A PROSPECTIVE RANDOMIZED COMPARISON OF THE BIOFREEDOMTM BIOLIMUS A9TM DRUG COATED STENT VERSUS THE GAZELLE* BARE METAL STENT IN PATIENTS AT HIGH RISK FOR BLEEDING

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1) Safety: Non inferiority of the BioFreedom* to the Gazelle* Bare Metal Stent in patients treated with one month DAPT only followed by aspirin alone. The non-inferiority will be assessed by the composite endpoint of CD, MI and ST at 1 year.2)...

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

Summary

ID

NL-OMON38988

Source
ToetsingOnline

Brief title
LEADERS FREE

Condition

- Coronary artery disorders

Synonym
atherosclerosis, Coronary Artery Disease

Research involving
Human

Sponsors and support

Primary sponsor: Biosensors SA
Source(s) of monetary or material Support: Biosensors Europe;S.A.

Intervention

Keyword: angina, bare metal stent, drug coated stent, high bleeding

Outcome measures

Primary outcome

Primary Endpoints:

Safety:

1. The composite of cardiac death, myocardial infarction and definite/probable

stent thrombosis at one year.

Efficacy:

2. The incidence of clinically driven target lesion revascularization at one

year.

Secondary outcome

Secondary Endpoints: [At all protocol defined follow-up time points (1, 2 and 4

months and 1 and 2 years) unless otherwise indicated]

1. Primary endpoints at 2 years

2. Bleeding per BARC criteria

a. BARC 3 to 5

b. All BARC

c. By vascular access site (Femoral/Radial)

3. All individual components of the primary endpoint (see below)

a. Cardiac Death

b. Myocardial infarction (according to the Third universal definition Q

wave, Non-Q wave and all Myocardial Infarction

c. Stent Thrombosis, per ARC definition of definite and probable

4. Stent Thrombosis per ARC definition

a. Definite, Probable and Possible

b. Definite

5. Urgent TLR

6. Clinically driven TLR at times points other than the primary endpoint

7. Clinically driven target vessel revascularization

8. All cause mortality

9. Primary endpoints at 1 year, in patients with at least 1 lesion treated with

a trial stent of 3mm or less in nominal diameter

10. Cost effectiveness (1 year; in predefined European countries)

11. Quality of Life (1 year; in predefined European countries)

Study description

Background summary

Atherosclerosis and coronary artery thrombosis are a major cause of premature death worldwide, and are source of loss of disability-adjusted life years. Treatment goals for patients with CAD are improvement in survival and a reduction in the risk of heart attack and symptoms of coronary disease. Balloon angioplasty with stent implantation of narrowed coronary lesions that cause a lack of blood supply to the heart can improve a patient's functional status and outcome.
Stents have been continuously improved in order to ensure better outcomes for patients. Currently, most stents are covered with a drug to reduce the risk of re-narrowing. One of the drugs which are widely used is Biolimus A9*, a strong

anti-inflammatory agent, which suppresses the growth of certain cells in the arteries.
In order to prevent blood from clotting within the stent, the blood needs to be modified slightly. This is accomplished through the simultaneous treatment with two antiplatelet drugs (Aspirin plus either Clopidogrel or Prasugrel or Ticagrelor). The type of stents covered with drugs called *drug-eluting stents* require a longer (6 to 12 months) treatment with double antiplatelet drugs than the stents not covered with a drug, the so-called *bare-metal stents (BMS)*. BMS require only one month of the double antiplatelet treatment because the time necessary for the artery to heal is shorter with bare metal stents than with drug-eluting stents.
While the prolonged double treatment does not cause any harm in most patients, there are some patients in whom the advantage of diminishing the risk of re-narrowing is offset by the increased bleeding risk due to the longer time that they need to take double antiplatelet treatment. A new generation of stents, called *drug coated stents* has been developed. . While in *drug-eluting stents* the drug is embedded in a synthetic polymer, which is attached to the metal backbone of the stent, in *drug coated stents* there is not any polymer used, but the stent is directly coated with the drug. This new stent has the potential to combine the benefit of being coated with a drug that prevents re-narrowing with the advantage of not requiring the prolonged dual anti-platelet treatment, because the healing process is possibly faster than with a drug eluting stent.
The stents used in this study are either the latest generation of stents, the drug coated stents, or uncovered stents, the bare-metal stents (BMS).
The Leaders free study will examine the risk/benefit of prolonged dual blood thinning medication in angioplasty and stented patients where increased risk for bleeding is not currently known. The study examines the shorter use of DAPT in comparison to the usual use after DES implantation.

Study objective

1) Safety: Non inferiority of the BioFreedom* to the Gazelle* Bare Metal Stent in patients treated with one month DAPT only followed by aspirin alone. The non-inferiority will be assessed by the composite endpoint of CD, MI and ST at 1 year.
2) Efficacy: Superiority of the BioFreedom* to the Gazelle* Bare Metal Stent as assessed by TLR at 1 year.

Study design

Prospective, multi center, multi-national, double blinded, randomized, trial designed to enroll 2456 patients at up to seventy centers worldwide. Patients will be randomized at 1:1 ratio to the stent treatment. All patients will be followed for 2 years.

