

# The Evolution of SFA Treatment Strategy with IN.PACT DCB

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CONTROVERSIES & UPDATES  
IN VASCULAR SURGERY

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# Background

- While the endovascular approach has emerged as a first-line therapy for peripheral artery disease management, no single device modality has emerged as a “gold standard”<sup>1,2</sup>
- Angioplasty and stenting is plagued by high restenosis rates, 20-40% at 12 months<sup>3-7</sup>
- DCBs have demonstrated improved outcomes over PTA at 1 and 2 years in randomized trials,<sup>8-14</sup> with the IN.PACT Admiral DCB showing sustained treatment benefit through 4 years<sup>15</sup>
- Efficacy of DCBs in complex lesions i.e. high plaque burden, calcium, lesion length, is associated with a dependence on bailout stenting<sup>16,17</sup>

1. Conrad MF, et al. J Vasc Surg. 2006.  
2. Bisdas T, et al. J Vasc Surg. 2015.  
3. Krakenberg H, et al. Circulation. 2007.  
4. Laird J, et al. Circ Cardiovasc Interv. 2010.  
5. Matsumura J, et al. J Vasc Surg. 2013.  
6. Lammer J, et al. JACC 62(15):1320-7.











7. Dake M, et al. Circ Cardiovasc Interv 2011.  
8. Tepe G. et al., Circulation. 2015.  
9. Laird et al., J Am Coll Cardiol. 2015.  
10. Rosenfield et al., N Engl J Med. 2015.  
11. Laurich C. LEVENT II 2 Year Results, SVS 2015.  
12. Krishnan, P. et al., Circulation. 2017

13. Schroeder, H. et al., Circulation. 2017.  
14. Brodmann M, ILLUMENATE EU RCT 2 Year Results VIVA 2017  
15. Schneider, P. IN.PACT SFA 4 Year Results, VIVA 2017  
16. Scheinert D, IN.PACT Global LL, EuroPCR 2015  
17. Tepe G. IN.PACT Global CTO, CX 2016

# Worldwide Available DCBs











Multiple Drug-coated balloons (DCBs) on the market.

Only similarity between platforms is the **Drug-paclitaxel**, everything else differs!

Manufacturer	DCB	Drug	Dose ( $\mu\text{g}/\text{mm}^2$ )	Excipient
 BARD	Lutonix	Paclitaxel	2.0	Polysorbate/Sorbitol
Medtronic	IN.PACT	Paclitaxel	3.5	Urea
 Spectranetics®	Stellarex	Paclitaxel	2.0	Polyethylene Glycol
 Boston Scientific	Ranger	Paclitaxel	2.0	Citrate Ester
 BIOTRONIK	Passeo-18 Lux	Paclitaxel	3.0	BTHC
 BRAUN SHARING EXPERTISE	SeQuent Please OTW	Paclitaxel	3.0	Resveratrol
 iVascular therapies for living	Luminor	Paclitaxel	3.0	Ester
 COOK®	Advance 18 PTX	Paclitaxel	3.0	none
 Aachen Resonance	Elutax SV	Paclitaxel	2.2	none
 BIOSENSORS	BioPath (FREEWAY)	Paclitaxel	3.0	Shellac
 CARDIONOVUM®	Legflow	Paclitaxel	3.0	Shellac

# Worldwide Available DCBs

DCBs have demonstrated promising results at 1- and 2-years in randomized trials  
Longer-term data for commercially available DCBs are limited

Manufacturer	DCB	Dose ( $\mu\text{g}/\text{mm}^2$ )	Excipient	RCT Data
 BARD	Lutonix	2.0	Polysorbate/Sorbitol	1- and 2-year
Medtronic	IN.PACT	3.5	Urea	1-, 2-, 3-, 4-year
 Spectranetics®	Stellarex	2.0	Polyethylene Glycol	1- and 2-year
 Boston Scientific	Ranger	2.0	Citrate Ester	<b>FDA-approved</b>
 BIOTRONIK	Passeo-18 Lux	3.0	BTHC	
 BRAUN SHARING EXPERTISE	SeQuent Please OTW	3.0	Resveratrol	
 iVascular therapies for living	Luminor	3.0	Ester	
 COOK®	Advance 18 PTX	3.0	none	
 Aachen Resonance	Elutax SV	2.2	none	
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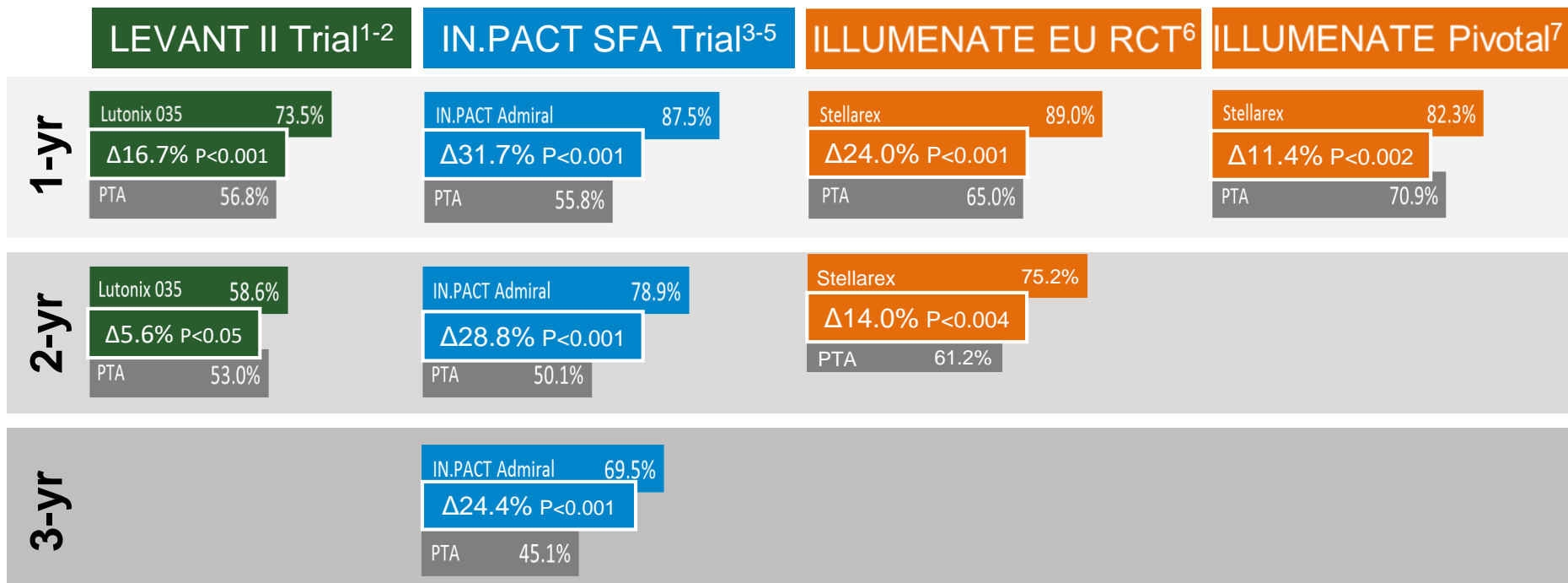
1. Tepe G. et al., Circulation. 2015.
2. Laird et al., J Am Coll Cardiol. 2015.
3. Rosenfield et al., N Engl J Med. 2015.
4. Laurich C. LEVENT II 2 Year Results, SVS 2015.

