Medtronic

Engineering the extraordinary

5-Year Results from the IN.PACT Global Study Pre-specified Cohorts

In-Stent Restenosis, Chronic Total Occlusions, and Long Lesions

Gunnar Tepe MD

Department of Diagnostic and Interventional Radiology at

RoMed Clinic Rosenheim, Rosenheim, DE

Disclosure

<<Firstname Lastname>>

- ❑ I have the following potential conflicts of interest to report:
  - ❑ Receipt of grants/research support
  - ❑ Receipt of honoraria and travel support
  - ❑ Participation in a company-sponsored speaker bureau
  - ❑ Employment in industry
  - ❑ Shareholder in a healthcare company
  - ❑ Owner of a healthcare company
- ❑ I do not have any potential conflict of interest

Background

- The treatment of peripheral arterial disease (PAD) in patients with multiple comorbidities is challenging and remains a global health concern, impacting approximately 236 million people worldwide.[1]
- Drug-coated balloons (DCB) emerged as a novel endovascular treatment option a decade ago; numerous randomized controlled trials (RCTs)[2-6] and a meta-analysis[7] have demonstrated the superiority of DCB over uncoated percutaneous transluminal angioplasty (PTA) balloons for the treatment of PAD.
- Patients with more complex lesions, such as in-stent restenosis (ISR), lesions longer than 15 cm, and long chronic total occlusions (CTO) are usually excluded from RCTs.
- Prior to the current study, there were no long-term data available on DCBs for treatment of femoropopliteal artery disease in these distinct populations.
- This is a presentation of prospectively collected 5-year data from pre-specified in-stent restenosis, long lesion and chronic total occlusion cohorts from a large global DCB study.

1. Song P, et al., Lancet Glob Health. Aug 2019;7(8):e1020-e1030.
2. Tepe G, et al., JACC Cardiovasc Interv. Jan 2015;8(1 Pt A):102-8.
3. Scheinert D, et al., J Endovasc Ther. Feb 2015;22(1):14-21.
4. Rosenfield K, et al., N Engl J Med. Jul 9 2015;373(2):145-53.
5. Krishnan P, et al., Circulation. Sep 19 2017;136(12):1102-1113.
6. Jia X, et al., JACC Cardiovasc Interv. Sep 26 2016;9(18):1941-9.
7. Katsanos K, et al., Endovasc Ther. Apr 2016;23(2):356-70.

Robust Clinical Program

IN.PACT DCB Portfolio - Clinical Data for the SFA

RCTs + Pivotal Registration Studies

- IN.PACT SFA (EU+US) RCT†
- IN.PACT Japan RCT†
- IN.PACT China†
- Gender Subset
- Diabetic Subset

