Latest data from the IN.PACT clinical trial programme

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on behalf of the RANGER SFA investigators

Disclosure

Speaker's name: Dierk Scheinert

I have the following potential conflicts of interest to report:

Advisory Board /Consultant:

Abbott, Biotronik, Boston Scientific, Cook Medical, Cordis, CR Bard, Gardia Medical/Allium, Medtronic, TriReme Medical, Trivascular, Upstream Peripheral Technologies

IN.PACT Clinical Trial Program

29 Trials (12 RCT), ~4,500 Patients, Jointly covering the full spectrum of PAD

IN.PACT DCB Clinical Program

RCTs + Approval Studies

- IN.PACT SFA RCT
  - Gender Subset
  - Diabetic Subset
- IN.PACT JAPAN RCT
- IN.PACT CHINA
- IN.PACT BTK RCT
- IN.PACT AV Access RCT

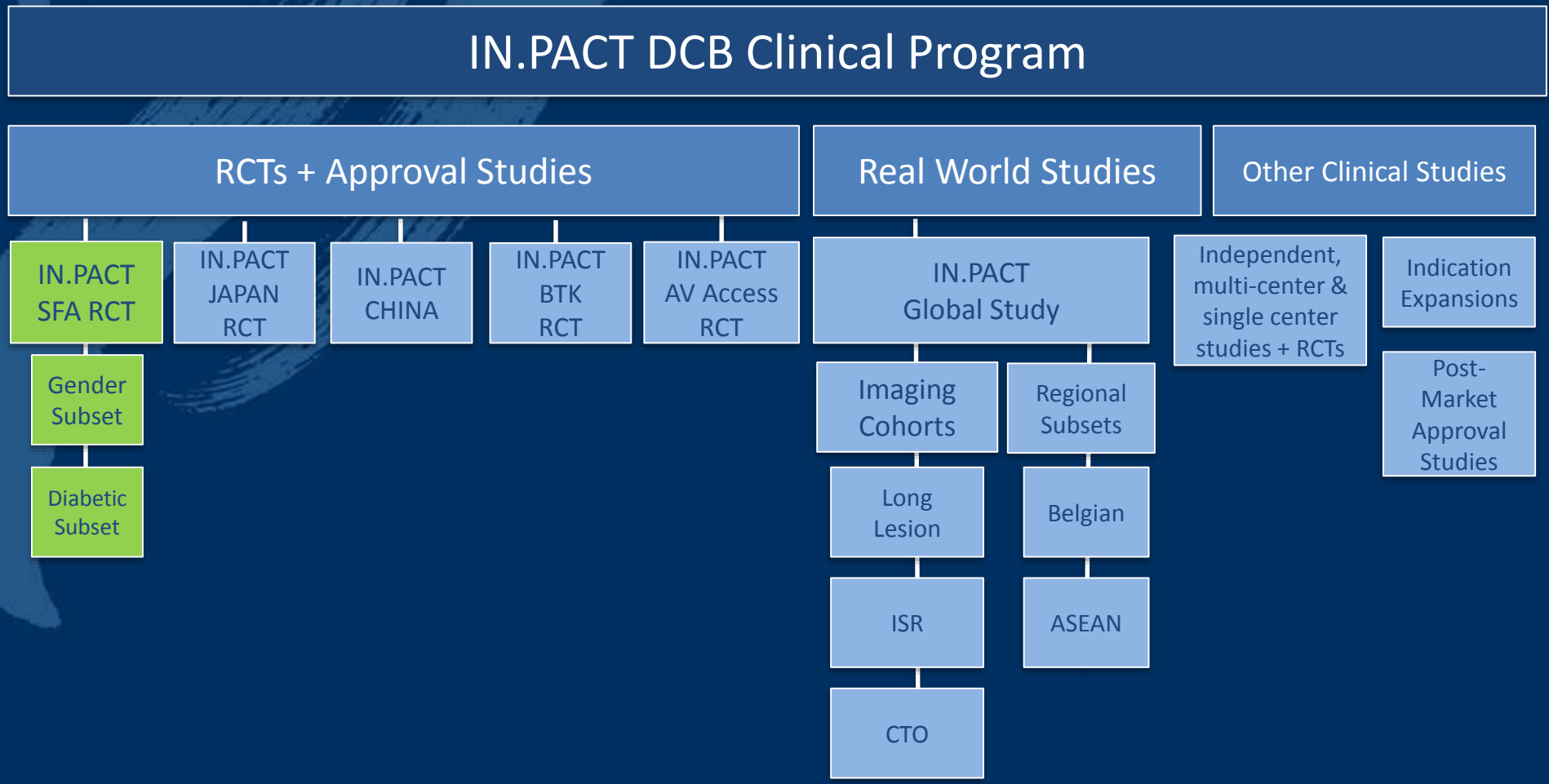
Real World Studies

- IN.PACT Global Study
  - Imaging Cohorts
    - Long Lesion
    - ISR
    - CTO
  - Regional Subsets
    - Belgian
    - ASEAN

Other Clinical Studies

- Independent, multi-center & single center studies + RCTs
- Indication Expansions
- Post-Market Approval Studies

IN.PACT Clinical Trial Program



IN.PACT SFA Trial Summary

IN.PACT SFA Trial	
Study Type	Prospective, Multicenter, Randomized, Controlled, Pivotal Trial
Primary Endpoints	Efficacy: Primary Patency[1] Safety: Safety Composite[2]
Rigor + Quality	• Independent adjudication by Clinical Events Committee & Imaging Core Labs • External Monitoring
Patients	331 patients
Sites	57 sites (US, EU)
Key Eligibility Criteria	• Single lesions ≤18 cm, CTO ≤10 cm • TASC A-C • SFA + Proximal Popliteal • No ISR, Ca^{++}

1. Freedom from CD-TLR and DUS-derived restenosis (PSVR ≤2.4) at 12m.
2. Composite 30-day freedom for device-and procedure-related mortality and 12-month freedom from major target limb amputation and CD-TVR.

