Safety and Clinical Performance of the Drug Eluting Resorbable Coronary Magnesium Scaffold System (Freesolve®) in the Treatment of Subjects with de Novo Lesions in Native Coronary Arteries: BIOMAG-II: A randomized controlled trial.

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

Summary

ID

NL-OMON57035

Source
ToetsingOnline

Brief title
BIOMAG-II study

Condition

- Coronary artery disorders

Synonym
Coronary artery disease, Coronary stenosis

Research involving
Human

Sponsors and support

Primary sponsor: BIOTRONIK Nederland B.V.
Source(s) of monetary or material Support: BIOTRONIK AG

Intervention

Keyword: Percutaneous Coronary Intervention, Resorbable Coronary Magnesium Scaffold

Outcome measures

Primary outcome

Target Lesion Failure (TLF) at 12 months, a composite of Cardiac Death, Target Vessel Q-wave or non-Q wave MI, and clinically driven Target Lesion Revascularization (TLR).

see also CIP section 7.7

Secondary outcome

* Safety Objective: Cardiac death at 1, 6, 12, 24, 36, 48 and 60 months; target vessel MI (TV-MI) at 6, 12, 24, 36, 48 and 60 months; definite/probable scaffold thrombosis at 1, 6, 12, 24, 36, 48 and 60 months;

*Performance Objective: clinically driven TLR at 1, 6, 12, 24, 36, 48 and 60 months; procedure success.

* A powered secondary endpoint analysis in the diabetic population will be performed to support a diabetic indication for Freesolve.

* A powered secondary endpoint analysis evaluating cumulative TLF rates between 1- and 5-years post-procedure will be performed.

* TLF, composite of Cardiac Death, Target Vessel Q-wave or non-Q wave MI, and clinically driven TLR at 1, 6, 12, 24, 36, 48 and 60 months.

* TVF, a composite of Cardiac Death, Target Vessel Q-wave or non-Q wave MI, and clinically driven Target Vessel Revascularization (TVR) at 1, 6, 12, 24, 36, 48 and 60 months.

* Cardiac death at 1, 6, 12, 24, 36, 48 and 60 months.

* Cardiovascular death at 1, 6, 12, 24, 36, 48 and 60 months.

* All-cause mortality at 1, 6, 12, 24, 36, 48 and 60 months.

* Target vessel MI in accordance to protocol defined peri-procedural MI and 3rd universal definitions for non-periprocedural MI at 1, 6, 12, 24, 36, 48 and 60 months.

* Any MI (including non-target vessel territory) at 1, 6, 12, 24, 36, 48 and 60 months.

* Clinically driven TLR at 1, 6, 12, 24, 36, 48 and 60 months.

* Clinically driven TVR at 1, 6, 12, 24, 36, 48 and 60 months.

* Definite or probable scaffold thrombosis rate at 1, 6, 12, 24, 36, 48 and 60 months (according to ARC-2 definition).

* Procedure success defined as achievement of < 30% final residual diameter stenosis (by Quantitative Coronary Angiography (QCA) or visual estimation of the target lesion, without the occurrence of cardiac death, Q-wave or non-Q-wave MI, or repeat revascularization of the target lesion during the hospital stay.

* Device Success defined as a final residual diameter stenosis of <30% by QCA or visual estimation using the assigned device only with:

- successful delivery of the device to the target lesion site in the coronary

artery and

- appropriate device deployment and

- successful removal of the delivery system

see also CIP section 7.8

Study description

Background summary

Standard of care treatment of coronary artery disease with drug-eluting stents (DES:Drug Eluting Stents) delivers good clinical outcomes with low target lesion failure (TLF) and stent thrombosis rates. Nevertheless, the use of DES presents some limitations, mainly due to the permanent presence of foreign material (metal) in the vessel wall. In particular, there is a long-term risk of stent failure, thrombosis, chronic inflammation due to the metal or polymer components and neoatherosclerosis. Moreover the metal cage can impair the vessel geometry, access and flow into side branches and can inhibit normal vasomotor function, which may hinder compensatory positive re-modelling and limits use of imaging and future treatment options. Bioresorbable scaffolds (BRS) were developed to overcome these problems, enabling vessel restoration and reducing long term risks. BRS are meant to provide a temporary drug eluting scaffold, which supports the vessel after implantation, limiting acute recoil and negative re-modelling, and enables a natural biologic reconstruction of the arterial wall and restoration of the vascular function once the scaffold is resorbed.
The ability of scaffolds to meet these expectations, however, have been partly questioned by suboptimal results of the Absorb Bioresorbable Vascular Scaffold (BVS) (Abbott Vascular, Santa Clara, CA) showing higher incidence of scaffold thrombosis and target vessel-related myocardial infarction. Notably, while Absorb BVS consists solely of a poly-L-lactic acid (PLLA) polymer which resorbs over a period of more than 24 months, other scaffolds have different materials and designs. In particular, the Magmaris (here after referred to also as DREAMS 2G= 2nd generation) consists of a magnesium (Mg) alloy which resorbs in approximately 12 months. Data from clinical trials thus far have demonstrated the clinical safety and performance of Magmaris and have not shown the same safety concerns as Absorb. DREAMS 2G gained CE-Mark in 2016 and since then is marketed as Magmaris.

