EuroIntervention

First human use of the TAXUS Petal paclitaxel-eluting bifurcation stent

John A. Ormiston[1]*, MB, ChB; Thierry Lefèvre[2], MD; Eberhard Grube[3], MD; Dominic J. Allocco[4], MD; Keith D. Dawkins[4], MD

1. Mercy Angiography, Mercy Hospital, Auckland, New Zealand; 2. ICPS, Institut Cardiovasculaire, Paris Sud, Massy, France; 3. HELIOS Heart Center, Siegburg, Germany; 4. Boston Scientific Corporation, Natick, MA, USA

Dr. Ormiston: Principal Investigator, Honoraria, BSC Scientific Advisory Board; Dr. Lefèvre: BSC Speakers Bureau; Dr. Grube: BSC Speakers Bureau, BSC Scientific Advisory Board; Dr. Allocco: Full-time employee and stockholder of BSC; Dr. Dawkins: Full-time employee and stockholder of BSC

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Abstract

Aims: This first human use (FHU) study in bifurcation lesions evaluated safety and feasibility of the TAXUS Petal paclitaxel-eluting dedicated bifurcation stent.

Methods and results: This prospective, single-arm, multicentre study had a composite primary endpoint of 30-day death, myocardial infarction (MI), and target vessel revascularisation (TVR). Angiographic and intravascular ultrasound follow-up was at six months with clinical follow-up through five years. Mean age (N=28) was 60.9±9.3 years and 17.9% of patients had medically treated diabetes. Main branch (MB) lesion length was 13.8±5.9 mm with 4.4±2.5 mm in the side branch (SB). TAXUS Petal was successfully implanted in 89.3% of patients (25/28). On a per device basis, 73.5% (25/34) of Petal deployments were successful. The primary endpoint occurred in one patient (3.7%, in-hospital non–Q-wave MI). Through one year, TVR was 11.1%, target lesion revascularisation was 7.4%, and there were no deaths, Q-wave MIs, or stent thromboses. In-segment late loss (n=21) was 0.47±0.45 mm (proximal MB), 0.41±0.57 mm (distal MB), and 0.18±0.39 mm (SB).

Conclusions: The requirement for rotational alignment made delivery of this first generation TAXUS Petal stent challenging and accounted for the relatively low device delivery success. Clinical and angiographic outcomes were satisfactory when successful delivery was achieved.

** Corresponding author: Mercy Angiography, Mercy Hospital, Newmarket, PO Box 9911, Auckland 1031, New Zealand*
E-mail: johno@mercyangiography.co.nz

Introduction

Coronary bifurcation disease remains one of the outstanding challenges of treatment with percutaneous coronary intervention (PCI), and may account for up to 20% of all lesions encountered in daily practice1. Compared with simple lesions, bifurcations have been associated with lower procedural success rates, higher adverse event rates, and poorer angiographic outcomes[1-3]. The less favourable outcomes associated with bifurcation compared with nonbifurcation lesions may in part result from the inability of current devices and techniques to scaffold adequately and preserve the side-branch (SB) ostium, which is a common site for restenosis[4-6]. Compromise of the SB during stent implantation is also common as many techniques, such as provisional T-stenting, do not allow the operator to maintain a usable wire in the SB[1,2]. The use of drug-eluting stents (DES) has resulted in significantly improved outcomes compared with bare metal stents (BMS)[3]. A variety of dedicated bifurcation stents, both BMS and DES, have been studied with variable results and to date none has become widely used[4]. The TAXUS® Petal™ (Boston Scientific Corporation, Natick, MA, USA) paclitaxel-eluting dedicated bifurcation stent has a side aperture mid-stent with deployable struts to scaffold the SB ostium so as to prevent occlusion after main branch (MB) stenting and deliver paclitaxel to the side-branch ostium, a frequent site of bifurcation restenosis[5]. We describe below the results of the first-human-use (FHU) study intended to evaluate safety and feasibility of this novel drug-eluting dedicated bifurcation stent.

Methods

Device description

The characteristics of the TAXUS Petal dedicated bifurcation stent (Figure 1A) have been described previously[5]. Briefly, this paclitaxel-eluting stent, which is an improved version of the bare metal AST Petal[6], is made of platinum chromium and includes a main branch (MB) section with a side branch (SB) aperture (petal) that provides mechanical scaffolding of the SB ostium by means of outwardly deploying strut elements that extend up to 2 mm. The novel platinum chromium alloy is stronger and more radiopaque than stainless steel alone. In this pilot study of a new device, use of an 8 Fr guide catheter was recommended in the directions-for-use (DFU). The stent delivery system is a dual-side exchange catheter with a MB wire lumen and a SB (side sheath) wire lumen (Figure 1B). Four radiopaque markers assist with proper alignment of stent and petal (Figure 2). A cylindrical-shaped balloon deploys the stent into the MB while a secondary gumdrop-shaped balloon connected to the same inflation lumen deploys the petal into the ostium of the SB. TAXUS Petal uses the same drug and polymer as the TAXUS Express and TAXUS Liberté stents[7]. One stent size (3.0 mm×16 mm) with 1 µg/mm^2 of paclitaxel was available for this study.