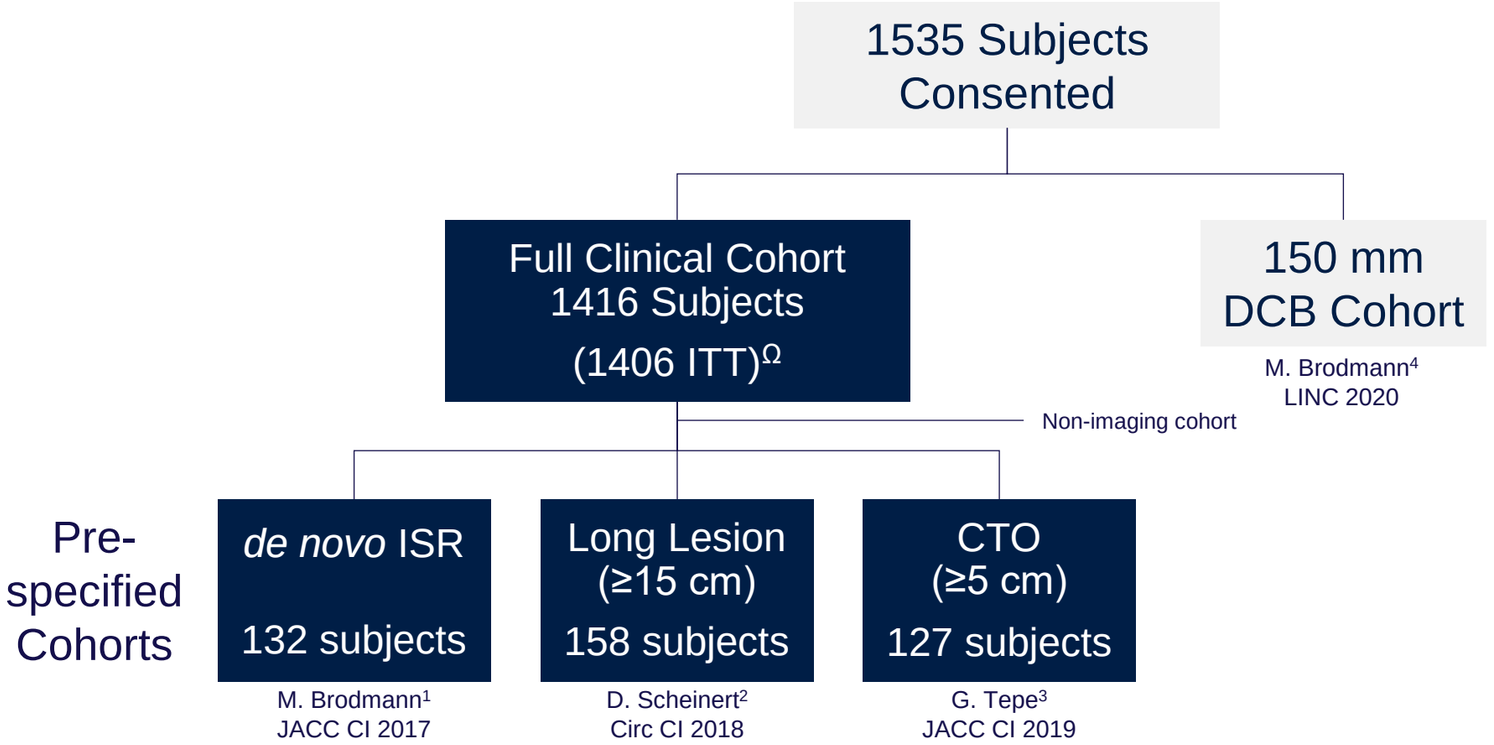
Real-World Studies

- IN.PACT Global Study‡
- Pre-specified Imaging Cohorts
- Regional Subsets
- Long Lesion †
- Belgian
- ISR[1]
- Asian
- CTO[1]

† Angiographic and DUS core lab adjudicated with clinical events committee oversight
‡ Clinical events committee oversight

IN.PACT Global Study†

- Real-world
- Prospective
- Multicenter (64 global sites)
- Single arm
- Complex femoropopliteal lesions
- Independently adjudicated ‡
- Prospective analysis of imaging cohorts with core lab §



This presentation includes 5-year outcome data on the 417 subjects who comprise the pre-specified ISR, long lesion, and CTO cohorts

† Sponsored by Medtronic plc
‡ Independent adjudication performed by Syntactx Clinical Events Committee, New York, NY, US
§ VasCore DUS Core Lab, Boston, MA, US, and SynvaCor Angiographic Core Lab, Springfield, IL, US

Ω Of the 1416 ITT subjects, 10 subjects did not receive a DCB

1. Brodmann et al. JACC Cardiovasc Interv. 2017;10:2113-23.
2. Scheinert et al. Circ Cardiovasc Interv. 2018;11:e005654.
3. Tepe et al. JACC Cardiovasc Interv. 2019;12:484-93.
4. Brodmann M, IN.PACT Global 150mm Cohort 3-Year Outcomes, LINC 2020.

Medtronic

IN.PACT Global Study

Independently Assessed Outcomes

Effectiveness	Freedom from clinically driven target lesion revascularization† through 60 months
Safety	Composite of freedom from device- and procedure-related death through 30 days, and freedom from major target limb amputation & clinically driven target vessel revascularization‡ through 60 months

† Any re-intervention within the target lesion(s) due to symptoms or drop of ABI of ≥ 20% or > 0.15 when compared to post-index procedure baseline ABI.
‡ Any re-intervention within the target vessel due to symptoms or drop of ABI of ≥ 20% or > 0.15 when compared to post-index procedure baseline ABI

