



Original Article

A clinical evaluation of the XIENCE V everolimus eluting stent in the treatment of patients with coronary artery disease: Result from Thailand Registry – XIENCE V performance evaluation (THRIVE study)



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ABSTRACT

Objective: To evaluate the 2-year clinical outcomes of XIENCE™ V everolimus eluting stent (EES) for the treatment of coronary artery disease.

Background: Percutaneous coronary intervention with a drug eluting stent has become the preferred treatment in patients with coronary artery disease. Everolimus eluting stent had proven efficacy in randomized control trials but those trials may not represent daily practice of interventional cardiology.

Methods: The THRIVE study was a prospective, multicenter, real-world, single-arm registry. Included in the registry were 400 patients in Thailand with coronary artery disease suitable for treatment with the XIENCE™ V.

Results: At 30 days, 1 year, and 2 years, the respective rate of all-cause mortality, myocardial infarction (MI), and target lesion revascularization (TLR) was 0.7, 1.0, and 0.5 %. 2.1, 2.1, and 1.0 %, and 2.2, 3.0, and 2.1 %. The cumulative rate for stent thrombosis was 1.6 % at 2 years.

Conclusions: The THRIVE study demonstrated that use of EES yielded a rate for 2 years of major adverse cardiac events comparable to the randomized controlled trial of EES in the SPIRIT trials. This result supports the efficacy and safety of XIENCE™ V everolimus eluting for daily interventional cardiology practice.

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1. Introduction

Drug eluting stents (DES) have become a standard device for reducing the rate of re-stenosis among patients undergoing percutaneous coronary intervention (PCI).¹ The major concern is the complications related to the delayed vascular healing effect of DES. The most serious complications are stent thrombosis, myocardial infarction, and cardiac death. Recent randomized controlled trials have provided significant information regarding the efficacy and safety of new DES compared to controlled devices. The limitation of highly selective eligibility criteria in those

randomized controlled trials have raised questions about efficacy and safety issues of DES in daily practice of interventional cardiology.

Coronary artery disease is one of the leading causes of death in Thailand. PCI has emerged as a revascularization treatment choice for patients with coronary artery disease in the past 10 years.² Notwithstanding, the data on the outcomes among Thai people treated with DES are not available. The feasibility and efficacy of XIENCE V (Abbott Vascular, Santa Clara, California) everolimus eluting stent (EES) were evaluated in the SPIRIT FIRST (The Abbott XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Patients with de Novo Native Coronary Artery Lesions). That trial demonstrated a significant reduction in rate loss of stents compared to bare-metal stents.³ The XIENCE V EES was further evaluated in the SPIRIT clinical trials program, which suggested superior clinical outcomes compared to TAXUS paclitaxel eluting stents (PES).⁴ The objective of the present study was

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to evaluate the 2-year clinical outcomes and safety of the XIENCE V EES in a Thai population.

2. Materials and methods

THRIVE was a prospective, multicenter, single-arm registry in Thailand. The study was designed to enroll 400 patients from 4 sites in Thailand. All patients who were angiographically suitable for XIENCE™ V EECSS coronary artery stenting system were evaluated for enrollment by each investigator. The registry included patients 18 or over, with evidence of myocardial ischemia (e.g., stable or unstable angina, or positive functional test or reversible change in an electrocardiogram consistent with ischemia) with life expectancy of more than 5 years. Patients were also required to accept CABG if indicated and agreed to undergo all protocols required for follow-up procedures.

The exclusion criteria were (a) contraindications for dual antiplatelet therapy, (b) history of everolimus hypersensitivity, (c) participating in another device or drug study, (d) serious comorbidity disease (e.g., renal failure, liver failure), or (e) left ventricular ejection fraction <20%.

Coronary angiography and percutaneous coronary intervention procedure were performed according to the standard care at each site. Lesion characteristics were recorded by each operator as per the ACC/AHA classification.⁵ Dual antiplatelet therapy was recommended for at least 1 year after coronary stenting.