5. Krishnan, P. et al., Circulation. 2017
6. Schroeder, H. et al., Circulation. 2017.
7. Brodmann M, ILLUMENATE EU RCT 2 Year Results VIVA 2017
8. Schneider, P. IN.PACT SFA 4 Year Results, VIVA 2017

# FDA Approved Drug-Coated Balloons

## Summary of Multicenter RCTs

- LEVANT II: PSVR  $\leq 2.5$  and freedom from TLR<sup>1-2</sup>
- IN.PACT SFA: PSVR  $\leq 2.4$  and freedom from CD-TLR<sup>3-5</sup>
- ILLUMENATE EU and US RCTs: PSVR  $\leq 2.5$  and freedom from CD-TLR<sup>6-7</sup>



Primary patency rates derived from respective trials' Kaplan Meier estimates.

1. Rosenfield K, et al. NEJM:373:145-53 (2015).  
 2. Presented by Laurich C, SVS Chicago, USA 2015.  
 3. Tepe G, et al. Circ 131:495-502 (2015).  
 4. Laird J, et al. JACC 66:2329-38 (2015).  
 5. Presented by Krishnan P. VIVA 2016

6. Schroeder H. et al Circ 2017; Presented by Brodmann M. VIVA 2017  
 7. Krishnan, P., et al. Circulation 2017.

# IN.PACT SFA TRIAL OVERVIEW

**Objective:** Assess the safety and efficacy of IN.PACT™ Admiral™ DCB vs. standard PTA for the treatment of superficial femoral and proximal popliteal artery disease due to claudication and rest pain



## IN.PACT SFA I

150 subjects enrolled at 13 EU sites Sep 2010-Apr 2011



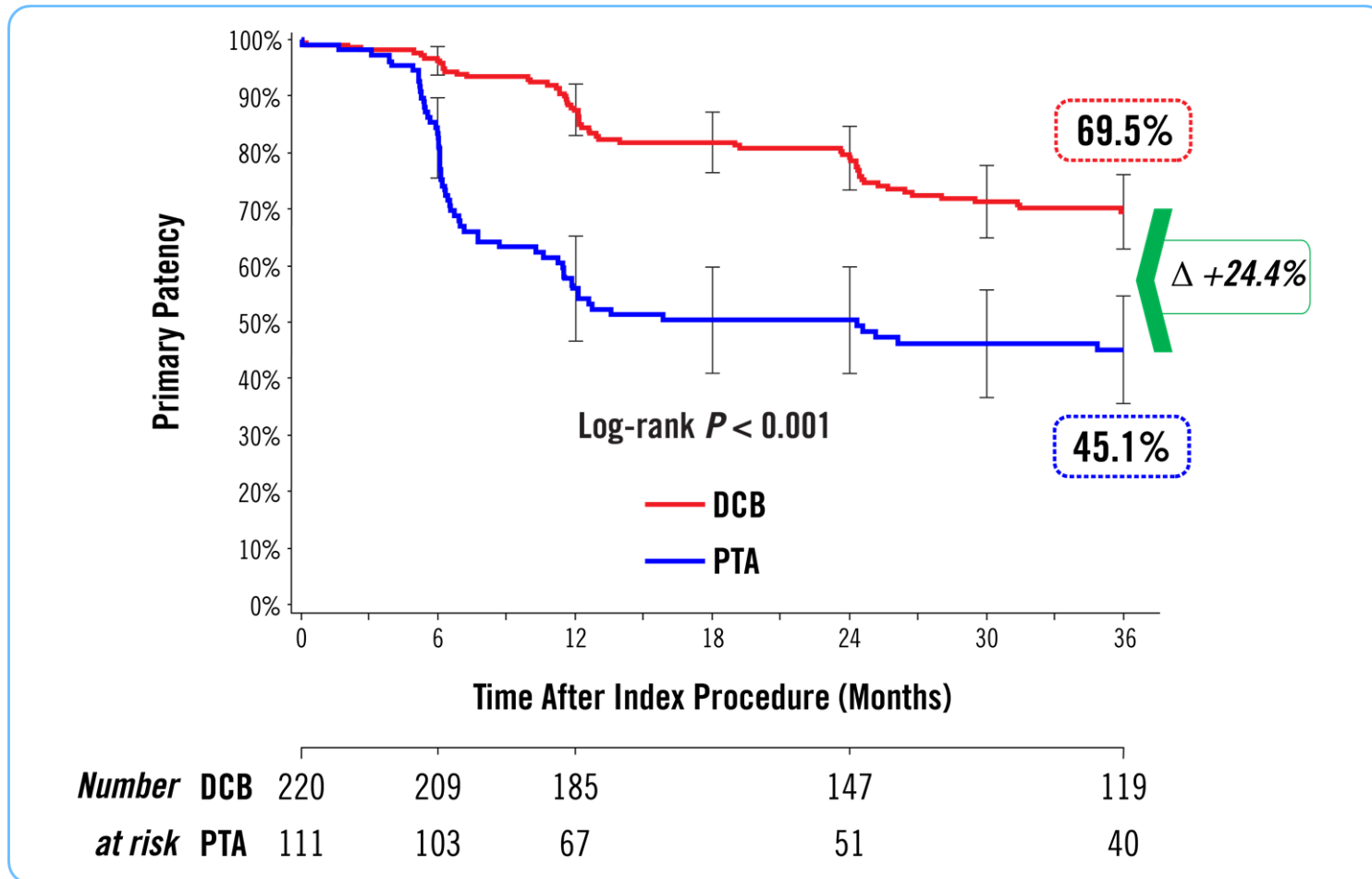
## IN.PACT SFA II

181 subjects enrolled at 44 US sites Apr 2012-Jan 2013

- Prospective, multicenter EU and US, randomized (2:1), single-blinded trial
- 331 patients enrolled:
  - IN.PACT™ Admiral™ DCB (n = 220) vs. PTA (n = 111)
- Rutherford Clinical Category 2-4
- Lesion lengths 4-18 cm or occlusions  $\leq$  10 cm
- Subjects followed up to 5 years
- Independent and blinded core labs and clinical events committee:
  - Duplex Ultrasound Core Lab: VasCore DUS Core Laboratory; Boston, MA, USA
  - Angiographic Core Lab: SynvaCor Angiographic Core Laboratory; Springfield, IL, USA
  - Clinical Events Committee and Data Safety Monitoring: HCRI; Boston, MA, USA

