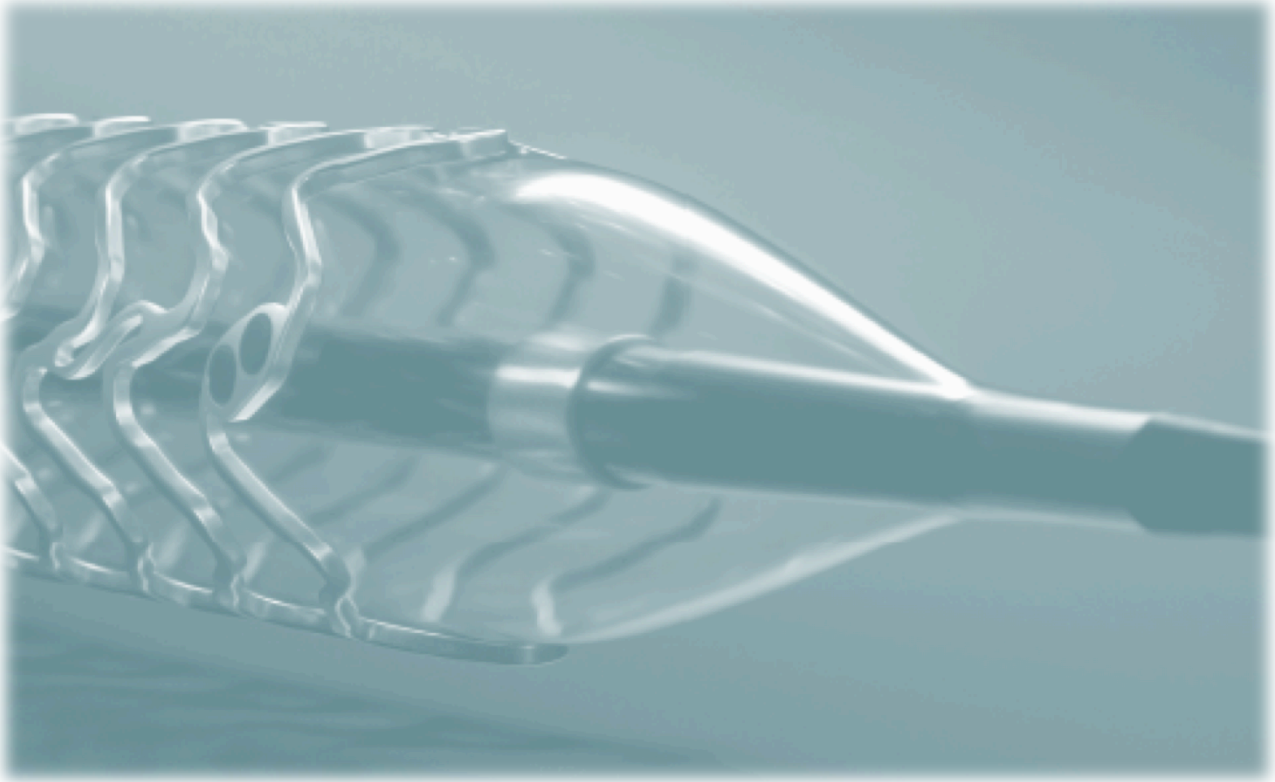
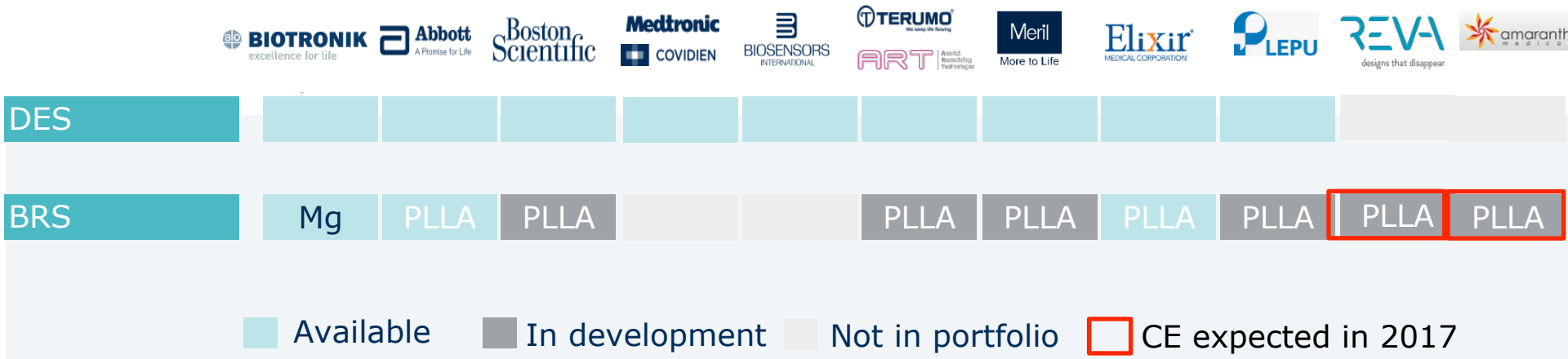
PALAIS DES CONGRES BIARRITZ 8/9/10 JUIN 2016

APPAC ACTUALISATIONS ET PERSPECTIVES EN PATHOLOGIE CARDIOVASCULAIRE



Bioresorbable magnesium scaffold MAGMARIS

BRS Overview



In 2016 BIOTRONIK completes the stent portfolio with launching a BRS

BIOTRONIK is the only one offering a Magnesium based BRS

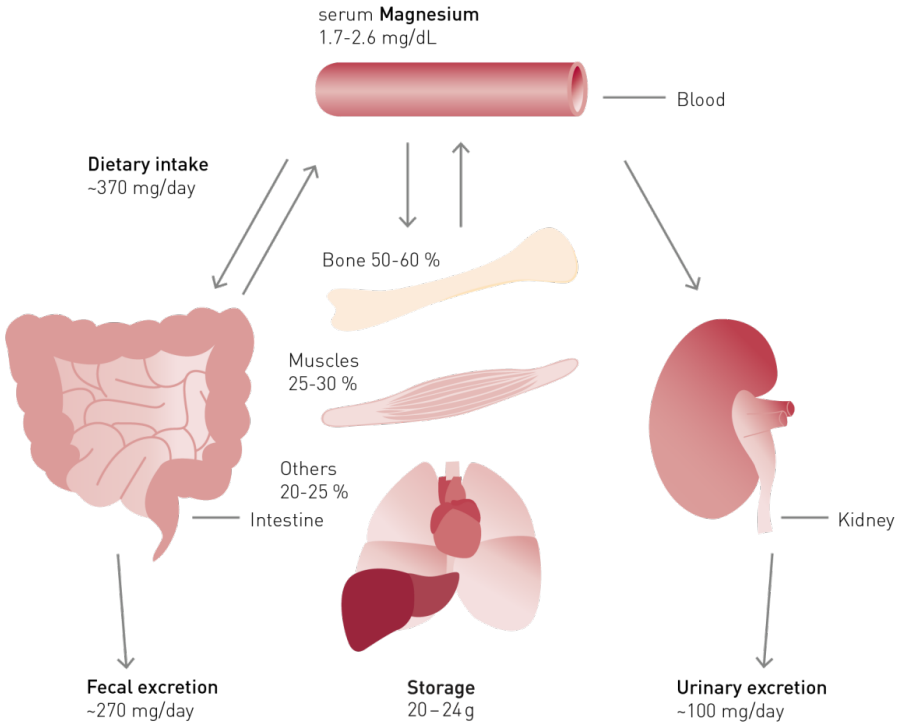
Available and upcoming BRS

Product	Magmaris	Absorb (GT1)	DESolve	Fantom
Availability	CE Q2 2016	2012;(2015): CE Planned: Japan, China, US	2013: CE	Expected CE 2016
Material	**Magnesium**	PLLA	PLLA	Desaminotyrosine-derived polycarbonate
Scaffolding time	**Up to 3m**	6-12m	1-3m	Up to 3m
Resorption time	**1y**	3-4y	~2y	3-4y
Number of sizes	6	14	12	4
Diameter [mm]	3.0; 3.5	2.5; 3.0; 3.5	2.5; 3.0; 3.25; 4.0	2.5; 3.0
Length [mm]	15; 20; 25	8; 12; 18; 23; 28	14; 18; 28	18; 24
Marker	Tantalum	Platinum	Pt/Ir	Not needed
Struts thickness/ width [µm]	150/150	150/**180**	150 **DESolve CX will have a strut thickness of 120 µm**	**125**
Crossing profile [mm]	1.5	1.45	1.4	1.27
Drug	Sirolimus	Everolimus	Novolimus	Sirolimus

