IN.PACT SFA Trial and IN.PACT Global Study: Study Design and Clinical Data Overview

Creating rigorous studies to produce meaningful data for use in everyday clinical practice.

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The IN.PACT SFA Trial is a level 1 clinical evidence trial evaluating the safety and effectiveness of the IN.PACT™ Admiral™ drug-coated balloon (DCB; Medtronic plc) versus standard percutaneous transluminal angioplasty (PTA) for the treatment of superficial femoral artery (SFA) and proximal popliteal artery lesions.

The IN.PACT Global Study is a single-arm study that reflects a complex, real-world patient population. Both the IN.PACT SFA Trial and the IN.PACT Global Study were designed with utmost attention to clinical rigor, and each has a prospective, multicenter design. Although IN.PACT SFA is a randomized controlled trial and IN.PACT Global is a single-arm study,

TABLE 1. COMPLEMENTARY STUDY DESIGNS

	IN.PACT SFA Trial	IN.PACT Global Study
Study type	Randomized controlled pivotal trial	Single-arm study
Primary endpoints	Efficacy: primary patency* Safety: safety composite†	Efficacy: freedom from CD-TLR‡ (all patients) Efficacy: primary patency (imaging cohort) Safety: safety composite†
Rigor and quality	Prospective, multicenter Independent clinical events committee (blinded in IN.PACT SFA) Independent core lab adjudication (blinded in IN.PACT SFA) External monitoring	
No. of patients	331 (220 DCB arm)	> 1,500 > 150, ISR subset > 150, long lesion subset > 150, CTO subset
No. of sites and location	57 (US + EU)	~67 global
Key eligibility criteria	Single lesions ≤ 18 cm, CTO ≤ 10 cm TASC A–C SFA + proximal popliteal No ISR, Ca^{++}	Single or multiple lesions ≥ 2 cm All TASC SFA + full popliteal ISR, Ca^{++}

Abbreviations: CD-TLR, clinically driven target lesion revascularization; CTO, chronic total occlusion; ISR, in-stent restenosis.
**Freedom from CD-TLR‡ and DUS-derived restenosis (PSVR ≤ 2.4) at 12 months.*
†Composite 30-day freedom from device- and procedure-related mortality and 12-month freedom from major target limb amputation and CD-TVR.
‡Defined as reintervention at target lesion due to symptoms or drop of ankle-brachial index/tibial-brachial index of ≥ 20% or > 0.15 when compared to postprocedure baseline ankle-brachial index/tibial-brachial index.

TABLE 2. SELECT BASELINE, LESION, AND PROCEDURAL CHARACTERISTICS		
Patient and Procedural Characteristics	**IN.PACT SFA Trial (n = 220 patients)**	**IN.PACT Global Study (n = 655 patients)**
Male sex	65% (143/220)	67.2% (440/655)
Diabetes	40.5% (89/220)	41.2% (269/653)
Coronary artery disease	57% (122/214)	43.3% (270/624)
Current smoker	38.6% (85/220)	33.6% (220/655)
Predilatation	96.4% (212/220)	75.4% (494/655)
Provisional stenting	7.3% (16/220)	24.7% (160/648)

they both utilize adjudication of major adverse events, including target lesion and target vessel revascularizations, by independent clinical events committees. In the IN.PACT SFA Trial and the imaging cohort of the IN.PACT Global Study, there is also interpretation of target lesion restenosis by independent core laboratories (blinded in the IN.PACT SFA Trial), as well as external monitoring (Table 1). The 12-month data from the IN.PACT SFA Trial were recently published, and 12-month data from the first 655 enrolled IN.PACT Global Study patients were presented at the Vascular Interventional Advances conference this past November.

