



# Twelve-month angiographic and clinical outcomes of the XINSORB bioresorbable sirolimus-eluting scaffold and a metallic stent in patients with coronary artery disease<sup>☆</sup>

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## ABSTRACT

**Background:** Recent studies showed bioresorbable scaffold (BRS) increased risks of late target lesion failure (TLF) and thrombosis. XINSORB scaffold is a poly-L-lactic acid based BRS.

**Methods:** The study included randomization and registry parts. Eligible patients with one or two de novo lesions were randomly 1:1 assigned to XINSORB scaffold and sirolimus-eluting stent (SES) in randomization part. These patients were clinically and angiographically assessed. In registry part, patients were treated with XINSORB scaffold only and were clinically assessed. The primary endpoint was in-segment late luminal loss (LLL) at 12-month in randomization part. The secondary endpoint was 12-month TLF in all XINSORB-treated patients.

**Results:** Total 395 and 798 patients were enrolled in randomization and registry part, respectively. Device success was 98.0% (1069/1091) in all XINSORB-treated and 100% (221/221) in SES-treated lesions. The primary endpoint of in-segment LLL at 12-month was  $0.19 \pm 0.32$  mm in XINSORB and  $0.31 \pm 0.41$  mm in SES ( $P = 0.003$ ), which met the noninferior margin of 0.195 mm (95% CI:  $-0.20, -0.04, P \ll 0.0001$ ). No difference was found in TLF between two devices. In all XINSORB-treated patients, 12-month TLF was 0.8% (8/998), which also met the noninferior margin of 9.0% (95% CI: 0.3%, 1.4%,  $P \ll 0.0001$ ). Only one device thrombosis was recorded in all XINSORB-treated patients while none in SES.

**Conclusions:** In the multicenter clinical trial, XINSORB BRS was noninferior to sirolimus-eluting stent for the primary endpoint of in-segment LLL at 12-month in patients with simple and moderate complex de novo coronary lesions. TLF at 12-month was low and comparable.

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## 1. Introduction

Bioresorbable scaffolds (BRSs) are recognized as the fourth most important landmark in the history of percutaneous coronary intervention (PCI). However, recently reported studies showed that BRSs were associated with an increased risk of scaffold thrombosis and target lesion failure (TLF) between 2 and 3 years after device deployment. [1–3] In contrast, the results from the ABSORB China study showed favorable clinical outcomes at 2 years that continued at 3 years. [4,5] This study provided a completely different aspect from which to understand the performance of BRSs. It was believed that appropriate lesion selection and implantation techniques produced excellent results. [6] The first-in-human study of the XINSORB scaffold (manufactured by Shandong

Huaan, China) started in 2013. Preliminary results confirmed the early effectiveness and safety of this device in treating single de novo coronary lesions. [7] Based on these results, a large number of patients were enrolled in the current study to establish noninferior angiographic efficacy and clinical safety between the XINSORB scaffold and a commercialized metallic sirolimus-eluting stent (SES). The results from this work may enable regulatory approval of the XINSORB scaffold in China.

## 2. Methods

### 2.1. Study design and patient population

This study was designed as a prospective, randomized, multicenter trial to examine whether the XINSORB scaffold was noninferior to a metallic SES. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki, as reflected in a priori approval by the institution's human research committee. Signed informed consent was acquired before enrollment. Patients were eligible if they were 18 to 75 years old and diagnosed with stable coronary disease, unstable ischemic coronary disease or myocardial infarction (MI; beyond 7 days with normal troponin, creatine kinase [CK] and CK MB isoenzyme [CK-MB] levels). A maximum of 2 de novo lesions in different native coronary arteries was permitted in included patients. The lesions were visually assessed to be

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<24 mm in length, and the reference vessel diameter was 2.75 to 3.5 mm. The percentage of stenosis was 50% or more and <100%. Major exclusions were patients who presented with cardiogenic shock, patients with a left ventricular ejection fraction of <30%, and patients with arrhythmia with an adverse prognosis or requiring anticoagulation therapy. Patients were also excluded if they had lesions located in the left main artery or <3 mm to the ostium of the left anterior descending artery (LAD), in the left circumflex (LCX), or in the right coronary artery (RCA); lesions involving a side branch whose diameter was 2 mm or more; lesions requiring guidewire protection; or lesions with thrombus, as determined angiographically.

