



# Clinical and Regulatory Review of ZENFLUXION™ Drug-coated PTA Balloon Catheter “SFA Clinical Study Using the ZENFLUXION™ Drug-coated PTA Balloon Catheter in a Chinese Patient Population”

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## Abstract

**Purpose:** To confirm the safety and effectiveness of the ZENFLUXION™ Drug-coated PTA Balloon Catheter manufactured by Zhejiang Zylox Medical Device Co., Ltd. as a treatment for de novo and native artery restenotic lesions in the superficial femoral artery (SFA) and/or proximal popliteal artery in Chinese subjects.

**Materials and Methods:** ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA China (ClinicalTrials.gov identifier NCT02118532) was a single- arm, independently adjudicated, prospective, premarket study that enrolled 143 subjects (mean age 66.8±7.7 years; 107 men) at 15 centers. The predominant risk factors were hypertension (104, 72.7%) and diabetes mellitus (66, 46.2%). The majority of subjects were classified as Rutherford category 2 or 3 [69 (48.3%) and 55 (38.5%), respectively]; 19 (13.3%) subjects had critical limb ischemia (Rutherford category 4). The mean lesion length was 10.4±6.51 cm; more than half of the lesions (75, 52.4%) were chronic total occlusions. Calcification was found in 66 (46.2%) lesions. Outcomes at 12 months were compared with DCB safety and effectiveness performance goals derived from the literature.

The 30-day primary safety outcome was a composite of freedom from device- and procedure-related mortality, major target limb amputation, and clinically-driven target lesion revascularization (CD-TLR).

**Results:** The primary safety outcome was 99.3% at 30 days. Follow-up compliance at 12 months was 92.6%. Estimated 1-year primary patency using Kaplan-Meier analysis was 90.9% and freedom from CD-TLR was 97.1%. The rate of CDTLR at 12 months was 2.9%. The Rutherford category status improved significantly ( $p<0.001$ ) between baseline and 12 months. In addition, a comparison clinical study was applied in order to evaluate and review the compliance of data collected with European medical device directive MDD 93/42/EEC, Medical device Regulation MDR 2017/745 and BS EN ISO 14155:2020; the evaluation shall take into consideration the state of the art for ZENFLUXION™ Drug-coated PTA Balloon Catheter manufactured by Zhejiang Zylox Medical Device Co., Ltd .

### Conclusion:

Results from ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA China demonstrated high rates of patency and low rates of CD-TLR in Chinese subjects through 12 months despite patient and lesion complexity. These data are consistent with the results of ZENFLUXION™ Drug-coated PTA Balloon Catheter trials. Based on the assessment applied; it has been noted that the statistical significant has been considered during this clinical trial; selection of patient was optimum, the assessment was applied for the clinical study where adequate clinical performance, outcomes, clinical safety and clinical benefits were addressed correctly according to MDD 93/42/EEC, Medical device Regulation MDR 2017/745 and BS EN ISO 14155:2020 for ZENFLUXION™ Drug coated PTA Balloon Catheter manufactured by Zhejiang Zylox Medical Device Co., Ltd .

**Keywords:** ZENFLUXION™, PTA Balloon Catheter, Chinese subjects.

## Introduction

In 2010, an estimated 202 million people were living with peripheral artery disease (PAD) worldwide.<sup>1</sup> However, limited data are available on the prevalence of PAD in China, with published reports suggesting rates ranging from 2.5% to 20%, varying between urban and rural areas.<sup>2-5</sup>

Over the decades, the original endovascular treatment for symptomatic lower limb PAD, percutaneous transluminal angioplasty (PTA), was supplanted by bare metal and drug-eluting stents (DES). However, their efficacy has been limited in complex lesions, whether they are long, heavily calcified, or occurring in areas already treated by a stent. In addition, the long-term consequences of a permanent metal-lic implant and stent fracture remain unknown.<sup>6,7</sup>

Drug-coated balloons (DCBs) were developed to overcome the challenges of PTA and stenting, particularly in the superficial femoral (SFA) and popliteal arteries. Randomized controlled trials (RCTs) have shown DCBs to be both safe and effective for the treatment of lesions in the femoropopliteal segment.<sup>8-14</sup> These trials, however, have been composed almost entirely of Caucasian subjects. While several DCB trials are ongoing in Asian populations [LTX DCB China (NCT02720003), Ranger China (NCT029440710), Biolux P4 China (NCT02912715), and Ranger Japan (NCT03064126)], there is still a paucity of published clinical results in Asian populations. Only the AcoArt I study<sup>15,16</sup> and the MDT-2113

(IN.PACT) SFA Japan trial<sup>17,18</sup> have been published through late 2018. The 12-month results of the ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA China study are now presented.

