Percutaneous coronary interventions of bifurcation lesions
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Chapter 4

The Tryton Side Branch Stent™ for the treatment of coronary bifurcation lesions

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Chapter 4

ABSTRACT

Coronary bifurcation lesions account for approximately 15 percent of all percutaneous coronary interventions (PCI) performed. Although clinical outcomes after PCI have been improved considerably, PCI of bifurcation lesions remains to be associated with adverse clinical events, when compared with non-bifurcation PCI. Therefore, several dedicated bifurcation devices have been developed to improve clinical outcomes. The Tryton Side Branch Stent™ is such device and is used in combination with a regular tubular balloon expandable stent in the main branch. Multiple single and multicenter registries and a patient pooled analysis including 900 patients have shown promising results regarding clinical outcomes after bifurcation PCI with Tryton. The pivotal Tryton IDE randomized trial is currently underway comparing the Tryton stent with side branch balloon angioplasty as side branch treatment in bifurcation lesions challenging the current dogma of provisional single stent strategy as treatment for coronary bifurcation lesions.
INTRODUCTION

Coronary bifurcation lesions account for approximately 15 percent of all percutaneous coronary interventions (PCI) performed. Although clinical outcomes have been improved with drug-eluting stents (DES), PCI of bifurcation lesions is still associated with the occurrence of in-stent restenosis and stent thrombosis (ST) when compared with non-bifurcation lesions. The current consensus to treat bifurcation lesions is to use the single stent approach with provisional stenting of the side branch (SB) as bailout in cases were this is deemed necessary (in case of SB flow compromise or significant (ostial) stenosis with ST-segment elevations for instance). This consensus is based on multiple randomized trials comparing single- with two-stent techniques. However, this current dogma of single stenting has recently been criticized because patients with extensive SB disease, requiring proper revascularization of the SB (see figure 1), were most likely excluded from those trials, while a considerable amount of patients without SB involvement have been randomized to an unnecessary complex two stent strategy.

To aim for improvement of clinical outcomes after bifurcation stenting, several dedicated bifurcation stents have been developed. Most of these devices are main branch (MB) stents crossing the SB allowing easy SB access and providing some sort of ostial SB scaffolding, facilitating the provisional single stenting approach. Although clinical results from some of these devices seem to be very promising, clinical results are limited to small registry studies and none of these devices are currently compared with regular balloon-expandable (drug-eluting) stents in a randomized trial. Other dedicated bifurcation devices are SB stents facilitating a two-stent approach rather than the single-stent approach. The Tryton Side Branch Stent™ (Tryton Medical, Durham, NC, USA) is such device and is a SB first stent, which is used in combination with a regular DES in the MB. The stent is currently being investigated in the Tryton IDE randomized trial comparing the device with balloon angioplasty as SB treatment, both in combination with DES in the MB. This makes the Tryton stent the first, and thus far the only, dedicated bifurcation stent which challenges the current dogma of provisional single stenting in the setting of a highly controlled randomized trial. In the current report we will describe the device and discuss the available clinical data so far.

