Foundational Pipeline: 2-Year FORTITUDE 150 µm BRS Program Clinical Update

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	*Company*
• Grant/Research Support • Consulting Fees/Honoraria	Medtronic, Mitralign, Millipede, Amaranth Medical, Valtech Cardio, Spectranetics, Acist Medical, Abbott Vascular, Keystone Heart, ICS, InnovHeart, Mitraltech

All TCT 2017 faculty disclosures are listed online and on the app.

Amaranth's BRS: Summary of Clinical Program

Status Update (n = 206)

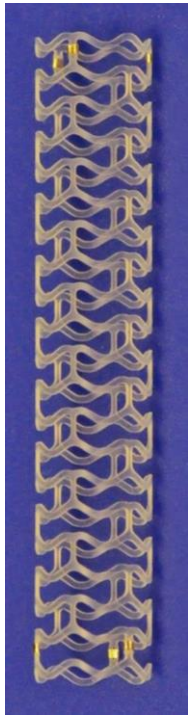
STUDY NAME	DEVICE TYPE	ENROLLMENT STATUS	# PATIENTS ENROLLED	ANGIO-OCT FOLLOW UP	LATEST FOLLOW UP
MEND I	FORTITUDE 150-µm BARE	Completed	13	2-Years Completed	4-Years Completed
FORTITUDE (Colombia)	FORTITUDE 150-µm SES	Completed	42	2-Years Completed	>2-Year Ongoing
FORTITUDE (Italy)	FORTITUDE 150-µm SES	Completed	21	2-Years Completed	>2-Year Ongoing
RENASCENT II[#]	APTITUDE 115-µm SES	Completed	60	9-Months **Completed**	2-Year Ongoing
RENASCENT III (Up to 2 Lesions)	MAGNITUDE 98-µm SES	Completed	70	9-Months Ongoing	>9-Months Ongoing