Study design and data management

This prospective, single-arm, multicentre study (Clinicaltrials.gov Identifier NCT00497367) was designed to enrol 45-60 patients in two phases. Monitors verified all data and an independent Clinical Events Committee (CEC, Appendix 1) adjudicated events. There was no protocol-mandated roll-in phase. Interim safety and performance criteria in Phase 1 patients were assessed at 30 days, including external input by an Independent Data Reviewer (Appendix 2). A determination was then made as to whether/how to proceed (enrol more complex patients in Phase 2, repeat Phase 1, or end the study). The study was supported by Boston Scientific Corporation.

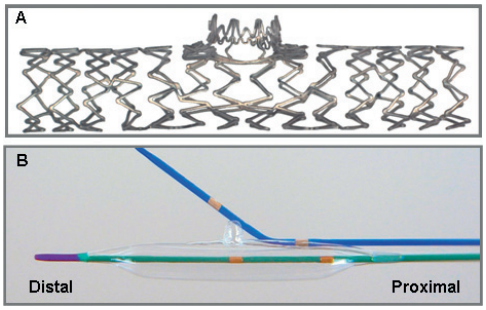

Figure 1. TAXUS Petal stent (A) and delivery system (B).

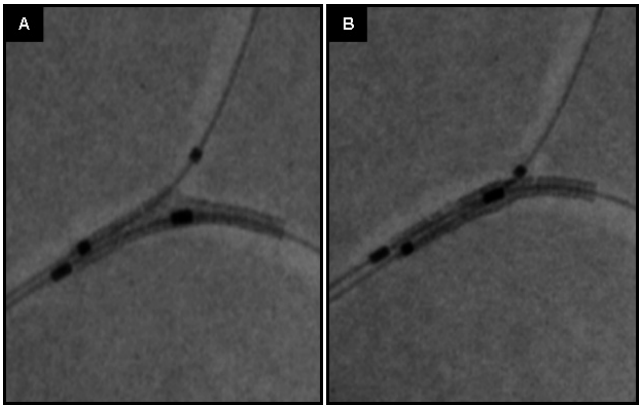

Figure 2. Correct and incorrect alignment of TAXUS Petal stent. Dual balloon and dual wire system with four marker bands ensure correct alignment (A). Figure B is 180° out of alignment.

Patient selection, procedure, and follow-up

Eligible patients (≥18 years) had a *de novo* bifurcation lesion in a native coronary artery and clinical and angiographic indications for PCI. Key lesion inclusion criteria included a bifurcation takeoff angle ≥30° and ≤90°; main branch reference vessel diameter (RVD) ≥3.0 to ≤3.5 mm with MB lesion length ≤20 mm; side branch RVD ≥2.25 to ≤3.5 mm with lesion length ≤14 mm. Placement of one additional planned MB stent and one additional planned SB stent was allowed. A maximum of one non-target lesion, located in a different vessel distribution from the target lesion, could also be treated. The non-target lesion was to be successfully treated first, either with a TAXUS stent or a bare metal stent. Kissing balloon post-dilatation was required for all procedures. Key exclusion criteria included excessive target lesion tortuosity, left main lesions, moderate or severe target lesion calcification, previous treatment of the target vessel with a BMS within nine months of the procedure or at any time with a DES or vascular brachytherapy, documented MI <72 hours before the procedure, cerebrovascular accident <6 months before the procedure, and allergy or contraindication to aspirin, clopidogrel, ticlopidine, platinum, or stainless steel. Study enrolment occurred following successful predilatation of the target lesion.

Before catheterisation patients were pretreated with ≥300 mg aspirin plus ≥300 mg clopidogrel or 500 mg ticlopidine. After the

procedure patients received aspirin at a dose level according to the institutional standard of care for at least one year and 75 mg clopidogrel daily (or 250 mg ticlopidine twice a day) for six months with one year recommended. Clinical follow-up was scheduled at 30 days, six months (both office visits), and then annually through five years (telephone interview allowed).

