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Dedicated Bifurcation Stent for the Treatment of Bifurcation Lesions Involving Large Side Branches

Outcomes From the Tryton Confirmatory Study

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ABSTRACT

OBJECTIVES The aim of this study was to prospectively study and confirm the safety and efficacy of the Tryton Side Branch Stent in the treatment of coronary artery bifurcations involving large side branches (SBs).

BACKGROUND The TRYTON Pivotal randomized controlled trial (RCT) was designed to compare the Tryton stent with standard provisional SB stenting in large vessels. The trial inadvertently enrolled patients with too small SBs (<2.25 mm). The overall trial did not meet its primary endpoint, because of an increased rate of periprocedural myocardial infarction in the Tryton stent arm. A post hoc analysis restricted to the intended population showed that the trial would have met its endpoint if only patients with SBs ≥2.25 mm in diameter (by core laboratory quantitative coronary angiography) had been enrolled.

METHODS The Tryton Confirmatory Study was a prospective, single-arm extension of the TRYTON Pivotal RCT that enrolled an additional 133 patients treated with the Tryton Side Branch Stent. It was designed to confirm the results of the post hoc analysis and emphasized the inclusion of appropriately sized SBs. The primary endpoint was noninferiority with regard to periprocedural myocardial infarction (creatine kinase myocardial band 3 times the upper limit of normal) compared with a performance goal based on the TRYTON Pivotal RCT.

RESULTS Among the 133 enrolled patients, 132 (99.2%) had SBs ≥2.25 mm. Baseline clinical and angiographic parameters were similar in this study and the RCT. Periprocedural myocardial infarction occurred in 10.5% of patients, which was numerically lower than the provisional group in the TRYTON Pivotal RCT (11.9%). The 95% confidence bounds did not extend beyond the pre-defined performance goal of 17.9%, meeting the noninferiority primary endpoint.

CONCLUSIONS The Tryton Confirmatory Study, in conjunction with the post hoc analysis of the intended population in the TRYTON Pivotal RCT, supports the safety and efficacy of the Tryton Side Branch Stent for treatment of bifurcation lesions involving large SBs. (J Am Coll Cardiol Intv 2016;9:1338–46) © 2016 by the American College of Cardiology Foundation.

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Bifurcation lesions are common and represent up to 20% of coronary lesions treated with percutaneous coronary intervention (PCI) (1,2). Bifurcation PCI is associated with a lower procedural success rate and a higher risk for adverse cardiac events (1,2). Data from multiple randomized controlled trials (RCTs) support a provisional 1-stent strategy over a systematic 2-stent strategy for bifurcation lesions (3–11); however, none of these studies was restricted to true bifurcation lesions involving large side branches (SBs).

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The Tryton Pivotal RCT compared a dedicated bare-metal stent, designed to specifically secure and treat the bifurcation SB, with SB balloon angioplasty alone (provisional stenting) for the treatment of de novo true bifurcation lesions (12). The intended study population was specified as patients with bifurcations involving large SBs (≥2.5 mm by visual assessment); however, more than one-half of the enrolled lesions had diameters <2.25 mm by quantitative coronary angiography (QCA). This corresponds to a lesion <2.5 mm by visual assessment (12). The trial failed to show noninferiority to balloon angioplasty alone with regard to its primary endpoint, target vessel failure (a composite of cardiac death, myocardial infarction, and target vessel [main vessel or SB] revascularization), despite superior angiographic results (lower diameter stenosis) at 9 months (12). The failure to meet the primary endpoint was due mainly to an increased incidence of periprocedural myocardial infarction (PPMI) in the Tryton stent group. A post hoc analysis of the intended population restricted to lesions involving SBs with a reference vessel diameter ≥2.25 mm demonstrated superior angiographic results and a numeric reduction in target vessel failure within the noninferiority margin; however, because of the nature (retrospective, non-prespecified) of this subanalysis, an additional prospective study was required to validate these findings (13).

The Tryton Confirmatory Study was designed in collaboration with the U.S. Food and Drug Administration to: 1) confirm the results seen in the intended population of the Tryton Pivotal RCT (patients with a reference diameter ≥2.25 mm); and 2) confirm the ability of physicians to enroll appropriate patients (with appropriately sized SBs).

