JOURNAL OF ENDOVASCULAR THERAPY
A SAGE Publication
An official publication of the ISEVS

Journal of Endovascular Therapy
2020, Vol. 27(6) 946–955

DOI: 10.1177/1526602820948240
www.jevt.org
SAGE

Three-Year Results of the IN.PACT SFA Japan Trial Comparing Drug-Coated Balloons With Percutaneous Transluminal Angioplasty

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Abstract

Purpose: To evaluate the 3-year safety and effectiveness of the MDT-2113 (IN.PACT Admiral) drug-coated balloon (DCB) vs percutaneous transluminal angioplasty (PTA) in a Japanese population with femoropopliteal occlusive disease. **Materials and Methods:** The multicenter, prospective, IN.PACT SFA Japan randomized controlled trial (*ClinicalTrials.gov* identifier NCT01947478) was an independently adjudicated study evaluating Japanese participants randomized 2:1 to DCB (n=68) or PTA (n=32). The effectiveness endpoint was primary patency through 36 months, defined as freedom from clinically-driven target lesion revascularization (CD-TLR) and freedom from restenosis (by duplex ultrasound). The effectiveness endpoint was evaluated using the Kaplan-Meier method; estimates are presented with the 95% confidence intervals (CIs). The safety composite endpoint was freedom from device- and procedure-related death through 30 days and freedom from major target limb amputation and clinically-driven target vessel revascularization through 36 months. **Results:** Primary patency by Kaplan-Meier estimate was higher in the DCB group (68.9%, 95% CI 57.5% to 80.2%) vs the PTA group (46.9%, 95% CI 29.6% to 64.2%) at 36 months (log-rank p=0.001). The CD-TLR rates were 14.9% (10/67) for the DCB group and 20.7% (6/29) for PTA (p=0.554). The safety composite endpoint occurred in 83.6% (56/67) of DCB participants and 75.9% (22/29) of PTA participants (p=0.402). All-cause death was similar between groups at 36 months [DCB 6.0% (4/67) vs PTA 6.9% (2/29), p>0.999), with no device- or procedure-related deaths in either group. **Conclusion:** The final report of the IN.PACT SFA Japan trial showed that the IN.PACT Admiral DCB is safe and had durable outcomes through 3 years in Japanese participants with femoropopliteal occlusive disease.

Keywords

amputation, balloon angioplasty, drug-coated balloon, femoropopliteal segment, mortality, restenosis, target lesion revascularization

Introduction

Traditional endovascular approaches to the treatment of atherosclerotic disease in the femoropopliteal arteries include percutaneous transluminal angioplasty (PTA) with an uncoated balloon and implantation of a bare metal stent or stent-graft.[1] Recently, drug-eluting stents (DES) and drug-coated balloons (DCBs) that transfer paclitaxel to the vessel wall during revascularization have been added to the suite of tools available to interventionists, helping to prevent restenosis after treatment.[2,3]

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Multiple prospective studies have demonstrated the safety and effectiveness of DCBs for the treatment of patients with peripheral artery disease, including those with complex lesions that are often excluded from randomized controlled trials (RCTs).[4–25] Despite the accumulation of short-term evidence supporting DCB use in a broad range of patients, there is still little evidence on DCB outcomes beyond 2 years. Three-year outcomes have been reported from the prospective, single-arm IN.PACT Global study (mean lesion length 12.1 cm),[26] the ILLUMENATE US and EU trials (mean lesion lengths 8.0 and 7.2 cm, respectively),[27] and the DEBATE-ISR RCT of patients with diabetes and in-stent restenosis (ISR; mean lesion length 13.2 cm).[15] Five-year outcomes have been published from the THUNDER (mean lesion length 7.4 cm) and the IN.PACT SFA (mean lesion length 8.9 cm) RCTs.[24,28] Five-year outcomes have been reported for AcoArt I (mean lesion length 14.7 cm).[29] Beyond these studies, there is a need for more evidence on the long-term safety and efficacy of DCB use in patients with femoropopliteal occlusive disease.

Additionally, most prospective DCB studies have enrolled participants from sites in Europe or the United States, meaning that devices have not been thoroughly examined in different geographies or ethnicities or in the full range of baseline variables in a real-world population. A more global approach means that a broader variable set is tested, from vessel size to distribution of comorbidities. Furthermore, though a clinical trial setting does control for many variables, strict follow-up and medical therapy are not fully standardized and are left to the discretion of the treating physician. As such, testing medical devices in geographical regions with different standards of care is important. To date, only 5 prospective DCB studies have included populations from outside Europe and the United States; there is a distinct need for DCB studies that are focused on populations outside these geographical regions, including in Asia. Of these 5 studies, 2 are the large and single-arm studies IN.PACT Global and ILLUMENATE Global.[7,18] The remaining 3 studies were conducted in Asia and include the prospective, multicenter, single-arm IN.PACT SFA China study and 2 RCTs, AcoArt I and IN.PACT (MDT-2113) SFA Japan.[14,21,25,29,30] Previous reports from the IN.PACT SFA Japan trial have shown DCBs are safe and effective in an exclusively Japanese population, with a high rate of patency and low rate of clinically-driven target lesion revascularization (CD-TLR) through 2 years.[25,30] This, the final IN.PACT SFA Japan report, is the first to publish 3-year DCB outcomes in an Asian population.