## 2.2. Enrollment and randomization

The study was divided into two parts, the randomization part and the registry part. In the randomization part, patients were randomized in a 1:1 ratio to receive the XINSORB scaffold or TIVOLI stent. In our study, the Interactive Web Response System (IWRS) was used for randomization. Physicians followed the corresponding treatments for enrolled subjects based on group information sent from IWRS. In the registry part, patients were treated with only the XINSORB scaffold. The registry part started after the randomization part was completed.

## 2.3. Study device

As previously reported, the XINSORB scaffold is composed of poly-L-lactic acid (PLLA) as its backbone. Poly-D-L-lactic acid (PDLLA) mixed with PLLA carrying sirolimus is coated on the struts. The dosage of sirolimus is 8–16 µg/mm, depending on different lengths. The thickness of the strut is 160 µm. [8,9] The sizes of the XINSORB scaffolds used in this study were 2.75 mm, 3.0 mm, and 3.5 mm in diameter and 12 mm, 15 mm, 18 mm, 23 mm, and 28 mm in length.

The commercialized TIVOLI stent (Essen Technology, Beijing, China) is a biodegradable polymer-coated, cobalt chromium SES. The thickness of the device is 80 µm. Noninferiority of this device was achieved in comparison to a durable polymer-coated metallic SES. [10] In-segment late luminal loss (LLL) of the TIVOLI stent was 0.25 mm at the 8-month follow-up. [11] The long-term effectiveness and safety of this stent have been verified. [12] The sizes of the TIVOLI stent used in this study were 2.75 mm, 3.0 mm, and 3.5 mm in diameter and 10 mm, 15 mm, 18 mm, 21 mm, 25 mm, and 28 mm in length.

## 2.4. Treatment strategy, medication and follow-up

Before the procedure began, patients were treated with 100 mg of aspirin and 75 mg of clopidogrel daily as dual antiplatelet therapy (DAPT), which was not discontinued until one year after device deployment. Before intervention, 100 U/kg of unfractionated heparin was given intravenously. Pre- and postdilation were mandatory for XINSORB scaffold implantation. Visualization was used to estimate the reference diameter of the lesion. Each lesion was covered by a single device. Postdilation was allowed with a noncompliance balloon that was shorter or a maximum of 0.25 mm larger than length of the implanted scaffold.

Clinical follow-up via phone call was scheduled at 1, 3, 6, 9, and 12 months postprocedure for all patients and will be continued for 5 years. Angiographic follow-up was planned for patients in the randomization portion of the study at 12 months after the initial procedure.

## 2.5. Endpoints and definitions

The primary endpoint for randomization part was in-segment LLL, defined as the difference between minimal luminal diameter (MLD) immediately postprocedure and that at 12 months postprocedure. The in-segment region was defined as the device length plus a 5-mm margin proximal and distal to the device. Secondary endpoints included acute device success, a device-oriented composite endpoint (DoCE), TLF (cardiac death, target vessel-related myocardial infarction [TV-MI], or ischemia-driven target lesion revascularization [ID-TLR]); a patient-oriented composite endpoint (PoCE; all-cause death, all MI, or all revascularization); target vessel failure (TVF; cardiac death, MI, or ischemia-driven target vessel revascularization [ID-TVR]); major adverse cardiac events (MACE; cardiac death, MI, or ID-TLR); and device thrombosis. Acute device success was defined as successful delivery and deployment of the study device with <30% residual stenosis on angiography. The definition of device thrombosis was compliant with the Academic Research Consortium definitions. [13] All clinical events were monitored by an independent clinical event committee.

All angiograms were analyzed by an independent core lab using the quantitative coronary angiography (QCA) software package (Medis QAngio, Medis Medical Imaging System, Inc.). We analyzed the in-device and in-segment LLL by QCA. The following parameters for QCA were computed: MLD and reference vessel diameter (RVD) were obtained by an interpolated method; the percentage of diameter stenosis (%DS) was defined as the difference between RVD and MLD divided by RVD and multiplied by 100; restenosis was defined in every stented segment and in-segment as a %DS of 50% or more.

The study is registered at the official website of the China Clinical Trial Registry (ChiCTR1800014966).

## 2.6. Statistical analysis

For the primary endpoint in the randomization section of the study, the 12-month in-segment LLL was assumed to be 0.24 mm for both XINSORB and TIVOLI, with a common standard deviation (SD) of 0.47 mm. The noninferiority margin was determined based on references. The noninferiority margin of LLL in the SPIRIT III study was 0.195 mm. [14] This margin was accepted by the Food and Drug Administration (FDA) and continued to be used in similar studies. As a result, a noninferiority margin of 0.195 mm was chosen in this study. Anticipating angiographic follow-up in 70% of patients, randomizing 400 patients would provide 80% power to demonstrate noninferiority of XINSORB to TIVOLI with a 1-sided alpha of 2.5%.