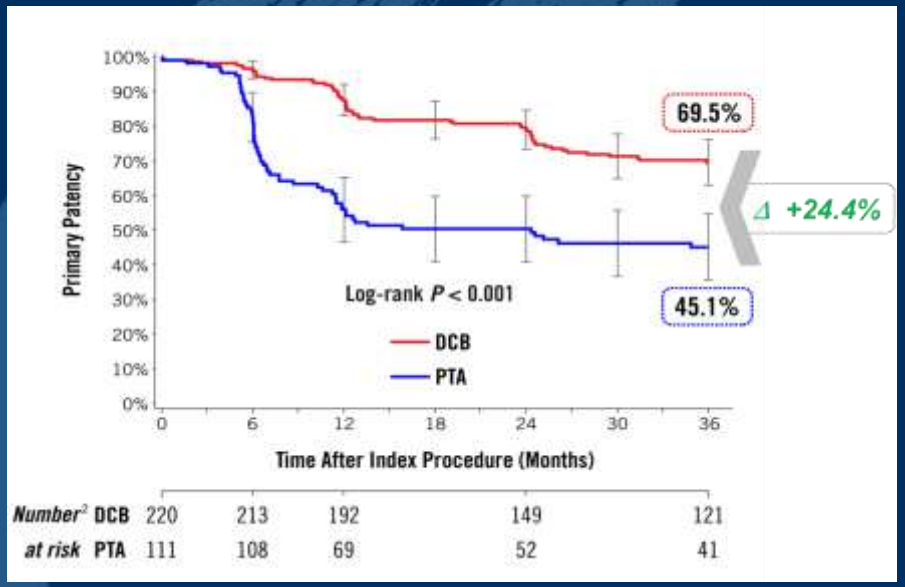
Results for the DCB Arm (n=220)			
	1 Year	2 Year	3 Year
Lesion Length (Mean ± SD, cm)	8.94 ± 4.89		
Primary Patency (KM)	87.5%	78.9%	69.5%
Primary Safety Endpoint[1] / Composite	95.7%	87.4%	81.2%
CD-TLR[2]	2.4%	9.1%	15.2%
Major Amputation Target Limb	0.0%	0.0%	0.0%
Thrombosis	1.4%	1.5%	2.0%

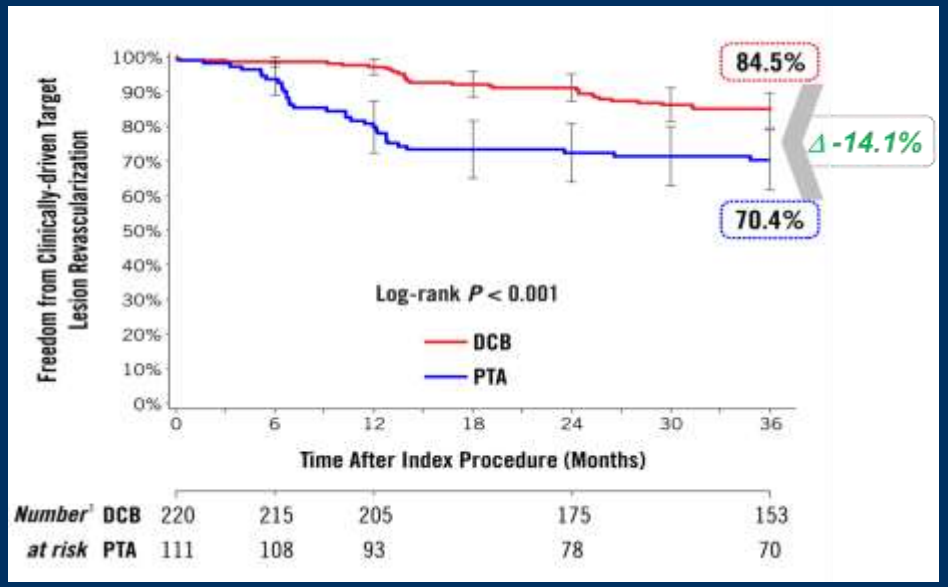
1. Composite of 30-day freedom from device- and procedure-related mortality & 12-month freedom from major target limb amputation/clinically-driven TVR.
2. Any re-intervention within the target lesion(s) due to symptoms or drop of ABI of ≥ 20% or > 0.15 when compared to post-index procedure baseline ABI.

1Y Results: Tepe G, presented at Charing Cross London 2014. Tepe G, et al. Circ :131:495-502 (2015). 2Y Results: Laird JR, presented at TCT San Francisco 2015. Laird JR, et al. J Am Coll Cardiol: 66:2329-38 (2015). Note: 1 year results updated from interval to cumulative KM calculations. 3Y Results: Krishnan P, presented at VIVA Las Vegas 2015.

IN.PACT SFA Trial:
3-year Outcomes Summary[1]

Baseline clinical and lesion characteristics were well matched.



