HMP Global

Cardiovascular CME

DCB for PAD in 2026 with a Changing Landscape of Safety and Effectiveness



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Faculty Disclosures

- **Peter Schneider, MD**: Consultant—Medtronic, Boston Scientific, Cagent, Acotec, Abbott, Endologix, Shockwave Medical, Healthcare Inroads, BD, Stryker, Cordis
- **Prakash Krishnan, MD**: Consultant—Abbott, Medtronic, BD, Gore, Philips, Stryker, Shockwave Medical, Cook Medical
- **John Winscott, MD**: Consultant/Speakers Bureau—J&J MedTech, Medtronic, Shockwave Medical, Stryker, Asahi, Rhevera Medical

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Program Information

- This program is provided by HMP Education, an HMP Global company
- HMP Education, LLC acknowledges Medtronic and its support

Learning Objectives

- Differentiate the mechanisms, design characteristics, and clinical applications of paclitaxel- and limus-based drug-coated balloons
- Evaluate current clinical evidence supporting drug-coated balloon use, including long-term outcomes and comparative data
- Apply vessel preparation, patient and lesion selection, and procedural techniques to optimize long-term outcomes with DCBs (drug-coated balloons)

DCB = drug-coated balloon.

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Cardiovascular CME

DCB 101: Everything You Need to Know about DCB

Peter Schneider, MD



What Is the Purpose of Drug Delivery?

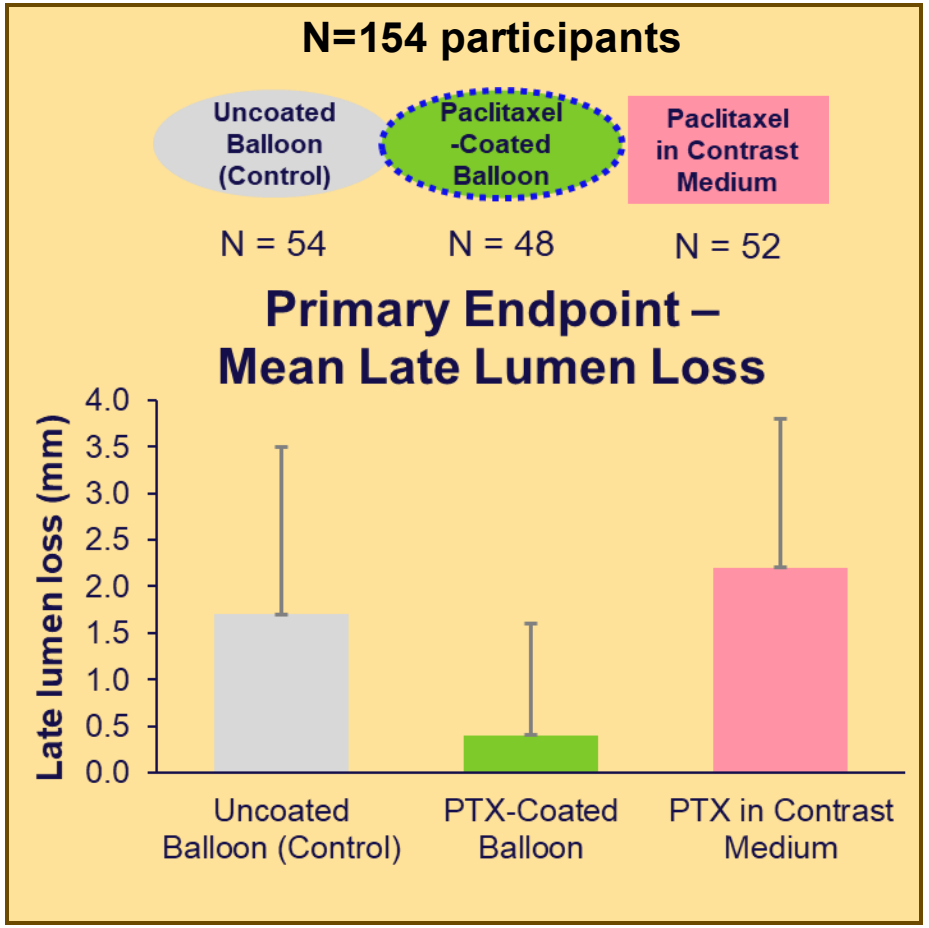
- Improve quality of life?
- Improve walking distance?
- Heal wounds?
- Decrease amputation rate?
- Reduce re-interventions?

THUNDER Trial:

Local Delivery of Paclitaxel to Inhibit Restenosis during Angioplasty of the Leg

- **First in-human study**
- Previous studies in cell culture and swine demonstrated an inhibitory effect
  - Multicenter
  - Randomized controlled trial
  - Core lab adjudicated

Enrollment between June 2004–June 2005

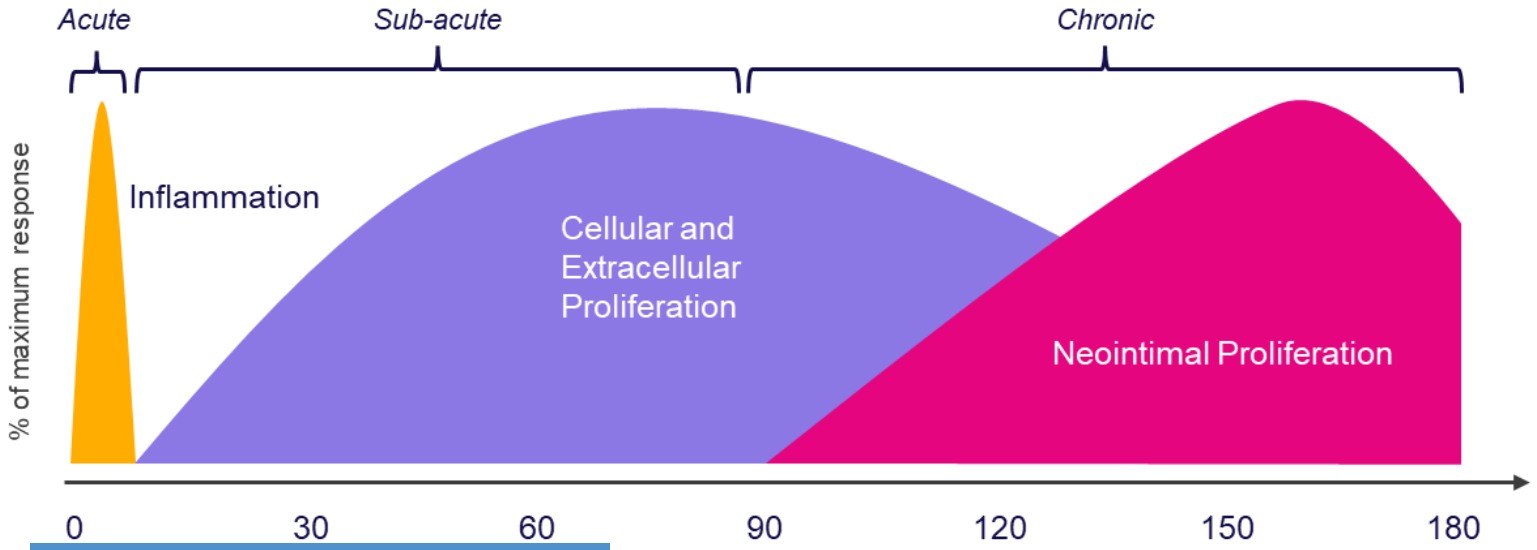


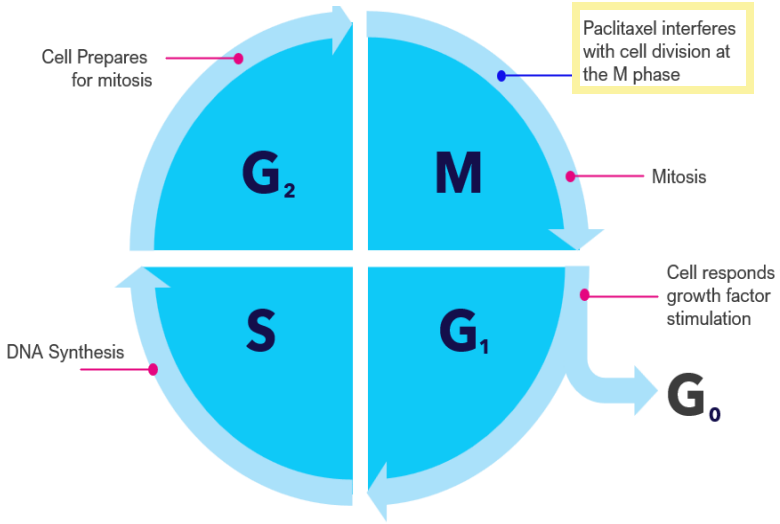
- Paclitaxel-coated balloons significantly reduced late lumen loss (*P*<.001) and angiographic restenosis at 6 months (*P*=.01) compared to uncoated balloons
- No significant increase in adverse events
- Paving the way for further paclitaxel DCB research

PTX = paclitaxel.

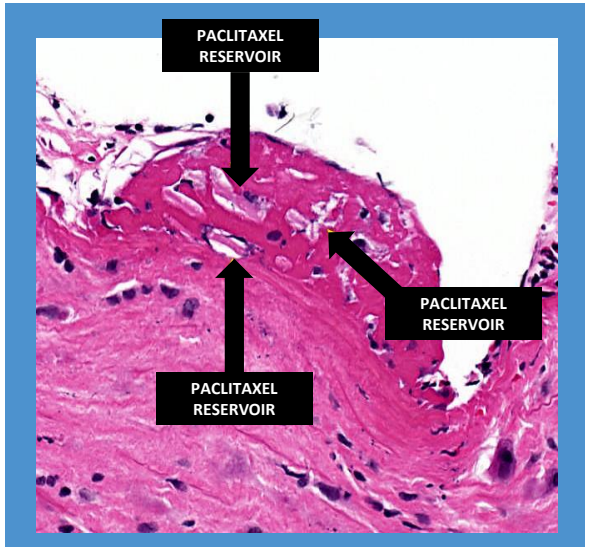
Tepe G, et al. *N Engl J Med*. 2008;358(7):689-699.

Restenotic Cascade and Paclitaxel Mechanism of Action



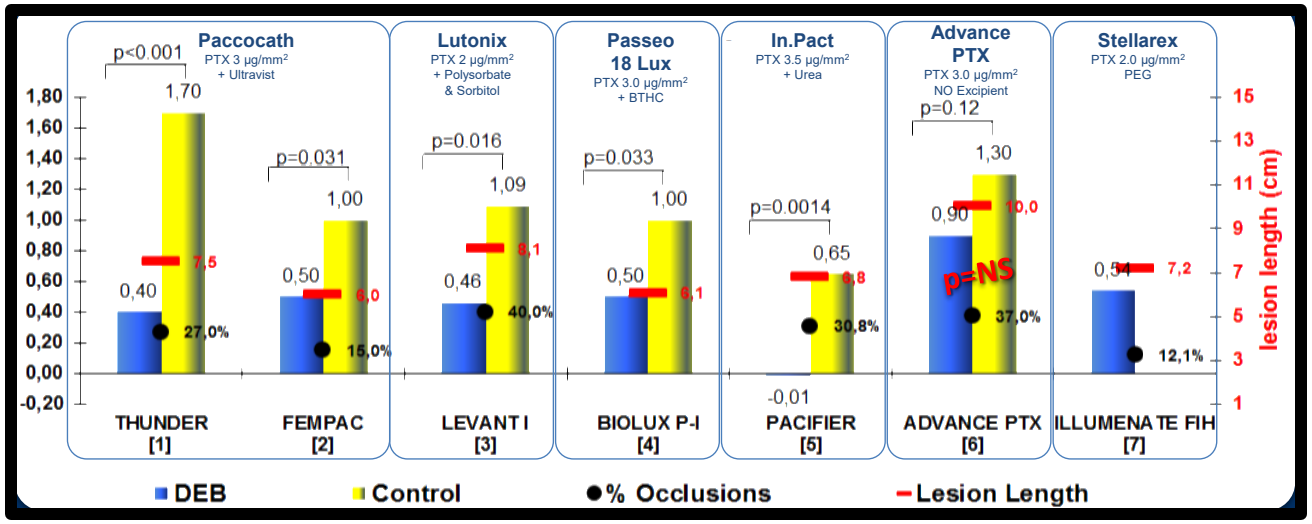


Strong anti-proliferative, moderate anti-inflammatory



- Paclitaxel is hydrophilic and readily adsorbed into the artery wall
- Crystals act as reservoirs

6-month angiogram:
Reduced late lumen loss



DEB = drug-eluting balloon; NS = not significant; BTHC = butyryl-tri-hexyl citrate; PEG = polyethylene glycol.

Deloose K. Presented at: Charing Cross 2018; April 15-18, 2018; London, United Kingdom. Forrester JS, et al. *J Am Coll Cardiol.* 1991;17(3):758-769. Henry M, et al. *J Indian Coll Cardiol.* 2017;7(Suppl 1):S19-S26.

Drug-Eluting Technology for Lower Extremity Revascularization

	DCB	DES
Femoral-popliteal	Paclitaxel: Lutonix, IN.PACT Stellarex, Ranger, Surveil, Chocolate Touch Numerous CE mark–approved devices Limus: Clinical studies	Paclitaxel: Zilver, Eluvia DRS in development Limus: Sirocco, Strides, Stroll—failed trials
Below-the-Knee	Paclitaxel: Lutonix, IN.PACT, Biolux-failed trials, Stellarex and Ranger stopped Acotec (PTX) in clinical trial, Limus: MedAlliance, Concept, Surmodics in clinical trials	Paclitaxel: SAVAL (SES) trial failed, PADI (DES) Limus: BE coronary DES (off-label) DRS: LIFE-BTK (approved), Reva, R3 (in clinical trials)

DES = drug-eluting stent; CE = Conformité Européenne; DRS = drug-eluting resorbable scaffold; SES = sirolimus-eluting stent; BE = balloon-expandable.

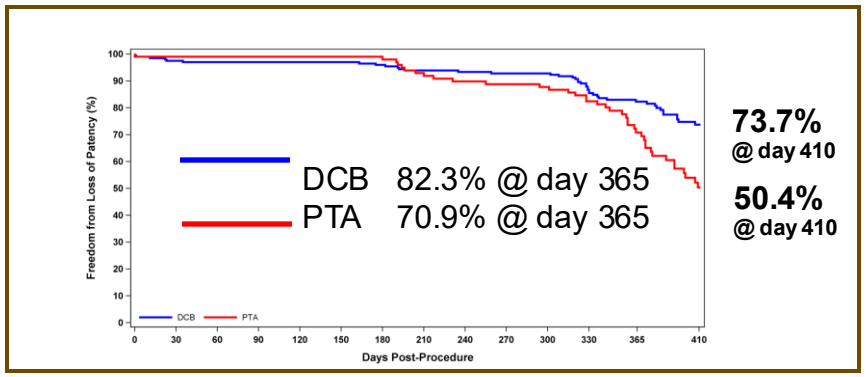
A Lot to Expect of Any Potential Solution…

- Deliverable by balloons
- Treat lesions ATK and BTK
- Manage a wide range of presentations
  - CLTI/claudication
  - Tissue loss vs intact skin integrity
- ISR, calcification, occlusion

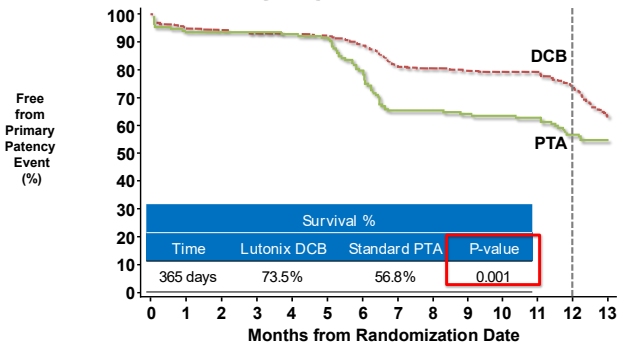
ATK = above-the-knee; BTK = below-the-knee; CLTI = chronic limb-threatening ischemia; ISR = in-stent restenosis.

Paclitaxel Efficacy: 1-Year Patency in Pivotal Trials

Illumenate

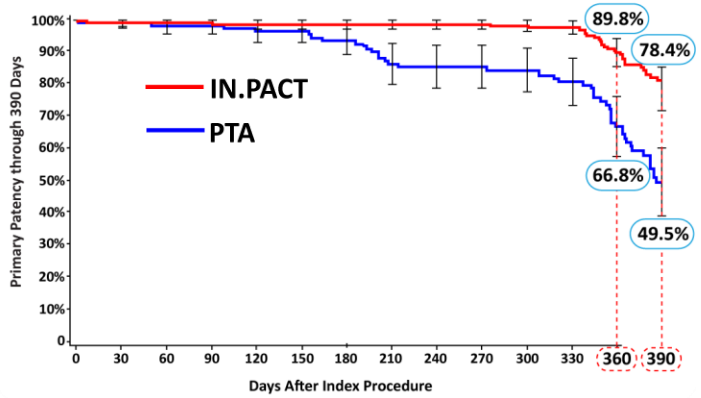


Levant

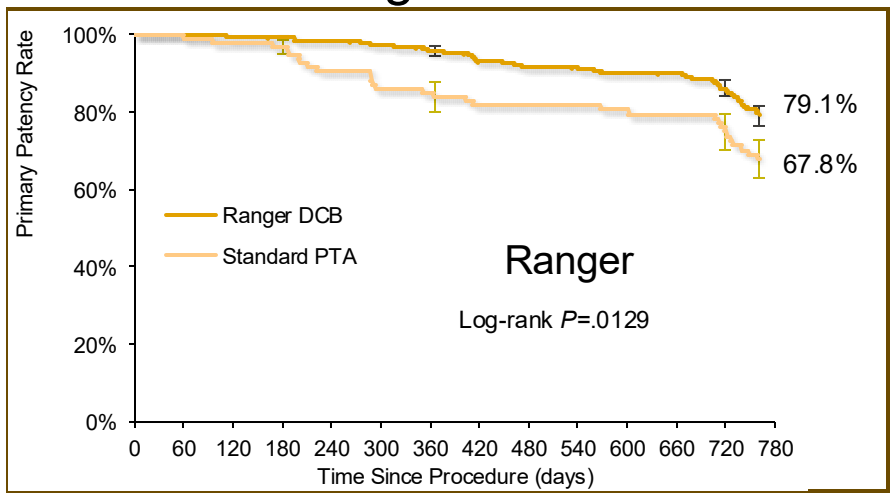


Proportions-based difference was 65.2% for DCB vs. 52.6% for standard PTA → 12.6% difference

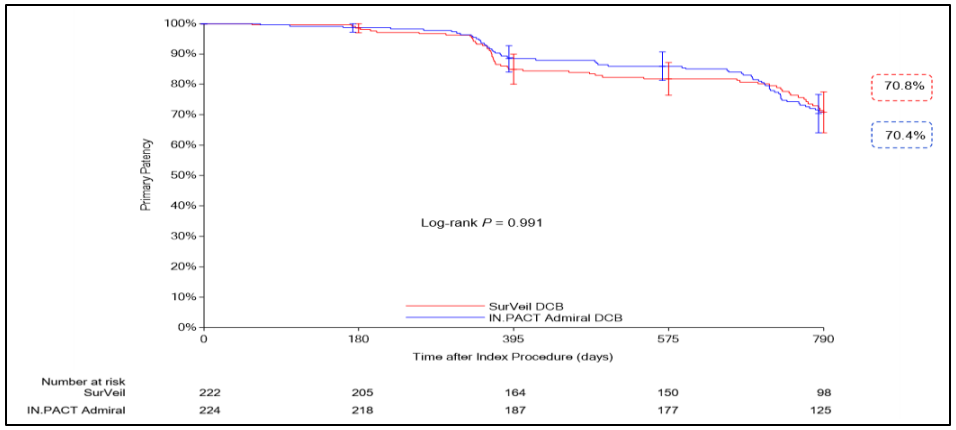
IN.PACT SFA



Ranger



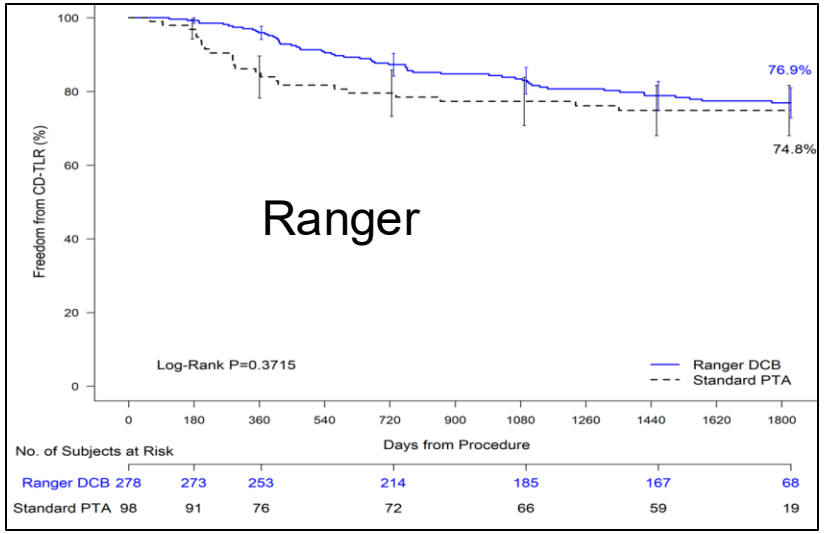
Transcend Trial: Surveil vs IN.PACT

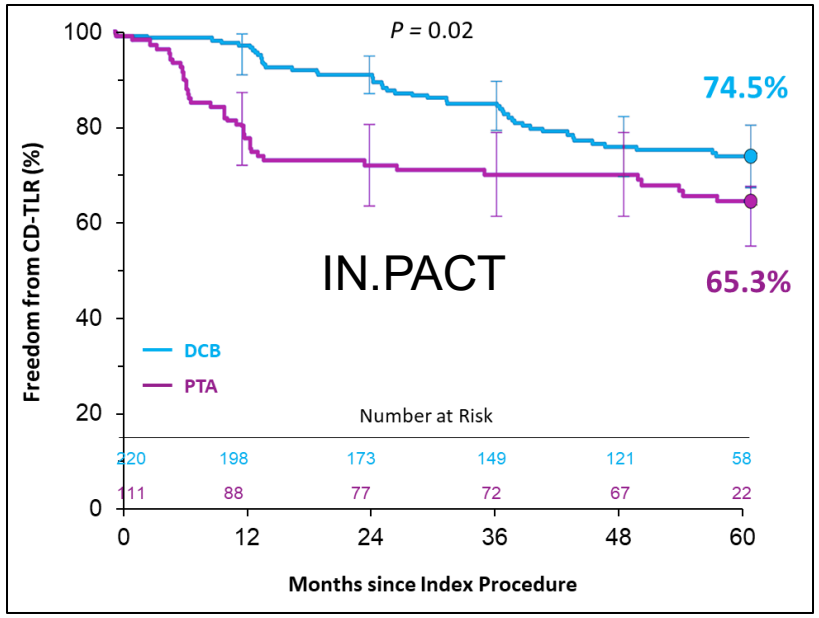


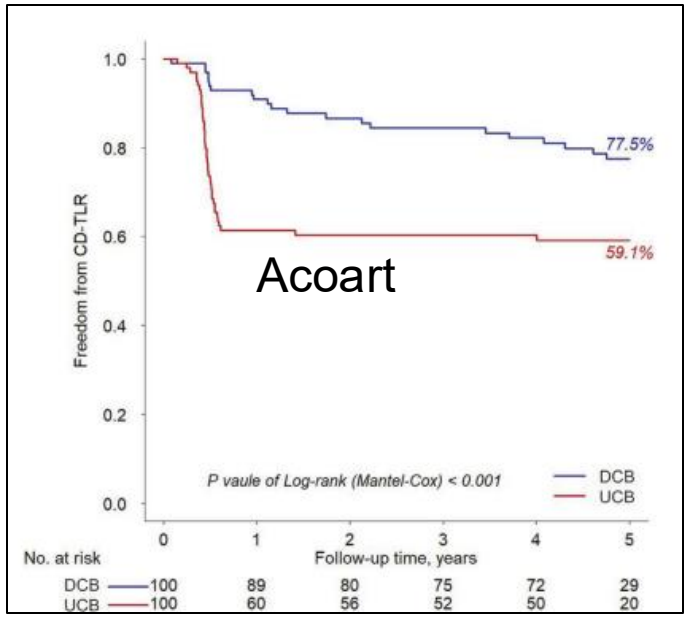
PTA = percutaneous transluminal angioplasty; SFA = superficial femoral artery.

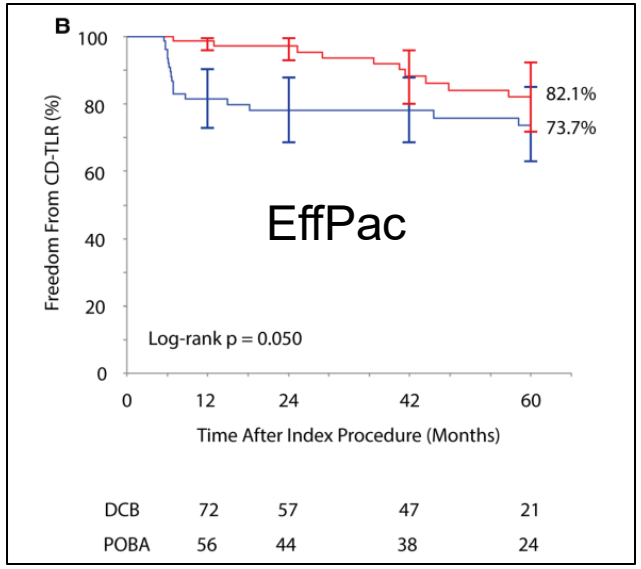
Lyden. Presented at: Transcatheter Cardiovascular Therapeutics (TCT); October 29–November 2, 2016; Washington, D.C. Sachar R. Presented at: VIVA; October 3-7, 2021; Las Vegas, Nevada. Rosenfield K, et al. *N Engl J Med*. 2015;373(2):145-153. Tepe G, et al. *Circulation*. 2015;131(5):495-502. Rosenfield. Presented at: VIVA; November 6-8, 2020; Virtual.

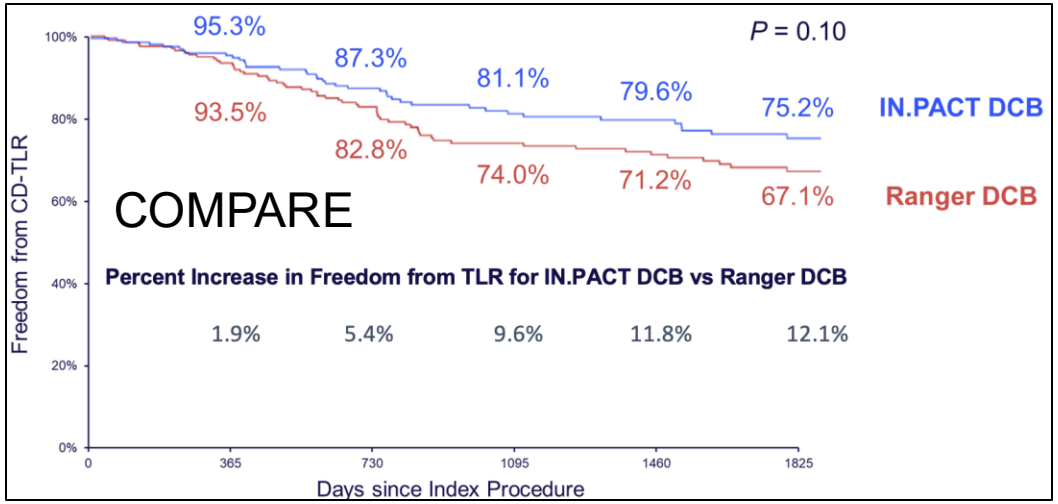
5-Year Results from Paclitaxel DCB RCTs: Freedom from CD-TLR









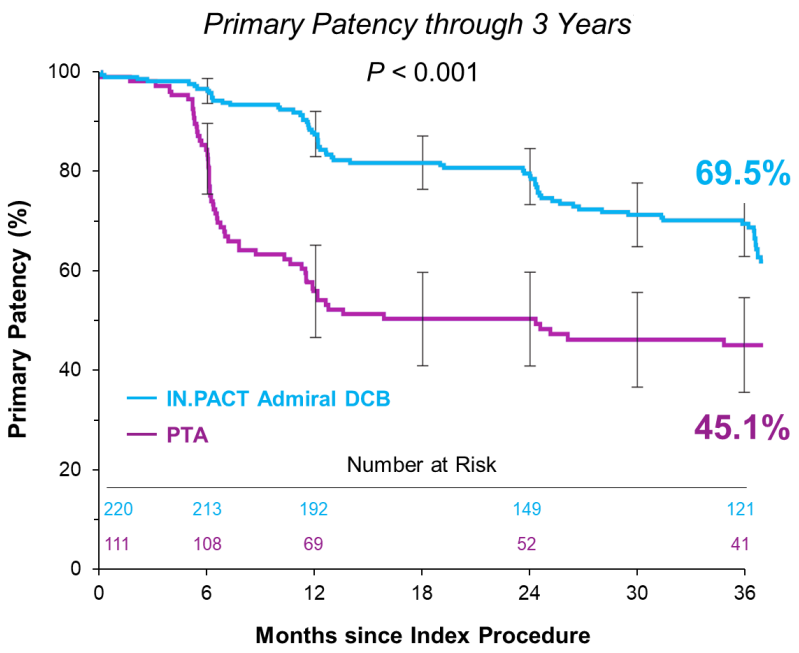


RCTs = randomized clinical trials; CD-TLR = clinically-driven target lesion revascularization.

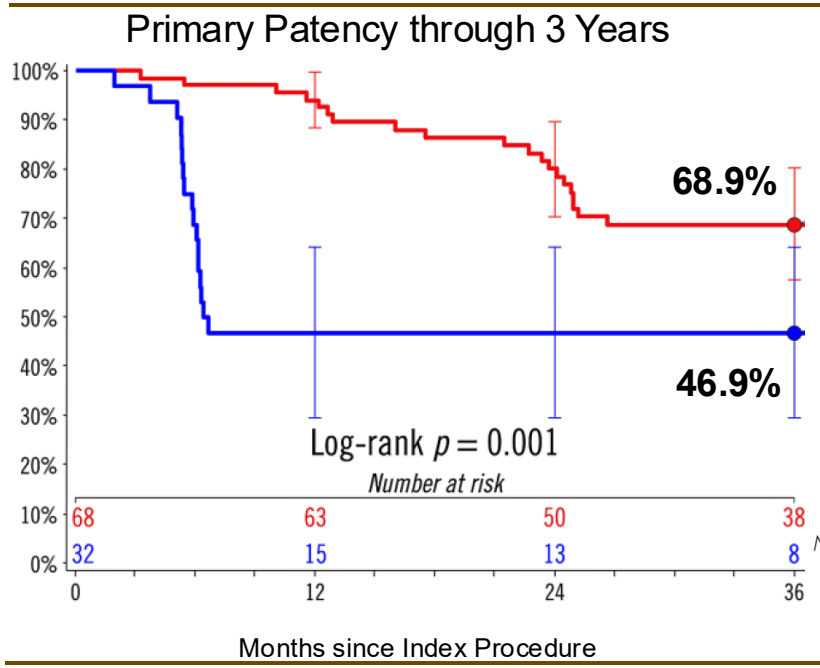
Teichgräber U, et al. *Cardiovasc Intervent Radiol*. 2022;45(12):1774-1783. Xu Y, et al. *J Vasc Surg*. 2021;74:756-762. Brodmann M. Presented at: LINC; May 28-31, 2024; Leipzig, Germany. Laird JA, et al. *Circ Cardiovasc Interv*. 2019;12(6):e007702. Steiner S. Presented at: LINC; May 28-31, 2024; Leipzig, Germany.

