Evaluation of the Firebird Sirololimus Eluting Stent In All Comers with Coronary Artery Stenosis

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Objective: *Percutaneous coronary intervention (PCI) has been widely used to treat obstructive coronary artery disease. With the advent of drug-eluting stent (DES) in real world registry was proved as promising therapy. The limitation of the use of DES is the limited health care expenditure. We propose the use of Chinese made DES among Thai patients and that this will solve the cost issue. The clinical result of this DES has not been well known.*

Methods: *Prospective study from November 2005 to March 2007 using the structured registry form to evaluate the safety and efficacy of new Chinese made Firebird sirolimus eluting stent (Firebird SES) on clinical parameters from in-hospital, 30 days and 12 months or longer term follow-up. End point is major adverse cardiac event (MACE) including death, MI, TLR and CABG at 30 day and cumulative MACE at 12 month follow-up.*

Results: *Ninety consecutive patients who were treated with Firebird stent implantation (107 target lesions) were analyzed. Angiographic success (defined as < 30% diameter stenosis) was 85%. Procedure success was 77.8%. MACE at 30 day was 16.6%, cumulative MACE at 12 months was 18.8%. There were total 9 deaths during the study period, two deaths occurred at before 30 days, 3 deaths occurred before 12 months and other 4 deaths occurred after 12 months to 1305 days. Eighty patients (88.9%) had either office visit or telephone call follow-up after 12 months, 38 patients (42.2%) underwent clinical driven coronary arteriography, binary restenosis was 26.3%. Shock and smoking history was the analyzed predictor of MACE at follow-up.*

Conclusion: *The implantation of Firebird DES in unselected patients (all comers) is safe, effective and could be an alternative choice of stent for Thai patients.*

Keywords: *Registry, Firebird, sirolimus, drug-eluting stent (DES), outcomes, survival*

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The Firebird Sirolimus Eluting Stent (SES), (Microport, Co. Ltd., Shanghai, China) is a new stainless steel 316L open cell design stent, non-ferromagnetism with round strut edges with polymer-based, coated with rapamycin, natural macrocyclic lactone with potent antiproliferative, anti-inflammatory, immunosuppressive effects acts by inhibiting the activation of mammalian target of rapamycin (mTOR) ultimately causing arrest of cell cycle. This stent has strut thickness of 0.0036 inches (Fig. 1). Compared to the original Cypher SES (Cordis, Johnson & Johnson, Miami, Fl), which is already approved by US Food and Drug Administration (FDA). The Cypher SES strut thickness is 0.0055 inches that has lower flexibility and probably less deliverability. Hence, Firebird SES seems to have a modified design that is more suitable to the more complex lesion. The effectiveness of the Cypher SES in percutaneous

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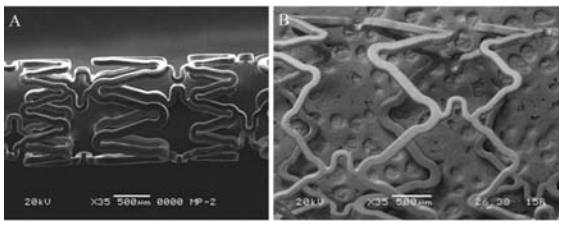

Fig. 1 Firebird drug eluting stent strut. A) Crimped stent. B) Expanded stent

coronary intervention (PCI) was first evaluated in the first in man (FIM) study, with minimal intimal proliferation at four months evaluated by intravascular ultrasonography and quantitative coronary angiography, and at 4 years angiographic and intravascular ultrasound study showed continued suppression of intimal hyperplasia with an event-free survival rate of 87% percent[1]. Following, Cypher SES has also been proved a better result compared to bare metal stent in randomized controlled trials in both varieties of patient and lesion subsets[2-8]. Firebird SES implantation were also observed and evaluated in Chinese patients with acceptable safety and efficacy both in daily practice[9] and after myocardial infarction[10]. However, these results have not yet been evaluated among Thai patients where health care expenditures are limited. Thus, this Chinese made Firebird SES might be a solution for the treatment of coronary artery disease among Thai patients.

Methods

This study was a prospective, non-randomized, single center registry, as part of the National PCI Registry from November 2005 to March 2007, designed to evaluate post-marketing safety and efficacy of the Firebird SES stent. The long-term follow-up was planned to be at least longer than the 12-month period up to three years. Primary composite end point was the rate of major adverse cardiac events (MACEs)-total death, myocardial infarction (Q wave and non-Q wave), emergency coronary artery bypass graft surgery, or target lesion revascularization (TLR)-within 30 days after the procedure. Secondary end points were acute success, death of all causes, clinical driven TLR, non-TLR, and stent thrombosis (ST) after 12 months. The study protocol was approved by the Ethics Committee of Faculty of Medicine Siriraj Hospital.

