Drug Coated Balloon Treatment for Patients with Intermittent Claudication: New Insights from the IN.PACT Global Study Long Lesion (≥ 15 cm) Imaging Cohort

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Potential Conflicts of Interest

Speaker's Name: Prof. Dr. med. Dierk Scheinert

☑ **I have the following potential conflicts of interest to report:**

Consulting:

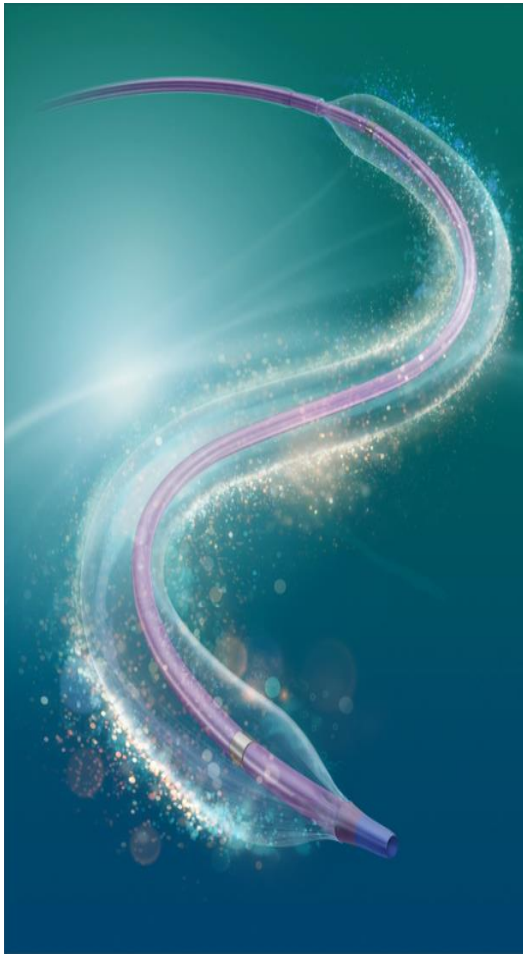
Abbott, Alvimedica, Angioslide, Atheromed, Biotronik, Boston Scientific, Cook Medical, Cordis, CR Bard, Gardia Medical, Hemoteq, Intact Vascular Inc, Medtronic/Covidien, Ostial Inc, TriReme Medical, TriVascular, Upstream Peripheral Technologies

Stockholder:

iDEV Technologies

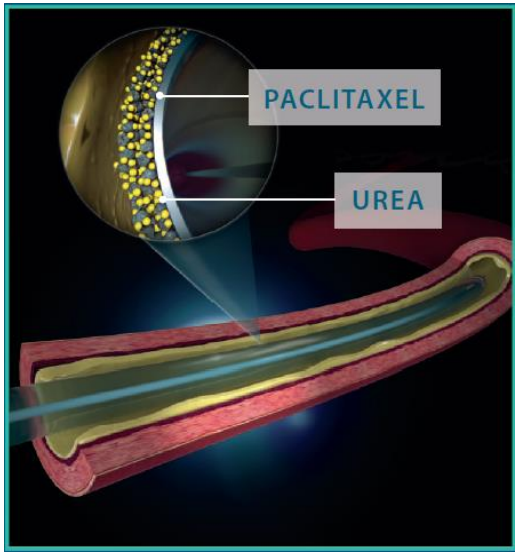
IN.PACT Admiral Drug-Coated Balloon System

DCB Components	IN.PACT Admiral	
Platform	PTA Balloon	Admiral® PTA balloon **4-7 mm diameters** **40, 60, 80, 120, 150 mm lengths**
Drug	Paclitaxel	Proven anti-proliferative drug **3.5 µg/mm²**
Excipient	Urea	Facilitates drug transfer **Naturally occurring, non-toxic**
Coating Process	Medtronic	Reliable, scalable, uniform drug coating process



