Efficacy of IN.PACT™ Admiral™ Drug-Coated Balloon - Highlights of the IN.PACT Admiral Clinical Program

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Disclosure

Speaker name: Yi Yang, MD

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I have the following potential conflicts of interest to report:

- ☐ Consulting
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)

- ☑ I do not have any potential conflict of interest

Background

- Numerous randomized trials with drug-coated balloons (DCBs) have shown improved outcomes of DCB over PTA[1-15]
- Published results of the IN.PACT SFA Trial have demonstrated superiority of the IN.PACT Admiral DCB over percutaneous transluminal angioplasty (PTA)[1,2, 9-13]
- Long-term data from randomized trials for DCBs available in the U.S. are limited

Primary Patency

	1-Year	2-Year	3-Year
IN.PACT SFA IN.PACT™ DCB	87.5%[1]	79.0%[1]	69.5%[2]
Levant II Lutonix™* DCB	73.5%[3]	58.6%[4]	Not Reported
ILLUMENATE Stellarex™* DCB	82.3%[5]	72.1%[6]	Not Reported
AcoArt I Orchid™* DCB	76.1%[7]	64.6%[8]	Not Reported

CD-TLR

	1-Year		1-Year	2-Year	3-Year
IN.PACT SFA IN.PACT™ DCB	2.4%[9]	9.1%[10]	15.2%[11]	23.4%[12]	25.5%[13]
Levant II Lutonix™* DCB	12.3%[3]	18.0%[4*]	Not Reported	Not Reported	Not Reported
ILLUMENATE Stellarex™* DCB	7.9%[5]	Not Reported	Not Reported	28.2%[14]	Not Reported
AcoArt I Orchid™* DCB	7%[15]	13%[15]	Not Reported	Not Reported	21%[15]

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1. Schneider P et al. Circ-CI 2018;11:1-8.
2. Schneider P. IN.PACT SFA Four-Year Results. VIVA 2017.
3. Laird J, et al. Circ-CI 2019; 12: e007702.
4. Lyden S, ILLUMENATE Four-Year Results, LINC 2020
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Product Overview

	MDT IN.PACT Admiral DCB	Becton Dickinson Lutonix™* 035 DCB	Philips Stellarex™* DCB	Acotec AcoArt™* Orhid™* DCB
Drug	Paclitaxel	Paclitaxel	Paclitaxel	Paclitaxel
Dose Density	3.5 µg/mm^2	2.0 µg/mm^2	2.0 µg/mm^2	3.3 µg/mm^2
Excipient	Urea	Polysorbate, Sorbitol	Polyethylene Glycol (PEG)	Mg-stearate
Uncoated Balloon	Admiral Xtreme™ PTA balloon catheter	Clearstream™*	0.035 PTA	Iris™*

Factors that can influence clinical performance of DCBs:

- Balloon Material
- Excipient / Excipient Interaction with Drug
- Drug Dose Delivered to Tissue
- Drug Form Delivered Tissue (Soluble vs. Solid Phase)

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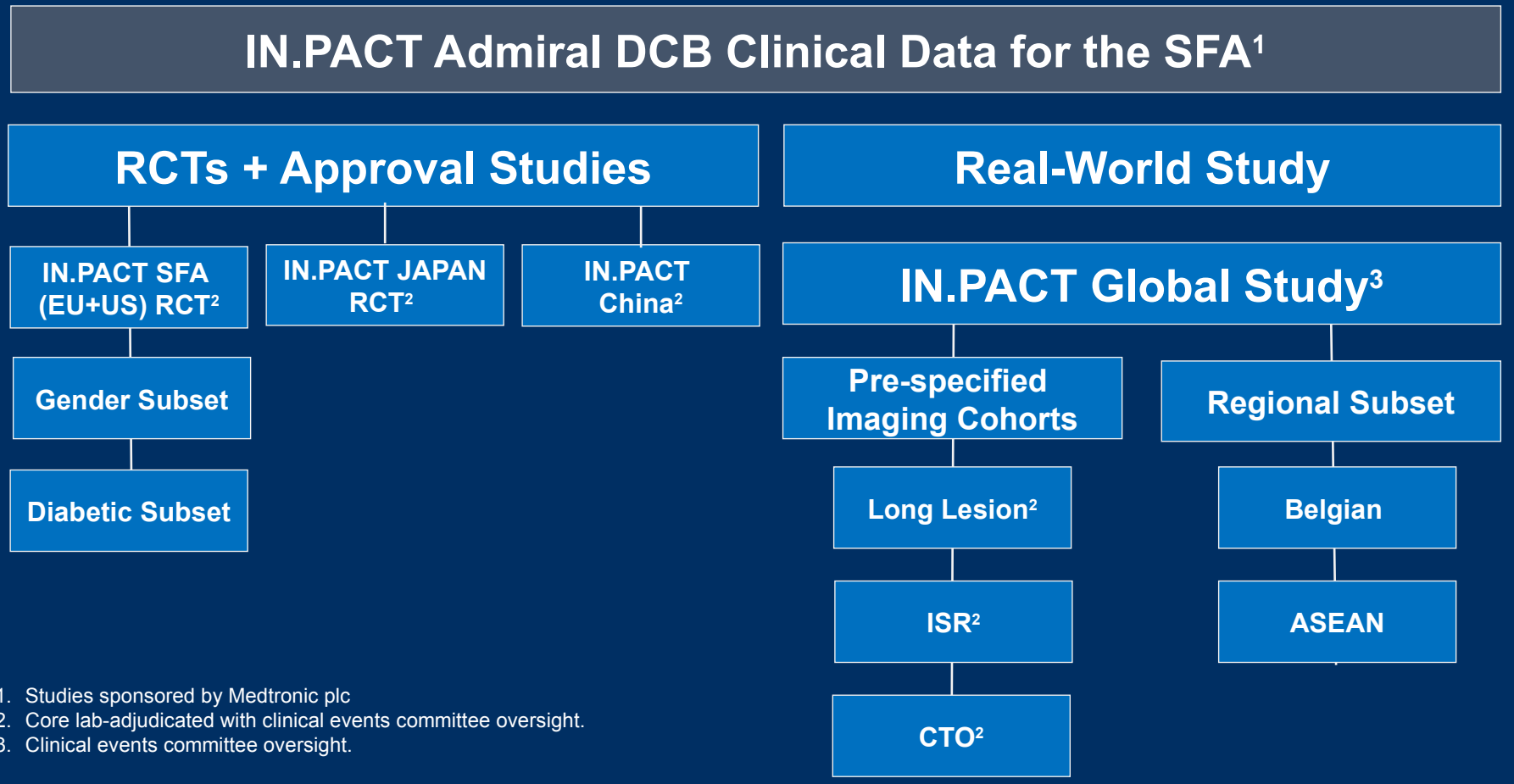
IN.PACT Admiral DCB Clinical Program