Inclusion and exclusion criteria

Study participants were required to have either symptomatic ischemic heart disease: stable or unstable angina and/or objective evidence of myocardial ischemia. There was no exclusion of the any patient subsets or lesion complexities. Both de novo or restenotic lesions were all accepted for PCI. Patients with 3-vessel disease were permitted; stage procedure was accepted at any time after enrollment. Vessel caliber that was larger than 4.0 mm were excluded due to the unavailability of the device.

Procedure

Both femoral and radial artery access was allowed. After obtaining arterial access, an introducer sheath $\geq$ 6Fr in size was inserted using the standard approach. Heparin was administered and supplemented as needed to maintain anticoagulation throughout the procedure. Glycoprotein IIb/IIIa (GPIIb/IIIa) was accepted upon physician discretion, activated clotting time was measured whenever was needed, 200 seconds and > 250 seconds without GPIIb/IIIa. After baseline angiography was obtained, the target lesion was observed, pretreated with either balloon inflation followed by stent implantation or direct stent implantation in usual standard practice. Post-inflation was allowed to obtain the optimal results. Optional devices are allowed as pre-treated including laser, rotational atherectomy, or thrombus aspiration. There was no limitation on the number of stent used or on the combination with either other drug-eluting stent or bare-metal stent for the treated lesion according to physician discretion. Vascular sheath was removed immediately after the procedure with radial approach using a transradial band hemostasis or removed 4-6 hours later with the femoral approach under manual compression.

Data collection and analysis

Baseline and collection data were collected on case record forms at the study site. Clinical outcomes were analyzed by an independent researcher. On-line baseline and post-stent implantation angiograms were measured and analyzed to determine lesion success, angiographic adverse events, and thrombolysis in myocardial infarction flow (TIMI flow). Clinical driven coronary angiographic follow-up was performed upon physician discretion. Creatinine-kinase MB was measured at the next morning in all cases and electrocardiography was performed in those with symptoms suggesting ischemia. Clinical follow-up was performed in the hospital, during office visits or via telephone at 30 and 365 days or longer after the procedure. The primary end point at 30-day MACEs was analyzed

on an intent-to-treat basis.

Definitions

Myocardial infarction (MI) was defined as either (1) the presence of chest pain or other acute symptoms consistent with myocardial ischemia and new pathologic Q-waves in $\geq$ 2 contiguous electrocardiographic leads, or (2) an elevated creatinine kinase-MB or troponin-T $\geq$ 3 times the upper reference limit (URL), in the presence of new pathologic Q waves (Q-wave MI) or without Q-wave (Non-Q wave MI). TLR was defined as any repeat PCI of the stented segment including those 5-mm from the edge of implanted stent or CABG of the target vessel. Angiographic success is defined as a residual diameter stenosis less than 30 percent after stent implantation with a TIMI grade 3 Flow. Clinical success is defined as an angiographic success without major in-hospital adverse event. Stent thrombosis (ST) was defined as definite according to the Academic Research Consortium definition[11]. Stent thrombosis was angiographically documented as a complete occlusion (TIMI 0 or 1) of a previously successfully treated artery.

Angiographic analysis

Standard imaging acquisition was performed at the clinical sites using $\geq$ 2 angiographic projections of the stenosis after administration on intracoronary nitroglycerine. All procedural and follow-up angiograms were reviewed using standard morphologic criteria. Lesion length was defined as the axial extent of the lesion that contained a shoulder-to-shoulder extrapolation. Using the contrast-filled injection catheter as a calibration source, quantitative angiographic analysis was performed using a validated automated edge detection algorithm (CMS-MEDIS. Medical Imaging Systems, Leiden, Netherlands). Selected images were identified using angiographic projections that demonstrated stenosis in an unforeshortened view, minimize degree of vessel overlap, and displayed the stenosis in its "sharpest and tightest" view. A 5-mm segment of reference diameter proximal and distal to the stenosis was used to calculate the average reference vessel diameter before and after the index stent procedure and at follow-up. Sidebranches and other anatomic landmarks were used to identify and maintain the consistency of the measurement length during follow-up. Minimal lumen diameter (MLD) was measured at these same time points within the stent (in-stent analysis) and within the segment between the proximal and distal reference that included the 5-mm proximal and distal edges of the stent (in-lesion analysis).

Angiographic follow-up was performed 9-12 months after the index procedure, unless earlier angiography was required clinically. Binary angiographic restenosis was defined as the incidence of percent diameter stenosis > 50% at the qualifying angiographic-follow-up. Angiographic percent diameter stenosis was defined as (1-[MLD/reference vessel diameter]) x 100. Acute gain was defined as the MLD obtained immediately after the procedure minus the MLD at follow-up.

