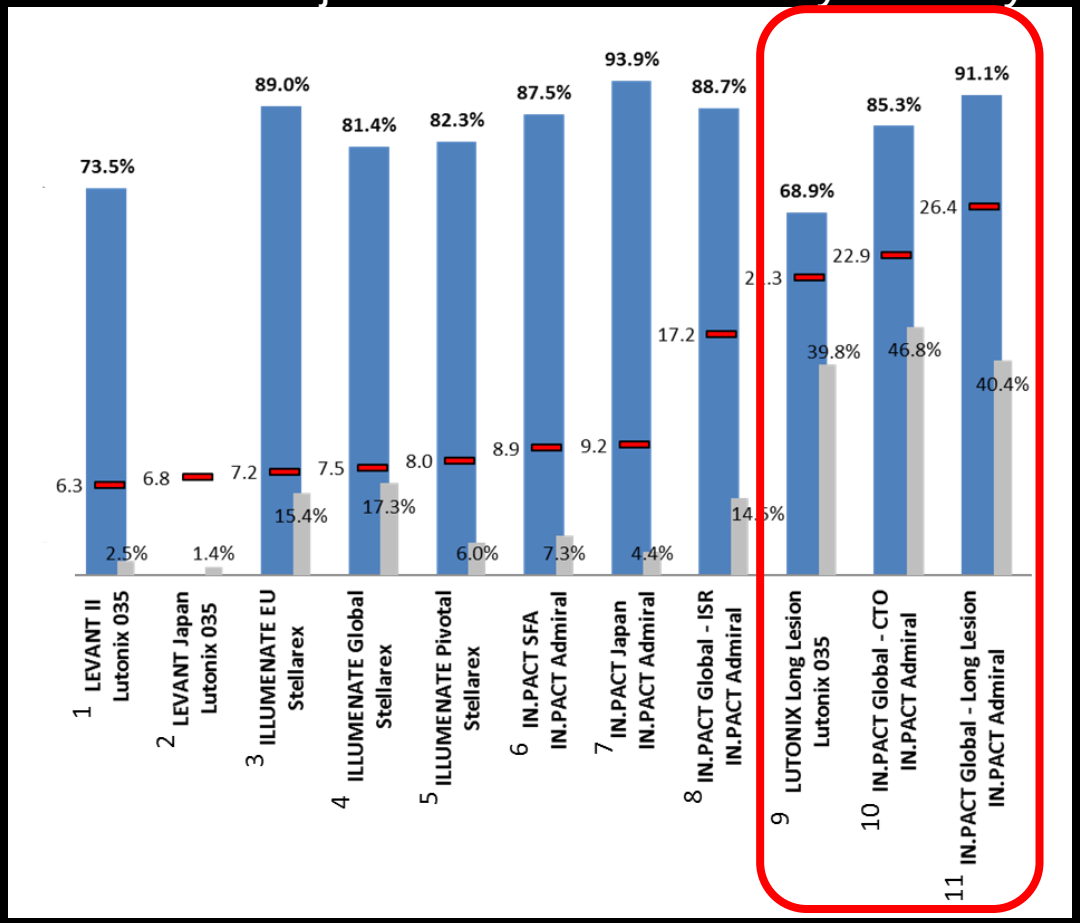
# DCB IN THE SFA: ARE THEY ALL THE SAME?

**Dr. Konstantinos Katsanos, *MSc, MD, PhD, EBIR***

*Asst. Prof. Interventional Radiology*
*School of Medicine, Patras University Hospital, GR*
*Honorary Consultant Interventional Radiologist*
*Guy's and St. Thomas' Hospitals, London, UK*

# DCB Data Synopsis

## Core Lab-adjudicated 12-mo Primary Patency Rates by Kaplan Meier Estimate




Key

- Patency Rate %
- Lesion Length (cm)
- Bail-out Stent Rate %

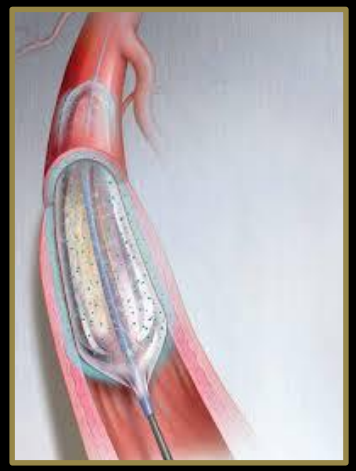
**Primary patency definitions:**

LEVANT PSVR ≤ 2.5 & FF TLR;
IN.PACT PSVR ≤ 2.4 & FF CD-TLR;
ILLUMENATE PSVR ≤ 2.5 & FF CD-TLR.


1. *Rosenfield K, et al. New Engl J Med 373:145-53 (2015).*
2. *PMDA Report on Lutonix 035 Japan randomized trial, Tables 12 and 14, July 14, 2017.*
3. *Schroeder H, et al. Circ 135:2227-2236 (2017).*
4. *Presented by Zeller T, LINC Leipzig, Germany 2017.*
5. *Presented by Lyden S, TCT Washington DC, USA 2016.*
6. *IN.PACT™ Admiral Instructions for Use, M052624T001_Rev1F_EN, Figure 10.*
7. *Iida O, et al. J Endovasc Ther 25:109-17 (2018).*
8. *Presented by Brodmann M, VIVA Las Vegas, USA 2015. *14.5% reflects provisional stent rate during DCB treatment of 100% in-stent restenosis cohort.*
9. *Lutonix Instructions for Use BAW1387400r3 section 10.5.*
10. *Presented by Tepe G, Charing Cross London, UK 2016.*
11. *Presented by Scheinert D, EuroPCR Paris, France 2015.*

# DCB Device Overview

## FDA-Approved Devices



| | Lutonix 035 (Bard) | IN.PACT Admiral (MDT) | Stellarex (Spectranetics) |
|---|---|---|---|
| Configurations | 4-7mm diameter<br>40-150mm length | 4-7mm diameter<br>40-150mm length | 4-6mm diameter<br>40-120mm length |
| Platform | Lutonix PTA | Admiral PTA | Stellarex PTA |
| Drug and Dosage | Paclitaxel 2.0µg/mm$^2$ | Paclitaxel 3.5µg/mm$^2$ | Paclitaxel 2.0µg/mm$^2$ |
| Excipient / Coating | Sorbitol / Polysorbate | Urea | Polyethylene Glycol |
| Commercial Availability | Worldwide | Worldwide | Worldwide |
| US Indication | SFA & PA + ISR<br>≤300mm lesions;<br>AV Access | SFA & PA + ISR<br>≤180mm lesions | SFA & PA<br>≤180mm lesions |

# DCB Multicenter RCTs

Potential differences in patient populations, lesion characteristics, study definitions, follow-up regimens, clinical events committees, core labs, etc.

| | LEVANT II Trial[1-2] | | IN.PACT SFA Trial[3-5] | | IN.PACT Japan Trial[6] | | ILLUMENATE EU RCT[7] | | ILLUMENATE Pivotal[8] | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Lutonix 035 | PTA | IN.PACT | PTA | IN.PACT | PTA | Stellarex | PTA | Stellarex | PTA |
| **Key Patient Variables** | (n=316) | (n=160) | (n=220) | (n=111) | (n=68) | (n=32) | (n=222) | (n=72) | (n=200) | (n=100) |
| Age (years) | 67.8y | 69.0y | 67.5y | 68.0y | 73.3y | 74.2y | 67y | 69y | 68.3y | 69.8y |
| RCC ≥4 (%) | 7.9% | 8.1% | 5.0% | 6.3% | 4% | 3% | 2% | 1% | 4.0% | 5.0% |
| Men (%) | 61.1% | 66.9% | 65.0% | 67.6% | 74% | 81% | 72% | 68% | 56.0% | 64.0% |
| DM (%) | 43.4% | 41.9% | 40.5% | 48.6% | 59% | 56% | 37% | 36% | 49.5% | 52.0% |
| ABI | 0.74 | 0.73 | 0.769 | 0.744 | 0.76 | 0.74 | 0.72 | 0.69 | 0.75 | 0.76 |
| **Key Lesion Variables** | (n=316) | (n=160) | (n=220) | (n=111) | (n=68) | (n=32) | (n=254) | (n=79) | (n=200) | (n=100) |
| RVD (mm) | 4.8mm | 4.8mm | 4.6mm | 4.7mm | 4.8mm | 4.7mm | 5.0mm | 4.8mm | 4.9mm | 5.2mm |
| Length (cm) | 6.3cm | 6.3cm | 8.9cm | 8.8cm | 9.2cm | 8.9cm | 7.2cm | 7.1cm | 8.0cm | 8.9cm |
| CTO (%) | 20.6% | 21.9% | 25.8% | 19.5% | 16% | 16% | 19% | 19% | 19.0% | 18.0% |
| Severe $Ca^{2+}$ (%)* | 10.4% | 8.1% | 8.1% | 6.2% | 7% | 9% | 13% | 10% | 43.9% | 43.0% |
| **Key Procedural Variables** | | | | | | | | | | |
| Pre-dilation (%) | 100.0% | 100.0% | 96.4% | 85.6% | 100% | 100% | 100% | 99% | 100.0% | 100.0% |
| Diss. Grade ≥D(%) | 0.0% | 0.0% | 0.0% | 0.9% | 0% | 0% | 1% | 0% | 20.0% | 12.0% |
| Bail-out Stent (%) | 2.5% | 6.9% | 7.3% | 12.6% | 4% | 3% | 15% | 11% | 6.0% | 6.0% |

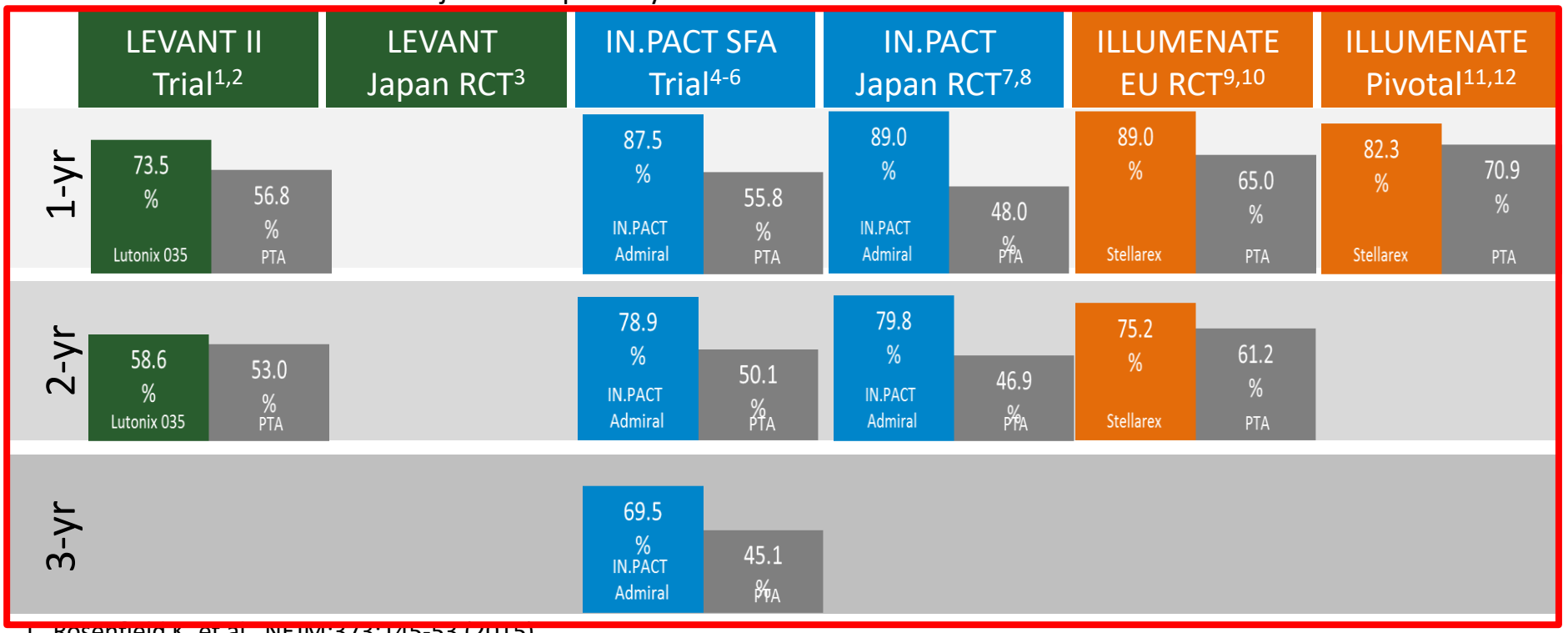
Definitions of Severe Ca2+ differ between trials. Additionally, ILLUMENATE Pivotal Study uses a different angiographic core lab (Beth Israel Deaconess Medical Center) than the other studies (SynvaCor). This difference may also influence reported rate of dissection Grade ≥D.