INTRODUCTION TO THE DEVICE

Specifications

The Tryton Side Branch Stent is a slotted-tube balloon expandable stent. The stent is made of cobalt-chromium with a strut thickness of 84 micron (0.0033”). Currently, only a bare metal version is available. The stent is 5 or 6 Fr-compatible (depending on the stent
Figure 1. Case example of a bifurcation lesion with extensive side branch involvement, treated with Tryton Side Branch Stent. Panel (A) shows a ramus circumflex (RCx) - marginal branch coronary bifurcation lesion with extensive side branch (SB) disease. Because the side branch was considered the ‘culprit,’ a provisional single stent strategy of the main branch (MB) was considered inappropriate and the chosen strategy was to approach this lesion with a multi-stent strategy. Both branches were wired and the SB ostium predilated, after which the Tryton Side Branch Stent was positioned from the proximal RCx into the marginal branch and successfully deployed (B). Note that the stent is mounted on a tapered balloon (B and C). After Tryton placement there were still stenoses distally in the marginal branch and in the distal MB (D). An everolimus DES was advanced through the Tryton into the SB (E) and deployed without difficulties (F). Hereafter, an everolimus DES was advanced into the RCx through the proximal MB zone of Tryton, crossing the side branch (G). After final kissing balloon inflation (I), the final angiogram showed an excellent result (J). Figure from Grundeken et al, Int J Cardiol 2013.
size, see table 1) using a single rapid exchange system over a conventional 0.014” guide-wire. The stent is mounted on a single delivery balloon either with a uniform diameter of 2.5 mm or with stepped diameters ranging from 2.5 to 3.5 mm in the SB and 3.0 to 4.0 mm in the MB (table 1). The stent is available in different lengths: the regular Tryton stent is 19 mm in length (18 mm for the larger sizes), while the recently developed short version has a length of 15 mm (only available for larger diameter sizes).

| Table 1. Available stent sizes of the Tryton Side Branch Stent |
|-------------------------|------------------|-----------------|-----------------|-----------------|-----------------|
| Balloon               | Diameter (mm)   | Length (mm)    | Recommended guiding catheter | Nominal pressures (atm) | RBP (atm) |
| Regular Tryton        | SB - MB          |                 |                             |                               |           |
| Straight              | 2.5 - 2.5        | 19              | 5Fr                         | 8                             | 14        |
| Stepped               | 2.5 - 3.0        | 19              | 5Fr                         | 10                            | 14        |
| Stepped               | 2.5 - 3.5        | 19              | 5Fr                         | 10                            | 14        |
| Tryton: larger sizes  |                 |                 |                             |                               |           |
| Stepped               | 3.0 - 3.5        | 18              | 6Fr                         | 8                             | 14        |
| Stepped               | 3.5 - 4.0        | 18              | 6Fr                         | 10                            | 14        |
| Tryton short:         |                 |                 |                             |                               |           |
| Stepped               | 3.0 - 3.5        | 15              | 6Fr                         | 8                             | 14        |
| Stepped               | 3.5 - 4.0        | 15              | 6Fr                         | 10                            | 14        |

Atm: atmosphere, MB: main branch, RBP: rated burst pressure, SB: side branch,

**Tri-ZONE design**

The stent design consists of three zones (the "Tri-ZONE™ technology"), a distal SB zone, a central transition zone and a proximal main branch zone (figure 2) 16, 17. The distal SB zone has the standard design of a conventional tubular balloon expendable stent and scaffolds the SB. It has four circumferential out-of-phase zigzag hoops linked together by one (small stent size) or two (larger stent sizes) connectors. The central transition zone consists of three panels, which can be independently deformed to accommodate to a wide range of carinal anatomy. The transition zone should be placed at the level of the carina and provides both scaffolding and coverage of the SB ostium. The proximal main branch zone is composed of three undulating fronds terminating in the proximal circumferential “wedding” band, connecting the wedding bands with the panels of the transition zone. The function of the proximal zone is to anchor the stent in the proximal MB using the wedding bands while minimizing the amount of metal and allowing easy delivery of the MB stent.
First, both the main and side branch are wired and predilated in one or both branches, according to operator’s preferences, after which the Tryton stent is advanced into the SB. The stent delivery system has four radio-opaque markers for optimal positioning of the stent: the distal and proximal markers indicating the distal and proximal end of the stent and the two middle markers indicating the transition zone. The stent is positioned in such a way that the carina lies in-between the two middle markers, without the need for rotational orientation (see figures 1 and 3). After deployment of the stent, it is generally recommended to postdilate the proximal part of the Tryton stent to ensure adequate apposition of the wedding bands to the vessel wall. Hereafter, the guidewire positioned
in the SB is retracted and advanced into the distal MB in-between the fronds of Tryton’s proximal MB zone, which is facilitated by the specific design of this part of the stent with the paucity of struts simplifying recrossing. After adequate advancement of the wire into the distal MB, the ‘trapped’ MB wire could be retracted. Then, the MB is predilated according to operator’s preference and a regular DES is advanced and deployed in the MB, crossing the SB. Finally, it is recommended to advance a guidewire into the SB, fenestrating the MB stent struts, finalizing the procedure with final kissing balloon inflation, although final kissing can not be achieved in about 20% of the cases in daily clinical practice 18 (Figure 3).