Intervention

The patient will undergo coronary angioplasty as normal and the stent used will be for:

Group A. Biosensors Gazelle* Bare Metal Coronary Stent: a stent which has not been covered with a drug. It has been commercially approved (CE Mark 2146002CE01).

Group B. Biosensors BioFreedom* Coronary Stent: is very similar to the Gazelle stent and is made by the same company, but coated with the drug Biolimus A9*, which has proved to be efficient in preventing artery re-narrowing.

+ One month of Aspirin plus either Clopidogrel/ Parasugrel/Ticagreolor for groupe A and group B, followed by single Antiplatelet therapy indefinetely

The post-procedure tests and examination as well as the follow-up will be the same for both groups and are part of the hospital routine.

Study burden and risks

Before and after the procedure the patient will take two blood-thinning medications to prevent blood from clotting within the stents. These drugs, Aspirin and Clopidogrel (or Prasugrel or Ticagrelor), are used routinely following stent placement.
Patient may also get other medications.

Follow-up: at 1, 2 and 4 months as well as at 1 and 2 years.
Without patient's problems, 2- and 4-month as well as 2-year Follow-Up may be done over the telephone.
The Follow Up at 1 month and 1 year should be done at the hospital.

Blood samples (about 2 tablespoons) will be collected for the study before procedure and at discharge.
This will be done whether the patient participate in this study or not and are routine for the procedure.
For the women of child-bearing potential, a pregnancy test to rule out pregnancy will be performed up to 7 days before stent placement.
Only testings that are standard of care at the site hospital for patients with study condition will be performed.

Risk:
A small number of people will have complications from their treatment. The risk of a problem varies depending on patient overall health and individual heart condition. As with any treatment of narrowing of one or more coronary artery

lesions, the major complications are
• Death: than 1%
• Stroke: 0.5%
• Heart Attack:2-5%
• Bleeding (major and minor): 2-5% The potential risk of receiving stents coated with a drug combined with only one month double antiplatelet treatment, is the risk of a blockage of the stent(s), called stent thrombosis and the potential risk of heart attack or death due to this blockage. The known risk of receiving a stent without a drug in comparison to a drug-eluting stent is the more frequent (up to 20%) re- narrowing of the coronary arteries.

Other risks for both stents include the fact that occasionally coronary angioplasty cannot be performed because of technical difficulties with the inability to pass the balloon or stent across the narrowed artery.

During the procedure, X-rays are use to direct the stent to the correct position. No additional radiation will be used in the study; exposure to the radiation will be part of the normal care and should carry no extra risks.
High doses of x-ray has the potential to cause skin damage, however, we do not anticipate this procedure will exceed the accepted threshold.

Benefit:
The information gathered in the study may help to improve the treatment given to patients with an increased bleeding risk and coronary artery disease in the future.

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

Any indication for PCI-S in patients deemed at high risk for bleeding and candidates for 1 month DAPT. This includes candidates with stable angina, silent ischemia, ACS (STEMI and non-STEMI), non-native lesions and in-stent restenosis. Patients must provide written informed consent.
Reasons of unsuitability for > 1 month dual antiplatelet treatment must include one or MORE of the following:
1. Adjunctive oral anticoagulation treatment planned to continue after PCI
2. Age >= 75 years old
3. Baseline Hgb <11 g/dl (or anemia requiring transfusion during the 4 weeks prior to randomization)
4. Any prior intracerebral bleed
5. Any stroke in the last 12 months
6. Hospital admission for bleeding during the prior 12 months
7. Non skin cancer diagnosed or treated < 3 years
8. Planned daily NSAID (other than aspirin) or steroids for >30 days after PCI
9. Planned surgery that would require interruption of DAPT (within next 12 months)
10. Renal failure defined as: Creatinine clearance <40 ml/min
11. Thrombocytopenia (PLT <100,000/mm3)
12. Severe chronic liver disease defined as: patients who have developed any of the following: variceal hemorrhage, ascites, hepatic encephalopathy or jaundice
13. Expected non-compliance to prolonged DAPT for other medical reasons

Exclusion criteria

1. Pregnant and breastfeeding women
2. Patients expected not to comply with 1 month DAPT
3. Patients requiring a planned staged PCI procedure more than one week after the index

procedure
4. Procedure planned to require non-study stents, or stand-alone POBA or stand-alone atherectomy
5. Active bleeding at the time of inclusion
6. Reference vessel diameter <2.25 - >4.0mm
7. Cardiogenic shock
8. Compliance with long-term single anti-platelet therapy unlikely
9. A known hypersensitivity or contraindication to aspirin, clopidogrel (or prasugrel, or ticagrelor if applicable), stainless steel, zinc, Biolimus A9TM or a sensitivity to contrast media, which cannot be adequately pre-medicated
10. PCI during the previous 12 months for a lesion other than the target lesion of the index procedure
11. Participation in another clinical trial (12 months after index procedure)
12. Patients with a life expectancy of < 1 year
13. Patients under judicial protection, tutorship or curatorship (for France only)

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-06-2013
Enrollment:	50
Type:	Actual

Medical products/devices used

Generic name:	Biosensors BioFreedom BA9 Drug Coated Coronary Stent

Registration:	No

Ethics review

Approved WMO Date:	14-05-2013
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	19-12-2013
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)

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	NCT01623180
CCMO	NL43274.075.13