DRUG-COATED BALLOONS SHOW SUPERIOR THREE-YEAR OUTCOMES VS. ANGIOPLASTY: RESULTS FROM IN.PACT SFA RANDOMIZED TRIAL

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Medtronic
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Drug-coated Balloons Show Superior Three-Year Outcomes versus Angioplasty: Results from the IN.PACT SFA Randomized Trial

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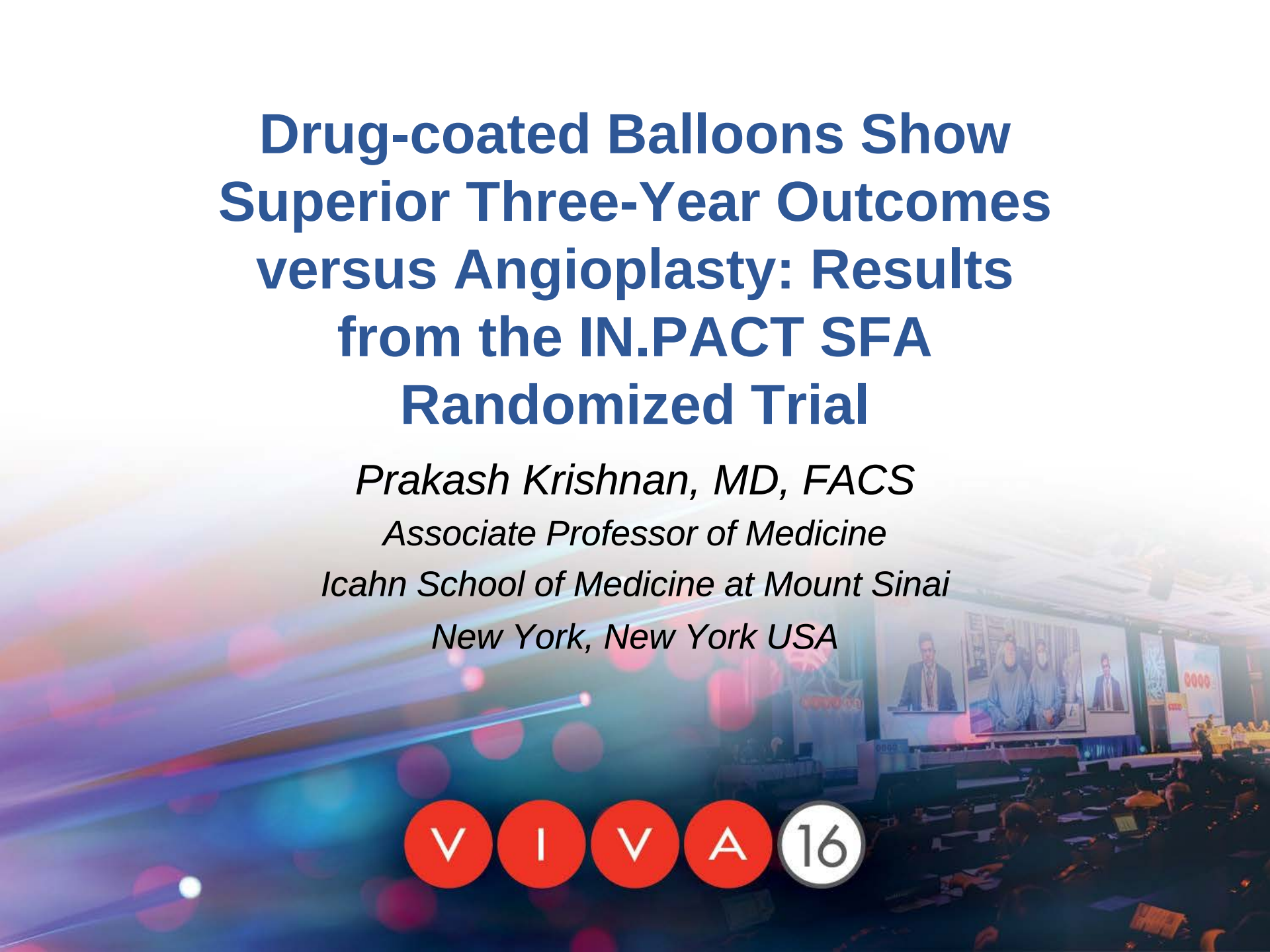

Background

- Drug-coated balloons have significantly changed the treatment landscape for femoropoplieal artery disease
- IN.PACT™ Admiral™ DCB has demonstrated best in class patency results at 1 and 2 years

		1-Year	2-Year	3-Year
Primary Patency	**IN.PACT DCB** [1]	87.5%	78.9%	?
	LUTONIX DCB [2,3]	73.5%	58.6%	?
CD-TLR	**IN.PACT DCB** [1]	2.4%	9.1%	?
	LUTONIX DCB [2,3]	12.3%	18.0%	?

