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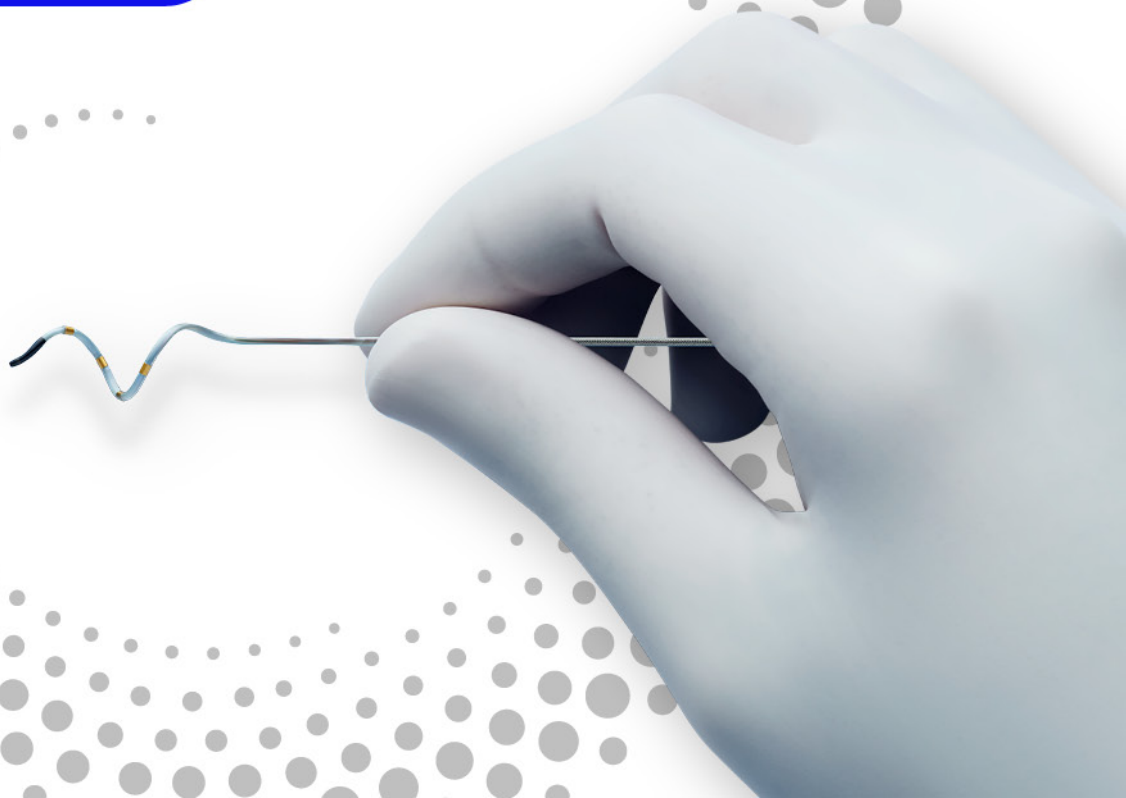

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Long-term outcomes after paclitaxel-coated balloon angioplasty of femoropopliteal arteries in Asian patients of the IN.PACT Global Study

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Abstract

Objectives: The long-term data on the use of drug-coated balloons (DCBs) for femoropopliteal atherosclerotic lesions in the real-world setting are limited, even more so for racially and geographically distinct populations. The present analysis reports the 5-year safety and effectiveness outcomes of a DCB in the Asian subset of the prospective, real-world IN.PACT Global Study.

Methods: The IN.PACT Global Study was a prospective, multicenter, international, single-arm study designed to assess the long-term safety and effectiveness of the IN.PACT Admiral DCB in real-world participants with femoropopliteal artery disease. The present analysis included 114 Asian participants (138 lesions) treated in South Korea and Singapore. Assessments through 5 years included freedom from clinically driven target lesion revascularization, the safety endpoint (a composite of freedom from device- and procedure-related mortality through 30 days; and freedom from major target limb amputation and clinically driven target vessel revascularization within 60 months after the index procedure) and major adverse events.

Results: In this prespecified Asian subset, there was a high incidence of diabetes mellitus (54.4%), hypertension (78.1%), coronary artery disease (43.9%), and concomitant below-the-knee vascular disease of target leg (39.5%). Mean lesion length was 17.4 ± 12.4 cm; 26.8% were in-stent restenosis, and more than half of the lesions were totally occluded (51.4%) and calcified (54.3%). The 5-year Kaplan–Meier estimate of freedom from clinically driven target lesion revascularization was 77.1% (95% confidence interval: 67.0%–84.5%). The safety composite endpoint was 76.0%; the cumulative

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incidence of all-cause mortality was 19.9%, and no major target limb amputations were reported through 5 years.

Conclusions: This subset analysis of Asian participants from the IN.PACT Global Study demonstrated consistent results with the previously reported data of the IN.PACT Admiral DCB. The data confirm the durable clinical effectiveness and safety profile of the DCB through 5 years for femoropopliteal atherosclerotic disease in this real-world population.

