BIOTRONIKS * Acute performance Of a Drug Eluting Absorbable Metal Scaffold (DREAMS 2G) in patients with de Novo Lesions in NatiVE Coronary Arteries: BIOSOLVE-III

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The study objective is to assess the acute clinical performance of the drug eluting absorbable metal scaffold (DREAMS 2G)

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

Summary

ID

NL-OMON42722

Source
ToetsingOnline

Brief title
BIOSOLVE-III

Condition

- Coronary artery disorders

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

Research involving
Human

Sponsors and support

Primary sponsor: Biotronik
Source(s) of monetary or material Support: Biostronik AG

Intervention

Keyword: coronary artery disease, DREAMS 2G, drug-eluting absorbable metal scaffold

Outcome measures

Primary outcome

The primary endpoint of this study is acute performance of the DREAMS 2G

assessed by Procedure Success.

Procedure Success is defined as achievement of a final diameter stenosis of

<30% by QCA (using any percutaneous method) without the occurrence of death,

Q-wave or non-Q-wave MI, or repeat revascularization of the target lesion

during the hospital stay.

Secondary outcome

Clinical endpoints:

* Target Lesion Failure (TLF*) at 1, 6 12, 24 and 36-months post procedure.

* Scaffold thrombosis rate at 1,6, 12, 24 and 36-months (according to ARC

definition)

* TLF is a composite of cardiac death, target vessel Q-wave or non-Q wave

Myocardial Infarction (MI)**, Coronary Artery Bypass Grafting (CABG),

clinically driven TLR.

**Myocardial infarction will be adjudicated according to the Society for

Cardiovascular Angiography and Interventions (SCAI) for a definition of

Clinically Relevant Myocardial Infarction After Coronary Revascularization (for

peri-procedural MIs)

Angiographic endpoints:

* Binary in-scaffold and in-segment restenosis rate at 12-months

* % in-scaffold and in-segment diameter stenosis at 12-months

* In-segment Late lumen loss at 12-months

* In-scaffold Late lumen loss at 12-months

Study description

Background summary

In comparison to Bare Metal Stents (BMS), Drug-Eluting Stents (DES) have shown reduced restenosis rate but have been associated with an increased risk of late thrombotic events which can*t be limited by prolonged dual antiplatelet therapy (DAPT). Bioabsorbable Vascular Scaffolds (BVS) have been developed to overcome the limitations of BMS and DES, and to avoid creation of a permanently caged vessel segment with inhibited vasomotion and vessel remodeling, chronic vessel wall inflammation or long-term stent crushing and fractures. Furthermore BVS provide improved non-invasive vessel lumen imaging by computer tomography or magnetic resonance technology and facilitate surgical or interventional target vessel and lesion reintervention.

The first Absorbable Metallic Scaffold (AMS) with magnesium alloy has been introduced by Biotronik AG as an alternative to polymeric scaffolds. It has a high mechanical strength and properties comparable to stainless steel stents in terms of its low elastic recoil (<8%), high collapse pressure (0.8 bar), and minimal shortening after inflation (<5%)
The AMS device has been improved by using a different magnesium alloy with a slower degradation time and by changing the strut shape in cross section from rectangular to square, thus improving scaffolding properties. A drug-polymer matrix with paclitaxel has been added to inhibit neo-intimal proliferative

response.
The improved AMS: DREAMS (Drug Eluting Absorbable Metal Scaffold) was tested in the BIOSOLVE-I study. In this prospective, multi-center, first-in-man trial the DREAMS showed an excellent clinical safety profile with no cardiac death or scaffold thrombosis up to 12-month follow-up.
However, even so the refinement of the device resulted in significant improvements compared to the bare AMS and the TLF rates were comparable to contemporary drug eluting stents and the ABSORB BVS, late lumen loss results were not comparable to the DES and BVS and required enhancement of the device.
Thus DREAMS 1G was further improved to DREAMS 2G (2nd generation), which has a more flexible and stronger scaffold backbone design, higher bending flexibility, and higher radial force. Radiopaque markers were also added for better x-ray visibility of the scaffold. Furthermore, the drug-polymer coating has been changed from Paclitaxel to Sirolimus in combination with a bioresorbable PLLA-polymer to decrease neo-intima formation more effectively. This same drug-polymer coating is also successfully used in the commercially available Orsiro sirolimus eluting coronary stent system (Biotronik AG).

DREAMS 2G is currently under investigation in the BIOSOLVE-II study (BIOTRONIK * Safety and Clinical Performance of the Drug Eluting Absorbable Metal Scaffold DREAMS 2G in the Treatment of Subjects with de novo lesions in native coronary arteries). It is the first study to assess the safety and performance of a novel sirolimus-eluting absorbable magnesium scaffold.
123 subjects have been enrolled from October 2013 to May 2015.
The 6-month results of the BIOSOLVE-II trial are expected later this year.

