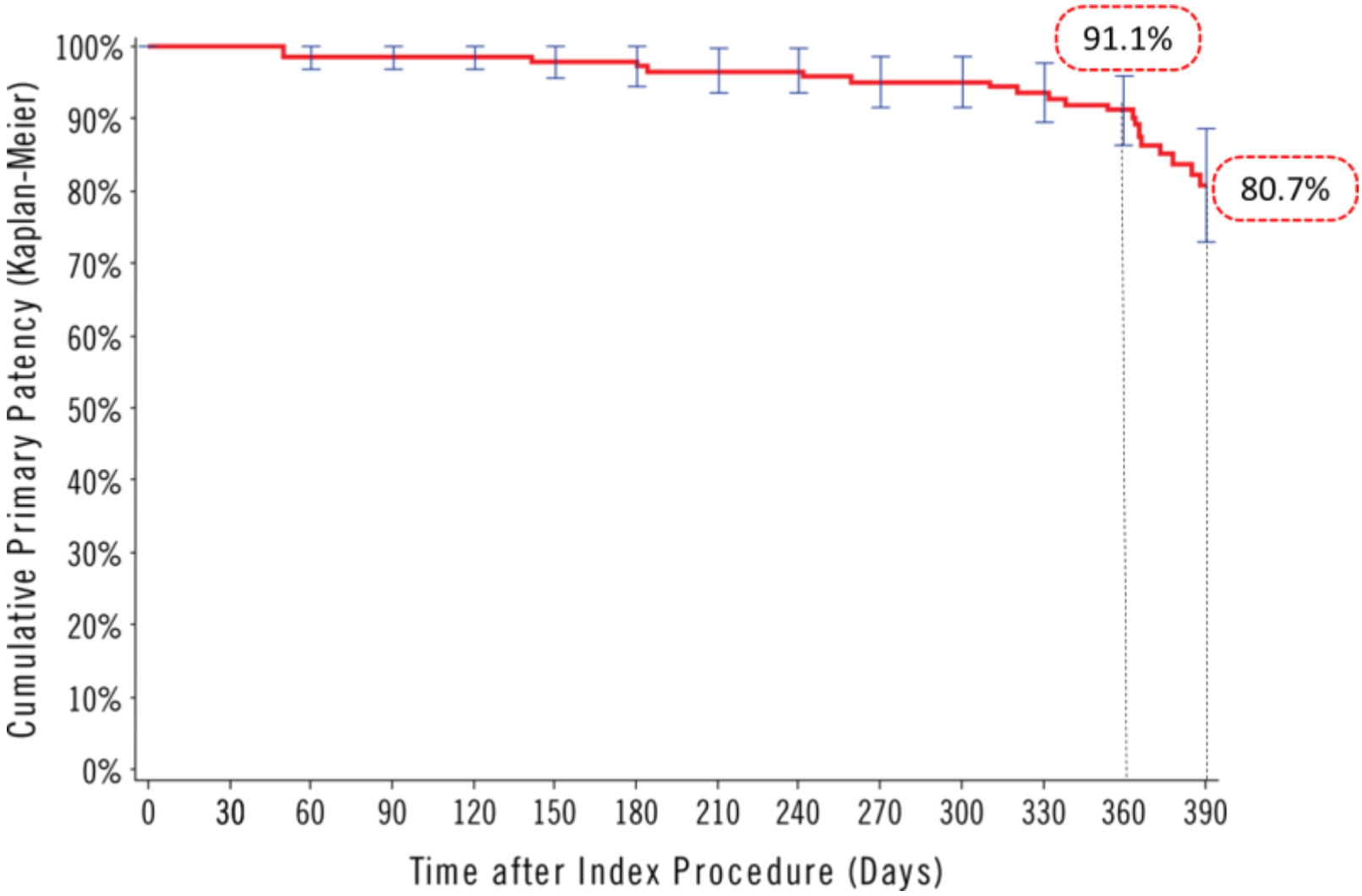
Lesions (N)	164
Lesion Type: de novo restenotic (no ISR) ISR	 83.2% (134/161) 16.8% (27/161) 0.0% (0/161)
Lesion Length	**26.40 ± 8.61 cm**
Total Occlusions	60.4% (99/164)
Calcification Severe	71.8% (117/163) 19.6% (32/163)
RVD (mm)	4.594 ± 0.819
Diameter Stenosis (pre-treatment)	90.9% ± 14.2
Dissections: 0	37.9% (61/161)
A-C	47.2% (76/161)
D-F	14.9% (24/161)

Device Success [1]	99.5% (442/444)
Procedure Success [2]	99.4% (155/156)
Clinical Success [3]	99.4% (155/156)
Pre-dilatation	89.8% (141/157)
Post-dilatation	39.1% (61/156)
Provisional Stent - LL 15-25 cm: - LL > 25 cm:	40.4% (63/156) 33.3% (33/99) 52.6% (30/57)

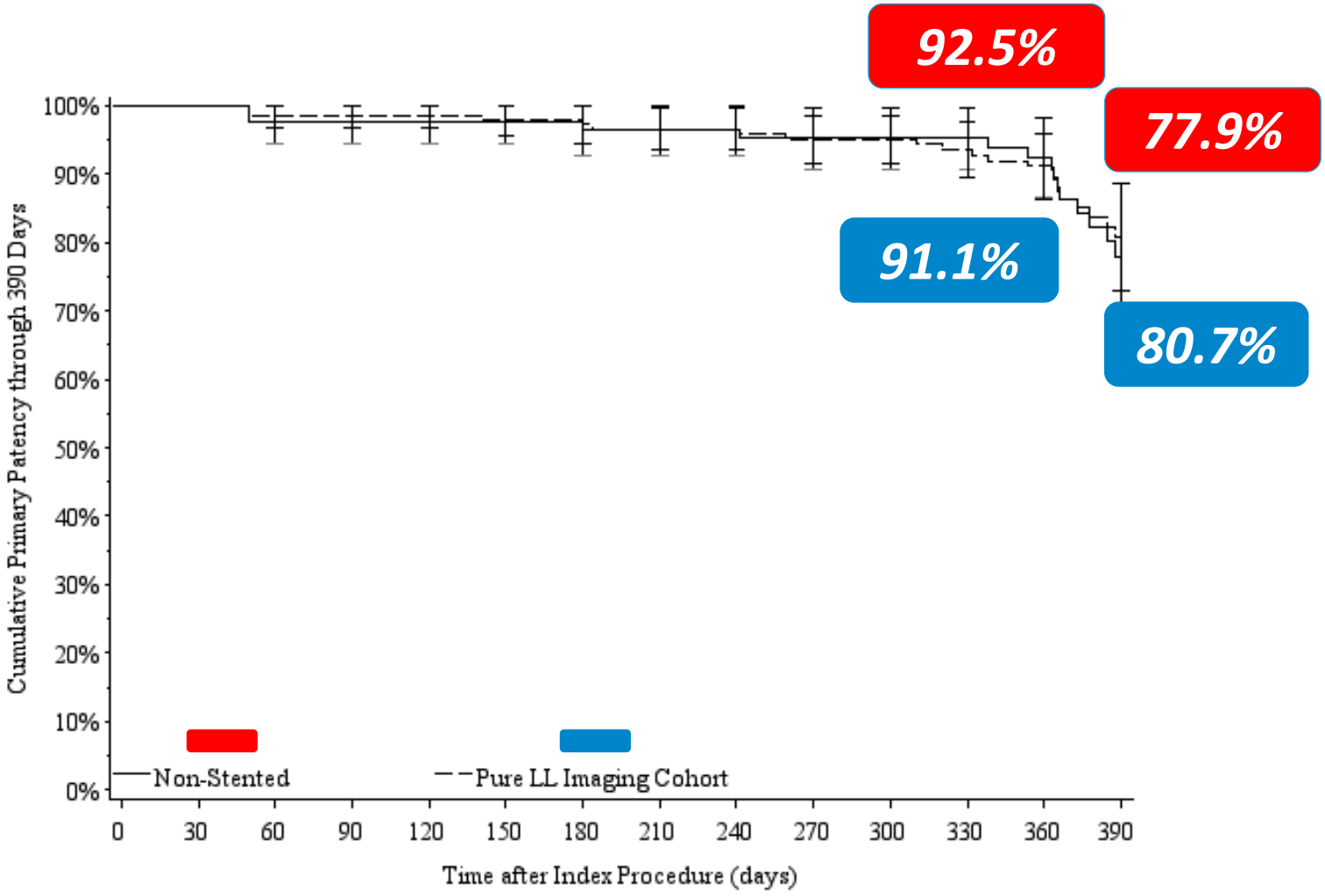
1. *Device success: successful delivery, inflation, deflation and retrieval of the intact study balloon device without burst below the RBP*
2. *Procedure success: residual stenosis of ≤ 50% (non-stented subjects) or ≤ 30% (stented subjects) by core lab (if core lab was not available then the site reported estimate was used)*
3. *Clinical success: procedural success without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or TVR) prior to discharge*