KEYWORDS

Asian, clinically driven target lesion revascularization, drug-coated balloons, paclitaxel, peripheral artery disease, real-world

1 | INTRODUCTION

Endovascular strategies have become first-line therapies for revascularization to treat peripheral artery disease (PAD). More specifically, angioplasty with paclitaxel drug-coated balloons (DCBs) has yielded favorable clinical outcomes as compared with uncoated standard percutaneous transluminal angioplasty (PTA) in the treatment of femoropopliteal lesions.[1–4] Asian patients with PAD represent a geographically distinct patient population, however, DCB data on this population are not well represented in the literature. A few reports from randomized controlled trials (RCT) and single-arm studies have shown encouraging results of DCB treatment in Asian patients through 1–3 years[5–9] and recently through 5 years in the AcoArt I study.[10] However, lesions included in RCTs are predominantly short, less complex and exclude broader patient populations that are seen in everyday practice.

The IN.PACT Global Study was a prospective, real-world study evaluating the long-term safety and effectiveness of the IN.PACT Admiral paclitaxel-coated balloon (Medtronic) in the treatment of atherosclerotic disease of the superficial femoral artery (SFA) and/or the entire popliteal artery. Outcomes of the full clinical cohort have been reported through 5 years.[11–14] While these reports are vital for understanding real-world clinical evidence, the patients represented in these studies were primarily from Europe and the United States. The Asian subset of the IN.PACT Global Study represents a geographically and racially distinct patient population that is typically underrepresented in previous analyses. Furthermore, long-term DCB data are limited for this particular subset of the patient population. The present analysis is the first report on the long-term safety and effectiveness of DCB angioplasty through 5 years in an Asian patient population with complex lesions.

2 | METHODS

2.1 | Study design

The IN.PACT Global Study was a prospective, multicenter, international, single-arm clinical study designed to assess the safety and effectiveness of a paclitaxel DCB for the treatment of real-world patients. In the full cohort, 1535 participants were enrolled across 64 sites in Europe, the Middle East, Asia, North Africa, Australia, Canada, and Latin America from 2012 to 2014. Details of the study design and outcomes from the full clinical cohort have been previously reported.[11–14] The present IN.PACT Global subset analysis included 114 participants enrolled at six sites in South Korea and Singapore. The study included participants with intermittent claudication and/or rest pain because of obstructive disease of the femoropopliteal artery with lesions located in the full native SFA and/or full popliteal artery (P1–P3). Participants were followed for a total of 60 months (Figure 1). Participants were followed with hospital visits at 6, 12, 24, and 36 months and telephone follow-ups at 30 days, 48, and 60 months. At all hospital follow-up visits, participants underwent a standard physical examination, including hospital standard of care blood laboratory test, review of medication, blood pressure measurement (ankle-brachial index; ABI), and determination of the Rutherford Category (RC). In addition, participants were asked to complete the Walking Impairment Questionnaire (WIQ) and the EuroQol health status measurement tool in five dimensions (EuroQol-5D) as per the institution's standard of care. All adverse events were recorded and documented at all visits throughout the conduct of the study. At 48 and 60 months, participants had phone follow-up to assess the occurrence of reintervention, adverse events, and health status. To verify safety information, investigational sites were also asked to obtain vital status from study participants who withdrew or were lost to follow-up. These vital status results are labeled as such when that additional data are included.

An independent Clinical Events Committee (CEC; Syntactx) adjudicated all major adverse events (MAEs) including clinically driven target lesion revascularizations (CD-TLRs), and clinically driven target vessel revascularizations (CD-TVRs) through 60 months after the index procedure.

The institutional review board or ethics committee at each study site approved the study protocol. Informed consent was obtained from all participants before enrollment. The study was conducted in accordance with the Declaration of Helsinki, good clinical practice guidelines, and applicable laws as specified by all relevant governmental bodies. The trial was registered on the National Institutes of Health website (*ClinicalTrials. gov* identifier: NCT01609296).