Follow-up QCA and IVUS were scheduled at six months; IVUS was to be performed in the MB and in the SB if possible. Quantitative coronary angiography (performed using software from Medis Medical Imaging Systems, Leiden, The Netherlands) of the target lesion was performed in accordance with consensus guidelines on analysis of bifurcation lesions[8]. Paired analyses were conducted on patients for whom both procedure and 6-month data were available. All QCA and IVUS data were analysed by independent core laboratories (Appendix 2).

Ethics Review Committees of participating institutions approved the protocol and patients provided written informed consent before enrolment. The study was conducted under Good Clinical Practice conditions and in compliance with regulations for the participating countries.

Endpoints

The primary endpoint was a composite 30-day safety endpoint of death, myocardial infarction (MI), and target vessel revascularisation ([TVR], see Appendix 3 for definitions). Secondary endpoints included device success, technical success, and clinical procedural success (Appendix 3); death, MI, revascularisation, and stent thrombosis (ST) at six months and annually through five years; and quantitative coronary angiography (QCA) and intravascular ultrasound (IVUS) analyses at six months.

Statistical methods

Patient, lesion, procedural characteristics, and event rates were analysed with SAS System Software, Version 8.2 or higher (SAS Institute, Cary, NC, USA) using descriptive statistics for continuous variables and frequency tables or proportions for discrete variables. No formal statistical testing was done in this single-arm, hypothesis-generating study.

Results

Patient, lesion, and procedural characteristics

The TAXUS Petal FHU study enrolled 28 patients total at three sites in New Zealand, France, and Germany (Appendix 4). Baseline demographics and lesion characteristics are shown in Table 1 and Table 2, respectively. Procedural, technical, and device performance are shown in Table 3. The Petal stent was successfully implanted in 25/28 patients (89.3%), reflecting a success rate of 73.5% (25/34) per device attempt. Wire wrap (twisting together of the wires which prevented further stent advancement), wire bias (wire position guiding the stent SB component away from the SB), and the oval cross-sectional shape of the device made it challenging to achieve correct rotational alignment. In all successful cases, however, wire access to the side branch was maintained after deployment. Table 4 provides information on the seven cases where at least one Petal stent was not successfully implanted. In cases with at least one unsuccessful attempt, moderate/severe calcification was more frequent than in cases where the first

Table 1. Baseline clinical characteristics.

Characteristic	All patients (N=28)
Male	82.1% (23)
Age (yr)	60.93±9.32
Cardiac history	
Stable angina	71.4% (20)
Unstable angina	14.3% (4)
Silent ischaemia	14.3% (4)
Left ventricular ejection fraction[a]	66.6±10.7
Previous myocardial infarction	28.6% (8)
Previous percutaneous coronary intervention	28.6% (8)
Previous coronary artery bypass graft	3.6% (1)
Cardiac risk factors	
Current smoking	25.0% (7)
Diabetes, medically treated[b]	17.9% (5)
Hypertension	75.0% (21)
Hyperlipidaemia[c]	81.5% (22)
Family history of coronary artery disease	46.4% (13)

Data are%(n) or mean±SD; a: N=25; b: Insulin and/or oral medication; c: N=27

Table 2. Baseline lesion characteristics.

Characteristic	All patients (N=28)	
Medina classification		
0.1.0	17.9% (5)	
0.1.1	7.1% (2)	
1.0.0	14.3% (4)	
1.0.1	7.1% (2)	
1.1.0	32.1% (9)	
1.1.1	21.4% (6)	
Target lesion vessel		
Left anterior descending artery	78.6% (22)	
Circumflex	7.1% (2)	
Right coronary artery	14.3% (4)	
	Main branch	**Side branch**
Reference vessel diameter (mm)	2.91±0.28	2.23±0.33
Minimum lumen diameter (mm)	1.18±0.38	1.31±0.55
Percent diameter stenosis	59.67±12.33	41.59±20.77
Lesion length (mm)	13.83±5.86	4.35±2.45[a]

Data are % (n) or mean±SD a: N=10 patients who had side branch disease per the Medina classification (core lab determination). Lesion characteristics were determined by quantitative coronary angiography.

Table 3. Procedural characteristics and performance.