Medtronic

IN.PACT Global: Pre-specified Cohorts

Baseline Patient Characteristics Reflective of Real-world Patients

Characteristics	*de novo* ISR N=132 Subjects	Long Lesion (≥15 cm) N=158 Subjects	CTO (≥ 5 cm) N=127 Subjects
Age (Years)	67.8 ± 10.1	69.6 ± 10.7	67.4 ± 10.5
Male	68.9 (91/132)	66.5 (105/158)	68.5 (87/127)
Diabetes	35.6 (47/132)	41.4 (65/157)	29.4 (37/126)
Hypertension	81.7 (107/131)	87.3 (138/158)	81.6 (102/125)
Hyperlipidemia	72.3 (94/130)	76.2 (115/151)	63.9 (78/122)
Current Smoker	35.6 (47/132)	34.2 (54/158)	49.6 (63/127)
Obesity†	18.2 (24/132)	21.9 (34/155)	20.0 (25/125)
Coronary Heart Disease	37.0 (47/127)	51.9 (80/154)	23.9 (28/117)
Carotid Artery Disease	19.7 (23/117)	22.2 (30/135)	19.0 (19/100)
Renal Insufficiency‡	9.8 (11/112)	14.3 (21/147)	9.9 (11/111)

Data are presented as % (n/N) or mean±standard deviation

† BMI ≥ 30 kg/m2
‡ Baseline serum creatinine ≥ 1.5 mg/dl

IN.PACT Global: Pre-specified Cohorts

Additional Baseline Characteristics

Characteristics	*de novo* ISR N=132 Subjects	Long Lesion (≥15 cm) N=158 Subjects	CTO (≥ 5 cm) N=127 Subjects
Previous Peripheral Revascularization	100.0 (132/132)	55.7 (88/158)	33.1 (42/127)
Concomitant BTK Disease	43.0 (55/128)	47.9 (68/142)	41.5 (49/118)
Ankle-brachial Index †	0.7 ± 0.2	0.7 ± 0.2	0.6 ± 0.2
Rutherford Category			
2	32.8 (43/131)	21.7 (34/157)	26.0 (33/127)
3	58.0 (76/131)	61.8 (97/157)	63.0 (80/127)
4	7.6 (10/131)	10.2 (16/157)	8.7 (11/127)
5	1.5 (2/131)	6.4 (10/157)	2.4 (3/127)

Data are presented as % (n/N) or mean±standard deviation

† ABI for all target limbs treated during the 1st index procedure are included (can be bilateral)

Medtronic

IN.PACT Global: Pre-specified Cohorts

Lesion Characteristics

Lesion Characteristics	*de novo* ISR N=132 Subjects N=150 Lesions† N=145 Lesions‡	Long Lesion (≥15 cm) N=158 Subjects N=162 Lesions† N=165 Lesions‡	CTO (≥ 5 cm) N=127 Subjects N=129 Lesions† N=128 Lesions‡
Lesion Type † De novo Restenotic (non-stented) In-stent Restenosis	 0.0 (0/150) 0.0 (0/150) 100.0 (150/150)	 83.3 (135/162) 16.7 (27/162) 0.0 (0/162)	 92.2 (119/129) 7.8 (10/129) 0.0 (0/129)
Lesion Length ‡ (cm)	17.1 ± 10.5	26.4 ± 8.6	22.8 ± 9.7
Occluded ‡	33.8 (48/142)	60.0 (99/165)	100.0 (124/124)
Occluded Lesion Length‡ (cm)	4.9 ± 9.5	9.0 ± 10.9	11.8 ± 8.1
Calcification ‡ Severe ‡	59.4 (79/133) 8.3 (11/133)	72.0 (118/164) 19.5 (32/164)	71.2 (89/125) 3.2 (4/125)
RVD† (mm)	5.2 ± 0.6	5.1 ± 0.6	5.1 ± 0.7
Diameter Stenosis‡ (%)	84.5 ± 15.1	90.7 ± 14.3	100.0 ± 0.0

Data are presented as % (n/N) or mean±standard deviation

† Site reported data
‡ Angiographic core lab reported. Lesions for Subjects 10220-049, 10220-043 and 13015-073 are not counted as they don't have core lab data.