* Colombo A. First Report Investigation, TCT 2016

[#] Colombo A. Late Breaking Clinical Trial, PCR 2017

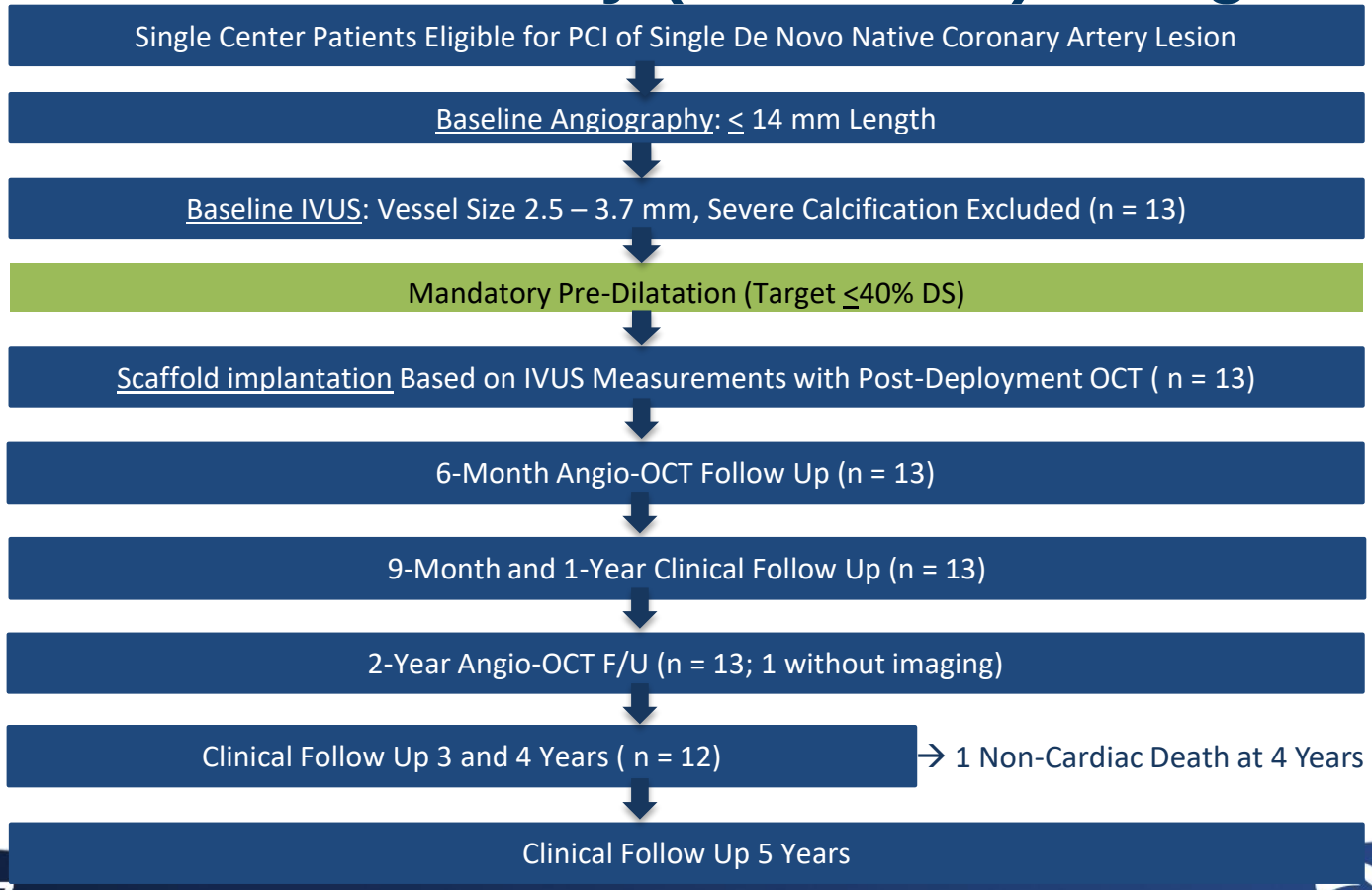
Amaranth Medical BRS Characteristics

Design Feature	Bare FORTITUDE®	Sirolimus FORTITUDE®
Polymer	Ultra High MW-Poly-L-Lactide (PLLA)	
Diameters	2.75 and 3.5 mm	2.75, 3.0, 3.5, and 3.75 mm
Lengths	13 and 18 mm	
Wall Thickness	150 – 200 µm*	150 µm
Surface Coverage Area (at RBP)	≤ 25%	23%
Drug Coating	None	1:1 Poly D L-lactide:Sirolimus
Drug Content	n/a	101 to 160 µg*
Drug Density	n/a	96 µg/cm^2
Inflation Pressures	Nominal: 7 to 8 ATM RBP: 16 ATM	Nominal: 6 to 8 ATM RBP: 15 to 17 ATM
Guide Catheter Size	7 – 8 French Compatible*	6 French Compatible