ABBREVIATIONS AND ACRONYMS

MB = main branch

PCI = percutaneous coronary intervention

PPMI = periprocedural myocardial infarction

QCA = quantitative coronary angiography

RCT = randomized controlled trial

SB = side branch

METHODS

STUDY POPULATION. Inclusion and exclusion criteria were the same as in the Tryton Pivotal RCT and have been described in detail (7). Briefly, patients with symptoms or objective evidence of ischemia due to a significant (≥50% narrowing) true bifurcation lesion (Medina classification 1,1,1; 1,0,1; or 0,1,1) (14) located in a de novo native coronary artery with an SB 2.5 to 3.5 mm in diameter and a main branch (MB) 2.5 to 4.0 mm in diameter were enrolled. Lesion length was restricted to ≤28 mm in the MB (treatable with a single stent) and ≤5 mm in the SB. Lesion evaluation was based on visual estimates of the baseline angiography. Important exclusion criteria were 1) ST-segment elevation myocardial infarction within 72 h or non-ST-segment elevation myocardial infarction within 7 days preceding the index procedure; 2) left ventricular ejection fraction <30%; 3) impaired renal function (serum creatinine >2.5 mg/dl or >221 mmol/l) or current dialysis treatment; 4) left main coronary artery disease (protected or unprotected); 5) trifurcation lesions; 6) a total occlusion of the target vessel (MB or SB); 7) severely calcified lesion(s); 8) the presence of excessive tortuosity; and 9) angiographic evidence of thrombus.

STUDY DEVICE AND IMPLANTATION. The Tryton stent is a dedicated bare-metal cobalt chromium thin-strutted SB stent mounted on a standard stent delivery balloon. The Tryton stent has 3 zones: 1) an SB zone (5.5 to 6.5 mm) to be deployed within the SB; 2) a transition zone (4.5 mm) to be positioned at the SB ostium; and 3) an MB zone (8 mm) (**Figure 1**).

The implantation technique includes the following steps: 1) lesion preparation (SB pre-dilation was mandated and MB pre-dilation was optional); 2) placement of the Tryton Side Branch Stent in the SB; 3) placement of a commercially available drug-eluting stent in the MB; and 4) simultaneous final kissing balloon inflation. Implantation of an unplanned

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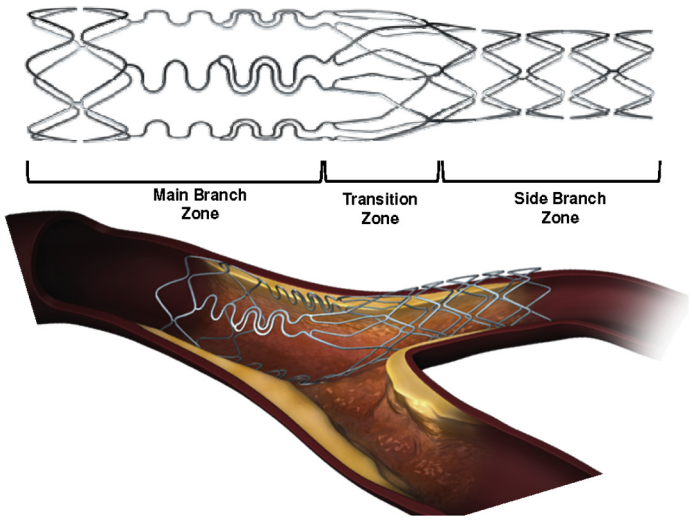
FIGURE 1 The Tryton Side Branch Stent



The Tryton Side Branch Stent is a cobalt chromium, thin-strut, bare-metal stent that is composed of 3 zones: 1) side branch (SB) zone; 2) transition zone; and 3) main branch (MB) zone. The SB zone is a conventionally slotted tube for insertion into the SB. The transition zone is composed of 3 panels that flare and rotate to accommodate a wide spectrum of bifurcation angle and large variation in SB and proximal MB diameters. When used in conjunction with a main vessel stent, the Tryton Side Branch Stent is designed to provide adequate radial strength and coverage across the carina. The MB zone has a minimal metal-to-artery ratio that is intended as an open path for an MB stent that will lock the Tryton Side Branch Stent in place. The Tryton stent is mounted on a standard balloon delivery system; sizes available during the time of the study were (MB/SB) 2.5/2.5 mm, 3.0/2.6 mm, 3.5/2.5 mm, 3.5/3.0 mm, and 4.0/3.5 mm.

additional stent in the SB was allowed in cases of TIMI (Thrombolysis in Myocardial Infarction) flow grade <3, vessel dissection type B or worse, or residual stenosis >80%.

STUDY DESIGN. The Tryton Confirmatory Study was a prospective single-arm extension of the Tryton Pivotal RCT that enrolled an additional 133 patients treated with the Tryton Side Branch Stent and an approved drug-eluting stent in the MB. The study mirrored the Tryton Pivotal RCT protocol, which has previously been described in detail (12). The study was approved by the Institutional Review Board at each participating site, and all patients provided written informed consent.