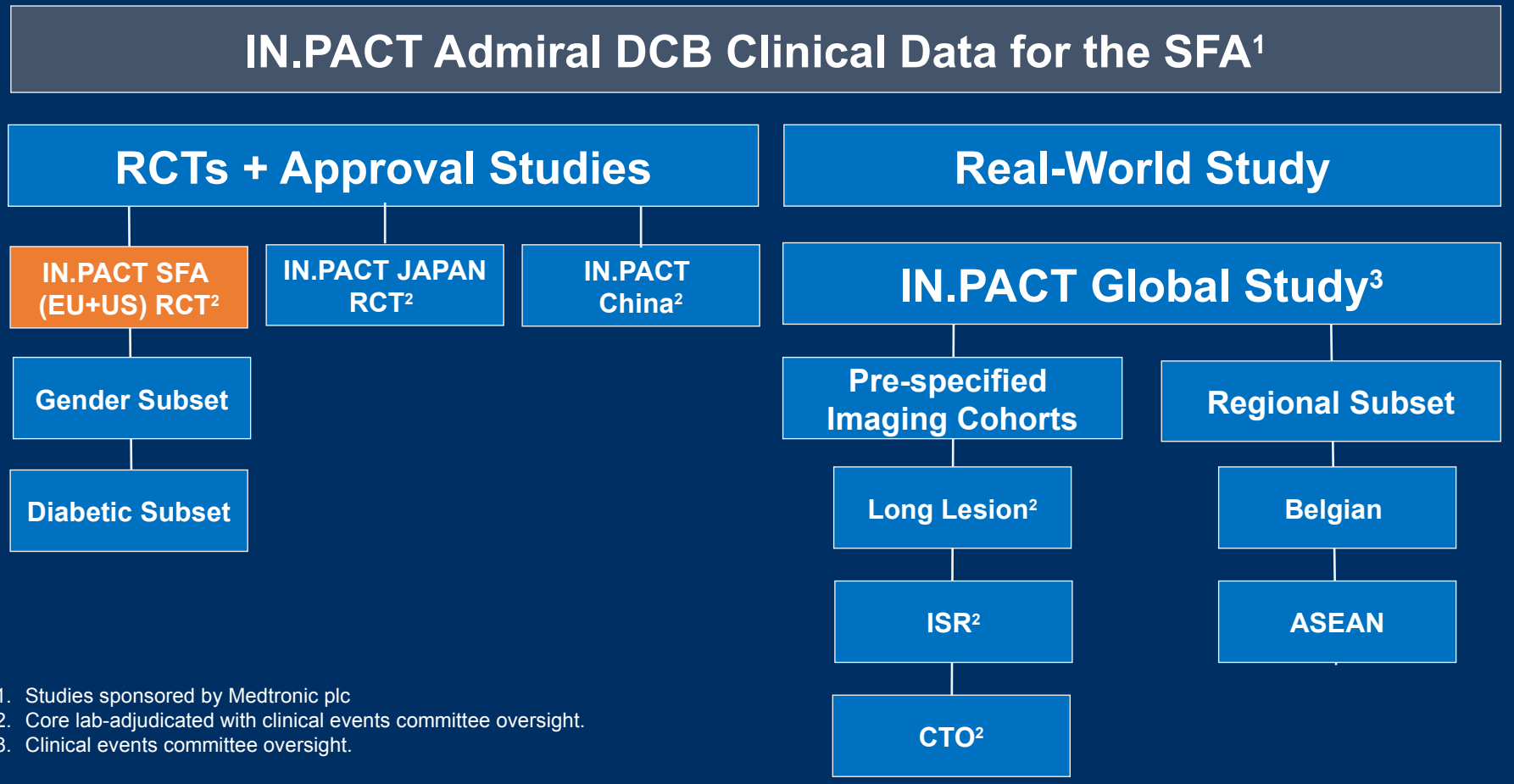
Robust Adjudicated Series of 1837 Patients



1. Studies sponsored by Medtronic plc
2. Core lab-adjudicated with clinical events committee oversight.
3. Clinical events committee oversight.