Medtronic

IN.PACT Global: Pre-specified Cohorts

Procedure Characteristics

Procedural Characteristics	*de novo* ISR N=132 Subjects N=150 Lesions Ω	Long Lesion (≥15 cm) N=158 Subjects N=162 Lesions Ω	CTO (≥ 5 cm) N=127 Subjects N=129 Lesions Ω
Device Success †	99.6 (283/284)	99.6 (444/446)	99.3 (289/291)
Procedure Success ‡	99.3 (149/150)	99.4 (160/161)	100.0 (128/128)
Clinical Success §	98.5 (130/132)	99.4 (156/157)	98.4 (124/126)
Pre-dilatation	64.4 (85/132)	89.2 (141/158)	94.5 (120/127)
Post-dilatation	25.8 (34/132)	38.9 (61/157)	49.6 (63/127)
Provisional Stent	13.3 (20/150)	39.1 (63/161)	46.5 (60/129)

Data are presented as % (n/N)
† Device success defined as successful delivery, inflation, deflation and retrieval of the intact study balloon device without burst below the RBP.
‡ Procedure success defined as residual stenosis of ≤ 50% (non-stented subjects) or ≤ 30% (stented subjects).

§ Clinical success defined as procedural success without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or TVR) prior to discharge.
Ω Site reported data
CTO: Chronic Total Occlusion; ISR: In-Stent Restenosis