Magnesium (Mg) is a natural element of the human body

4th more abundant cation

Mg concentration in the blood serum is 1.7 - 2.6 mg/dl[1]



Mg levels are regulated by the collaborative actions of the

- **intestine**
- **kidneys**
- **Bones[1,2]**

~10 mg
1 BIOTRONIK Mg Scaffold 95% resorbed over 12 months

[1]Blaine et al. (2015). Clinical Journal of the American Society of Nephrology 10(7):1257-72;
[2]de Baaij et al. (2015). Physiological reviews;95(1):1-46;

Mg is taken up in significant quantities on a daily basis

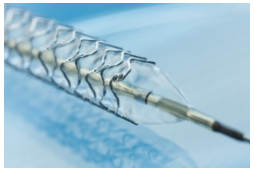
Recommended daily intake[1]:
Men: 420 mg
Women: 320 mg

Mg concentration in drinking water and food composition[3] defines magnesium intake

156 mg
1 cup of cooked spinach[4]

26 mg
1 liter bottle of *evian* water[5]

The BIOTRONIK Mg Scaffold does not contribute to the recommended daily intake

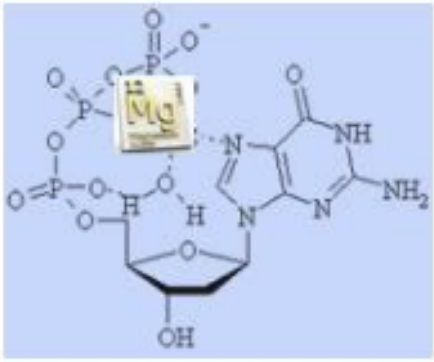


~10 mg
1 BIOTRONIK Mg Scaffold 95% resorbed over 12 months

References: [1]Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes (1997). Washington, DC: National Academies Press. [2] King et al. (2005). J Am Coll Nutr;24(3):166-71; [3]Swaminathan et al. (2003). The Clinical Biochemist Reviews;24(2):47; [4]Qu et al. (2013). PLoS One 8, no. 3, e57720. [5]Website: http://www.evian.com/de_ch/

Magnesium in the human body

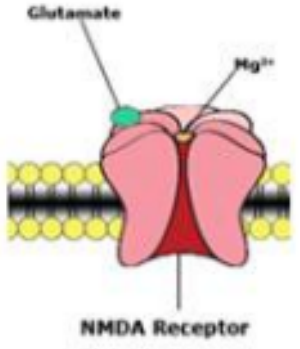
Mg means energy



Mg is crucial to hundreds of enzymatic reactions

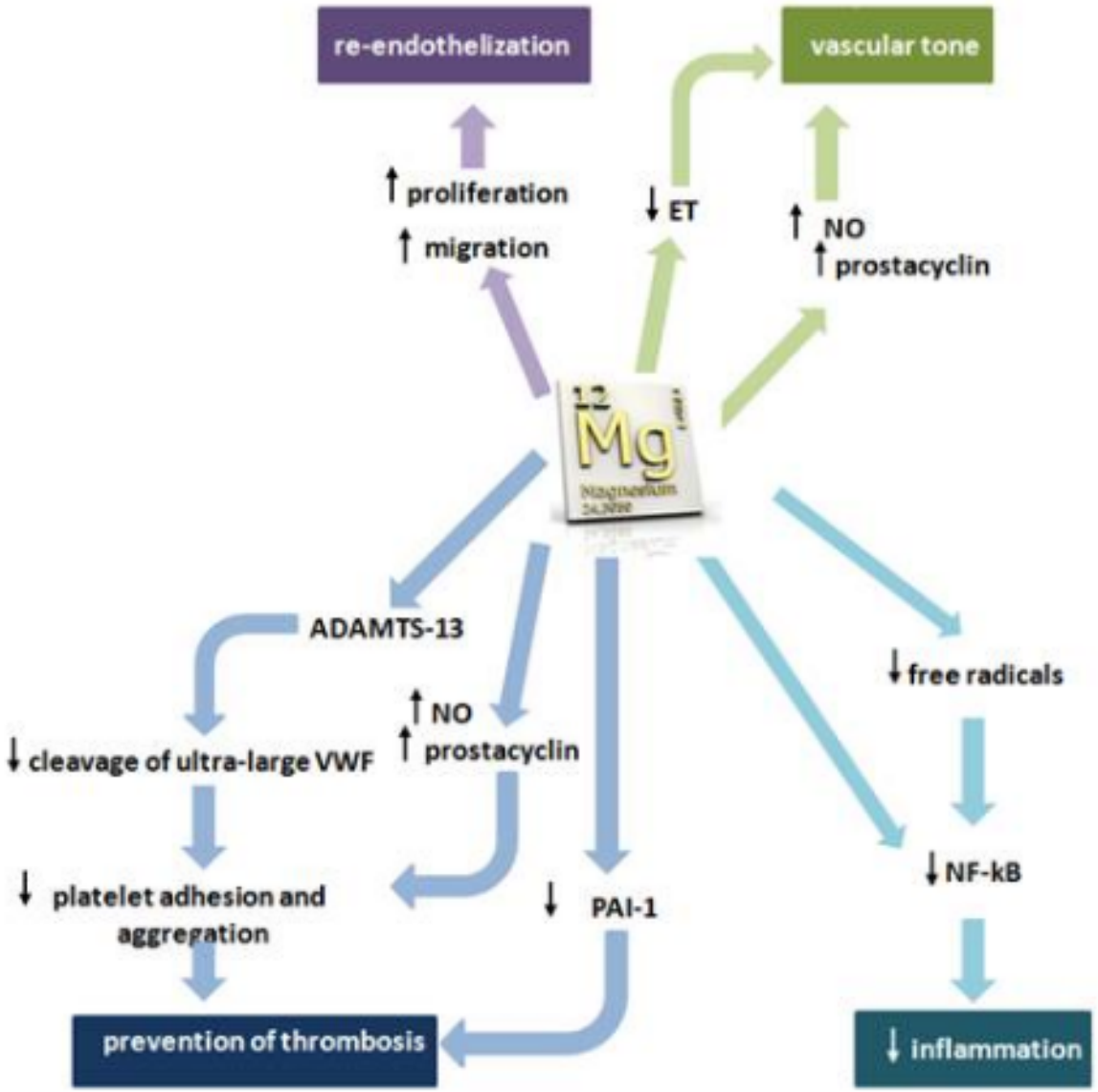
Mg stabilizes membranes and macromolecules

