IN.PACT SFA: A Prospective Randomized Trial of a Drug-Coated Balloon for Femoropopliteal Lesions– Two-Year Outcomes

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On behalf of the IN.PACT SFA Trial investigators

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support	• WL Gore, Medtronic
• Consulting Fees/Honoraria	• Abbott Vascular, Bard Peripheral Vascular, Boston Scientific, Cordis, Medtronic
• Major Stock Shareholder/Equity	• Syntervention, AngioSlide, BioCardia, Endoluminal Sciences, Reflow Medical, Eximo, Shockwave Medical, Ostial, PQ Bypass

Background

- SFA disease remains a challenge to manage with no evidence-based standard treatment defined
- PTA is associated with high incidence of restenosis when used for anything but focal, noncomplex lesions
- Reported long-term patency rates with stents range from 60-75%[1-2], but concerns persist about in-stent restenosis and stent fractures
- Promising early results with drug-coated balloons in randomized trials, but longer term results are lacking

1. Dake MD et al. *J Am Coll Cardiol.* 2013;61:2417-27. 2. Rocha-Singh KJ, et al. *Catheter Cardiovasc Interv.* 2015

IN.PACT SFA Trial Overview

***Objective*: 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**

- **Prospective, multicenter EU and US, randomized (2:1), single-blinded trial**
- **331 patients enrolled:**
  IN.PACT DCB (n = 220) *vs.* PTA (n = 111)
- **Rutherford Clinical Category 2-4**
- **Lesion lengths 4-18 cm or occlusions ≤ 10 cm**
- **Subjects followed up to 5 years**
- **Independent and blinded Duplex Ultrasound Core Lab,[1] Angiographic Core Lab,[2] and Clinical Events Committee[3]**

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***

Baseline Clinical Characteristics

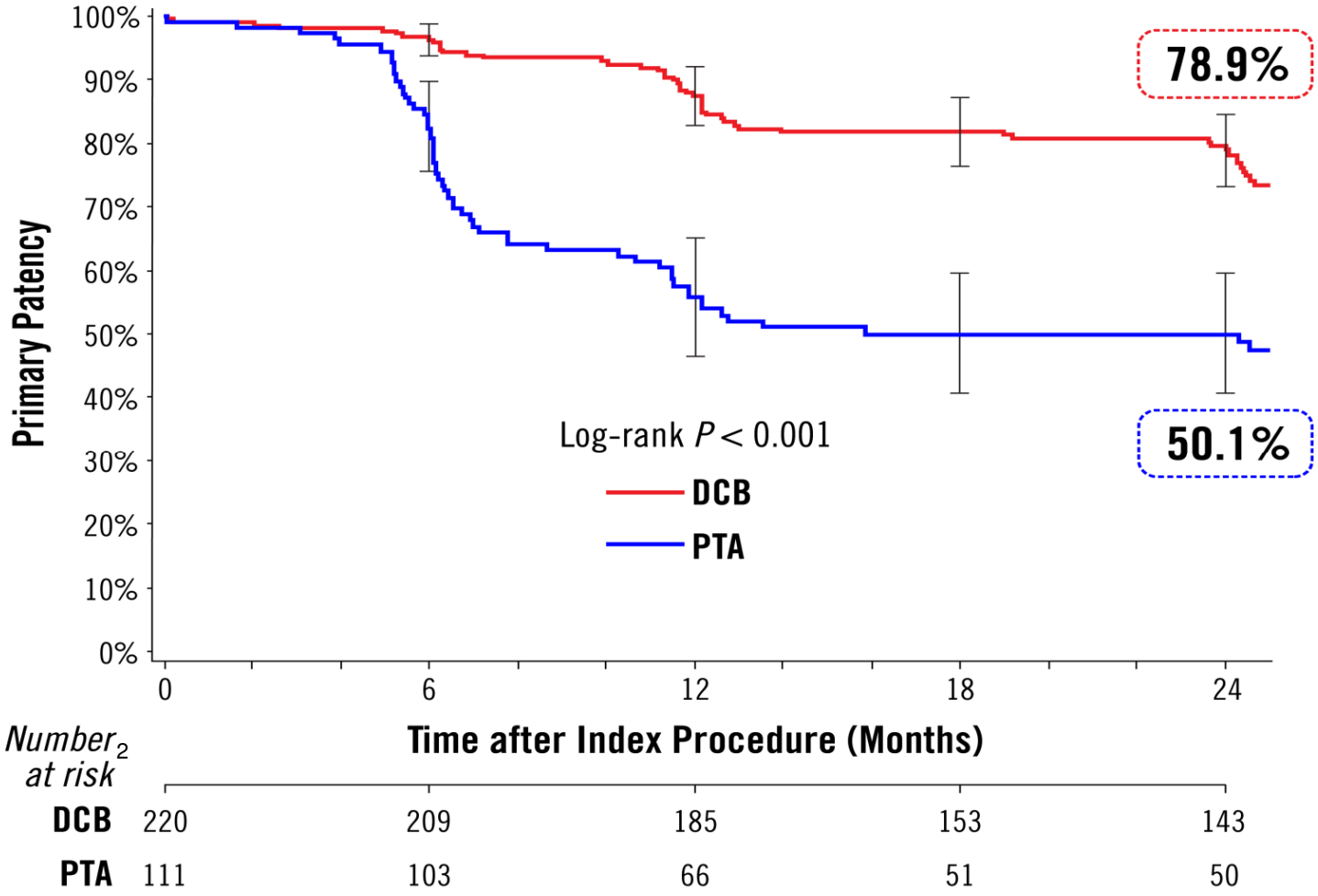
	IN.PACT n = 220 subjects	PTA n = 111 subjects	p
Age, Y ± SD	67.5 ± 9.5	68.0 ± 9.2	0.612
Male, % (n)	65.0% (143/220)	67.6% (75/111)	0.713
Diabetes, % (n)	40.5% (89/220)	48.6% (54/111)	0.161
Hypertension, % (n)	91.4% (201/220)	88.3% (98/111)	0.431
Current smoker, % (n)	38.6% (85/220)	36.0% (40/111)	0.719
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