IN.PACT DCB in the Femoropopliteal Artery: Similar Results across Geographies

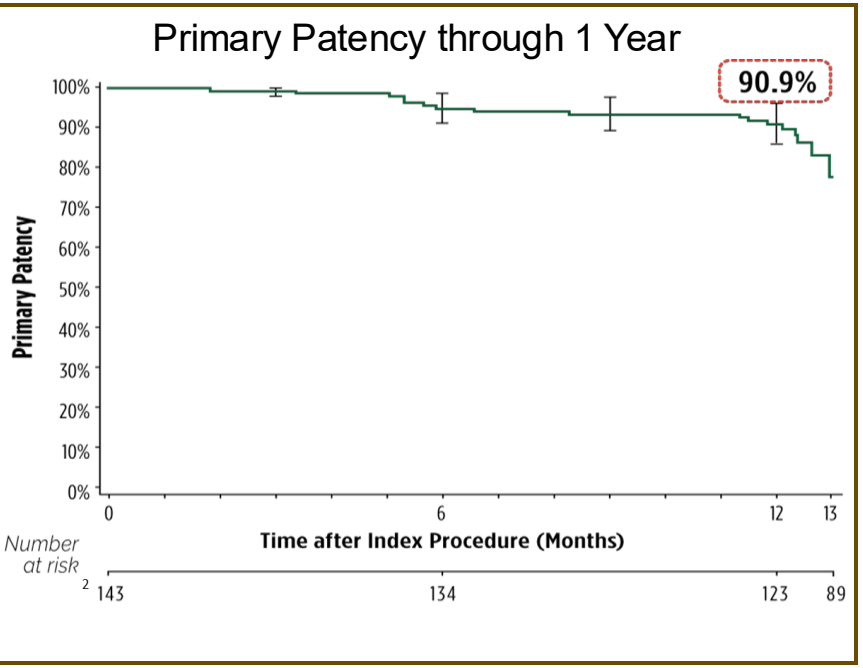
IN.PACT SFA (EU+US) RCT



IN.PACT JAPAN RCT



IN.PACT China



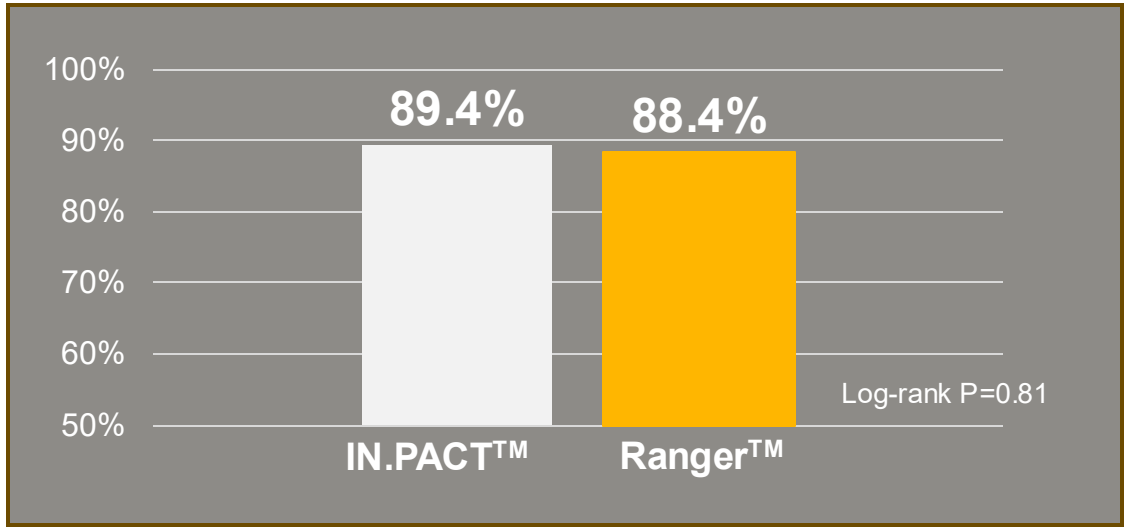
Schneider PA, et al. *Circ Cardiovasc Interv*. 2018;11(1):e005891. Soga Y, et al. *J Endovasc Ther*. 2020;27(6):946-955. Chen Z, et al. *J Endovasc Ther*. 2019;26:471-478.

Consistent DCB Results across Geographies

12-month patency comparable for low-dose and high-dose DCBs

COMPARE

Randomized Controlled Trial (Europe)

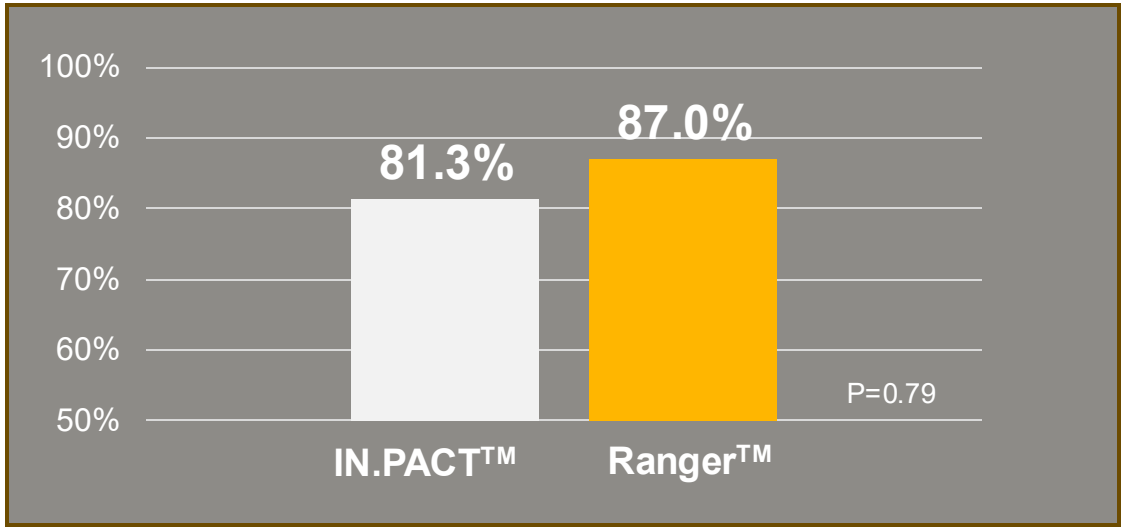


Head-to-head Prospective, RCT (1:1) N=414

	Mean lesion length	CTO	Mod-Severe Ca (PACSS 3/4)	Diabetes
Ranger	**124 mm**	**41%**	**51%**	**31%**
IN.PACT	**128 mm**	**43%**	**57%**	**37%**

PROSPECT-MONSTER

Propensity Score-matched Analysis (Japan)



Multicenter Propensity Score-Matched Analysis N=521

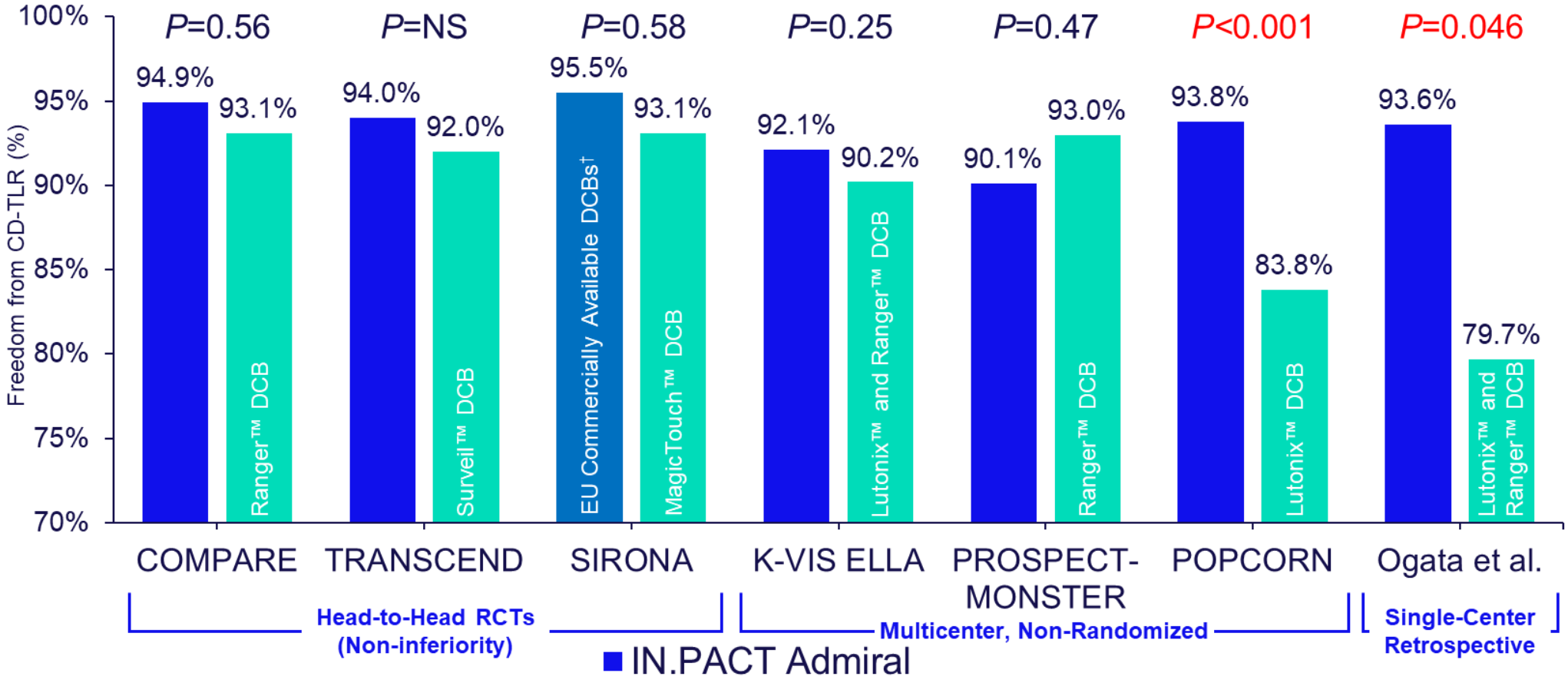
	Mean lesion length	CTO	Mod-Severe Ca (PACSS 3/4)	Diabetes
Ranger	**185 mm**	**45%**	**46%**	**72%**
IN.PACT	**179 mm**	**47%**	**45%**	**71%**

CTO = chronic total occlusion; Ca = calcium; PACSS = Peripheral Arterial Calcium Scoring System.

Steiner S, et al. *Eur Heart J*. 2020;41(27):2541-2552. Nakama T, et al. *JACC Cardiovasc Interv*. 2023;16(21):2655-2665.

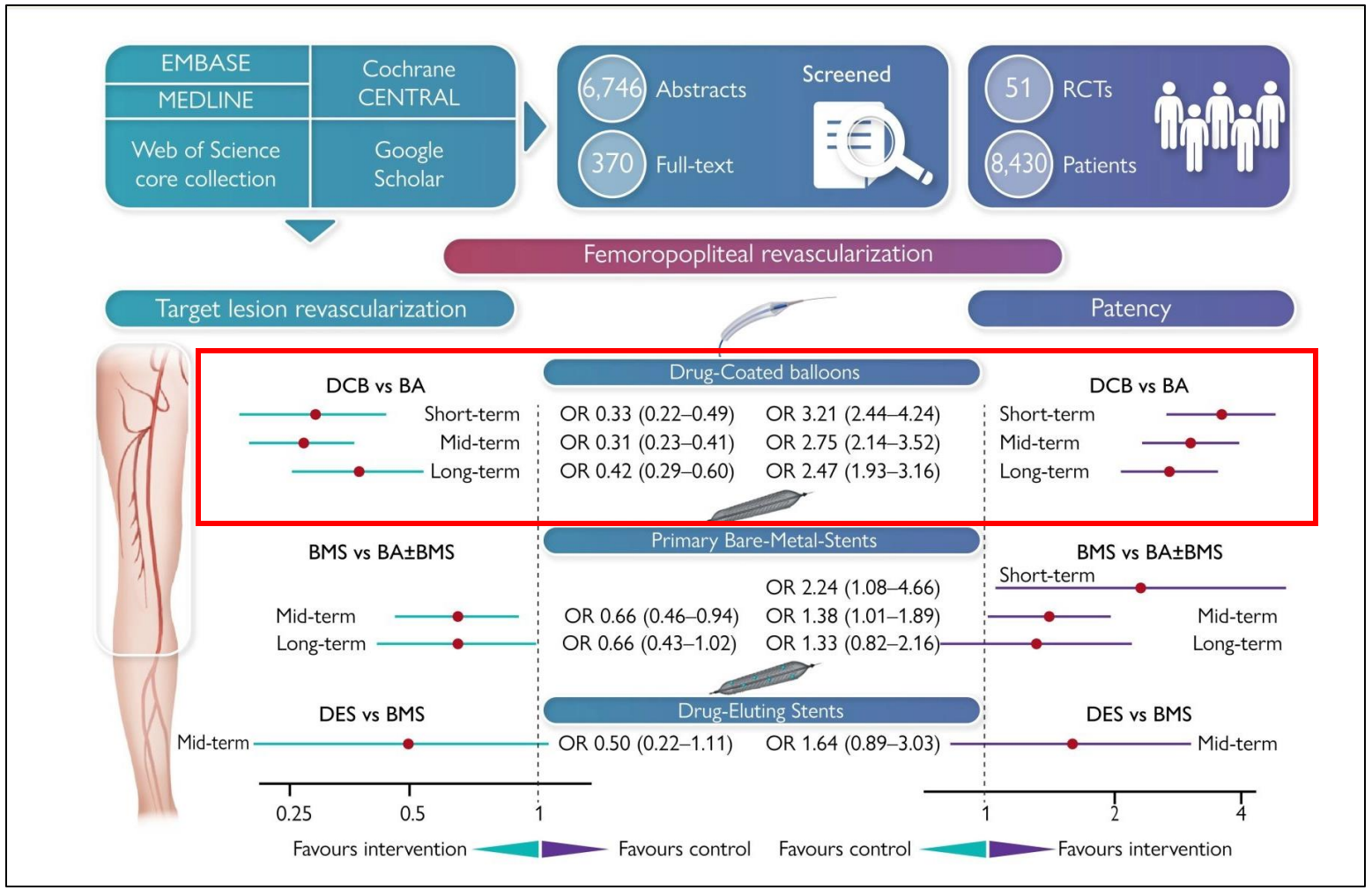
More Comparative Studies

Freedom from Clinically Driven Target Lesion Revascularization at 12 Months



Steiner S, et al. *Eur Heart J*. 2020;41(27):2541-2552. Brodmann, et al. *Eur J Vasc Endovasc Surg*. 2025;69(3):452-462. Rosenfield, et al. Presented at: LINC; 2021. Teichgräber, et al. Presented at: Charing Cross; 2025. Tomoi, et al. *J Endovasc Ther*. 2022. Fujihara, et al. *CVIR Endovasc*. 2023;6(1):41. Lee, et al. *Yonsei Med J*. 2024;66. Ogata, et al. *Circ J*. 2025;89(5):566-573. Nakama T, et al. *JACC Cardiovasc Interv*. 2023;16(21):2655-2665.

Meta-Analysis of Femoropopliteal Treatments



PTX: Improved patency and decreased TLR

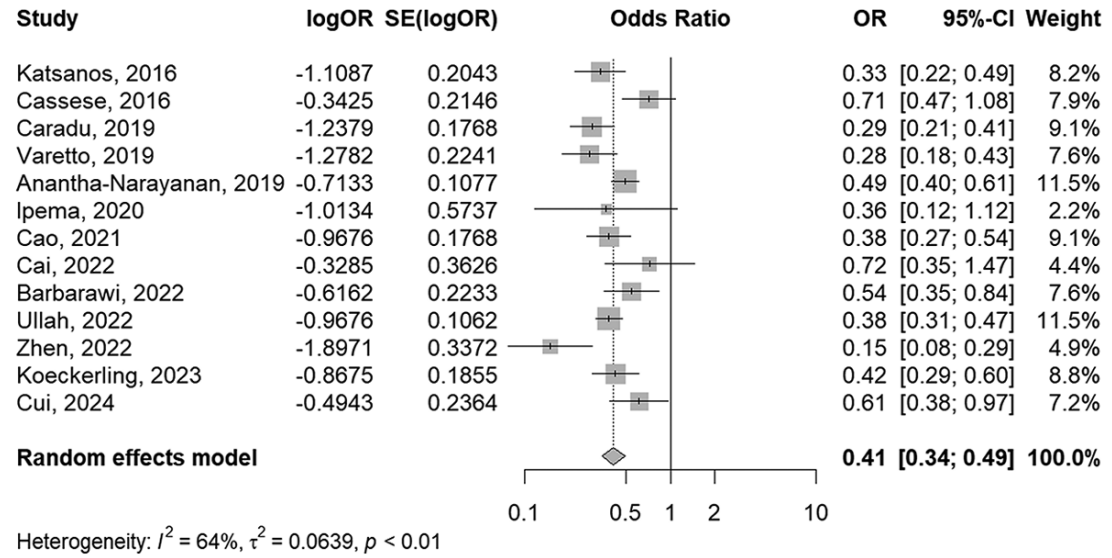
DCB vs plain balloon

TLR = target lesion revascularization; BA = balloon angioplasty; BMS = bare metal stent; OR = odds ratio.
Koeckerling D, et al. *Eur Heart J*. 2023;44(11):935-950.

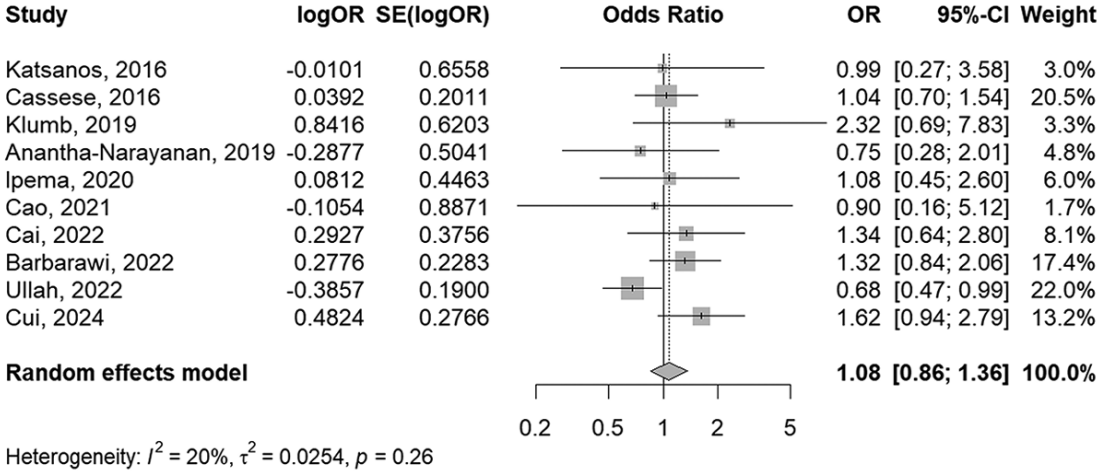
Comparison of Clinical Outcomes of Drug-Coated Balloons Angioplasty vs. Plain Old Balloons Angioplasty for Peripheral Arterial Disease: An Umbrella Meta-Analysis

13 meta-analyses

Reduced TLR with DCB



No difference in major amputation



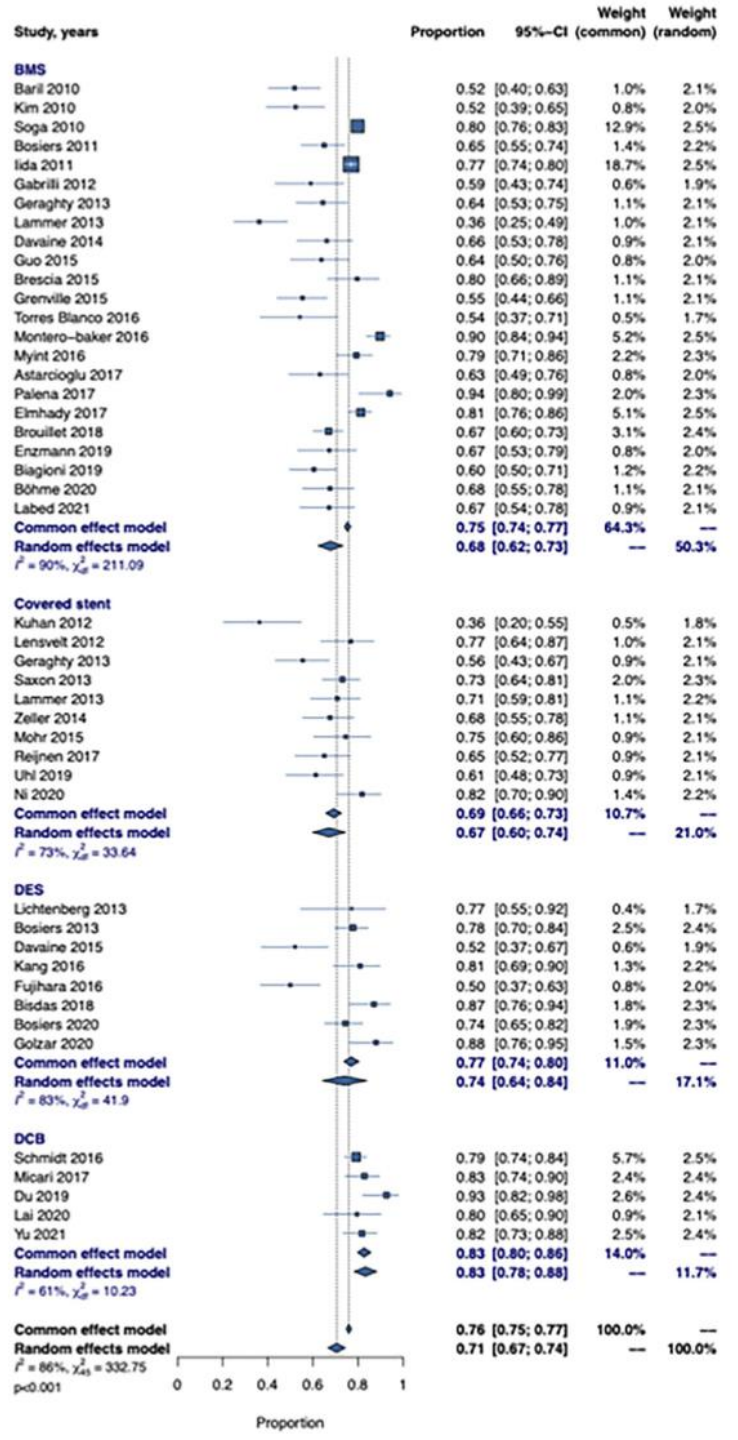
SE = standard error; CI = confidence interval.
Li J, et al. *Front Cardiovasc Med*. 2024:11:1511268.

Systematic Review and Meta-Analysis of Clinical Outcomes after Endovascular Treatment in Patients with Femoropopliteal Lesions Greater than 150 mm

2010-2021; 4847 patients

Primary Patency at One Year

BMS	68% [0.62-0.73]
Covered stent	67% [0.60-0.74]
DES	74% [0.64-0.84]
DCB	83% [0.78-0.88]



Dubosq-Lebaz M, et al. *J Endovasc Ther*. 2025;32(3):593-604.

Global Algorithm for the Endovascular Treatment of Chronic Femoropopliteal Lesions: An Interdisciplinary Expert Opinion Statement

FIGURE 1 Delphi Consensus for the Lesion Preparation and Definitive Treatment Tools

	Lesion preparation					Definitive treatment				
	POBA	Atherectomy	Lithotripsy	Specialty balloons	Thrombectomy	DCB	BMS	Interwoven stents	DES	Covered stents
Mobile Segments: distal SFA & popliteal artery PACSS I-II (non-CTO)	1 (G)	2 (G)	-1 (M)	1 (G)	-1 (G)	2 (G)	-1 (G)	2 (G)	-1 (M)	-1 (G)
Mobile Segments: distal SFA & popliteal artery PACSS III-IV (non-CTO)	-1 (G)	1 (G)	2 (G)	1 (G)	-1 (G)	1 (G)	-1 (G)	2 (G)	-1 (P)	-1 (G)
Short <15 TASC A&B ; PACSS I-II; intraluminal & fibrotic lesions	1 (G)	2 (G)	-1 (G)	-1 (G)	-1 (G)	2 (G)	1 (G)	1 (G)	1 (G)	-1 (G)
Short <15 TASC A&B ; PACSS I-II; fresh & organized thrombus	-2 (G)	-1 (G)	-2 (G)	-1 (G)	2 (G)	2 (G)	1 (G)	-1 (M)	1 (G)	1 (G)
Short <15 TASC A&B; PACSS I-II; subintimal passage	1 (G)	-2 (G)	-1 (G)	1 (M)	-2 (G)	2 (G)	1 (G)	2 (G)	2 (G)	-1 (M)
Short <15 TASC A&B ; PACSS III-IV; Diffuse calcification	-1 (M)	2 (G)	2 (G)	1 (G)	-2 (G)	1 (G)	1 (G)	2 (G)	1 (G)	-1 (G)
Short <15 TASC A&B ; PACSS III-IV; Eccentric calcification	-1 (G)	2 (G)	1 (G)	1 (G)	-2 (G)	1 (G)	1 (M)	2 (G)	1 (G)	-1 (G)
Short <15 TASC A&B ; PACSS III-IV subintimal passage	1 (G)	-1 (G)	1 (G)	1 (G)	-2 (G)	1 (G)	1 (G)	2 (G)	1 (G)	-1 (P)
Long >15 cm TASC C&D ; PACSS I-II; intraluminal passage	1 (G)	1 (G)	-1 (M)	1 (M)	-1 (M)	2 (G)	1 (G)	1 (G)	2 (G)	1 (M)
Long >15 cm TASC C&D; PACSS I-II; subintimal passage	1 (G)	-2 (G)	-1 (G)	-1 (P)	-2 (G)	2 (G)	1 (G)	2 (G)	2 (G)	1 (G)
Long >15 cm TASC C&D; PACSS III-IV; intraluminal passage	-1 (M)	2 (G)	2 (G)	1 (G)	-1 (G)	2 (G)	1 (G)	2 (G)	2 (G)	1 (M)
Long >15 cm TASC C&D ; PACSS III-IV; subintimal passage	1 (G)	-2 (G)	1 (G)	1 (G)	-2 (G)	1 (G)	1 (G)	2 (G)	1 (G)	1 (M)
Short ISR non-CTO ; Tosaka I class	1 (G)	2 (G)	-2 (G)	1 (M)	-1 (G)	2 (G)	-1 (G)	-1 (M)	-1 (M)	1 (M)
Long ISR and stent occlusions; Tosaka II-III class	-1 (G)	2 (G)	-1 (G)	1 (M)	1 (G)	2 (G)	-1 (G)	-1 (M)	1 (M)	1 (G)

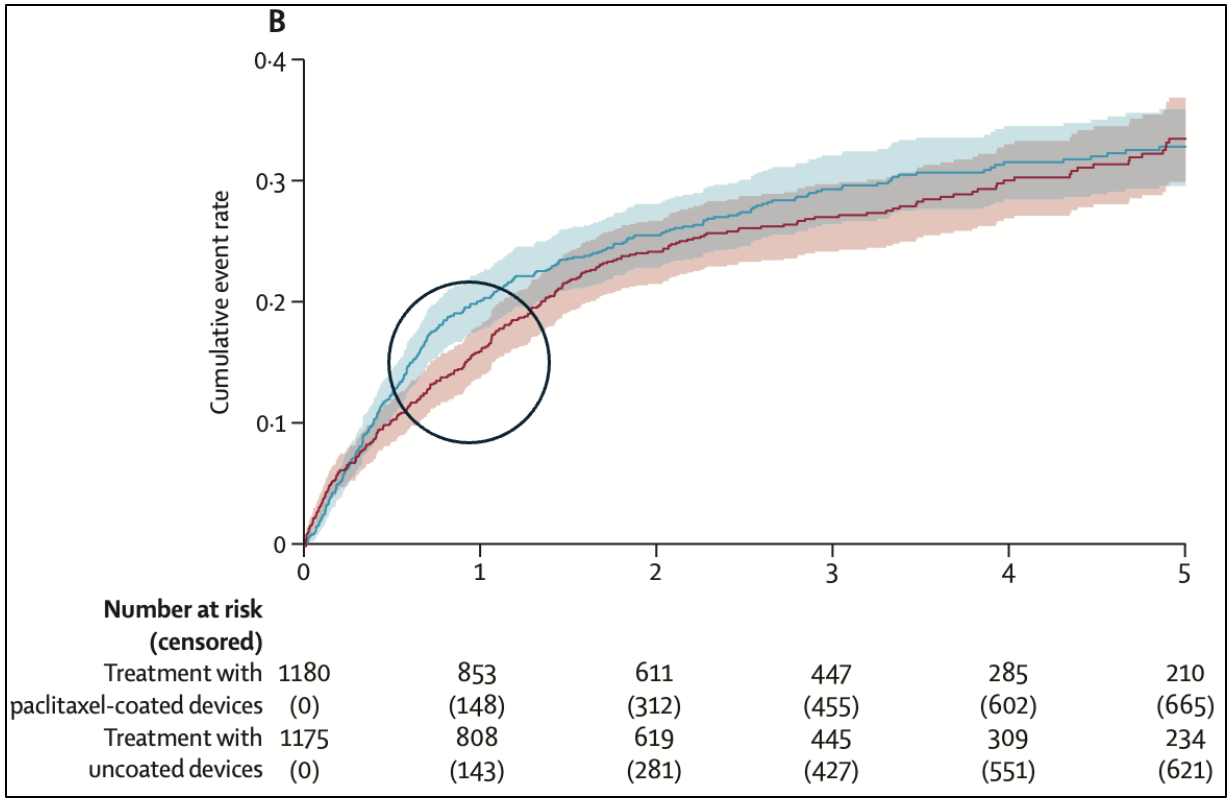
2 = strong recommendation
1 = Weak recommendation
-1 = Weak Warning
-2 = Strong warning

(G) for good agreement: 80-100%
(M) for moderate agreement: 60-79%
(P) for poor agreement: <60%

Korosoglou G, et al. *JACC Cardiovasc Interv*. 2025;18(5):545-557.

Paclitaxel Efficacy in SWEDEPAD

SWEDEPAD 1: CLTI



Re-intervention: Reduced after drug, but only at 1 year

SWEDEPAD 2: Claudication

	Treatment with paclitaxel-coated devices (n=565)		Treatment with uncoated devices (n=571)		Hazard ratio* (95% CI)	p value
	Events, n	Event rate, percentage per 100 person-years	Events, n	Event rate, percentage per 100 person-years		
Ipsilateral amputation						
Up to 5 years	16	0·71 (0·41–1·16)	11	0·47 (0·24–0·85)	1·58 (0·73–3·45)	0·24
Up to 1 year	8	1·44 (0·62–2·83)	3	0·53 (0·11–1·55)	3·46 (0·86–13·9)	0·062
Complete follow-up	20	0·66 (0·41–1·02)	17	0·54 (0·32–0·87)	1·28 (0·66–2·47)	0·46
Death						
Up to 5 years	104	4·57 (3·73–5·54)	77	3·28 (2·59–4·10)	1·47 (1·09–1·98)	0·010
Up to 1 year	15	2·68 (1·50–4·42)	12	2·11 (1·09–3·69)	1·27 (0·57–2·81)	0·56
Complete follow-up	154	5·01 (4·25–5·87)	146	4·61 (3·89–5·42)	1·18 (0·94–1·48)	0·16
Ipsilateral amputation or death						
Up to 5 years	112	4·99 (4·11–6·00)	85	3·66 (2·93–4·53)	1·44 (1·08–1·92)	0·011
Up to 1 year	21	3·77 (2·34–5·77)	14	2·47 (1·35–4·15)	1·58 (0·79–3·17)	0·19
Complete follow-up	163	5·41 (4·61–6·30)	152	4·87 (4·12–5·70)	1·19 (0·95–1·48)	0·13
Target vessel reintervention						
Up to 5 years	145	7·83 (6·60–9·21)	151	8·06 (6·83–9·45)	0·96 (0·76–1·20)	0·71
Up to 1 year	68	12·98 (10·08–16·45)	79	15·09 (11·95–18·80)	0·86 (0·62–1·19)	0·37
Complete follow-up	166	7·00 (5·97–8·15)	165	6·80 (5·80–7·92)	1·01 (0·81–1·25)	0·93
Ipsilateral reintervention						
Up to 5 years	149	8·12 (6·87–9·53)	155	8·36 (7·09–9·78)	0·96 (0·77–1·21)	0·74
Up to 1 year	73	14·01 (10·98–17·61)	82	15·72 (12·50–19·51)	0·90 (0·66–1·24)	0·53
Complete follow-up	171	7·27 (6·22–8·44)	170	7·08 (6·06–8·23)	1·01 (0·82–1·25)	0·90

Re-intervention: No difference

Falkenberg M, et al. *Lancet*. 2025;406(10508):1103-1114. Nordanstig J, et al. *Lancet*. 2025;406(10508):1115-1127.