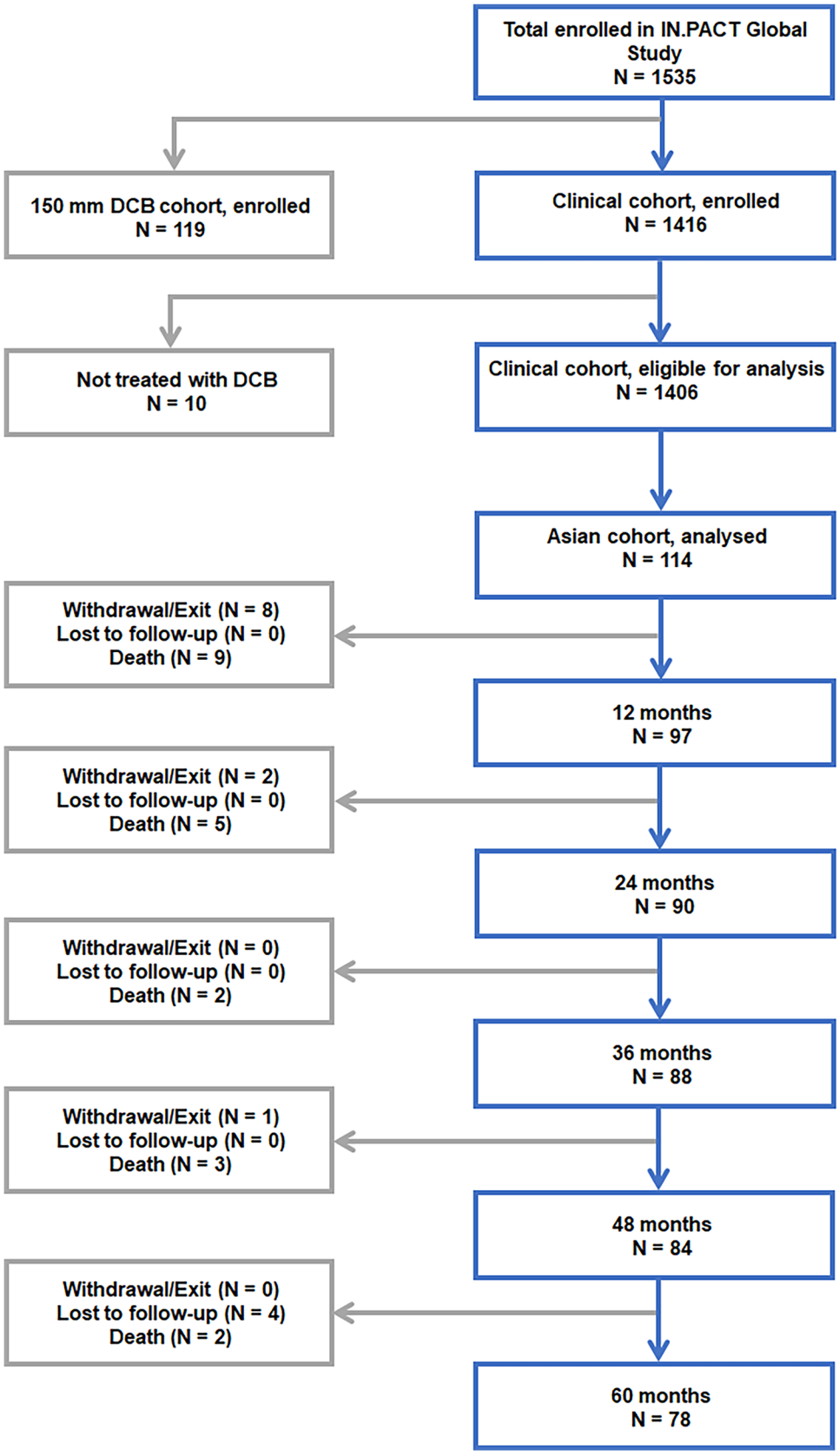

FIGURE 1 Participant flow through 60 months in the IN.PACT Global Study Asian cohort [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Baseline demographic and clinical characteristics in the IN.PACT Global Asian subset participants[a]

	IN.PACT admiral DCB (*N* = 114, participants)
Participant characteristics	
Age, years	67.9 ± 10.7 (114)
Male	86.0% (98/114)
Obesity, BMI ≥ 30 kg/m^2	4.4% (5/114)
Hypertension	78.1% (89/114)
Hyperlipidemia	40.4% (46/114)
Diabetes mellitus	54.4% (62/114)
Insulin-dependent diabetes mellitus	12.3% (14/114)
Carotid artery disease	6.2% (7/113)
Coronary artery disease	43.9% (50/114)
Current smoker	29.8% (34/114)
Renal insufficiency, baseline serum creatinine ≥ 1.5 mg/dl	19.6% (22/112)
On dialysis	8.8% (10/114)
Below-the-knee vascular disease of target leg, stenotic/occluded	39.5% (45/114)
Previous peripheral revascularization	50.0% (57/114)
Previous limb amputation	5.3% (6/114)
Rutherford Category	
0	0.0% (0/114)
1	0.0% (0/114)
2	36.0% (41/114)
3	57.0% (65/114)
4	6.1% (7/114)
5[b]	0.9% (1/114)
6	0.0% (0/114)
ABI, per participant	0.61 ± 0.18 (109)

Note: Continuous data are presented as the mean ± standard deviation (number of participants with data); categorical data are given as the percentage (number/number of participants with data).

Abbreviation: ABI, ankle-brachial index; BMI, body-mass index; DCB, drug-coated balloon.

[a]Summaries are based on non-missing assessments. In some cases, baseline demographic or clinical data were not available, and therefore the total number of participants for that variable is <114.

[b]One participant classified as Rutherford Category 5 was enrolled and included in this analysis due to protocol violation.

2.2 | Treatment device and medical therapy

The IN.PACT Admiral DCB is indicated for de novo, restenotic, or in-stent restenotic lesions up to 360 mm with reference vessel diameters of 4–7 mm in the superficial femoral or popliteal arteries. The coating

TABLE 2 Lesion and procedural characteristics in the IN.PACT Global Asian subset participants[a]

