Update on IN.PACT DCB Clinical Evidence:

IN.PACT SFA &
IN.PACT Global Studies Results

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Disclosures

Speaker: Prof. Seung-Woon Rha

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 speakers‘ bureau
- ❑ Employment in industry
- ❑ Shareholder in a healthcare company
- ❑ Owner of a healthcare company

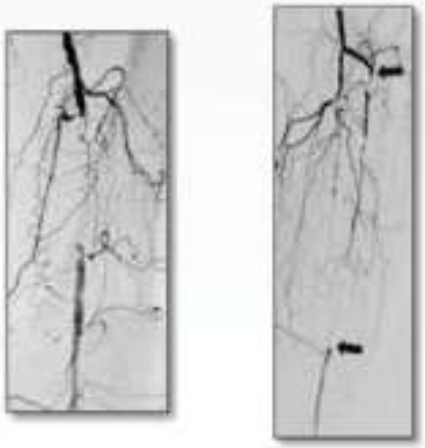
❑ I do not have any potential conflict of interest

Technology of IN.PACT Admiral

Background – Unmet Clinical Needs

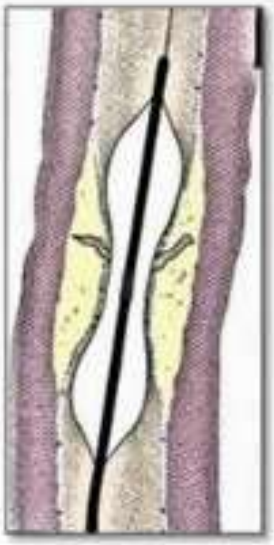
De Novo Lesions

Small vessels(BTK) high movement or flexion Sites(SFA/POP)



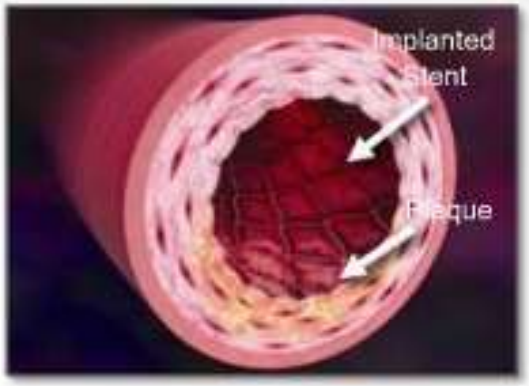
Stent should not be placed or It may not be ideal

Restenosis After POBA



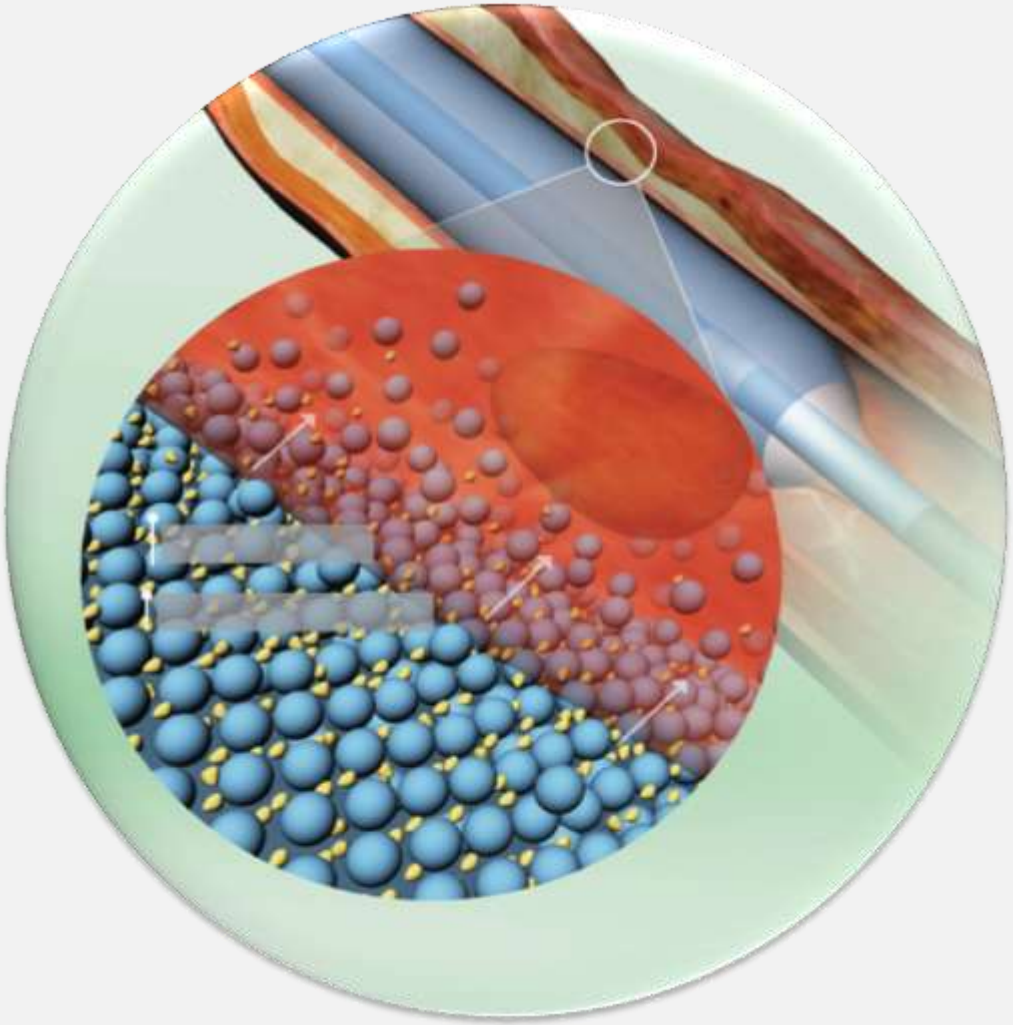
Anti-proliferative therapy desired

In-Stent Restenosis



Stent-in-stent not desired

IN.PACT Holding the Promise



DES-like efficacy

with

BMS-like safety

with

PTA-like deliverability

with

Nothing left behind

Drug Eluting Balloon Technology

Component	Function	Design Goal	Example
Platform	• PTA Dilatation • Drug Carriers	• Easy-to-use • Highly deliverable • Full size matrix	• PTA balloons
Drug	• Restenosis prevention	• Potent anti-proliferative • Hydrophobic • Lipophilic	• Paclitaxel • Sirolimus
Excipient	• Drug retention • Release control	• Hydrophilic • Biocompatible	• Contrast Media • Natural agents • Custom Polymers
Coating Process	• Apply drug/excipient formulation to balloon surface	• Uniform mix and layer • Reproducibility • Scalability	• Dip • Spray • Custom Application

IN.PACT Technology Overview

- **A proven balloon platform utilising Medtronic's proprietary FreePac® coating technology, offering rapid drug transfer and consistent quality**

Platform	**Invatec®**	Proven PTA balloon line
Drug	**Paclitaxel**	Hydrophobic, lipophilic, proven anti-proliferative
Excipient	**Urea**	Hydrophilic, naturally occurring, non-toxic
Coating process	**Medtronic®**	Uniformity + stability + release controlled and scalable

Paclitaxel

- **Antiproliferative** action on SMC known since 1988
  - Natural substance from the taxus brevifolia (yew tree)
  - Approved to cure ovarian cancer in US in 1992
  - Normally used at doses up to 300mg/day in cancer therapy
- **Hydrophobic**: limited wash out
- **Lipophilic**: attracted by lipids and proteins (protein-bound)

Rowinsky and Donehower (1995), Axel et al. (1997), Margolis et al. (2007)

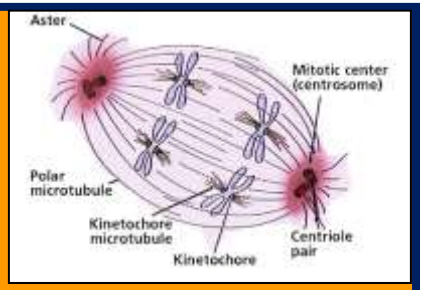
Paclitaxel is the right choice for DEB

Paclitaxel is…

- **Proven** — Long history of use as anti-proliferative
- **Potent** — Strong inhibitor of cell division
- **Retained** — In tissue up to 6 months
- **Durable** — Induces permanent effect

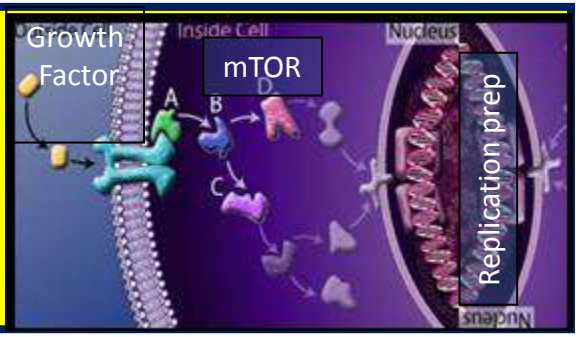
Paclitaxel

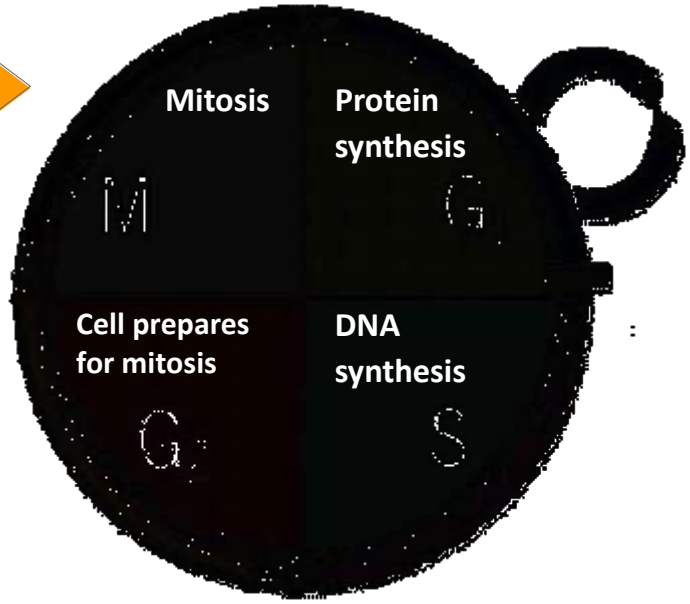
Interferes with cell division at the M phase, after DNA synthesis has occurred.



Rapamycin

Interferes with cell growth at the G1/S transition, before DNA synthesis.





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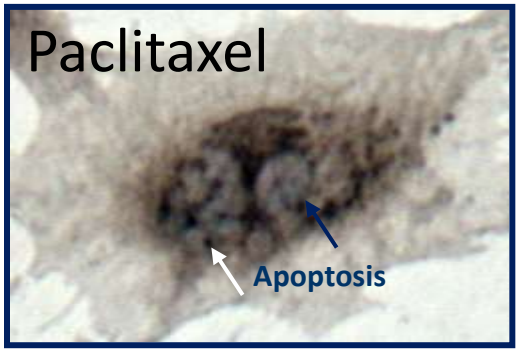
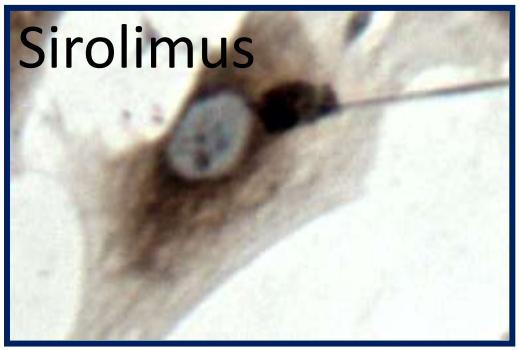




Why Paclitaxel works for DEB

Paclitaxel is more lipophilic and requires shorter tissue absorption time than limus.