Mg regulates some ion channels

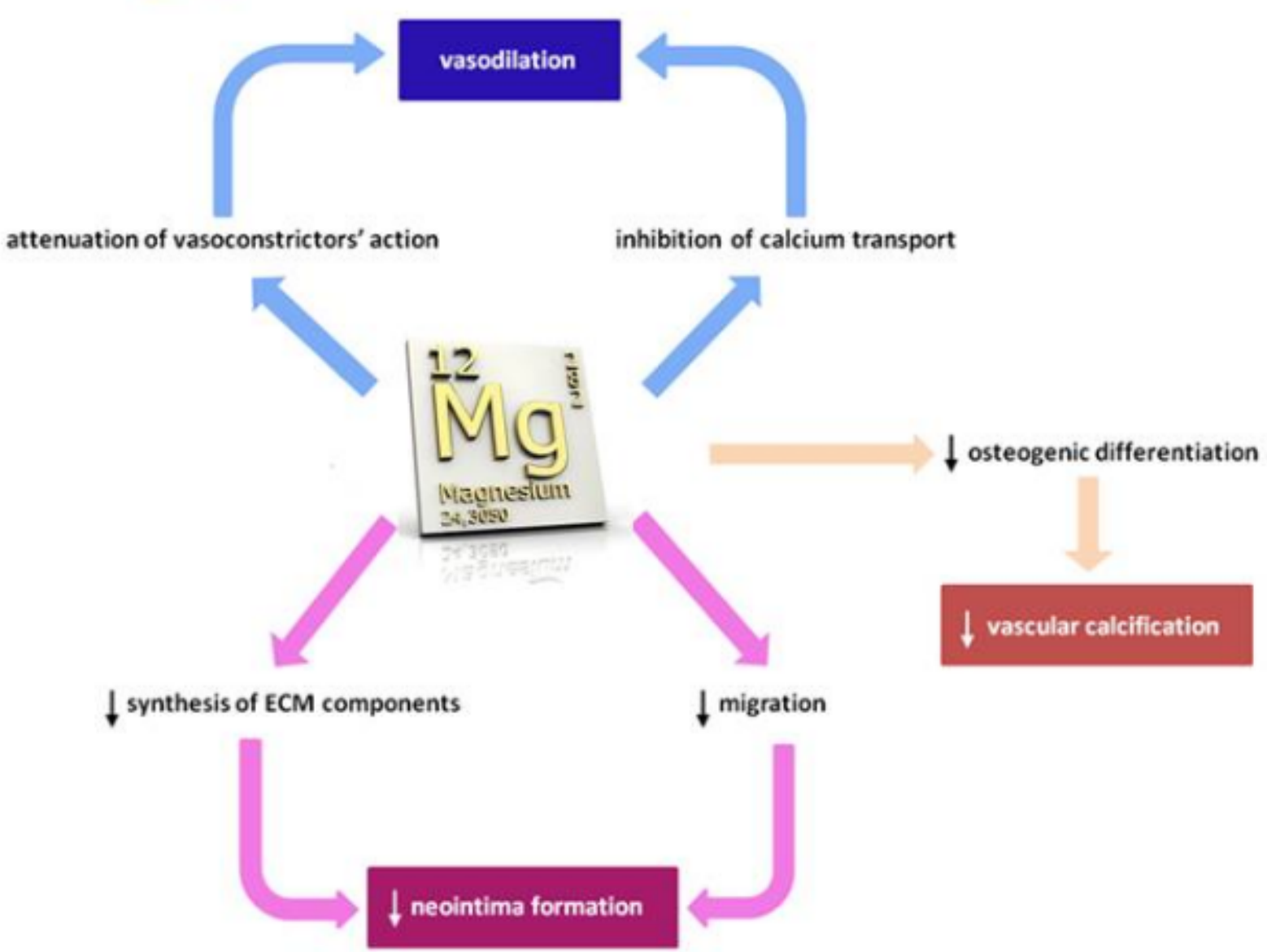


Mg is a natural calcium antagonist

Magnesium and the endothelium



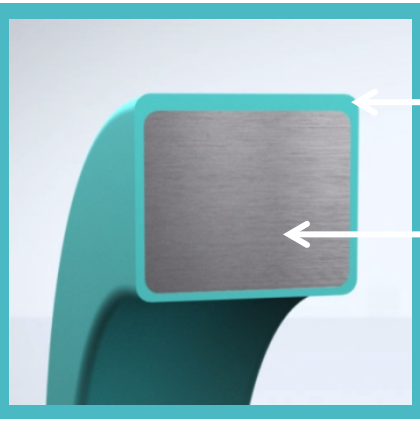
Magnesium and vascular smooth muscle cells



Magmaris description

Mg Backbone *resorbable*

Double eye radiopaque marker (Tantalum) *permanent*



BIOlute Coating *resorbable*

Mg Backbone *resorbable*

Magmaris components

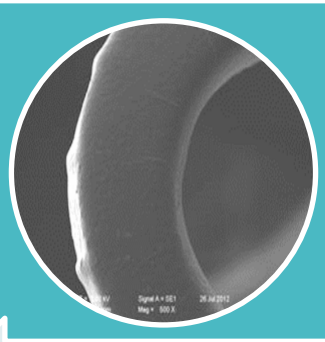
Backbone

Mg alloy

Tantalum markers

6-crown & 2-link design

150µm strut thickness



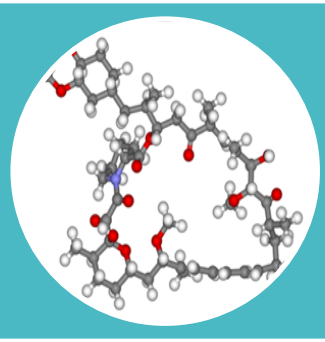
BIOlute

Coating

PLLA

Proven resorption profile

Proven technology identical to Orsiro coating



Drug

Limus

1.4 µg/mm² same as for Orsiro

Release kinetics comparable to Orsiro

Delivery system

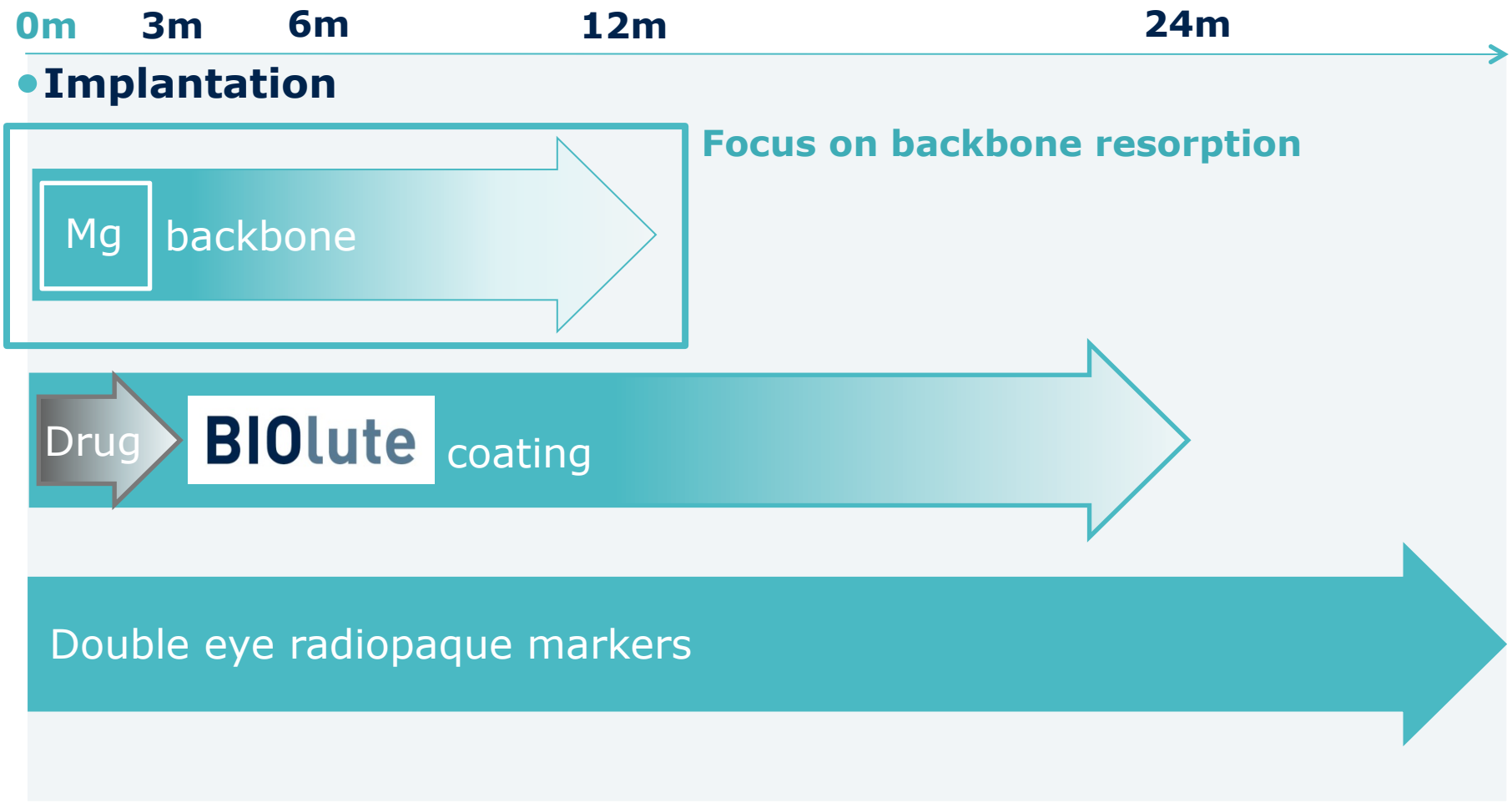
RX, 0.014”

