IN.PACT Global 4-Year Outcomes for DCB Alone vs DCB with Provisional Stenting

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DISCLOSURE

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- ❑ 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: Complex Disease

- Bare metal stent (BMS) studies in the SFA demonstrate improved outcomes over percutaneous transluminal angioplasty (PTA) but longer lesion length is a predictor of lower patency at 12 months (35-65%)[1-2] and is associated with higher stent fractures.[3,4]
- The clinical evidence for real-world drug-coated balloon studies has expanded; however, bailout stent rates in complex lesions remain notable.[5-10]
- As previously reported, the IN.PACT Global study outcomes elucidated the IN.PACT™ Admiral™ drug-coated balloon (DCB) can be safely followed by a provisional BMS with sustained freedom from CD-TLR through 3 years.[11,12]

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7. Tepe G, IN.PACT Global CTO Charing Cross London, UK 2016.
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IN.PACT Global Study
Overview

Real-world, prospective, multicenter, single arm, independently-adjudicated femoropopliteal study*

- **1535** patients consented
- **64** sites in EU, Mid-East, Latin America, Asia
- Independent adjudication by Clinical Events Committee[1]
- Prospective subset analysis with core lab[2] reported results (*de novo* ISR, long lesions ≥15 cm, CTOs ≥5 cm)
- Safety and effectiveness data on 150 mm DCB

Complex, Real-World Lesions

✓ Bilateral disease	✓ SFA and Popliteal Artery	✓ RCC 2-4
✓ Multiple lesions	✓ TASC A,B,C,D	✓ De novo ISR, Long Lesions, CTOs

* Sponsored by Medtronic plc

1. Independent adjudication performed by Syntactx Clinical Events Committee, New York, NY, US
2. VasCore DUS Core Lab, Boston, MA, US, and SynvaCor Angiographic Core Lab, Springfield, IL, US

