# IN.PACT BTK Randomized Study: 9-Month Primary Outcomes

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# DISCLOSURE

- Speaker name: Francesco Liistro
- I have the following potential conflicts of interest to report:
- Consulting: Medtronic, ACOTEC Ltd, Biotronic, Boston Scientific
- 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

1. The insight gained from previous below-the-knee (BTK) drug-coated balloon (DCB) studies, including IN.PACT DEEP, provided an opportunity to affect a new balloon and BTK study design.  As a result, the novel IN.PACT BTK Study was initiated.
2. Through years of research and development, a new .014 BTK DCB balloon consistent with the 3.5 µg/mm$^2$ drug formulation used in the IN.PACT SFA, Global, and AV trials, was utilized.
3. Rigorous procedural and DUS requirements for optimal vessel results before enrollment were included to more accurately assess the effect of drug.
4. Extensive angiographic sub-segmental measurements of each target lesion were performed to improve late lumen loss assessment.

# IN.PACT BTK STUDY*
## OVERVIEW

Purpose: To assess the safety and effectiveness of the IN.PACT 014 paclitaxel-coated balloon (DCB) versus conventional PTA for the treatment of CLI patients with chronic total occlusions (CTOs) in the infrapopliteal arteries

- Prospective, multicenter, randomized (1:1) feasibility study
- Independent Duplex Ultrasound Core Lab (DUS)[1], Angiographic Core Lab[2], Data Safety Monitoring Board and Clinical Events Committee (CEC)[3]
- 50 CLI patients with infrapopliteal CTOs enrolled at 9 sites across 5 European Countries and followed through 36 months[4]
- No formal hypothesis test is specified for this feasibility study. Descriptive statistics will be reported.

*Sponsored by Medtronic plc

1. Vascore DUS Core Laboratory, Boston, MA, US
2. Beth Israel Deaconess Medical Center, Boston, MA, US
3. Data Safety Monitoring Board and Clinical Events Committee services provided by Syntactx, Belgium
4. Sponsor intends to extend follow-up through 60 months

# IN.PACT BTK STUDY
## KEY ELIGIBILITY CRITERIA

### Inclusion

- Rutherford Class 4 and 5
- Infrapopliteal arteries above the ankle
- Single or multiple total occlusions with total lesion length ≥ 40 mm
- Infection grade 0-2 and ischemia grade 2-3 according to WIfI
- RVD 2-4 mm
- Evidence of adequate distal run-off through the foot

### Exclusion

- Planned target limb amputation
- Inflow impaired or non re-established
- Prior stents(s) or bypass surgery in the target vessel
- Previous DCB within 6 months prior to procedure
- Infection grade 3 and ischemia grade 0-1 according to WIfI
- Documented active osteomyelitis, excluding the phalanges

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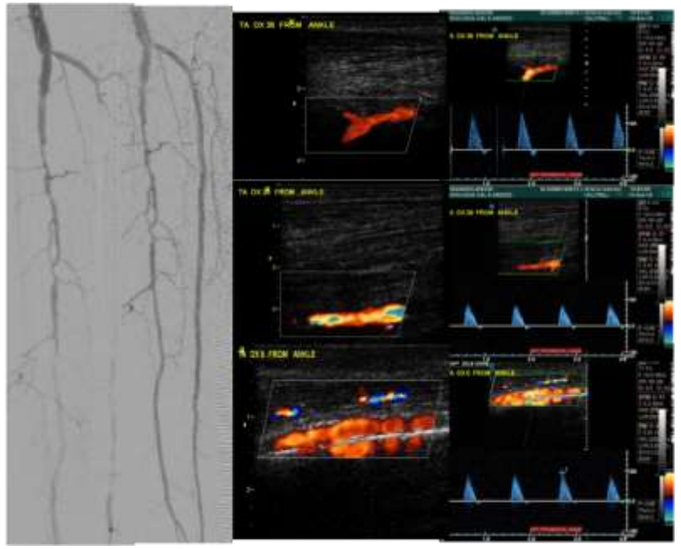
**Most challenging lesions were purposefully included**

