BIOTRONIK- *A Prospective, Randomized, Multicenter Study to Assess the SaFety and Effectiveness of the Orsiro SiroLimus Eluting Stent in the Treatment Of Subjects With up to two de novo Coronary Artery Lesions* - IV

Published: 08-07-2014
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To evaluate the safety and effectiveness of Orsiro for the treatment of subjects with up to 2 de novo atherosclerotic coronary artery lesions.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Observational invasive

Summary

ID

NL-OMON44708

Source
ToetsingOnline

Brief title
BIOFLOW-IV

Condition

- Coronary artery disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
coronary stenosis, narrowing of the arteries which supply the heart with blood

Research involving

Human

Sponsors and support

Primary sponsor: Biotronik
Source(s) of monetary or material Support: Study Sponsor - BIOTRONIK AG / Ackerstrasse 6 / 8180 - Buelach / Switzerland

Intervention

Keyword: Coronary Artery Disease, Drug-Eluting Stent, Percutaneous Coronary Intervention, Randomized Controlled Trial

Outcome measures

Primary outcome

The primary endpoint for the main randomized controlled trial (RCT) is the 12-month target vessel failure (TVF) rate, defined as any clinically-driven revascularization of the target vessel (TVR), target vessel Q-wave or non-Q wave myocardial infarction (MI), emergent CABG, or cardiac death -. The primary endpoint will be evaluated for all subjects who are randomized to one of the study stents (Orsiro or Xience Prime/Xpedition). The RCT will be considered complete with regard to the primary endpoint after all subjects have completed the 12-month follow-up.

Secondary outcome

The below listed endpoints will be evaluated for events that occurred prior to discharge, 1-, 6- and 12-months and 2-, 3-, 4- and 5-years post procedure. Subjects who are randomized but who do not receive a study stent (Orsiro or XIENCE) will be followed through 12 months only. Starting with the 2-year follow-up, follow-up will be limited to the implanted population.

1. Rate of clinically-driven target lesion revascularization (TLR)

2. Rate of clinically-driven TVR

3. Rate of target lesion failure (TLF), defined as composite of cardiac death, target vessel Q-wave or non-Q wave MI, emergent CABG, any clinically-driven TLR

4. Rate of TVF

5. Rate of Q-wave and non-Q-wave MI

6. Rate of cardiac death

7. Rate of non-cardiac death

8. Rate of all death

9. Rate of cardiac death or MI

10. Rate of all death or MI

11. Rate of all death, MI and TVR

12. Rate of stent thrombosis (definite or probable by ARC definitions)

13. Rate of cerebrovascular disease

Periprocedural endpoints measured in the RCT and HuPK sub-study are listed below.

1. Technical success rate

2. Clinical procedural success rate

Study description

Background summary

Since the first Percutaneous Transluminal Coronary Angioplasty (PTCA), this procedure has become a widely accepted treatment modality for Coronary Artery Disease (CAD). For the majority of CAD, treatment with PTCA provides high initial procedural success, symptomatic relief, improvement in functional capacity, and survival rates quite similar to those of Coronary Artery Bypass Grafting (CABG). However, all percutaneous techniques, regardless of the mode of intervention, have rather high rates of repeat interventions at long-term follow up. The first type of stent used in Percutaneous Coronary Intervention (PCI), were Bare Metal Stents (BMS), designed to address the limitations of PTCA. BMS reduced the angiographic and clinical restenosis rates in de novo lesions compared to PTCA alone and decreased the need for CABG. BMS substantially reduced the incidence of abrupt artery closure, but restenosis occurred in about 20%-40% of all cases, necessitating repeat procedures. The invention of Drug Eluting Stents (DES) significantly improved on the principle of BMS by adding an antiproliferative drug, which is either directly immobilized on the stent surface or released from a polymer matrix to inhibit neointimal hyperplasia. This allows for controlled release of the drug at the site of injury. The polymer drug carriers currently used on DES are either biodegradable or non-biodegradable. Non-biodegradable polymers reside on the surface of the stent indefinitely. In contrast biodegradable polymers dissolve after a certain period of time, leaving only the BMS platform in the vessel wall. The introduction of DES greatly reduced the incidence of restenosis and resulted in a better safety profile as compared to BMS with systemic drug administration. These advantages and a lower cost compared to surgical interventions have made DES an attractive option to treat coronary artery disease.
This study will collect data prospectively on subjects that are randomly assigned to be implanted with either the Biotronik Orsiro or the Abbott Xience Prime* / Xience Xpedition* stent. The Xience Prime and Xience Xpedition stents differ in the delivery system. The stent itself is exactly the same. All investigational devices have received the CE mark and are available on the market. By comparing two different products of the latest generation, we expect to gain more knowledge on the safety and efficacy of the Orsiro stent. The built evidence through this study may also provide useful insights for the continuous development of drug eluting stents.