Procedural characteristics (N=28)	
Pre-dilatation	100.0% (28)
MB only	53.6% (15)
SB only	0.0% (0)
MB and SB	46.4% (13)
Post-dilatation	100.0% (28)
Number of post-dilatations	1.96±1.48 (28)
Kissing balloon post-dilatation performed successfully	100.0% (28)
Procedure time (min)	70.6±20.1 (28)
Total fluoroscopy time (min)	19.3±9.5 (28)
Total amount of contrast used (mL)	296.5±80.6 (26)
Additional main branch stenting[a]	28.0% (7)[b]
Side branch stenting[c]	25.0% (7)

Table 3. Procedural characteristics and performance.(continued)

Technical performance (N=28)	
Technical success[d]	96.4% (27)
Post procedure % diameter stenosis ≥30% in MB	3.6% (1)
Post procedure % diameter stenosis ≥50% in SB	3.6% (1)
Post procedure TIMI <3 in MB	0.0% (0)
Post procedure TIMI <3 in SB	0.0% (0)
Procedural performance (N=28)	
Clinical procedural success[e]	92.9% (26)
In-hospital death	0.0% (0)
In-hospital myocardial infarction (MI)	3.6% (1)
In-hospital target vessel revascularisation (TVR)	0.0% (0)
Technical failure	3.6% (1)
Device performance (N=28)	
TAXUS Petal stent implanted[f]	89.3% (25)

Data are % (n) or mean±SD (n); a: Among patients with a Petal stent, 28.0% (7/25) received a non-Petal stent in the MB; 57.1% (4/7) of these additional MB stents were unplanned; b: One patient received both a planned and an unplanned additional MB stent; c: Among seven patients with additional SB stents implanted (T-stenting), one stent was unplanned; d: Defined as residual lesion percent diameter stenosis <30% (MB) and <50% (SB ostium) and TIMI flow 3 (MB & SB) attained with any device; e: Defined as no in-hospital death, MI, or TVR associated with MB or SB; f: On a per device basis, 73.5% (25/34) of attempts to place a Petal stent were successful; MB: main branch; SB: side branch; TIMI: thrombolysis in myocardial infarction

attempt was successful (6/7, 85.7% vs. 5/21, 23.8%; P=0.007). Depending on lesion anatomy, additional non-study stents were placed as necessary. Among patients receiving a Petal stent, 28.0% (7/25) received an additional MB stent and 28.0% (7/25) received a SB stent, all of which were TAXUS Liberté.

In Phase 1 of the study (11 July – 21 November, 2007), the Petal stent was successfully implanted in 14/16 patients (87.5%), reflecting a success rate of 14/20 (70.0%) per device attempt. Additionally, device delivery was challenging in several cases where implantation was ultimately successful. After careful consideration of this initial Phase 1 experience, 12 additional patients with lesion criteria as in Phase 1 were enrolled (7 April – 30 June, 2008) to assess whether delivery difficulties improved as operators gained experience with the device. Enrolment in the study was terminated after 28 patients due to shelf-life expiration of study devices.

Clinical outcomes at 30 days, 6-months, and 1-year

Clinical outcomes are shown in Table 5. The composite primary endpoint at 30 days occurred in one patient (3.7%) and consisted of an in-hospital non–Q-wave MI thought to be secondary to stenting over a second side branch. Through one year, the TLR rate was 7.4% (n=2) and there were no deaths, Q-wave MIs, or STs. One of the two TLRs occurred in a Petal stent but the other was in a main branch stent of a patient in whom Petal implantation had failed. The other two patients without Petal stents had no major events. One patient withdrew consent after the unsuccessful Petal implantation.

Table 4. Cases with unsuccessful implantation of a Petal stent.