Materials and Methods

Study Design

IN.PACT (MDT-2113) SFA Japan was a phase III, multicenter, prospective RCT conducted in Japan. Methods have been previously reported.[25] This single-blinded trial evaluated the MDT-2113 device (IN.PACT Admiral DCB; Medtronic plc, Santa Rosa, CA, USA) compared with standard uncoated PTA to report safety and effectiveness; participants were randomly assigned in a 2:1 ratio to treatment with a DCB or PTA. The trial was registered on the National Institutes of Health website (*ClinicalTrials.gov* identifier NCT01947478).

A Clinical Events Committee (CEC) reviewed and adjudicated all major adverse events through 36 months post-intervention. Independent core laboratories analyzed procedural and follow-up duplex ultrasonography images (VasCore, Massachusetts General Hospital, Boston, MA, USA) and angiograms (SynvaCor, Springfield, IL, USA). The CEC and independent core laboratories were blinded through the 36-month follow-up duration. The trial was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice Guidelines, and applicable laws as specified by all relevant governmental authorities. Independent oversight was provided by a data safety monitoring board.

Participant Population

Participants were enrolled in this study if they were between the ages of 20 and 85 years, with symptoms of claudication and/or ischemic rest pain (Rutherford categories 2–4) referable to a stenotic (70%–99%) lesion between 4- and 20-cm long or an occlusion ≤10 cm long involving the superficial femoral and/or proximal popliteal arteries. Lesions were required to undergo successful predilation before inclusion in the trial. Prior to enrollment, written informed consent was obtained from all participants according to the protocols approved by the institutional review boards at each investigational site.

The trial enrolled 100 participants randomized to receive treatment with DCB (n=68) or PTA (n=32). Demographic, clinical, and lesion characteristics have been reported and were well matched between groups (Table 1).[25] The mean lesion length was 9.15±5.85 cm in the DCB group and 8.89±6.01 cm in the PTA group. Intravascular ultrasound was used in 39.7% (27/68) of DCB procedures and 25.0% (8/32) of PTA procedures, and the provisional stent rate was 4.4% (3/68) in the DCB group and 3.1% (1/32) in the PTA group (Table 2). Participant flow through 36 months is shown in Figure 1. Among participants still eligible for evaluation at 36 months, the rate of within and out of window follow-up was 95.1% (58/61) in the DCB group and 100% (27/27) in the PTA group.

Study Endpoints Through 36 Months

The primary effectiveness and safety endpoints were previously reported through 12 and 24 months.[25,30] Through 36 months, the effectiveness endpoint was primary patency,

Table 1. Baseline Participant and Lesion Characteristics.[a]

Characteristic	DCB (68 Participants, 68 Lesions)	PTA (32 Participants, 32 Lesions)	p
Age, y	73.3±7.4	74.2±6.1	0.539
Men	73.5 (50/68)	81.3 (26/32)	0.461
Obesity (BMI ≥30 kg/m^2)	4.4 (3/68)	0 (0/32)	0.549
Diabetes mellitus	58.8 (40/68)	56.3 (18/32)	0.831
Insulin dependent	14.7 (10/68)	18.8 (6/32)	0.771
Current smoker	26.5 (18/68)	31.3 (10/32)	0.639
Carotid artery disease	18.5 (12/65)	16.1 (5/31)	>0.999
Coronary heart disease	50.0 (34/68)	50.0 (16/32)	>0.999
Renal insufficiency	8.8 (6/68)	12.5 (4/32)	0.722
Previous peripheral revascularization	57.4 (39/68)	59.4 (19/32)	>0.999
Below-the-knee involvement	33.8 (23/68)	34.4 (11/32)	>0.999
Previous limb amputation	1.5 (1/68)	0 (0/32)	>0.999
ABI/TBI	0.76±0.15	0.74±0.17	0.384
Rutherford category			0.623
2	54.4 (37/68)	59.4 (19/32)	
3	41.2 (28/68)	37.5 (12/32)	
4	4.4 (3/68)	3.1 (1/32)	
Lesion type[b]			0.085
De novo	91.2 (62/68)	100 (32/32)	
Restenotic (nonstented)	8.8 (6/68)	0.0 (0/32)	
Proximal popliteal involvement	1.5 (1/68)	3.1 (1/32)	0.540
Severe calcification[c,d]	7.4 (5/68)	9.4 (3/32)	0.708
Lesion length, cm[c,e]	9.15±5.85	8.89±6.01	0.838
Total occlusions[c]	16.2 (11/68)	15.6 (5/32)	>0.999
TASC II classification[c]			0.852
A	57.4 (39/68)	56.3 (18/32)	
B	23.5 (16/68)	21.9 (7/32)	
C	19.1 (13/68)	21.9 (7/32)	
Reference vessel diameter, mm[c]	4.84±0.75	4.68±0.66	0.280
Lesion diameter, mm[c]	0.97±0.73	0.90±0.59	0.610
Diameter stenosis, %[c]	80.2±14.1	80.7±12.5	0.861

Abbreviations: ABI, ankle-brachial index; BMI, body mass index; DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty; TASC II, TransAtlantic Inter-Society Consensus II; TBI, toe-brachial index.

