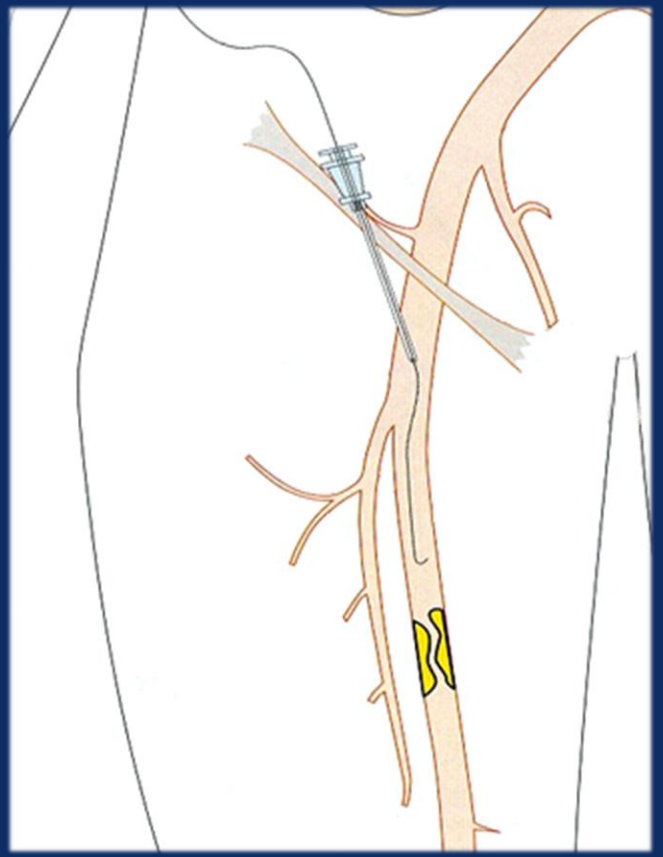
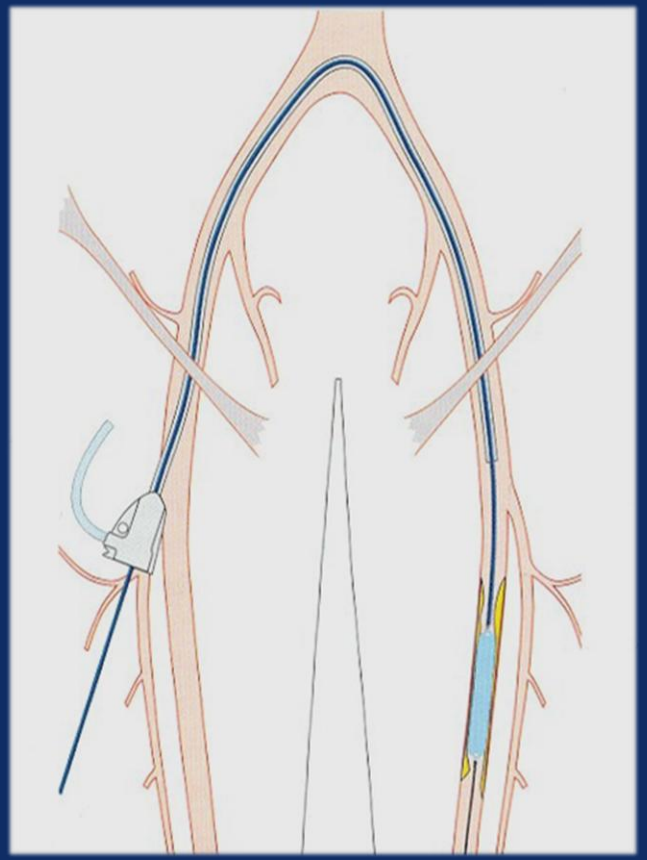
Femoropopliteal Intervention

Access for Treatment of SFA
Antegrade Access



- Distal lesions, very calcified lesions
- Better steerability and pushability
- Shorter devices and wires

Access for Treatment of SFA
Cross-over technique



- Easier punture
- Less complications
- Accessability of very proximal SFA lesions
- Compression bandage on the contralateral leg

Classification of femoropopliteal lesions *TASC*

Type A	• Single stenosis ≤ 10cm • Single occlusion ≤5cm		Endovascular
Type B	• Multiple lesions, Each ≤ 5cm • Single stenosis or occlusions ≤ 15cm, Not involving the infrageniculate popliteal artery • Single or multiple lesions in the Absence of continuous tibial vessels to improve inflow for a distal bypass • Heavily calcified occlusion ≤ 5cm • Single popliteal stenosis	 	Endovascular

Classification of femoropopliteal lesions *TASC*

Type C	• Multiple stenosis or occlusions totaling > 15cm with or without heavy calcification • Recurrent stenosis or occlusions that need treatment after two endovascular interventions		Endovascular or surgery depending on the risk benefit
Type D	• Chronic total occlusions of CFA or SFA (> 20cm, involving the popliteal artery) • Chronic total occlusion of popliteal artery and proximal trifurcation vessels		Surgery

Treatment strategies

Balloon angioplasty (PTA)

Stainless steel stent

Nitinol stent

Graft stent

Drug-eluting balloon (Paclitaxel)

Drug-eluting stent (Everolimus, Sirolimus or Paclitaxel)

Bio-degradable stent

Cryoplasty / Laser angioplasty

Atherectomy

Factors Influencing the Patency of SFA Interventions

Positive	Negative	Noncontributory
< 2 cm lesions	Occlusions	Age
Non-calcified	Segments stented > 10 cm	Race
> 3.5 mm diameter vessel	> 30% residual stenosis	
Non-smokers	Poor tibial run-off	
Low CRP	Creatinine > 1.3	

Guidewires for PTA

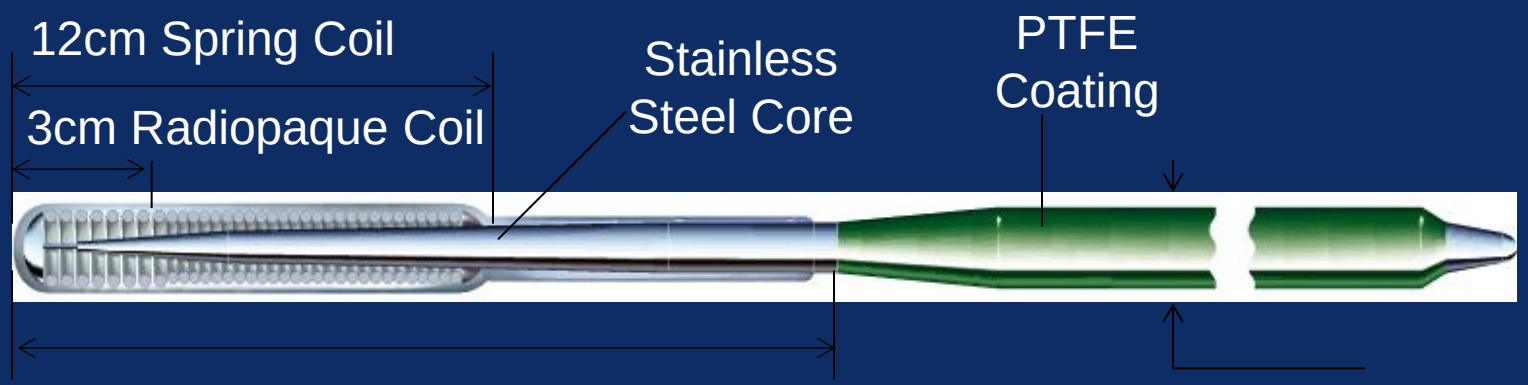
	Abbott	Asahi	Boston	Cook	Covidien
014	Command Command E S	Regalia XS Astato XS	Journey V-14 Victory 014	HydroST Approach CT O	Nitrex
018	Connect Connect Flex Connect 250 T	Treasure 12 Treasure Floppy Astato 30	V-18 Victory 018		

**Underline; CTO wires*

Guidewire Command

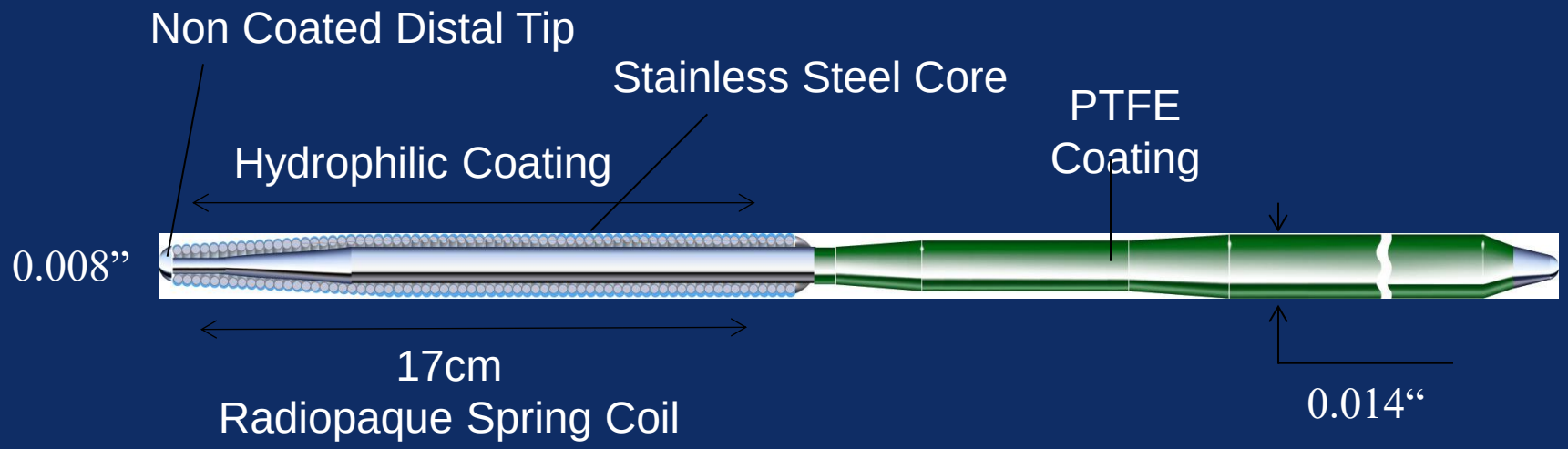
Wire	Command	Command ES
Shape		
Tip stiffness(g)	2.8	3.5
Tip diameter	014’	
Length(Cm)	190, 300	
Feature	stainless steel with nitinol tip	

Guidewire Regalia



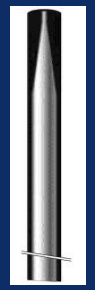
Tip Stiffness 1g
Length 180, 300 cm

Guidewire Astato 20

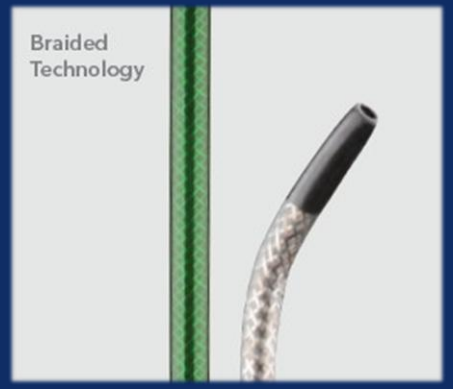


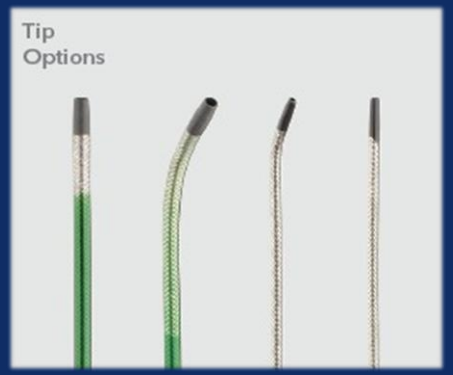
Tip Stiffness 20g
Length 180, 300 cm

Guidewire V-14, V-18

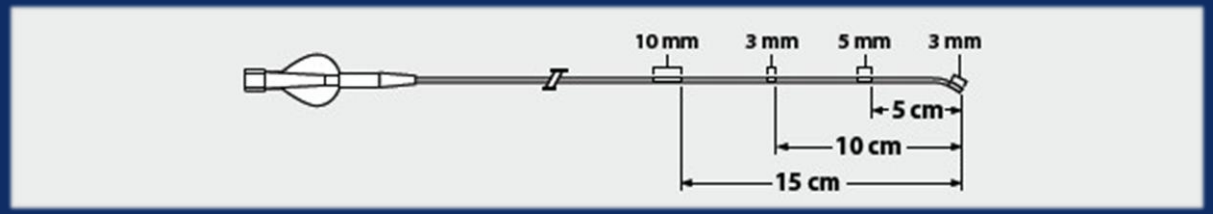
Wire	V-14	V-18
		
Tip Stiffness (g)	3 (long Taper) 6 (short Taper)	7.6 (Short Taper) 6.7 (Long Taper)
Tip Diameter (in)	014’	018’
Length (Cm)	145, 195, 300	145, 195, 300

Support Catheter CXI

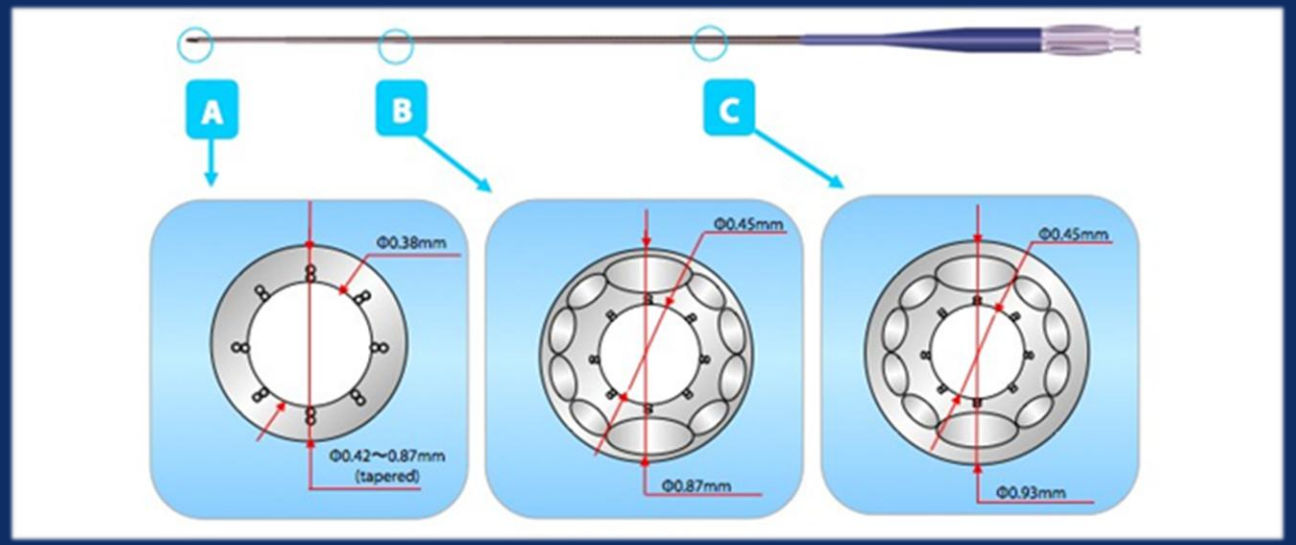




- Pushability with braided stainless steel shaft
- Hydrophilic coated distal part
- Tapered tip(0.018”) delivers great support to wire
- Diameter / length: 2.6Fr / 90 and 150cm
- Tip Configuration: straight or angled



Support Catheter Corsair



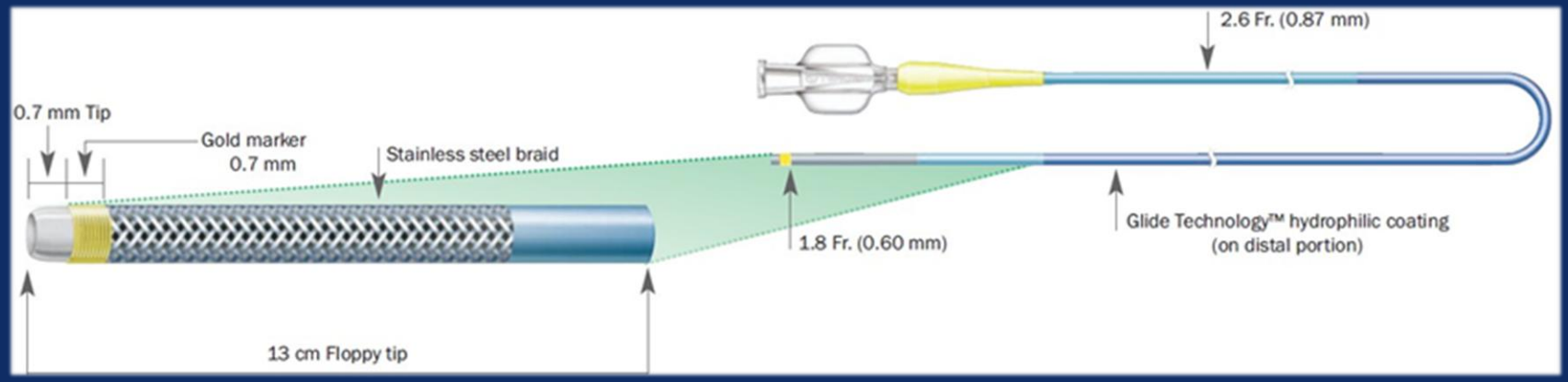
Pushability, Trackability, Support – SHINKA - Shaft

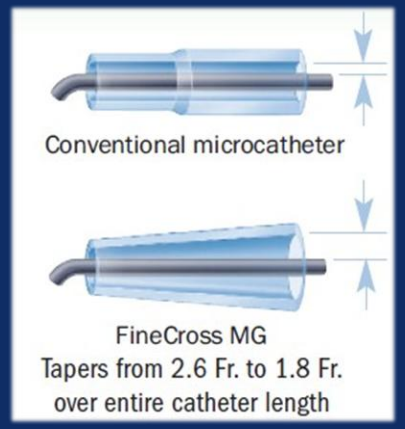
Lubricity - Hydrophilic Polymer Coating, PTFE Inner Layer

Maneuverability - Tapered Soft tip and Tungsten Braiding

Diameter / length: 2.6Fr / 135 and 150cm

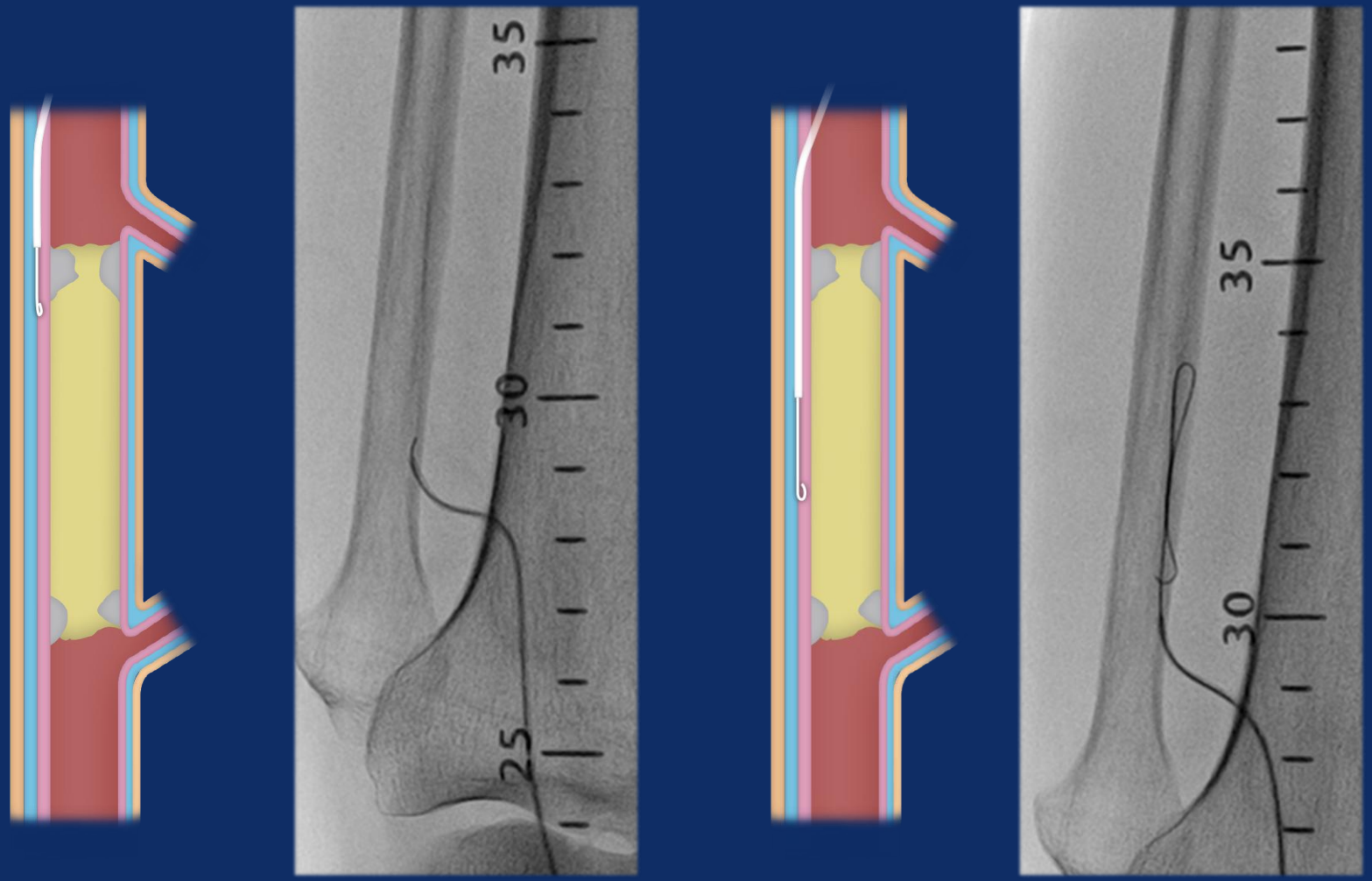
Support Catheter FineCross



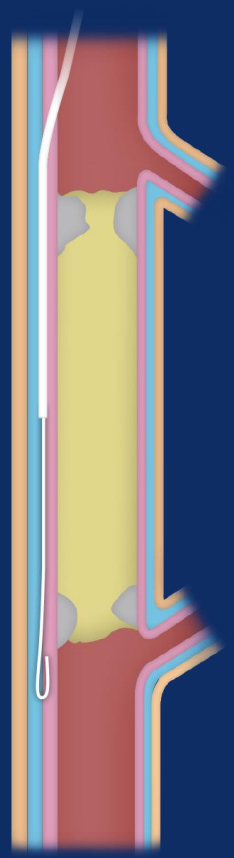


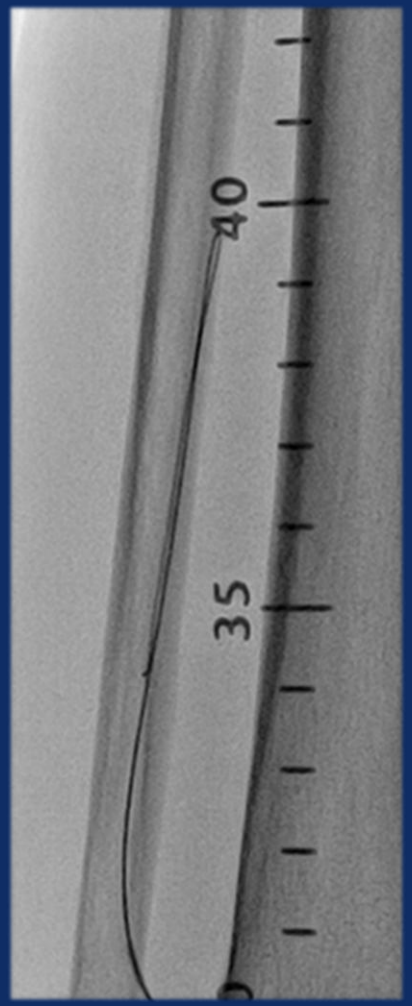
- Stainless steel braid structure
- Hydrophilic coating, PTFE inner layer
- Catheter length 130 cm / 150 cm
- Diameter / length: 2.6Fr / 130 and 150cm

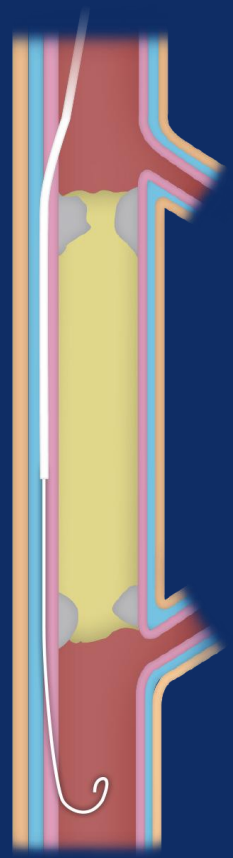
Subintimal Approach

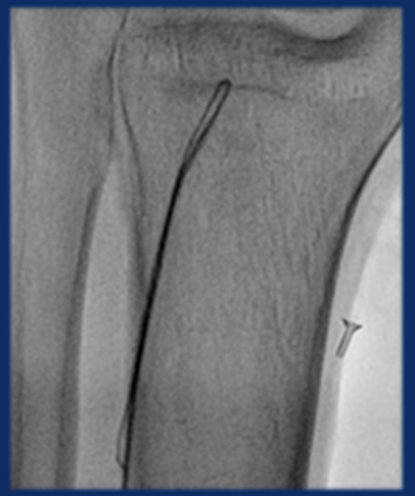


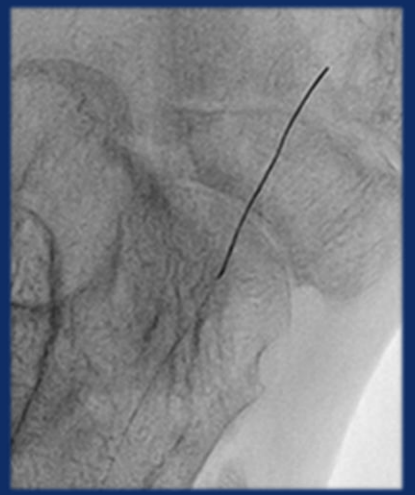
Subintimal Approach









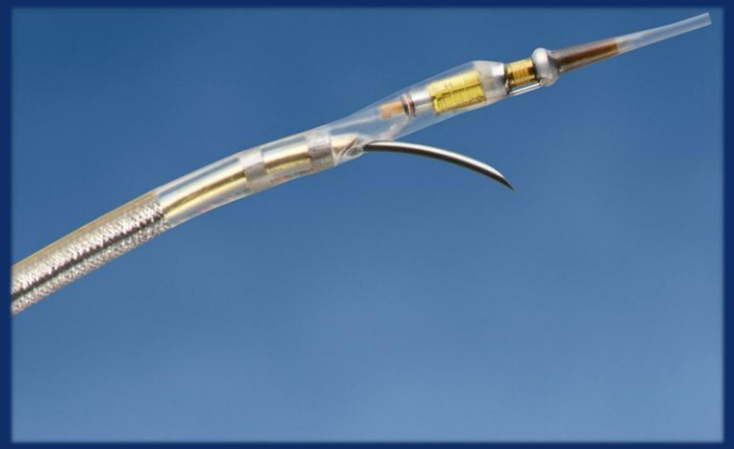


Re-entry Catheter

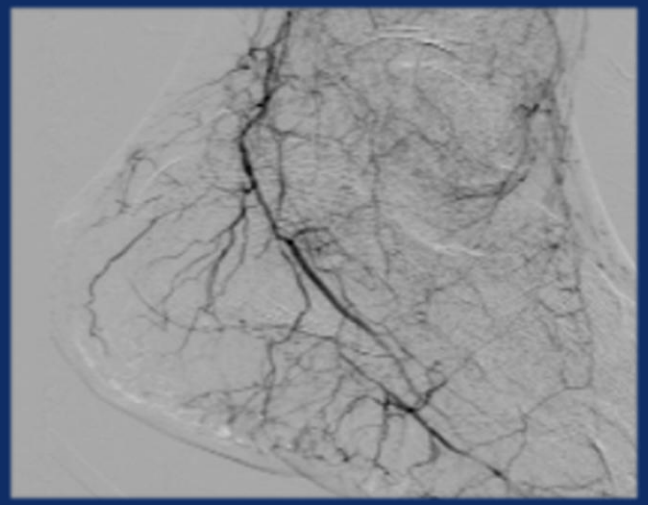
Re-entry catheter	Enter true lumen from subintimal space
Outback	Premounted needle on a 6 Fr catheter with fluoroscopic orientation
Pioneer	IVUS guided, premounted needle, orient needle to 12 o'clock, color flow in true lumen
Enteer	Flat balloon orients itself in subintimal space and points needle toward true lumen, 0.018 compatible
Offroad	Conical balloon 5.4 mm, when inflated points toward true lumen, microcatheter lancet

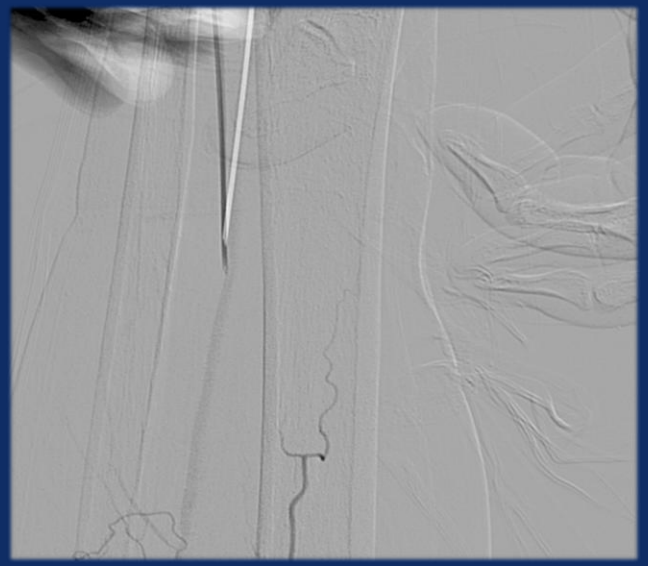
Schneider et al. J Vasc Surg 2013

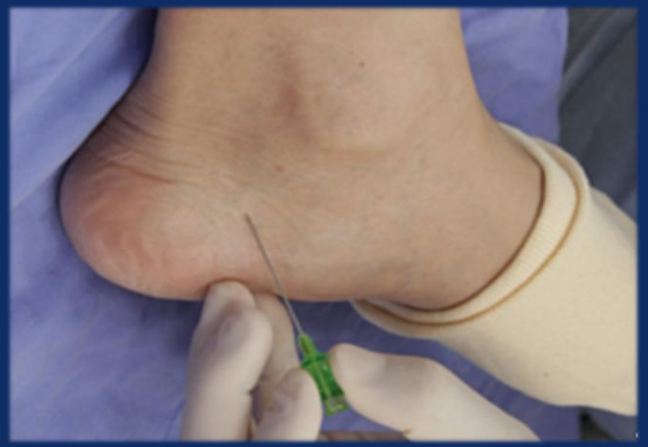
Re-entry Catheter

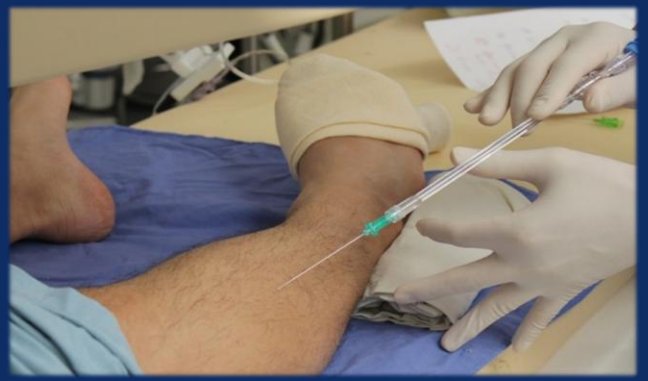
Pioneer	Outback
8F compatible 0.014” wire (2) IVUS-guided (Volcano)	6F compatible 0.014” wire (1 or 2) Fluoro-guided
	