The primary efficacy endpoint for IN.PACT SFA was primary patency (defined as freedom from clinically driven target lesion revascularization (CD-TLR) and duplex ultrasound (DUS)-derived restenosis (peak systolic velocity ratio [PSVR] ≤ 2.4) at 12 months. For IN.PACT Global, the primary efficacy endpoint in the clinical cohort is freedom from CD-TLR within 12 months. In the imaging cohort of the IN.PACT Global Study, the primary efficacy endpoint is primary patency within 12 months, defined as freedom from CD-TLR and freedom from restenosis as determined by DUS PSVR ≤ 2.4. Both studies were analyzed with a composite safety endpoint defined as 30-day freedom from device- and procedure-related mortality and 12-month freedom from major target limb amputation and clinically driven target vessel revascularization (CD-TVR).

Select baseline, lesion, and procedural characteristics of the patients who were treated in the two studies are shown in Table 2.

PATIENT POPULATION COMPARISON

Compared to the IN.PACT SFA Trial, the first 655 subjects enrolled in the IN.PACT Global Study tended to have higher Rutherford classification scores, longer

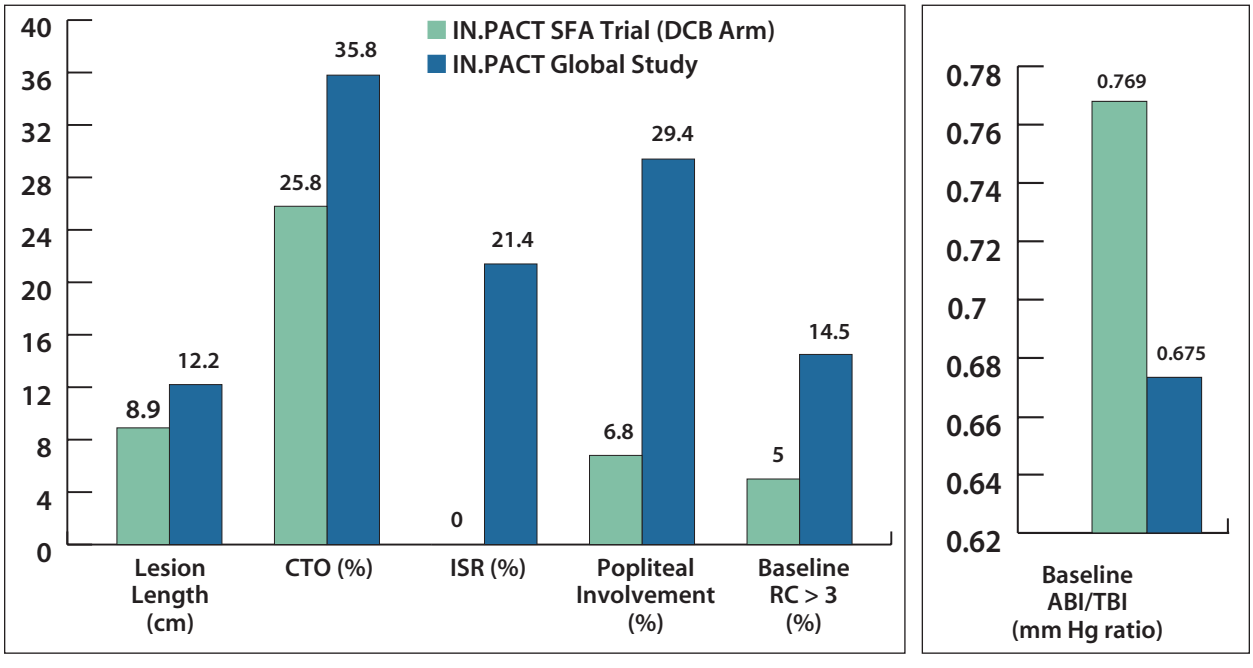

Figure 1. IN.PACT SFA Trial and IN.PACT Global Study patient population comparison.