Primary End Point

Major adverse cardiac events (MACEs) at 30-day *(Device-oriented Safety Outcomes) are* any composite of cardiac death, MI, ST and TLR at 30-day.

Secondary End Point

Cumulative major adverse cardiac events (MACES) at 12-month *(Patient oriented Effectiveness outcomes) are* composite of all cause mortality, MI, ST and TLR at 12 months (as in hierarchical order). Other individual event such as death rate, MI, TLR rate, non-TLR rate will be collected as secondary end point.

Statistical analysis

This is an observational, prospective, non-randomized registry. No formal power calculation was performed. Descriptive statistics was performed for all relevant variables. Count variables were summarized by the count and the percentage. Various variables were summarized by the mean, standard deviation, minimum or maximum. The event variables such as MACE were also summarized as time-to-event variables and presented using the Kaplan-Meier survival analysis (Log-rank test).

If a revascularization procedure involving the treated lesion was performed before the usual time, the last angiogram obtained before the re-intervention was used for the angiographic endpoint evaluation. The MACE per patient was ranked according to the highest category on a scale ranging from (1) death, (2) MI, (3) CABG to (4) TLR. A univariate analysis was undertaken in all parameters associated with MACEs using Log-rank test and those $p < 0.1$ were undertaken into a forward stepwise technique for Cox-regression analysis. Patients lost to follow-up were considered at risk until the date of last contact, at which point they were censored. All listed authors participated in the enrolment of the patients, and/or data interpretation. The data was processed and analyzed by a statistician who was blinded to the treatment. The author of this manu-

script has full access to the data.

List of cases contribution:

Interventional cardiologists who work at Her Majesty Cardiac Center contributed cases for the registry (ordered alphabetically): operator A = 11 (12.2%), B = 56 (62.2%), C = 2 (2.2%), D = 1 (1.1%), E = 19 (21.1%) and F = 1 (1.1%).

Results

Baseline demographics and lesion characteristics

Among the ninety patients enrolled, baseline demographic and clinical characteristics (Table 1) showed a mean age of 64.2 years; 63.3% were men and 36.7% had a history of diabetes mellitus. Fifty-three percent of our patients had chronic stable angina, 18.8% had prior history of myocardial infarction, and 42.2% had prior treatment with PCI. Baseline lesion characteristics are listed in Table 2. Among 107 lesions treated with Firebird stent implantation, 89% were de novo lesion while 15% were infarct-related arteries. Left main target was 8.4%, 46.8% were left anterior descending artery, 11.2% were in-stent restenotic lesion. Lesion morphology type was B2 in 35.5% and type C in 46.7%. Among the target lesions treated in this cohort, 41.1% had the narrowed segments longer than 20 mm, 14% were located at the ostial segment of the vessel treated, 36.4% were bifurcation, and 14% had small vessel caliber than 2.5mm. Glycoprotein IIb/IIIa were administered in 6.5% of the procedure.

Procedural strategies

For the procedural strategy (Table 3), stents were deployed at 13.6 barr, 15.6% underwent multivessel coronary stenting, 19.3% were direct stenting without pre-dilatation at the target lesion, while 83.2% received post-stent inflation to optimize the scaffolding of the stent to vessel wall at a mean inflation of 15.4 barr. Due to long lesion segment, 23.4% received overlapping stents to cover the lesion length in which 10.3% of these overlapping stents were a combination of either Firebird stent with other drug-eluting stent or with bare metal stent. Overall device success was 100%. The angiographic success (residual % DS $\leq$ 30% with TIMI 3 flow) was observed in 91 (85%) of the treated targets (n = 107).

Post-PCI cardiac markers were collected in nearly all enrolled cases. According to the ARC definition, CK-MB $\geq$ 3X URL (defined as MI) was founded in 13 patients (15.3%) and considered as post-procedural MI (Table 3). After subtracting the cases with MI from the above-mentioned angiographic successes, the net procedural success was achieved in 77.8% of the total cohort (Table 4).

Table 1. Baseline Demographics and Clinical Characteristics of All Treated Patients (n = 90)

Patient characteristics	
Number of patients	90
Age, y (range, mean $\pm$ SD)	34-84, 64.2 $\pm$ 11.0
Age 80-89 y, n (%)	6 (6.7)
Male sex, m (%)	57 (63.3)
Height, cm (range, mean $\pm$ SD)	140-180, 170.0 $\pm$ 8.5
Weight, kg (range, mean $\pm$ SD)	38-95, 65.6 $\pm$ 11.3
Prior coronary artery by pass grafting, n (%)	6 (6.7)
Prior MI, n (%)	17 (18.8)
Prior PTCA, n (%)	38 (42.2)
Left ventricle dysfunction (EF <30%)*, n (%)	5 (5.6)
Stable angina, n (%)	48 (53.3)
STEMI, n (%)	8 (8.9)
Hypertension, n (%)	63 (70.0)
Hypercholesterolemia, n (%)	71 (78.9)
Diabetes mellitus, n (%)	33 (36.7)
Smokers, n (%)	8 (8.9)