In order to ensure 6F guiding catheter compatibility, the crossing profile of the DREAMS 2G has been reduced to 1.5mm.
The BIOSOLVE-III study will be conducted in order to proof easy deliverability and acute performance in regards to procedure success with the improved DREAMS 2G.
Even so the DREAMS 2G starts to lose its mechanical integrity at around 3 month, studies with the predecessor devices have shown the ability of positive remodeling at later time points. Since those subject cohorts have been rather small, results are only indicating the possibility of positive remodeling.
Therefore the BIOSOLVE-III trial aims to assess 12-month LLL, % diameter stenosis and binary restenosis rate as secondary endpoints in a larger population

Study objective

The study objective is to assess the acute clinical performance of the drug eluting absorbable metal scaffold (DREAMS 2G)

Study design

This is a prospective, multi-center trial to be conducted in up to 7 investigational sites.
Up to 61 subjects will be enrolled in order to ensure 60 evaluable study subjects.
Clinical follow-up visits will take place at 1, 6, and 12 months and annually until 3 years post procedure.
All subjects will undergo angiographic follow-up at 12months.

Intervention

Percutaneous transluminal coronary angioplasty (PTCA) including concomitant anticoagulation medication according to protocol and implantation of the DREAMS 2G scaffold.

Study burden and risks

The use of the DREAMS scaffold may lead to undesirable effects or discomfort. The same risks associated with treatment with an authorised stent or balloon may occur. No increased incidence is expected based on earlier studies with the preceding product and similar products. Some of the risks can also occur during the control angiograms at 12 months.

Complications of the heart:
Occlusion of coronary arteries with decreased supply of blood to the heart with heart attack in extreme cases, re-stenosis (renewed narrowing of a treated vessel), cardiogenic shock (abnormal function of the heart chamber), chest pain, cardiac tamponade (accumulation of fluid inside the pericardial space, adversely affecting the function of the heart), perforation or dissection (rupture) of the coronary artery, of the aorta or of the heart, emergency heart surgery, pericardial effusion (abnormal accumulation of fluid inside the pericardial space), development of an aneurysm (pathological distension of an artery), death
Cardiac arrhythmias:
Ventricular tachycardia (accelerated heart rate); ventricular or atrial fibrillation (uncoordinated contraction of the muscle of the heart chambers); bradycardia (reduced heart rate)
Complications due to the scaffold:
Failure to place the scaffold at the intended site, detachment of the scaffold from the introduction system, faulty placement of the scaffold, deformation of the scaffold, embolisation of the scaffold (detachment of the scaffold from the catheter with subsequent displacement), scaffold thrombosis (formation of a blood clot inside the scaffold) or occlusion, breaking of scaffold, movement of the scaffold, insufficient attachment of the scaffold to the vascular wall or compression of the scaffold, problems while inflating the balloon, rupture or small hole in the balloon of the introduction system, problems deflating the balloon, difficulties in retracting the equipment, embolisation (detachment and

displacement) of the catheter material
Events affecting the airways:
Acute pulmonary oedema (accumulation of fluid inside the lungs), heart failure (inability of the heart to pump a sufficient amount of blood), respiratory insufficiency or respiratory failure (inability of the lungs to provide enough oxygen to the tissue)
Events affecting the vessels:
Bruising at the access site, drop / increase in blood pressure, pseudo-aneurysm (hematoma that forms as the result of a leaking hole in an artery), formation of arteriovenous fistula (abnormal connection between an artery and a vein), retroperitoneal (in the posterior abdominal cavity) bruising, rupture or perforation of the vascular wall, re-stenosis, thrombosis (blood clot inside the vessel) or occlusion, vascular cramps, disturbed peripheral circulation, rupture of the vascular wall, distal embolism (occlusion of the vessel due to material that has become detached from a blood clot)
Bleeding events:
Bleeding at the access site or other bleeding events that require a transfusion or another form of treatment
Events affecting the nervous system:
Stroke or transient ischemic attack (TIA) of the brain causing neurological deficits, damage to the nerves
Allergic reactions:
Allergic reactions to the contrast medium, to the platelet aggregation inhibitor (drug to prevent the formation of blood clots), to the scaffolding material, to the polymer coating or sirolimus or its breakdown products
There is a possibility of adverse reactions of the body to the medicinal component of DREAMS. The exceedingly low quantity of sirolimus in blood plasma means that the classical side effects triggered by the medication are less relevant than during systemic treatment and occur significantly less frequently. The following undesirable effects are known: Abnormal liver values, anaemia (low blood count), joint pains, diarrhoea, hypercholesterolaemia, hypersensitivity reaction, including anaphylactic reaction, hypertriglyceridaemia, hypokalaemia (reduced blood potassium level), infections, interstitial pulmonary disease (disease affecting the tissue of the lungs), lymphoma or other malignant diseases, thrombocytopenia (platelet deficiency in the blood)
As with any product, new and previously unknown side effects may occur when using the test product.
The control angiogram scheduled at 12 months harbours risks or can lead to discomfort. The use of X-ray radiation is necessary to carry out the angiogram. Experience with patients receiving similar treatment has shown that the total additional X-ray radiation lasts between about 5-10 minutes. This corresponds to a radiation dose of about 4-6 millisievert (mSv; depending on X-ray system used); as a comparison: the average exposure to natural radiation per year amounts to about 2.5 mSv.
Please tell the employees of the study staff about all symptoms, diseases or injuries that occur during the course of the clinical study. If any of these

are serious, inform the study staff immediately, if necessary by telephone.