All serious adverse events were adjudicated by an independent clinical events committee (Harvard Cardiovascular Research Institute, Boston, Massachusetts). A data and safety monitoring board had access to all study data. All data were analyzed by independent consulting biostatisticians. An independent angiographic core laboratory (Cardiovascular Research Foundation, New York, New York) analyzed all angiograms using a conventional single-vessel algorithm analysis. All patients were required to receive dual-antiplatelet therapy (unless they developed contraindications) for 12 months. Clinical assessment was performed at 30 days and 12 months post-enrollment. The study emphasized proper SB selection (i.e., SB reference diameter ≥2.5 mm by visual assessment).

STUDY ENDPOINTS. The primary endpoint was PPMI after PCI, defined as creatine kinase myocardial band elevation >3 times the upper limit of normal within 48 h after PCI. Patients were compared against a performance goal derived in close collaboration with the Food and Drug Administration from the corresponding rate from the angioplasty-only arm (provisional approach) in the intention-to-treat and per protocol analysis populations in the TRYTON Pivotal RCT (12,13). Only patients with SBs ≥2.25 mm by QCA were included in calculating the performance goal. This rate was then adjusted upward by 6.0% to allow for sample variability, resulting in a performance goal of 17.9% (11.9% + 6.0%). Noninferiority of the Tryton Side Branch Stent was defined as a 1-sided 95% confidence bound of the PPMI rate that did not exceed this performance goal.

Secondary endpoints included the following: all-cause and cardiac mortality, myocardial infarction, major adverse cardiac events (a composite of death, myocardial infarction, emergent bypass surgery, or target lesion revascularization), target vessel failure (cardiac death, target vessel myocardial infarction, or target vessel revascularization), and stent thrombosis. Secondary angiographic endpoints included device success (<30% residual stenosis in the SB) and lesion success (<50% residual stenosis).

STATISTICAL ANALYSIS. The primary endpoint was evaluated by the approximate normal method. Continuous data are presented as mean ± SD and were compared using analysis of variance and the modified Student *t* test or the Kruskal-Wallis test, as appropriate. Categorical variables were compared using the chi-square or Fisher exact test. We performed statistical analyses using SAS version 9.1 (SAS Institute, Cary, North Carolina) and considered p values <0.05 to indicate statistical significance.

RESULTS

PATIENTS AND ENROLLMENT. From July 2014 to July 2015, the Tryton trial enrolled 133 patients from 28 sites (13 in the United States and 15 in Europe). Of those patients, 132 (99.2%) had SB diameters ≥2.25 mm as assessed by QCA. The baseline clinical

characteristics of the patients are presented in Table 1 alongside the patients in the RCT who had SB diameters ≥2.25 mm by QCA. No significant differences were present in baseline characteristics, except for the prevalence of hypertension, which was significantly more common in the Tryton Confirmatory Study population compared with the Tryton SB group (but not the provisional group) of the RCT. In contrast to the RCT, which enrolled about 10% patients with non-true bifurcation lesions, all study patients had true bifurcation lesions (Table 2).

PROCEDURAL AND ANGIOGRAPHIC OUTCOMES. Among the 133 enrolled patients, 132 (99.2%) received the study stent in the SB. Procedure, device, and lesion success rates were significantly higher with the Tryton stent in both the confirmatory study and the RCT compared with patients who had the provisional strategy ($p < 0.001$ for all) (Table 3). The need for additional stenting in the SB (bailout stenting) was required in 3 patients (2.3%; 1 dissection, 2 inadequate lesion coverage) who received the Tryton stent. Procedures were on average longer and required more contrast and radiation when the Tryton stent strategy was used compared with the provisional 1-stent strategy (Table 3).

CLINICAL OUTCOMES. Clinical outcomes are summarized in Table 4. No patient died during the procedure or within 30 days post-procedure. The primary endpoint, PPMI, occurred in 10.5% of the patients. This was numerically lower than the provisional group in the Tryton Pivotal RCT (11.9%) (Figure 2). The 95% confidence bounds did not extend beyond the pre-defined performance goal of 17.9%, and the noninferiority primary endpoint was met.