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 Las Vegas, USA 2016.
6. Iida O, et al. J Endovasc Ther 25:109-17 (2018).
7. Schroeder H, et al. Circ 135:2227-2236 (2017).
8. Presented by Lyden S, TCT Washington DC, USA 2016.

# DCB Multicenter RCTs

## Primary Patency by Kaplan Meier Estimates, ITT Basis

- LEVANT Studies: Subject-level patency defined as PSVR ≤ 2.5 and freedom from TLR[1-3]
- IN.PACT Studies: Subject-level patency defined as PSVR ≤ 2.4 and freedom from CD-TLR[4-8]
- ILLUMENATE EU: Lesion-based patency defined as PSVR ≤ 2.5 and freedom from CD-TLR[9,10]
- ILLUMENATE Pivotal: Subject-level patency defined as PSVR ≤ 2.5 and freedom from CD-TLR[11,12]



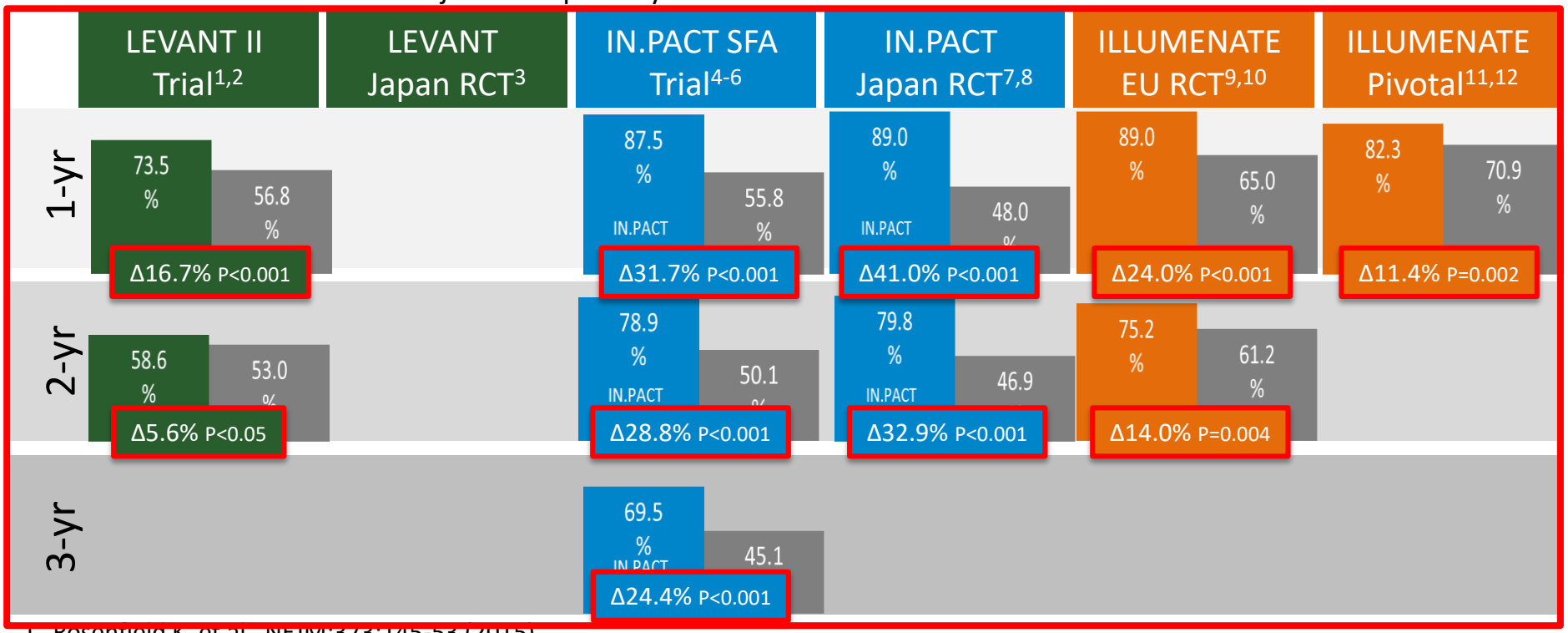


1. Rosenfield K, et al. NEJM:373:145-53 (2015).
2. Presented by Laurich C, SVS Chicago, USA 2015.
3. Proportion-based primary patency of 58.0% and 62.9% for Lutonix 035 and PTA, respectively, were provided in PMDA Report on Lutonix 035 Japan randomized trial, Tables 12 and 14, July 14, 2017; Kaplan Meier estimates are unavailable.
4. Tepe G, et al. Circ 131:495-502 (2015).
5. Laird J, et al. JACC 66:2329-38 (2015).
6. Schneider P, et al. Circ Cardiovasc Interv 11:e005891 (2018).
7. Iida O, et al. J Endovasc Ther 25:109-17 (2018).
8. Presented by Iida O, LINC Leipzig, Germany 2018.
9. Schroeder H, et al. Circ 135:2227-2236 (2017).
10. Presented by Brodmann M, VIVA Las Vegas, USA 2017.
11. Presented by Lyden S, TCT Washington DC, USA 2016.
12. Stellarex IFU Rev 07/2017 Table 7.

# DCB Multicenter RCTs

## Primary Patency by Kaplan Meier Estimates, ITT Basis

- LEVANT Studies: Subject-level patency defined as PSVR ≤ 2.5 and freedom from TLR[1-3]
- IN.PACT Studies: Subject-level patency defined as PSVR ≤ 2.4 and freedom from CD-TLR[4-8]
- ILLUMENATE EU: Lesion-based patency defined as PSVR ≤ 2.5 and freedom from CD-TLR[9,10]
- ILLUMENATE Pivotal: Subject-level patency defined as PSVR ≤ 2.5 and freedom from CD-TLR[11,12]



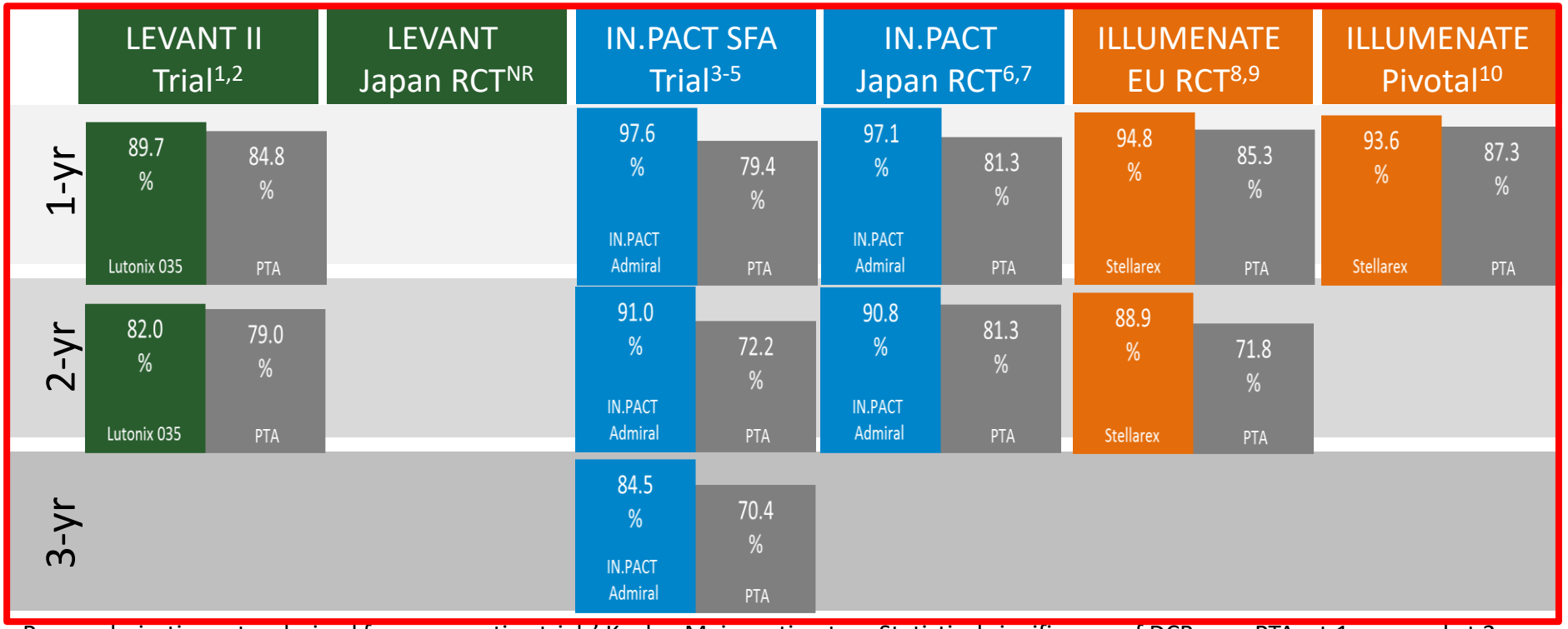


1. Rosenfield K, et al. NEJM:373:145-53 (2015).
2. Presented by Laurich C, SVS Chicago, USA 2015.
3. Proportion-based primary patency of 58.0% and 62.9% for Lutonix 035 and PTA, respectively, were provided in PMDA Report on Lutonix 035 Japan randomized trial, Tables 12 and 14, July 14, 2017; Kaplan Meier estimates are unavailable.
4. Tepe G, et al. Circ 131:495-502 (2015).
5. Laird J, et al. JACC 66:2329-38 (2015).
6. Schneider P, et al. Circ Cardiovasc Interv 11:e005891 (2018).
7. Iida O, et al. J Endovasc Ther 25:109-17 (2018).
8. Presented by Iida O, LINC Leipzig, Germany 2018.
9. Schroeder H, et al. Circ 135:2227-2236 (2017).
10. Presented by Brodmann M, VIVA Las Vegas, USA 2017.
11. Presented by Lyden S, TCT Washington DC, USA 2016.
12. Stellarex IFU Rev 07/2017 Table 7.