*Depending on scaffold size

MEND I FIM Study (Bare BRS) Design



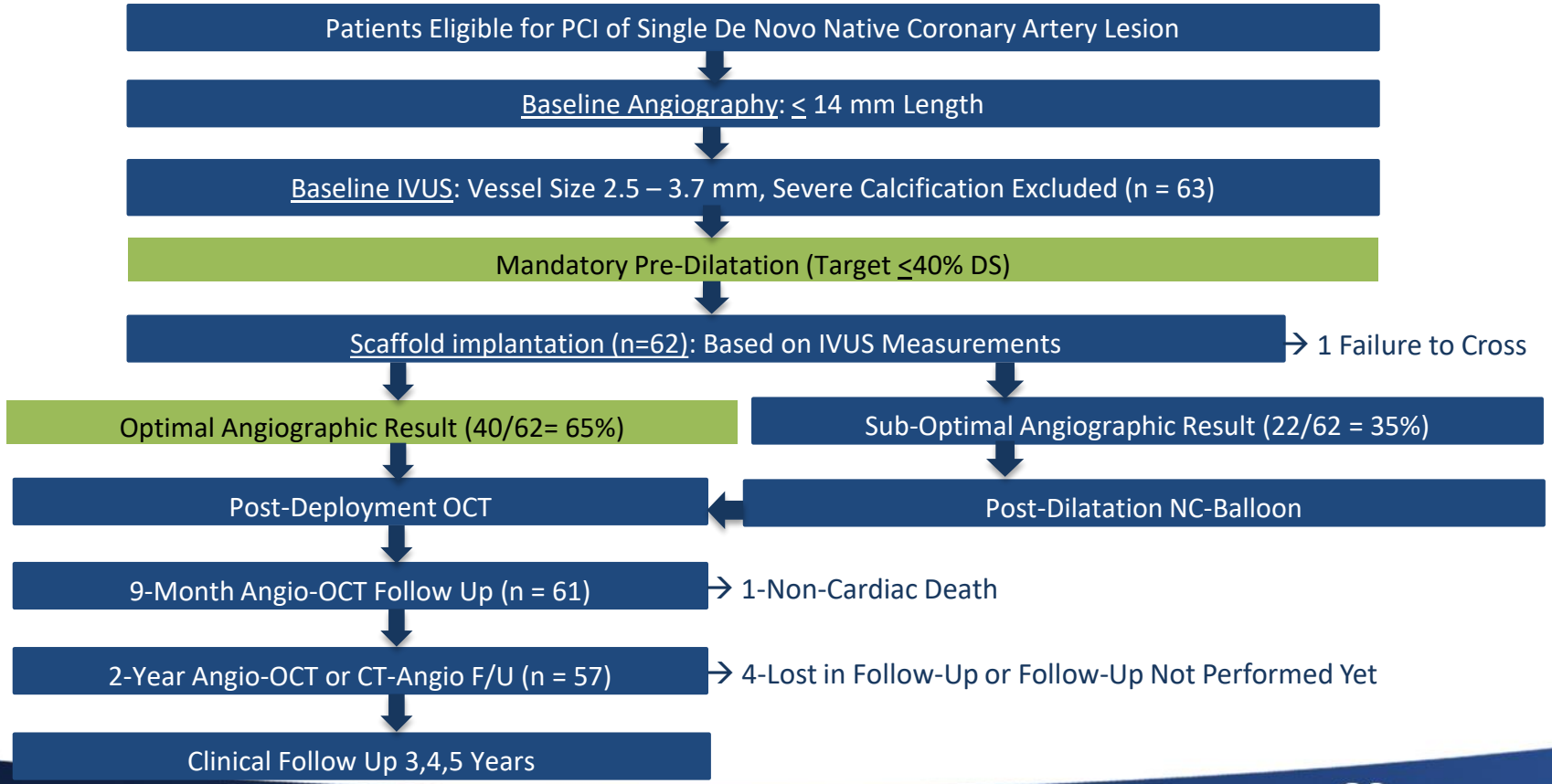
2-Year Angiographic Analysis

QCA Measurements Mean ± SD	Baseline Procedure (n = 13)	Post-BRS Implantation (n = 13)	6-Month Follow-Up (n = 13)	2-Year Follow-Up (n = 12)
In-Segment Analysis				
Interpolated RVD (mm)	3.0 ± 0.4	2.8 ± 0.4	2.7 ± 0.3	2.7 ± 0.4
MLD (mm)	1.2 ± 0.4	2.5 ± 0.4	1.9 ± 0.6	2.3 ± 0.5
Diameter Stenosis (%)	58.0 ± 11.4	10.5 ± 7.6	31.9 ± 17.8	15.3 ± 7.0
In-Scaffold Analysis				
Acute Gain (mm)	---	1.6 ± 0.3	---	---
Late Lumen Loss (mm)	---	---	0.9 ± 0.4	0.5 ± 0.5
Binary Restenosis (%)	---	---	0%	7.7% (1/13)