*Left ventricular dysfunction (n = 67), the other data were missing. MI = myocardial infarction, PTCA = percutaneous transluminal coronary angioplasty, EF = ejection fraction, STEMI = ST-segment elevation myocardial infarction

Clinical follow-up and clinical driven coronary arteriography

During the first 12 month follow-up, there were 5 cumulative deaths and one patient lost to follow-up. Eighty patients (88.9%) came back for follow-up after 12 months either via office visit, chart review or home call. Mean follow-up was 925.8 days, median 1,041 days (range 225-1,305 days). Thirty-eight patients (42.2%) were eligible for repeat coronary arteriography due to recurrent angina. Binary restenosis (>50% diameter stenosis) was observed in 10 patients (26.3%). Repeat intervention was performed as an intention to treat basis (Table 4).

Primary end point

Table 5 lists the first 30-day MACEs as 16.6%. In detail, there was 1.1% mortality, 16.6% had myocardial infarction, subacute ST (2.2%). One patient had

Table 2. Baseline Lesion Characteristics (n = 107)

Lesion Characteristics	
Number of lesions	107
Lesion location, n (%)	
LM	9 (8.4)
Left anterior descending artery	50 (46.8)
Right coronary artery	34 (31.8)
Left circumflex coronary artery	19 (17.8)
SVG	3 (2.8)
Restenotic lesions, n (%)	12 (11.2)
Infarct-related artery, n (%)	16 (15.0)
B_2 Type, n (%)	38 (35.5)
C Type, n (%)	50 (46.7)
Proximal segment, n (%)	49 (45.8)
Bifurcation lesion, n (%)	39 (36.4)
Chronic total occlusion, n (%)	15 (14.0)
Calcified lesion, n (%)	25 (23.4)
Ostial location, n (%)	15 (14.0)
Small vessel diameter < 2.5 mm, n (%)	15 (14.0)
Long lesion length > 20 mm, n (%)	44 (41.1)
Use GPIIb/IIIa inhibitor, n (%)	7 (6.5)

LM = left main, SVG = saphenous vein graft, GPIIb/IIIa = glycoprotein IIb/IIIa

Table 3. Procedural Characteristics

Procedure characteristics	
Direct stenting	21 (19.3%)
Stent size, mm (mean ± SD)	2.97 ± 0.4
Stent length, mm	21.52 ± 0.8
Post-dilation after stent deployment	89 (83.2)
Dissection at stent edge, n (%)	4 (3.7)
Stent deployment pressure, atm (mean ± SD)	13.6 ± 3.5
Final balloon size, mm (mean ± SD)	3.07 ± 0.5
Final balloon pressure, atm (mean ± SD)	15.4 ± 4.1
Number of stents per patient	1.51
Multivessel coronary intervention, n (%)	18 (16.5)
Overlap stents, n (%)	25 (23.4)
Hybrid stents, n (%)	11 (10.3)
Stent length, range (mean ± SD)	13-100 (27.8 ± 15.7)
Total stent length ≥ 34 mm, n (%)	20 (18.7)
Post-TIMI 3 Flow	107 (100)
Clopidogrel, n (%)	90 (100)
Aspirin, n (%)	88 (98.9)
Post-CK-MB*, ng/ml (mean ± SD)	15.45 ± 53.9
Post-CK-MB* ≥3 xURL, n (%)	13 (15.3)
Post-CK-MB* ≥5 xURL, n (%)	8 (9.4)

*n = 85, the other 5 were missing, xURL =times the upper reference limit

urgent non-TVR on other vessel with in-lesion complication and required urgent CABG (1.1%).

Secondary end points

Table 5 lists the cumulative MACES at 12 months was 18.8%. There were four additional deaths during follow-up. Cumulative death at 12- month follow-up was 5.5%. TLR was 3.3% and non-TLR was 12.2% (Table 5). There was no late ST upon this 12-month follow-up. After 12 months, 4 additional deaths occurred. For univariate analysis, the patients demographic were analyzed, including gender, age, age > 80, atyherogenic risk, patient's symptoms, lesion morphology, vessel size, stent length > 34 mm, CK-MB post PCI, all the procedural parameters. Only shock and smoking history were found to be significance. Then we applied the Cox-regression analysis. Characteristics found to be associated with MACEs in multivariate analysis were shock (p = 0.0001) and smoking history (p = 0.061) (Table 6). The MACE-free survival curve was shown in Fig. 2.