# DCB Multicenter RCTs

## Freedom from Revascularization

- LEVANT Studies: LEVANT II reported all TLR;[1,2] LEVANT Japan revascularization rate not reported (NR).
- IN.PACT Studies: TLR due to symptoms or drop of ABI of ≥20% or >0.15 compared to baseline[3-7]
- ILLUMENATE Studies: TLR due to an increase in RCC >1 category or deterioration in the ABI by >0.15 compared to baseline[8-10]



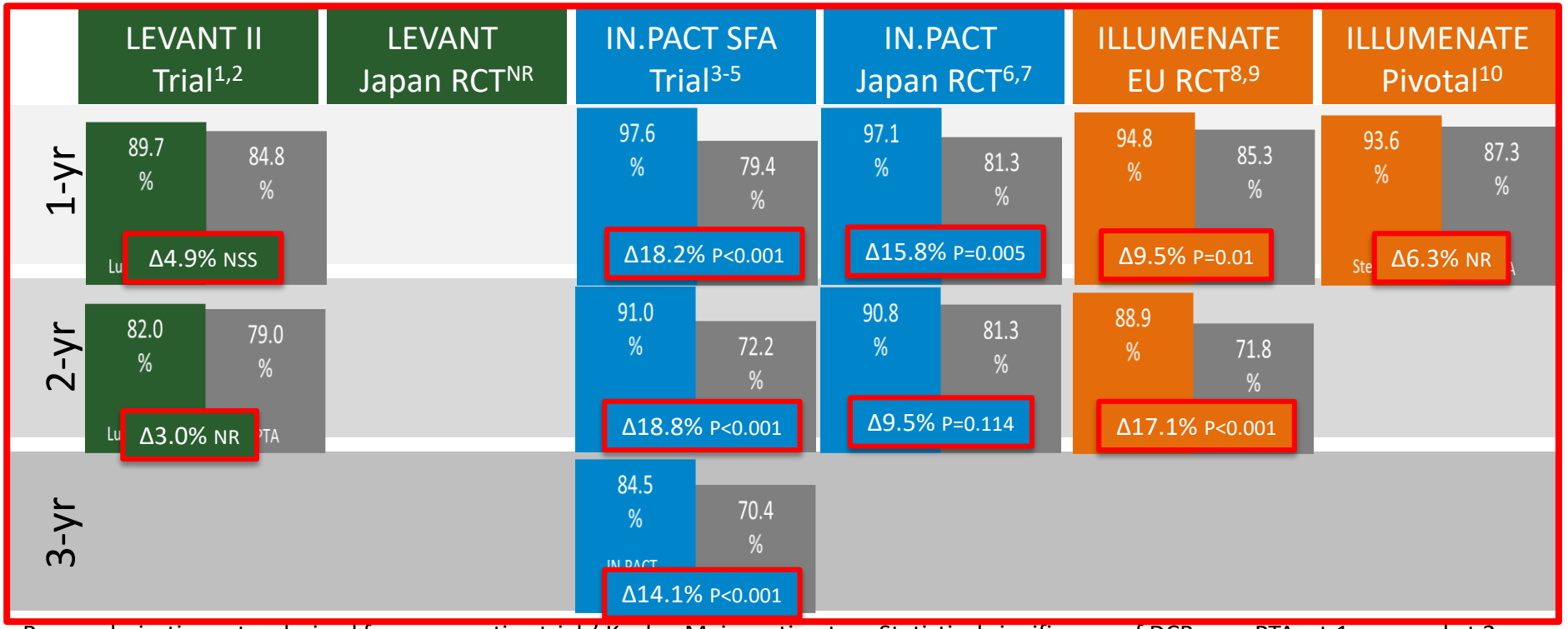

Revascularization rates derived from respective trials' Kaplan Meier estimates. Statistical significance of DCB over PTA at 1 year and at 2 years for ILLUMENATE Pivotal RCT and LEVANT II, respectively, not reported (NR). Difference in revascularization rate between DCB and PTA at 1 year in LEVANT II not statistically significant (NSS).


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. Schneider P, et al. Circ Cardiovasc Interv 11:e005891 (2018).
6. Iida O, et al. J Endovasc Ther 25:109-17 (2018).
7. Presented by Iida O, LINC Leipzig, Germany 2018.
8. Schroeder H, et al. Circ 135:2227-2236 (2017).
9. Presented by Brodmann M, VIVA Las Vegas, USA 2017.
10. Presented by Lyden S, TCT Washington DC, USA 2016.

# DCB Multicenter RCTs

## Freedom from Revascularization

- LEVANT Studies: LEVANT II reported all TLR;[1,2] LEVANT Japan revascularization rate not reported (NR).
- IN.PACT Studies: TLR due to symptoms or drop of ABI of ≥20% or >0.15 compared to baseline[3-7]
- ILLUMENATE Studies: TLR due to an increase in RCC >1 category or deterioration in the ABI by >0.15 compared to baseline[8-10]

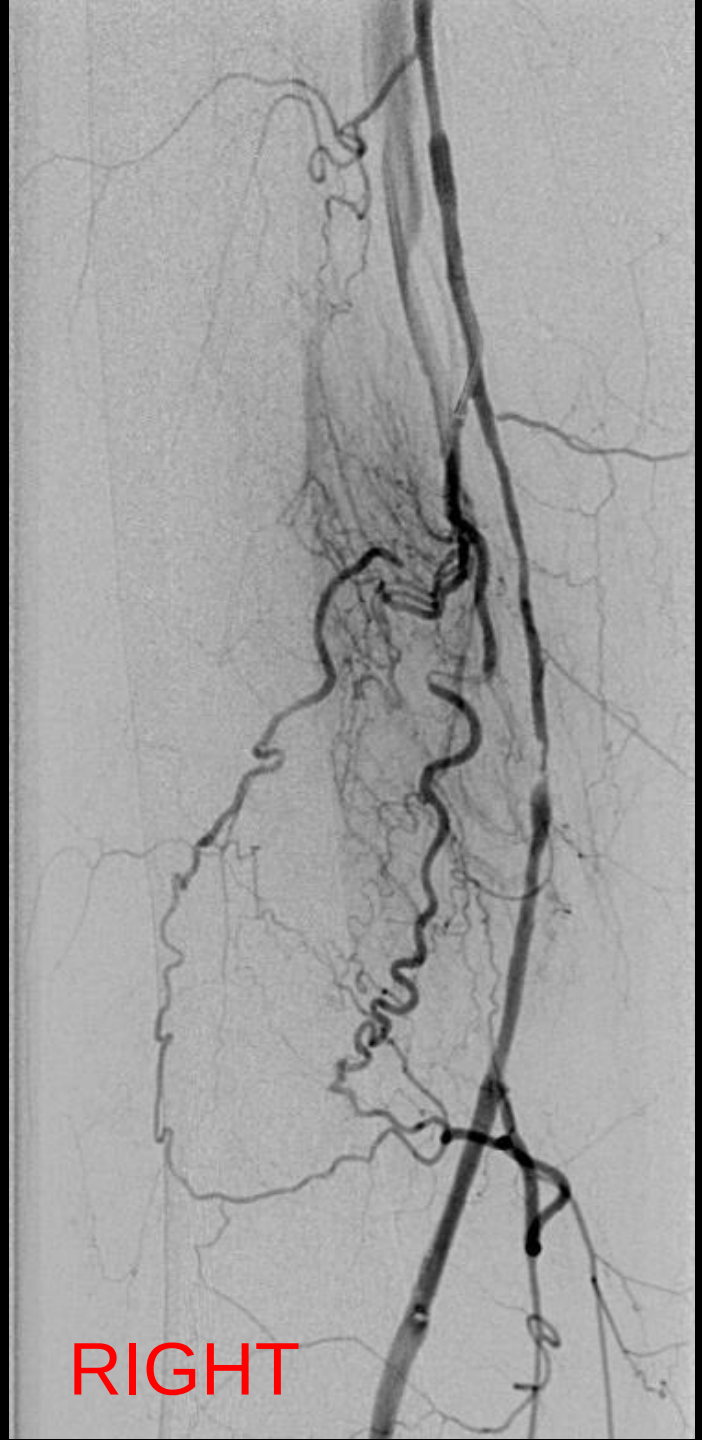


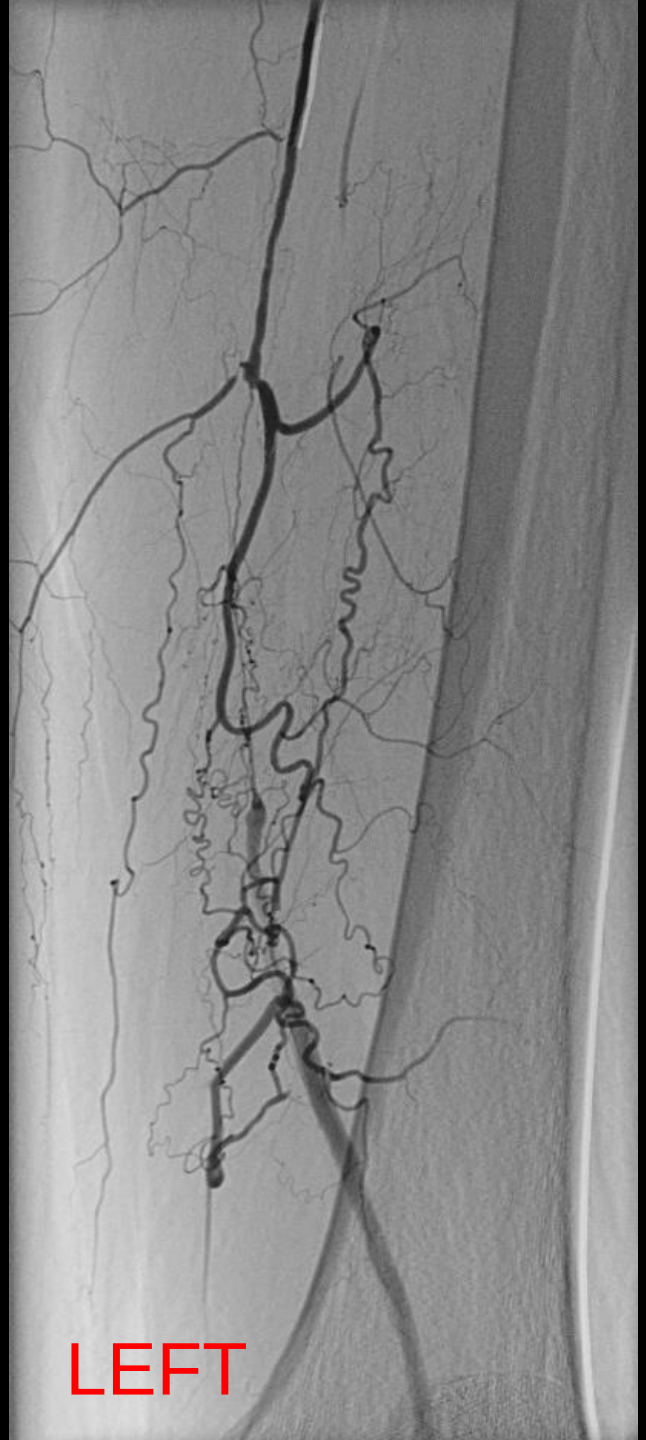

Revascularization rates derived from respective trials' Kaplan Meier estimates. Statistical significance of DCB over PTA at 1 year and at 2 years for ILLUMENATE Pivotal RCT and LEVANT II, respectively, not reported (NR). Difference in revascularization rate between DCB and PTA at 1 year in LEVANT II not statistically significant (NSS).


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. Schneider P, et al. Circ Cardiovasc Interv 11:e005891 (2018).
6. Iida O, et al. J Endovasc Ther 25:109-17 (2018).
7. Presented by Iida O, LINC Leipzig, Germany 2018.
8. Schroeder H, et al. Circ 135:2227-2236 (2017).
9. Presented by Brodmann M, VIVA Las Vegas, USA 2017.
10. Presented by Lyden S, TCT Washington DC, USA 2016.