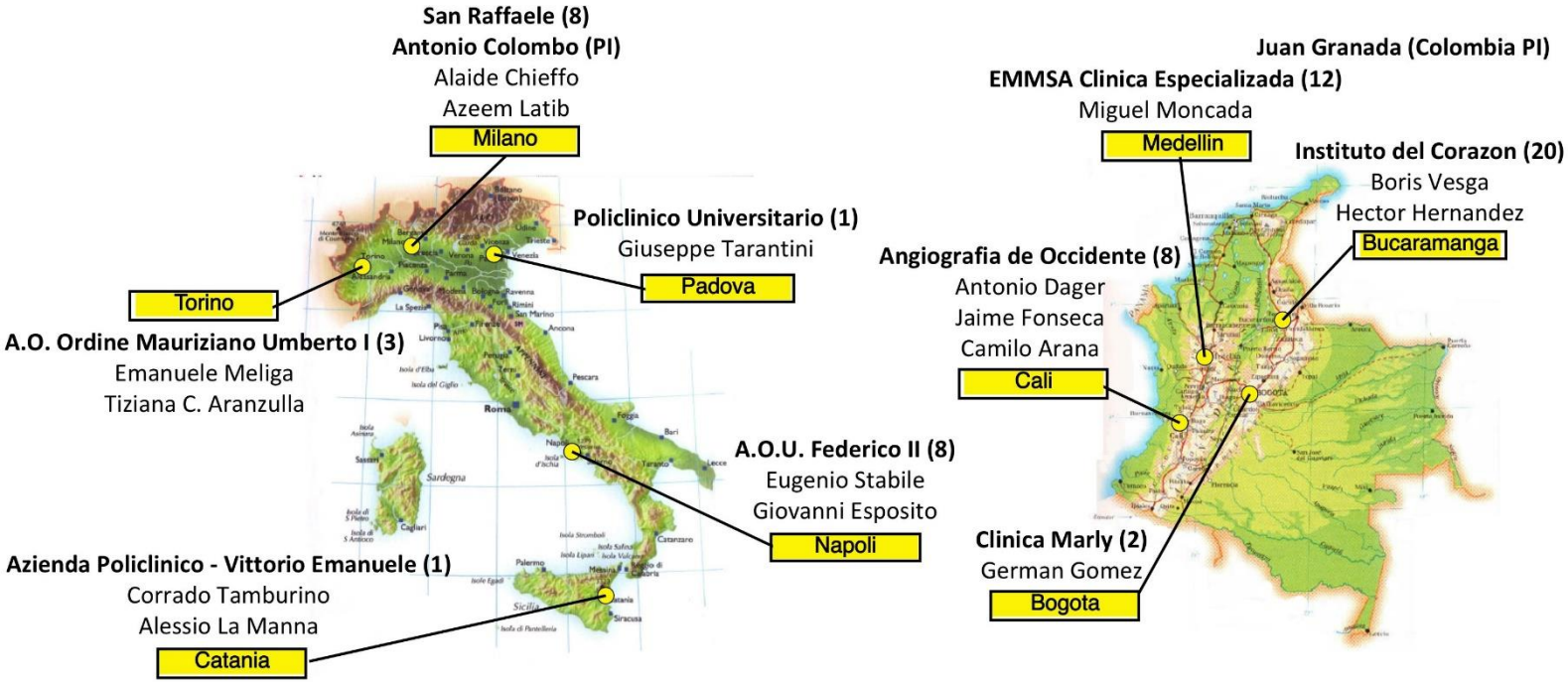
4-Year Safety End-Points

Safety Endpoints % (n)	<1-Month (n = 13)	1 to 9 Months (n = 13)	1 to 4 Years (n = 13)
Target Vessel Failure **(Cardiac Death, TV-MI, or ID-TLR)**	0%	7.7% (1)	0%
All Death **Cardiac Death** Non-Cardiac Death	0% **0%** 0%	0% **0%** 0%	7.7% (1) **0%** 7.7% (1)
Target Vessel MI Q-wave MI Non-Q-wave MI	**0%** 0% 0%	**0%** 0% 0%	**0%** 0% 0%
Ischemia Driven TLR PCI CABG	**0%** 0% 0%	**7.7% (1)** 0% 7.7% (1)	**0%** 0% 0%
ARC Stent Thrombosis Definite or Probable Possible	 0% 0%	 0% 0%	 0% 0%

FORTITUDE® Study (MEND II/RENASCENT) Design



Enrollment in Italy and Colombia: Investigators (Number of Patients)



Baseline Clinical Characteristics

Baseline Characteristics	FORTITUDE® BRS (n = 63) Mean ± SD or % (n)
Male	77.8% (49)
Age (Years)	63.7 ± 11.0
History of Smoking	60.3% (38)
Medically Treated Diabetes • Insulin Requiring • Non-Insulin Requiring	31.7% (20) 30.0% (6) 70.0% (14)
Medically Treated Hypertension	81.0% (51)
History of Renal Disease	9.5% (6)
Clinical Presentation • Stable Angina • Acute Coronary Syndrome • Silent Ischemia	 61.3% (38) 35.5% (22) 3.2% (2)
Previous MI	38.1% (24)
History of PCI	60.3% (38)
History of CABG	4.8% (3)
LVEF	55% ± 8.5%

Angiographic Lesion Characteristics

Baseline Characteristics	FORTITUDE® BRS (n = 63) Mean ± SD or % (n)
Target Artery • LAD • LCX • RCA	 38.1% (24) 27.0% (17) 34.9% (22)
Lesion Location • Proximal-Mid	 92% (58)
Reference Vessel Diameter (mm)	2.9 ± 0.5
QCA Diameter Stenosis	60.1% ± 10.1%
QCA Length (mm)	12.5 ± 3.0
ACC/AHA Lesion Class • Type B1-C	 88.9% (56)
Any Bifurcation/Side Branch	12.7% (8)
Calcification • Moderate-Severe	 9.5% (6)
Pre-Procedure TIMI 3 Flow	95.2% (60)

Device Implantation: Procedural Endpoints

Index Procedure Characteristics (QCA)	FORTITUDE® BRS (n = 63) Mean ± SD or % (n)
Pre-Procedure Diameter Stenosis	60.1% ± 10.1%
Pre-Dilatation Prior to Implant	100% (63)
Single Post-Dilatation using NC Balloon	34.9% (22)
Max. Scaffold Deployment Inflation Pressure (ATM)	12.3 ± 2.8 (62)
Final In-Segment Diameter Stenosis	14.1% ± 10.9%
Failure to Cross Due to Severe Calcification/Tortuosity	1.6% (1)
Distal Dissection Treated with DES[1]	4.8% (3)
Clinical Device Success[2]	98.4% (62)
Clinical Procedure Success[3]	96.8% (61)

[1] Non-flow limiting dissections identified distal and outside of scaffold; BRS-DES overlap not required