- Longer tissue retention rates after delivery.[1]
- Limus DEBs have not yet shown they can suppress cell proliferation.[2]

➡ **Quick Absorption**

Lovich, Creel, Hong, Hwang, and Edelman (2001), Zou, Cao, Xi, and Zhang (2009)

Why Paclitaxel works for DEB

Paclitaxel is a more potent inhibitor of cell profileration than limus.

- Paclitaxel permanently eliminates or inhibits proliferating cells.[5]
- Limus drugs temporarily stop cell proliferation [5]

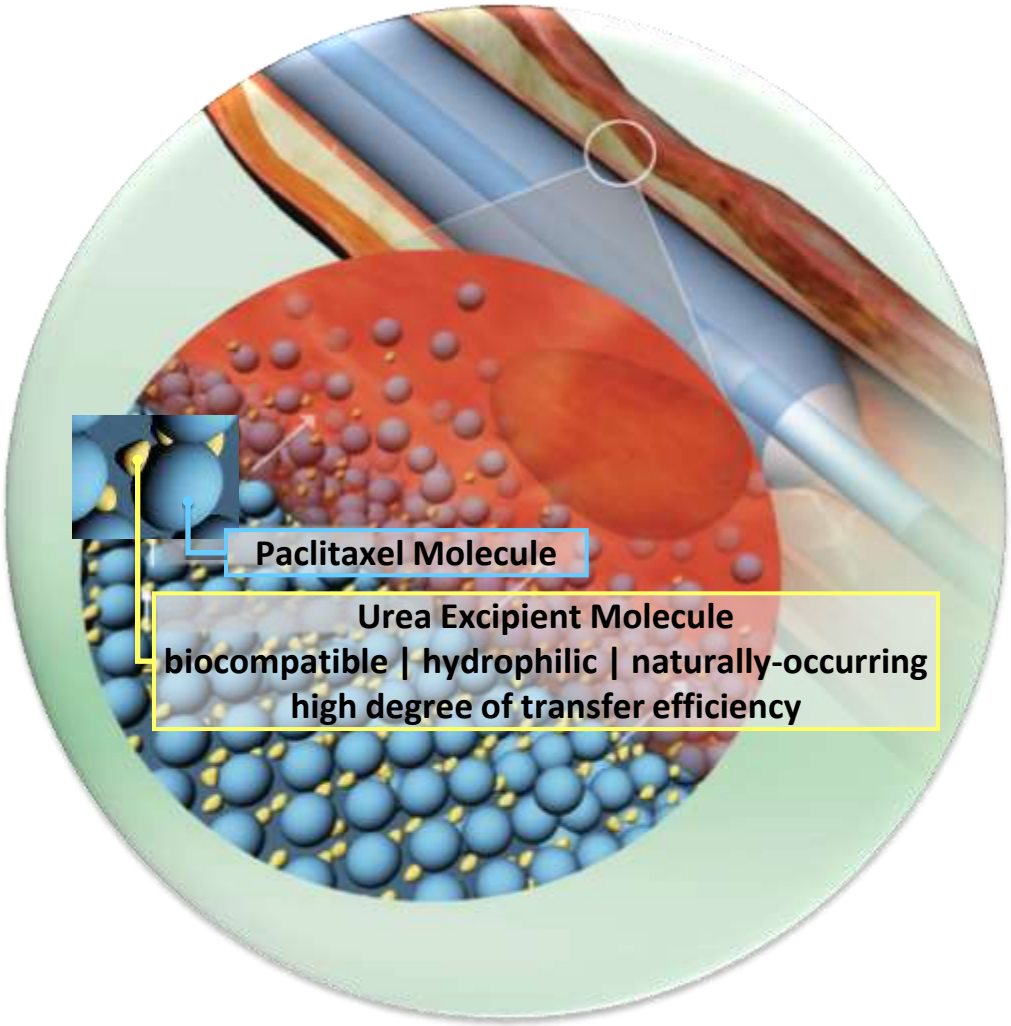
➡ More Potent

Krucoff et al. (2008), Schnorr et al. (2010)

IN.PACT –
The Only Known Natural Excipient

	IN.PACT™	Paccocath™ Prototype in early studies	Lutonix Moxy	Medrad Cotavance	Eurocor Freeway
Drug	Paclitaxel	Paclitaxel	Paclitaxel	Paclitaxel	Paclitaxel
Excipient	Urea (100% natural)	Ultravist (Contrast Media)	?	Ultravist (Contrast Media)	Shellac (Resin)

IN.PACT DEB with FreePac Coating



IN.PACT™

- Medtronic-Invatec DEB balloon line

FreePac™

- Proprietary hydrophilic coating formulation
  - **Urea** facilitates improved drug transfer efficiency from balloon
  - **Urea** facilitates Paclitaxel absorption into the vessel wall

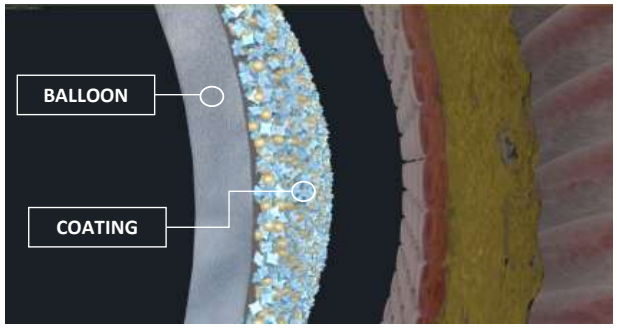
Coating Technology

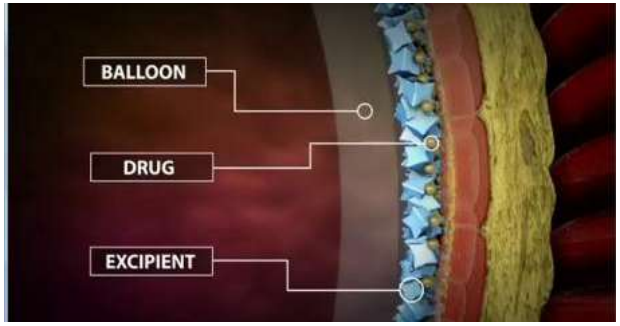
IN.PACT's proprietary coating technology provides advantages over first generation coating technologies

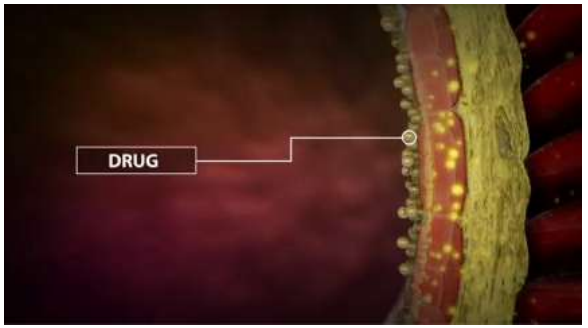
Competitors' First-Generation DEB Coatings	Medtronic Invatec's Proprietary DEB Coating Process
• Standard dipping process • Layer and mix inconsistent	• Automated, controlled drug dispersing • Layer and mix uniformity • Large-scale reproducibility

IN.PACT Mechanism of Action: Dilatation + Drug Delivery

- Mechanical drug transfer
- Lipophilic drug redistribution and sequestration
- Sustained retention of low drug levels for extended neointimal inhibition

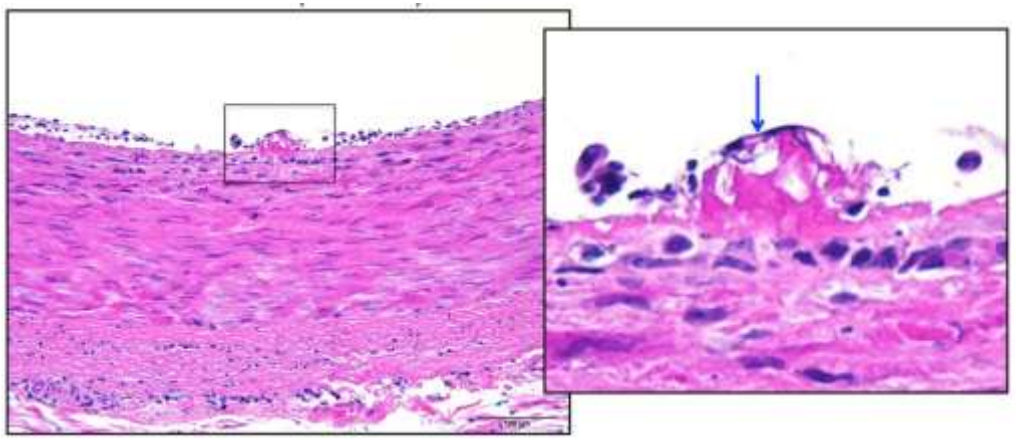






Histology Confirms Transfer of PTX

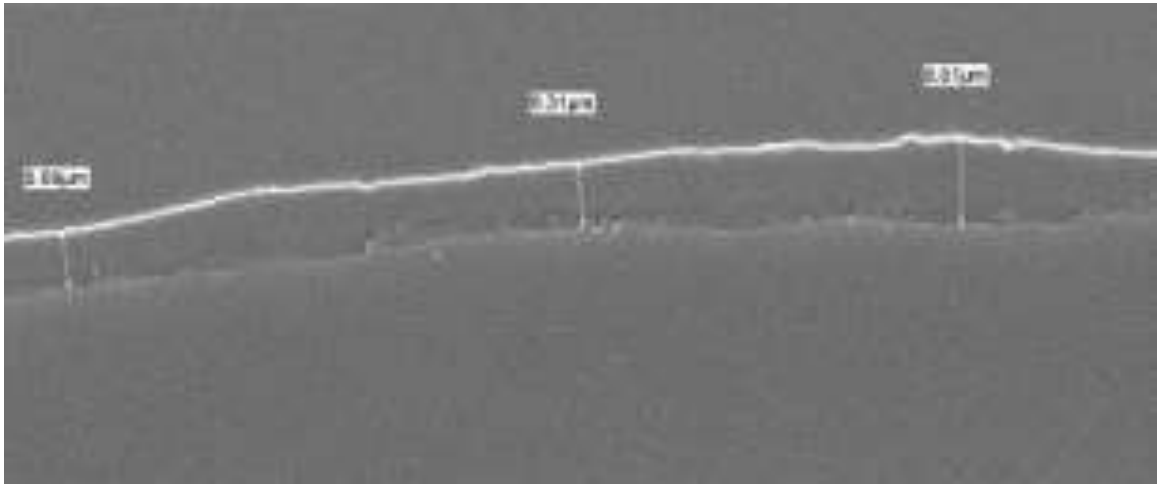
High (20x and 40x) power images of crystalline material (yellow arrows) within fibrin. Sections shown are stained by Hematoxylin & Eosin (H&E)



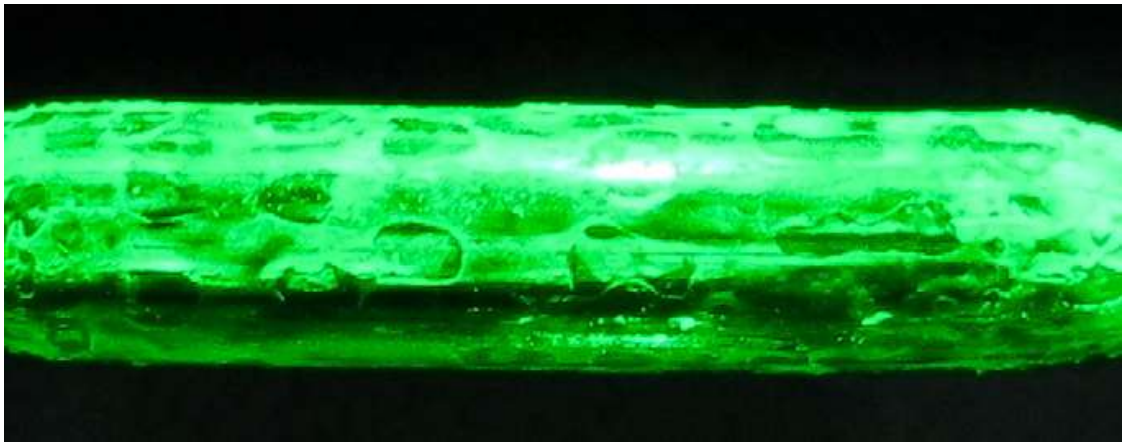
Paclitaxel crystals provide a source for extended drug release to the intima

