BIOFLOW-V: BIOTRONIK * A Prospective Randomized Multicenter Study to Assess the SaFety and Effectiveness of the Orsiro SiroLimus Eluting Coronary Stent System in the Treatment Of Subjects With up to Three De Novo or Restenotic Coronary Artery Lesions * V

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To assess the safety and efficacy of the Orsiro Sirolimus Eluting Coronary Stent System in the treatment of subjects with up to three native de novo or restenotic (standard PTCA only) coronary artery lesions compared to the Xience coronary stent...

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

Summary

ID

NL-OMON43649

Source
ToetsingOnline

Brief title
BIOFLOW-V

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 Target lesion failure (TLF) rate at 12 months post*index procedure. TLF is defined as all cardiac death, target vessel Q-wave or non*Q-wave myocardial infarction (MI), or clinically driven target lesion revascularization (TLR).

Secondary outcome

Secondary endpoints include the following measures:

1. Device success, defined as attainment of < 30% residual stenosis of the target lesion using the assigned study stent only.

Note: Post-dilatation is allowed to achieve device success.

2. Lesion success, defined as attainment of < 30% residual stenosis of the target lesion using any percutaneous method.

3. Procedure success, defined as attainment of < 30% residual stenosis of the target lesion using the assigned study stent only without occurrence of in-hospital major adverse cardiac events (MACE; composite of all-cause death,

Q-wave or non*Q-wave MI, and any clinically-driven TLR).

The following secondary clinical endpoints will be evaluated prior to discharge, at 1, 6 and 12 months and annually thereafter through 5 years follow-up:

4. Death.

5. MI

6. Cardiac death or MI.

7. MACE and individual MACE components (MACE: composite of all-cause death, Q-wave or non*Q-wave MI, and any clinically-driven TLR).

8. TLF and individual TLF components (TLF: composite of cardiac death, target vessel Q-wave or non*Q-wave MI, and any clinically-driven TLR).

9. Target vessel failure (TVF) and individual TVF components (TVF: composite of cardiac death, target vessel Q-wave or non*Q-wave MI, and any clinically-driven TVR).

10. Stent thrombosis (all, definite, definite/probable, probable, possible) according to Academic Research Consortium (ARC) criteria for acute, subacute, late, very late and cumulative stent thrombosis.

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 stent system. 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 assess the safety and efficacy of the Orsiro Sirolimus Eluting Coronary Stent System in the treatment of subjects with up to three native de novo or restenotic (standard PTCA only) coronary artery lesions compared to the Xience coronary stent system.

Study design

BIOFLOW-V is a prospective, multicenter, randomized, controlled trial combining data on the randomized subjects with data from two historical studies by

employing a Bayesian approach.
Subjects with coronary artery disease (CAD) that qualify for percutaneous coronary intervention (PCI) with stenting will be screened per the protocol inclusion and exclusion criteria to achieve a total of 1,334 randomized subjects. Eligible subjects will be randomized in a 2:1 ratio to undergo percutaneous coronary revascularization with either the Orsiro Sirolimus Eluting Stent System (treatment group) or the Xience Everolimus Eluting Stent System (control group).
BIOFLOW-V randomized subjects will be combined with historical Orsiro, Xience Prime* and Xience Xpedition* randomized subjects from the BIOFLOW-II and BIOFLOW-IV trials by employing a Bayesian statistical approach. Only subjects that meet all clinical and angiographic eligibility criteria of the BIOFLOW-V trial will be included in the analysis.

Intervention

The Orsiro or Xience stent is chosen at random, which makes this an interventional study.

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. An additional ECG will be collected during this visit according to standard of care. 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
The collected data will provide more knowledge to the long term safety and efficacy of the Orsiro SES and the Xience
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 on the market 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

1.Subject is *18 years or the minimum age required for legal adult consent in the country of enrollment.
2.Subject is an acceptable candidate for PCI.
3.Subject is an acceptable candidate for CABG.
4.Subject has clinical evidence of ischemic heart disease, stable or unstable angina pectoris or documented silent ischemia.
5.Subject is eligible for dual anti-platelet therapy treatment with aspirin plus either, clopidogrel, prasugrel, ticagrelor or ticlopidine.
6.Subject has provided written informed consent.
7.Subject is willing to comply with study follow-up requirements.
stents.

Exclusion criteria

1.Subject has clinical symptoms and/or electrocardiogram (ECG) changes consistent with acute ST elevation myocardial infarction (STEMI) within 72 hours prior to the index procedure.
2.Subject is hemodynamically unstable.
3.Subject is pregnant and/or breastfeeding or intends to become pregnant during the duration of the study.
4.Subject has a known allergy to contrast medium that cannot be adequately pre-medicated, or any known allergy to thienopyridine, aspirin, both heparin and bivalirudin, L-605 cobalt-chromium (Co-Cr) alloy or one of its major elements (cobalt, chromium, tungsten and nickel), acrylic, fluoropolymers, silicon carbide, PLLA, sirolimus or everolimus.
5.Revascularization of any target vessel within 9 months prior to the index procedure or previous PCI of any non-target vessel within 30 days prior to the index procedure.
6.Planned treatment of a lesion not meeting angiographic inclusion and exclusion criteria during the index procedure or after the index procedure.
7.Planned surgery within 6 months of index procedure unless dual antiplatelet therapy can be maintained throughout the peri-surgical period.
8.History of a stroke or transient ischemic attack (TIA) within 6 months prior to the index procedure.
9.Subjects with active bleeding disorders, active coagulopathy, or any other reason, who are ineligible for DAPT.
10.Subject will refuse blood transfusions.
11.Subject has documented left ventricular ejection fraction (LVEF) < 30% as evaluated by angiography, echocardiogram, radionuclide ventriculography or any non-invasive imaging

method within 90 days prior to the index procedure.
12.Subject is dialysis-dependent.
13.Subject has impaired renal function (i.e., blood creatinine > 2.5 mg/dL or 221 *mol/L determined within 7 days prior to the index procedure).
14.Subject has leukopenia (i.e. < 3,000 white blood cells/mm3), thrombocytopenia (i.e. < 100,000 platelets/mm3) or thrombocytosis (i.e. > 700,000 platelet/mm3).
15.Subject is receiving oral or intravenous immunosuppressive therapy (inhaled steroids are permitted), or has known life-limiting immunosuppressive or autoimmune disease (e.g., human immunodeficiency virus, systemic lupus erythematosus; diabetes mellitus is permitted).
16.Subject is receiving chronic anticoagulation (e.g. coumadin, dabigatran, apixaban, rivaroxaban or any other agent).
17.Subject has life expectancy of < 1 year.
18.Subject is participating in another investigational (medical device or drug) clinical study. Subjects may be concurrently enrolled in a post-market study, as long as the post-market study device, drug or protocol does not interfere with the investigational treatment or protocol of this study.
19.In the investigator*s opinion, subject will not be able to comply with the follow-up requirements.

Study design

Design

Study phase:	4
Study type:	Interventional
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):	23-10-2015
Enrollment:	80
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	17-08-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-10-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-09-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-11-2016
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	NCT02389946
CCMO	NL52331.060.15

Study results

Date completed:	03-12-2020
Results posted:	21-01-2022
Actual enrolment:	17

Summary results
Trial is onging in other countries

First publication
05-11-2021