- Unique DCB designs and variable clinical outcomes across technology platforms support there being no class effect
- Presentation of the 3-year results will answer the question of continued durability of the IN.PACT Admiral DCB

1. Laird JR, et al. 24-Month Results of IN.PACT SFA. J Am Coll Cardiol 2015;66:2329-38.
2. Rosenfield K, et al. 12-Month Results of LEVANT2 Trial. New Engl J Med 2015; 373:145-53.
3. LEVANT 2 2-Year Results. Presented by Laurich C, SVS Chicago 2015.

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IN.PACT SFA Trial

Overview

<u>Objective</u>: 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

Robust Level 1 Evidence

- Prospective, multicenter EU and US, randomized (2:1), single-blinded trial
- 331 patients enrolled:
  IN.PACT DCB (n = 220) *vs.* PTA (n = 111)

Rigorous and Unbiased

- Independent and blinded Duplex Ultrasound Core Lab,[1] Angiographic Core Lab,[2] and Clinical Events Committee[3]
- Independent Safety Monitoring Board
- External monitoring with 100% source data verification

Durability of Outcomes

- Subjects followed up to 5 years

1. VasCore DUS Core Laboratory, Boston, MA, US;
2. SynvaCor Angiographic Core Laboratory, Springfield, IL, US;
3. Clinical Events Committee and Data Safety Monitoring services provided by HCRI, Boston, MA, US

IN.PACT SFA: Investigators and Sites

IN.PACT SFA I

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

M. Brodmann, Graz, Austria
G. Tepe, Rosenheim, Germany
T. Zeller, Bad Krozingen, Germany
D. Scheinert, Leipzig, Germany
A. Micari, Palermo, Italy
I. Baumgartner, Bern, Switzerland
S. Sixt, Hamburg, Germany
G. Sorropago, Mercogliano, Italy
P. Peeters, Bonheiden, Belgium
F. Vermassen, Gent, Belgium
C. Trani, Rome, Italy
M. Bosiers, Dendermonde, Belgium
J. Van den Berg, Lugano, Switzerland

IN.PACT SFA II

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

P. Krishnan, New York, NY, USA
C. Metzger, Kingsport, TN, USA
A. Jain, Fremont, CA, USA
R. Sachar, Raleigh, NC, USA
N. Farhat, Elyria, OH, USA
L. Garcia, Boston, MA, USA
R. Malhotra, Glendale, AZ, USA
S. Germanwala, Longview, TX, USA
A. Pershad, Phoenix, AZ, USA
B. Bigelow, Indianapolis, IN, USA
J. Zidar, Raleigh, NC, USA
S. Ahanchi, Norfolk, VA, USA
R. Feldman, Ocala, FL, USA
R. Kovach, Brown Mills, NJ, USA
M. Goodwin, Naperville, IL, USA
L. Marone, Pittsburgh, PA, USA
M. Shishehbor, Cleveland, OH, USA
D. Chew, Des Moines, IA, USA
P. Soukas, Providence, RI, USA
M. Garcia, Newark, DE, USA
M. Mewissen, Milwaukee, WI, USA
R. Brown, Waco, TX, USA
C. Walker, Houma, LA, USA
N. Strickman, Houston, TX, USA
R. Fairman, Philadelphia, PA, USA
S. Laster, Kansas City, MO, USA
W. Gray, New York, NY, USA
V. Ramaiah, Phoenix, AZ, USA
P. Alden, Minneapolis, MN, USA
C. Stinis, La Jolla, CA, USA
R. Dave, Camp Hill, PA, USA
R. Gallino, Washington, DC, USA
G. Ansel, Columbus, OH, USA
M. Schermerhorn, Boston, MA, USA
M. Hunter, Cincinnati, OH, USA
M. Dake, Stanford, CA, USA
J. Benenati, Miami, FL, USA
P. Schneider, Honolulu, HI, USA
R. Serry, Poway, CA, USA
J. Angle, Charlottesville, VA, USA
K. Gupta, Kansas City, KS, USA
P. Jones, Chicago, IL, USA
G. Petrossian, Roslyn, NY, USA
A. Patel, Morristown, NJ, USA

IN.PACT SFA Trial
Blinded, Independently Assessed Outcomes

Primary Efficacy Endpoint	**Primary patency within 12 months, defined as freedom from clinically-driven TLR and DUS-derived restenosis (PSVR ≤ 2.4)**
Primary Safety Endpoint	**Freedom from device- and procedure-related death through 30 days, and freedom from target limb major amputation and clinically-driven TVR within 12 months**