Mortality during registry

Table 7 lists the total 9 deaths. There was one death within 30 days, another 4 deaths were found within 12 months period. There were 4 additional deaths after 12 months. After chart reviewed, we concluded only two cardiac deaths (2.2%) from these nine cumulative deaths.

Discussion

As mentioned, the earlier clinical trials of Cypher SES were promising[1]. This study confirms the longevity of the optimal outcomes observed in patients treated with sirolimus-eluting Bx Velocity stents 4 years after implantation. Cumulative event-free survival rate was 87% for the total population. Grayson et al report the North West Quality Improvement Programme (NWQIP) in Cardiac Intervention PCI registry, in-hospital MACE (death, Q-wave MI, CABS, cerebrovascular accident) was 1.3%. Independent variables identified with an increased risk of developing MACE were advanced age, female sex, cerebrovascular disease, cardiogenic shock and treatment of the left main stem or graft lesions during PCI[12]. In-hospital mortality form NWQIP was 1.3%. However, there is concern that those

Table 4. Acute and Long-term Clinical and Angiographic Outcomes (n = 90)

Efficacy measures, n (%)	Outcome, n (%)
Acute success	
Device	107 (100)
Lesion (Diameter Stenosis ≤ 30 percent)	91 (85)
Procedural (No MACEs)	70 (77.8)
Post procedure lesion characteristics	
Reference vessel diameter, mm (mean ± SD)	3.06 ± 0.5
Minimal luminal diameter, mm (mean ± SD)	2.72 ± 0.5
Percent diameter stenosis (mean ± SD)	10.9 ± 8.0
Acute gain, mm (mean ± SD)	1.44 ± 0.4
Post-procedure ST-elevation MI, n (%)	2 (2.2)
Clinical-driven CAG, n (%)	38 (42.2)
range 5-1081 day	
<30 Day, n (%)	2 (5.3)
31-180 Day, n (%)	9 (23.7)
181-365 Day, n (%)	6 (15.8)
>12 Months, n (%)	21 (55.3)
Binary restenosis, n (%)	10 (26.3)
Follow-up, day (mean ± SD, median, range)	925.8 ± 281.4 (1,041, 225-1,305)

Table 5. Cumulative MACEs at In-Hospital, 30 Days, 365 Days and 1,305 Days

Event	In-Hospital	30-Day	31-365 Day	366-1,305 Day
MACEs, n (%)	13 (14.4)	15 (16.6)	17 (18.8)	-
Death, n (%)	1 (1.1)	1 (1.1)	5 (5.5)	9(10)
Any MI (CK-MB ≥ 3xURL), n (%)	13 (14.4)	15 (16.6)	15 (16.6)	15 (16.6)
ST, n (%)	1 (1.1)	2 (2.2)	2 (2.2)	2 (2.2)
TLR, n (%)	0	2 (2.2)	3 (3.3)	12 (13.3)
CABG, n (%)	0	1 (1.1)	2 (2.2)	2 (2.2)
Non-TVR, n (%)	0	1 (1.1)	11 (12.2)	35 (38.8)

MACEs = major adverse cardiac events, MI = myocardial infarction, xURL =times the upper reference limit, CK-MB = creatine kinase MB, ST = stent thrombosis, TLR = target lesion revascularization, CABG = coronary artery bypass graft surgery, non-TVR = non target vessel revascularization

Table 6. Multivariate Predictors for Cumulative Major Adverse Cardiac Events at Follow-up

	HR (95% CI)	p-value
Smoker	3.11 (1.23-7.84)	0.016
Cardiogenic shock	11.46 (2.95-44.1)	<0.001

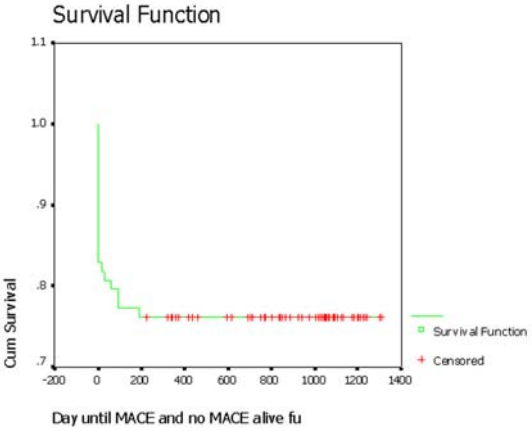

Fig. 2 Kaplan Survival Curve of Major Adverse Cardiac Events

results might not be translated into daily practice. The Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH) registry reported the real world registry of 508 consecutive patients with de novo lesions exclusively treated with SES. Ong et al reported low adverse events after SES implantation in sequential registry of 9.7 percent at one year, and the rate of clinical driven reintervention of 3.7 percent[13]. Rate of MACEs was 15.4 percent at two years follow-up. The two-year risk of target vessel revascularization in the SES group was 8.2%[14]. From our cohort of the use of Firebird SES, which is a non-US sirolimus eluting stent, in all comers who were patients who underwent PCI, the device success and clinical success is acceptable. The deployment of this stent system is safe and effective, despite the unfavorable patient clinical profiles and lesion characteristics as mentioned earlier. Both 30-day and 12-month MACEs were higher than RESEARCH registry at 16.6% and 18.8%. These higher MACEs could be explained from the higher periprocedural MI rate in our cohort. However, there is an inconsistency in the definition used for major adverse events in many clinical trials mentioned earlier which could lead to substantially different results and