TABLE 1 Baseline Clinical Characteristics

	Confirmatory Study	RCT With Side Branch Diameter ≥2.25 mm			
	Tryton (n = 133)	Tryton (n = 146)	Provisional (n = 143)	p Value*	p Value†
Age, yrs	65.6 ± 9.5	64.5 ± 10.7	65.2 ± 9.2	0.36	0.72
Male	93/133 (69.9)	116/146 (79.5)	117/143 (81.8)	0.07	0.02
Current smoker	28/133 (21.1)	25/146 (17.1)	22/142 (15.5)	0.40	0.23
Diabetes mellitus	34/132 (25.8)	37/146 (25.3)	41/143 (28.7)	0.94	0.79
Hypertension	34/132 (82.0)	100/146 (68.5)	109/142 (76.8)	<0.001	<0.001
Hypercholesterolemia	94/132 (71.2)	104/144 (72.2)	107/139 (77.0)	0.85	0.47
Previous myocardial infarction	43/133 (32.3)	43/145 (29.7)	57/141 (40.4)	0.63	0.60
Previous PCI	53/133 (39.8)	54/146 (37.0)	62/143 (43.4)	0.62	0.96
Previous CABG	3/133 (2.3)	5/145 (3.4)	5/143 (3.5)	0.55	0.50
Previous TIA/CVA	9/133 (6.8)	13/146 (8.9)	8/143 (5.7)	0.51	0.69
History of congestive heart failure	8/133 (6.0)	2/146 (1.4)	0/143 (0.0)	0.04	<0.001
Atrial fibrillation	10/133 (7.5)	18/146 (12.3)	12/143 (8.4)	0.18	0.35
Left ventricular ejection fraction, %	56.3 ± 9.5	57.1 ± 9.4	56.8 ± 10.7	0.48	0.68
Clinical presentation					
Stable angina	98/133 (73.7)	108/146 (74.0)	98/143 (68.5)	0.96	0.61
Unstable angina	24/133 (18.0)	28/146 (19.2)	34/143 (23.8)	0.81	0.42
Functional test showing ischemia	34/53 (64.2)	50/81 (61.7)	46/72 (63.9)	0.78	0.85
Access site					
Femoral	71/133 (53.4)	94/146 (64.4)	88/143 (61.5)	0.06	0.06
Radial	62/133 (46.6)	51/146 (34.9)	55/143 (38.5)	0.047	0.053
Other	0/133 (0.0)	1/146 (0.7)	1/143 (0.7)	0.34	0.34
Number of vessels with ≥50% stenosis					
1	84/133 (63.2)	91/146 (64.4)	90/143 (61.5)	0.89	0.92
2	46/133 (34.6)	47/146 (32.2)	39/143 (27.3)	0.67	0.32
3	3/133 (2.3)	8/146 (5.5)	14/143 (9.8)	0.17	0.03
Medina classification					
1,1,1	95/133 (71.4)	95/146 (65.2)	94/143 (65.7)	0.25	0.22
1,0,1	15/133 (11.3)	26/146 (17.8)	21/143 (14.7)	0.12	0.18
0,1,1	23/133 (17.3)	24/146 (16.4)	27/143 (18.9)	0.85	0.93
1,1,0 or 1,0,0 or 0,1,0 or 0,0,1	0/133 (0.0)	1/146 (0.7)	1/143 (0.7)	0.34	0.34
Antiplatelet therapy pre-loading before index procedure	118/133 (88.7)	127/146 (87.0)	119/143 (83.2)	0.66	0.32

Values are mean ± SD or n/N (%). *Tryton group in the confirmatory study versus Tryton group in the RCT. †Tryton group in the confirmatory study versus provisional group in the RCT.

CABG = coronary artery bypass graft surgery; CVA = cerebrovascular accident; PCI = percutaneous coronary intervention; RCT = randomized controlled trial; SB = side branch; TIA = transient ischemic attack.

TABLE 2 Quantitative and Qualitative Angiographic Findings at Baseline and After Procedure