Schienert, D EuroPCR 2015 presentation

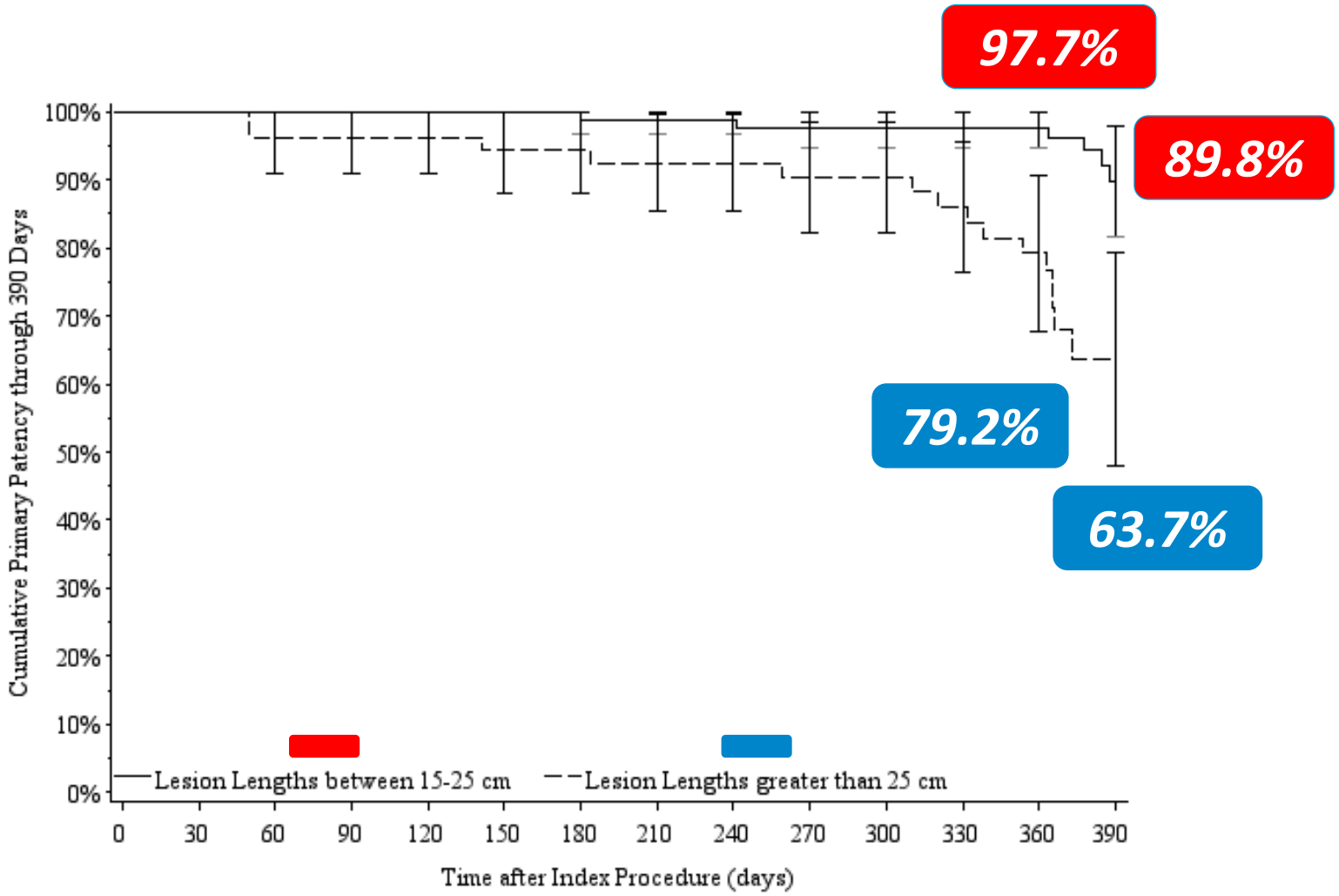
IN.PACT Global Long Lesion Imaging Cohort: Kaplan-Meier Estimate of Primary Patency



IN.PACT Global Long Lesion Imaging Cohort: Primary Patency in Non-stented Subgroup

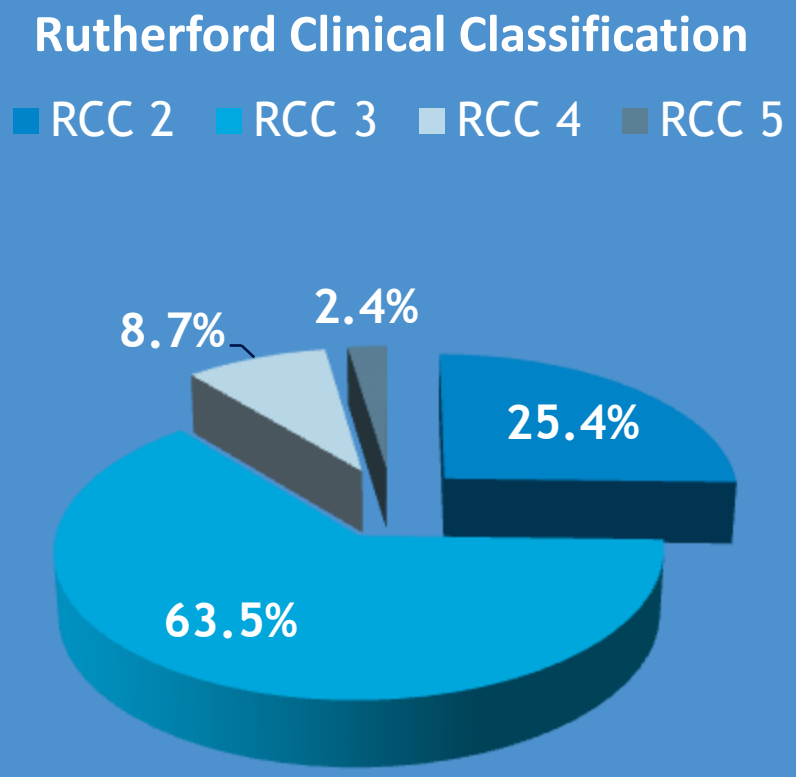


IN.PACT Global Long Lesion Imaging Cohort: Primary Patency by Lesion Length Subgroup



Baseline Clinical Characteristics

Characteristics	N = 126 Subjects
Age (Y, Mean ± SD)	67.5 ± 10.4
Male % (n)	69.0% (87/126)
Diabetes % (n)	29.6% (37/125)
Hypertension % (n)	82.3% (102/124)
Hyperlipidemia % (n)	64.5% (78/121)
Current Smoker % (n)	49.2% (62/126)
Obesity % (n)	20.2% (25/124)
Coronary Heart Disease % (n)	24.1% (28/116)
Carotid Artery Disease % (n)	19.2% (19/99)
Renal Insufficiency[1] % (n)	10.0% (11/110)
Previous Peripheral Revascularization % (n)	33.3% (42/126)
Concomitant BTK Disease % (n) (n)	41.0% (48/117)
ABI[2] (Mean ± SD)	0.595 ± 0.180



1. Baseline serum creatinine ≥1.5 mg/dL.
2. The ABI for both target limbs treated during both index procedures are included for bilateral subjects.