[a]Continuous data are presented as the means ± standard deviation; categorical data are presented as the percent (number/sample).

[b]Site-reported.

[c]Assessed per lesion by core laboratory.

[d]Severe calcification defined as calcification with circumference ≥180° (both sides of vessel at the same location) and length greater than or equal to half of the total lesion length.

[e]Normal-to-normal by core laboratory quantitative vascular analysis.

defined as freedom from CD-TLR and freedom from restenosis as determined by a duplex ultrasound–derived peak systolic velocity ratio ≤2.4. Each component of the endpoint was independently adjudicated by the blinded CEC (for CD-TLR) or by the core laboratories (for restenosis). CD-TLR was defined as reintervention at the target lesion due to symptoms or decrease in ankle-brachial index (ABI) ≥20% or >0.15 vs the postprocedure ABI. At 36 months following the index procedure, the safety composite endpoint was freedom from (1) device- and procedure-related death through 30 days, (2) major target limb amputation through 36 months, and (3) clinically-driven target vessel revascularization (CD-TVR) through 36 months.

Other endpoints included major adverse events (a composite endpoint that included all-cause death, CD-TVR, major target limb amputation, and thrombosis at the target lesion site) at 36 months. Thrombosis was defined as a total occlusion due to rapidly evolving thrombus formation confirmed by sudden onset of symptoms and documented by duplex ultrasound and/or angiography. Additional assessments included individual components of the composite major adverse events endpoint and primary sustained clinical improvement (defined as freedom from target limb amputation, freedom from TVR, and an improvement shift of 1 Rutherford category at 36 months). Functional assessments included general appraisal through