FreePac Uniformity

Longitudinal Coating Thickness Uniformity+/- 6%



Circumferential Coating Uniformity +/- 2%



Drug Delivery :

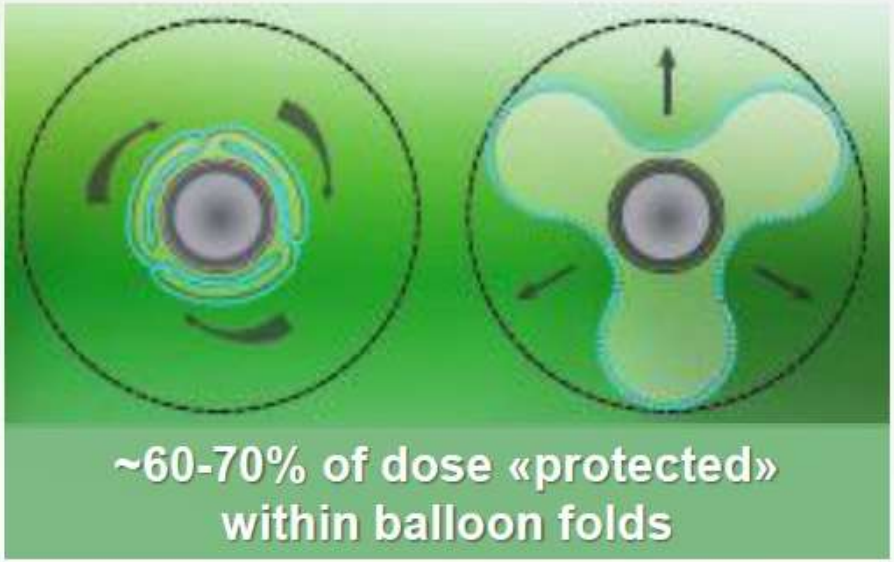
What Happens to the drug during the procedure?

DEB advancement → ~ 20% of Drug lost during DEB delivery to the target lesion *(in-vitro GLP studies)**

DEB inflation → ~ 20% of Drug delivered to the vessel wall *(in-vivo GLP PK Studies)**

DEB retrieval → ~ 10-20% found on balloon surface after removal *(in-vitro / in-vivo GLP studies)**

~ 40-50% wash-out



~60-70% of dose «protected» within balloon folds

*data on file at Medtronic (GLP Study FS208; In Vitro Report RE-11050-001; GLP Study PS516)

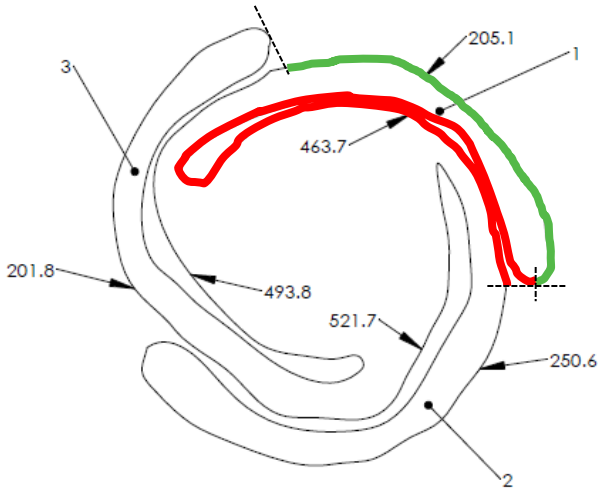
FreePac Durability:

Coating Protected By Balloon Folds

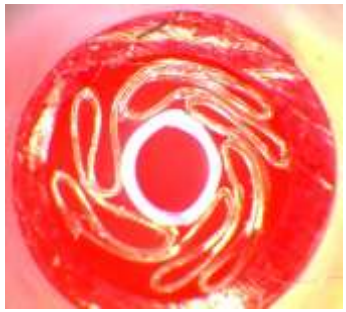
3 Fold Design (2-4mm diameters)

Red ≈ 70%
Covered balloon surface

Green ≈ 30%
Non-covered balloon surface

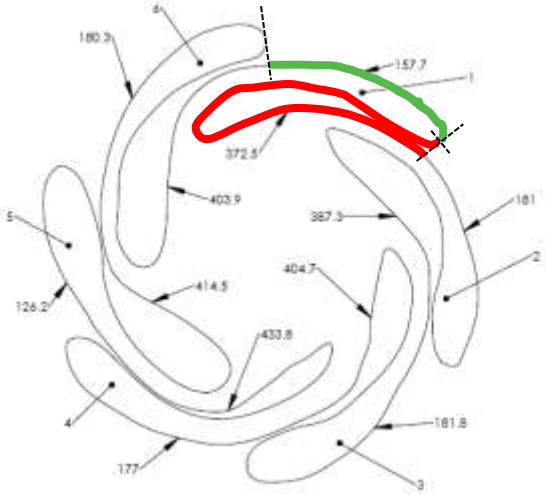


6 Fold Design (5-7mm diameters)



Red ≈ 60%
Covered balloon surface

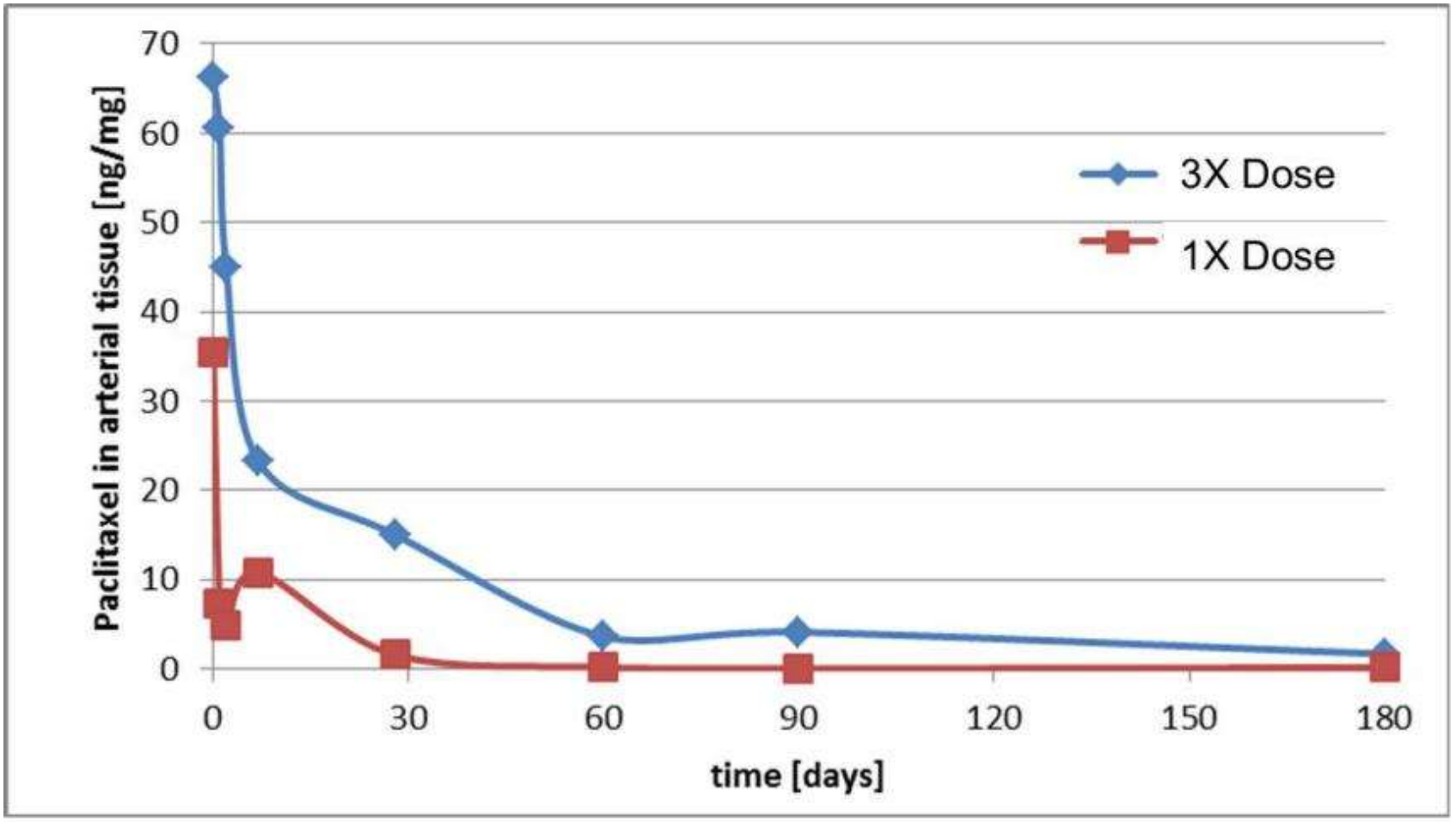
Green ≈ 40%
Non-covered balloon surface



FreePac Drug Transfer Efficiency

Therapeutic dose delivered in 30-60 seconds

Detectable therapeutic levels remain up to 180 days



IN.PACT SFA Clinical data

IN.PACT SFA Trial Overview

IN.PACT SFA I
150 subjects enrolled at 13 EU sites
Sep 2010 - Apr 2011

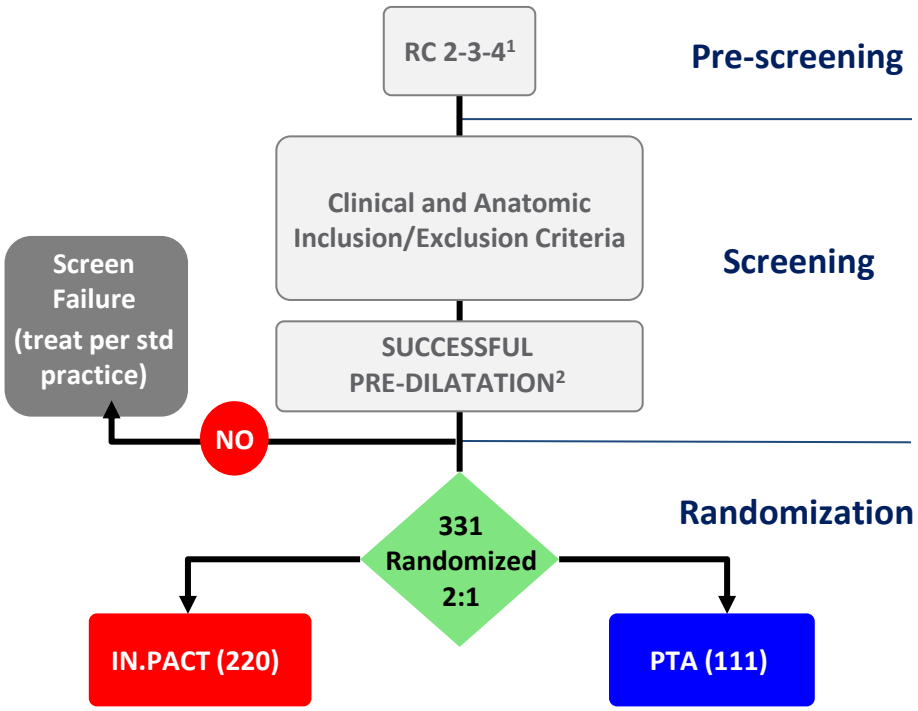
IN.PACT SFA II
181 subjects enrolled at 44 US sites
Apr 2012 - Jan 2013