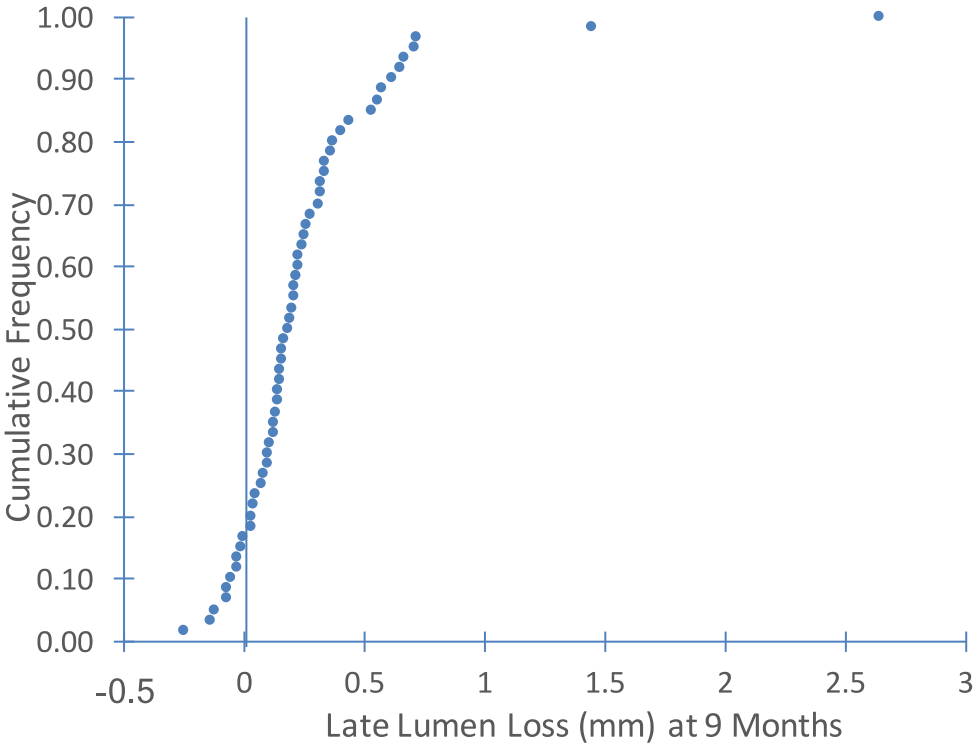
[2] Defined as successful delivery and deployment of the scaffold at the intended target lesion with final residual stenosis of <50% of the target lesion by QCA after the index procedure.

[3] Defined as clinical device success with any adjunctive device without the occurrence of major adverse clinical events related to ischemia up to day of discharge.

9-Month Angiographic Analysis

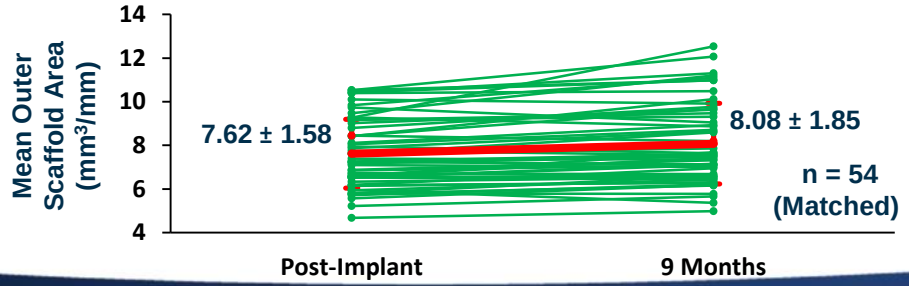
QCA Measurements Mean ± SD	Baseline Procedure (n = 63)	Post-BRS Implantation (n = 63)	9-Month Follow-Up (n = 61)	p-Value
In-Segment Analysis				
Interpolated RVD (mm)	2.9 ± 0.5	2.9 ± 0.4	2.8 ± 0.5	0.0009
MLD (mm)	1.1 ± 0.3	2.5 ± 0.5	2.4 ± 0.5	<0.0001
Late Lumen Loss (mm)	---	---	0.17 ± 0.49	---
Diameter Stenosis (%)	60.1 ± 10.1	14.1 ± 10.9	15.6 ± 13.3	<0.0001
In-Scaffold Analysis				
Interpolated RVD (mm)	---	3.1 ± 0.4	2.9 ± 0.4	<0.0001
MLD (mm)	---	2.8 ± 0.4	2.5 ± 0.5	<0.0001
Acute Gain (mm)	---	1.6 ± 0.4	---	---
Late Lumen Loss (mm)	---	---	0.29 ± 0.43	
Diameter Stenosis (%)	---	9.4 ± 5.4	14.3 ± 12.0	0.0019
Binary Restenosis (%)	---	---	1.6% (1/61)	---