IN.PACT Global Study
Blinded, Independently Assessed Outcomes

Effectiveness

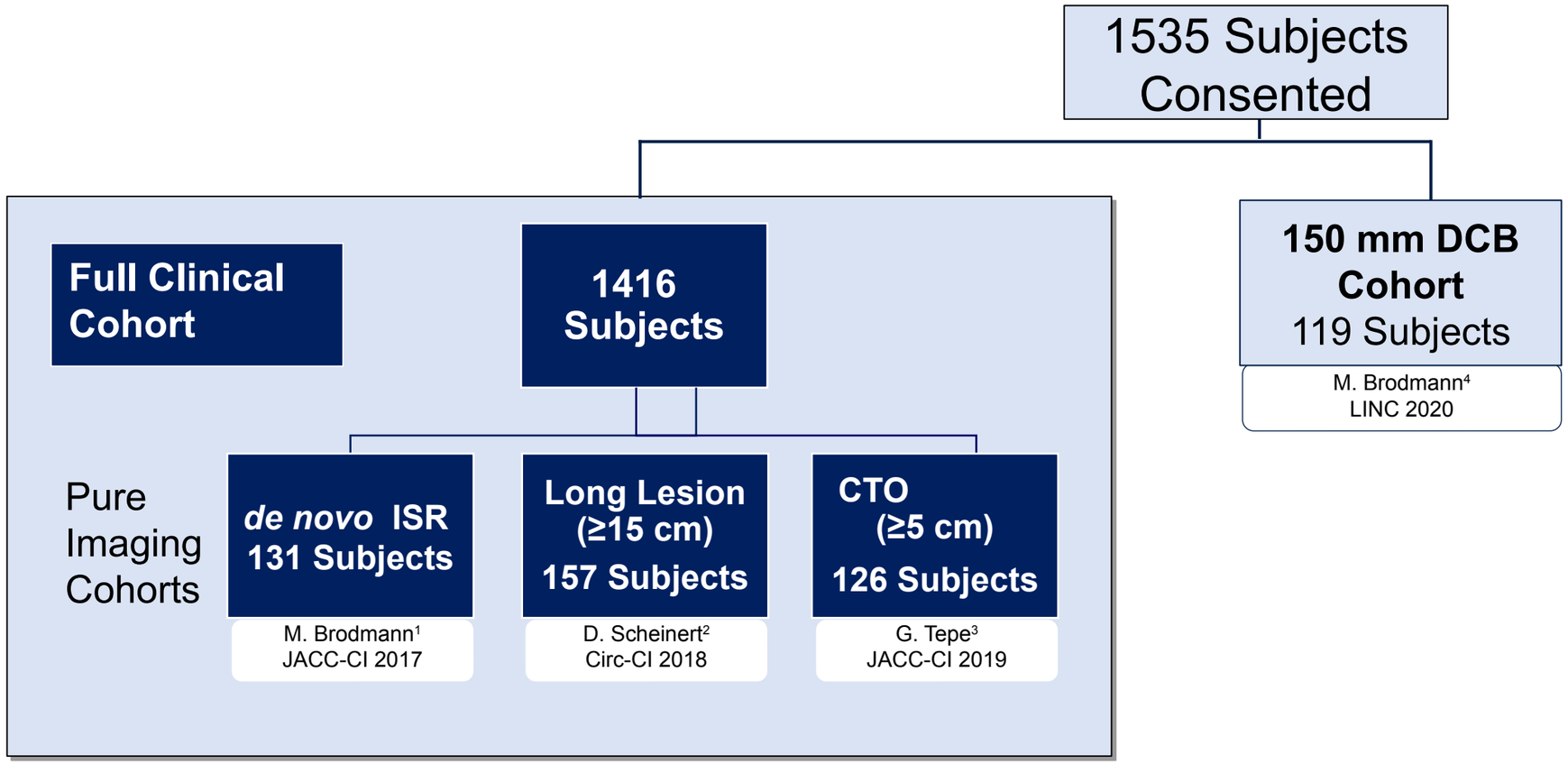
- Freedom from clinically-driven[1] target lesion revascularization measured through 48 months

Safety

- Freedom from device-and procedure-related death through 30 days, and freedom from major target limb amputation & clinically-driven[1] target vessel revascularization (TVR) measured through 48 months

1. Clinically-driven defined as any re-intervention due to symptoms or drop of ABI of ≥ 20% or > 0.15 when compared to post-index procedure baseline ABI.

IN.PACT Global Study
Architecture



This presentation includes outcome data on the 1406 ITT subjects who comprise the IN.PACT Global Clinical Cohort

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

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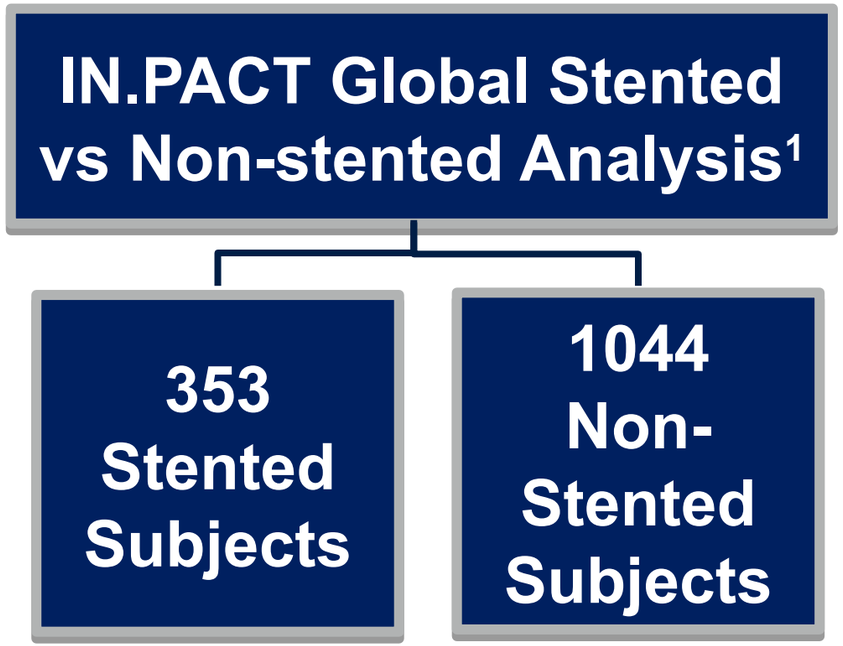
IN.PACT Global Study
Stented vs Non-stented Analysis from the Full Cohort