Table 7. Clinical Characteristics of the 9 Patients Who Died

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Age, y	65	60	74	41	61	78	81	84	80
Gender	F	M	M	M	F	M	M	F	M
LVEF (%)	> 30	> 30	> 30	> 30	< 30	> 30	> 30	> 30	< 30
DM	No	Yes	No	No	No	Yes	Yes	Yes	Yes
Clinical at index intervention	Late MI	Stable	Stable, old MI	ACS	Stable	ACS, ESRD	ACS, ESRD	ACS	ACS
Location	ostLAD	mRPL	pLAD	mLAD	mLAD	mRCA	OM	LADD	d-RCA, RPD
Overlap stent	Yes	No	No	No	No	No	Yes	No	No
Total stent length, mm	62	23	33	29	23	13	36	18	33
ST	No	No	No	Yes	No	No	No	No	No
Clinical driven coronary angiography	No	No	No	Yes	No	Yes, TVR (CABG) Day 17	No	No	No
Cause of death	Cardiac	Non-cardiac	Unk	Urgent PCI, urgent CABG	Non-cardiac	Non-cardiac Pneu-monia	Non-cardiac	Cardiac	Non-cardiac (pneu-monia)
Time of death after pro-cedure, day	2	63	93	96	193	431	616	975	1134

conclusions[15]. We choose the newly developed consensus criteria for clinical endpoints that may provide more consistency and facilitate the evaluation of the safety and effectiveness of this device, which was proposed by the Academic Research Consortium definition (ARC)[11]. Two different composite MACEs were identified, device safety composite and patient-oriented composite. ARC defined MI as any increased in troponin-T or CK-MB level $\geq$ 3 times the upper reference limit (xURL). Surprisingly 14.4% of our patients had increased CK-MB without angina, but was considered as myocardial infarction, reached end point at 30 day. The other observation was high incidence of diabetes mellitus (36.7%) and small vessel caliber (14.0%) with long lesions (41.1%) in our group, which could explain the rather high cumulative incidence of MACEs at both 30 days and 12 months including the long-term outcomes after follow-up. Secondly, the definition of death in this study is death from all causes, according to the introduction of ARC that considers all-cause mortality the most unbiased method to report deaths in a clinical trial or observational study, even though it may be less specific than deaths adjudicated as cardiac in origin. Death at 30 day was (1.1%) and the cumulative death was 5.5%, which was actually due to the non-cardiac caused in origin.

The non-TLR, non-TVR of this cohort was 12.2% at 12 months and higher (38.8%) at longer follow-up due to the real clinical situation in which patient might complain of more symptoms during the late follow-up period. Eighty patients had complete follow-up, only 1 case was lost to follow-up at 6-month period. The cumulative incidence of MACEs to 1,305 days after implantation was 21.3 percent.

Our study could not show whether predictor of MACEs that reached statistical significance (Table 6). The variables tested to reach statistical significances were shock and the smoking history.

The incidence of clinically driven TLR at 12 months was low (3.3%) and increased to 13.3% after 12 months, which is quite similar to the RESEARCH registry (8.2%). In the RAVEL trial, Morice et al reported some non-significant late catch-up effect was noted in the SES arm, with six TLR versus none in the bare group seen between the one- and three-year follow-ups[2].

Clinical driven coronary arteriography was performed in 38 patients (42.2 percent) due to recurrent angina. The incidence of binary restenosis of those

who consented for controlled coronary arteriography was 26.3%, despite those greater complexities of the subgroup mentioned. Compared to the Firebird registry reported from China, Liu et al reported the pilot study on Firebird stent implantation in 84 patients, cumulative 12 month MACEs was 4.8% and the TLR rate was 2.4%. These results seem to be better than our registry, though the MI definition was different to those defined as ARC[16] Zhang et al[9] reported that in the off-label use of Firebird among 384 patients, the cumulative MACEs free survival at three years was 92%. After 3 years, DM patients had significantly higher rates of MACE (13.7% vs. 6.4%, $p < 0.05$) and TVR (9.8% vs. 4.0%, $p < 0.05$) and the cumulative MACE free survival rate was very significantly much lower in the DM group (86.4% vs. 93.6%, $p < 0.05$). ST occurred in 7 patients (1.4%) at the end of 3 years' follow-up.