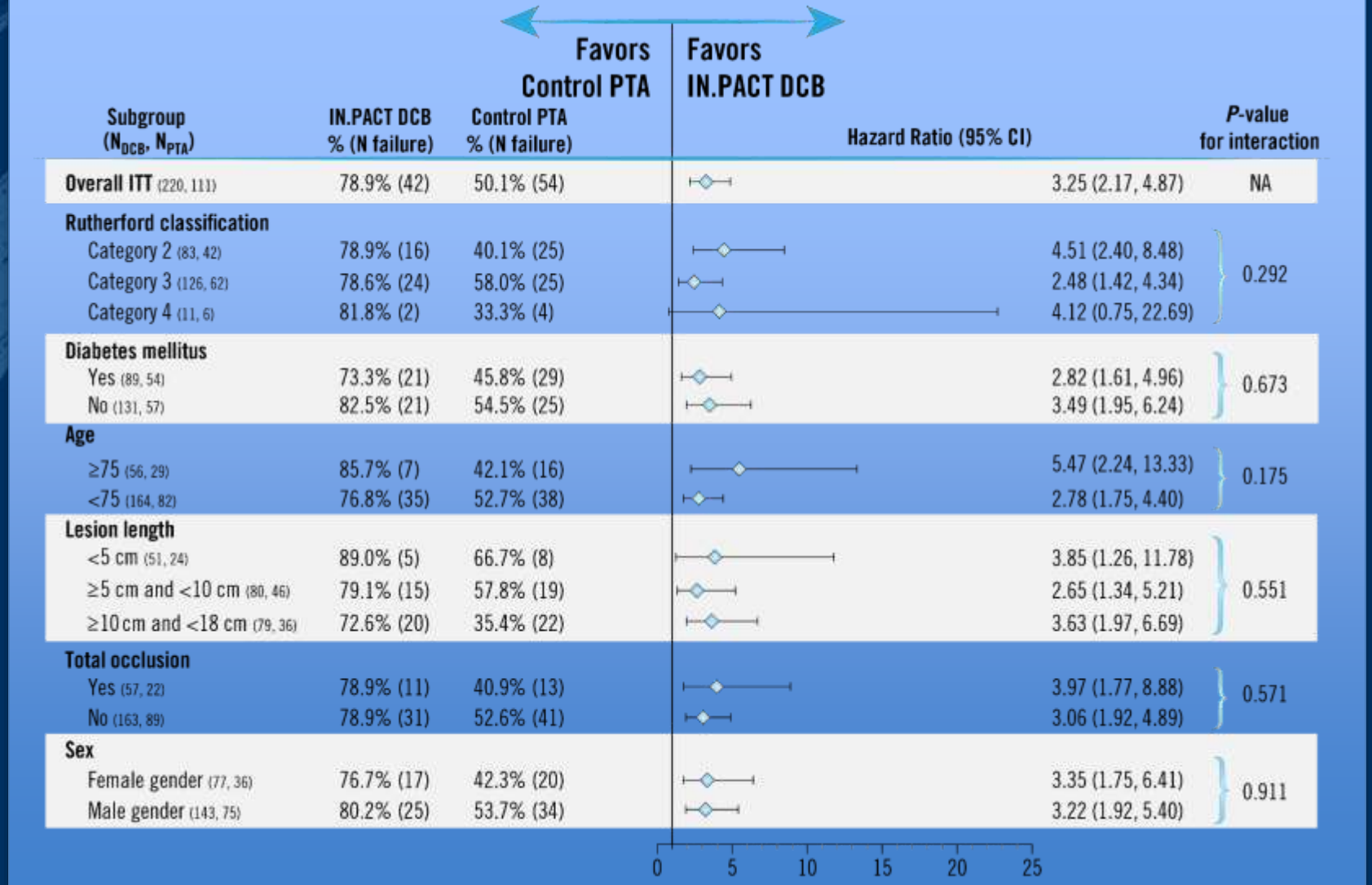


First and only independently adjudicated, randomized pivotal IDE trial to demonstrate durable, superior treatment effect with a DCB over PTA through three years. Primary patency benefit was sustained to 3 years with minimal to no late catch up. Data support IN.PACT™ Admiral™ as a first-line treatment for symptomatic femoropopliteal disease

1. Krishnan P, presented at VIVA Las Vegas 2015.

IN.PACT SFA Trial:

Subgroup Primary Patency through 2 Years



Subgroup (N_{DCB}, N_{PTA})	IN.PACT DCB % (N failure)	Control PTA % (N failure)	Hazard Ratio (95% CI)	*P*-value for interaction
Overall ITT (220, 111)	78.9% (42)	50.1% (54)	3.25 (2.17, 4.87)	NA
Rutherford classification				
Category 2 (83, 42)	78.9% (16)	40.1% (25)	4.51 (2.40, 8.48)	0.292
Category 3 (126, 62)	78.6% (24)	58.0% (25)	2.48 (1.42, 4.34)	
Category 4 (11, 6)	81.8% (2)	33.3% (4)	4.12 (0.75, 22.69)	
Diabetes mellitus				
Yes (89, 54)	73.3% (21)	45.8% (29)	2.82 (1.61, 4.96)	0.673
No (131, 57)	82.5% (21)	54.5% (25)	3.49 (1.95, 6.24)	
Age				
≥75 (56, 29)	85.7% (7)	42.1% (16)	5.47 (2.24, 13.33)	0.175
<75 (164, 82)	76.8% (35)	52.7% (38)	2.78 (1.75, 4.40)	
Lesion length				
<5 cm (51, 24)	89.0% (5)	66.7% (8)	3.85 (1.26, 11.78)	0.551
≥5 cm and <10 cm (80, 46)	79.1% (15)	57.8% (19)	2.65 (1.34, 5.21)	
≥10 cm and <18 cm (79, 36)	72.6% (20)	35.4% (22)	3.63 (1.97, 6.69)	
Total occlusion				
Yes (57, 22)	78.9% (11)	40.9% (13)	3.97 (1.77, 8.88)	0.571
No (163, 89)	78.9% (31)	52.6% (41)	3.06 (1.92, 4.89)	
Sex				
Female gender (77, 36)	76.7% (17)	42.3% (20)	3.35 (1.75, 6.41)	0.911
Male gender (143, 75)	80.2% (25)	53.7% (34)	3.22 (1.92, 5.40)	

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

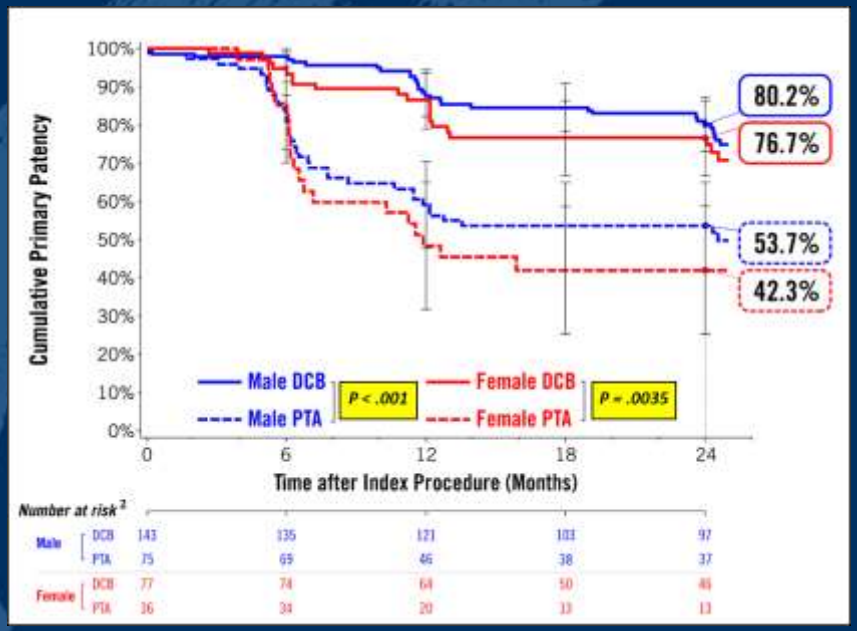
1. TBI allowed / used in cases of incompressible vessels in IN.PACT SFA II phase