## Materials and Methods

### Study Design

The ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA Clinical Study for the Treatment of Atherosclerotic Lesions in the SFA and/or Proximal Popliteal Artery using the ZENFLUXION™ Drug-coated PTA Balloon Catheter in a Chinese Patient Population was an independently adjudicated, prospective, multicenter, single-arm, premarket study designed to confirm the safety and effectiveness of the ZENFLUXION™ Drug-coated PTA Balloon Catheter in Chinese subjects. The 15 participating sites and principal investigators are listed in Supplemental Table 1 (available in the online version of the article). After completion of the clinical trial, the product name was updated to ZENFLUXION™ Drug-coated PTA Balloon Catheter, though it will be referred to as the ZENFLUXION™ Drug-coated PTA Balloon Catheter in this report. The ZENFLUXION™ Drug-coated PTA Balloon Catheter is coated with the antiproliferative agent paclitaxel (3.5 µg/mm<sup>2</sup>) in a urea excipient.

As an open label study, blinding procedures were not applicable. An independent clinical events committee adjudicated major adverse events. Duplex ultrasonography studies were reviewed by

an independent vascular ultrasound core laboratory (VasCore, Massachusetts General Hospital, Boston, MA, USA), while angiograms were evaluated by the Beth Israel Deaconess Imaging Laboratory (Beth Israel Deaconess Medical Center, Boston, MA, USA). This study was conducted in compliance with the 2008 version of the Declaration of Helsinki, the international standard ISO 14155:2011 ("Clinical Investigation of medical devices for human subjects"), and applicable China laws and regulations. Prior to enrolling subjects in this study, the ethics committee or institutional review board at each site approved the study protocol. This study is registered on the National Institutes of Health website (*ClinicalTrials.gov*; identifier NCT02118532).

Subjects were excluded from the trial if they had a stroke or myocardial infarction within 3 months prior to the index procedure; known allergies or hypersensitivities to components of the procedure (heparin, aspirin, contrast media, paclitaxel); or surgeries that took place within 30 days prior to or scheduled after the procedure. Angiographic exclusion criteria included aneurysm, thrombus, severe calcium, instant restenosis, failure to cross the target lesion, a grade D or higher flow-limiting dissection, or residual stenosis >70% after predilation. A full list of inclusion and exclusion criteria is available on the *ClinicalTrials.gov* website.

### ***Treatment, Medical Therapy, and Follow-up***

In this trial, there was no mandatory medication prescribed, although dual antiplatelet therapy was recommended. In general, a minimum of 75 mg of clopidogrel was given daily for at least 3 days prior to the index procedure; if this was not feasible, a 300-mg bolus of clopidogrel was administered within 24 hours prior to the procedure (or a 500-mg ticlopidine bolus if allergic to clopidogrel). Prior to the procedure, a 500-mg loading dose of aspirin was given if not already on a 75 mg/d regimen. As appropriate, heparin was administered during the procedure to maintain an activated clotting time 250 seconds. Additional information is provided in

Supplemental Table 2 (available in the online version of the article).

Lesions were predilated with a standard uncoated PTA balloon sized 1 mm smaller than the reference vessel diameter (RVD). After successful predilation, an ZENFLUXION™ Drug-coated PTA Balloon Catheter sized to match the RVD and slightly longer than the lesion length was delivered to the target site. The DCB was inflated across the lesion at or beyond nominal pressure for at least 3 minutes. More than one DCB could be used in the study to treat a given lesion. If there was a residual stenosis >50%, a translesion gradient >10 mmHg, and/or a flow limiting dissection (grade D or higher) then postdilation was performed with a PTA balloon shorter than the full lesion length. If postdilation was unsuccessful even with a long inflation time of 3 minutes, provisional stenting was allowed, but not with a DES.