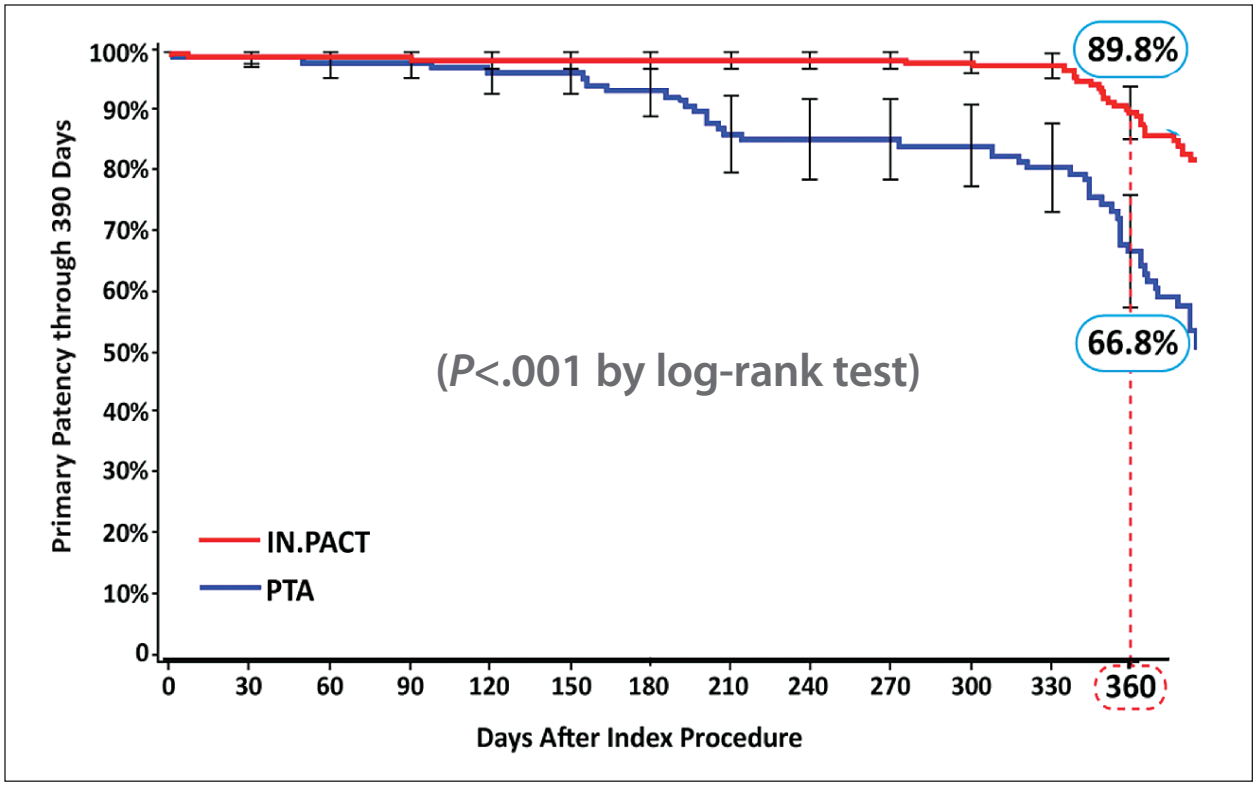

Figure 2. Twelve-month primary patency rates from the IN.PACT SFA Trial. Primary patency is defined as freedom from CD-TLR and restenosis as determined by DUS PSVR ≤ 2.4.

lesions, greater involvement of the popliteal artery, and included patients with in-stent restenosis* (ISR) (Figure 1). ISR is a very important potential application for DCBs. The IN.PACT Global Study included a large number of femoropopliteal ISR lesions (21.4% in the first 655 subjects) and will provide important data regarding this challenging clinical problem.

TWELVE-MONTH OUTCOMES FROM IN.PACT SFA AND IN.PACT GLOBAL

Figure 2 shows a Kaplan-Meier analysis of primary patency in the DCB-treated and PTA-treated arms of the IN.PACT SFA Trial. At 360 days, 89.8% of patients in the DCB group achieved primary patency compared to 66.8% who underwent standard PTA ($P < .001$).

Table 3 compares safety and efficacy outcomes at 12 months in the two arms of the IN.PACT SFA Trial. The data indicate significant improvement in most outcomes for the DCB arm as compared to the PTA arm in the IN.PACT SFA Trial. The results of DCB use in IN.PACT SFA are remarkably good, despite the fact that lesions were longer (mean lesion length, 8.9 cm) in this trial than in previous randomized DCB trials. The most striking finding from IN.PACT SFA was the remarkably low CD-TLR rate (2.4%), which is lower than those reported in any previous SFA device trial.

