Mg-BRS. Estudios BIOMAG

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Potential advantages of BRS

Bioresorption

1) Thrombosis 2) Side Branch jailing 3) Grafts 4) MSCT fup

Expansive vessel remodeling

Endothelial function and vessel phisiology restoration

Resorbable Magnesium Scaffold

Clinical trials with Magmaris (RMS)		
	24 months (Full cohort) BIOSOLVE-IV[1] (n=2,066) 6.8% TLF**	Definite/probable scaffold thrombosis 0.8%Δ
	36 months (First cohort) BIOSOLVE-IV[2] (n=1,075) 8.2% TLF**	Definite/probable scaffold thrombosis 0.6%°
	36 months BIOSOLVE-II/-III[3] (n=184) 6.4% TLF**	Definite/probable scaffold thrombosis 0.0%
	60 months BIOSOLVE-II[4] (n=123) 8.0% TLF**	Definite/probable scaffold thrombosis 0.0%

- Good safety and efficacy profile with low rates of thrombosis and TLF
- In-scaffold late lumen loss not comparable to contemporary DES

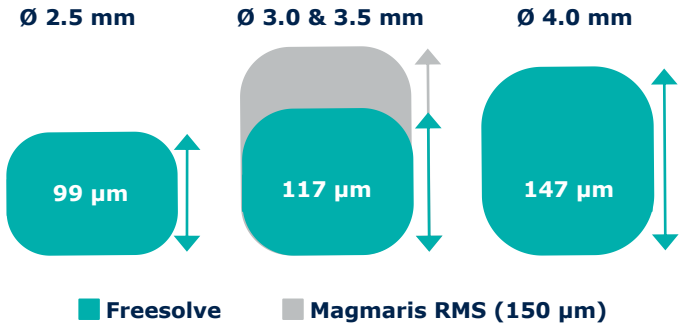
Freesolve RMS

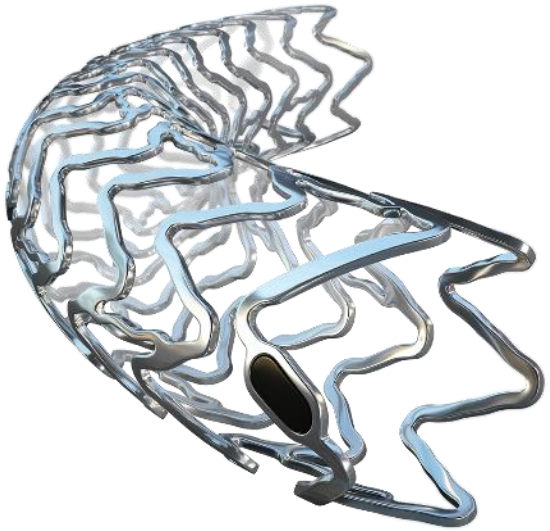
1. Increased durability of radial support, maintained resorption time of 12 month

BIOmag® Proprietary Alloy

- 93.75 wt% magnesium
- 6.25 wt% aluminum

2. Reduced strut thickness[1]

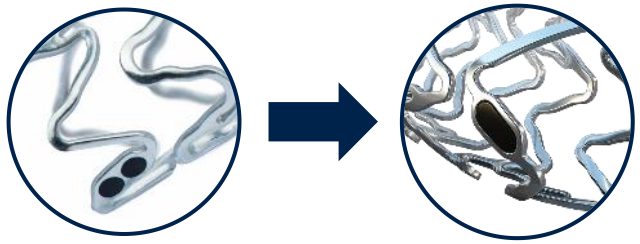




Freesolve

5. BIOlute®
Recubrimiento reabsorbible

3. Improved radiopacity[2]



Magmaris

Freesolve: marcador de tantalio

4. Increased size portfolio

mm	ø 2.5	ø 3.0	ø 3.5	ø 4.0
13	X	X	X	X
18	X	X	X	X
22	X	X	X	X
26		X	X	X
30		X	X	X
35		(X)	(X)	(X)
40		(X)	(X)	(X)

(X): Available at a later stage

1. BIOTRONIK data on file, compared to Magmaris. 2. BIOTRONIK data on file, BIOMAG-I case angiogram, courtesy of Prof. M. Haude, Rheinland Klinikum, Neuss, Germany 2021. BIOmag and BIOlute are a trademark or registered trademark of the BIOTRONIK Group of Companies, DREAMS 3G is the project name, the product is not CE marked.