Purpose: To compare outcomes of standalone IN.PACT Admiral DCB usage versus IN.PACT Admiral DCB followed by provisional stenting



1. 19 subjects were excluded from this analysis due to incomplete stent information

25.3%
Provisional stent rate*

Reason for Provisional Stenting† (N=455 Lesions)	
Persistent Residual Stenosis ≥ 50%	59.2% (221/373)
>10 mmHg Trans Lesion Gradient	0.5% (2/373)
Flow-Limiting Dissection	53.6% (200/373)
Other	5.1% (19/373)

* Per subject rate; † Lesion based

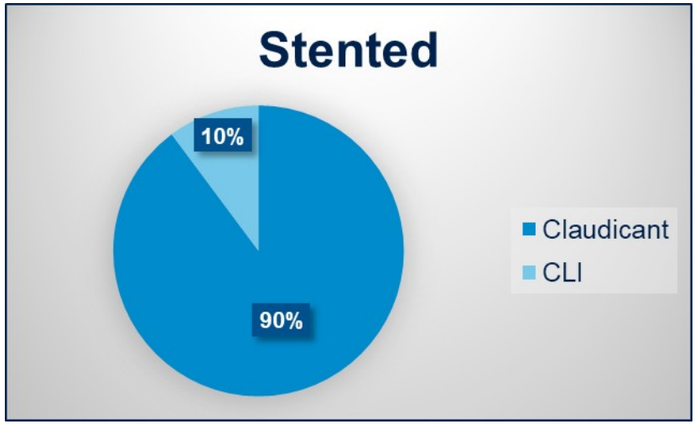
IN.PACT Global Study
Stented vs Non-stented Analysis

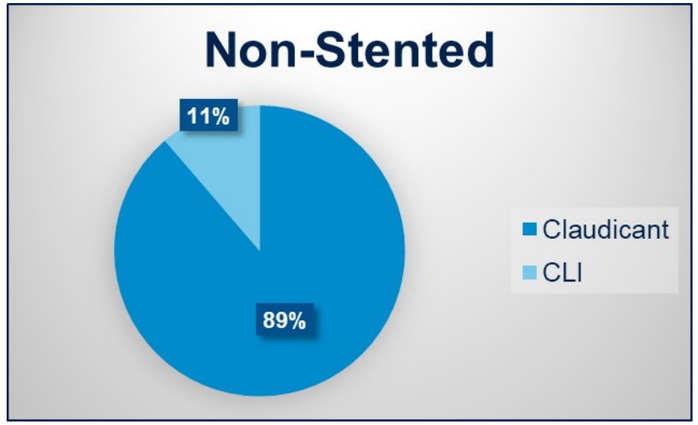
Baseline Characteristics	IN.PACT DCB Stented (N=353 Subjects)	IN.PACT DCB Non-Stented (N=1044 Subjects)	p-value (Stented vs Non-Stented)
Age (Y, Mean ± SD)	67.8 ± 10.3	68.8 ± 10.0	0.122
Male (%)	71.1% (251/353)	66.7% (696/1044)	0.130
Diabetes (%)	36.0% (127/353)	41.0% (426/1040)	0.102
Hypertension (%)	84.7% (299/353)	83.1% (863/1039)	0.508
Hyperlipidemia (%)	68.8% (238/346)	70.9% (715/1008)	0.454
Current Smoker (%)	32.0% (113/353)	31.8% (332/1044)	0.947
Obesity (BMI ≥ 30 kg/m^2(%)	21.1% (74/351)	20.4% (210/1031)	0.760
Coronary Heart Disease (%)	37.2% (128/344)	41.6% (408/980)	0.160
Carotid Artery Disease (%)	15.9% (49/308)	21.6% (190/880)	0.032
Renal Insufficiency[1] (%)	10.6% (32/302)	11.4% (103/906)	0.753
Previous Peripheral Revas (%)	46.5% (164/353)	54.7% (571/1044)	0.008
ABI[2] (Mean ± SD)	0.643 ± 0.215	0.691 ± 0.217	< 0.001