IN.PACT Admiral DCB Clinical Program

Robust Adjudicated Series of 1837 Patients



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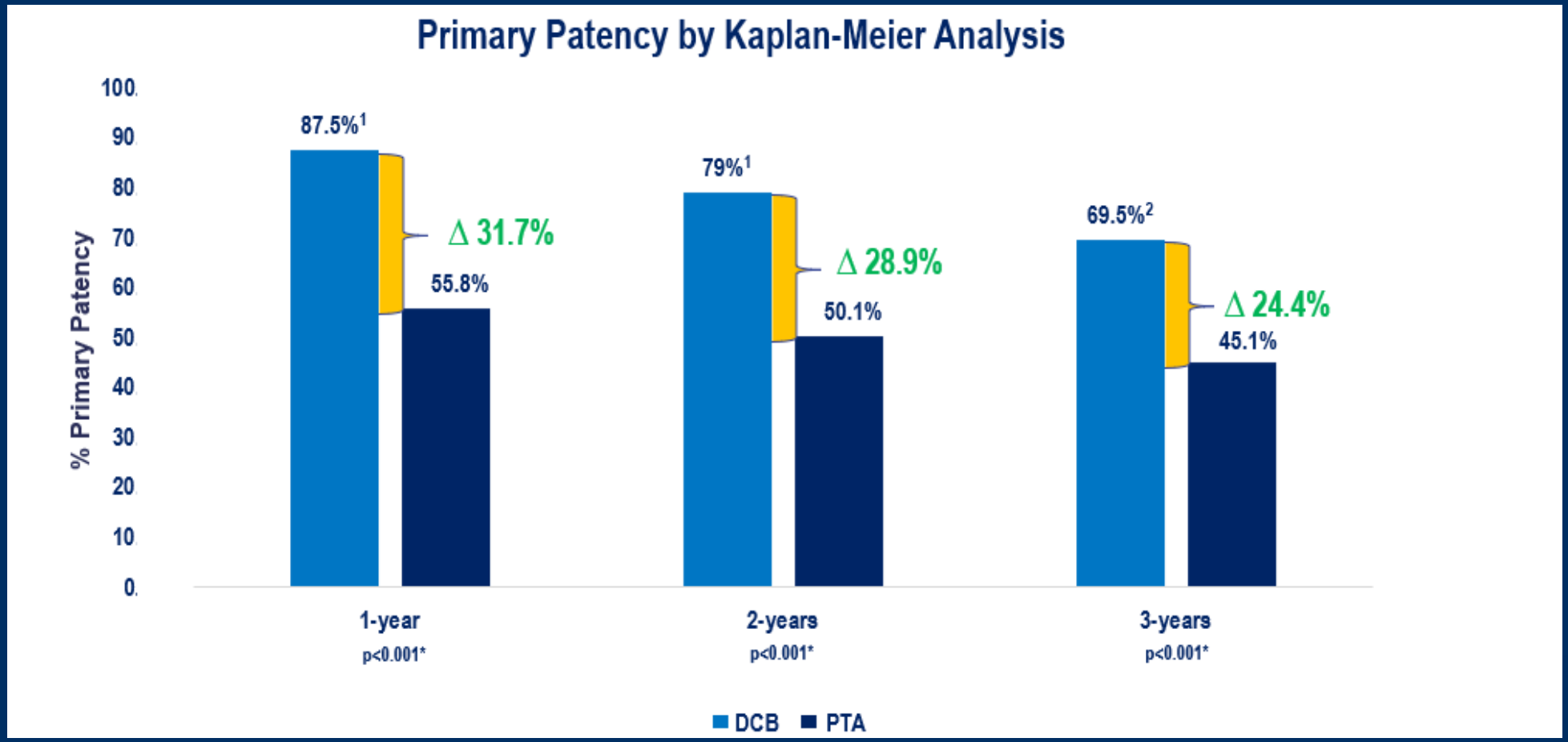
IN.PACT SFA Trial
Baseline Characteristics

	IN.PACT n = 220 subjects	PTA n = 111 subjects	P-value
Age, Y ± SD	67.5 ± 9.5	68.0 ± 9.2	0.612
Male, % (n)	65.0% (143/220)	67.6% (75/111)	0.713
Diabetes, % (n)	40.5% (89/220)	48.6% (54/111)	0.161
Current Smoker, % (n)	38.6% (85/220)	36.0% (40/111)	0.719
Rutherford Class, % (n) 2 3 4 5	 37.7% (83/220) 57.3% (126/220) 5.0% (11/220) 0.0% (0/220)	 37.8% (42/111) 55.9% (62/111) 5.4% (6/111) 0.9% (1/111)	0.898
Lesion Length (cm ± SD)	8.94 ± 4.89	8.81 ± 5.12	0.815
Total Occlusions, % (n)	25.8% (57/221)	19.5% (22/113)	0.222
Calcification, % (n)	59.3% (131/221)	58.4% (66/113)	0.907
Severe Calcification, % (n)	8.1% (18/221)	6.2% (7/113)	0.662
Provisional Stenting, % (n)	7.3% (16/220)	12.6% (14/111)	0.110

Laird J, et al. Circ Cardiovasc Interv 2019; 12: e007702.