# IN.PACT SFA TRIAL

## PRIMARY PATENCY<sup>1</sup> RESULTS THROUGH 3 YEARS

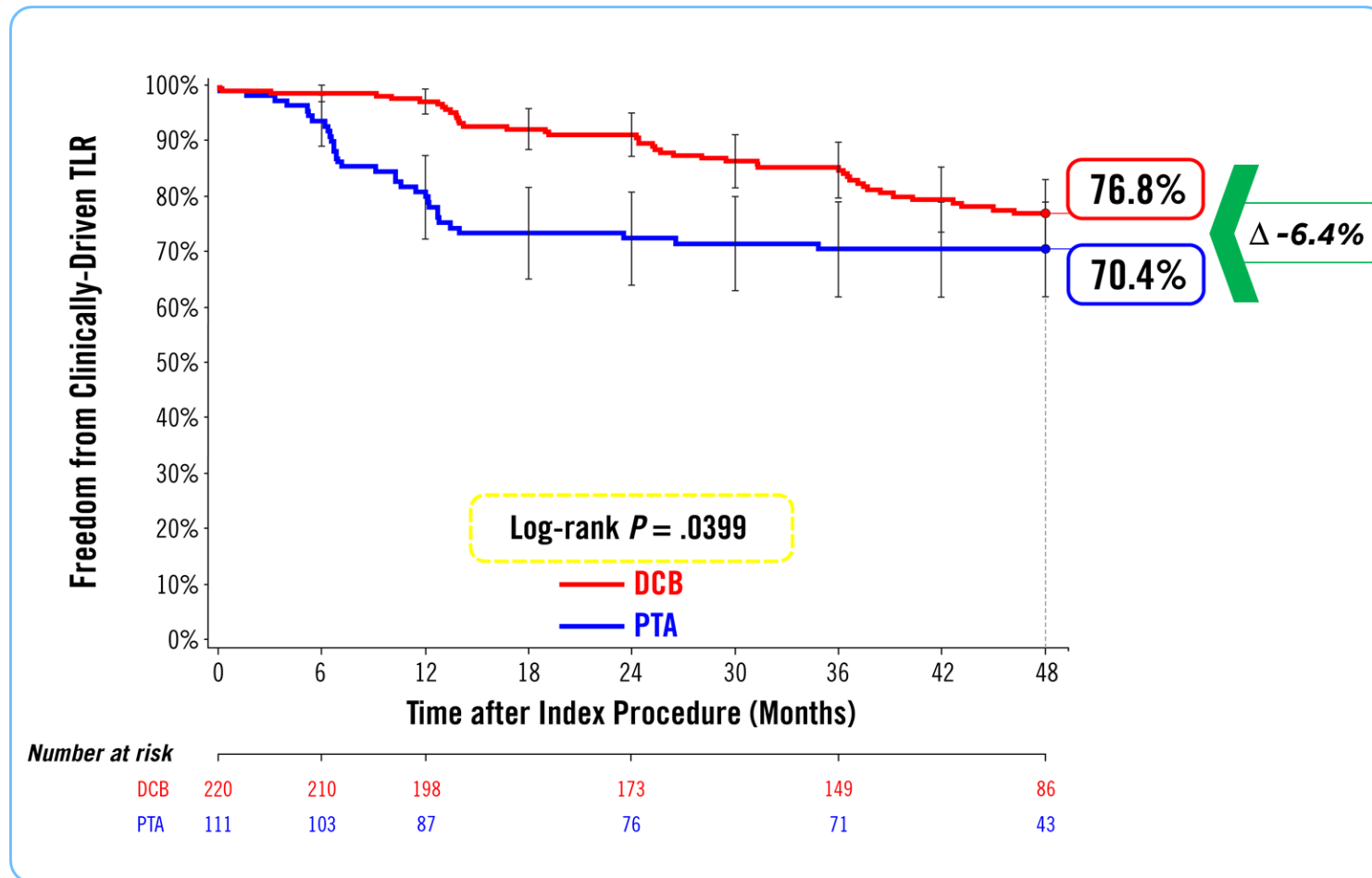


1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR  $\leq 2.4$ ) or clinically-driven target lesion revascularization through 36 months (adjudicated by a Clinical Events Committee blinded to the assigned treatment)

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

# IN.PACT SFA TRIAL

## FREEDOM FROM CD-TLR<sup>1</sup> THROUGH 4 YEARS



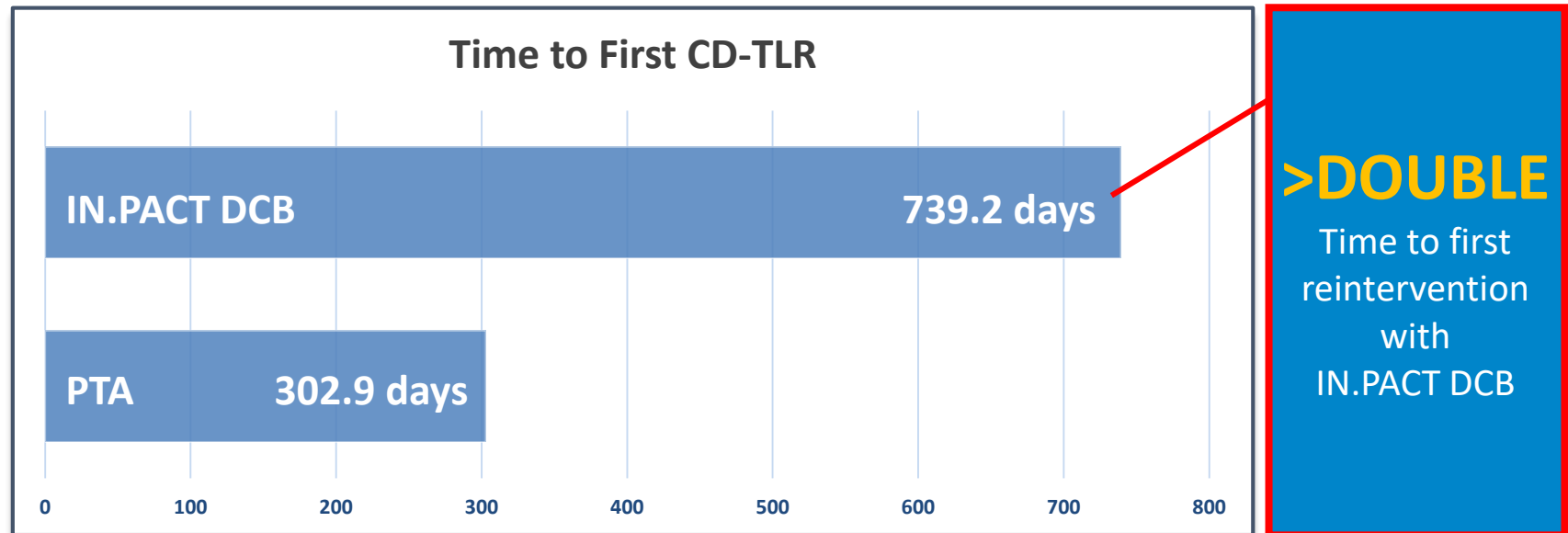
Clinically-driven TLR adjudicated by an independent Clinical Event Committee, blinded to the assigned treatment based on any re-intervention at the target lesion due to symptoms or drop of ABI of  $\geq 20\%$  or  $>0.15$  when compared to post-procedure baseline ABI



# IN.PACT SFA TRIAL

## ADDITIONAL OUTCOMES THROUGH 4 YEARS

	IN.PACT DCB (N=220)	PTA (N=111)	P-value <sup>†</sup>
Clinically-driven TLR [1]	23.4% (43/184)	31.1% (32/103)	0.164
Any TLR [2]	24.5% (45/184)	34.0% (35/103)	0.100
<b>Time to First CD-TLR</b>	<b>739.2 ± 384.0</b>	<b>302.9 ± 213.0</b>	<b>&lt; 0.001</b>



# IN.PACT SFA TRIAL

## SAFETY OUTCOMES THROUGH 4 YEARS

	IN.PACT DCB (N=220)	PTA (N=111)	P-value†
<b>Primary Safety Composite</b> <sup>[1]</sup>	73.4% (135/184)	64.1% (66/103)	0.108
<b>Major Adverse Events</b> <sup>[2]</sup>	38.0% (70/184)	40.8% (42/103)	0.705
<b>All-cause Death</b>	13.0% (24/184)	6.8% (7/103)	0.116
<b>Device- or Procedure-related Death</b>	0.0% (0/219)	0.0% (0/111)	>0.999
<b>Clinically-driven TVR</b>	26.6% (49/184)	35.9% (37/103)	0.108
<b>Target Limb Major Amputation</b>	0.0% (0/184)	0.0% (0/103)	>0.999
<b>Thrombosis</b>	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 48 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