SWEDEPAD Trial Design

- No validation of operators or technique
- Milder disease morphology
- Indications for TLR?
- No core lab, imaging, or patency data
- Remote follow-up after 1 year
- "RCT"—but registry style
- Multiple different devices used
- Lost to follow-up/crossover data missing
- Different results in concurrent SWEDEVASC

Devices Swedepad 1

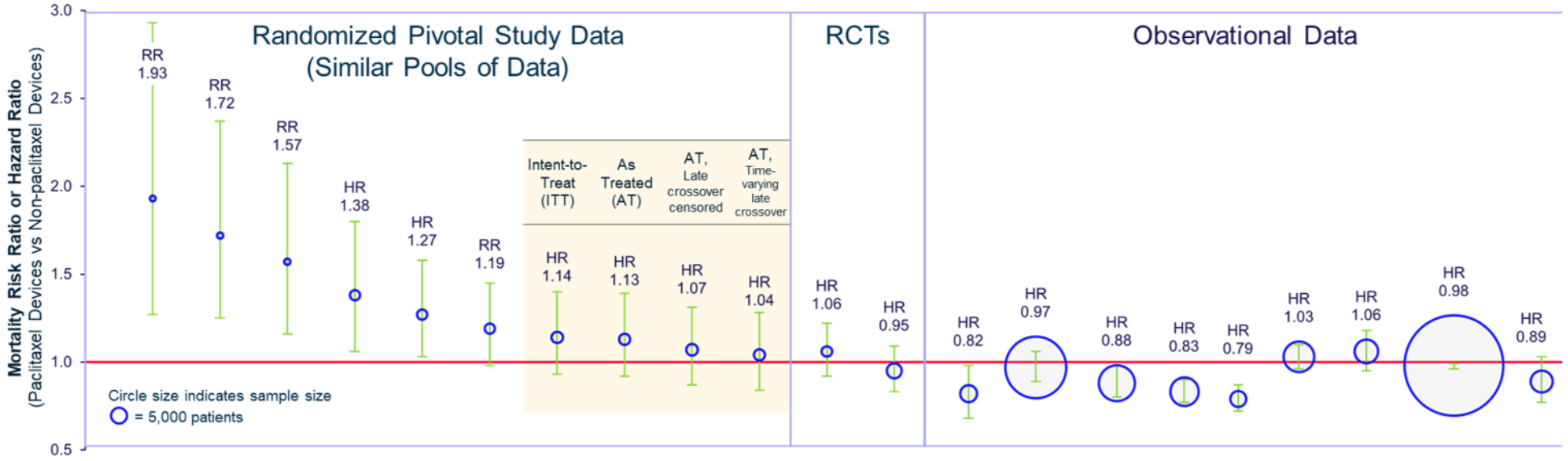
Brand	Frequency	Percent
Freeway (Eurocor)	103	4·5%
IN.PACT (Medtronic)	227	9·9%
Lutonix (BD)	1026	44·9%
Zilver PTX (COOK)	302	13·2%
Eluvia (Boston Scientific)	56	2·5%
Passeo Lux (Biotronic)	178	7·8%
BioPath (Biosensors)	61	2·7%
Ranger (Boston Scientific)	284	12·4%
Stellarex (Philips)	16	0·7%
SeQuent (Braun)	18	0·8%
Advance PTX (COOK)	4	0·2%
Xience Prime (Abbot, Everolimus*)	3	0·1%
Resolute Integrity (Medtronic, Zotarolimus*)	1	0·0%
LegFlow (Cardionovum)	4	0·2%
Total	2283	100·0%

Devices Swedepad 2

Brand	Frequency	Percent
Freeway (Eurocor)	43	4·6%
IN.PACT Admiral (Medtronic)	197	20·9%
Lutonix (BD)	367	38·9%
Zilver PTX (Cook Medical)	171	18·1%
Eluvia (Boston Scientific)	37	3·9%
Passeo Lux (Biotronik)	42	4·5%
BioPath (Biosensors)	33	3·5%
Ranger (Boston Scientific)	35	3·7%
Stellarex (Philips)	2	0·2%
SeQuent Please (Braun)	15	1·6%
Advance PTX (Cook)	1	0·1%
Total	943	100·0%

Falkenberg M, et al. *Lancet*. 2025;406(10508):1103-1114. Nordanstig J, et al. *Lancet*. 2025;406(10508):1115-1127.

Mortality in Randomized Controlled Trials Using Paclitaxel-Coated Devices for Femoropopliteal Interventional Procedures: An Updated Patient-Level Meta-Analysis



Study	Katsanos	FDA - VS	FDA + VS	VIVA-NAMSA		Dinh	LIMR-NAMSA 2023 Analysis				SWEDE-PAD	VOYAGER-PAD	VQI Vision	BARMER	BARMER		VQI Delta	Optum	VA Data-base	SAFE-PAD	FAIR Health
Year	2018	2019	2019	2019	2020	2021	ITT	AT	LCC	TVLC	2020	2021	2020	2020	2020		2021	2021	2021	2022	2023
Patients	863	971	1,035	2,185	2,185	2,288	2,666	2,667	2,667	2,667	2,289	4,316	5,436	64,771	23,122	14,792	4,912	16,796	10,505	168,553	8978
Follow-up, yrs	4-5	≤ 5	≤ 5	4	4	5	4.9 Years *				2.5‡	2.6 *	1.1 *	7.7 *	2.7 *		1.8 *	2.7 *	1.7 *	3.5 *	4

UPDATE: Paclitaxel-Coated Devices to Treat Peripheral Arterial Disease Unlikely to Increase Risk of Mortality - Letter to Health Care Providers

July 11, 2023

The U.S. Food and Drug Administration (FDA) is informing health care providers about updated information associated with paclitaxel-coated devices used to treat peripheral arterial disease (PAD).

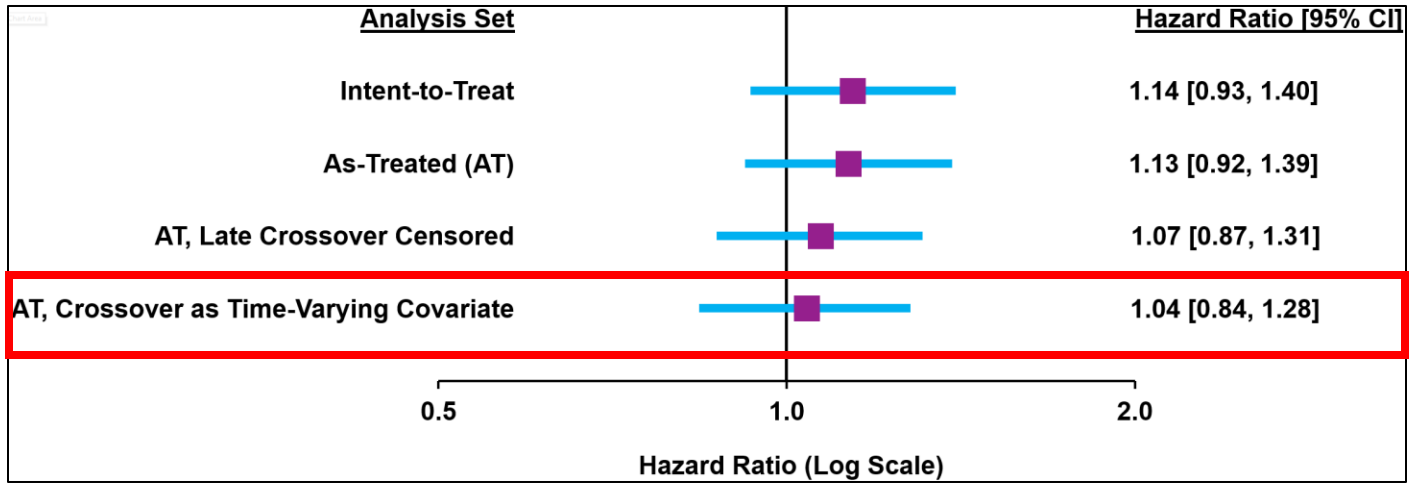
Based on the FDA's review of the totality of the available data and analyses, we have determined that the data does not support an excess mortality risk for paclitaxel-coated devices.

FDA Update
July 11, 2023

***Median follow-up; ‡Mean follow-up.**

Parikh SA, et al. *Lancet*. 2023;402(10415):1848-1856.

Final Patient Level Updated Meta-Analysis



Mortality in randomised controlled trials using paclitaxel-coated devices for femoropopliteal interventional procedures: an updated patient-level meta-analysis

Sahil A Parikh, Peter A Schneider*, Christopher M Mullin, Tyson Rogers, William A Gray**

What Went Wrong?

Summary-level meta-analysis
Small control groups
Not powered for mortality
Treatment bias after randomization
Crossover effect
Ascertainment bias: Lost to follow-up
Unexpected confounder: Lesion length

↓

Dose response (biologic gradient)
No proposed mechanism


Peripheral Arteries

Eur J Vasc Endovasc Surg (2026) 71, 928–941

EJVES Open Access

SYSTEMATIC REVIEW

Editor's Choice – Dynamic Risk of Death following Application of Paclitaxel Coated Devices in the Femoropopliteal Artery: A Contemporary Meta-analysis of Randomised Controlled Trials

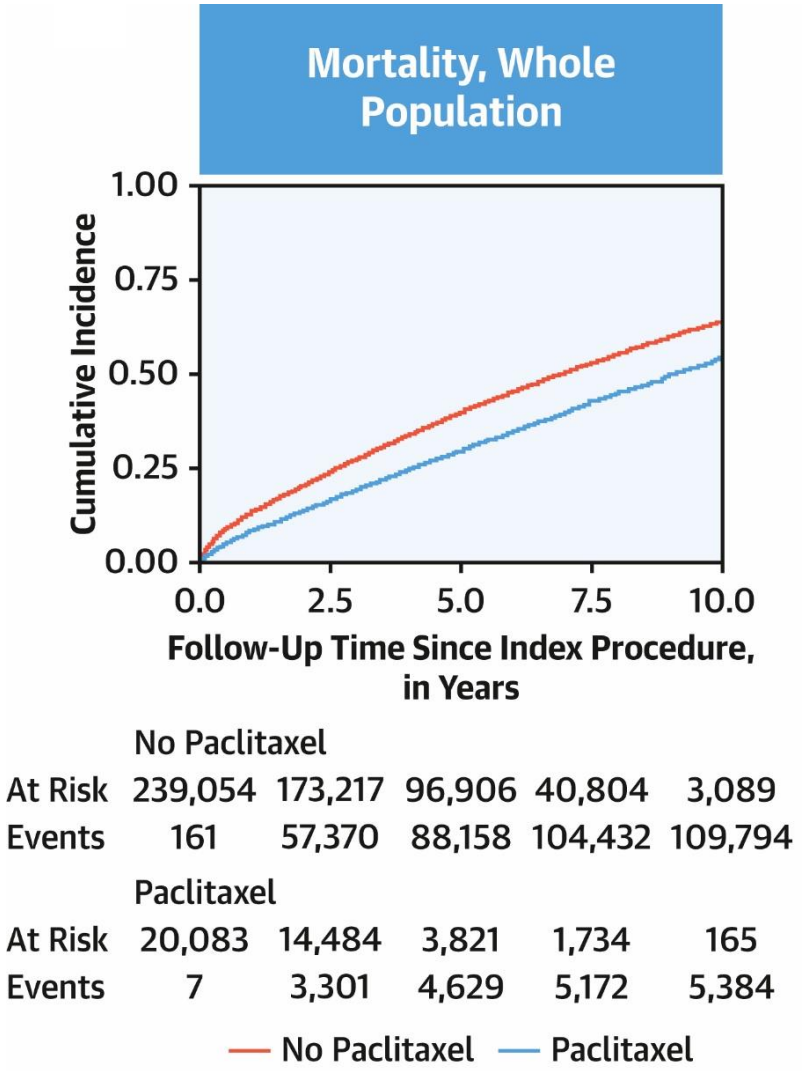
Konstantinos Katsanos [a,*], Stavros Spiliopoulos [b], Athanasios Saratzis [c,d], Ulf Teichgräber [e], Hany Zayed [d,f], Panagiotis Kitrou [a], Miltiadis Krokidis [g], Dimitrios Karnabatidis [a]

AT = as-treated.

Parikh SA, et al. *Lancet*. 2023;402(10415):1848-1856. Katsanos K, et al. *J Am Heart Assoc*. 2018;7(24):e011245. Katsanos K, et al. *Eur J Vasc Endovasc Surg*. 2026;71:928-941.

Latest Real-World Data from France

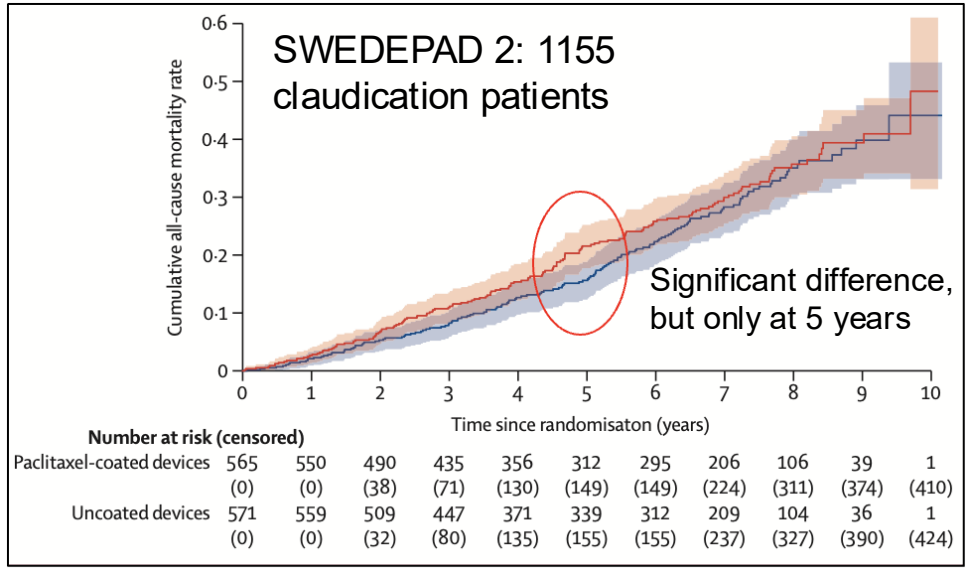
- DETECT: **D**rug **E**lu**T**ing d**E**vices Fren**C**h safe**T**y Survey
- Nationwide cohort study
- Individual data from the French National Data Information System
- 259,137 patients (20,083 treated with PCD)
- Median follow-up: 4.1 years
- PCD was associated with a lower risk of mortality (HR: 0.86, *P*<.001)

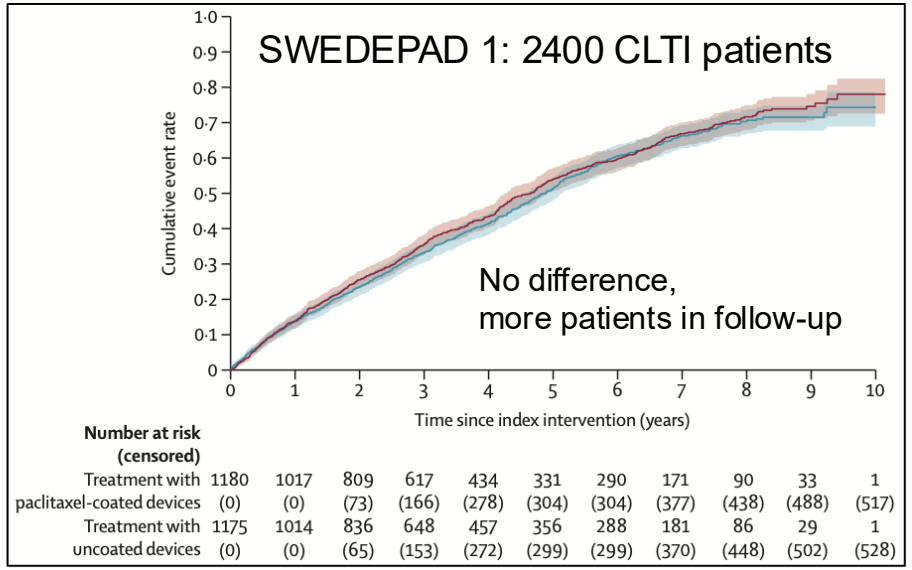


PCD = paclitaxel-coated device.

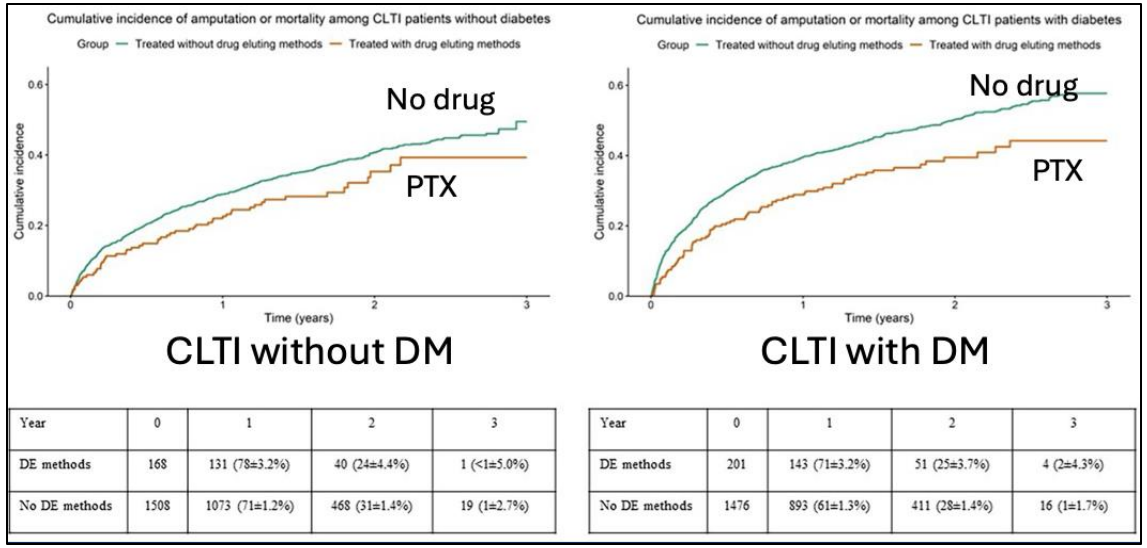
Wargny M, et al. *J Am Coll Cardiol*. 2024;83(13):1207-1221.

SWEDEPAD 1 and 2 and Mortality





SWEDEVASC Registry

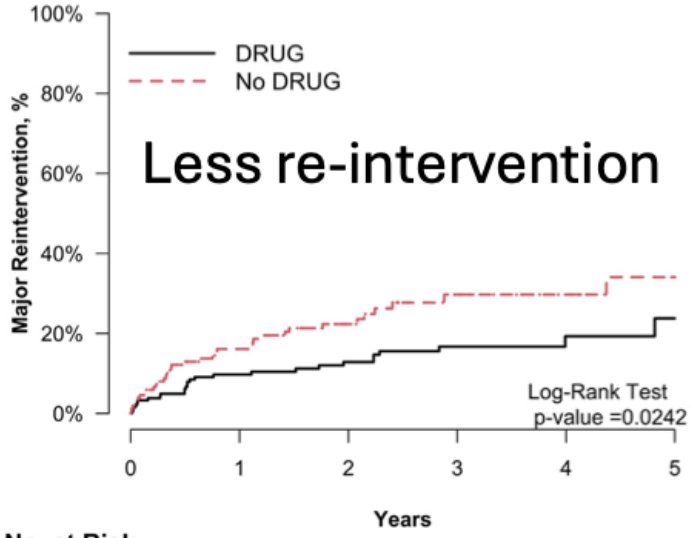


3353 CLTI patients
Lower risk of amputation and death with PTX

DM = diabetes mellitus.

Fransson T, et al. *J Endovasc Ther*. 2025;32(6):2196-2207. Falkenberg M, et al. *Lancet*. 2025;406(10508):1103-1114. Nordanstig J, et al. *Lancet*. 2025;406(10508):1115-1127.

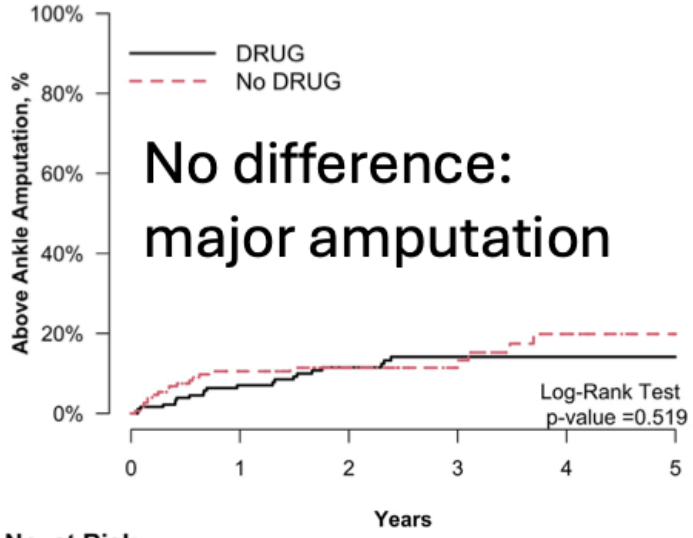
Paclitaxel in BEST-CLI



No. at Risk

DRUGS	186	129	104	65	31	16
No DRUGS	155	101	63	34	23	10

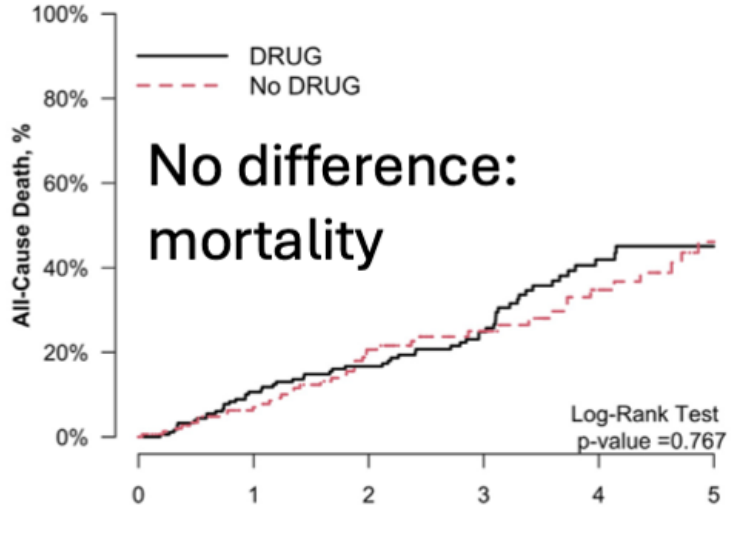
Fig 1. Major reinterventions using ENDO-drug vs ENDO-No drug in patients with femoropopliteal (FP) disease.



No. at Risk

DRUGS	186	134	110	72	36	20
No DRUGS	155	110	77	48	29	16

Fig 2. Above-ankle amputations in patients with femoropopliteal (FP) disease treated with ENDO-drug vs ENDO-No drug.



No. at Risk

DRUGS	186	152	129	87	43	22
No DRUGS	155	124	87	56	35	18

Fig 3. Mortality in patients with femoropopliteal (FP) disease treated with for ENDO-drug vs ENDO-No drug.

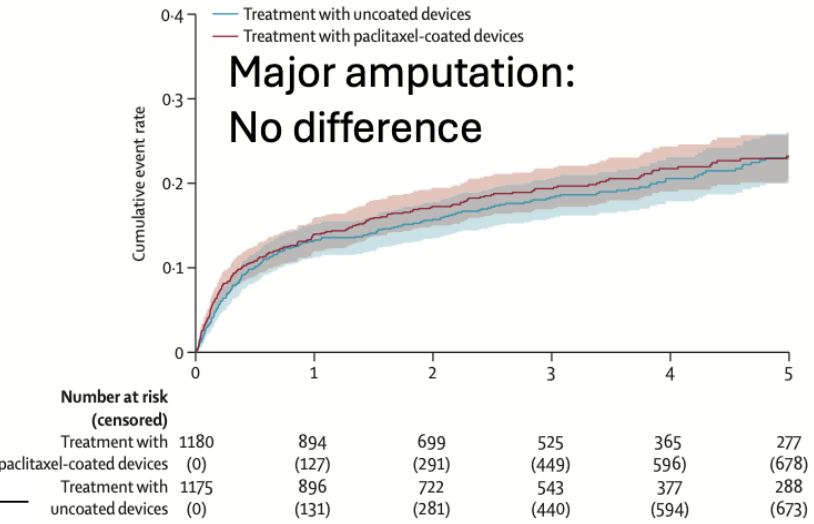
Siracuse JJ, et al. *J Vasc Surg*. 2025;82(4):1375-1382.

Paclitaxel: No Increase in Amputation Risk or Mortality Risk in CLTI

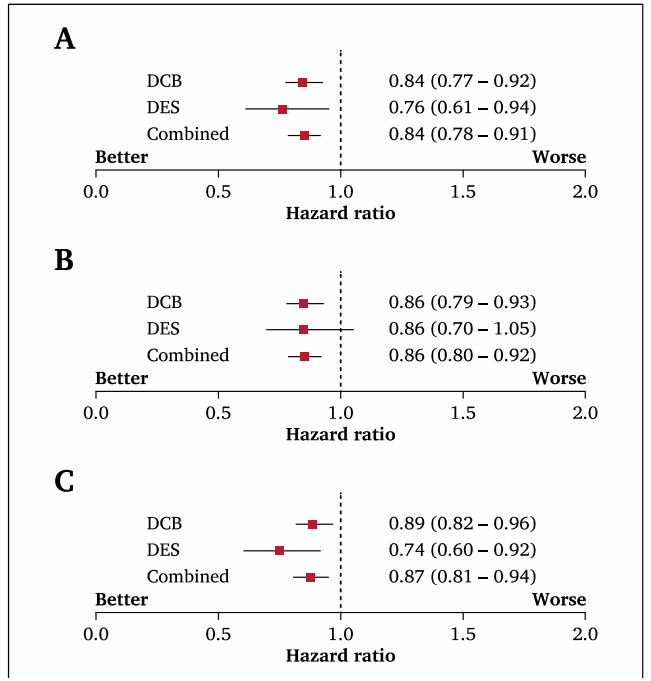
Risk of amputation in over 160,000 patients in SAFE-PAD: HR 0.86

Event	Max Follow-Up Time, days	Cumulative Incidence (95% CI)		Sub-distribution HR (95% CI)	Cause-Specific HR (95% CI)
		Non-Drug-Coated Devices (N=97,969)	Drug-Coated Devices (N=70,584)		
Amputation	365	9.76 (9.55, 9.98)	8.29 (8.06, 8.52)		
	730	11.32 (11.09, 11.56)	9.82 (9.57, 10.08)	0.86 (0.83, 0.89)	0.86 (0.83, 0.89)
	1095	12.15 (11.89, 12.42)	10.70 (10.41, 11.00)		
	Max§	12.35 (12.06, 12.65)	11.05 (10.67, 11.44)		

SWEDEPAD 1: RCT of 2400 CLTI patients



Barmer Insurance: 14,738 CLTI patients



Lower risk of death, amputation

Risk of MALE in 4316 VOYAGER PAD patients was similar: HR 1.07

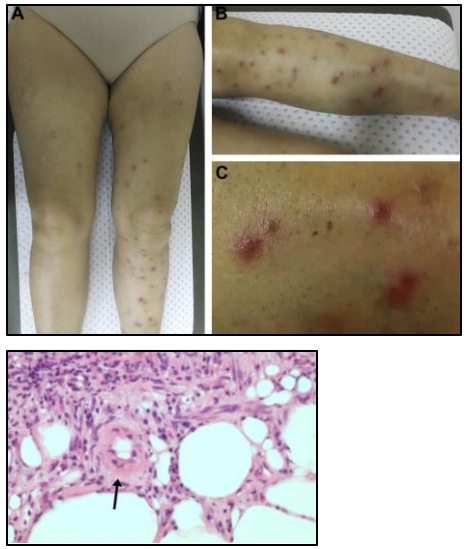
	Total Population				Weighted Analysis Population			
	DCD	Non-DCD			DCD	Non-DCD		
	3.5 y KM Rate	3.5 y KM Rate	HR (95% CI)	*P* Value	3.5 y KM Rate	3.5 y KM Rate	HR (95% CI)	*P* Value
All-cause mortality								
Overall	10.2	13.8	0.76 (0.61-0.95)	0.02	12.1	12.9	0.95 (0.83-1.09)	0.49
Overall-stabilized weights	10.2	13.8			12.1	12.9	0.95 (0.77-1.18)	0.66
DCB vs uncoated PTA	10.1	14.0	0.75 (0.56-1.01)	0.06	12.1	12.6	0.99 (0.82-1.20)	0.93
DES vs BMS	12.9	13.6	0.82 (0.51-1.32)	0.42	17.5	13.4	1.04 (0.84-1.28)	0.75
MALE	6.5	6.3	1.07 (0.82-1.41)	0.60	6.6	6.5	1.08 (0.90-1.30)	0.39
UILR	23.5	23.5	0.97 (0.85-1.12)	0.71	21.5	24.6	0.84 (0.76-0.92)	0.0003

***Max follow-up for all-cause repeat hospitalization is 1170 days for the non-DCD group and 1158 days for the DCD group; †Max follow-up for repeat lower extremity endovascular revascularization is 1159 days for the non-DCD group and 1166 days for the DCD group; ‡Max follow-up for surgical revascularization is 1147 days for the non-DCD group and 1136 days for the DCD group; §Max follow-up for amputation is 1162 days for the non-DCD group and 1166 days for the DCD group.**

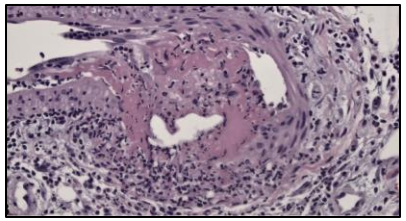
MALE = major adverse limb event; DCD = drug-coated devices; UILR = unplanned index limb revascularization; KM = Kaplan-Meier.

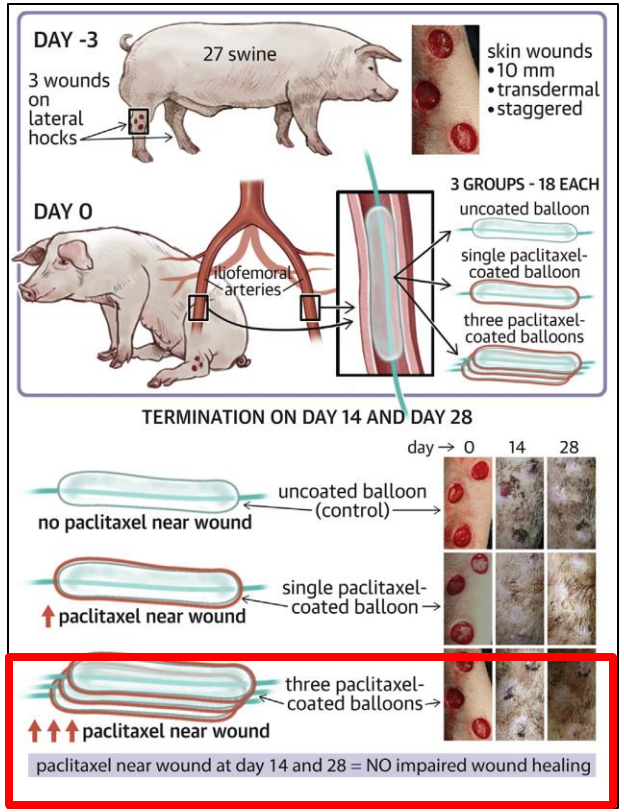
Heidemann, et al. *Eur J Vasc Endovasc Surg*. 2020;60(4):549-558. Falkenberg, et al. *Lancet*. 2025;406:1103. Hess, et al. *J Am Coll Cardiol*. 2021;78:1768-1778. Secemsky, et al. *JAMA Intern Med*. 2021;181:1071.