Tepe, G CharringCross 2016 presentation

Lesion/Procedural Characteristics

Lesion Characteristics	N = 128 Lesions
Lesion Type: % (n) De novo Restenotic (non-stented) In-stent Restenosis	 92.2% (118/128) 7.8% (10/128) 0.0% (0/128)
Lesion Length (cm ± SD)	22.90 ± 9.75
Occluded Lesion Length (cm ± SD)	11.97 ± 8.11
Calcification % (n)	71.2% (89/125)
RVD (mm ± SD)	5.056 ± 0.657
Diameter Stenosis (% ± SD)	100.0 ± 0.0
Dissections: 0 A-C D-F	 32.8% (42/128) 43.8% (56/128) 23.4% (30/128)

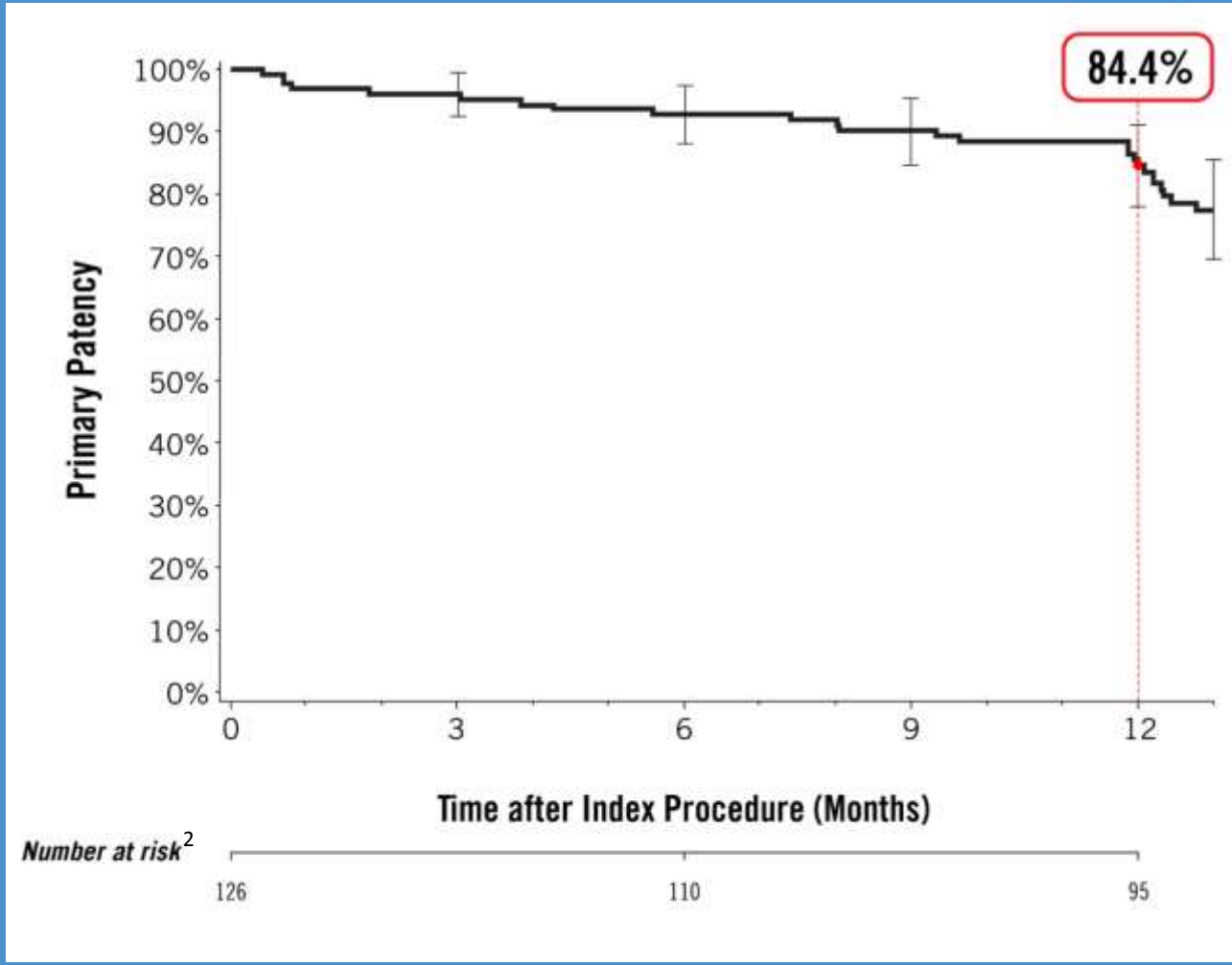
Procedural Characteristics	N = 126 Subjects N = 128 Lesions
Device Success[1] % (n)	99.3% (283/285)
Procedure Success[2] % (n)	100% (125/125)
Clinical Success[3] % (n)	99.2% (124/125)
Pre-dilatation % (n) Post-dilatation % (n)	94.4% (119/126) 50.0% (63/126)
Provisional Stent % (n)	46.8% (59/126)

1. Device success defined as successful delivery, inflation, deflation and retrieval of the intact study balloon device without burst below the RBP.

2. Procedure success defined as residual stenosis of ≤ 50% (non-stented subjects) or ≤ 30% (stented subjects) by core lab (if core lab was not available then the site-reported estimate was used).

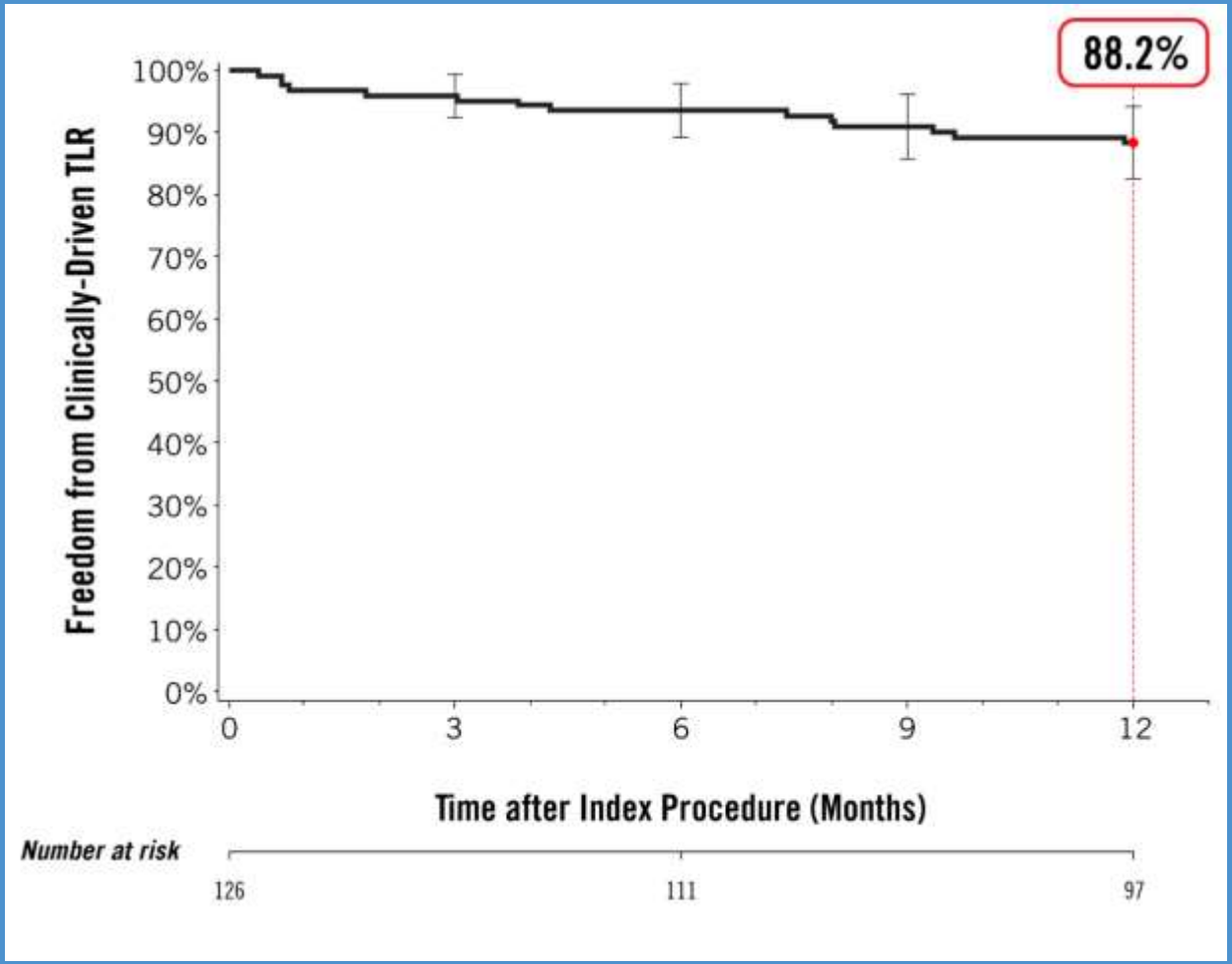
3. Clinical success defined as procedural success without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or TVR) prior to discharge.