- ***MAEs (including all individual components of the primary endpoints and key secondary endpoints) are adjudicated by the blinded CEC through 5 years***
- ***Restenosis is assessed by the blinded Duplex and Angiographic Core Labs through the 3-year follow-up visits***

IN.PACT SFA Trial

Baseline Clinical Characteristics

	IN.PACT n = 220 subjects	PTA n = 111 subjects	P-value
Age, Y ± SD	67.5 ± 9.5	68.0 ± 9.2	0.612
Male, % (n)	65.0% (143/220)	67.6% (75/111)	0.713
Diabetes, % (n)	40.5% (89/220)	48.6% (54/111)	0.161
Hypertension, % (n)	91.4% (201/220)	88.3% (98/111)	0.431
Current smoker, % (n)	38.6% (85/220)	36.0% (40/111)	0.719
Rutherford class, % (n) **2** **3** **4** **5**	 37.7% (83/220) 57.3% (126/220) 5.0% (11/220) 0.0% (0/220)	 37.8% (42/111) 55.9% (62/111) 5.4% (6/111) 0.9% (1/111)	0.898
ABI / TBI, ± SD [1]	0.769 ± 0.228	0.744 ± 0.189	0.308

1. TBI allowed in cases of incompressible vessels in IN.PACT SFA II phase

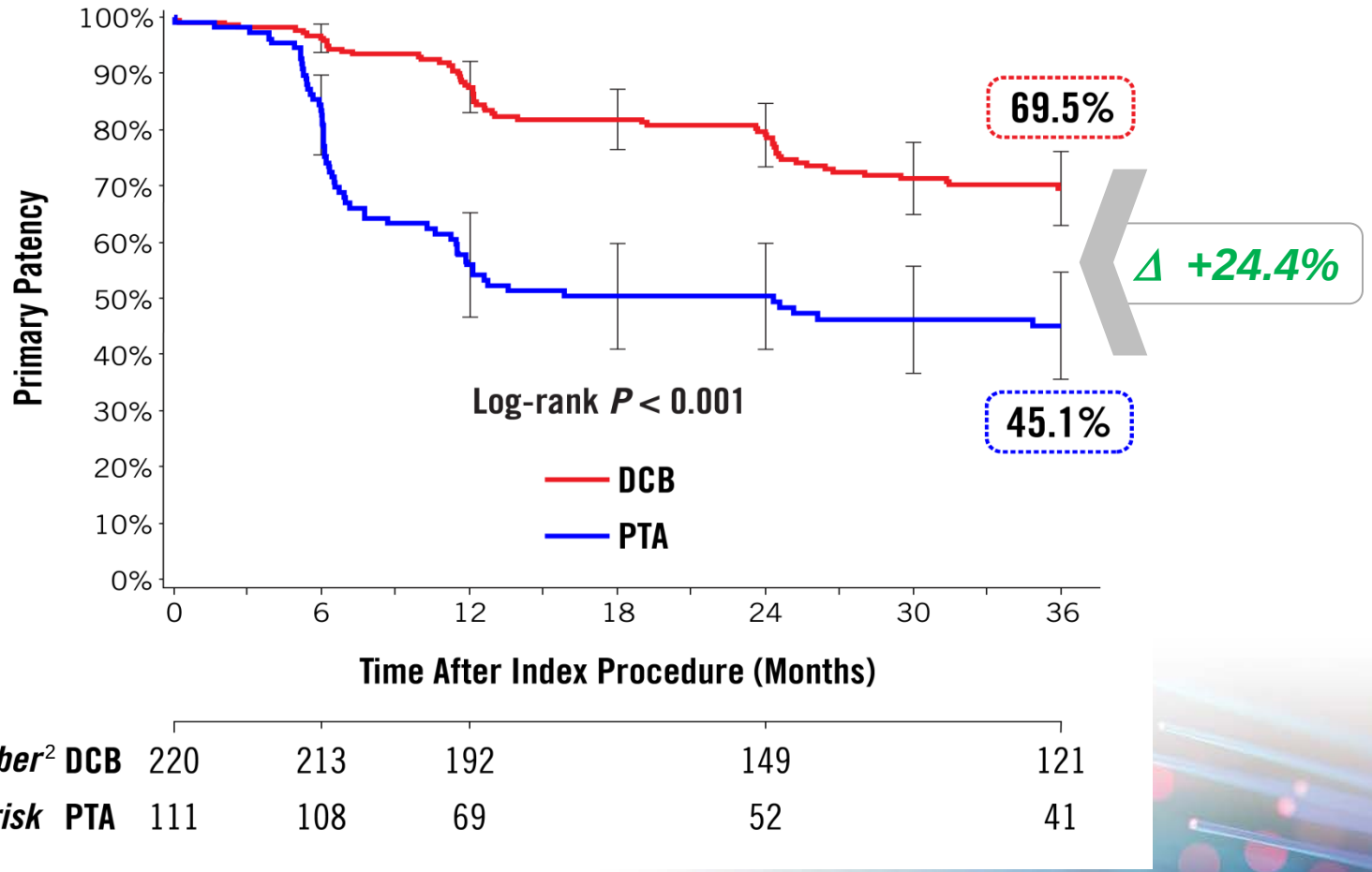
IN.PACT SFA Trial

Baseline Lesion Characteristics

	IN.PACT n = 220 Subjects, n = 221 Lesions	PTA n = 111 Subjects, n = 113 Lesions	P-value
Lesion length (cm ± SD)	8.94 ± 4.89	8.81 ± 5.12	0.815
Total occlusions, % (n)	25.8% (57/221)	19.5% (22/113)	0.222
Calcification, % (n)	59.3% (131/221)	58.4% (66/113)	0.907
Severe calcification, % (n)	8.1% (18/221)	6.2% (7/113)	0.662
Provisional stenting, % (n)	7.3% (16/220)	12.6% (14/111)	0.110

IN.PACT SFA Trial

Primary Patency[1] Through 3 Years



1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) and 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 each 30-day window

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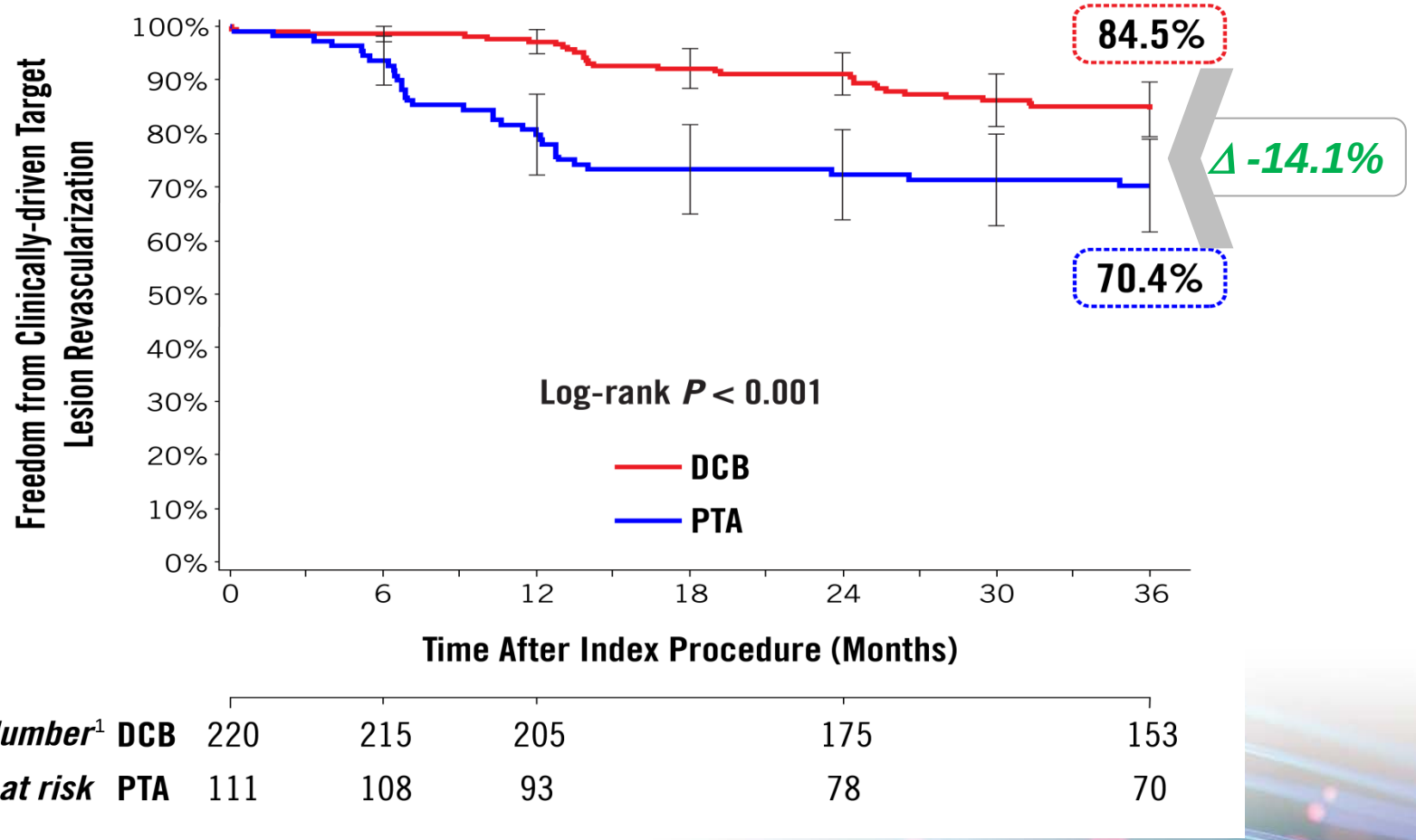
IN.PACT SFA Trial