Retrograde Puncture
Tibial Access

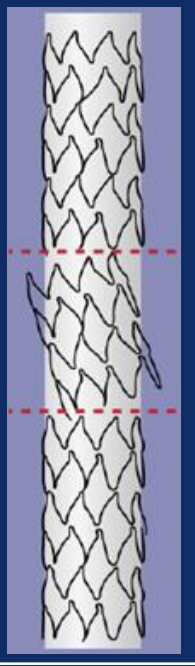








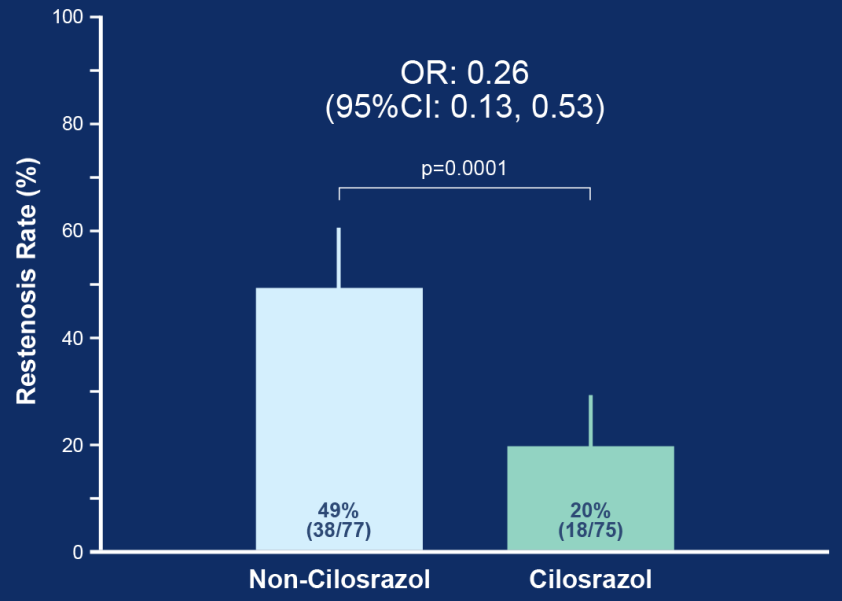
Stent Fracture

Type I	Type II	Type III	Type IV
			
Single stent fracture	Multiple single stent fracture, different site	Multiple single stent fracture, complete transverse linear fracture	Complete transverse linear Type III fracture with stent displacement

STOP-IC Aspirin vs. Aspirin + Cilostazol

After Endovascular Therapy; Randomized Study

12 Months Results of 77 without Cilostazol vs. 75 with Cilostazol



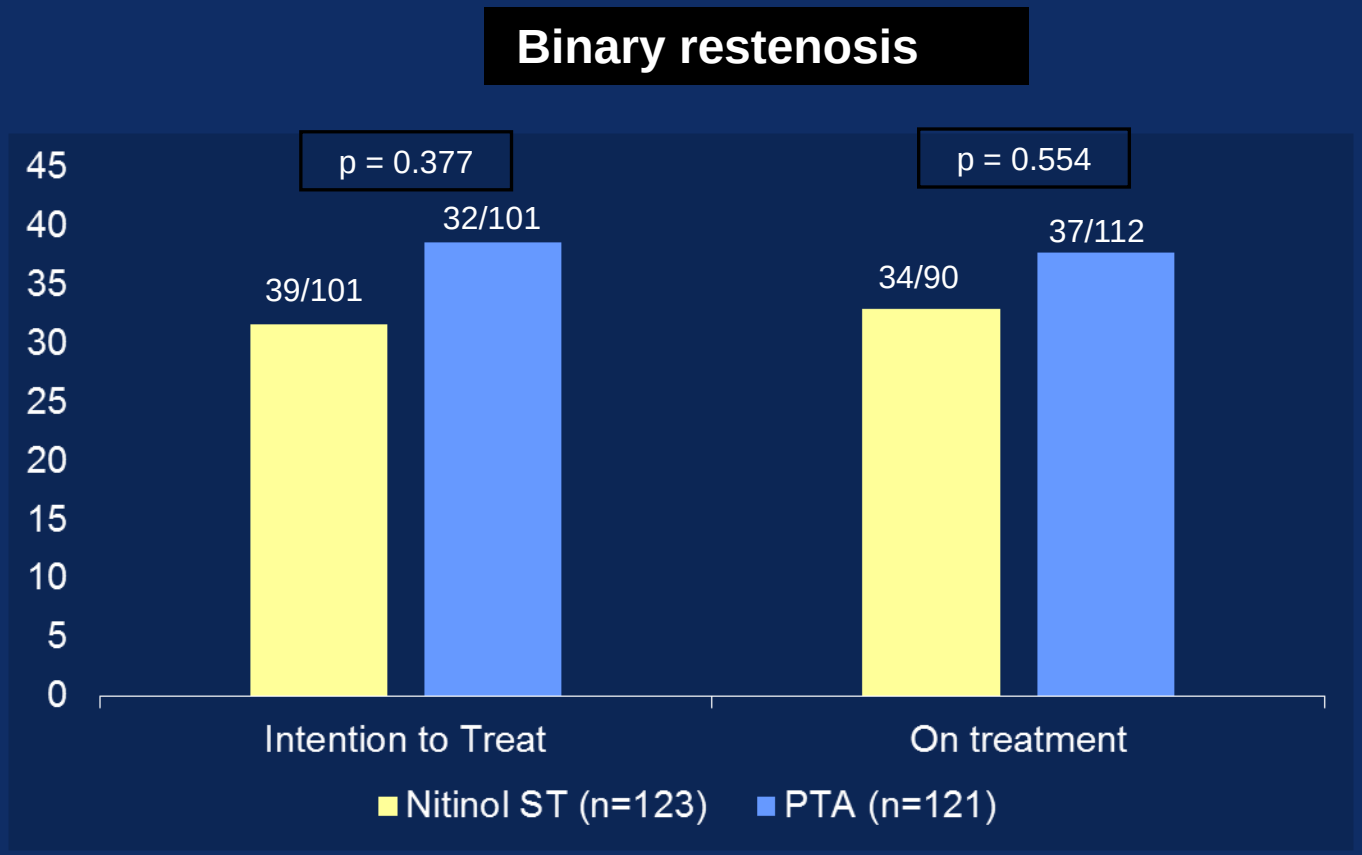
Conclusion Cilostazol reduced angiographic restenosis after percutaneous transluminal angioplasty with provisional nitinol stenting for femoropopliteal lesions.

Iida O et al. Circulation. 2013

FAST Nitonol Stent vs. PTA

SFA Lesions up to 10 cm

Lesion length 45mm ST vs. 44mm PTA



Krankenberg H et al. Circulation. 2007

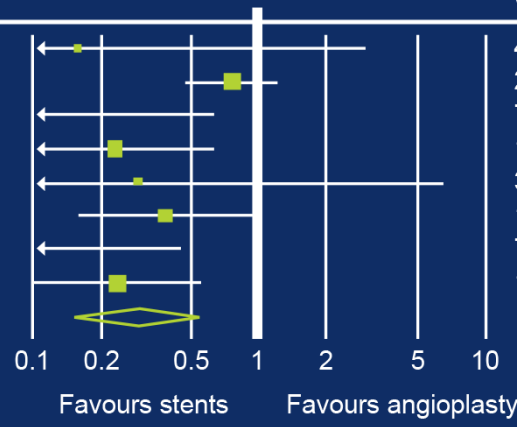
Routine vs. Provisional Stenting

Meta-Analysis of Randomized Trials

Lesion length 45.8mm ST vs. 43.3mm Provisional + PTA

Immediate technical failure

Study name	Stent type	Time point	Risk ratio	Lower limit	Upper limit	P-value	Failure / total: Stent	Failure / total: Angioplasty	Relative weight
Vroegindeweij	Palmaz	1997	0.16	0.01	2.95	0.218	0/24	3/27	4.2
IntraCoil	Nitinol	2001	0.77	0.48	1.25	0.291	25/177	32/175	24.1
Cejna	Palmaz	2001	0.08	0.01	0.63	0.016	1/77	12/77	7.5
Becquemin	Palmaz	2003	0.23	0.08	0.66	0.006	4/115	17/112	15.9
Saxon	Stent graft	2003	0.29	0.01	6.60	0.439	0/15	1/13	3.7
Vlabahn	Stent graft	2005	0.39	0.16	0.95	0.038	6/97	16/100	18.1
Schilinger	Nitinol	2006	0.06	0.01	0.44	0.006	1/51	17/53	7.7
Krankenberg	Nitinol	2007	0.24	0.10	0.56	0.001	6/123	25/121	18.7
Summary risk ratio			0.28	0.15	0.54	0.000			



Conclusion Despite the higher immediate success, routine stenting was not associated with a significant reduction in the rate of restenosis or TVR.

Kasapis C et al. Eur Heart J. 2009

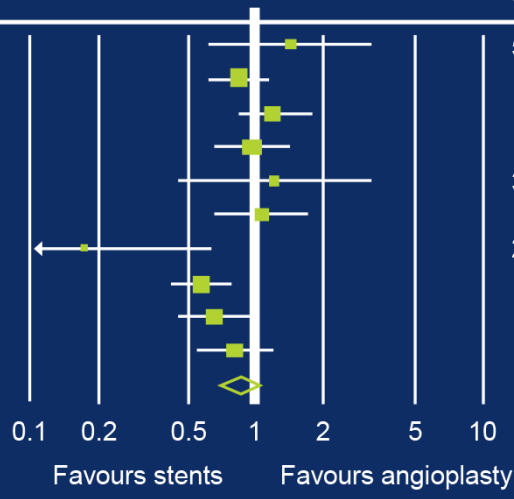
Routine vs. Provisional Stenting

Meta-Analysis of Randomized Trials

Lesion length 45.8mm ST vs. 43.3mm Provisional + PTA

Restenosis

Study name	Stent type	Time point	Risk ratio	Lower limit	Upper limit	P-value	Failure / total Stent	Failure / total Angioplasty	Relative weight
Vroegindeweij	Palmaz	1997	1.45	0.64	3.29	0.378	9/24	7/27	5.1
Zdanowski	Strecker	1999	0.86	0.63	1.16	0.321	10/12	8/8	14.3
IntraCoil	Nitinol	2001	1.22	0.84	1.78	0.288	40/97	31/92	12.6
Cejna	Palmaz	2001	0.98	0.66	1.46	0.929	26/56	26/55	12.0
Grimm	Palmaz	2001	1.23	0.46	3.26	0.682	8/30	5/23	3.9
Becquemin	Palmaz	2003	1.07	0.67	1.72	0.769	26/75	21/65	10.3
Saxon	Stent graft	2003	0.17	0.05	0.65	0.009	2/15	10/13	2.3
Vlabahn	Stent graft	2005	0.58	0.43	0.80	0.001	34/97	60/100	14.1
Schilinger	Nitinol	2006	0.66	0.46	0.95	0.025	21/46	36/52	12.8
Krankenberg	Nitinol	2007	0.82	0.56	1.20	0.304	32/101	39/101	12.5
Summary risk ratio			0.85	0.69	1.06	0.146			



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Kasapis C et al. Eur Heart J. 2009

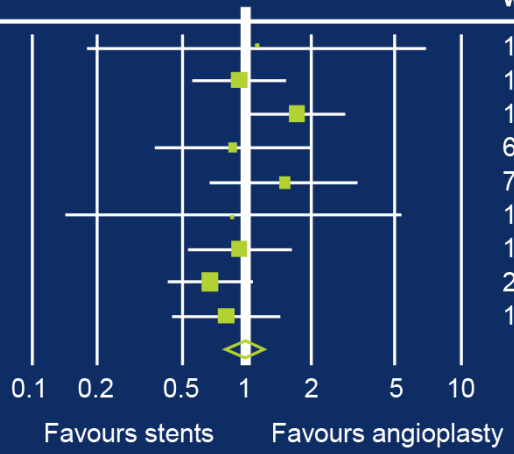
Routine vs. Provisional Stenting

Meta-Analysis of Randomized Trials

Lesion length 45.8mm ST vs. 43.3mm Provisional + PTA

Target vessel revascularization

Study name	Stent type	Time point	Statistics for each study: Risk ratio	Lower limit	Upper limit	P-value	Failure / total: Stent	Angioplasty	Relative weight
Zdanowski	Strecker	1999	1.13	0.18	7.09	0.894	2/15	2/17	1.5
IntraCoil	Nitinol	2001	0.93	0.56	1.54	0.771	24/146	25/141	17.2
Cejna	Palmaz	2001	1.75	1.03	2.96	0.037	28/77	16/77	16.2
Grimm	Palmaz	2001	0.88	0.37	2.06	0.762	8/30	7/23	6.6
Becquemin	Palmaz	2003	1.51	0.68	3.36	0.306	14/115	9/112	7.6
Saxon	Stent graft	2003	0.87	0.14	5.32	0.877	2/15	2/13	1.5
Vlabahn	Stent graft	2005	0.93	0.54	1.62	0.805	19/97	21/100	14.8
Schilinger	Nitinol	2006	0.69	0.44	1.08	0.104	17/46	28/52	21.0
Krankenberg	Nitinol	2007	0.82	0.46	1.47	0.497	17/114	21/115	13.5
Summary risk ratio			0.98	0.78	1.23	0.889			



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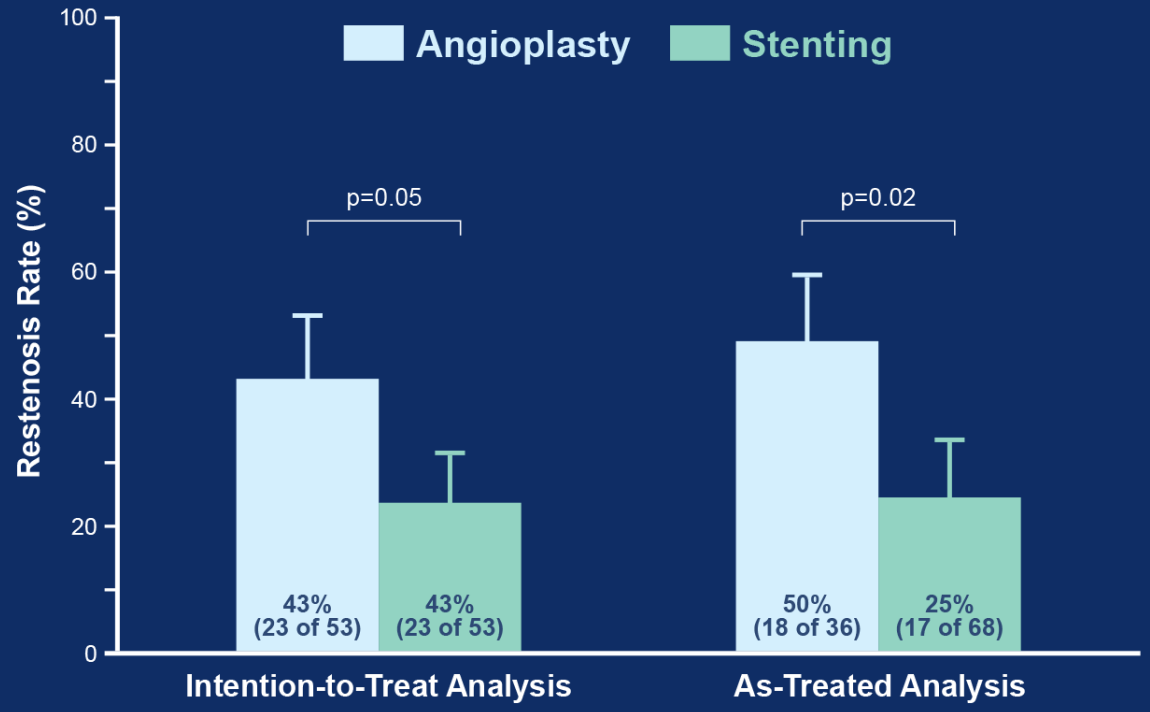
Kasapis C et al. Eur Heart J. 2009

Nitinol Stent vs. PTA Randomized

Intermittent Claudication and Chronic CLI of SFA

Lesion length 132mm ST vs. 127mm PTA



Schillinger M et al. NEJM. 2006

Nitinol Stent vs. PTA Randomized

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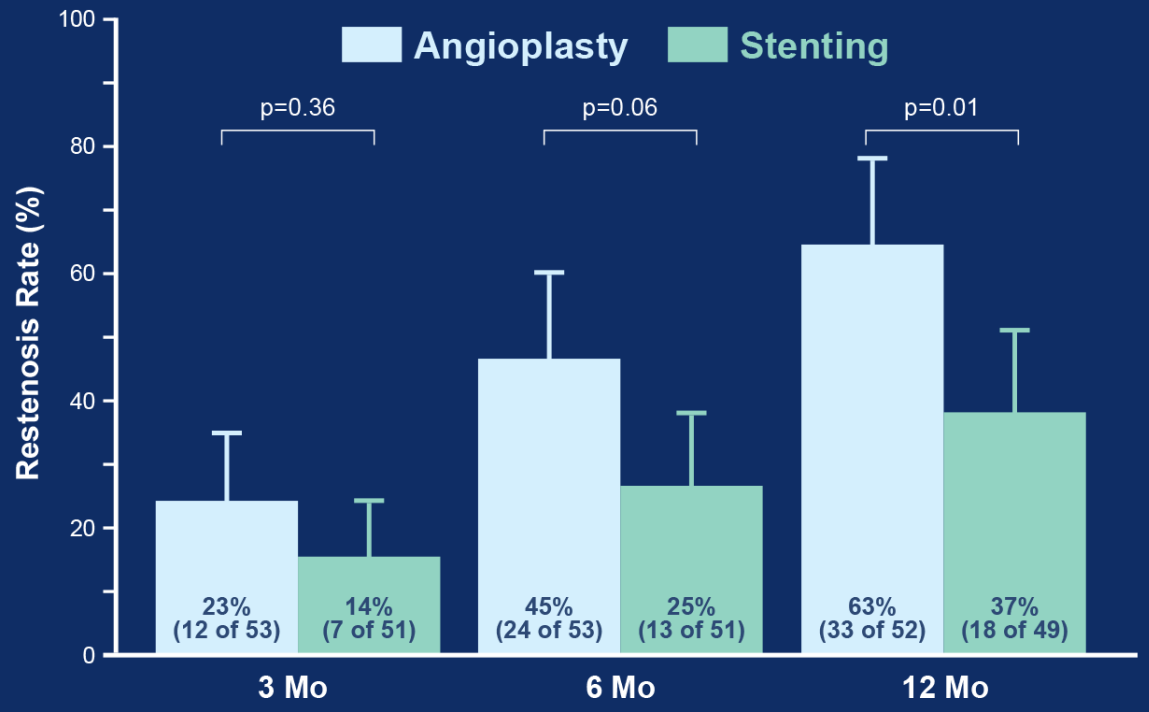
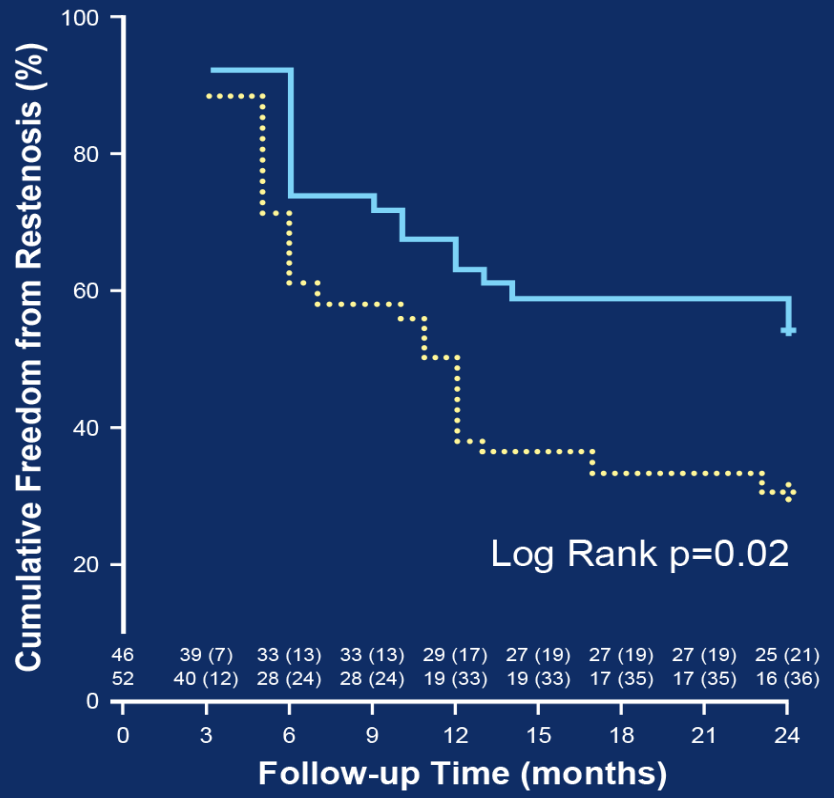


Schillinger M et al. NEJM. 2006

Primary ST vs. PTA with Optional ST

Sustained Benefit at 2 Years

Lesion length 112mm ST vs. 93mm PTA



Schillinger M et al. Circulation. 2007

Primary ST vs. PTA with Optional ST

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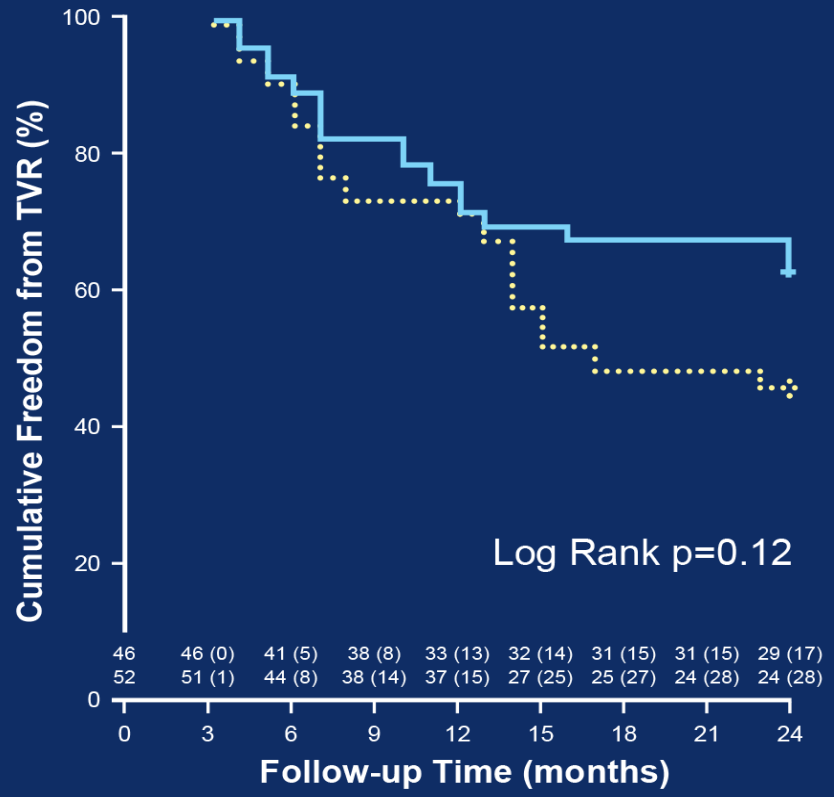
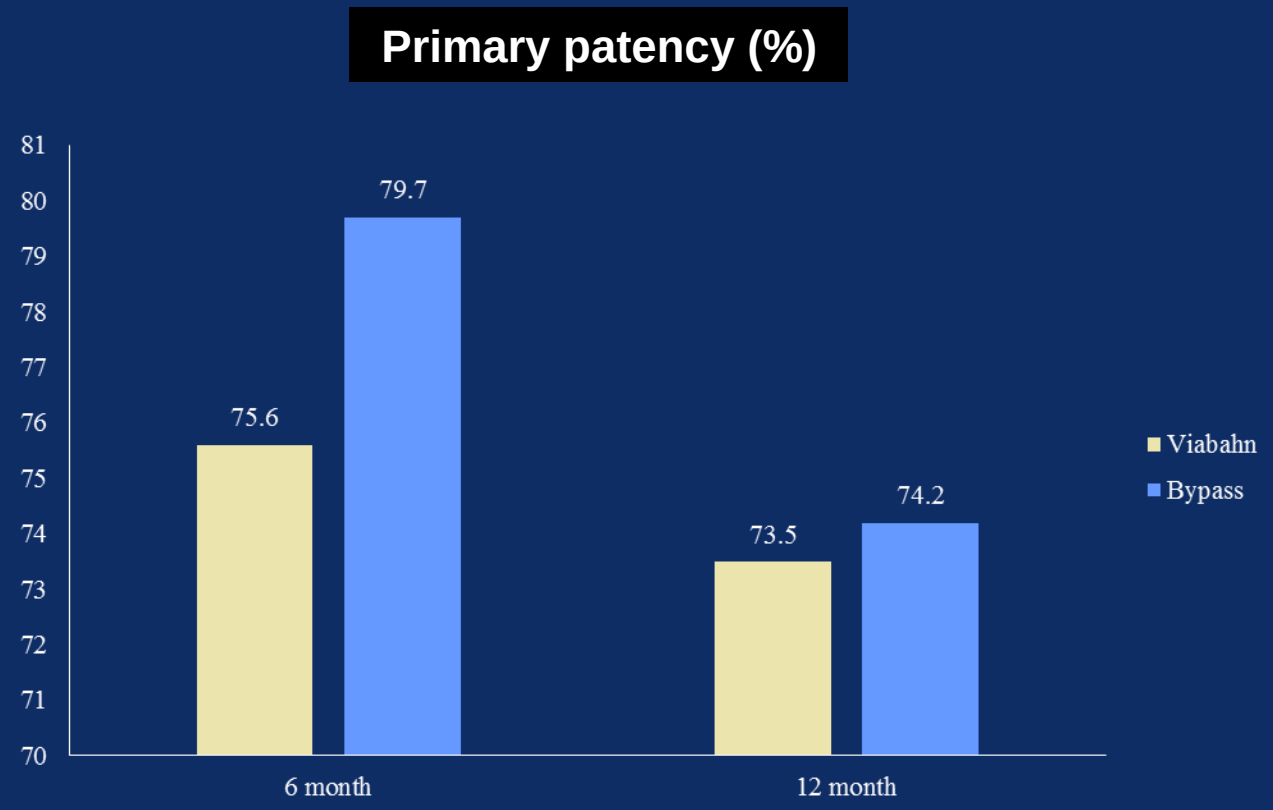


Schillinger M et al. Circulation. 2007

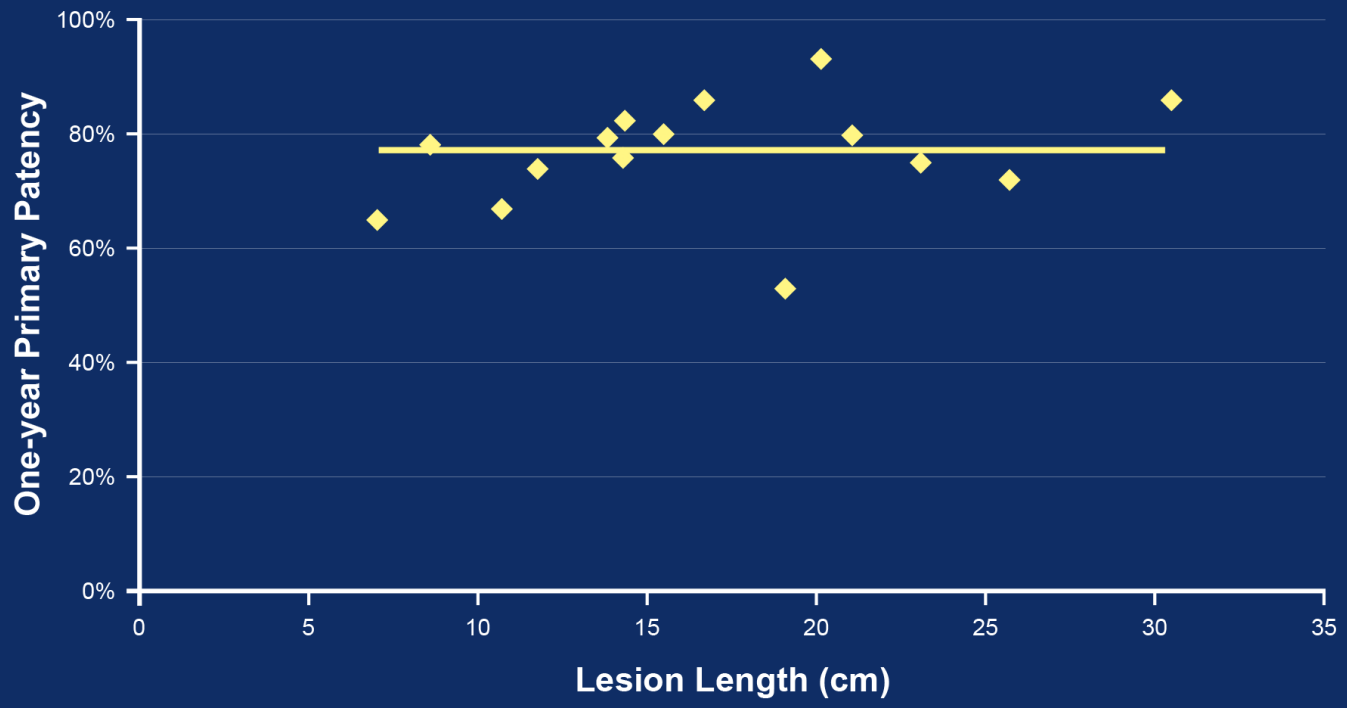
Viabahn Graft Stent

Stented length: 25.6±15 cm



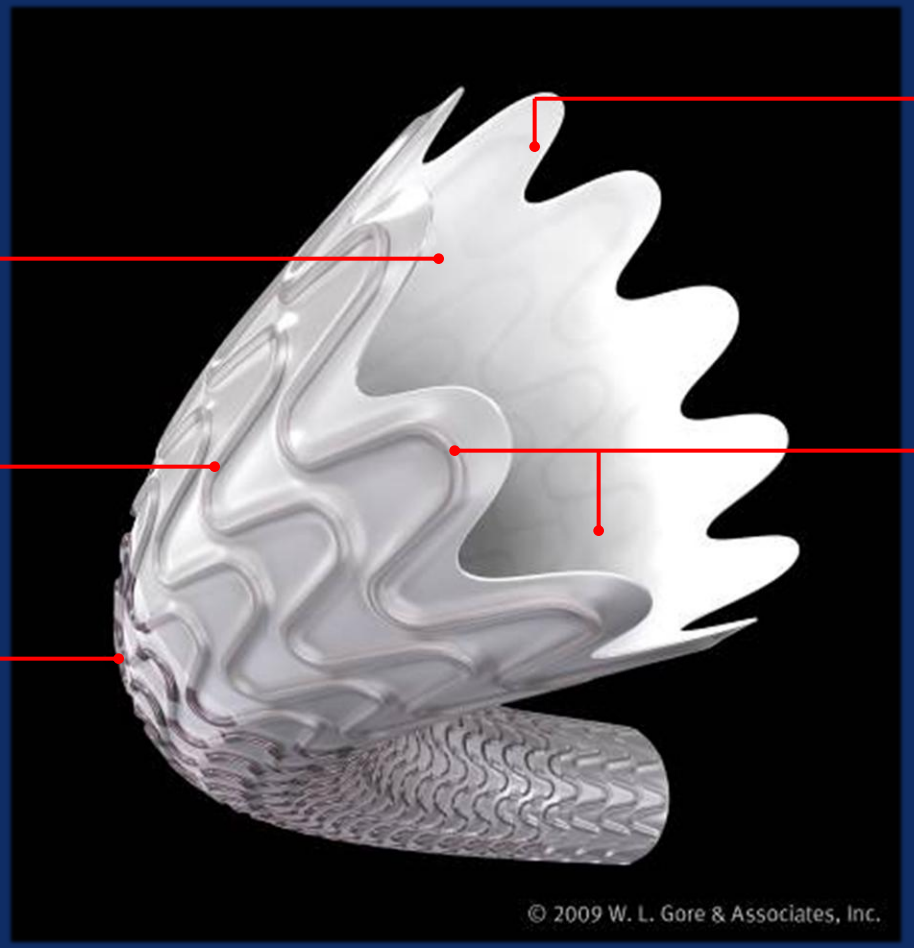
Jet K et al. J Vasc Surg. 2007

Viabahn 1-year Primary Patency
Based on Lesion Length
988 Limbs in 15 Independent Studies



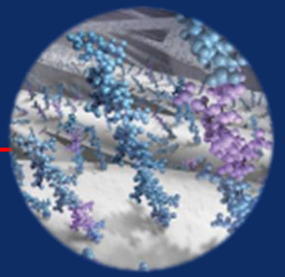
Patient demographics, lesion characterization, and patency definitions may differ among studies.
Studies include at least 30 limbs.