Despite these positive results, iterative improvement of Magmaris to enhance performance and usability led to the development of the 3rd generation scaffold, DREAMS 3G (here after referred to also as Freesolve® Sirolimus-Eluting Coronary Resorbable Magnesium Scaffold (RMS) System). This scaffold is built with a refined magnesium alloy and enhances some scaffold properties, such as radial strength, scaffolding time and marker visibility, broadens the size range and reduces crossing profile and strut thickness. All these changes are meant to improve overall clinical outcomes. The Dreams 3G (Freesolve scaffold) obatained CE-mark in February 2024.
In order to demonstrate the safety and efficacy of Freesolve with respect to the current state of the art devices for treatment of coronary artery disease, drug eluting stents, a head-to-head comparison of Freesolve with the Xience DES will be performed in the BIOMAG-II randomized controlled trial.
This is to comply with the current regulation for medical devices (MDR) for the collection of Post Market Clinical Follow Up (PMCF) data.

Study objective

The study aims to assess the safety and efficacy of the Freesolve scaffold in de novo coronary artery lesions compared to the Xience coronary stent system during standarfd clinical use. This is in the context of the MDR and the legal obligation to collect PMCF data.

Study design

A prospective, international, multi-center, randomized controlled, non-inferiority trial.

Intervention

Percutaneous coronary intervention (PCI) with either the Freesolve or the Xience stent.

Study burden and risks

As with any subjects undergoing percutaneous coronary intervention, subjects may experience adverse events and/or outcomes that are listed in the IFU and are not expected to differ from other contemporary drug eluting stent implantation procedures.
Potential adverse events related to the oral administration of sirolimus include, but are not limited to, abnormal liver function tests, anemia, arthralgia, diarrhea, hypercholesterolemia, hypersensitivity (including anaphylactic/ anaphylactoid type reactions), hypertriglyceridemia, hypokalemia, infections, interstitial lung disease, thrombocytopenia, leukopenia, lymphoma, and other malignancies. Since these events have been observed after oral systemic administration of sirolimus, it is deemed extremely unlikely that they

could occur after sirolimus-eluting scaffold implantation, even if they cannot be ruled out completely. Current literature gives no indication that these adverse events ever occurred specifically as a result of sirolimus-eluting stent/scaffold implantation. None of them were reported for DREAMS 3G in BIOMAG-I. Appropriate contraindications and warnings are included in the IFU provided with the study device.
In summary (see also CIP section 6, tabel 6), the device- and procedure-related adverse events/ side-effects identified in clinical data of DREAMS 3G are within the range of similar and benchmark devices or single occurrences. Therefore, the identified adverse events/ side-effects are deemed acceptable and do not have a negative impact on the benefit-risk ratio. No previously unknown side-effects were identified during the clinical evaluation of DREAMS 3G and risks were consistent across the intended patient population of DREAMS 3G.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

See CIP section 7.12.
1. Subject is >=18 years and <= 80 years old.
2. Written informed consent provided by subject before any study related procedure.
3. Subject is elegible for PCI according to current applicable guidelines.
4. Subject is an acceptable candidate for coronary artery bypass surgery.
5. Subjects with stable or unstable angina pectoris, documented silent ischemia/abnormal physiologic testing or hemodynamically stable non-ST elevation myocardial infarction (NSTEMI) patients without angiographic evidence of thrombus at target lesion.
Note: STEMI patients may be eligible for the study for treatment of selected non-culprit lesions, if:
* Subject and target lesion(s) meet all inclusion and no exclusion criteria and consent occurs at least >= 72 hours after successful treatment of the culprit lesion causing STEMI.
* Subject is hemodynamically stable with documented declining cardiac biomarkers.
* Target lesion(s) to be treated are not located in the culprit vessel(s) and are not culprit lesion(s).
6. Subject is elegible for DAPT therapy for at least 6-months.
7. Documented left ventricular ejection fraction (LVEF) >= 30% within 6 months prior to or during the procedure.
8. Subject is willing and able to comply with protocol requirements, including completion of study visits for the duration of the study.