# Case

- 63-year-old male
- Smoker, old MI, non-diabetic
- Short-distance claudication (RIII)
- Bilateral symptoms
- Right ABPI: 0.7 - Left ABPI: 0.5
- Statin 20mg OD, Aspirin 75mg OD
- Post-procedure Clopidogrel 75mg OD for 6 mon


RIGHT

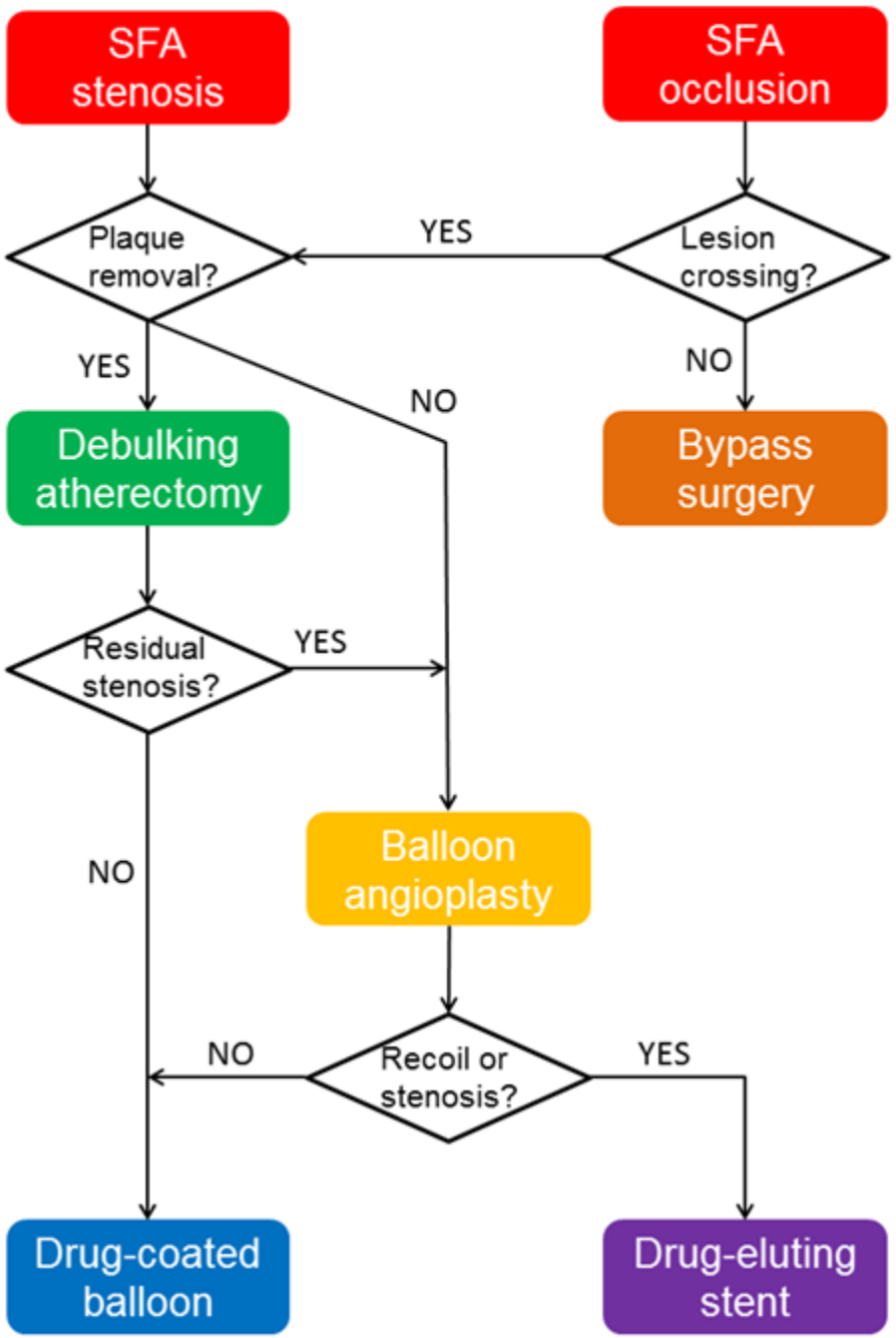

LEFT

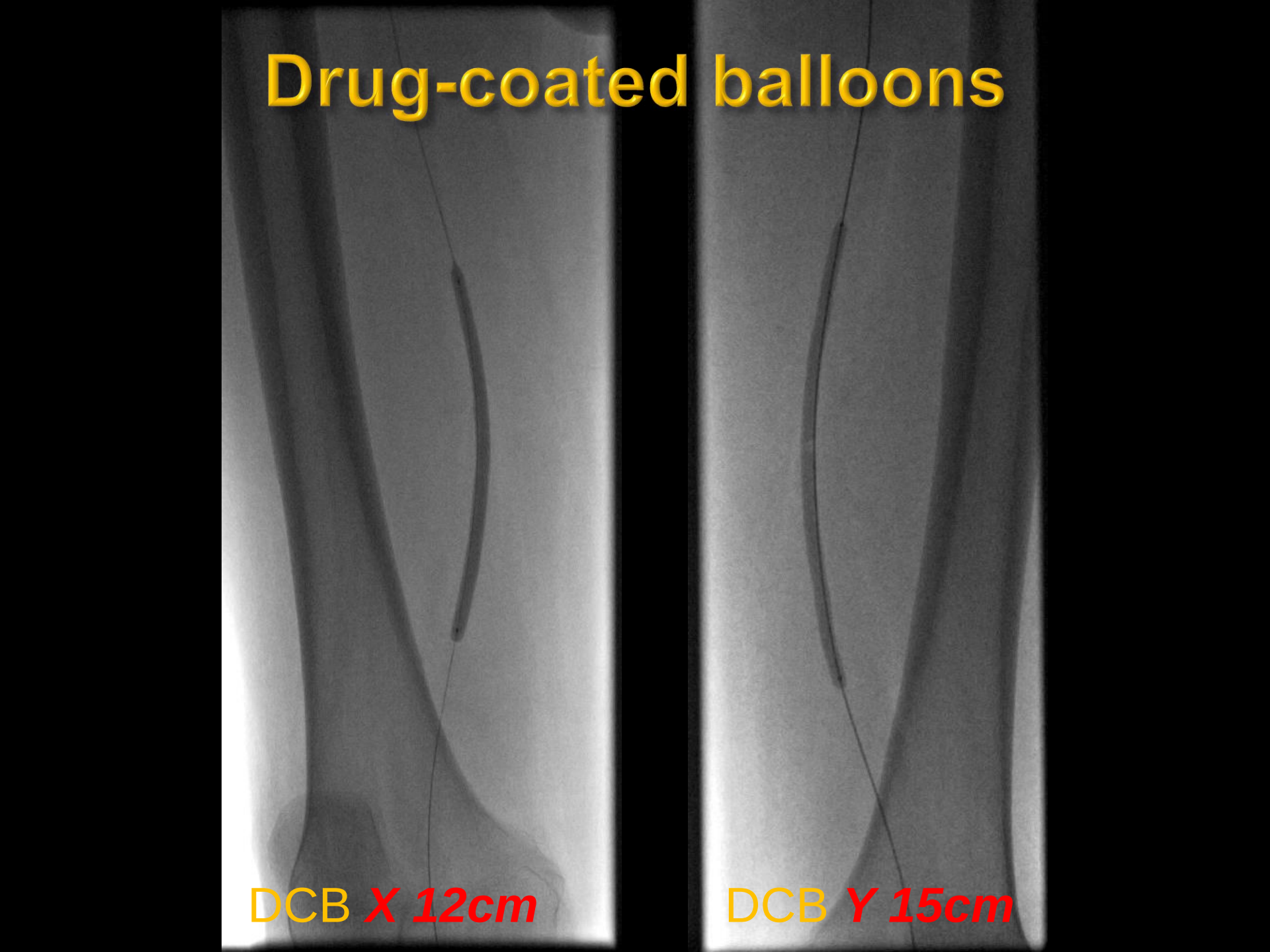
Access & crossing

Lesion preparation

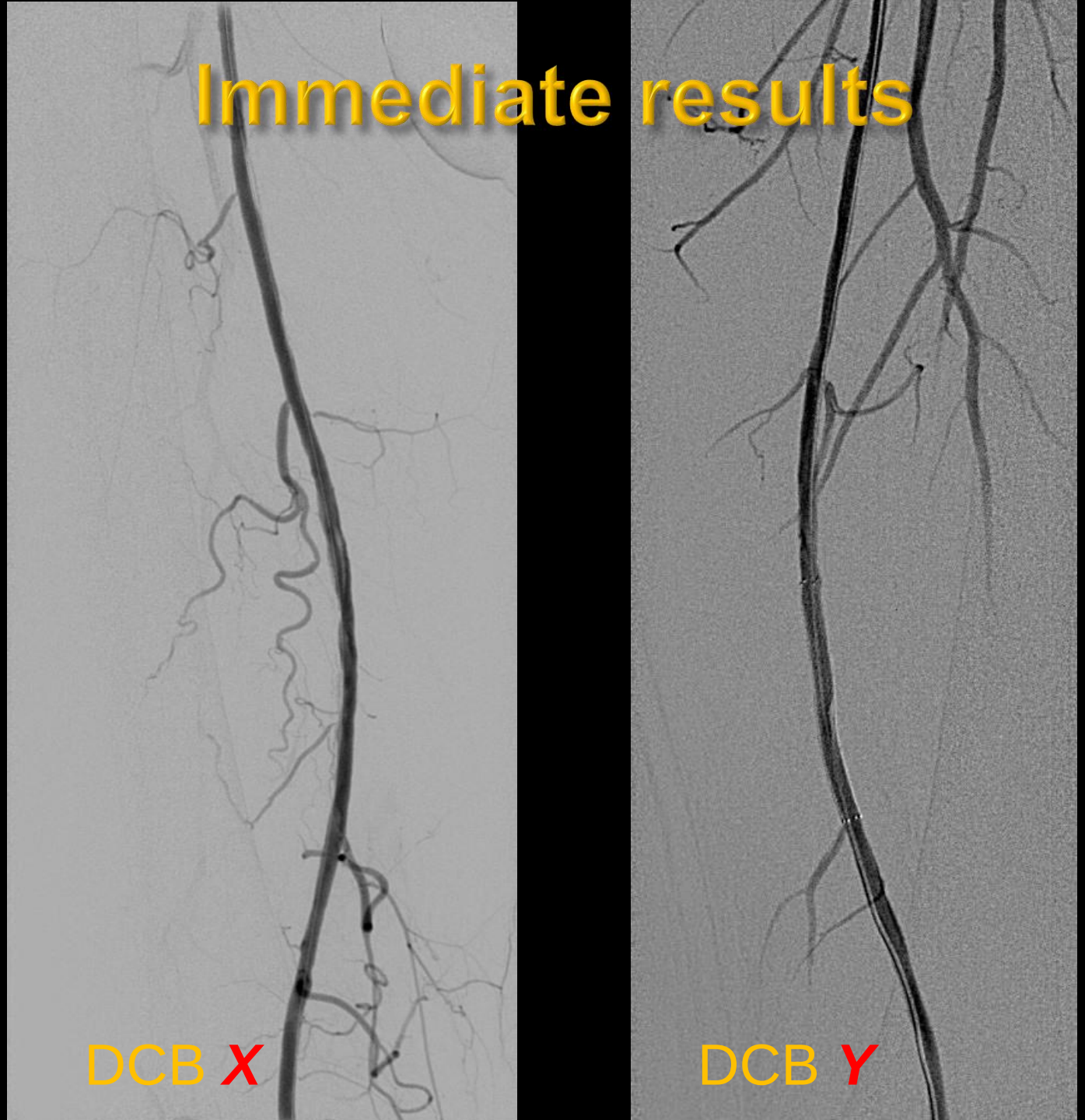
Drug application

(Stent or scaffold?)