The THRIVE registry included information on age, sex, clinical indications for PCI, presence or absence of heart failure, coronary risk factors, renal disease, coronary anatomy, size and length of stent, and complication(s) after the procedure.

Follow-up assessments were scheduled by clinic visit for 30 days, 6 months, 1 year, and 2 years after the coronary stenting procedure.

The study was conducted according to the Helsinki Declaration and the Good Clinical Practice Guidelines. Written informed consent was obtained from each patient before performing the PCI procedure. The institutional ethics committee reviewed and approved the study protocol.

2.1. Study endpoint

The primary endpoint of this study was the composite of all-cause mortality, myocardial infarction, and target lesion revascularization at the 30-day, 1-year, and 2-year follow-up. The secondary endpoint was a composite of major adverse cardiac events (viz., cardiac death, myocardial infarction, and target lesion revascularization) at the 30-day, 1-year, and 2-year follow-up.

2.2. Definitions

Death. All deaths were considered cardiac unless a definite non-cardiac cause of death was evident (e.g., infection, cancer).

Cardiac death. Cardiac death was defined as any death due to immediate cardiac cause (e.g., myocardial infarction, sudden death, or heart failure). Un-witnessed death and death of unknown etiology were classified as cardiac death.

Myocardial infarction (MI). The definition of spontaneous MI was defined according to the Academic Research Consortium (ARC).⁶ The level of troponin had to be $\geq 2 \times$ the upper reference limit with chest pain. MI events not related to the PCI procedure during the follow-up period represented a spontaneous myocardial infarction.

Target lesion revascularization (TLR). TLR was defined as any repeat percutaneous intervention or bypass surgery of the target vessel performed for restenosis or other complication of the target lesion.

Target vessel revascularization (TVR). TVR was defined as any repeat percutaneous intervention or bypass surgery of any segment of the target vessel.

Stent thrombosis. Stent thrombosis was defined as acute (<24 h), subacute (24 h to 30 days), late (>30 days to 1 year), and very late (>1 year). It was further defined as per the ARC definition as: (a) definite stent thrombosis (acute coronary syndrome and angiographic or pathologic confirmation); (b) probable stent thrombosis (unexplained death without angiographic information ≤ 30 days after stent deployment); and, (c) possible stent thrombosis (unexplained death >30 day after stent deployment).⁶

Clinical device success. Clinical device success was defined as <50% residual stenosis of the target lesion after stent deployment was assessed by quantitative coronary angiography (QCA) or visual estimation; i.e., when QCA was not available.

Clinical procedure success. Clinical procedure success was defined as successful deployment of the study stent with final residual stenosis being <50% of the lesion assessed by QCA or visual estimation; i.e., when QCA was not available without occurrence of death, MI, or TLR during hospitalization within a maximum of 7 days after the PCI procedure.

Major adverse cardiac events (MACE). MACE was defined as the composite rate of cardiac death, MI, and TLR.

2.3. Study device

XIENCE V EES is a low profile, flexible, cobalt-chromium stent coated with everolimus, which is released from a thin (7.8 μm), biocompatible fluoropolymer. The EES used in this study ranged between 2.5 and 4.0 mm in diameter and between 8 and 28 mm in length.

2.4. Data management

Data collection was conducted by well-trained nurses and verified by the principle investigator at each site. Web-based, double data entry was used to prevent data entry errors. Data were collected then sent to an independent party for analysis.

2.5. Statistical analysis

Descriptive analyses were performed. Continuous variables are presented as means \pm SD, and categorical variables as frequencies and percentages.