Endoprosthesis Description



Contoured proximal edge

Propaten Bioactive Surface



Ultra-thin wall ePTFE tube

Unique, durable bonding film

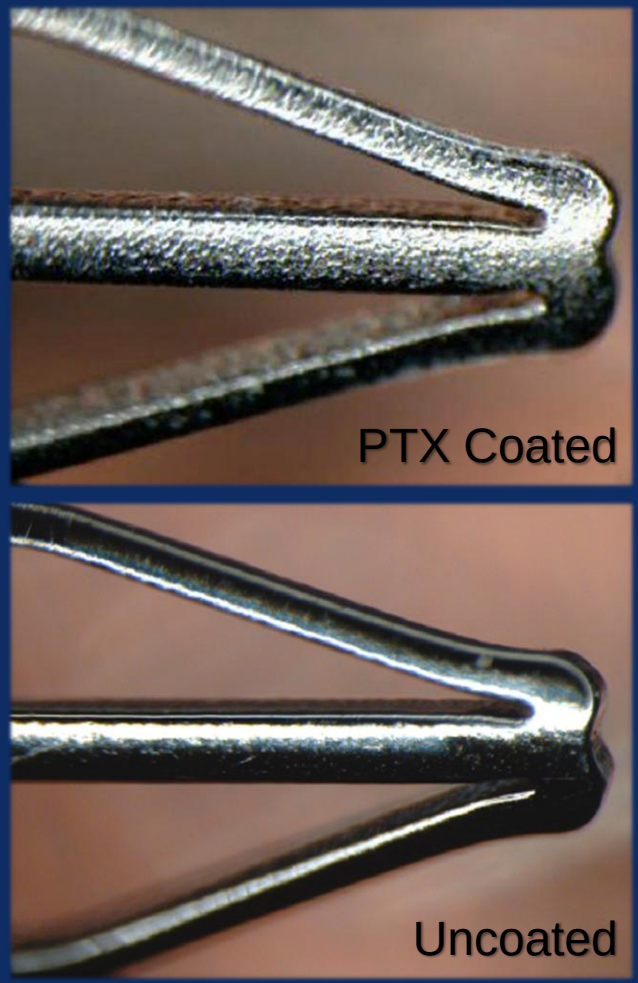
Polished nitinol support

Lengths:
2.5, 5, 10, 15 cm

Diameters:
5 – 13 mm

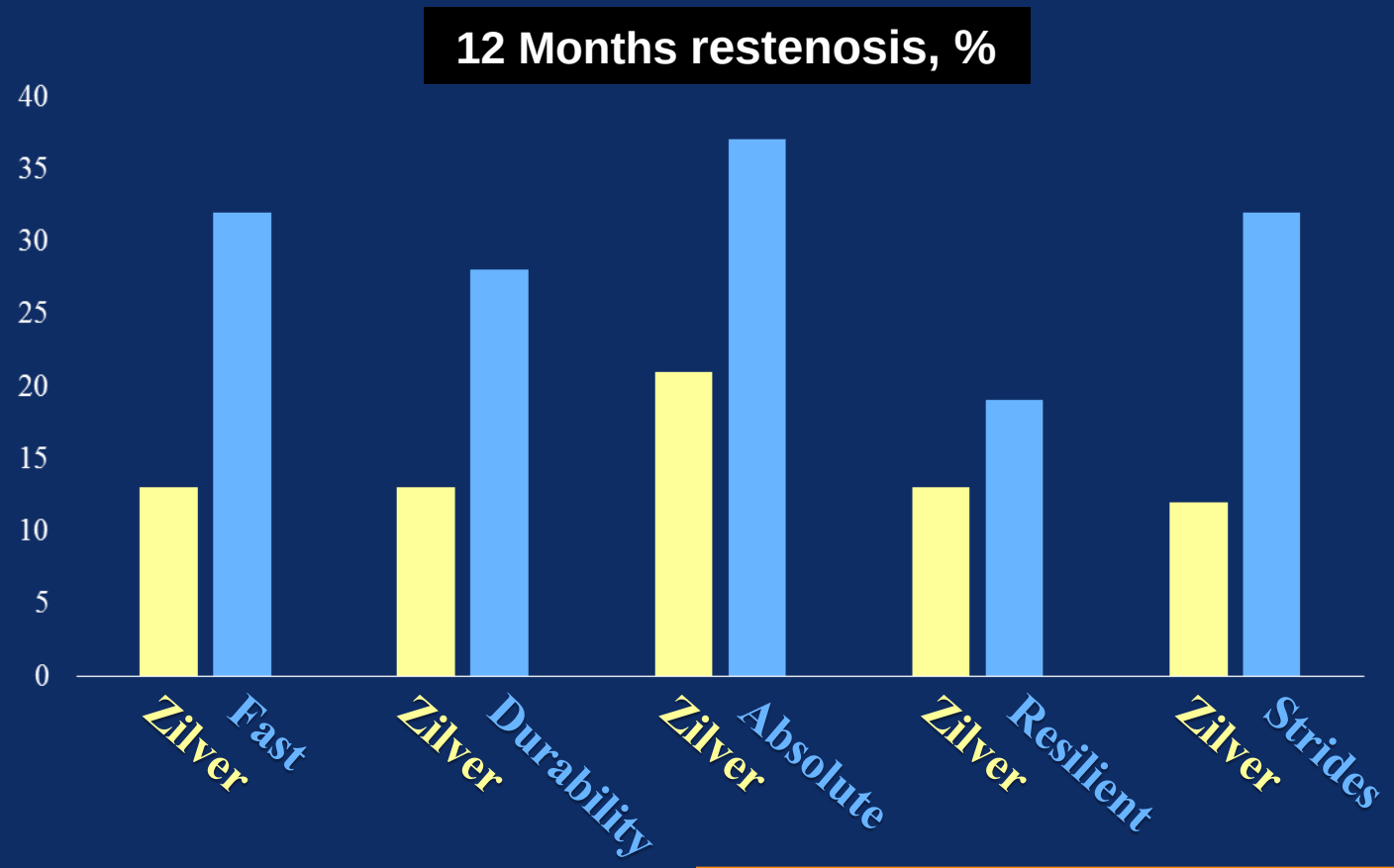
Zilver® PTX® Drug Eluting Stent

- Designed for the SFA
- CE Marked
  - Investigational in the US and Japan
- Dual therapy stent
  - Mechanical support:
  - Zilver® Flex™ Stent Plaftorm
  - coating: Paclitaxel only
  - No polymer or binder
  - 3 µg/mm^2 dose density
- Sponsor: Cook Medical



Zilver PTX for de novo Lesion

Matching comparison with other stent trials

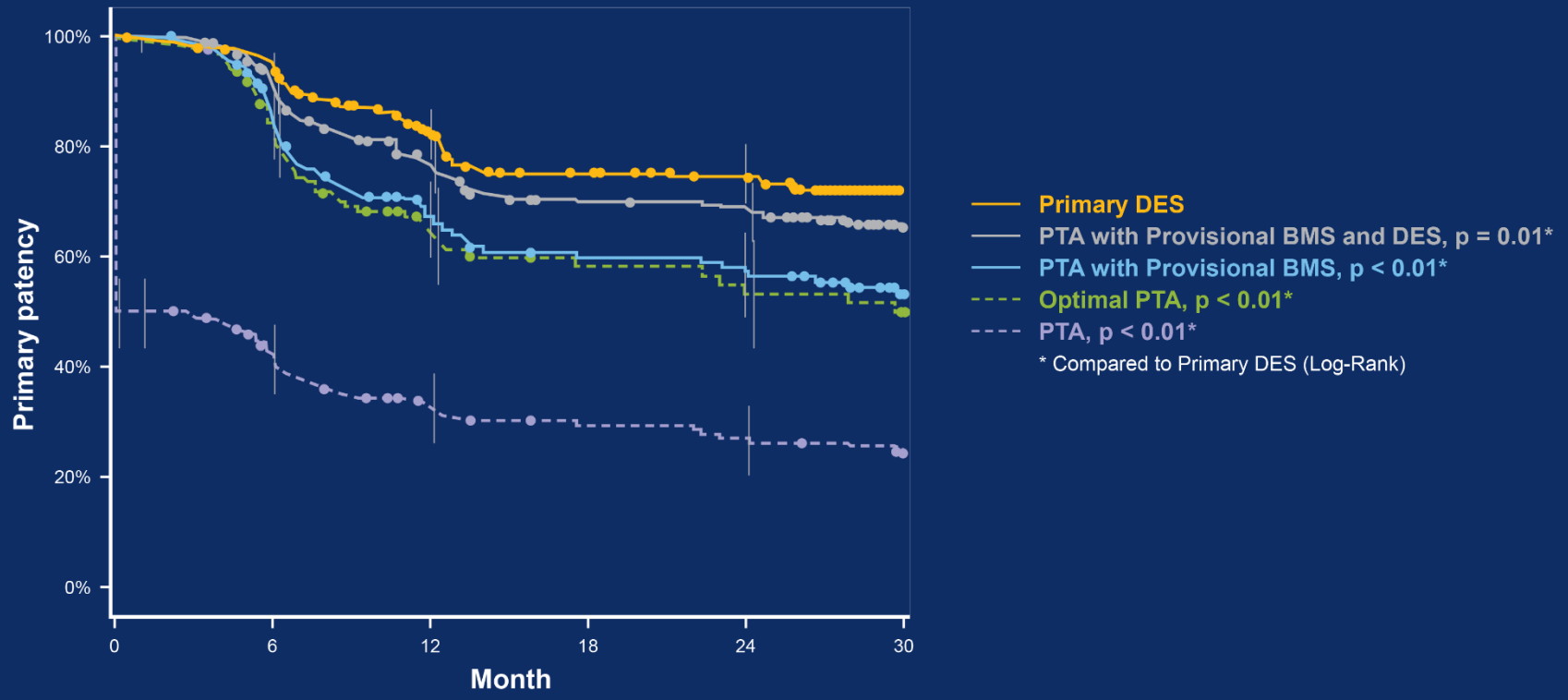


Dake MD et al. J Endovasc Ther. 2011

Zilver PTX vs. PTA/Provisional BMS

Randomized and Single-Arm Clinical Studies

2 Year Follow-Up of 236 Primary DES vs. 238 Primary PTA and 59 Provisional BMS vs. Provisional DES

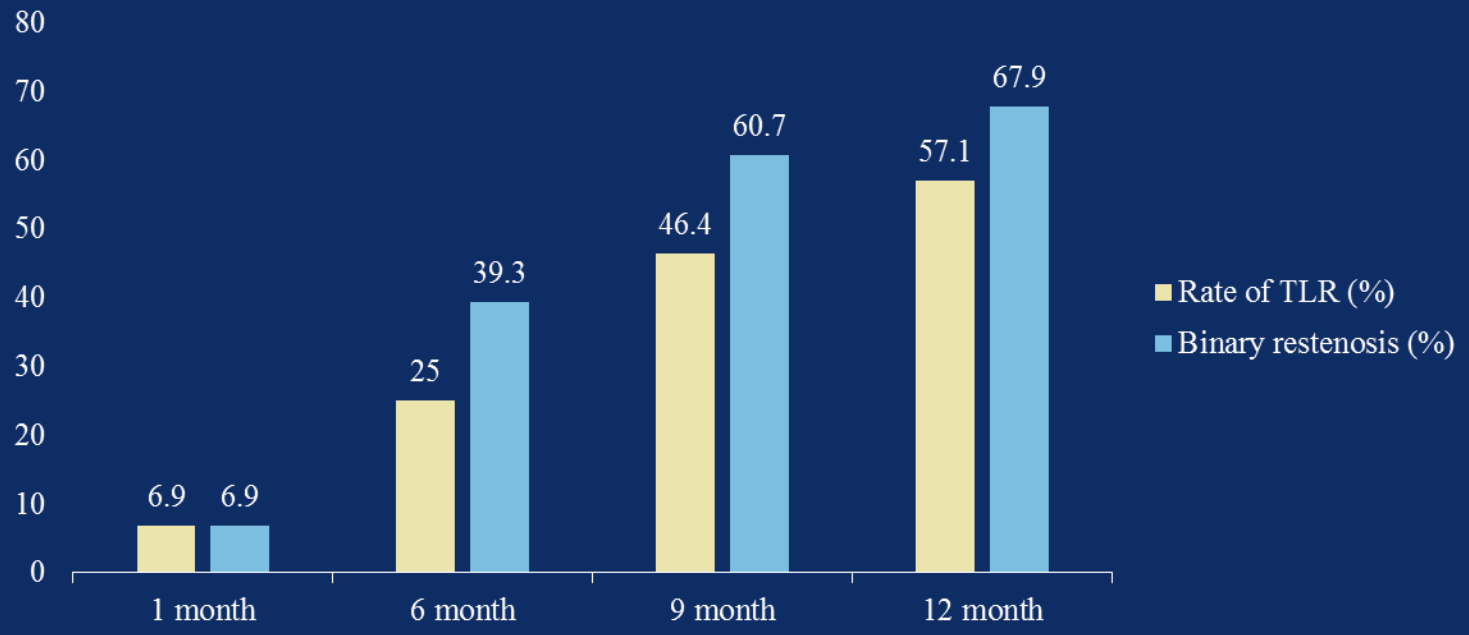


Dake MD et al. J Am Coll Cardiol. 2013

Biodegradable Igaki-Tamai Stent

First-generation PLLA fully Bioresorbable Stent

SFA de novo Lesions of 30 Patients



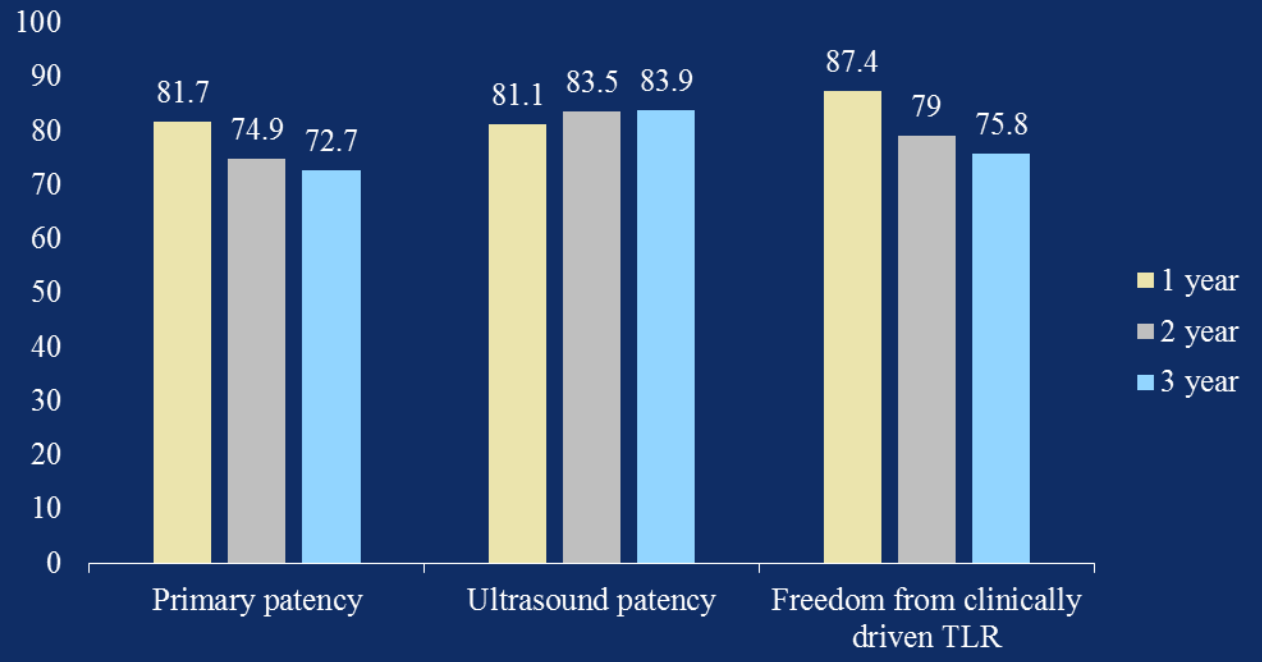
Conclusion The first fully bioresorbable stent shows angiographic results similar to those of metal stents in occlusive lesions of the SFA.

Werner M et al. JACC Cardiovasc Interv. 2014

SMART Nitinol Self-expanding Stent

Obstructive SFA Disease

3 year outcomes for 250 stented patients



Conclusion Patients treated with a Nitinol stent show sustained clinical and quality of life improvements at 3 years, with a low, 3.6% rate of stent fracture.

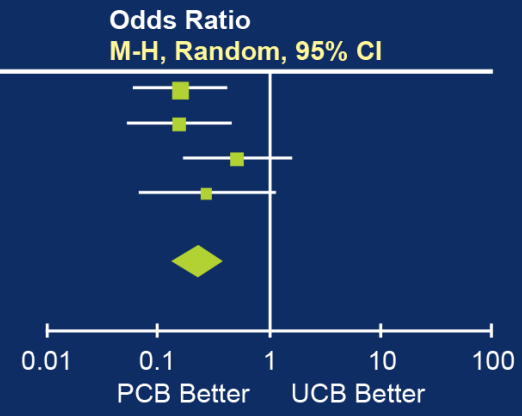
Jaff MR. International Symposium on Endovascular Therapy 2014

Paclitaxel-Coated vs. Uncoated Balloon
Meta-Analysis of Randomized Trials

Target lesion revascularization

Study or Subgroup	PCB Events	PCB Total	UCB Events	UCB Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
THUNDER	7	48	28	54	32.1%	0.16 [0.06, 0.42]	2008
FemPac	6	45	21	42	27.3%	0.15 [0.05, 0.44]	2008
LEVANT I	6	47	10	45	24.7%	0.51 [0.17, 1.55]	2010
PACIFIER	3	40	9	39	16.0%	0.27 [0.07, 1.09]	2011
Total (95% CI)		**180**		**180**	**100.0%**	**0.23 [0.13, 0.40]**	
Total events	22		68				

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 3.19$, df = 3 (P = 0.36); $I^2 = 6\%$
Test for overall effect: Z = 5.09 (P < 0.00001)
Heterogeneity(exact): $Chi^2 = 3.26$, df = 3 (P = 0.35)
Test for overall effect (exact): P < 0.00001



Conclusion In femoropopliteal arterial disease, PCB therapy is associated with superior antirestenotic efficacy as compared with UCB angioplasty with no evidence of a differential safety profile

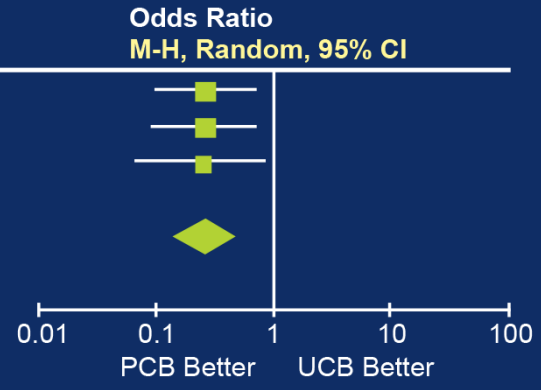
Salvatore C et al. Circ Cardiovasc Interv. 2012

Paclitaxel-Coated vs. Uncoated Balloon
Meta-Analysis of Randomized Trials

Binary restenosis

Study or Subgroup	PCB Events	PCB Total	UCB Events	UCB Total	Weight	Odds Ratio M-H, Random, 95% CI
THUNDER	7	41	21	48	38.8%	0.26 [0.10, 0.71]
FemPac	10	31	22	34	36.1%	0.26 [0.09, 0.73]
PACIFIER	4	40	12	39	25.1%	0.25 [0.07, 0.86]
Total (95% CI)		**112**		**121**	**100.0%**	**0.26 [0.14, 0.48]**
Total events	21		55			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.01$, df = 2 (P = 1.00); $I^2 = 0\%$
Test for overall effect: Z = 4.27 (P < 0.0001)
Heterogeneity(exact): $Chi^2 = 0.004$, df = 2 (P = 0.99)
Test for overall effect (exact): P < 0.00001



Conclusion In femoropopliteal arterial disease, PCB therapy is associated with superior antirestenotic efficacy as compared with UCB angioplasty with no evidence of a differential safety profile

Salvatore C et al. Circ Cardiovasc Interv. 2012

Paclitaxel-Coated vs. Uncoated Balloon
Meta-Analysis of Randomized Trials

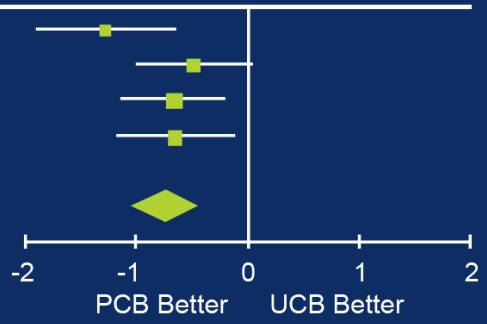
Late lumen loss

Study or Subgroup	PCB Mean	SD	Total	UCB Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
THUNDER	0.4	1.2	41	1.7	1.8	48	19.6%	-1.30 [-1.93, -0.67]
FemPac	0.5	1.1	31	1	1.1	34	25.2%	-0.50 [-1.04, 0.04]
LEVANT I	0.4	1.1	39	1.09	1	35	29.7%	-0.69 [-1.17, -0.21]
PACIFIER	-0.05	1.1	40	0.61	1.3	39	25.5%	-0.66 [-1.19, -0.13]
Total (95% CI)			**151**			**156**	**100.0%**	**0.75 [-1.06, -0.45]**

Total events

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 3.95$, df = 3 (P = 0.27); $I^2 = 24\%$

Test for overall effect: Z = 4.78 (P < 0.00001)



Conclusion In femoropopliteal arterial disease, PCB therapy is associated with superior antirestenotic efficacy as compared with UCB angioplasty with no evidence of a differential safety profile

Salvatore C et al. Circ Cardiovasc Interv. 2012

DEBATE-SFA Randomized Trial

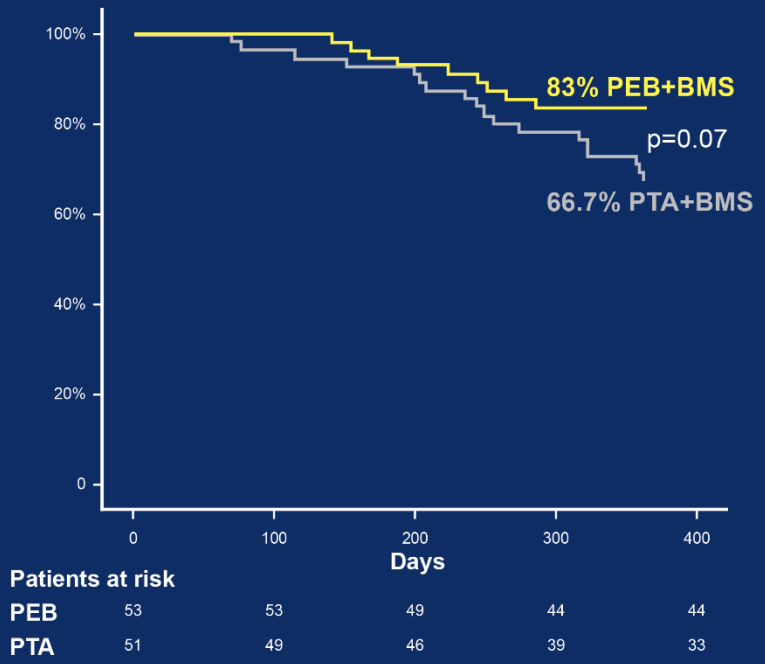
PEB+BMS vs. PTA+BMS with intermittent claudication or CLI

12-Month Results from 55 Lesion vs. 55 Lesion

12-month target lesion evaluation

	PEB+BMS	PTA+BMS	P Value
Restenosis	9 (17.0)	26 (47.3)	0.008
RVD, mm	5.11±0.6	5.05±0.5	0.5
MLD, mm	3.59±1.42	2.12±1.47	<0.001
DS, %	20.7	41.2	<0.001
Late lumen loss, mm	0.86	1.68	<0.001

Freedom from TLR



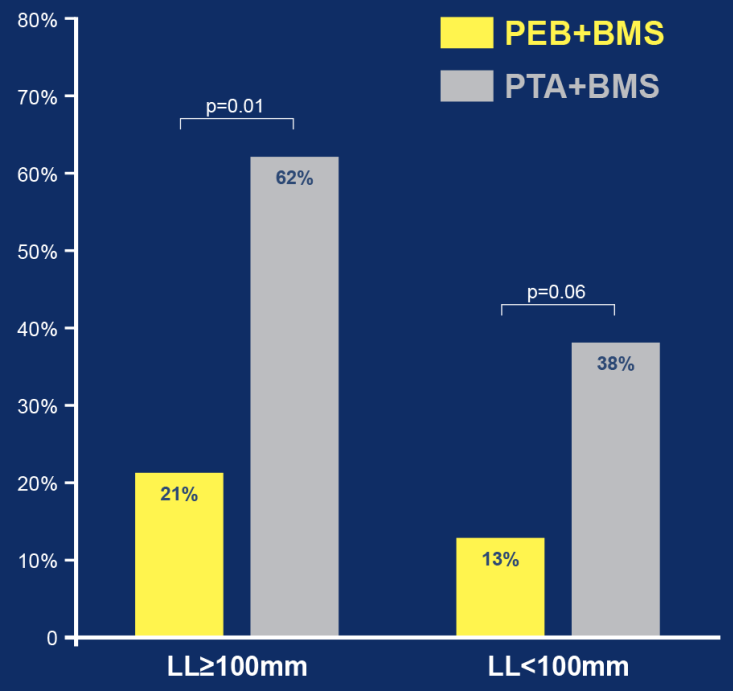
Liistro F et al. J Am Coll Cardiol Intv. 2013

DEBATE-SFA Randomized Trial

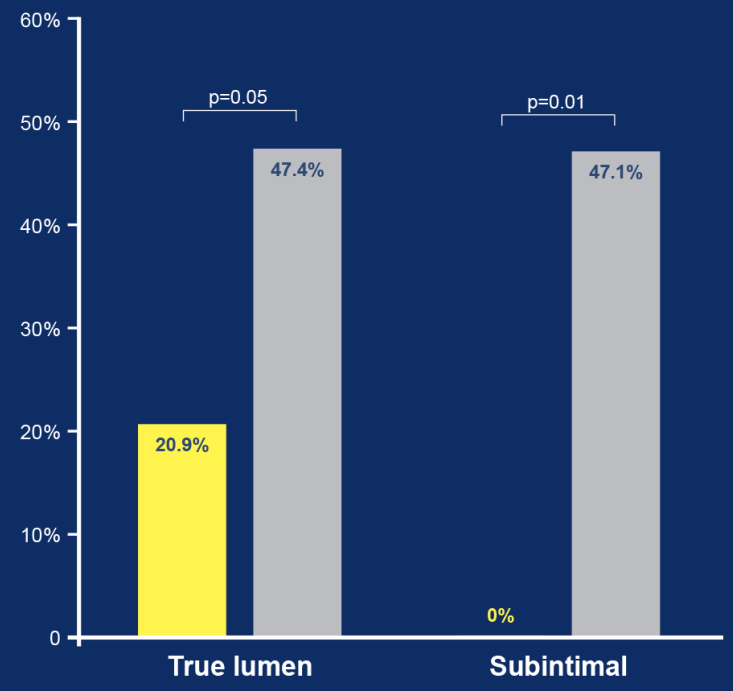
PEB+BMS vs. PTA+BMS with intermittent claudication or CLI

12-Month Results from 55 Lesion vs. 55 Lesion

Restenosis and lesion length



Restenosis and technique

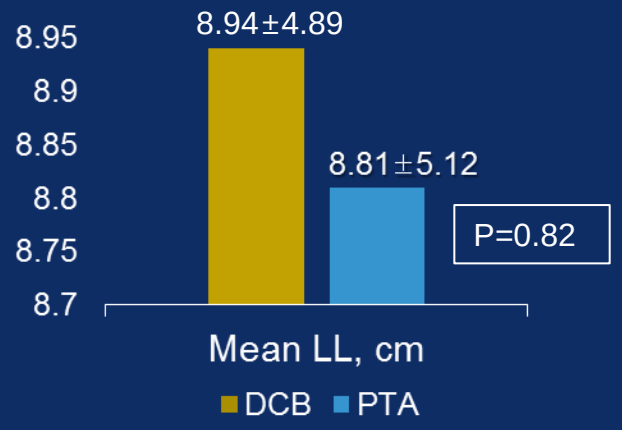


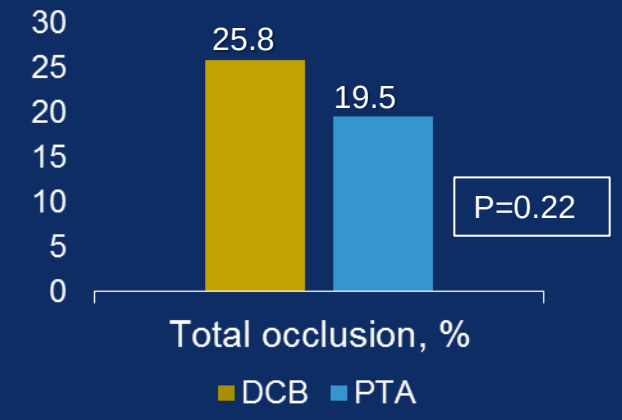
Liistro F et al. J Am Coll Cardiol Intv. 2013