6F compatible

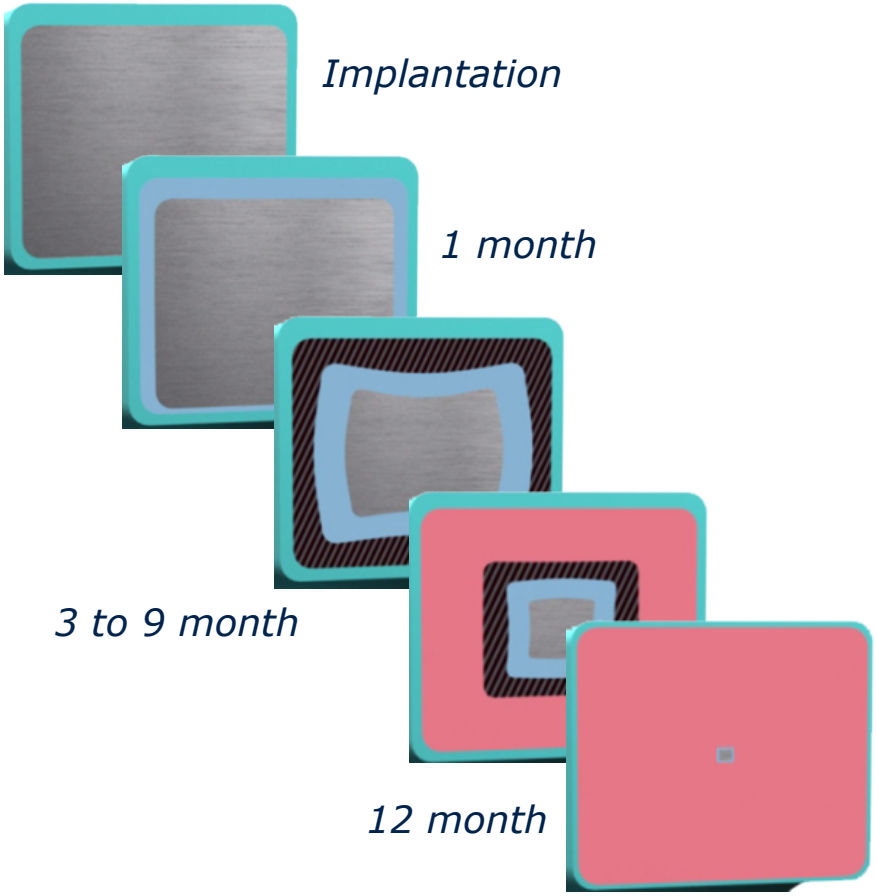
Adapted from Orsiro system

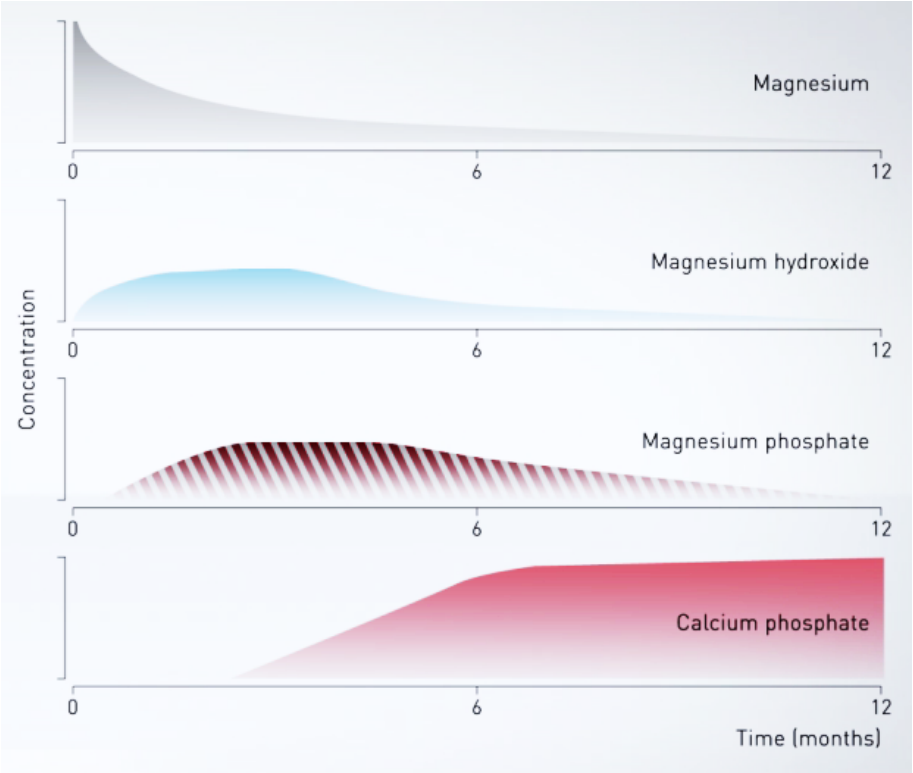
A combination of proven Orsiro elements and the benefits of a resorbable Magnesium Scaffold

Magmaris resorption process over time

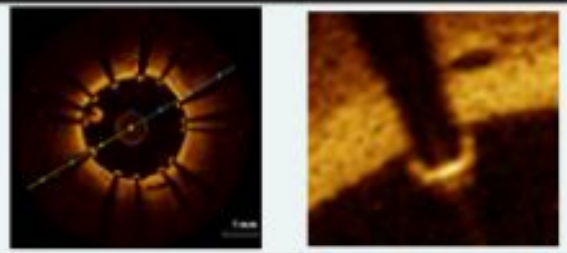
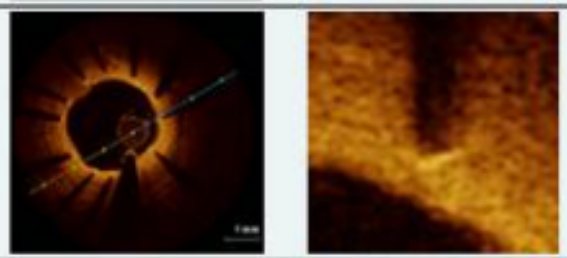
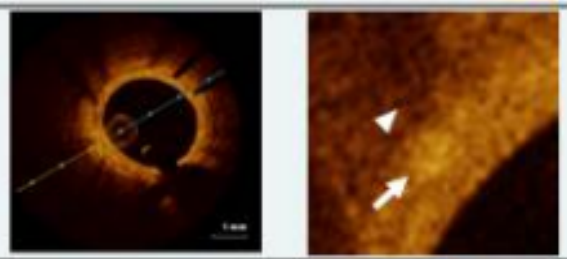
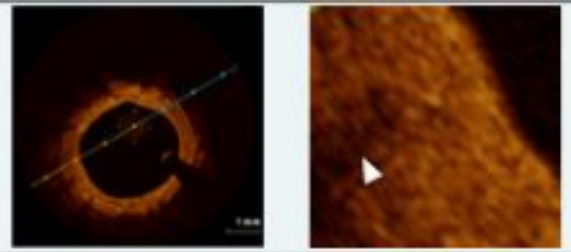