- Prospective
- Multicenter
- Randomized (2:1)
- Single-blinded
- Subjects followed up to 5 years

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

1. VasCore DUS Core Laboratory, Boston, MA, US
2. SynvaCor Angiographic Core Laboratory, Springfield, IL, US
3. CEC and DSMB services provided by HCRI, Boston, MA, US

IN.PACT SFA Trial Design



IN.PACT SFA
Aggregate dataset from Phase I and II

Primary Endpoints:

- **Efficacy**[3]: 12-month Primary Patency
- Freedom from clinically-driven TLR and duplex ultrasound derived restenosis (PSVR ≤2.4)
- **Safety**[4]: 30-day device/procedure death, 12-month amputation, 12-month clinically-driven TVR

Summarized Key Inclusion Criteria:

- Rutherford 2-3-4
- SFA and proximal popliteal
- Lesion length 4-18 cm
- Total occlusion ≤10 cm

1. With symptoms of claudication and/or rest pain and angiographic evidence of SFA/PPA stenosis
2. Pre-dilatation mandatory for all subjects in IN.PACT SFA II phase only
3. Primary Efficacy Analysis on all ITT non-stented subjects based on superiority assumption of DCB vs. PTA
4. Primary Safety Analysis on all ITT non-stented subjects based on non-inferiority of DCB vs. PTA

Key Eligibility Criteria

Key Inclusions

- RC 2-3-4
- Lesion in SFA and/or PPA
- Single *de novo* or non-stented restenotic lesion:
  - 70%-99% occluded with total length ≥ 4 cm and ≤ 18 cm; or
  - 100% occluded total length ≤ 10 cm
  - Combination and tandem lesions allowed if criteria above met and lesion gap ≤ 3 cm
- Successful inflow treatment

Key Exclusions

- RC 5-6
- Lesion extending below P1
- In-stent restenosis, post-DCB restenosis, or previous bypass
- Contralateral SFA/PPA disease requiring treatment at index; Failure to successfully treat non-target lesions in contralateral limb
- Major intervention performed or planned ≤ 30 days of index*
- Unsuccessful lesion crossing
- Unsuccessful pre-dilatation*

* IN.PACT SFA I phase did not include pre-dilatation requirement for all subjects and did not exclude major interventions within 30 days prior to index procedure

Baseline Clinical Characteristics

	IN.PACT DCB (220 Subjects)	PTA (111 Subjects)	p-Value
Age (Y)	67.5 ± 9.5	68.0 ± 9.2	0.612
Male Gender (%)	65.0% (143/220)	67.6% (75/111)	0.713
Diabetes (%)	40.5% (89/220)	48.6% (54/111)	0.161
Hypertension (%)	91.4% (201/220)	88.3% (98/111)	0.431
Hyperlipidemia (%)	84.5% (186/220)	82.0% (91/111)	0.637
Current Smoker (%)	38.6% (85/220)	36.0% (40/111)	0.719
Coronary Artery Disease (%)	57.0% (122/214)	55.0% (60/109)	0.813
Carotid Artery Disease (%)	34.9% (73/209)	31.7% (32/101)	0.610
ABI / TBI [1]	0.769 ± 0.228	0.744 ± 0.189	0.308
Rutherford Stage (%) 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

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

Baseline Angiographic Characteristics

	IN.PACT DCB (N=220 Subjects, N=221 Lesions)	PTA (N=111 Subjects, N=113 Lesions)	p-Value
Lesion Type [1] *De novo*	95.0% (209/220)	94.6% (105/111)	0.875
Restenotic	5.0% (11/220)	5.4% (6/111)	
# Patent Runoff Vessels 0	3.3% (7/212)	4.5% (5/112)	0.042
1	13.7% (29/212)	26.8% (30/112)	
2	41.5% (88/212)	33.0% (37/112)	
3	41.5% (88/212)	35.7% (40/112)	
Prox. Popliteal Involvement (%)	6.8% (15/221)	7.1% (8/113)	1.000
Lesion Length (cm) [2]	8.94 ± 4.89	8.81 ± 5.12	0.815
RVD (mm)	4.647 ± 0.841	4.681 ± 0.828	0.728
MLD pre (mm)	0.900 ± 0.776	0.933 ± 0.771	0.711
Diameter Stenosis pre (%)	81.1 ± 15.5	81.3 ± 13.7	0.946

1. Site-reported
2. Normal-to-normal by Core Lab QVA evaluation

Baseline Lesion Characteristics

	IN.PACT DCB (N=220 Subjects, N=221 Lesions)	PTA (N=111 Subjects, N=113 Lesions)	p-Value
Eccentric Lesion (%)	6.3% (14/221)	3.5% (4/113)	0.442
Ulcerated Plaque (%)	3.2% (7/221)	5.3% (6/113)	0.376
Calcification (%) Severe	59.3% (131/221) 8.1% (18/221)	58.4% (66/113) 6.2% (7/113)	0.097 0.662
Thrombus (%)	0.5% (1/221)	0.9% (1/113)	1.000
Aneurysm (%)	0.0% (0/221)	0.0% (0/113)	>0.999
Total Occlusions (%)	25.8% (57/221)	19.5% (22/113)	0.222
TASC Lesion Type (%) **A** **B** **C** **D**	 56.6% (125/221) 30.8% (68/221) 12.2% (27/221) 0.5% (1/221)	 62.8% (71/113) 26.5% (30/113) 10.6% (12/113) 0.0% (0/113)	0.275

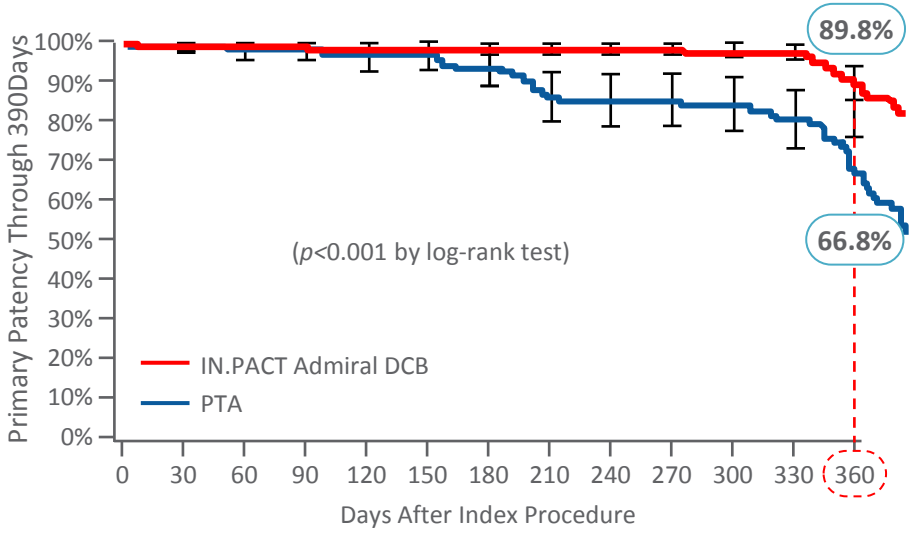
Baseline Procedural Characteristics

	IN.PACT DCB	PTA	p-Value
Pre-dilatation (%)	96.4% (212/220)	85.6% (95/111)	<0.001
Post-dilatation (%)	26.8% (59/220)	18.9% (21/111)	0.135
Dissections (%) 0 **A-C** **D-F**	36.2% (80/221) 63.8% (141/221) 0.0% (0/221)	38.9% (44/113) 60.2% (68/113) 0.9% (1/113)	0.360
Provisional Stenting (%)	7.3% (16/220)	12.6% (14/111)	0.110
MLD post (mm)	3.903 ± 0.750	3.862 ± 0.732	0.632
Diameter Stenosis post (%)	19.9 ± 10.4	19.1 ± 10.3	0.535
Device Success (%) [1]	99.0% (308/311)	98.5% (128/130)	0.302
Procedural Success (%) [2]	99.5% (219/220)	98.2% (109/111)	0.111
Clinical Success (%) [3]	99.1% (218/220)	97.3% (108/111)	0.103

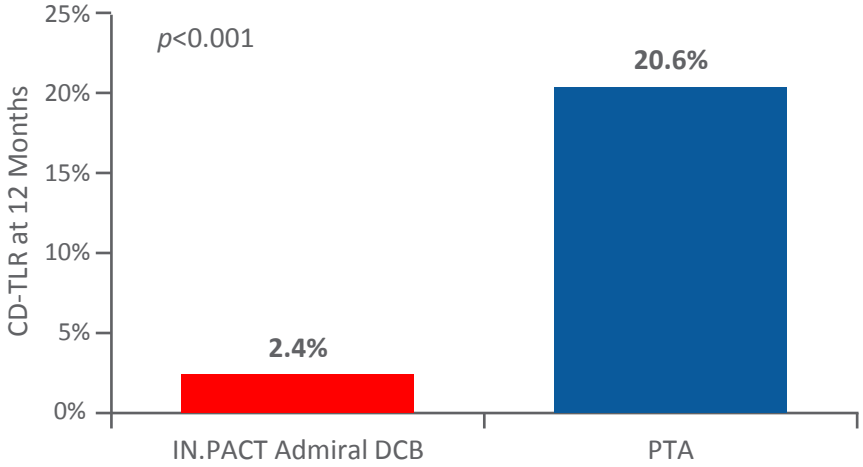
1. Device success: Successful delivery, inflation, deflation, and retrieval of the intact study balloon without burst < RBP
2. Procedural success: Residual DS ≤ 50% for non-stented subjects or ≤ 30% for stented subjects
3. Clinical success: Procedural success without procedural complications (death, major target limb amputation, thrombosis of target lesion, or TVR) prior to discharge

12-month Effectiveness Outcomes

Primary Patency Kaplan Meier (All ITT)[1]



Clinically-Driven Target Lesion Revascularization (CD-TLR)[2]



1. Primary patency is defined as freedom from clinically-driven TLR and freedom from restenosis as determined by DUS PSVR ≤2.4
2. Clinically-driven TLR defined as any re-intervention due to symptoms or drop of ABI/TBI of >20% or >0.15 compared to post-procedure ABI/TBI

12-month Effectiveness Outcomes

	IN.PACT DCB	PTA	p-Value
Primary Patency (PSVR ≤ 2.4)	82.2% (157/191)	52.4% (54/103)	<0.001
Clinically-driven TLR [1]	2.4% (5/207)	20.6% (22/107)	<0.001
All TLR [2]	2.9% (6/207)	20.6% (22/107)	<0.001
Primary Sustained Clinical Improv. [3]	85.2% (167/196)	68.9% (73/106)	<0.001
ABI / TBI [4]	0.951 ± 0.221	0.886 ± 0.169	0.002

1. Clinically-driven TLR adjudicated by an independent Clinical Events Committee, blinded to the assigned treatment, based on any re-intervention at the target lesion due to symptoms or drop of ABI/TBI of ≥20% or >0.15 when compared to post-procedure baseline ABI/TBI
2. All TLR includes clinically-driven and incidental or duplex-driven TLR
3. Freedom from target limb amputation, TVR, and increase in Rutherford class at 12 months post-procedure
4. TBI allowed / used in cases of incompressible vessels in IN.PACT SFA II phase