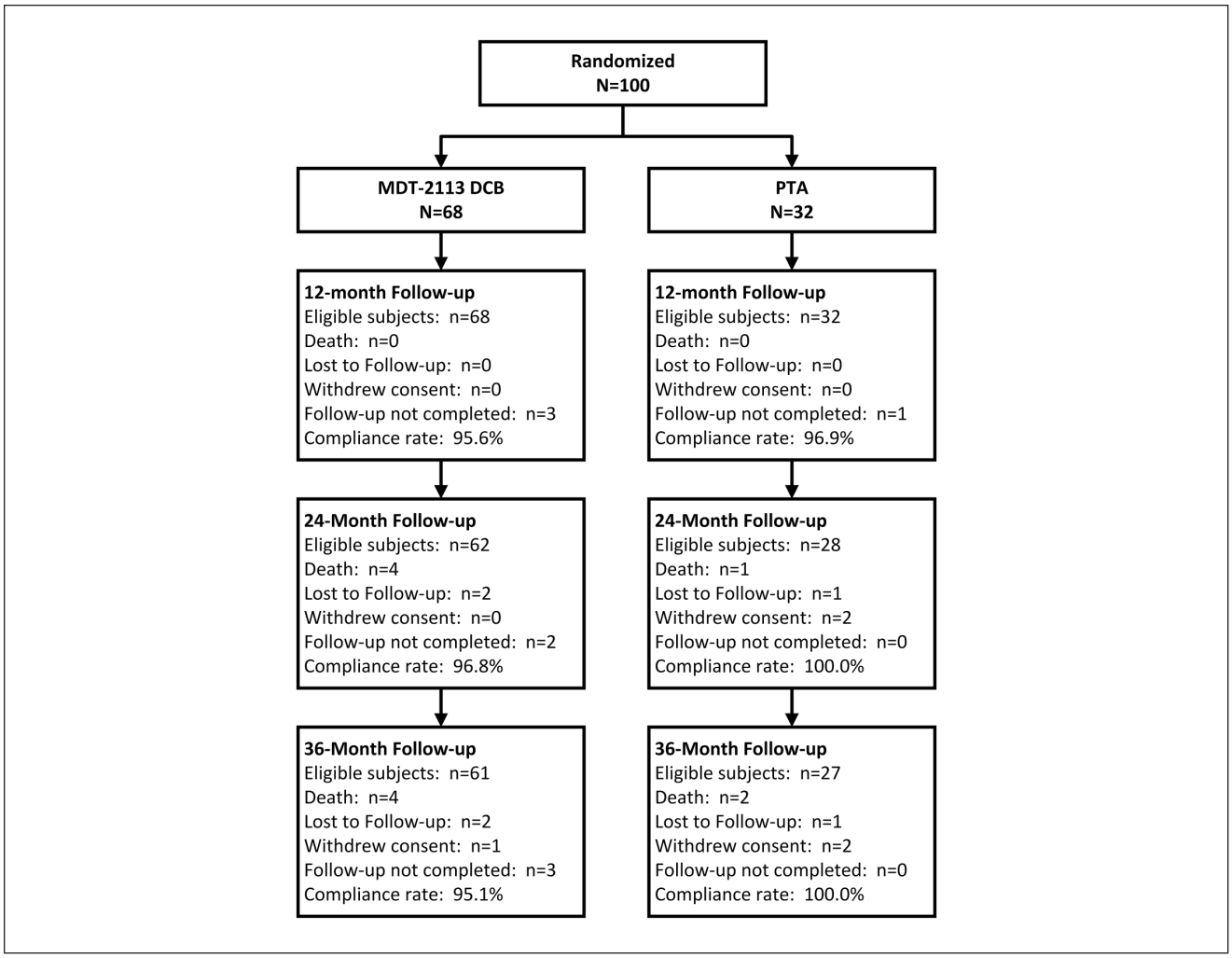

Figure 1. Participant flow in the MDT-2113 SFA Japan trial through 36 months. Values for death, lost to follow-up, and withdrew consent are cumulative; other exits were due to progressive dementia and PTA for other disease. Compliance rates include follow-up completed in and outside of the follow-up window. DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty; SFA, superficial femoral artery.

the administration of the EuroQOL (EQ-5D), a 5-dimension generic health status questionnaire, a 6-minute walk test, and evaluation of walking capacity using the Walking ImpairmentQuestionnaire (WIQ).

Statistical Analysis

The planned enrollment of 100 participants was not powered for any of the endpoints, though the trial design and endpoint assessments were the same as the IN.PACT SFA trial. The IN.PACT (MDT-2113) SFA Japan trial was intended to demonstrate consistent effectiveness and safety outcomes for the Japanese cohort compared with other studied geographies in the IN.PACT SFA trial.

All analyses were based on the intent-to-treat principle. For baseline characteristics and outcomes, continuous variables were described as mean ± standard deviation and were compared using independent *t* tests for between-group differences and paired *t* tests for changes from baseline; dichotomous and categorical variables were summarized as the counts and percentages and were compared using the Fisher exact or Cochran-Mantel-Haenszel test, respectively. The Kaplan-Meier method was used to evaluate time-to-event data for primary patency and freedom from CD-TLR over the 36-month follow-up period; estimates are given with the 95% confidence intervals (CI). Differences in the survival curves between groups were assessed using the log-rank test. There was no correction for multiple comparisons. The level of statistical significance was set at $p<0.05$. Statistical analyses were performed using SAS software (version 9.4; SAS Institute, Cary, NC, USA).

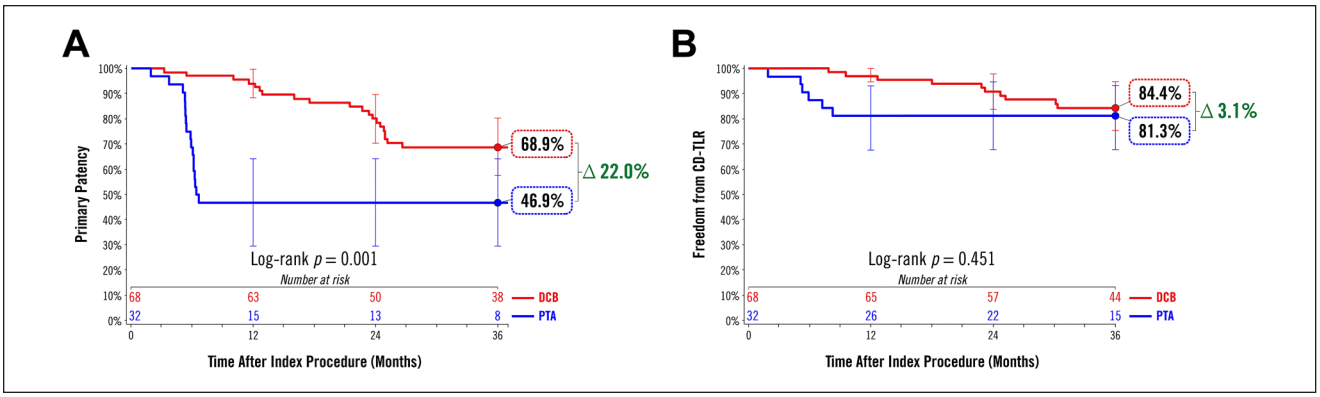

Figure 2. Kaplan-Meier analyses of (A) primary patency and (B) freedom from clinically-driven target lesion revascularization (CD-TLR) through 36 months. Bars represent the 95% confidence intervals. DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty.