	Confirmatory Study	RCT With Side Branch Diameter ≥2.25 mm			
	Tryton (n = 133)	Tryton (n = 146)	Provisional (n = 143)	p Value†	p Value‡
True bifurcation*	133/133 (100)	132/146 (90.4)	132/143 (92.3)	<0.001	<0.001
Main branch					
Vessel location					
Left anterior descending	100/133 (75.2)	104/146 (71.2)	94/143 (65.7)	0.46	0.17
Left circumflex	27/133 (21.1)	29/146 (19.9)	36/143 (25.2)	0.93	0.70
Right	5/133 (3.8)	13/146 (8.9)	13/143 (9.1)	0.08	0.07
Baseline					
Reference vessel diameter, mm	3.12 ± 0.37	3.09 ± 0.35	3.06 ± 0.34	0.49	0.16
MLD, mm	0.93 ± 0.35	1.12 ± 0.39	1.05 ± 0.38	<0.001	0.007
Diameter stenosis, %	70.21 ± 10.41	63.82 ± 11.96	65.62 ± 11.52	<0.001	<0.001
Lesion length, mm	17.23 ± 7.89	16.14 ± 6.84	16.05 ± 6.53	0.22	0.18
Thrombus	2/133 (1.5)	0/146 (0.0)	2/143 (1.4)	0.23	0.59
Tortuosity					
Moderate	6/133 (4.5)	0/146 (0.0)	3/143 (2.1)	0.009	0.02
Severe	1/133 (0.8)	0/146 (0.0)	2/143 (1.4)	0.29	0.95
Calcification					
Moderate	24/133 (18.0)	17/146 (11.6)	22/143 (15.4)	0.13	0.22
Severe	15/133 (11.3)	3/146 (2.1)	5/143 (3.5)	0.002	<0.001
Post-procedure					
Reference vessel diameter, mm	3.18 ± 0.44	3.16 ± 0.36	3.11 ± 0.35	0.68	0.15
In-segment MLD, mm	2.42 ± 0.41	2.50 ± 0.35	2.49 ± 0.36	0.08	0.13
In segment diameter stenosis, %	23.74 ± 8.45	20.62 ± 7.29	19.82 ±7.59	0.001	<0.001
In-stent MLD, mm	2.74 ± 0.39	2.89 ± 0.38	2.82 ± 0.34	0.001	0.07
In-stent diameter stenosis, %	13.50 ± 8.68	20.62 ± 7.29	19.82 ± 7.59	<0.001	<0.001
In-segment acute gain, mm	1.49 ± 0.48	1.38 ± 0.46	1.45 ± 0.44	0.052	0.47
In-stent acute gain, mm	1.81 ± 0.47	1.77 ± 0.46	1.78 ± 0.40	0.47	0.57

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DISCUSSION

Drawn from 133 additional patients, the Tryton Confirmatory Study confirmed and extended the finding of the large SB post hoc analysis of the Tryton Pivotal RCT. The principal findings of the Tryton Confirmatory Study are as follows: 1) among patients undergoing PCI of true bifurcation lesions with an SB diameter ≥2.25 mm, the Tryton 2-stent strategy was noninferior to the standard 1-stent provisional approach in terms of PPMI; and 2) appropriate selection of patients who may benefit from receiving the Tryton Side Branch Stent is possible.

The intention-to-treat analysis of the Tryton Pivotal RCT demonstrated that the Tryton Side Branch Stent was associated with superior angiographic outcomes but failed to meet the pre-specified noninferiority criteria (12). The high rate of the composite endpoint, target vessel failure, in the Tryton group was driven by a higher incidence of PPMI. A closer look at the data revealed that 59% of the patients had SBs that were smaller than the pre-specified inclusion criteria. These patients had a disproportionally high incidence of procedure-related creatine kinase myocardial band elevation (13). Patients with too small SBs assigned to the provisional (control) group were treated with appropriately sized angiography balloons, whereas those assigned to the Tryton group were treated with a stent mounted on an oversized balloon. A post hoc analysis of the intended study population (i.e., patients with SB diameters ≥2.25 mm) instead showed a numeric reduction in target vessel failure, which was within the pre-specified noninferiority margin, and superior angiographic outcomes at 9 months (13). The present study, which was designed in collaboration with the Food and Drug Administration to validate the post hoc analysis, confirms the safety and efficacy of the Tryton Side Branch Stent for the treatment of bifurcation lesions with SBs ≥2.25 mm in diameter.

The Tryton Side Branch Stent is the first dedicated bifurcation stent to be compared head to head with the provisional technique in a multicenter RCT. The Tryton Pivotal RCT was also the largest RCT to exclusively studied bifurcation lesions (12). The pivotal randomized trial (12) and its large SB post hoc analysis (13), in conjunction with the present study, not only demonstrate the safety and efficacy of the Tryton Side Branch