IN.PACT SFA Randomized Trial

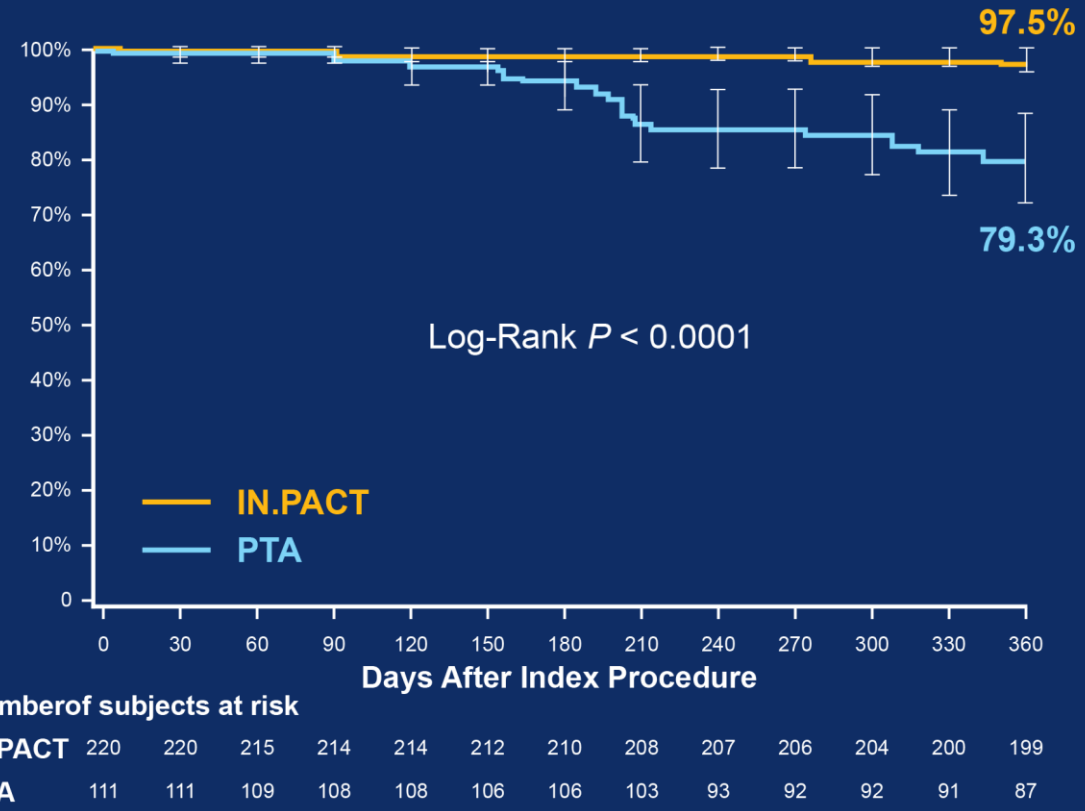
DCB vs. Standard PTA of symptomatic femoropopliteal disease

12-Month Results from 207 DCB vs 109 PTA





Freedom from clinically-driven TLR



Numberof subjects at risk

IN.PACT	220	220	215	214	214	212	210	208	207	206	204	200	199
PTA	111	111	109	108	108	106	106	103	93	92	92	91	87

Tepe G et al. Circulation. 2015

IN.PACT SFA Randomized Trial

DCB vs. Standard PTA of symptomatic femoropopliteal disease

12-Month Results from 207 DCB vs 109 PTA

Outcome	DCB (n=220)	PTA (n=111)	*P* Value
Primary efficacy – primary patency, % (m/n)	82.2 (157/191)	52.4 (54/103)	<0.001
12-month efficacy outcomes			
All TLR, % (m/n)	2.9 (6/207)	20.6 (22/107)	<0.001
Clinically driven TLR, % (m/n)	2.4 (5/207)	20.6 (22/107)	<0.001
Clinically driven TVR, % (m/n)	4.3 (9/207)	23.4 (25/107)	<0.001
Primary sustained clinical improvement, % (m/n)	85.2 (167/196)	68.9 (73/106)	<0.001
ABI/TBI	0.951±0.221#	0.886±0.169	0.002

Tepe G et al. Circulation. 2015

IN.PACT SFA Randomized Trial

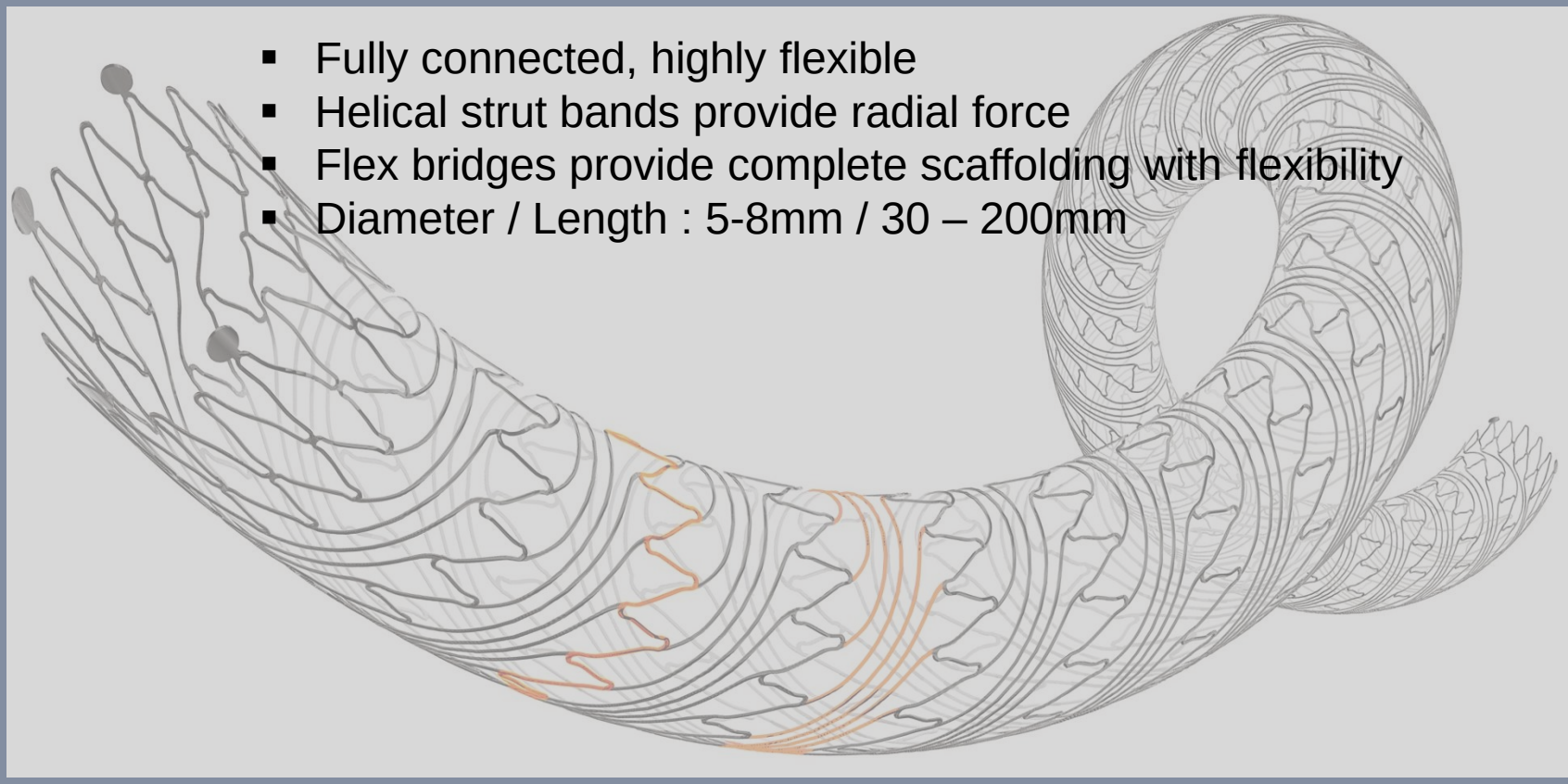
DCB vs. Standard PTA of symptomatic femoropopliteal disease
12-Month Results from 207 DCB vs 109 PTA

Outcome	DCB (n=220)	PTA (n=111)	*P* Value
12-month safety outcomes			
30-day device- and procedure-related death, % (m/n)	0.0 (0/218)	0.0 (0/111)	>0.999
Target limb major amputation, % (m/n)	0.0 (0/207)	0.0 (0/107)	>0.999
All-cause death, % (m/n)	1.9 (4/207)	0.0 (0/107)	0.93
Thrombosis, % (m/n)	1.4 (3/207)	3.7 (4/107)	0.10
12-month functional outcomes			
Change from baseline by EQ-5D Index	0.1059±0.2089#	0.0730±0.1951	0.095
Walking impairment, %	72.7±31.4#	73.6±29.5	0.590
Change in 6MWT from baseline to 12 mo, m	38.7±92.1#	59.1±102.3	0.878

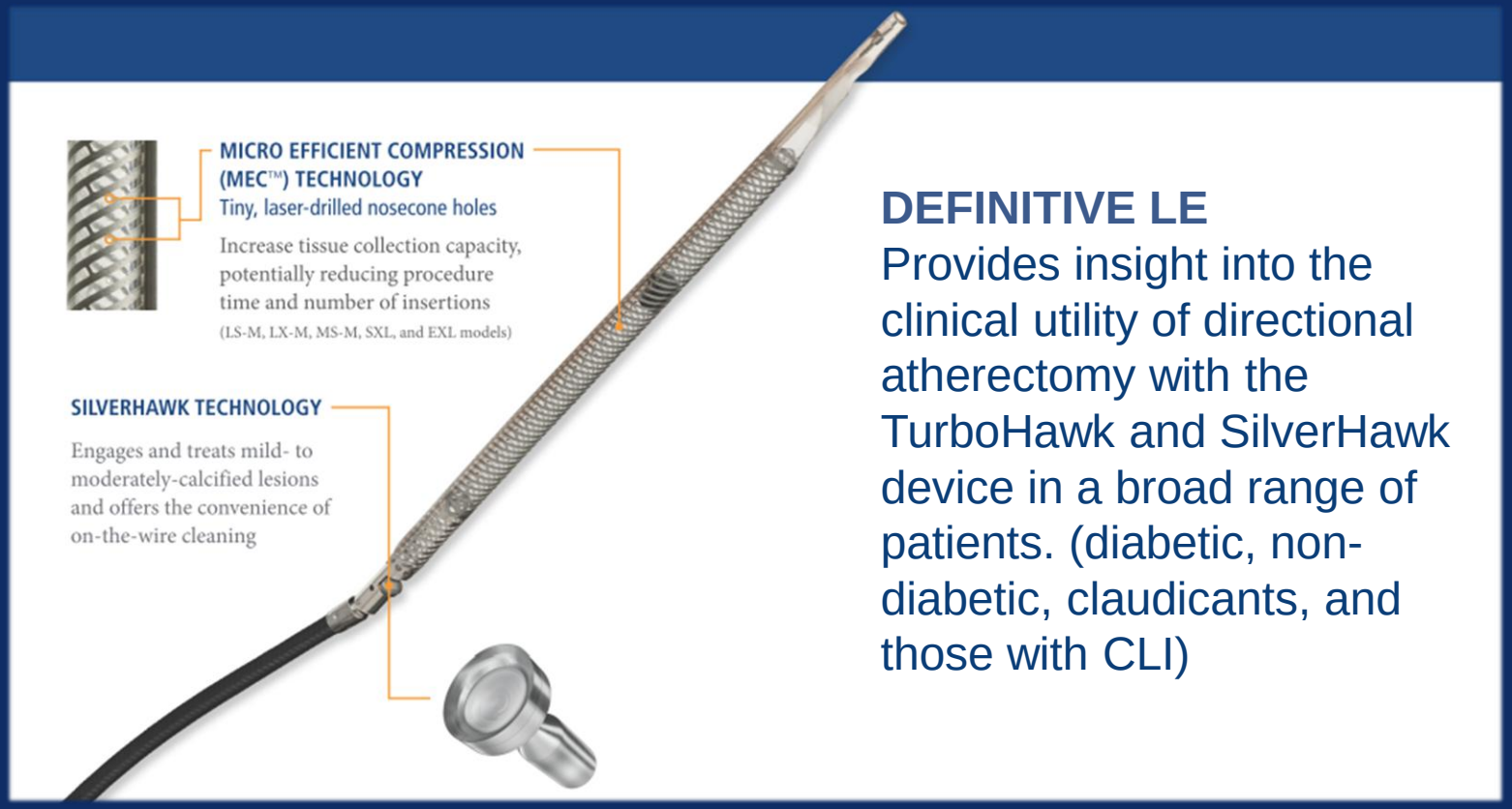
Tepe G et al. Circulation. 2015

SMART® Flex
Nitinol Self Expanding Stent

- Fully connected, highly flexible
- Helical strut bands provide radial force
- Flex bridges provide complete scaffolding with flexibility
- Diameter / Length : 5-8mm / 30 – 200mm



SilverHawk Directional Atherectomy



DEFINITIVE LE

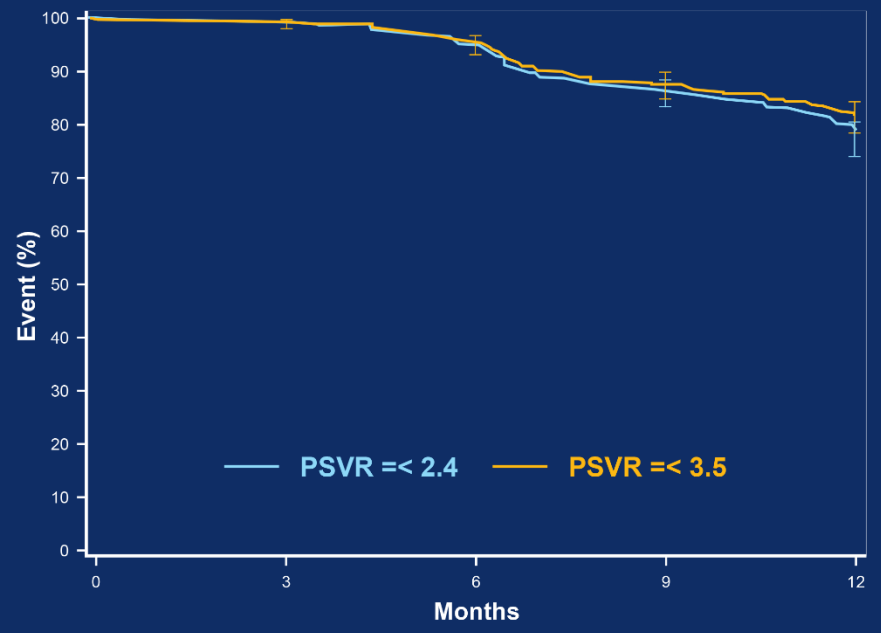
Provides insight into the clinical utility of directional atherectomy with the TurboHawk and SilverHawk device in a broad range of patients. (diabetic, non-diabetic, claudicants, and those with CLI)

DEFINITIVE LE

Revascularization Using Directional Atherectomy

12 Month Prospective Results

Patency outcomes: Claudicant cohort



81% (78.3-84.4)

78% (74.0-80.6)

Conclusion The DEFINITIVE LE study demonstrated that DA is a safe and effective treatment modality at 12 months for a diverse patient population with either claudication or CLI.

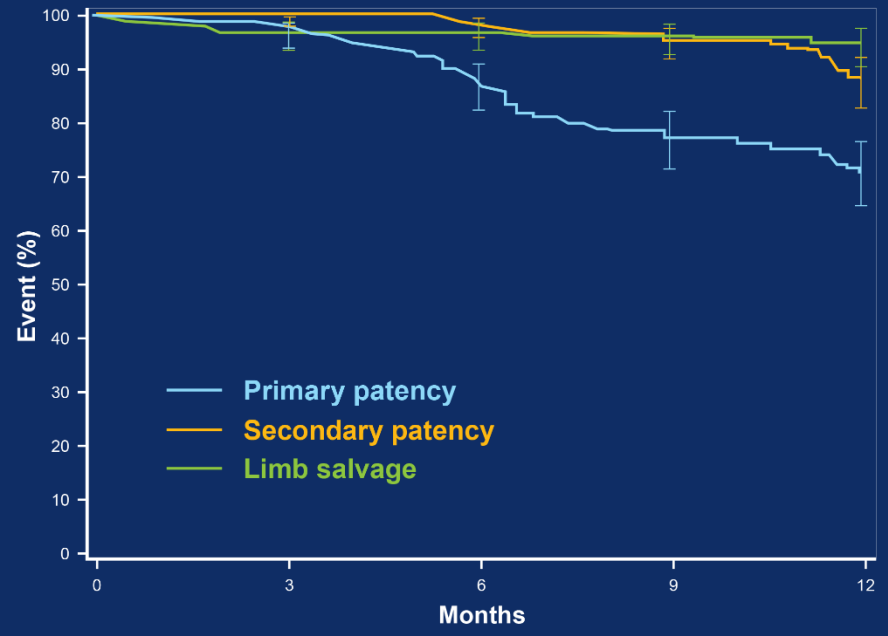
McKinsey et al. J Am Coll Cardiol Intv. 2014

DEFINITIVE LE

Revascularization Using Directional Atherectomy

12 Month Prospective Results

Endpoint outcomes: CLI cohort



95% (90.7-97.4)

88% (82.9-92.1)

71% (64.6-76.5)

Conclusion The DEFINITIVE LE study demonstrated that DA is a safe and effective treatment modality at 12 months for a diverse patient population with either claudication or CLI.

McKinsey et al. J Am Coll Cardiol Intv. 2014

DEFINITIVE LE

Revascularization Using Directional Atherectomy

12 Month Prospective Results

Patency outcomes: Diabetic vs. Nondiabetic claudicants

	Months	0	3	6	9	12
Diabetic	At risk	345	331	309	261	150
	Patency (95% CI)	100 (100.0 100.0)	99 (96.5 99.4)	95 (92.2 97.0)	85 (80.6 88.5)	77 (71.7 81.4)
Non-Diabetic	At risk	398	376	346	309	167
	Patency (95% CI)	100 (100.0 100.0)	99 (98.1 100.0)	95 (92.1 96.7)	88 (83.6 90.5)	78 (72.9 82.1)

Conclusion DA was shown to be noninferior for treating PAD in patients with diabetes compared with those without diabetes.

McKinsey et al. J Am Coll Cardiol Intv. 2014

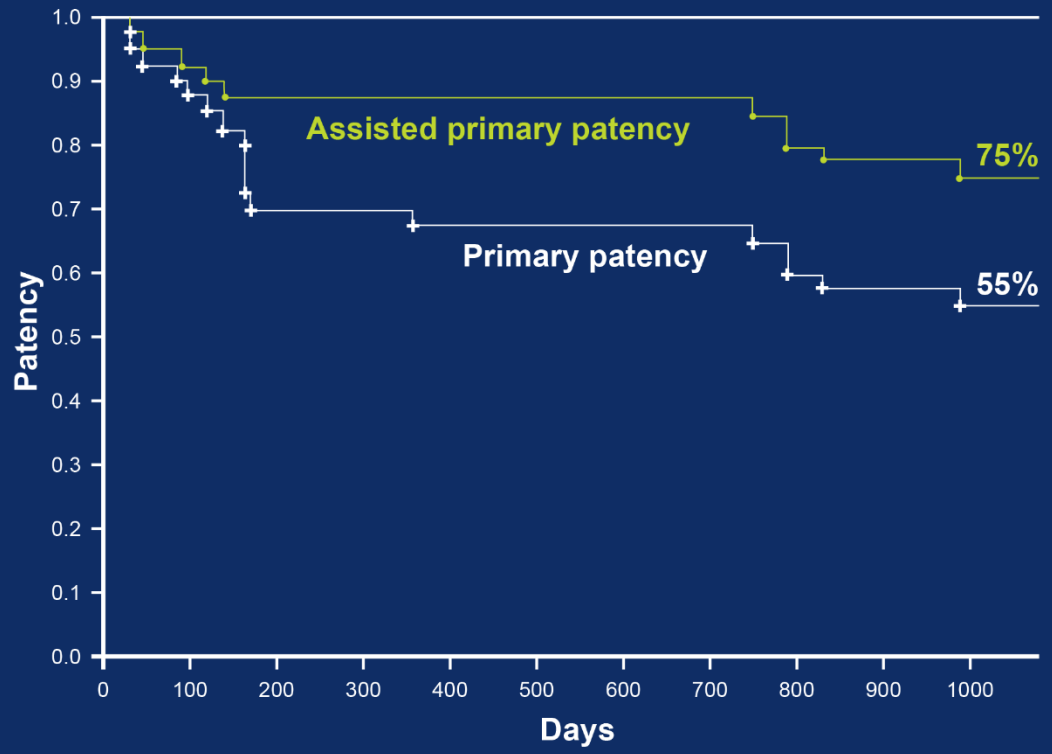
SFA Patency Comparison

Study	Device	Mean Length, cm	Patency, %	Patency Definition
DEFINITIVE LE	DA	8.1	75	PSVR ≤ 2.4
RESILIENT	BMS	6.2	81.3	PSVR <2.5
DURABILITY II	BMS	8.9	77.2	PSVR <2.0
STRIDES	DES	9.0	68	PSVR <2.5
Zilver RCT	DES	5.4	83.1	PSVR <2.0
Italian Registry	DCB	7.6	83.7	PSVR <2.5
LEVANT I	DCB	8.1	67	PSVR <2.5

Directional Atherectomy

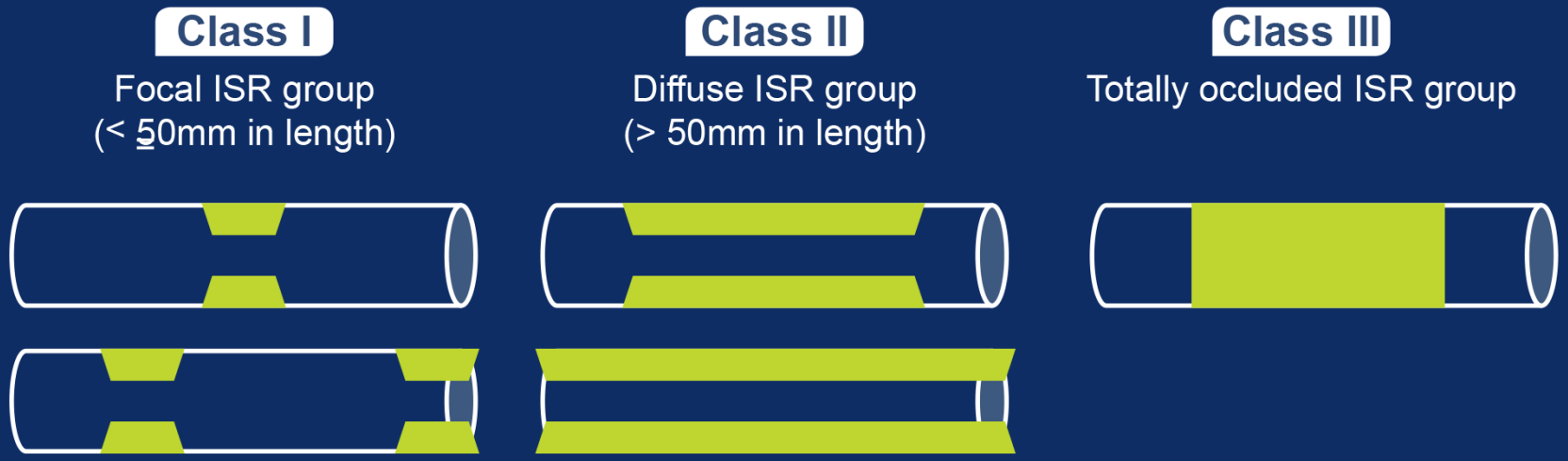
Calcified Stenotic Lesion of SFA, TASC B and C

3-Year Results of 59 Lesion, Mean Lesion Length 7.9cm



Minko P et al. Cardiovasc Intervent Radiolol. 2014

ISR Classification

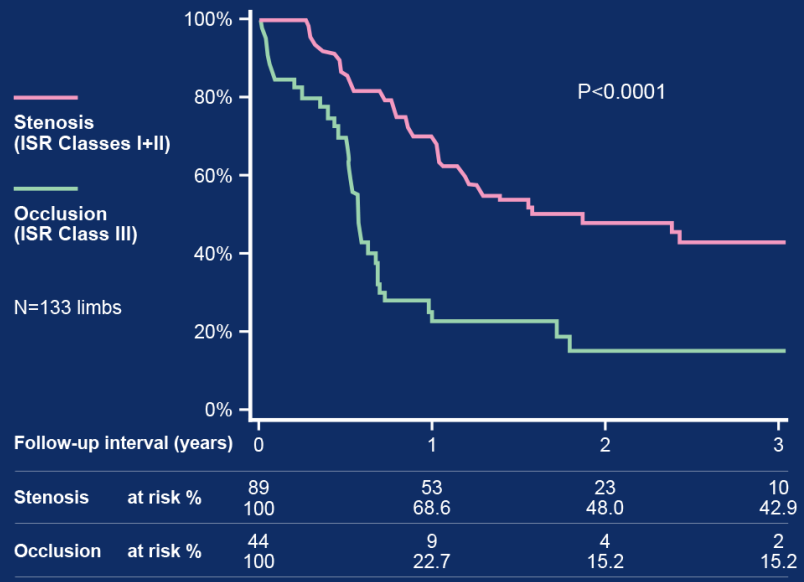


Atushi Tosaka. J Am Coll Cardiol 2012

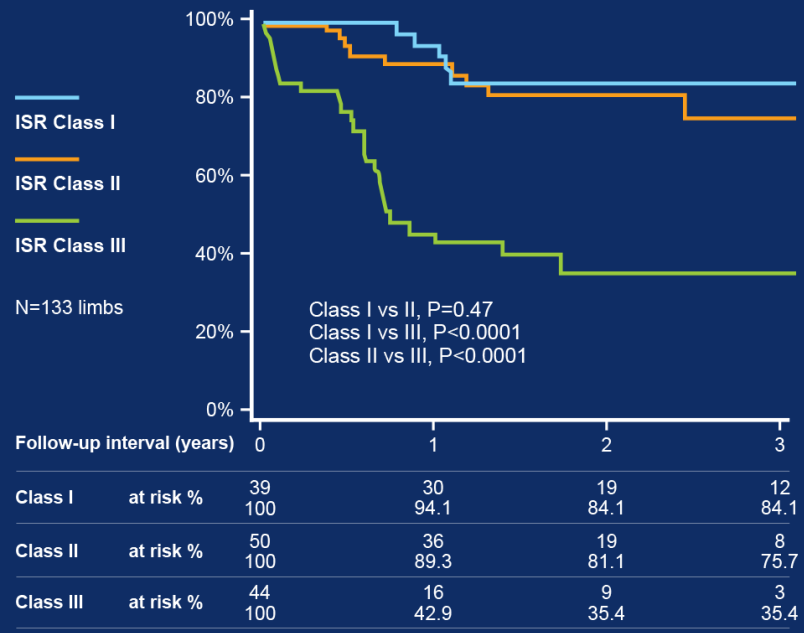
Classification and Clinical Impact

Freedom From Recurrent ISR

By ISR class



By stenosis and occlusion

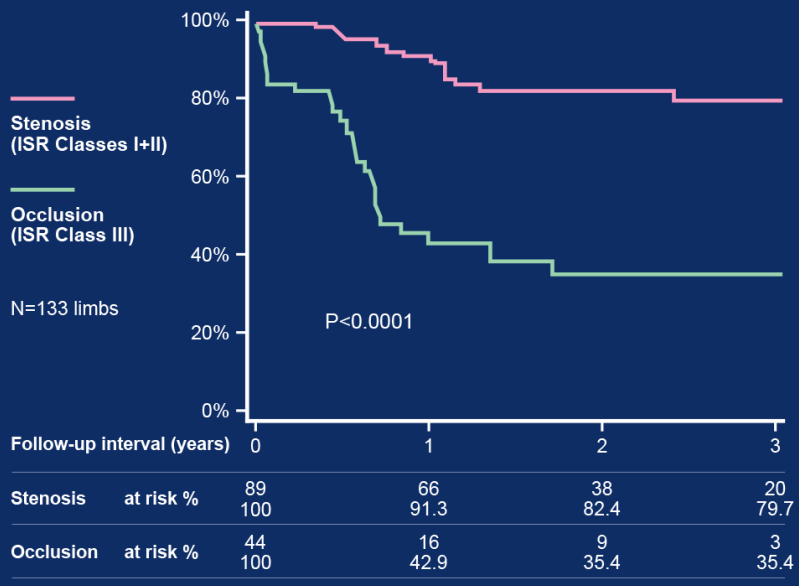


Atushi Tosaka. J Am Coll Cardiol 2012

Classification and Clinical Impact

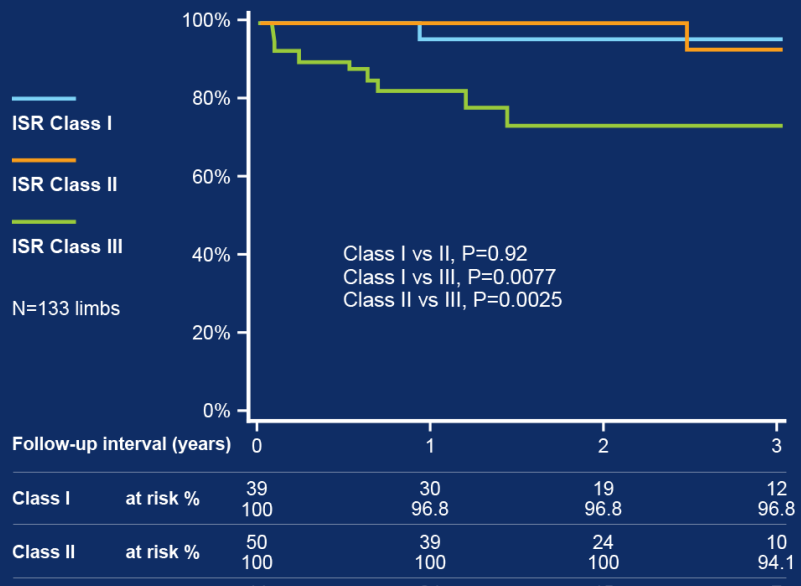
Freedom From Recurrent Occlusion

By ISR class



Stenosis	at risk %	89 100	66 91.3	38 82.4	20 79.7
Occlusion	at risk %	44 100	16 42.9	9 35.4	3 35.4

By stenosis and occlusion



Class I	at risk %	39 100	30 96.8	19 96.8	12 96.8
Class II	at risk %	50 100	39 100	24 100	10 94.1
Class III	at risk %	44 100	24 82.0	15 74.0	7 74.0

Atushi Tosaka. J Am Coll Cardiol 2012

Predictors of Recurrent ISR

After POBA for ISR

	Univariate Analysis		*Multivariate Analysis*	
Variables	HR (95% CI)	P value	HR (95% CI)	P value
ISR class III	2.90 (1.83-4.56)	<0.01	2.44 (1.33-4.48)	<0.01
Lesion Length (mm)	1.004 (1.002-1.007)	<0.01	1.001 (0.998-1.005)	0.50
Reference vessel diameter (mm)	0.62 (0.44-0.87)	<0.01	0.63 (0.44-0.89)	<0.01
Early restenosis	1.92 (1.13-3.23)	0.02	1.60 (0.94-2.73)	0.09