	IN.PACT admiral DCB (*N* = 114 participants) (*N* = 138 lesions)
Preprocedure	
Lesion type	
De novo	73.2% (101/138)
Restenotic, nonstented	0.0% (0/138)
ISR	26.8% (37/138)
Vessel[b]	
SFA	91.3% (126/138)
PA	29.7% (41/138)
SFA + PA	21.0% (29/138)
Calcification	54.3% (75/138)
None	45.7% (63/138)
Mild	31.9% (44/138)
Moderate	8.0% (11/138)
Moderately severe	6.5% (9/138)
Severe[c]	8.0% (11/138)
RVD, mm	5.6 ± 0.9 (138)
Total occlusion	51.4% (71/138)
Diameter stenosis, %	89.6 ± 13.9 (138)
Lesion length, cm	17.4 ± 12.4 (138)
Procedure	
Predilatation	91.2% (104/114)
Postdilatation	43.9% (50/114)
Provisional stent rate per lesion	16.7% (23/138)
Number of provisional stents per lesion	1.5 ± 0.8 (23)
Spot stenting[d]	8.7% (2/23)
Partial lesion coverage[e]	56.5% (13/23)
Whole lesion coverage	34.8% (8/23)
Reason for provisional stenting	
Persistent residual stenosis ≥ 50%	30.4% (7/23)
>10 mmHg trans lesion gradient	0.0% (0/23)
Flow-limiting dissection[f]	78.3% (18/23)
Total provisional stent length per lesion, mm	156.1 ± 124.9 (23)
Stent length/lesion length ratio per lesion	0.6 ± 0.5 (23)
Postprocedure	
Residual stenosis, %	14.8 ± 12.3 (138)

TABLE 2 (Continued)

	IN.PACT admiral DCB (*N* = 114 participants) (*N* = 138 lesions)
Dissection grade[f]	
0, no dissection	38.4% (53/138)
A-C	46.4% (64/138)
D-F	15.2% (21/138)
Device success[g]	99.7% (346/347)
Procedural success[h]	99.3% (137/138)
Clinical success[i]	99.1% (113/114)

Note: Continuous data are presented as the mean ± standard deviation (observations with data); categorical data are given as the percentage (number/observations with data).

Abbreviations: DCB, drug-coated balloon; ISR, in-stent restenosis; PA, popliteal, RVD, reference vessel diameter; SFA, superficial femoral artery.

[a]Summaries are based on nonmissing assessments.

[b]Multiple lesion locations are reported in a single target limb, the total lesion locations could be more than the total number of target limbs.

[c]Severe calcification was defined as calcification with circumference ≥180° (both sides of the vessel at the same location) and a length greater than or equal to half of the total lesion length.[15] The calcium analysis was participant-based.

[d]Spot stenting was defined as the use of the single shortest stent in which minimal length was sufficient to cover the residual stenosis but did not cover the entire original length of the target lesion.

[e]Partial lesion coverage was defined as the use of a stent length longer than the residual stenosis but shorter than the original length of the target lesion.

[f]Dissection classification was based on the National Heart, Lung, and Blood Institute classification.[16] Dissection D-F are considered flow-limiting dissections.

[g]Device success was defined as successful delivery, inflation, deflation, and retrieval of the intact study balloon device without burst below the rated burst pressure. This analysis is device (balloon)-based.

[h]Procedural success was defined as residual stenosis ≤50% for nonstented participants or ≤30% for stented participants by core laboratory assessment (site-reported estimate was used if core laboratory assessment was not available). This analysis is lesion-based.

[i]Clinical success was defined as procedural success without complications (death, major target limb amputation, thrombosis of the target lesion, or target vessel revascularization) before discharge. This analysis is participant-based.

of this DCB includes paclitaxel as the antiproliferative agent at a dose of 3.5 μg/mm^2, with urea as the excipient. At the time when this study was conducted, available IN.PACT Admiral DCB sizes included 4.0-7.0 mm diameters and 40-, 60-, 80-, 120-, and 150-mm lengths. A minimum balloon inflation time of 180 s was required for the DCB. To avoid geographic miss, DCB length was chosen to exceed the target lesion length by 10 mm at the proximal and distal edges.

Dual antiplatelet therapy (DAPT) was required consistent with standard clinical practice, including aspirin (ASA) indefinitely and DAPT for 1 month (3 months for stented participants).

2.3 | Endpoints and assessments

Assessments through 60 months included freedom from CD-TLR, the safety endpoint (a composite of freedom from device- and procedure-related mortality through 30 days; and freedom from major target limb amputation and CD-TVR within 60 months after the index procedure), and the incidence of MAEs (all-cause mortality, CD-TVR, major target limb amputation, and thrombosis at the target lesion site). CD-TLR was defined as any reintervention within the target lesion(s) because of symptoms or drop of ABI of ≥20% or >0.15 when compared with post-index procedure baseline ABI. CD-TVR was defined as any reintervention within the target vessel due to symptoms or drop of ABI ≥ 20% or >0.15 when compared with the postprocedure baseline ABI. All repeat interventions on the target limbs including TLR, TVR, and the clinically driven status were reviewed and adjudicated by the independent CEC.

Other assessments included device success, procedural success, clinical success, and functional outcomes through 36 months including changes in RC, walking capacity using the WIQ and quality of life using the EuroQol-5D index. Device success was defined as successful delivery, inflation, deflation, and retrieval of the intact study balloon device without burst below the rated burst pressure. Procedural success was defined as residual stenosis ≤50% for nonstented participants or ≤30% for stented participants by core laboratory assessment (site-reported estimate was used if core laboratory assessment was not available). Clinical success was defined as procedural success without complications (death, major target limb amputation, thrombosis of the target lesion, or target vessel revascularization) before discharge. The device success analysis was device (balloon)-based, the procedural success analysis was lesion-based and the clinical success analysis was participant-based.