Resorption process of the Magnesium backbone

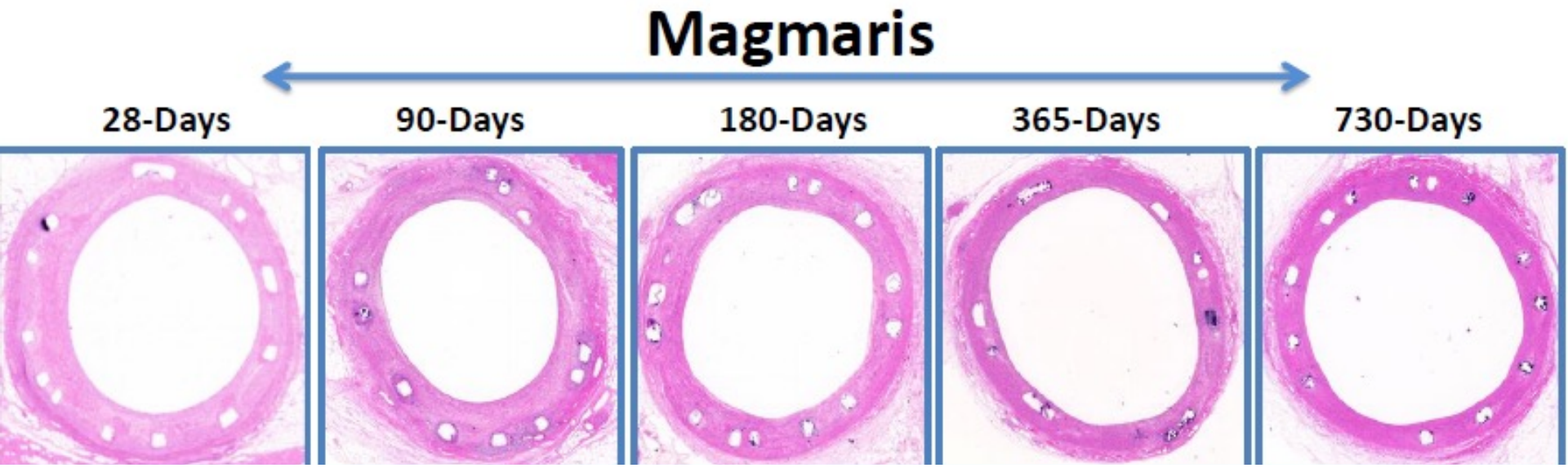




OCT Classification During Strut Resorption

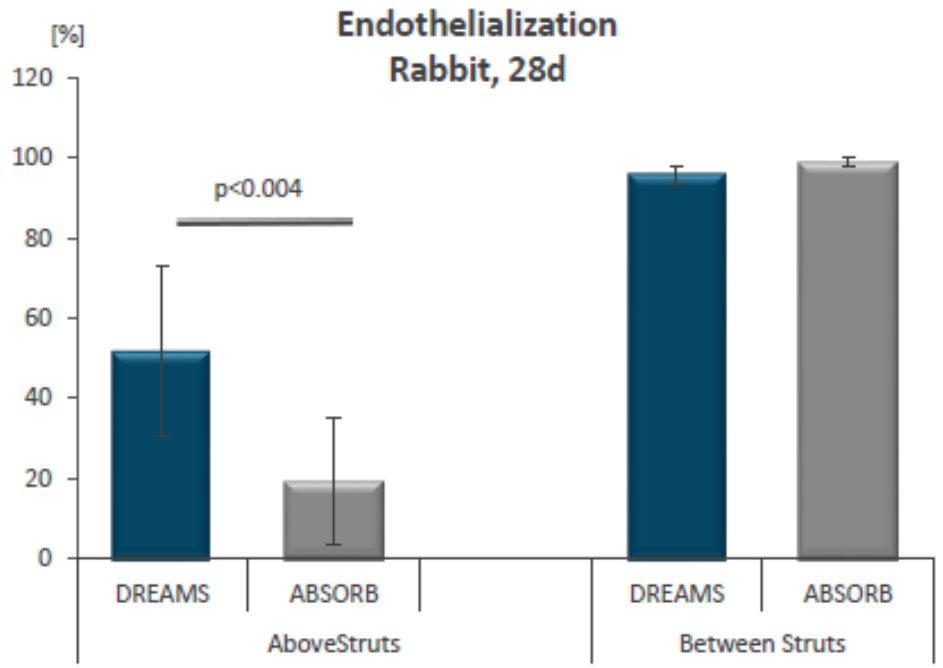
Classification	Time point	OCT appearance	Mg resorption [%]	characterization
1	Post implantation		0%	Appearance like a permanent metallic stent, bright reflection with complete attenuation
2	180 days		65%	Detectable reflection with attenuation showing diffuse boders
3	365 days		95%	Brighter, diffuse region (arrow) with attenuation (arrowhead)
4	730 days		100%	No bright regions, minimal attenuation (arrowhead)

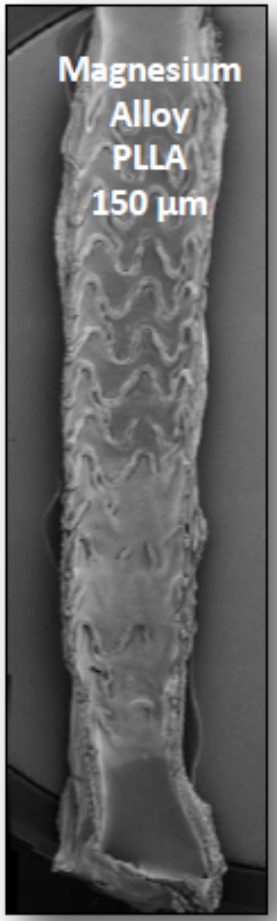
Representative histology up to 2 years



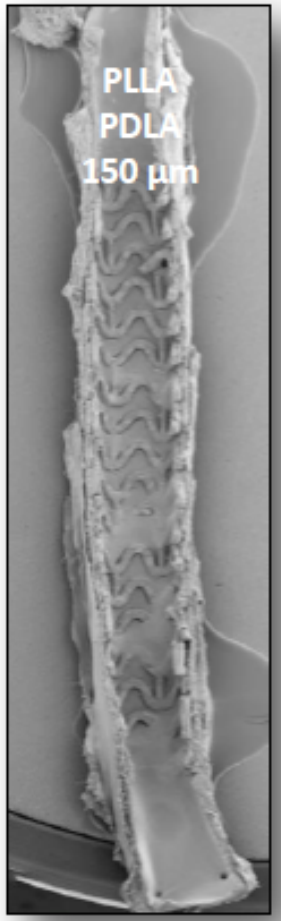
Endothelialization of BRS not only Depends on Strut Dimensions

Vessel surface coverage of BRS struts determines pace of re-endothelialization





DREAMS

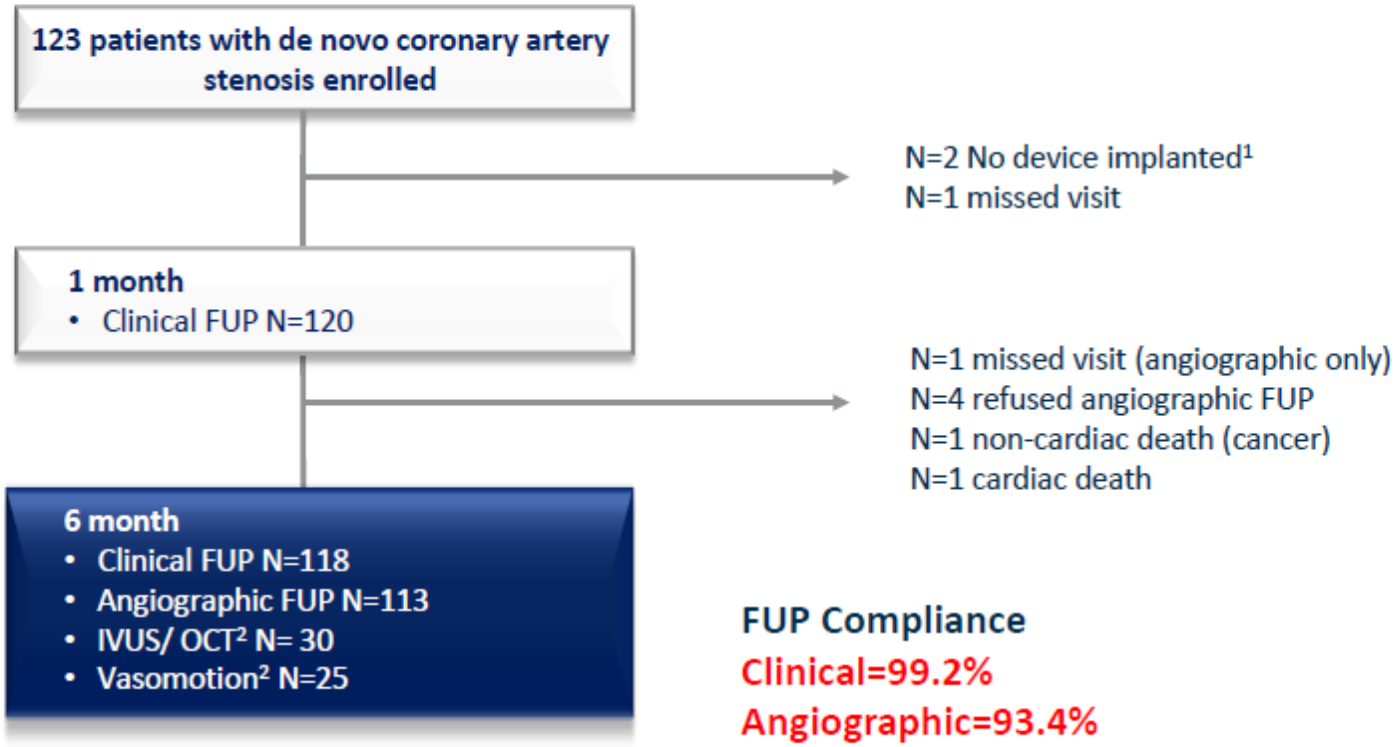


ABSORB

BIOSOLVE II – 6 mo

BIOSOLVE-II

Patient Flow



1. 2 subject who did not receive a DREAMS 2G were only considered for procedure and device success calculation as defined in the protocol
2. Subgroup only