Atushi Tosaka. J Am Coll Cardiol 2012

DEB for treatment of SFA ISR

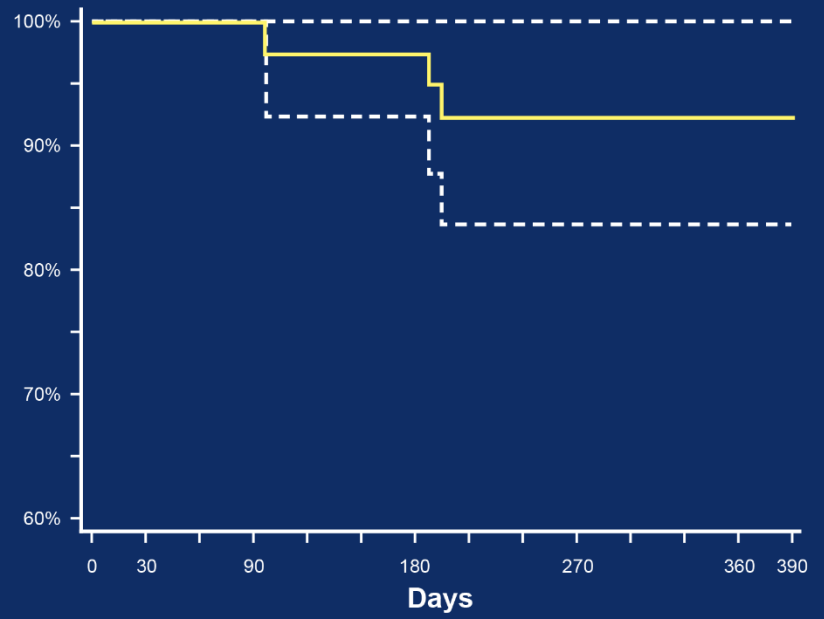
Final post-dilation with paclitaxel-eluting balloons

12-Month Results of 39 Consecutive Patients

Procedural characteristics

Stent diameter, mm	6 (6-6.5)
Stent length, mm	150 (95-262.5)
Lesion length, mm	82.9 ± 78.9
DEB diameter, mm	6 (5-6)
Number of DEB	2 (1-2)
Procedural success	39 (100)

Freedom from TLR



Dotted lines = 95% confidence interval

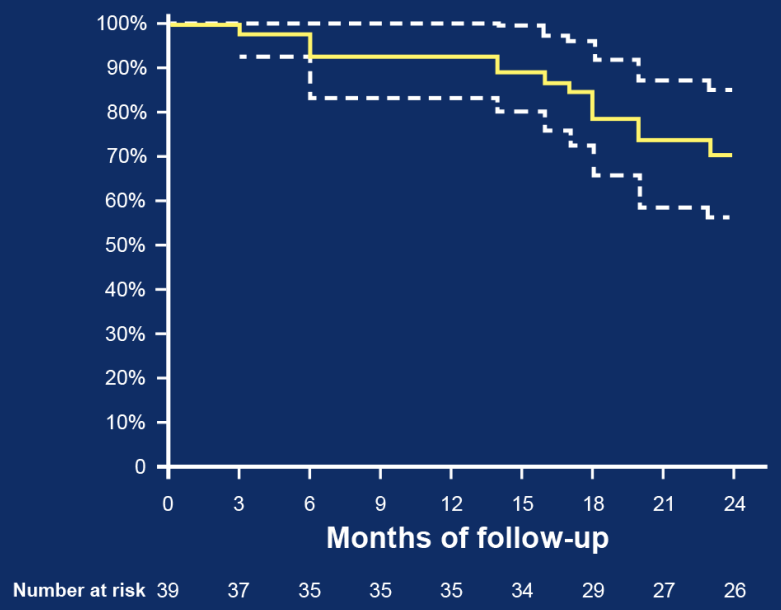
Stabile E. et al. J Am Coll Cardiol 2012

DEB for treatment of SFA ISR

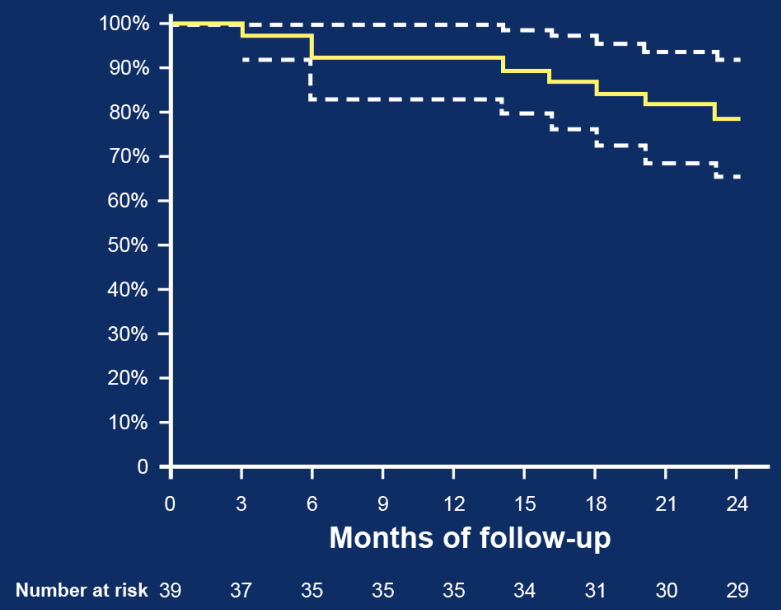
Final post-dilation with paclitaxel-eluting balloons

2-Year Follow Up of 39 Consecutive Patients

Primary patency



Freedom from TLR



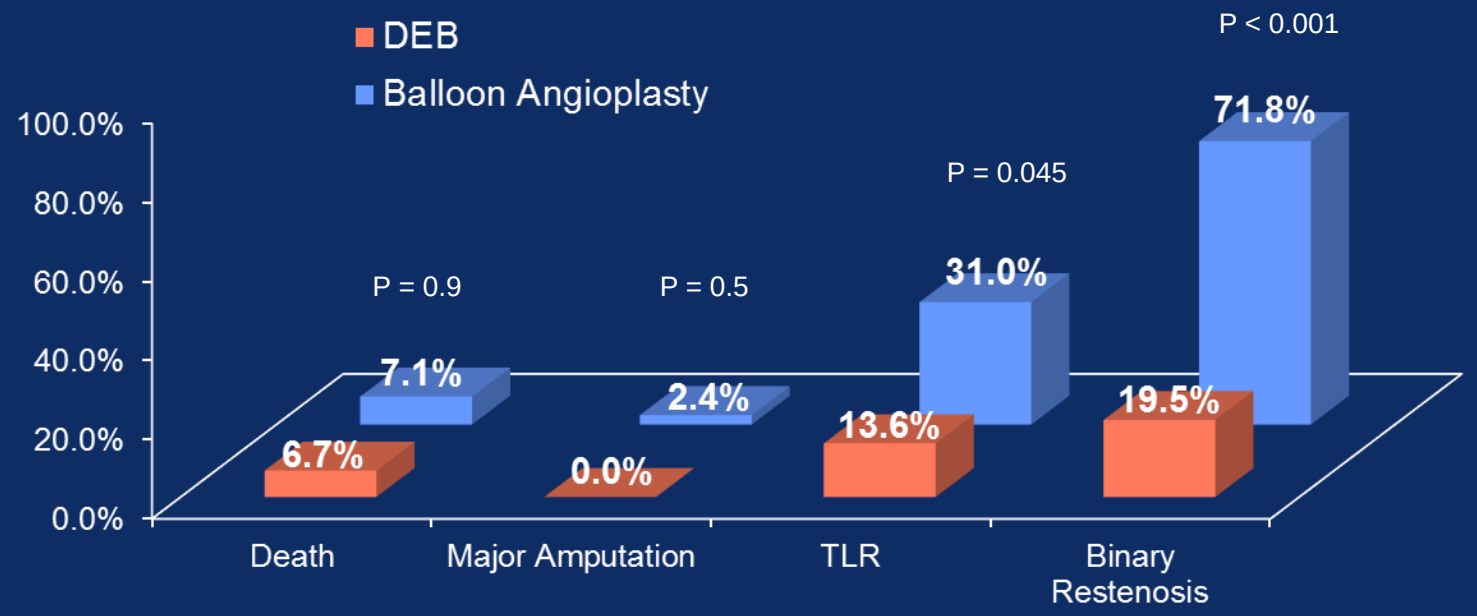
Dotted lines = 95% confidence interval

Virga V et al. JACC Cardiovasc Interv. 2014

DEBATE-ISR

DEB vs. Standard Angioplasty to Reduce Recurrent Restenosis in Diabetics with Femoropopliteal ISR

44 patients with claudication or CLI treated with paclitaxel eluting balloon



Conclusion Use of DEBs to treat diabetic patients with femoropopliteal ISR appears to reduce recurrent restenosis and repeat angioplasty at 1 year.

Liistro F et al. J Endovasc Ther. 2014

Treatment of ISR in SFA

PTA	Up to 73% restenosis rates at 6-month 49.9% to 84.8% at 12-month	***J.Laird et al. JACC 2012 P.Dick et al. Radiology 2008***
Cutting Balloon	65% restenosis rates at 6-month	***A. Tosaka et al. JACC 2012***
Atherectomy	46% restenosis rates at 12-month	***T.Zeller et al. JACC 2006***
Graft stents	62%~85.1% primary patency at 12-month	***TS. Monahan et al. Journal of Vasc Surg 2011 P.Soukas Oral presentation LINC 2011***
ELCA/PTA+HFH-Graft stents	48% primary patency at 12-month	***J.Laird et al. Cath and Cardiovasc Interv 2012***
PTA + Brachytherapy	79.8% primary patency at 12-month	***M.Werner et al. JEVT 2012***
DES	81% freedom from TLR at 12-month 61% freedom from TLR at 24-month	***Thomas Zeller JACC Cardiovasc Interv 2013***
DEB	92% freedom from TLR at 12-month	***Stabile JACC 2013***

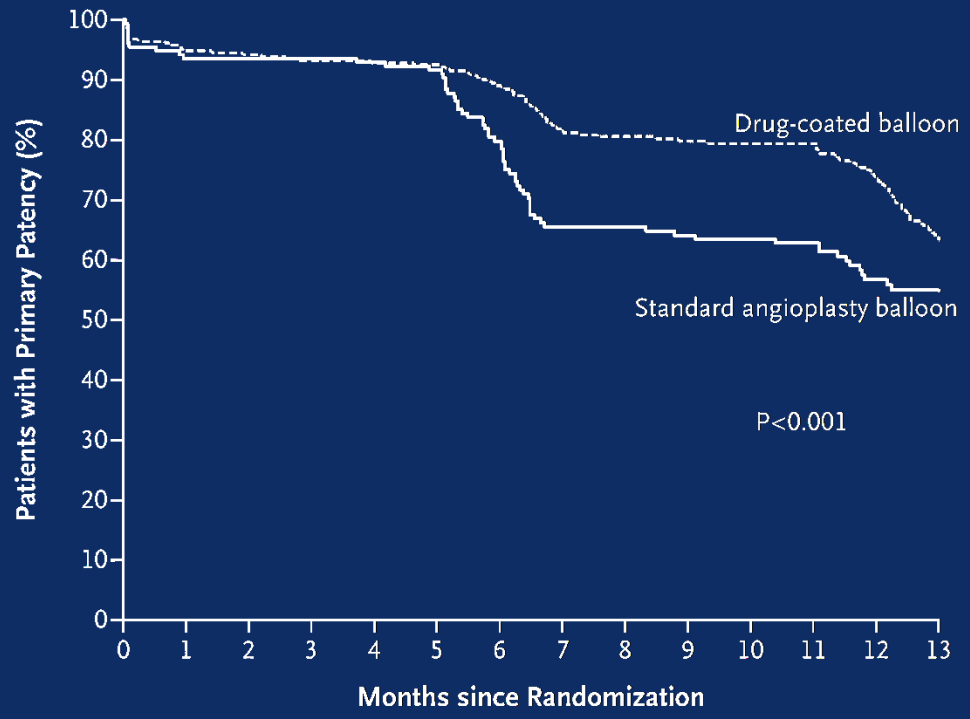
New Trial of Treatment in SFA

LEVANT 2 trial

Paclitaxel-Coated Balloon for Femoropopliteal Artery Disease

12 Month Randomized Results

Patency outcomes: Drug-coated balloon vs. Conventional angioplasty



Conclusion DCB was higher than the rate with angioplasty with a standard balloon in a rate of primary patency at 12 months.

Kenneth R et al. N Engl J Med. 2015

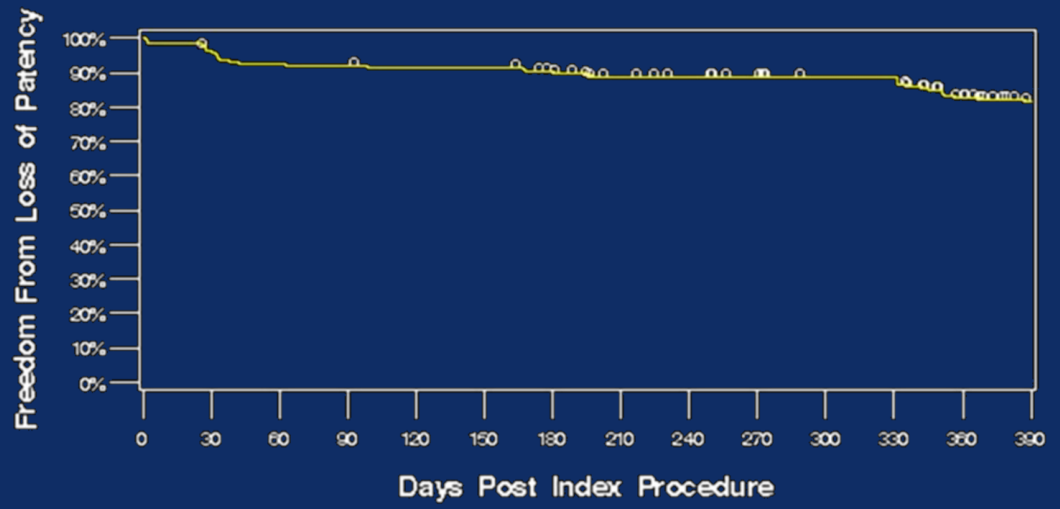
SUPERB trial

Wire-Interwoven Nitinol Stent for Femoropopliteal Artery

12 Month Randomized Results

Composite outcome of death, TLR, limb salvage

Interval	[0, 90)	[90, 180)	[180, 270)	[270, 360)	[360, 390)
# At Risk	264	242	234	215	188
# Censored	21	4	5	14	3
# Events	1	4	14	13	16
% Survived	1.000	0.996	0.979	0.920	0.863
Standard Error	0.000	0.004	0.009	0.018	0.023



Conclusion Primary endpoint was achieved in 99.2% of patients(*P*<0.001). Primary patency at 12 months was achieved in 78.9% of population (*P*<0.001).

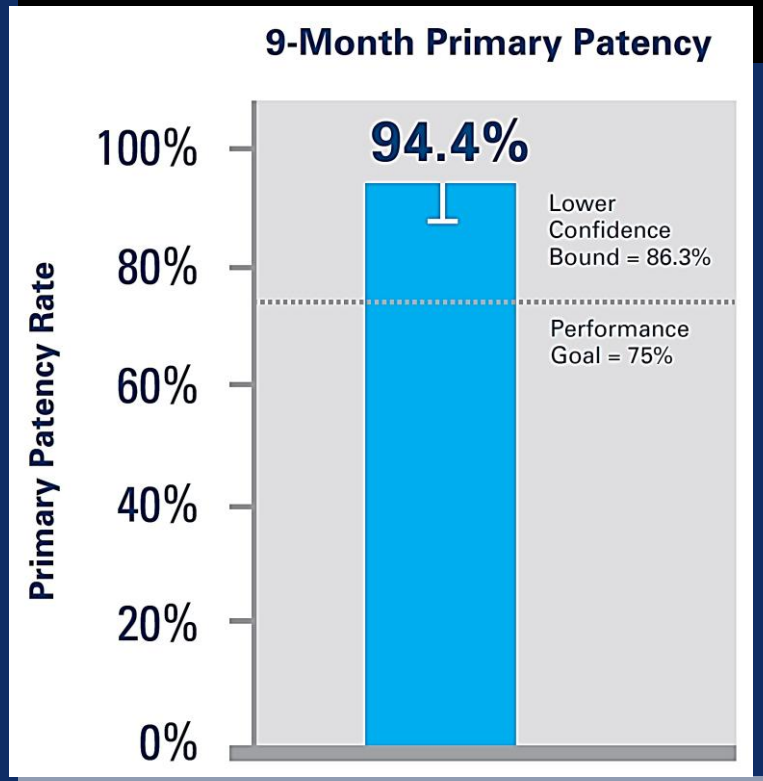
Lawrence G et al. Circ Cardiovasc Interv. 2015

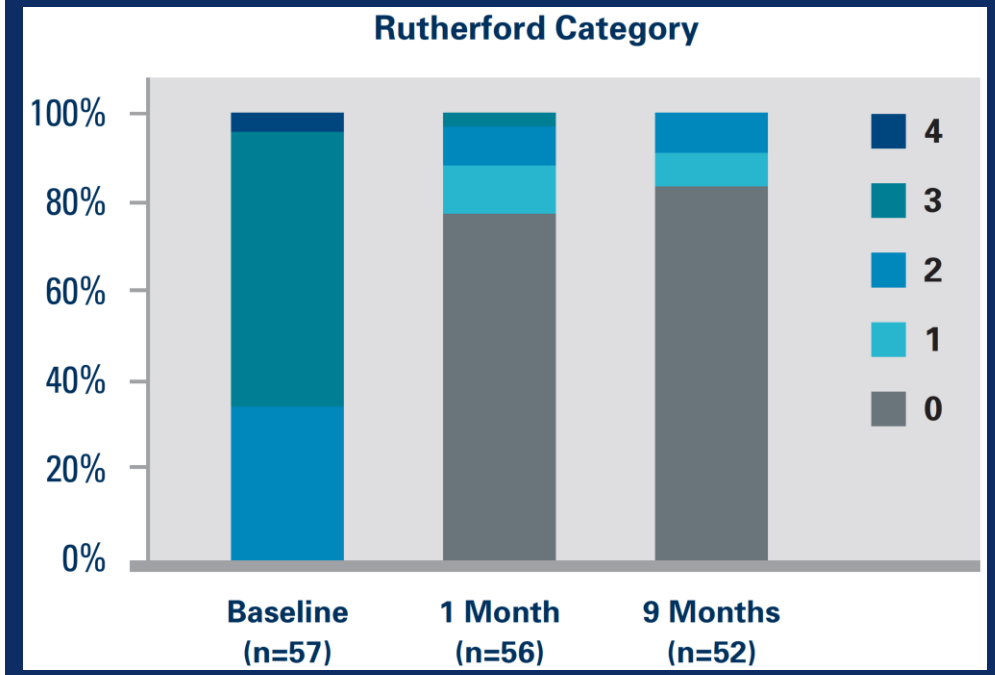
MAJESTIC trial

Paclitaxel-Eluting Self-Expanding Stent for Femoropopliteal Artery

9 Months Primary patency

Patency outcomes: Phase 2





Conclusion Primary patency was achieved in 94.4% of patients. TLR rate at 9 months was achieved in 3.6% of population.

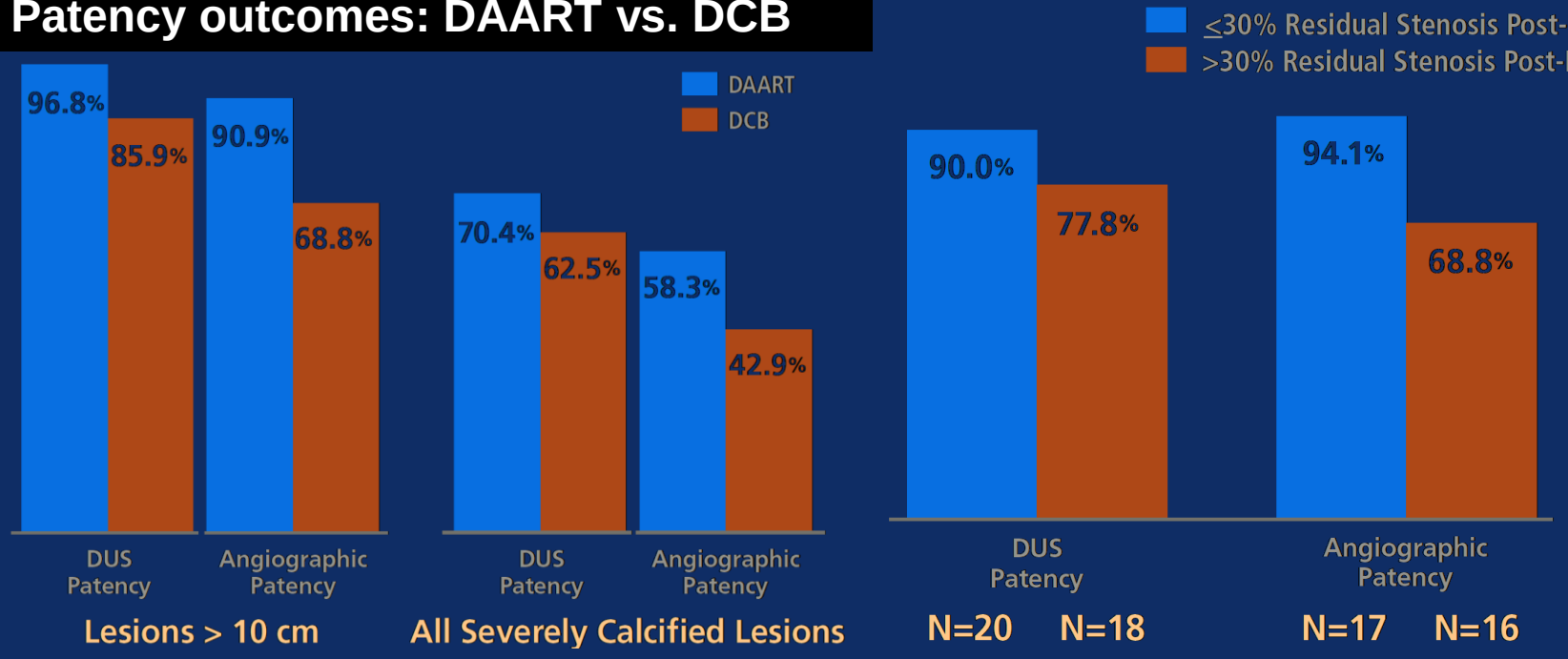
ClinicalTrials.gov, NCT01820637

DEFINITIVE AR trial

Revascularization Using Directional Atherectomy combine with Drug Coated Balloon angioplasty

12 Month Prospective Results

Patency outcomes: DAART vs. DCB



Conclusion The DEFINITIVE AR study demonstrated that DA is a safe and effective treatment modality at 12 months for a diverse patient population with either claudication or CLI.

ClinicalTrials.gov, NCT01366482

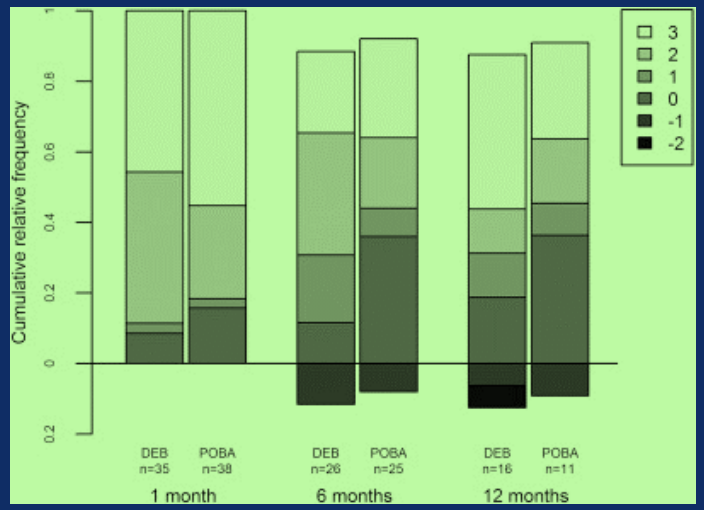
PACUBA trial

Paclitaxel-eluting balloon versus standard balloon angioplasty in ISR of the SFA and proximal popliteal artery

12 Month Prospective Results

	DEB(95% CI)	PTA(95% CI)
Primary patency rate		
6 months	58.8%(0.44-0.78)	31.3%(0.18-0.52)
12 months	40.7%(0.25-0.64)	13.4%(0.05-0.36)*
Freedom from clinically drive TLR		
6 months	88.2%(0.78-0.99)	83.8%(0.72-0.97)
12 months	49.0%(0.32-0.75)	22.1%(0.10-0.47)

Rutherford-Becker Score



***Log-rank p=0.02**

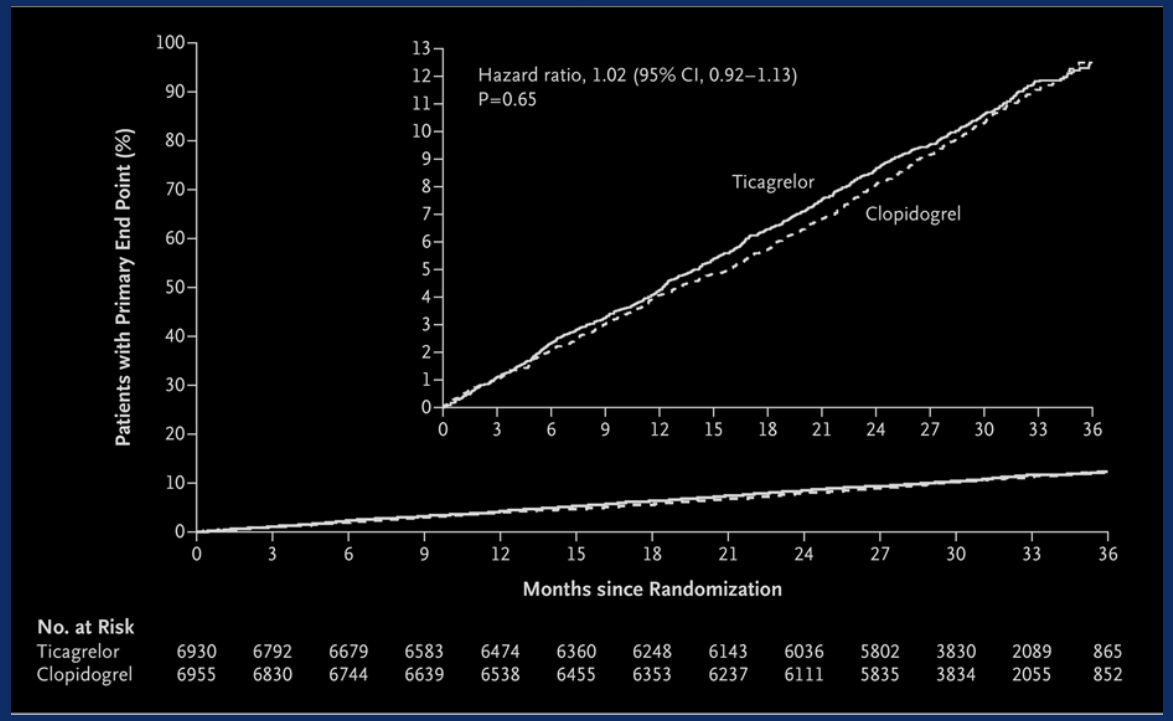
Conclusion When treating peripheral arterial disease in patients with ISR in the femoropopliteal artery, paclitaxel-eluting balloon angioplasty provides significantly higher patency rates than standard PTA.

Kinstner C et al. JACC Cardiovasc Interv. 2016

EUCLID trial

Ticagrelor versus Clopidogrel in symptomatic peripheral arterial disease

30 Month Prospective Results



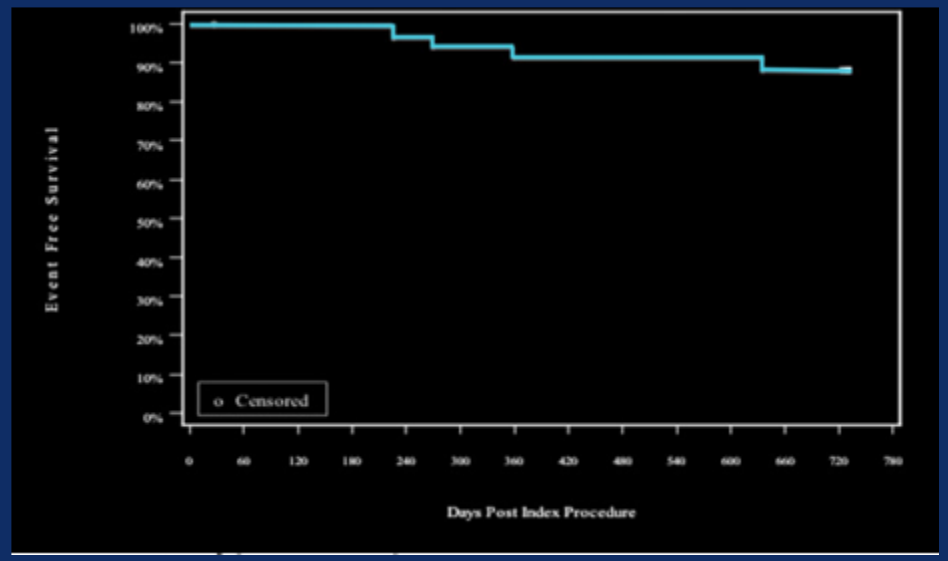
Conclusion Ticagrelor was not shown to be superior to clopidogrel for the reduction of cardiovascular events.