Freedom from CD-TLR through 3 Years



1. Number at risk represents the number of evaluable subjects at the beginning of the each 30-day window

IN.PACT SFA Trial

Effectiveness Outcomes through 3 Years

	IN.PACT DCB (N=220)	PTA (N=111)	P-value†
Clinically-driven TLR [1]	15.2% (30/197)	31.1% (32/103)	0.002
All TLR [2]	16.2% (32/197)	34.0% (35/103)	< 0.001
Time to First CD-TLR	542.9 ± 278.2	302.9 ± 213.0	< 0.001
Primary Sustained Clinical Improvement [3]	68.7% (114/166)	52.6% (51/97)	0.012
ABI / TBI [4]	0.917 ± 0.231	0.894 ± 0.194	0.429

1. 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 ≥20% or >0.15 when compared to post-procedure baseline ABI
2. Any TLR includes clinically-driven and incidental or duplex driven TLR
3. Freedom from target limb amputation, target vessel revascularization (TVR), and increase in Rutherford class
4. TBI allowed / used in case of incompressible vessels in IN.PACT SFA II phase

† Unless otherwise indicated, all tests were for superiority using the Fisher's exact test for binary variables and t-test for continuous variables.

IN.PACT SFA Trial

Safety Outcomes through 3 Years

3-Year Outcomes	IN.PACT DCB N=220	PTA N=111	P-value†
Primary Safety Composite [1]	81.2% (160/197)	64.1% (66/103)	< 0.001‡
Major Adverse Events [2]	27.9% (55/197)	37.9% (39/103)	0.089
All-cause Death *	10.7% (21/197)	1.9% (2/103)	0.006
Device- or Procedure-related Death	0.0% (0/197)	0.0% (0/103)	N/A
Clinically-driven TVR	18.8% (37/197)	35.9% (37/103)	0.002
Target Limb Major Amputation	0.0% (0/197)	0.0% (0/103)	N/A
Thrombosis	2.0% (4/197)	4.9% (5/103)	0.283

1. Freedom from 30-day device and procedure-related death and target limb major amputation and clinically-driven TVR within 36 months
2. Composite of death, clinically-driven TVR, target limb major amputation, and thrombosis

* No deaths were adjudicated as device- or procedure-related by the CEC; Median post-index days to death: 610 days in DCB vs. 637 days in PTA

† P-values are based on Fisher's exact test for superiority with significance level of 0.05