Study objective

To evaluate the safety and effectiveness of Orsiro for the treatment of subjects with up to 2 de novo atherosclerotic coronary artery lesions.

Study design

BIOFLOW-IV is a prospective, international multicenter, randomised controlled trial to assess Orsiro for the treatment of subjects with up to 2 de novo atherosclerotic coronary artery lesions. All subjects will be randomised 2:1

to receive the BIOTRONIK Orsiro SES or the Abbott Xience Prime* / Xience Xpedition* EES. The randomisation will be stratified for diabetes.

Approximately 555 subjects at up to ca. 50 sites in Japan and Europe are proposed to demonstrate the safety and effectiveness of Orsiro.
A randomized controlled trial (RCT) at up to ca.50 sites in Japan and Europe aims to enter 555 subjects. All subjects will be randomised 2:1 to receive the Orsiro or the Xience Prime* / Xience Xpedition*.
During study enrolment phase, all patients will be screened according to the protocol inclusion and exclusion criteria. All patients consented will undergo angiographic assessment during the index procedure a spart of standard clinical care.
Clinical telephone follow up visits will take place at 1, 6 months and annually for 5 years post procedure. At 12 months an outpatient visit at the site is required to assess the clinical status.

Protocol mandated angiographic follow-up is not required; however, patients requiring re-intervention for the target vessel(s) during the 5 year follow up period will undergo angiographic assessment at the time of re-intervention as standard of care. Angiographic data and images collected during the index procedure and during re-intervention (if applicable) must be forwarded to the Angiographic Core Laboratory for analysis.

This clinical trial is designed to be performed in accordance with the Declaration of Helsinki 2008, ISO 14155 (E), the Pharmaceutical Affairs Laws and regulations related to clinical trials in Japan (Japanese Good Clinical Practice), and Local and National regulations.

Study burden and risks

The nature and extent of the burden, risks and benefits associated with participation are described for baseline and follow up.

Baseline
All baseline examinations prior to randomization are according to standard clinical care.
Implantation of the devices will not bring additional risk to the subjects, then otherwise experience in standard clinical care.
None of the study patients will have any planned additional invasive or non-invasive examinations/procedures during the PTCA procedure.
All diagnostic examinations post-procedure are according to standard clinical care. The study does not include any additional study specific invasive or non-invasive examination(s).

In summary we conclude that the anticipated rate of events for study patients and regular patients are equal.
A complete description of associated possible adverse events and correct usage

of the Orsiro and the Xience Prime/Xpedition stents are described in each device instructions for use.

Follow up
During follow up all patients will be requested to return for an outpatient visit at 12 months, to assess their clinical status. This will be done according to standard clinical practice.
A standard ECG will be collected during this visit. No blood samples will be drawn.
In summary, there are no anticipated increased risks associated with the follow up visit at 12 months.
All other follow up visits will be done by telephone interview and will not bring any additional risk to the patient(s).

Benefits
In this clinical investigation all subjects will have a more frequent medical follow up then otherwise provided in standard clinical care. This may be beneficial for the long term clinical outcome of the patient.
The collected data will provide more knowledge to the long term safety and efficacy of the Orsiro SES and the Xience Prime*/Xience Expedition* EES.

Conclusion
Except for the randomization at baseline and the mandatory physical examination at 12 month follow up, all study patients will receive equal treatment as non-study patients with the same diagnose.
The stents used in this study are available and used in standard clinical care.
The study may, but is not certain to bring a direct benefit to the individual patient by the more intense medical follow up.
The knowledge gained through the study might help to improve the therapy for future patients.
In summary we conclude that the study patients will experience no plausible additional risk by participating in this clinical study.