# IN.PACT SFA TRIAL

## SUMMARY

Only independently-adjudicated, randomized, pivotal trial to demonstrate a superior treatment effect of DCB over PTA through four years

- Highly statistically significant primary patency benefit of IN.PACT™ Admiral™ DCB over PTA at three years
  - Primary patency difference by Kaplan-Meier estimate: 24.4% (p<0.001)
- Favorable freedom from CD-TLR of IN.PACT™ Admiral™ DCB over PTA through four years
  - Numerically favorable difference by proportion rate: 7.7% (p=0.164)  
Statistically favorable difference by Kaplan-Meier estimate: 6.4% (p=0.0399)
  - Significantly longer time to first reintervention for DCB compared to PTA (739.2 ± 384.0 days v 302.9 ± 213.0 days; p<0.001)
- Continued safety of IN.PACT™ Admiral™ DCB through four years
  - Lower thrombosis rate than PTA control (2.0% v 4.9%; p=0.29)
  - No amputations in either study arm
- These data stress the importance of follow-up beyond common 1- and 2-year intervals, especially for drug therapies

# DCB “Real-World” Registries

Global registries include real-world patients and lesions

	Global <sup>1</sup>	Long Lesion <sup>2</sup>	Long Lesion <sup>3</sup>	CTO <sup>4</sup>	ISR <sup>5</sup>	Clinical <sup>6</sup>	ILLUMENATE Global <sup>7</sup> Stellarex
<b>Key Inclusion Criteria</b>	RCC ≤4 SFA & PA	RCC 2-4 SFA & PA Lesions ≥14cm	RCC 2-4 SFA & PA Lesions ≥15cm	RCC 2-4 SFA & PA CTOs	RCC 2-4 SFA & PA ISR	RCC 2-4 SFA & PA	RCC 2-4 SFA & PA
<b>Key Patient Characteristics</b>							
Age (years)	68.3y	67.6y	69.5y	67.5y	67.8y	68.6y	68.2y
RCC ≥4 (%)	9.0%	6.1%	16.7%	11.1%	10.0%	11.0%	8.6%
Men (%)	67.6%	73.7%	66.2%	69.0%	69.5%	67.8%	73.0%
DM (%)	39.5%	36.4%	41.0%	29.6%	35.1%	39.9%	33.7%
<b>Key Lesion Characteristics</b>							
Length (cm)	10.1cm	21.3cm	26.4cm	22.9cm	17.2cm	12.1cm	7.5cm
CTO (%)	31.2%	52.1%	60.4%	100.0%	34.0%	35.5%	31.3%
Ca <sup>2+</sup> (%)	50.2%	78.9% <sup>2</sup>	71.8%	71.0%	59.1%	68.7%	56.2% <sup>7</sup>

1. Thieme, M., et al. (2017). JACC Cardiovasc Interv.

2. Bard Lutonix Instructions for Use BAW1387400r3, Section 10.5. Moderate to severe calcification reported; amputations not reported (NR).

3. Presented by Scheinert D, PCR Paris, France 2015.

4. Presented by Tepe G, CX London, UK 2016.

5. Presented by Brodmann M, VIVA Las Vegas, USA 2015.

6. Presented by Jaff M, VIVA Las Vegas, USA 2016;

7. Presented by Zeller T, LINC Leipzig, Germany 2017. Moderate to severe calcification reported.

# DCB “Real-World” Registries

Similar outcomes despite potential differences in populations and lesions, as well as reliance on provisional stenting

	Global <sup>1</sup>	Long Lesion <sup>2</sup>	Long Lesion <sup>3</sup>	CTO <sup>4</sup>	ISR <sup>5</sup>	Clinical <sup>6</sup>	ILLUMENATE Global <sup>7</sup> Stellarex
<b>Follow-up</b>	691 subjects Complete follow-up CEC & site-reported outcomes	107 & 102 subjects for safety & effectiveness, respectively; Core lab-adjudicated	157 subjects Complete follow-up; Core lab-adjudicated	126 subjects Complete follow-up; Core lab-adjudicated	131 subjects Complete follow-up; Core lab-adjudicated	1406 subjects Complete follow-up; CEC & site-reported outcomes	371 subjects Complete follow-up; Core lab-adjudicated
<b>12-mo Outcomes</b>							
1° Patency (%)	NR	68.9%	91.1%	85.3%	88.7%	NR	81.4%
FF TLR/CD-TLR(%)	94.3%	87.8%	94.0%	89.1%	92.9%	92.6%	94.8%
<b>Bail-out Stent (%)</b>	<b>25.2%</b>	<b>39.8%</b>	<b>40.4%</b>	<b>46.8%</b>	<b>14.5%</b>	<b>25.3%</b>	<b>17.3%</b>
Amputations (%)	0.5% (3/632)	NR	0.0%	0.0%	0.0%	0.2% (3/1311)	0.3% (1/371)

1. Thieme, M., et al. (2017). JACC Cardiovasc Interv.

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# DCB “Real-World” Registries

Similar outcomes despite potential differences in populations and lesions, as well as reliance on provisional stenting

Consistently low frequency of major amputation across platforms

	Global <sup>1</sup>	Long Lesion <sup>2</sup>	Long Lesion <sup>3</sup>	CTO <sup>4</sup>	ISR <sup>5</sup>	Clinical <sup>6</sup>	ILLUMENATE Global <sup>7</sup> Stellarex
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<b>Amputations (%)</b>	<b>0.5% (3/632)</b>	<b>NR</b>	<b>0.0%</b>	<b>0.0%</b>	<b>0.0%</b>	<b>0.2% (3/1311)</b>	<b>0.3% (1/371)</b>

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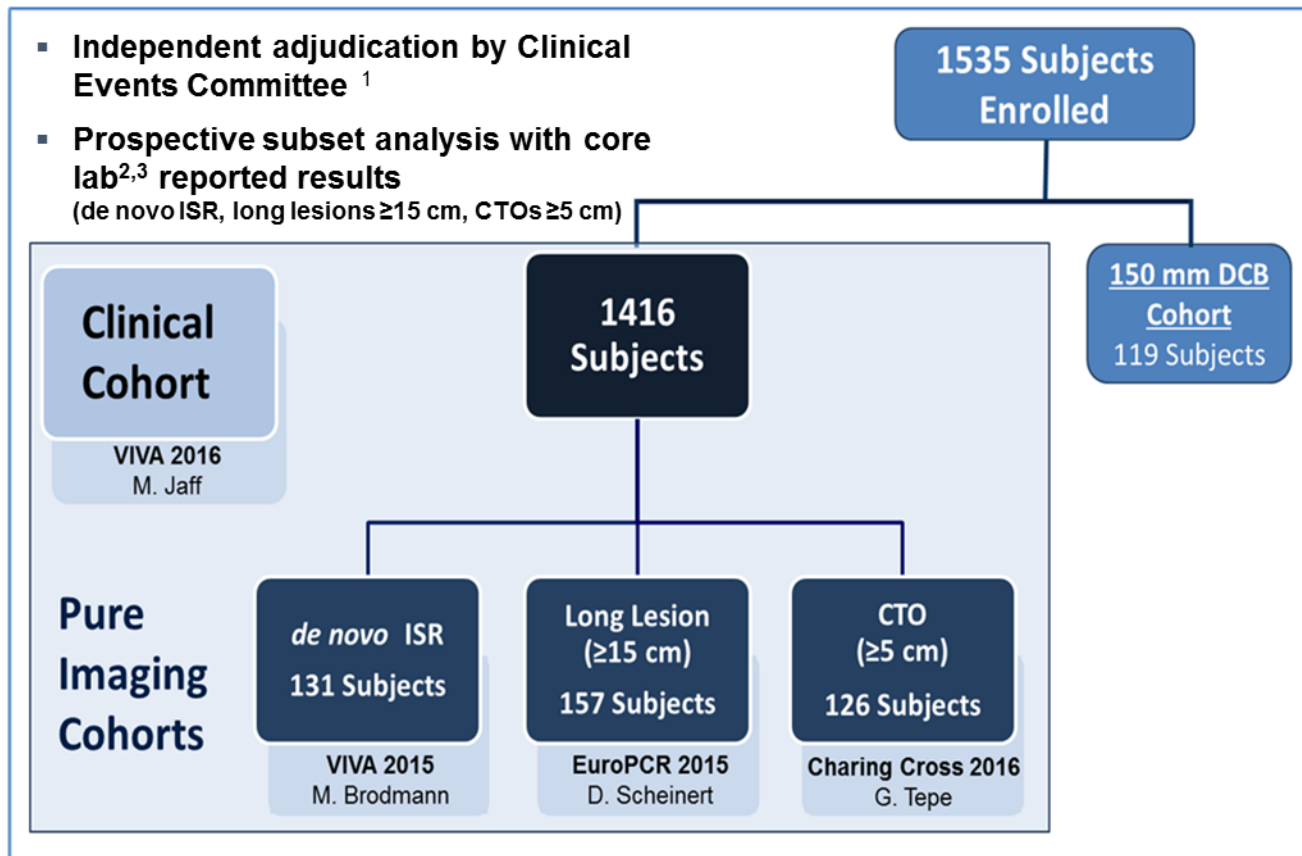
# IN.PACT Global Study OVERVIEW