# IN.PACT BTK STUDY
## Eligibility Before Enrollment and Randomization

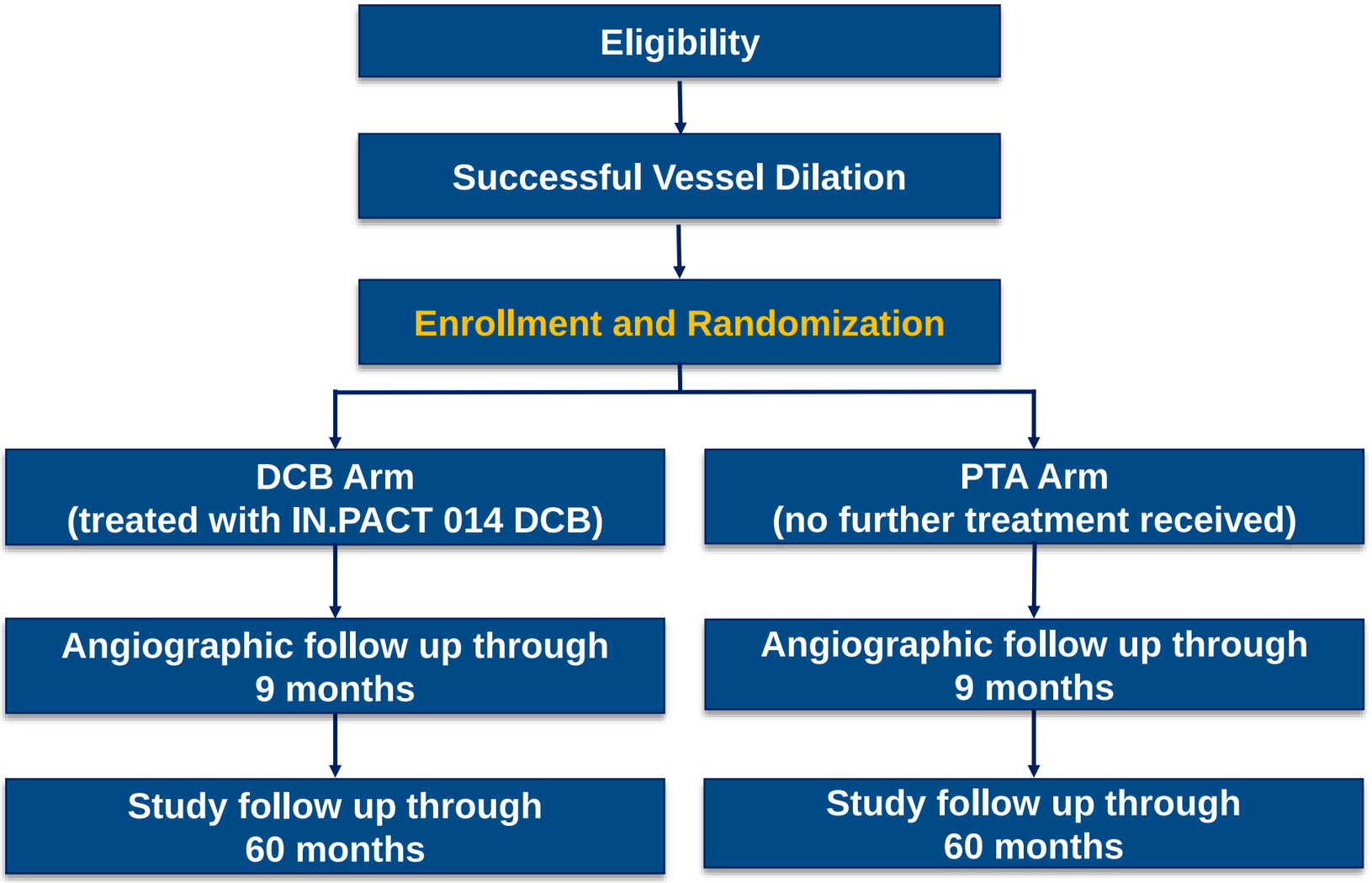
**Eligibility**

**Successful Vessel Dilation Criteria**

Defined as ≤30% residual stenosis documented by angiographic visual estimate and functional DUS assessment required (biphasic or triphasic wave signal with rapid take-off distal to the target lesion)