2.4 | Statistical analysis

Baseline demographics, clinical characteristics, and outcomes are reported or analyzed on a participant basis, lesion characteristics are reported on a lesion basis, and device characteristics are reported on a device basis. Data are summarized descriptively using percentages and frequencies for categorical variables and the mean, standard deviation (SD), and the number of observations for continuous variables. Time-to-event outcomes are summarized using survival curves and survival probabilities using the Kaplan–Meier method and the restricted mean survival time with a time horizon of 1800 days. The confidence intervals (CIs) for Kaplan–Meier estimates were derived for time-to-event outcomes using the log–log transformation. Annual cutoffs for the statistical analysis used 360 days per year (e.g., 1800 days for the 5-year cut-off). The denominator for binary endpoints used the sum of those with an event and those with follow-up of at least 1740 days for 60-month endpoints. Statistical analyses were performed using SAS version 9.4 (SAS Institute).

3 | RESULTS

3.1 | Participant population and baseline characteristics

The participants were followed through 60 months as shown in Figure 1. A total of 15 participants were lost to follow-up or withdrew, or exited for other reasons, and 21 died within the 60-month follow-up window. Of the remaining 78 participants available for the 60-month evaluations, 74 (94.9%) completed the 60-month follow-up call within the window.

Baseline demographics and lesion characteristics of the IN.PACT Global Asian cohort are reported in Tables 1 and 2. A summary of procedural below-the-knee run off vessel status is reported in Supporting Information: Table 1. The mean age of participants was 67.9 ± 10.7 years and 86.0% were male. A substantial percentage of participants had diabetes mellitus (54.4%), hypertension (78.1%), coronary artery disease (43.9%), concomitant below-the-knee vascular disease of target leg (39.5%), and lesions affecting both SFA and popliteal (21.0%). Mean lesion length was 17.4 ± 12.4 cm. Among lesions, 26.8% were in-stent restenosis (ISR), 51.4% were total occlusions, and 54.3% were calcified.

Provisional stents were implanted in 16.7% of lesions in this Asian cohort (Table 2). The reasons for provisional stenting were persistent residual stenosis ≥50% (30.4%) and flow-limiting dissection (78.3%). Device success was achieved with 99.7% of devices used (Table 2). Procedural success was achieved in 99.3% of lesions and clinical success was achieved in 99.1% of participants.

3.2 | Medication compliance

Medication compliance data through 36 months are provided in Supporting Information: Table 2.

3.3 | Effectiveness and safety outcomes

The Kaplan–Meier freedom from CD-TLR was 77.1% (95% CI: 67.0% to 84.5%) through 60 months (Figure 2). The restricted mean survival time to the first occurrence of CD-TLR was 1551.8 ± 49.8 days with a time horizon of 60 months (Table 3). The causes of CD-TLR and CD-TVR are reported in Supporting Information: Table 3. The 5-year estimate of the safety endpoint, a composite of freedom from device- and procedure-related mortality through 30 days and freedom from major target limb amputation and CD-TVR within 60 months after the index procedure was 76.0% (Table 3). There were no device- or procedure-related deaths through 30 days. The 5-year cumulative incidence rates of MAE and all-cause death were 38.1% and 19.9%, respectively (Table 3). After the vital status update, 94.7% (108/114) of the participants had vital status information and the freedom from all-cause mortality including this information by Kaplan–Meier estimate was 79.4% (95% CI: 70.6% to 85.8%) through 5 years (Figure 3). None of the participants had major amputation of the target limb and only one participant had an occurrence of thrombosis throughout the 5 years follow-up (Table 3). Key outcomes of the Asian cohort and the full clinical cohort of the IN.PACT Global Study are shown side by side in Table 4.

3.4 | Functional outcomes

Data on functional outcomes were available through 36 months. At baseline, there were no participants in the RC 0 or RC 1 categories. At 36 months, more than half of the participants were asymptomatic (RC 0, Figure 4A). Changes in the RC between baseline and 36 months were statistically significant ($p < 0.001$) and the majority of participants (81.1%, 60/74) had improvements of ≥1 RC (Figure 4B). The mean change from baseline in the EuroQol-5D index score at 36 months was 0.187 ± 0.396 ($n = 30$, $p = 0.015$). The overall walking