**Figure 3.** Deployment sequence of the Tryton Side Branch Stent for a de novo coronary bifurcation lesion. (A) First, both branches are wired. (B) Predilatations of the side branch (and main branch) are performed according to the operator’s discretion. (C) Positioning of the Tryton stent is done by using the two middle radio-opaque markers (arrows) on the delivery system, ensuring that the carina is in-between these two markers. (D) After accurate positioning, the stent is deployed after which the delivery system is removed (note the taperd design of the delivery balloon). (E) A deployed Tryton stent. After deployment, the guidewire in the side branch (the green wire) is retracted and advanced into the proximal main branch. (F, G and H) A workhorse stent is positioned and placed in the main branch. (I) The procedure is completed with final kissing balloon inflation. Figure from Grundeken et al, EuroIntervenion 2013.

**CLINICAL PROFILE AND POST-MARKETING FINDINGS**

**First-in-man study**

The first-in-man (FIM) trial enrolled 30 patients in three centers from different European countries with stable coronary artery disease and a de novo coronary bifurcation lesion 19,20. Six-month clinical follow-up was available in all patients. Angiographic success, defined as <30% residual stenosis and Thrombolysis In Myocardial Infarction (TIMI) 3 flow in both MB and SB post-procedure, was achieved in 96.7%. Six-month major adverse cardiac event (MACE, defined as the composite of cardiac death, myocardial infarction (MI), coronary bypass graft surgery (CABG) or target lesion revascularization (TLR)) rate was 9.9%. Two patients experienced an MI (6-month MI rate of 6.6%) and only one a TLR.
(6-month TLR rate of 3.3%). No cases of ST were observed. Angiographic follow-up at 6 months was performed in 23 (78%) patients. Quantitative coronary angiography (QCA) demonstrated a late lumen loss (LLL) of only 0.17±0.35 in the SB, which was comparable to the LLL in the proximal (0.25±0.43) and distal (0.00±0.31) MB. No restenosis of the SB was observed. This study showed that the technique is safe and feasible. A limitation of the study was that half of the patients (47%) were treated for a bifurcation lesion in which the SB was not significantly involved (Medina 2 1.0.0, 1.1.0, and 0.1.0), which might be an explanation for the comparable LLL of the bare-metal Tryton compared with that of the DES in the MB.

**Registries**

**Rotterdam-Poznan registry**
In the Rotterdam-Poznan registry, two centers (Rotterdam, The Netherlands, and Poznan, Poland) collaborated and combined their clinical registry data including 96 patients with 100 bifurcation lesions in their study. The aim of the study was to investigate the performance of the Tryton stent in a more “real-world” setting. In contrast with the FIM, more complex lesions and patients were evaluated, including patients presenting with ST-segment elevation MI (STEMI), left main bifurcation lesions, saphenous vein graft/native vessel anastomoses, and chronic total occlusions. Furthermore, the vast majority of patients (76%) had significant disease in the SB (i.e. Medina 0.0.1, 1.0.1, 0.1.1, and 1.1.1). Angiographic success (<30% residual stenosis and TIMI 3 flow in MB and SB post-procedure) rate was 95%, while procedural success (angiographic success in the absence of in-hospital MACE) rate was 94%. The median duration of follow-up was six months. MACE (cardiac death, MI, CABG or TLR) occurred in eight patients (8%). Only three experienced an MI (3%), while TLR was observed in 4 patients (4%). Again, no ST was observed. This study confirmed the promising results of the FIM study and showed that similar clinical results could be achieved in daily clinical practice.