Table 2. Procedural Characteristics and Outcomes.[a]

	DCB (68 Participants, 68 Lesions)	PTA (32 Participants, 32 Lesions)	p
Predilation[b]	100 (68/68)	100 (32/32)	>0.999
Postdilation[b]	23.5 (16/68)	18.8 (6/32)	0.796
Provisional stenting[b]	4.4 (3/68)	3.1 (1/32)	0.759
IVUS use during index procedure	39.7 (27/68)	25.0 (8/32)	0.181
Balloons used per participant[b]	1.4±0.5	1.1±0.2	<0.001
Dissection			0.235
None	26.5 (18/68)	28.1 (9/32)	
A-C	73.5 (50/68)	71.9 (23/32)	
D-F	0 (0/68)	0 (0/32)	
Hospitalization, d[b]	2.0±1.0	2.1±1.2	0.778
Lesion length treated, cm[c]	13.4±5.1	13.7±5.6	0.800
Device success[d]	100 (97/97)	97.1 (33/34)	0.260
Procedure success[e]	97.1 (66/68)	100 (32/32)	>0.999
Clinical success[f]	97.1 (66/68)	100 (32/32)	>0.999

Abbreviations: DCB, drug-coated balloon; IVUS, intravascular ultrasound; PTA, percutaneous transluminal angioplasty.
[a]Continuous data are presented as the means ± standard deviation; categorical data are presented as the percent (number/sample).
[b]Site-reported.
[c]Assessed per lesion and reported by the core laboratory.
[d]Device success was defined as successful delivery, inflation, deflation, and retrieval of the intact study balloon without burst below the rated burst pressure; device-based analysis.
[e]Procedure success was defined as residual diameter stenosis ≤50% for nonstented participants and ≤30% for stented participants by core laboratory assessment; lesion-based analysis.
[f]Clinical success was defined as procedure success without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or target vessel revascularization) before discharge; participant-based analysis.

Results

Effectiveness Outcomes

As previously reported, acute procedure success was 97.1% or higher by all measures (Table 2).[25] At 36 months, the Kaplan-Meier estimate of primary patency was 68.9% (95% CI 57.5% to 80.2%) in the DCB group and 46.9% (95% CI 29.6% to 64.2%) in the PTA group (log-rank p=0.001; Figure 2A). The freedom from CD-TLR estimate was 84.4% (95% CI 75.4% to 93.3%) in the DCB group and 81.3% (95% CI 67.7% to 94.8%) in the PTA group (log-rank p=0.451; Figure 2B). Time to first CD-TLR was 20.4±8.1 months in the DCB group and 5.6±2.2 months in the PTA group (p<0.001). Primary sustained clinical improvement through 36 months occurred in 70.0% (42/60) of DCB participants and 70.4% (19/27) of PTA participants (p>0.999).

Safety Outcomes

Safety outcomes are reported in Table 3. The primary safety composite endpoint (freedom from device- and

Table 3. Effectiveness and Safety Outcomes at 36 Months.[a]

Outcome	DCB (68 Participants, 68 Lesions)	PTA (32 Participants, 32 Lesions)	Difference [95% CI]	p
CD-TLR[b]	14.9 (10/67)	20.7 (6/29)	–5.8 [–24.7 to 9.3]	0.554
Time to first CD-TLR, mo (number of participants with CD-TLR within 36 months)	20.4±8.1 (10)	5.6±2.2 (6)	14.8 [8.9 to 20.8]	<0.001
Primary sustained clinical improvement[c]	70.0 (42/60)	70.4 (19/27)	–0.4 [–19.0 to 21.0]	>0.999
ABI/TBI	0.91±0.14 (58)	0.94±0.12 (27)	–0.029 [–0.092 to 0.034]	0.363
Change from baseline[d]	0.15±0.17 (58)	0.20±0.18 (27)	–0.045 [–0.125 to 0.035]	0.263
Safety composite[e]	83.6 (56/67)	75.9 (22/29)	7.7 [–8.3 to 27.0]	0.402
Major adverse events[f]	20.9 (14/67)	31.0 (9/29)	–10.1 [–30.0 to 7.6]	0.306
Death (all-cause)	6.0 (4/67)	6.9 (2/29)	–0.9 [–16.4 to 8.8]	>0.999
CD-TVR	16.4 (11/67)	24.1 (7/29)	–7.7 [–27.0 to 8.3]	0.402
Major target limb amputation	0 (0/67)	0 (0/29)	NA	>0.999
Thrombosis	1.5 (1/67)	0 (0/29)	1.5 [–10.3 to 8.0]	>0.999
Death (device- and procedure-related at 30 days)	0 (0/68)	0 (0/32)	NA	>0.999
Any TLR	14.9 (10/67)	24.1 (7/29)	–9.2 [–28.4 to 6.6]	0.382
Any TVR	16.4 (11/67)	24.1 (7/29)	–7.7 [–27.0 to 8.3]	0.402

Abbreviations: ABI, ankle-brachial index; CD-TLR, clinically-driven target lesion revascularization; CD-TVR, clinically-driven target vessel revascularization; CI, confidence interval; DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty; TBI, toe-brachial index; TLR, target lesion revascularization; TVR, target vessel revascularization.

[a]Continuous data are presented as the means ± standard deviation and categorical data are presented as the proportion (number/sample) unless otherwise indicated. Differences are reported with 95% CI; "36 months" refers to 1080 days.

[b]CD-TLR was defined as any reintervention within the target lesion(s) due to symptoms or drop in ABI/TBI ≥20% or >0.15 compared with postprocedure baseline ABI/TBI.