Totalmente reabsorbido después de 12 meses

>99 % de los struts no son visibles a los 12 meses[2]

Entorno preclínico[1]

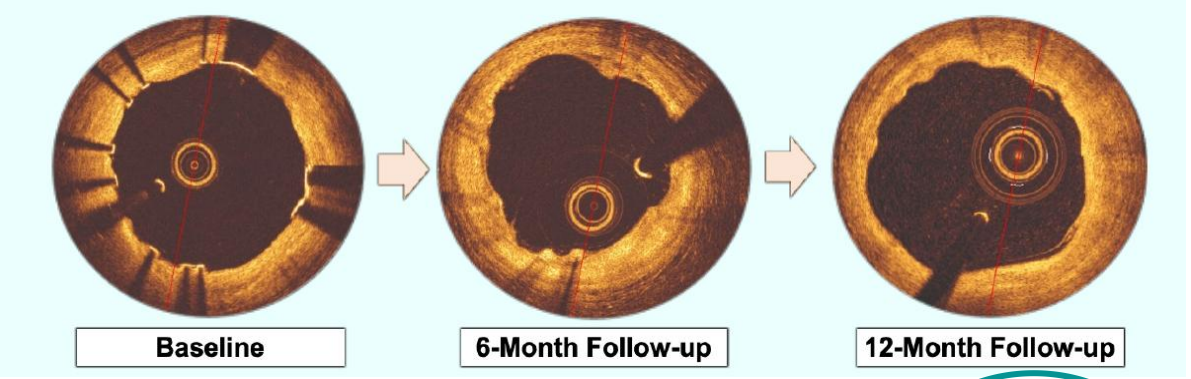
Al año, el scaffold estaba casi completamente degradado (99,6 %).

Puntos temporales	DREAMS 3G	Magmaris[b]	Valor p
28 d[a]	16,8 %±5,4 %	14,2 %±6,8 %	0,04
90 d	42,6 %±7,9 %	37,5 %±7,8 %	0,31
120 d	45,7 %±6,0 %	33,5 %±9,0 %	<0,01
180 d	64,9 %±4,0 %	n.d.[c]	n.d
365 d	99,6 %±0,5 %	n.d	n.d

99,6 %
del magnesio se reabsorbe en 12 meses[1]

Entorno clínico: Análisis BIOMAG-I[2]

El análisis de OCT reveló que el 99,3 % de los struts se habían degradado completamente a los 12 meses (lo que confirma los datos preclínicos).



99,3 %
de los struts se habían degradado completamente a los 12 meses[2]

a. Días; b. Scaffold de magnesio reabsorbible; c. No disponible. 1. Masaru Seguchi et al. Preclinical evaluation of the degradation kinetics of third generation resorbable magnesium scaffolds. EuroIntervention ; 2023; 18-publicación online previa a la versión impresa, enero 2023. DOI: 10.4244/EIJ-D-22-00718. 2. Twelve-months vessel healing profile following the novel resorbable magnesium scaffold implantation: an intravascular OCT analysis of the BIOMAG-I trial, presentado en el congreso de ESC 2023.

Safety and Clinical Performance of the Sirolimus Eluting Resorbable Coronary Magnesium Scaffold System (DREAMS 3G) in the Treatment of Subjects With de Novo Lesions in Native Coronary Arteries, BIOMAG-I First-In-Human Trial

BIOMAG-I

EuroIntervention
The Official Journal of EuroPCR and the European Association of Percutaneous Coronary Interventions (EAPCI)

Link to study publication →

CAUTION: Investigational Device. Limited by United States law to investigational use.

Study Design

BIOMAG-I First-In-Human Trial

Study objective

Assessment of the safety and clinical performance of DREAMS 3G in patients with *de novo* coronary artery lesions

Primary endpoint

In-scaffold late lumen loss **(LLL) at 6-month** post-procedure

Clinical endpoints at 1, 6, 12, 24, 36, 48 and 60 months

- Target Lesion Failure (TLF*)
- Cardiac death
- Target vessel MI**
- Clinically driven target lesion revascularization
- Clinically driven target vessel revascularization
- Definite/probable scaffold thrombosis (ARC-2 def.)