Baseline Lesion Characteristics

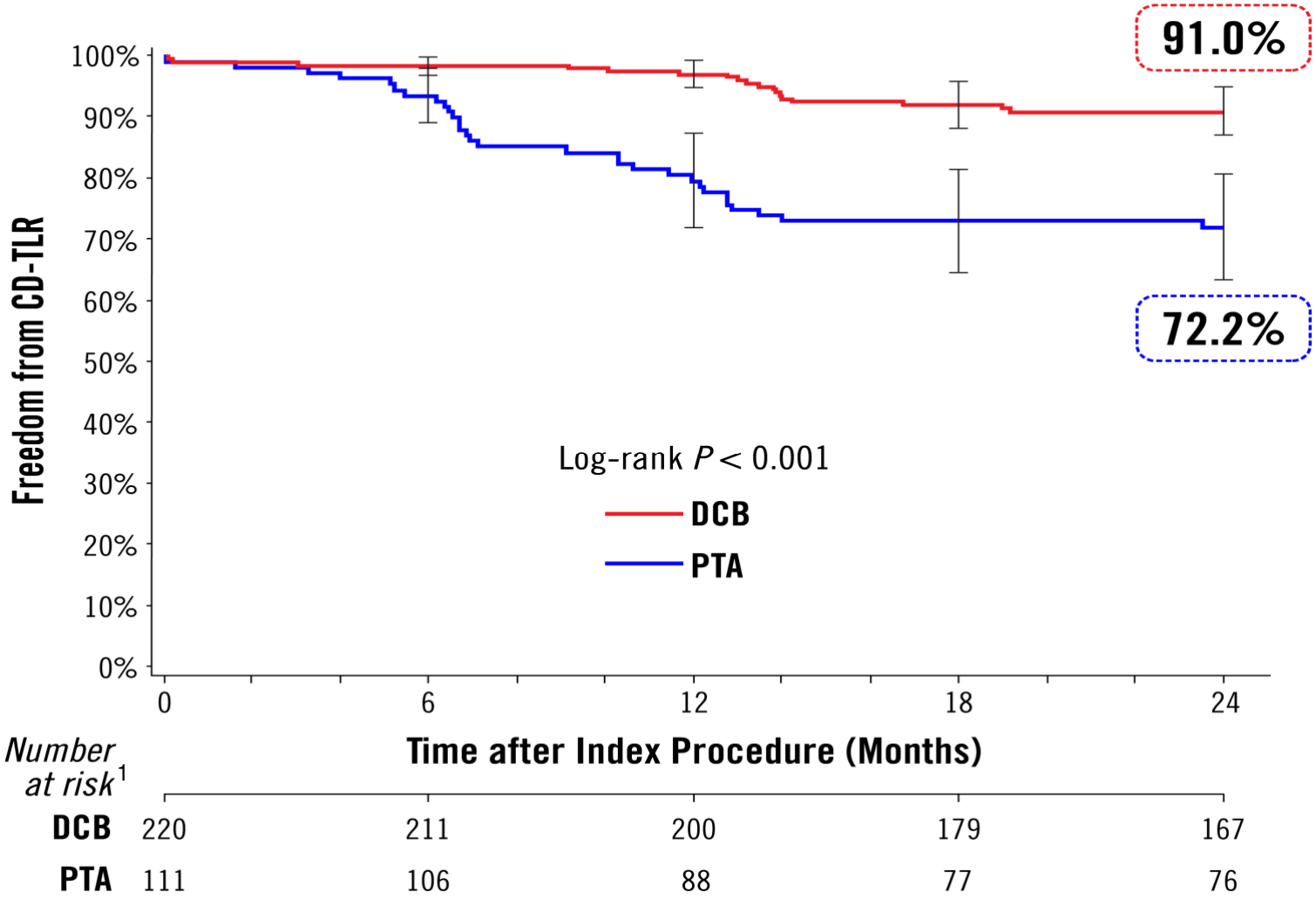
	IN.PACT n = 220 Subjects, n = 221 Lesions	PTA n = 111 Subjects, n = 113 Lesions	p
Lesion length (cm ± SD)	8.94 ± 4.89	8.81 ± 5.12	0.815
Total occlusions, % (n)	25.8% (57/221)	19.5% (22/113)	0.222
Calcification, % (n)	59.3% (131/221)	58.4% (66/113)	0.907
Severe calcification, % (n)	8.1% (18/221)	6.2%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