# IN.PACT BTK STUDY
## ARCHITECTURE



# IN.PACT BTK STUDY
## ENDPOINTS

| | |
|---|---|
| **Effectiveness Endpoint** | ▪ Late Lumen Loss* (LLL) 9 months after the index procedure |
| **Safety Endpoint** | ▪ Composite of 30-day freedom from device- and procedure-related mortality and freedom from major target limb amputation through 9-months and freedom from clinically-driven TLR through 9-months |

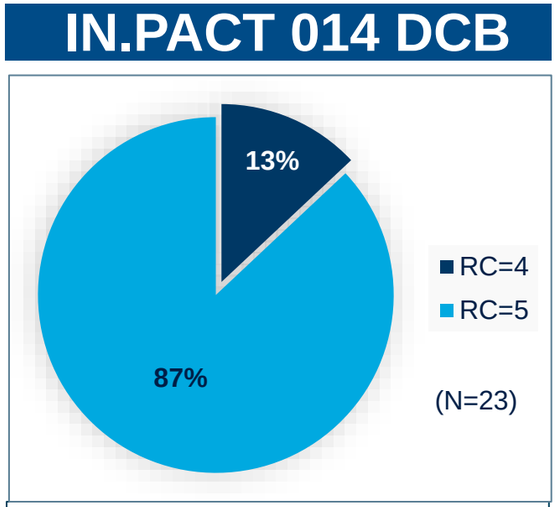
***Prospectively defined by the Angiographic Core Lab to use classic and subsegmental LLL measurement methods**

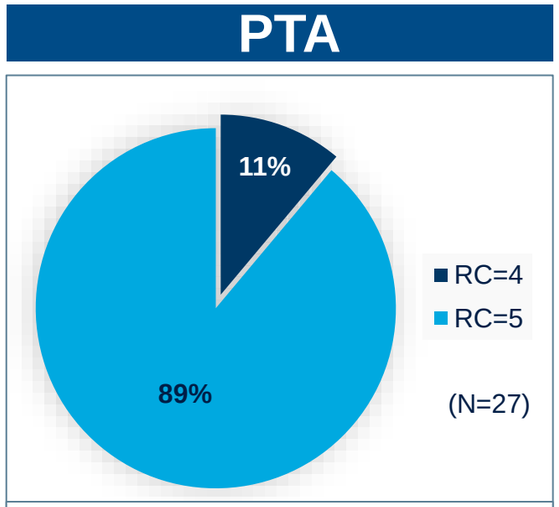
# IN.PACT BTK STUDY
## BASELINE CLINICAL CHARACTERISTICS

| | IN.PACT 014 DCB (N=23 Subjects) | PTA (N=27 Subjects) | P-value |
|---|---|---|---|
| Age (years) mean ± SD | 73.1 ± 7.4 | 69.6 ± 9.4 | 0.107 |
| Male % (n) | 82.6% (19/23) | 74.1% (20/27) | 0.515 |
| Obesity (BMI ≥ 30 kg/m$^2$) % (n) | 22.7% (5/22) | 26.9% (7/26) | 1.000 |
| Hypertension % (n) | 82.6% (19/23) | 77.8% (21/27) | 0.736 |
| Hyperlipidemia % (n) | 72.7% (16/22) | 80.0% (20/25) | 0.732 |
| **Diabetes Mellitus %** (n) | **73.9% (17/23)** | **96.3% (26/27)** | **0.039** |
| Insulin Treated % (n) | 39.1% (9/23) | 74.1% (20/27) | 0.021 |
| Current smoker % (n) | 17.4% (4/23) | 11.5% (3/26) | 0.692 |
| Ischemic Heart Disease % (n) | 43.5% (10/23) | 34.6% (9/26) | 0.569 |
| Bilateral PAD % (n) | 54.5% (12/22) | 63.6% (14/22) | 0.760 |
| Previous Target Limb Peripheral Revascularization % (n) | 30.4% (7/23) | 33.3% (9/27) | 1.000 |
| Previous Target Limb Minor Amputation % (n) | 13.0% (3/23) | 40.7% (11/27) | 0.056 |