Real-world, prospective, multicenter, single arm study with independent adjudication to expand clinical evidence of the IN.PACT™ Admiral™ DCB in the treatment of patients with femoropopliteal lesions



## All-comers RCC 2-4

Bilateral disease  
Multiple lesions  
SFA and Popliteal  
TASC A, B, C, D  
De novo ISR  
Long Lesions  
CTOs

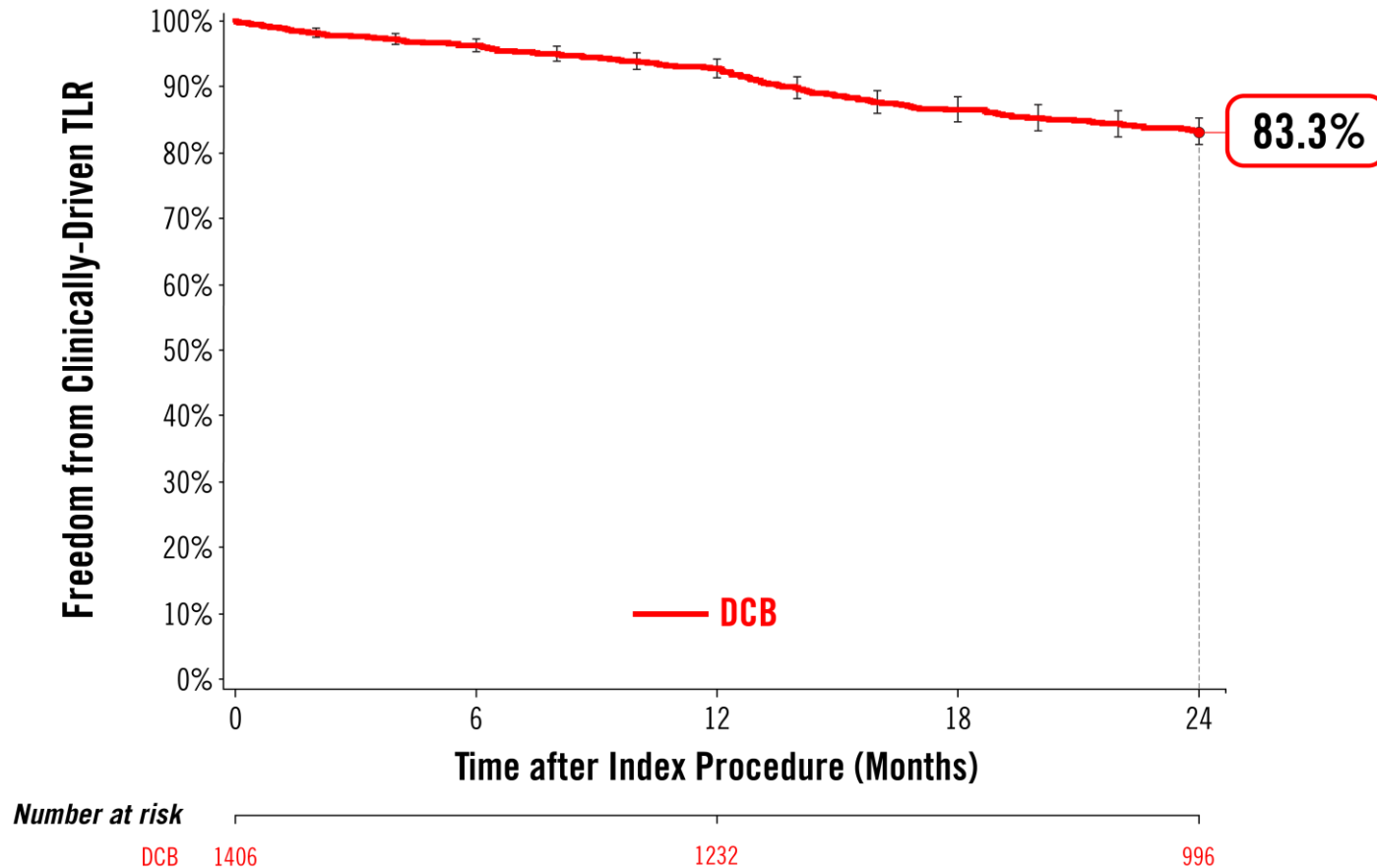


\*Analysis is based on the 1406 ITT subjects.

<sup>1</sup>Syntactx Clinical Events Committee, New York, NY, US; <sup>2</sup>VasCore DUS Core Lab, Boston, MA, US; <sup>3</sup>SynvaCor Angiographic Core Lab, Springfield, IL, US  
Jaff, M. VIVA 2016