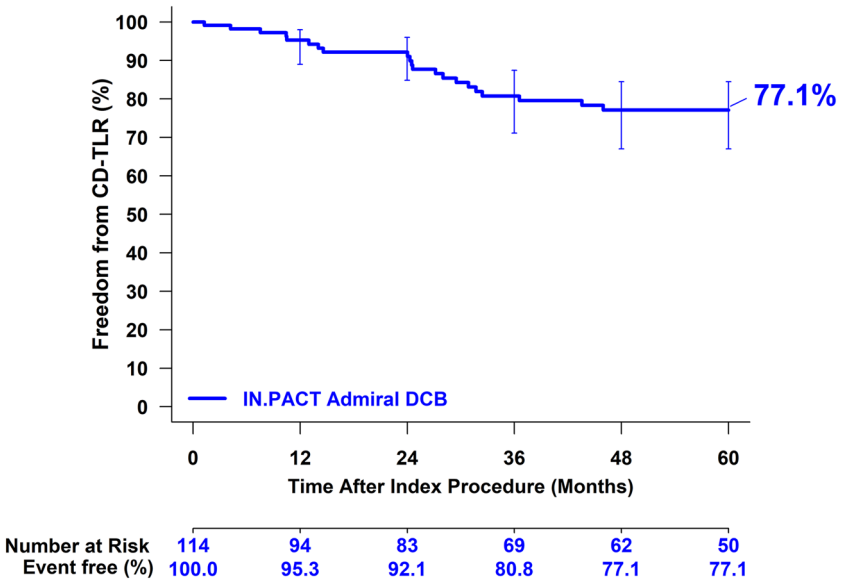

FIGURE 2 Kaplan–Meier estimate of freedom from CD-TLR through 60 months in the IN.PACT Global Study Asian subset. Bars represent the 95% confidence intervals. CD-TLR, clinically driven target lesion revascularization; DCB, drug-coated balloon. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 3 Safety outcomes through 60 months in the IN.PACT Global Asian subset participants

Parameters	IN.PACT DCB (*N* = 114 participants)
Safety parameters[a]	
Safety composite endpoint—Freedom from:	76.0%
Device- and procedure-related death through 30 Days	0.0% (0)
Target limb major amputation within 60 months	0.0% (0)
CD-TVR[b] within 60 months	24.0% (22)
Cumulative complications within 60 months[a]	
MAE composite (death, major target limb amputation, CD-TVR[b], thrombosis)	38.1% (40)
All-cause death	19.9% (21)
CD-TVR[b]	24.0% (22)
Major target limb amputation	0.0% (0)
Thrombosis	0.9% (1)
CD-TLR[c]	22.9% (21)
Any TVR	24.0% (22)
Any TLR	22.9% (21)
Other major secondary endpoints	
Restricted mean survival time to first CD-TLR (days) through 60 months	1551.8 ± 49.8 (21)

Note: Cumulative incidence are given as the percentage (number of participants with events); restricted mean survival time is presented as the mean ± standard error (number of participants with events). All target lesion revascularizations and adverse events were adjudicated by the independent Clinical Events Committee.

Abbreviations: ABI, ankle-brachial index; CD, clinically driven; DCB, drug-coated balloon; TLR, target lesion revascularization; TVR, target vessel revascularization.

[a]Percentages are cumulative incidence or event-free survival based on Kaplan–Meier estimate (number of participants with events).

[b]CD-TVR is defined as any reintervention at the target vessel due to symptoms or drop of ABI ≥ 20% or >0.15 when compared with post-index procedure baseline ABI.

[c]CD-TLR is defined as any reintervention within the target lesion due to symptoms or drop in ABI ≥ 20% or >0.15 when compared with post-index procedure baseline ABI.

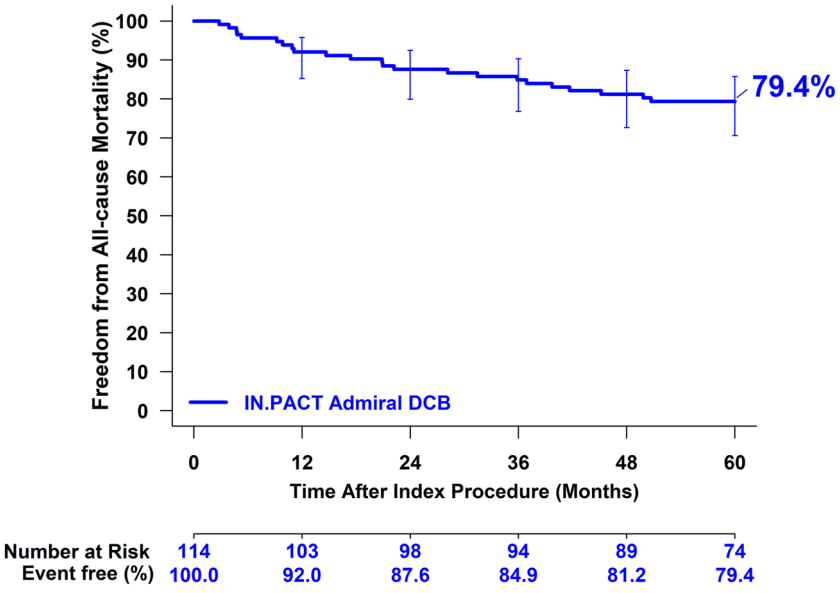

FIGURE 3 Kaplan–Meier estimate of freedom from all-cause mortality through 60 months with the vital status update in the IN.PACT Global Study Asian subset. Bars represent the 95% confidence intervals. DCB, drug-coated balloon. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 4 Summary of key baseline characteristics and 5-year outcomes in the IN.PACT global study Asian cohort subset and full clinical cohort