[c]Primary sustained clinical improvement was defined as freedom from target limb amputation, freedom from TVR, and improvement of at least 1 Rutherford category at 36 months.

[d]Changes from baseline to 36 months were significantly different in both the DCB ($p<0.001$) and PTA ($p<0.001$) groups.

[e]Primary safety composite was defined as freedom from the following after the index procedure: (1) device- and procedure-related death through 30 days, (2) major target limb amputation through 36 months, and (3) CD-TVR through 36 months.

[f]Major adverse events were defined as all-cause mortality, CD-TVR, major target limb amputation, and thrombosis at the target lesion site.

procedure-related death through 30 days as well as major target limb amputation and CD-TVR through 36 months) was 83.6% (56/67) in the DCB group and 75.9% (22/29) in the PTA group (p=0.402). The rate of CD-TVR was 16.4% (11/67) in the DCB group and 24.1% (7/29) in the PTA group. There was 1 death between the 24- and 36-month follow-up periods. One participant in the PTA group died at 29.7 months of an unknown cause that was determined to be unrelated to the study device or procedure after independent adjudication by the CEC. Other deaths in the study that occurred prior to the 24-month time point included 4 deaths in the DCB group due to infection (n=1) and cancer (n=3) and 1 death in the PTA group due to infection.

Functional Outcomes

There were functional improvements in both groups at 36 months. The mean ABI/TBI change from baseline was 0.15±0.17 for the DCB group ($p<0.001$) and 0.20±0.18 for the PTA group ($p<0.001$). No significant difference was observed comparing the change from baseline between groups (p=0.263). Most participants in both groups also showed improvement in the Rutherford category at 36 months (Table 4). An improvement of ≥1 Rutherford category occurred in 86.2% (50/58) of the DCB group and 88.9% (24/27) of the PTA group.

Table 4. Changes in Rutherford Category per Participant at 36 Months.[a,b]

Change	DCB (n=58)	PTA (n=27)
–4	3.4 (2)	0 (0)
–3	17.2 (10)	11.1 (3)
–2	51.7 (30)	70.4 (19)
–1	13.8 (8)	7.4 (2)
0	10.3 (6)	11.1 (3)
+1	3.4 (2)	0 (0)
+2	0 (0)	0 (0)
+3	0 (0)	0 (0)
+4	0 (0)	0 (0)

Abbreviations: DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty.

[a]Categorical data are presented as the percentage (count).

[b]p=0.983 for comparison between groups from baseline to 36 months.

Discussion

The IN.PACT (MDT-2113) SFA Japan trial was the first RCT of a DCB in an Asian population with midterm

Table 5. IN.PACT SFA Japan Outcomes at 12, 24, and 36 Months.[a]

	12 Months[25]			24 Months[30]			36 Months		
Outcome	DCB	PTA	p	DCB	PTA	p	DCB	PTA	p
Primary patency	93.9[b]	46.9[b]	<0.001[c]	79.8[b]	46.9[b]	<0.001[c]	68.9[b]	46.9[b]	0.001[c]
Freedom from CD-TLR	97.1[b]	81.3[b]	0.005[c]	90.8[b]	81.3[b]	0.114[c]	84.4[b]	81.3[b]	0.451[c]
CD-TLR	2.9 (2/68)	18.9 (6/32)	0.012	9.1 (6/66)	20.7 (6/29)	0.177	14.9 (10/67)	20.7 (6/29)	0.554
All-cause death	0 (0/68)	0 (0/32)	>0.999	6.1 (4/66)	3.4 (1/29)	>0.999	6.0 (4/67)[d]	6.9 (2/29)	>0.999
Major target limb amputation	0 (0/68)	0 (0/32)	>0.999	0 (0/66)	0 (0/29)	>0.999	0 (0/67)	0 (0/29)	>0.999
Thrombosis	0 (0/68)	0 (0/32)	>0.999	0 (0/66)	0 (0/29)	>0.999	1.5 (1/67)	0 (0/29)	>0.999

Abbreviations: CD-TLR, clinically-driven target lesion revascularization; DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty.
[a]Data are presented as the percent (number/sample) unless otherwise indicated.
[b]Kaplan-Meier estimate in percent.
[c]Log-rank p.
[d]There were 66 evaluable participants at 2-year follow-up and 67 evaluable participants at 3-year follow-up. There were no deaths in the DCB group between 2 and 3 years.

outcomes. There were no safety concerns through 3 years, including all-cause mortality, major target limb amputation, or thrombosis. The rate of all-cause death was low and similar between treatment groups at 3 years. The rate of thrombosis was also low, and there were no major target limb amputations in either group.