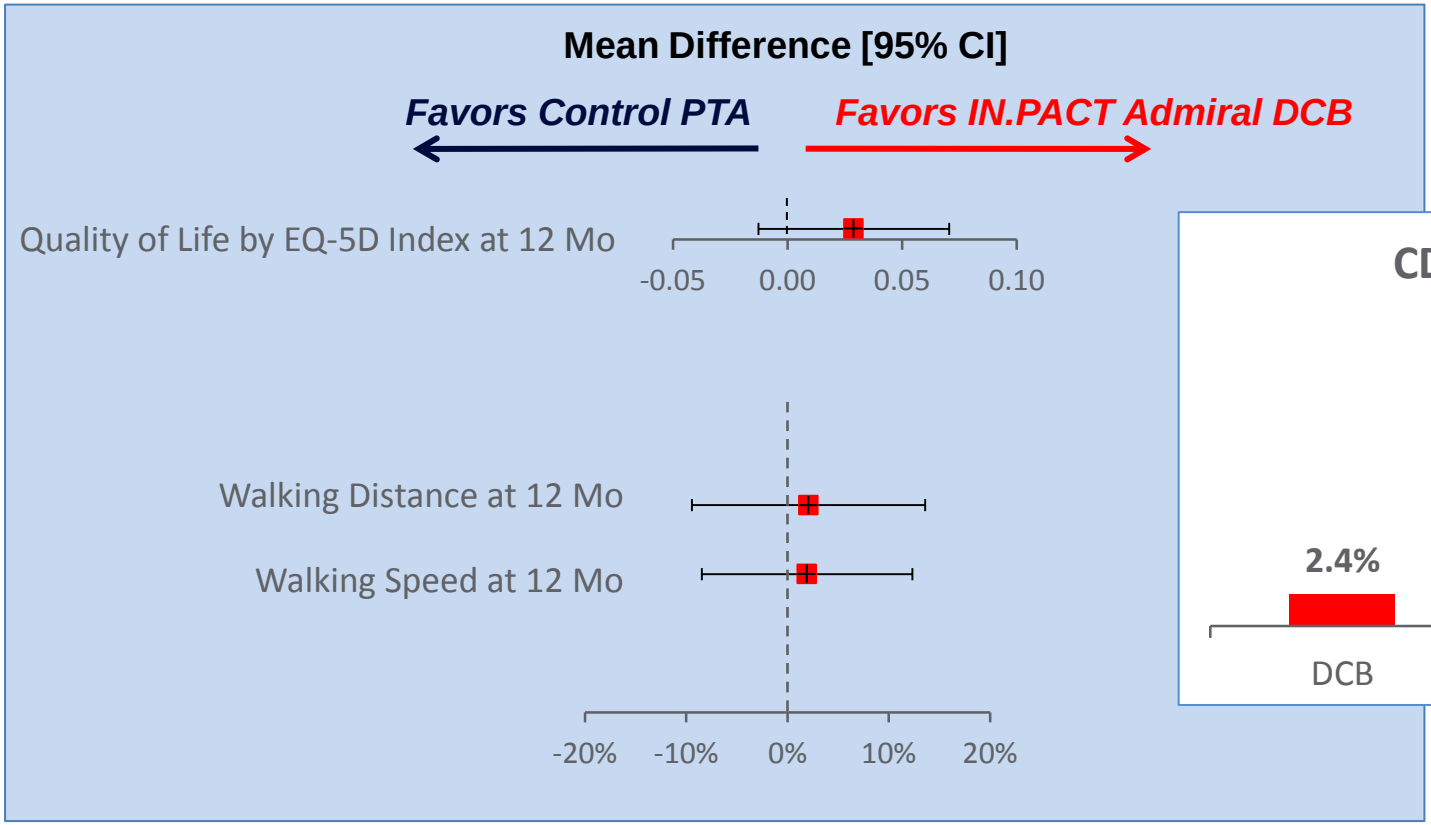
12-month Safety Outcomes

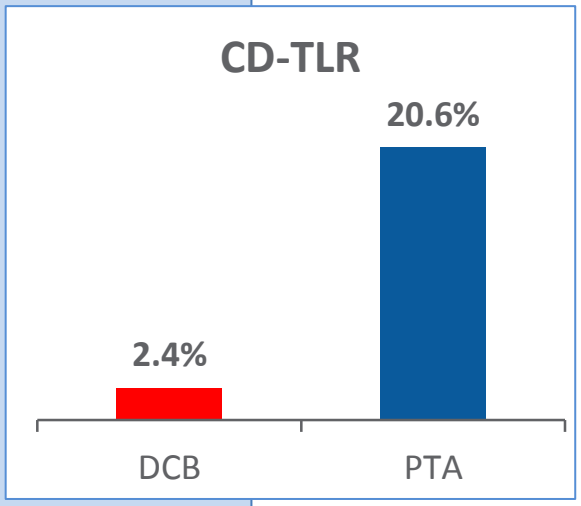
	IN.PACT DCB	PTA	p
Primary Safety Composite [1]	95.7% (198/207)	76.6% (82/107)	<0.001
30-day Device- and Proc.-related Death	0.0% (0/218)	0.0% (0/111)	>0.999
12-month Clinically-driven TVR	4.3% (9/207)	23.4% (25/107)	<0.001
12-month Target Limb Major Amputation	0.0% (0/207)	0.0% (0/107)	>0.999
Additional 12-month Safety Endpoints	**IN.PACT DCB**	**PTA**	**p**
Major Adverse Events [2]	6.3% (13/207)	24.3% (26/107)	<0.001
All-cause Death	1.9% (4/207)	0.0% (0/107)	0.926
Thrombosis	1.4% (3/207)	3.7% (4/107)	0.096

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

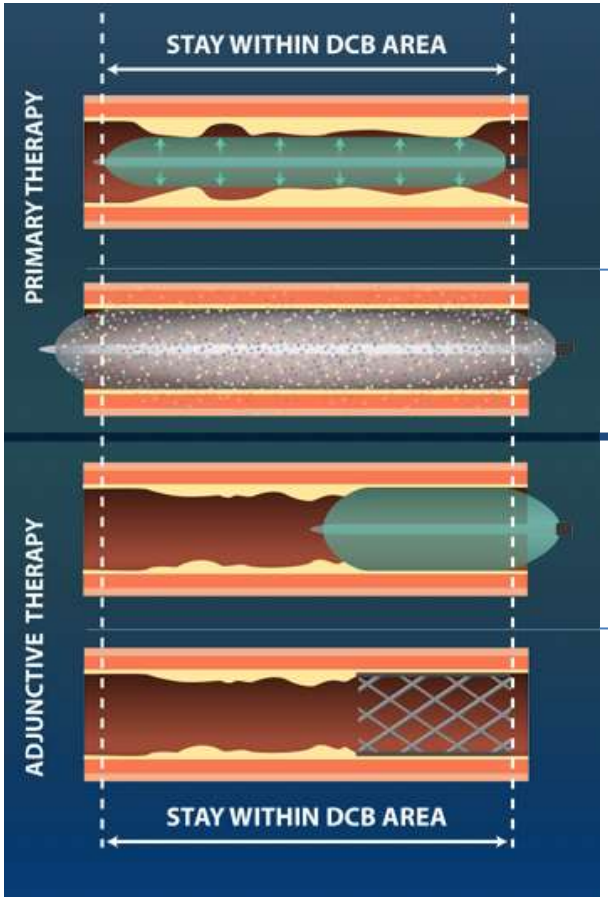
IN.PACT SFA Functional Outcomes Trend in Favour of DCB

***DCB** patients required **88%** fewer re-interventions to achieve the same level of function*





DCB and Minimizing Geographical Miss



1. **PRE-DILATATION**
   - Required for all lesions prior to DCB procedure
   - Size - Diameter: 1 mm less than RVD
   - Size - Length: should not be greater than planned DCB length

2. **DRUG-COATED BALLOON**
   - DCB diameter RVD = 1:1; length 1 cm beyond lesion on both ends
   - Inflation: Time ≥ 3 minutes; Pressure < RBP as required to reach full DCB expansion

3. **POST-DILATATION**
   - If residual stenosis ≥ 50% or flow-limiting dissection
   - Standard or high pressure PTA balloon diameter 1:1 to RVD
   - Short/focal length as necessary to treat the extent of residual stenosis or dissection

4. **PROVISIONAL SPOT STENTING**
   - For persistent residual stenosis ≥ 50% or flow-limiting dissection
   - Minimum length as necessary to fully treat the residual stenosis or dissection

Landmark Publication

Circulation

Original Article

Drug-Coated Balloon versus Standard Percutaneous Transluminal Angioplasty for the Treatment of Superficial Femoral and/or Popliteal Peripheral Artery Disease: 12-Month Results from the IN.PACT SFA Randomized Trial

Gunnar Tepe[1]; John Laird[2*]; Peter Schneider[3]; Marianne Brodmann[4]; Prakash Krishnan[5]; Antonio Micari[6]; Christopher Metzger[7]; Dierk Scheinert[8]; Thomas Zeller[9]; David J. Cohen[10]; David B. Snead[11]; Beaux Alexander[11]; Mario Landini[11]; Michael R. Jaff[12]

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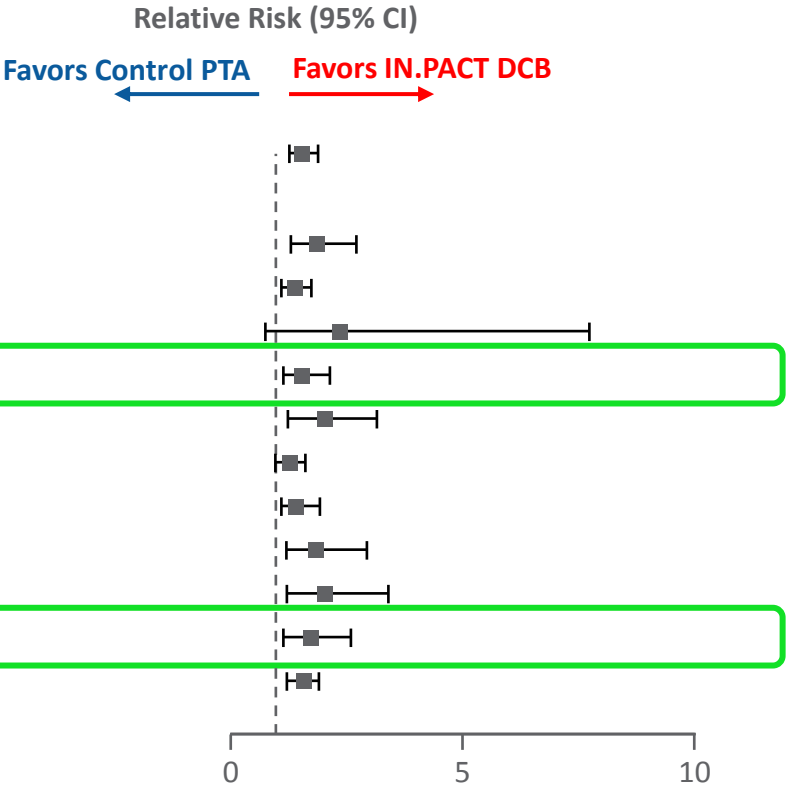
IN.PACT SFA Trial