	Asian cohort (*N* = 114, participants) (*N* = 138 lesions)	Clinical cohort (*N* = 1406 participants) (*N* = 1774 lesions)[14]
Key baseline characteristics		
Age, years	67.9 ± 10.7 (114)	68.6 ± 10.1 (1396)
Obesity, BMI ≥ 30 kg/m^2	4.4% (5/114)	20.5% (285/1391)
Diabetes mellitus	54.4% (62/114)	39.9% (560/1402)
Hyperlipidemia	40.4% (46/114)	70.5% (960/1362)
Lesion length, cm	17.4 ± 12.4 (138)	12.1 ± 9.5 (1774)
In-stent restenosis	26.8% (37/138)	18.0% (320/1774)
RVD, mm	5.6 ± 0.9 (138)	5.2 ± 0.7 (1774)
Total occlusion	51.4% (71/138)	35.5% (630/1774)
Calcification	54.3% (75/138)	68.7% (1217/1772)
Severe	8.0% (11/138)	10.2% (181/1772)
Vessel		
SFA	91.3% (126/138)	87.6 (1554/1774)
PA	29.7% (41/138)	27.3 (484/1774)
Procedural outcomes		
Predilatation	91.2% (104/114)	78.0% (1097/1406)
Postdilatation	43.9% (50/114)	35.1% (491/1397)
Provisional stent rate per lesion	16.7% (23/138)	21.2% (373/1762)
60-month outcomes[a]		
Freedom from CD-TLR[b]	77.1% (21)	69.4% (366)
Major target limb amputation	0.0% (0)	1.7% (19)
Thrombosis	0.9% (1)	5.7% (73)
Freedom from all-cause death with vital status update	79.4% (23)	78.9% (289)

Note: Continuous data are presented as the mean ± standard deviation (observations with data); categorical data are given as the percentage (number/observations with data). All target lesion revascularizations and adverse events were adjudicated by the independent Clinical Events Committee.

Abbreviations: ABI, ankle-brachial index; BMI, body-mass index; CD, clinically driven; PA, popliteal artery; RVD, reference vessel diameter; SFA, superficial femoral artery; TLR, target lesion revascularization.

[a]Kaplan-Meier based estimates are provided as survival percentage using freedom from event rates (number of participants with events) or cumulative incidence percentage (number of participants with events).

[b]CD-TLR is defined as any reintervention within the target lesion due to symptoms or drop in ABI ≥ 20% or >0.15 when compared to post-index procedure baseline ABI.

impairment score was 61.2 ± 32.4% (*n* = 29) at 36 months compared with 36.8 ± 25.1% (*n* = 112) at baseline.

4 | DISCUSSION

Randomized trials have shown added clinical benefit of DCB compared with PTA in Asian patients through midterm follow-up.[5–8] While these findings are important, the long-term safety and effectiveness of this device for the treatment of Asian patients with complex lesions seen in real-world settings are not well understood. Results of the present analysis demonstrated sustained clinical effectiveness of DCB angioplasty with a freedom from CD-TLR rate of 77.1% and a restricted mean survival time of over 4 years to the first reintervention (1551.8 days). The majority of the patients remained asymptomatic with a significant improvement in RC. There were no safety concerns as demonstrated by low mortality rates, no major amputations, and only one thrombosis through 5 years.

There are only a handful of published long-term reports for endovascular therapies in the femoropopliteal vessel bed. At the time of writing this article, 5-year outcomes were reported by only one real-world DCB study (IN.PACT Global Study, clinical cohort),[14]

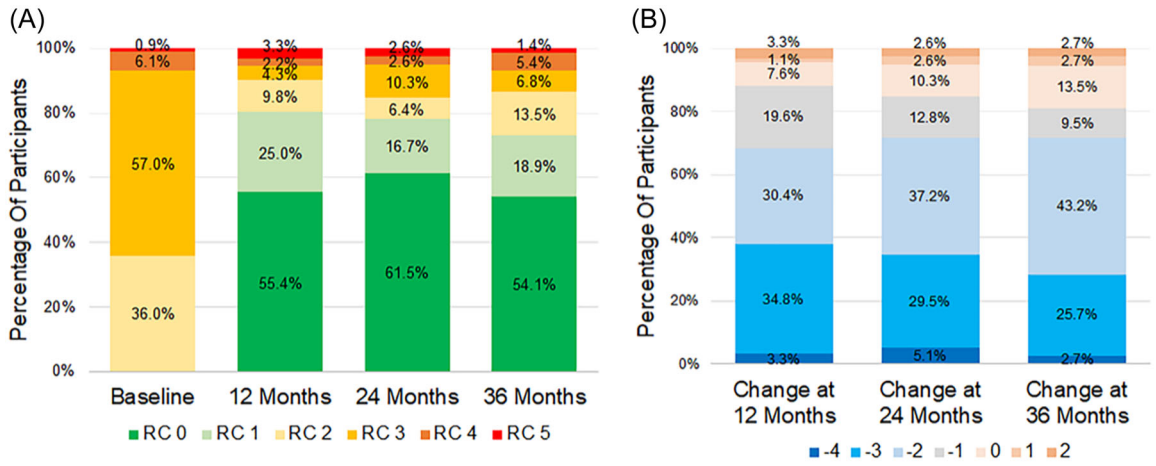

FIGURE 4 (A) Rutherford Category (RC) status at baseline and follow-up intervals. (B) Changes in RC at the follow-up intervals compared with baseline to illustrate the percentage of participants showing improvement ($p < 0.001$ for change in RC at all time points). [Color figure can be viewed at wileyonlinelibrary.com]