# IN.PACT BTK STUDY
## BASELINE CLINICAL CHARACTERISTICS

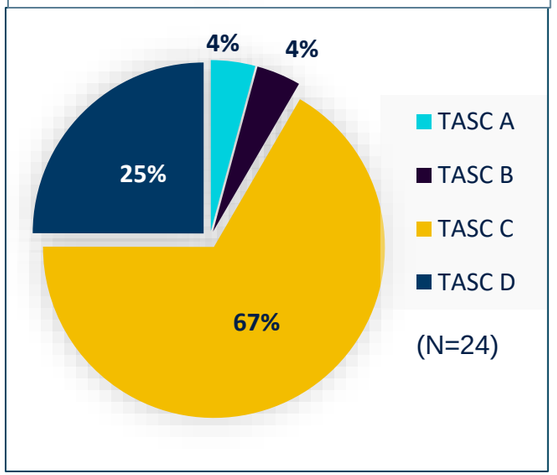
**Rutherford Category[1]**

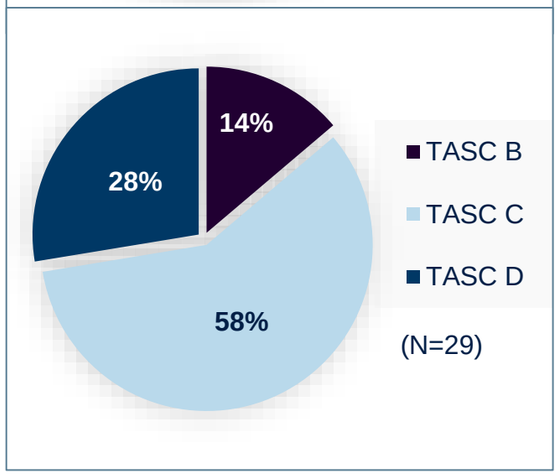



**P- value = 1.000**

**TASC II[2]**




**P- value = 0.504**

1. Site reported
2. Core lab reported

# IN.PACT BTK STUDY
## BASELINE LESION CHARACTERISTICS

| Lesion Characteristics[1] | IN.PACT 014 DCB (N=23 Subjects N=24 Lesions) | PTA (N=27 Subjects N=29 Lesions) | P-value |
|---|---|---|---|
| Inflow in the Target Vessel < 30% RS (subject level), %(n) | 90.0% (18/20) | 87.5% (21/24) | 1.000 |
| Lesion Length (mm ± SD) | 215.41 ± 83.81 | 218.19 ± 80.43 | 0.806 |
| Total Occluded Lesion Length (mm ± SD) | 159.00 ± 84.66 | 136.43 ± 72.82 | 0.353 |
| Diameter Stenosis (% ± SD) | 97.59% ± 6.69 | 96.33% ± 8.64 | 0.473 |
| Reference Vessel Diameter (mm ± SD) | 2.80 ± 0.54 | 2.71 ± 0.39 | 0.835 |
| Minimum Lumen Diameter (mm ± SD) | 0.06 ± 0.19 | 0.09 ± 0.21 | 0.511 |
| Calcification %(n) | 54.1% (13/24) | 41.4% (12/29) | 0.410 |
| Mod/Severe and Severe[2] %(n) | 41.6% (10/24) | 27.6% (8/29) | -- |