BIOSOLVE-II

Inclusion/ Exclusion Criteria

Inclusion Criteria*

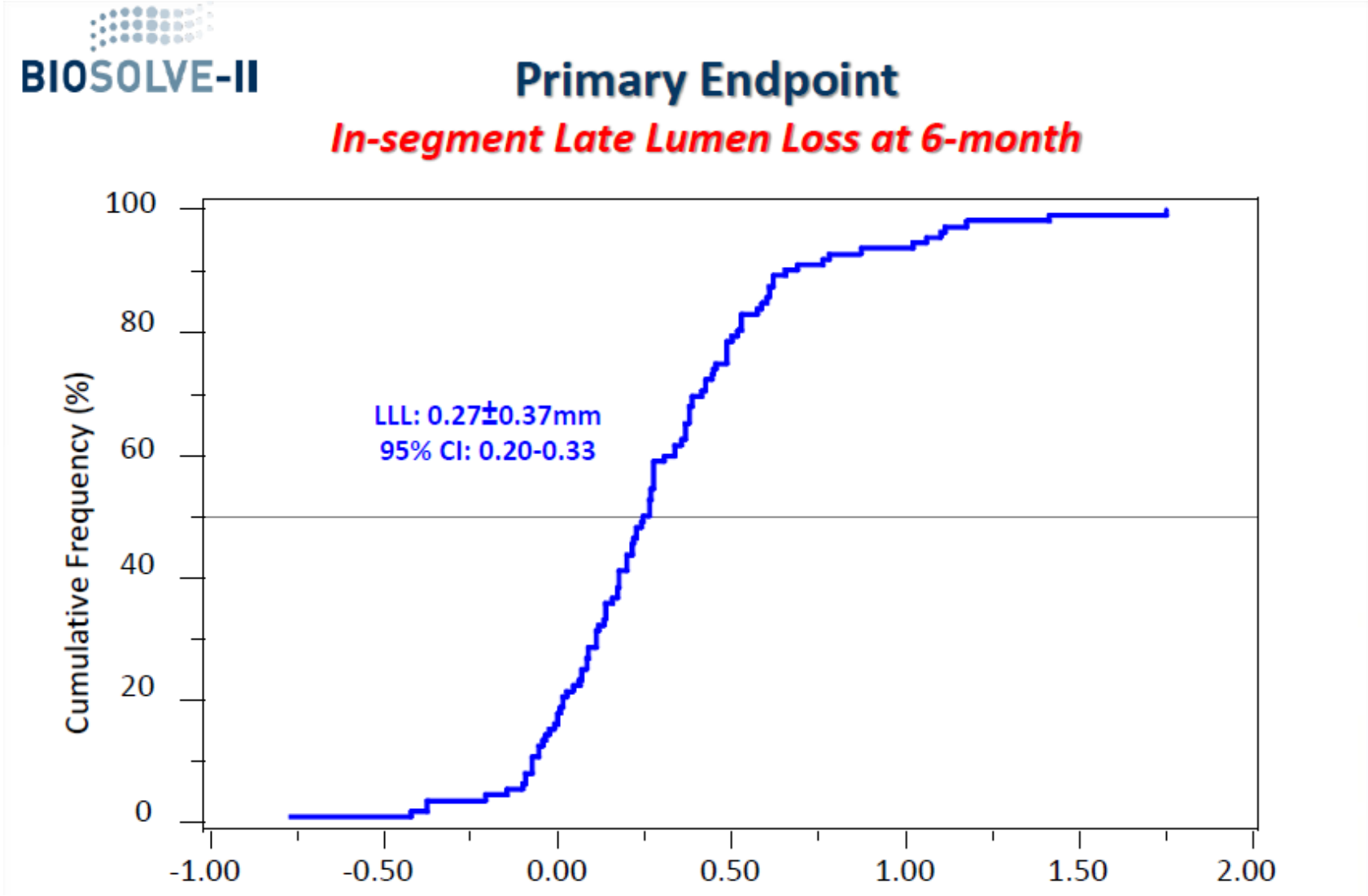
- Maximum of two single de novo lesions in two separate coronary arteries
- Target RVD by visual estimation, 2.2-3.7 mm (after NITRO)
- Target lesion length by visual estimation ≤ 21 mm
- Target lesion stenosis by visual estimation ≥ 50% - < 100%

*list truncated

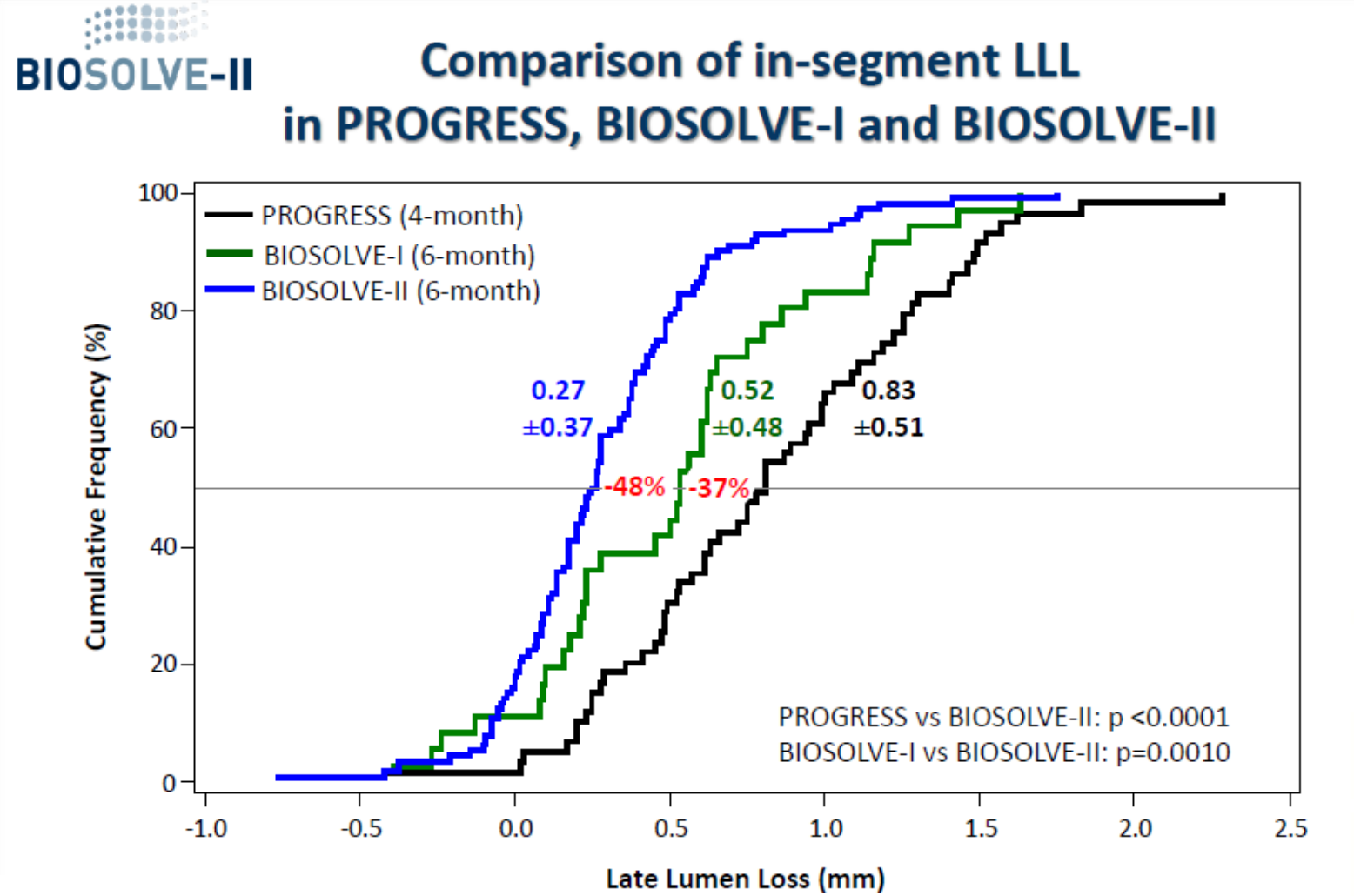
Exclusion Criteria*

- Evidence of myocardial infarction within 72 hours prior to index procedure
- LVEF <30%
- Thrombus in the target vessel (visualized by QCA)
- Severe calcification
- Patients with three-vessel disease, where all three vessels require treatment
- Previous CABG in the target vessel
- Additional coronary lesion in the same vessel, which requires treatment
- Totally occluded coronary artery (TIMI flow 0)
- Target lesion involves a side branch (vessel diameter > 2.0 mm), a bifurcation or is located 5 mm next to a bifurcation
- Ostial lesions
- Unsuccessful pre-dilatation