Primary Patency[1] Results through 2 Years



1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) or clinically-driven target lesion revascularization through 24 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 30-day window prior to each follow-up interval

Freedom from CD-TLR through 2 Years



1. Number at risk represents the number of evaluable subjects at the beginning of the 30-day window prior to each follow-up interval

IN.PACT SFA Trial
Effectiveness Outcomes Through 2 Years

2-Year Outcomes	IN.PACT n = 220	PTA n = 111	p*
Clinically-driven TLR [1]	9.1% (18/198)	28.3% (30/106)	< 0.001
All TLR [2]	10.1% (20/198)	29.2% (31/106)	< 0.001
Primary Sustained Clinical Improvement [3]	76.9% (133/173)	59.2% (61/103)	0.003
ABI / TBI [4]	0.924 ± 0.261	0.938 ± 0.184	0.611

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. All 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 in cases 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 2 Years

2-Year Outcomes	IN.PACT n = 220	PTA n = 111	p*
Primary Safety Composite [1]	87.4% (173/198)	69.8% (74/106)	< 0.001
Major Adverse Events [2]	19.2% (38/198)	31.1% (33/106)	0.023
All-cause Death †	8.1% (16/198)	0.9% (1/106)	0.008
Device- or Procedure-related Death	0.0% (0/198)	0.0% (0/106)	> 0.999
Clinically-driven TVR	12.6% (25/198)	30.2% (32/106)	< 0.001
Target Limb Major Amputation	0.0% (0/198)	0.0% (0/106)	> 0.999
Thrombosis	1.5% (3/198)	3.8% (4/106)	0.243

1. Freedom from 30-day device and procedure-related death and target limb major amputation and clinically-driven TVR within 12 (24) months
2. Composite of death, clinically-driven TVR, target limb major amputation, and thrombosis