Up to 116 subjects with *de novo* coronary artery stenosis

1-month Clinical FUP

6-month
Clinical and angiographic FUP (mandatory)
IVUS and OCT (mandatory)

12-month
Clinical and angiographic FUP (mandatory)
IVUS & OCT (mandatory)
Vasomotion (if subject consents)

24-month Clinical FUP

36-month Clinical FUP

48-month Clinical FUP

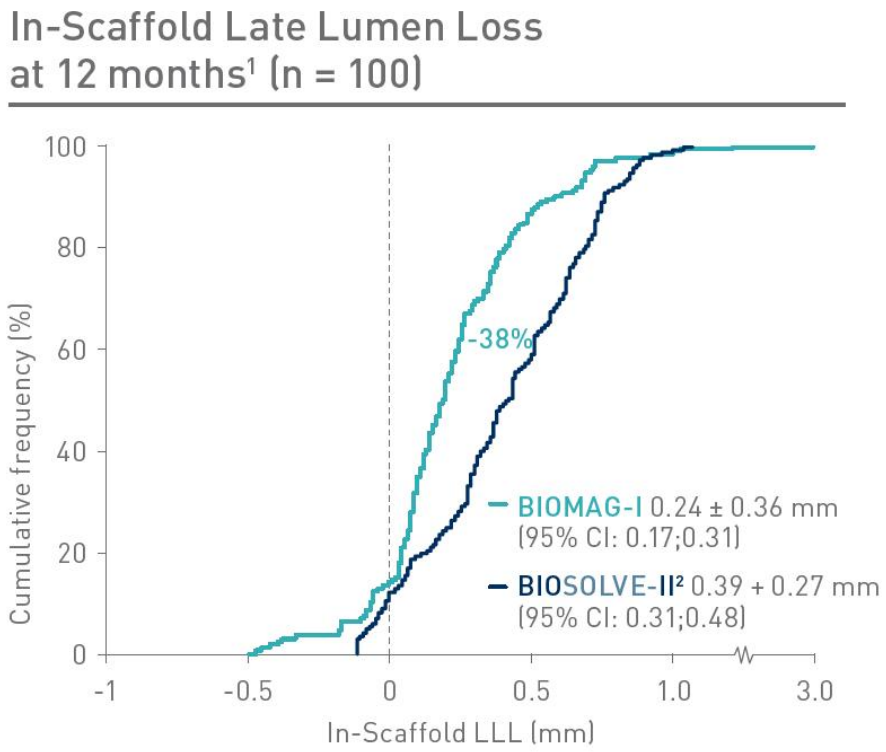
60-month Clinical FUP

ClinicalTrials.gov identifier: NCT04157153; * composite of cardiac death, target vessel myocardial infarction, and clinically driven target lesion revascularization;
** peri-procedural target vessel MI according to SCAI definition and non-peri-procedural target vessel MI according to Universal MI definition.

Late Lumen Loss at 12 months

BIOMAG-I FIH trial

In-Scaffold Late Lumen Loss at 12 months



FREESOLVE has an improved angiographic in-scaffold LLL compared to its precursor[2] Magmaris at 12-month follow-up

1. Haude, M "1-Year Clinical Outcomes of the new resorbable Magnesium scaffold DREAMS 3G, from the first in-human BIOMAG-I study" presented at EuroPCR May 2023; 2. Haude M, et al., Sustained safety and performance of the second-generation drug-eluting absorbable metal scaffold in patients with de novo coronary lesions: 12-month clinical results and angiographic findings of the BIOSOLVE-II first-in-man trial. Eur Heart J 2016;37:2701-2709. 3. Byrne RA, et al., Report of a European Society of Cardiology-European Association of Percutaneous Cardiovascular Interventions task force on the evaluation of coronary stents in Europe: executive summary. Eur Heart J 2015;36:2608-262.