1. Baseline serum creatinine ≥ 1.5 mg/dl
2. ABI for all target limbs treated during the 1st index procedure including subjects with bilateral disease

IN.PACT Global Study
Stented vs Non-stented Analysis

Baseline Rutherford Category	Stented (N=353 Subjects)	Non-Stented (N=1044 Subjects)	P-value
1	0.0% (0/353)	0.1% (1/1041)	0.840
2	30.3% (107/353)	31.6% (329/1041)	
3	59.5% (210/353)	57.0% (593/1041)	
4	6.8% (24/353)	9.0% (94/1041)	
5	3.4% (12/353)	2.3% (24/1041)	
6	0.0% (0/353)	0.0% (0/1041)	





IN.PACT Global Study
Stented vs Non-stented Analysis

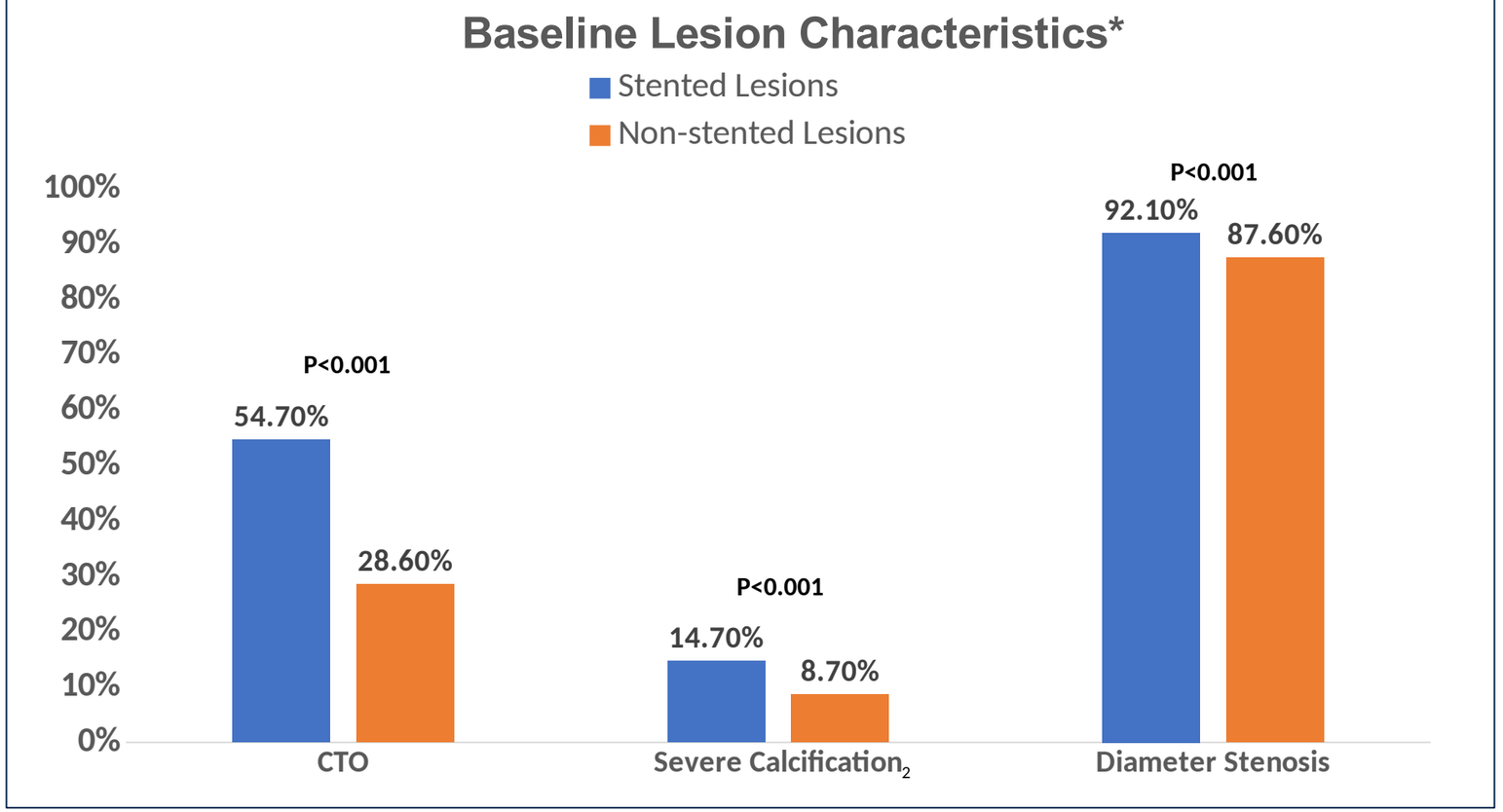
Baseline Lesion Characteristics*	IN.PACT DCB Stented (N=353 Subjects) (N=455 Lesions)	IN.PACT DCB Non-Stented (N=1044 Subjects) (N=1306 Lesions)	p-value (Stented vs Non-Stented)
Lesion Length (cm ± SD)	**15.37 ± 10.68**	**10.97 ± 8.83**	< 0.001
Total Occlusions % (n)	54.7% (249/455)	28.6% (373/1306)	< 0.001
Occluded Lesion Length (cm ± SD)	7.93 ± 10.46	3.33 ± 7.40	< 0.001
Calcification % (n) **Severe [1] % (n)**	73.8% (336/455) 14.7% (67/455)	66.7% (870/1304) 8.7% (113/1304)	0.005 < 0.001
Diameter Stenosis (% ± SD)	92.1% ± 11.6	87.6% ± 12.3	< 0.001
RVD (mm ± SD)	5.209 ± 0.651	5.187 ± 0.687	0.540