Primary Patency[1] Results through 1 Year



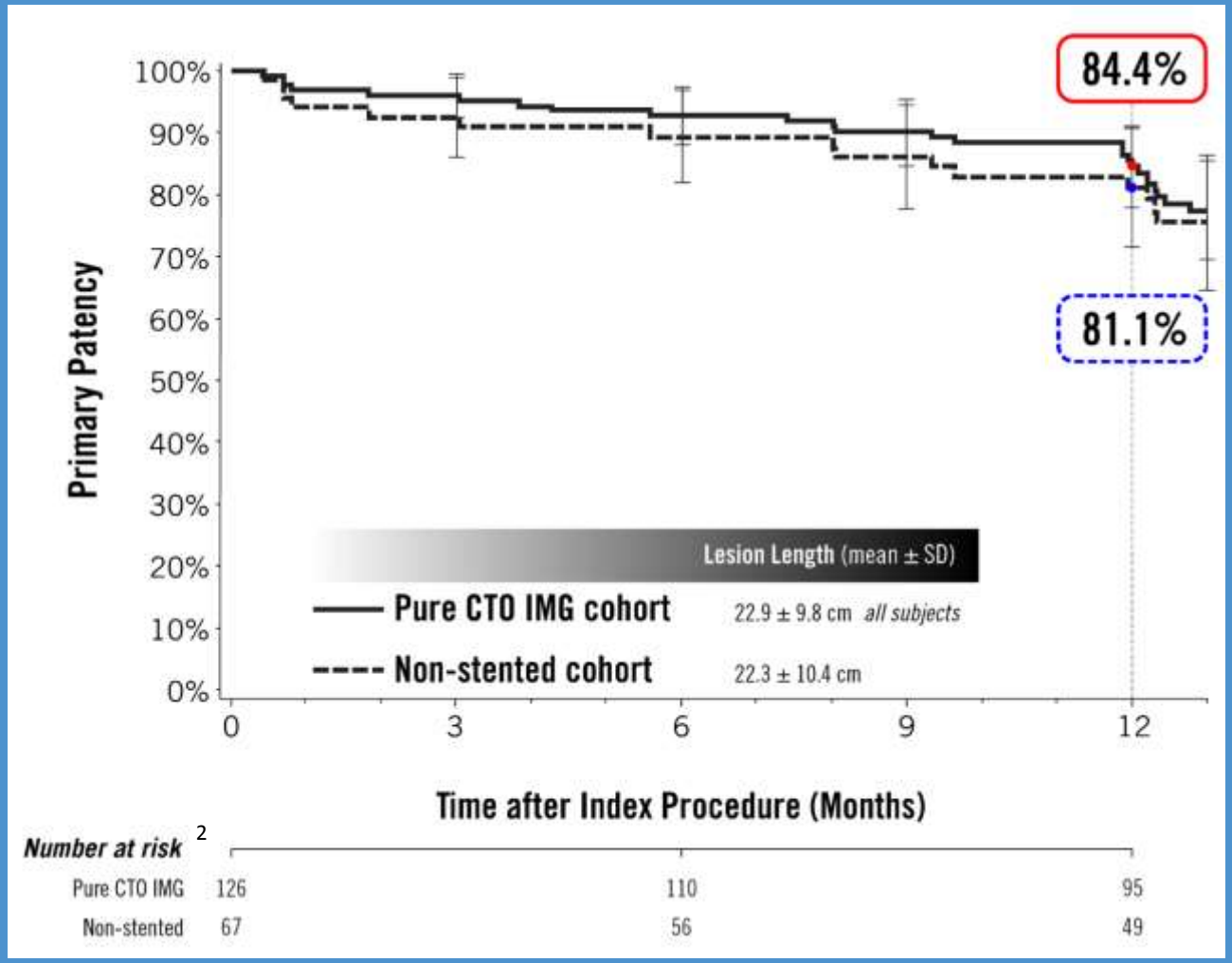
1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) or clinically-driven target lesion revascularization through 12 months (adjudicated by a Clinical Events Committee)
2. Number at risk represents the number of evaluable subjects at the beginning of the 30-day window and prior to each follow-up interval

Freedom from CD-TLR at 1 Year



Number at risk represents the number of evaluable subjects at the beginning of the 30-day window prior to each follow-up interval

Primary Patency[1] in Non-Stented Subgroup through 1 Year



1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) or clinically-driven target lesion revascularization through 12 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 and prior to each follow-up interval

Safety Outcomes at 1 Year

	N = 126 subjects
Clinically-Driven TLR [1]	12.2% (14/115)
Clinically-Driven TVR [2]	12.2% (14/115)
Primary Safety Endpoint [3]	87.8% (101/115)
Major Adverse Events [4]	16.5% (19/115)
Death (all-cause)	4.3% (5/115)
Major Target Limb Amputation	0.0% (0/115)
Thrombosis	4.3% (5/115)

1. Any re-intervention within the target lesion(s) due to symptoms or drop of ABI of ≥ 20% or > 0.15 when compared to post-index procedure baseline ABI.
2. Any re-intervention within the target vessel due to symptoms or drop of ABI ≥ 20% or > 0.15 when compared to post-index procedure baseline ABI.
3. Composite of 30-day freedom from device- and procedure-related mortality and 12-month freedom from major target limb amputation and clinically-driven TVR.
4. Major Adverse Events: Composite of death, major target limb amputation, clinically-driven TVR, and thrombosis.