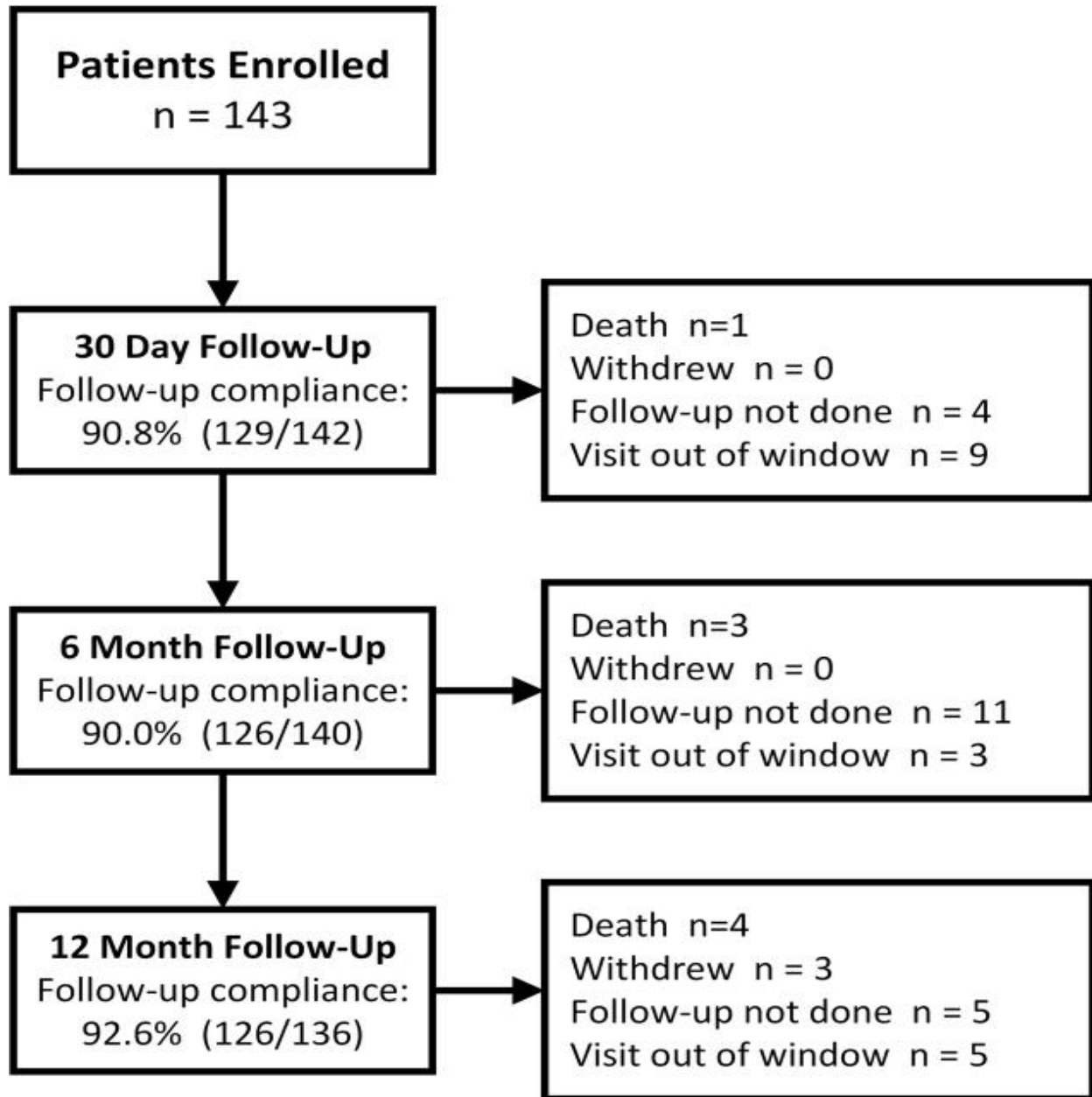
Subjects were followed by their treating physician at 30 days, 6 months, and 12 months. These office visits included duplex ultrasound and assessment of adverse events. Functional testing included the Walking Impairment Questionnaire (WIQ), 6-minute walk test (6MWT), and EuroQol-5 dimensional quality of life test (EQ-5D). If a reintervention was required, PTA and provisional stenting were used.

### ***Qualitative and Quantitative Angiography***

Procedure angiograms were independently reviewed by observers blinded to the clinical outcomes. Lesion length was defined as the shoulder-to-shoulder lumen narrowing that was to be treated. RVD and percent diameter stenosis were determined using quantitative angiographic methods (CMS Medis, Leiden, the Netherlands). Dissections were graded using the National Heart, Lung and Blood Institute grading system.<sup>19</sup>

### ***Enrolled Subjects***

Between March 2014 and August 2015, 143 subjects (mean age 66.8±7.7 years; 107 men) were enrolled at 15 centers in China. Patient flow through 12-month follow-up is shown in Figure 1.