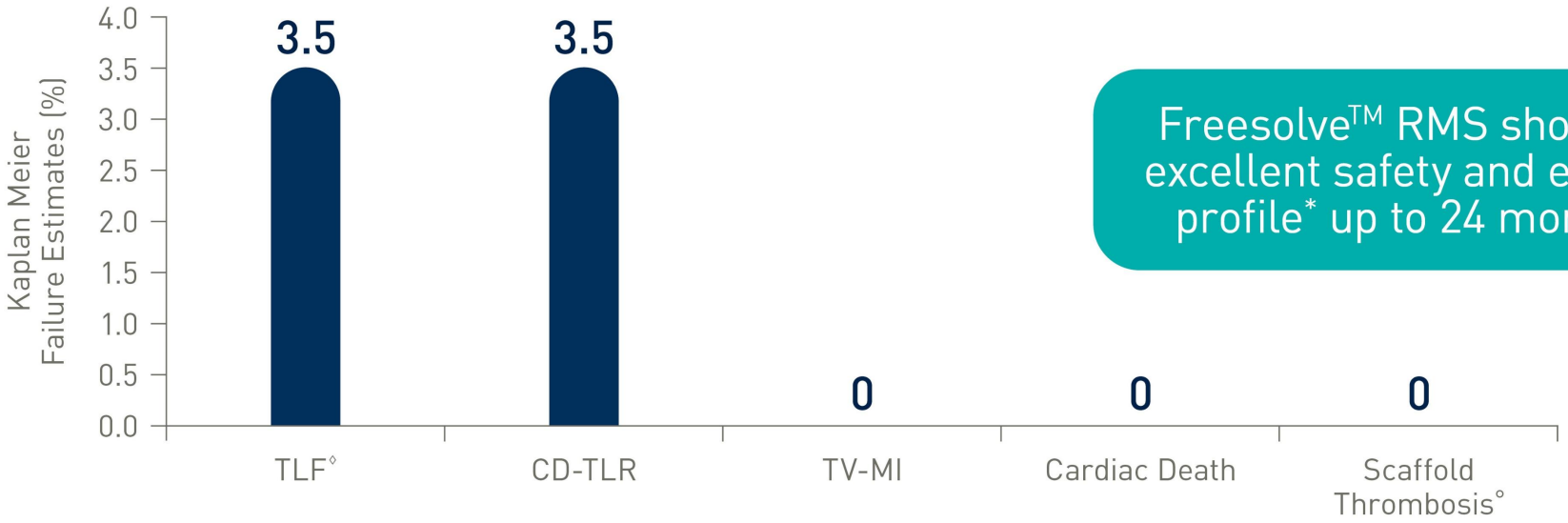
Resultados clínicos a los 24 meses de seguimiento

BIOMAG-I

BIOTRONIK
excellence for life

BIOMAG-I 24-month data

First-In-Human trial for new generation RMS



Freesolve™ RMS shows an excellent safety and efficacy profile* up to 24 months.[1]