Table 5 summarizes key IN.PACT SFA Japan outcomes between 12 months and the final follow-up at 36 months. Results are consistent with what has been reported from other DCB trials in Asian populations at 12 and 24 months. Efficacy outcomes at 12 months were consistent with IN.PACT SFA China (90.9% primary patency, 2.9% CD-TLR), which is remarkable considering that the prevalence of total occlusions was so much higher in IN.PACT SFA China (52.4%) compared with IN.PACT SFA Japan (16.2%).[14,25] Safety outcomes were also similar between the 2 trials, with consistent rates of all-cause mortality (2.9% IN.PACT SFA China) and thrombosis at 12 months (2.2% IN.PACT SFA China).[14,25] At 24 months, primary patency in IN.PACT SFA Japan was higher than in the AcoArt I trial of Chinese patients (64.6%), though AcoArt I may have enrolled a more challenging patient population.[21,30] The DCB group in AcoArt I had longer lesions (mean length 14.7 cm) and a higher percentage of patients with total occlusions (57.0%) compared with IN.PACT SFA Japan. Other 24-month outcomes were consistent between the studies, including rates of CD-TLR (13.5% AcoArt I) and all-cause mortality (8.3% AcoArt I).[21,30]

To date, the only other DCB studies that have published 36-month results are IN.PACT SFA, IN.PACT Global, REAL-PTX, ILLUMENATE EU, and ILLUMENATE US (Table 6). All-cause mortality in the DCB group from IN.PACT SFA Japan (6.0%) was within range of IN.PACT SFA (10.7%), IN.PACT Global (11.6%), REAL-PTX (10.7%), ILLUMENATE EU (9.4%), and ILLUMENATE US (10.1%).[6,26,27,31] All-cause mortality from the DCB group in IN.PACT SFA Japan was also consistent with studies of other endovascular modalities that have reported outcomes at 36 months, including MAJESTIC (DES, 3.6%), RESILIENT (BMS, 10.0%), DURABILITY II (BMS, 10.1%), and STROLL (BMS, 10.1%).[32–35] The rate of thrombosis after DCB angioplasty in IN.PACT SFA Japan, while low (1.5%), was consistent with what has been reported for DCBs at 36 months (IN.PACT SFA 2.0%, IN.PACT Global 5.6%, not reported in REAL-PTX, ILLUMENATE EU, or ILLUMENATE US).[6,26,27,31]

Efficacy outcomes from IN.PACT SFA Japan were consistent with other DCB studies at 36 months (Table 6). Primary patency was very similar between DCB groups in IN.PACT SFA Japan (68.9%), IN.PACT SFA (69.5%), ILLUMENATE EU (67.5%), and ILLUMENATE US (64.2%).[6,27] Freedom from CD-TLR in the IN.PACT SFA Japan trial (84.4%) was consistent with IN.PACT SFA (84.5%) and higher than IN.PACT Global (76.9%), as well as REAL-PTX (71.3% in the DCB arm and 68.9% in the DES arm).[6,26,31] The potential difference in CD-TLR between these studies may be due to underlying clinical and lesion characteristics of the patient population. The IN.PACT Global Study was a prospective, single-arm trial that was open to patients with complex lesions, including ISR and total occlusions. The inclusion of patients with challenging lesions may have contributed to a higher need for revascularization in IN.PACT Global compared with IN.PACT SFA Japan. Mean lesion lengths in the DCB groups were 9.2 cm in IN.PACT SFA Japan, 12.1 cm in IN.PACT Global, and higher in REAL-PTX (15.0 cm in the DCB arm and 15.6 cm in DES arm). The percentages of patients with total occlusions and ISR were higher in IN.PACT Global (35.5% occlusions, 18.0% ISR) and highest in REAL-PTX (occlusions were 53.3% in the DCB arm

Table 6. 36-Month Outcomes Across Studies of Endovascular Interventions.

Study	Study Device	N	Mean Lesion Length, cm	Primary Patency,[a,b] %	Freedom From CD-TLR,[a] %	CD-TLR, % (n/N)	All-Cause Death, % (n/N)	Major Amputation, % (n/N)	Thrombosis, % (n/N)
IN.PACT SFA Japan									
DCB	IN.PACT Admiral	68	9.2	68.9	84.4	14.9 (10/67)	6.0 (4/67)	0 (0/67)	1.5 (1/67)
PTA	Uncoated balloon	32	8.9	46.9	81.3	20.7 (6/29)	6.9 (2/29)	0 (0/29)	0.0 (0/29)
IN.PACT SFA RCT[6]									
DCB	IN.PACT Admiral	220	8.9	69.5	84.5	15.2 (30/197)	10.7 (21/197)	0 (0/197)	2.0 (4/197)
PTA	Uncoated balloon	111	8.8	45.1	70.4	31.1 (32/103)	1.9 (2/103)	0 (0/103)	4.9 (5/103)
IN.PACT Global Clinical Cohort[26]									
DCB	IN.PACT Admiral	1406	12.1	NR	76.9	22.9 (289/1262)	11.6 (147/1262)	1.0 (12/1262)	5.6 (71/1262)
REAL-PTX[31]									
DCB	IN.PACT Admiral or Pacific, or Lutonix	75	15.0	42.4	71.3	NR	10.7 (8/75)	NR	NR
DES	Zilver-PTX	75	15.6	56.7	68.9	NR	4.0 (3/75)	NR	NR
ILLUMENATE EU[27]									
DCB	Stellarex	222	7.2	67.5	NR	NR	9.4 (18/192)	0 (0/175)	NR
PTA	Uncoated balloon	72	7.1	59.9	NR	NR	8.5 (5/59)	0 (0/54)	NR
ILLUMENATE US[27]									
DCB	Stellarex	200	8.0	64.2	NR	NR	10.1 (18/178)	0 (0/162)	NR
PTA	Uncoated balloon	100	8.9	51.0	NR	NR	11.0 (10/91)	0 (0/81)	NR
MAJESTIC[34]									
DES	Eluvia	57	7.1	NR	85.3[c]	14.8[c]	3.6 (2/56)	0 (0/56)	NR
RESILIENT RCT[33]									
BMS	LifeStent	134	7.0	NR	75.5[c]	NR	10.0[d]	NR	NR
PTA	Uncoated balloon	72	6.4	NR	41.8[c]	NR	8.3[d]	NR	NR
DURABILITY II[35]									
BMS	EverFlex	287	8.9	60.0	70.0	31.1 (80/257)	10.1 (26/257)	0.8 (2/257)	NR
STROLL[32]									
BMS	SMART	250	7.7	72.7	78.5	21.5[a]	10.1[a]	0.8[a]	NR