Cumulative Frequency Distribution
9-Month In-Scaffold Late Lumen Loss



9-Month In-Scaffold OCT Measurements

OCT Measurements Mean ± SD or %	Post-BRS Implantation (n = 55)	9-Month Follow-Up (n = 61)	Difference (Post vs. 9-Month)
Mean Lumen Area (mm^3/mm)	7.018 ± 1.634	6.324 ± 1.961	-0.694 (-9.9%)
Mean Outer Scaffold Area (mm^3/mm)	7.624 ± 1.563	8.042 ± 1.880	0.418 (5.5%)
Percent NIH Volume (%)	---	9.1 ± 7.1	---
Post-Implantation Strut Fracture (%)			
OCT Volumetric Measurements Mean ± SD or %	**Percent Covered Struts (At 9 Months)**	**Percent Uncovered Struts (At 9 Months)**	**Total**
Percent Apposed per Patient (%)	94.282 ± 7.055	4.067 ± 5.629	98.3%
Percent "Malapposed" of Total Struts (%)	0.581 ± 1.752	0.178 ± 0.724	0.8%
Percent "Orifice of Branch" of Total Struts (%)	0.776 ± 1.422	0.117 ± 0.275	0.9%
Total	95.6%	4.4%	100%



9-Month Safety End-Points

Safety Endpoints % (n)	In Hospital (n=63)	Discharge to 30 Days (n=63)	9 Months (n=61)
Target Vessel Failure **(Cardiac Death, TV-MI, or ID-TLR)**	3.2% (2)	0%	4.9% (3)
All Death	0%	0%	1.6% (1)
Cardiac Death	**0%**	**0%**	**0%**
Non-Cardiac Death	0%	0%	1.6% (1)
Target Vessel MI	**3.2% (2)**	**0%**	**3.3% (2)**
Q-wave MI	0%	0%	0%
Non-Q-wave MI	3.2% (2)[1]	0%	3.3% (2)
Ischemia Driven TLR	**0%**	**0%**	**1.6% (1)**
PCI	0%	0%	1.6% (1)
CABG	0%	0%	0%
ARC Stent Thrombosis			
Definite or Probable	0%	0%	0%
Possible	0%	0%	0%

[1]Peri-procedural asymptomatic enzymatic raise

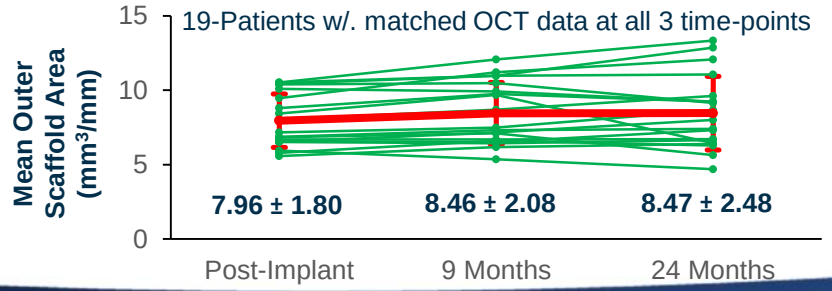
2-Yr Angio Analysis (49 Pts QCA or CT)

QCA Measurements Mean ± SD	9-Month (n= 61)	2-Years (n = 30)
In-Segment Analysis		
Interpolated RVD (mm)	2.8 ± 0.5	2.9 ± 0.5
MLD (mm)	2.4 ± 0.5	2.4 ± 0.6
Late Lumen Loss (mm)	0.17 ± 0.49	0.15 ± 0.62
Diameter Stenosis (%)	15.6 ± 13.3	18.5 ± 12.9
In-Scaffold Analysis		
MLD (mm)	2.5 ± 0.5	2.5 ± 0.5
Late Lumen Loss (mm)	0.29 ± 0.43	0.27 ± 0.37
Diameter Stenosis (%)	14.3 ± 12.0	17.5 ± 12.8
Binary Restenosis	1.6% (1/61)	6.7% (2/30)
CT Angio Analysis	**9-Month (n= 0)**	**2-Year (n= 18)**
Angio Restenosis >50% (n) %	N/A	5.6% (1/18)
Cumulative Binary Restenosis (%)	1.6% (1/61)	8.3% (4/48)

2-Year Matched In-Scaffold OCT Measurements

OCT Measurements Mean ± SD or %	Post-BRS Implantation (n = 19)	9-Month Follow-Up (n = 19)	2-Year Follow-Up (n = 19)	Difference (Post vs. 2-Year)
Mean Lumen Area (mm^3/mm)	7.508 ± 1.935	6.952 ± 2.106	6.528 ± 2.234	-0.980 (-13.1%)
Mean Outer Scaffold Area (mm^3/mm)	7.961 ± 1.798	8.455 ± 2.076	8.466 ± 2.476	0.504 (6.3%)
Percent NIH Volume (%)	---	5.8 ± 4.0	9.5 ± 5.6	---