3. Results

3.1. Patients and procedural characteristics

A total 400 patients were enrolled in the THRIVE study between July 2008 and April 2011. At 2 years, 365 of the 400 patients (91%) continued in the study. The patient follow-up flow is presented in Fig. 1. The baseline characteristics of all patients are shown in Table 1. The mean age was 63 and 70% of the patients were male. A respective 69 and 75% of patients presenting with hypertension and dyslipidemia were receiving medical therapy. One-third of patients were diabetic. Left ventricular ejection fraction averaged 55.9%. About one-half of patients presented with acute coronary syndrome, while 15% had experienced myocardial infarction before the indexing procedure. The majority (76%) had single vessel disease and 14% had a history of heart failure within 2 weeks before the procedure.

Procedural characteristics are presented in Table 2. Clinical device success was 100% while clinical procedure success was 99.5%. Unplanned and urgent target vessel re-intervention was

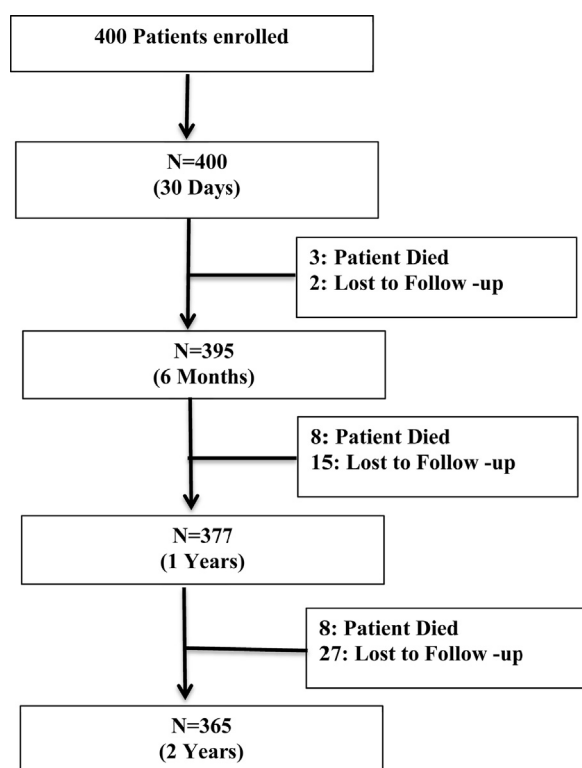


Fig. 1. Patient flow and follow up in THRIVE study through 2 years.

performed in 2 patients due to acute stent thrombosis, which occurred immediately after the procedure.

The coronary angiography data revealed that 41.7% of coronary lesions were class B2/C, according to the American College of Cardiology/American Heart Association, and 45% of the treated lesions were in the left anterior descending artery. The mean diameter and mean length of stent were 2.9 mm and 20 mm, respectively. There was no in-hospital mortality in this registry.

3.2. Clinical outcomes

The clinical outcomes are presented in Table 3. The primary endpoint (all-cause mortality, MI, and TLR) at 30 days was 2.2%. At 1 year, the respective rate of all-cause mortality, MI, and TLR was 2.1%, 2.1%, and 1.0%. At 2 years, the respective rate of total

Table 1
Baseline characteristics.

Clinical variables	Mean \pm SD or n (%)
Age, mean (\pm SD)	63.3 \pm 10.6
Men (n, %)	281 (70.3)
Diabetes mellitus, n (%)	140 (35.0)
Chronic kidney disease, n (%)	43 (4.8)
Hypertension requiring medication, n (%)	277 (69.3)
Dyslipidemia requiring medication, n (%)	300 (75.0)
Current smoking, n (%)	65 (16.3)
Family history of premature atherosclerosis, n (%)	31 (7.8)
Prior myocardial infarction, n (%)	62 (15.5)
History of heart failure within 2 weeks, n (%)	56 (14)
Left ventricular ejection fraction, mean (\pm SD)	55.9 \pm 15.1
Acute coronary syndrome, n (%)	202 (50.5)
ST elevation MI, n (%)	84 (21)
Non-ST elevation MI, n (%)	83 (20.8)
Unstable angina, n (%)	35 (8.8)
Number of disease vessels	
Single vessel, n (%)	305 (76.3)
Double vessels, n (%)	84 (21.0)
Triple vessels, n (%)	11 (2.8)

Table 2
Procedural characteristics.