Pt	MC	TLV	Main branch					Side branch					Petal stent		Non-Petal stent		MACE
			RVD (mm)	LL (mm)	MLD (mm)	% DS	Cal.	RVD (mm)	LL (mm)	MLD (mm)	% DS	Angle	Attempt	Implant	MB	SB	
1	0.1.0	LAD	3.18	9.62	1.42	55.39	Mod.	2.83	8.75	1.86	34.34	30°	2	1	0	0	None
	First Petal stent removed after multiple unsuccessful attempts at delivery. Delivery of second Petal stent challenging, but ultimately successful; technical and procedural success[a] with this second stent.																
2	1.1.0	LAD	3.27	17.79	1.32	59.63	Mod.	2.65	9.81	1.44	45.75	30°	2	1	TL[b]	0	None
	First Petal stent removed after multiple unsuccessful attempts at delivery. Delivery of second Petal stent challenging, but ultimately successful; technical and procedural success[a] with this second stent. Additional MB stent placed as planned after Petal deployment.																
3	1.0.1	LAD	2.68	13.25	1.35	49.44	Mod.	2.10	4.06	0.57	72.86	40°	2	0	TL	0	None
	First Petal stent removed after multiple unsuccessful attempts at delivery. Attempted delivery of second Petal stent also unsuccessful despite numerous attempts. TAXUS Liberté stent placed in MB; residual stenosis of 30% in the MB and 70% in the SB.																
4	1.1.0	R-PDA	2.48	13.44	0.86	65.36	Mod.	2.14	2.02	1.42	33.64	80°	2	0	TL	0	TLR
	First Petal stent removed after multiple unsuccessful attempts at delivery. Attempted delivery of second Petal stent also unsuccessful despite numerous attempts. TAXUS Liberté stent placed in MB with good result. CYPHER stent placed for treatment of in-stent restenosis on day 183 post-procedure.																
5	1.1.1	LAD	3.01	19.61	0.72	76.12	N/M	2.33	4.02	0.71	69.53	35°	2	1	TL[b]	TL	None
	First Petal stent removed after multiple unsuccessful attempts at delivery. Delivery of second Petal stent challenging, but ultimately successful. Additional MB stent placed as planned after Petal deployment.																
6	1.1.0	LAD	2.38	25.57	0.88	63.27	Mod.	1.66	3.90	1.01	39.16	40°	1	0	CY[b]	0	None
	Challenging delivery complicated by dissection and threatened abrupt closure which led to abandonment of attempt at Petal delivery. CYPHER stent placed in MB; technical and procedural success[a]																
7	1.1.1	LAD	2.93	5.57	0.96	67.18	Sev.	2.19	3.75	0.87	60.27	90°	2	1	0	TL	None
	First Petal stent could not be positioned correctly; technical and procedural success[a] with second stent																

a: Defined in Appendix 3; b: Two stents were placed; Cal.: calcification; CY: CYPHER; DS: diameter stenosis; LAD: left anterior descending artery; LL: lesion length; MACE: major adverse cardiac events; MB: main branch; MC: Medina classification (core lab determination); MLD: minimum lumen diameter; Mod.: moderate; N/M: none/mild; Pt: patient; R-PDA: right posterior descending artery; RVD: reference vessel diameter; SB: side branch; Sev.: severe; TL: TAXUS Liberté; TLR: target lesion revascularisation; TLV: target lesion vessel

Table 5. Clinical outcomes.

Outcome (N=28)	30 Days (N=27)	6 Months (N=27)	1 Year (N=27)
All death, MI, or TVR	3.7% (1)	14.8% (4)	14.8% (4)
All death	0.0% (0)	0.0% (0)	0.0% (0)
Myocardial infarction	3.7% (1)	3.7% (1)	3.7% (1)
Q-wave MI	0.0% (0)	0.0% (0)	0.0% (0)
Non–Q-wave MI	3.7% (1)[a]	3.7% (1)[a]	3.7% (1)[a]
TVR, overall[b]	0.0% (0)	11.1% (3)	11.1% (3)
TLR, overall	0.0% (0)	7.4% (2)[c]	7.4% (2)[c]
TLR, main branch	0.0% (0)	7.4% (2)	7.4% (2)
TLR, side branch	0.0% (0)	3.7% (1)	3.7% (1)
TVR, non-TLR	0.0% (0)	3.7% (1)	3.7% (1)
Stent thrombosis[d]	0.0% (0)	0.0% (0)	0.0% (0)

Data are cumulative for each time point; a: Thought to be secondary to stenting over a second side branch; b: All TVR were percutaneous coronary interventions; c: One TLR occurred at 183 days (in a non-Petal stent) and one at 185 days post intervention; one TLR involved both the main branch and the side branch; d: Per Academic Research Consortium definitions definite/probable[20]; Data are binary rates; MI: myocardial infarction; TLR: target lesion revascularisation; TVR: target vessel revascularisation

QCA and IVUS results

At six months, angiographic follow-up among patients who received the Petal stent was 84% (21/25); QCA results are presented in Table 6. In-segment late loss was 0.47±0.45 mm (proximal MB), 0.41±0.57 mm (distal MB), and 0.18±0.39 mm (SB). Among patients with binary restenosis, MB restenosis was located just proximal to the Petal stent (two cases) or in the body of the Petal stent distal to the SB aperture (two cases). Side branch restenosis was at the SB ostium (two cases, one of which occurred in one of the patients with proximal MB restenosis). None of these cases of restenosis were related to placement of a second nearby/overlapping stent. As shown in Table 7, there were no cases of incomplete stent apposition observed with IVUS post-procedure or at 6-months. Mean lumen area in the SB was 3.83±2.14 (n=15) post-procedure and 3.72±0.97 (n=12) at 6-month follow-up.