OCT Volumetric Measurements Mean ± SD or %	Percent Covered Struts (At 2 Years)	Percent Uncovered Struts (At 2 Years)	Total
Percent Apposed per Patient (%)	90.881 ± 9.099	8.016 ± 8.389	98.9%
Percent "Malapposed " of Total Struts (%)	0.223 ± 0.834	0.290 ± 1.143	0.5%
Percent "Orifice of Branch" of Total Struts (%)	0.526 ± 0.919	0.064 ± 0.211	0.6%
Total	91.6%	8.4%	100%

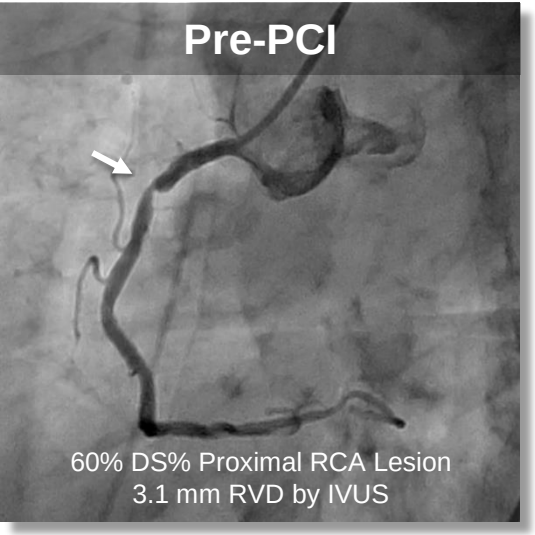


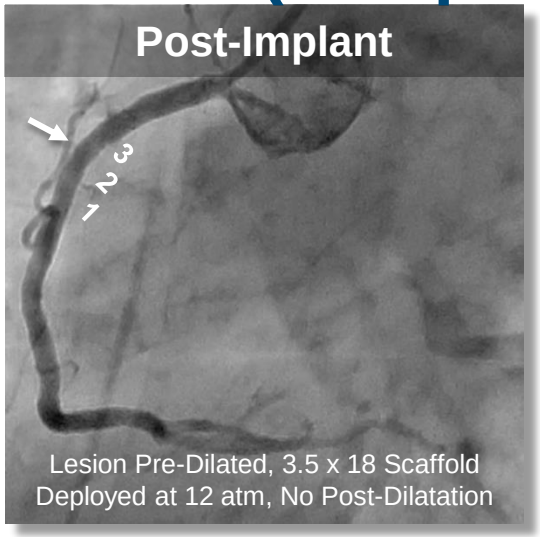
2-Year Safety End-Points

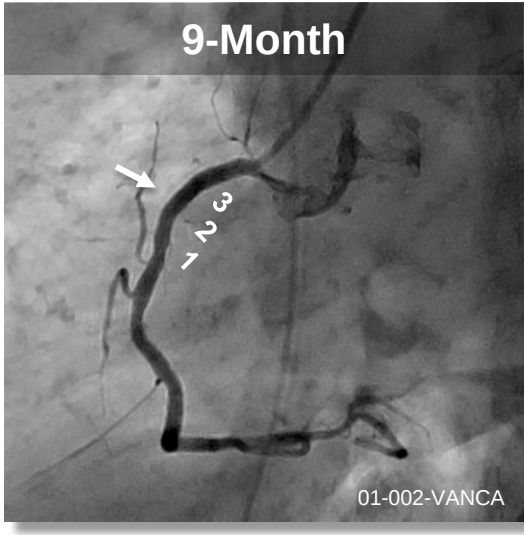
Safety Endpoints % (n)	<1-Month (n = 63)	1 to 9 Months (n = 61)	9 to 24 Months (n = 57)
Target Vessel Failure **(Cardiac Death, TV-MI, or ID-TLR)**	3.2% (2)	1.6% (1)	5.3% (3)
All Death **Cardiac Death** Non-Cardiac Death	0% **0%** 0%	1.6% (1) **0%** 1.6% (1)	0% **0%** 0%
Target Vessel MI Q-wave MI Non-Q-wave MI	**3.2% (2)** 0% 3.2% (2)[1]	**0%** 0% 0%	**0%** 0% 0%
Ischemia Driven TLR PCI CABG	**0%** 0% 0%	**1.6% (1)** 1.6% (1)[2] 0%	**5.3% (3)** 5.3% (3)[3] 0%
ARC Stent Thrombosis Definite or Probable Possible	 0% 0%	 0% 0%	 1.8% (1)[3] 0%