* Data is site reported per lesion

1. Severe calcium definition used by study sites and core laboratory is bilateral calcium at the same location (also measured in sections), ≥ half of the total lesion length, ≥180° (both sides of the vessel at the same location). Dattilo, R; J Invasive Cardiol 2014;26(8):355360

IN.PACT Global Study
Stented vs Non-stented Analysis

Complexity at Baseline



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IN.PACT Global Study

Stented vs Non-stented Analysis

Procedural Characteristics*	IN.PACT DCB Stented (N=353 Subjects) (N=455 Lesions)	IN.PACT DCB Non-Stented (N=1044 Subjects) (N=1306 Lesions)	p-value (Stented vs Non-Stented)
Device Success[1] % (n)	99.3% (911/917)	99.4% (2053/2065)	0.801
Procedure Success[2] % (n)	97.5% (344/353)	99.9% (1042/1043)	< 0.001
Clinical Success[3] % (n)	96.6% (341/353)	99.2% (1035/1043)	< 0.001
Pre-dilatation % (n) Post-dilatation[4] % (n)	90.4% (319/353) 60.1% (212/353)	73.7% (769/1044) 26.7% (279/1044)	< 0.001 < 0.001
Dissections: D E F	 12.3% (56/455) 9.5% (43/455) 2.4% (11/455)	 1.7% (22/1305) 0.5% (7/1305) 0.0% (0/1305)	--
Stent Coverage (Operator Def) Spot Stenting Partial Lesion Coverage Whole Lesion Coverage	 24.4% (91/373) 37.8% (141/373) 37.8% (141/373)	N/A	N/A