Angiographic inclusion criteria:
1. Subjects with a maximum of two single de novo target lesions each in separate native coronary arteries.
2. Target vessel must have a reference vessel diameter between 2.5-4.2mm by visual estimation (may be assisted by QCA, IVUS or OCT).
3. Target lesion must be <= 28 mm in length by visual estimation (may be assisted by QCA, IVUS or OCT) (or < 20 mm for target lesion(s) to be treated with a study device < 3.0 mm in diameter) and must be amenable to treatment with a single study device.
Target lesion stenosis >= 50% and < 100% by visual estimation (may be assisted by QCA, IVUS or OCT).
4. Target lesion stenosis >= 50% and < 100% by visual estimation (may be assisted by QCA, IVUS or OCT). Target lesion stenosis < 70% by visual estimation, should have clinical justification for treatment as per local standards.
5. Target lesion must have a Thrombolysis In Myocardial Infarction (TIMI) flow

>=1.

Exclusion criteria

See CIP section 7.13
1. Subject is pregnant and/or breastfeeding or intends to become pregnant during the duration of the study.
2. Subject has clinical symptoms and/or electrocardiogram (ECG) changes consistent with STEMI < 72 hours prior to the index procedure. Note: Hemodynamically stable non-STEMI (NSTEMI) subjects are eligible for study enrollment.
3. Subject has undergone prior PCI within the target vessel during the last 12 months prior to the index procedure or prior PCI within a non-target vessel < 72 hours prior to the index procedure if successful and uncomplicated.
4. Subject is on dialysis or with impaired renal function (serum creatinine > 2.5 mg/dl or 221 µmol/L, determined within 72 hours prior to the index procedure).
5. known allergy to contrast medium, aspirin, P2Y12 inhibitors, heparin, bivalirudin, sirolimus, everolimus, poly L-lactide, the scaffold material (magnesium, aluminium, tantalum), or Xience stent material (cobalt, chromium, tungsten, nickel, methacrylic polymer, and fluoropolymer).
6. 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).
7. Life expectancy less than 1 year.
8. Planned surgery or dental surgical procedure within 6 months after index procedure, unless DAPT can be maintained.
9. In the investigator*s opinion subject will not be able to comply with the follow-up requirements.
10. Subjects under oral anticoagulation therapy (OAC) prior to index procedure unless DAPT + OAC (i.e. triple therapy) can be maintained for a minimum of 1 month.
11. Subject has had a stroke or transient ischemic attack (TIA) within 6 months prior to the index procedure.
12. Subject with active bleeding disorders, active coagulopathy, or any other reason, who is ineligible for DAPT.
13. Subject is currently participating or plans to participate in another study with an investigational device or an investigational drug.

Angiographic exclusion criteria
1. Target vessel has been previously treated and the target lesion is within 5 mm proximal or distal to the previously treated lesion.
2. Left main coronary artery disease.
3. Target lesion was totally occluded (100% stenosis).

4. Thrombus in target vessel.
5. Future planned staged PCI either in target or non-target vessel.
6. Ostial target lesion within the left descending (LAD), left circumflex (LCx), or right coronary artery (within 5.0 mm of vessel origin).
7. Target lesion involves a side branch >= 2.0 mm in diameter that requires a two-device strategy after pre-dilatation.
8. Target lesion is located in or supplied by an arterial or venous bypass graft.
9. Target lesion with excessive tortuosity proximal to or within the lesion based on visual estimation or heavily calcified target lesion which cannot be adequately pre-dilated by a non-compliant and/or cutting/scoring balloon as described in angiographic exclusion criteria 10.
10. The target lesion requires treatment with the device other than the non-compliant balloon and/or cutting/scoring balloon prior to scaffold/stent placement (including but not limited to atherectomy devices, intravascular lithotripsy, drug-coated balloons etc.)
11. Target vessel was treated with brachytherapy any time prior to the index procedure.
12. Unsuccessful pre-dilatation, defined as residual stenosis > 20% (by visual estimation) and / or angiographic complications (e.g. distal embolization, side branch closure, flow-limiting dissections)

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-01-2025
Enrollment:	120
Type:	Actual

Medical products/devices used

Generic name:	Freesolve
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	03-10-2024
Application type:	First submission
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	NCT05540223
CCMO	NL86352.100.24