IN.PACT SFA Trial

Sustained Benefit – Primary Patency through 3 Years

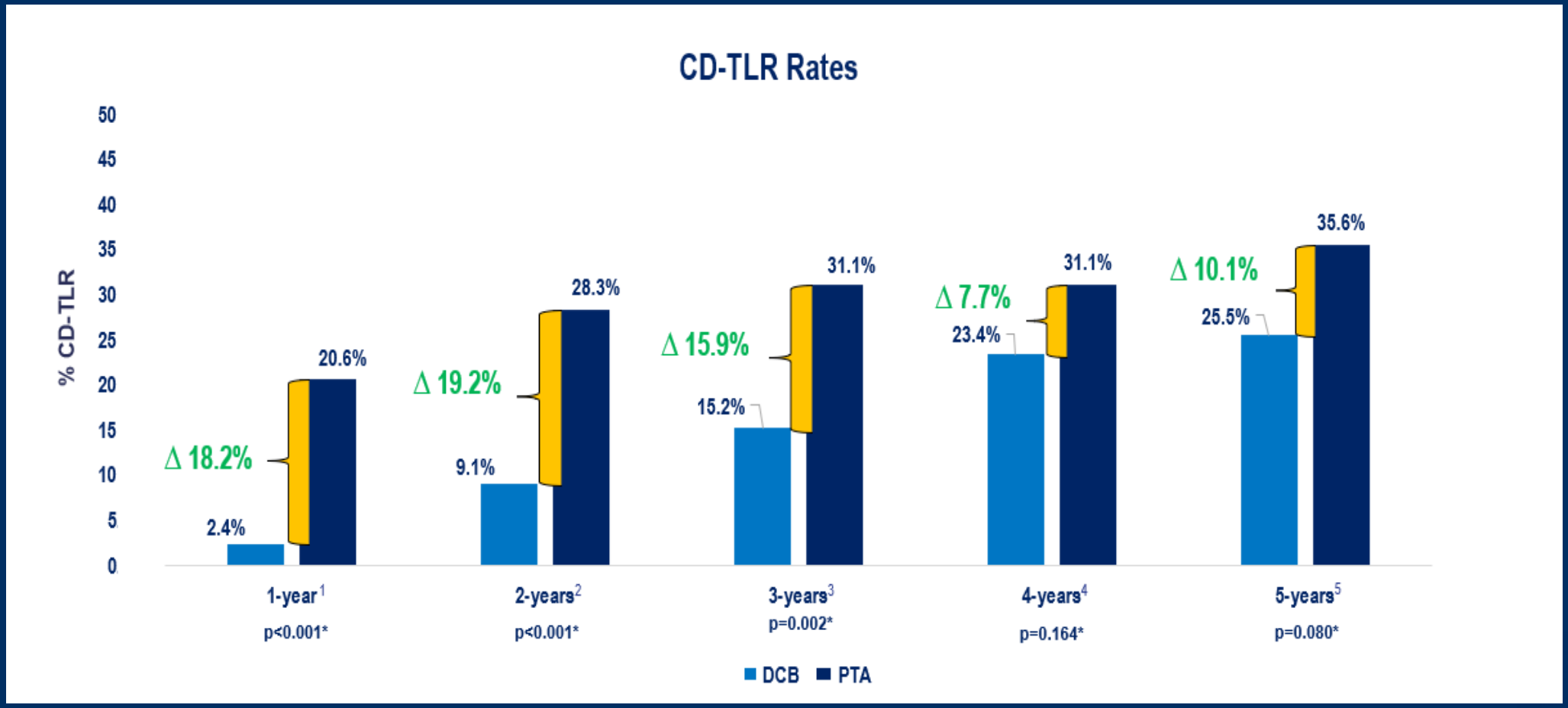


1. Laird J, et al. Circ Cardiovasc Interv 2019; 12: e007702.
2. Schneider P. et al. Circ-CI 2018;11:1-8.

* p-value compares DCB to PTA.

IN.PACT SFA Trial

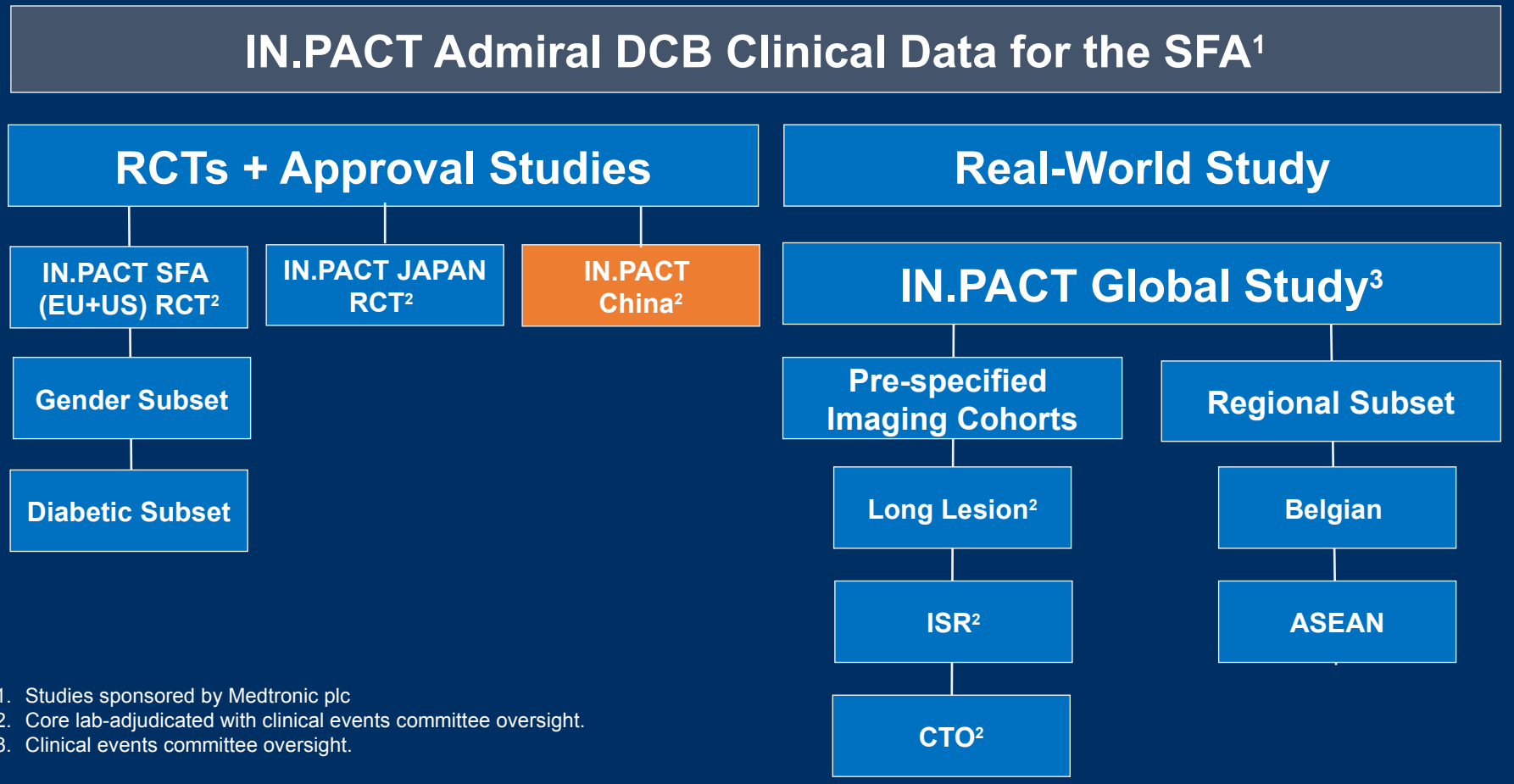
Sustained Benefit – CD-TLR through 5 Years