Discussion

This FHU study evaluated safety and clinical performance of the TAXUS Petal bifurcation stent, which was designed to provide mechanical scaffolding and drug delivery to the SB ostium. Results showed that treatment is feasible in bifurcation lesions though the requirement for rotational alignment made delivery more challenging than with conventional stents. Through one year the TLR rate was 7.4% (2/28) with no deaths, Q-wave myocardial infarctions, or stent thromboses. In-segment late loss at six months was 0.47 mm in the proximal MB, 0.41 in the distal MB, and 0.18 mm in the SB. Binary restenosis was 9.5%. Net volume obstruction was 11.4% in the MB and 7.8% in the SB. Thus, as assessed by 1-year clinical follow-up and 6-month QCA and IVUS, outcomes were satisfactory with the TAXUS Petal stent in patients where successful delivery was achieved.

There are few clinical data available with other drug-eluting dedicated bifurcation stents[4]. AXXESS Plus is a biolimus-eluting, self-expanding nitinol stent designed for the treatment of bifurcation

Table 6. Quantitative coronary angiography outcomes.

	Main branch (MB) Proximal	Main branch (MB) Distal	Side branch (SB)
Pre-procedure (N=28)			
Reference vessel diameter (mm)	3.32±0.39	2.51±0.30	2.23±0.33
Minimum lumen diameter (mm)	1.28±0.59	1.08±0.55	1.31±0.55
Percent diameter stenosis	61.72±16.70	56.72±20.74	41.59±20.77
MB-SB angulation (degrees)	NA	NA	48.57±16.99
Post-procedure (N=28)			
Reference vessel diameter (mm)	3.31±0.37	2.48±0.33	2.22±0.34
Minimum lumen diameter, in-stent (mm)	3.04±0.30a	2.67±0.29	NA
Minimum lumen diameter, analysis segment (mm)	2.83±0.41	2.25±0.37	1.70±0.38
Acute gain, in-stent (mm)	1.74±0.57[a]	1.59±0.55	NA
Acute gain, analysis segment (mm)	1.55±0.61	1.17±0.58	0.39±0.45
Percent diameter stenosis, in-stent	8.68±7.86[a]	–8.73±13.26	NA
Percent diameter stenosis, analysis segment	14.59±7.53	9.53±7.20	23.08±13.66
MB-SB angulation (degrees)	NA	NA	46.96±13.83
6-months (N=21)[b]			
Reference vessel diameter (mm)	3.13±0.34	2.43±0.29	2.11±0.29
Minimum lumen diameter, in-stent (mm)	2.55±0.26[c]	2.05±0.57	NA
Minimum lumen diameter, analysis segment (mm)	2.31±0.55	1.89±0.56	1.61±0.47
Late loss, in-stent (mm)	0.44±0.26[c]	0.62±0.60	NA
Late loss, analysis segment (mm)[d]	0.47±0.45	0.41±0.57	0.18±0.39
Percent diameter stenosis, in-stent	18.34±8.61[c]	15.17±22.43	NA
Percent diameter stenosis, analysis segment	26.33±16.00	22.40±20.41	23.91±19.87
MB-SB angulation (degrees)	NA	NA	46.00±14.10
Binary restenosis, in-stent	0.0% (0)[c]	9.5% (2)	NA
Binary restenosis, analysis segment	9.5% (2)	9.5% (2)	9.5% (2)

Data are mean ±SD;% (n); a: N=27; b: The three patients who did not receive a Petal stent plus four patients who did receive a Petal stent did not return for angiographic follow-up and are not included here; c: N=20; d: Late loss in the SB was 0.05±0.47 mm (n=7) among patients with SB disease per the Medina classification and 0.24±0.34 mm (n=14) among those without SB disease; NA: not applicable or data not available

Table 7. Intravascular ultrasound outcomes.

	Main branch	Side branch[a]
Post-procedure		
Incomplete stent apposition	0.0% (0/23)	0.0% (0/15)
Minimum lumen diameter (mm)	2.44±0.29 (23)	1.78±0.78 (15)
Vessel area (mm^2)	16.26±3.19 (23)	11.43±3.20 (13)
Stent area (mm^2)	7.77±1.09 (23)	4.38±1.48 (15)
Lumen area (mm^2)	7.77±1.09 (23)	3.83±2.14 (15)
6-month follow-up		
Incomplete stent apposition	0.0% (0/19)	0.0% (0/12)
Minimum lumen diameter (mm)	2.17±0.57 (19)	1.98±0.27 (12)
Vessel area (mm^2)	17.38±3.01 (19)	10.85±3.21 (10)
Stent area (mm^2)	7.97±1.11 (19)	4.03±0.83 (12)
Lumen area (mm^2)	7.06±1.12 (19)	3.72±0.97 (12)
Neointimal area (mm^2)	0.91±0.53 (19)	0.31±0.53 (12)
In-stent net volume obstruction (%)	11.40±6.48 (19)	7.81±12.07 (12)