**Figure 1.** Enrollment in the ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA China study, showing deaths, subjects lost to follow-up, visits not completed, and withdrawals through 12 months.

Patient characteristics are listed in Table 1. Diabetes mellitus was highly prevalent (66, 46.2%), a third of the subjects were smokers (52, 36.4%). The majority of subjects were categorized as Rutherford category 2 and 3 [69 (48.3%) and 55 (38.5%), respectively]; 19 (13.3%) subjects had critical limb ischemia (CLI;

Rutherford category 4). Mean lesion length was  $10.4 \pm 6.51$  cm, and 17 (11.9%) lesions were severely calcified as determined by the angiographic core laboratory. All lesions except one were de novo. More than half the lesions were occlusions (75, 52.4%), and the mean diameter stenosis was 89.0%.

### **Study Outcomes**

The primary effectiveness outcome was primary patency within 12 months of the index procedure, defined as freedom from clinically-driven target lesion revascularization (CD-TLR) and freedom from restenosis determined by a duplex ultrasound peak systolic velocity ratio  $\geq 2.4$ . This endpoint was evaluated against a performance goal of 50%<sup>20</sup> in all subjects who did not receive a stent [intent-to-treat (ITT) population]. This number was generated when the ZENFLUXION<sup>TM</sup> Drug-coated PTA Balloon Catheter China study was designed in 2013. Eleven clinical trials<sup>21–31</sup> examining DCB, DES, bare metal stents, and PTA were assessed, and the treatment differences between the non-DES devices with and without provisional stenting were evaluated. To assess the 12-month primary patency performance in DCB and PTA separately, the published data were combined, both unweighted and as a weighted average of the individually calculated 12-month rates of primary patency, TLR, and binary restenosis. The unweighted rate calculated the proportion of the number of patients with the event over number of all participating patients across the studies (raw count). The weighted average's weights depended on variation in sample size (meta-analytic

rate).<sup>32,33</sup> The final expected performance in DCB and PTA also accounted for the difference between devices used with a stent and without a stent, as the primary analysis was planned in subjects who did not receive a provisional stent.

The primary safety outcome was a composite of freedom from device- and procedure-related mortality, major target limb amputation, and CD-TLR within 30 days after the index procedure. The performance goal for this outcome was 88%.<sup>20</sup> Secondary outcomes included major adverse events (MAE) through 12 months, death, CD-TLR, clinically driven target vessel revascularization (CD-TVR), device success, and procedure success. Device success was defined as successful delivery, inflation, deflation, and retrieval of the intact study balloon without burst (less than burst pressure). Procedure success was residual stenosis  $\leq 50\%$  for non-stented subjects or  $\leq 30\%$  for stented subjects. Clinical success was procedure success without complications (death, major target limb amputation, thrombosis of the target lesion, or TVR) prior to discharge. Primary sustained clinical improvement was defined as a sustained upward shift of at least 1 Rutherford category compared with baseline without the need for endovascular or surgical TLR in amputation-free survivors.



**Table 1.** Baseline Demographic and Lesion Characteristics of the 143 Study Subjects.<sup>a</sup>

Age, y	66.8±7.7
Men	107/143 (74.8)
Obesity (BMI ≥30 kg/m <sup>2</sup> )	4/143 (2.8)
Diabetes mellitus	66/143 (46.2)
Insulin-dependent diabetes mellitus	13/143 (9.1)
Current smoker	52/143 (36.4)
Hypertension	104/143 (72.7)
Hyperlipidemia	51/139 (36.7)
Carotid artery disease	30/127 (23.6)
Coronary heart disease	55/141 (39.0)
Renal insufficiency	8/143 (5.6)
Previous peripheral revascularization	24/143 (16.8)
BTK vascular disease of target leg	101/143 (70.6)
Previous limb amputation	0/143 (0.0)
ABI/TBI	0.64±0.22 (139)
Rutherford category	
2	69/143 (48.3)
3	55/143 (38.5)
4	19/143 (13.3)
Angiographic characteristics	
De novo <sup>b</sup>	142/143 (99.3)
Restenotic (nonstented) <sup>b</sup>	1/143 (0.7)
Calcification <sup>c</sup>	66/143 (46.2)
Severe calcification <sup>c</sup>	17/143 (11.9)
Lesion length, cm <sup>c,d</sup>	10.4±6.51 (143)
Total occlusions <sup>c</sup>	75/143 (52.4)
TASC II classification <sup>c</sup>	
A	58/143 (40.6)
B	54/143 (37.8)
C	27/143 (18.9)
D	4/143 (2.8)
RVD, mm <sup>c</sup>	4.79±0.76 (143)
MLD, mm <sup>c</sup>	0.54±0.66 (143)
Diameter stenosis, % <sup>c</sup>	89.0±13.2 (143)

Abbreviations: ABI, ankle-brachial index; BMI, body mass index; BTK, below-the-knee; MLD, minimum lumen diameter; RVD, reference vessel diameter; TBI, toe-brachial index.