Particulate Embolization after PTX DCB





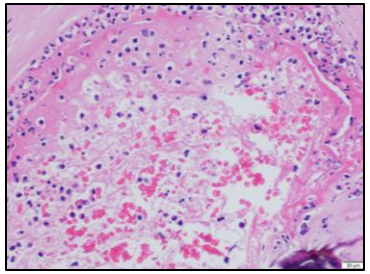




The no-flow phenomenon following drug-coated balloon angioplasty in a patient with chronic limb-threatening ischemia and a history of below-knee amputation

Mituso Sobajima (MD, PhD) *, Teruhiko Imamura (MD, PhD, FJCC), Atsuko Fukuo (MD), Yohei Ueno (MD, PhD), Hiroshi Onoda (MD, PhD), Hiroshi Ueno (MD, PhD), Koichiro Kinugawa (MD, PhD, FJCC)





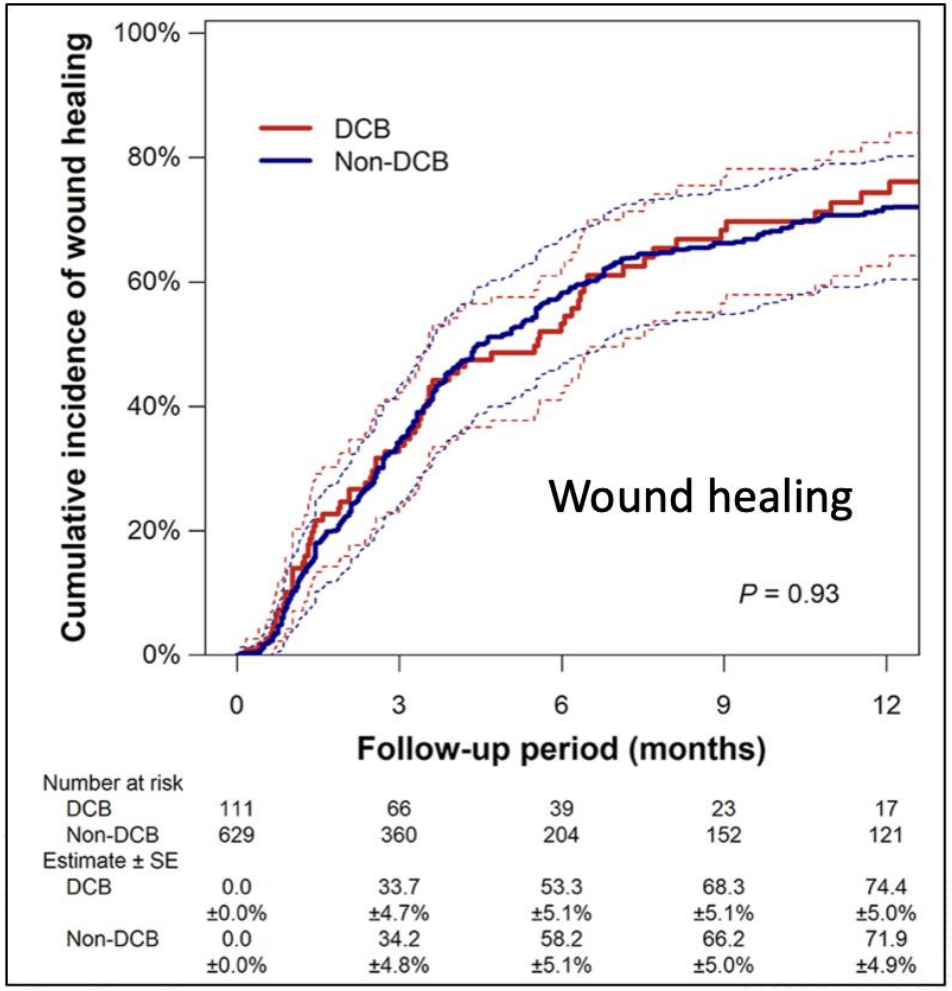
Healing not impaired in distal extremity wounds in presence of paclitaxel overdose.

Downstream Paclitaxel Released Following Drug-Coated Balloon Inflation and Distal Limb Wound Healing in Swine

Juan F. Granada, MD,[a] Marco Ferrone, MD,[a,b,c] Gilberto Melnick, MD,[a,d] Lesley Crookall, BMLSc,[a] Daniel Schulz-Jander, PhD,[a] Stefan Tunev, DVM,[a] Robert J. Melder, DSc,[a] Grzegorz L. Kaluza, MD, PhD[a]

Thomas SD, et al. *J Vasc Surg*. 2014;59:520-523. Sobajima M, et al. *J Cardiol Cases*. 2023;27:132-135. Hawkins K, et al. *JAAD Case Rep*. 2022;23:1-3. Granada JF, et al. *J Am Coll Cardiol Basic Trans Science*. 2021;6(5):416-427.

Roles of Angioplasty with Drug-Coated Balloon for Chronic Ischemia in Wound Healing



Number at risk					
DCB	111	66	39	23	17
Non-DCB	629	360	204	152	121
Estimate ± SE					
DCB	0.0 ±0.0%	33.7 ±4.7%	53.3 ±5.1%	68.3 ±5.1%	74.4 ±5.0%
Non-DCB	0.0 ±0.0%	34.2 ±4.8%	58.2 ±5.1%	66.2 ±5.0%	71.9 ±4.9%

FF = freedom from.

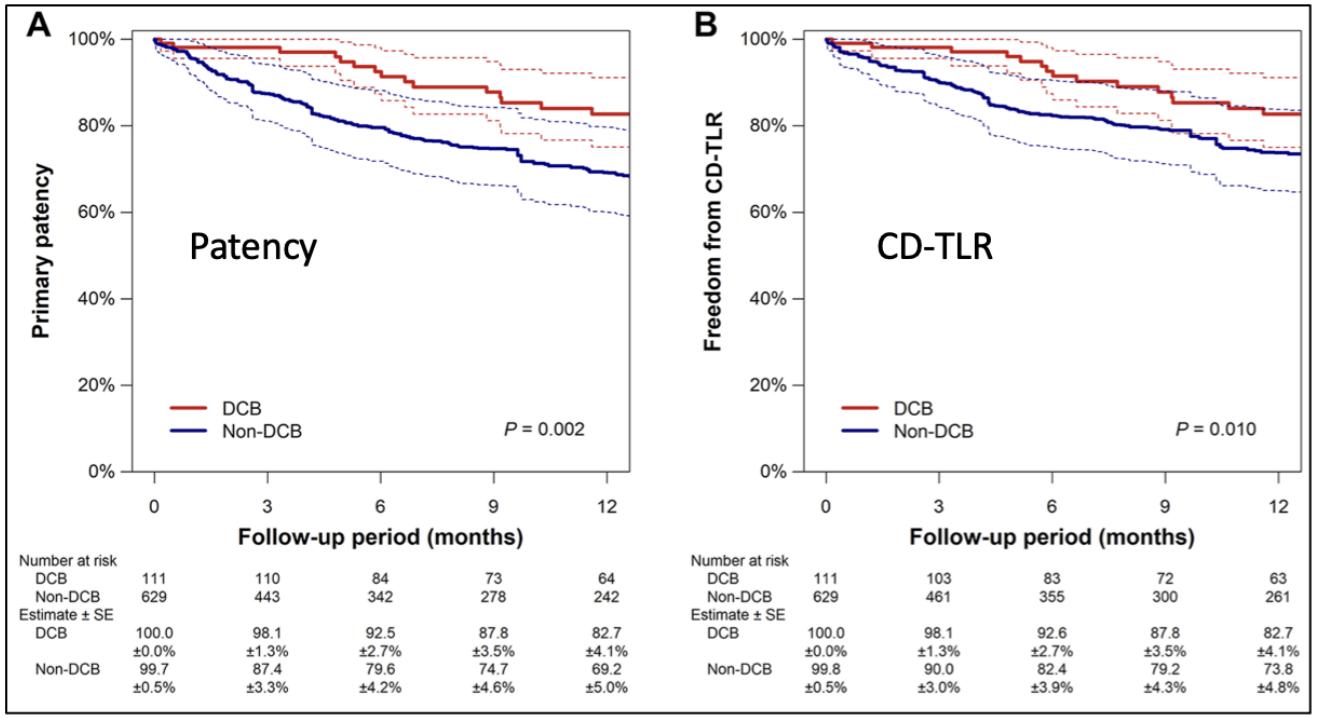
Hata Y, et al. *J Endovasc Ther*. 2021;28(5):778-787.

RADISH Trial

980 CLTI patients, propensity-matched

Same wound healing

Better patency, FF CD-TLR with DCB



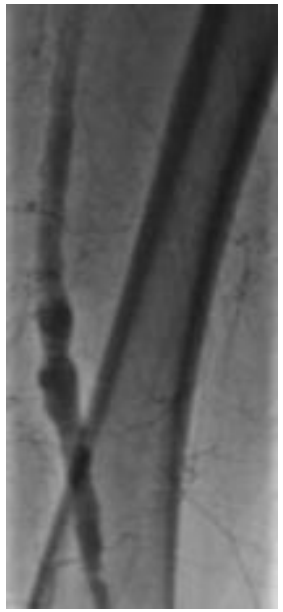
Number at risk					
DCB	111	110	84	73	64
Non-DCB	629	443	342	278	242
Estimate ± SE					
DCB	100.0 ±0.0%	98.1 ±1.3%	92.5 ±2.7%	87.8 ±3.5%	82.7 ±4.1%
Non-DCB	99.7 ±0.5%	87.4 ±3.3%	79.6 ±4.2%	74.7 ±4.6%	69.2 ±5.0%

Number at risk					
DCB	111	103	83	72	63
Non-DCB	629	461	355	300	261
Estimate ± SE					
DCB	100.0 ±0.0%	98.1 ±1.3%	92.6 ±2.7%	87.8 ±3.5%	82.7 ±4.1%
Non-DCB	99.8 ±0.5%	90.0 ±3.0%	82.4 ±3.9%	79.2 ±4.3%	73.8 ±4.8%

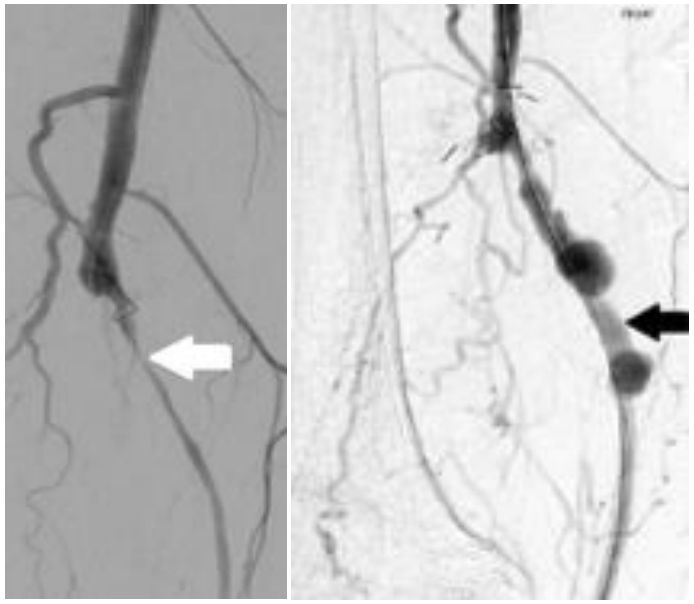
No evidence of decreased wound healing

What About Local Complications?

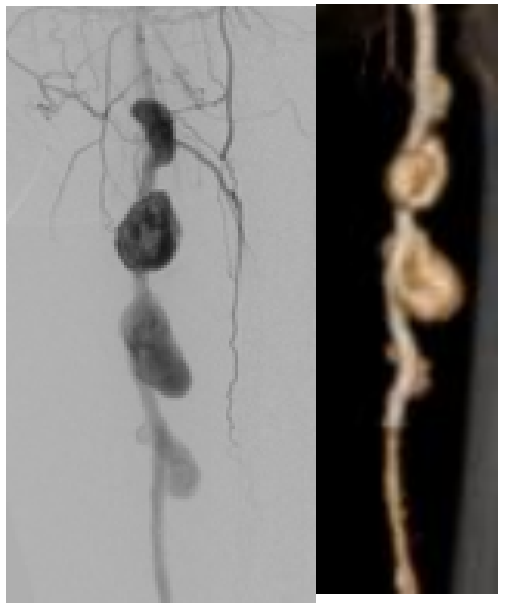
Case reports: No clear incidence



DCB after atherectomy



DCB of vein graft stenosis



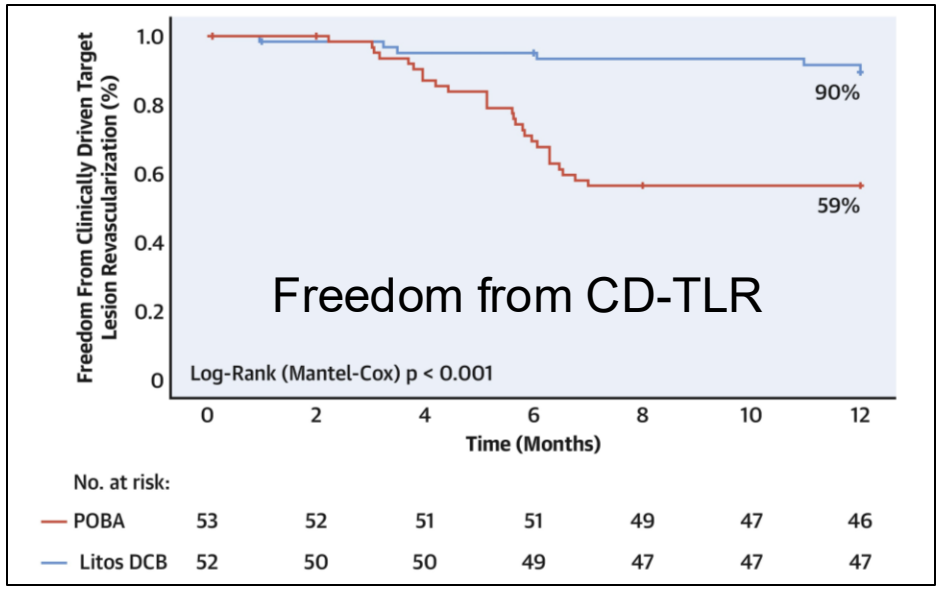
DCB after subintimal crossing

Avadhani SA, et al. *JACC Case Rep*. 2021;3(3):425-426. Chen W, et al. *Vasc Endovascular Surg*. 2021;55(4):410-414. Dinh K, et al. *Radiol Case Rep*. 2021;16(12):3628-3630.

Paclitaxel DCB for BTK

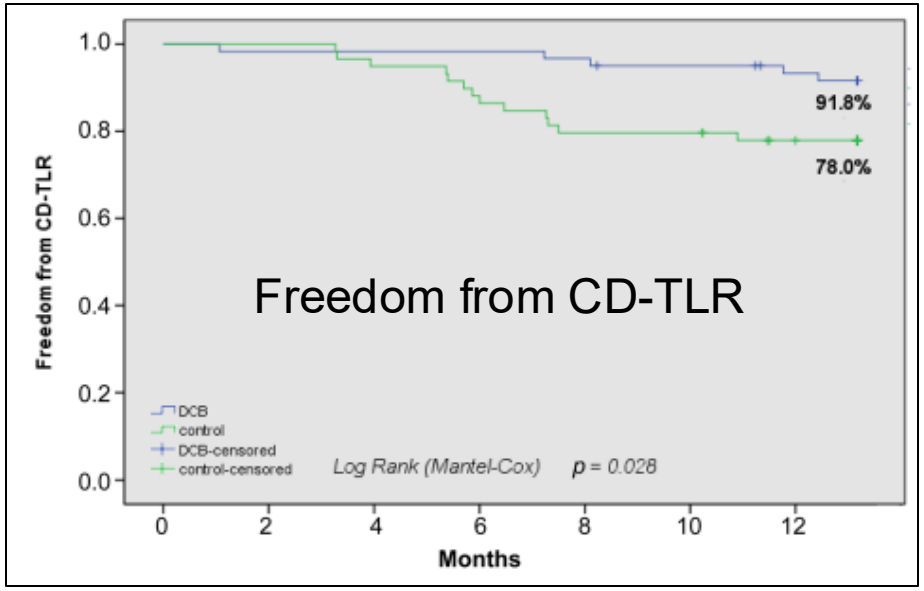
Randomized Controlled Trial of Acotec Drug-Eluting Balloon Versus Plain Balloon for Below-the-Knee Angioplasty

105-patient RCT, 1 site
Lesion length: 17-19 cm
Occlusions: 67-68%



Long-term Outcomes of the AcoArt II–BTK Trial: Drug-Coated Balloon Angioplasty Compared With Uncoated Balloons for the Treatment of Infrapopliteal Artery Lesions

120-patient RCT, 11 sites
Lesion length: 17-18 cm
Occlusions: 75-83%



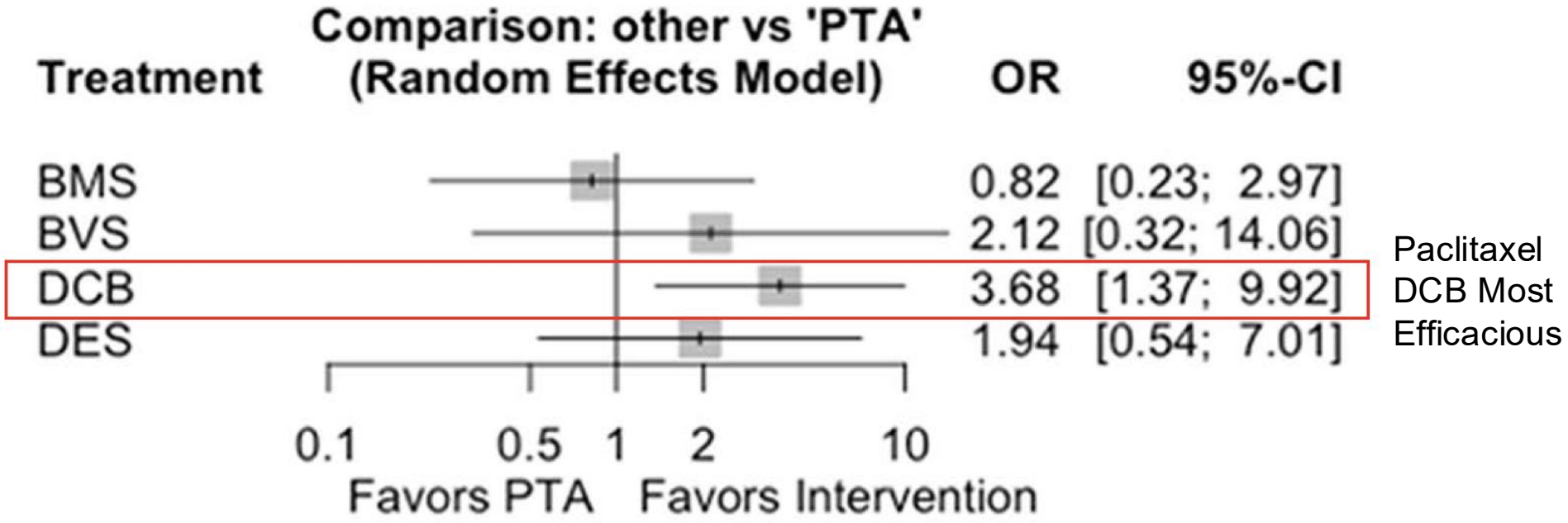
Primary patency at 6 months: DCB 75%, PTA 28%

Liistro F, et al. *JACC Cardiovasc Interv*. 2020;13(19):2277-2286. Jia X, et al. *J Endovasc Ther*. 2021;28(2):215-221.

Safety and Efficacy of Endovascular Treatment Modalities for Below-the-Knee Arterial Disease: A Systematic Review and Network Meta-Analysis

PRISMA 2005-2025
23 studies, 3091 patients with CLTI

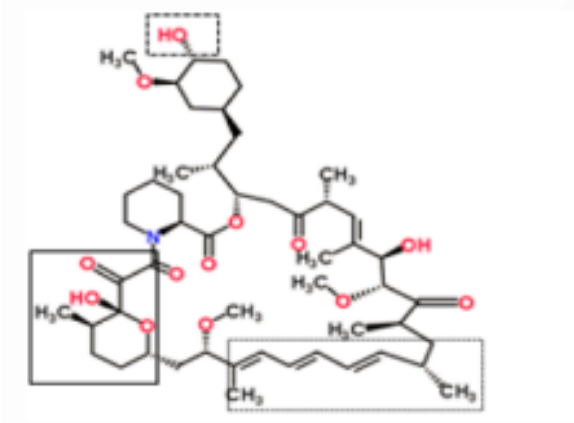
Primary efficacy endpoint at 6 months:
Freedom from major amputation, target lesion occlusion, and CD-TLR



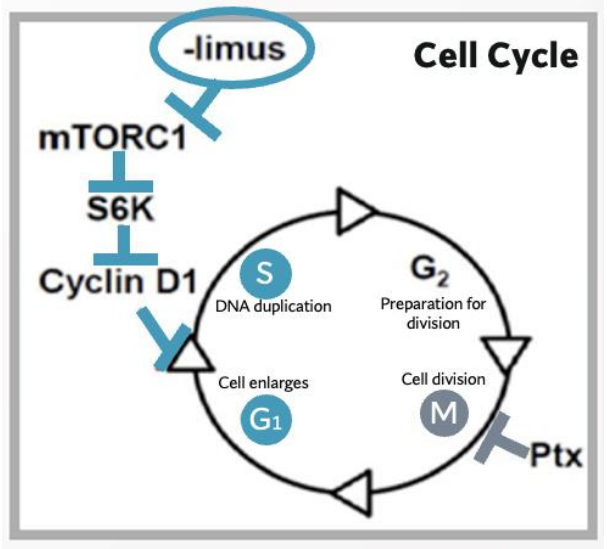
Paclitaxel DCB Most Efficacious

Tirziu D, et al. *J Endovasc Ther*. 2026;33(4):2139-2155.

Mechanism of Sirolimus



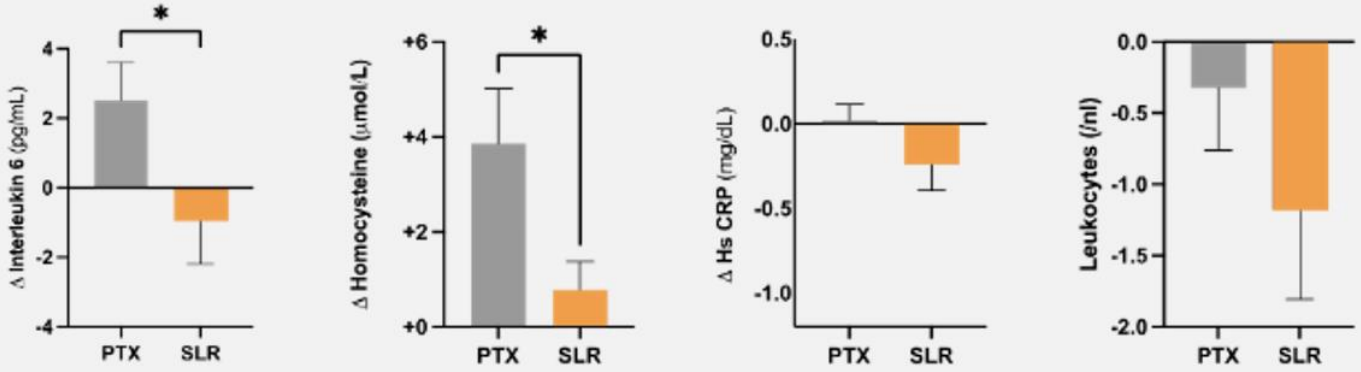
Sirolimus blocks cells at the G1/S phase interface, **stopping cells from dividing and growing**; the block is removed when the concentration falls below a critical threshold (**reversible**)



LIMUS FLOW Study Single Center RCT, 70 patients, Germany

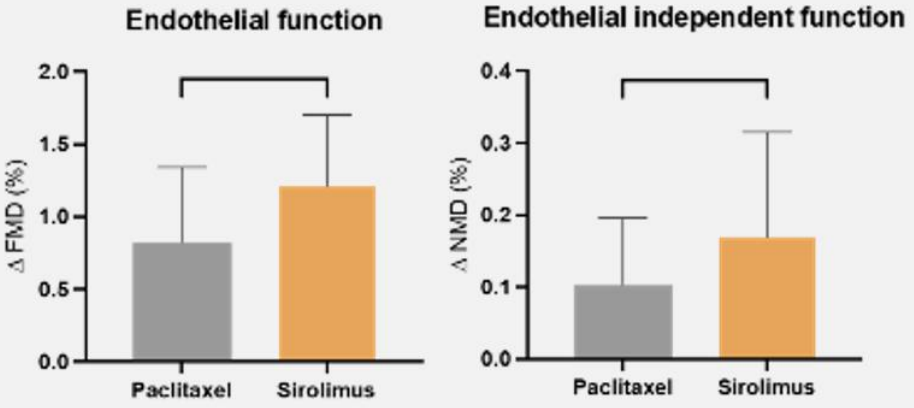
Markers of inflammation after 1 month

Sirolimus leads to decreased inflammation compared to PTX



Endothelial function in the target vessel 12M

Sirolimus leads to greater improvement than PTX



Habib A, Finn A. *Interv Cardiol Clin*. 2016;5(3):321-329. Gupta ML, et al. *Proc Natl Acad Sci U S A*. 2003;100:6394-6397. Rammos C. Presented at: LINC; January 28-30, 2025; Leipzig, Germany.

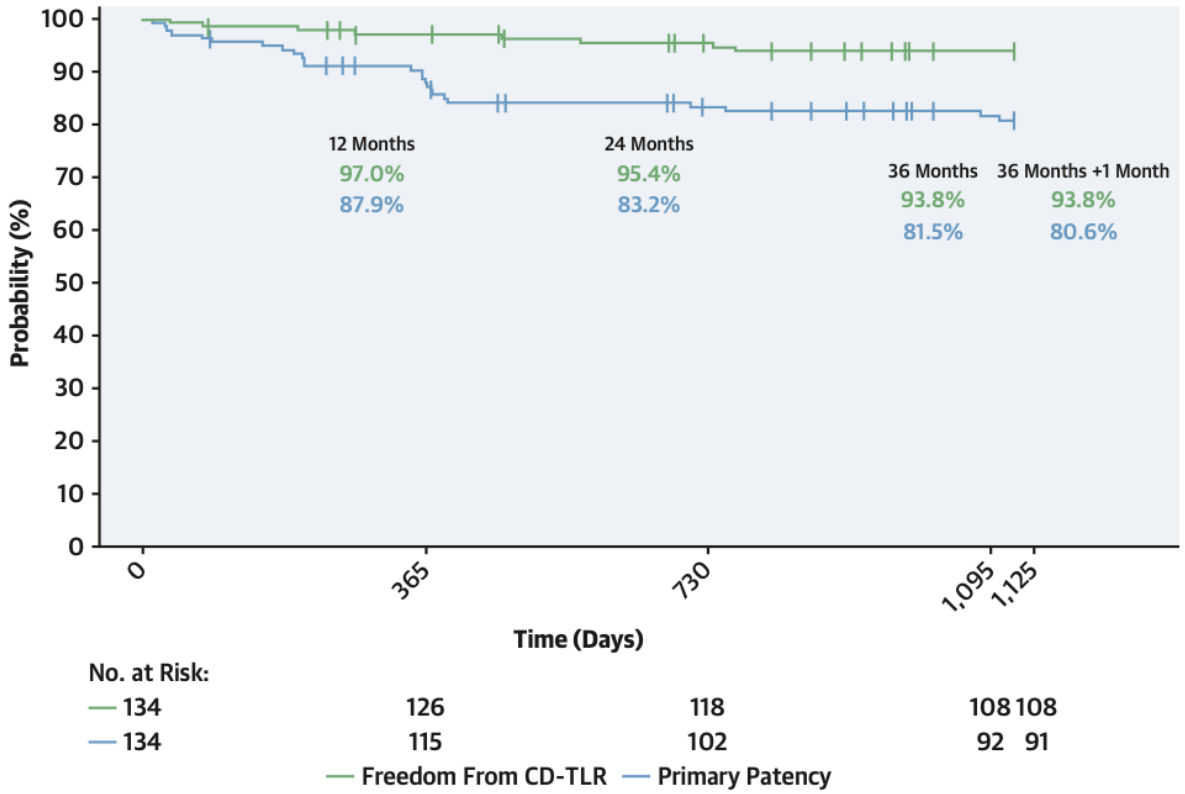
SELUTION Japan: 3-Year Results

Treatment of Symptomatic Femoropopliteal Disease With a Sirolimus-Eluting Balloon: 3-Year Outcomes of the SELUTION SFA JAPAN Study, N = 134

Patient Population

- Age: 73.8 ± 6.9 years
- Japanese: 100%
- Rutherford Classification 2-4
- Diabetes mellitus: 60.3%
- Renal insufficiency: 6.9%
- Mean lesion length: 127.4 mm
- Occlusions: 17.2%
- Moderate to severe calcification: 26.9%

Freedom From CD-TLR and Primary Patency Through 3 Years



- At 3 years the primary patency rate was 81.5% (95% CI: 73.7%-87.2%); the freedom from CD-TLR rate was 93.8% (95% CI: 88.0%-96.9%); and the major adverse event rate was 14.2%.
- These results demonstrated the durability of the SELUTION sirolimus-eluting balloon and suggest it is a safe and effective treatment option for femoropopliteal disease in symptomatic patients.

Soga Y, et al. *JACC Cardiovasc Interv*. 2025;18(21):2629-2637.

SirPAD Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Sirolimus-Coated Balloon Angioplasty for Infrainguinal Artery Disease

44 vascular centers in Switzerland
1252 patients enrolled; 15 operators; all infrainguinal arteries included in treatment zone
30% of patients underwent BTK angioplasty
LL: 140-150 mm, occlusions: 56-58%
Tissue loss: 23-25%, stent required: 35-40%

Fontaine classification — no./total no. (%)		
Stage I	4/626 (0.6)	8/624 (1.3)
Stage IIa	69/626 (11.0)	60/624 (9.6)
Stage IIb	337/626 (53.8)	344/624 (55.1)
Stage III	57/626 (9.1)	70/624 (11.2)
Stage IV	159/626 (25.4)	142/624 (22.8)
Acute limb ischemia at target limb — no. (%)	64 (10.2)	59 (9.4)

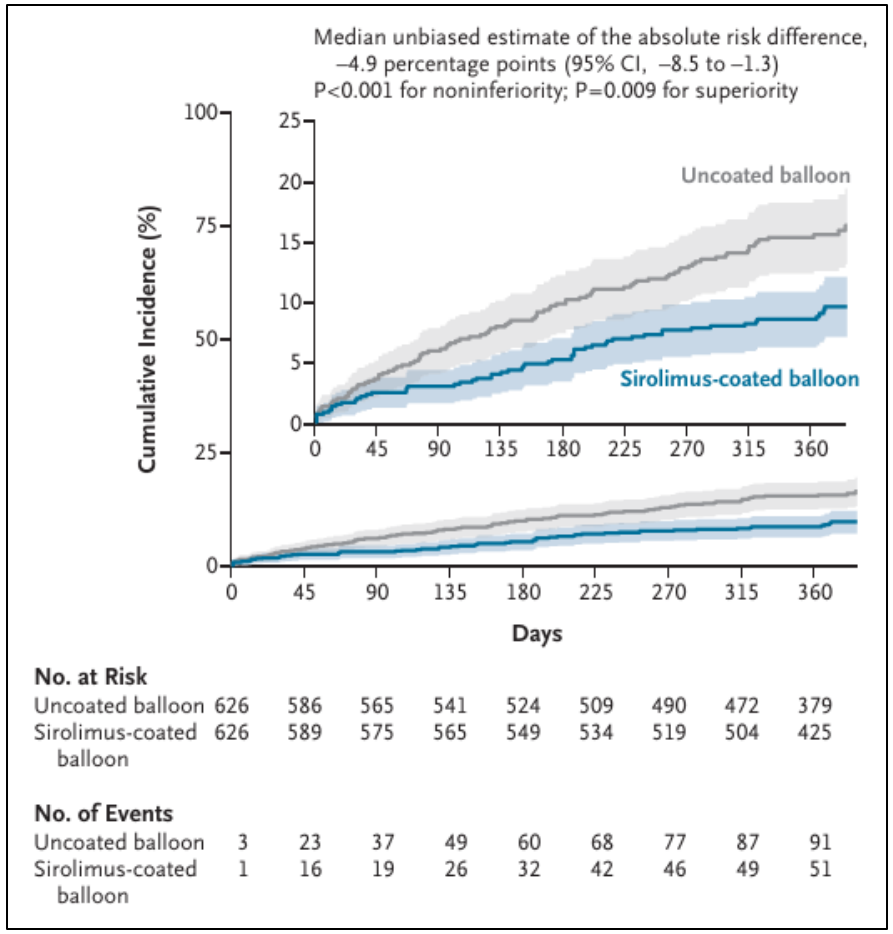
Table 2. Procedural Data and Characteristics of the Target Lesions.

Variable	Sirolimus-Coated Balloon (N=626)	Uncoated Balloon (N=626)
Target lesion — no. (%)		
Common femoral artery	34 (5.4)	28 (4.5)
Superficial femoral artery	360 (57.5)	362 (57.8)
Deep femoral artery	2 (0.3)	2 (0.3)
Popliteal artery	219 (35.0)	235 (37.5)
Arteries below the knee	191 (30.5)	188 (30.0)
Tibiofibular trunk	57 (9.1)	66 (10.5)
Peroneal artery	43 (6.9)	50 (8.0)
Anterior tibial artery	79 (12.6)	63 (10.1)
Posterior tibial artery	52 (8.3)	49 (7.8)
Bypass or bypass anastomosis	9 (1.4)	6 (1.0)
Details of the target lesion — no. (%)		
Not previously treated	451 (72.0)	453 (72.4)
Restenosis after previous angioplasty	77 (12.3)	87 (13.9)
Restenosis after previous stent placement	45 (7.2)	35 (5.6)
In-stent occlusion	53 (8.5)	51 (8.1)
Median length of the target lesion (IQR) — mm*	150 (80–200)	143 (60–212)
Total occlusion of the target lesion — no./total no. (%)	350/622 (56.3)	361/623 (57.9)
Lack of technical success of treatment of the index target lesion — no. (%)	11 (1.8)	6 (1.0)
Persistent occlusion	4 (0.6)	3 (0.5)
Persistent lumen stenosis of >50%	5 (0.8)	3 (0.5)
Other reason	2 (0.3)	0
Bailout stent placement — no. (%)	222 (35.5)	250 (39.9)

Barco S, et al. *N Engl J Med*. 2026;395(6):561-570.