Hiatt R et al. N Engl J Med. 2016

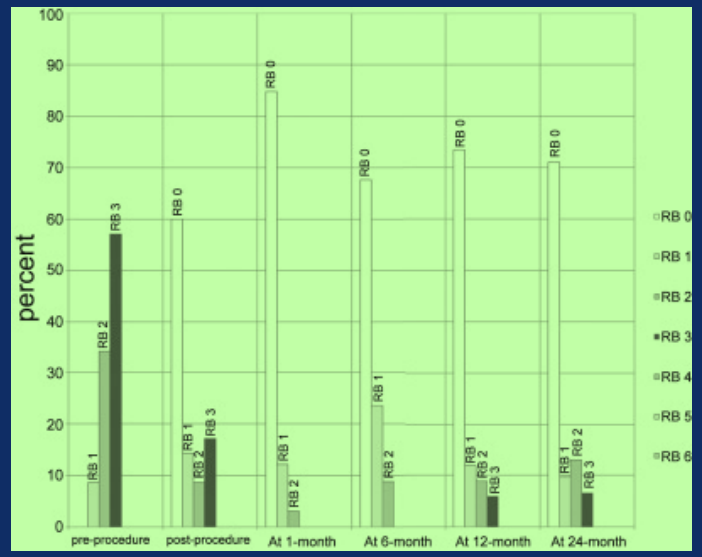
ESPRIT 1 trial

Bioresorbable Everolimus-Eluting Vascular Scaffold for peripheral artery disease
2-year Prospective Results

Freedom from any TLR through 24 months



Rutherford-Becker Score



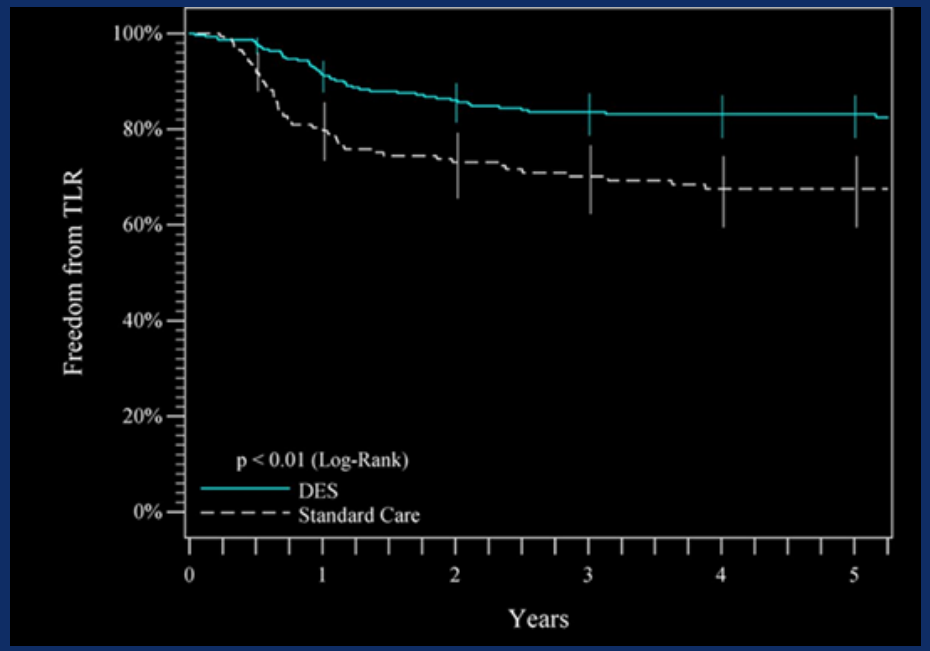
Conclusion The 1-year and 2-year freedom from TLR seems comparable to results of DEB and DES for peripheral arteries

Lammer J et al. JACC Cardiovasc Interv. 2016

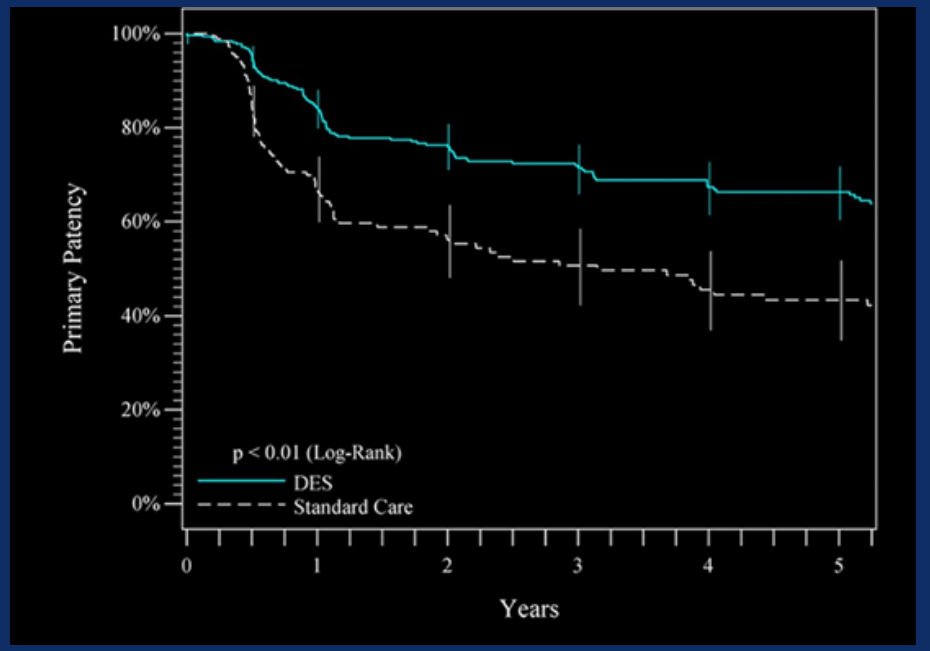
Zilver PTX randomized trial

5-year Prospective Results

Freedom from any TLR through 5 years



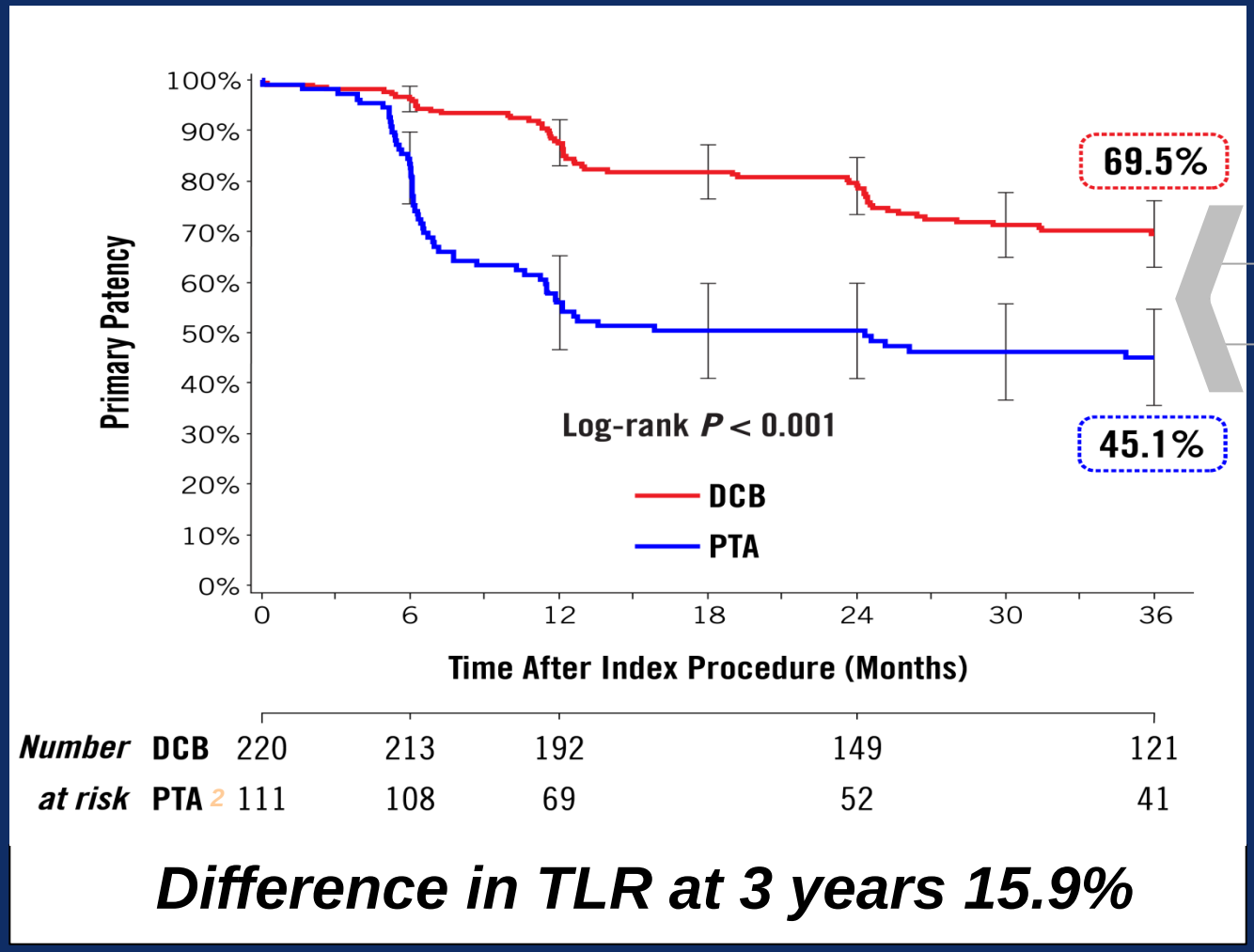
Primary patency through 5 years



Conclusion The Zilver PTX DES provided sustained safety and clinical durability in comparison with standard endovascular treatments.

Dake M et al. Circulation. 2016

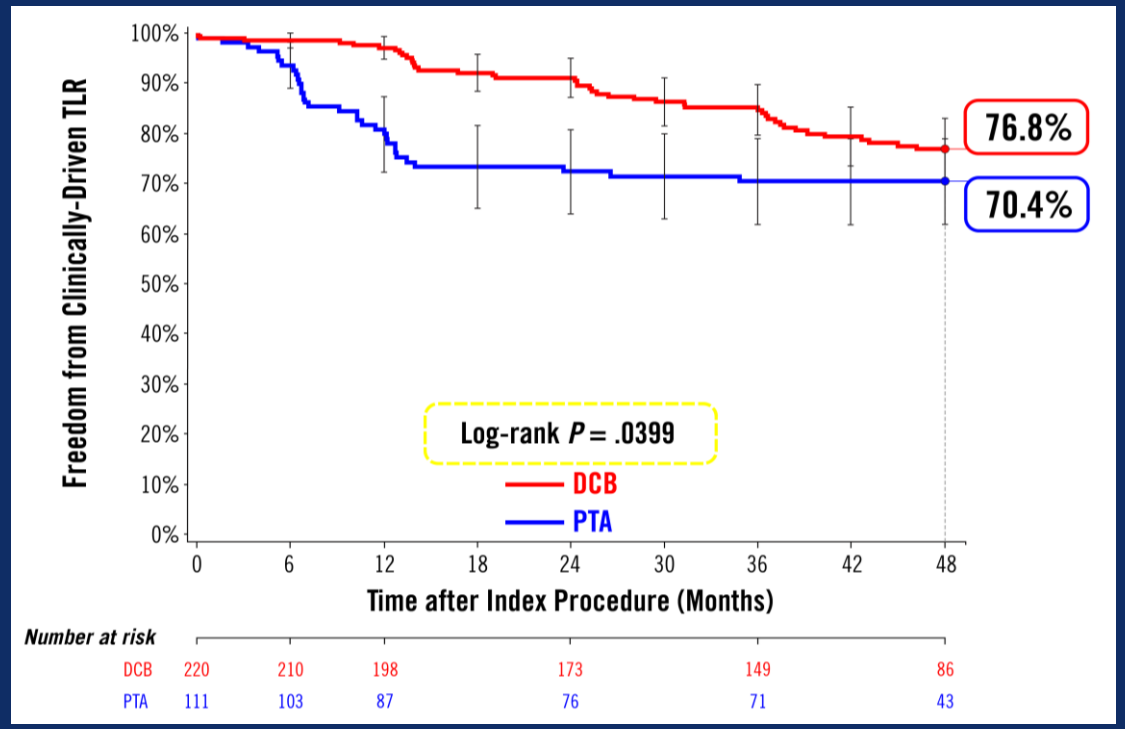
IN.PACT SFA Trial
Primary Patency Through 3 Years



Difference in TLR at 3 years 15.9%

Schneider. TCT 2017.

IN.PACT SFA Trial
Freedom From CD-TLR Through 4 Years



	IN.PACT DCB (N=220)	PTA (N=111)	P-value†
Time to CD-TLR	739.2 ± 384.0	302.9 ± 213.0	< 0.001

Schneider. TCT 2017.

IN.PACT SFA Trial
Safety Outcomes Through 4 Years

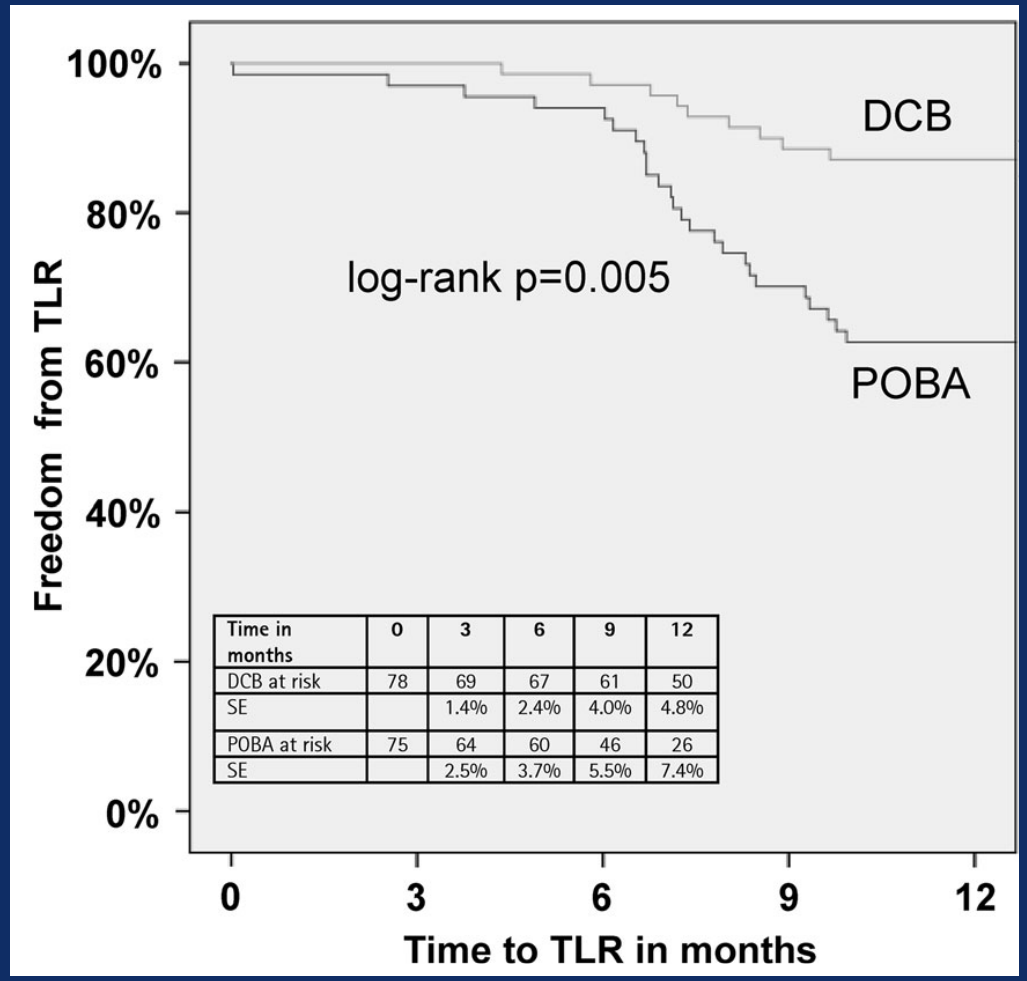
	IN.PACT DCB (N=220)	PTA (N=111)	P-value†
Primary safety composite [1]	73.4% (135/184)	64.1% (66/103)	0.108
Major adverse events [2]	38.0% (70/184)	40.8% (42/103)	0.705
All-cause death	13.0% (24/184)	6.8% (7/103)	0.116
Device-related death	0.0% (0/219)	0.0% (0/111)	>0.999
Target limb major amputation	0.0% (0/184)	0.0% (0/103)	>0.999
Thrombosis	2.2% (4/184)	4.9% (5/103)	0.290

1. *Freedom from 30-day device and procedure-related death and target limb major amputation and clinically-driven TVR within 36 months*
2. *Composite of death, clinically-driven TVR, target limb major amputation, and thrombosis*

† P-values are based on Fisher's exact test for superiority with significance level of 0.05

Schneider. TCT 2017.

CONSEQUENT Trial
Freedom from CD-TLR

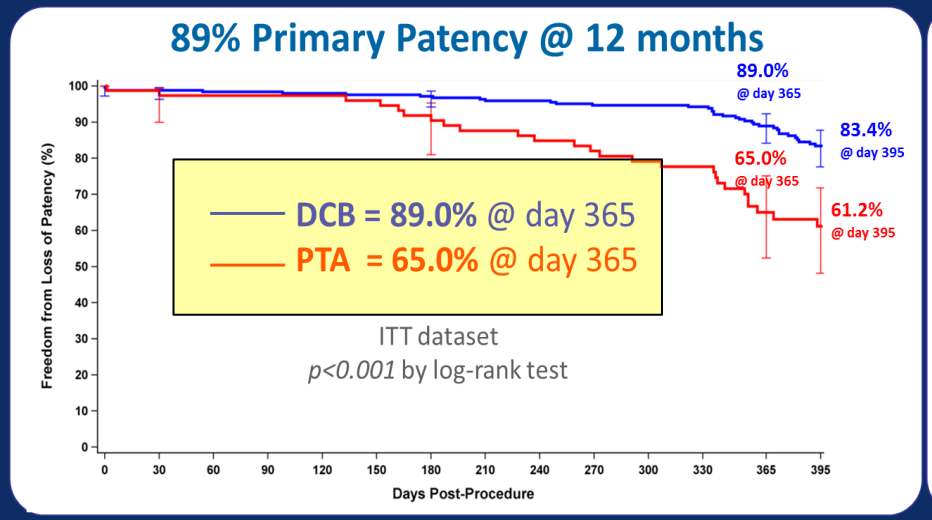


Time in months	0	3	6	9	12
DCB at risk	78	69	67	61	50
SE		1.4%	2.4%	4.0%	4.8%
POBA at risk	75	64	60	46	26
SE		2.5%	3.7%	5.5%	7.4%

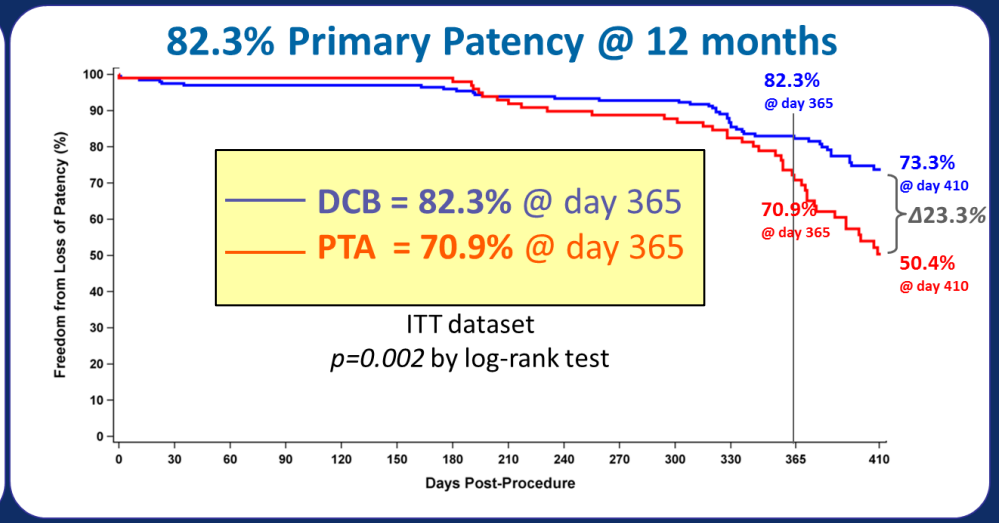
Tepe et al. Cardiovasc Intervent Radiol 2017;40: 1535

ILLUMENATE: 2 RCTs
Good Patency at 12 Months

EU RCT[1]



US Pivotal[2]



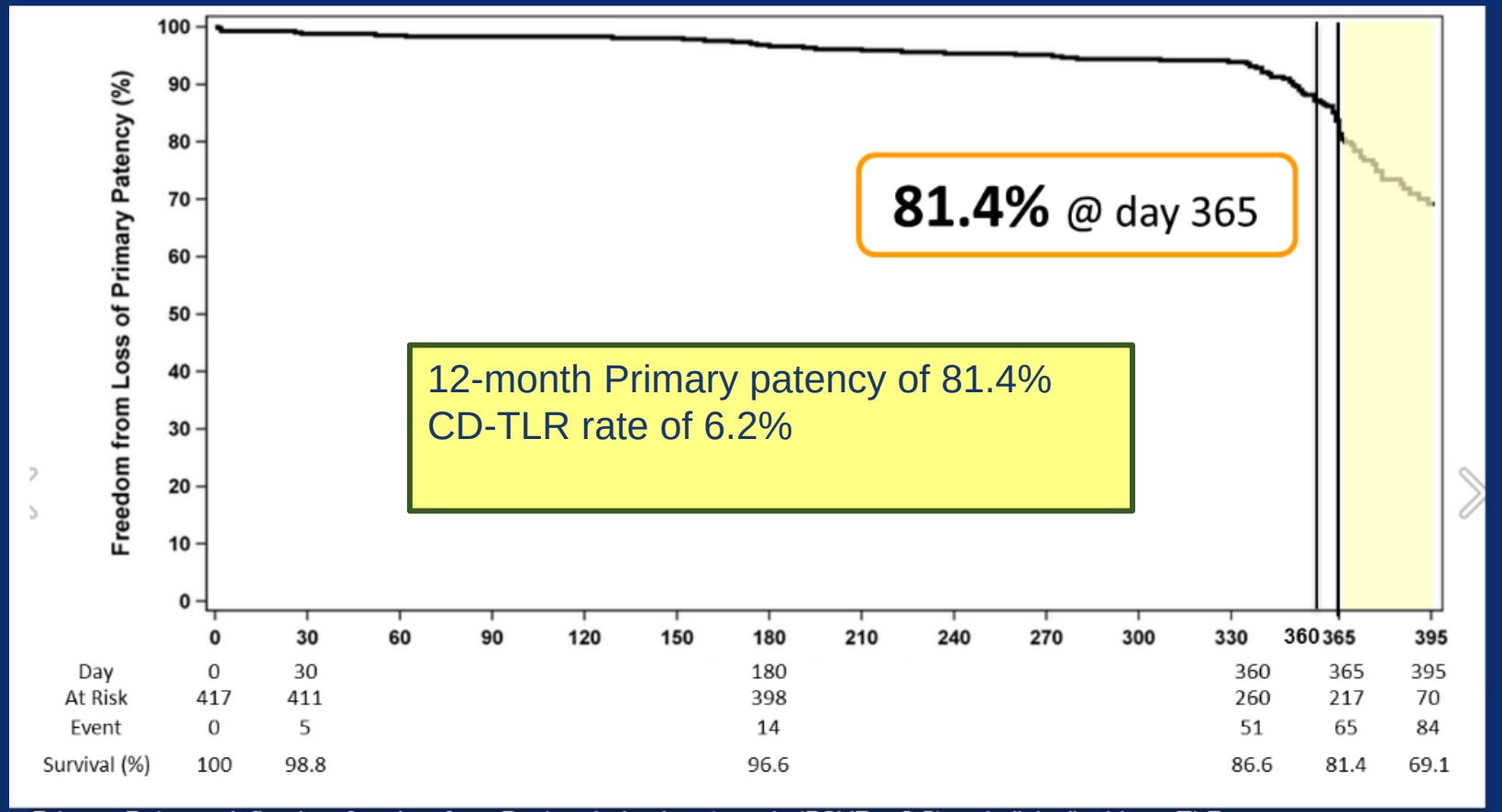
[ǂ] Core-lab adjudicated (VascCore Core laboratory - Boston, MA, USA) Duplex derived Primary Patency based on PSVR ≤2.5 . KM survival estimates at 365 days
[≠] freedom from CEC adjudicated clinically driven TLR by KM survival estimates at 365 days

1. Schroeder H, Werner M, Meyer DR, Reimer P, Krüger K, Jaff MR, Brodmann M; ILLUMENATE EU RCT Investigators. Circulation. 2017 Jun 6;135(23):2227-2236.
2. Krishnan P, Faries P, Niazi K, Jain A, Sachar R, Bachinsky WB, Cardenas JA, Werner M, Brodmann M, Mustapha JA, Mena-Hurtado CI, Jaff MR, Holden AH, Lyden SP. Stellarex Drug-Coated Balloon for Treatment of Femoropopliteal Disease: 12-Month Outcomes from the Randomized ILLUMENATE Pivotal and Pharmacokinetic Studies. *Circulation*. 2017;136:1102-1113

M. Weinberg Oral Presentation. TCT 2017

ILLUMENATE Global: Similar 1-Year Patency

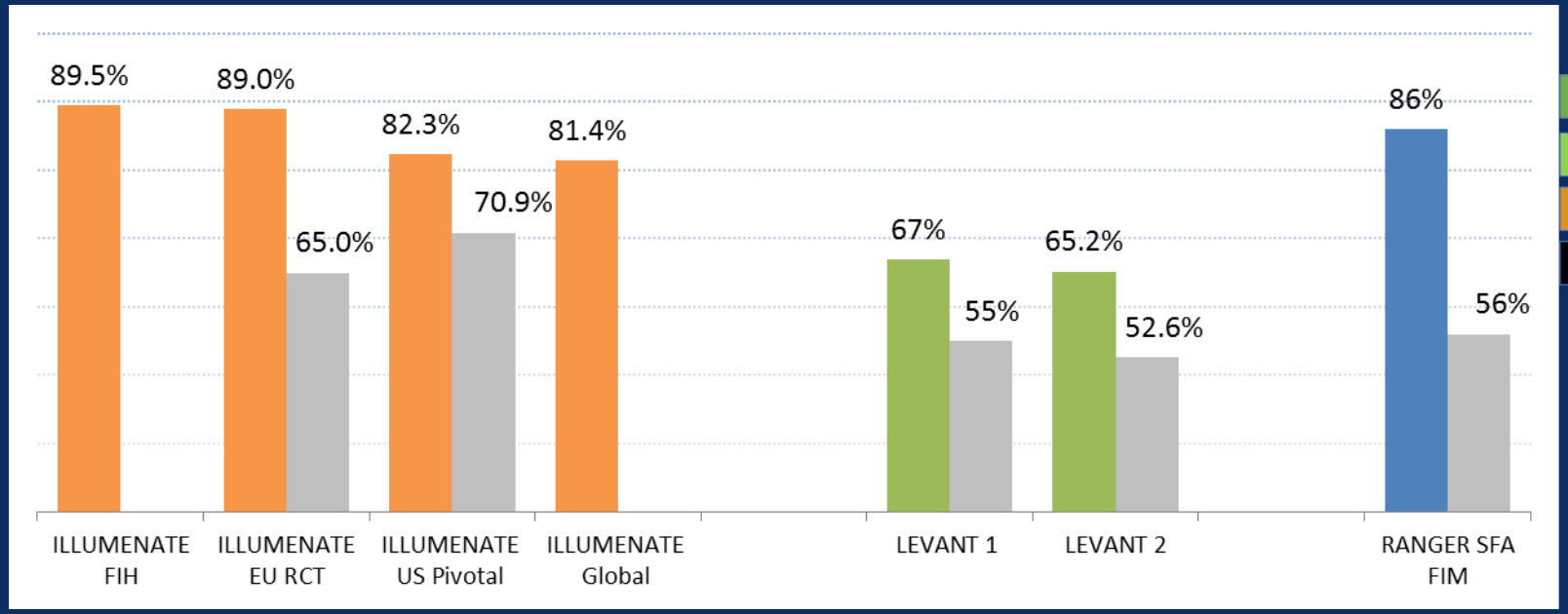
Primary Patency through 1 year



Primary Patency defined as freedom from Duplex derived restenosis (PSVR ≤ 2.5) and clinically-driven TLR

Zeller T. Oral Presentation. LINC 2017

Primary Patency at 1 year
Core Lab Adjudicated



N = 1,078 patients

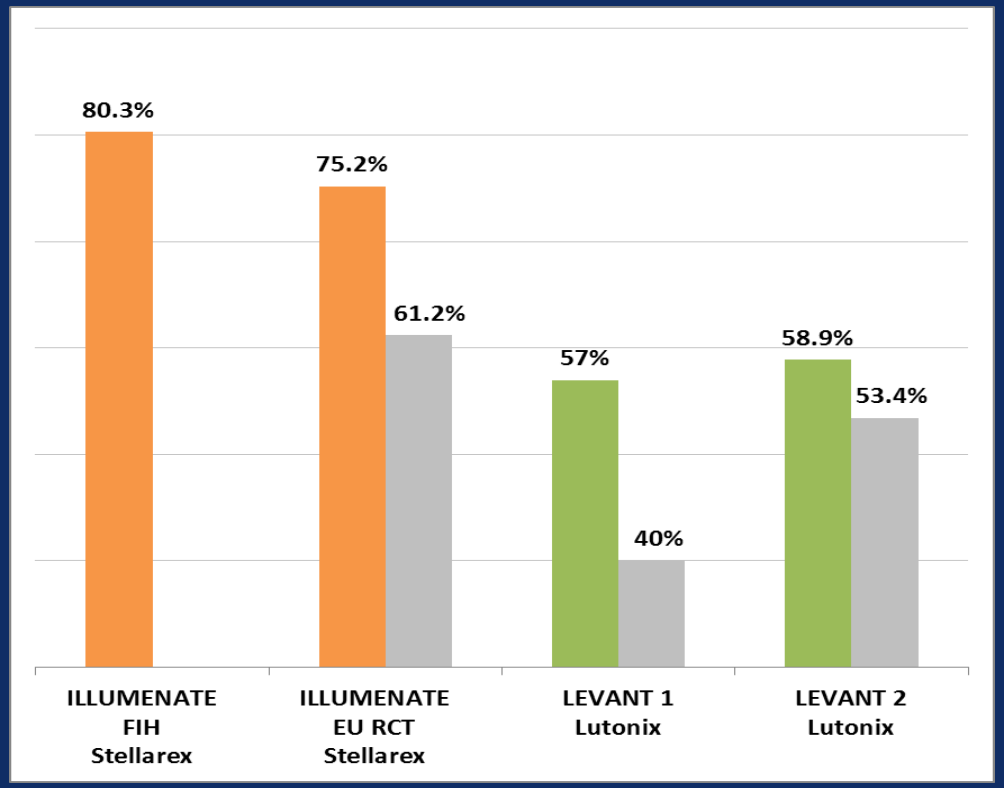
N = 577 patients

N = 105 patients

1. Schroeder H. et al. Catherization and Cardiovascular Interventions . 2015;86:278-86
2. Schroeder H. et al. Circulation. 2017 Jun 6;135(23):2227-2236.
3. Krishnan P. et al. *Circulation*. 2017;136:1102-1113
4. Zeller T. Oral Presentation LINC 2017
5. Scheiert D. et al. J Am Coll Cardiol Interv 2014;7:10-19
6. Rosenfield New England Journal of Med. 2015;373:145-53
7. Scheinert D. Oral Presentation. Charing Cross 2017