‡ 10% Non-inferiority Test Margin with one-sided 97.5005% CL

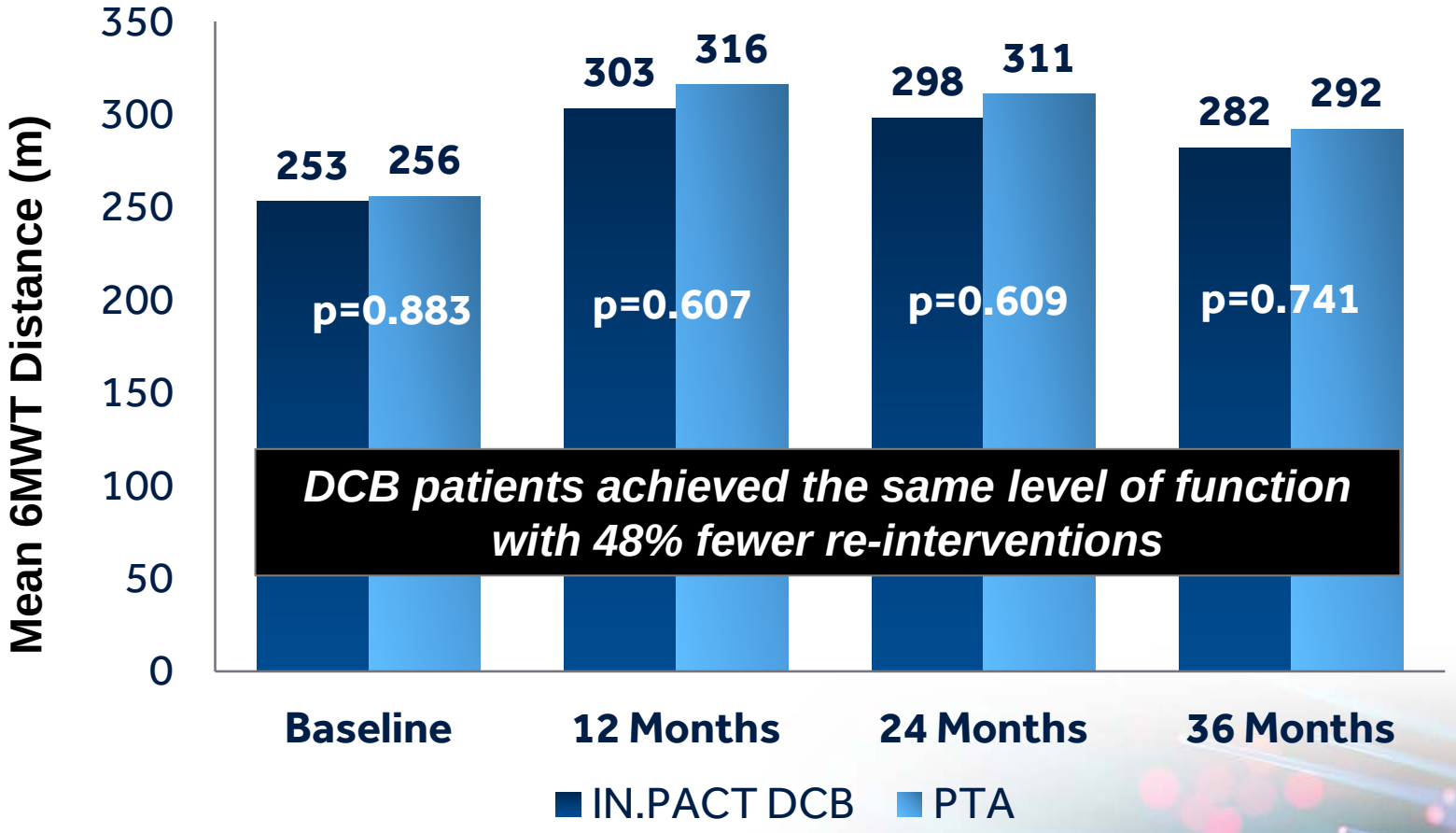
All-Cause Mortality through 3 Years

Causes of Death Through 3 Years	Treatment Group	Days to Death	CEC Adjudication	
			Procedure-Related (Y/N)	Device-Related (Y/N)
Cardiac-related				
Acute Diastolic Congestive Heart Failure	DCB	540	NO	NO
Cardiac Arrest	DCB	568	NO	NO
Cardiac Arrest	DCB	610	NO	NO
CAD	DCB	615	NO	NO
Ischemic Cardiomyopathy	DCB	699	NO	NO
Cardiac Arrest	DCB	907	NO	NO
Malignancy				
Metastatic Colon Cancer	**PTA**	397	NO	NO
GI Cancer	DCB	561	NO	NO
Worsening Pre-existing Carcinoma	**PTA**	877	NO	NO
Respiratory-related				
Acute Respiratory Failure	DCB	657	NO	NO
Hypoxic Respiratory Failure	DCB	681	NO	NO
Acute Respiratory Failure	DCB	1051	NO	NO
Other				
Infarction of Right Cerebral Hemisphere In Anterior & Medial Flow Region	DCB	127	NO	NO
Biliary Sepsis	DCB	168	NO	NO
Perforated Transverse Colon Secondary to Cecal Volvulus	DCB	314	NO	NO
Sepsis	DCB	374	NO	NO
Deterioration of General Condition	DCB	603	NO	NO
Dementia	DCB	679	NO	NO
Septic Shock	DCB	756	NO	NO
Hemorrhagic Stroke	DCB	788	NO	NO
Gastric Perforation	DCB	1055	NO	NO
Unknown				
Sudden Death	DCB	287	NO	NO
Unknown	DCB	541	NO	NO