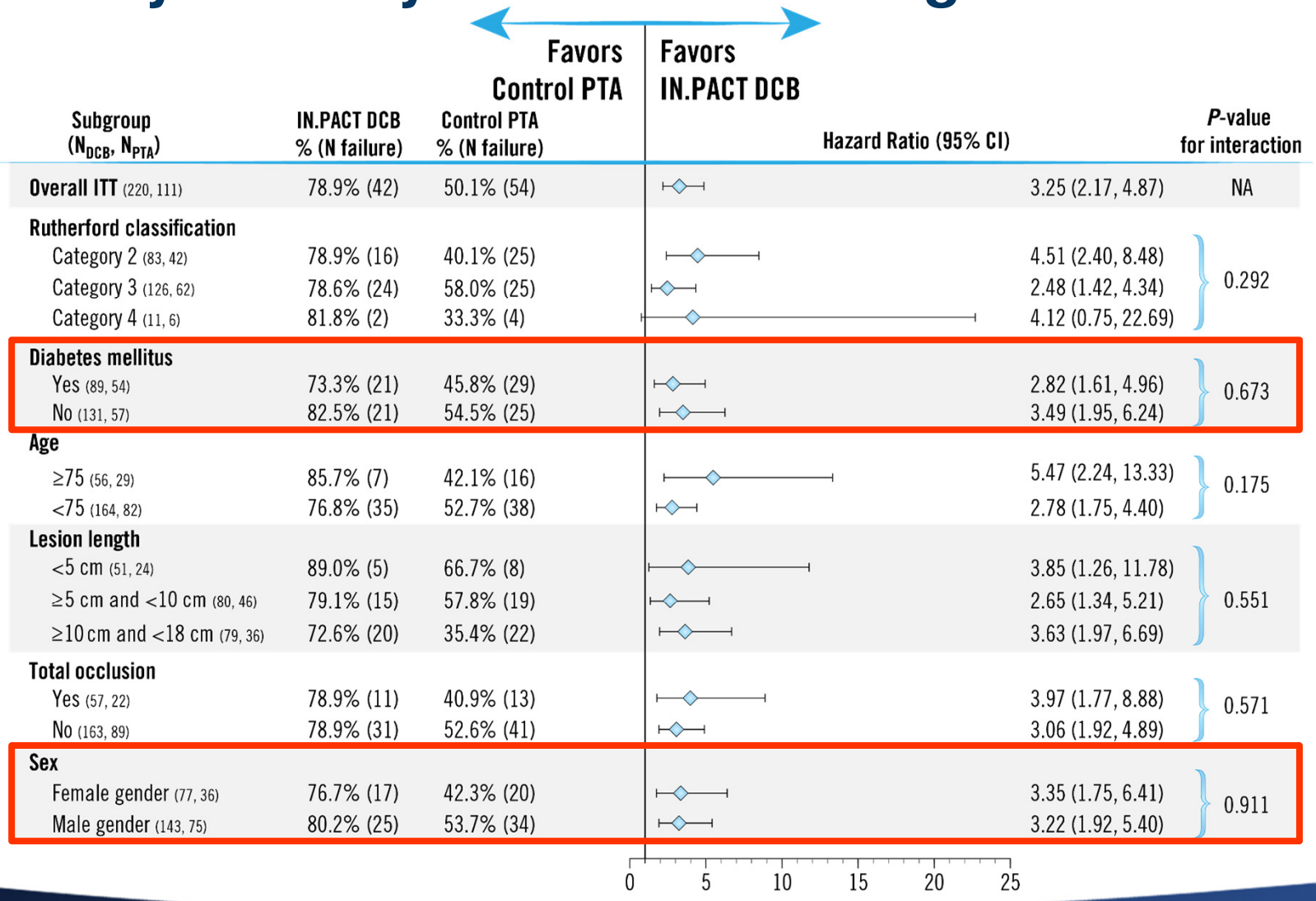
* *p*-values are based on Fisher's exact test for superiority with significance level of 0.05

† No deaths were adjudicated as device- or procedure-related by the CEC; Median post-index days to death: 564.5 days in DCB vs. 397 days in PTA

All-cause Mortality Through 2 Years

Causes of Death Through 2 Years	Treatment Group	Days to Death	CEC Adjudication	
			Procedure-related	Device-related
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
Malignancy				
Metastatic Colon Cancer	PTA	540	NO	NO
GI Cancer	DCB	561	NO	NO
Respiratory-related				
Acute Respiratory Failure	DCB	657	NO	NO
Hypoxic Respiratory Failure	DCB	681	NO	NO
Other				
Infarction of the Right Cerebral Hemisphere in the Anterior and 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
Unknown				
Sudden Death	DCB	287	NO	NO
Unknown	DCB	541	NO	NO