In this study, although there was a trend toward fewer events in SES-treated patients after 30-day and between one and two years, the beneficial effect seen with SES at two years was driven primarily by the reduction in events in the first year. Thus, once the important beneficial effect of neointimal suppression had occurred during the period after stenting, the next step was to detect whether a later rebound phenomenon (as seen in porcine models) occurred in humans.

In our registry, we did not observe any late catch-up phenomenon such as seen with radioactive stents and brachytherapy. In fact, during the second year, a trend toward a lower TVR rate was seen. In addition to the previously described events, approximately 12% of patients in our cohort required repeat intervention for progressive disease in a previously non-treated vessel (non-TLR) and the non-TLR rate was even higher later during the follow-up (38.8%). It is imperative that intensive risk factor reduction, both physical and pharmaceutical, is implemented to reduce the potential for progression of remote lesions. Lastly, subacute ST was founded in 2 cases (2.2%), however there was no further ST during long-term follow-up to 1,301 days in our cohort. This is the safety issue regard to the more conflicting report concerning the ST, especially when clopidogrel is discontinued. However, observation and interpretation of this rare and unexpected late complication requires a much larger sample size and longer-term follow-up.

Conclusion

The Firebird SES is the first indigenously designed and evaluated "low cost" DES from Asia to have similar results as the more expensive US brand SES. It promised strong impact in health care system for improving outcomes while limiting health care expenditure in CAD patients.

Limitation of this present study evaluating Firebird SES is the small sample sizes and need for complete controlled coronary arteriography among all enrolled patients and more complexity of the patient subsets and lesion complexities. The real world CAD patients enrolled in this study reflects the necessity to more preventive measures to attack CAD patients at earlier stages.

In conclusion, the implantations of Firebird SES achieve the objective in terms of its safety and efficacy and could be used in all comers who are constrained by limited health care expenditures.

Reference

1. Sousa JE, Costa MA, Abizaid A, et al. Four-year angiographic and intravascular ultrasound follow-up of patients treated with sirolimus-eluting stents. Circulation 2005;111:2326-9.
2. Morice MC, Serruys PW, Sousa JE, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. N Engl J Med 2002;346:1773-80.
3. Meier B, Sousa E, Guagliumi G, et al. Sirolimus-eluting coronary stents in small vessels. Am Heart J 2006;151:1019 e1-7.
4. Moses JW, Leon MB, Popma JJ, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. N Engl J Med 2003;349:1315-23.
5. Moussa I, Leon MB, Baim DS, et al. Impact of sirolimus-eluting stents on outcome in diabetic patients: a SIRIUS (SIRolImUS-coated Bx Velocity balloon-expandable stent in the treatment of patients with de novo coronary artery lesions) substudy. Circulation 2004;109:2273-8.
6. Nakamura S, Muthusamy TS, Bae JH, Cahyadi YH, Udayachalerm W, Tresukosol D. Impact of sirolimus-eluting stent on the outcome of patients with chronic total occlusions. Am J Cardiol 2005;95:161-6.
7. Schofer J, Schluter M, Gershlick AH, et al. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-SIRIUS). Lancet 2003;362:1093-9.
8. Schampaert E, Cohen EA, Schluter M, et al. The Canadian study of the sirolimus-eluting stent in the treatment of patients with long de novo le-

sions in small native coronary arteries (C-SIRIUS). J Am Coll Cardiol 2004;43:1110-5.
9. Zhang Q, Xu B, Yang YJ, et al. Long-term efficacy and safety of Chinese made sirolimus eluting stents: results, including off label usage, from two centres over three years. Chin Med J (Engl) 2008;121:1670-4.
10. Gao H, Yan HB, Zhu XL, et al. Firebird sirolimus eluting stent versus bare mental stent in patients with ST-segment elevation myocardial infarction. Chin Med J (Engl) 2007;120:863-7.
11. Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007;115:2344-51.
12. Grayson AD, Moore RK, Jackson M, et al. Multivariate prediction of major adverse cardiac events after 9914 percutaneous coronary interventions in the north west of England. Heart 2006;92:658-63.
13. Lemos PA, Serruys PW, van Domburg RT, et al. Unrestricted utilization of sirolimus-eluting stents compared with conventional bare stent implantation in the "real world": the Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH) registry. Circulation 2004;109:190-5.
14. Ong AT, van Domburg RT, Aoki J, Sonnenschein K, Lemos PA, Serruys PW. Sirolimus-eluting stents remain superior to bare-metal stents at two years: medium-term results from the Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital (RESEARCH) registry. J Am Coll Cardiol 2006;47:1356-60.
15. Kip KE, Hollabaugh K, Marroquin OC, Williams DO. The problem with composite end points in cardiovascular studies: the story of major adverse cardiac events and percutaneous coronary intervention. J Am Coll Cardiol 2008;51:701-7.
16. Liu HB, Xu B, Gao RL, et al. Outcomes of using Firebird rapamycin eluting stents in routine coronary intervention practice: one-year results from the pilot study of Firebird in China registry. Chin Med J (Engl) 2006;119:609-11.