**eTryton registry**
The eTryton registry study is a European multi-center study including 302 patients from 15 centres with stable coronary artery disease undergoing PCI of a coronary bifurcation disease using the Tryton stent. Procedural success (Tryton deployment at the intended site without in-hospital MACE) was 94.4%. Six-month follow-up was available for 296 patients (98%). MACE (cardiac death, MI, and TLR) occurred in 19 patients (6.4%), with 14 patients experiencing an MI (of which 11 periprocedural and three spontaneous). TLR occurred in only 10 patients (3.4%), while only one ST was observed (0.3%). This study confirmed again the safety and feasibility of the device showing remarkably similar clinical outcomes compared with the previous studies (MACE rates of 9.9%, 8% and 6.4% and
TLR rates of 3.3%, 4%, and 3.4%, respectively). Furthermore, the study showed that these findings were not restricted to a limited number of (experienced) operators, but can be expanded to multiple centers with different operators across Europe.

Amsterdam single centre registry

The Amsterdam single centre registry included 91 patients in whom an attempt was performed to place a Tryton stent for the treatment of coronary bifurcation lesions. No restrictions concerning in- or exclusion criteria applied. Almost half of the patients (41%) had an acute coronary syndrome as indication for PCI of which a considerable amount was STEMI (16%). Relatively complex lesions were evaluated including left main bifurcations, chronic total occlusions, saphenous venous graft/ native vessel anastomosis, and in-stent restenosis of a previous failed provisional approach. Successful stent placement at the intended site was obtained in 95%. In four patients successful stent placement could not be performed due to severe calcifications. Median follow-up duration was six months. Target vessel failure (cardiac death, MI, and TVR) occurred in 9.7%, whereas MI occurred in 2 patients (2.2%). TLR was performed in 3 patients (4.5%) and only one probable ST was observed (1.1%). These results again resembled the findings of the previous observational studies. Furthermore, the study showed that failure to place the stent was primarily caused by severe calcifications, which might preclude the use of the stent in severely calcified lesions. The study also showed that the Tryton technique can be easily introduced and adopted in a centre where the provisional single-stent technique was the default strategy before the availability of Tryton.

Patient-level pooled analysis

In order to confirm the findings from these smaller registry studies, and to evaluate clinical outcomes beyond six months, a patient-level pooled analysis including individual patient data from 8 (published and unpublished) clinical registries comprising 905 patients was performed. Target vessel failure (cardiac death, MI and clinically indicated TVR) rates were 6.5% (six months) and 8.5% (one year) (figure 4). MI rates were 3.0% at six months and 4.3% at one year, whereas TLR rates were 3.2% (six months) and 5.4% (one year). Only four STs were observed (2 probable and 2 definite) resulting in a 1-year ST rate 0.5%. These findings again confirmed the good clinical performance and safety of the Tryton stent in combination with conventional stents in the MB. Furthermore, a sub-analysis was performed on this patient-pooled dataset on patients with long SB lesions. The data presented in this study suggested that treatment of long SB lesions with the Tryton stent in combination with additional SB stenting is safe and feasible and that the Tryton stent can facilitate a multi-stent approach in patients with complex bifurcation disease including long SB lesions in which an a-priori multi-stent approach is warranted (figure 1).
Chapter 4