IN.PACT Admiral DCB

Mechanism of Action

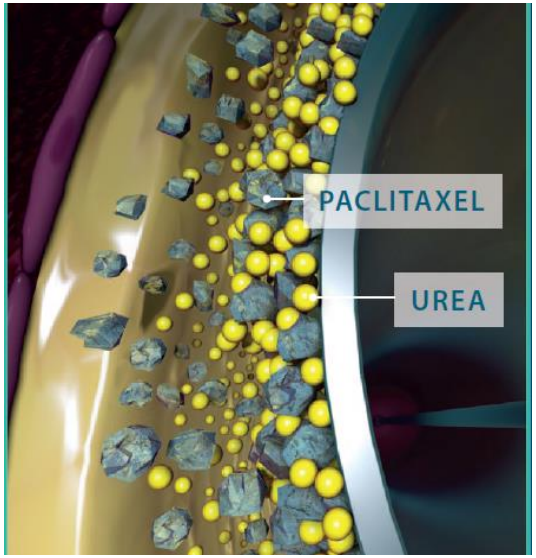


DCB matrix coating:

- Paclitaxel + Urea

During transit to lesion:

- Majority of matrix protected within folds of the balloon



DCB inflation:

- Matrix contacts blood
- Blood hydrates urea
- Urea releases paclitaxel
- Due to its hydrophobic and lipophilic properties, paclitaxel binds to vessel wall

Paclitaxel penetration:

- Through vessel wall deep into the media and adventitia
- Interferes with SMC proliferation
- Can remain in the vessel wall for over 180 days at therapeutic levels[1]

Duration of drug in tissue leads to neointimal control

1. Data on file at Medtronic (GLP Study FS208; GLP Study PS516)

Background

- Complex lesion types including **long lesions, chronic total occlusions and in-stent restenosis** remain unmet clinical needs, with no current treatment standard identified.
- Longer lesion length is a predictor of lower patency at 12 months post-procedure (35-65%) when associated with “gold standard” therapies of PTA and stenting.[1-2]
- High patency and low TLR rates reported at 12 months from the IN.PACT SFA Trial demonstrate that the IN.PACT Admiral drug-coated balloon reduces the risk of restenosis; this remains to be demonstrated in long lesions.

1. Lammer J et al. J Am Coll Cardiol 2013;62:1320-7; 2. Bosiers M et al. J Vasc Surg 2011;54:1042-50

IN.PACT Global Clinical Study

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

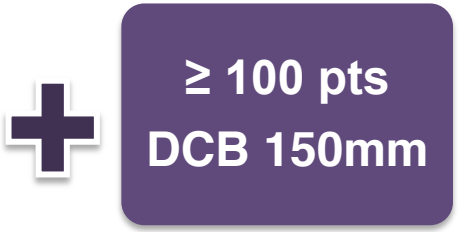
All-comers (RCC 2-4)

- ☑ Bilateral disease
- ☑ Multiple lesions
- ☑ SFA and Popliteal
- ☑ TASC A, B, C, D
- ☑ *de novo* ISR
- ☑ Long Lesions
- ☑ CTOs

- **1538 patients enrolled**
- **64 sites in EU, Mid-East, Latin America, Asia**
- **Independent adjudication by Clinical Events Committee[1]**
- **Prospective subset analysis with core lab[2,3] reported results**
  (*de novo* ISR, long lesions ≥15 cm, CTOs ≥5 cm)
- **Safety and effectiveness data on 150 mm DCB**

1. Syntactx Clinical Events Committee, New York, NY, US
2. VasCore DUS Core Lab, Boston, MA, US
3. SynvaCor Angiographic Core Lab, Springfield, IL, US

IN.PACT Global Study Patient Cohorts
1538 patients enrolled



*ISR is not an approved indication in the US

IN.PACT Global Study

Key Eligibility Criteria

- **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

*Primary Endpoints**

Safety

- **Composite**
  - 30-day freedom from device- and procedure-related mortality
  - 12-month freedom from major target limb amputation and clinically-driven TVR

Efficacy

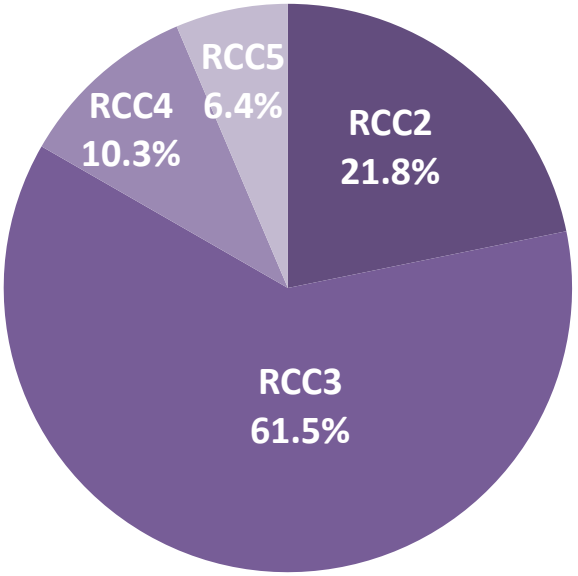
- **Imaging Cohort: 12-Month Primary Patency**
  - Freedom from clinically-driven TLR and freedom from restenosis as determined by DUS PSVR ≤ 2.4.