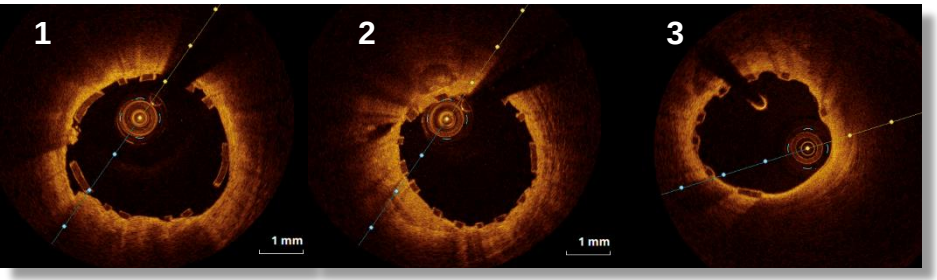
[1]Peri-procedural asymptomatic enzymatic raise. [2]Clinically driven restenosis. [3]Includes the ST case patient, patient stopped all medications close to the 24-month follow up visit (8 days prior to event).

FORTITUDE® (150-µm) Clinical Case

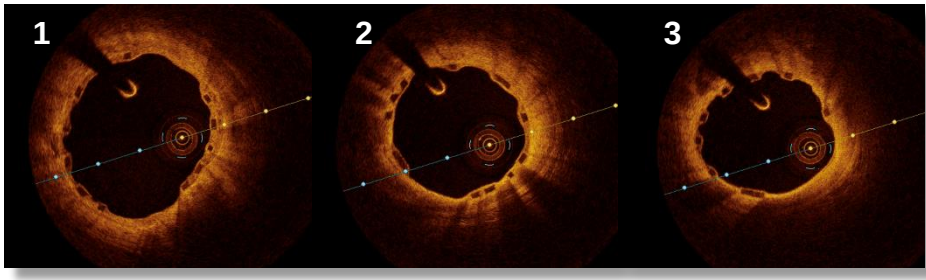






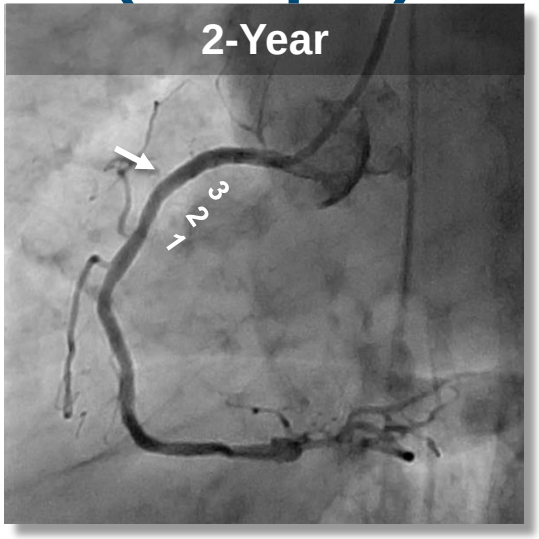


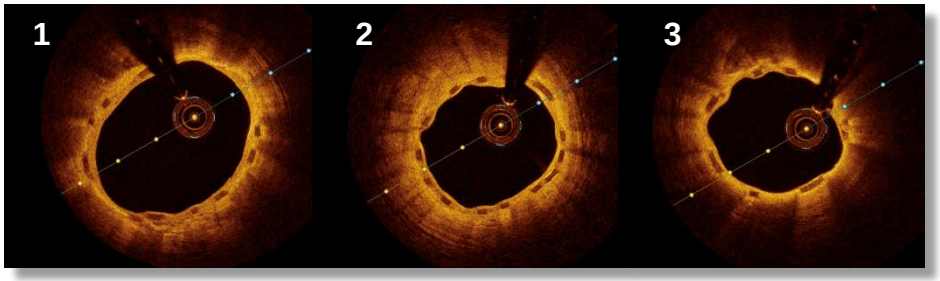
Post-Implant



9-Month

FORTITUDE® (150-µm) Clinical Case





2-Year

Case Courtesy of Boris Vesga, Instituto del Corazon, Bucaramanga, Colombia

FORTITUDE Study: Conclusions

- **The FORTITUDE Study, an international, multi-center investigation of the clinical performance of the 1st generation (150-µm) Amaranth BRS showed:**
  - ✓ **High clinical device success rate (98.4%)**
  - ✓ **Low MACE rates at 9-months (4.9%; 2 out 3 events related to peri-procedural MIs)**
  - ✓ **Low angiographic binary restenosis (1.6%) and late loss (0.27 ± 0.41 mm)**
  - ✓ **High levels of strut coverage (96%) and scaffold stability (1.7% late discontinuities) in OCT at 9-months**
  - ✓ **At 2-years, imaging analysis showed that the FORTITUDE BRS continued to show stable mechanical stability, strut apposition and low restenosis rates (5.3%).**
- **Due to the unique polymer features, future generation scaffolds have the potential to match the biological performance of current metallic DES**