12-month Subgroup Analyses

IN.PACT SFA 12-month Subgroups – Primary Patency

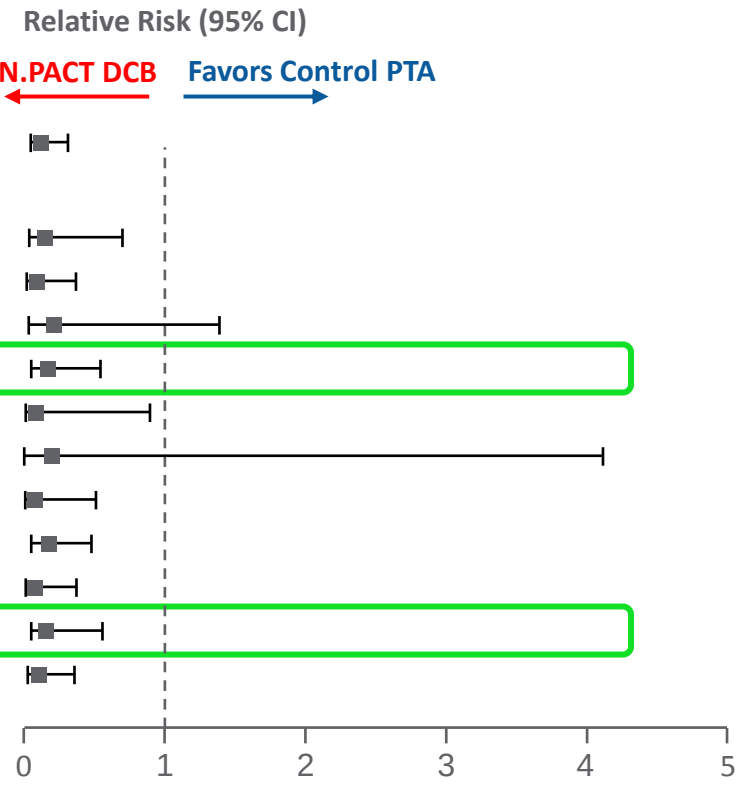
	Control PTA %	IN.PACT DCB %
Overall ITT	52.4%	82.2%
Subgroups		
Rutherford Category 2	43.6%	82.2%
Rutherford Category 3	59.6%	82.4%
Rutherford Category 4	33.3%	80.0%
Diabetes Mellitus	49.0%	77.3%
Age ≥75	42.3%	84.4%
Lesion Length <5 cm	73.9%	93.3%
Lesion Length ≥5 cm and <10 cm	57.1%	83.3%
Lesion Length ≥10 cm and <18 cm	39.4%	74.6%
Total Occlusion	40.9%	83.3%
Female Gender	43.8%	75.7%
Male Gender	56.3%	86.0%



There were no significant treatment-by-subgroup interactions (*P*>0.15). The 95% confidence intervals were unadjusted for multiplicity.

IN.PACT SFA 12-month Subgroups – CD-TLR

	IN.PACT DCB %	Control PTA %
Overall ITT	2.4%	20.6%
Subgroups		
Rutherford Category 2	2.6%	17.1%
Rutherford Category 3	1.7%	20.3%
Rutherford Category 4	9.1%	50.0%
Diabetes Mellitus	3.7%	23.1%
Age ≥75	0.0%	17.9%
Lesion Length <5 cm	0.0%	4.2%
Lesion Length ≥5 cm and <10 cm	1.4%	20.5%
Lesion Length ≥10 cm and <18 cm	5.3%	32.4%
Total Occlusion	1.9%	38.1%
Female Gender	4.1%	25.7%
Male Gender	1.5%	18.1%



There were no significant treatment by subgroup interactions (P>0.15) except in diabetes mellitus (P=0.027). The 95% confidence intervals were unadjusted for multiplicity.

Female Gender Subgroup

Effectiveness Outcomes

	IN.PACT DCB	PTA	p-Value
Primary Patency (PSVR ≤ 2.4)	75.7% (53/70)	43.8% (14/32)	0.004
Clinically-driven TLR [1]	4.1% (3/74)	25.7% (9/35)	<0.001
All TLR [2]	4.1% (3/74)	25.7% (9/35)	<0.001

1. Clinically-driven TLR adjudicated by an independent Clinical Events 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

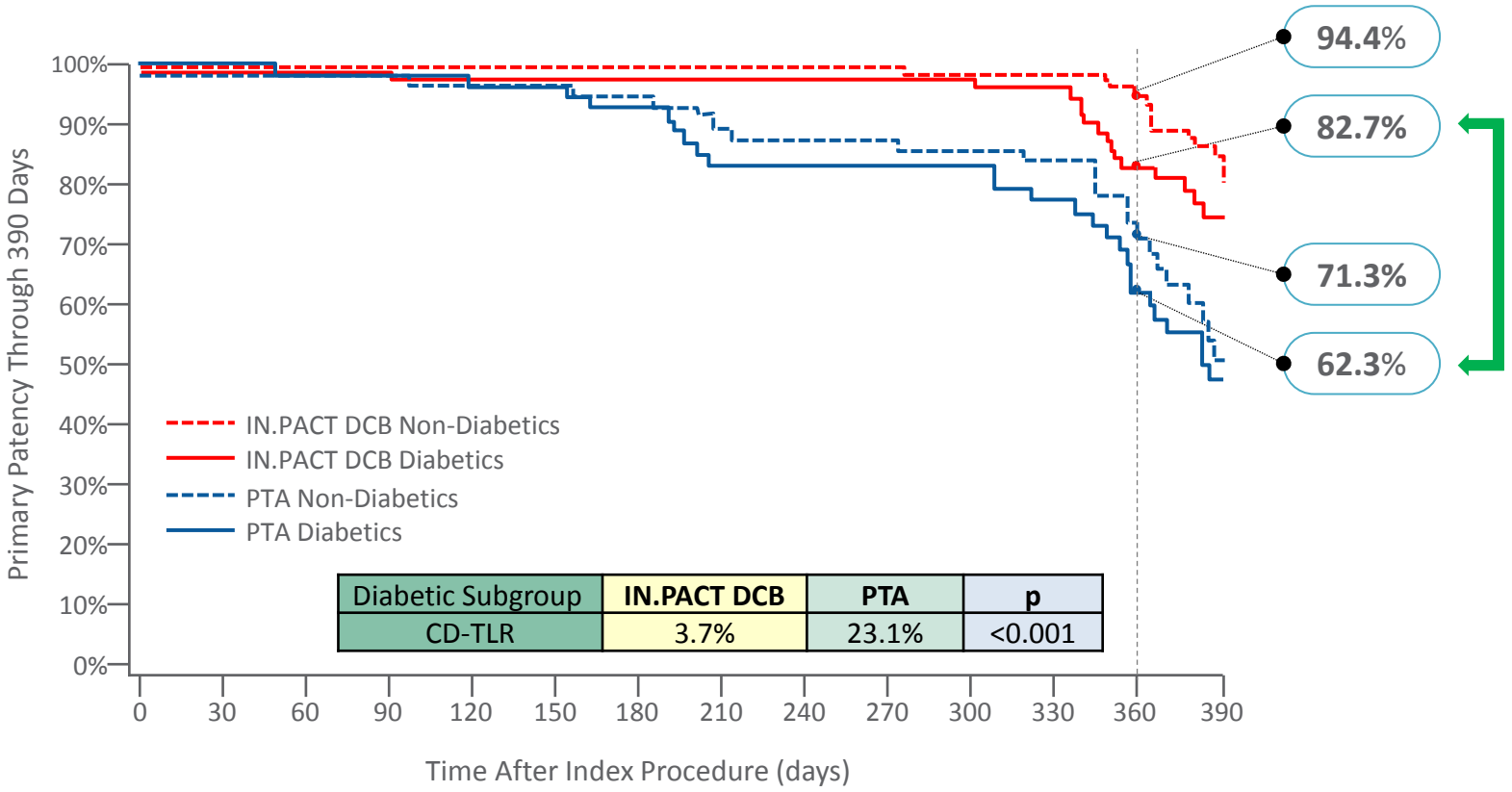
Female Gender Subgroup

Safety Outcomes

	IN.PACT DCB	PTA	p-Value
Primary Safety Composite [1]	94.6% (70/74)	68.6% (24/35)	<0.001*
30-day Device- and Proc.-related Death	0.0% (0/76)	0.0% (0/36)	>0.999
12-month Clinically-driven TVR	5.4% (4/74)	31.4% (11/35)	<0.001
12-month Target Limb Major Amputation	0.0% (0/74)	0.0% (0/35)	>0.999
Additional 12-month Safety Endpoints	**IN.PACT DCB**	**PTA**	**p-Value**
12-month Major Adverse Events [2]	5.4% (4/74)	31.4% (11/35)	<0.001
All-cause Death	0.0% (0/74)	0.0% (0/35)	>0.999
Thrombosis	1.4% (1/74)	0.0% (0/35)	0.755

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

IN.PACT SFA Primary Patency – Diabetics vs. Non-Diabetics



Diabetic Subgroup	IN.PACT DCB	PTA	p
CD-TLR	3.7%	23.1%	<0.001

Conclusions

- Robust level 1 evidence
- IN.PACT Admiral: Lowest TLR and highest patency ever reported in an SFA trial
- DCB patients required 88% less re-interventions to achieve the same level of function
- DCB response consistent in men vs. women
- Potential to become standard of care for fem-pop treatment, including diabetic patients
- No DCB class effect

The IN.PACT Global Study:

Early Results of Prospective Outcomes Using the IN.PACT® Admiral® DCB in an Unrestricted, Real World Environment

IN.PACT Global Clinical Study

Background

- 1-year DCB performance in femoropopliteal vessels is well characterized in TASC A-B lesions through recent large scale RCTs
- Questions remain as to consistency of DCB performance in TASC C-D lesions
- IN.PACT Global is a real-world study with >1500 patients enrolled
- Current analysis will provide insights into IN.PACT® Admiral® DCB performance across all TASC lesion categories and lesions ≥15 cm*

* Lesions ≥18 cm are not indicated in the United States.

IN.PACT Global Clinical Study

Objectives

- Characterize IN.PACT® Admiral® DCB clinical outcomes in a real-world patient population
- Allow for ample subset analyses and have ability to detect low event rates
- Evaluate the efficacy of the IN.PACT® Admiral® DCB in the treatment of:
  - *de novo* ISR lesions
  - Long lesions (≥ 15 cm)
  - CTOs (≥ 5 cm) based on Core Lab assessment
- Collect effectiveness and safety data of subjects receiving the 150mm IN.PACT® Admiral® DCB

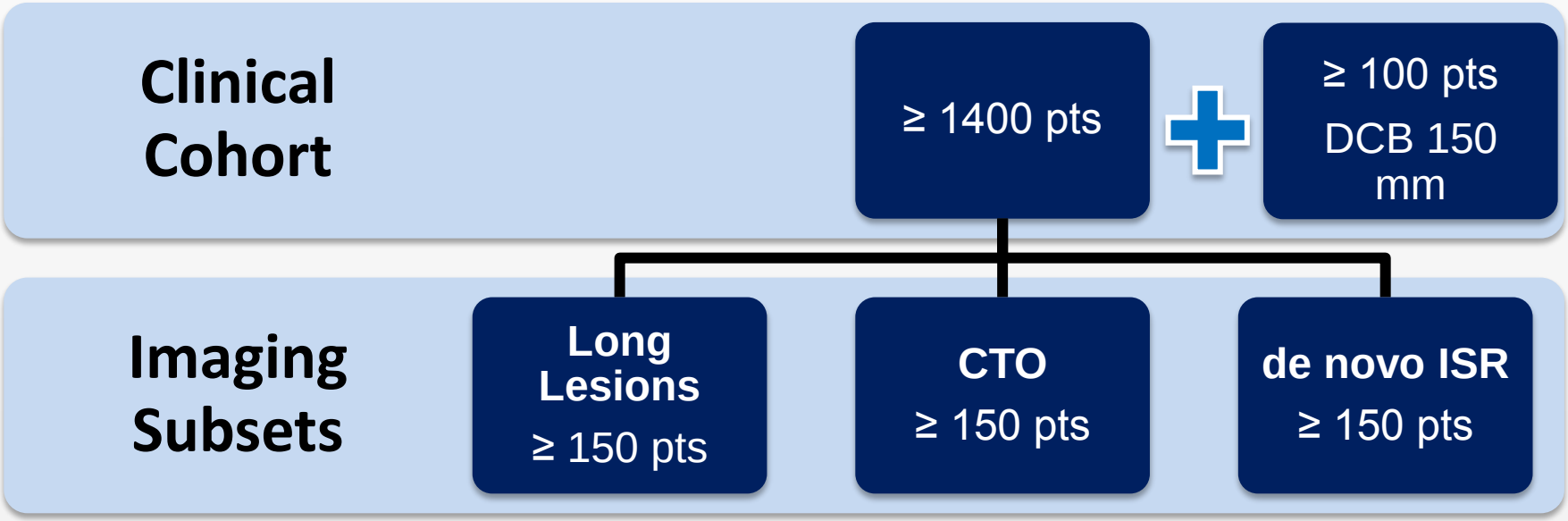
IN.PACT® Admiral® DCB Clinical Outcomes

Real-World Patient Population

IN.PACT SFA	IN.PACT GLOBAL
RCT	Single-arm
331 patients	1500+ patients
57 sites (US, EU)	~67 sites Global
Systematic pre-dil	Pre-dil at physician's discretion
Single lesions vs. Multiple lesions TASC A-C vs. Any TASC SFA / P1 vs. Full fem-pop No severe Ca++ or ISR vs. Ca++ and ISR included	

IN.PACT Global Study

Patient Cohorts



Study Design

Sites need to be assessed by Corelab before they can enroll patients into the imaging cohort.