1. Lesion characteristics are core lab reported
2. Dattilo, R; J Invasive Cardiol 2014;26(8):355360

# IN.PACT BTK STUDY
## PROCEDURAL CHARACTERISTICS

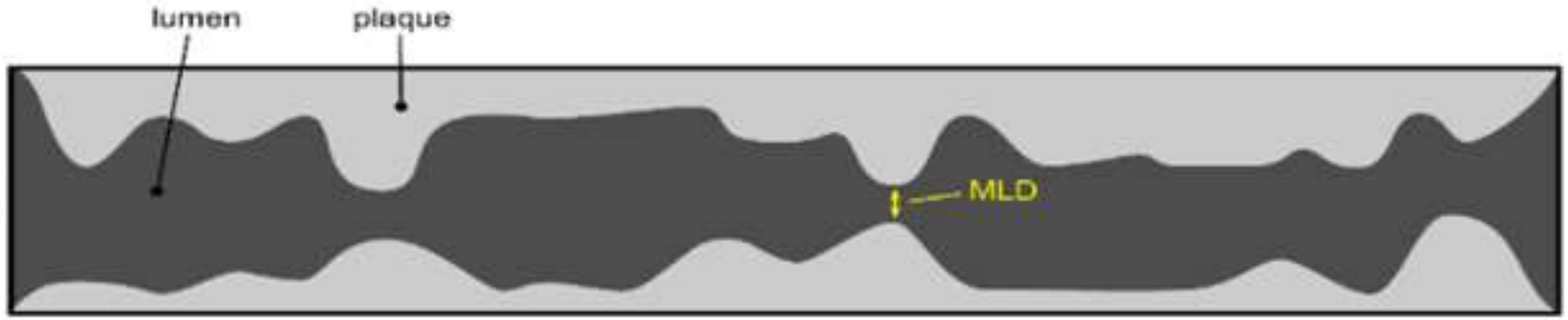
| Characteristics | IN.PACT 014 DCB (N=23 Subjects) (N=25 Lesions) | PTA (N=27 Subjects) (N=30 Lesions) | P-value |
|---|---|---|---|
| Lesions Received Post-dilation, %(n) | 36.0% (9/25) | 10.0% (3/30) | 0.026 |
| Provisional Stent %(n) | 8.0% (2/25) | 3.3% (1/30) | 0.586 |
| Balloon Diameter (all balloons used, mm±SD) | 3.0 ± 0.3 | 2.9 ± 0.4 | 0.187 |

| | (N=23 Subjects N=24 Lesions) | (N=27 Subjects N=29 Lesions) | P-value |
|---|---|---|---|
| Dissections* % (n) | | | 0.108 |
| No | 45.8% (11/24) | 72.4% (21/29) | |
| A | 0.0% (0/24) | 0.0% (0/29) | |
| B | 45.8% (11/24) | 24.1% (7/29) | |
| C | 4.2% (1/24) | 3.4% (1/29) | |
| D | 4.2% (1/24) | 0.0% (0/29) | |
| E - F | 0.0% (0/24) | 0.0% (0/29) | |

*Dissections are core lab reported

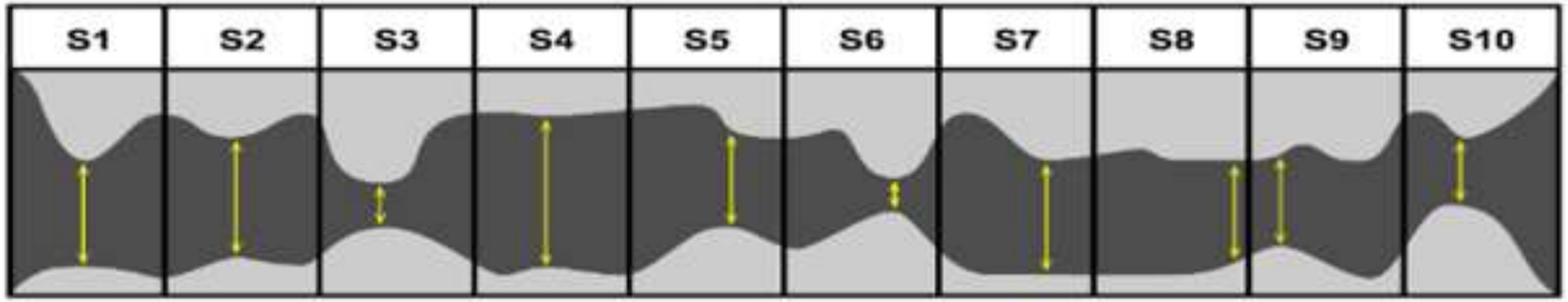
# IN.PACT BTK STUDY
## ANGIOGRAPHIC[1] MEASUREMENTS FOR LATE LUMEN LOSS

**Classic**




Segmental measurements **along the entire lesion** allow for better assessment of late lumen loss compared to measurement at one single point in the lesion.