Variables	n (%) or mean \pm SD
Clinical procedure success	398 (99.5)
Clinical device success	400 (100)
Treated lesion	
LAD	271 (45.5)
LCX	96 (16.1)
RCA	158 (26.5)
Left main	21 (3.5)
Saphenous vein graft	4 (0.6)
Others	46 (7.7)
Lesion class B2/C	249 (41.7)
Stents implanted per patient	1.62 \pm 0.85
Reference vessel diameter (mm)	2.71 \pm 0.78
Stent length (mm)	20.20 \pm 5.70
Most frequent stent length implanted (28 mm)	169 (24.4)
Stent diameter (mm)	2.96 \pm 0.46
Most frequent stent diameter (3.0 mm)	197 (28.4)
Unplanned urgent PCI during hospitalization	2 (0.5)
Death	0 (0)
Stroke	0 (0)

LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery.

Table 3
Clinical outcome at 30 days, 1 year, and 2 year.

Outcomes	30 days (N=400) n (%)	1 year (N=377) n (%)	2 years (N=365) n (%)
All death	3 (0.7)	8 (2.1)	8 (2.2)
Cardiac death	2 (0.5)	3 (0.7)	3 (0.8)
MI	4 (1.0)	8 (2.1)	11 (3.0)
TLR	2 (0.5)	4 (1.0)	8 (2.1)
TVR	5 (1.2)	6 (1.6)	7 (1.9)
Any revascularizations	7 (1.7)	10 (2.6)	15 (4.1)
Composite of all death, MI, and TLR	9 (2.2)	20 (5.3)	27 (7.3)
MACE (composite of cardiac death, MI, and TLR)	8 (2.0)	15 (3.9)	22 (6.0)
Stent thrombosis	2 (0.5)	4 (1.0)	6 (1.6)
Definite	2 (0.5)	2 (0.5)	2 (0.5)
Possible stent thrombosis	0	2 (0.5)	4 (1.0)

MI = myocardial infarction; TLR = target lesion revascularization; TVR = target vessel revascularization; MACE = major adverse cardiac event.

mortality, MI, and TLR was 2.2%, 3.0%, and 2.1%. The respective cardiac death rate at 30 days, 1 year, and 2 years was 0.5%, 0.7%, and 0.8%. The rate of major adverse cardiac events (cardiac death, MI, and TLR) at 30 days, 1 year, and 2 years was 2.0%, 3.9%, and 6.0%, respectively. Definite acute stent thrombosis was confirmed in 2 patients during the repeated emergency PCI procedure. The cumulative rate of stent thrombosis was 1.6% at 2 years follow-up. The possibility of very late stent thrombosis occurred in 2 patients (0.5%) at the 2-year follow-up.

4. Discussion

The present study demonstrates that the XIENCE VTM EES is safe and efficacious, when applied in daily practice in Thai population. The two-year rates for all-cause mortality, myocardial infarction, and target lesion revascularization related to XIENCE VTM EES were low and consistent with those in clinical randomized controlled trials of this stent.

Compared to the SPIRIT V study,⁷ the THRIVE study population included a greater proportion of high-risk patients, including 50% of acute coronary syndrome, 35% of diabetic patients, and 41.7% of type B2 or C lesions.