TABLE 2 Continued

	Confirmatory Study	RCT With Side Branch Diameter ≥2.25 mm			
	Tryton (n = 133)	Tryton (n = 146)	Provisional (n = 143)	p Value†	p Value‡
Side branch					
Vessel location					
Left anterior descending	100/133 (75.2)	106/146 (72.6)	93/143 (65.0)	0.62	0.18
Left circumflex	28/133 (21.1)	27/146 (18.5)	37/143 (25.9)	0.59	0.80
Right	5/133 (3.8)	13/146 (8.9)	13/143 (9.1)	0.08	0.055
Baseline					
Reference vessel diameter, mm	2.49 ± 0.20	2.53 ± 0.23	2.52 ± 0.22	0.12	0.24
MLD, mm	0.89 ± 0.31	1.06 ± 0.34	1.15 ± 0.35	<0.001	<0.001
Diameter stenosis, %	64.15 ± 12.15	58.13 ± 12.74	54.11 ± 14.34	<0.001	<0.001
Lesion length, mm	5.94 ± 2.53	4.80 ± 1.24	4.60 ± 0.86	<0.001	<0.001
Thrombus	0/133 (0.0)	0/146 (0.0)	0/143 (0.0)	–	–
Tortuosity					
Moderate	12/133 (9.0)	0/146 (0.0)	0/143 (0.0)	<0.001	<0.001
Severe	2/133 (1.5)	0/146 (0.0)	2/143 (1.4)	0.14	0.42
Calcification					
Moderate	11/133 (8.3)	7/146 (4.8)	6/143 (4.2)	0.24	0.12
Severe	2/133 (1.5)	1/146 (0.7)	2/143 (1.4)	0.51	0.68
Angulation, °					
0–45	109/133 (82.0)	128/146 (87.7)	108/143 (75.5)	0.18	0.94
>45–90	24/133 (18.0)	16/146 (11.0)	32/143 (22.4)	0.09	0.72
>90	0/133 (0.0)	2/146 (1.4)	3/143 (2.1)	0.18	0.13
Post-procedure					
Reference vessel diameter, mm	2.55 ± 0.25	2.61 ± 0.26	2.54 ± 0.27	0.050	0.75
In-segment MLD, mm	2.26 ± 0.32	2.33 ± 0.27	1.74 ± 0.48	0.051	<0.001
In segment diameter stenosis, %	11.32 ± 8.44	10.71 ± 6.82	30.89 ± 18.78	0.51	<0.001
In-stent MLD, mm	2.47 ± 0.34	2.59 ± 0.27	–	0.001	–
In-stent diameter stenosis, %	2.98 ± 9.80	0.57 ± 8.24	–	0.028	–
In-segment acute gain, mm	1.37 ± 0.41	1.26 ± 0.36	0.59 ± 0.48	0.02	<0.001
In-stent acute gain, mm	1.58 ± 0.43	1.53 ± 0.36	–	0.30	–

Values are n/N (%) or mean ± SD. *Medina classification 1,1,1; 1,0,1; or 0,1,1 as per angiographic core laboratory analysis. †Tryton group in the confirmatory study versus Tryton group in the RCT. ‡Tryton group in the confirmatory study versus provisional group in the RCT.

MLD = minimal lumen diameter; RCT = randomized controlled trial.

Stent but also offer insights regarding what bifurcations should be treated with such technology. Indeed, although provisional stenting should be the treatment of choice for small SBs (<2.5 mm by visual assessment) that supply small myocardial territories, large SBs represent a condition in which acute, short-term, and midterm patency of an SB could be seen as extremely important. Indeed, among the 279 patients with SBs ≥2.25 mm receiving Tryton stents from both the Tryton Confirmatory Study and the Tryton Pivotal RCT, the need for an additional stent in the SB was 4-fold lower compared with patients undergoing a provisional approach (1.4% vs. 5.6%). Paired with the superior 9-month angiographic patency (12), these findings are extremely important, especially if bifurcation stenting is envisioned for even larger SBs, such as the left main coronary artery.

Procedural, device, and lesion success were significantly higher with the Tryton stent compared with the provisional approach. Specifically, achievement of final diameter stenosis <30% with the intended initial strategy (~95% for the Tryton stent vs. ~35% for the provisional approach) was superior in the Tryton group compared with the provisional arm. In contrast, procedures with the Tryton Side Branch Stent were longer, with more contrast used compared with the provisional approach. Actually, Tryton Side Branch Stent implantation took about 10 minutes more and required about 30 ml more contrast on average. This finding is not surprising, considering that the Tryton Side Branch Stent represents a true "2-stent" approach, compared with the provisional strategy, being the simplest "1-stent approach"; however, when compared with the data from landmark studies using a 2-stent approach such as the Nordic-Baltic Bifurcation Study IV, procedural time, fluoroscopic time, and amount of contrast were similar (15). That being said, procedural length and