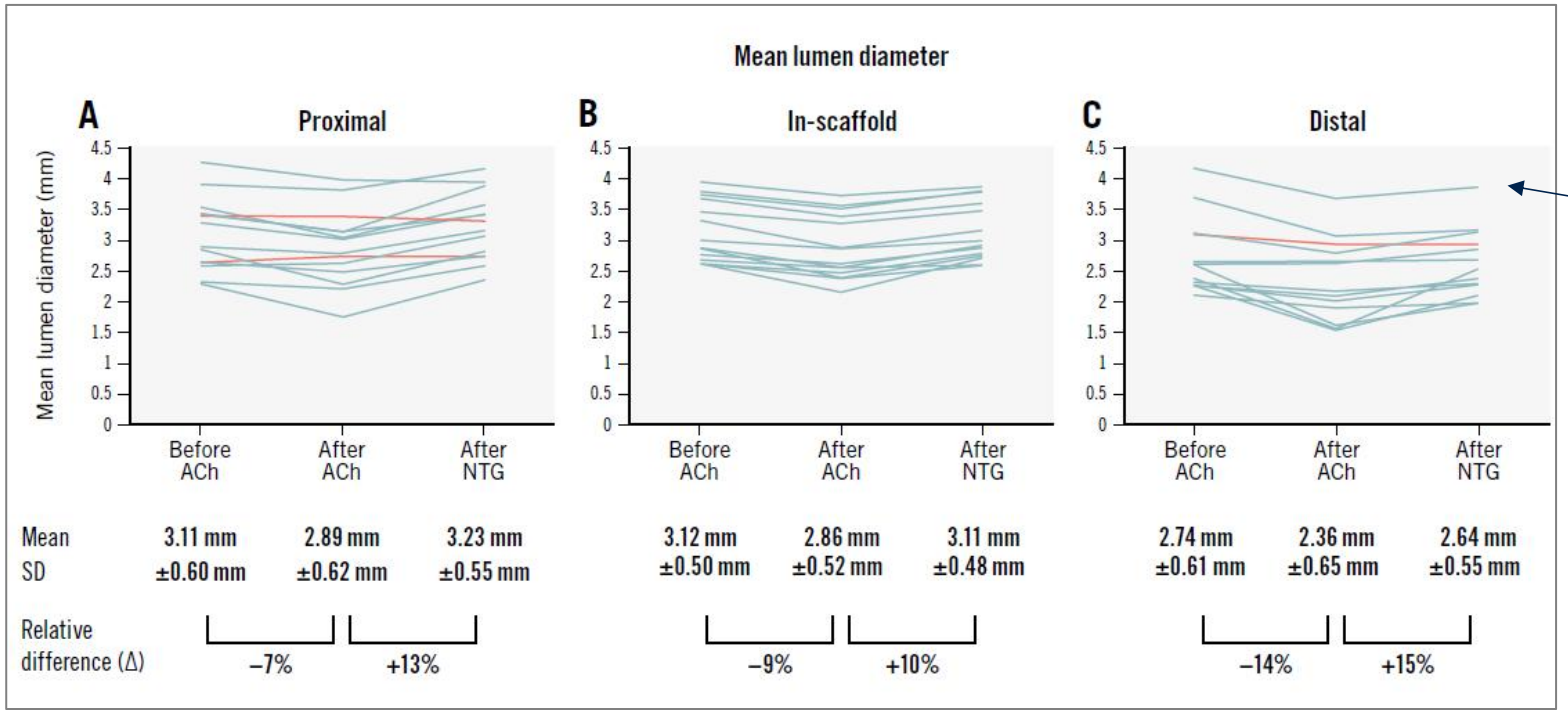
* Based on low Target Lesion Failure and definite or probable Scaffold Thrombosis (Kaplan-Meyer estimate). ◊ TLF is defined as a composite of Cardiac Death, TV-MI, emergent Coronary Artery Bypass Grafting (CABG), and CD-TLR. Peri-procedural MI according to SCAI definition and spontaneous MI according to 3rd universal MI definition. ° Definite or probable Scaffold Thrombosis. All endpoint related events have been adjudicated by an independent clinical event committee; 1. Haude M, «BIOMAG-I: two-year clinical outcomes of the resorbable magnesium Scaffold-DREAMS 3G», presented at EuroPCR, May 2024.

A los 24 meses de seguimiento, DREAMS 3G muestra una **tasa baja de TLF (3,5 %) y de TLR guiada clínicamente (3,5 %), ningún infarto de miocardio, ninguna muerte cardíaca y ninguna trombosis del scaffold confirmada o probable.**

Vasomotion assessment at 12 months after Freesolve implantation

Assessment on 14 patients from BIOMAG-I FIH study

The 12-month results showed the return of vasomotion in all tested patients



Each line represents data of 1 patient.

- **All patients had vasomotion after either ACh or NTG in the scaffolded segment** (change in the lumen diameter of at least 3.0%)
- The proximal segment in 2 patients and the distal segment in 1 patient showed no vasomotion (orange lines)

ACh: acetylcholine
NTG: nitroglycerine

*Freesolve demonstrates significantly **lower in-scaffold LLL** compared to its precursor device Magmaris at 6 and 12 month follow-up[1] which is now on the level of contemporary DES[2]

*Very **good safety and efficacy profile** at 24 months

- Low TLF (3.5% all of them TLR)
- No MI or scaffold thrombosis

Programa clínico

BIOMAG-I en curso hasta 2027; FSI CE **BIOMAG-II** previsto para abril de 2024

BIOMAG-I	116	Europa	Primer estudio en humanos (FIM)	LLL in-scaffold a los 6 meses	Fase de Seguimiento
BIOMAG-II	1859	Países CE y APAC	RCT	TLF a los 12 meses	Fase de reclutamiento
BIOMAG LL	100	Países CE	Estudio previo a la comerciali-zación	TLF a los 12 meses (por confirmar)	Planificado para comenzar en el 4to trimestre de 2024
Registro RMS	1106	Todo el mundo	Registro	TLF a los 12 meses	En curso