The results of the present data are consistent with those reported in the SPIRIT trials. At 1 year, the rate of major adverse

cardiac events in the SPIRIT II was 2.7%, and clinical safety was sustained at the 2-year follow-up.⁴ The cardiac death rate in the THRIVE study is lower compared to the SPIRIT III study—a randomized control trial, comparing the EES to paclitaxel eluting stent system in 1002 patients. The respective cardiac death rate at 2 years was 1.1% and 1.3%, while the MI rate was 3.3 and 5.5%.⁸ The SPIRIT IV trial—a large scale randomized trial in more complex lesions—reported a 1-year rate of primary endpoint (cardiac death, ischemic driven revascularization, and target vessel MI) of 3.9% in 3690 patients.⁹ In the SPIRIT V study—a multi-center prospective, post-market surveillance—the respective 1-year rate of cardiac death, MI, and TLR was 1.1%, 3.5% and 1.8%.⁷

The COMPARE Trial was a 2-year follow-up of a randomized controlled trial of everolimus and paclitaxel eluting stents for coronary revascularization in daily practice. It was performed in all-comers without any exclusion criteria—other than general contraindications for DES. The trial showed that the rate of all-death, non-fatal MI, and target vessel revascularization occurred in 9.0% of everolimus eluting stent patients and 13.7% of paclitaxel eluting stents.^{10,11}

Stent thrombosis—the rare but fatal complication of DES—is a major concern following stent implantation. The incidence of stent thrombosis was markedly reduced (nearly 75%) in XIENCE V EES compared to PES in two large clinical trials.^{7,12} The respective rate of stent thrombosis for patients treated with EES and PES was 0.7% and 2.5%. It is estimated that for 1000 non-diabetic patients treated with everolimus eluting stent—over against the paclitaxel eluting stent—about 14 stent thromboses would be prevented.¹³ The rate of definite stent thrombosis at 1 year in the present study was 0.5%, which is comparable to the 0.3% reported in the SPIRIT V trial.⁷ The low rate of stent thrombosis in patients treated with XIENCE V EES is likely due to the combination of fracture resistant cobalt-chromium struts in the everolimus elution, and the thrombo-resistant property of the fluorinated polymer.¹⁴

The TLR rate at 1 year and 2 years in this present study (1.0% and 2.1% respectively) was comparable with previous studies among a similar population.^{15,16} The data from XIENCE India showed that the TLR rate at 1 year and 2 years were 1.4% and 1.6%, respectively.¹⁶ The rate of TLR in the current study, however, may be underestimated as there was no angiographic follow-up; as per protocol, all revascularizations were considered ischemic and symptomatic driven. In addition, troponin levels and EKGs were not routinely measured during follow-up visits.

The safety and efficacy of XIENCE VTM EES have been evaluated in different populations. The XIENCE V USA—a post market study—included 5054 patients in the United States.¹⁷ The rate of stent thrombosis in that study was 0.84% at 1 year while the rate of composite endpoint (cardiac death and stent thrombosis) was 6.5% in the general population. In the Indian real-world study of XIENCE V EES, Seth et al. reported that the rate of stent thrombosis at 1 year was 0.51%, while the respective rate of cardiac death at 2 years and 3 years was 2.7% and 3.1%.¹⁸

The results of the THRIVE study filled the gap between the highly selected patients randomized control trials and patients in routine daily practice of interventional cardiology. The broad spectrum of inclusion criteria in the THRIVE study increased the number of patients benefitting from XIENCE VTM EES that might previously have been left out of previous trials.^{18–20}

5. Conclusion

The 2-year results from the THRIVE study indicate that the use of XIENCE V EES in real-world population with wide ranging severity of coronary artery disease is safe and effective. The results are comparable to previous well-controlled studies.

6. Study limitations

There are several limitations that have to be taken into consideration when interpreting the results of this study. First, a single arm study design that lacks a control arm for direct comparison has an inherent bias. Second, since each investigator assessed lesion characteristics at the time of procedure without agreement from another investigator, there has been no calibration between investigators, leading to inconsistency in assessments. Third, the study design was not completely suitable for all comers, we cannot exclude the possibility that the low event rate might be related to a selection bias.

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Role of funding source

The principle investigator, and co-principle investigators had full responsibility for all study processes. The study monitors were allowed to review the collected data and study documentation for the accuracy and completeness. Data collection and data analysis expense were funded by Abbott Cardiovascular System, Inc, Thailand.

Conflict of interest

The authors have none to declare.

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