***This presentation includes outcome data on the subjects enrolled in the ≥ 150 mm Long Lesion Imaging cohort**

IN.PACT Global Long Lesion Imaging Cohort: Baseline Clinical Characteristics

Characteristic	N=157 Subjects
Age (Y)	69.5 ± 10.7
Male Gender (%)	66.2% (104/157)
Diabetes (%)	41.0% (64/156)
Insulin Dependent Diabetes Mellitus (%)	21.8% (34/156)
Hypertension (%)	87.9% (138/157)
Hyperlipidemia (%)	76.7% (115/150)
Current Smoker (%)	34.4% (54/157)
Obesity (BMI ≥ 30 kg/m²) (%)	22.1% (34/154)
Coronary Heart Disease (%)	52.3% (80/153)
Carotid Artery Disease (%)	22.4% (30/134)
Renal Insufficiency[1] (%)	14.4% (21/146)
Previous Peripheral Revasc. (%)	55.4% (87/157)
Concomitant BTK Disease (%)	47.5% (67/141)
ABI	0.669 ± 0.232 (147)

Rutherford Clinical Category



1. Baseline serum creatinine ≥1.5 mg/dL

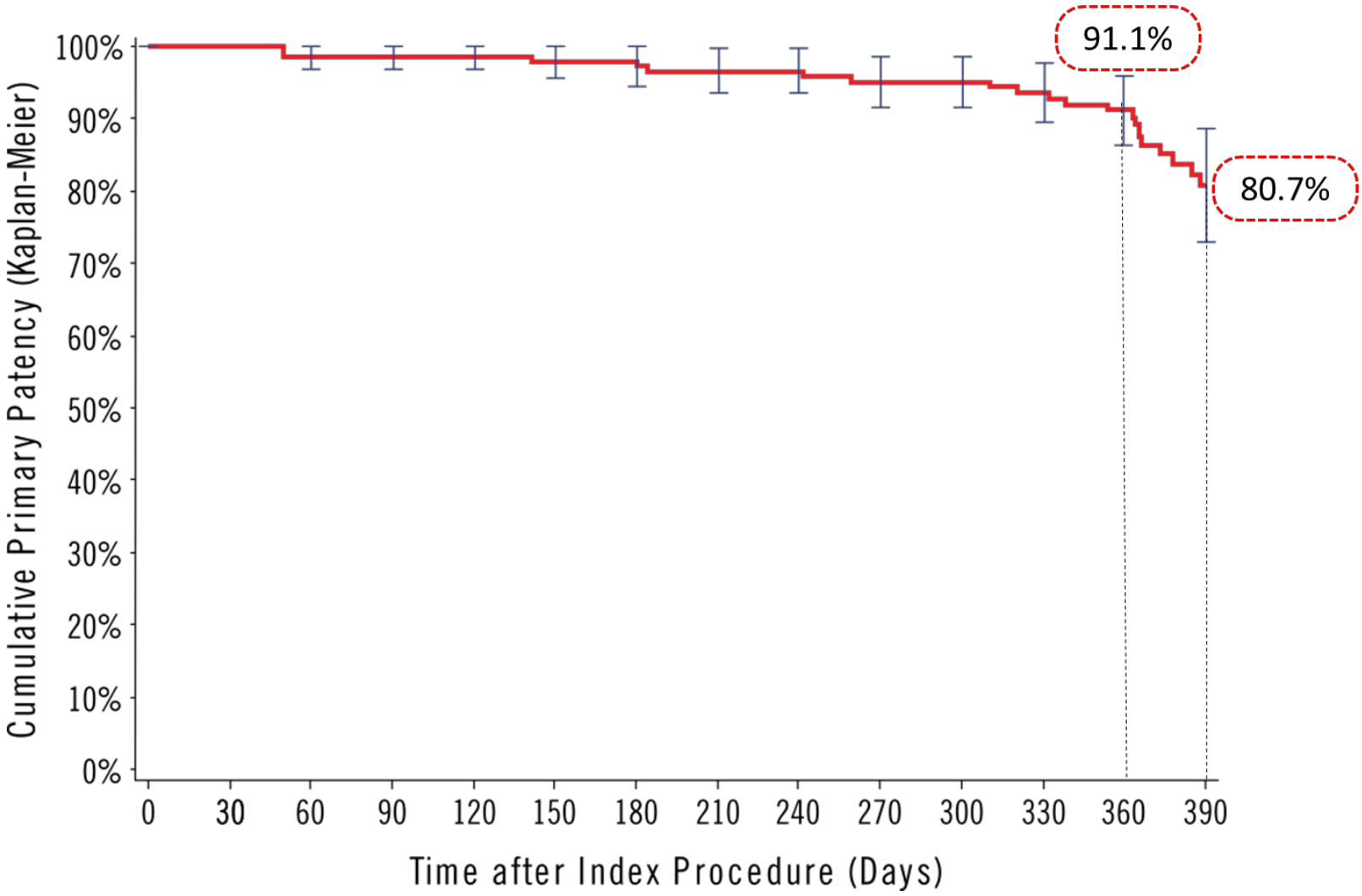
IN.PACT Global Long Lesion Imaging Cohort: Lesion/Procedural Characteristics