1. Tepe G. et al. Circ 2015;131:495-502.
2. Laird J.R. et al. JACC 2015;66:2329-2338
3. Schneider P. et al. Circ-CI 2018;11:1-8.
4. Schneider P. VIVA 2017.
5. Laird J, et al. Circ Cardiovasc Interv 2019; 12: e007702.

* p-value compares DCB to PTA.

IN.PACT China Study



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IN.PACT China Study

Select Baseline and Procedural Characteristics

Patient Characteristics	N=143 Subjects
Age, Y ± SD	66.8 ± 7.7
Male Gender (%)	74.8% (107/143)
Diabetes Mellitus (%)	46.2% (66/143)
Current Smoker (%)	36.4% (52/143)

Lesion Characteristics	N=143 Subjects N=143 Lesions
Lesion Type [1] De novo Restenotic (non-stented)	 99.3% (142/143) 0.7 % (1/143)
Lesion length (cm ± SD) [2]	10.40 ± 6.51
Total occlusions, % (n) [2]	52.4% (75/143)
Severe calcification, % (n) [2]	11.9% (17/143)

1. Site-reported
2. Normal-to-normal by Core Lab QVA evaluation

Procedural Characteristics		N=143 Subjects N=143 Lesions
Pre-Dilatation (%) [1]		100% (143/143)
Post-dilatation (%) [1]		14.0% (20/143)
Dissections (%)	0	18.9% (27/143)
	A	0.0% (0/143)
	B-C	55.3% (79/143)
	D	25.9% (37/143)
	E-F	0.0% (0/143)
Provisional Stenting (%) [1]		4.2% (6/143)
Device Success (%) [3]		97.6% (206/211)
Procedural Success (%) [4]		91.5% (130/142)
Clinical Success (%) [5]		89.4% (127/142)

3. Device success: Successful delivery, inflation, deflation and retrieval of the intact study balloon without burst < RBP
4. Procedural success: Residual stenosis ≤ 50% for non-stented subjects or ≤ 30% for stented subjects
5. Clinical success: Procedural success without procedural complications (death, major target limb amputation, thrombosis of target lesion or TVR) prior to discharge

IN.PACT China Study

Safety and Efficacy Endpoints

	DCB	95%CI	Performance Goal	p-value
Primary Efficacy Primary Patency [1]	**88.6% (109/123)**	[81.6%, 93.6%]	50%	< 0.001

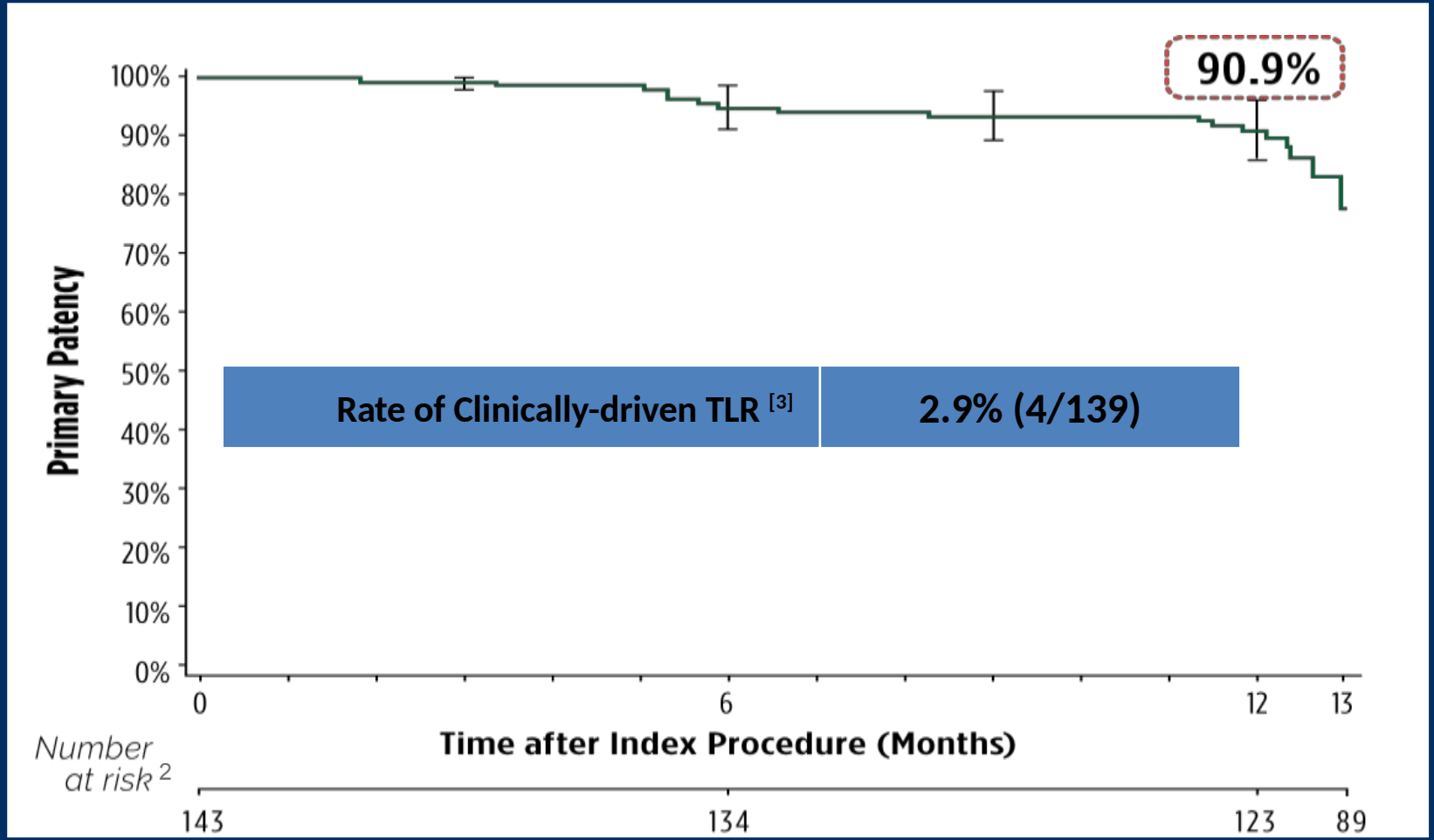
	DCB	95%CI	Performance Goal	p-value
Primary Safety Composite [2]	**99.3% (141/142)**	[96.1%, 100.0%]	88%	< 0.001