**Sub-Segmental[2]**




1. Beth Israel Deaconess Angiographic Core Lab, Boston, MA, USA
2. Sub-segmental late lumen loss is the average of late lumen loss for each of the 10 sub-segments. Late Lumen Loss defined as the difference between minimum lumen diameter (MLD) immediately after index procedure and minimum lumen diameter at follow up. (MLD Post Procedure – MLD Follow Up).

# IN.PACT BTK STUDY
## EFFECTIVENESS ENDPOINT THROUGH 9 MONTHS

| 9-Month Angiographic Outcome[1] | IN.PACT 014 DCB (N=23 Subjects N=24 Lesions) | PTA (N=27 Subjects N=29 Lesions) | P-value |
|---|---|---|---|
| **Sub-Segmental Late Lumen Loss[2]** (Mean mm ± SD) | **0.59 ± 0.94** | **1.26 ± 0.81** | **0.017** |
| **Classic Late Lumen Loss** (Mean mm ± SD) | **0.89 ± 0.77** | **1.31 ± 0.72** | **0.070** |

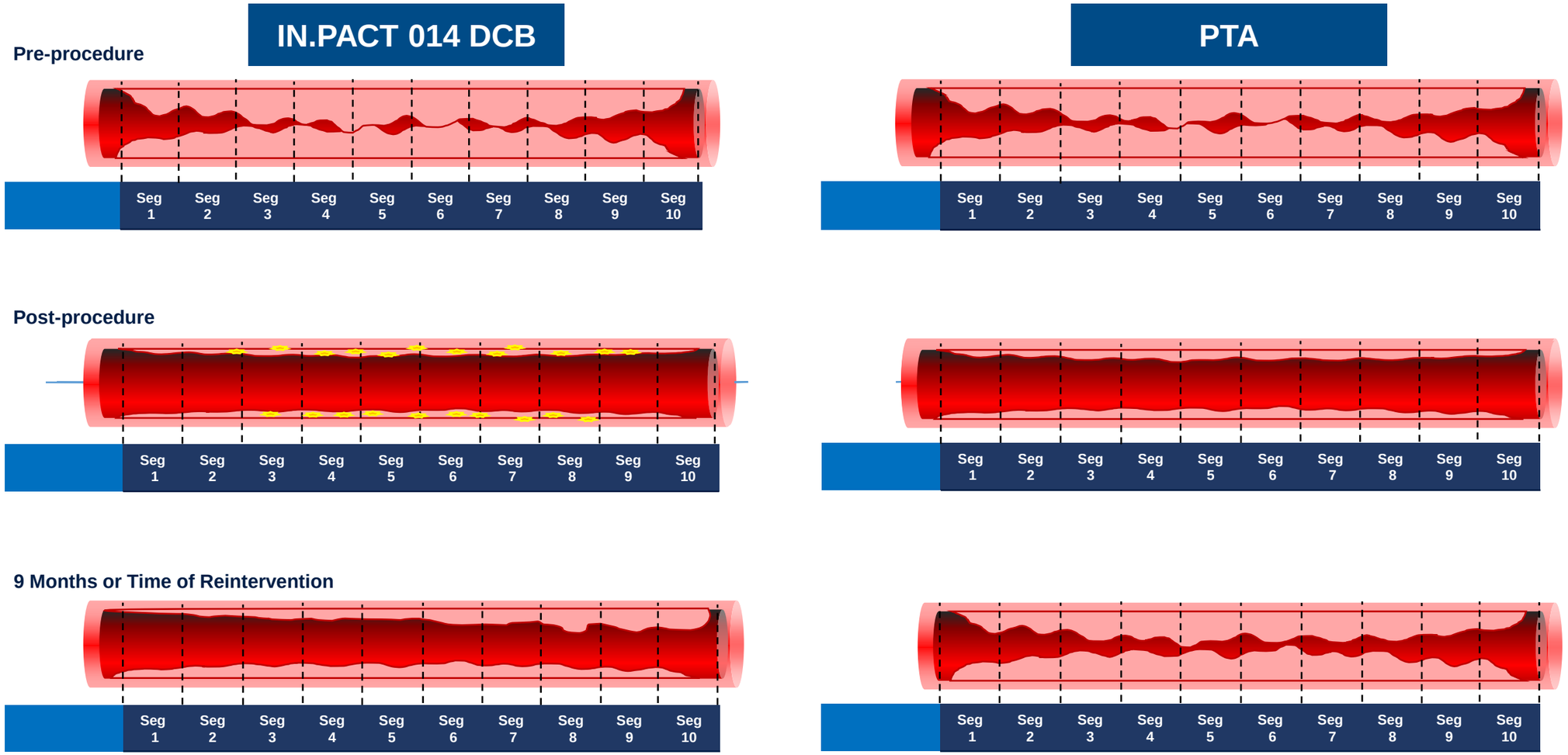
1. Beth Israel Deaconess Angiographic Core Lab, Boston, MA, USA
2. Sub-segmental late lumen loss is the average of late lumen loss for each of the 10 sub-segments. Late Lumen Loss defined as the difference between minimum lumen diameter (MLD) immediately after index procedure and minimum lumen diameter at follow up. (MLD Post Procedure – MLD Follow Up)