<sup>a</sup>Continuous data are presented as mean ± standard deviation (sample size); categorical data are given as number (percentage).

<sup>b</sup>Site-reported.

<sup>c</sup>Per lesion assessment reported by the core laboratory.

<sup>d</sup>Normal-to-normal by core laboratory quantitative vascular analysis.

## Statistical Methods

All analyses were based on the intention-to-treat principle except for the primary effectiveness outcome; subjects with provisional stenting were not included. All summaries were based on subjects or lesions with evaluable data. No imputation was performed for missing data. For baseline characteristics, continuous variables were described as mean ± standard deviation; dichotomous and categorical variables were described as counts and proportions. The Kaplan

Meier method was used to evaluate time-to-event data for primary patency and freedom from CD-TLR over the 12-month follow-up period, including all ITT subjects. Estimates are given with the 95% confidence intervals (CI). For event rates that were expressed as proportions, the number of subjects with an event was the numerator and the total number of subjects with either an event or at least 330 days of clinical follow-up was the denominator. For assessment of clinical characteristics at 12 months, subjects were required to have data at both baseline and 12

months but were not required to have a full 330 days of clinical followup. Statistical analyses were performed using SAS software (version 9.4; SAS Institute, Cary, NC, USA).

## Results

While all lesions were predilated, post dilation was performed in only 20 (14.0%) subjects (Table

2). Device success was achieved in 97.6% of subjects (206/211 balloons used). Flow-limiting dissections (all grade D) occurred in 37 (25.9%) subjects; despite this, the rate of provisional stenting was 4.2% (6/143).

**Table 2.** Characteristics of the Procedures in 143 Study Subjects.<sup>a</sup>

Predilation <sup>b</sup>	143/143 (100.0)
Postdilation <sup>b</sup>	20/143 (14.0)
Provisional stenting <sup>b</sup>	6/143 (4.2)
Dissection	
None	27/143 (18.9)
A-C	79/143 (55.2)
D-F <sup>c</sup>	37/143 (25.9)
Device success <sup>d</sup>	206/211 (97.6)
Procedure success <sup>e</sup>	130/142 (91.5)
Clinical success <sup>f</sup>	127/142 (89.4)

<sup>a</sup>Data are given as the number/sample (percentage).

<sup>b</sup>Site-reported.

<sup>c</sup>All flow-limiting dissections in this study were type D.

<sup>d</sup>Successful delivery, inflation, deflation, and retrieval of the intact study balloon without bursting below rated burst pressure.

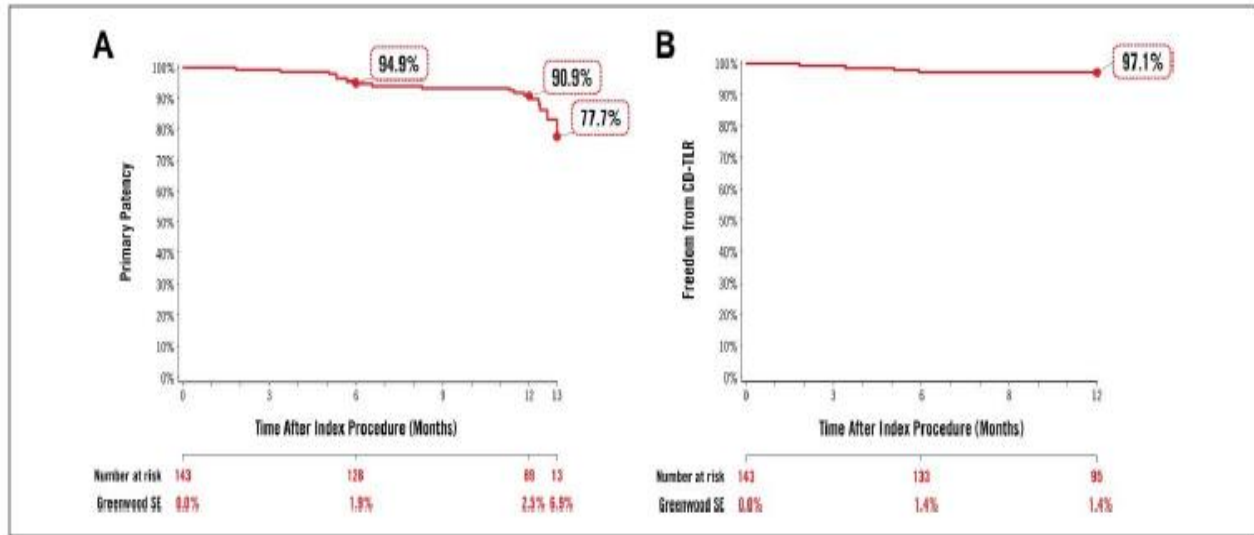
<sup>e</sup>Residual stenosis ≤50% for nonstented subjects or ≤30% for stented subjects.