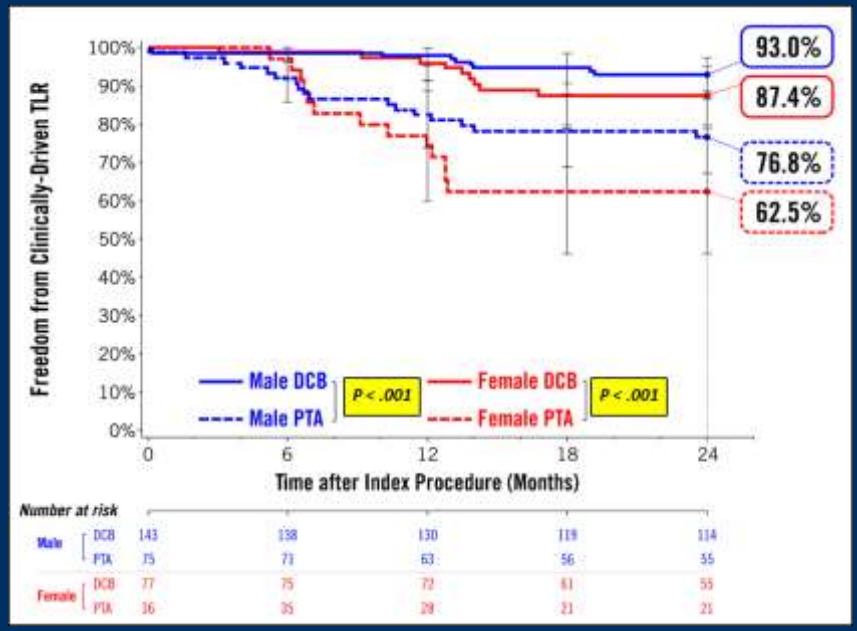
1Y Results: Tepe G, presented at Charing Cross London 2014. Tepe G, et al. Circ :131:495-502 (2015). 2Y Results: Laird JR, presented at TCT San Francisco 2015. Laird JR, et al. J Am Coll Cardiol: 66:2329-38 (2015). Note: 1 year results updated from interval to cumulative KM calculations. 3Y Results: Krishnan P, presented at VIVA Las Vegas 2015.

IN.PACT SFA Trial: 2-year Outcomes

By Gender Summary[1]

Baseline clinical characteristics were well matched between groups and lesion/procedural characteristics had no difference between groups





A significant patency benefit favoring IN.PACT Admiral DCB over PTA was demonstrated in both women and men. Primary patency benefit was sustained to 2 years with no late catch up for either gender. High primary patency and low CD-TLR rates were achieved in women, despite smaller RVDs.

1. Schneider P, presented at Charing Cross London 2016.

IN.PACT SFA Trial

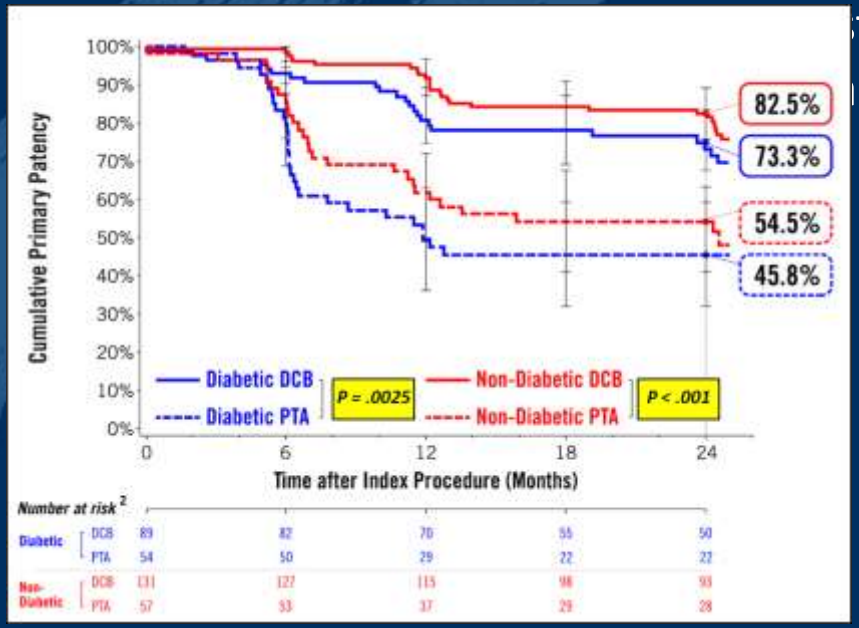
Baseline Clinical Characteristics

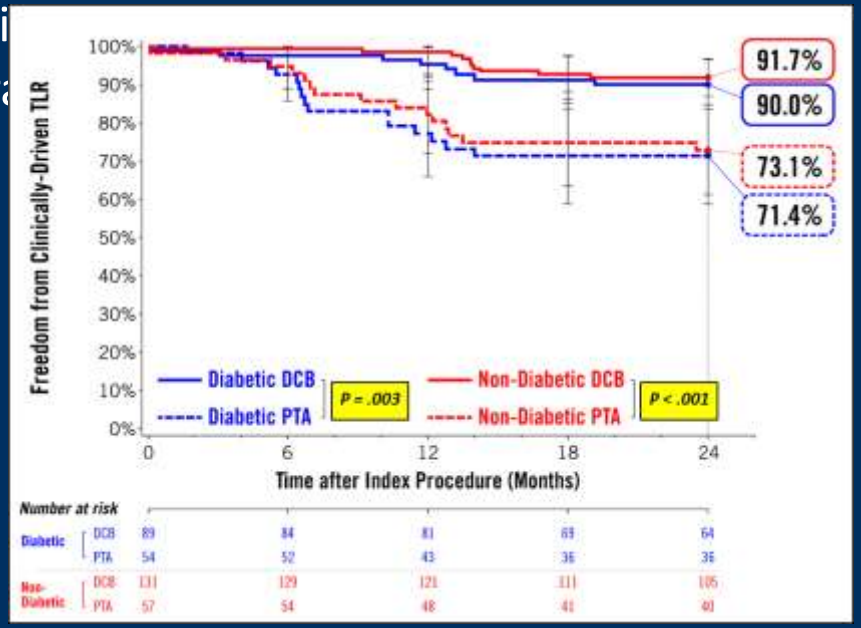
	IN.PACT n = 220 subjects	PTA n = 111 subjects	P-value
Age, Y ± SD	67.5 ± 9.5	68.0 ± 9.2	0.612
Male, % (n)	65.0% (143/220)	67.6% (75/111)	0.713
Diabetes, % (n)	40.5% (89/220)	48.6% (54/111)	0.161
Hypertension, % (n)	91.4% (201/220)	88.3% (98/111)	0.431
Current smoker, % (n)	38.6% (85/220)	36.0% (40/111)	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 / used in cases of incompressible vessels in IN.PACT SFA II phase

1Y Results: Tepe G, presented at Charing Cross London 2014. Tepe G, et al. Circ :131:495-502 (2015). 2Y Results: Laird JR, presented at TCT San Francisco 2015. Laird JR, et al. J Am Coll Cardiol: 66:2329-38 (2015). Note: 1 year results updated from interval to cumulative KM calculations. 3Y Results: Krishnan P, presented at VIVA Las Vegas 2015.