Tryton left main multi-center registry

The Tryton left main multi-center registry evaluated the safety and feasibility of the Tryton stent for the treatment of left main coronary artery bifurcation disease. Procedural and clinical data were retrospectively collected from 52 patients from nine European centers. Patients included were generally of high surgical risk and in some cases deemed not to be surgical candidates due to comorbidities. Procedural success was 98% (there was one delivery failure and there were no device-related complications). Postprocedural QCA measurements showed an adequate acute gain of 1.52±0.86 mm of the left main and 0.92±0.47 mm of the SB. Interestingly, the investigators assessed whether Tryton was implanted with adequate depth by measuring the relative distance from the carina to the middle markers. The authors concluded that appropriate implantation could only be achieved in 38% of the cases, because most operators (43%) chose to keep as much as transition zone as possible in the MB to ensure adequate scaffolding of the SB by the distal zone of the stent. Six-month clinical follow-up was available in all except one patient. MACE (cardiac death, MI and ischaemia-driven TVR) occurred in 11 patients (22%). Five patients experienced an MI (10%), while six patients needed a TVR (12%), with SB involvement in all cases. Accurate Tryton positioning did not predict for
TVR: in two of the six TVR cases, the Tryton stent was positioned too deep, in two other cases Tryton was positioned too proximal, whereas in the remaining two cases Tryton was positioned correctly. This study showed that the Tryton stent is feasible for left main bifurcation treatment with optimal acute angiographic results and with acceptable six month outcomes. Importantly to note is that all patients were treated with the 3.5-2.5 mm Tryton device. Larger sized Tryton stents currently available (table 1) could have resulted in better apposition and improvement of clinical outcomes. Therefore, the same study group set-up a prospective registry with baseline and six-month IVUS measurements to assess whether outcomes are indeed better with the larger sized Trytons available. Furthermore, feasibility of the Tryton stent for left main bifurcation treatment will further improve with the Tryton Short version which became available recently, since the use of the first generation of the Tryton stent in left main PCI was hampered by the minimal required landing zone of 10 mm needed to have sufficient space for the proximal MB zone, while most left mains are longer. Ultimately, randomized studies will be needed comparing Tryton with other (two-)stent techniques and CABG for the treatment of left main bifurcation disease to assess whether the Tryton stent indeed improves clinical outcomes in this specific high-risk lesion subgroup.

Clinical outcomes in “off-label” use

Tryton only in Medina 0,0,1 lesions

It is explicitly instructed by the IFU always to use the Tryton stent in conjunction with an approved balloon-expandable coronary stent. Implantation of Tryton alone, without MB stent, is contraindicated because the three fronds of the proximal MB zone are not designed to provide radial strength. However, it has been proposed in a recent publication to use Tryton only, without MB stent, in bifurcation lesions in which the SB ostium is involved, without significant stenoses of the MB (i.e. Medina 0,0,1 lesions) \(^{28}\). The rationale behind this strategy is that with single ostial stenting using a conventional stent it is technical challenging to adequately cover the SB ostium without having struts protruded in the MB. With Tryton, the SB ostium is adequately scaffolded, while the specific design of the main branch zone minimizes the amount of metal in the main branch. In this publication, a small case series of 12 patients (median follow-up 868 days) was described with only one patient experiencing an event (TLR of the SB) after 427 days. No deaths, MIs or STs were observed. This study was limited by the lack of angiographic follow-up and intravascular imaging which would have given more insights in the safety and efficacy of this new strategy. Particularly of interest would be to evaluate if the three fronds of the MB zone are well apposed during follow-up, despite their low radial strength, since mall-apposition of these fronds might result in late stent thrombosis. Although encouraging, the results need to be confirmed in larger studies, including angiographic and intravascular follow-up.
Other publications on “off-label” use
There has been several cases published in which the Tryton is used “off-label”. In one case, two adjacent bifurcations were treated with two Trytons (one implanted in the circumflex artery and the other in the first diagonal branch) with only one 30mm regular DES as MB stent, placed from the left main to the mid-left anterior descending artery, covering both proximal zones of both Tryton stents at once. Another case involved a failed provisional single stent approach of a left anterior descending artery / first diagonal branch bifurcation, eight months earlier treated with a single BMS. The patient returned with recurrent chest pains based on in-stent restenosis (ISR) of the previous placed BMS with significant ostial SB stenosis. The ISR was treated by implanting a Tryton stent from the proximal MB into the SB through the BMS stent after several predilatations. Both the bare metal side branch and the restenosed MB stent were postdilated with drug-eluting balloons. The angiographic result was good after 8 months follow-up. Both cases illustrated the flexibility of the device to adjust to different anatomies and clinical settings.