TABLE 3 Procedural and Device Characteristics

	Confirmatory Study	RCT With Side Branch Diameter ≥2.25 mm			
	Tryton (n = 133)	Tryton (n = 146)	Provisional (n = 143)	p Value§	p Value‖
Procedure success*	117/131 (89.3)	125/143 (87.4)	95/142 (66.9)	0.62	0.003
Device success†	122/130 (93.8)	135/143 (94.4)	51/142 (35.9)	0.84	<0.001
Lesion success‡	133/133 (100)	141/141 (100)	120/142 (84.5)	–	<0.001
Pre-dilation of the main vessel	124/133 (93.2)	129/144 (89.6)	114/142 (80.3)	0.28	0.02
Pre-dilation of the side branch	131/133 (98.5)	139/146 (95.2)	86/138 (62.3)	0.12	<0.001
Final kissing balloon technique					
Attempted	133/133 (100)	134/146 (91.8)	128/143 (89.5)	<0.001	<0.001
Not attempted	0/133 (0.0)	7/146 (4.8)	11/143 (7.7)	0.01	0.001
Unsuccessful	9/133 (6.8)	5/146 (3.4)	4/143 (2.8)	0.20	0.12
Tryton stent successfully delivered	132/133 (99.2)	142/146 (97.3)	1/143 (0.7)	0.21	<0.001
2.5/2.5 × 19 mm	9/132 (6.8)	81/142 (5.6)	–	<0.001	–
3.0/2.5 × 19 mm	53/132 (40.2)	40/142 (28.2)	–	0.04	–
3.5/2.5 × 19 mm	36/132 (27.3)	51/142 (35.9)	1/1 (100.0)	0.12	–
3.5/3.0 × 18 mm	32/132 (24.2)	40/142 (28.2)	–	0.46	–
4.0/3.5 × 18 mm	2/132 (1.5)	3/142 (28.2)	–	0.71	–
Additional stent in side branch	3/133 (2.3)	1/146 (0.7)	8/143 (5.6)	0.27	0.76
Nontarget lesion treated	10/133 (7.5)	21/146 (14.4)	23/143 (16.1)	0.07	0.003
Additional nonstudy stent implanted					
0	107/133 (80.5)	109/146 (74.7)	100/143 (69.9)	0.25	0.09
1	23/133 (17.3)	29/146 (19.9)	33/143 (23.1)	0.58	0.36
2	2/133 (1.5)	6/146 (4.1)	7/143 (4.9)	0.19	0.16
≥3	1/133 (0.8)	2/146 (1.4)	3/143 (2.1)	0.62	0.67
Bare metal stent	2/30 (6.7)	3/47 (6.4)	0/56 (0.0)	0.96	0.34
Drug-eluting stent	28/30 (93.3)	44/47 (93.6)	56/56 (100.0)	0.96	0.34
Adjunctive devices	2/133 (1.5)	3/146 (2.1)	1/143 (0.7)	0.73	0.92
Rotational atherectomy	0/2 (0.0)	0/3 (0.0)	1/1 (100.0)	–	0.44
Cutting or AngioSculpt balloon	0/2 (0.0)	0/3 (0.0)	0/1 (0.0)	–	–
Other	2/2 (100)	3/3 (100.0)	0/1 (0.0)	–	0.44
Procedure time, min	64.6 ± 26.2	68.7 ± 30.1	55.9 ± 27.3	0.22	0.007
Fluoroscopic time, min	23.3 ± 11.4	24.0 ± 13.8	11.6 ± 5.4	0.64	<0.001
Contrast volume, ml	248.2 ± 85.6	269.2 ± 98.3	227.0 ± 88.7	0.058	0.044

Values are n/N (%) or mean ± SD. *Achievement of final in-stent diameter <50% in side branch with assigned study device. †Achievement of final in-stent residual stenosis <30% (by quantitative coronary angiography) in side branch using the assigned study device without malfunction. ‡Achievement of final in-stent diameter of <50% (by quantitative coronary angiography) within the side branch. §Tryton group in the confirmatory study versus Tryton group in the RCT. ‖Tryton group in the confirmatory study versus provisional group in the RCT.

RCT = randomized controlled trial.

resource use should be weighed against the benefits of acute and midterm (9-month) SB patency.

The Tryton Pivotal RCT and the subsequent Tryton Confirmatory Study are studies with a unique design and scientific process that illustrate important concepts in RCT planning: 1) the importance of selecting a clinically appropriate target population; 2) the importance of enrolling the intended population from which the scientific hypothesis was derived; and 3) the importance of selecting clinically meaningful endpoints. Similar to our study, many other trials have initially failed to meet their primary endpoints (16-18) to subsequently succeed (19,20) after readjustments of the targeted population or the primary endpoints, leading to approval for the population in which the study device or drug was shown to be favorable. However, designing trials on the basis of subgroup findings may not always confirm the initial subgroup results (21,22), illustrating the need and value for well-conducted, prospective studies to validate or invalidate subgroup findings. The Tryton Confirmatory Study used a unique design, combining the rigor of a prospective registry with identical inclusion and exclusion criteria as the Tryton Pivotal RCT with the statistical advantages of using a historical cohort as the comparator (i.e., the control group in the Tryton Pivotal Trial as the performance goal).