IN.PACT SFA Trial Subgroups
Primary Patency Outcomes through 2 Years



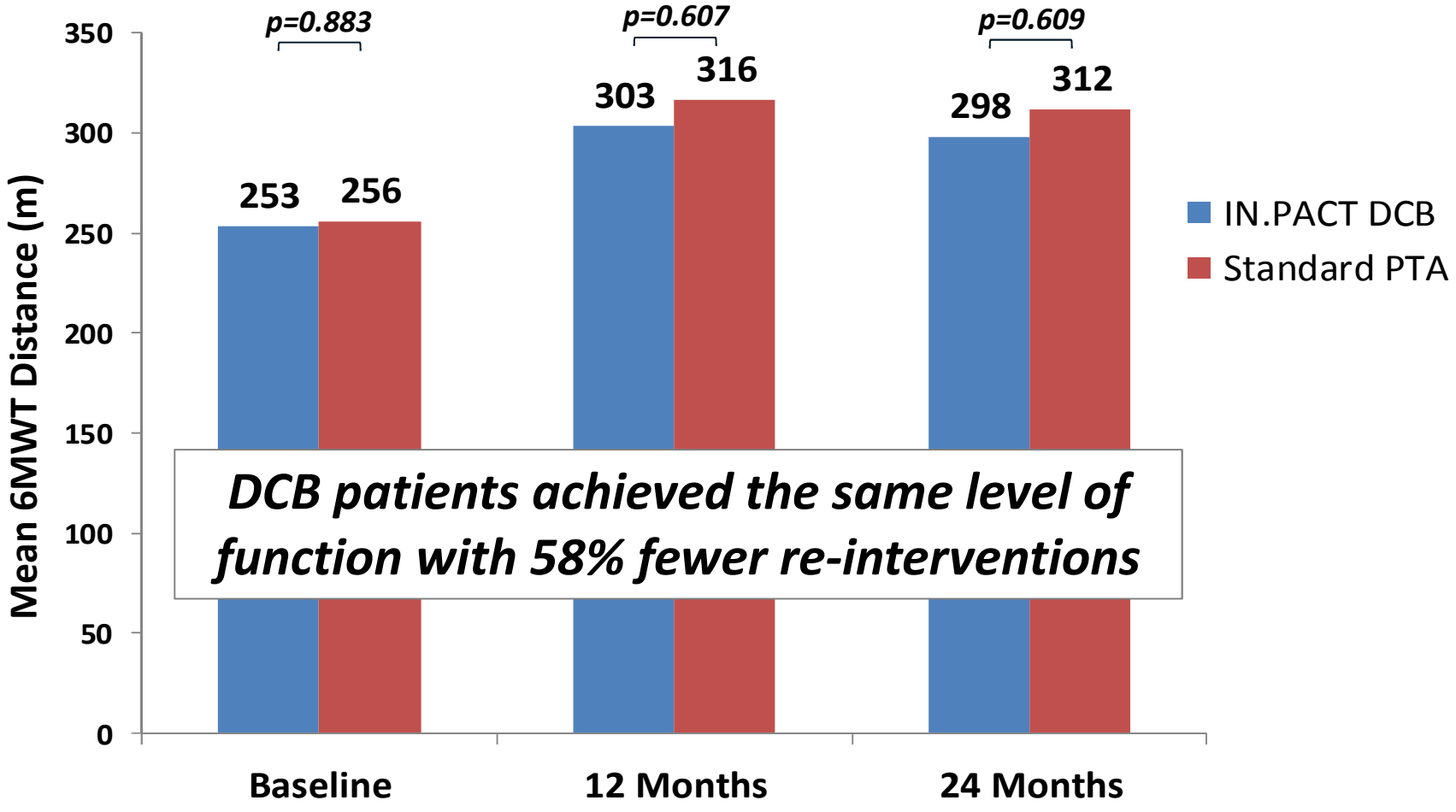
IN.PACT SFA Trial Subgroups
Primary Patency at 2 Years by Gender

Gender Subgroup (N_{DCB}, N_{PTA})	IN.PACT % (N failure)	PTA % (N failure)	p
Female (77, 36)	76.7% (17)	42.3% (20)	< 0.001
Male (143, 75)	80.2% (25)	53.7% (34)	< 0.001