IN.PACT SFA Trial: 2-year Outcomes By Diabetic Status Summary[1]

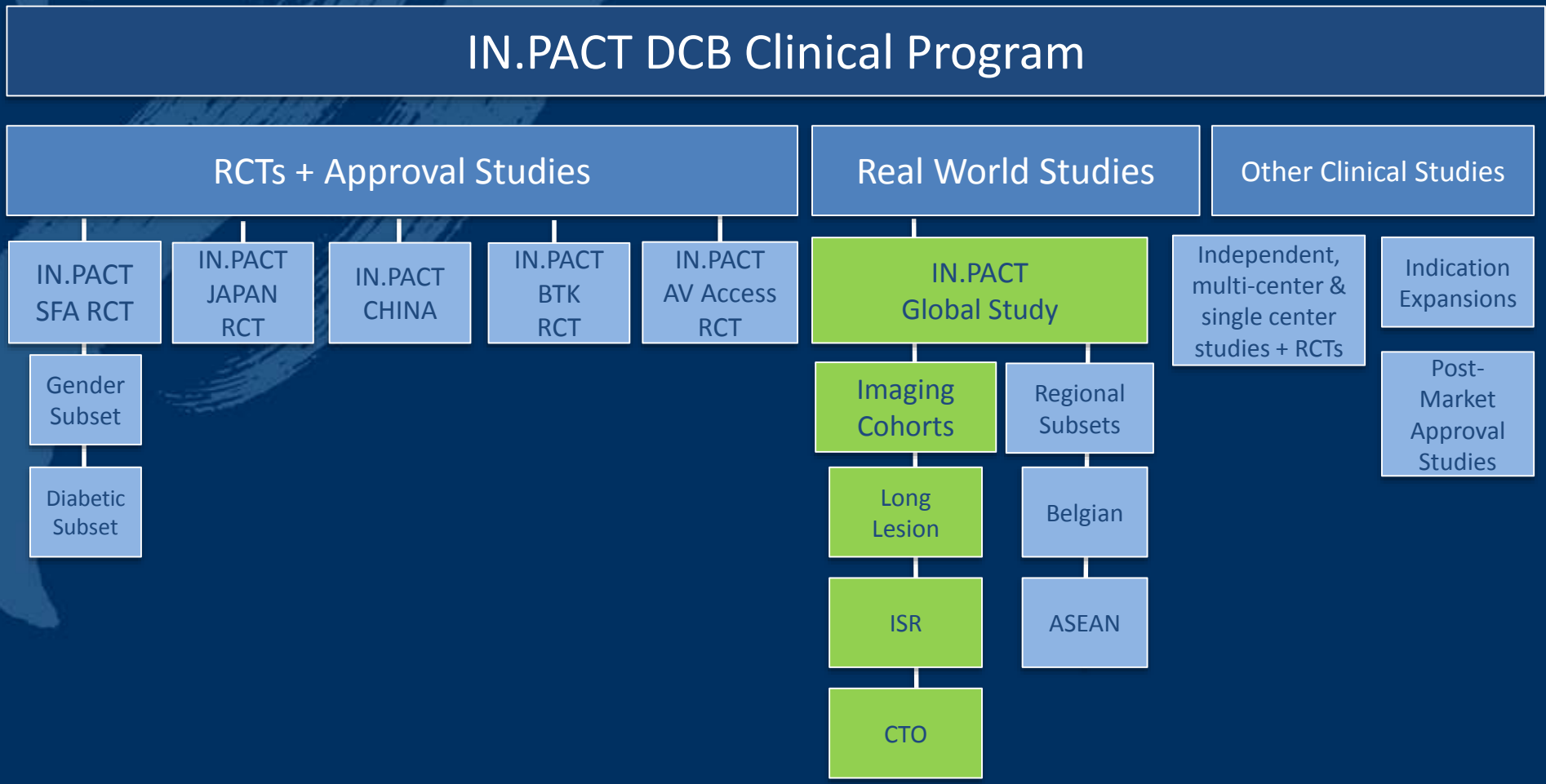




A significant patency benefit favoring IN.PACT Admiral DCB over PTA was demonstrated in both diabetic and non-diabetic subsets. Primary patency benefit was sustained to 2 years with no late catch up for either subset. IN.PACT Admiral DCB is significantly more effective than PTA in diabetic patients who typically present with advanced, complex PAD.

1. Schneider P, presented at Charing Cross London 2016.

IN.PACT Clinical Trial Program



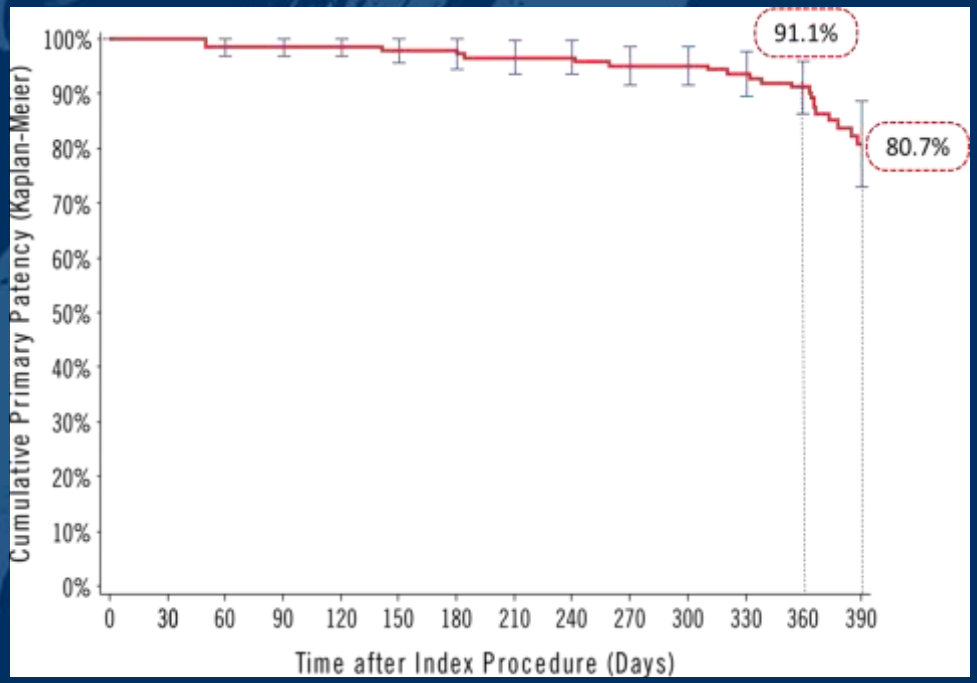
IN.PACT Global Study Summary[1]