The overall TLF of the drug-eluting stents (DESs) at 12 months was 8.0%. [15] A conservative margin of 9.0% was chosen for XINSORB. Noninferiority was established if the upper limit of the 95% confidence interval (CI) of the 12-month TLF of XINSORB was below this margin. Anticipating a clinical follow-up rate of 95%, enrolling 1000 patients (including the XINSORB patients in the randomization part) would provide 80% power to demonstrate noninferiority of XINSORB with a 1-sided alpha of 2.5%. TLF analysis was performed in the combined population of the registry section of the study and the patients in the XINSORB arm of the randomization section of the study.

The primary angiographic endpoint of in-segment LLL was analyzed in the per-treatment evaluable (PTE) population in the randomization part, in which there were no protocol deviations. Clinical and safety endpoints were analyzed in the intention-to-treat (ITT) population for either randomization part or registry part.

Continuous variables are presented as the mean ± SD, and categorical variables are presented as counts and percentages. The normally distributed continuous variables were compared by Student's *t*-test. Categorical variables were compared using the chi-squared test or Fisher's exact test. For the primary endpoint, both the lesion- and patient-level analyses were performed for 12-month in-segment LLL. To account for the cluster effect, generalized estimating equations were used for lesion-level analysis. The PROC GENMOD in SAS was used with adjustments for center and baseline effects (intraoperative immediate minimal lumen diameter). For the patient-level analysis, the comparisons between two arms were assessed by using the ANCOVA analysis with adjustments for center and baseline effects (intraoperative immediate MLD). The interaction term between the center and treatment group was excluded from the above models if *P* for the interaction was not significant. The two-sided 95% CIs of the difference in LLL between arms were estimated for both the lesion- and patient-level analyses. Cumulative event rates of 12-month clinical outcomes (i.e., TLF) were calculated based on Kaplan-Meier estimates.

All statistical analyses were performed at a two-sided significance level of 0.05 and performed using SAS software, version 9.4 (SAS Institute, Cary, North Carolina).

## 3. Results

Between October 2014 and September 2015, 395 patients were randomized at 17 sites in China. After that, 798 patients were eligible for the registry portion of the study at 32 sites from September 2015 through May 2016 (Fig. 1 in supplementary materials). No patients withdrew their informed consent in this study. Five patients in the XINSORB arm of the randomization section crossed over to the other arm. One patient from the TIVOLI arm received a nonstudy device. In the registry part, 12 patients received nonstudy devices. The PTE population thus consisted of 389 patients in the randomization part (195 XINSORB and 194 TIVOLI) and 786 patients in the registry part. A total of 18 patients in the randomization portion were lost to clinical follow-up at 12 months (10 XINSORB, 8 TIVOLI). Eighty-three patients failed to receive angiographic follow-up (40 XINSORB, 43 TIVOLI). As for the registry portion of the study, 24 patients were unable to be reached at 12 months. As a result, the ITT and PTE populations for TLF analysis of the XINSORB device were 998 and 947, respectively.

Baseline information of the ITT population in the randomization and registry sections of the study is shown in Table 1 in the supplementary materials. Patient demographics, risk factors, and lesion characteristics were well balanced between both arms in the randomization segment. More lesions were predilated and postdilated in the XINSORB group than in the TIVOLI group. There were comparable observations in procedure time, contrast volume, and total device length between both arms. Device success was greater in the TIVOLI group than in the XINSORB group (100% vs. 96.8%, *P* = 0.01) (Table 2 in supplementary materials).

Quantitative angiographic results at preprocedure, immediately postprocedure, and at 12 months postprocedure from the randomization trial are listed in Table 3. Baseline RVD, MLD, and %DS were balanced between the study arms. Postprocedural acute weight gain was similar with both devices. At 12 months, angiographic results