Intravascular imaging studies
Ferrante et al. first published on intravascular imaging evaluation of the Tryton stent. They performed an optical coherence (OCT) assessment of the MB and SB acutely after treatment of a bifurcation lesion of the circumflex artery - marginal obtuse branch using Tryton in combination with a Promus everolimus-eluting stent (Boston Scientific Corporation, Natick, USA). They showed that there was good stent apposition in both distal MB and SB. In the proximal MB, where proximal Tryton and the Promus stent were overlapping, the OCT images also showed good apposition with a maximum strut separation from the vessel wall of 160 μm, corresponding to the ~170 μm combined strut thickness of the Tryton and Promus stents. A subsequent report from the same study group including nine patients evaluated the acute results of the Tryton stent in combination with a regular DES with OCT. The study confirmed good apposition of the overlapping DES and Tryton stents in the proximal MB zone, with 19% malapposed struts comparing well with the 10% found in the distal MB. However, at the level of the side branch ostium, the rate of malapposed struts was higher (33%), with more malapposed struts in the luminal half towards the SB compared with the luminal half opposite the SB (48% and 15%, respectively) (figure 5). The authors acknowledged that drawing conclusions from these findings was difficult since only a limited number of patients was included and, more importantly, a direct comparator was lacking and therefore it was difficult to appreciate the percentage of malapposed struts in the luminal half towards the SB. Until now, only one intravascular imaging follow-up study is published. The PYTHON (Prospective evaluation of the Tryton SB stent with an additional Xience-V Everolimus-eluting stent in coronary bifurcation lesions) study prospectively enrolled 20 consecutive patients with bifurcation disease, all with significant ostial SB involve-
Eighteen patients (90%) returned for 9-month follow-up angiography of whom 16 were treated with Tryton. QCA showed an in-stent LLL of the proximal MB of 0.34 (interquartile range [IQR]: 0.17-0.46), a LLL of the distal MB of 0.29 (IQR: 0.24-0.48) and a LLL of the SB of 0.57 (IQR: 0.29-0.73). OCT imaging could be obtained in 13 patients at 9 months, while in 3 patients this was precluded by severe stenosis. A per-strut analysis

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**Figure 5.** Optical coherence tomography evaluation of a patient treated with the Tryton stent. Panel (A) shows a three-dimensional optical coherence tomography (3D-OCT) reconstruction, immediately post-procedure, looking from outside the vessel at the side branch (SB) ostium, showing an open ostium without struts jailing the SB. Panel (B) shows a 3D-OCT of the same lesion from the same view, at 17 months follow-up. The ostium is still wide open without stenoses. Panel (C) show an OCT still frame of the distal main branch (MB), postprocedure. Panel (D) shows an OCT still frame at the same level as in panel (D), at 17 month follow-up. Panel (E) shows an OCT still frame just proximal of the carina, showing some non-apposed side branch (NASB) struts (white arrows). Panel (F) shows the same still frame 17 months later, with some coverage of the NASB struts. Panel (G) shows an OCT still frame a little more proximal from panels E and F, showing a wide open SB ostium, with some malapposed struts which are fully covered at 17 months, as shown in panel (H). Panel (I) shows the proximal MB with good apposition of the two layers of stent struts, which are fully covered at 17 months (Panel (J)). Panel (K) shows the follow-up angiogram at 17 months with a good angiographic result of both MB and SB. The dotted lines indicating the positioned of the OCT still frames.
showed that the ratio of uncovered to total stent struts was 4.0±5.8% in the proximal MB, 0.7±1.3% in the distal MB, and 2.5±3.6% in the ostial side branch area, while there were no uncovered struts in the SB. There were only 1.85 free floating struts per patient seen in the SB ostium area. The LLL in the proximal and distal MB compared very well with the 0.20-0.30mm LLL regularly found in DES OCT studies. Importantly, the authors found that the LLL of the SB was considerably higher (0.57mm) compared with the LLL of the SB in the FIM study (0.17mm). These differences could at least partly be explained by the fact that in the PYTHON study only bifurcation lesions with significant SB stenosis were included whereas in the FIM also patients with bifurcation lesions without SB involvement were included. Furthermore, the authors showed that in some cases the SB ostium was pinched on angiography with a crushed appearance of the Tryton on OCT in the SB ostium, potentially provoking excessive neointimal growth. The in-stent LLL of the SB of 0.57mm compared very well with previous findings of BMS studies showing a LLL of 0.80-1.00mm \(^{34,35}\). The authors of the PYTHON study concluded that the results did not fulfil the expectations of a dedicated bifurcation stent and that a drug-eluting version of Tryton is desired. However, it has to be pointed out that none of the struts in the SB were uncovered, and that less than two free floating struts per patient in the bifurcation region were observed with only a 2.5% ratio of uncovered to total stent struts. These latter findings may explain why ST rates were low in the various clinical studies endorsing the stent’s safety profile.