IN.PACT GLOBAL Study	
Study Type	Prospective, Multicenter, Single-Arm Study
Primary Endpoints	Efficacy: Freedom from CD-TLR (All Subjects)[4] Efficacy: Primary Patency[2] (Imaging Cohort) Safety: Safety Composite[3]
Rigor + Quality	• Independent adjudication by Clinical Events Committee and Imaging Core Labs (Imaging Cohort)[5] • External Monitoring
Patients	1535 patients
Sites	64 sites (Global OUS)
Key Eligibility Criteria	• Single or multiple lesions ≥2 cm • All TASC • SFA + Full Popliteal • ISR, Ca^{++}, CTO

Results for the IN.PACT Global Study Full Clinical Cohort (n=1406)	
	1 Year
Lesion Length (Mean ± SD, cm)	12.09 ± 9.54
Primary Safety Endpoint[3]	92.1%
Freedom from CD-TLR	92.6%
CD-TLR[2]	7.5%
Major Amputation Target Limb	0.2%
Thrombosis	2.9%

1. Jaff M, presented at VIVA Las Vegas 2016.
2. Freedom from CD-TLR and DUS-derived restenosis (PSVR ≤2.4) at 12m.
3. Composite 30-day freedom for device-and procedure-related mortality and 12-month freedom from major target limb amputation and CD-TVR.
4. Defined as TLR due to symptoms or drop of ABI/TBI of >20% or >0.15 when compared to post-procedure baseline ABI/TBI.
5. IN.PACT Global Study: Only imaging cohort Core Lab Adjudicated (Long lesions, CTO, ISR).

IN.PACT Global Study:
Long Lesion Imaging Cohort, 12 M Results[1]



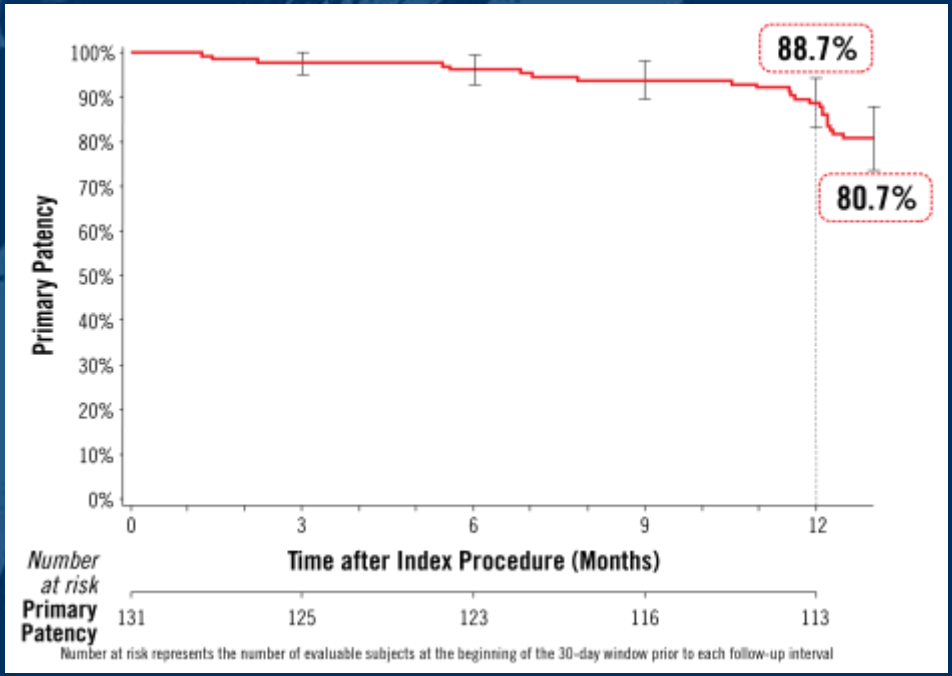
Safety Outcomes	
Clinically-Driven TLR[2]	**6.0% (8/134)**
Primary Safety Endpoint[3]	94.0% (126/134)
Major Adverse Events[4]	11.9% (16/134)
Death (all-cause)	4.5% (6/134)
Major Target Limb Amputation	0.0% (0/134)
Thrombosis	3.7% (5/134)
Any TLR	6.0% (8/134)
Any TVR	6.0% (8/134)

Results demonstrate remarkable overall effectiveness and safety for patients treated with the IN.PACT Admiral DCB with a mean lesion length of **26.4 cm**. The 360-day primary patency rate of **91.1%** and the CD-TLR rate of **6.0%** are unmatched for this complex patient subgroup.

1. Scheinert D, presented at EuroPCR 2015.
2. 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
3. Composite of 30-day freedom from device- and procedure-related mortality and 12-month freedom from major target limb amputation and clinically-driven TVR
4. Major Adverse Events: Composite of death, major target limb amputation, clinically-driven TVR, and thrombosis

IN.PACT Global Study:

ISR Imaging Cohort, 12 M Results[1]