IN.PACT SFA Trial

3-Year Functional Outcomes

6-Minute Walk Test*



*Data collected in IN.PACT SFA II phase only

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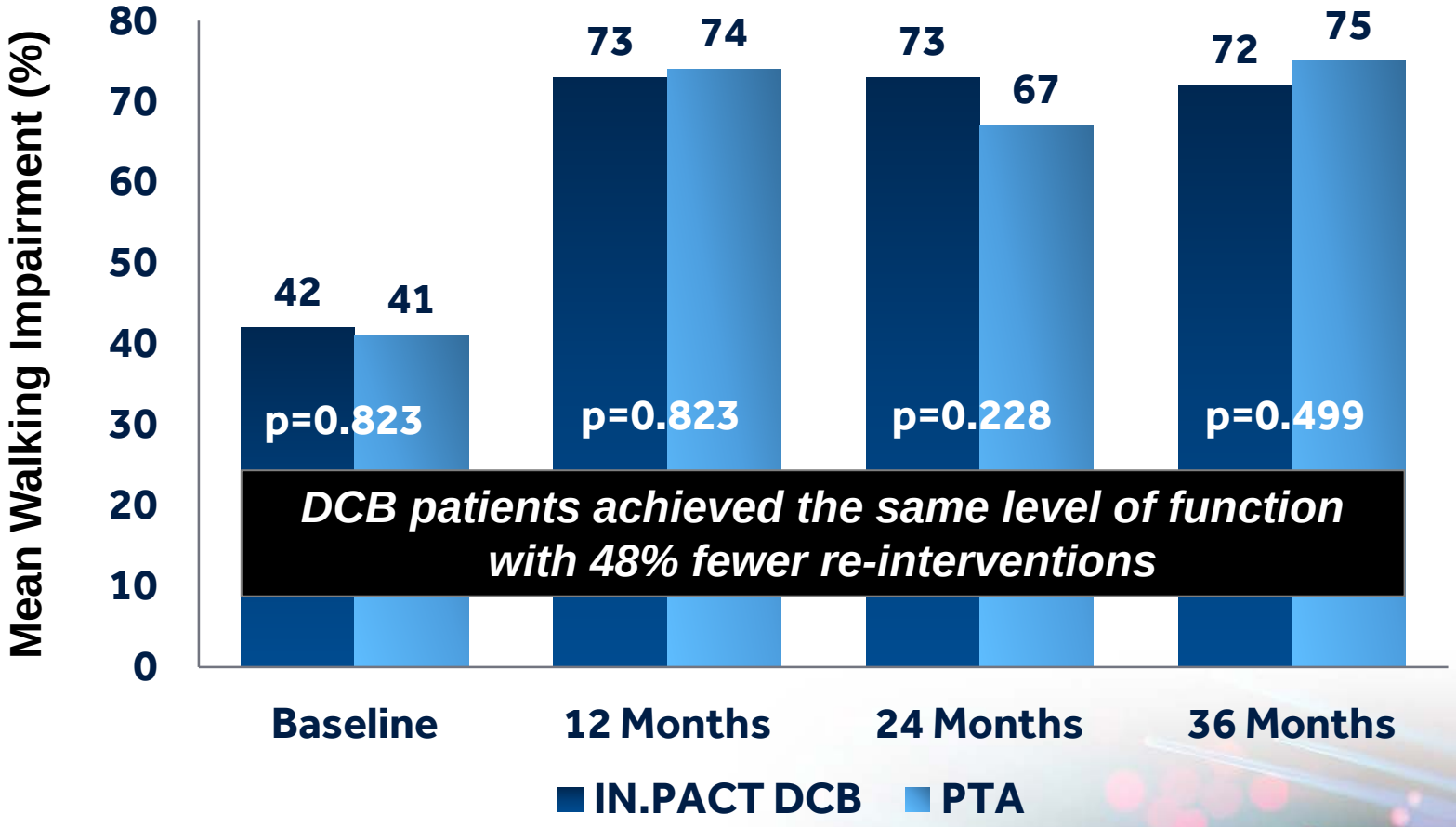
IN.PACT SFA Trial

3-Year Functional Outcomes

Walking Impairment



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IN.PACT SFA Trial

Summary

Superior 3-year patency and low intervention rates with the IN.PACT™ Admiral™ Drug-Coated Balloon

Durability

- First independently adjudicated, randomized pivotal IDE trial to show durable treatment effect with a DCB through three years

Safety

- Results demonstrate long-term safety of IN.PACT Admiral DCB

Paradigm Shift

- Data support IN.PACT™ Admiral™ as a first-line treatment for symptomatic femoropopliteal disease

IN.PACT™ Admiral™ Drug-Coated PTA Balloon Catheter
Brief Statement

Indications for Use:
The IN.PACT™ Admiral™ Paclitaxel-Coated PTA Balloon catheter is indicated for percutaneous transluminal angioplasty, after appropriate vessel preparation, of de novo, restenotic, or in-stent restenotic lesions with lengths up to 180 mm in superficial femoral or popliteal arteries with reference vessel diameters of 4-7 mm.