Diseño del estudio BIOMAG-II

Estudio prospectivo, aleatorizado y controlado, internacional, multicéntrico, de no inferioridad

Diseño

- Estudio multicéntrico internacional, prospectivo, aleatorizado y controlado, de no inferioridad frente a la familia Xience.
- **Indicación**: DREAMS 3G está indicado para su uso con el objetivo de ampliar el diámetro luminal como parte del tratamiento de lesiones de novo en arterias coronarias nativas de pacientes con cardiopatía isquémica.
- Diámetro vascular de referencia entre 2,5-4,2 mm y longitud máxima de la lesión de ≤ 28 mm.

Objetivo principal

- Fallo de la lesión tratada a los 12 meses

Objetivos secundarios:

- Objetivos clínicos en todos los puntos temporales de seguimiento
- Éxito de la intervención
- Éxito del dispositivo
- Resultados informados por los pacientes
  - Encuesta EuroQoL 5D (EQ-5D-3L) para evaluar el estado de salud general
  - Seattle Angina Questionnaire versión corta (SAQ-7) para cuantificar las limitaciones físicas causadas por la angina de pecho
  - Escala del trastorno de ansiedad generalizada (GAD-7) para evaluar la ansiedad (solo fuera de Estados Unidos)

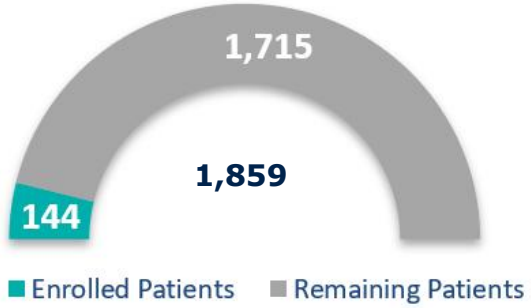
Investigador clínico coordinador: Prof. Dr. Michael Haude, Neuss, Alemania

BIOMAG-II will compare the advantages of an RMS to a permanent DES

The BIOMAG-II RCT progresses well, with >140 Enrollments!

Main Facts

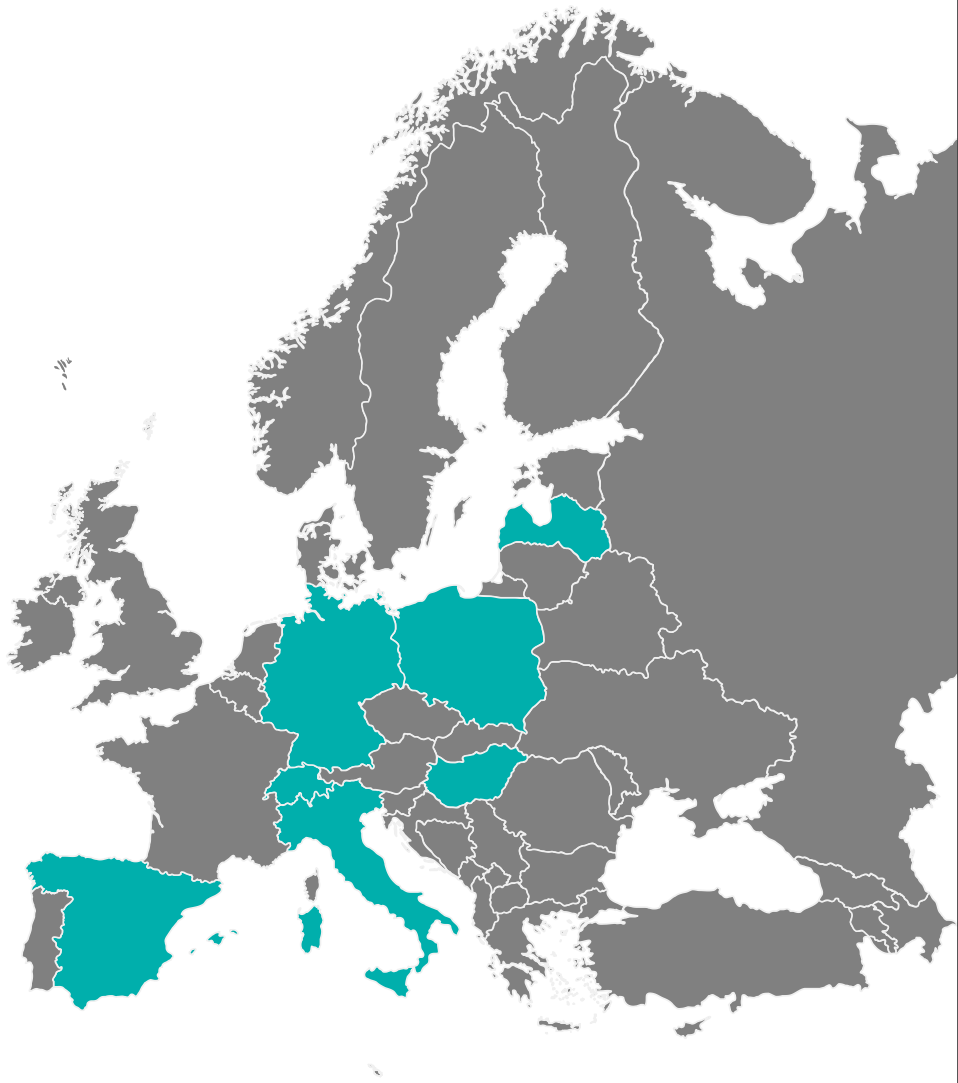
- **2:1 RCT Freesolve vs DES** (Xience)
- **1,859 Subjects** with de novo coronary artery stenosis
- Primary Endpoint: Target Lesion Failure at 12-month
- First Subject In: May 2024