Potential Benefits:
Compared to a 'normal' permanent stent, the DREAMS scaffold does not remain inside your coronary arteries but is absorbed over time. You may benefit from this form of treatment, as it allows the same section of the vessel to be retreated with a stent at a later point in time without having to apply multiple layer of stents, or if necessary the vessel can be treated with a bypass. In addition, the risk of a later blood clot may be reduced, as no stent remains inside the vessel at which a blood clot could later develop. Furthermore, inflammation caused by the stent remaining inside the vessel may be prevented, which could lead to a reduction in the development of new stenosis (atherosclerosis). Another potential benefit is that lateral branches that branch off from the narrowing being treated are blocked less or only temporarily, which in turn improves blood supply to the vessel. As the scaffold is absorbed over time, the mobility of the vessel is only reduced during the first 3-4 months. Moreover, non-invasive procedures such as an MRI or CT are easier to interpret, as there are no artefacts caused by metal; this could help prevent a potential coronary angiogram at a later point in time. However, as the function of the test product has not been demonstrated yet, it is also possible that you will not have the desired benefit from participating in this clinical study.
In addition, your health will be intensively monitored during the study visits. The health of your coronary arteries will be assessed as part of the planned control angiogram, which means that the progression of your disease can be controlled and newly developing stenosis can be detected and treated accordingly. Your participation in the study contributes to the development of potential and improved therapies for patients with atherosclerosis in 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

1.Subject is > 18 years and < 80 years of age
2.Written subject informed consent available prior to PCI
3.Subject with stable or unstable angina pectoris or documented silent ischemia
4.Subject eligible for PCI
5.Subject acceptable candidate for coronary artery bypass surgery
6.Subject with a maximum of two single lesions in two separate coronary arteries which have to be de novo lesions.
7.Reference vessel diameter between 2.7-3.8 mm by visual estimation, depending on the scaffold size used.
8.Target lesion length * 21 mm by visual estimation, depending on the scaffold size used.
9.Target lesion stenosis by visual estimation, assisted by QCA: > 50% - < 100%
10.Eligible for Dual Anti Platelet Therapy (DAPT)

Exclusion criteria

1.Pregnant 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 a *2 fold CK level or in absence of CK a *3 fold CKMB level above the upper range limit within 24 hours prior to the procedure
4.Left main coronary artery disease
5.Three-vessel coronary artery disease at time of procedure
6.Thrombus in target vessel
7.Subject is currently participating in another study with an investigational device or an investigational drug and has not reached the primary endpoint yet
8.Planned interventional treatment of any non-target vessel within 30 days post-procedure
9.Subject is on dialysis

10.Planned intervention of the target vessel after the index procedure
11.Ostial target lesion (within 5.0 mm of vessel origin)
12.Target lesion involves a side branch >2.0 mm in diameter
13.Documented left ventricular ejection fraction (LVEF) * 30%
14.Heavily calcified lesion
15.Target lesion is located in or supplied by an arterial or venous bypass graft
16.The target lesion requires treatment with a device other than the pre-dilatation balloon prior to scaffold placement (including but not limited to directional coronary atherectomy, excimer laser, rotational atherectomy, etc.)
17.Unsuccessful pre-dilatation, defined as minimal lumen diameter smaller than the respective crossing profile of DREAMS 2G and angiographic complications (e.g. distal embolization, side branch closure, extensive dissections that can*t be covered by a single scaffold), by visual estimation
18.Known allergies to: Acetylsalicylic Acid (ASA), Heparin, contrast medium, Sirolimus, Everolimus or similar drugs (i.e., ABT 578, Biolimus, Tacrolimus), PLLA, Silicon Carbide, Magnesium, Yttrium, Neodymium, Zirconium, Gadolinium, Dysprosium, Tantalum
19.Impaired renal function (serum creatinine > 2.5 mg/dl or 221 mmol/l) determined within 72 hours prior to intervention
20.Subject is receiving oral or intravenous immuno-suppressive therapy (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)
21.Proximal or distal to the target lesion located stenosis that might require future revascularization or imped run off detected during diagnostic angiography
22.Life expectancy less than 1 year
23.Planned surgery or dental surgical procedure within 6 months after index procedure
24.Subject with tortuous vessel that may impair scaffold placement in the region of obstruction or proximal to the lesion
25.In the investigators opinion subjects will not be able to comply with the follow-up requirements

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-05-2016
Enrollment:	12
Type:	Actual

Medical products/devices used

Generic name:	DREAMS 2G Drug-Eluting Coronary Scaffold System
Registration:	No

Ethics review

Approved WMO Date:	17-03-2016
Application type:	First submission
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	NL55318.078.15

Study results

Results posted: 20-07-2020

First publication
23-06-2020