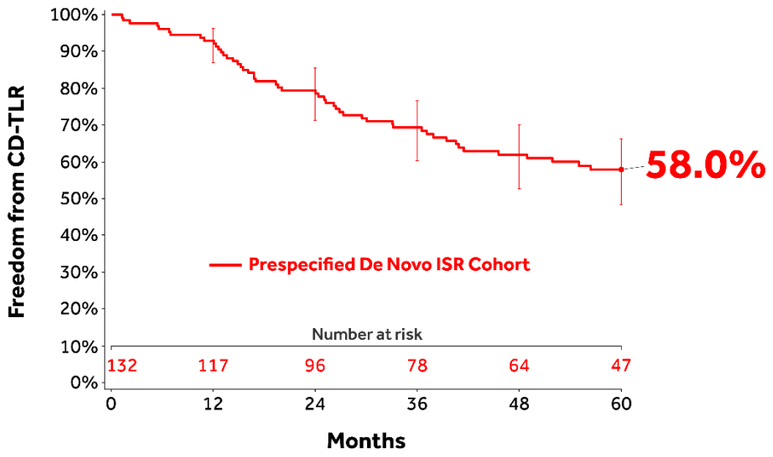
Medtronic

IN.PACT Global: Pre-specified Cohorts

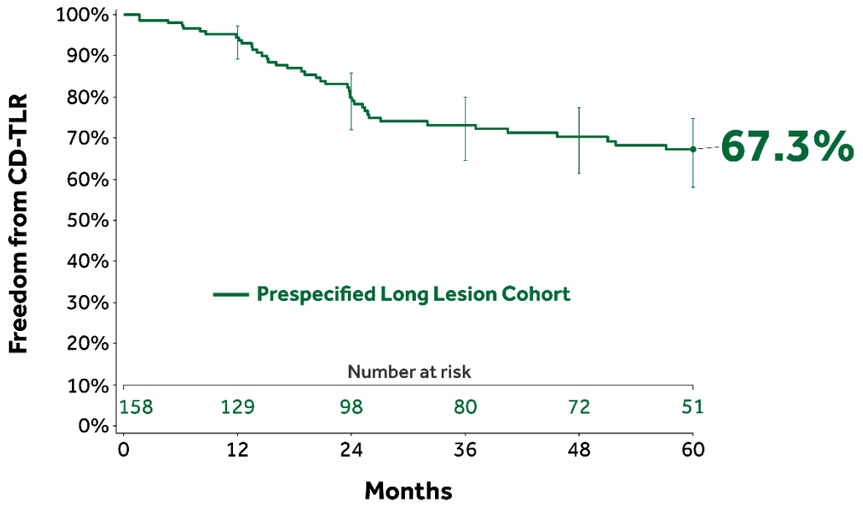
5-Year Effectiveness Outcomes

Freedom from CD-TLR through 5 Years

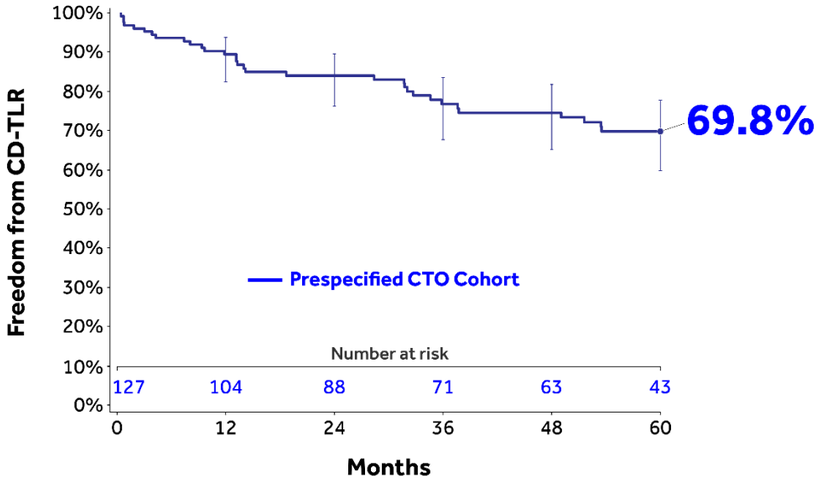
de novo ISR



Long Lesion



CTO



IN.PACT Global Full Cohort 5-year Freedom from CD-TLR rate: 69.4%

IN.PACT Global: Pre-specified Cohorts

Additional 5-Year Effectiveness Outcomes

Cumulative Incidence by Kaplan-Meier Estimate	*de novo* ISR N=132 Subjects	Long Lesion (≥15 cm) N=158 Subjects	CTO (≥ 5 cm) N=127 Subjects
CD-TLR† (%) (Number of subjects with event)	42.0 (50)	32.7 (41)	30.2 (32)
Any TLR‡ (%) (Number of subjects with event)	43.1 (51)	33.7 (42)	32.2 (34)

Reintervention Through 5 Years	*de novo* ISR N=132 Subjects	Long Lesion (≥15 cm) N=158 Subjects	CTO (≥ 5 cm) N=127 Subjects
Restricted Mean Survival Time to First CD-TLR (Days ± SD)	1354.6 ± 53.6	1437.0 ± 49.9	1465.5 ± 54.5

† Clinically driven TLR adjudicated by an independent Clinical Event Committee and defined as any re-intervention within the target lesion due to symptoms or drop of ABI of ≥20% or >0.15 when compared to post-procedure baseline ABI.
‡ Any TLR includes clinically driven and incidental or duplex driven TLR.

Medtronic

IN.PACT Global: Pre-specified Cohorts

5-Year Safety Outcomes

Kaplan-Meier Estimated %	*de novo* ISR N=132 Subjects	Long Lesion (≥15 cm) N=158 Subjects	CTO (≥ 5 cm) N=127 Subjects
Safety Composite† % (n) ‡	56.0 (52)	65.7(43)	69.8 (32)

† Safety composite endpoint consists of: Freedom from device- and procedure-related to 30 days, freedom from major target limb amputation within 60 months, and freedom from CD-TVR within 60 months.

‡ Percentage based on Kaplan-Meier estimate (number of subjects with event)

Medtronic

IN.PACT Global: Pre-specified Cohorts

Additional 5-Year Safety Outcomes

5-Year Kaplan-Meier Cumulative Incidence	*de novo* ISR N=132 Subjects	Long Lesion (≥15 cm) N=158 Subjects	CTO (≥ 5 cm) N=127 Subjects
Major Adverse Events †	53.1 (65)	48.9 (67)	43.0 (48)
CEC-Adjudicated All-cause Death	16.7 (20)	22.4 (30)	19.1 (20)
CD-TVR	44.0 (52)	32.7 (41)	30.2 (32)
Major Target Limb Amputation	0.8 (1)	1.7 (2)	0.0 (0)
Thrombosis	10.6 (13)	5.0 (7)	7.0 (8)

Data are presented as % (n) as cumulative incidence based on Kaplan-Meier Estimate (number of patients with events)
† CEC adjudicated Major Adverse Events (MAE) defined as all-cause death, clinically-driven TVR, major target limb amputation, thrombosis at the target lesion site through 60 months

CD-TVR: Clinically Driven Target Vessel Revascularization; CTO: Chronic Total Occlusion; ISR: In-Stent Restenosis