M. Weinberg Oral Presentation. TCT 2017

Primary Patency at 2 years
Core Lab Adjudicated



***Exact rates, KM estimate not reported**

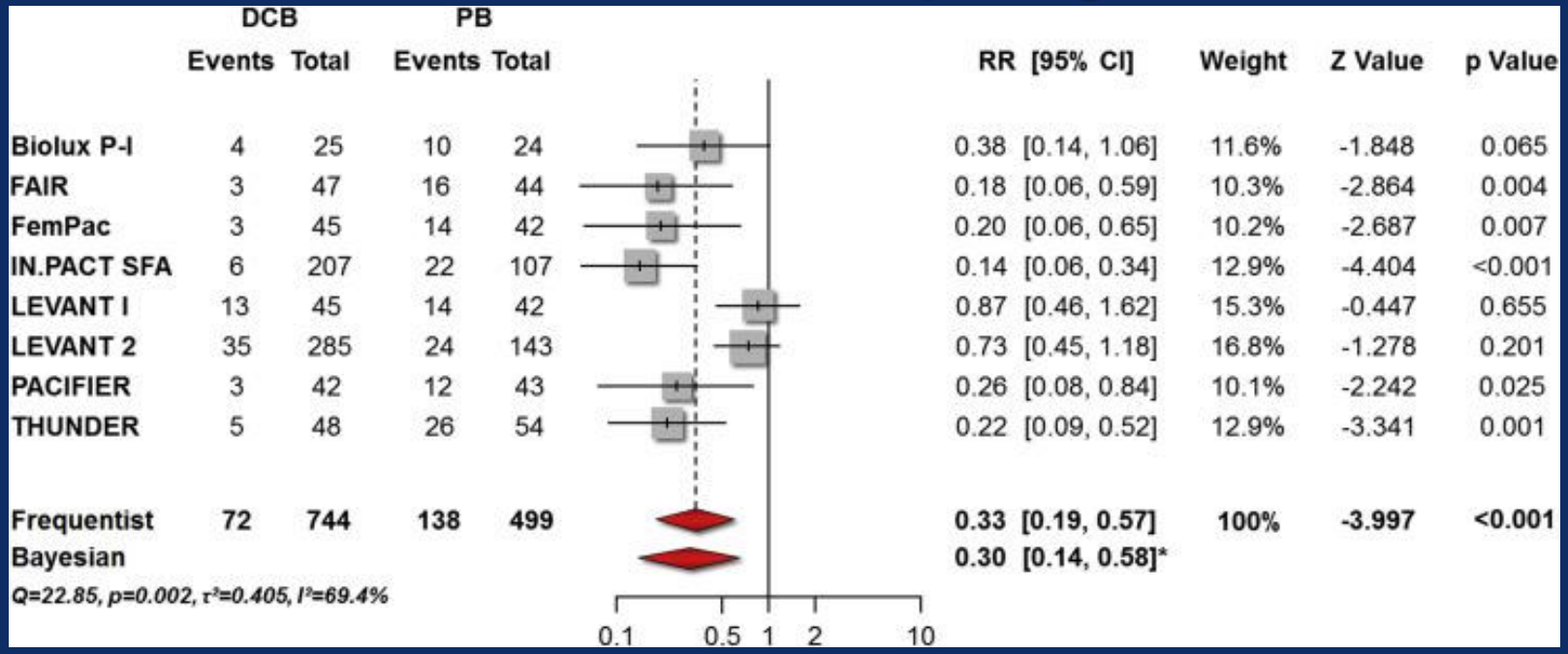
Schroeder H., et al. *Catheterization and cardiovascular interventions* 2015;86:278-86
M. Brodmann. ILLUMENATE European Randomized Trial: 2-year Results. Oral Presentation. VIVA September, 2017, Las Vegas, NV.
Scheinert et al. J Am Coll Cardiol Intv 2014; 7:10-9
Laurich C. Oral Presentation. *SVS*. 2015

M. Weinberg Oral Presentation. TCT 2017

DCB vs. Plain balloon angioplasty for Femoropopliteal artery disease

Meta-Analysis of Randomized Trials

Risk of TLR at 12 months comparing DCB with PB



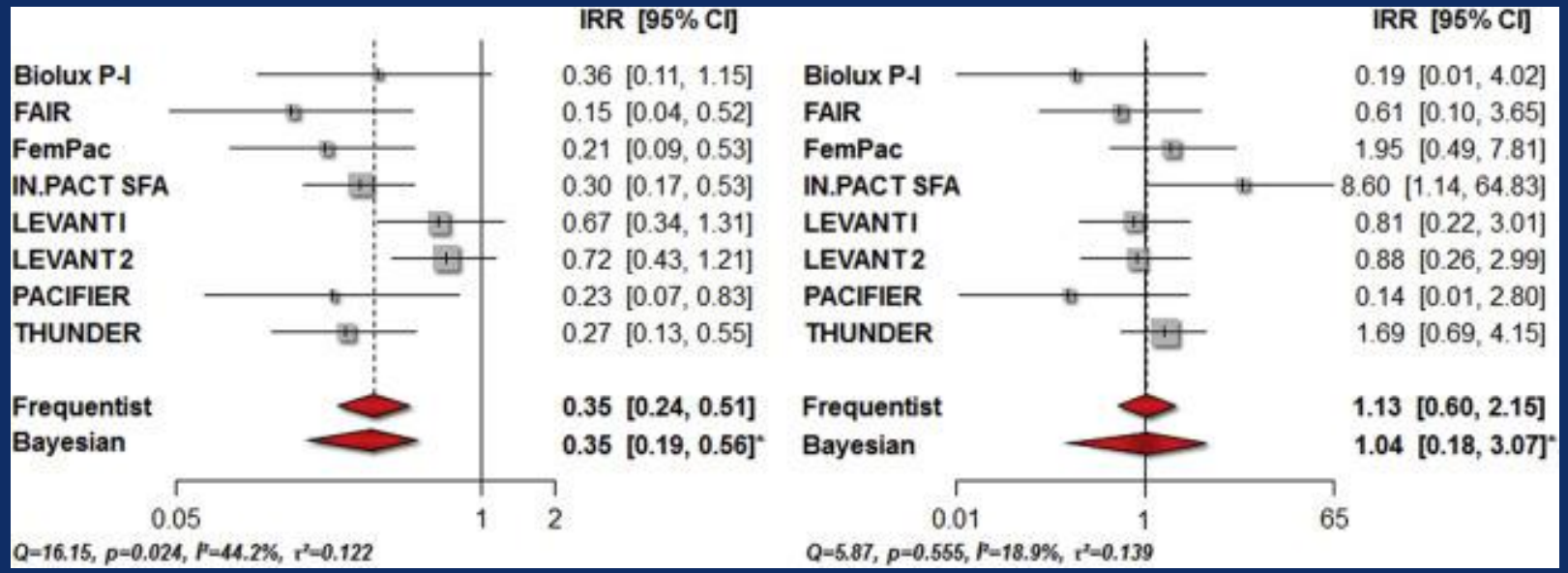
Conclusion DCB significantly reduce the risk of TLR as compared with PB without any effect on all-cause death.

Giacoppo D et al. JACC Cardiovasc Interv. 2016

DCB vs. Plain balloon angioplasty for Femoropopliteal artery disease

Meta-Analysis of Randomized Trials

Long-Term TLR and All-cause Death in DCB versus PB

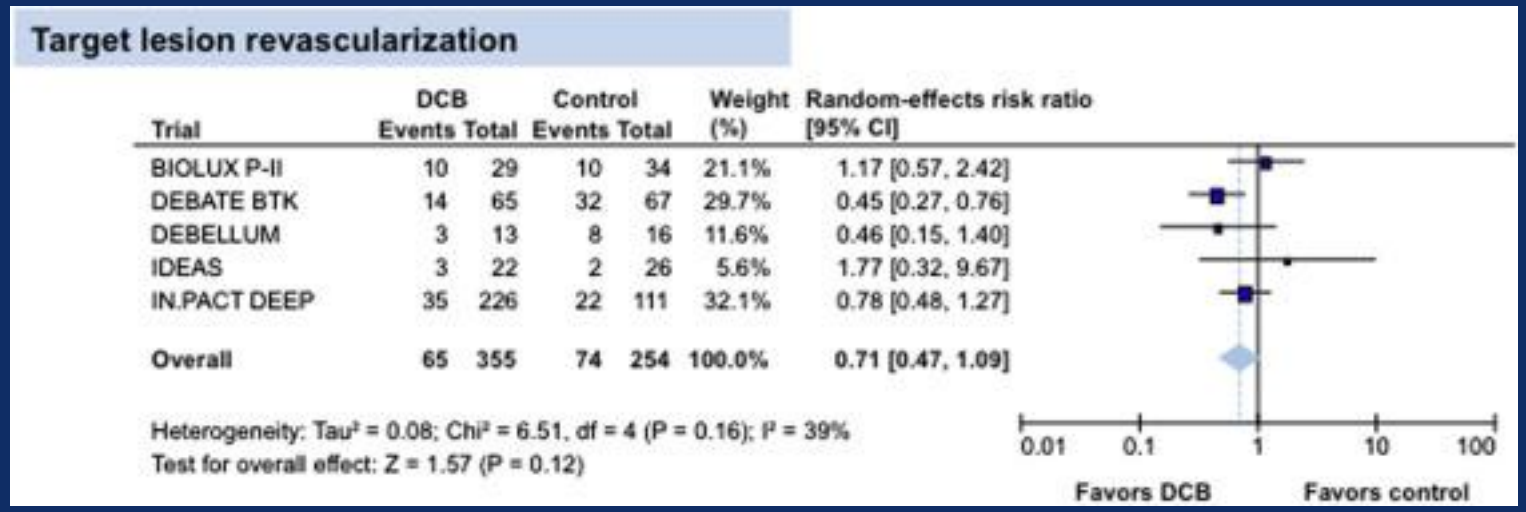


Conclusion DCB significantly reduce the risk of TLR as compared with PB without any effect on all-cause death.

Giacoppo D et al. JACC Cardiovasc Interv. 2016

DCB vs. Control(PB or DES) for infrapopliteal arteries

Meta-Analysis of Randomized Trials
Risk of TLR comparing DCB with control

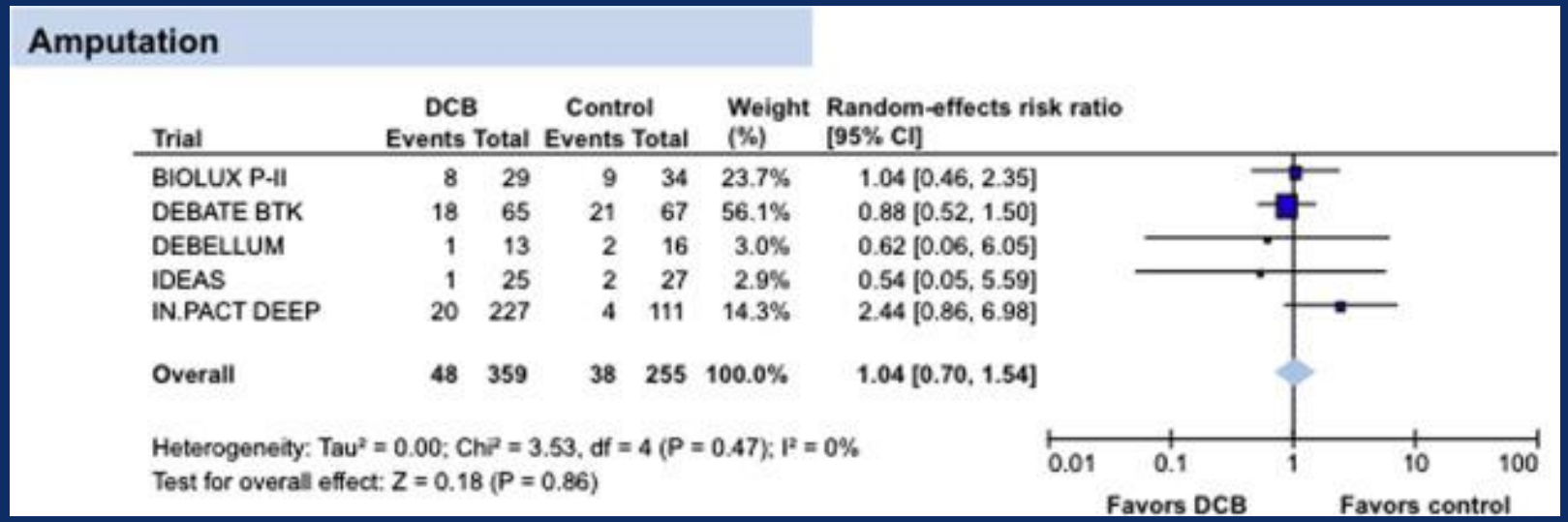


Conclusion The treatment of infrapopliteal arteries with DCBs is associated with similar outcomes and favorable angiographic efficacy at 1-year follow-up.

Cassese S et al. JACC Cardiovasc Interv. 2016

DCB vs. Control(PB or DES) for infrapopliteal arteries

Meta-Analysis of Randomized Trials
Risk of Amputation comparing DCB with control



Conclusion The treatment of infrapopliteal arteries with DCBs is associated with similar outcomes and favorable angiographic efficacy at 1-year follow-up.

Cassese S et al. JACC Cardiovasc Interv. 2016

DCB vs. Control(PB or DES) for infrapopliteal arteries

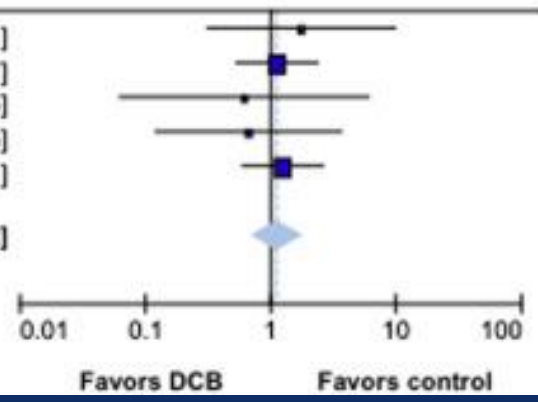
Meta-Analysis of Randomized Trials

Risk of Death comparing DCB with control

Death

Trial	DCB Events	DCB Total	Control Events	Control Total	Weight (%)	Random-effects risk ratio [95% CI]
BIOLUX P-II	3	29	2	34	7.5%	1.76 [0.32, 9.81]
DEBATE BTK	12	65	11	67	39.9%	1.12 [0.53, 2.37]
DEBELLUM	1	13	2	16	4.2%	0.62 [0.06, 6.05]
IDEAS	2	25	3	25	7.6%	0.67 [0.12, 3.65]
IN.PACT DEEP	23	227	9	111	40.7%	1.25 [0.60, 2.61]
Overall	**41**	**359**	**27**	**253**	**100.0%**	**1.14 [0.71, 1.82]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.97$, df = 4 (P = 0.91); $I^2 = 0\%$
Test for overall effect: Z = 0.54 (P = 0.59)



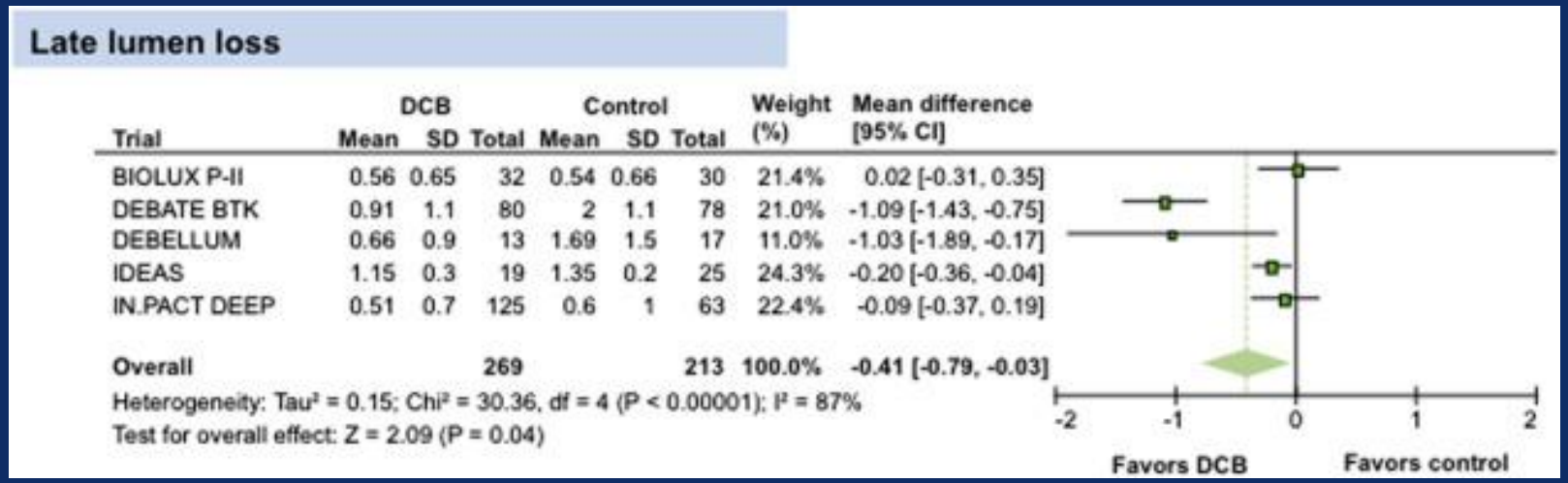
Conclusion The treatment of infrapopliteal arteries with DCBs is associated with similar outcomes and favorable angiographic efficacy at 1-year follow-up.

Cassese S et al. JACC Cardiovasc Interv. 2016

DCB vs. Control(PB or DES) for infrapopliteal arteries

Meta-Analysis of Randomized Trials

Risk of Late lumen loss comparing DCB with control



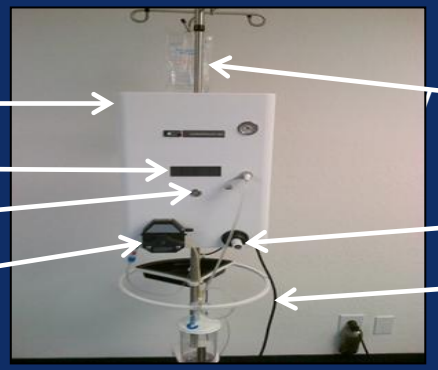
Conclusion The treatment of infrapopliteal arteries with DCBs is associated with similar outcomes and favorable angiographic efficacy at 1-year follow-up.

Cassese S et al. JACC Cardiovasc Interv. 2016

The Genesis™ System

Hardware

- Generator
- Timer
- ON/OFF Switch
- Irrigation Pump

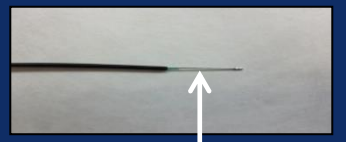


Pole

Transducer

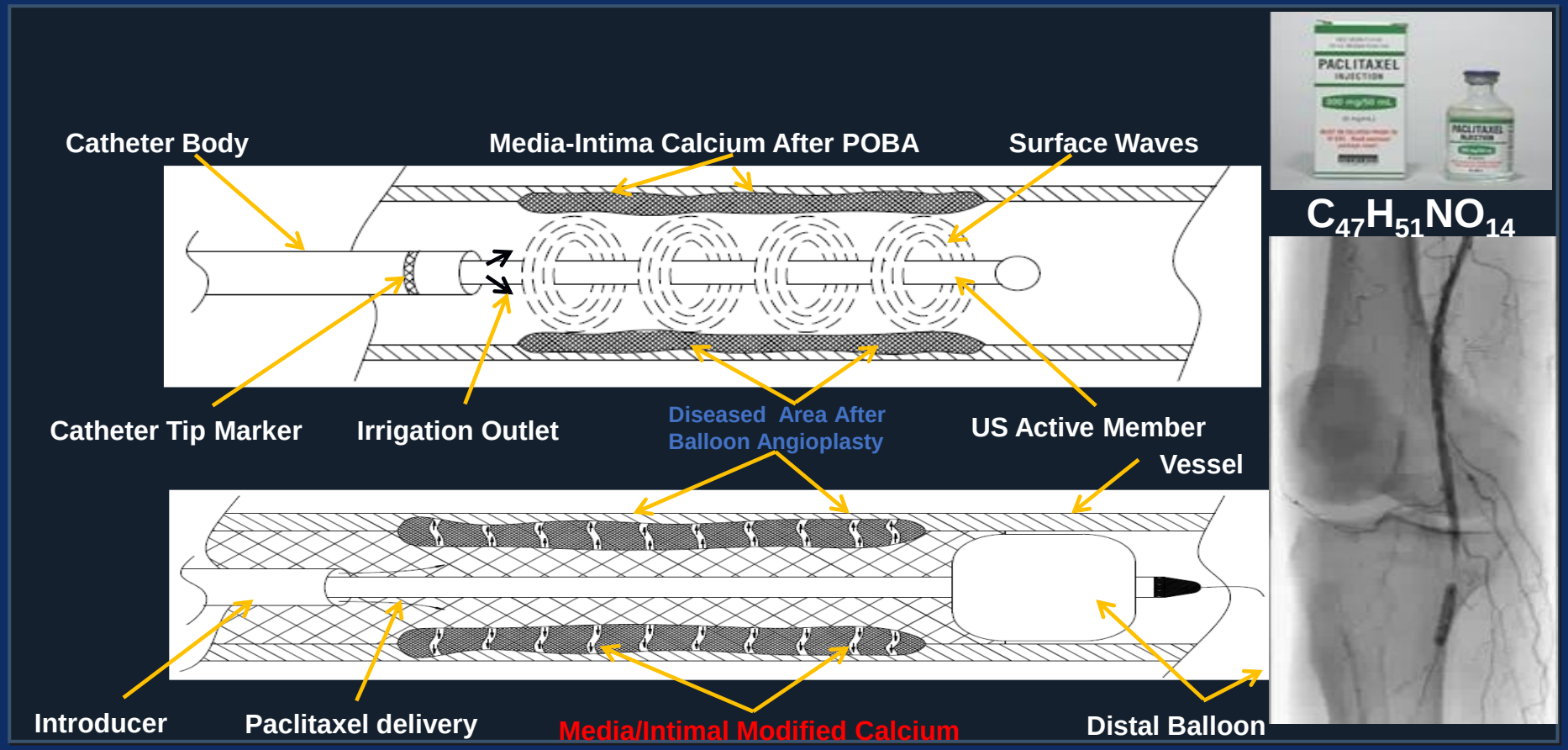
Foot switch cable

Catheter

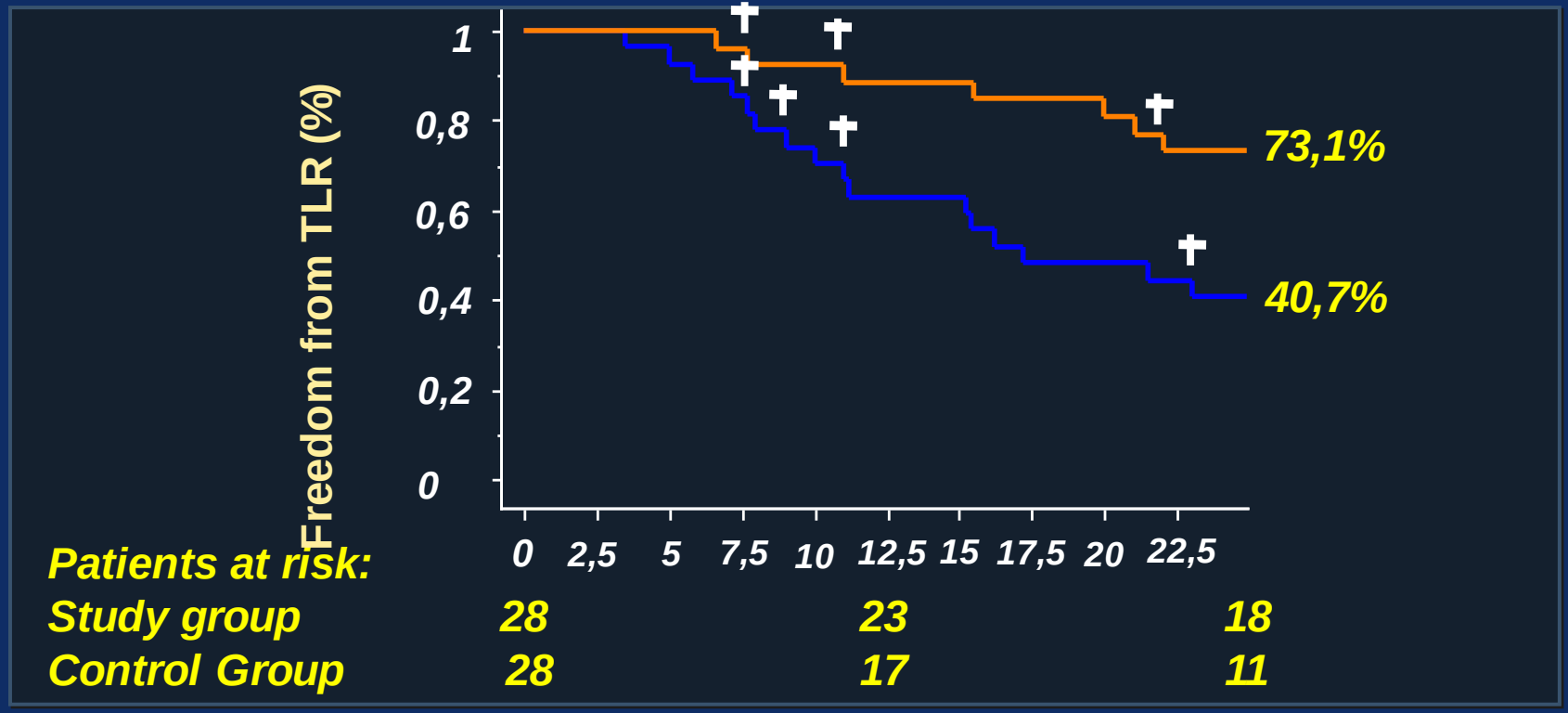


- .6 mm tip
- 1.6mm catheter
- RX any 0.014’guidewire
- 200 cm long
- 5F sheath compatible
- Ultrasound active member with adjustable length 10-100mm

Method of Action



PACUS trial
Freedom from TLR 24m FU



C. Giudice, Oral Presentation. TCT 2017

Serranator® Alto PTA Serration Balloon Catheter

- 4 embedded serrated metal strips
- Nylon, semi-compliant balloon
- 6F Sheath with 0.018” GW
- 4.0, 5.0, 6.0 mm balloon diameters
- 40, 80, 120 mm balloon lengths

Designed to create linear, interrupted scoring along the endoluminal surface

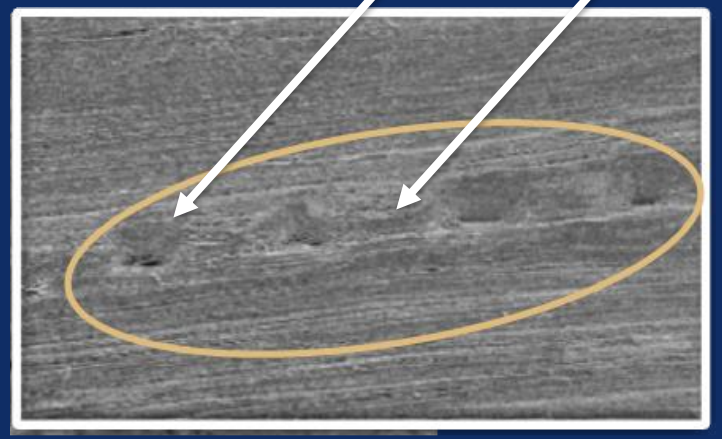
Serranator® Alto PTA Serration Balloon Catheter Mechanism of action

- As the Serranator inflates and contacts the artery wall, the strips create multiple interrupted lines of scoring (serrations)
- Serrations are responsive to the balloon’s energy, enabling predictable and controlled lumen expansion along the lines

Serranator® Alto PTA Serration Balloon Catheter
Mechanism of action

Scanning Electron Microscopy (SEM)
of porcine tissue at 7-days

Serrations create
linear and circumferential
expansion



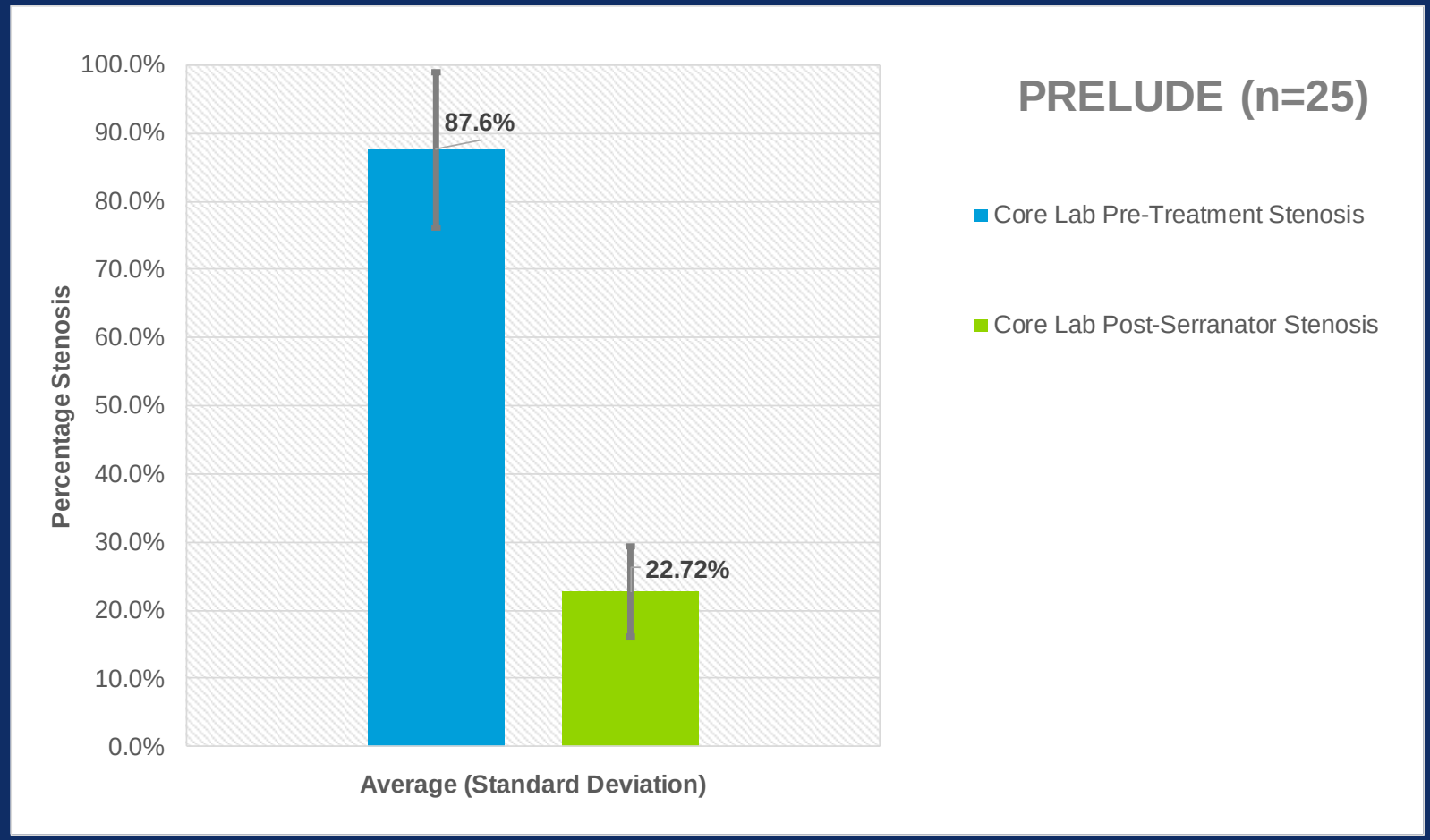
PRELUDE study
Result in calcification

Characteristic	Results
Degree of Calcification	
None/mild	11 (44%)
Moderate	7 (28%)
Severe*	7 (28%)
Avg. Lumen Gain	
Overall	3.36 mm
Severe Calcification	3.45 mm

* Severe calcification of target lesion: circumferential calcium and >50% of lesion length.