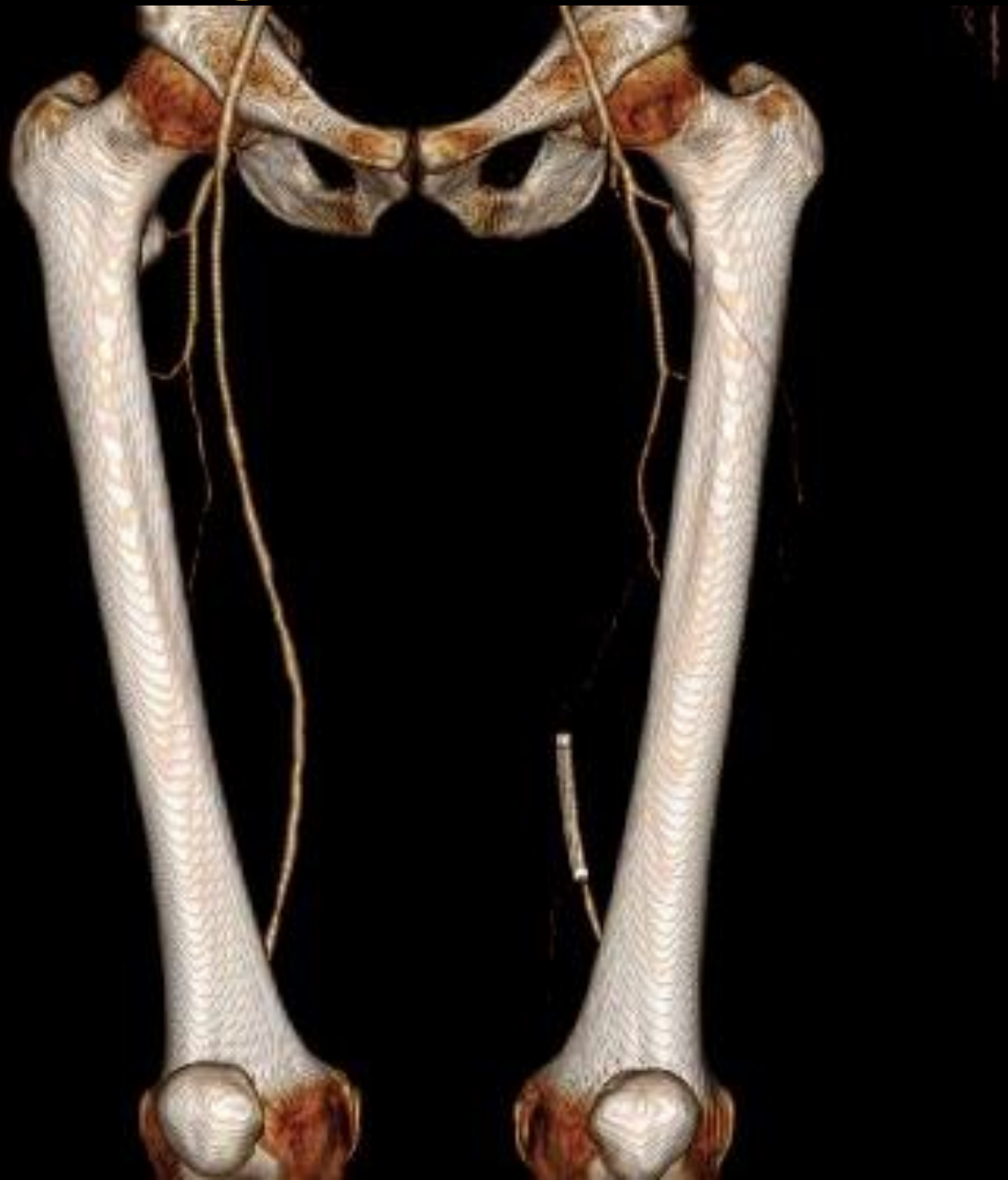



Drug-coated balloons
DCB X 12cm
DCB Y 15cm

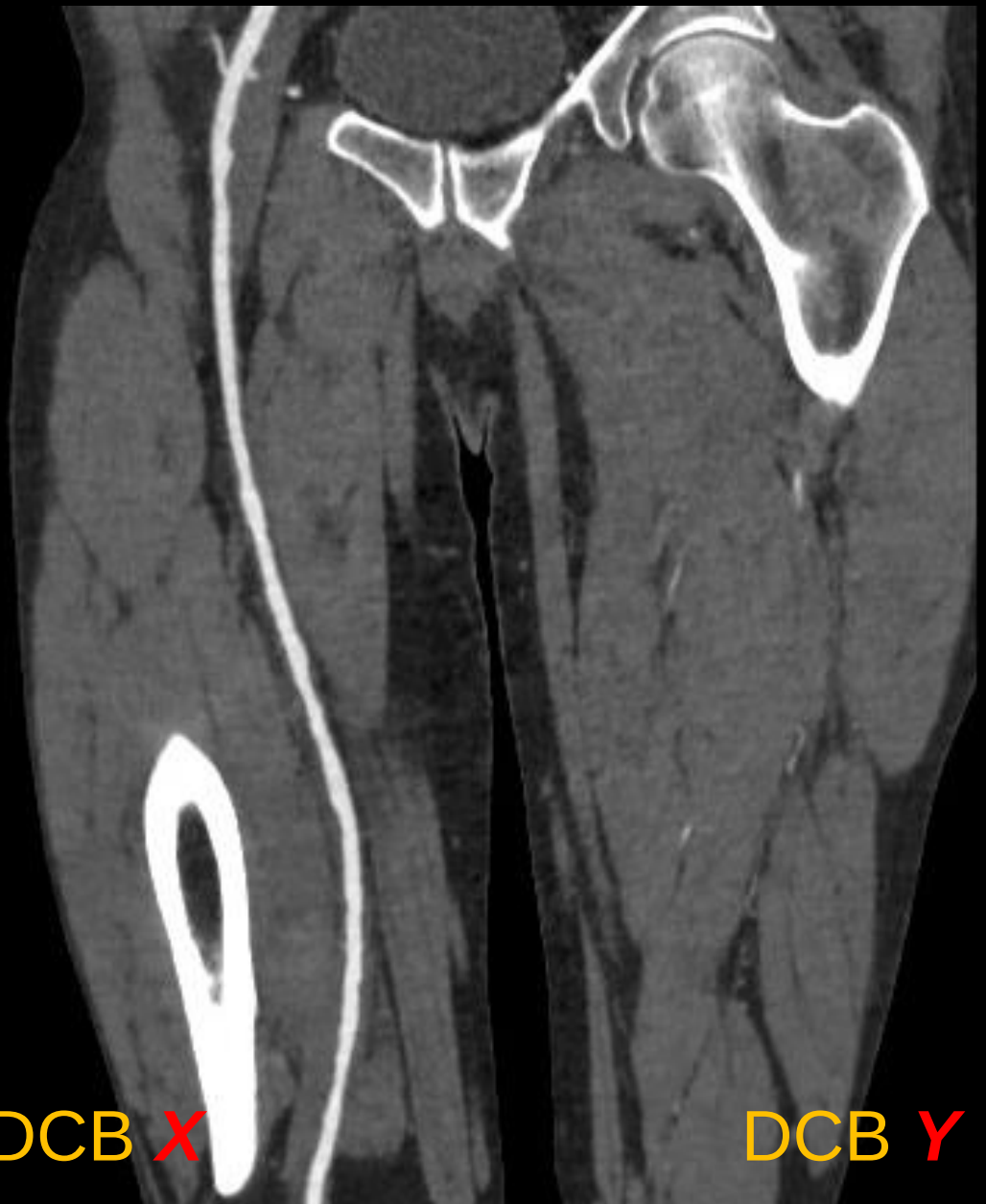
# Immediate results



# 2 years later

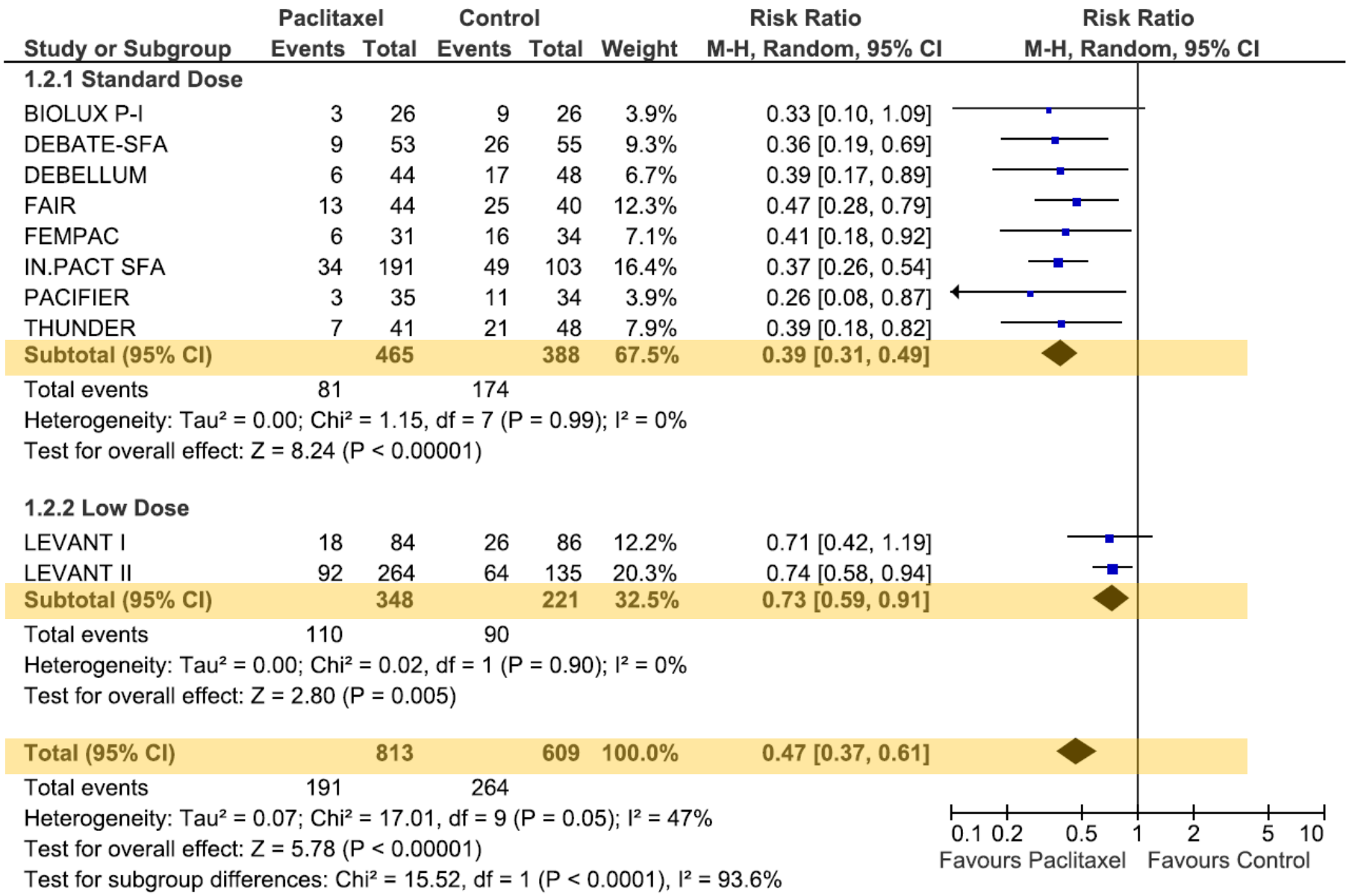


# 2-year FUP



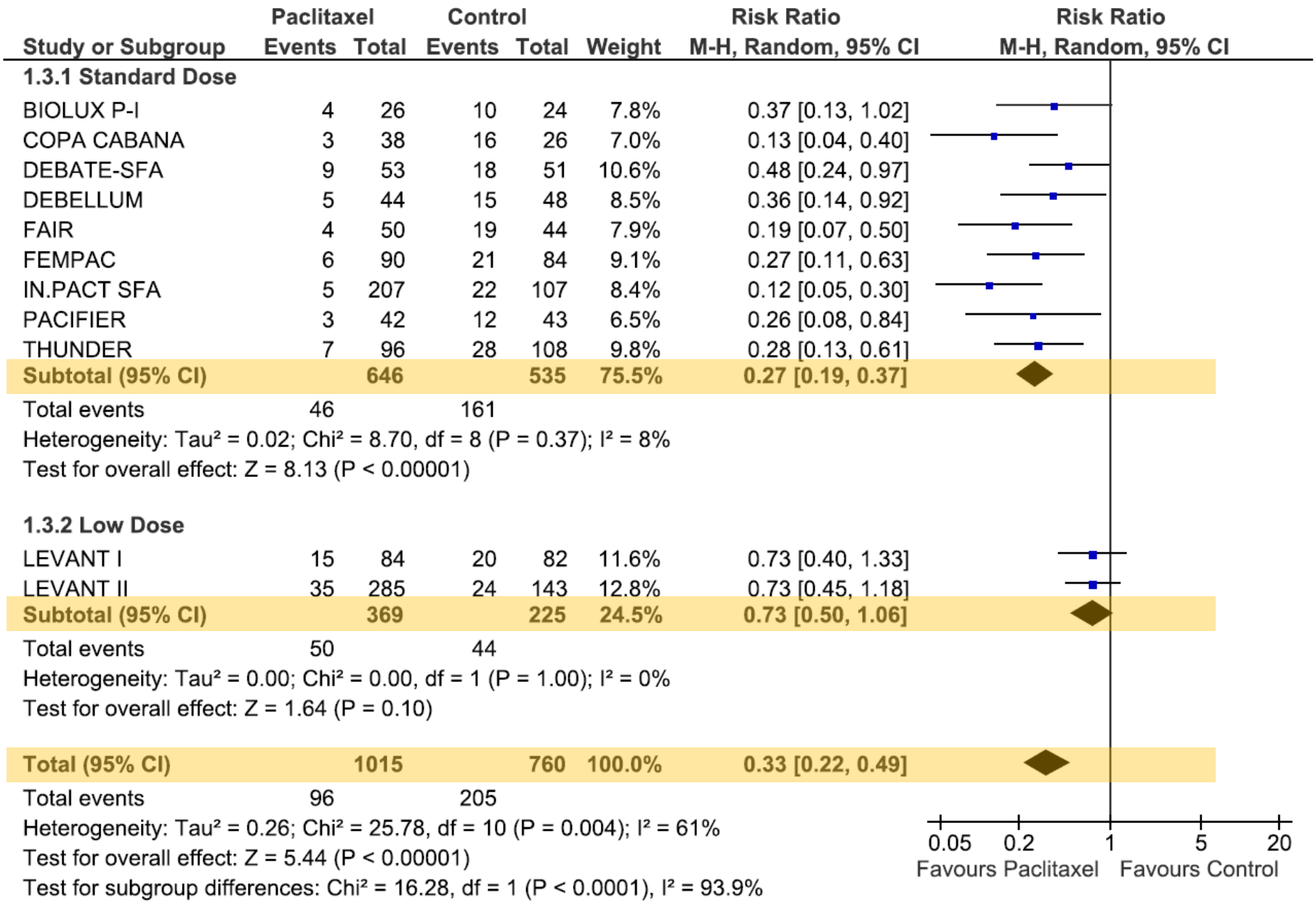
DCB *X*

DCB *Y*




# Binary vascular restenosis

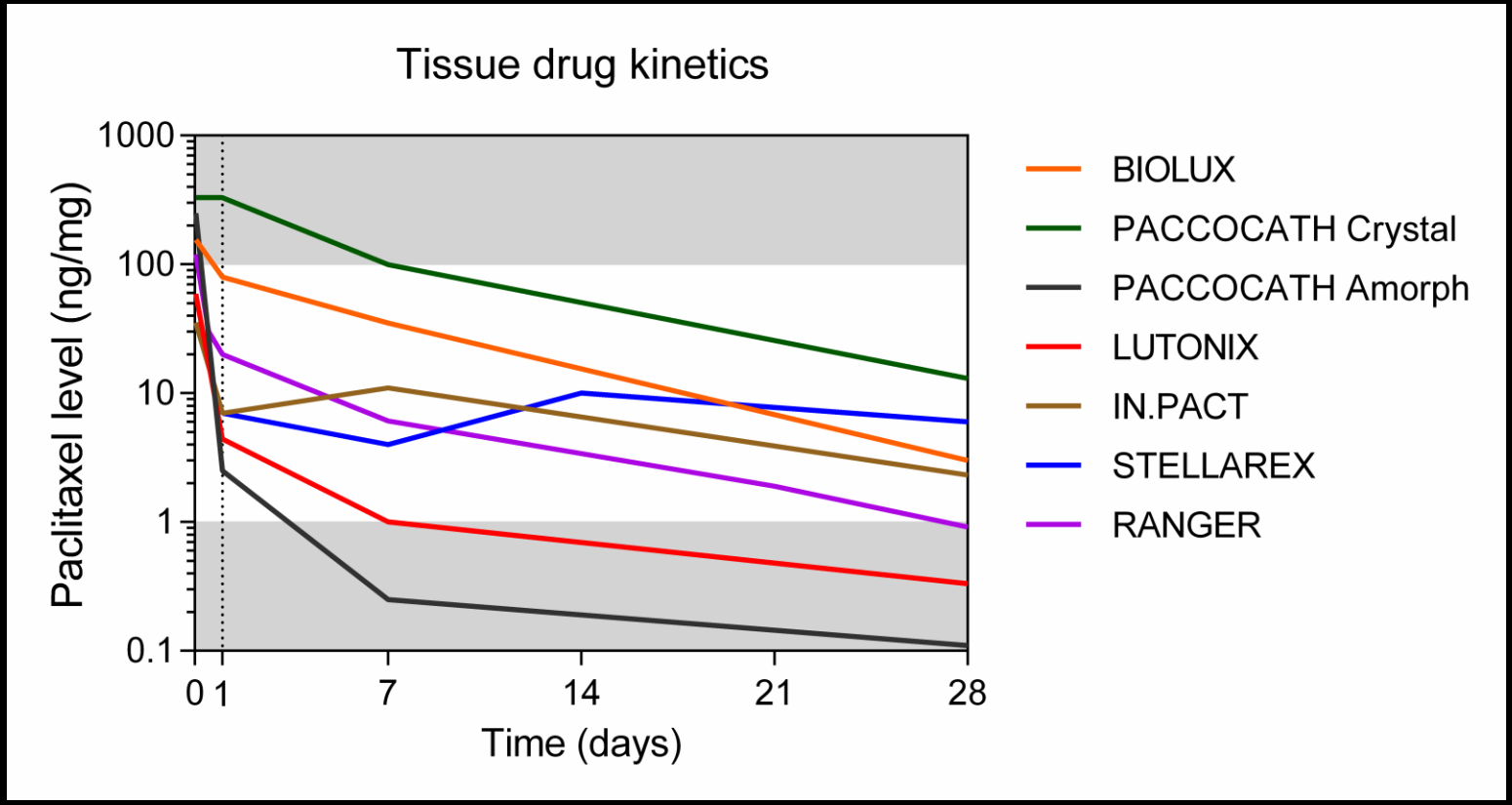
*JEVT 2016 Katsanos K, et al.*




# Target lesion revascularization

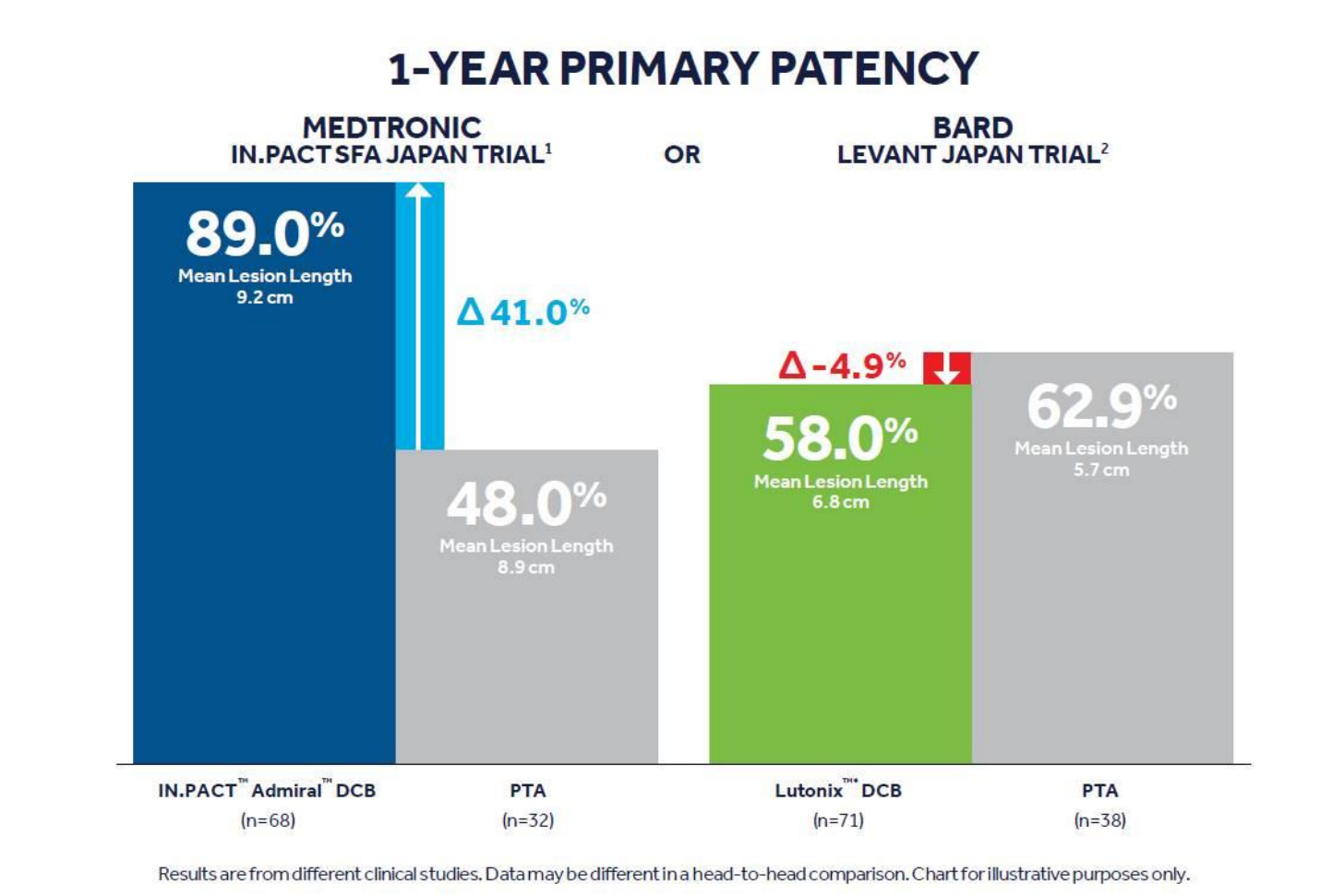
*JEVT 2016 Katsanos K, et al.*

# DCB tissue drug kinetics



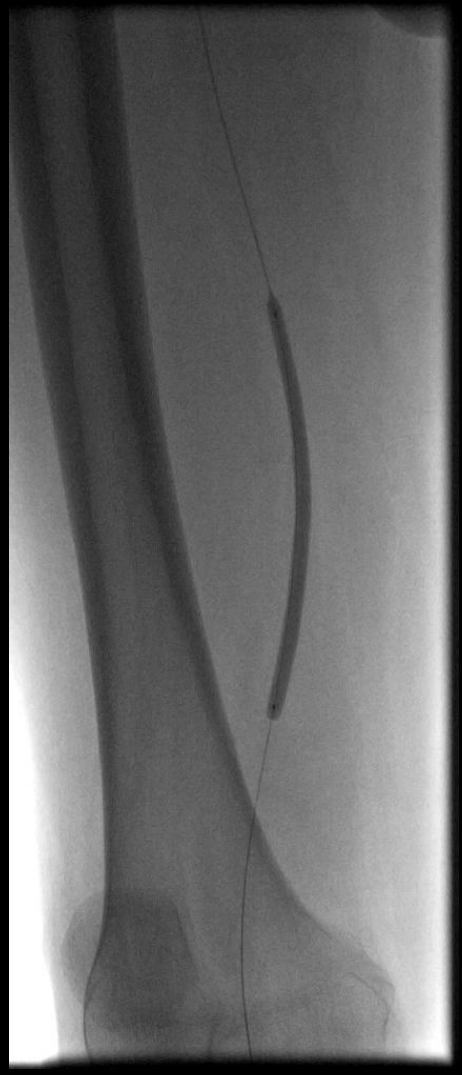

*Compiled commercial data Sept 2015*

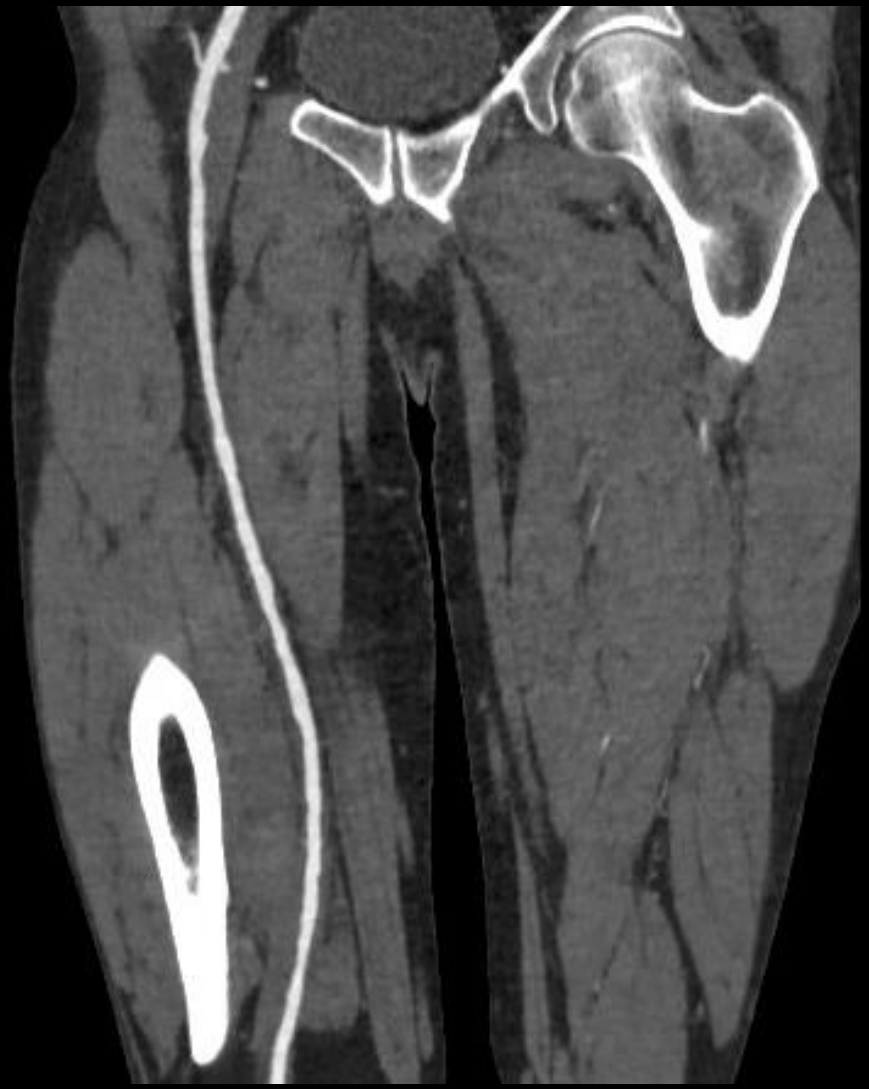
# JAPAN RCTs

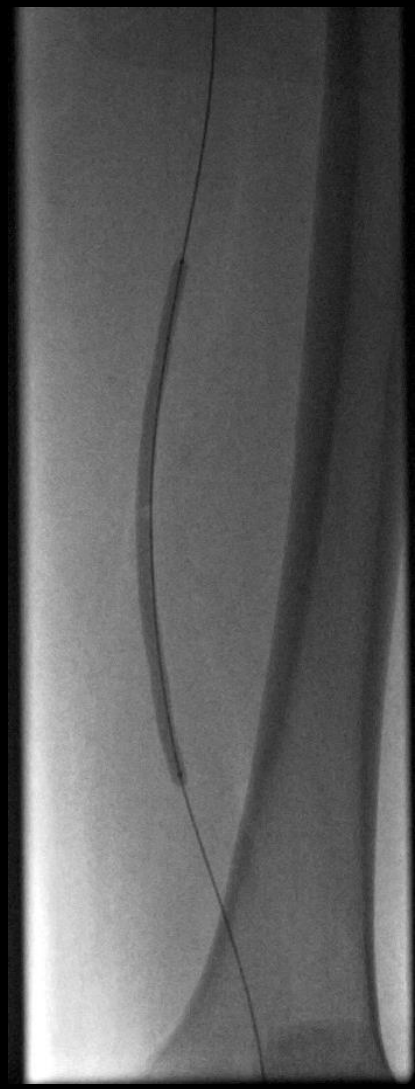