SirPAD Trial Sirolimus DCB

Outcome	Sirolimus-Coated Balloon (N=626)	Uncoated Balloon (N=626)	Absolute Risk Difference (95% CI)
			percentage points
Primary outcome			
Composite of unplanned major amputation affecting the target limb or endovascular or surgical target-lesion revascularization for critical limb ischemia at 1 yr — no. (%)	55 (8.8)	94 (15.0)	−4.9 (−8.5 to −1.3)†
Secondary efficacy outcomes			
Composite of any unplanned amputation affecting the target limb or target-lesion revascularization for critical or noncritical limb ischemia at 1 yr — no. (%)	144 (23.0)	193 (30.8)	−7.8 (−12.7 to −2.9)‡
Unplanned major amputation affecting the target limb at 1 yr — no. (%)	8 (1.3)	17 (2.7)	−1.4 (−3.1 to 0.2)
Unplanned minor amputation affecting the target limb at 1 yr — no. (%)	34 (5.4)	45 (7.2)	−1.8 (−4.5 to 1.0)
Any unplanned amputation affecting the target limb at 1 yr — no. (%)	37 (5.9)	55 (8.8)	−2.9 (−5.8 to 0.0)
Target-lesion revascularization for critical or noncritical limb ischemia at 1 yr — no. (%)	124 (19.8)	162 (25.9)	−6.1 (−10.7 to −1.4)
Target-lesion revascularization for critical limb ischemia at 1 yr — no. (%)	52 (8.3)	83 (13.3)	−5.0 (−8.4 to −1.5)
Target-lesion revascularization for noncritical limb ischemia at 1 yr — no. (%)	72 (11.5)	79 (12.6)	−1.1 (−4.7 to 2.5)

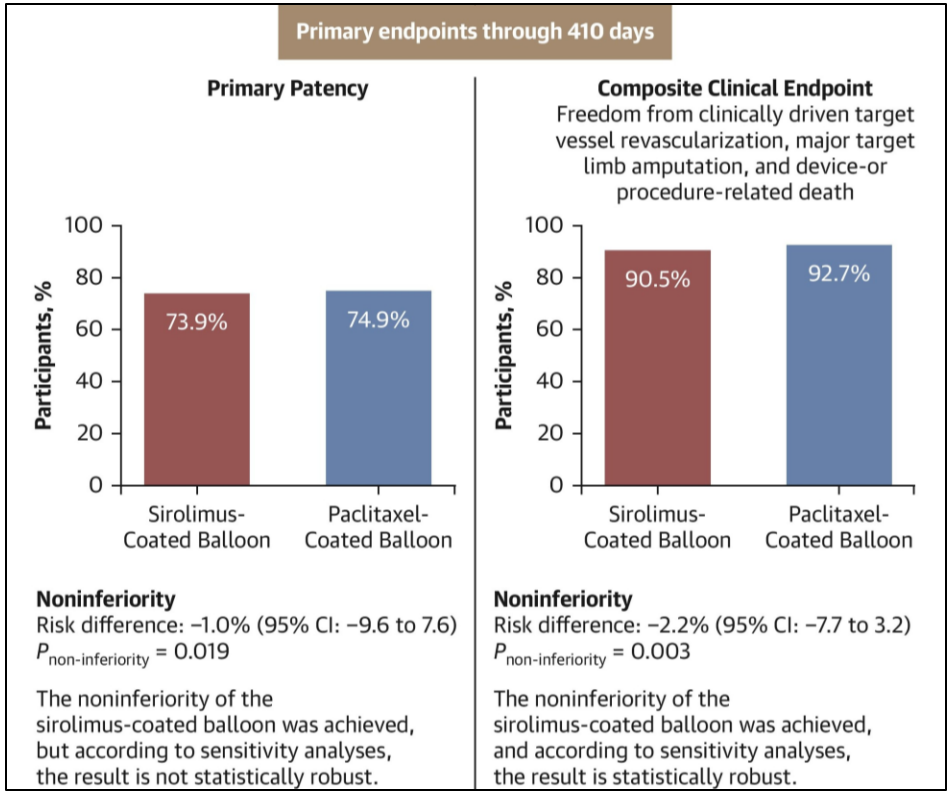


Barco S, et al. *N Engl J Med*. 2026;395(6):561-570.

SIRONA Trial: Noninferiority RCT of PTX vs Sirolimus DCBs

25 centers in Germany and Austria: 482 patients

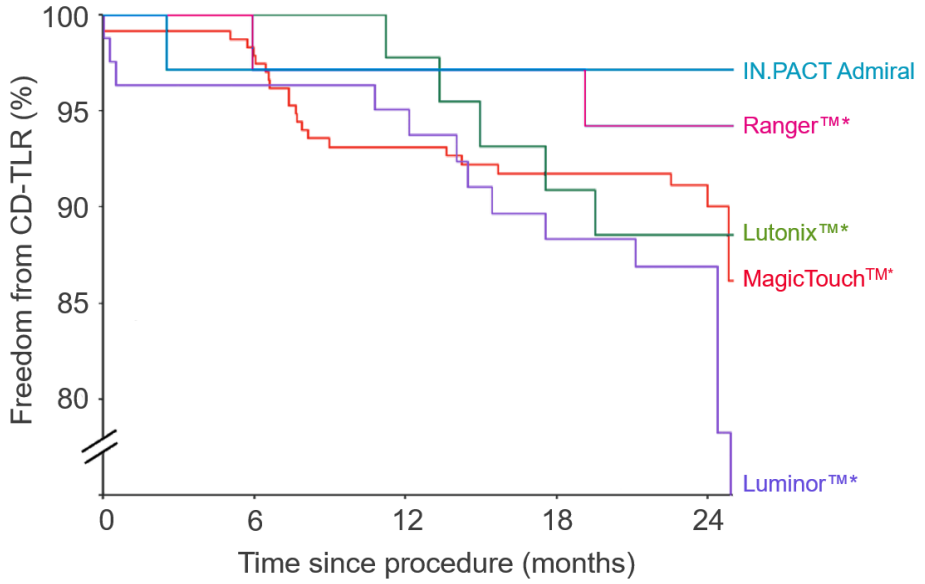
Lesion length 8.4 cm, CTO 33.2%



12-month primary patency:

Ranger and IN.PACT Trials: 82-83%

	Drug Dose	Excipient	No. of Balloons (n=325)
PCB			
Luminor 35	3.0 µg paclitaxel/mm²	Organic ester	106 (32.6)
Lutonix	2.0 µg paclitaxel/mm²	Polysorbate and sorbitol	59 (18.2)
Ranger	2.0 µg paclitaxel/mm²	Acetyltributyl-citrate	49 (15.1)
IN.PACT Admiral	3.5 µg paclitaxel/mm²	Urea	45 (13.8)
Stellarex	2.0 µg paclitaxel/mm²	Polyethylene-glycol	18 (5.5)
Orchid	3.0 µg paclitaxel/mm²	Magnesium- stearate	13 (4.0)
SeQuent Please OTW	3.0 µg paclitaxel/mm²	Resveratrol	11 (3.4)
IN.PACT Pacific	3.0 µg paclitaxel/mm²	Urea	3 (0.9)
ELUTAX	2.2 µg paclitaxel/mm²	Dextran	1 (0.3)
Combination			9 (2.8)
Unknown DCB type			4 (1.2)



Teichgräber U, et al. *JACC Cardiovasc Interv*. 2026;19(16):2251-2261. Teichgräber U, et al. *J Am Coll Cardiol*. 2026;88(8):780-796.

Conclusion: DCB 101

- Drug delivery has profoundly affected the management of lower occlusive extremity disease
- Paclitaxel reduces reintervention and is well established for femoral-popliteal treatment, but each device is different
- Quality of data with paclitaxel DCB in fem-pop segment is as good as or better than anything we have in the vascular field
- Well-suited to use in PAD due to anti-proliferative properties, crystalline microstructure providing long-term stability and residence in tissue through the re-stenotic cascade
- Patient-level analysis of pivotal paclitaxel RCTs, conducted with input from the FDA, demonstrated no mortality signal
  - Updated RCTs, meta-analyses, and real-world studies do not show mortality risk
- Promising technology for sirolimus delivery to reduce inflammation and improve vascular healing
  - Specific technology, including phospholipid coating and micro-reservoirs, enhances drug transfer, bioavailability, and tissue retention
- Current studies will provide evidence to assess this approach

HMP Global
Cardiovascular CME

Current Body of Evidence for DCBs

Prakash Krishnan, MD



Q1

Overview of Available Evidence

Paclitaxel has more randomized and long-term evidence than sirolimus

Level of evidence	Paclitaxel devices	Sirolimus devices
Proof of concept	THUNDER, FemPac	Limus FLOW mechanistic RCT (n=70); XTOSI pilot
Pivotal RCTs vs PTA	IN.PACT SFA, LEVANT 2, ILLUMENATE, RANGER II SFA	SirPAD (n=1,252, NEJM 2026); SELUTION4SFA, SELUTION4BTK, LIMES enrolling
Large real-world registries	IN.PACT Global, Lutonix Global, ILLUMENATE Global; Japan PMS	SELUTION SFA Japan (n=134), SUCCESS PTA (n=720), PRISTINE
Head-to-head RCTs	COMPARE (dose), TRANSCEND, IMPERIAL (DES)	SIRONA vs paclitaxel DCB (n=482)
Follow-up ≥5 years	IN.PACT SFA, IN.PACT Global, ILLUMENATE, Zilver PTX, COMPARE	None yet; longest is 3 years (SIRONA preliminary, SELUTION Japan)

NIH. Accessed November 4, 2026. https://clinicaltrials.gov/study/NCT04475783; NCT05132361; NCT05055297; NCT04772300.

Q1

Early Randomized and Feasibility Studies

Early paclitaxel trials assessed restenosis and TLR; sirolimus studies include mechanistic and feasibility endpoints

Paclitaxel

THUNDER

RCT · n=154 · fem-pop

59%

relative reduction in 5-yr TLR vs uncoated balloon (22.9% vs 55.6%)

Lower restenosis and TLR versus uncoated balloon

Paclitaxel

FemPac

RCT · n=87 · fem-pop

Replicated

lower late lumen loss and TLR vs uncoated balloon

Similar findings in an independent randomized trial

Sirolimus

Limus FLOW

Mechanistic RCT · n=70 · vs IN.PACT

40% vs 22%

improvement in endothelial function at 12 months (p=0.023); less inflammation at 30 days

Mechanistic rather than clinical efficacy endpoint

Sirolimus

XTOSI

Pilot · n=50 · fem-pop + BTK

92.9%

3-yr freedom from CD-TLR, fem-pop (77.8% BTK)

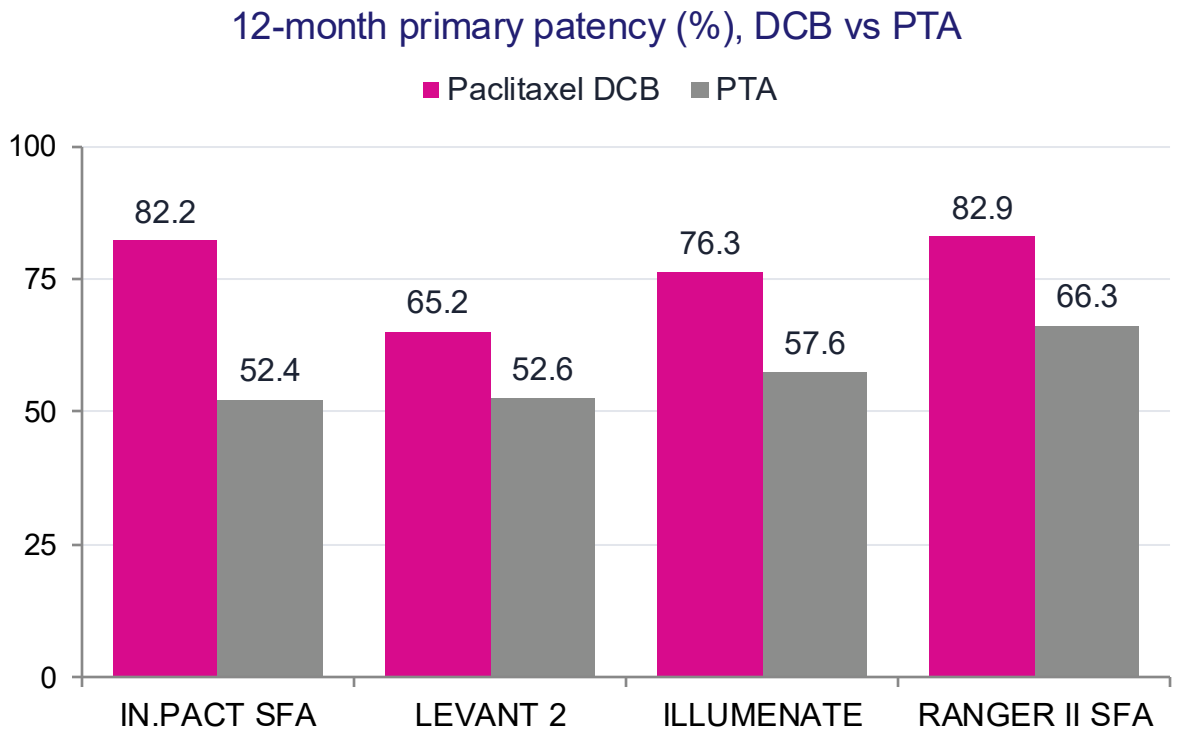
Small, single-arm study

Tepe G, et al. *N Engl J Med*. 2008;358:689-699. Werk M, et al. *Circulation*. 2008;118:1358-1365. Rammos C, et al. *J Am Heart Assoc*. 2026;15(19):e046944. Choke ETC, et al. *Ann Vasc Surg*. 2024;106:8-15.

Q1

Pivotal Randomized Trials vs PTA

Paclitaxel trials reported efficacy advantages over PTA; SirPAD assessed a clinical composite endpoint



Patency as defined in each primary report; RANGER II Kaplan-Meier 89.8% vs 74.0%.

Trial	n	12-mo outcome	Longer term
IN.PACT SFA	331	CD-TLR 2.4% vs 20.6%	5-yr freedom from CD-TLR 74.5% vs 65.3%
LEVANT 2	476	Safety 83.9% vs 79.0%	—
ILLUMENATE	300	CD-TLR 7.9% vs 16.8%	4-yr CD-TLR 28.2% vs 34.1% (NS)
RANGER II SFA	376	CD-TLR 5.5% vs 16.5%	—

SirPAD sirolimus DCB vs PTA · n=1252 all-comers, incl. BTK

Major amputation or CLI-driven TLR at 1 yr: 8.8% vs 15.0% (*P*=.009). The primary endpoint was clinical rather than patency-based.

Tepe G, et al. *Circulation*. 2015;131(5):495-502. Laird JA, et al. *Circ Cardiovasc Interv*. 2019;12(6):e007702. Rosenfield K, et al. *N Engl J Med*. 2015;373(2):145-153. Krishnan P, et al. *Circulation*. 2017;136(12):1102-1113. Krishnan P, et al. *Am J Cardiol*. 2024;227:83-90. Sachar R, et al. *JACC Cardiovasc Interv*. 2021;14(10):1123-1133. Barco S, et al. *N Engl J Med*. 2026;395(6):561-570.

Q1

Observational Registry Evidence

Paclitaxel registries have larger cohorts and longer follow-up; sirolimus data include smaller and more heterogeneous cohorts

Paclitaxel			Sirolimus		
IN.PACT Global n=1,406 · 64 sites	**69.4%**	5-yr freedom from CD-TLR (83.3% at 2 yr)	**SELUTION SFA Japan** n=134 · fem-pop	**97.0%**	12-mo freedom from CD-TLR; patency 87.9% (81.5% at 3 yr)
Lutonix Global n=691	**94.3%**	12-mo freedom from TLR (89.3% at 2 yr)	**SUCCESS PTA** n=720 · 27 sites	**91.1%**	12-mo freedom from CD-TLR; CLTI 90.3%
ILLUMENATE Global n=371	**94.8%**	12-mo freedom from CD-TLR; patency 81.4%	**PRISTINE** n=75 · all CLTI	**74%**	12-mo freedom from CD-TLR; patency 58%; wound healing 79%

Populations differ widely (SELUTION Japan: CLTI 2.2%; PRISTINE: 100% CLTI), and time points vary; registries are not directly comparable.

Zeller T, et al. *EuroIntervention*. 2022;18(11):e940-e948. Thieme M, et al. *JACC Cardiovasc Interv*. 2017;10(16):1682-1690. Schroë H, et al. *Catheter Cardiovasc Interv*. 2018;91(3):497-504. Iida O, et al. *JACC Cardiovasc Interv*. 2024;17(13):1547-1556. Soga Y, et al. *JACC Cardiovasc Interv*. 2025;18(21):2629-2637. Lichtenberg M. Presented at: Charing Cross Symposium; April 23-25, 2025; London, England. Tang TY, et al. *Cardiovasc Intervent Radiol*. 2024;47:863-874.

Q1

Randomized Device Comparisons

Direct comparisons allow assessment of relative efficacy; conclusions depend on endpoints and follow-up duration

COMPARE

Paclitaxel vs paclitaxel

Low-dose Ranger vs high-dose IN.PACT · n=414

12 mo Patency 83.0% vs 81.5% (noninferior)

Later 5-yr: freedom from CD-TLR 67.1% vs 75.2% (*P*=.096)

TRANSCEND

Paclitaxel vs paclitaxel

SurVeil vs IN.PACT · n=446

12 mo Primary efficacy 82.2% vs 85.9% (noninferior)

Later Long-term follow-up pending

IMPERIAL

Paclitaxel DES vs DES

Eluvia vs Zilver PTX · n=465

12 mo Patency 86.8% vs 77.5%

Later 5-yr: K-M patency 69.6% vs 67.4% (*P*=.48)

SIRONA

Sirolimus vs paclitaxel

MagicTouch vs paclitaxel DCB · n=482

12 mo Patency 73.8% vs 75.0% (noninferior)

Later 3-yr*: freedom from TLR 88.2% vs 80.2%

***Preliminary, pending event adjudication.**

Wittig T, et al. *EuroIntervention*. 2026;22(3):e186-e189. Brodmann M, et al. *Eur J Vasc Endovasc Surg*. 2025;69(3):452-462. Gray WA, et al. *Lancet*. 2018;392(10157):1541-1551. Teichgräber U, et al. *J Am Coll Cardiol*. 2026;88(8):780-796.

Q1

Paclitaxel DCB Meta-Analyses

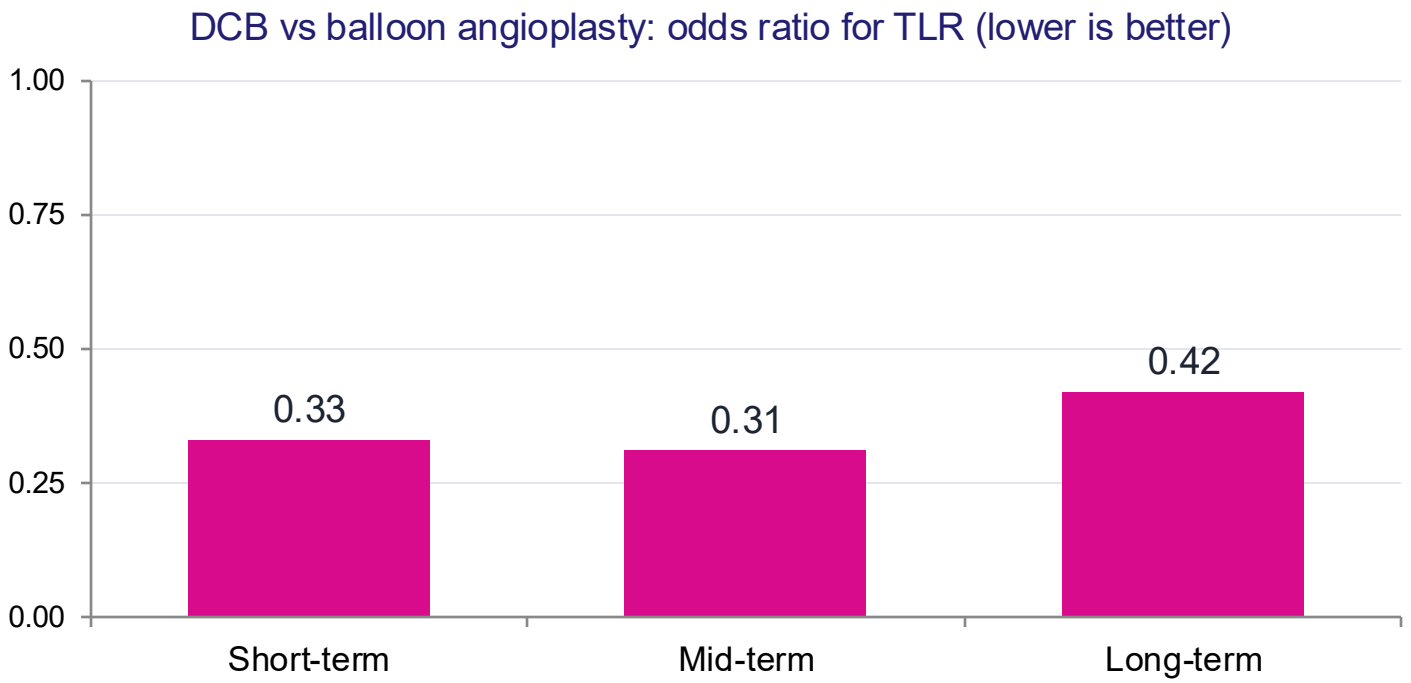
Meta-analyses report improved TLR and patency outcomes, with effect estimates varying by follow-up

1.39

RR for freedom from TLR at 24 months, DCB vs POBA (1.27–1.52); 8 RCTs, heterogeneity I^2 = 21%

51 RCTs

8430 patients in the femoropopliteal network meta-analysis; DCB showed favorable outcomes across included comparisons



Patency OR 3.21 → 2.75 → 2.47 over the same horizons: with decreasing effect estimates over time. DES vs BMS: TLR OR 0.50 (0.22–1.11), fewer trials.

POBA = plain old balloon angioplasty.

Klumb C, et al. *EClinicalMedicine*. 2019;16:42-50. Koeckerling D, et al. *Eur Heart J*. 2023;44:935-950.

Q1

Clinical Studies of Sirolimus Devices

Evidence includes randomized trials and registries, with limited long-term follow-up

Study	Design · Device	n	Key result
SIRONA	RCT vs paclitaxel DCB · MagicTouch, fem-pop	482	12-mo patency 73.8% vs 75.0% (noninferior); 3-yr TLR favors SCB, preliminary
SirPAD	RCT vs PTA · MagicTouch, infrainguinal	1252	Major amputation or CLI-TLR 8.8% vs 15.0% (*P*=.009)
SELUTION SFA Japan	Single-arm · SELUTION SLR, complex fem-pop	134	3-yr patency 81.5%; freedom from CD-TLR 93.8%
SUCCESS PTA	Real-world, 27 sites · SELUTION SLR	720	12-mo freedom from CD-TLR 91.1% (CLTI 90.3%)
ILLUMINA	First-in-human · NiTiDES sirolimus stent	—	2-yr patency 83.4%; freedom from CD-TLR 93.1%
LIFE-BTK	RCT vs PTA · everolimus resorbable scaffold, BTK	261	2-yr primary efficacy 68.8% vs 45.4%

SCB = sirolimus-covered balloon.

Teichgräber U, et al. *J Am Coll Cardiol*. 2026;88(8):780-796. Barco S, et al. *N Engl J Med*. 2026;395(6):561-570. Iida O, et al. *JACC Cardiovasc Interv*. 2024;17(13):1547-1556. Soga Y, et al. *JACC Cardiovasc Interv*. 2025;18(21):2629-2637. Lichtenberg M. Presented at: Charing Cross Symposium; April 23-25, 2025; London, England. Steiner S, et al. *JACC Cardiovasc Interv*. 2022;15(6):618-626. DeRubertis BG, et al. *Circulation*. 2025;152(15):1076-1086.

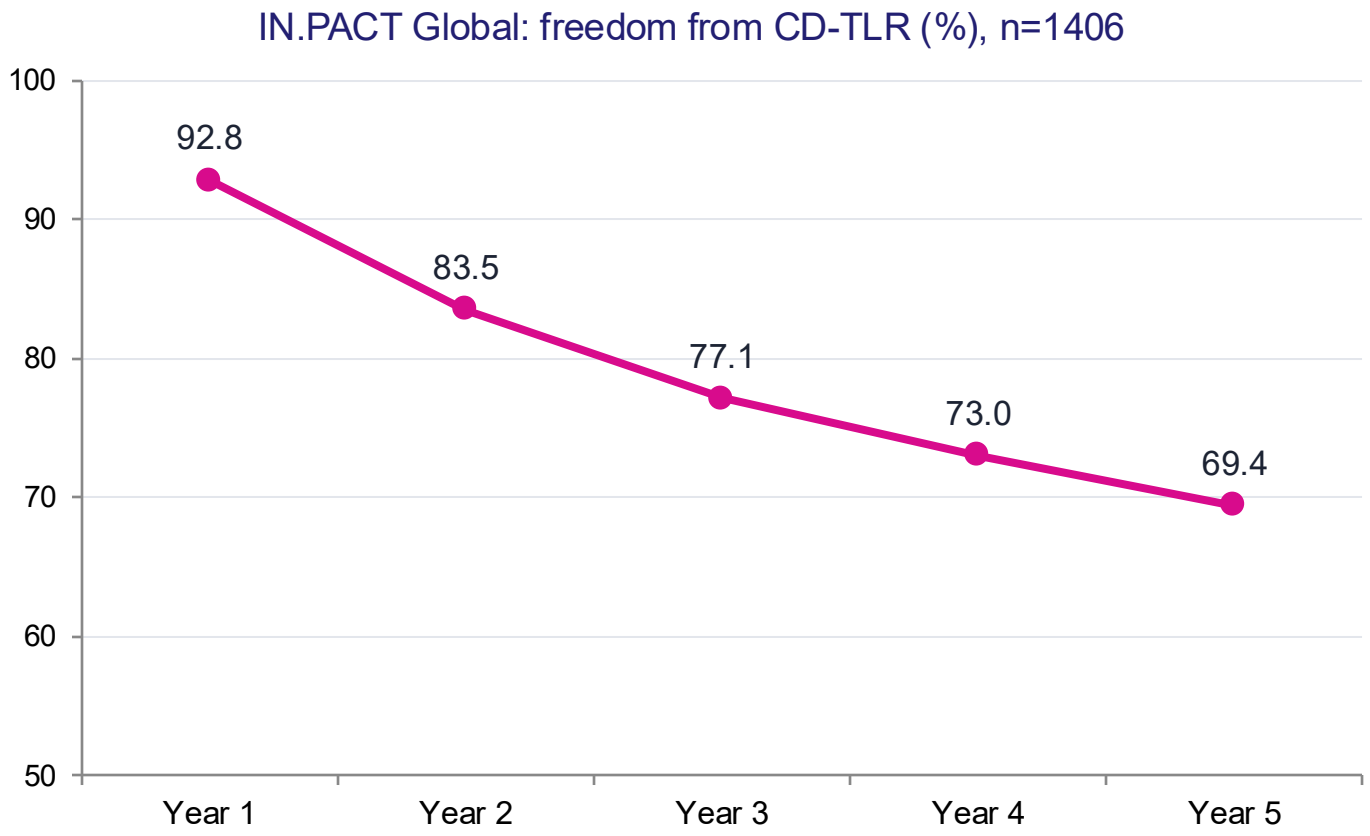
Long-Term Outcomes and Comparative Evidence

Efficacy and safety beyond 12 months

Q2

Outcomes beyond 12 Months

Freedom from reintervention decreases with longer follow-up in published cohorts



+9.2

points, 5-yr freedom from CD-TLR: IN.PACT DCB 74.5% vs PTA 65.3%

+15.5

points, 5-yr freedom from TLR: Zilver PTX 83.1% vs PTA/BMS 67.6%

366

IN.PACT Global patients re-intervened by 5 years: approximately one quarter of the cohort

Zeller T, et al. *EuroIntervention*. 2022;18(11):e940-e948. Laird JA, et al. *Circ Cardiovasc Interv*. 2019;12(6):e007702. Dake MD, et al. *Circulation*. 2016;133(15):1472-1483.

Q2

Paclitaxel Safety: Evidence and Regulatory Review

Subsequent analyses did not confirm the initial mortality signal; clinical use changed during the review period

2018

Signal

Summary-level meta-analysis suggests late mortality with paclitaxel devices; FDA warning follows.

2019–23

Pause

Medicare: DCB share of fem-pop revascularization falls sharply while plain PTA rises.

2023

Resolution

Patient-level, long-term data show no mortality signal; FDA updates its recommendations.

HR 1.03

Major amputation or death after fem-pop PVI during the safety-concern era vs before (1.01–1.04), Medicare

HR 0.85

Amputation-free survival, paclitaxel vs control in CLI (0.79–0.91); German insurance cohort, n=21,546

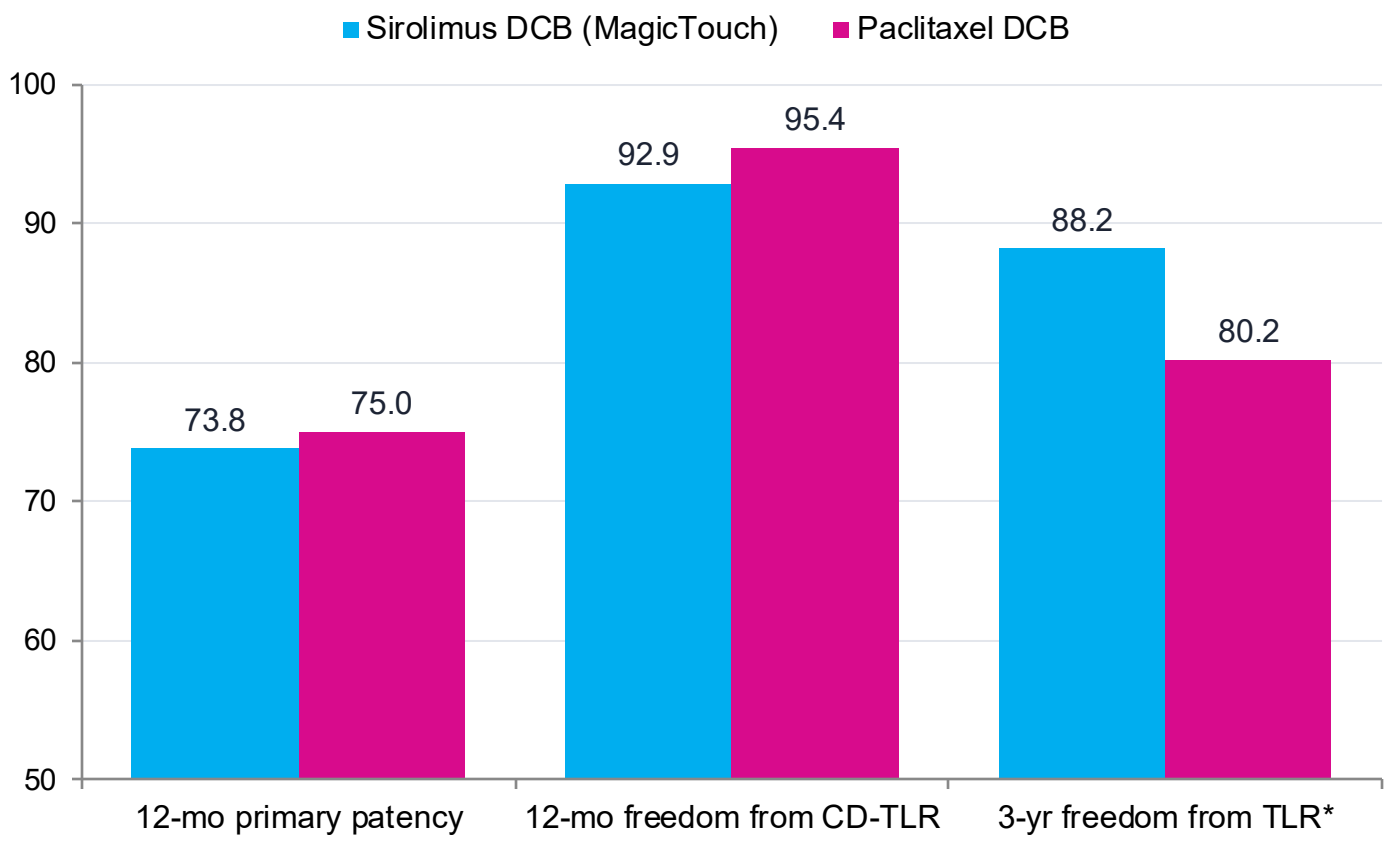
FDA = U.S. Food and Drug Administration; PVI = peripheral vascular intervention.

