TRYTON EXTENDED ACCESS REGISTRY

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To assure the continued safety and effectiveness of the Tryton Side Branch Stent* with main branch approved DES in the treatment of de novo native coronary artery bifurcation lesions with side branch diameter ranging from >=2.5 mm to =2.5 mm to

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON42141

Source
ToetsingOnline

Brief title
Tryton Extended access registry

Condition

- Coronary artery disorders

Synonym
Treatment of de novo Bifurcation Lesions Involving the Main Branch and Side Branch within the Native Coronary Circulation

Research involving
Human

Sponsors and support

Primary sponsor: Tryton Medical Inc.
Source(s) of monetary or material Support: Tryton Medical

Intervention

Keyword: Bifurcation, Coronary, Stent, Tryton

Outcome measures

Primary outcome

Primary Endpoint: Periprocedural MI after PCI CK-MB elevation with value >3 times the upper range limit within the first 48 hours after PCI.

Secondary outcome

Secondary Endpoints: Safety: 1.All-cause and cardiac mortality at 30 days, and 1 year FU; 2. Myocardial infarction (MI): Q-wave and non-Q-wave, cumulative and individual at 30 days to 1 year (presented in 2 ways, assessed per the modified ARC definition and then by the ARC definition); 3. Major Adverse Cardiac Event (MACE) defined as a composite of all cause death, MI (Q wave or non-Q wave, per modified ARC definition), emergent coronary artery bypass surgery (CABG), or target lesion revascularization (TLR) by repeat PTCA or CABG at hospital discharge, 30 days, and to 1 year; 4. The composite of cardiac death, myocardial infarction (Q wave or non-Q wave, per modified ARC definition) > 30 days post-procedure, stent thrombosis, and target vessel revascularization (main branch or side branch); 5. Rates of stent thrombosis using ARC definition of definite and probable stent thrombosis and categorized as early, late or very late, at 30 days to 1 year. Effectiveness: 1. Device success, defined as attainment of <30% residual stenosis within the side branch;

2. Lesion success defined as attainment of <50% residual stenosis using any percutaneous method;

3. Procedure success defined as lesion success without the occurrence of in-hospital MACE;

4. Clinically or ischemia-driven target lesion revascularization at 30 days and 1 year;

5. Clinically or ischemia-driven target vessel revascularization at 30 days and 1 year;

6. Clinically or ischemia-driven target vessel failure (defined as cardiac death, target vessel MI (Q wave or non-Q wave, per modified ARC definition) or target vessel revascularization TVR) at 30 days and 1 year;

7. Clinically or ischemia-driven target lesion failure (defined as cardiac death, target lesion MI (Q wave or non-Q wave, per modified ARC definition) or target lesion revascularization TLR) at 30 days and 1 year;

8. Target lesion failure (TLF) defined as cardiac death, target lesion MI (Q wave or non-Q wave, per modified ARC definition) and target lesion revascularization (TLR) at 30 days and 1 year.

Study description

Background summary

The Tryton IDE trial was a randomized (1:1), multi-center, active control, non-inferiority clinical trial to compare the Tryton stent with drug eluting stent (DES) to Provisional stent with DES in subjects with bifurcation disease. The goal was to demonstrate that the Tryton stent is safe and effective for its intended use. The primary endpoint was Target Vessel Failure (TVF) 9 months post-procedure. TVF is a composite endpoint consisting of three components: cardiac death, target vessel myocardial infarction (MI), and target vessel revascularization (TVR). The powered secondary endpoint was percent diameter stenosis of the side branch 9 months post-procedure. The trial was the first randomized trial specifically conducted in the bifurcation disease area. The trial did not meet its primary endpoint; the TVF rate for the Tryton arm was 17.4% compared to 12.8% for the Provisional arm, non-inferiority p=0.417. There are two main causes for this. First, upon examining the components, the main determinant of not meeting non-inferiority was the rate of target vessel MI;