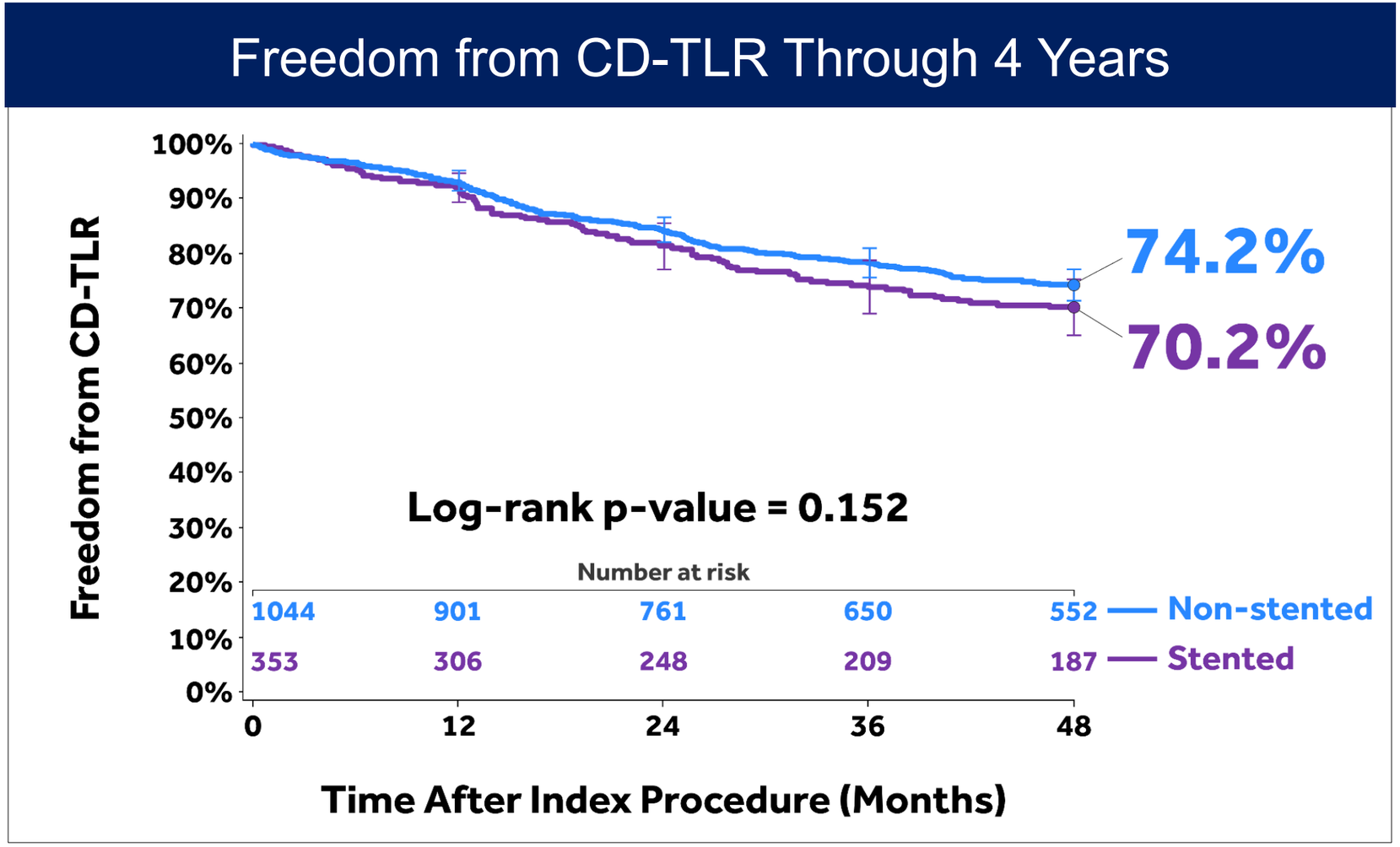
1. Device success defined as successful delivery, inflation, deflation and retrieval of the intact study balloon device without burst below the RBP.
2. Procedure success defined as residual stenosis of ≤ 50% (non-stented subjects) or ≤ 30% (stented subjects)
3. Clinical success defined as procedural success without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or TVR) prior to discharge.
4. Post-dilatation is not required and is performed at the discretion of the investigator. In the event a post-dilatation is performed, it must be done with a balloon shorter than the lesion length to avoid geographic miss when initial DEB dilatation results in any of the following: Residual stenosis ≥ 50% (by visual estimate); Trans-lesional gradient is >10 mm Hg; Presence of a flow-limiting dissection.