Outcomes from the first 655 patients enrolled in the IN.PACT Global Study are also presented in Table 3. The 12-month safety and efficacy outcomes from these subjects confirm the safety and effectiveness of IN.PACT Admiral in a complex, real-world patient population and reinforce the excellent outcomes from IN.PACT SFA. The CD-TLR rate was only 8.7%, despite the inclusion of longer and more complex lesions, with 14.5% patients at Rutherford classification > 3. The CD-TLR rate in the IN.PACT Global Study compares very favorably with the TLR rate seen in previous device trials (DCB, stent, atherectomy) that included shorter and less complex lesions.

The patients were predefined by sex in subgroups that were analyzed in the IN.PACT SFA Trial. The primary safety, primary effectiveness, and CD-TLR outcomes for these subgroups are shown in Table 4. The results of an interaction analysis indicate that the treatment differences between the IN.PACT Admiral DCB and PTA groups are consistent between men and women. This occurred despite the historically worse outcomes of endovascular procedures in women. These

*In-stent restenosis is not an approved indication in the United States.

TABLE 3. TWELVE-MONTH SAFETY AND EFFECTIVENESS OUTCOMES				
IN.PACT SFA Trial				IN.PACT Global Study
Outcomes	**IN.PACT Admiral (n = 220)**	**Standard PTA (n = 111)**	***P* Value**	**IN.PACT Admiral (n = 655)**
CD-TLR	2.4% (5/207)	20.6% (22/107)	< .001	8.7% (50/577)
All TLR	2.9% (6/207)	20.6% (22/107)	< .001	9% (52/577)
CD-TVR	4.3% (9/207)	23.4% (25/107)	< .001	9.5% (55/577)
Primary safety composite	95.7% (198/207)	76.6% (82/107)	< .001	89.6% (517/577)
Thrombosis	1.4% (3/207)	3.7% (4/107)	.096	3.8% (22/577)
Target limb major amputation	0% (0/207)	0% (0/107)	> .999	0.3% (2/577)
All-cause death	1.9% (4/207)	0% (0/107)	.926	3.3% (19/577)

TABLE 4. TWELVE-MONTH SAFETY AND EFFECTIVENESS OUTCOMES BY IN.PACT SFA PATIENT SEX SUBGROUP			
Women			
Outcome	**IN.PACT Admiral (n = 77)**	**Standard PTA (n = 36)**	***P* Value**
Primary safety endpoint	94.6% (70/74)	68.6% (24/35)	< .001
Primary effectiveness endpoint (primary patency)	75.7% (53/70)	43.8% (14/32)	.004
CD-TLR	4.1% (3/74)	25.7% (9/35)	< .001
Men			
Outcome	**IN.PACT Admiral (n = 143)**	**Standard PTA (n = 75)**	***P* Value**
Primary safety endpoint	96.2% (128/133)	80.6% (58/72)	< .001
Primary effectiveness endpoint (primary patency)	86% (104/121)	56.3% (40/71)	< .001
CD-TLR	1.5% (2/133)	18.1% (13/72)	< .001

findings are particularly important because another DCB trial (LEVANT 2), failed to show a benefit of DCB use in women who were treated with the Lutonix device (Bard Peripheral Vascular).

CONCLUSION

The IN.PACT SFA Trial was a well-conducted, large, prospective, randomized trial that confirmed the benefits of the IN.PACT Admiral DCB compared to standard PTA for patients with disease in the SFA and proximal popliteal arteries. Twelve-month primary patency was excellent, and there was an extremely low rate of CD-TLR. The IN.PACT Global Study has added to our understanding regarding the effectiveness of DCBs for more complex lesions often seen in real-world clinical practice. The 12-month outcomes on the first 655 subjects confirm the safety and effectiveness of IN.PACT Admiral in a complex, real-world patient population and reinforce the excellent outcomes from IN.PACT SFA. ■

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