CONCLUSIONS

Percutaneous coronary treatment of bifurcation lesions is still associated with an increased risk of ISR and ST when compared with non-bifurcation lesions. Although a considerable amount of bifurcation lesions can adequately be treated with the currently recommended provisional single stent technique, treatment of complex bifurcation lesions with extensive side branch involvement remains a challenge.

Several dedicated bifurcation stents such as the Tryton stent have been developed to improve clinical outcomes after bifurcation stenting. As outlined above, accumulating registry data over the past years suggests that the use of the Tryton stent for the treatment for complex bifurcation lesions is promising. However, based on the currently available data, the provisional single stent approach remains the ‘gold standard’ for treatment of coronary bifurcation lesions. Randomized data have to be awaited to fully appreciate the efficacy and safety profile of this novel device and to determine its role within the daily armamentarium of the interventionalist.
ALTERNATIVE DEVICES

As mentioned above, most dedicated bifurcation devices are MB first stents placed crossing the SB allowing easy access to the side branch, facilitating the provisional single stent approach. However, besides Tryton, there is one other dedicated bifurcation device developed and clinically tested which facilitates the two-stent approach. The Sideguard® stent (Capella Medical Devices Ltd, Galway, Republic of Ireland) is a self-expanding trumpet-shaped nitinol stent. The stent is placed in the SB first in combination with a conventional balloon-expandable tubular stent in the MB in a T-stent configuration. The Sideguard stent consists of three zones: the cup, designed to have complete wall apposition around the side-branch ostium, a transition zone, and a distal anchor zone. The stent is positioned using two distal and three proximal radio-opaque markers. Combined clinical results from the first (20 patients) and second (93 patients) generation Sideguard FIM studies showed a 6-month MACE rate of 10.8% 36. An IVUS substudy of SG-1 showed an increase in SB stent area from 3.9 to 4.6 mm² at six months follow-up, whereas no change in lumen area was observed (3.9 vs. 4.0 mm²), suggesting that the self-expanding properties of the nitinol stent compensates for the intimal hyperplasia within this BMS 37. More recently, a registry including 20 patients showed a MACE rate of 5% at 6 months 38. More clinical studies, including randomized studies, will be needed to further evaluate the performance of this self-expanding device.