BIOSOLVE II – 6 mo



BIOSOLVE II – 6 mo



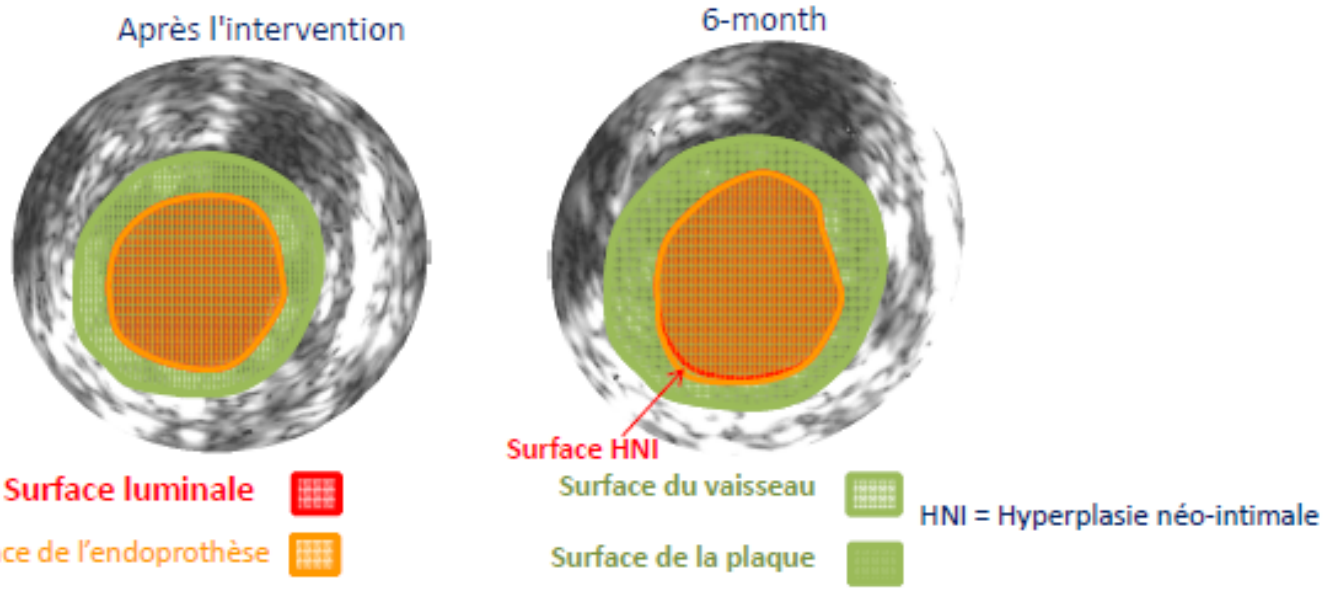
BIOSOLVE II – 6 mo

BIOSOLVE-II

QCA Results

	Baseline N=123	Post-Procedure N=121	6-month N=113
Lesion Length (mm)	12.61±4.53	NA	NA
In-segment RVD (mm)	2.68±0.40	2.69±0.39	2.55±0.41
In-scaffold RVD (mm)	NA	2.78±0.36	2.59±0.40
In-segment MLD (mm)	1.19±0.32	2.16±0.40	1.89±0.43
In-scaffold MLD (mm)	NA	2.45±0.32	2.00±0.44
In-segment acute gain (mm)	NA	0.96±0.40	NA
In-scaffold acute gain (mm)	NA	1.25±0.35	NA
In-segment DS (%)	55.2±10.3	19.7±8.3	25.9±12.3
In-scaffold DS (%)	NA	11.7±5.2	22.6±12.9
In-segment LLL (mm)	NA	NA	0.27±0.37
In-scaffold LLL (mm)	NA	NA	0.44±0.36
In-segment Binary Restenosis (%)	NA	NA	5.4
In-Scaffold Binary Restenosis (%)	NA	NA	5.4

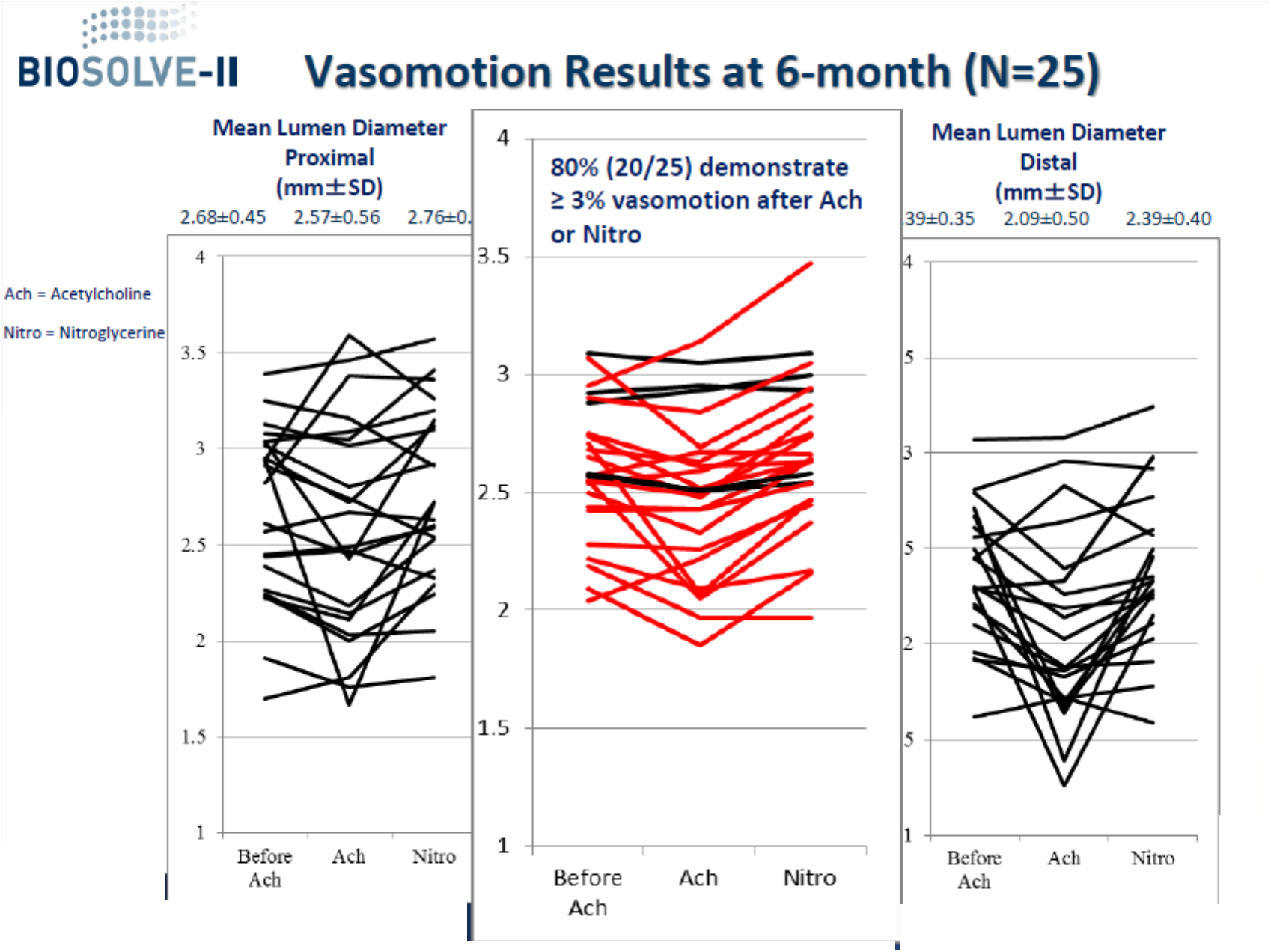
BIOSOLVE II – 6 mo



	Post procédure	6 mois	Δ6 mois vs post procédure [95 % IC]	valeur p
Surface du vaisseau (mm^2)	14,06±3,17	14,21±3,14	0,15[-0,13-0,42]	0,289
Surface de l'endoprothèse (mm^2)	6,24±1,15	6,21±1,22	-0,03[-0,29-023]	0,803
Surface de la plaque (mm^2)	7,76±2,41	8,06±2,23	0,29[0,11-0.47]	0,002
Surface HNI (mm^2)	NA	0,08±0,09	NA	NA