Data are % (n/N) or mean±SD (n); a: Difficulty passing the IVUS catheter into the side branch limited the number of patients.

lesions. In the first human use study (N=139), overall 6-month TLR was 7.5%, MI was 6.0%, and stent thrombosis was 2.2%[9]. In the follow-on single-arm, non-randomised DIVERGE study (N=302) at nine months TLR was 4.3%, MI was 4.3% and stent thrombosis was 1.0%[10]. Additional stenting, mostly DES, of one or both branches was performed in the majority of patients. It should be noted that the bifurcation lesions treated with Petal were less complex than in AXXESS and DIVERGE.

Dedicated bifurcation stents are not widely used in everyday practice and conventional stents remain the mainstay for PCI of bifurcation lesions. While variations in bifurcation anatomy preclude a single overarching approach, results from DES randomised controlled trials and registry data have supported the provisional strategy of stenting the MB and performing balloon angioplasty in the SB, with SB stenting reserved for cases where the initial SB result is suboptimal[11-17]. Routine DES implantation in both branches appears to offer no clear advantage over the provisional method with respect to restenosis in the MB or SB or repeat bifurcation revascularisation. With its projecting petal elements TAXUS Petal is designed to support the SB which may make the provisional stenting procedure safer by both maintaining wire access to the SB, and in addition, avoiding carina shift[18] during the intervention. Furthermore, long term outcomes may also improve through SB ostial support and minimisation of gaps between stents if a SB stent is required. As such, the support provided by the petal may preclude the requirement for a second stent or facilitate its placement if needed.

The results described here suggest that the Petal approach has promise, though the delivery difficulties must first be overcome. It became apparent during the course of the study that meticulous attention to wire management was important to maximise the likelihood of successful delivery. Passive rotational alignment was limited by the oval cross-sectional nature of the device. A major limitation to passive rotational alignment was wire bias where the wire curving into the SB directed the SB component of the stent away from the SB. Use of more or less stiff wires also at times reduced wire bias and enabled successful delivery. If wire wrap was observed or suspected, withdrawal of either the MB or SB wire into the Petal stent and subsequent re-advancement of the wire frequently resolved wire wrap and facilitated successful delivery of the stent though it should be noted that this approach may lead to an inability to re-access the vessel in the presence of dissection. In some cases, however, this first generation of the Petal stent could not be delivered despite the best efforts of an experienced operator. An improved version of the Petal stent incorporating a torquable shaft and a modified delivery system is under development. These modifications may make it easier for the operator to successfully deliver the device.

Limitations

Limitations to this study include the small number of patients typical of a first human use study which was insufficient to provide accurate estimates of clinical event rates, relatively low lesion complexity, and the absence of a randomised control group. The single available stent size made it difficult to enrol patients and some who met the enrolment criteria had limited SB disease. Additionally, because this study did not prospectively assign a particular SB treatment method, the use of additional stents was at operator discretion, resulting in a heterogeneous study population. Limitations of dedicated bifurcation devices in general include larger crossing profiles (8 Fr guide calibre for TAXUS Petal recommended in the DFU) with less flexibility compared with conventional stents. In addition, the requirement for two wires introduced new challenges to delivery and rotational alignment such as wire twisting (wrap) and wire bias, which sometimes may be addressed by careful guide wire management[19]. The oval cross sectional shape of the device also limited passive rotational alignment.

Conclusions

In this FHU study the TAXUS Petal dedicated bifurcation stent was delivered with an acceptable success rate though the requirement for rotational alignment made delivery more challenging than with conventional stents. Clinical, QCA, and IVUS outcomes were satisfactory in patients where successful delivery was achieved.

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Appendices

Appendix 1. Clinical events committee members.

Donald E. Cutlip, MD, Chair
Beth Israel Deaconess Medical Center, Boston, MA, USA

Julian Aroesty, MD
Beth Israel Deaconess Medical Center, Boston, MA, USA

Manish Chauhan, MD
Texas Cardiovascular Consultants, PA, Austin, TX, USA

Germano DiSciascio, MD
Campus Bio-Medico University, Rome, Italy

Kalon Ho, MD
Beth Israel Deaconess Medical Center, Boston, MA, USA

Joseph Kannam, MD
Beth Israel Deaconess Medical Center, Boston, MA, USA

Michel Vandormael, MD
Tampa Bay Heart Institute, Largo, FL, USA

Appendix 2. Sponsor and study personnel.