Kim JM, et al. *J Am Coll Cardiol*. 2025;85(6):645-648. Behrendt CA, et al. *Eur J Vasc Endovasc Surg*. 2020;59(4):587-596.

Q2

SIRONA: Results by Follow-Up and Comparator

Randomized comparison of sirolimus and paclitaxel DCBs (n=482; 25 sites in Germany and Austria)



Patency HR, sirolimus vs each paclitaxel DCB in SIRONA

Comparator	HR (95% CI)
All paclitaxel DCB	1.17 (0.84–1.63)
Luminor	1.01 (0.68–1.77)
Lutonix	1.31 (0.73–2.33)
Ranger	**1.78 (0.85–3.73)**
IN.PACT Admiral	**1.77 (0.76–4.08)**

HR >1 = higher loss of patency with sirolimus. Small subgroups, wide CIs.

***3-yr TLR: HR 0.60 (0.36–0.97), *P*=.03, preliminary, CX 2026, pending event adjudication. Freedom from major amputation 99.6% both arms.**

Teichgräber U, et al. *J Am Coll Cardiol*. 2026;88(8):780-796. Teichgräber U, et al. *CVIR Endovasc*. 2026;9:96.

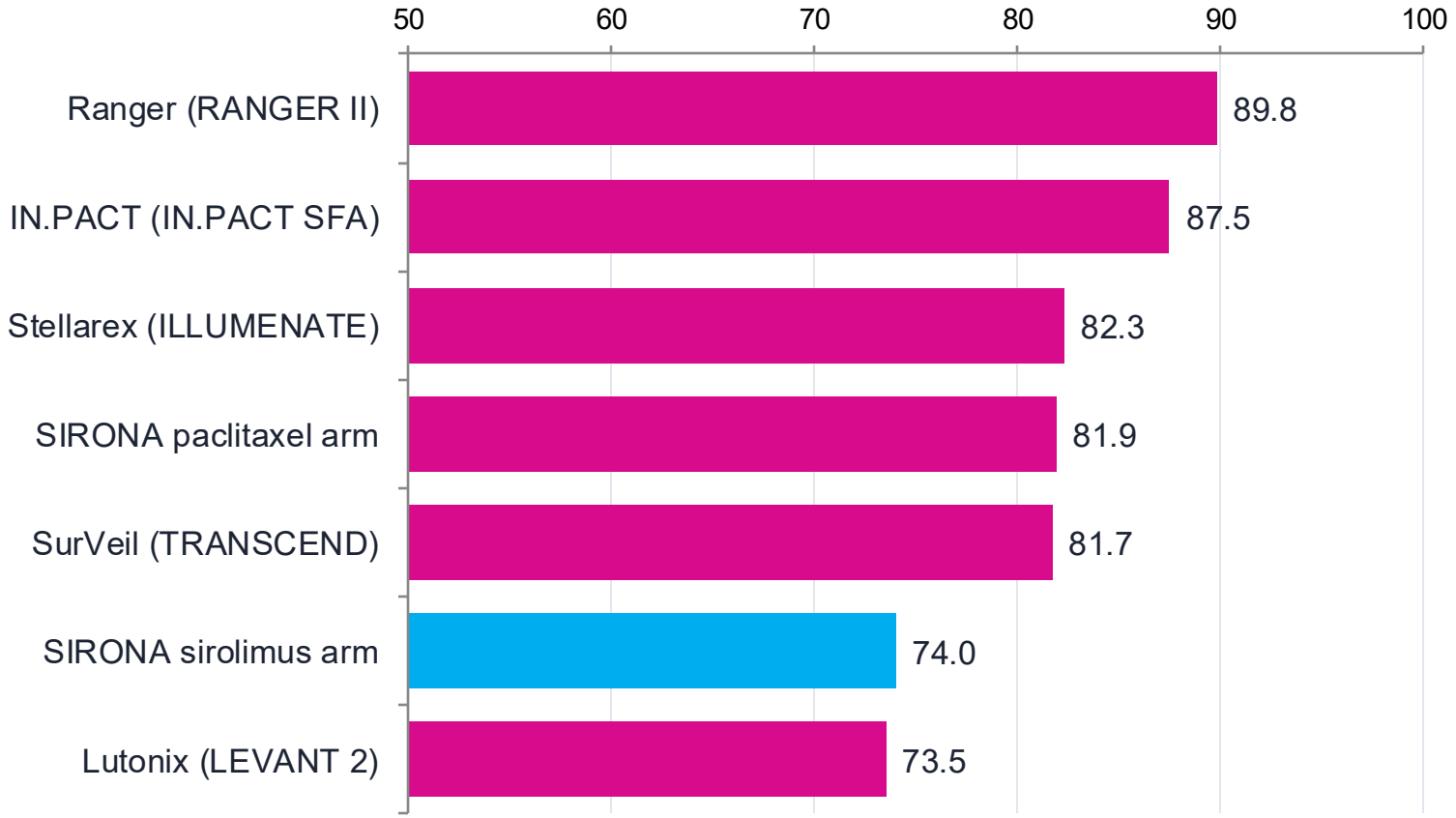
Selection of Comparative Trial Controls

Comparator, population, endpoints, and follow-up

Q3

Differences among Paclitaxel DCB Trials

12-month primary patency (Kaplan-Meier) across trial DCB arms spans more than 16 points



56.8-74.0%

12-month patency of the PTA control arms in the same IDE trials

How to read the spread

New devices should be compared with clinically relevant established platforms.

Interpret differences cautiously because patient populations and trial methods vary.

Cross-trial comparison; results from different trials are not directly comparable.
IDE = investigational device exemption.
Rosenfield K, et al. *N Engl J Med*. 2015;373(2):145-153. Laird JA, et al. *Circ Cardiovasc Interv*. 2019;12(6):e007702. Sachar R, et al. *JACC Cardiovasc Interv*. 2021;14(10):1123-1133. NIH. Accessed November 5, 2026. https://clinicaltrials.gov/study/NCT03421561; NCT03241459. Teichgräber U, et al. *J Am Coll Cardiol*. 2026;88(8):780-796.

Q3

Comparator Selection and Trial Design

PTA remains a common control despite established randomized evidence for paclitaxel DCBs

Plain PTA

Established control for initial evaluation; multiple RCTs have shown DCB efficacy advantages.

Best-in-class DCB

IN.PACT or Ranger, with 5-year RCT data. Relevant active comparators for noninferiority studies.

Complex-lesion standard

DES or DCB with vessel prep in long, calcified, CTO, ISR, CLTI, and BTK disease.

A fair comparison also needs

1. **Rigor** Core lab, independent CEC, source-data monitoring
2. **Population** Include complex lesions representative of clinical practice
3. **Endpoints** Patency + CD-TLR + amputation and survival
4. **Duration** At least 3 years for efficacy, 5 for safety
5. **Power** Prespecified individual-device comparisons

CEC = Clinical Events Committee.

Koeckerling D, et al. *Eur Heart J*. 2023;44:935-950.

Q3

What the Sirolimus Trials Compare Against

Among the 5 trials listed, SIRONA directly compares a sirolimus DCB with paclitaxel DCBs

1 of 5

sirolimus DCB RCTs with a paclitaxel DCB comparator

Comparison with PTA establishes efficacy relative to uncoated angioplasty but not relative performance vs active DCBs.

SIRONA	**vs Paclitaxel DCB**	Fem-pop · completed
SirPAD	**vs Plain PTA**	Infrainguinal · completed
SELUTION4SFA	**vs Plain PTA**	Fem-pop · enrolling
SELUTION4BTK	**vs Plain PTA**	BTK · enrolling
LIMES	**vs Plain POBA**	Infrapopliteal · enrolling

NIH. Accessed November 5, 2026. https://clinicaltrials.gov/study/NCT04475783; NCT05132361; NCT05055297; NCT04772300. Barco S, et al. *N Engl J Med*. 2026;395(6):561-570.

Conclusions

Q1 — Current body of evidence

- Paclitaxel: 4+ pivotal RCTs, a 51-RCT meta-analysis, global registries, head-to-head trials, and 5-year data, with consistently lower TLR than PTA
- Sirolimus: one large RCT vs PTA (SirPAD), one head-to-head RCT (SIRONA), and registries; follow-up ≤3 years

Q2 — Long-term and comparative evidence

- Benefit attenuates over time, and the mortality signal took years of patient-level data to resolve
- Results and relative treatment estimates may differ at later follow-up in COMPARE, IMPERIAL, and SIRONA

Q3 — Standard of comparison

- Direct comparisons with established individual DCB platforms are needed to establish relative efficacy
- Studies should include complex lesions, independent adjudication, and longer follow-up

Bottom line: Paclitaxel DCBs have a more extensive evidence base. Additional long-term randomized comparisons are needed to define the relative efficacy and safety of sirolimus DCBs.

HMP Global

Cardiovascular CME

Getting the Most out of Your DCB

John Winscott, MD



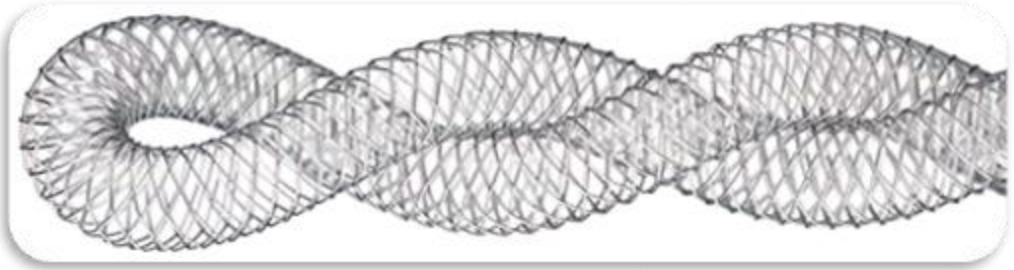
Background

- Movement away from scaffolds
- DCB has changed the treatment landscape
- Huge data gap in fem/pop treatment between trials and practice (6-12 cm vs >30 cm)
- “Vessel Prep” is a commonly used term but poorly defined

Vessel Prep

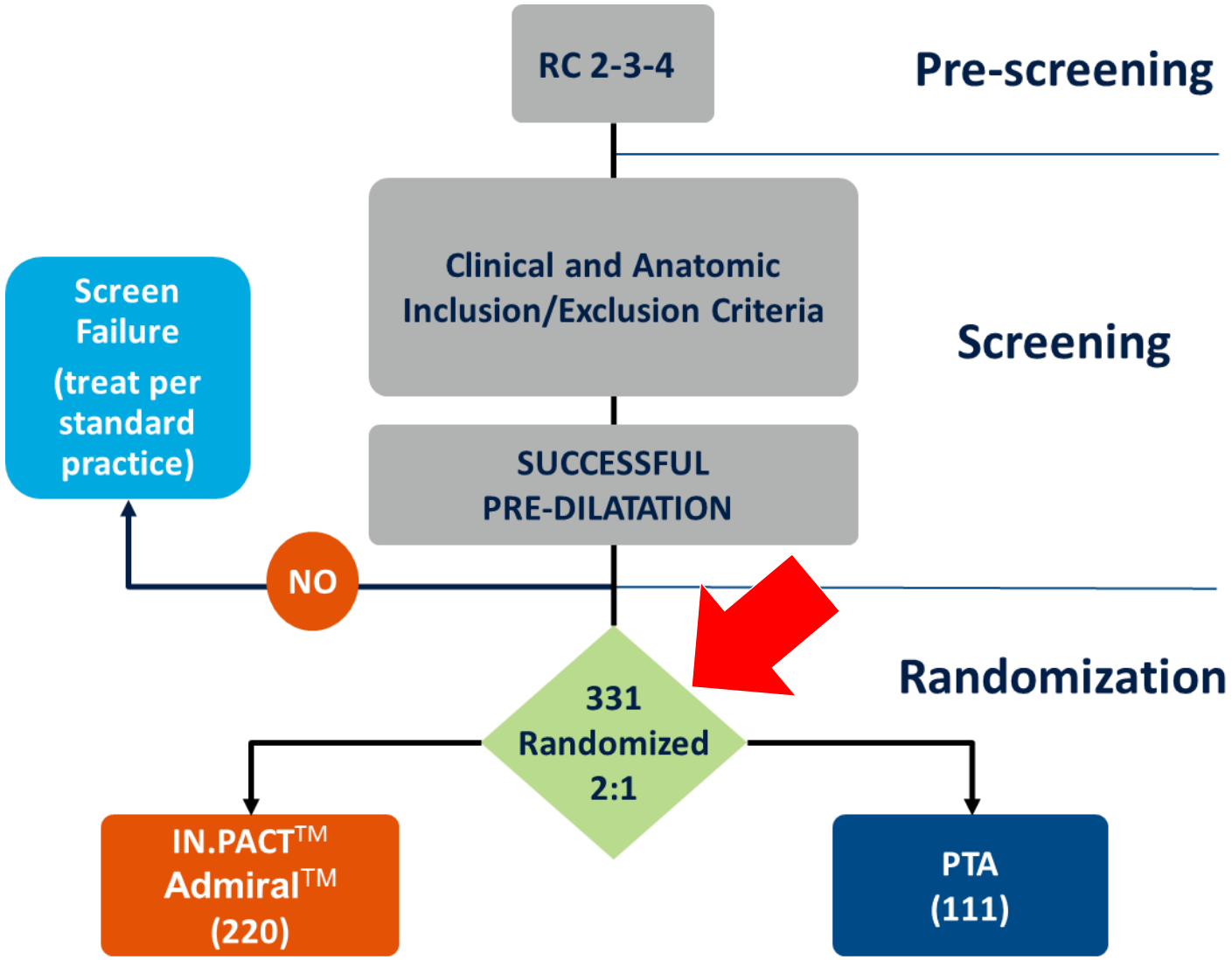
- Prepare for what?
  - DCB
  - Stent
- Goals of prep?
  - Create a channel
  - Easier equipment delivery
  - Better stent delivery/expansion
  - Lumen gain
  - Minimize dissection
  - More consistent drug uptake
- Potential for better long-term patency
- Prettier angiogram





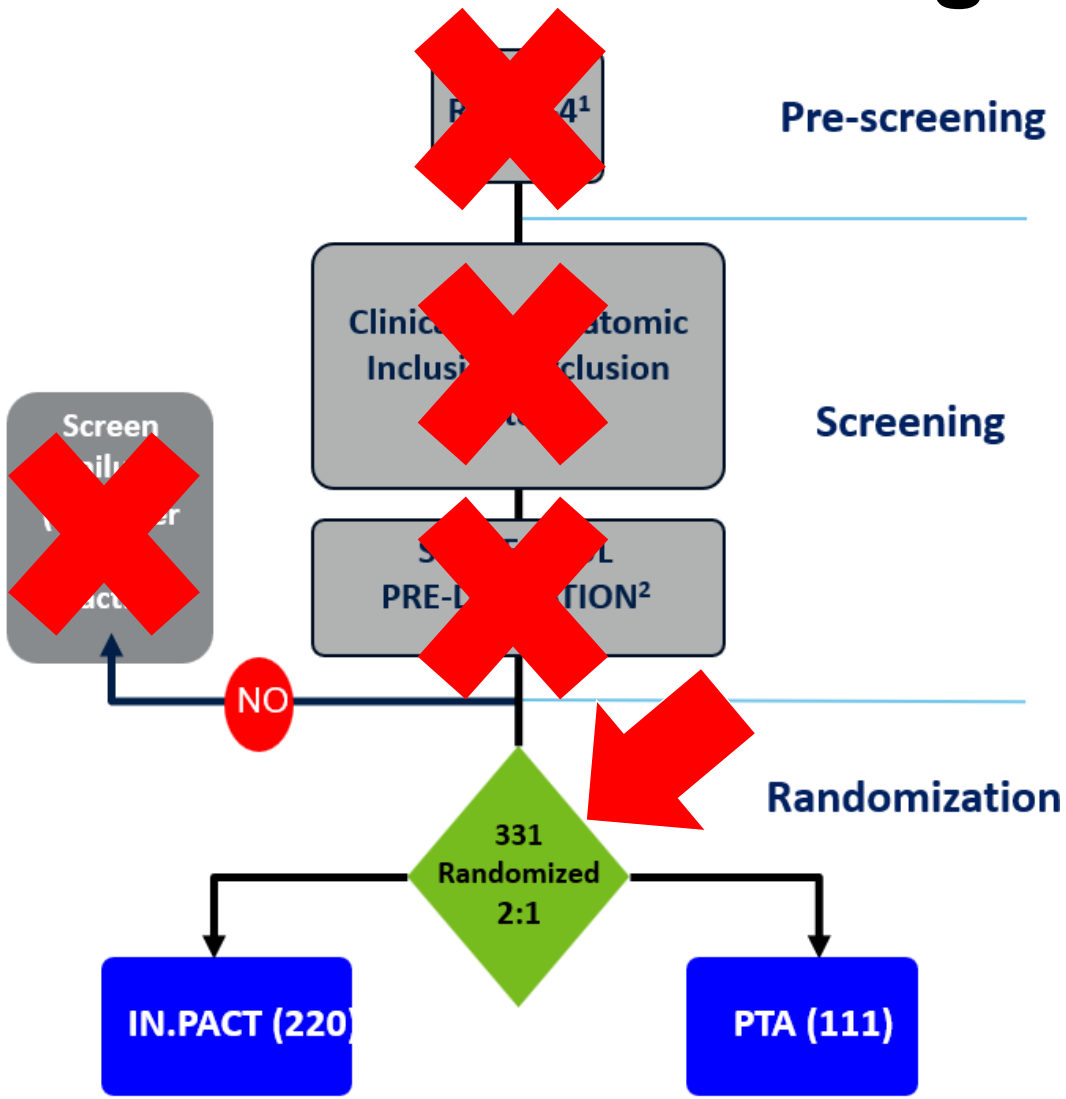


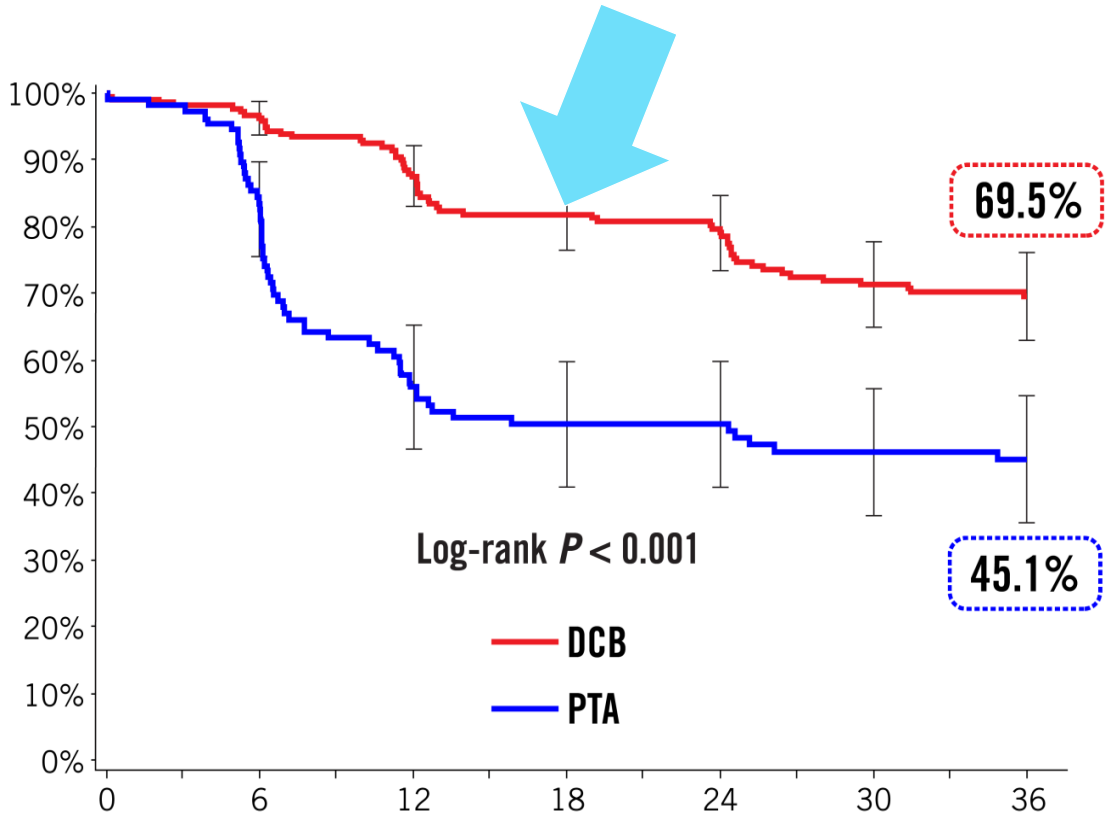




Laird JR, et al. *J Am Coll Cardiol*. 2015;66(21):2329-2338.

IN.PACT SFA Trial Design and Efficacy Outcomes





What if we could transform our real-world patients into IN.PACT SFA Trial patients?

Laird JR, et al. *J Am Coll Cardiol*. 2015;66(21):2329-2338.

Determinants of Drug-Coated Balloon Failure in Patients Undergoing Femoropopliteal Arterial Intervention

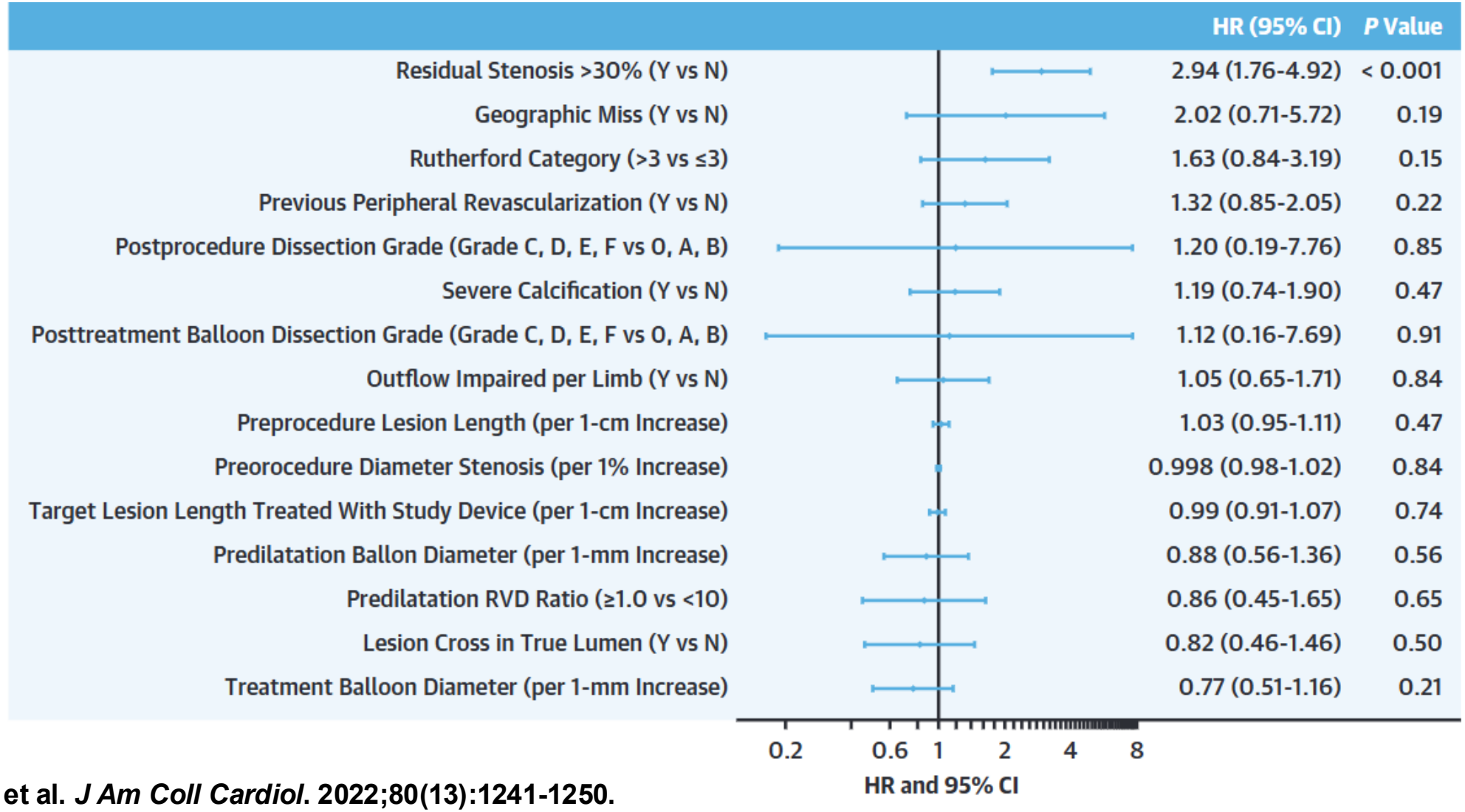
Prakash Krishnan, MD, Serdar Farhan, MD, Peter Schneider, MD, Haroon Kamran, MD, Osamu Iida, MD, Marianne Brodmann, MD, Antonio Micari, MD, Ravish Sachar, MD, Kasuki Urasawa, MD, Dierk Scheinert, MD, Kenji Ando, MD, Arthur Tarricone, DPM, Gheorghe Doros, PhD, Gunnar Tepe, MD, Hiroyoshi Yokoi, MD, John Laird, MD, Thomas Zeller, MD

Journal of the American College of Cardiology

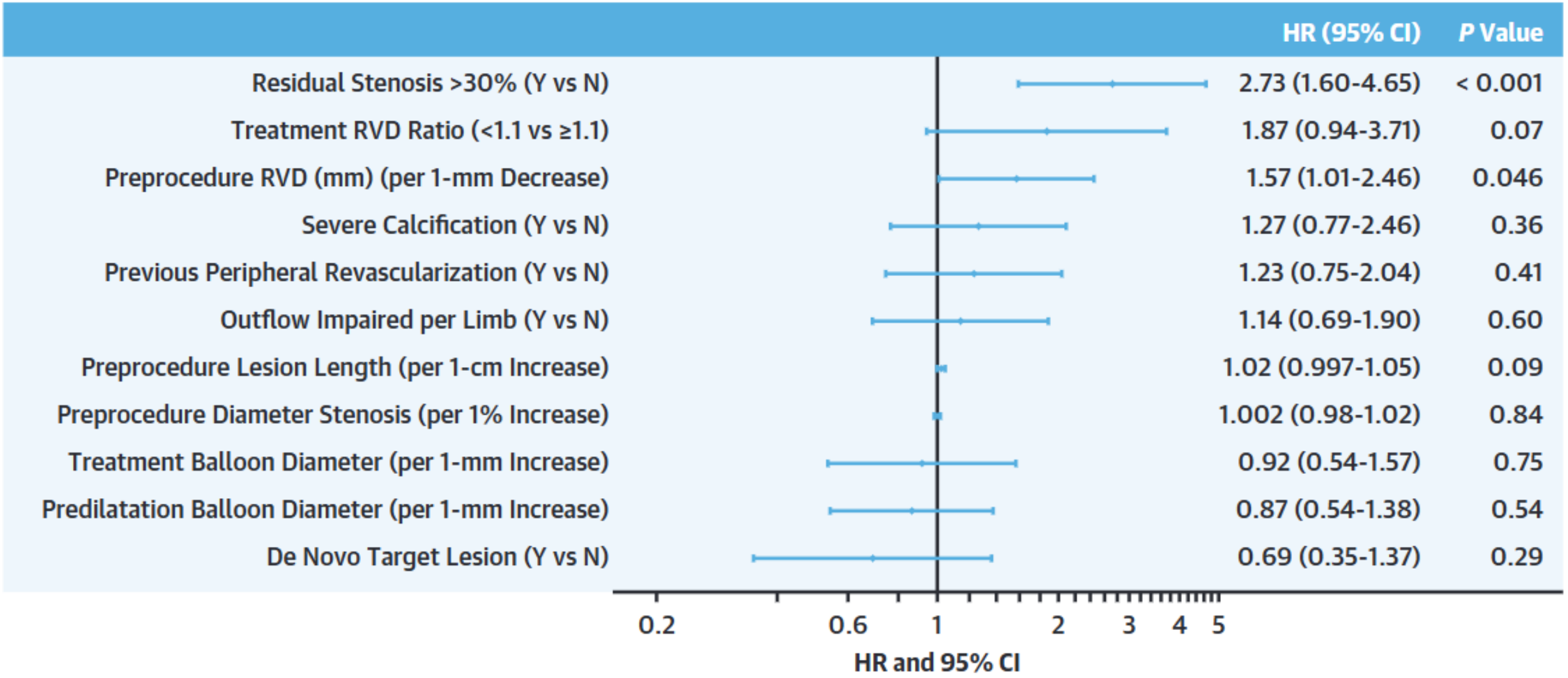
Volume 80, Issue 13, 27 September 2022, Pages 1241-1250

Krishnan P, et al. *J Am Coll Cardiol*. 2022;80(13):1241-1250.

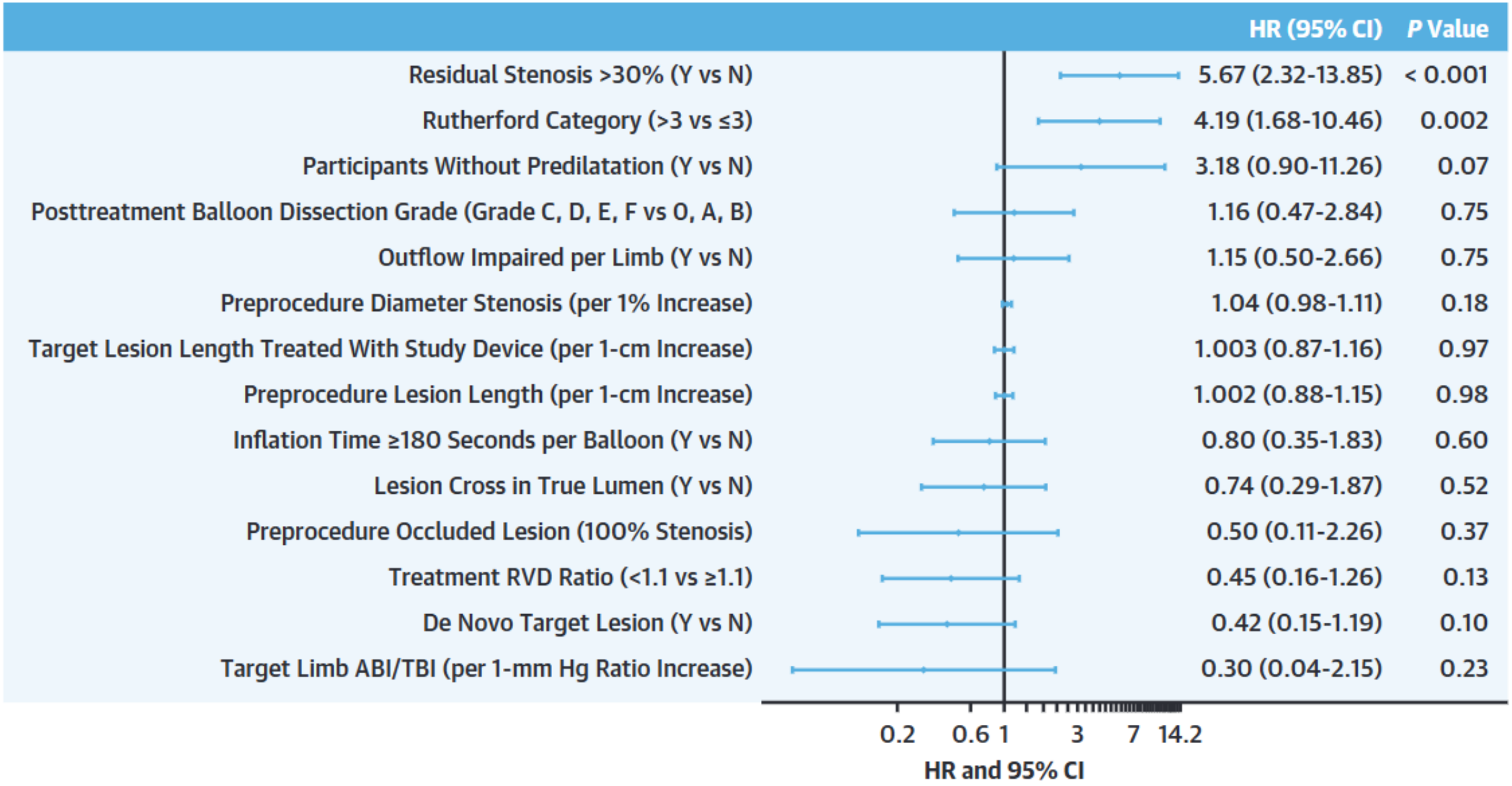
Predictors of Patency Loss, Binary Restenosis, and CD-TLR



Krishnan P, et al. *J Am Coll Cardiol*. 2022;80(13):1241-1250.