Primary endpoints met

1. Primary Patency is defined as freedom from clinically-driven TLR and freedom from restenosis as determined by duplex ultrasound (DUS) Peak Systolic Velocity Ratio (PSVR) ≤ 2.4 in ITT non-stented subjects.
2. Primary safety composite is defined as freedom from device- and/or procedure-related mortality, freedom from major target limb amputation and freedom from clinically-driven TLR within 30 days post-index procedure in ITT subjects.

IN.PACT China Study

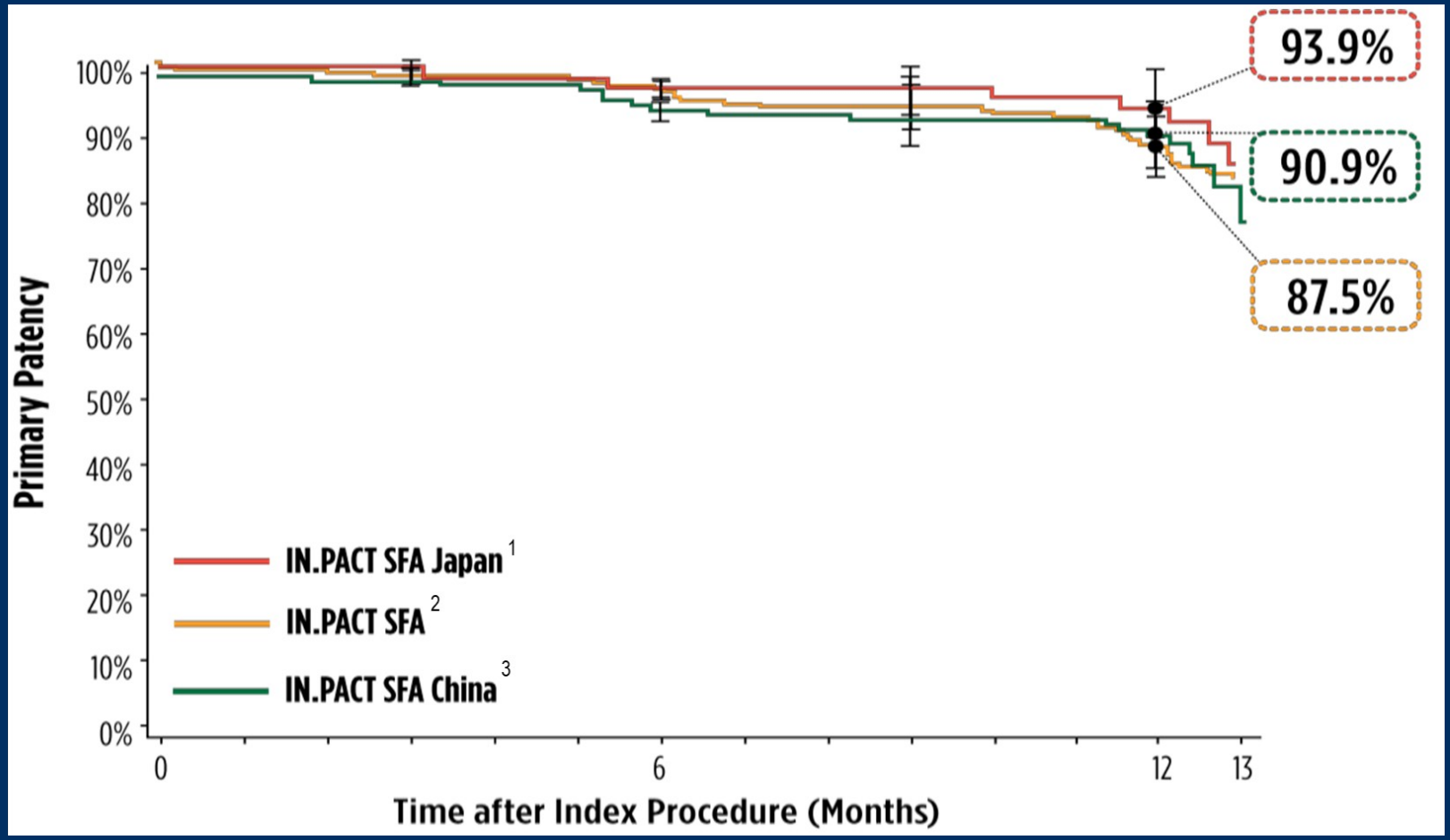
12-Month Patency[1] (ITT)



1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) and clinically-driven target lesion revascularization through 12 months (adjudicated by a CEC).
2. Number at risk represents the number of evaluable subjects at the beginning of the 30-day window prior to each follow-up interval.
3. Clinically-driven TLR is defined as any re-intervention at the target lesion due to symptoms or drop of ABI/TBI of ≥20% or >0.15 when compared to post-procedure baseline ABI/TBI.