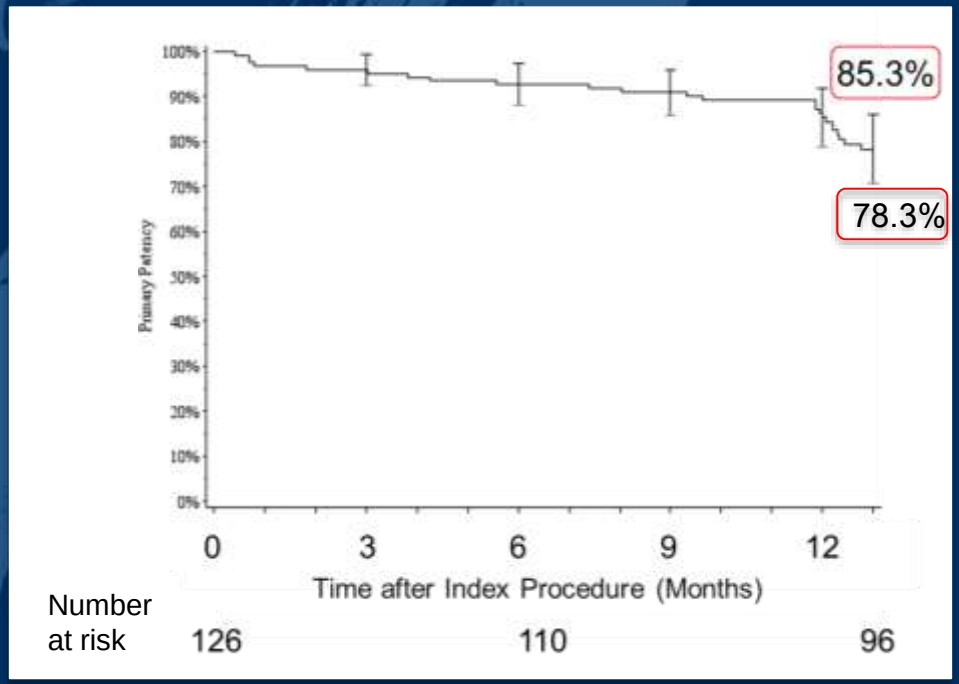


Safety Outcomes	
Clinically-Driven TLR[2]	**7.3% (9/124)**
Primary Safety Endpoint[3]	91.1% (113/124)
Major Adverse Events[4]	8.9% (11/124)
Death (all-cause)	0.0% (0/124)
Major Target Limb Amputation	0.0% (0/124)
Thrombosis	0.8% (1/124)
Any TLR	8.1% (10/124)
Any TVR	9.7% (12/124)

Results demonstrate remarkable effectiveness and safety for ISR patients treated with the IN.PACT Admiral DCB with a mean lesion length of **17.2 cm**. The 12-month primary patency rate of **88.7%** and the 12-month CD-TLR rate of **7.3%** are unmatched for this difficult to treat patient subgroup.

1. Broadmann M, presented at VIVA 2015.
2. 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
3. Composite of 30-day freedom from device- and procedure-related mortality and 12-month freedom from major target limb amputation and clinically-driven TVR
4. Major Adverse Events: Composite of death, major target limb amputation, clinically-driven TVR, and thrombosis

IN.PACT Global Study:
CTO Imaging Cohort, 12 M Results[1]

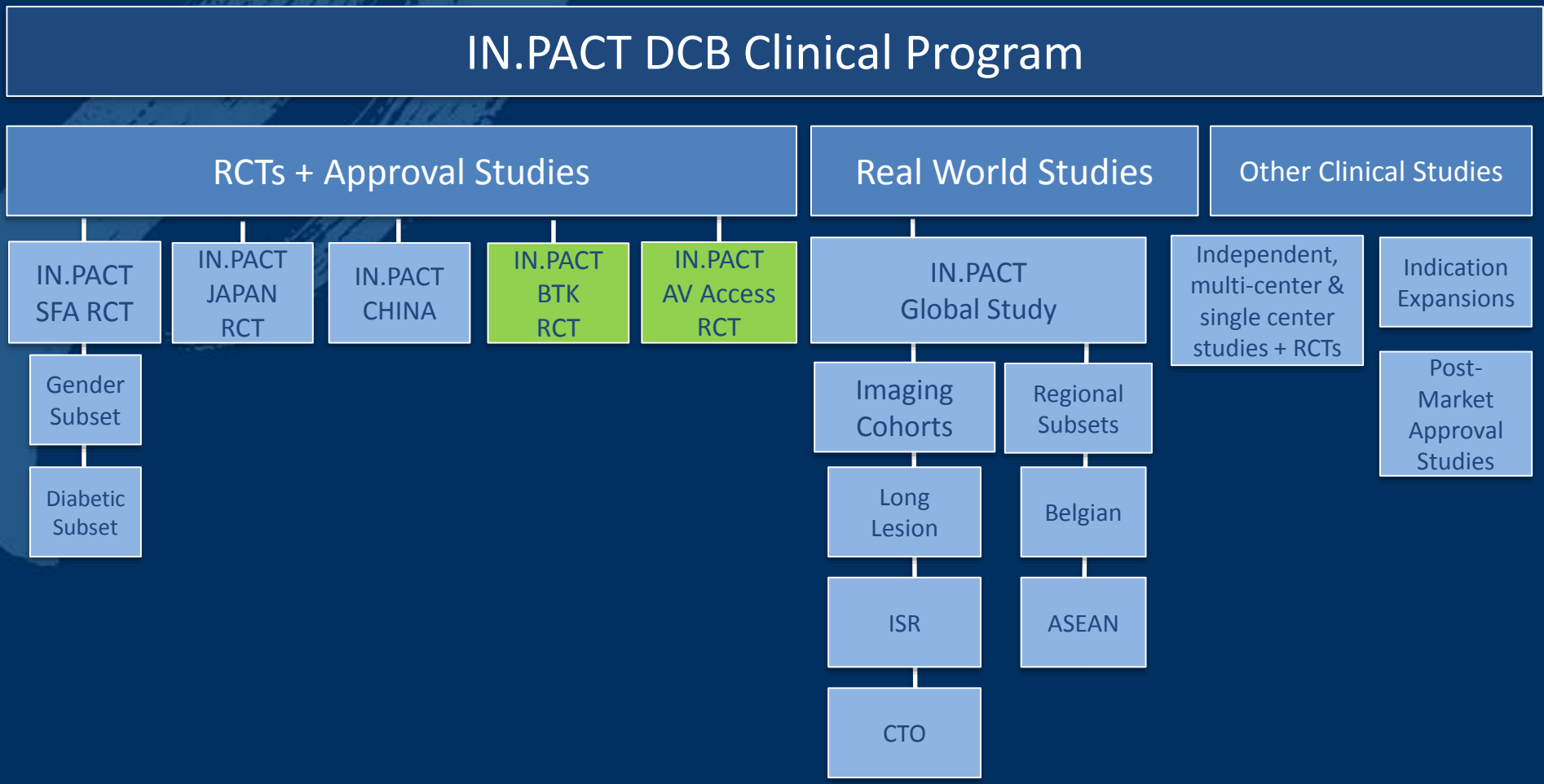


Safety Outcomes	
Clinically-Driven TLR[2]	**11.3% (13/115)**
Primary Safety Endpoint[3]	88.7% (102/115)
Major Adverse Events[4]	15.7% (18/115)
Death (all-cause)	4.3% (5/115)
Major Target Limb Amputation	0.0% (0/115)
Thrombosis	4.3% (5/115)
Any TLR	12.2% (14/115)
Any TVR	12.2% (14/115)