# IN.PACT BTK STUDY
## FUNCTIONAL FLOW RETAINED IN DCB GROUP

| Absence of Target Lesion Occlusion at 9 Months | DCB (N=24 lesions*) | PTA (N=29 lesions*) | P value |
|---|---|---|---|
| **Functional Flow by DUS at 9 months[1]** | **84.6% (11/13)** | **60.0% (6/10)** | 0.341 |

1. Functional flow defined as the absence of target lesion occlusion (no Flow) as assessed by duplex ultrasound

# IN.PACT BTK STUDY
## ANGIOGRAPHIC SUB-SEGMENTAL MLD RESULTS



# IN.PACT BTK STUDY
## 9-MONTH SAFETY OUTCOMES

| 9-Month Safety Outcomes | IN.PACT 014 DCB (N=23 Subjects) | PTA (N=27 Subjects) | P-value |
|---|---|---|---|
| **Safety Composite Endpoint[1] %(n)** | **91.3% (21/23)** | **87.5% (21/24)** | **1.000** |
| ▪ Device- and Procedure-related Death through 30 Days %(n) | 0.0% (0/23) | 3.7% (1/27) | 1.000 |
| ▪ Target Limb Major Amputation within 270 Days %(n) | 0.0% (0/23) | 0.0% (0/23) | >0.999 |
| ▪ Clinically-driven TLR within 270 Days %(n) | 8.7% (2/23) | 8.7% (2/23) | 1.000 |
| **All-cause Death %(n)** | **4.3% (1/23)** | **8.0% (2/25)** | **1.000** |
| **Thrombosis at Target Lesion site %(n)** | **4.3% (1/23)** | **4.2% (1/24)** | **1.000** |

1. Safety composite endpoint consists of: Freedom from device- and procedure-related mortality within 30 days, freedom from major target limb amputation within 270 days and freedom from CD- TLR within 270 days.

# SUMMARY

- The IN.PACT 014 BTK DCB demonstrates effectiveness through 9 months compared to percutaneous transluminal angioplasty (PTA) in a complex population

| Sub-segmental Late Lumen Loss | |
|---|---|
| 0.59 mm (DCB) | P = 0.017 |
| 1.26 mm (PTA) | |

| Classic Late Lumen Loss | |
|---|---|
| 0.89 mm (DCB) | P = 0.070 |
| 1.31 mm (PTA) | |

- The total re-occlusions at 9-month follow-up were numerically significantly lower in those treated with the DCB vs PTA
- There were no safety concerns from the outcomes of the IN.PACT 014 BTK Study and results support consistency of full IN.PACT Clinical Program
  - Safety composite was 91.3% (DCB) compared to 87.5% (PTA)
  - **No major amputations** within 9 months in either arm
  - Low all-cause death 4.3% (DCB), 8.0% (PTA)
- This novel, randomized, feasibility study with a .014 BTK balloon utilizing the 3.5 µg/mm$^2$ IN.PACT drug formulation and enhanced study design provides opportunity to affect future BTK studies and treatment algorithms

# THANK YOU