Sponsor: Boston Scientific Corporation, Natick, MA, USA

Angiography Core Lab: Beth Israel Deaconess Medical Center, Boston, MA, USA

Intravascular Ultrasound Core Lab: MedStar Research Institute, Washington, DC, USA

Independent Data Reviewer: Adam Greenbaum, MD, Farmington Hills, MI, USA

Appendix 3. Cardiac event and procedural definitions in the TAXUS Petal first human use study.

CARDIAC EVENT

Event: Myocardial infarction (MI)

Definition: Myocardial infarction was defined as follows:

1. Q-wave MI: Development of new (i.e., not present on the subject's ECG before allocation) pathological Q-waves in two or

more leads lasting ≥0.04 seconds with CK-MB/troponin levels elevated above normal.

2. Non-Q-Wave MI: Elevation of post-procedure CK levels >2x ULN with positive CK or, if the assay for CK-MB was not performed, elevation of CK levels >2x ULN with positive troponin.

Drawing a CK-MB or troponin was mandated if CK was greater than 2x ULN. If no CK-MB or troponin was drawn, CK >2x ULN was considered an MI. ULN was determined per local laboratory specifications.

For subjects undergoing bypass surgery post-procedure, a perioperative MI was defined as follows:

a) Total CK-MB >5x upper limits of local laboratory normal -OR-

b) Presence of new pathologic Q waves (as defined above)

Event: Stent thrombosis

Definition: Academic Research Consortium definitions definite/probable[20]

Event: Target lesion revascularisation (TLR)

Definition:

Target lesion revascularisation was defined as any ischaemia-driven repeat percutaneous intervention (to improve blood flow) of the target lesion or bypass surgery of the target lesion.

A target lesion revascularisation was considered ischaemia-driven if the target lesion diameter stenosis was ≥50% by QCA and any of the following were present:

1. The subject has a positive functional study corresponding to the area served by the target lesion.
2. The subject has ischaemic ECG changes at rest in a distribution consistent with the target lesion.
3. The subject has ischaemic symptoms referable to the target lesion.

A target lesion revascularisation for a lesion with a diameter stenosis <50% might also be considered ischaemia-driven by the CEC if there was a markedly positive functional study or if there were ECG changes corresponding to the area served by the target lesion.

A target lesion revascularisation was considered as ischaemia-driven if the lesion diameter stenosis was ≥70% even in the absence of clinical or functional ischaemia.

An ischaemia-driven TLR was considered if the angiogram and TLR would have been performed for clinical indications in the absence of this protocol.

Event: Target vessel revascularisation (TVR)

Definition: Target vessel revascularisation was defined as any ischaemia-driven repeat percutaneous intervention (to improve blood flow) of the target vessel or bypass surgery of the target vessel.

A target vessel revascularisation was considered ischaemia-driven if the target vessel diameter stenosis was ≥50% by QCA and any of the following were present:

1. The subject has a positive functional study corresponding to the area served by the target vessel.
2. The subject has ischaemic ECG changes at rest in a distribution consistent with the target vessel.
3. The subject has ischaemic symptoms referable to the target lesion.

A target vessel revascularisation for a lesion with a diameter stenosis less than 50% might also be considered ischaemia-driven by the CEC if there was a markedly positive functional study or if there were ECG changes corresponding to the area served by the target lesion.

PROCEDURAL EVENT

Event: Clinical procedural success

Definition: Technical success with no in-hospital death, MI or TVR associated with the MB or SB

Event: Device success

Definition: Successful delivery and deployment of the stent to the target lesion, including petal deployment and apposition in the SB with no petal balloon rupture or stent embolisation, and successful retrieval of the stent delivery system with <30% MB stenosis and <50% stenosis in the SB ostium

Event: Technical success

Definition: <30% MB stenosis and <50% SB ostium stenosis with TIMI flow 3 (MB & SB) attained with any device

CEC: Clinical Events Committee; CK: creatine kinase; ECG: electrocardiogram; MB: main branch; QCA: quantitative coronary angiography; SB: side branch; ULN: upper limit of normal

Appendix 4. Investigators and institutions participating in the TAXUS Petal first human use study.

John Ormiston, Principal Investigator, Mercy Hospital and Auckland City Hospital, Auckland, New Zealand

Thierry Lefèvre, Institut Cardiovasculaire, Paris Sud, Massy, France

Eberhard Grube, Helios Klinikum Siegburg, Siegburg, Germany

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