Lesions (N)	164
Lesion Type: de novo restenotic (no ISR) ISR	 83.2% (134/161) 16.8% (27/161) 0.0% (0/161)
Lesion Length	**26.40 ± 8.61 cm**
Total Occlusions	60.4% (99/164)
Calcification Severe	71.8% (117/163) 19.6% (32/163)
RVD (mm)	4.594 ± 0.819
Diameter Stenosis (pre-treatment)	90.9% ± 14.2
Dissections: 0	37.9% (61/161)
A-C	47.2% (76/161)
D-F	14.9% (24/161)

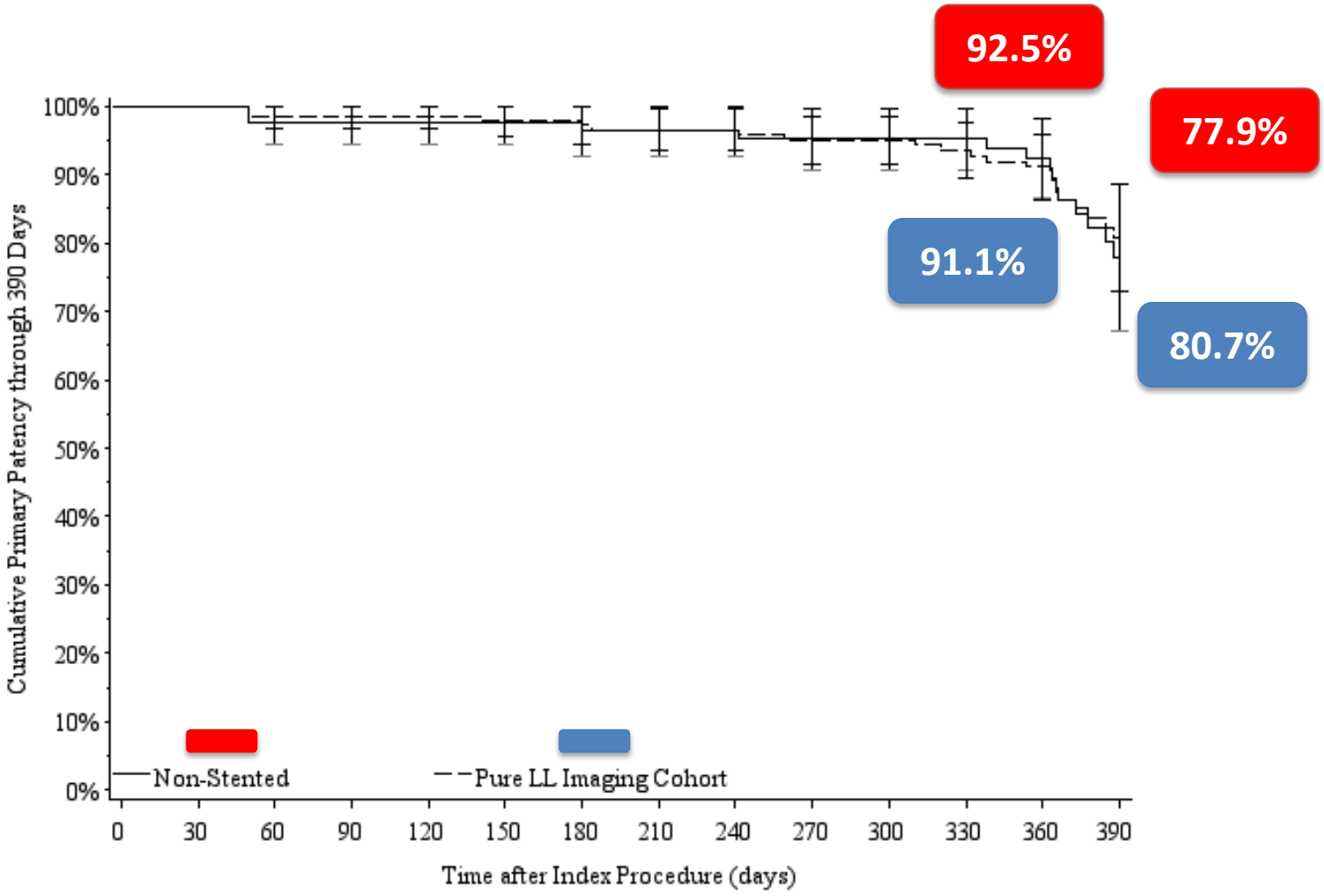
Device Success [1]	99.5% (442/444)
Procedure Success [2]	99.4% (155/156)
Clinical Success [3]	99.4% (155/156)
Pre-dilatation	89.8% (141/157)
Post-dilatation	39.1% (61/156)
Provisional Stent - LL 15-25 cm: - LL > 25 cm:	40.4% (63/156) 33.3% (33/99) 52.6% (30/57)