Contraindications
The IN.PACT Admiral DCB is contraindicated for use in:

- Coronary arteries, renal arteries, and supra-aortic/cerebrovascular arteries
- Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system
- Patients with known allergies or sensitivities to paclitaxel
- Women who are breastfeeding, pregnant or are intending to become pregnant or men intending to father children. It is unknown whether paclitaxel will be excreted in human milk and whether there is a potential for adverse reaction in nursing infants from paclitaxel exposure.

Warnings

- Use the product prior to the Use-by Date specified on the package.
- Contents are supplied sterile. Do not use the product if the inner packaging is damaged or opened.
- Do not use air or any gaseous medium to inflate the balloon. Use only the recommended inflation medium (equal parts contrast medium and saline solution).
- Do not move the guidewire during inflation of the IN.PACT Admiral DCB.
- Do not exceed the rated burst pressure (RBP). The RBP (14 atm [1419 kPa]) is based on the results of in vitro testing. Use of pressures higher than RBP may result in a ruptured balloon with possible intimal damage and dissection.
- The safety and effectiveness of using multiple IN.PACT Admiral DCBs with a total drug dosage exceeding 20,691 µg of paclitaxel in a patient has not been clinically evaluated in the IN.PACT SFA Trial.

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IN.PACT™ Admiral™ Drug-Coated PTA Balloon Catheter
Brief Statement

Precautions

- This product should only be used by physicians trained in percutaneous transluminal angioplasty (PTA).
- This product is designed for single patient use only. Do not reuse, reprocess, or resterilize this product. Reuse, reprocessing, or resterilization may compromise the structural integrity of the device and/or create a risk of contamination of the device, which could result in patient injury, illness, or death.
- Assess risks and benefits before treating patients with a history of severe reaction to contrast agents.
- The safety and effectiveness of the IN.PACT Admiral DCB used in conjunction with other drug-eluting stents or drug-coated balloons in the same procedure or following treatment failure has not been evaluated.
- The extent of the patient's exposure to the drug coating is directly related to the number of balloons used. Refer to the *Instructions for Use* (IFU) for details regarding the use of multiple balloons and paclitaxel content.
- The use of this product carries the risks associated with percutaneous transluminal angioplasty, including thrombosis, vascular complications, and/or bleeding events
- Vessel preparation using only pre-dilatation was studied in the clinical study. Other methods of vessel preparation, such as atherectomy, have not been studied clinically with IN.PACT Admiral DCB.
- This product is not intended for the expansion or delivery of a stent

Potential Adverse Effects

The potential adverse effects (e.g. complications) associated with the use of the device are: abrupt vessel closure; access site pain; allergic reaction to contrast medium, antiplatelet therapy, or catheter system components (materials, drugs, and excipients); amputation/loss of limb; arrhythmias; arterial aneurysm; arterial thrombosis; arteriovenous (AV) fistula; death; dissection; embolization; fever; hematoma; hemorrhage; hypotension/hypertension; inflammation; ischemia or infarction of tissue/organ; local infection at access site; local or distal embolic events; perforation or rupture of the artery; pseudoaneurysm; renal insufficiency or failure; restenosis of the dilated artery; sepsis or systemic infection; shock; stroke; systemic embolization; vessel spasms or recoil; vessel trauma which requires surgical repair.

Potential complications of peripheral balloon catheterization include, but are not limited to the following: balloon rupture; detachment of a component of the balloon and/or catheter system; failure of the balloon to perform as intended; failure to cross the lesion.

Although systemic effects are not anticipated, potential adverse events that may be unique to the paclitaxel drug coating include, but are not limited to: allergic/immunologic reaction; alopecia; anemia; gastrointestinal symptoms; hematologic dyscrasia (including leucopenia, neutropenia, thrombocytopenia); hepatic enzyme changes; histologic changes in vessel wall, including inflammation, cellular damage, or necrosis; myalgia/arthralgia; myelosuppression; peripheral neuropathy.

Refer to the Physician's Desk Reference for more information on the potential adverse effects observed with paclitaxel. There may be other potential adverse effects that are unforeseen at this time.

Please reference appropriate product Instructions for Use for a detailed list of indications, warnings, precautions and potential adverse effects. This content is available electronically at www.manuals.medtronic.com.

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician.

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www.peripheral.medtronicendovascular.com/international

www.aortic.medtronicendovascular.com

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