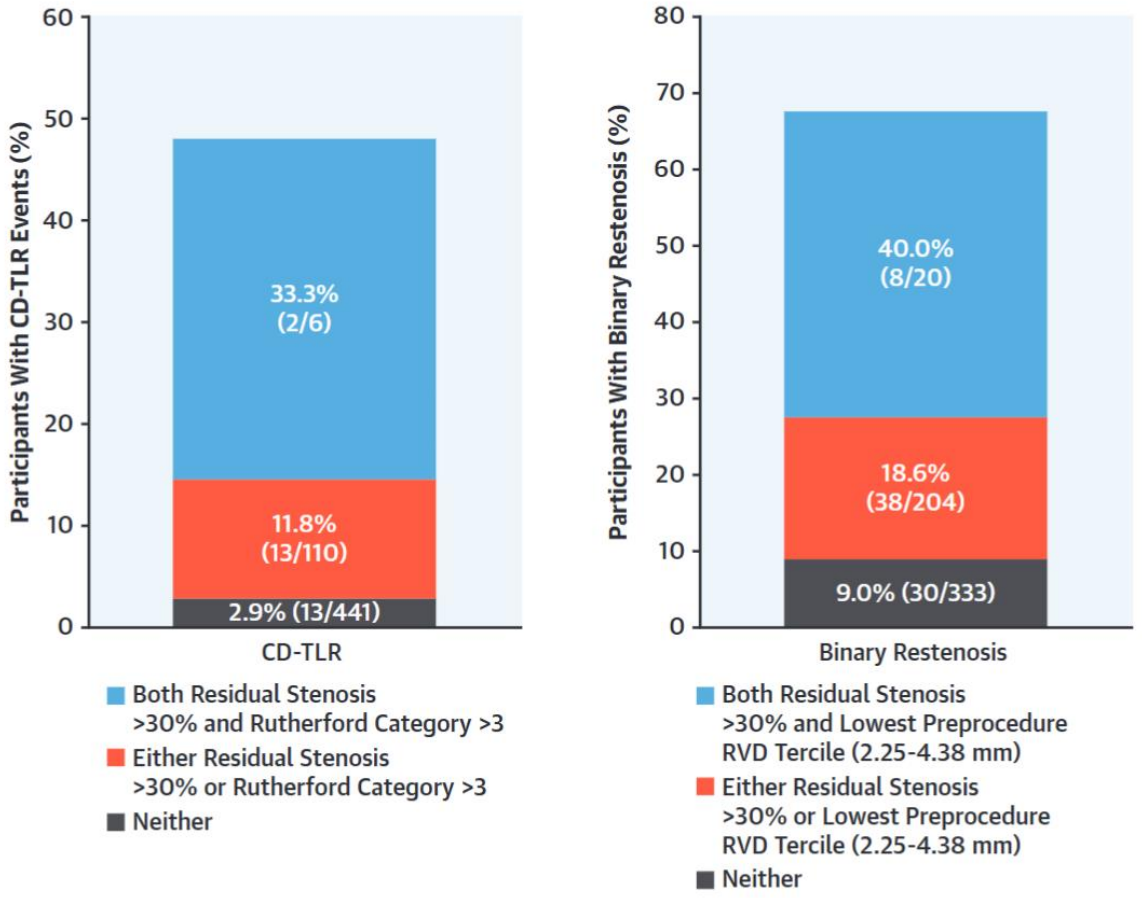


Krishnan P, et al. *J Am Coll Cardiol*. 2022;80(13):1241-1250.



Krishnan P, et al. *J Am Coll Cardiol*. 2022;80(13):1241-1250.

CENTRAL ILLUSTRATION **Independent Predictors of Clinically Driven Target Lesion Revascularization and Binary Restenosis**



Krishnan P, et al. J Am Coll Cardiol. 2022;80(13):1241-1250.

A patient-level pooled analysis of randomized clinical trials and the prespecified imaging cohorts of a prospective single-arm study was used to identify the predictors of drug-coated balloon failure, including binary restenosis and CD-TLR. Influential procedural characteristics were evaluated by an independent angiographic core laboratory. Among the factors found to be statistically significant in multivariable models (residual stenosis >30%, Rutherford clinical category >3, and smaller RVD), participants with 2 risk factors had a higher risk of CD-TLR or binary restenosis than participants with only 1 risk factor or no risk factors.

RVD = reference vessel diameter.

Krishnan P, et al. *J Am Coll Cardiol*. 2022;80(13):1241-1250.

Sizing

- Vessel diameter matters (SFA–P1)
- DCB trials reference vessel diameter
  - LUTONIX 4.8 cm and 4.8 cm
  - IN.PACT 4.6 cm and 4.7 cm
  - RANGER 5.0 cm and 4.5 cm
  - COMPARE 4.9 cm and 4.8 cm
- DA + DCB (REALITY) 5.3 cm
- IVL (DISRUPT PAD III) 5.4 cm

Peripheral IVL System Components



Peripheral IVL Clinical Programs

	Disrupt PAD I	Disrupt PAD II	Disrupt BTK	Disrupt PAD III RCT	Disrupt PAD III OS	Disrupt PAD+	Disrupt BTK II
Status	Enrollment completed	Enrollment completed	Enrollment completed	Enrollment completed	Enrollment completed	Enrollment completed	Enrollment ongoing
Study Design	Single arm, safety, and performance	Single arm, safety, and effectiveness	Single arm, pilot	RCT, safety, and effectiveness	Single arm, observational study	Single arm, safety, and effectiveness	Single arm, safety, and effectiveness
Study Conduct	CEC, ACL	CEC, ACL	ACL	CEC, ACL	ACL	CEC, ACL	CEC, ACL
# of Patients	35	60	20	306	1,373	37	250
# of Sites	3	8	3	45	32	8	Up to 40
Regions	NZ, EU	NZ, EU	NZ, EU	U.S., NZ, EU	U.S., NZ, EU	NZ, AU, U.S.	U.S., Germany

ACL = angiographic core lab; NZ = New Zealand; EU = European Union; U.S. = United States; AU = Australia.

DISRUPT PAD III RCT

Largest long-term Level 1 evidence in the treatment of heavily calcified femoropopliteal lesions

Study Flow

Calcified *de novo* femoropopliteal lesions

- **IVL** N = 153
- **PTA** N = 153

IN.PACT DCB +/- stent

Procedural Success & 30-day F/U

Presented at VIVA 2020

1-Year Primary Patency + 2-Year F/U

Presented at SCAI 2022

Endpoints

Primary: Procedural success (Residual stenosis ≤ 30% without flow-limiting dissection)

Powered Secondary: Primary patency at 1-year (freedom from CD-TLR + freedom from restenosis determined by duplex US + freedom from provisional stenting)

Design

Prospective Multicenter Single-Blind RCT

45 Global Sites

306 SFA/Popliteal Lesions

83%* Severe Calcification†

129mm* Avg. Calcified Length

Angiographic core-lab adjudicated

*IVL arm; †PARC definition.
F/U = follow-up.
Tepe G, et al. *J Soc Cardiovasc Angiogr Interv*. 2022;1(4):100341.

Key Eligibility Criteria

Inclusion

- Rutherford category 2, 3, or 4 of the target limb
- Target lesion is de novo SFA or popliteal artery
- Target lesion
  - RVD ≥4.0 mm and ≤7.0 mm
  - Stenosis ≥70% by visual estimate
  - Length ≤180 mm for lesions 70-99% stenosis
  - CTO lesion length ≤100 mm of the total ≤180 mm target lesion
- Calcification ≥ moderate defined as presence of fluoroscopic evidence of calcification
  - On parallel sides of the vessel and
  - Extending >50% of lesion length (if length ≥50 mm) or minimum calcification of 20 mm (if length <50 mm)

Exclusion

- Rutherford category 0, 1, 5, and 6
- Significant stenosis (>50%) or occlusion of inflow tract before target zone not successfully treated
- Planned target limb major amputation
- Renal disease (SCr >2.5 mm/dL) or on dialysis
- In-stent restenosis within 10 mm of target zone

Tepe G, et al. *J Soc Cardiovasc Angiogr Interv*. 2022;1(4):100341.

Study Endpoints

Primary Endpoint: Procedural success

- Residual stenosis ≤30% without flow-limiting dissection (≥ grade D) prior to DCB +/- stenting by angiographic core lab

Secondary Effectiveness Endpoint: Primary patency at 1 year

- Freedom from CD-TLR and freedom from restenosis determined by DUS or angiogram ≥50% stenosis
- Acute PTA failure* requiring a stent at any time during the index procedure was counted as a loss of primary patency per protocol

Additional 1-year secondary endpoints

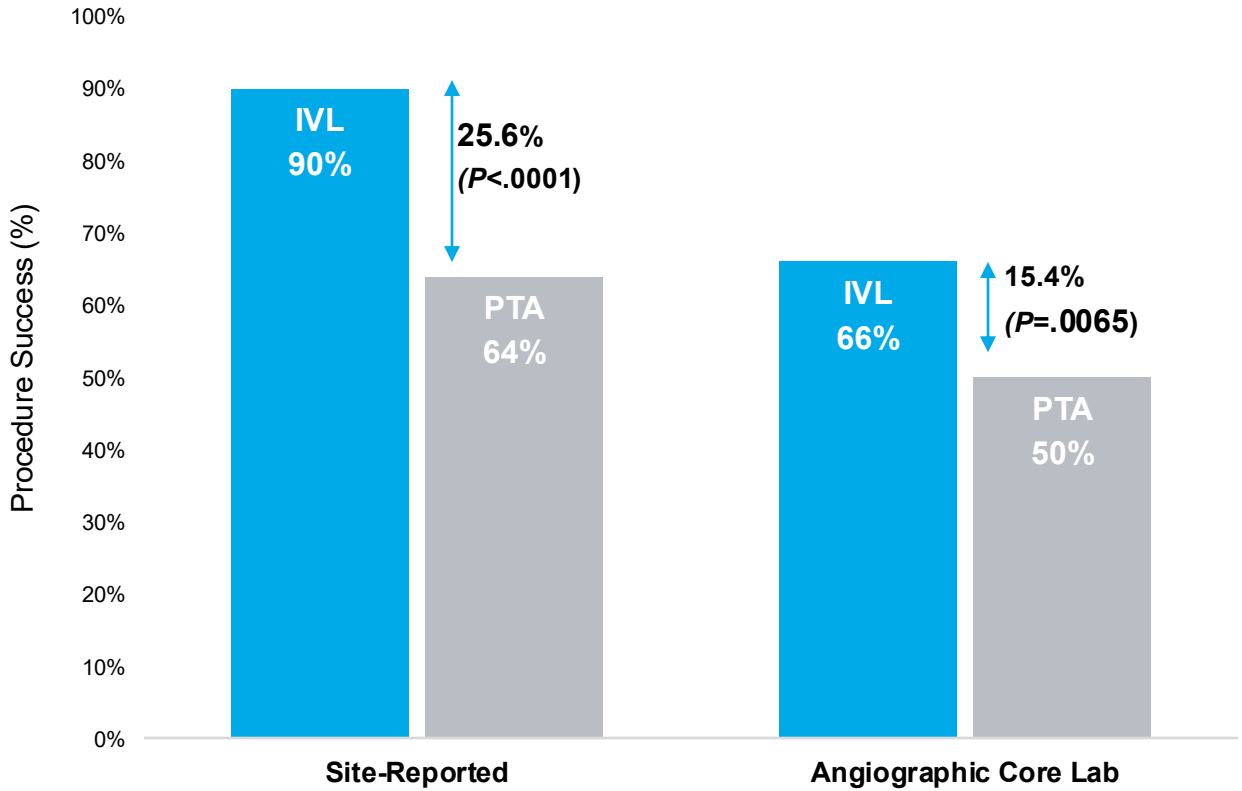
- Major adverse events†, ABI, RC, WIQ, EQ-5D

*PTA failure defined as residual stenosis ≥50% by visual estimate, or unresolved flow-limiting (≥grade D) dissection, and trans-lesional gradient >10 mm Hg; †MAE: Need for emergency surgical revascularization of target limb, unplanned target limb major amputation, thrombus or distal emboli requiring intervention to improve flow, perforations that require intervention, including bail-out stenting.

DUS = Duplex ultrasound; ABI = ankle-brachial index; RC = Rutherford Category; WIQ = Walking Impairment Questionnaire; EQ-5D = EuroQol 5-Dimension; MAE = major adverse event.

Tepe G, et al. *J Soc Cardiovasc Angiogr Interv*. 2022;1(4):100341.

PAD III

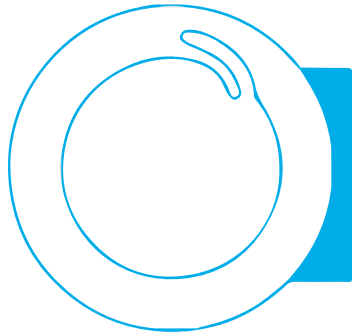


Procedural Success = Residual stenosis ≤30%
without flow-limiting dissections prior to DCB +/- stenting



44%

Lower Max Pressure
(6.3 atm vs 11.3 atm) *P*<.0001



77%

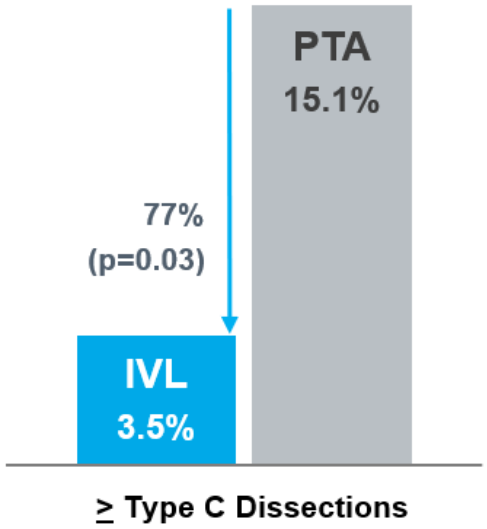
Reduction in Type ≥ C Dissections
(3.5% vs 15.1%) *P*=.03

Tepe G, et al. *J Soc Cardiovasc Angiogr Interv*. 2022;1(4):100341.

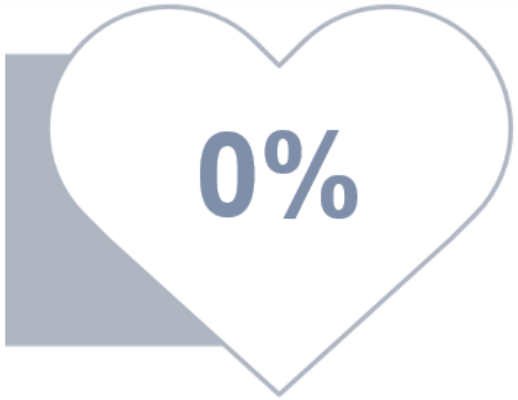
PAD III

Reduced Dissections

77% Reduction
in Type ≥ C Dissections



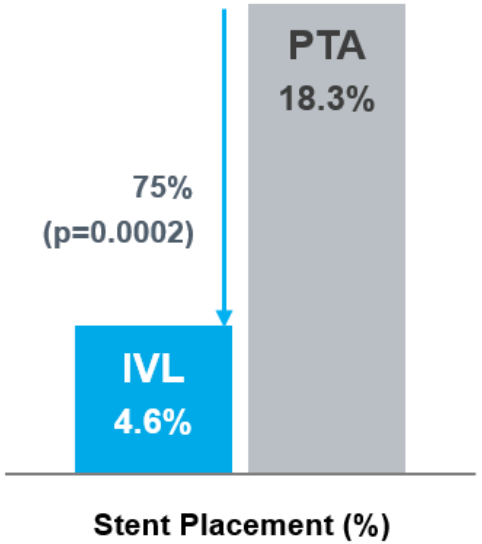
Low Complications



Embolization
Perforations
Thrombus
No Flow

Reduced Bailout Stenting

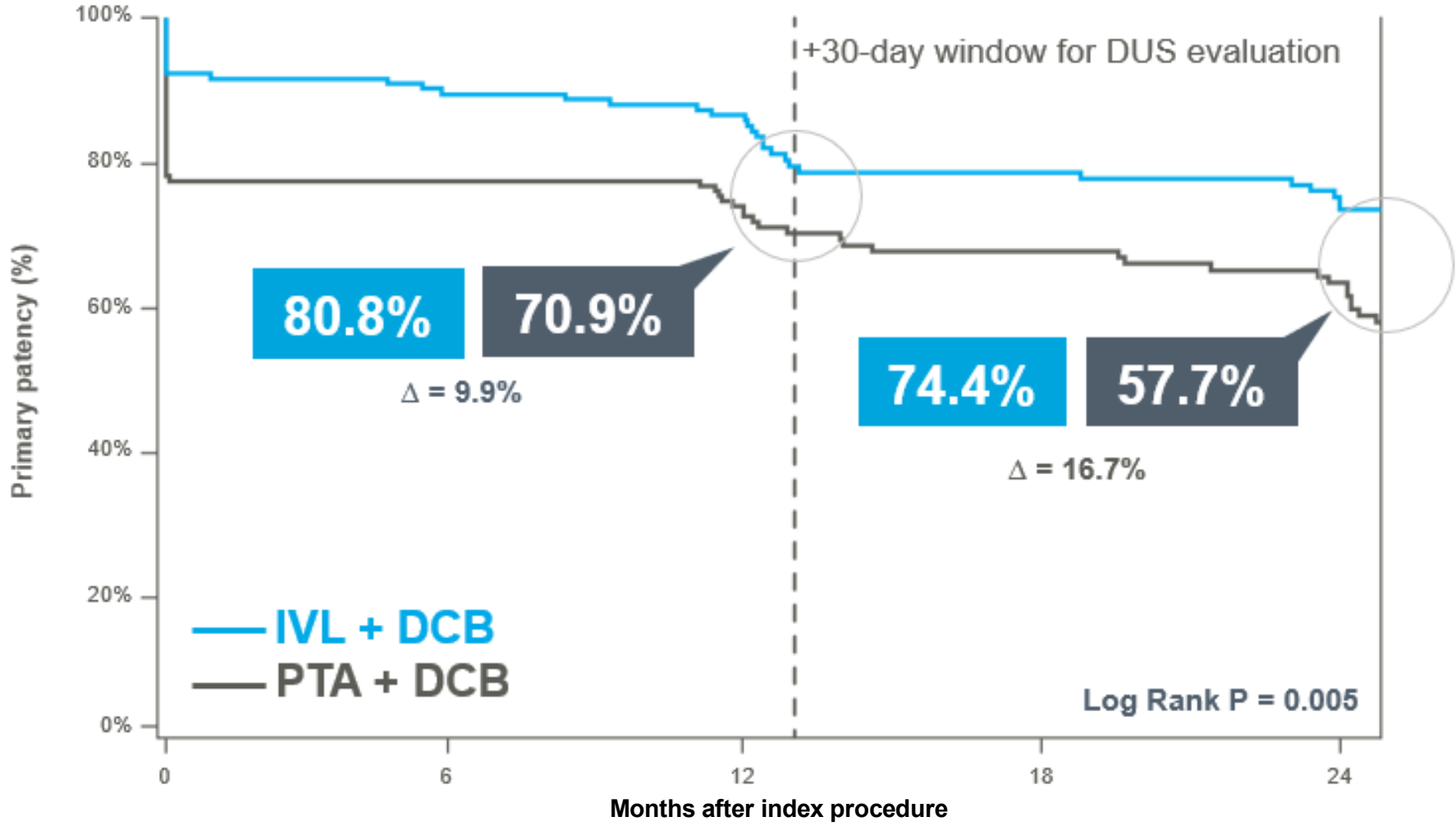
75% Reduction
in Bailout Stenting



Embolic protection: Utilized in 1.3% of cases in IVL treatment arm.
Provisional stent: Utilized if residual stenosis ≥50% by visual estimate or unresolved ≥ type D dissection, and trans-lesional gradient > 10 mmHg

Tepe G, et al. *J Soc Cardiovasc Angiogr Interv*. 2022;1(4):100341.

PAD III



Primary Patency defined as freedom from provisional stenting at index procedure, freedom from clinically-driven target lesion revascularization, and freedom from restenosis determined by duplex ultrasound.

Tepe G, et al. *J Soc Cardiovasc Angiogr Interv*. 2022;1(4):100341.

DISRUPT PAD III Observational Study

Design

OBJECTIVE:
Assess 'real-world' peri-procedural outcomes of IVL for treatment of calcified, stenotic, peripheral arteries

DESIGN:
Prospective, Multicenter, Single-Blind, Observational Study

KEY INCLUSION:
RC 2-6
Moderate-severe calcification*
Ilio-femoral, femoral, popliteal and infrapopliteal arteries

1,373	1,677	30	3
Patients	Lesions	Sites	Countries

Study Flow

November 2017 – June 2021
N = 1,373 patients; 1,677 lesions

IVL treatment +/- adjunctive technology†

1,531/1,677 lesions (91.3%)
Evaluable **angiographic core lab** data could be cross-referenced with site-reported information

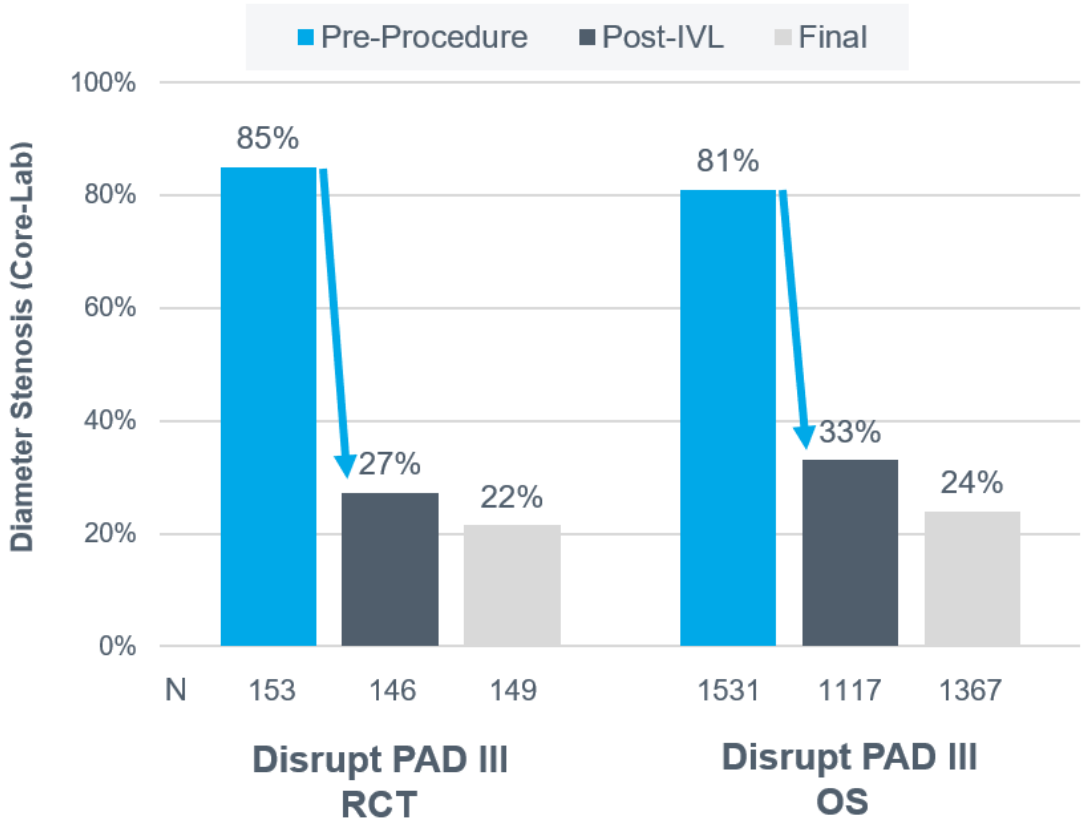
N = 1,262 patients
N = 1,531 lesions (core lab assessment)

***Presence of fluoroscopic evidence of calcification by PARC definition: 1) on parallel sides of the vessel and 2) extending ≥50% the length of the lesion if lesion is >50 mm in length; or extending for minimum of 20 mm if lesion is <50 mm in length. †At operator's discretion.**

Armstrong E. Presented at: VIVA; October 29–November 3, 2022; Las Vegas, Nevada.

	DISRUPT PAD III RCT	DISRUPT PAD III OS
N	153	1367
Vessels	SFA/Pop	Iliac, CFA, SFA/Pop, Infrapop
Dissection (Type D-F)	0%	0.7%
Perforation	0%	0.2%
Embolization	0%	0%
Slow Flow/ No Reflow	0%	0%
Abrupt Closure	0%	0%
Thrombus	0%	0%

Final Angiographic Complications (Core-Lab)



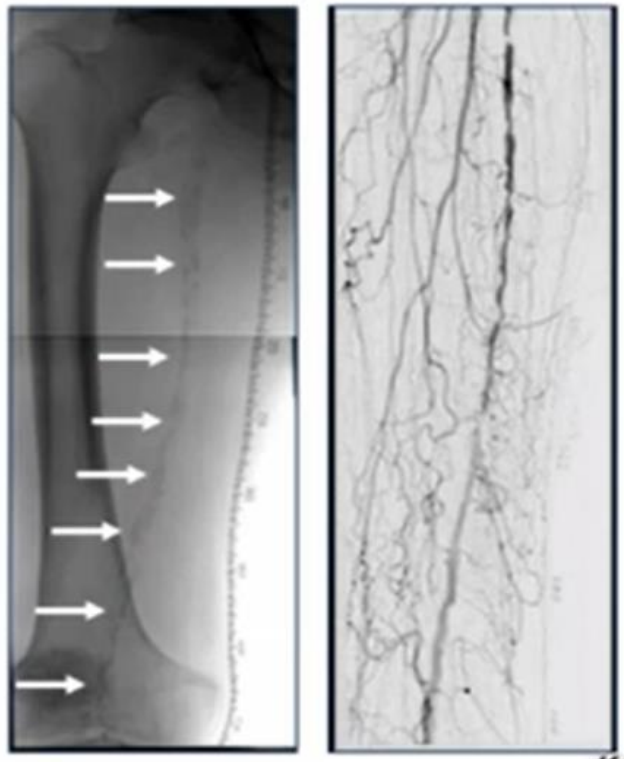
Tepe G, et al. *J Soc Cardiovasc Angiogr Interv*. 2022;1(4):100341. Armstrong E. Presented at: VIVA; October 29–November 3, 2022; Las Vegas, Nevada.

Directional Atherectomy before Paclitaxel-Coated Balloon Angioplasty in Complex Femoropopliteal Disease: The VIVA REALITY Study

Rocha-Singh KJ, et al. *Catheter Cardiovasc Interv*. 2021;98(3):549-558.

Defining “Complex” Lesion Morphologies: Challenging REALITY Inclusion Criteria

- Femoropopliteal lesion lengths: 8-36 cm
- Long chronic total occlusion lesion lengths: >10 cm
- Bilateral vessel wall calcification required in all lesions



Fluoroscopic Image

DSA Image

Rocha-Singh K. Presented at: VIVA; October 29–November 3, 2022; Las Vegas, Nevada.

REALITY: Long Calcified Lesions

Diabetes Mellitus: **84.3%**

Prior Peripheral Vascular Disease: **74.5%**

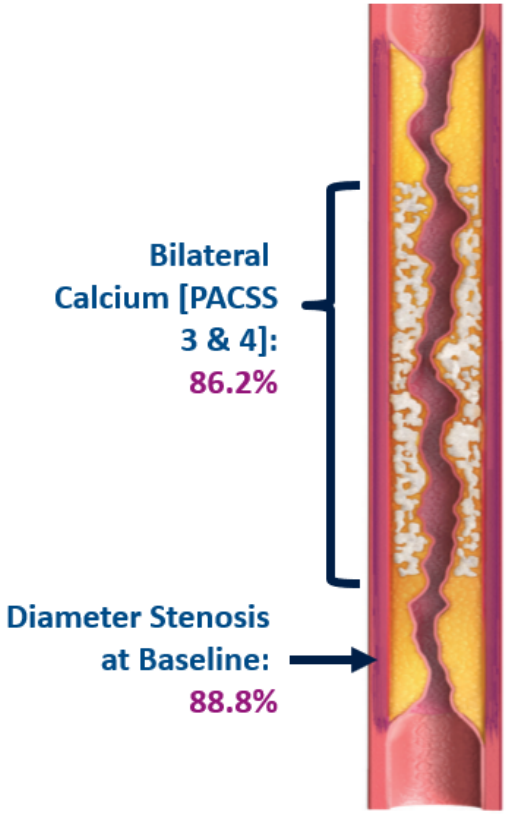
History to Coronary Artery Disease: **61.8%**

Bilateral Calcium

- **86.2%** Bilateral Calcium [PACSS 3&4]
- **67.6%** Bilateral Calcium ≥5cm [PACSS 4]

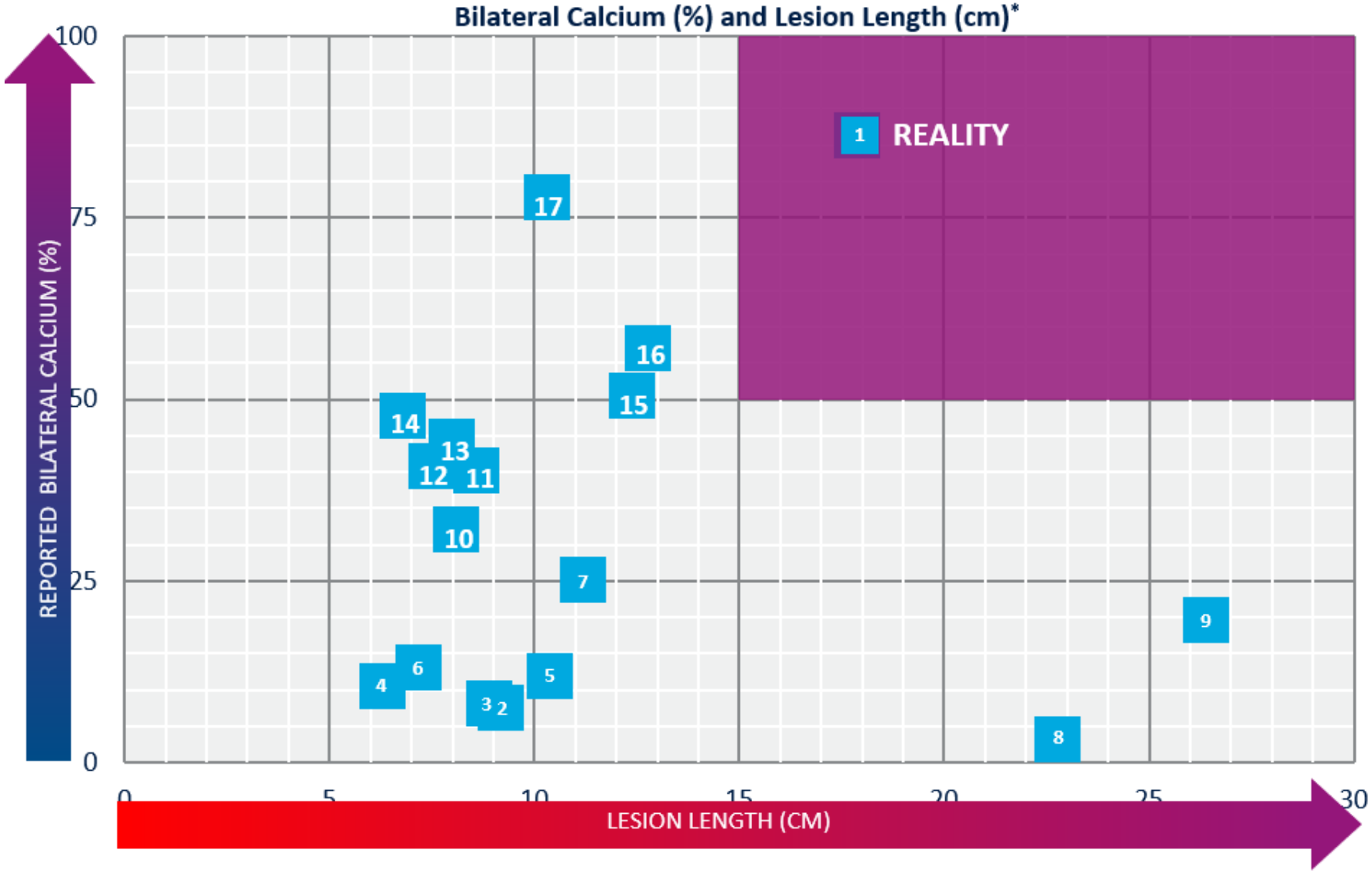
Average Lesion Length: **17.9 cm**

Chronic Total Occlusions: **39.0%**



*Vessel imagery is for illustration purposes only.