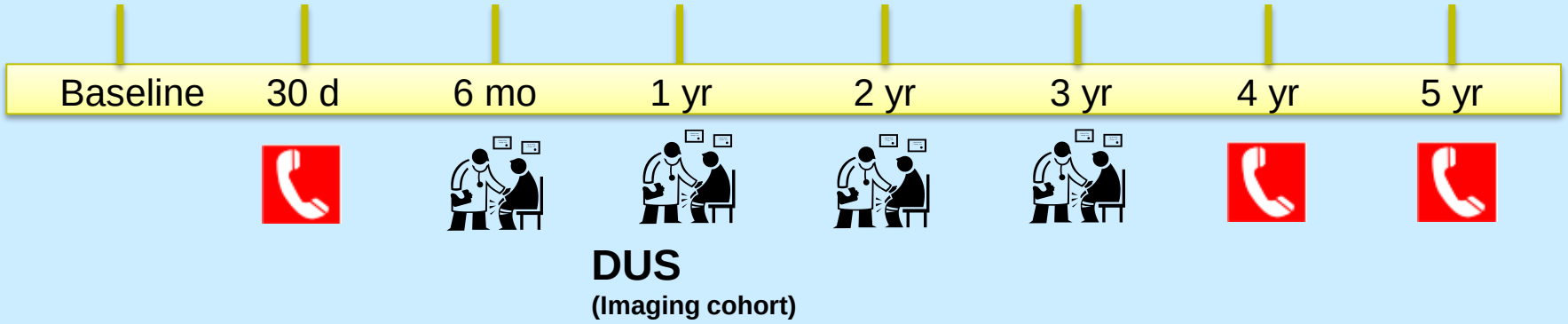
Prospective, Multi-center, Single-Arm Study

Clinical Cohort

n = 800 to 1500 patients in approx. 80 sites

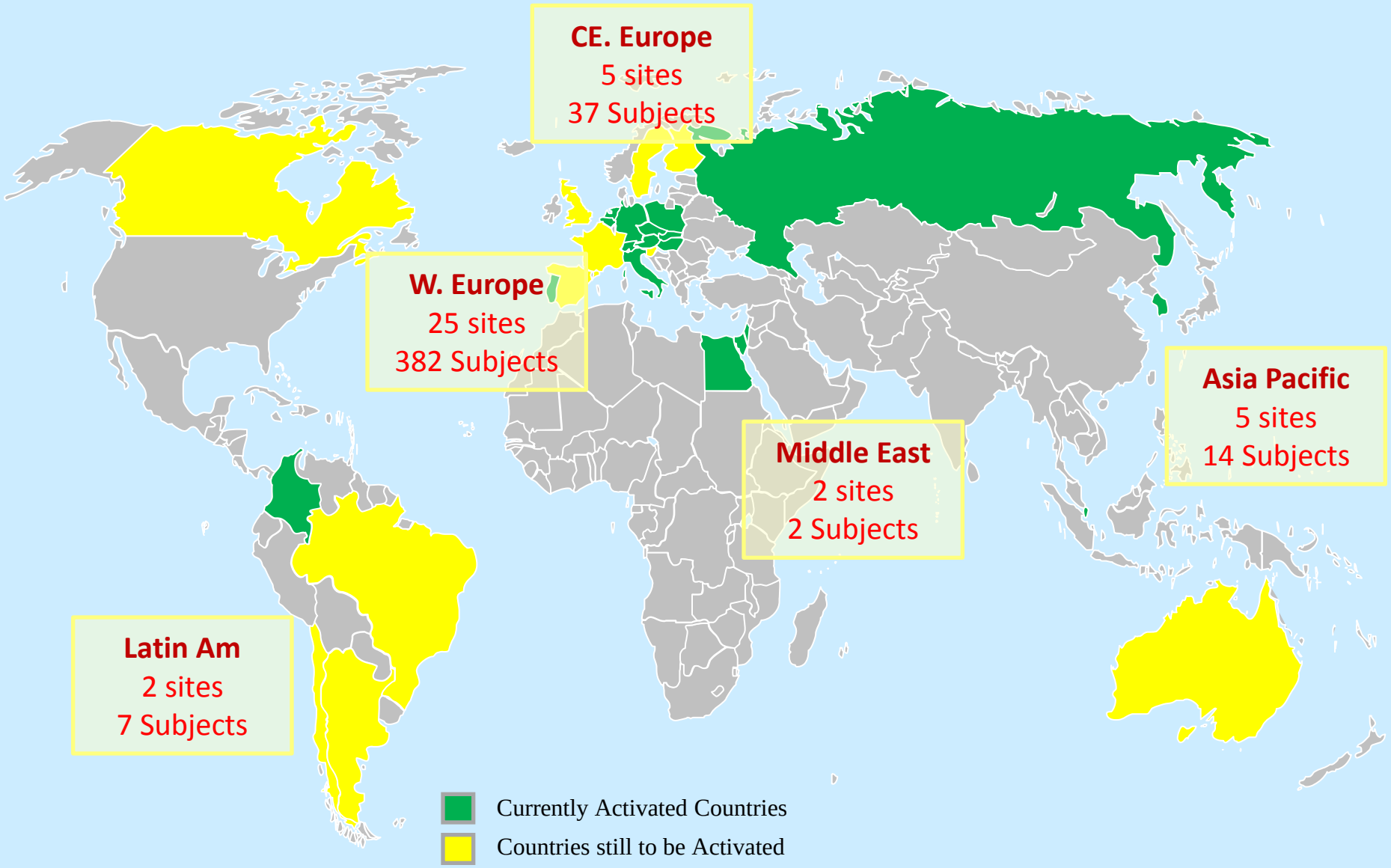
Imaging Cohort

n = 450 patients
First 150 De novo ISR
First 150 LL
First 150 CTO



DUS
(Imaging cohort)

Global Enrollment Distribution



* As of March 20th, 2013

Asia Pacific Enrollment

- YonSei Univ Severance Hospital (Choi)
- Korea Univeristy Guro Hospital (Rha SW)
- Samsung Medical Center (Do)
- Ajou University (Won)
- Asan Medical Center (Lee)

- Changi Hospital (Kum)

* As of March 20th, 2013

IN.PACT Global Study

*Primary Endpoints**

Efficacy	Safety
• Clinical cohort: 12-month Freedom from clinically-driven TLR [1] • Imaging cohort: 12-month Primary Patency [2]	• Composite - 30-day freedom from device- and procedure-related mortality - 12-month freedom from major target limb amputation and clinically driven TVR

*This presentation includes outcome data, including CD-TLR, on the first 655 subjects enrolled

1. 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.
2. Freedom from clinically-driven target lesion revascularization (TLR) and freedom from restenosis as determined by DUS Peak Systolic Velocity Rate (PSVR) ≤ 2.4. Primary Patency of the de novo ISR, long lesion ≥ 15 cm and CTO ≥ 5 cm will be calculated separately.

IN.PACT Global Study

Patient Population

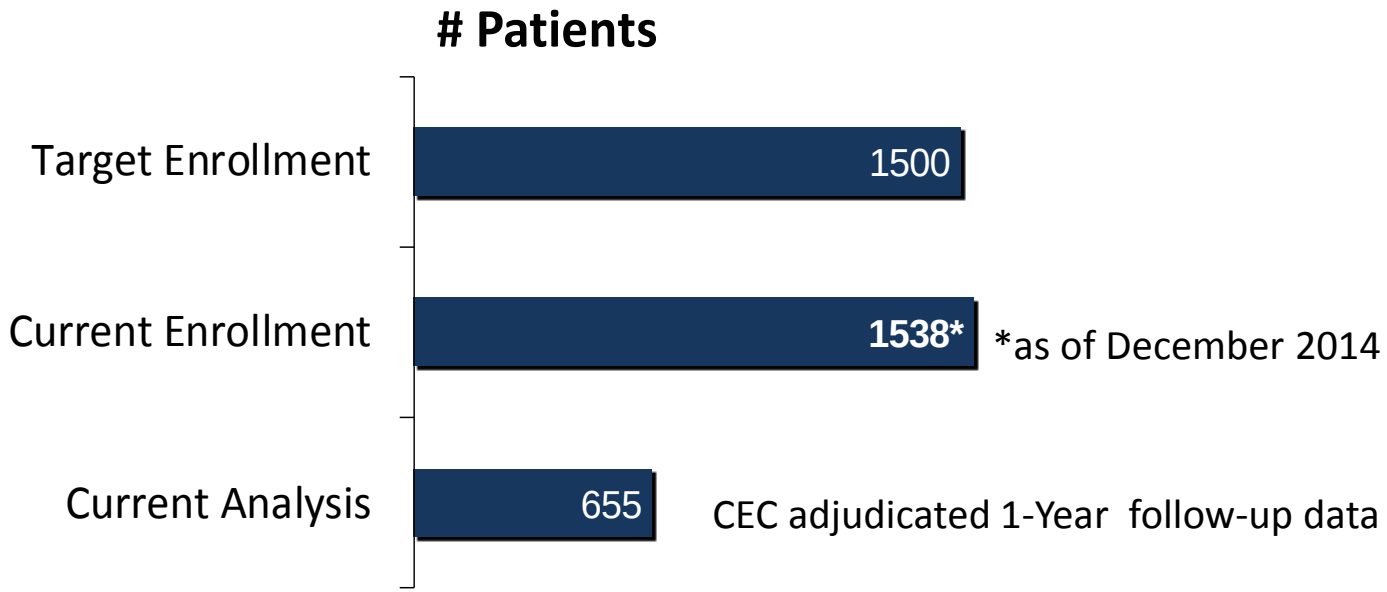
Key Eligibility Criteria

- IN.PACT Global inclusion and exclusion criteria are intended to allow for evaluation of the IN.PACT Admiral DCB in a complex, real-world patient population

Inclusion Criteria	Exclusion Criteria
• Rutherford Class 2, 3 and 4 • Lesion(s) in SFA and/or Popliteal artery • Single or multiple stenosis or occlusions of any length ≥ 2 cm • De novo or restenotic (in-stent or not in-stent) • At least one infrapopliteal run-off vessel	• Rutherford Class 5 and 6 • Acute or sub-acute thrombus in the target vessel • Previous bypass surgery to the target lesion • Failure to successfully cross the target lesion with a guide wire