FIVE-YEAR VIEW: THE TRYTON IDE TRIAL AND BEYOND

Currently, the Tryton Investigational Device Exemption (IDE) randomized trial is running. With this study, the company is applying for approval by the food and drug administration (FDA) for use of this device within the US. In this trial the Tryon stent in combination with a DES in the MB (352 patients) is compared with balloon angioplasty of the SB in combination with a DES in the MB (352 patients). The trial has a non-inferiority design and its primary endpoint is nine-month target vessel failure, defined as the composite of cardiac death, target vessel MI, and TVR. The powered secondary endpoint is nine-month in-segment percentage diameter stenosis of the SB. Most important inclusion criteria were that the bifurcation lesions has to involve both MB and SB (Medina 1,1,1, 0,1,1, or 1,0,1), that reference vessel diameters should be between 2.5 and 4.0 mm of the MB and between 2.5 and 3.5 mm of the SB, and that lesion lengths should be ≤28 mm (MB) and ≤5 mm (SB). Most important exclusion criteria were left main disease, totally occluded lesions, and severely calcified lesions. At present, all patients have been recruited and the study is in its follow-up phase. The primary results are expected to be
presented by the end of 2013. If the primary endpoint will be met, the device will most likely be approved in the US.

This pivotal trial is the first ever randomized clinical trial involving a dedicated bifurcation stent. Furthermore, it is the largest trial ever on the treatment of bifurcation lesions. Half of the patients will have a 9-month re-angiography and an additional 96 patients will have a baseline and 9-month IVUS evaluated. So it is legitimate to state that the results of this trial will be robust and will give valuable insights in bifurcation stenting, both for the provisional technique as well as for the Tryton technique. The results of this trial will bring us closer to the answer whether dedicated bifurcation devices supporting the two-stent technique will shift the current paradigm of single stenting and make the two-stent approach the preferred strategy, especially in bifurcation lesions in which the side branch is involved.

Irrespective of the trial results, the device might be further improved in the future. The most obvious improvement would be to add a drug on the surface of the stent. However, coating the whole stent with a drug will probably increase the risk of ST, as shown in a meta-analysis comparing single with two stent techniques using conventional stents \(^{39}\), probably due to delayed strut coverage at the level of the carina where the MB DES and SB DES are in close proximity and where flow is highest \(^{40}\). More intravascular imaging studies are needed not only to globally measure the mean of neointimal growth within the SB part of Tryton, but also to reveal patterns of neo-intimal growth relative to the SB origin. This information is vital to determine where the drug is most needed to find an optimal balance between prevention of neointimal hyperplasia and the occurrence of (late) ST.

Another future improvement of the device might be the development of a bioresorbable version. Currently, several tubular bioresorbable scaffolds have been developed and clinically evaluated showing promising results \(^{46-48}\). The bioresorbable technology might be applied to the proximal MB zone only: the part which is only needed during stent placement to anchor the stent but its presence is not longer needed after adequate MB stent placement. A fully bioresorbable Tryton is an exciting thought, although this may be technically somewhat challenging to develop.

**KEY ISSUES**

- Coronary bifurcation lesions accounts for approximately 15 percent of all percutaneous coronary interventions performed and are associated with an increased risk of adverse clinical events during follow-up when compared with non-bifurcation lesions.
Dedicated bifurcation devices such as the Tryton Side Branch Stent have been developed to improve clinical outcomes.

The stent has a specific stent design (the Tri-ZONE technology): a distal side branch (SB) zone scaffolding the SB, a central transition zone with three panels to adjust to the wide variety of carinal anatomies and to provide scaffolding of the SB ostium, and a proximal main branch (MB) zone with two wedding bands anchoring the stent and a minimum amount of metal allowing easy delivery of the MB stent.

Until now, only observational data is available on the Tryton stent confirming the safety and feasibility of the stent with promising clinical results as shown in a large patient-pooled analysis showing a target vessel failure rate of 8.5% at one year.

Currently, the pivotal Tryton IDE trial is running comparing Tryton with balloon angioplasty as side branch treatment, both in combination with a conventional DES in the MB, challenging the current dogma of single stenting in bifurcation lesions.

REVIEW CRITERIA

A systematic search of the PubMed database was performed on June 2013 for articles written in English using (“Tryton” AND “stent”) as search term without further restrictions. This search identified 16 articles which were all scrutinized in full text. All articles were used and cited in the current article. We did not use unpublished data solely presented on scientific conferences.
REFERENCE LIST