# IN.PACT Global Study

## FREEDOM FROM CD-TLR<sup>1</sup> THROUGH 2 YEARS



1. Number at risk represents the number of evaluable subjects at the beginning of the each 60-day window



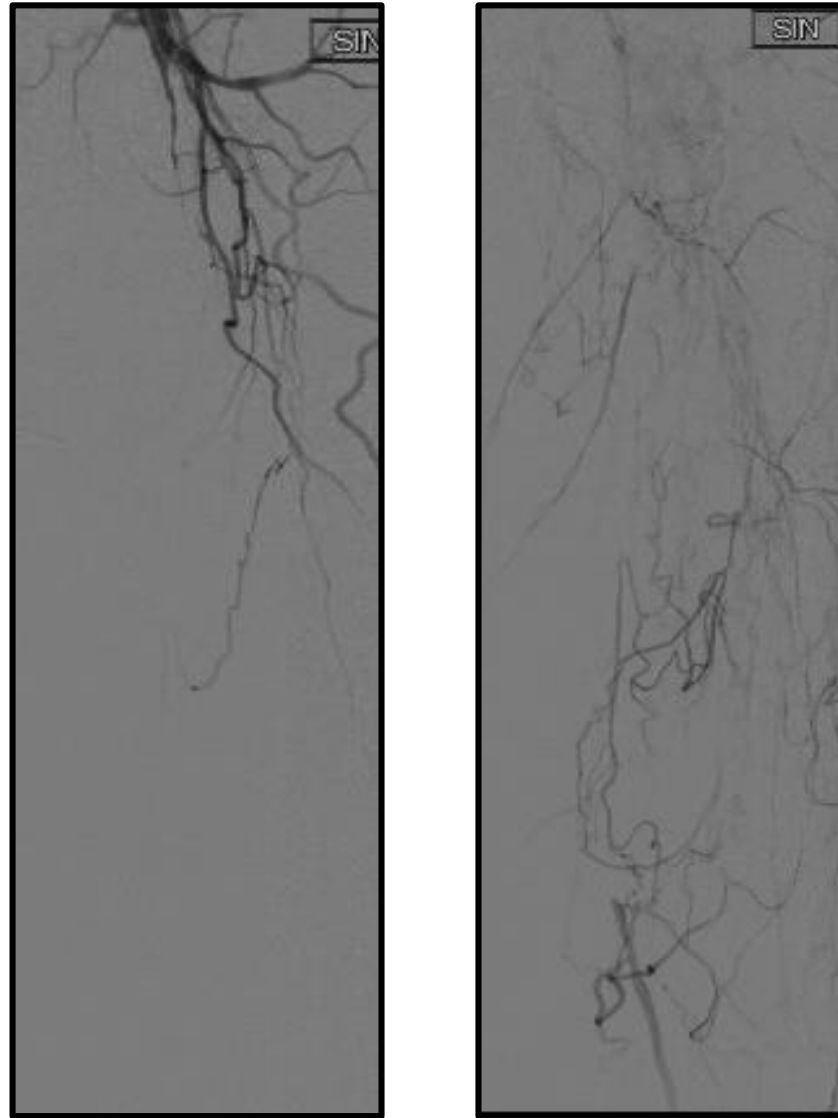
# IN.PACT Global Study

## 2-YEAR OUTCOMES ACROSS IN.PACT STUDIES

Consistent performance of the IN.PACT™ Admiral™ DCB across SFA studies, with durable safety and effectiveness outcomes through 2 years.

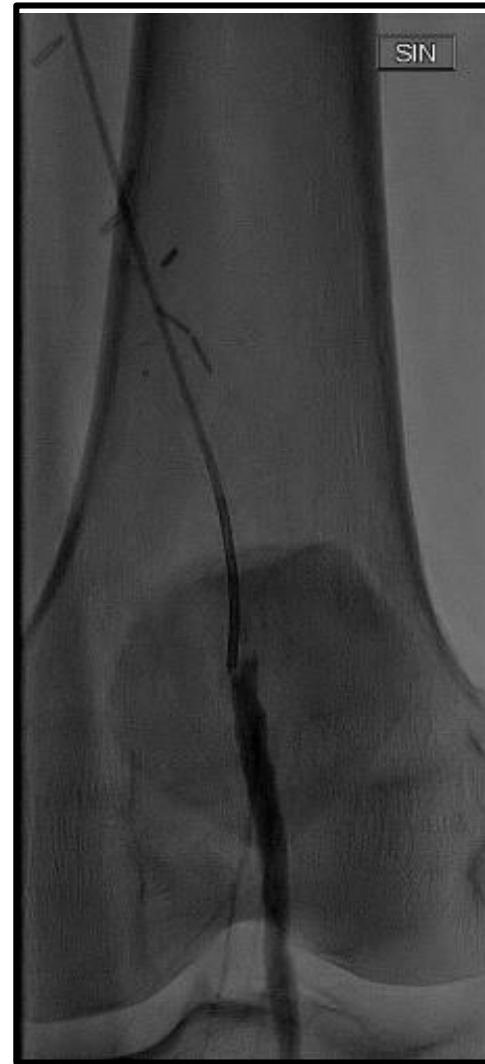
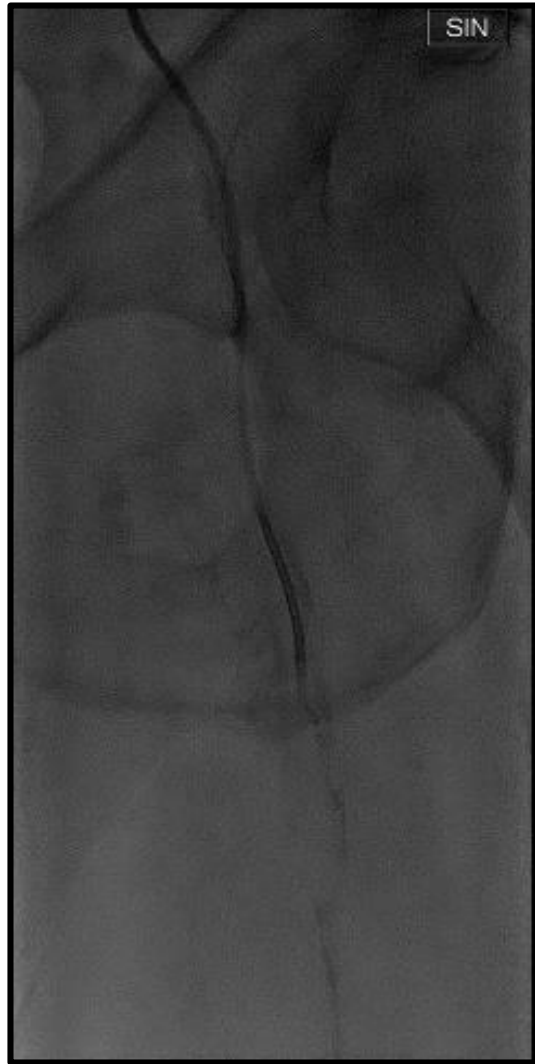
	IN.PACT SFA (DCB ARM) (N=220)	IN.PACT Global Clinical Cohort (N= 1406)
Lesion Length (Mean ± SD, cm)	8.94 ± 4.89	12.09 ± 9.54
In-stent Restenosis (ISR) %	0.0%	18.0%
Chronic Total Occlusion (CTO) %	25.8%	35.5%
Primary Patency (KM @ 720 days)	78.9%	N/A
<b>CD-TLR</b>	<b>9.1%</b>	<b>16.9%</b>
Thrombosis	1.5%	4.5%
Major Amputation Target Limb	0.0%	0.7%

