BIOTRONIK-Safety and Clinical PerFormance of the Drug ELuting Orsiro Stent in the Treatment of Subjects With single de novo Coronary Artery Lesions - II

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To compare the BIOTRONIK Orsiro Limus Eluting Stent System (LESS) with the Abbott Xience Prime* Llimus Eluting Stent System (LESS) with respect to in-stent Late Lumen Loss (LLL) in a non-inferiority study in de novo coronary lesions at 9 months.

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

Summary

ID

NL-OMON35790

Source
ToetsingOnline

Brief title
BIOFLOW-II

Condition

- Coronary artery disorders

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

Intervention

Keyword: Coronary Artery disease, Drug Eluting Stent, Limus

Outcome measures

Primary outcome

In-stent LLL at 9 months post procedure by core laboratory QCA analysis

Secondary outcome

1. Clinically driven Target Lesion Revascularization (TLR) at 1, 6 and 12

months post-procedure

2. Clinically driven Target Vessel Revascularization (TVR) at 1, 6 and 12

months post-procedure

3. Target Lesion Failure (TLF), composite of cardiac death, target vessel

Q-wave or non-Q wave Myocardial Infarction (MI), Coronary Artery Bypass

Grafting (CABG), clinically driven TLR

4. Target vessel failure (TVF), composite of cardiac death, MI and clinically

driven TVR

5. Composite of all-cause mortality and all MI

6. All serious adverse device effects (SADEs)

7. All target vessel MI*s

8. All cardiac deaths

9. Definite stent thrombosis at 1, 6, 12 months and annually up to 5 years post

procedure

10. In-segment LLL at 9 months post-procedure

11. In-stent and in-segment (proximal and distal) minimum lumen diameter (MLD)

at 9 months post-procedure

12. In-stent and in-segment binary restenosis rate angiographically assessed (*

50% diameter stenosis) at 9 months post procedure

13. In-stent and in-segment percent diameter stenosis (% DS)

IVUS Subgroup

1. Neointimal hyperplasia volume at 9 months post-procedure

2. Incomplete stent apposition

OCT Subgroup

1. Neointimal hyperplasia volume at 9 months post-procedure

2. Strut coverage at 9 months post procedure (%)

3. Stent apposition at baseline and 9 months post procedure

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 immobilised 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 has 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* stent. Both investigation 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 vs. the *Golden Standard* Xience Prime* stent. In addition, OCT and IVUS subgroup analyses will be performed. Taken together this will contribute to expand the knowledge of drug eluting stents in interventional cardiology. The built evidence through this study may also provide useful insights for the continuous development of drug eluting stents.

Study objective

To compare the BIOTRONIK Orsiro Limus Eluting Stent System (LESS) with the Abbott Xience Prime* Llimus Eluting Stent System (LESS) with respect to in-stent Late Lumen Loss (LLL) in a non-inferiority study in de novo coronary lesions at 9 months.

Study design

A prospective, multicenter, international, two-arm, non-inferiority, randomised controlled clinical study enrolling up to 440 subjects. All subjects will be randomised 2:1 to receive the BIOTRONIK Orsiro LESS or the Abbott Xience Prime* LESS. The randomisation will be stratified for diabetes.

Clinical follow up visits will take place at 1, 6 and 12 months and annually for 5 years post procedure. At 9 months all subjects will undergo an

angiographic follow up to assess the in-stent LLL.
Up to 60 pre-specified subjects will have an additional IntraVascular UltraSound (IVUS) examination at both baseline and at the 9 months follow up visit.

Up to 60 pre-specified subjects will have an additional Optical Coherence Tomography (OCT) examination at both baseline and at the 9 month follow up visit.

A subgroup subject will only be allocated to either IVUS or OCT. Both IVUS and OCT will be conducted exclusively at pre-specified centres according to a pre-specified allocation scheme.

This study is designed to be performed in accordance with the Declaration of Helsinki, ISO 14155:2011(E), ICH-GCP, Local and National Regulations.