W. Gray MD, Oral Presentation. TCT 2017

PRELUDE study
Pre- and Post-stenosis



W. Gray MD, Oral Presentation. TCT 2017

EffPac-RCT Trial

Efficacy: Target Lesion Revascularization (TLR)

	LUMINOR®	POBA	Relative Risk, 95% CI (LUMINOR® vs. POBA)	Number needed to treat (NNT)	p value
TLR 6M (%)	1.3 (1/76)	17.1 (13/76)	0.082 [CI: 0.012; 0.560]	7	<0.001
TLR 12M (%)	1.3 (1/76)	18.7 (14/75)	0.077 [CI: 0.011; 0.526]*	6	<0.001

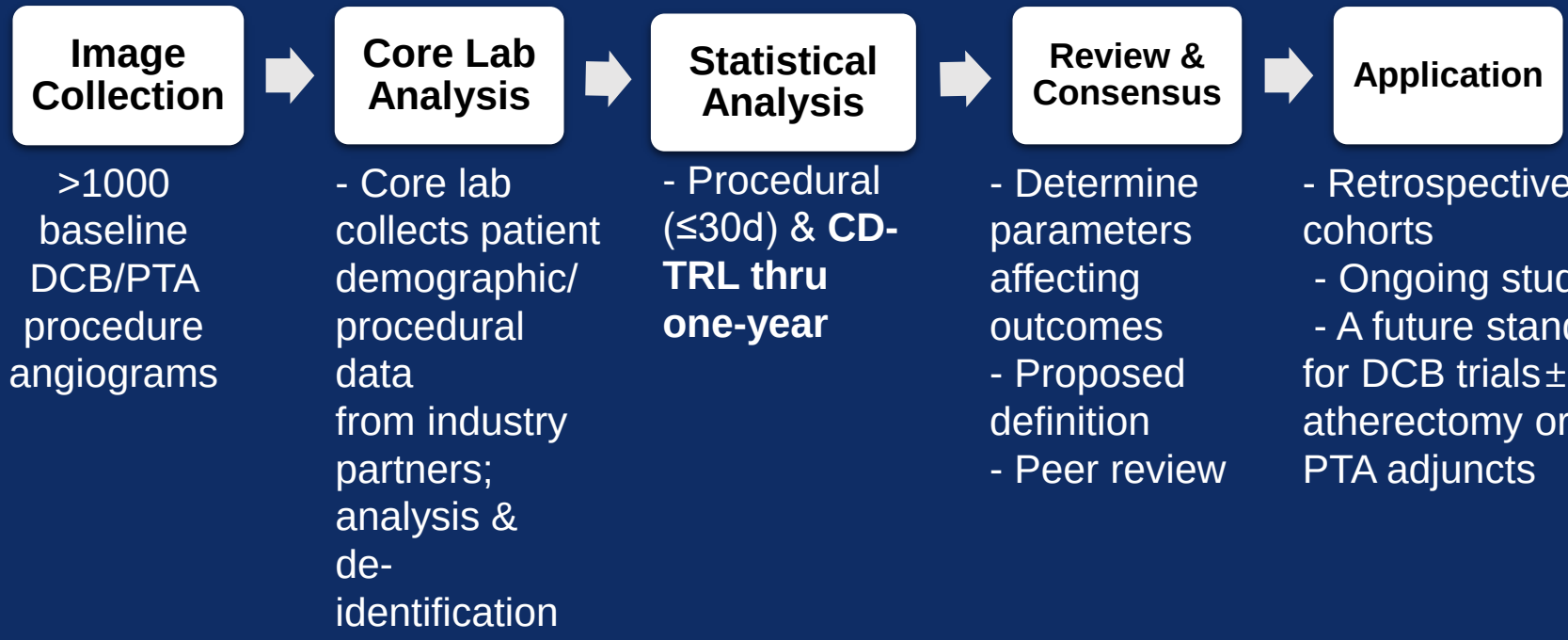
Efficacy: Patency

	LUMINOR®	POBA	Relative Risk, 95% CI (LUMINOR® vs. POBA)	Number needed to treat (NNT)	p value
Patency 6M (%)	94.7 (72/76)	75.0 (57/76)	1.26 [CI: 1.100; 1.443]	6	<0.001
Patency 12M (%)	90.3 (65/72)	65.3 (47/72)	1.38* [CI: 1.146; 1.664]	4	<0.001

Marcus Thieme MD, TCT 2018

The VIVA Calcium Scale Unification Project: Proposed Investigational Plan

IN.PACT RTC/Global Japan IP SFA ILLUMENATE RCT/ ILLUMENATE Global SFA-LONG Study

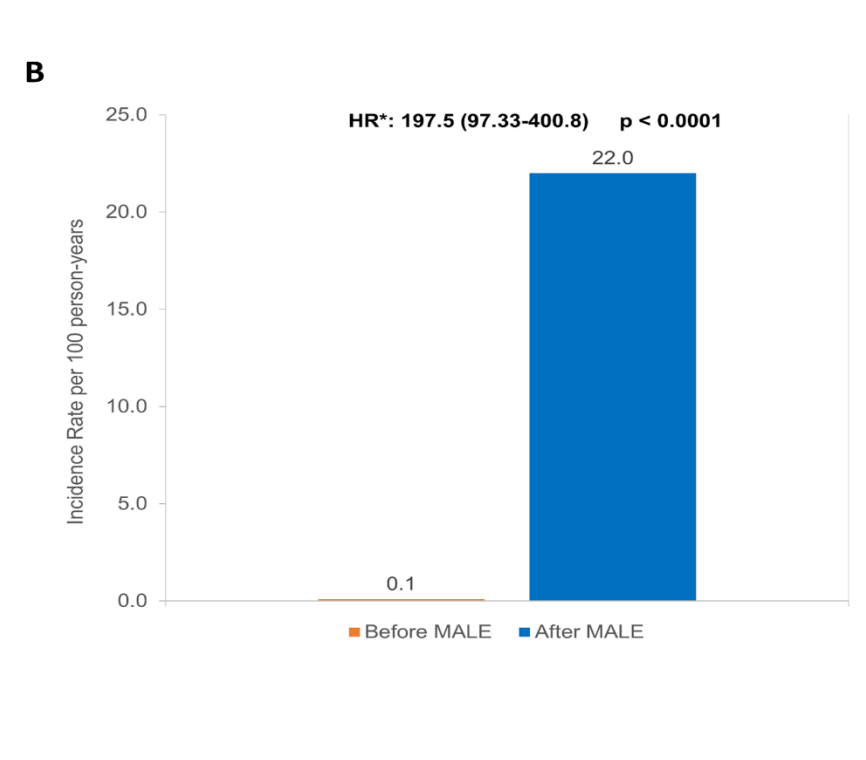


Courtesy of Krishna Rocha-Singh, MD

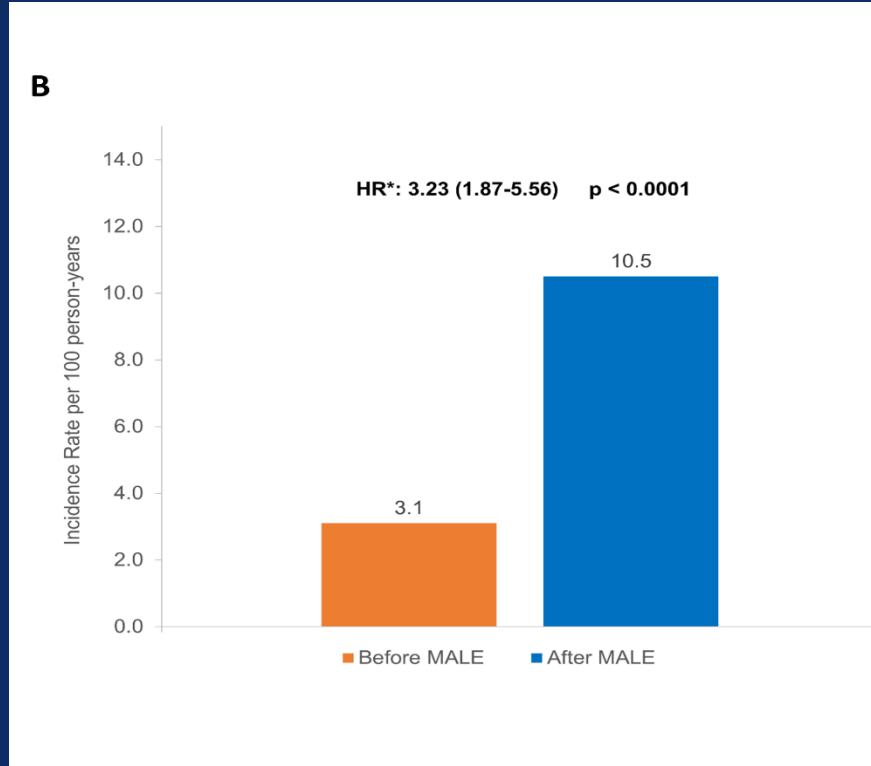
Jeffrey J. Popma MD TCT 2018

High Rate of Amputation & Death after MALE in PAD : Results from COMPASS

Incidence of Vascular Amputation



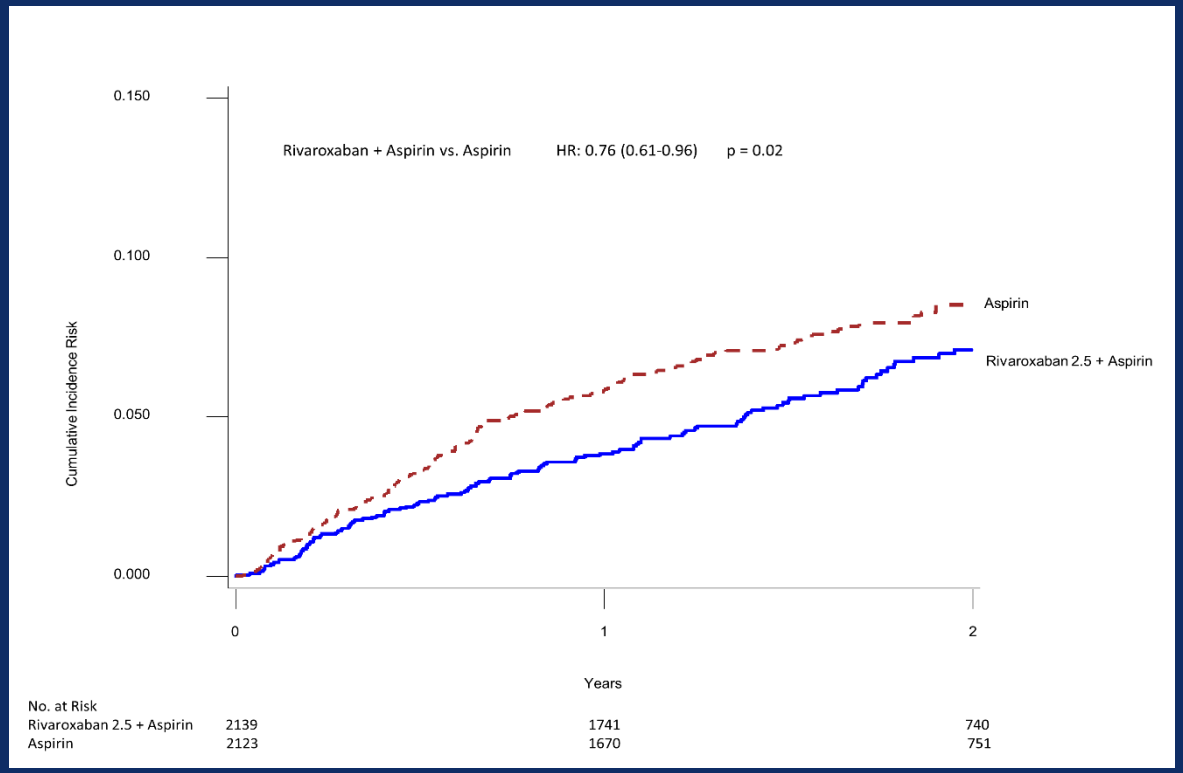
Incidence of Death



Conclusion: **MALE is associated with a poor prognosis: 3 fold increase in death,200 fold increase in amputation.**

Anand SS et al, J Am Coll Cardiol. 2018 May 22;71(20):2306-2315

High Rate of Amputation & Death after MALE in PAD : Results from COMPASS

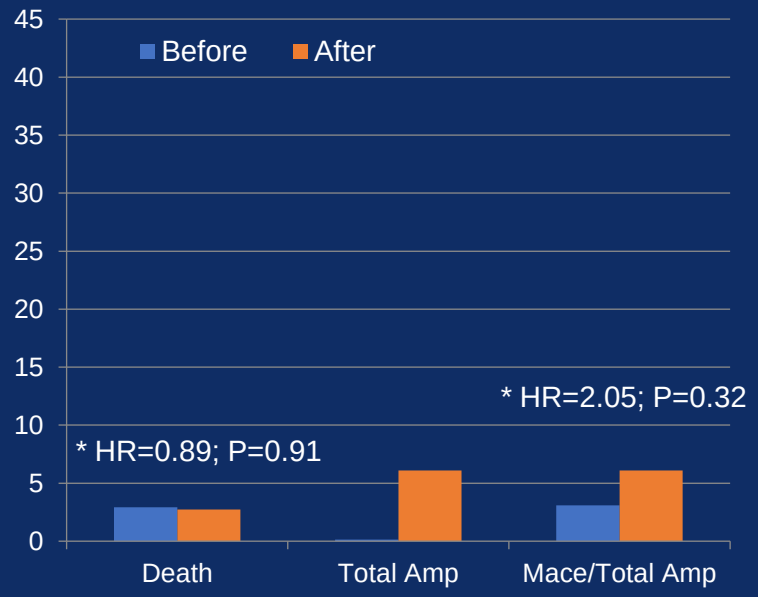


Conclusion: **Compared to aspirin, Riva/Aspirin combination prevents MALE, vascular interventions, and total peripheral vascular outcomes**

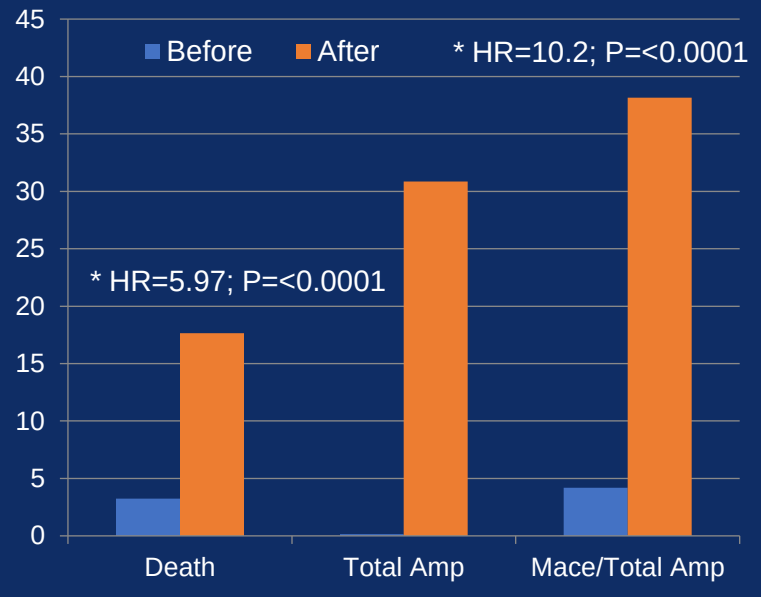
Anand SS et al, J Am Coll Cardiol. 2018 May 22;71(20):2306-2315

High Rate of Amputation & Death after MALE in PAD : Results from COMPASS

Riva/Aspirin



Aspirin Only



*HR determined by time-dependent Cox model

Conclusion: **Outcomes after MALE are worse for aspirin-treated patients**

Anand SS et al, J Am Coll Cardiol. 2018 May 22;71(20):2306-2315

DES vs DCB Revascularization in Patients wiith Femoropopliteal Arterial Disease

REAL PTX: randomized 150-patient trial of paclitaxel-based devices that included lesions ≤ 30 cm, CTOs, and severe calcification.

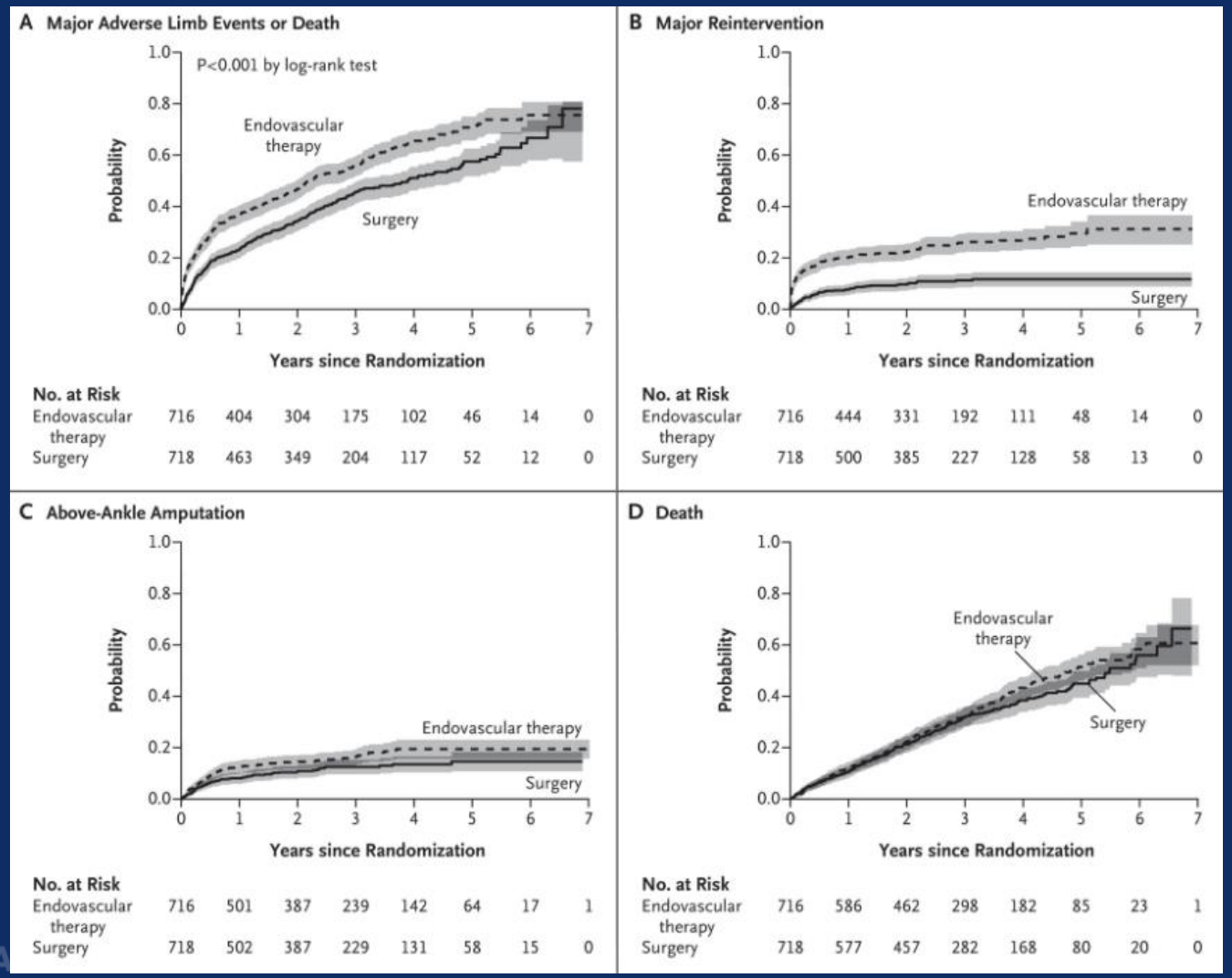
- One in four DCB patients required bailout stenting
- Primary patency was similar at 12 months, but by 36 months a trend favored DES over DCB (54% vs 38%; *P* = 0.17)
- In lesions > 10 cm, restenosis accrued over time in both treatment groups but there was a numerically lower patency rate for DCB at 3 years

Conclusion: The head-to-head comparison suggests equivalent results at 12 months, with a patency advantage for DES at 36 months.

Bausback Y, et al. J Am Coll Cardiol. 2019;73:667-679.

Surgery or Endovascular Therapy for Chronic Limb-Threatening Ischemia

randomized 1830 patient with CLTI and infra-inguinal peripheral artery disease

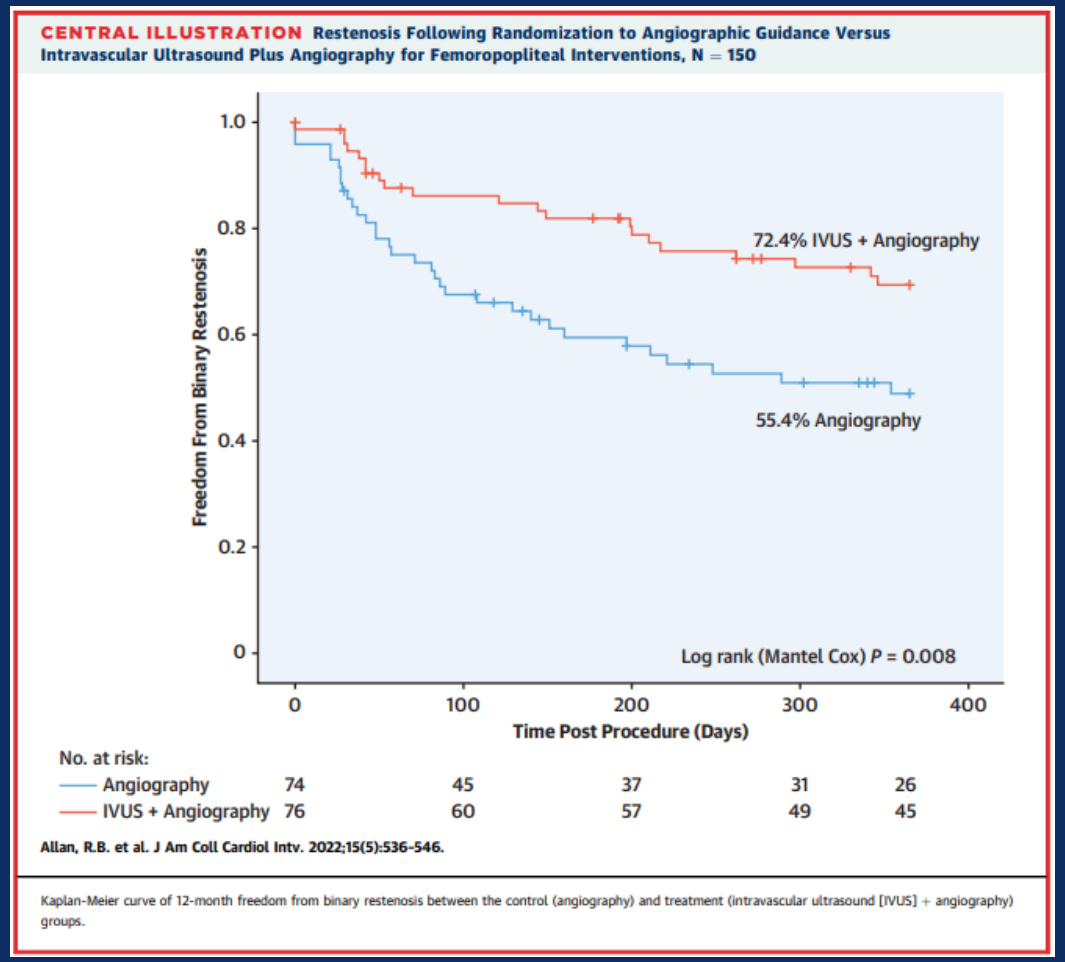


Conclusion: In patients with CLTI, initial bypass surgery was associated with a lower incidence of major adverse limb events or death than initial endovascular intervention.

Alik Farber, et al.
N Engl J Med 2022; 387:2305-2316.

IVUS guided Femoropopliteal intervention

IVUS guidance vs Angiographic guidance

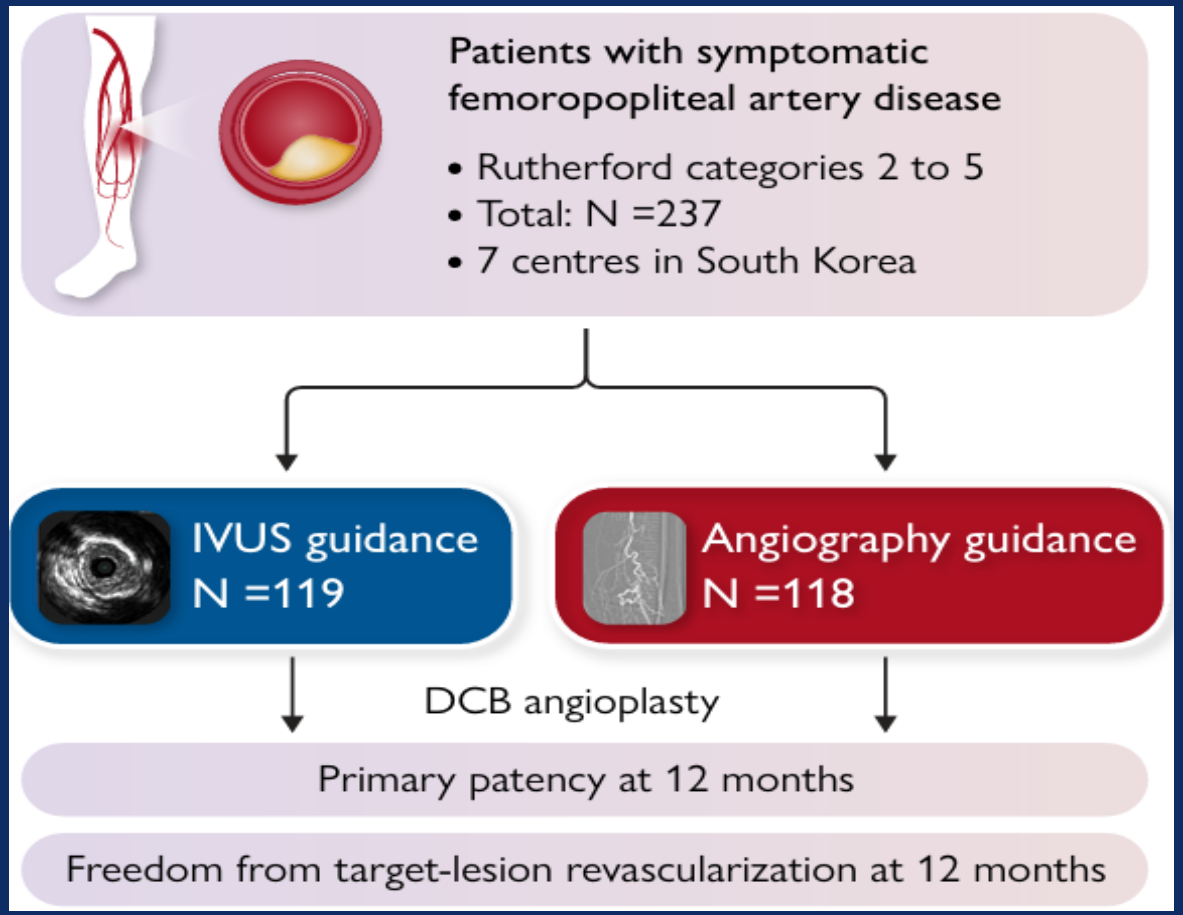


- **Randomized 150-patient trial o f IVUS guidance or Angiograph ic guidance**

- **Conclusion**
- The use of IVUS resulted in a significant reduction in the rate of restenosis after endovascular intervention

Allan, R.B. et al.
J Am Coll Cardiol Intv. 2022;15(5):536-546.

IVUS-DCB trial

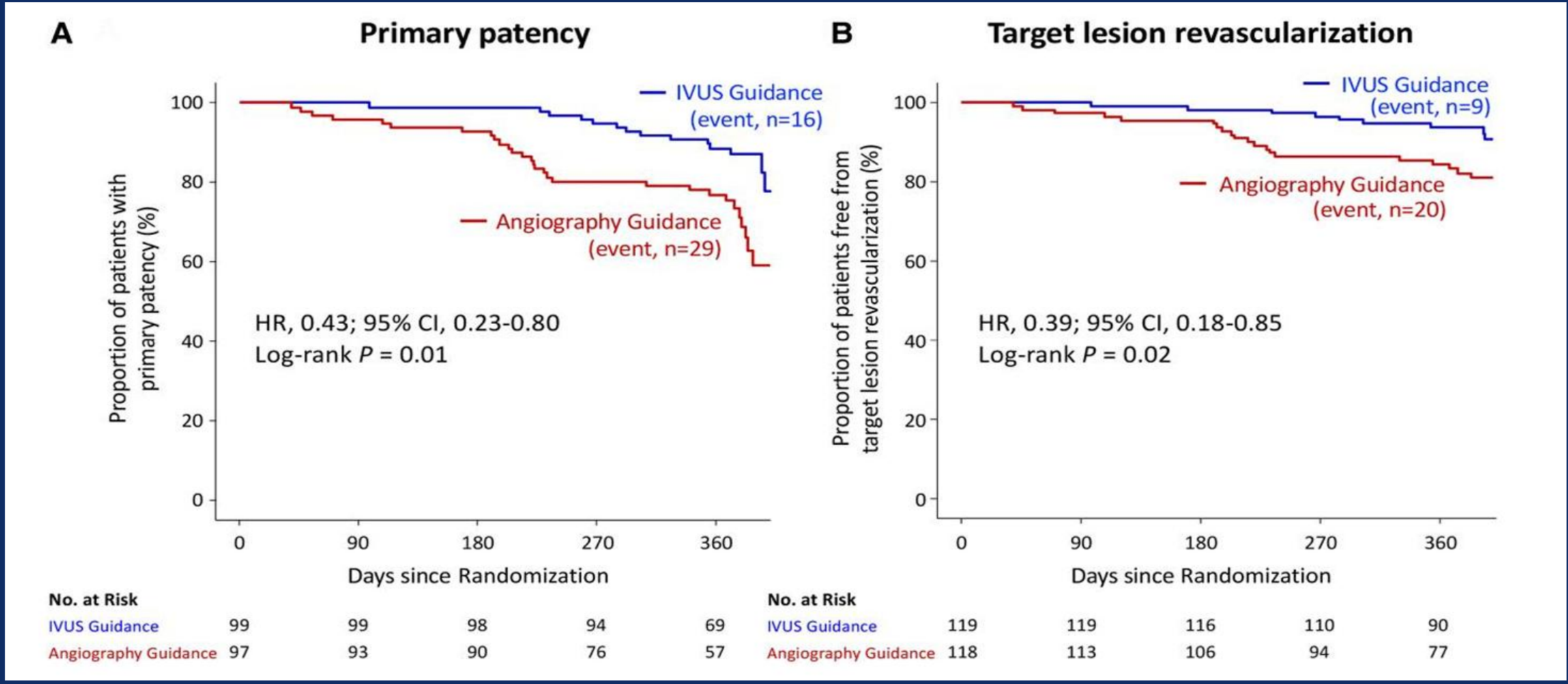


- **Primary endpoint**
- Primary patency defined as the abscnce of clinically-driven target lesion revascularization(CD-TLR)
- binary restenosis on imaging studies(DUS, CT, Angiography) at 12 month follow-up

- **Secondary endpoints**
- Freedom from CD-TLR
- Sustained clinical improvement(improved Sx≥1 Rutherford category, no CD TLR)
- Sustained Hemodynamic improvement(ABI≥0.15, no CD TLR)
- Mortality
- Major amputations
- Major bleeding

Young-Guk Ko. European Heart Journal (2024) 45, 2839–2847

IVUS-DCB



Conclusion: IVUS guidance significantly improved the outcomes of DCB angioplasty for FPA disease in terms of primary patency, freedom from CD TLR, and sustained clinical and hemodynamic improvement at 12months

Young-Guk Ko. European Heart Journal (2024) 45, 2839–2847