Rocha-Singh K. Presented at: VIVA; November 6-8, 2020; Virtual.



*Calcium definitions differ across studies. These are angiographic core lab-adjudicated reported calcium results.
This graph is for illustration purposes only.
Rocha-Singh K. Presented at: VIVA; November 6-8, 2020; Virtual.

Lesion and Procedure Metrics

Lesion Metrics:	
Lesion Length (mm)	179.36 ± 81.40
Lesion Length ≥150 mm	55.6%
MLD (mm) at Baseline	0.57 ± 0.61
Chronic total occlusions at Baseline	39.0%
Chronic total occlusion length (mm)	226.0 ± 86.0
Procedure Metrics:	
Diameter Stenosis (%) at Baseline	88.8 ± 11.7
Diameter Stenosis (%) Post-DA Treatment	40.4 ± 14.9
Diameter Stenosis (%) Post DA+DCB Treatment	28.1 ± 12.0
Procedural Success	57.6%

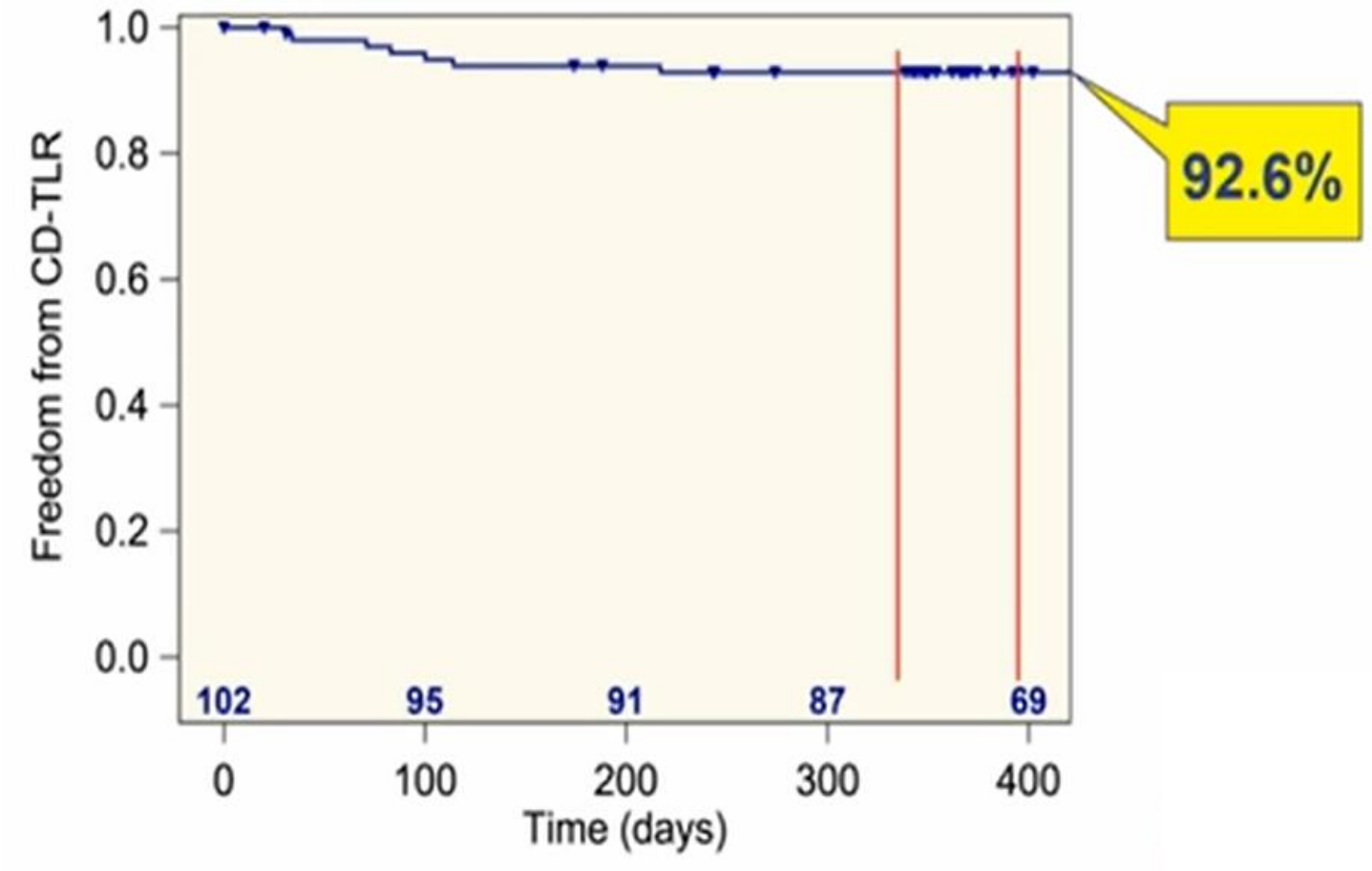
***Procedural Success defined as ≤30% post-DA+DCB as assessed by the angiographic core lab.**
Rocha-Singh K. Presented at: VIVA; October 29–November 3, 2022; Las Vegas, Nevada.

Lesion Calcium Severity Assessment

PACSS Score	
Grade 0	1.0%
Grade 1	2.9%
Grade 2	0.0%
Grade 3	18.6%
Grade 4: Bilateral vessel wall Ca^{2+} ≥5 cm	67.6%
Not assessable	8.8%
Type of calcification	
Type A: Intimal	0.0%
Type B: Medial	1.0%
Type C: Intimal + medial Ca^{2+} (mixed)	86.3%
Not assessable	12.7%
PACSS Index: [(total bilateral calcification length/lesion length) x100]	**55.7 ± 26.2**

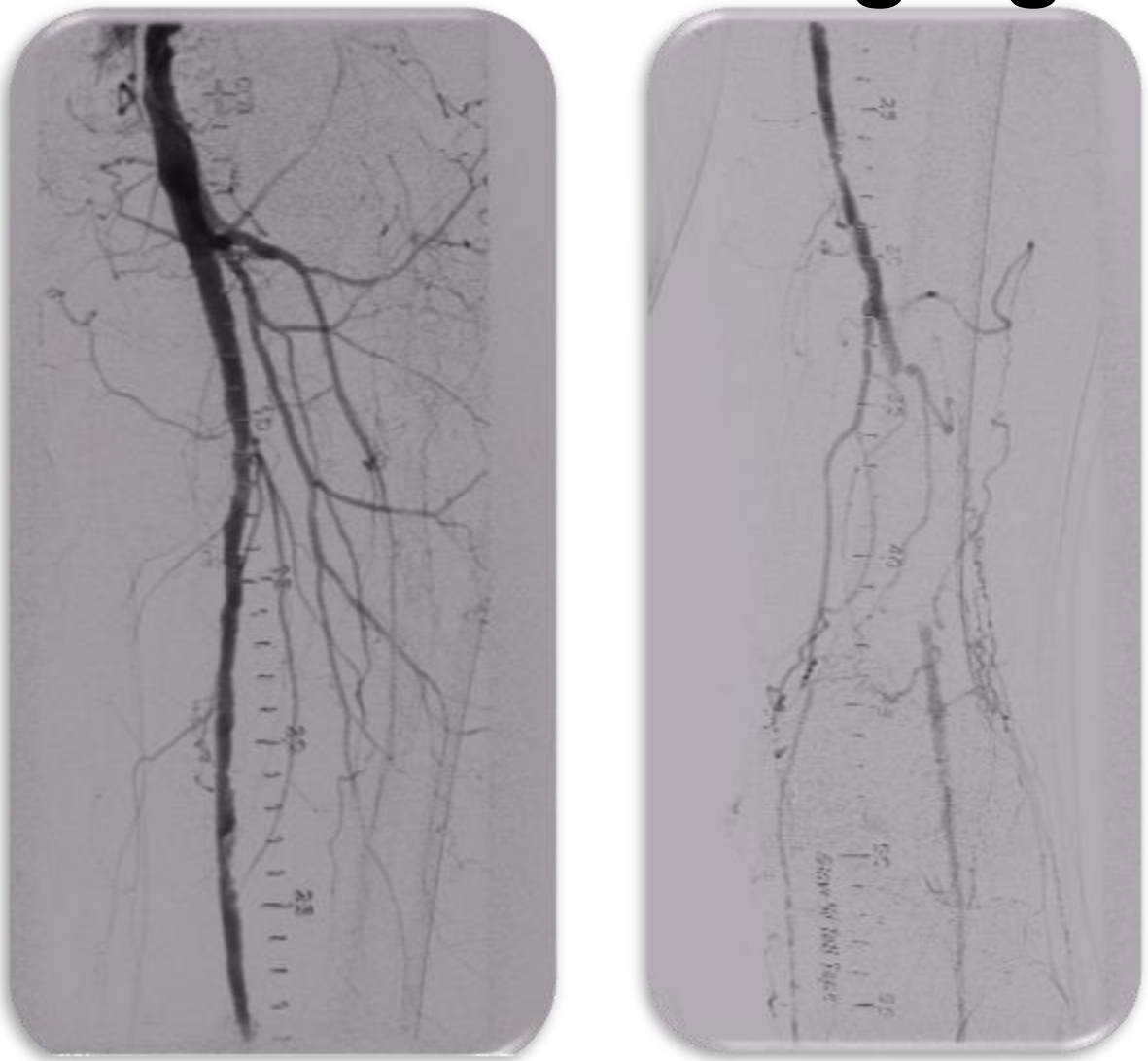
Rocha-Singh K. Presented at: VIVA; October 29–November 3, 2022; Las Vegas, Nevada.

12-Month Freedom from CD-TLR



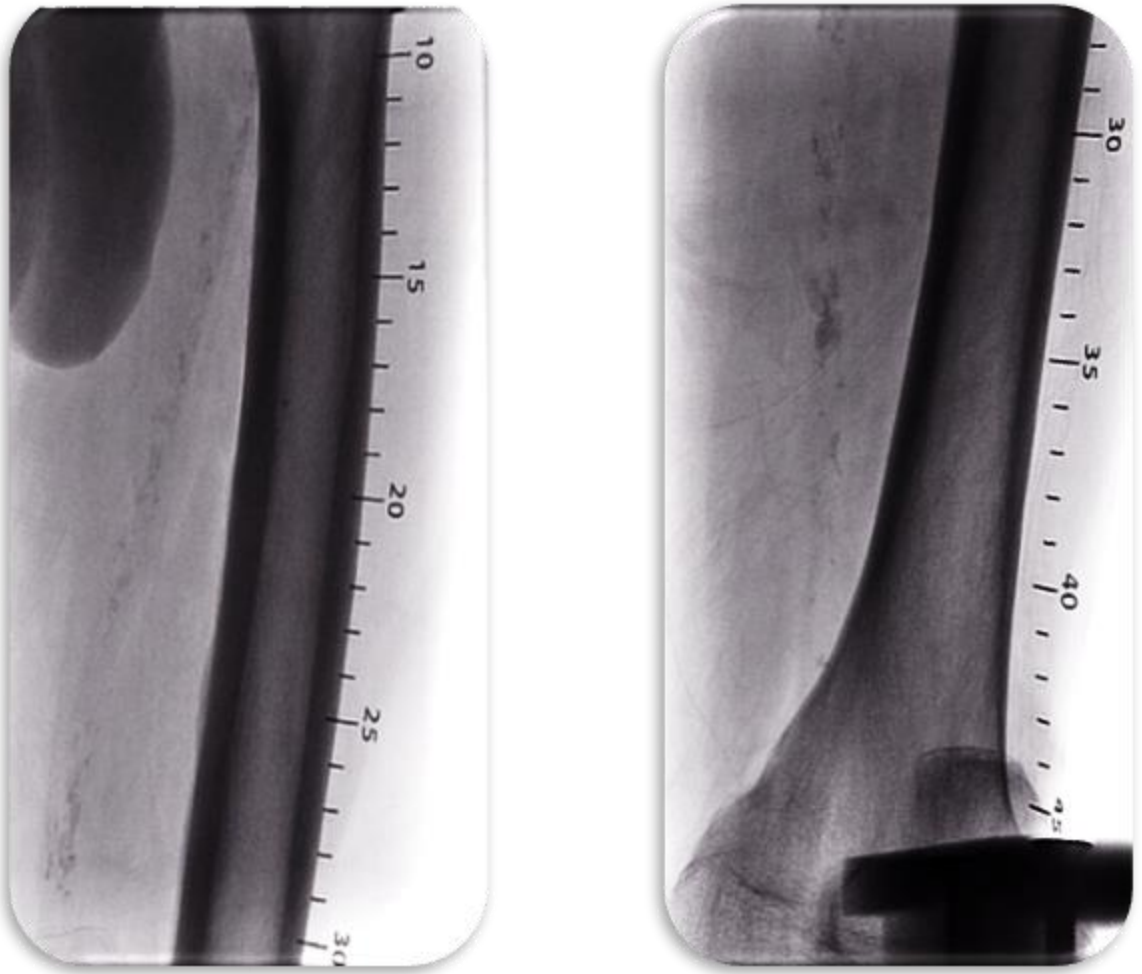
Rocha-Singh K. Presented at: VIVA; October 29–November 3, 2022; Las Vegas, Nevada.

Patient #19: Initial Angiography



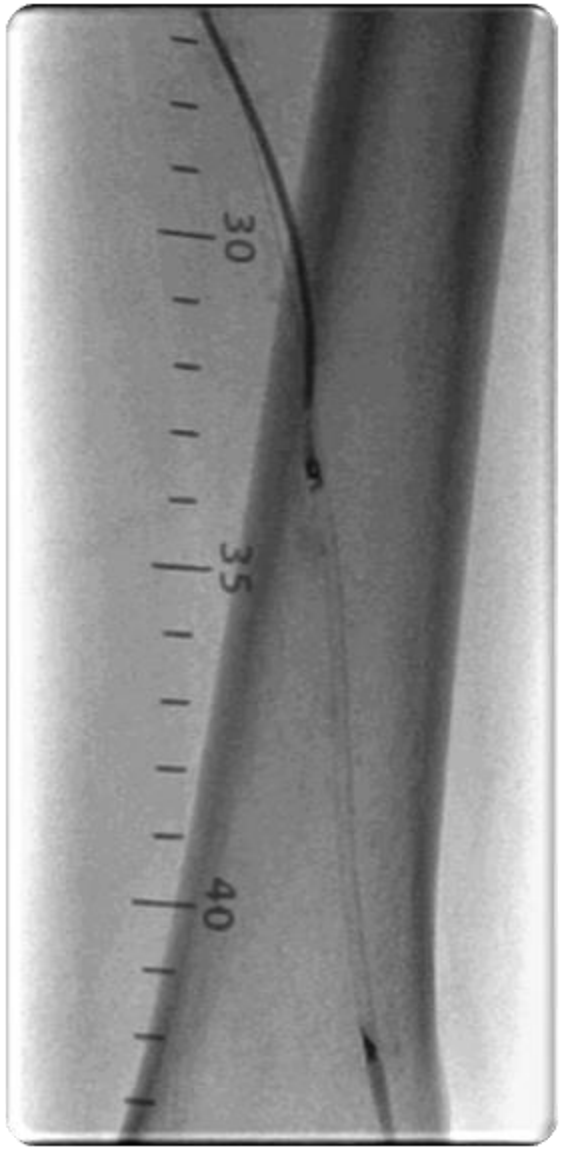
Images courtesy of Dr. John Winscott.

Fluoroscopy of Calcium
PACSS Grade 4
PACSS Index >80%



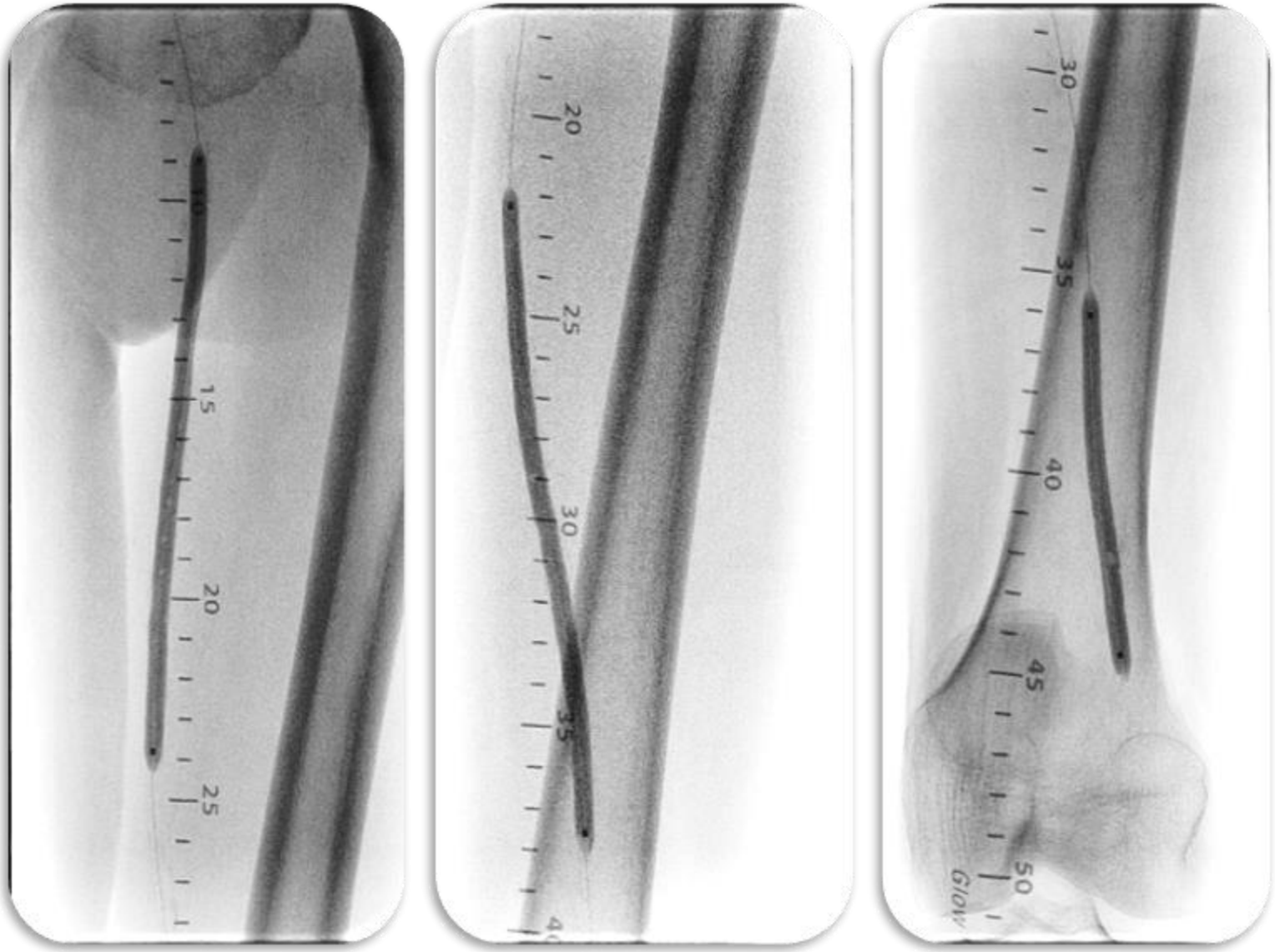
Images courtesy of Dr. John Winscott.

7F Directional Atherectomy System



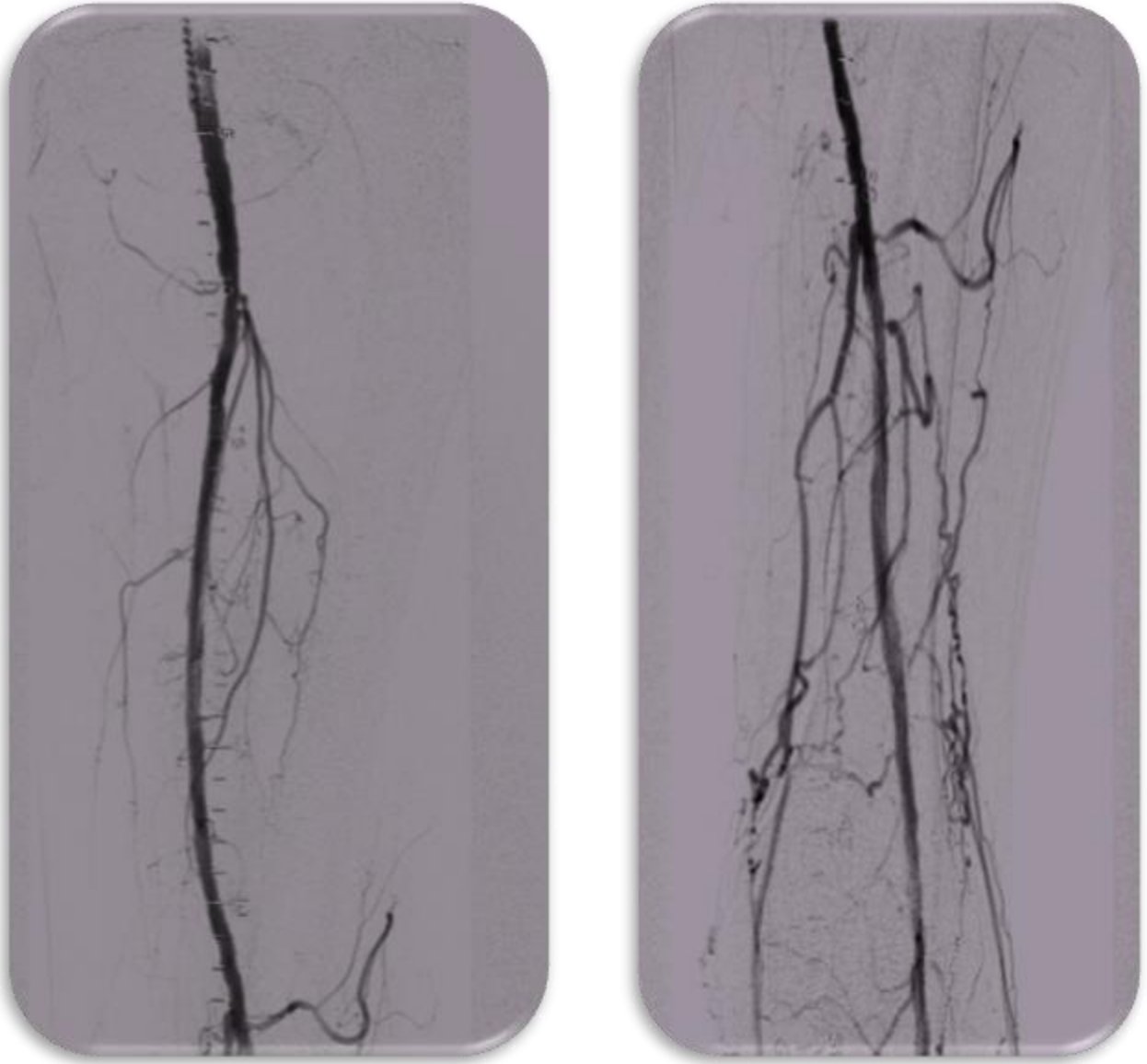
Video courtesy of Dr. John Winscott.

6 mm DCBs



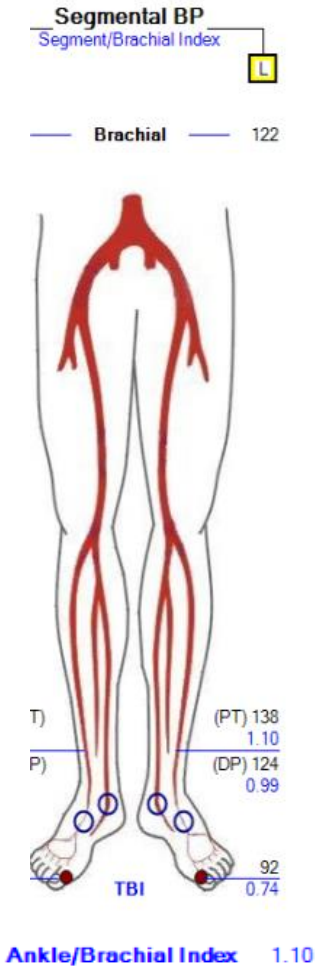
Images courtesy of Dr. John Winscott.

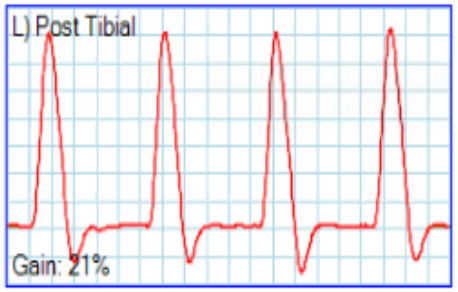
Post-Treatment Angiography

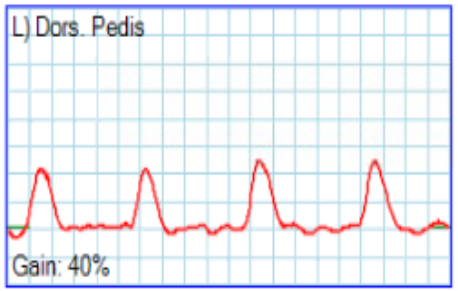


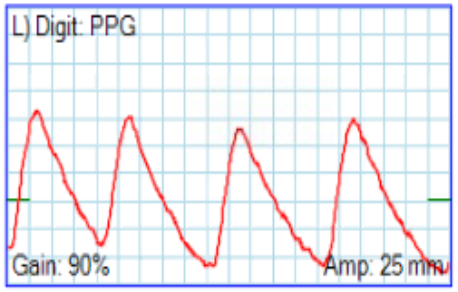
Images courtesy of Dr. John Winscott.

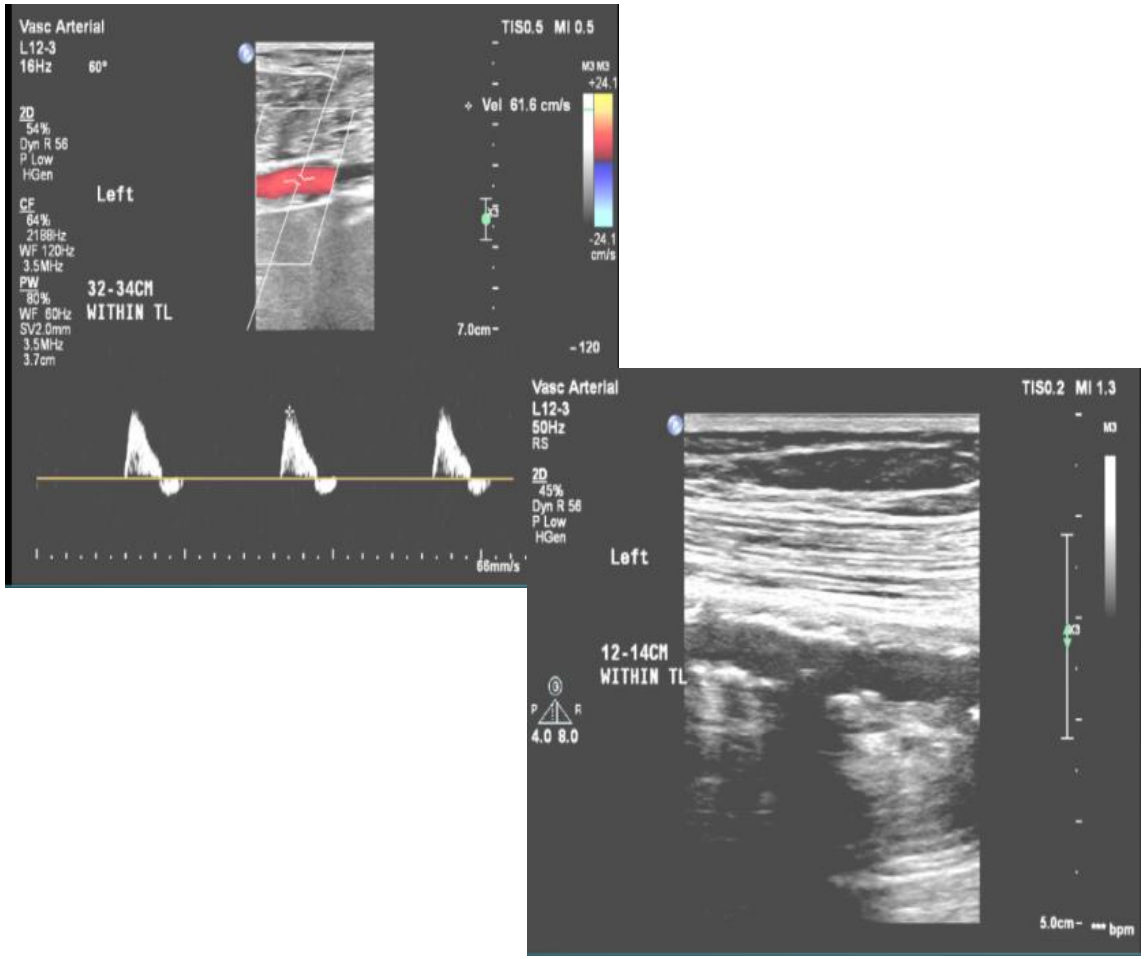
Patient #19: 12-Month ABI and Duplex US





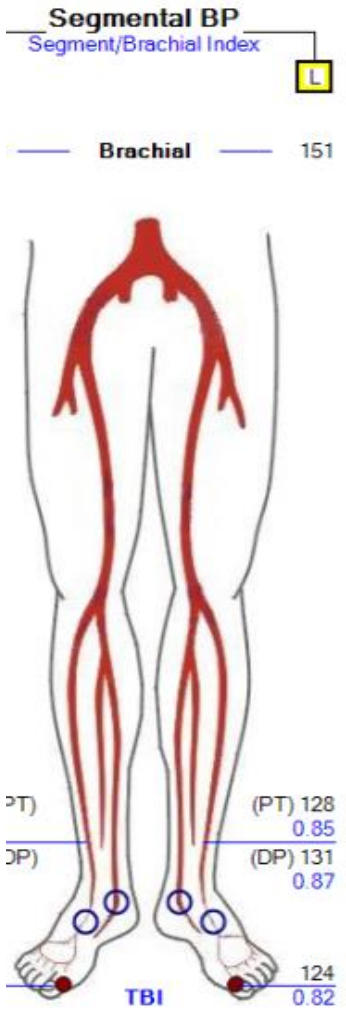


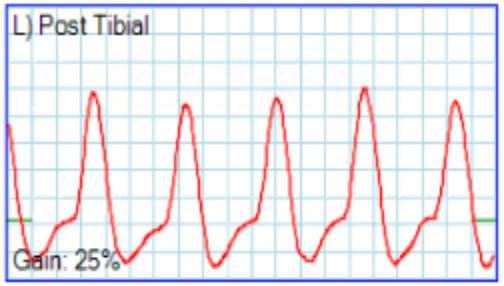


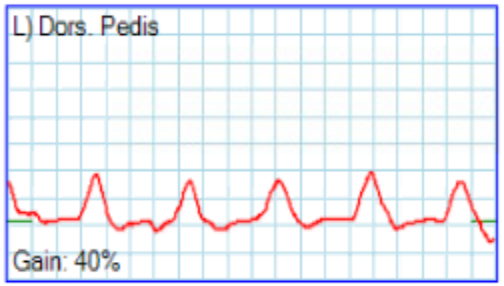


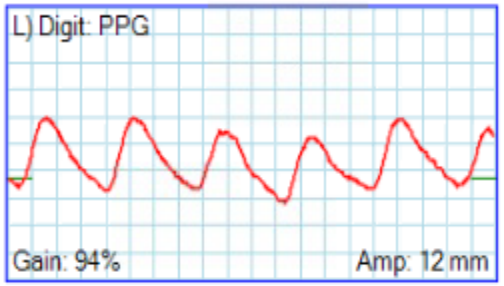
US = ultrasound; PT = posterior tibial; DP = dorsalis pedis; TBI = toe-brachial index; PPG = photoplethysmography.
Images courtesy of Dr. John Winscott.

Patient #19: ABI at 8-Year Follow-Up









Ankle/Brachial Index 0.87

My SFA Strategy

- Goals of treatment
  - <30% residual stenosis
  - No/minimal dissection
  - No scaffold
  - Optimal environment for DCB
- Will device cross?
  - Yes…Atherectomy +/- IVL then DCB
  - No…IVL +/- Atherectomy then DCB

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Cardiovascular CME

Panel Discussion