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

Clinical Inclusion Criteria
1. Subject must provide written informed consent
2. Subject is * 18 years and * 80 years old
3. For subject less than 20 years of age enrolled at a Japanese site, the patient and the patient*s legal representative must provide written informed consent before any study-specific tests or procedures are performed
4. Subject, target vessel(s) and lesion(s) are eligible for percutaneous coronary intervention (PCI)
5. Subject is an acceptable candidate for coronary artery bypass grafting (CABG)
6. Subject has clinical evidence of ischemic heart disease and/or a positive functional study, stable or unstable angina pectoris or documented silent ischemia, attributable to the target lesions
7. Subject is eligible for dual anti-platelet therapy (DAPT) treatment with acetylsalicylic acid (ASA) plus either, Clopidogrel, Prasugrel, Ticlopidine, or Ticagrelor. For subjects enrolled at a Japanese site, DAPT with ASA plus either Clopidogrel or Ticlopidine;Angiographic Inclusion Criteria
1. The target reference vessel diameter (RVD) is * 2.50 mm and * 3.75 mm assessed either visually or by online Quantitative Coronary Angiography.
2. Target lesion length is * 26 mm (assessed either visual estimate or by online Quantitative Coronary Angiography) and can be covered by one study stent
3. Single de novo lesion with * 50% and < 100% stenosis in up to 2 coronary arteries
4. Target vessel(s) Thrombolysis in Myocardial Infarction (TIMI) flow * 2

Exclusion criteria

Clinical Exclusion Criteria;1. Subject has evidence of myocardial infarction within 72 hours prior to the index procedure
2. Subject with a *2 fold CK level or in absence of CK *3 fold CKMB level above the upper range limit within 24 hours prior to the procedure
3. Documented recent left ventricular ejection fraction (LVEF) * 30%
4. Subject is receiving oral or intravenous immunosuppressive therapy (i.e., inhaled steroids are not excluded) or has known life-limiting immunosuppressive or autoimmune disease (e.g., human immunodeficiency virus, systemic lupus erythematosus, but not including diabetes mellitus)
5. Subject has impaired renal function (i.e., serum creatinine > 2.5 mg/dl or 221 mmol/l, determined within 72 hours prior to intervention)
6. Target vessel(s) or side branch has been treated with any type of PCI (e.g., balloon angioplasty, stent, cutting balloon, atherectomy) within 12 months prior to the index procedure
7. The target lesion requires treatment with a device other than the pre-dilatation balloon prior to stent placement (including but not limited to, directional coronary atherectomy, excimer laser, rotational atherectomy, cutting balloon etc.)
8. Planned intervention of non-target vessel(s) within 30 days after the index procedure
9. Planned intervention of target vessel(s) after the index procedure
10. Subject has a known allergy to contrast medium (that cannot be adequately premedicated), acetylsalicylic acid (ASA), heparin, PLLA, sirolimus, everolimus, cobalt chromium, nickel, or silicon carbide.
11. Subject is currently participating in another (medical device or drug) clinical study that has not reached the primary endpoint
12. Subject is pregnant and/or breast-feeding female or female who intends to become pregnant during the time of the study
13. Subject has serious medical illness (e.g., cancer, congestive heart failure) that may reduce life expectancy to less than 12 months
14. Planned surgery or dental surgical procedure within 6 months after index procedure
15. Three-vessel coronary artery disease at time of procedure
16. In the investigators opinion subject will not be able to comply with the follow up requirements;Angiographic Exclusion Criteria;1. Target lesion is located in the left main stem
2. Target lesion is located in or supplied by an arterial or venous bypass graft
3. Target lesion involves a side branch > 2.0 mm in diameter by visual estimate or by online quantitative coronary angiography
4. Ostial target lesion (within 5.0mm of vessel origin)
5. Thrombus, or possible thrombus, present in the target vessel
6. Heavily calcified lesion
7. Proximal or distal to the target lesion located stenosis that might require future revascularization or impede run off;Note: Multiple focal stenosis will be considered as a single lesion if they can be completely covered with 1 stent

Study design

Design

Study phase:	4
Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-07-2014
Enrollment:	120
Type:	Actual

Medical products/devices used

Generic name:	Orsiro (Sirolimus Eluting Stent System
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	08-07-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-08-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	26-05-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-10-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-10-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
ClinicalTrials.gov	NCT01939249
CCMO	NL47384.100.14

Study results

Date completed:	22-01-2020

Results posted:	25-11-2020
Actual enrolment:	83

Summary results
Trial is onging in other countries

First publication
12-10-2020