IN.PACT SFA Trial Subgroups
Primary Patency at 2 Years
by Diabetic Status

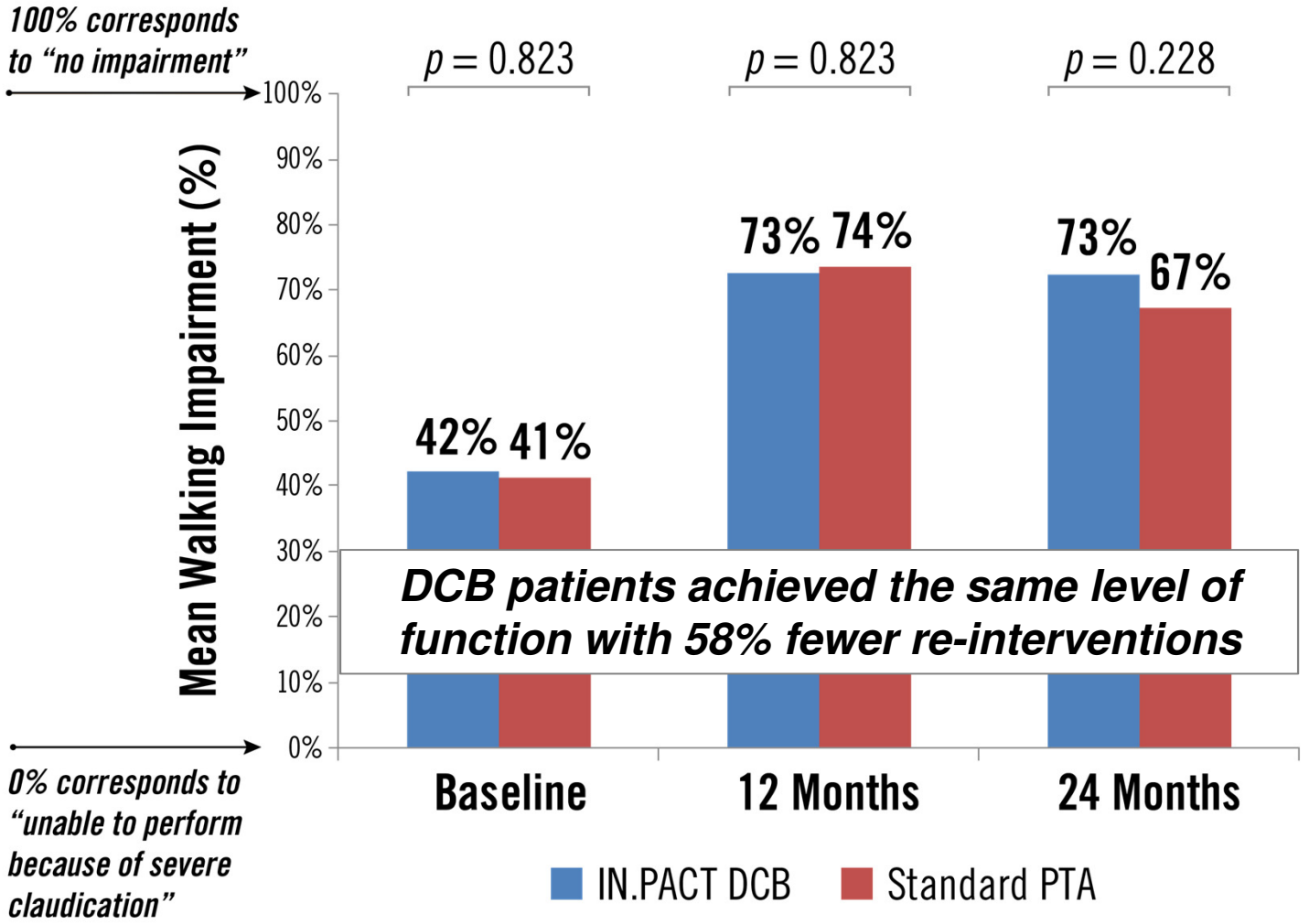
Diabetes Subgroup (N_{DCB}, N_{PTA})	IN.PACT % (N failure)	PTA % (N failure)	p
Diabetic (89, 54)	73.3% (21)	45.8% (29)	< 0.001
Non-diabetic (131, 57)	82.5% (21)	54.5% (25)	< 0.001

2-year Functional Outcomes: 6 Minute Walk Test*



*Data collected in IN.PACT SFA II phase only

2-year Functional Outcomes: Walking Impairment



Conclusions

Two-year results demonstrate durability and continued superiority of the IN.PACT Admiral DCB over PTA

- Sustained durability of IN.PACT Admiral DCB treatment effect with no late catch-up through 2 years

2-Year Results	DCB	PTA	Δ	p-value
Primary Patency	**78.9%**	50.1%	**28.8%**	<0.001
CD-TLR	**9.1%**	28.3%	**19.2%**	<0.001

- Consistent, durable results in subgroups including females and diabetics
- IN.PACT Admiral DCB subjects had similar functional outcomes with 58% fewer re-interventions
- Potential to drive a paradigm shift in SFA interventions