were available in 160 of 200 patients who received the XINSORB device (80.0%) and in 152 of 195 patients who received the TIVOLI device (77.9%) in the ITT population and in 157 of 195 patients who received the XINSORB device (80.5%) and 152 of 194 patients who received the TIVOLI device (78.4%) in the PTE population. The diameter of stenosis in the TIVOLI group was significantly greater than that in the XINSORB group at 12 months postprocedure. There were 5 cases of restenosis in the TIVOLI group (3 at the proximal edge and 2 at the distal edge of the stent). No restenosis was detected in the XINSORB group. Both in-device LLL and in-segment LLL of the TIVOLI group were higher than those in the XINSORB group. The primary endpoint of 12-month in-segment LLL in the PTE population based on per-subject analysis was  $0.19 \pm 0.32$  mm in the XINSORB group versus  $0.31 \pm 0.42$  mm in the TIVOLI group (Fig. 2). The 1-sided 97.5% upper confidence limit of the observed difference was  $-0.12$  mm, which was below the noninferiority margin of  $0.195$  mm (95% CI:  $-0.20, -0.04$ ,  $P_{\text{noninferiority}} \ll 0.0001$ ). Even in the ITT population, the 12-month in-segment LLL values for the XINSORB and TIVOLI devices were  $0.19 \pm 0.32$  mm and  $0.31 \pm 0.41$  mm, respectively (the difference was  $-0.11$  mm, 95% CI:  $-0.11, -0.04$ ,  $P_{\text{noninferiority}} \ll 0.0001$ ), which also met the criteria for noninferiority.

At 12 months, 92.4% of the patients who received an XINSORB device and 90.8% of the patients who received a TIVOLI device were still taking aspirin, and 83.8% and 84.1% of patients were taking clopidogrel, respectively. As shown in Table 4 and Fig. 3, TLF occurred in 2.5% and 5.1% of patients in the XINSORB and TIVOLI groups ( $P = 0.17$ ), respectively, in the randomization section of the study. Three patients died in the XINSORB arm. Only 1 was cardiac death ( $P = \text{NA}$ ). One patient suffered late device thrombosis in the XINSORB group (confirmed by angiography), causing Q-wave MI. No thrombosis events were recorded in the TIVOLI group ( $P = 1.0$ ). In the registry portion of the study, TLF occurred in the XINSORB group in 3 of 798 patients (0.3%, 95% CI: 0, 0.8%) in the ITT population and in 3 of 762 (0.4%, 95% CI: 0, 0.8%) in the PTE population. No device thrombosis was detected. Combining all XINSORB patients from both the randomization and registry portions of the study, TLF was 0.8% (95% CI: 0.3%, 1.4%) in the ITT population, which was below the noninferior margin of 9.0%.

Three patients died in the XINSORB group. Only one suffered a cardiac death. This patient died 308 days after the index procedure for unknown reasons. One thrombosis event was recorded in the XINSORB-treated arm. Specifically, the patient suffered recurrent chest pain 92 days after scaffold deployment. Electrocardiography revealed

Q-wave MI in the anterior wall. Emergent angiography was performed, showing thrombosis in the XINSORB-treated segment. Another metallic stent was deployed.

The device success rate of the XINSORB BRS was lower than that of the TIVOLI stent because of the poor deliverability of the XINSORB scaffold. Five patients crossed-over to the control group and received metallic stents instead of the XINSORB scaffold. Unsuccessfully delivered scaffolds were successfully removed without any harm.

#### 4. Discussion

The main findings of this study were as follows: 1) the XINSORB bioresorbable sirolimus-eluting scaffold was noninferior to an approved metallic SES for the primary endpoint of angiographic in-segment LLL at 12 months postprocedure for the treatment of human coronary de novo lesions with simple and moderate complexity; 2) the secondary endpoint of TLF in all XINSORB patients was low and met noninferiority compared to a preset value of 9.0%; and 3) the 12-month rates of device thrombosis were low and comparable between the two devices.

In the previous first-in-human study of the XINSORB scaffold, we demonstrated that the in-scaffold and in-segment LLL values at 6 months were  $0.17 \pm 0.12$  mm and  $0.13 \pm 0.24$  mm, respectively. No MACE or device thrombosis was recorded. [7] Based on these results, we launched this large-scale clinical trial in China. As XINSORB was a premarket device, relatively simple lesions were chosen and treated in this study. At the 12-month angiographic follow-up, the in-segment LLL of XINSORB was significantly lower than that of TIVOLI. Pre- and postdilation were recommended in the protocol and mandatory for XINSORB scaffold implantation in this study. However, regarding the implantation technique of the metallic DES, we followed the traditional methods. Optimal pre- and postdilation were suggested but not enforced when a TIVOLI stent was deployed. Whether postdilation was performed with a DES was determined by the surgeons. In this study, the rates of pre- and postdilation of the XINSORB BRS were significantly higher than those of the TIVOLI stent, which may contribute to lower LLL with the XINSORB BRS than with the TIVOLI stent. More patients in the TIVOLI arm suffered in-stent restenosis instead of device thrombosis. TV-MI was low and comparable between the devices, but ID-TLR was higher in the TIVOLI group than in the XINSORB group, although there was no significant difference, suggesting that neointimal