First-of-its-kind independently-adjudicated CTO data. Remarkable effectiveness and safety confirm IN.PACT™ Admiral™ DCB as a stand-alone device for CTO treatment: Mean lesion length of **22.8 cm** (occluded length of **11.86 cm**). 12-month primary patency of **85.3%** overall. CD-TLR of **11.3%.**

1. Tepe G, presented at Charing Cross 2016 updated per Medtronic Data on file.
2. 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
3. Composite of 30-day freedom from device- and procedure-related mortality and 12-month freedom from major target limb amputation and clinically-driven TVR
4. Major Adverse Events: Composite of death, major target limb amputation, clinically-driven TVR, and thrombosis

IN.PACT Clinical Trial Program Upcoming Studies



IN.PACT BTK

Study Enrolling!

Efficacy & Safety of IN.PACT 0.014 DCB vs. PTA in infrapopliteal CTOs

- ☑ Prospective
- ☑ Multicenter (Europe)
- ☑ Randomized (1:1) n=60
- ☑ Corelab
- ☑ Clinical Events Committee
- ☑ Wound care protocol

Key Eligibility Criteria:

- Documented CLI in the target limb with RC 4 or 5
- RVD 2-4 mm
- Successful pre-dilatation of the (entire) target lesion
- No prior stent(s) or bypass surgery within the target vessel(s)[1]

Primary Endpoint:

Late lumen loss (LLL) at 9 months

Secondary Endpoints:

- Composite Safety Endpoint[2]
- MAE rate
- Status of wound healing[3]
- Thrombosis at the target lesion
- Clinical & device success[4]

[1] including stents placed within target vessels during the index procedure prior to randomization; [2] A composite of freedom from device- and procedure-related mortality within 30 days, freedom from major target limb amputation and freedom from clinically-driven TLR within 9 months post-index procedure; [3] Status defined as completely healed - improvement - unchanged – worsened; [4] Device success is defined as successful drug delivery, balloon inflation, deflation and retrieval of the intact study device without burst below the rated burst pressure (RBP). Clinical success is defined as residual stenosis of ≤ 30% without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or TVR)

IN.PACT AV Access IDE Trial

- ☑ Prospective
- ☑ Global, Multicentre
- ☑ Randomized (1:1)
- ☑ Corelab
- ☑ Clinical Events Committee

Design:

- Prospective, global, multicenter, randomized, single-blinded study
- ~30 Global Sites (US, Japan & New Zealand)
- 330 patients
- 24 month follow-up
- 1:1 randomization
- Lesions up to 10 cm in length in the AVF

Study starting in second half of 2017

Purpose:

Evaluate the safety and efficacy of the **IN.PACT™ AV Access DCB compared to PTA** for treatment of subjects presenting with **de-novo or non-stented restenotic obstructive lesions of native AVF** in the upper extremity.

Primary Safety Endpoint: **Serious Adverse Event Rate through 30 Days**[1]

Primary Efficacy Endpoint: **Primary Patency Rate through 6 Months**[2]

Principal Investigators:

- Robert Lookstein, MD (New York, USA)
- Andrew Holden (Auckland, New Zealand)
- Hiroaki Haruguchi, MD (Tokyo, Japan)

[1] Defined as the Serious Adverse Event (SAE) rate involving the AV access circuit through 30 days post-procedure. [2] Defined as freedom from clinically-driven target lesion revascularization (CD-TLR) or access circuit thrombosis measured at 6 months post-procedure.

IN.PACT DCB Clinical Program in the SFA

	IN.PACT SFA (DCB Arm) (N= 220)	IPA SFA Diabetic (DCB Arm) (N=89)	IPA SFA Female (DCB Arm) (N=77)	IN.PACT Global Long Lesion Imaging Cohort (N= 157)	IN.PACT Global ISR Imaging Cohort (N= 131)	IN.PACT Global CTO Imaging Cohort (N=126)	IN.PACT Global Clinical Cohort (N=1406)
Lesion Length (Mean ± SD, cm)	8.94 ± 4.89	9.87 ± 5.21	8.69 ± 4.90	26.40 ± 8.61	17.17 ± 10.47	22.83 ± 9.76	12.09 ± 9.54
Primary Patency[1] (KM @ 360 days)	87.5%	80.7%	86.6%	91.1%	88.7%	85.3%	N/A
Primary Safety Endpoint[2]	95.7%	92.7%	94.6%	94.0%	91.1%	87.7%	92.1%
CD-TLR[3]	**2.4%**	**3.7%**	**4.1%**	**6.0%**	**7.3%**	**11.3%**	**7.5%**
Major Amputation Target Limb	0.0%	0.0%	0.0%	0.0%	0.0%	4.3%	2.9%
Thrombosis	1.4%	2.4%	1.4%	3.7%	0.8%	0.0%	0.2%

1. Freedom from CD-TLR and DUS-derived restenosis (PSVR ≤2.4) at 12m.
2. Composite of 30-day freedom from device- and procedure-related mortality & 12-month freedom from major target limb amputation/clinically-driven TVR.
3. 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.

Conclusions

IN.PACT Admiral DCB effective across patient populations and varying lesion complexities

- Beneficial DCB treatment effect in historically challenging female patients is unique to the IN.PACT Admiral DCB.
- IN.PACT DCB is significantly more effective than PTA in diabetic patients who typically present with advanced, complex PAD.
- Robust evidence supporting the benefit of IN.PACT DCB for complex lesion subsets including very long lesions, CTO, and ISR
- The need for clinically supported treatment options for BTK and AVF still remains.
    - The upcoming IN.PACT BTK and IN.PACT AV Access trials will provide evidence to demonstrate safety and efficacy of IN.PACT DCB in these challenging disease states.

Latest data from the IN.PACT clinical trial programme

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on behalf of the RANGER SFA investigators