however, the vast majority of these events were clinically silent, transient elevations in peri-procedural CK-MB enzymes. Second, upon examining the size of the side branch vessel by the core lab, it was discovered that approximately 60% of treated subjects had a side branch vessel of less than 2.5 mm by QCA (inclusion criterion 10b, Side branch reference vessel diameter must be >=2.5 mm to <= 3.5 mm by visual estimate). This was due primarily to participating investigators inadvertently overestimating the size of the side branch vessel by greater than the anticipated 10% increase relative to the angiographic core lab determination. When a subset of subjects with side branch vessel of at least 2.25 mm (10% less than the 2.5 mm visual estimation inclusion criterion) was examined, the TVF rate in the Tryton arm was 11.3% relative to 15.6% in the Provisional arm (the upper 95% confidence limit excludes the prospectively determined non-inferiority delta chosen for the full cohort). The data suggest smaller side branches reflect less myocardium at risk and raise the possibility of clinically silent restenosis, impacting clinically driven TVR rates. In addition, patients with smaller side branches assigned to the Tryton arm were subjected to far greater over-stretch, which may lead to increased peri-procedural CKMB elevation (study defined MI) and restenosis. The powered secondary endpoint of in-segment % diameter stenosis in the side branch at 9 months was 31.6% for the Tryton stent and 38.6% for the Provisional Control, (p = 0.002), demonstrating superiority for the Tryton stent in the complete ITT population, thus meeting the pre-specified powered secondary (efficacy) endpoint. In a similar analysis of the angiographic cohort of patients with side branch vessel diameters at least 2.25mm by QCA, the in-segment % diameter stenosis of the side branch at 9 months was 30.4% for Tryton stents and 40.6% for Provisional controls (p= 0.004), demonstrating superiority of Tryton for the pre-specified efficacy endpoint in this subset of patients as well. * A critical long-term consequence for patients with side branch disease is restenosis at the ostium, which means the patient has symptoms and may need re-intervention in the ostium of the side branch. A decrease in % diameter stenosis in the side branch reduces the likelihood of that which is an important benefit to the patient. Another potential benefit of Tryton is maintaining that access to the side branch for future downstream treatment. In order to confirm the acceptable safety profile of the Tryton Side Branch Stent as demonstrated in the >=2.25mm SB RVD subset of the primary IDE study, Tryton will prospectively collect additional clinical data on approximately 133 subjects in the EXTENDED Access Registry. Tryton believes that an open-label registry approach is appropriate in the Tryton stent setting. While the Tryton trial did not meet its primary endpoint, due to clinically silent, transient peri-procedural elevations in CK-MB enzymes, the clinical literature has debated whether CK-MB enzyme elevations are clinically meaningful, as the majority of these events were not associated with clinical sequelae. In addition, the specific threshold for concern has also been debated in the literature, with values of 3x, 5x, 8x, and even 10x the normal level proposed. Aside from the transient CK-MB enzymes, the safety profile of the Tryton stent appears acceptable, with no cardiac death out to 9 months, low stent thrombosis and low TVR. The TRYTON EXTENDED Access Registry is therefore focused on the

peri-procedural CK-MB elevations and will compare Tryton rates of peri-procedural events to a performance goal derived from the performance of the provisional stenting control group from the >=2.25mm SB RVD subset of the primary IDE study. As well the incidental enrollment of subjects outside of the >2.5 mm side branch visual RVD intended study population will be monitored. Changes to the EXTENDED Access Registry protocol are centered around the study design changes that remove the active control, (randomization) as the registry is a single arm study with the endpoint focused on Periprocedural Target Vessel Failure (TVF) of cardiac death and myocardial infarction (Q wave and non Q wave) at 48hours as a follow-up to the original IDE study. The registry study will only require 30 day and 1 year telephone follow-up therefore, removes the need for longer-term follow-up of 6,and 9 months and 2, 3, 4 and 5-year time points. Additionally, the registry has no angiographic or IVUS interventions as no sub studies are required. All pre-procedure and post procedure lab testing and screening remains the same and the Tryton treatment algorithm remain the same with additional detail in the predilatation steps only. Several changes to grammar and miscellaneous terminology have been corrected throughout.

Study objective

To assure the continued safety and effectiveness of the Tryton Side Branch Stent* with main branch approved DES in the treatment of de novo native coronary artery bifurcation lesions with side branch diameter ranging from >=2.5 mm to <=3.5 mm and main branch diameter ranging from >=2.5 mm to <=4.0 mm

Study design

TRYTON EXTENDED Access is designed to enroll up to 133 subjects treated with the Tryton Side Branch Stent* with main branch approved DES for treatment of native coronary artery bifurcation disease.

Intervention

Treatment with the Tryton Side Branch StentTM plus approved main branch DES

Study burden and risks

Known risks are associated with balloon inflation and stent implantation, including death (0.2 - 0.5%), heart attack (4 - 5%), or emergency surgery (0.5%). Other risks include (but are not limited to): • Cardiac events such as inadequate or impaired blood flow to the heart causing chest pain or discomfort (angina or angina symptoms), impaired pumping ability of the heart, re-narrowing of a treated heart artery, collection of blood around the lining of the heart, injury or tear in a heart artery, tear or puncture in a heart wall, weakening and bulging in a heart artery, or an unexpected need for immediate heart surgery. • Irregularities in the heart rhythm such as very