IN.PACT China Study

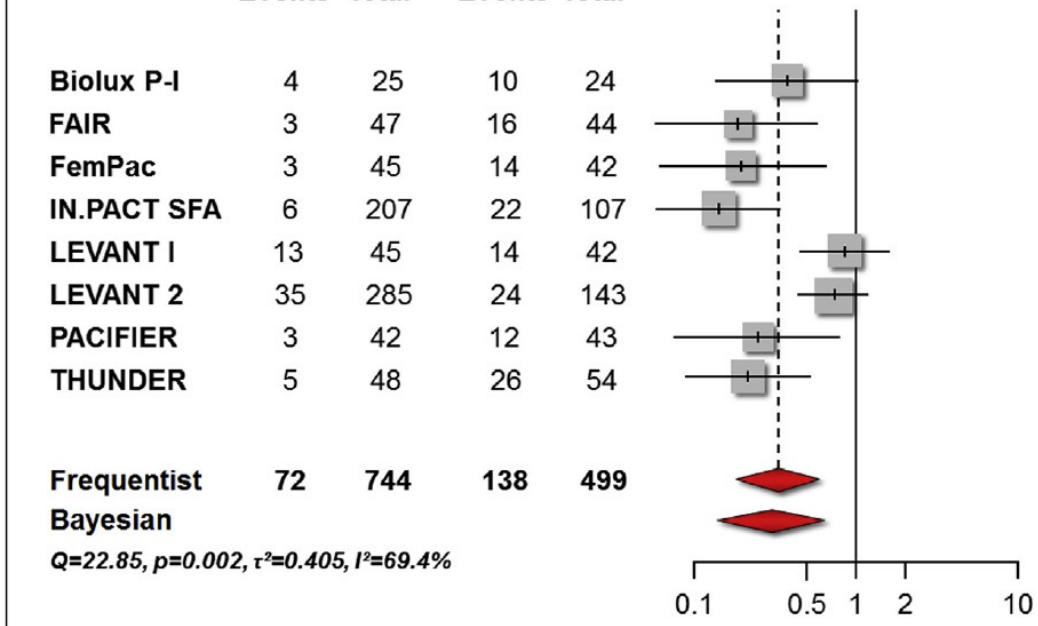
Consistent Patency Across IN.PACT Studies



1. Iida O, et al. J Endoasc Ther. 2017; 25: 109-117
2. Tepe G, et al. Circulation 2015; 131: 495-502.
3. Chen Z, et al. J Endovasc Ther. 2019; 26: 471-8.

Meta-analysis*
Results favor DCBs

FIGURE 1 Risk of Target Lesion Revascularization. Risk at 12 Months Comparing DCB With PB