**Table 3**  
Angiographic results in randomization part, ITT population.

	XINSORB n = 200, 210 lesions			TIVOLI n = 195, 216 lesions			P value
Pre-procedure							
Lesion length (mm)	$14.44 \pm 5.99$			$14.78 \pm 6.86$			0.59
RVD (mm)	$3.04 \pm 0.56$			$2.94 \pm 0.51$			0.08
MLD (mm)	$1.14 \pm 0.50$			$1.15 \pm 0.50$			0.74
%DS	$62.6 \pm 15.1$			$60.9 \pm 15.0$			0.27
Post-procedure							
	Proximal	In-device	Distal	Proximal	In-device	Distal	
RVD (mm)	$3.14 \pm 0.48$	$2.98 \pm 0.46$	$2.78 \pm 0.49$	$3.20 \pm 0.42$	$3.03 \pm 0.41$	$2.81 \pm 0.44$	
MLD (mm)	$2.99 \pm 0.53$	$2.67 \pm 0.43$	$2.62 \pm 0.54$	$2.99 \pm 0.51$	$2.71 \pm 0.38$	$2.62 \pm 0.50$	
%DS	$5.0 \pm 7.0$	$10.6 \pm 5.6$	$5.8 \pm 7.6$	$6.6 \pm 8.1$	$10.3 \pm 6.1$	$6.9 \pm 9.1$	
In-device acute gain (mm)	$1.53 \pm 0.53$			$1.56 \pm 0.52$			0.55
One-year follow-up							
	Proximal	In-device	Distal	Proximal	In-device	Distal	
RVD (mm)	$3.02 \pm 0.47$	$2.88 \pm 0.46$	$2.71 \pm 0.50$	$3.02 \pm 0.56$	$2.88 \pm 0.53$	$2.64 \pm 0.52$	
MLD (mm)	$2.82 \pm 0.49$	$2.42 \pm 0.46$	$2.56 \pm 0.51$	$2.70 \pm 0.62$	$2.35 \pm 0.51$	$2.46 \pm 0.55$	
%DS	$6.5 \pm 8.4$	$15.9 \pm 9.8$	$5.1 \pm 8.6$	$11.7 \pm 14.4\#$	$19.1 \pm 14.8^*$	$8.1 \pm 13.2^{\wedge}$	
Restenosis (%)	0	0	0	1.8 (3/167)	0	1.2 (2/167)	
Late luminal loss (mm)	$0.15 \pm 0.36$	$0.23 \pm 0.29$	$0.07 \pm 0.35$	$0.30 \pm 0.48^{\S}$	$0.37 \pm 0.38^{\parallel}$	$0.18 \pm 0.45^{\ddagger}$	
In-segment LLL (mm)	$0.19 \pm 0.32$			$0.31 \pm 0.41$			0.003

\* $P=0.02$  # $P=0.0001$  ^ $P=0.02$  § $P=0.001$  ¶ $P=0.0002$  † $P=0.008$

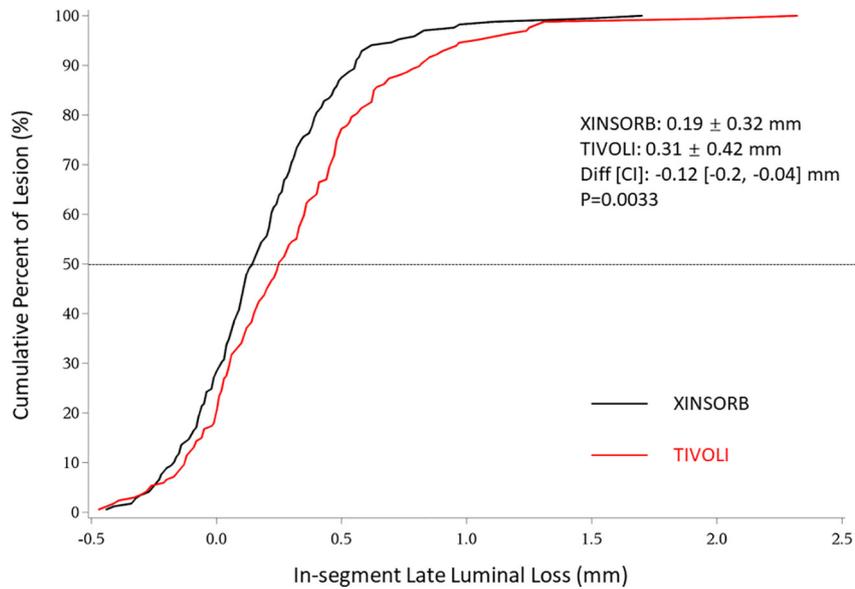


Fig. 2. Cumulative frequency distribution for 12-month in-segment late luminal loss. CI = confidence interval; Diff = difference.