NA= Non Applicable

BIOSOLVE II – 6 mo



BIOSOLVE II – 6 mo

BIOSOLVE-II

Clinical Results

TLF rate at 6-month

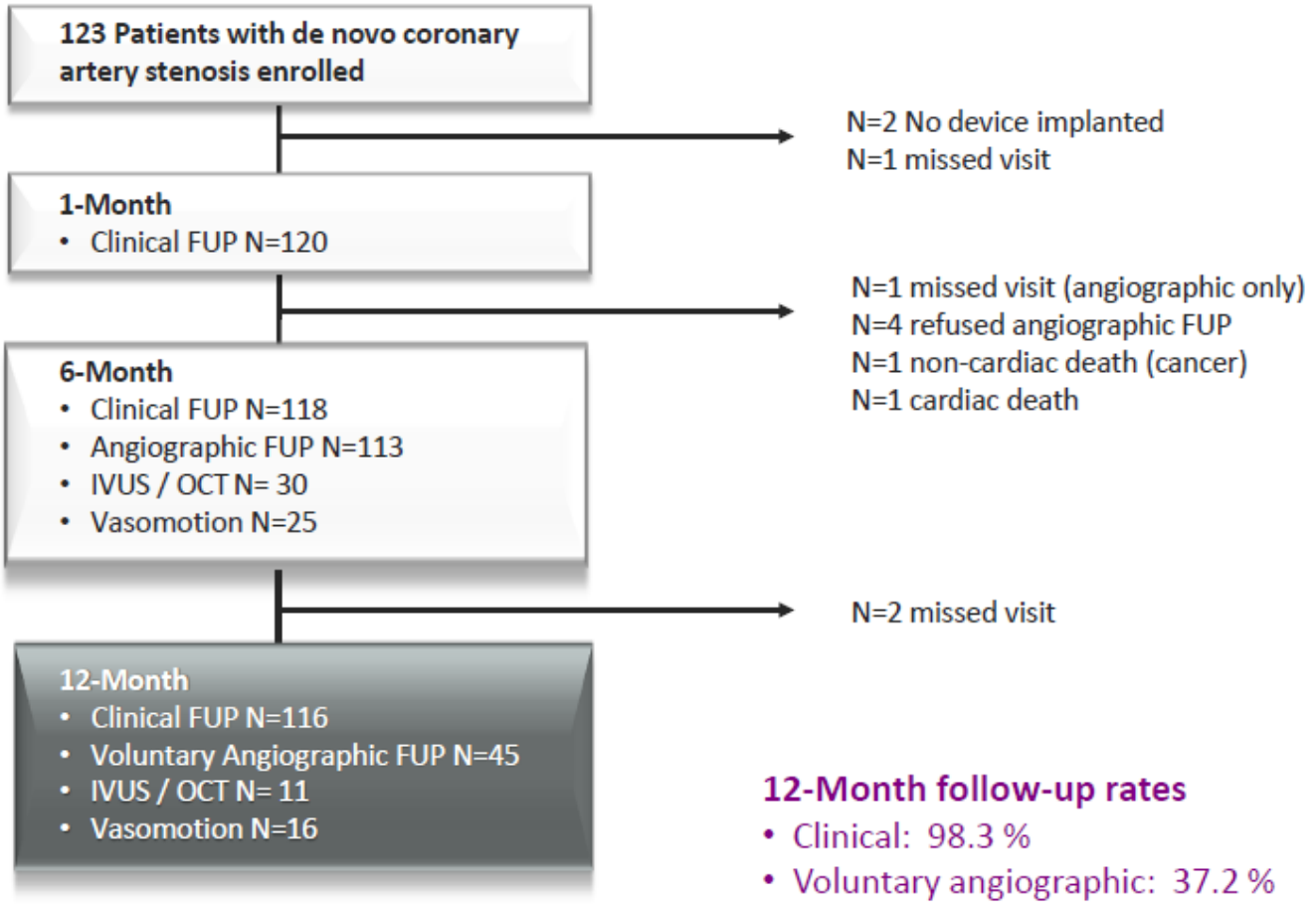
	N=120	%	95% CI
TLF[1]	4	3.3	1.3-8.3
Cardiac Death	1[2]	0.8	0.0-4.6
Target Vessel MI	1	0.8	0.0-4.6
Clinically driven TLR	2	1.7	0.2-5.9
CABG	0	0.0	0.0-3.1
Scaffold Thrombosis Definite or probable	0	0.0	0.0-3.1

1. Composite of cardiac death, target vessel myocardial infarction, clinically driven target lesion revascularization and CABG
2. 58 old smoker, CV RF: hypertension and hyperlipidemia, stable angina CCS Class II, treated with a DREAMS 2G 3.0x20mm in the distal RCA. Patient experienced an unwitnessed death 134 days post procedure. Since a cardiac cause could not be ruled out, patient was adjudicated as cardiac death by the Clinical Event Committee

BIOSOLVE II – 12 mo

Patient flow

BIOSOLVE-II



12-Month follow-up rates

- Clinical: 98.3 %
- Voluntary angiographic: 37.2 %

BIOSOLVE II – 12 mo QCA

Serial QCA data in 42 patients at post-procedure, 6 and 12-month follow-up

	Baseline	Post-Procedure	6-Month	12-Month
Lesion length (mm)	12.84 ± 4.71	NA	NA	NA
In-segment RVD (mm)	2.74 ± 0.35	2.75 ± 0.35	2.60 ± 0.38	2.60 ± 0.44
In-scaffold RVD (mm)	NA	2.84 ± 0.37	2.66 ± 0.34	2.64 ± 0.41
In-segment MLD (mm)	1.22 ± 0.33	2.25 ± 0.41	2.01 ± 0.38	1.96 ± 0.41
In-scaffold MLD (mm)	NA	2.54 ± 0.33	2.14 ± 0.38	2.10 ± 0.41
In-segment acute gain (mm)	NA	1.00 ± 0.38	NA	NA
In-scaffold acute gain (mm)	NA	1.29 ± 0.34	NA	NA
In-segment DS (%)	55.2 ± 10.9	18.7 ± 6.8	22.6 ± 9.2	24.7 ± 10.6
In-scaffold DS (%)	NA	10.4 ± 6.0	19.6 ± 8.4	20.4 ± 8.6
In-segment LLL (mm)	NA	NA	0.20 ± 0.21	0.25 ± 0.22
In-scaffold LLL (mm)	NA	NA	0.37 ± 0.25	0.39 ± 0.27
In-segment binary restenosis (%)	NA	NA	0.0	2 (4.8)
In-scaffold binary restenosis (%)	NA	NA	0.0	0 (0.0)

Data are mean SD or n (%).

BIOSOLVE II – 12 mo clinical

Clinical Results until 12-month follow-up

	6-month N=120	%	12-month N=118	%
TLF[1]	4	3.3	4	3.4
Cardiac Death	1[2]	0.8	1[2]	0.8
Target Vessel MI	1	0.8	1	0.8
Clinically driven TLR	2	1.7	2	1.7
CABG	0	0.0	0	0
Scaffold Thrombosis Definite or probable	0	0.0	0	0.0

1. Composite of cardiac death, target vessel myocardial infarction, clinically driven target lesion revascularization and CABG
2. 58 old smoker, CV RF: hypertension and hyperlipidemia, stable angina CCS Class II, treated with a DREAMS 2G 3.0x20mm in the distal RCA. Patient experienced an unwitnessed death 134 days post procedure. Since a cardiac cause could not be ruled out, patient was adjudicated as cardiac death by the Clinical Event Committee

Magmaris Clinical Program