* Site reported

IN.PACT Global Study

Stented vs Non-stented Analysis

Effectiveness Outcome Through 4 Years



IN.PACT Global Study
Stented vs Non-stented Analysis

Additional Effectiveness Outcomes Through 4 Years

4-Year Outcomes*	IN.PACT DCB Stented (N=353 Subjects)	IN.PACT DCB Non-Stented (N=1044 Subjects)	p-value (Stented vs Non-Stented)
Any TLR[1]	30.8% (97)	26.2% (241)	0.112
Time to first CD-TLR[2] (days)	562.8 ± 359.5 (94)	573.1 ± 370.4 (237)	0.818

* For Clinical/Safety endpoints, percentages are based on Kaplan-Meier Estimate (number of patients with events)
1. Any TLR includes clinically-driven and incidental or duplex driven TLR
2. Number of CD-TLR within 1440 days

IN.PACT Global Study
Stented vs Non-stented Analysis

Safety Outcomes Through 4 Years

4-Year Outcomes*	IN.PACT DCB Stented (N=353 Subjects)	IN.PACT DCB Non-Stented (N=1044 Subjects)	p-value (Stented vs Non-Stented)
Primary Safety Composite[1]	68.7% (99)	72.8% (252)	0.158

* For Clinical/Safety endpoints, percentages are based on Kaplan-Meier Estimate (number of patients with events)

1. Safety composite endpoint consists of: Freedom from device- and procedure-related death to 30 days, freedom from target limb amputation within 1440 days; and freedom from clinically-driven TLR within 48 months.

IN.PACT Global Study
Stented vs Non-stented Analysis

Additional Safety Outcomes Through 4 Years

4-Year Outcomes*	IN.PACT DCB Stented (N=353 Subjects)	IN.PACT DCB Non-Stented (N=1044 Subjects)	p-value (Stented vs Non-Stented)
Major Adverse Events[1]	41.5% (138)	38.5% (376)	0.265
All-cause Death	14.8% (48)	15.1% (146)	0.832
CD-TVR	30.4% (96)	26.7% (246)	0.191
Major Target Limb Amputation	1.6% (5)	0.9% (8)	0.277
Thrombosis	6.4% (21)	5.1% (49)	0.356

* For Clinical/Safety endpoints, percentages are based on Kaplan-Meier Estimate (number of patients with events)

1. CEC adjudicated Major Adverse Events (MAE) defined as all-cause death, clinically-driven TVR, major target limb amputation, thrombosis at the target lesion site at 1440 days

Summary
IN.PACT Global Stented vs Non-stented Analysis

- In this **complex lesion subset** from the IN.PACT Global study, the IN.PACT Admiral DCB demonstrates durable safety and effectiveness through 4 years.

- In the event of sub-optimal angioplasty results (i.e., persistent residual stenosis >50%, flow limiting dissection), the IN.PACT Admiral DCB can be safely followed by provisional BMS with the **expectation of similar outcomes** through **4 years** compared to lesions treated with DCB alone.

FF CD-TLR	70.2% DCB + prov. BMS 74.2% DCB alone	P=0.152
Primary Safety Composite	68.7% DCB + prov. BMS 72.8% DCB alone	P=0.158