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

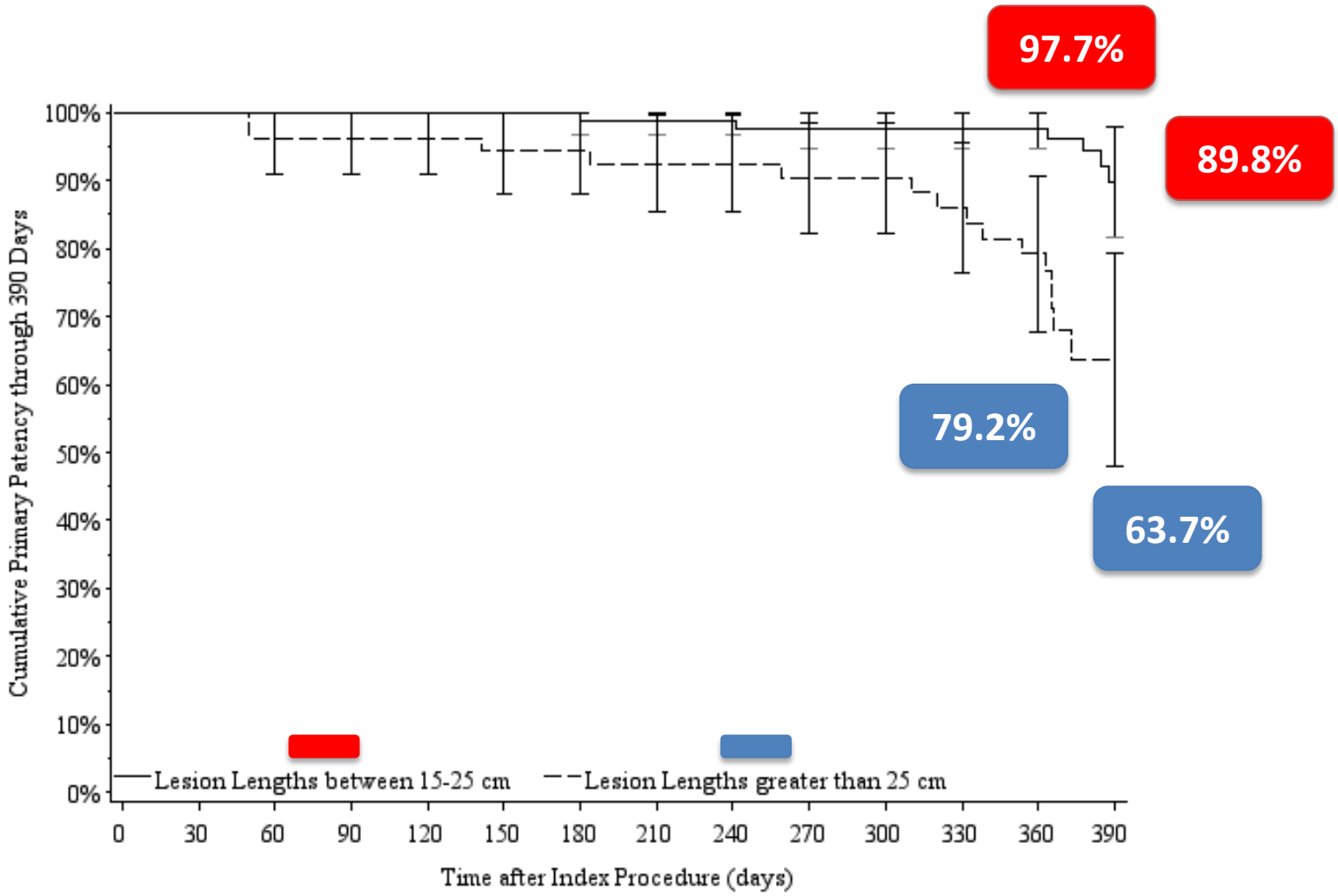
IN.PACT Global Long Lesion Imaging Cohort: Kaplan-Meier Estimate of Primary Patency