IN.PACT Global Study

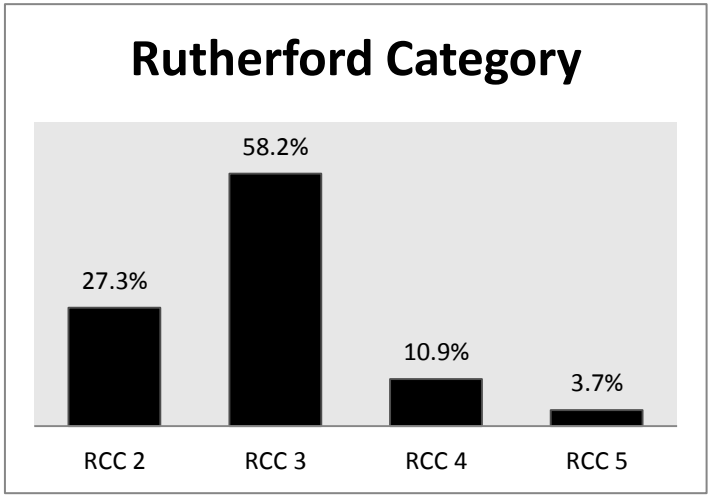
Status



1st enrollment May 2012

Baseline Clinical Characteristics

N	655
Age (Y)	69.2 ± 10.2
Male Gender (%)	67.2% (440/655)
Diabetes (%)	41.2% (269/653)
Hypertension (%)	83.6% (546/653)
Hyperlipidemia (%)	73.1% (470/643)
Current Smoker (%)	33.6% (220/655)
Obesity (BMI ≥ 30 kg/m²) (%)	20.6% (134/649)
Coronary Artery Disease (%)	43.3% (270/624)
Carotid Artery Disease (%)	21.5% (122/568)
Renal Insufficiency [1] (%)	11.8% (70/595)
Previous Peripheral Revasc. (%)	57.3% (375/655)
Concomitant BTK Disease	45.7% (283/619)
ABI	0.675 ± 0.233



1. Baseline serum creatinine ≥1.5 mg/dL

Lesion/Procedural Characteristics

Lesions (N)	763
Lesions per Patient (N)	1.16
Lesion Type: de novo restenotic (no ISR) ISR	 70.6% (539/763) 8.0% (61/763) **21.4% (163/763)**
Lesion Length	**12.23 ± 9.59 cm**
Total Occlusions	35.8% (273/763)
Severe Calcification	10.4% (79/761)
RVD (mm)	5.164 ± 0.684
Diameter Stenosis (pre-treatment)	88.7% ± 12.2
Dissections: 0 A-C D-F	60.2% (459/762) 33.9% (258/762) 5.9% (45/762)

Pre-dilatation	75.4% (494/655)
Post-dilatation	31.0% (201/648)
Provisional Stent	**24.7% (160/648)**
Device Success [1]	99.4% (1264/1271)
Procedure Success [2]	99.8% (646/647)
Clinical Success [3]	99.5% (644/647)

1. Device success: successful delivery, inflation, deflation and retrieval of the intact study balloon device without burst below the RBP
2. Procedure success: residual stenosis of ≤ 50% (non-stented subjects) or ≤ 30% (stented subjects) by core lab (if core lab was not available then the site reported estimate was used)
3. Clinical success: procedural success without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or TVR) prior to discharge)

12-month Outcomes (655 Patients)

Clinically-driven TLR [1]	8.7% (50/577)
Primary Safety Endpoint [2]	89.6% (517/577)
Major Adverse Events [3]	13.5% (78/577)
Death (all-cause)	3.3% (19/577)
Major Target Limb Amputation	0.3% (2/577)
Thrombosis	3.8% (22/577)
Any TLR	9.0% (52/577)
Any TVR	9.9% (57/577)

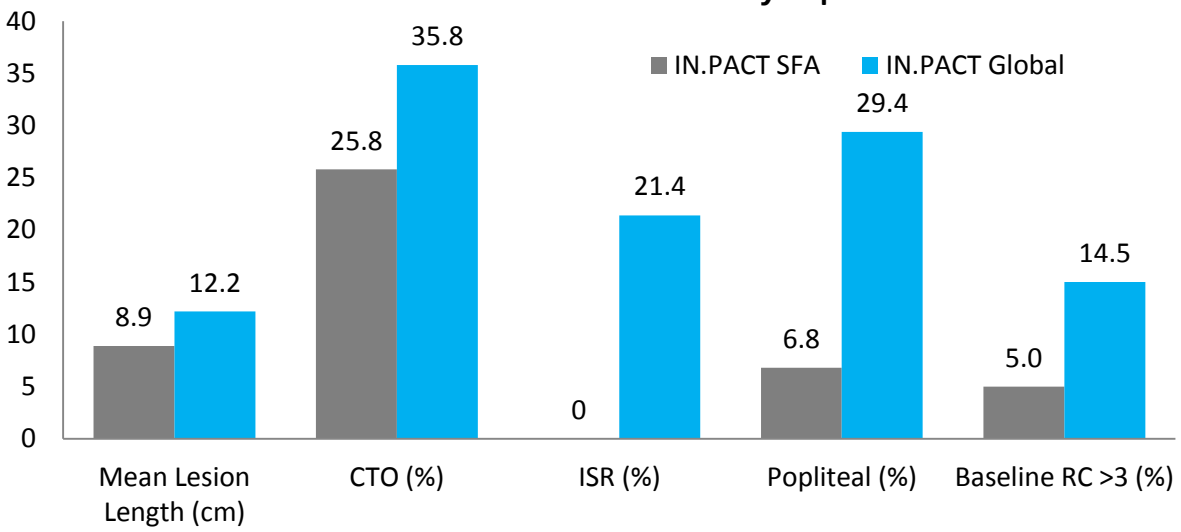
1. Any re-intervention within the target lesion(s) due to symptoms or drop of ABI of ≥ 20% or > 0.15 when compared to post-index procedure baseline ABI. This endpoint will be reported on a lesion basis
2. Composite of 30-day freedom from device- and procedure-related mortality and 12-month freedom from major target limb amputation and clinically-driven TVR
3. Major Adverse Events: Composite of death, major target limb amputation, clinically-driven TVR, and thrombosis

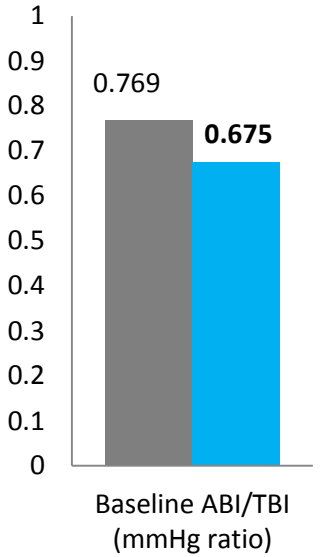
IN.PACT Global Study & IN.PACT SFA Trial

Patient Population Comparison

IN.PACT Global confirms safety and effectiveness of IN.PACT® Admiral ® DCB in a complex, real-world patient population.

- IN.PACT Global evaluated a more complex patient population that IN.PACT SFA, including long lesions, chronic total occlusions, in-stent restenosis, popliteal and a higher Rutherford classification.





IN.PACT® Admiral ® DCB is not approved for use in ISR

IN.PACT Global Study & IN.PACT SFA Trial

Outcomes Comparison

- IN.PACT Global evaluated a more complex patient population that IN.PACT SFA, including long lesions, chronic total occlusions, in-stent restenosis, popliteal and a higher Rutherford classification.

Key Population Differences

Characteristic	IN.PACT SFA (DCB Arm)	IN.PACT Global
Mean Lesion Length	8.9 cm	12.2 cm
Chronic Total Occlusion (CTO)	25.8%	35.8%
In-Stent Restenosis (ISR)	0.0%	21.4%
Baseline Rutherford Classification (RC) > 3	5.0%	14.5%

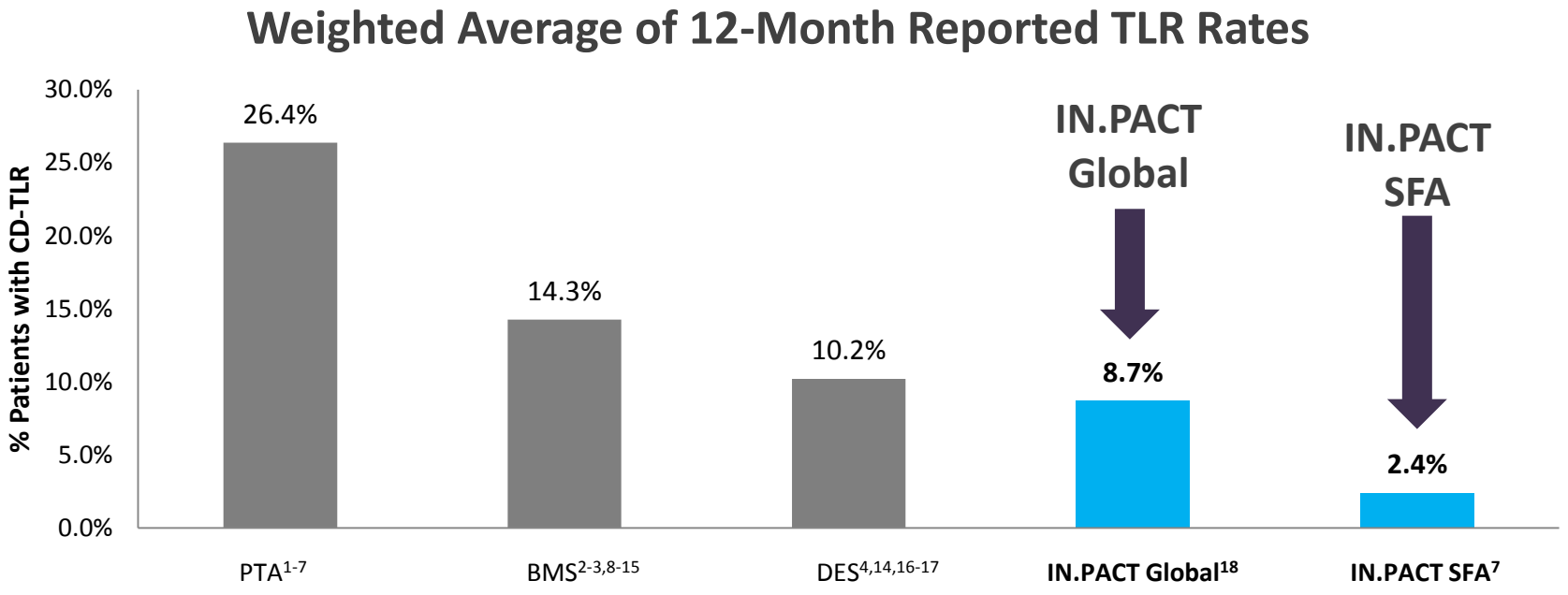
Outcomes (12-Month)

Outcome	IN.PACT SFA (DCB Arm) n = 220	IN.PACT Global n = 655
CD-TLR	2.4%	8.7%
CD-TVR	4.3%	9.5%
Thrombosis	1.4%	3.8%
Target Limb Major Amputation	0.0% (0)	0.3% (2)

IN.PACT Admiral is not approved for use in ISR

IN.PACT Global Study

Clinically-driven TLR



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IN.PACT Global Study

Key Takeaways

- IN.PACT Global is a rigorous, independently adjudicated study, **setting a new standard** in the real-world assessment of femoropopliteal revascularization
- IN.PACT Global confirms safety and effectiveness of the IN.PACT® Admiral® DCB in a **complex, real-world patient population**
- IN.PACT Global results reinforce market-leading outcomes from the IN.PACT SFA Trial and **support DCB as a front-line therapy in the treatment of SFA disease**
- Data from the long lesion imaging cohort will be presented in the late-breaking clinical trial session at EuroPCR

Thank You for Your Attention!

Korea University Guro Hospital, Seoul, Korea