>140
Enrollments
157

12
Sites

7
Countries



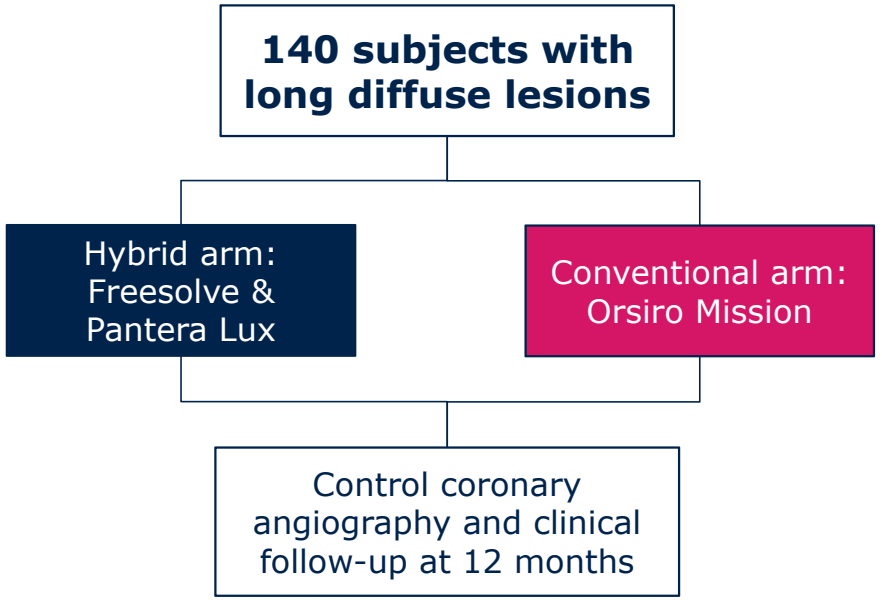
Status as of 23.10.2024

The BIOHYBRID pilot study

An RCT comparing hybrid strategy RMS/DCB vs DES only in long diffuse lesions

BIOHYBRID	140	Switzerland PI: Dr. Iglesias	1:1 RCT comparing hybrid strategy RMS/DCB vs DES only in long diffuse lesions	angioFFR at 12m	FPI Q4 2024

- The number of patients with de novo diffuse coronary artery disease is increasing in the recent years.
- PCI with newer-generation DES in these patients is known to be challenging and associated with an increased risk of stent failure.
- The aim of this pilot study is to **assess the feasibility** and **explore the safety and efficacy of an RMS / DCB hybrid approach** in long / diffuse CAD.



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- No MI or scaffold thrombosis

***Biomag II** a randomized controlled trial comparing Freesolve and Xience has started recruitment in May 2024

Muchas gracias