STUDY LIMITATIONS. First, this study was not an RCT; however, the inclusion and exclusion criteria were identical to the recently conducted Tryton

TABLE 4 Adverse Events During the Procedure and at 30 Days

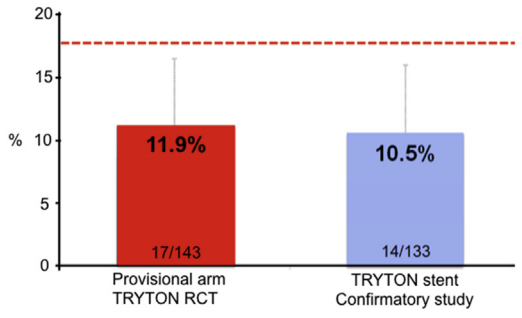
	Confirmatory Study	RCT With Side Branch Diameter ≥2.25 mm			
	Tryton (n = 133)	Tryton (n = 146)	Provisional (n = 143)	p Value†	p Value‡
Procedure					
Myocardial infarction	10.5 (14)	8.2 (12)	11.9 (17)	0.51	0.88
30 days					
Target vessel failure*	10.5 (14)	8.2 (12)	11.9 (17)	0.51	0.88
Death	0.0 (0)	0.0 (0)	0.0 (0)	–	–
Cardiac death	0.0 (0)	0.0 (0)	0.0 (0)	–	–
Noncardiac death	0.0 (0)	0.0 (0)	0.0 (0)	–	–
Target vessel myocardial infarction	10.5 (14)	8.2 (12)	11.9 (17)	0.51	0.88
Q-wave	1.5 (2)	0.7 (1)	0.0 (0)	0.51	0.51
Non-Q-wave	6.8 (9)	7.5 (11)	11.9 (17)	0.80	0.32
Clinically driven TVR	1.5 (2)	0.7 (1)	0.0 (0)	0.51	0.51
ARC-defined stent thrombosis	1.5 (2)	0.7 (1)	0.0 (0)	0.51	0.51

Values are % (n). *Composite of cardiac death, target vessel myocardial infarction, and clinically driven target vessel revascularization; revascularization. †Tryton group in the confirmatory study versus Tryton group in the RCT. ‡Tryton group in the confirmatory study versus provisional group in the RCT.

ARC = Academic Research Consortium; RCT = randomized clinical trial; TVR = target vessel revascularization.

Pivotal RCT. Therefore, a reliable optimal performance goal could be defined (on the basis of the group that was randomized to the provisional approach in the RCT). Second, only short lesions (<5 mm) with diameter stenoses >50% were enrolled. Whether our results can be extrapolated to more diffuse or physiologically significant (as assessed by fractional flow reserve) SB disease remains to be shown. Third, whether the use of the Tryton Side Branch Stent is cost effective, in light of procedure time, contrast use, and utilization of other resources was not addressed in this study. Last, the Tryton Side Branch Stent is a bare-metal stent. Whether a drug-eluting version would be superior remains to be established.

FIGURE 2 Primary Endpoint: Periprocedural Myocardial Infarction



Incidence of the pre-specified primary endpoint, periprocedural myocardial infarction, in patients enrolled in the Tryton Confirmatory Study **(blue)** compared with patients randomized to the provisional 1-stent control group in the Tryton Pivotal randomized controlled trial (RCT) **(red)**. Error bars represent 95% confidence limits, and the **dotted red line** indicates the pre-defined performance goal of 17.9%. Noninferiority to this performance goal was met (p = 0.014).

CONCLUSIONS

The Tryton Confirmatory Study, assessing the safety of the Tryton Side Branch Stent in the treatment of bifurcation lesions involving large SBs, met its primary endpoint (performance goal) related to PPMI. This finding confirms the safety and efficacy of the Tryton Side Branch Stent in the treatment of bifurcation lesions involving a large SB. In light of the higher procedural success rate, improved acute angiographic results, and higher rate of SB patency at 9-month follow-up compared with provisional stenting, the Tryton Confirmatory Study and the Tryton Pivotal RCT support the use of the dedicated Tryton Side Branch Stent in conjunction with standard drug-eluting stent in the treatment of bifurcation lesions involving large SBs.

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PERSPECTIVES

WHAT IS KNOWN? A post hoc analysis of the Tryton IDE randomized trial restricted to lesions involving large SBs (≥2.25 mm) demonstrated superior angiographic results and a numeric reduction in target vessel failure when the dedicated bifurcation Tryton stent was used compared with a stenting provisional strategy.

WHAT IS NEW? The Tryton confirmatory study prospectively confirmed the safety and efficacy of the dedicated bifurcation Tryton stent in the treatment of bifurcation lesion involving large SBs.

WHAT IS NEXT? Future investigation studying a drug-eluting stent version of the Tryton stent, especially for left main bifurcation lesion, or use in combination with bioresorbable vascular scaffold, are needed and could potentially improve long-term outcomes of such complex patient population.

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KEY WORDS bifurcation, PCI, side branch, stent, Tryton dedicated bifurcation stent