*1 - Medtronic data on file: 1-year Outcomes: Iida et al, JEVT, .25 (1) 109-117.*
*2 - Bard Data: 1-year outcomes from the LEVANT Japan Trial, PMDA Website (http://www.pmda.go.jp/medical_devices/2017/M20170830001/780045000_22900BZX00252000_A100_1.pdf)*

# Drug-coated balloons







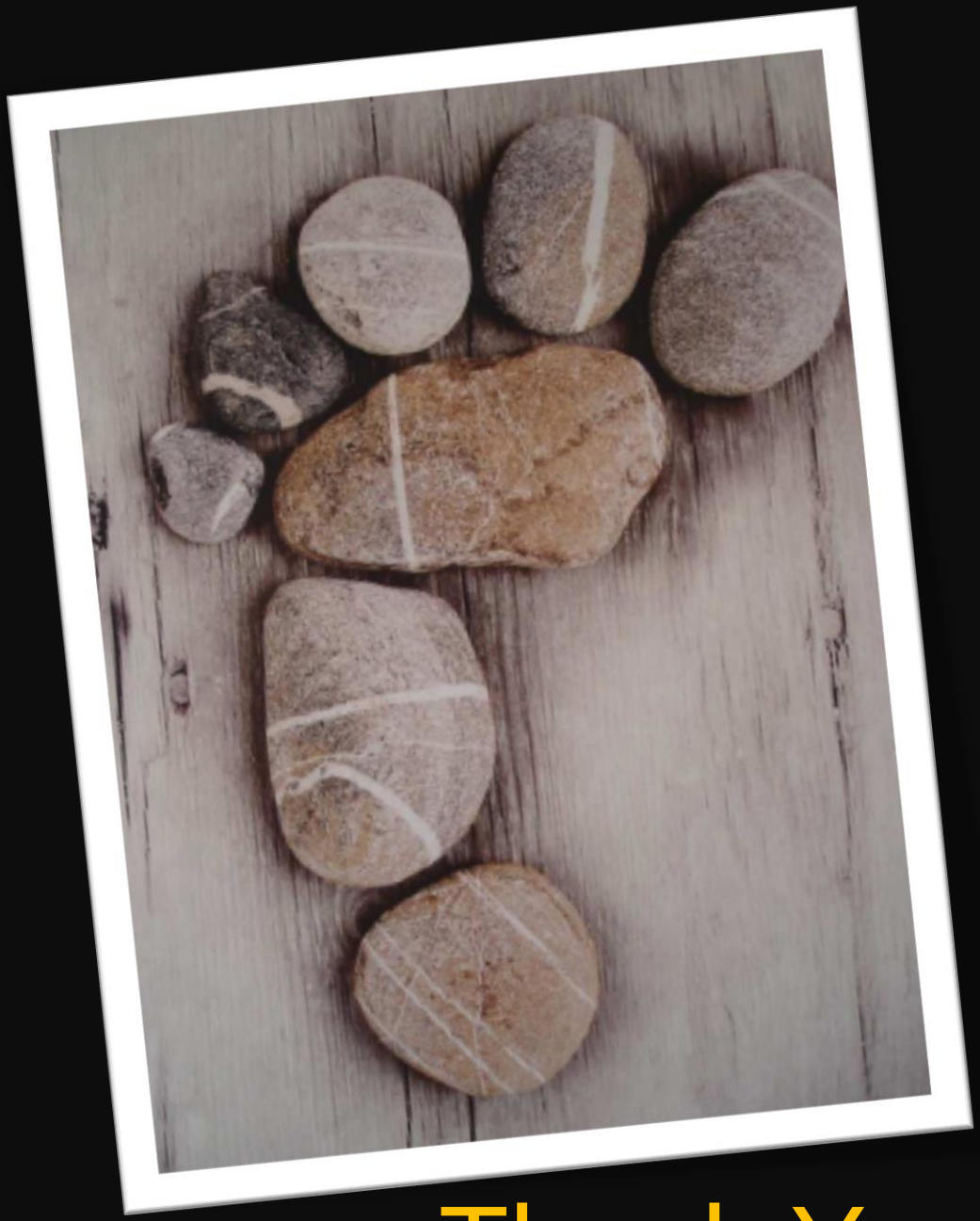
IN.PACT

2 years FUP

LUTONIX

# DCB are not all the same

- Clinical results may depend on vessel wall bioavailability of paclitaxel
- Clinical results may depend on the pharmacokinetic profile of individual devices



Thank You

# Femoropopliteal outcomes

**Table 1** Systematic review of femoropopliteal outcomes

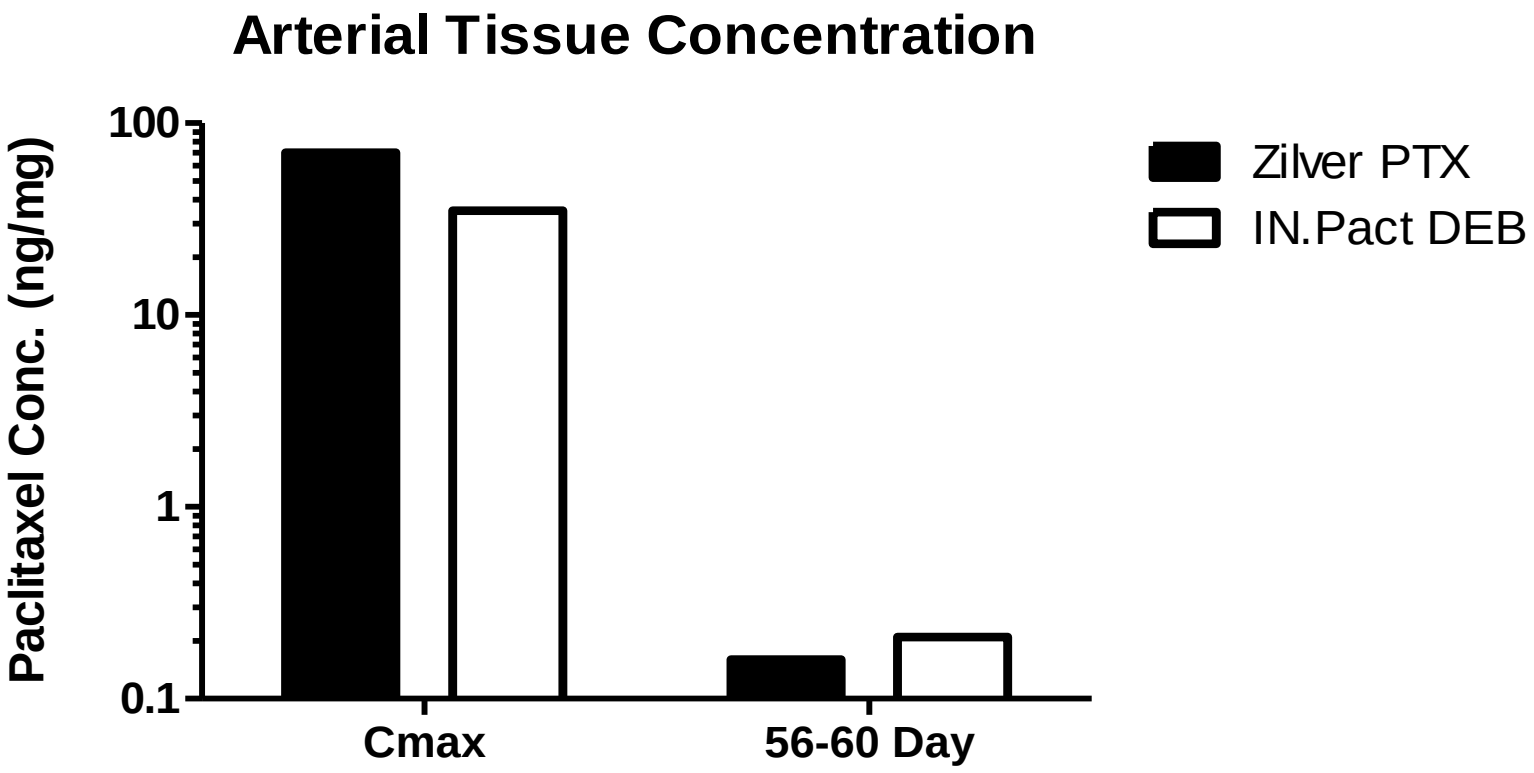
| Recanalization technology | Lesion length (range, cm) | Technical success (%; 95% CI) | Primary patency at 1 y [%; 95% CI] |
|---|---|---|---|
| Balloon angioplasty | 5–12 | 69 (59–78) | 57 (42–71) |
| Drug-coated balloons | 5–8 | | 81 (67–91)[a] |
| Nitinol stents | 5–18 | 94 (91–97) | 66 (60–72) |
| Drug-eluting stents | 5–10 | | 83 (77–90) |
| Covered stents | 11–26 | | 68 (60–75) |

Source: Adapted from Katsanos et al.[7]

Notes: Pooled analysis of control and treatment arms of major randomized trials, major single-arm prospective studies and large ($n > 50$ limbs) cohort studies (ABSOLUTE, FAST, RESILIENT, ASTRON, SIROCCO, STRIDES, ZILVER-PTX, THUNDER, FEMPAC, LEVANT I, PACIFIER, VIABAHN, and VIBRANT trials). Pooled proportional outcomes were calculated with a random effects (DerSimonian–Laird) meta-analytic model.