Lesion/Procedural Characteristics by Gender

No Differences Between Groups

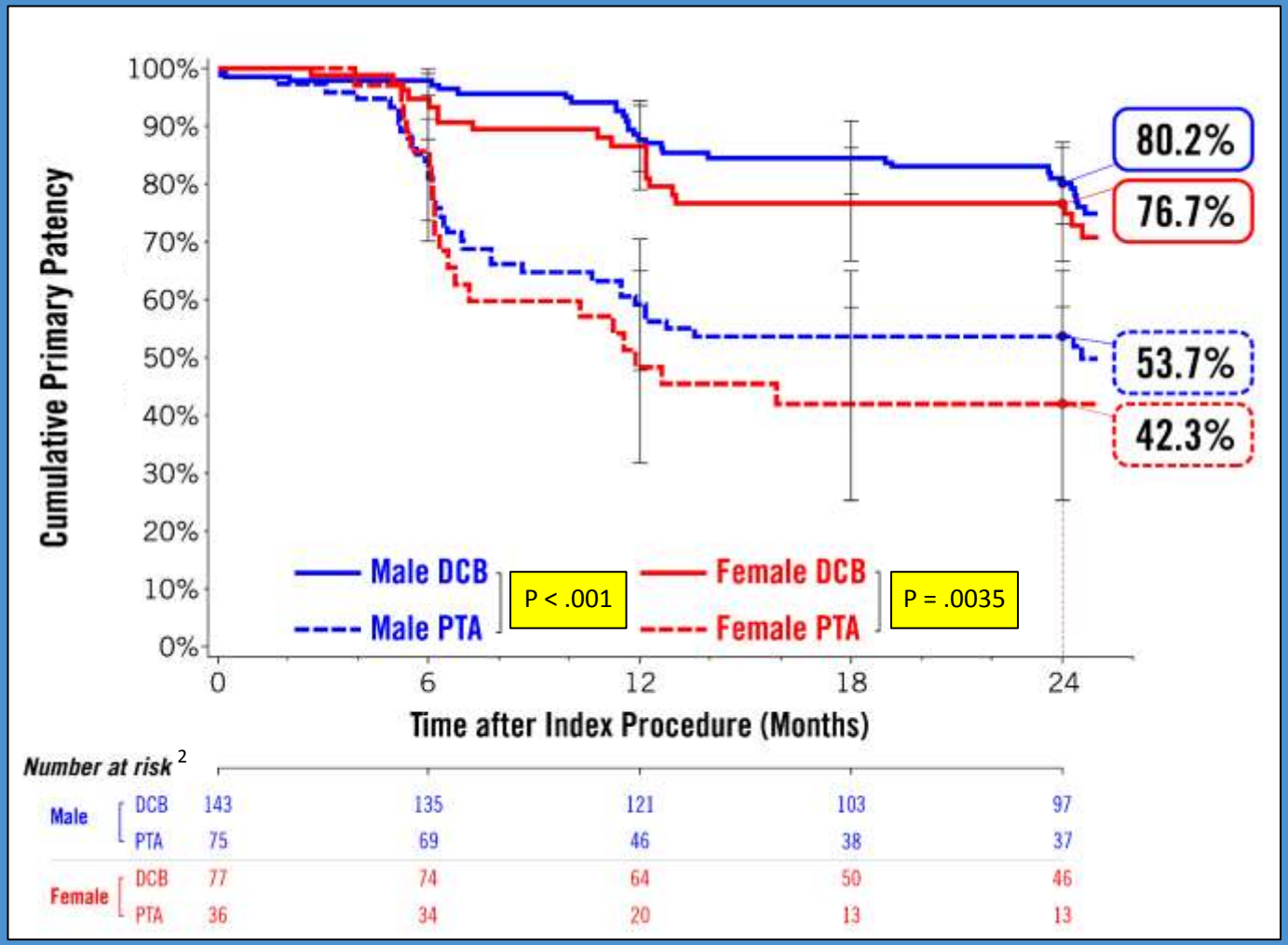
	Male			Female		
	DCB (N=143 Subjects) (N=144 Lesions)	**PTA (N=75 Subjects) (N=77 Lesions)**	**P-Value**	**DCB (N=76 Subjects) (N=77 Lesions)**	**PTA (N=36 Subjects) (N=36 Lesions)**	**P-Value**
Reference vessel diameter (mm)	4.785 ± 0.886	4.892 ± 0.771	NS	4.390 ± 0.682	4.229 ± 0.770	NS
Lesion length (cm ± SD)	9.08 ± 4.90	9.20 ± 5.22	NS	8.69 ± 4.90	7.97 ± 4.86	NS
Total occlusions	26.4%	22.1%	NS	24.7%	13.9%	NS
Calcification	63.9%	66.2%	NS	50.6%	41.7%	NS
Device success[1]	99.0%	97.7%	NS	99.1%	100.0%	NS
Procedure success[2]	99.3%	97.3%	NS	100.0%	100.0%	N/A
Clinical success[3]	98.6%	96.0%	NS	100.0%	100.0%	N/A

Schneider, P CharringCross 2016 presentation

1. Device success defined as successful delivery, inflation, deflation and retrieval of the intact study balloon device without burst below the RBP.
2. Procedure success defined as residual stenosis of ≤ 50% (non-stented subjects) or ≤ 30% (stented subjects) by core lab (if core lab was not available then the site-reported estimate was used).
3. Clinical success defined as procedural success without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or TVR) prior to discharge.

Primary Patency[1] Results through 2 Years

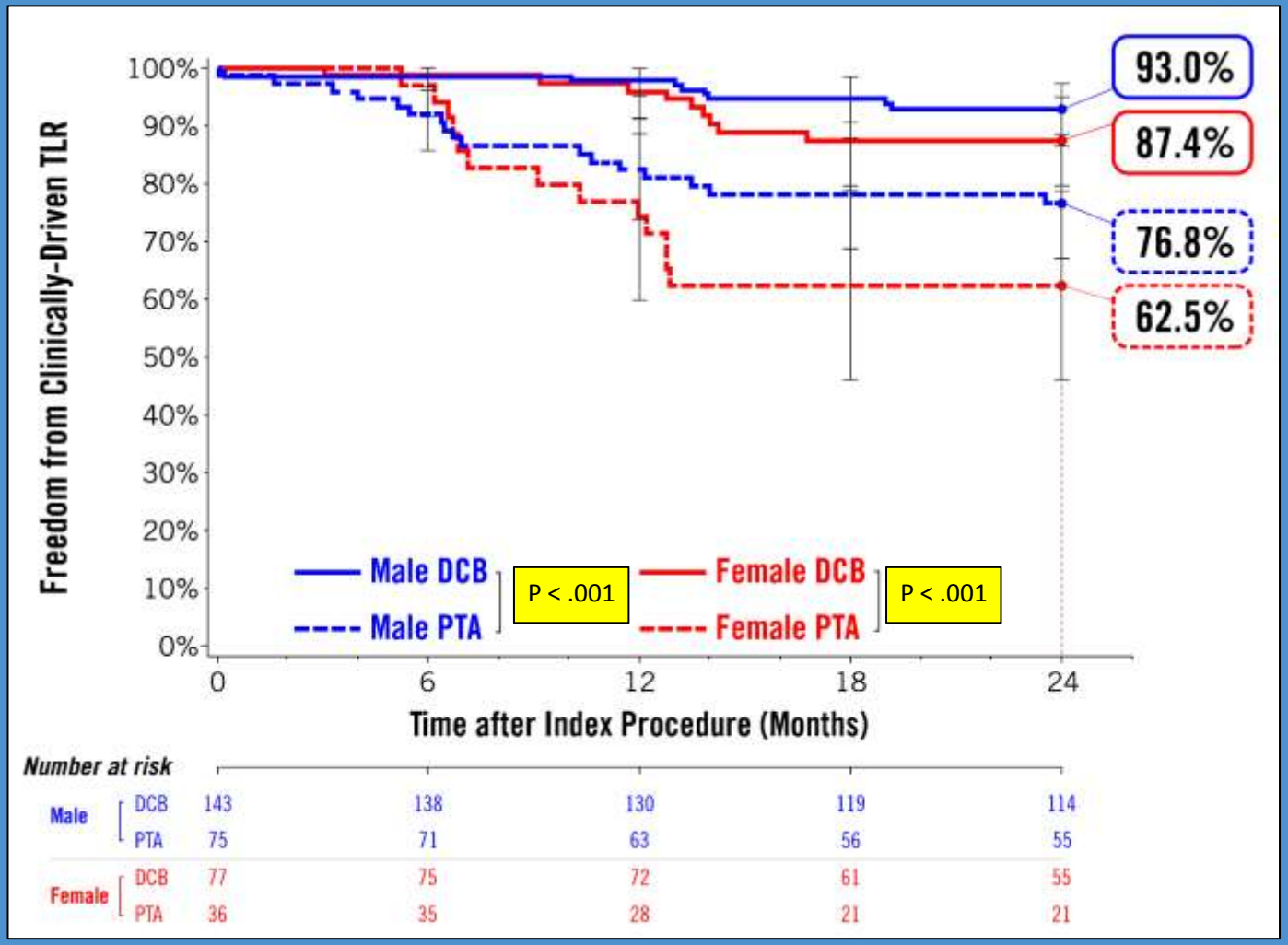
DCB Treatment is Effective in Both Male and Female Subgroups