Abbreviations: BMS, bare metal stent; CD-TLR, clinically-driven target lesion revascularization; DCB, drug-coated balloon; DES, drug-eluting stent; DUS, duplex ultrasonography; n/N, sample/population; NR, not reported; PSVR, peak systolic velocity ratio; PTA, percutaneous transluminal angioplasty; RCT, randomized controlled trial.

[a]Kaplan-Meier estimate.

[b]For IN.PACT SFA Japan, IN.PACT SFA RCT, IN.PACT Global Clinical Cohort, ILLUMENATE EU, and ILLUMENATE US, the endpoint was "primary patency," defined as freedom from CD-TLR and freedom from restenosis (DUS PSVR ≤2.4). For REAL-PTX, patency was defined as absence of CD-TLR (reintervention performed for ≥50% diameter stenosis as confirmed by angiography after documentation of clinical symptoms following the index procedure) or binary restenosis (DUS >2.4). For MAJESTIC, patency was reported only through 2 years. For DURABILITY II, endpoint was "stent patency," defined as PSVR <2.0. For STROLL, the endpoint was "target vessel patency," defined as freedom from CD-TLR and freedom from binary restenosis (eg, PSVR ≥2.5).

[c]Value refers to all TLRs.

[d]Calculated from probability of survival at 36 months.

and 52.0% in DES arm; ISR not reported) compared with IN.PACT SFA Japan (16.2% occlusions, 0% ISR).[25,26,31]

Limitations

The trial enrolled only Japanese participants, which not only limits the generalizability of findings from this specific study but also increases the range of populations that have been included in the IN.PACT clinical program. The number of enrolled participants was lower than other IN.PACT studies, and the trial was not fully powered. While the study evaluated mid-term outcomes through 3 years, other studies (eg, IN.PACT SFA, THUNDER, AcoArt I) have followed participants up to 5 years.[24,28,29]

Conclusion

The IN.PACT SFA Japan trial is the first RCT of a DCB in an Asian population with published midterm outcomes. Results of this final report show that treatment with the IN.PACT Admiral DCB is safe and has durable outcomes through 3 years in a population of Japanese participants with femoropopliteal occlusive disease.

Appendix

The principal investigators and institutions in Japan participating in the IN.PACT SFA Japan study: Shigeru Saito, MD, Shonan Kamakura General Hospital, Kamakura; Masato Nakamura, MD, Toho University Medical Center, Ohashi Hospital, Tokyo; Keisuke Hirano, MD, Yokohama Tobu Hospital, Yokohama; Osamu Iida, MD, Kansai Rosai Hospital, Amagasaki; Kazushi Urasawa, MD, Tokeidai Memorial Hospital, Sapporo; Naoto Inoue, MD, Sendai Kousei Hospital, Sendai; Hiroshi Ando, MD, Kasukabe Chuo General Hospital, Kasukabe; Junko Hone, MD, Kikuna Memorial Hospital, Yokohama; and Takuo Nakagami, MD, Omihachiman Community Medical Center, Omihachiman.

Authors' Note

This study was presented at the Leipzig Interventional Course (LINC) 2019; January 22–25, 2019; Leipzig, Germany.

Acknowledgments

The authors would like to thank the participants for their involvement in this study and recognize the principal investigators and institutions in Japan that enrolled participants in the study. The authors also thank Zachary Harrelson, PhD, for medical writing assistance and Bridget Wall, PhD, and Eric Fernandez, MD, for technical review.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Hong Wang and Hiroko Ookubo are full-time employees of Medtronic. Michael R. Jaff is a compensated advisor for Biotronix, Medtronic, Philips/Spectranetics, Sanofi, and Vactronix and is an equity investor of PQ Bypass.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by Medtronic.

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