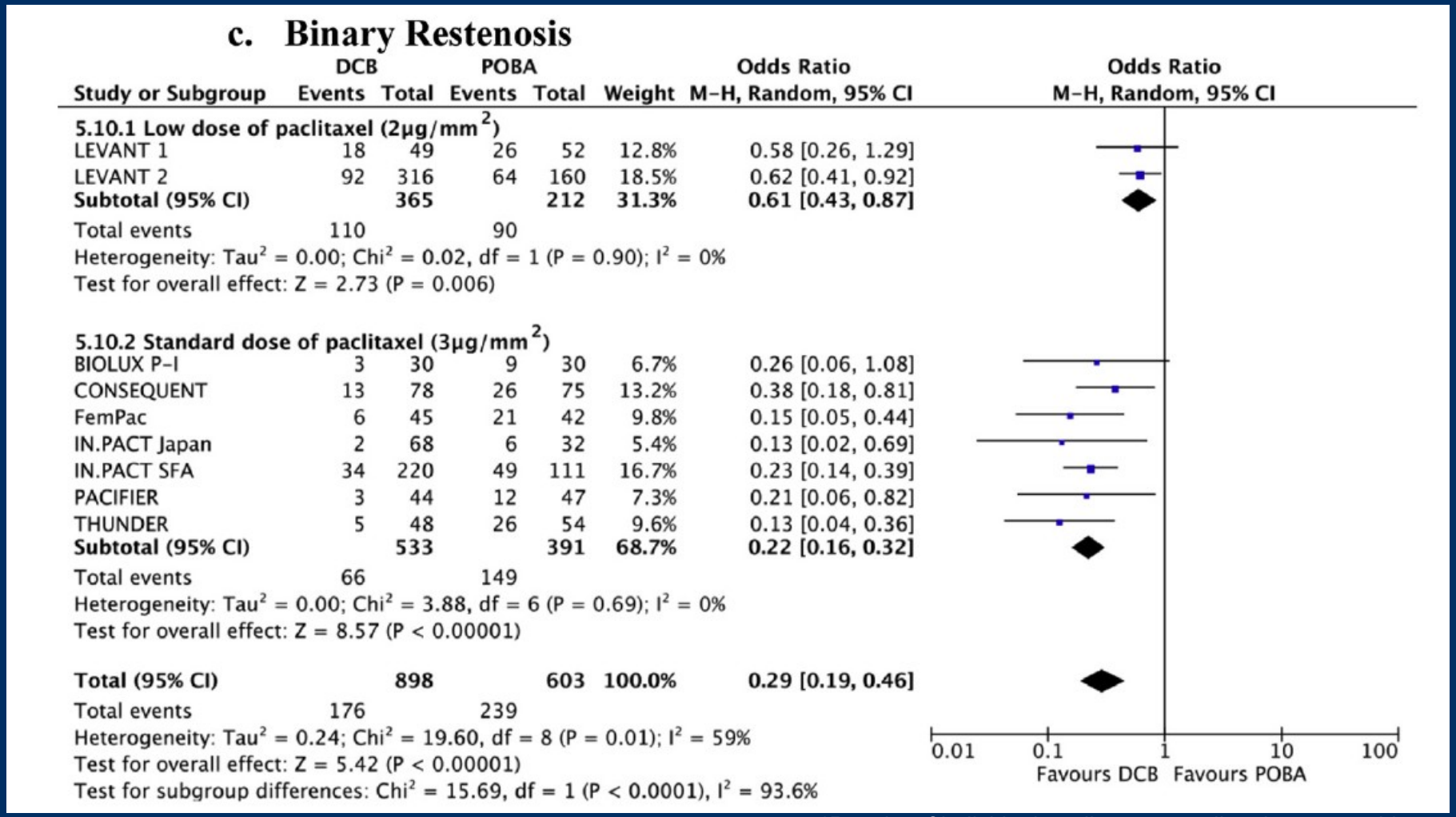


The forest plot illustrates the results of the main analysis: DCB compared with PB produced a 67% RR reduction in 12-month target lesion revascularization. Bayesian estimate (lower summary effect, RR: 0.30; 95% credible intervals: 0.14 to 0.58) was consistent. CI = confidence interval; DCB = drug-coated balloon; PB = plain balloon; RR = risk ratio. *Credible intervals for the Bayesian estimate.

Giacoppo D. et al., JACC Cardiovasc Interv. 2016 Aug 22;9(16):1731-42

*Results of individual studies are not directly comparable. Each individual study compares DCB against PTA

Meta-analysis*
Paclitaxel Dosage



Caradu C et al. Journal of Vascular Surgery 2019; 70: 981-95

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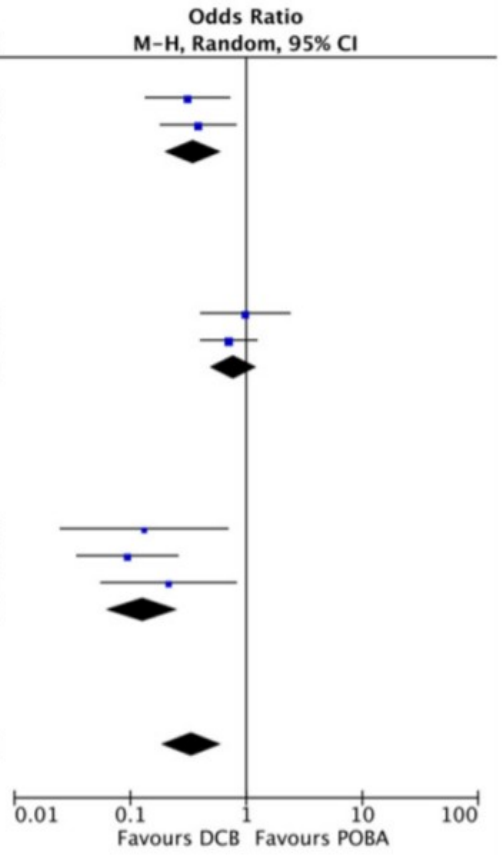
Meta-analysis*
Varying Excipients

B **Excipients**

a. Clinical Driven TLR

Study or Subgroup	DCB Events	DCB Total	POBA Events	POBA Total	Weight	Odds Ratio M-H, Random, 95% CI
5.7.1 Polyethylene glycol						
ILLUMENATE EU RCT	13	222	12	72	15.8%	0.31 [0.13, 0.72]
ILLUMENATE Pivotal and Pharmacokinetic Studies	15	220	16	100	16.8%	0.38 [0.18, 0.81]
Subtotal (95% CI)		**442**		**172**	**32.6%**	**0.35 [0.20, 0.61]**
Total events	28		28			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.14$, df = 1 (P = 0.71); $I^2 = 0\%$						
Test for overall effect: Z = 3.69 (P = 0.0002)						
5.7.2 Polysorbate and sorbitol						
LEVANT 1	13	49	14	52	15.3%	0.98 [0.41, 2.37]
LEVANT 2	35	316	24	160	18.9%	0.71 [0.40, 1.23]
Subtotal (95% CI)		**365**		**212**	**34.2%**	**0.78 [0.48, 1.24]**
Total events	48		38			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.38$, df = 1 (P = 0.54); $I^2 = 0\%$						
Test for overall effect: Z = 1.06 (P = 0.29)						
5.7.3 Urea						
IN.PACT Japan	2	68	6	32	8.4%	0.13 [0.02, 0.69]
IN.PACT SFA	5	220	22	111	14.0%	0.09 [0.03, 0.26]
PACIFIER	3	44	12	47	10.8%	0.21 [0.06, 0.82]
Subtotal (95% CI)		**332**		**190**	**33.2%**	**0.13 [0.06, 0.26]**
Total events	10		40			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.92$, df = 2 (P = 0.63); $I^2 = 0\%$						
Test for overall effect: Z = 5.59 (P < 0.00001)						
Total (95% CI)		**1139**		**574**	**100.0%**	**0.34 [0.18, 0.62]**
Total events	86		106			
Heterogeneity: $Tau^2 = 0.44$; $Chi^2 = 18.90$, df = 6 (P = 0.004); $I^2 = 68\%$						
Test for overall effect: Z = 3.46 (P = 0.0005)						
Test for subgroup differences: $Chi^2 = 17.40$, df = 2 (P = 0.0002), $I^2 = 88.5\%$						



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Summary

- Numerous randomized trials with drug-coated balloons (DCBs) have shown improved outcomes of DCB over PTA
- Outcomes from the IN.PACT Admiral Clinical Program are very consistent across different regions and patient populations
- Results support DCB as a first line strategy for the treatment of femoropopliteal disease

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