# Complex lesion



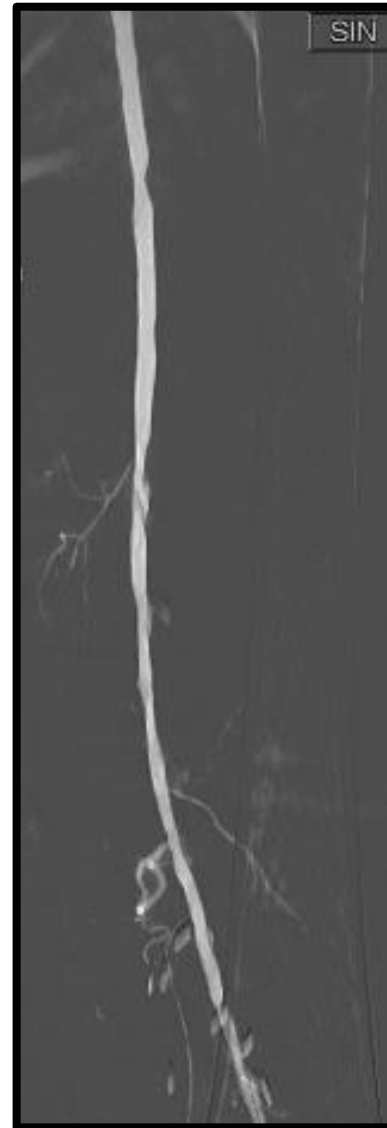
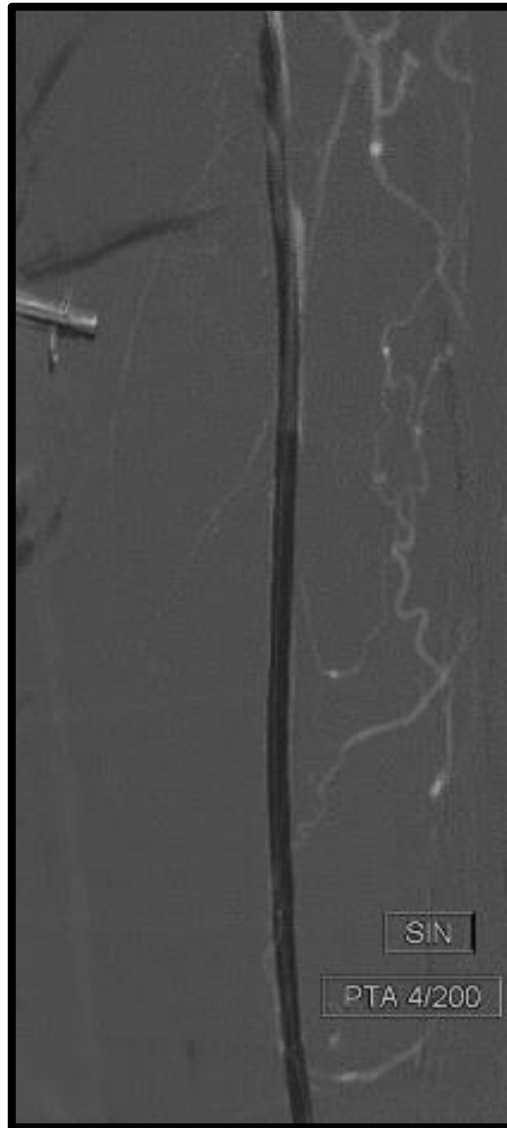
Long lesion (32 cm), with calcium

# Complex lesion



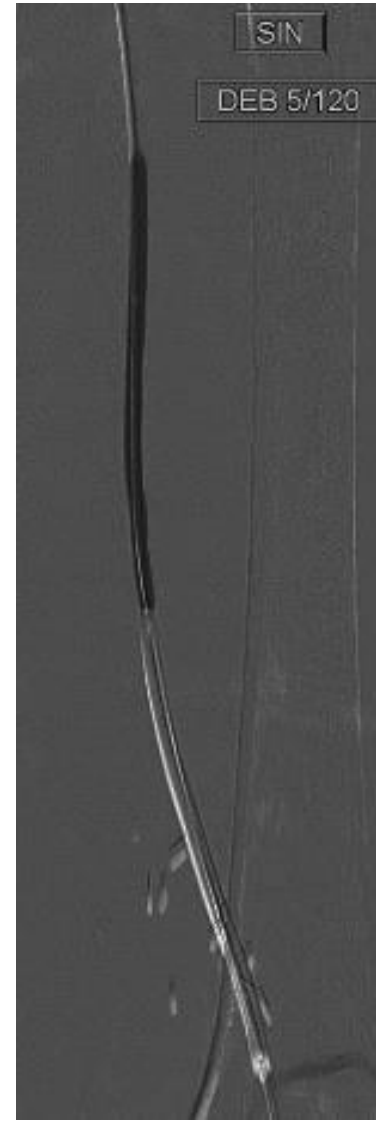
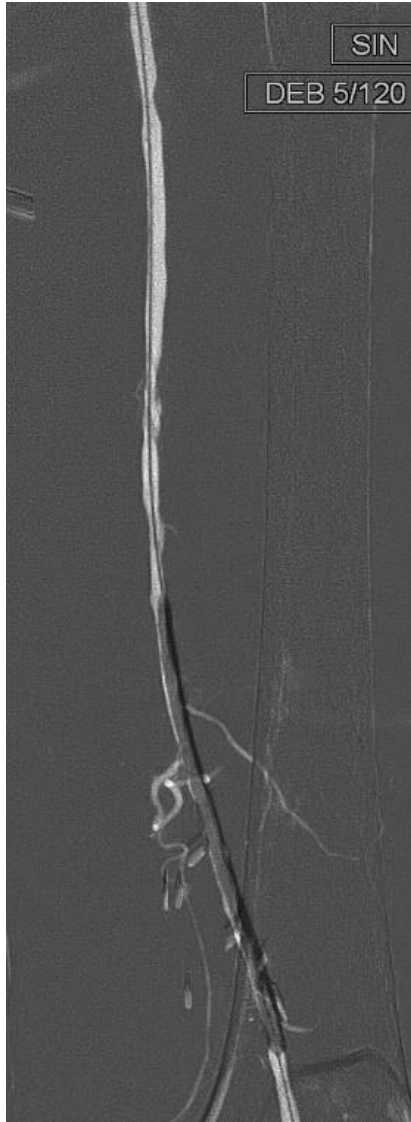
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# Complex lesion