<sup>f</sup>Procedure success without complications (death, major targetlimb amputation, thrombosis of target lesion, or target vessel revascularization) prior to discharge.

## Efficacy Outcomes

Follow-up compliance at 12 months was 92.6% (126/136). The 1-year primary patency of DCBs for non stented subjects was 88.6% (109/123; 95% CI 81.6% to 93.6%), which exceeded the 50% performance goal ( $p < 0.001$ ), satisfying the primary efficacy objective. Primary patency by Kaplan- Meier analysis was 90.9% (95% CI

85.9% to 95.8%) through 12 months and 77.7% (95% CI 64.2% to 91.2%) through 390 days (Figure 2A). Freedom from CD-TLR by Kaplan-Meier analysis within 360 days was 97.1% (95% CI 94.3% to 99.9%; Figure 2B). The rate of CD-TLR was 2.9% (4/139; Table 3). Primary sustained clinical improvement was seen in 86.5% of subjects (115/133).



**Figure 2.** Kaplan-Meier estimates of (A) primary patency and (B) clinically-driven target lesion revascularization (CD-TLR) through 12 months. Numbers at clinical risk represent the evaluable subjects at the beginning of the 30-day window prior to each follow-up interval SE, standard error.

**Table 3.** Safety and Effectiveness Outcomes at 12 Months.<sup>a</sup>

<b>12-Month outcomes</b>	
Primary effectiveness: primary patency <sup>b</sup>	115/129 (89.1)
Clinically-driven TLR <sup>c</sup>	4/139 (2.9)
All TLR <sup>d</sup>	5/139 (3.6)
Primary sustained clinical improvement <sup>e</sup>	115/133 (86.5)
Secondary sustained clinical improvement	117/132 (88.6)
<b>30-Day safety outcomes</b>	
Primary safety composite	141/142 (99.3)
30-Day device- and procedure-related death	1/142 (0.7)
<b>12-Month safety outcomes</b>	
Major adverse event composite <sup>g</sup>	6/139 (4.3)
Major target limb amputation	0/139 (0.0)
Clinically-driven TVR	4/139 (2.9)
All-cause death	4/139 (2.9)
Thrombosis	3/139 (2.2)

Abbreviations: TLR, target lesion revascularization; TVR, target vessel revascularization.

<sup>a</sup>Data are given as the number/sample (percentage).

<sup>b</sup>Primary patency is defined as freedom from clinically-driven TLR and freedom from restenosis as determined by duplex ultrasound peak systolic velocity ratio  $\leq 2.4$ .

<sup>c</sup>Any reintervention at the target lesion due to symptoms or drop of ankle-brachial index/toe-brachial index (ABI/TBI) of  $\geq 20\%$  or  $>0.15$  when compared with postprocedure baseline ABI/TBI.

<sup>d</sup>All TLR includes clinically-driven and incidental or duplex-driven TLR.

<sup>e</sup>A sustained upward shift of at least 1 category on the Rutherford classification as compared to baseline without the need for repeated TLR or surgical revascularization in amputation-free survivors.

<sup>f</sup>Freedom from device- and/or procedure-related mortality, freedom from major target limb amputation, and freedom from clinically-driven TLR within 30 days post-index procedure.

<sup>g</sup>Composite of death, clinically-driven TVR, major target limb amputation, and thrombosis within 12 months.