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*

Freedom from CD-TLR at 2 Years

DCB Treatment is Safe in Both Male and Female Subgroups



Number at risk represents the number of evaluable subjects at the beginning of the 30-day window prior to each follow-up interval

Lesion/Procedural Characteristics by Diabetic Status

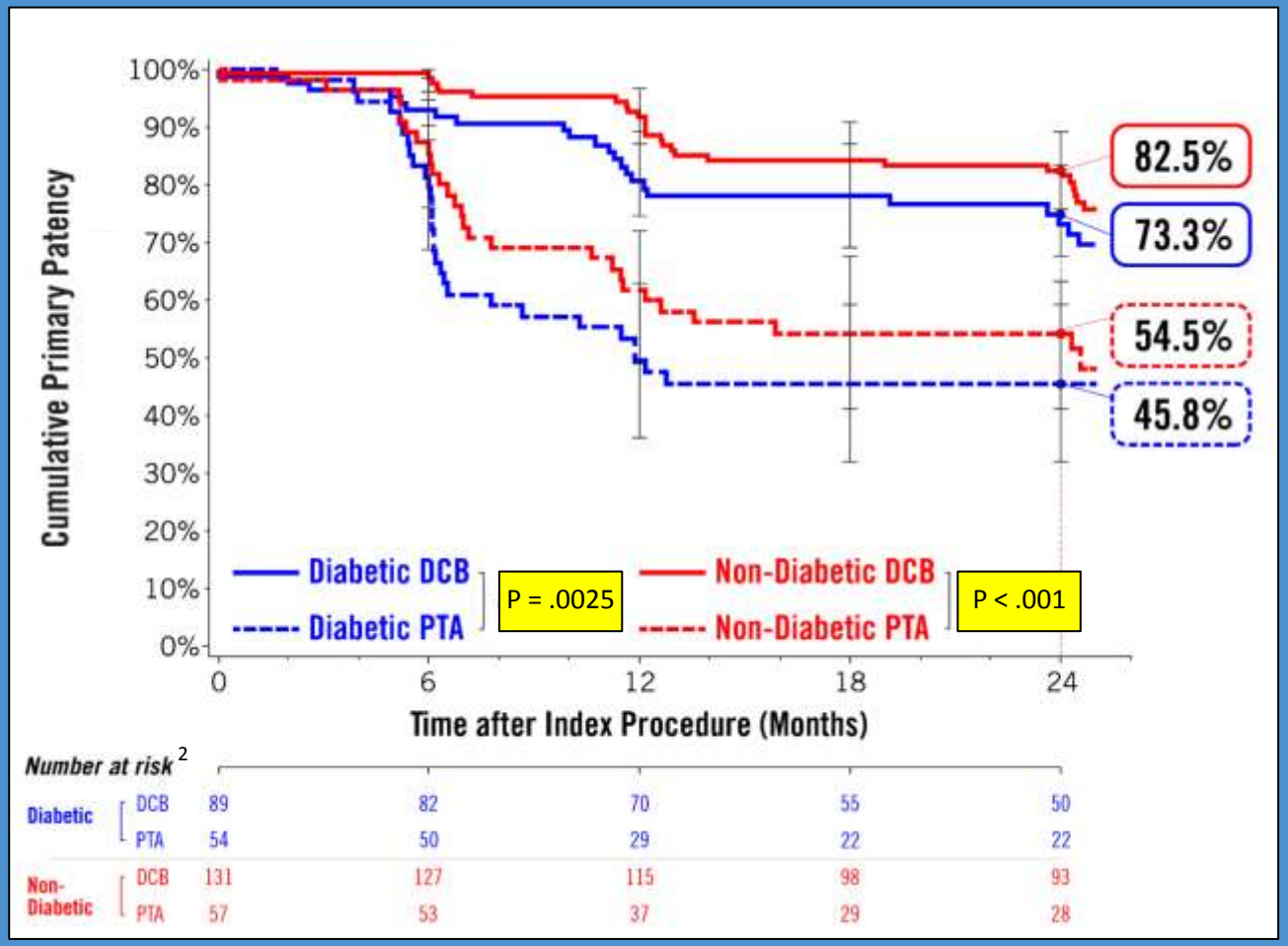
No Differences Between Groups

	Diabetic			Non-Diabetic		
	DCB (N=89 Subjects) (N=90 Lesions)	PTA (N=54 Subjects) (N=55 Lesions)	P-Value	DCB (N=130 Subjects) (N=131 Lesions)	PTA (N=57 Subjects) (N=58 Lesions)	P-Value
Lesion length (cm ± SD)	9.87 ± 5.21	9.34 ± 5.19	NS	8.31 ± 4.57	8.31 ± 5.04	NS
Total occlusions	20.0%	14.5%	NS	29.8%	24.1%	NS
Calcification	57.8%	61.8%	NS	60.3%	55.2%	NS
Severe calcification	7.8%	9.1%	NS	8.4%	3.4%	NS
Device success[1]	99.3%	98.4%	NS	98.9%	98.5%	NS
Procedure success[2]	100.0%	100.0%	N/A	99.2%	96.5%	NS
Clinical success[3]	98.9%	100.0%	NS	99.2%	94.7%	NS

1. Device success defined as successful delivery, inflation, deflation and retrieval of the intact study balloon device without burst below the RBP.
2. Procedure success defined as residual stenosis of ≤ 50% (non-stented subjects) or ≤ 30% (stented subjects) by core lab (if core lab was not available then the site-reported estimate was used).
3. Clinical success defined as procedural success without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or TVR) prior to discharge.

Primary Patency[1] Results through 2 Years

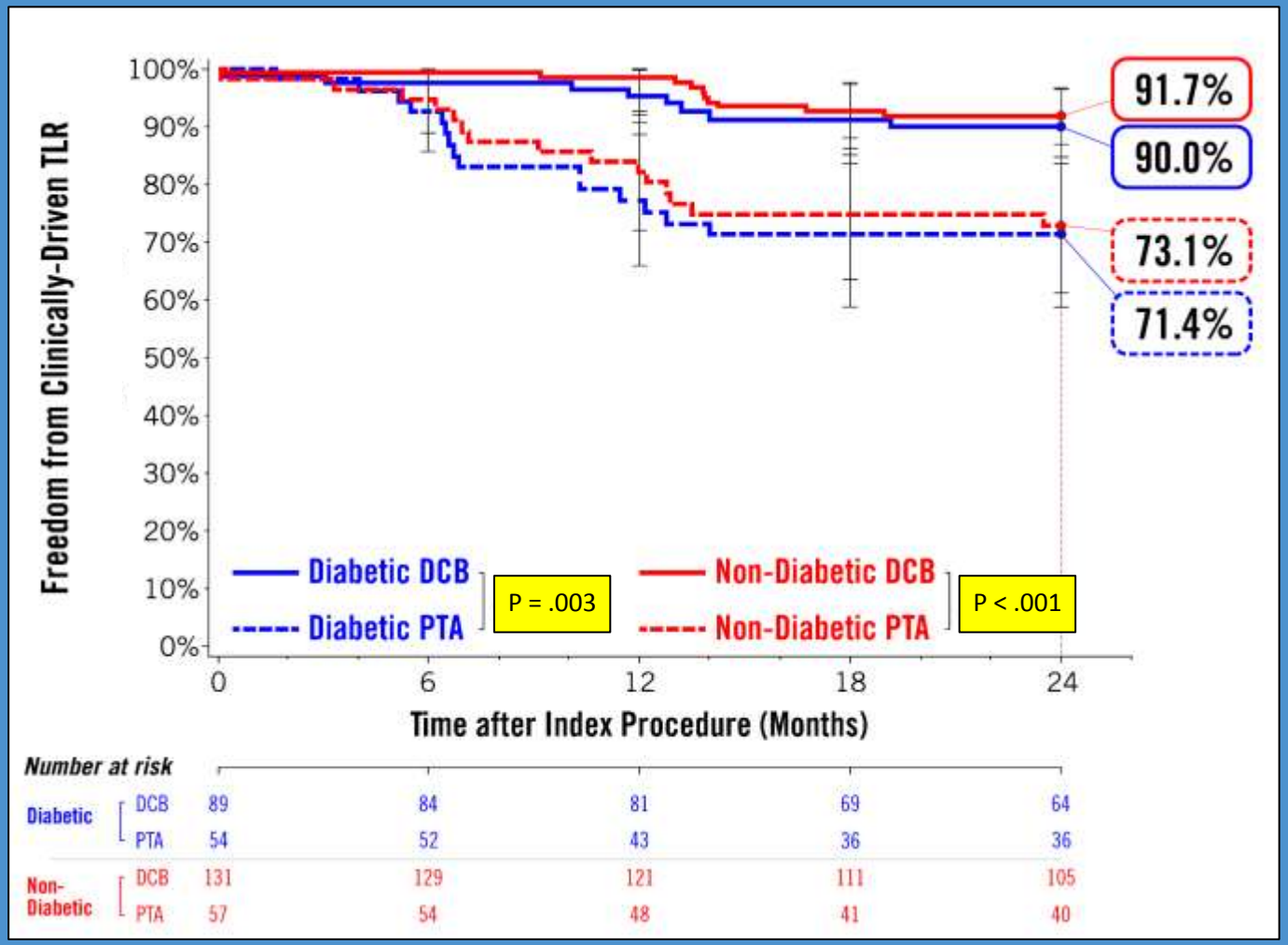
DCB Treatment is Effective in Patients With Diabetes