การประเมินผลการรักษาโรคหลอดเลือดโคโรนารีในผู้ป่วยทุกรายที่ได้รับการสอดฝัง ขดลวดค้ำยันผนังหลอดเลือดเคลือบยาไฟร์เบิรด

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วัตถุประสงค์: *ในปัจจุบันการรักษาผ่านสายสวนหลอดเลือดโคโรนารี เป็นการรักษาหนึ่งใช้กันทั่วไป ในผู้ป่วยหลอดเลือดโคโรนารีตีบตัน ร่วมกับการใช้ขดลวดค้ำยันผนังหลอดเลือดชนิดเคลือบยาต้านการตีบซ้ำ ทำให้ผลการรักษาจริงได้ผลดียิ่งขึ้น ข้อจำกัดได้แก่ขดลวดดังกล่าวมีราคาแพง ผู้วิจัยจะวิจัยผลการรักษาของขดลวดไฟร์เบิรดที่ผลิตจากประเทศจีน ซึ่งยังไม่ทราบผลการรักษาในผู้ป่วยไทยมาก่อน*

วิธีการ: *เป็นการวิจัยแบบไปข้างหน้าโดยใช้ข้อมูลจากทะเบียนการรักษาตั้งแต่เดือน พฤษจิกายน พ.ศ. 2548 ถึง มีนาคม พ.ศ. 2550 เพื่อศึกษาความปลอดภัยและผลการรักษาเมื่อใช้ขดลวดไฟร์เบิรด โดยประเมินผลทางคลินิกขณะอยู่ในโรงพยาบาล ที่ 30 วัน 1 ปี และติดตามผู้ป่วยต่อไปถึงภาวะแทรกซ้อน ทางหัวใจที่รุนแรงได้แก่อัตราเสียชีวิต กล้ามเนื้อหัวใจตายเฉียบพลัน การรักษาซ้ำ และการผ่าตัดต่อทางเบี่ยงหลอดเลือดโคโรนารี*

ผลการวิจัย: *ผู้ป่วย 90 รายได้รับการสอดฝังขดลวดไฟร์เบิรดที่หลอดเลือดโคโรนารี 107 ตำแหน่ง ผลการรักษาที่หลอดเลือดหายดี ร้อยละ 85 (อัตราการตีบน้อยกว่าร้อยละ 30) ไม่มีโรคแทรกซ้อนใด ๆ เท่ากับ ร้อยละ 77.8 ติดตาม ผู้ป่วยนาน 30 วัน เกิดโรคแทรกซ้อนรุนแรง ร้อยละ 16.6 ติดตามต่อไปอีกจนครบ 1 ปี เกิดโรคแทรกซ้อนรุนแรงสะสม ร้อยละ 18.8 ผู้ป่วยเสียชีวิต 9 ราย โดยเสียชีวิตในร.พ. 1 ราย ผู้ป่วย 4 ราย เสียชีวิตที่ 1 ปี และอีก 4 ราย เสียชีวิตเมื่อติดตามนาน 1,305 วัน มีผู้ป่วย 1 ราย เท่านั้นที่ติดตามไม่ได้ ผู้ป่วย 38 ราย (ร้อยละ 42.2) เกิดอาการทางคลินิกจนต้องเข้ารับการตรวจสวนหลอดเลือดหัวใจ พบอัตราตีบซ้ำร้อยละ 26.3 จากการวิเคราะห์ multivariate analysis พบว่าช้อคก่อนหรือระหว่างการรักษามีค่า Odd ratio เท่ากับ 11.46 ที่ค่าความเชื่อมั่นที่ร้อยละ 95 (2.95-44.1), p = 0.001 และภาวะสูบบุหรี่ ค่า Odd ratio เท่ากับ 3.11 ที่ค่าความเชื่อมั่นที่ร้อยละ 95 (1.23-7.84), p = 0.016 จะพยากรณ์การเกิดโรคแทรกซ้อนรุนแรงได้*

สรุป: *การสอดฝังขดลวดค้ำยันผนังหลอดเลือดโคโรนารีด้วยขดลวดไฟร์เบิรดปลอดภัยได้ผลดีในการรักษาผู้ป่วยโดยไม่จำกัดข้อบ่งชี้ อาจเป็นทางเลือกของขดลวดที่ใช้ได้กับผู้ป่วยไทยต่อไป*