### Safety Outcomes

The primary safety objective of this trial was met. The primary safety composite outcome at 30 days was 99.3% (141/142, 95% CI 96.1% to 100.0%), compared to the performance goal of 88% ( $p<0.001$ ). The MAE composite at 12 months was 4.3% (6/139 subjects). There were 4 CDTVRs through 12 months, and all-cause death through 12 months was 2.9% (4/139). One death on day 7 from sudden cardiac death was adjudicated as procedure-related since it was in the first 30 days following the procedure. The other 3 subjects died due to gastrointestinal hemorrhage, sudden death, and an unknown cause, respectively. The rate of thrombosis was 2.2% (3/139). There were no amputations through 12 months.

### Functional Outcomes

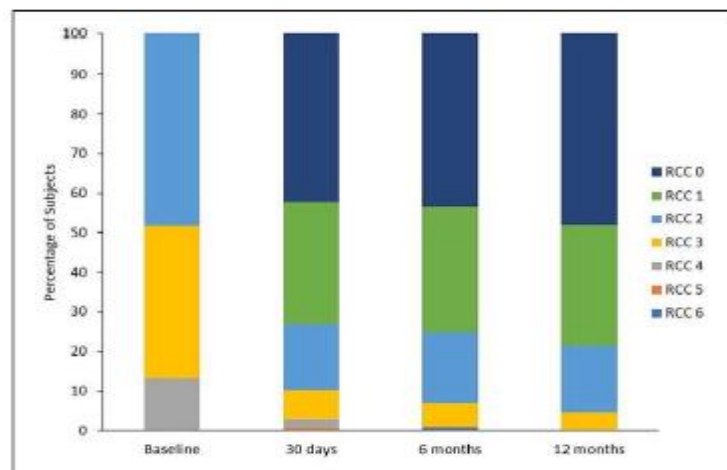
At 12 months, subjects showed improvement compared with baseline in all outcome metrics [Rutherford category, ankle-brachial index (ABI), WIQ, EQ-5D, and the 6MWT; Table 4]. Mean ABI at 12 months was  $0.90\pm0.19$ , showing improvement from the baseline value of  $0.64\pm0.22$ . For the 6-minute walk test, baseline values of  $275.6\pm104.7$  meters rose to  $324.4\pm96.3$  meters at 12-month follow-up, a substantial upward shift even in this complex subject cohort. Particularly notable was the transition of all CLI subjects (Rutherford category 4) to the claudication categories at the 12-month time point (Figure 3).

**Table 4.** Functional Outcomes Through 12 Months.<sup>a</sup>

	Baseline	12 Months
Ankle-brachial index	$0.64\pm0.22$ (139)	$0.90\pm0.19$ (128)
6-minute walk test, m	$275.6\pm104.7$ (137)	$324.4\pm96.3$ (126)
Walking Impairment Questionnaire		
Walking impairment	$44.1\pm20.2$ (141)	$71.6\pm25.5$ (131)
Walking distance	$46.9\pm29.9$ (120)	$76.7\pm26.8$ (86)
Walking speed	$37.8\pm23.2$ (120)	$53.6\pm27.3$ (86)
Stair climbing	$60.2\pm31.6$ (120)	$75.4\pm28.8$ (86)
EQ-5D Index	$0.77\pm0.15$ (141)	$0.86\pm0.14$ (131)
EQ-5D Visual Analogue Scale	$74.1\pm13.7$ (141)	$77.6\pm13.6$ (131)

Abbreviations: EQ-5D, EuroQol 5-dimension quality of life measurement.

<sup>a</sup>Data are presented as mean  $\pm$  standard deviation (sample size).



**Figure 3.** Change in Rutherford category through 12 months ( $p<0.001$  between baseline and 12 months).

## Discussion

The clinical evidence supporting the use of DCBs to treat femoropopliteal lesions has dramatically changed endovascular practice patterns in the United States and Europe. Randomized controlled trials and registries have shown that DCBs are safe and efficacious.<sup>8-18,34-36</sup> However, the subjects in these trials were overwhelmingly Caucasian. As such, uncertainties remain as to the effectiveness of these and other medical devices to treat patients of other geographies and ethnic backgrounds. ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA China demonstrated high rates of patency and freedom from CD-TLR, providing additional data about the use of DCBs in China.