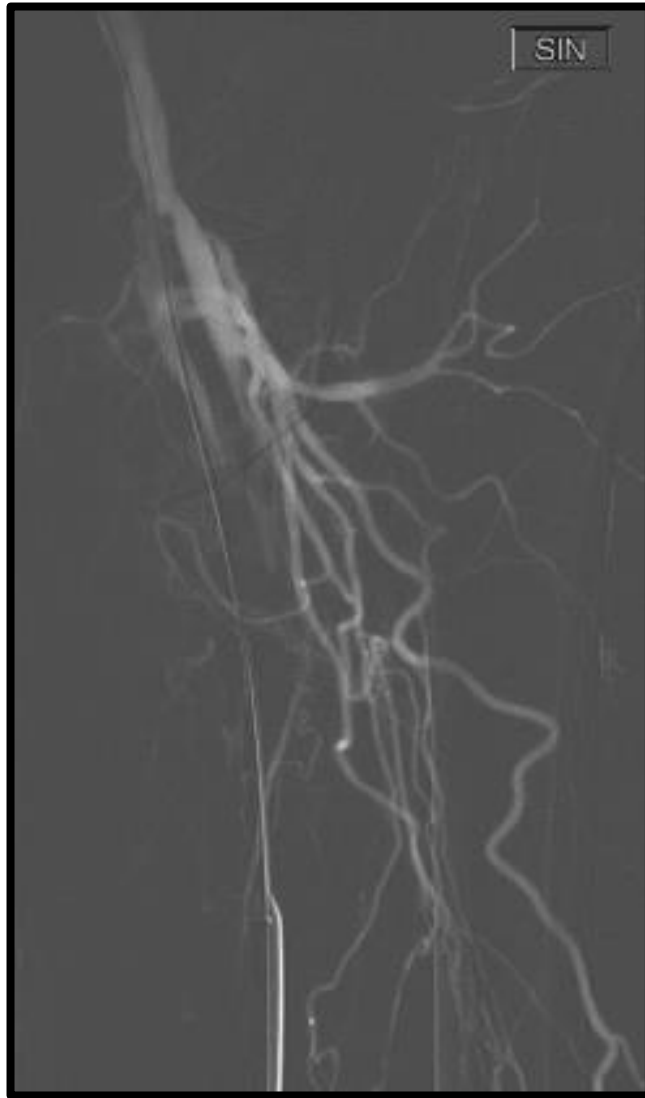
Predilation 4 x 200

# Complex lesion



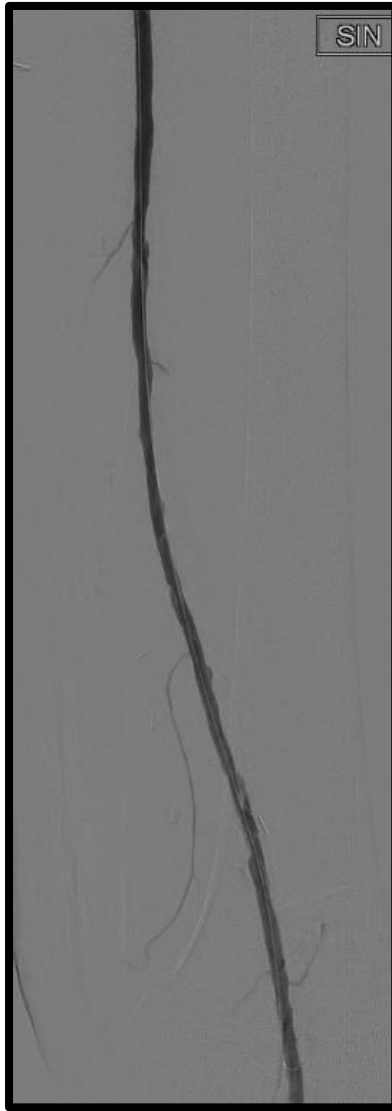
DCB 5 x 120 mm (n=3)  
Use of road-map to avoid geographical miss

# Complex lesion

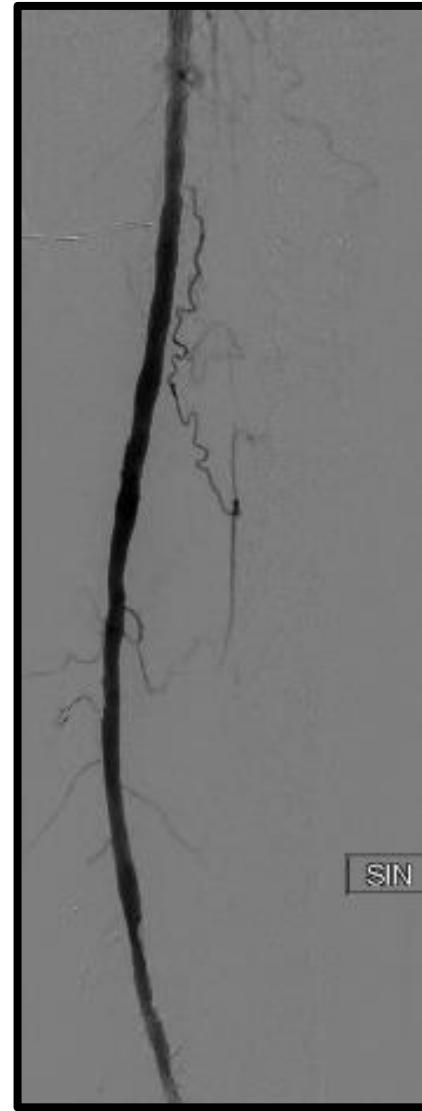


DCB 5 x 120 mm (n=3)  
Use of road-map to avoid geographical miss

# Complex lesion



Note filling of  
collaterals

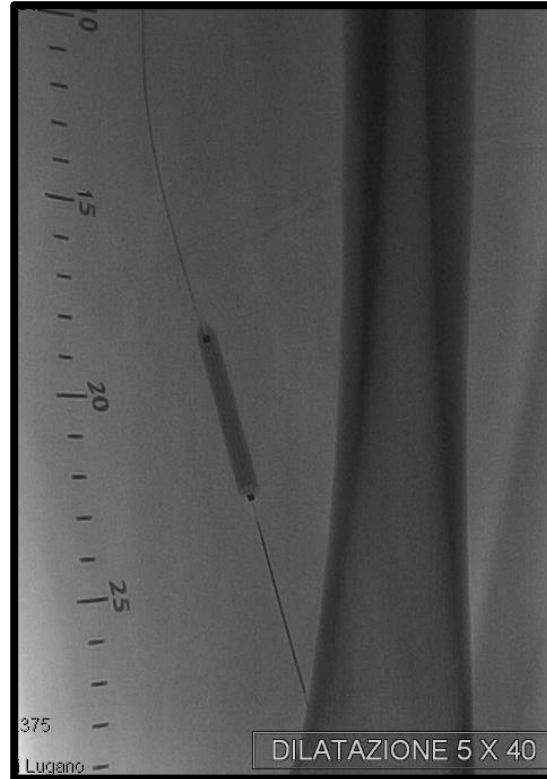


Acute result

@1 year

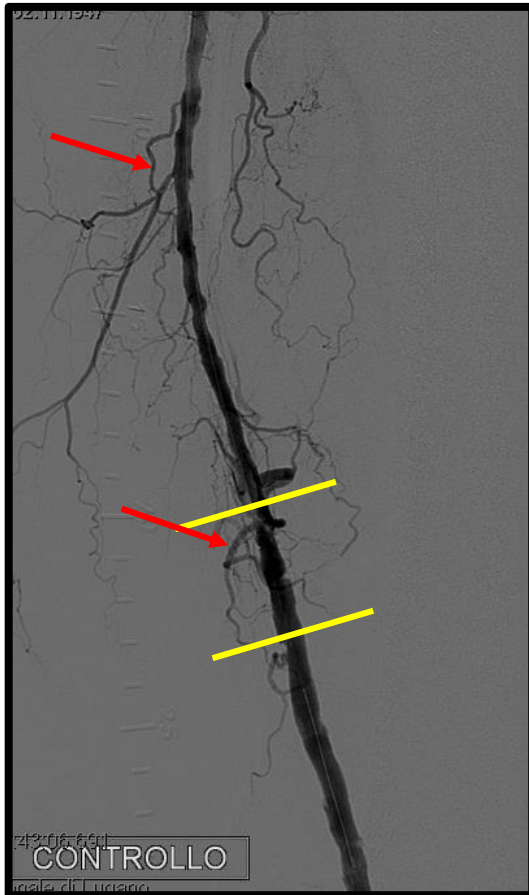
# Short occlusion- Long follow-up

Patient included in IN.PACT SFA trial (DCB arm)





# Short occlusion- Long follow-up



December 2010



April 2017

# Summary

- Endovascular procedures continue to be first line for the treatment of femoropopliteal disease
- Outcomes from RCTs of DCB demonstrate outstanding early results at 1 and 2 years, with variable longer term outcomes across platforms<sup>1-7</sup>
- IN.PACT DCB is the only platform to show sustained treatment benefit through 4 years<sup>8</sup>
- Results from the real-world DCB registries show complex lesions may still require stenting<sup>9,10</sup>
- When interpreting these data, it's important to consider patients of your specific practice to realistically anticipate use of stents and expected patency and/or reintervention rates

1. Tepe G. et al., Circulation. 2015.  
2. Laird et al., J Am Coll Cardiol. 2015.  
3. Rosenfield et al., N Engl J Med. 2015.  
4. Laurich C. LEVENT II 2 Year Results, SVS 2015.

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