[a]Reported primary patency rates are at 1 year with the exception of drug-coated balloons (6-month outcomes) and are based on the 50 or 70% restenosis threshold evaluable with either Duplex ultrasound or quantitative vascular angiography.

# Tissue paclitaxel kinetics




**Paclitaxel concentrations in arterial tissue are comparable with regard to $C_{max}$ values and concentrations at 2 months post-treatment**

*FDA Zilver Panel Meeting Summary 2012*

# Limitations of SFA RCTs so far

| Variable | ZILVER-PTX | DCB | Notes |
|---|---|---|---|
| CLI | 10% | 4-6% | DEBELLUM 36% |
| CTOs | 30% | 13-41% | ISR excluded |
| Length | 5.4cm | 4.0-8.1cm | Mostly TASC A & B |
| Stenting | 100% | Very low | IN.PACT SFA: 7.3 vs 11.6% |

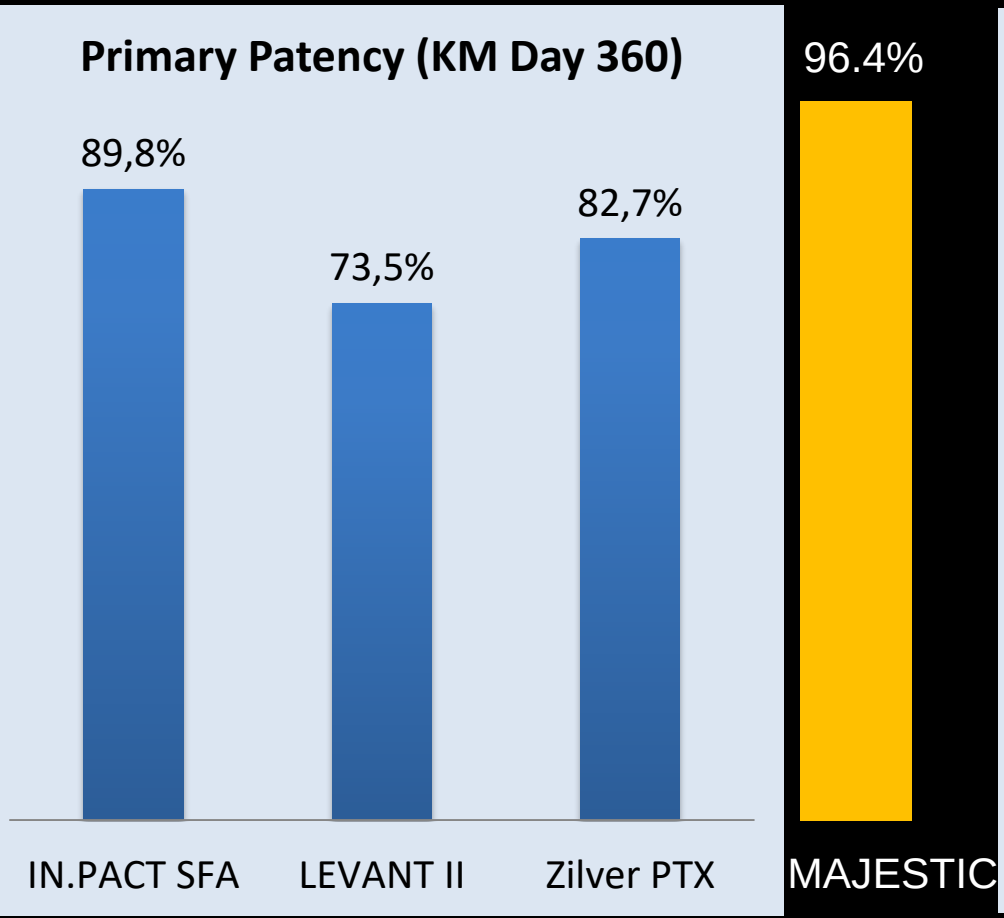
*DO NOT apply in long or complex SFA lesions !*

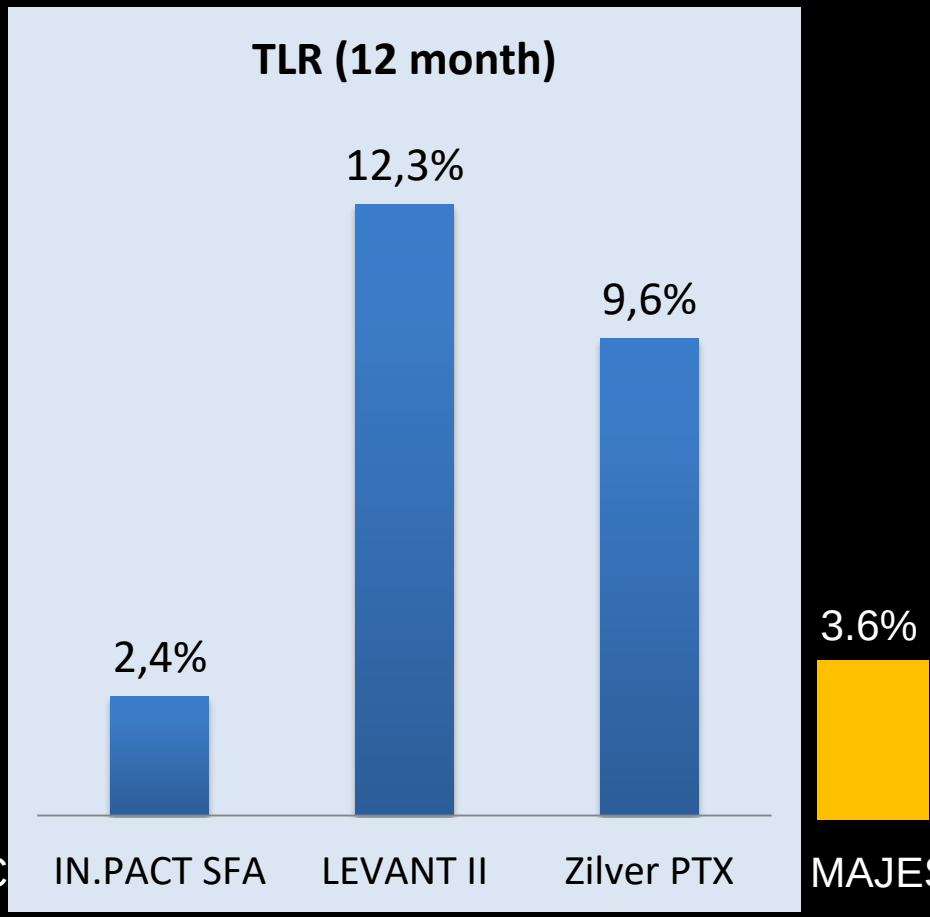
# Major RCTs

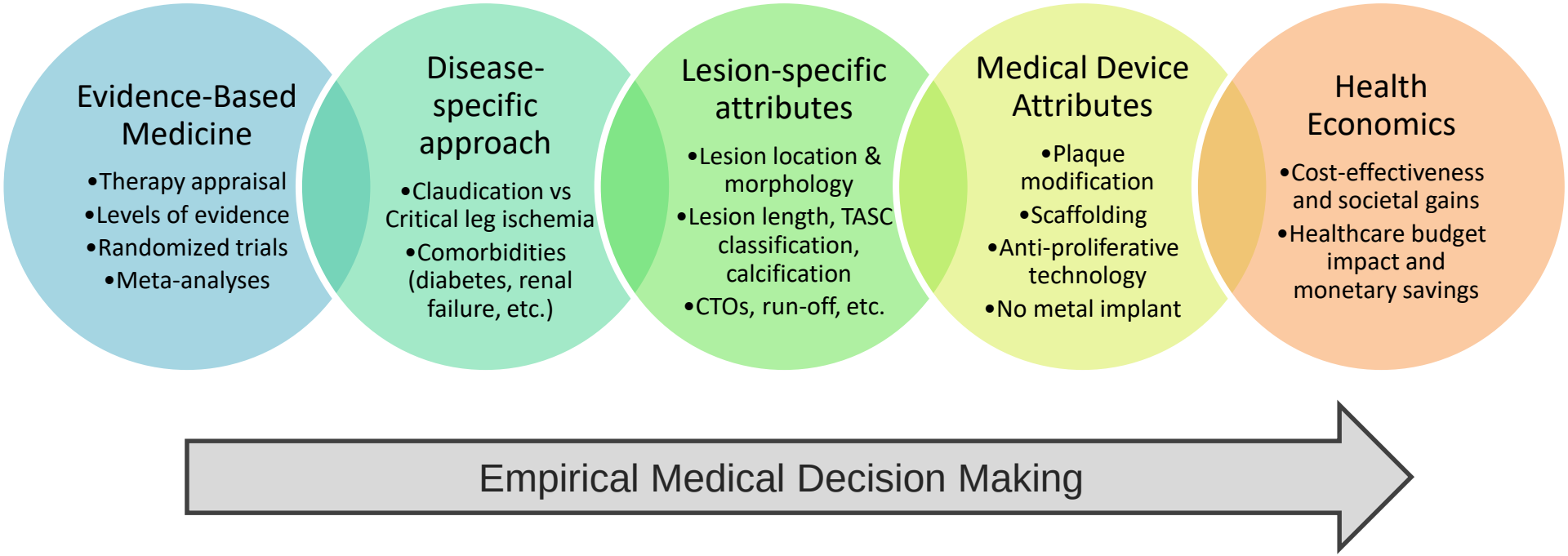
| | IN.PACT SFA | LEVANT II | Zilver PTX |
|---|---|---|---|
| Design | 2-phase multicenter, single blind, 2:1 RCT | multicenter, single blind, 2:1 RCT | multicenter, 1:1 RCT |
| # Patients | 331<br>EU, US | 476<br>EU, US | 479<br>US, Japan, Germany |
| Randomization | PTA | PTA | 1° PTA<br>2° BMS<br>(for suboptimal PTA) |

| | **IN.PACT SFA**<br>*IN.PACT Arm* | **LEVANT II**<br>*Lutonix Arm* | **Zilver PTX**<br>*Zilver PTX Arm* |
|---|---|---|---|
| Age (y) | 67.5 ± 9.5 | 67.8 ± 10 | 67.9 ± 9.6 |
| Male Gender | 65% | 61.1% | 65.7% |
| Diabetes | 40.5% | 43.4% | 49.6% |
| Lesion Length (cm) | 8.94 ± 4.89 | 6.27 ± 4.14 | 6.64 ± 3.89 |
| Total Occlusions | 25.8% | 20.6% | 32.8% |
| Severe Calcification* | 8.1% | 10.4% | 37.3% |
| RVD (mm) | 4.647 ± 0.841 | 4.8 ± 0.8 | 5.1 ± 0.9 |
| Diameter Stenosis(%) | 81.1 ± 15.5 | 80.5 ± 14.8 | 79.8 ± 17.0 |

# Major RCTs


Primary Patency (KM Day 360)
89,8%
73,5%
82,7%
96.4%
IN.PACT SFA
LEVANT II
Zilver PTX
MAJESTIC


TLR (12 month)
2,4%
12,3%
9,6%
3.6%
IN.PACT SFA
LEVANT II
Zilver PTX
MAJE


Evidence-Based Medicine
•Therapy appraisal
•Levels of evidence
•Randomized trials
•Meta-analyses
Disease-specific approach
•Claudication vs Critical leg ischemia
•Comorbidities (diabetes, renal failure, etc.)
Lesion-specific attributes
•Lesion location & morphology
•Lesion length, TASC classification, calcification
•CTOs, run-off, etc.
Medical Device Attributes
•Plaque modification
•Scaffolding
•Anti-proliferative technology
•No metal implant
Health Economics
•Cost-effectiveness and societal gains
•Healthcare budget impact and monetary savings
Empirical Medical Decision Making