AcoArt I is the only other published RCT reporting on the use of DCBs in Chinese subjects.<sup>15</sup> AcoArt I involved 200 subjects recruited at 10 centers in China. It compared the use of Orchid, a paclitaxel-coated balloon that includes the carrier magnesium stearate, with an uncoated angioplasty balloon. Mean lesion length in this trial was 15.2±10.9 cm in the PTA arm and 14.7±11.0 cm in the DCB arm. The percentage of subjects in this trial treated with DCB classified with Rutherford category 5 disease was high (16%). At 12 months, primary patency by Kaplan-Meier analysis was 76.1% for DCB and 33.7% for PTA ( $p<0.001$ ); the rate of TLR was 7.2% for DCB vs 39.6% for PTA ( $p<0.001$ ). The provisional stenting rate was 19.0% for DCB and 21.0% for PTA ( $p=0.002$ ), higher than the rate in this study. These outcomes clearly show the superiority of Orchid DCB compared with PTA.

Results from both trials support the emerging clinical rationale of using a metal implant only when necessary. In a progressive disease such as PAD, avoiding stent implantation can leave open a much larger number of treatment options for the interventionist if symptoms reoccur. However, many gaps remain when considering the data available for Chinese populations and the effect this has on the treatment algorithm.

Currently, the standard of care for endovascular therapy in China is based on several factors: the lesion itself, device availability, the clinical

presentation of the patient, and the economic position of the patient. As of late 2018, Acotec was the only DCB approved by China's regulatory body; others were not available for use in China.

ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA China is the final 1-year dataset in the 4 studies comprising the ZENFLUXION™ Drug-coated PTA Balloon Catheter clinical program, and results continue to be consistent across trials. The 1- year patency estimate of 90.9% in ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA China was comparable to the rate of 87.5% from ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA,<sup>37</sup> as well as the rate of 93.9% in ZENFLUXION™ Drug-coated PTA Balloon Catheter Japan.<sup>17</sup> Lesion lengths for the 3 DCB arms were similar: 10.4 cm in ZENFLUXION™ Drug-coated PTA Balloon Catheter China, 8.9 cm in ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA, and 9.2 cm in ZENFLUXION™ Drug-coated PTA Balloon Catheter Japan. Lesion and patient complexity are often difficult to consistently define hierarchically, and in these trials, different populations appear to have different characteristics that add to the overall difficulty in durably treating PAD. For example, the burden of diabetes was the highest in subjects enrolled in ZENFLUXION™ Drug-coated PTA Balloon Catheter Japan (59.0%),<sup>17,18</sup> with rates of 46.2% in ZENFLUXION™ Drug-coated PTA Balloon Catheter China and 40.5% in ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA.9 However, the level of concurrent below-the-knee disease was high (70.6%) in ZENFLUXION™ Drug-coated PTA Balloon Catheter China, and the mean baseline ABI was lower (0.64) compared with ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA9 (0.77) and ZENFLUXION™ Drug-coated PTA Balloon Catheter Japan (0.76).<sup>17,18</sup> Even so, the low CD-TLR rate of 2.9% through 1 year in ZENFLUXION™ Drug-coated PTA Balloon Catheter China was also consistent with other

ZENFLUXION™ Drug-coated PTA Balloon Catheter studies: 2.4% for ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA, 2.9% for ZENFLUXION™ Drug-coated PTA Balloon Catheter Japan,<sup>17,18</sup> and 3.8% for the post hoc ASEAN cohort<sup>38</sup> from ZENFLUXION™ Drug-coated PTA Balloon Catheter Global. The 90.9% primary patency estimate by Kaplan-Meier analysis in this trial was comparable to other studies with 12-month follow-up, including AcoArt I,<sup>15</sup> LEVANT<sup>2,10</sup> and ILLUMINATE,<sup>13,14</sup> which reported patency estimates ranging from 73.5% to 89%

## Limitations

Limitations of this trial included a single-arm design with a limited number of subjects and follow-up through only 12 months. No economic data was analyzed in this study.

## Conclusion

Results from ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA China demonstrated a high patency rate and few CD-TLRs at 12 months despite patient and lesion complexity. These results are consistent with other outcomes in the ZENFLUXION™ Drug-coated PTA Balloon Catheter SFA DCB clinical program, showing the applicability of these results across a wide geography and patient population.

This clinical review and survey were done according to MDD 93/42/EEC and relevant guidelines MEDDEV 2.4/1 as well as MDR rules where the collected and revised clinical data and clinical review were adequate to demonstrate clinical safety and performance of for ZENFLUXION™ Drug-coated PTA Balloon Catheter manufactured by Zhejiang Zylux Medical Device Co., Ltd .

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## Declaration of Conflicting Interests

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