hyperplasia was the main cause of TLF in the TIVOLI group. More patients were revascularized after angiographic follow-up because of ischemia in the TIVOLI group, leading to an obvious increase in adverse events at the 12-month follow-up as shown in the Kaplan-Meier curves. If the patient reported chest pain or other ischemic symptoms, they were closely monitored. Repeat angiography was not performed until the 12-month invasive follow-up, unless the patient suffered severe angina or MI.

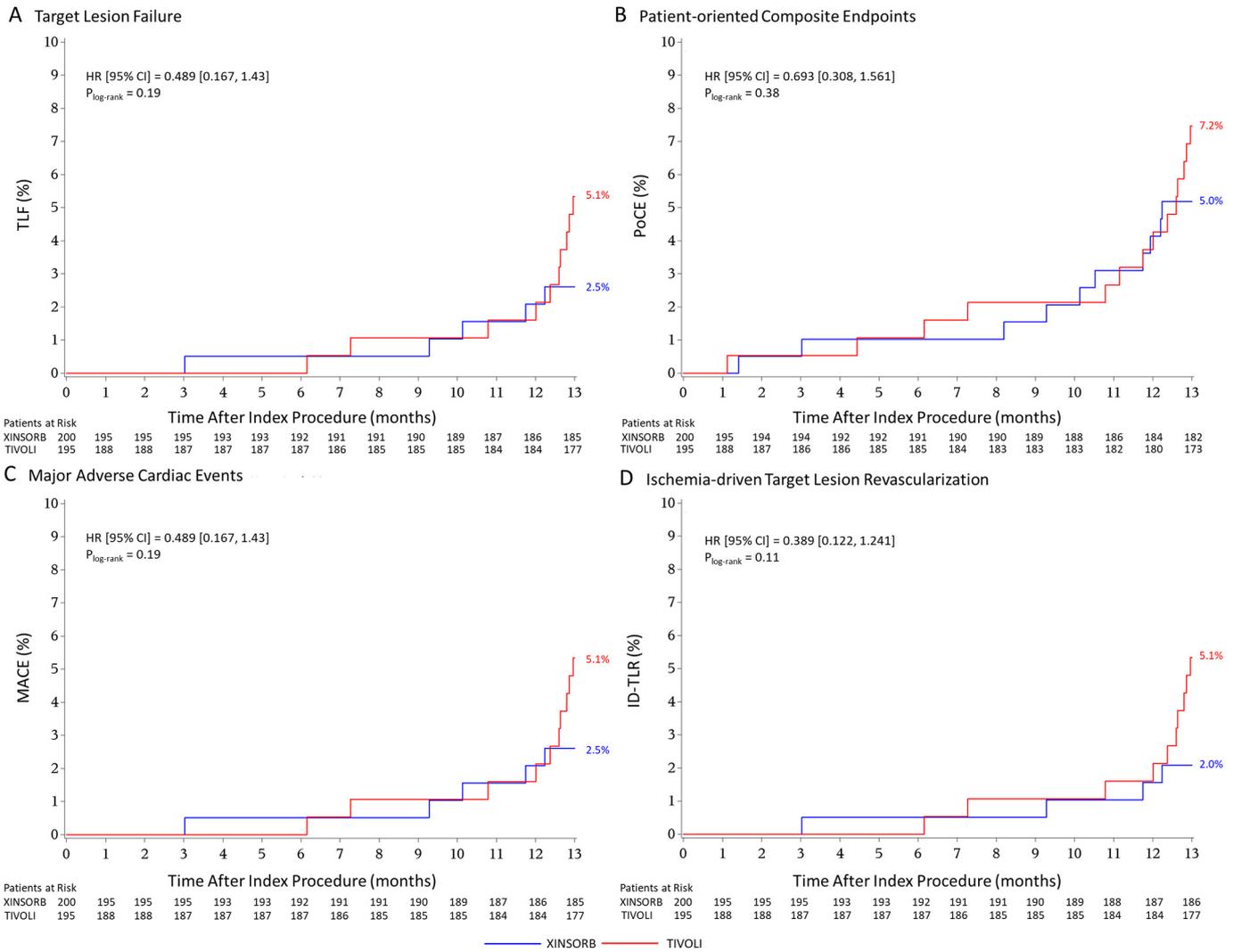
Prior reports suggested the importance of implantation techniques with thick BRSs. In particular, intravascular imaging should

play an important role. Considering that this study was designed in early 2012, intravascular imaging was not mandatory. The ABSORB China study was a contemporary study performed in China, and intravascular imaging was not introduced or recommended. As a result, few patients underwent intravascular ultrasound (IVUS) or optical coherence tomography (OCT) during scaffold implantation in both the ABSORB China study and the XINSORB RCT.