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*

Freedom from CD-TLR at 2 Years

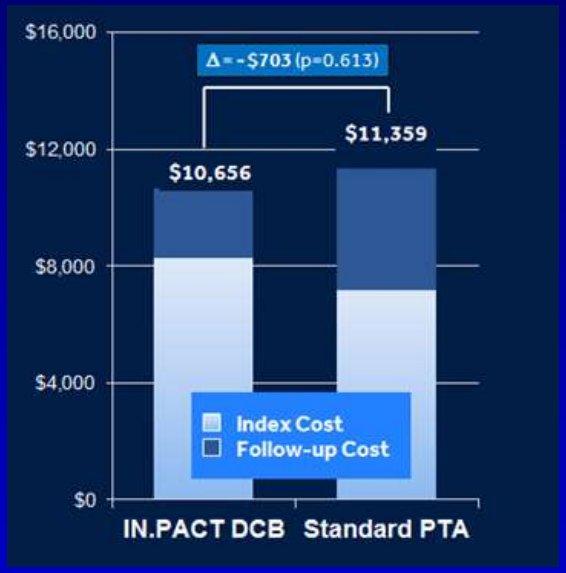
DCB Treatment is Safe in Patients With Diabetes



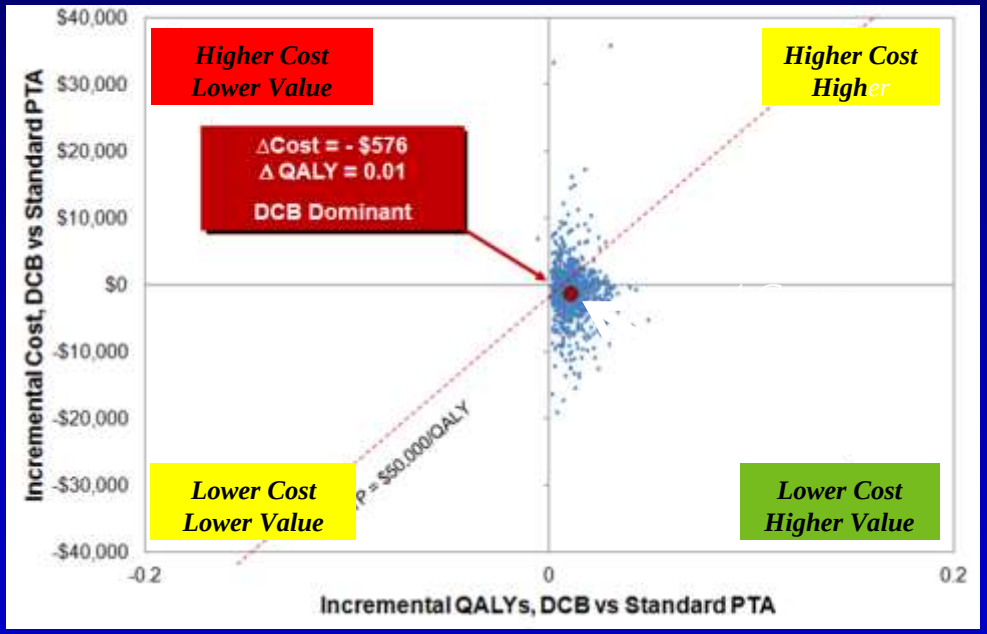
Number at risk represents the number of evaluable subjects at the beginning of the 30-day window prior to each follow-up interval

IN.PACT SFA Cost-Effectiveness study finds IN.PACT Admiral is cost-effective and "economically dominant" compared to PTA

Cost-Effective: Lower follow up costs for DCB exceed PTA's lower index costs



Economically Dominant: Providing Higher QALY with a Lower Cost compared to PTA



Cohen D. Late Breaking Clinical Trial Presentation, VIVA 2015

Lutonix Global SFA Real-World Registry Design

Enrollment

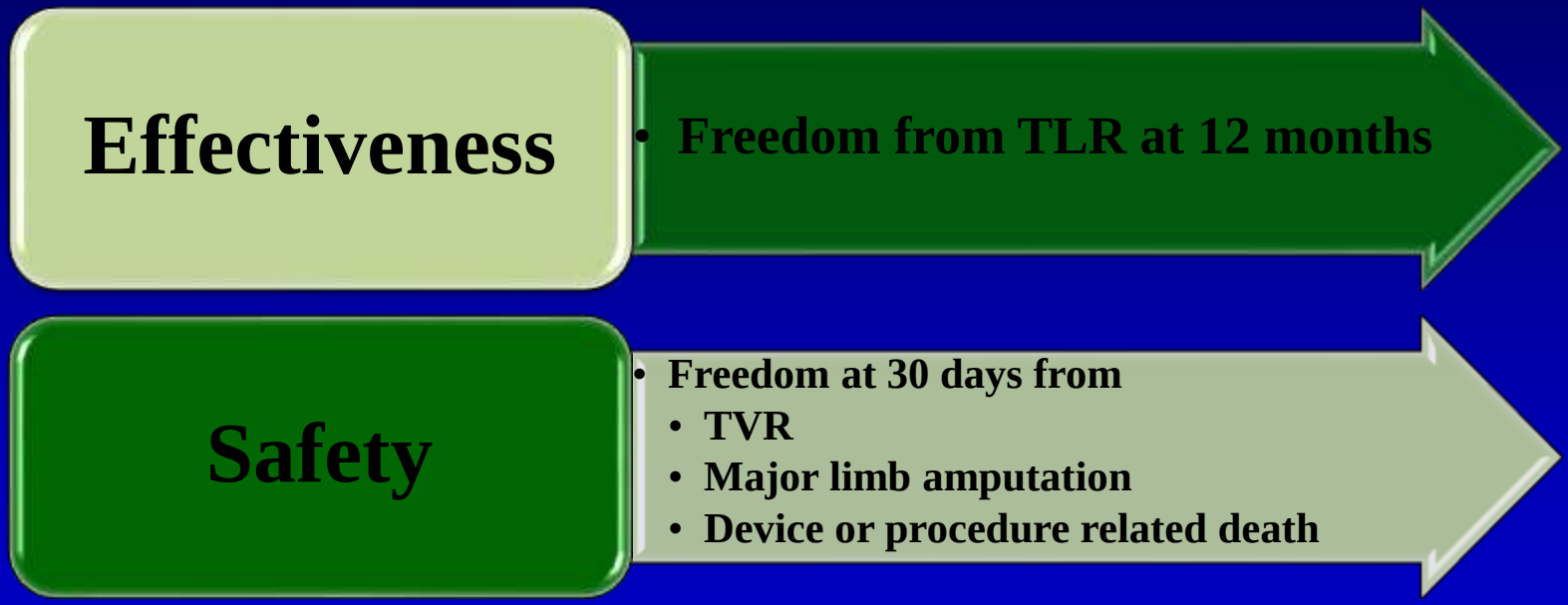
- Up to 1000 patients with femoro-popliteal lesions
- Registry to include up to 75 sites
- Follow up 1m, 6m, 12m and 24m by phone or at clinic
- Patient consent for 5 year F/U