one postmarket surveillance subset analysis (the Zilver PTX Japan Post-Market Surveillance Study),[17] and five RCTs (THUNDER, Zilver PTX, IN.PACT SFA RCT, AcoArt I, and EffPac).[10,18–21] The results of the present Asian cohort study were compared with that of the full clinical cohort (IN.PACT Global Study) for literature benchmarking purposes. Because the inclusion/exclusion criteria were the same in these two cohorts, participant characteristics were generally similar. However, some differences were observed; the Asian cohort had lower rates of obesity and hyperlipidemia, but a higher burden of diabetes mellitus, longer lesions, and higher percentages of ISR and total occlusion as compared with the full clinical cohort. In addition, despite the longer mean lesion length (17.4 cm) in the Asian cohort compared with the full clinical cohort (12.1 cm), the provisional stenting rate was lower (16.7% Asian cohort vs. 21.2% clinical cohort).[12] This provisional stenting rate of 16.7% was also lower than in other global studies; 25.2% in the Lutonix Global SFA Registry (mean lesion length 10.1 cm).[22] and 17.3% in the ILLUMENATE Global Study (mean lesion length 7.5 cm).[23] Despite a high proportion of diabetes and more complex lesions, the 5-year freedom from CD-TLR rate of 77.1% in the Asian cohort was favorable compared with the full clinical cohort (69.4%).[14] The freedom from CD-TLR rate in this study was also comparable to the Zilver PTX Japan Post-Market Surveillance Study (77.1% IN.PACT Global Asian Cohort vs. 73.4% Zilver PTX Japan Post-Market) with equivalent lesion lengths between these two studies (17.4 cm IN.PACT Global Asian Cohort vs. 17.8 cm Zilver PTX Japan Post-Market).[17] This 5-year freedom from CD-TLR rate of 77.1% was also comparable to DCB outcomes in RCTs: 79.0% in the THUNDER trial (mean lesion length 7.4 cm),[18] 74.5% in the IN.PACT SFA RCT (mean lesion length 8.9 cm),[20] 77.5% in the AcoArt I (mean lesion length 14.7 cm), [10] and 82.1% in the EffPac trial (mean lesion length 5.9 cm).[21] In the Zilver PTX randomized trial, the 5-year freedom from TLR was 83.1% for the Zilver PTX DES arm (mean lesion length 6.6 cm)[19] and carried the risk of ISR.

A summary-level meta-analysis reported an association between the use of paclitaxel devices and late mortality in PAD patients who had undergone femoropopliteal interventions.[24] In this Asian cohort study, all MAEs were adjudicated by an independent CEC throughout the 5-year follow-up period. No safety concerns were found in this study; there were no major target limb amputations and only one thrombosis through 5 years in this complex PAD population demonstrating a sustained safety profile of this DCB. The freedom from all-cause mortality rate was 79.4% including data from the vital status update through 5 years in this cohort. This rate was in line with other contemporary DCB studies: 80.8% in the DCB arm of the LEVENT 2 RCT,[25] 80.4% in the DCB arm of the meta-analysis of ILLUMENATE Pivotal and ILLUMENATE European RCTs,[26] 82.7% in the DCB arm of the AcoArt I RCT[10] and 78.9% in the full clinical cohort of IN.PACT Global Study.[14] The 19.9% cumulative incidence of 5-year all-cause mortality in the present study was similar or favorable to that of the 5-year mortality in the Zilver PTX Japan Post-Market Surveillance study (25.1%) or the Zilver PTX RCT for the Zilver PTX DES arm (19.1%), described as a low paclitaxel dose compared with DCBs.[17,27] The all-cause mortality rate of 19.9% in the present Asian cohort is also consistent with that of published epidemiologic studies that reported 5-year mortality rates of 10%–52% in PAD patients depending on the age and comorbidities.[28,29]

The study has several strengths including prespecified, prospective enrollment and analysis, a challenging lesion/patient population applicable to daily practice, independent adjudication throughout the study, long-term patient-level data, and a distinct patient subset underrepresented in previous reports. Yet, there were some limitations to this study; the study had no control arm, hence the results cannot support a direct comparison with other endovascular interventions and data available in the literature were used as reference comparisons. The study was also nonblinded as this is a single-arm study. Imaging data were not available for all patients

hence no anatomic outcomes were analyzed in this cohort. The participant population included in this analysis was from South Korea and Singapore and may not represent other Asian populations.

5 | CONCLUSIONS

This subset analysis of Asian participants in the IN.PACT Global Study, a prospective, multicenter, single-arm study, demonstrated consistent results with the previously reported data of the IN.PACT Admiral DCB. Given that improving the functional status and the quality of life of patients are primary goals of revascularization in claudicants and patients with rest pain, these results confirm a sustained, durable clinical efficacy of DCB angioplasty in this real-world Asian population.

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CONFLICT OF INTEREST

Jeremiah Menk, MS, is a full-time employee of Medtronic. The remaining authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request. The study sponsor (Medtronic) will evaluate on a study-by-study basis whether there is an opportunity to share clinical trial data with qualified scientific or medical researchers, consistent with the associated informed consent and applicable laws and regulations.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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