Study burden and risks

Risks

Both devices in this study have received the CE mark. Implantation of the devices will therefore not bring additional risk to the subjects, compared to treatment with any other drug eluting stent in standard clinical care. The anticipated adverse events in this study are those related to regular percutaneous interventions (PCI), with drug eluting stents. A complete description of the risks of implantation and correct usage of the Orsiro and the Xience Prime stents are described in each device Instructions for Use.

The additional Angiography and OCT/IVUS* FUP do provide extra risk for the patient in terms of risk for complications and an additional radiation dose.
The direct benefit for the patient is the chance for detection and pro-active treatment of a possible lesion and/or re-stenosis and thereby preventing a more serious event at a later stage.
*If medically indicated both IVUS and OCT are performed during PCI procedures in routine practice.

ECG*s will be required at screening and prior to discharge and one additional blooddraw may be taken prior to the angiographic follow up at 9 months post procedure.

Taken together, all subjects will have a more intense medical follow up then in standard practice, which may be beneficial to the long term clinical outcome for the individual.

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

1.Subject has provided a written informed consent
2.Subject is * 18 years and * 80 years old
3.Single de novo lesion with * 50% and <100% stenosis in up to 2 coronary arteries
4.Subject, target vessel(s) and lesion(s) are eligible for PCI with the Orsiro stent
5.The target lesion length is * 26 mm (assessed either visually or by online Quantitative Coronary Angiography (QCA)) and can be covered by one study stent
6.The target reference vessel diameter is * 2.25 mm and * 4.0 mm (assessed either visually or by online QCA)
7.Target vessel(s) TIMI flow * 2
8.Subject is an acceptable candidate for CABG
9.Clinical evidence of ischemic heart disease and/or a positive functional study, stable or unstable angina pectoris or documented silent ischemia

10. Eligible for Dual Anti Platelet Therapy (DAPT) treatment with Acetylsalicylic Acid (ASA) plus either, Clopidogrel, Prasugrel, Ticlopidine or Ticagrelor

Exclusion criteria

1.Pregnant and/or breast-feeding females or females who intend to become pregnant during the time of the study
2.Evidence of myocardial infarction within 72 hours prior to index procedure
3.Subjects with CK, CKMB(optional) and/or Troponin levels exceeding the normal range within 24 hours prior to the procedure
4.Unprotected left main coronary artery disease (stenosis >50%)
5.Three-vessel coronary artery disease at time of procedure
6.Thrombus in target vessel
7.Planned interventional treatment of any non-target vessel within 30 days post-procedure
8.Planned intervention of the target vessel after the index procedure
9.Ostial target lesion (within 5.0 mm of vessel origin)
10.Target lesion involves a side branch > 2.0 mm in diameter
11.Documented left ventricular ejection fraction (LVEF) * 30%
12.Heavily calcified lesion
13.Target lesion is located in or supplied by an arterial or venous bypass graft
14.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.)
15.Known allergies to: Acetylsalicylic Acid (ASA), Heparin, Contrast medium, Sirolimus, Everolimus or similar drugs (i.e., ABT 578, Biolimus,Tacrolimus); CoCr, PLLA, Silicon Carbide
16.Impaired renal function (serum creatinine > 2.5 mg/dl or 221 mmol/l, determined within 72 hours prior to intervention)
17.Subject is receiving oral or intravenous immunosuppressive therapy (e.g., 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)
18.Proximal or distal to the target lesion located stenosis that might require future revascularization or impede run off
19.Life expectancy less than 1 year
20.Planned surgery or dental surgical procedure within 6 months after index procedure
21.In the investigators opinion subject will not be able to comply with the follow-up requirements
22.Subject is currently participating in another study and has not reached the primary endpoint

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):	08-12-2011
Enrollment:	35
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	01-11-2011
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-06-2012
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	NCT01356888
CCMO	NL36465.100.11

Study results

Date completed: 23-03-2017

Actual enrolment: 28

Summary results
Trial is onging in other countries