IN.PACT Global Long Lesion Imaging Cohort: Primary Patency in Non-stented Subgroup



IN.PACT Global Long Lesion Imaging Cohort: Primary Patency by Lesion Length Subgroup



IN.PACT Global Long Lesion Imaging Cohort: Safety Outcomes

Clinically-Driven TLR [1]	6.0% (8/134)
Primary Safety Endpoint [2]	94.0% (126/134)
Major Adverse Events [3]	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)

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. 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 Long Lesion Imaging Cohort: Safety Outcomes by Lesion Length Subgroup

	LL 15-25 cm (N=100)	LL > 25 cm (N=57)
Clinically-Driven TLR [1]	**2.3% (2/87)**	**12.8% (6/47)**
Primary Safety Endpoint [2]	97.7% (85/87)	87.2% (41/47)
Major Adverse Events [3]	8.0% (7/87)	19.1% (9/47)
Death (all-cause)	3.4% (3/87)	6.4% (3/47)
Major Target Limb Amputation	0.0% (0/87)	0.0% (0/47)
Thrombosis	2.3% (2/87)	6.4% (3/47)
Any TLR	2.3% (2/87)	12.8% (6/47)
Any TVR	2.3% (2/87)	12.8% (6/47)

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. 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 Long Lesion Imaging Cohort: Results across IN.PACT Clinical Studies

Consistent clinical outcomes with the IN.PACT® Admiral® DCB across studies and complex femoropopliteal lesions.

	IN.PACT SFA (DCB Arm) N= 220	IN.PACT Global N= 655	IN.PACT Global Long Lesion Imaging Cohort N=157
Lesion Length (cm)	8.9	12.2	26.4
CD-TLR	**2.4%**	**8.7%**	**6.0%**
CD-TVR	4.3%	9.5%	6.0%
Thrombosis	1.4%	3.8%	3.7%
Target Limb Major Amputation	0.0%	0.3%	0.0%

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

IN.PACT Global Long Lesion Imaging Cohort: Conclusions

- The IN.PACT Global Study is a real-world trial including patients from more than 25 countries, with independent monitoring and independent core lab adjudication of effectiveness outcomes in imaging subgroups.
- Results demonstrate remarkable overall effectiveness and safety for patients treated with the IN.PACT Admiral DCB with a mean LL 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.
- A higher provisional stent rate was observed in patients with LL > 25 cm.
- Patients who did not require provisional stenting demonstrated primary patency at 360 days of 92.5%, which confirms the effectiveness of the IN.PACT Admiral DCB as a stand-alone device in long, complex SFA lesions.