All SAEs adjudicated
Study monitored

Inclusion

- Male or non-pregnant female ≥ 18 years
- Rutherford Class ≤ 4
- Stenotic or obstructive vascular lesions of the Fem-Pop artery treated per IFU
- At least one patent native outflow artery to the ankle free from significant lesion (≥ 50% stenosis) as confirmed by angiography

Lutonix Global SFA Real-World Registry Primary End Points



Lutonix Global SFA Real-World Registry

Lesion Characteristics

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)**
Number of Lesions treated %, (n/N)	
1	84.4% (583/691)
2	13.9% (96/691)
3 or more	1.7% (12/691)
Most Distal Lesion location %, (n/N)	
Proximal SFA	8.0% (55/690)
Mid SFA	24.8% (171/690)
Distal SFA	37.2% (257/690)
Proximal Popliteal	**16.8% (116/690)**
Mid Popliteal	**10.1% (70/690)**
Distal Popliteal	**3.0% (21/690)**

30%

Lutonix Global SFA Real-World Registry

12 Month Results

Measure	LUTONIX® DCB % (n/N)
Freedom from TLR	94.2% (599/636)
30 Day Safety	99.7% (678/680)

Lutonix Global SFA Real-World Registry

12 Month Secondary Outcomes

All Cause Death, % (n/N)	**2.5% (16/636)**
Major Index Limb Amputation, % (n/N)	**0.5% (3/632)**
Minor Index Limb Amputation, % (n/N)	**0.5% (3/630)**
Reintervention for Treatment of Embolization to the Distal Vasculature, % (n/N)	**0.5% (3/631)**
Reintervention for treatment of thrombosis of the target vessel, % (n/N)	**1.1% (7/631)**

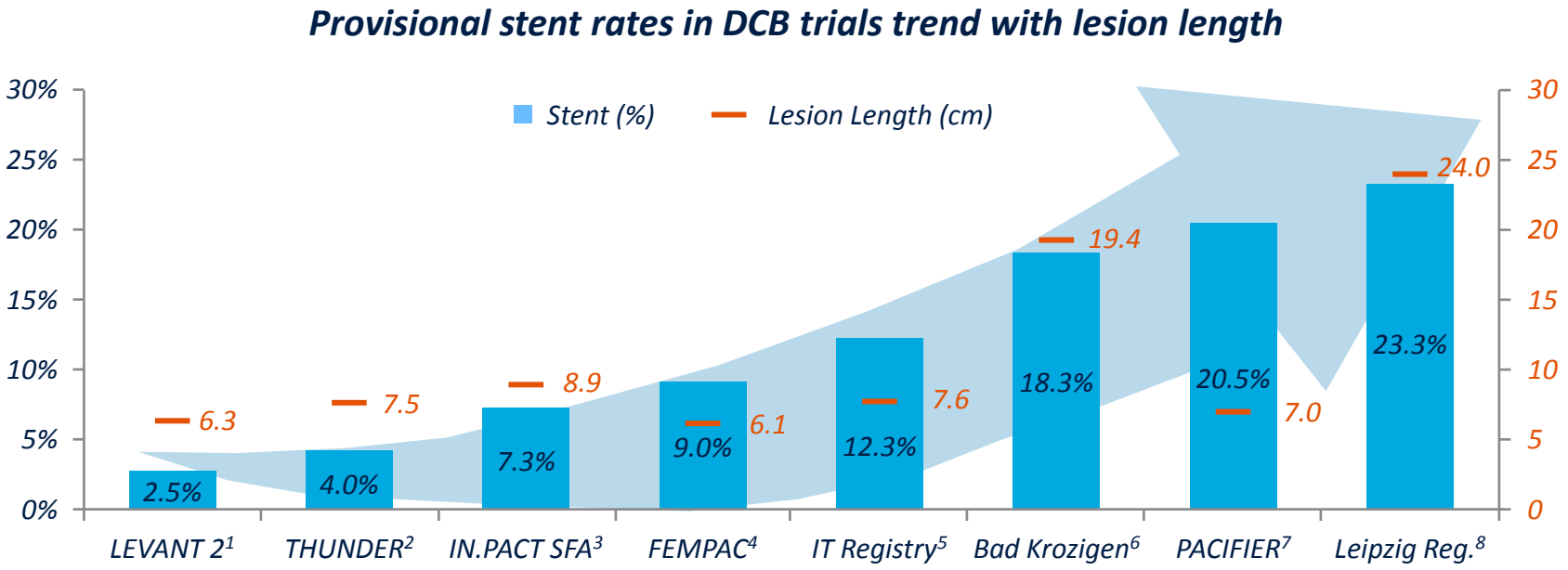
Baseline Lesion Characteristics
All Lesions vs Long Lesions (140 – 500 mm)

	All Lesions (23 – 500 mm)	Long Lesions (140 – 500 mm)
Total Lesion Length (mm)	101.2 ± 84.2 (685)	212.3 ± 65.3 (140)
Treated Length (mm)	136.6 ± 89.7 (685)	242.5 ± 83.3 (140)
Calcification, % (n/N)	50.2% (238/474)	57.5% (46/80)
Total Occlusion, % (n/N)	31.2% (214/686)	42.1% (59/140)
Lesion Locations, % (n/N)		
SFA, % (n/N)	70% (483/690)	66.5% (93/140)
Proximal Popliteal, % (n/N)	16.8% (116/690)	15.7% (22/140)
Mid & Distal Popliteal, % (n/N)	13.1% (91/690)	17.9% (25/140)
%DS post-treatment, %	14.6 ± 18.7 (680)	19.0 ± 21.0 (140)
Bail-out Stenting, % (n/N)	25.2% (174/691)	35.7% (50/140)
Dissection, % (n/N)	30.1% (135/448)	42.1% (45/107)

12 Month Results
All Lesions vs Long Lesions (140 – 500 mm)

Measure	All Lesions % (n/N)	Long Lesions % (n/N)
Freedom from TLR	**94.2% (599/636)**	**93.0% (119/128)**
30 Day Safety	**99.7% (678/680)**	**100.0% (138/138)**

SCAFFOLDS STILL NEEDED, LIKELY AT RATES PROPORTIONAL TO LESION COMPLEXITY



1. Rosenfield K TCT 2013; 2. Tepe G et al. N Engl J Med. 2008; 3. Tepe CX 2014; 4. Werk M et al. Circulation. 2008; 5. Micari A et al. J Am Coll Cardiol Intv. 2012; 6. Zeller T CX 2013 oral presentation; 7. Werk et al. Circ Cardiovasc Interv. 2012; 8. Schmidt A LINC 2013 oral presentation

Conclusions

- DCB data remain strong for primary patency from RCT data
  - InPact at 24 months 74%
- Real world registries suggest consistent pattern of patency comparable to the RCT
  - Long lesions
  - CTO
  - Gender
  - Diabetes
- Caveat some data not core lab adjudicated
- Caveats are the stent use is much higher than the RCT
- For “real-world” patients we must understand these differences in applying the data to our patients