fast or slow beating of the upper and/or the lower heart chambers, or disorganized beating of the lower heart chambers. • Stent events such as failure to place it in the desired spot in the heart artery, clot or obstruction within the stent, unintended movement of the stent in the heart artery, losing the stent in the circulation as it is placed, inadequate expansion or fit of the stent in the heart artery. • Respiratory events such as impaired ability of the lungs to provide oxygen for body tissues, fluid build-up in the lungs, or breathing difficulties. • Blood vessel events such as bleeding or blood collection at catheter entry site/s in groin, high or low blood pressure, abnormal area or weakness in wall of artery, abnormal connection between an artery and vein in the groin, injury or tear in artery in groin leading to the heart, air, tissue debris, or blood clot that moves to smaller vessels away from the heart and may block flow, spasm in a vessel. • Brain or nervous system events such as stroke, impaired brain function that improves over time, nerve injury in brain or in other body parts. • Bleeding events such as bruising, bleeding from the catheter groin site/s, or bleeding in other body parts requiring a blood transfusion or other treatment. • Kidney events such as impaired kidney function or kidney failure. • Allergic or immune system events such as sensitivities or body reactions to medications given such as contrast dye, heparin, aspirin, Plavix, drug/polymer in the stent or other drugs the doctor prescribes for treating the heart artery; or fever or infection.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients must meet ALL of the following criteria: General Inclusion Criteria 1. The patient must be >=18 and <= 90 years of age; 2. Symptomatic ischemic heart disease (CCS class 1-4, Braunwald Class IB, IC, IIB, IIC, IIIB, IIIC, and/or have objective evidence of myocardial ischemia); 3. Acceptable candidate for CABG; 4. Intent to treat the side branch of the target bifurcation based on angiographic evaluation; 5. The patient is willing to comply with specified follow-up evaluations; 6. The patient or legally authorized representative has been informed of the nature of the study, agrees to its provisions and has been provided written informed consent, approved by the appropriate Medical Ethics Committee (MEC) or Institutional Review Board (IRB). 7. Planned use of one of the following approved and commercially available drug-eluting stents for subject*s index procedure: CYPHER®, RESOLUTE Family of products, (ENDEAVOR® RESOLUTE or RESOLUTE INTEGRITY), PROMUS®, PROMUS ELEMENT Family of products (PROMUS® ELEMENT, or PROMUS ELEMENT PLUS, PROMUS® PREMIER, Family of products,),, XIENCE* V, or the XIENCE PRIME, Family of products (XIENCE EXPEDITION. PRIME, XIENCE XPEDITION or XIENCE PRO). Angiographic Inclusion Criteria 8. a)Single de novo lesion in a bifurcation involving both the main branch and the side branch with b) The bifurcation: main branch and side branch with a visual diameter stenosis >= 50% (Medina classification 1.1.1; 0.1.1; 1.0.1 by visual assessment); 9. Target lesion located in a native coronary artery; 10. a)Bifurcation lesion main branch reference vessel diameter must be >=2.5 mm to <= 4.0 mm b) Side branch reference vessel diameter must be >=2.5mm by visual estimate (>=2.25mm by QCA) and <3.5 mm by visual estimate (<3.25 mm by QCA) 11. a) Bifurcation lesion main branch lesion length <= 28 mm b) Side branch lesion length <= 5.0 mm (the ability to be treated with a single stent for both main and side branch); 12. Target lesion >=50% and <100% stenosed by visual estimate in both the main branch and side branch; Refer to Protocol 1.10 for full list of Inclusion Criteria

Exclusion criteria

Patients will be excluded if ANY of the following conditions apply: General Exclusion Criteria 1. Pregnant or nursing patients and those who plan pregnancy in the period up to 1 year following index procedure. Female patients of child-bearing potential must have a negative pregnancy test done within 7 days prior to the index procedure per site standard test; 2.

Patient has had a known diagnosis of STEMI acute myocardial infarction (AMI) within 72 hours preceding the index procedure or >72 hours preceding the index procedure and CK and CK-MB have not returned to within normal limits at the time of procedure; 3. Patients with non-STEMI within 7 days prior to index procedure with continued CK-MB elevation; 4. Patients with non-target lesion PCI within 14 days prior to index procedure with continued CK-MB elevation; Angiographic Exclusion Criteria 15. Left main coronary artery disease (protected and unprotected) 16. Trifurcation lesion; 17. Totally occluded target vessel (TIMI flow 0 or 1); 18. Severely calcified target lesion(s); 19. Highly calcified target lesion(s) requiring rotational atherectomy; 20. Target lesion has excessive tortuosity unsuitable for stent delivery and deployment; 21. Angiographic evidence of thrombus in the target lesion(s); Refer to Protocol 1.10 for full list of Exclusion Criteria.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-02-2015
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	Side Branch Stent
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	12-11-2014
Application type:	First submission

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-05-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-08-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL49704.078.14

Study results

First publication
21-11-2016