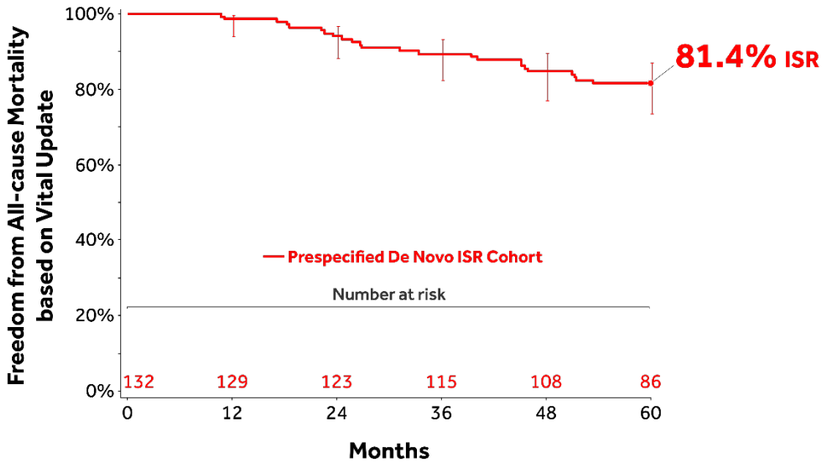
IN.PACT Global: Pre-specified Cohorts

All-Cause Death through 5 Years with Additional Vital Status

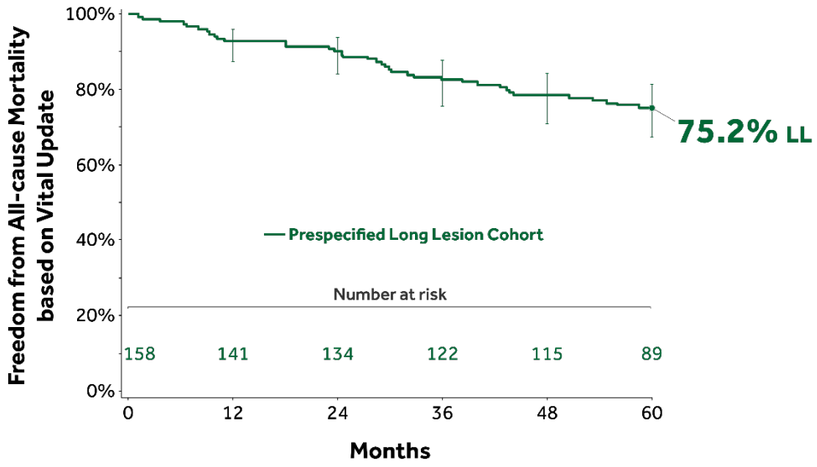
Freedom from All Cause Mortality through 5 Years

96.4% Vital Status Follow-up †

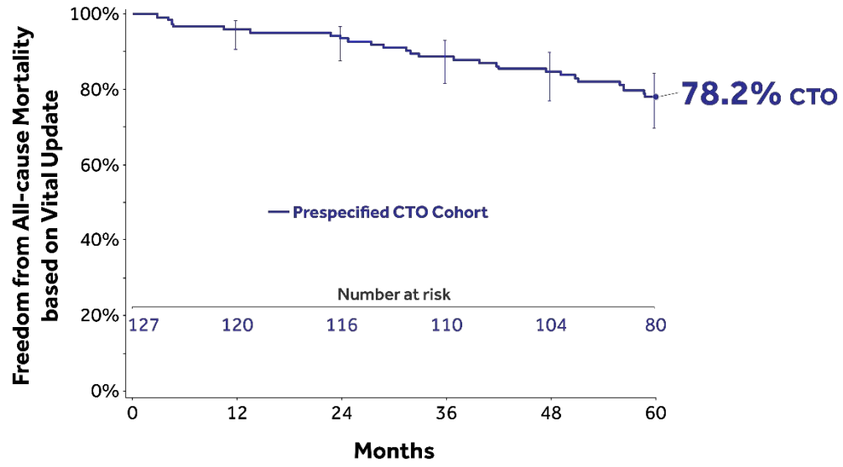
de novo ISR



Long Lesion



CTO



† Vital Status number based on the IN.PACT Global Study full ITT cohort

Conclusions

- Real-world data from the IN.PACT Global Study continue to confirm long-term clinical safety and effectiveness of the IN.PACT Admiral drug-coated balloon when used to treat complex lesions
- High 5-year freedom from clinically driven TLR was demonstrated in all three pre-specified cohorts, but it was slightly lower in the de novo ISR cohort highlighting the challenging nature of ISR lesions
  - 69.8% CTO
  - 67.3% Long Lesions
  - 58.0% de novo ISR
- No safety issues were reported in any of the cohorts. All-Cause Mortality with vital status at 5 years:
  - 81.4% de novo ISR
  - 75.2% Long Lesions
  - 78.2% CTO
- These data support incorporating the use of the IN.PACT Admiral DCB into clinical treatment algorithms for complex femoropopliteal disease.