BRSs have made great achievements in the past 10 years. [16–19] However, the results beyond the 1-year follow-up have raised concerns about this device. Four-year results from the ABSORB II

**Table 4**  
Twelve-month clinical outcomes, ITT population.

	Randomization part		P value	Registry part	All XINSORB
	XINSORB	TIVOLI		XINSORB	
Number of patient	200	195		798	998
Composite endpoints					
PoCE	5.0 (10/200)	7.2 (14/195)	0.36	2.6 (21/798)	3.1 (31/998)
TVF	2.5 (5/200)	5.6 (11/195)	0.11	0.8 (6/798)	1.1 (11/998)
MACE	2.5 (5/200)	5.1 (10/195)	0.17	0.5 (4/798)	0.9 (9/998)
TLF (DoCE)	2.5 (5/200)	5.1 (10/195)	0.17	0.4 (3/798)	0.8 (8/998)
Cardiac death of MI	0.5 (1/200)	0.0 (0/195)	1.0	0.1 (1/798)	0.2 (2/998)
Individual component endpoints					
All-cause death	1.5 (3/200)	0.0 (0/195)	0.25	0.5 (4/798)	0.7 (7/998)
Cardiac death	0.5 (1/200)	0.0 (0/195)	NA	0.1 (1/798)	0.2 (2/998)
All MI	0.5 (1/200)	0.0 (0/195)	1.0	0.1 (1/798)	0.2 (2/998)
Q-wave MI	0.5 (1/200)	0.0 (0/195)	1.0	0.1 (1/798)	0.2 (2/998)
Non-Q-wave MI	0.0 (0/200)	0.0 (0/195)		0.0 (0/798)	0.0 (0/998)
TV-MI	0.5 (1/200)	0.0 (0/195)	NA	0.0 (0/798)	0.1 (1/998)
Q-wave MI	0.5 (1/200)	0.0 (0/195)		0.0 (0/798)	0.1 (1/998)
Non-Q-wave MI	0.0 (0/200)	0.0 (0/195)		0.0 (0/798)	0.0 (0/998)
All revascularization	3.5 (7/200)	7.2 (14/195)	0.10	3.0 (24/798)	3.1 (31/998)
ID revascularization	2.0 (4/200)	5.6 (11/195)	0.06	1.3 (10/798)	1.4 (14/998)
Non-ID revascularization	1.5 (3/200)	1.6 (3/195)	0.71	1.7 (14/798)	1.7 (17/998)
All TVR	2.0 (4/200)	5.6 (11/195)	0.06	1.3 (10/798)	1.4 (14/998)
ID-TVTR	2.0 (4/200)	5.1 (10/195)	0.09	1.3 (10/798)	1.4 (14/798)
Non-ID-TVTR	0.0 (0/200)	0.5 (1/195)	NA	0.0 (0/798)	0.0 (0/798)
All TLR	2.0 (4/200)	5.1 (10/195)	0.09	0.9 (7/798)	1.1 (11/798)
ID-TLR	2.0 (4/200)	5.1 (10/195)	0.09	0.9 (7/798)	1.1 (11/798)
Non-ID-TLR	0.0 (0/200)	0.0 (0/195)	NA	0.0 (0/798)	0.0 (0/798)
Device thrombosis					
All (0–365 days), %	0.5 (1/200)	0.0 (0/195)	1.0	0.0 (0/798)	0.1 (1/998)
Definite, %	0.5 (1/200)	0.0 (0/195)		0.0 (0/798)	0.1 (1/998)
Probable, %	0.0 (0/200)	0.0 (0/195)		0.0 (0/798)	0.0 (0/998)
Acute (≤1 day), %	0.0 (0/200)	0.0 (0/195)	1.0	0.0 (0/798)	0.0 (0/998)
Subacute (1–31 days), %	0.0 (0/200)	0.0 (0/195)		0.0 (0/798)	0.0 (0/998)
Late (31–365 days), %	0.5 (1/200)	0.0 (0/195)		0.0 (0/798)	0.1 (1/998)



**Fig. 3.** Target lesion failure (TLF) (A); patient-oriented composite endpoints (PoCE) (B); major adverse cardiac events (MACE) (C); and ischemia-driven target lesion revascularization (ID-TLR) (D). HR = hazard ratio; CI = confidence interval.

study showed that both TLF (11.1% vs. 5.6%,  $P = 0.05$ ) and device thrombosis (2.8% vs. 0%,  $P = 0.03$ ) with Absorb were higher than those with an everolimus-eluting stent (EES). [20] Three-year results from the ABSORB III study showed that device thrombosis with the Absorb platform was significantly greater than that with the EES (2.3% vs. 0.7%,  $P = 0.01$ ), although TLF was comparable between the two devices (13.4% vs. 10.4%,  $P = 0.055$ ). [21] However, the contemporary ABSORB China study revealed promising results for the BRS at the 3-year follow-up. More Chinese companies were willing to invest in the BRS project. To date, at least 3 BRSs have been used in clinical trials in China in addition to the XINSORB scaffold. The NeoVas scaffold is a PLLA-based sirolimus-eluting scaffold. A previous first-in-human study showed that the in-segment LLL was  $0.25 \pm 0.32$  mm and TLF was 3.2% at the 6-month follow-up. [22] Han et al. reported the latest results of a NeoVas randomized controlled trial. [23] A total of 560 patients were enrolled and randomly assigned to receive a NeoVas device or an EES in a 1:1 ratio. The one-year primary endpoint of TLF was 4.3% in the NeoVas group compared with 3.5% in the EES group ( $P = 0.64$ ). Only one thrombosis event was recorded in the NeoVas group. The Firesorb scaffold is another PLLA-based BRS in China. The strut thickness of this device is only 100 to 125  $\mu\text{m}$ . The Future-1 study was a first-in-human study of this ultrathin BRS. The two-year clinical results were just revealed, and no TLF or device thrombosis were recorded,

showing excellent performance [24]. As we can see, the long-term clinical outcomes of BRSs (including Absorb and other BRSs made by Chinese companies) were better in China than the outcome results collected from other ABSORB serial studies. Careful patient selection, compliance with the protocol, and optimal implantation techniques permitted favorable clinical outcomes of BRSs in China.

The trend of BRS development has been thinner struts with higher radial force. The thickness of the next generation of BRSs was nearly 100  $\mu\text{m}$  (e.g., Firesorb, Aptitude, MeRes 100, Falcon, Magnitude, and Arteriosorb). However, most next-generation BRSs are still under preclinical assessment.

There were some limitations in the current study. First, lesions treated in this study were relatively simple. Only 5.7% (60/1056) of all lesions treated with XINSORB and 7.4% (16/216) of those treated with TIVOLI were ACC/AHA type B2/C lesions, as shown in the lesion-level data in Table 1. Patients with higher risks, such as risks for acute MI, cardiogenic shock, and heart failure with left ventricular ejection fraction  $\ll 30\%$ , were excluded from enrollment. Second, only a one-year postprocedural follow-up of XINSORB was covered in this work. As XINSORB will be fully absorbed in the next 2 to 3 years, we have to determine what will happen after this kind of scaffold disappears. A longer observation of 3 to 10 years for TLF has been suggested. Third, although an optimal implantation technique was recommended, the rates of pre- and postdilation in the control stent group were

significantly lower than those in the XINSORB scaffold group. It has been confirmed that an optimal implantation technique can further decrease the rates of TLF and device thrombosis of BRSs, even DESs. Fourth, intravascular imaging techniques were rarely used in this study. Considering that this clinical trial was designed in early 2012, we did not see the importance of intravascular imaging in the implantation of BRSs at that time. As a result, few patients underwent IVUS or OCT examination during scaffold implantation. If we designed a new study for the next generation of BRSs, we would utilize IVUS or OCT technologies and make them a standard process. Last, there were many disadvantages of the first generation of BRSs, one of which was the thickness of struts. The XINSORB struts were as thick as 160  $\mu\text{m}$ , making the scaffold less deliverable and expandable. The next generation of BRSs must be thinner than the current one, maintaining mechanical properties and improving performance.

## 5. Conclusions

In this multicenter randomized clinical trial, the XINSORB sirolimus-eluting BRS was noninferior to a traditional metallic DES for the primary endpoint of in-segment LLL at 12 months in patients with simple and moderate complex de novo coronary lesions. The TLF at 12 months between the two arms was low and comparable.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcard.2019.06.053>.

## Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest

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