The PROSPECT ABSORB Trial: Randomized Evaluation of Vulnerable Plaque Treatment with Percutaneous Coronary Intervention

Gregg W. Stone, MD

On behalf of Akiko Maehara, Ziad A. Ali, Claes Held, Mitsuaki Matsumura, Lars Kjøller-Hansen, Hans Erik Bøtker, Michael Maeng, Thomas Engstrøm, Rune Wiseth, Jonas Persson, Thor Trovik, Ulf Jensen, Stefan K. James, Gary S. Mintz, Ovidiu Dressler, Aaron Crowley, Ori Ben-Yehuda and David Erlinge
for the PROSPECT ABSORB Investigators

Disclosures

- In the past 12 months Gregg W. Stone has received speaker honoraria from Cook; served as a consultant to Valfix, TherOx, Robocath, HeartFlow, Gore, Ablative Solutions, Miracor, Neovasc, Abiomed, Ancora, Vectorious, Cardiomech; and has equity/options from Ancora, Qool Therapeutics, Cagent, Applied Therapeutics, Biostar family of funds, SpectraWave, Orchestra Biomed, Aria, Cardiac Success, Valfix

Background

- ACS most commonly arise from rupture and thrombosis of thin-cap lipid-rich coronary atheromas that have large plaque burden despite angiographically appearing mild
- Scaffold or stent treatment of such lesions may create a “neocap” of neointimal hyperplasia, thickening the fibrous cap and normalizing wall stress, thus stabilizing the high-risk plaque
- We thus sought to examine the outcomes of PCI of non-flow-limiting vulnerable plaques in a pilot randomized trial meant to inform a pivotal study

Virmani R et al. ATVB 2000;20:1262-75
Stone GW et al. NEJM 2011;364:226-35
McPherson JA et al. JACC Img 2012;5:S76–85

Methods

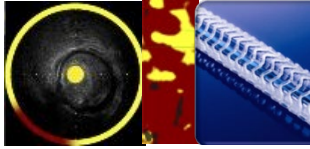
- The PROSPECT ABSORB RCT was embedded within the PROSPECT II natural history study
- After successful PCI of all flow-limiting lesions in pts with STEMI and NSTEMI, NIRS-IVUS imaging was performed of the prox 6-10 cm of all 3 coronary arteries
- Non-flow-limiting stenoses not intended for PCI were identified with the following site-assessed features:
  - Angiographic DS <70% (with negative FFR or iFR required if DS was >40%) with RVD 2.5-4.0 mm and lesion length ≤50 mm
  - IVUS plaque burden ≥65%
- Qualifying lesions (1 per pt) were randomized to treatment with an Absorb bioresorbable vascular scaffold (BVS) plus GDMT vs. GDMT alone
- 3-vessel angiography and NIRS-IVUS imaging were repeated at 25 months in all pts

Outcome Measures

- The primary powered effectiveness endpoint was the IVUS-derived minimum lumen area (MLA) at protocol-driven 25-month follow-up
- The primary (non-powered) safety endpoint was randomized target lesion failure (TLF; cardiac death, target vessel-related MI or clinically-driven TLR) at 24 months
- The secondary (non-powered) clinical effectiveness endpoint was randomized lesion-related major adverse cardiac events (MACE; cardiac death, MI, unstable angina, or progressive angina) at latest follow-up

PROSPECT II Organization, Leadership, Committees and Core Laboratories

- Coordinating PIs and Study Chairmen: David Erlinge and Gregg W. Stone
- AROs: CRF (Ori-Ben-Yehuda, Executive Director) and UCR (Jonas Oldgren, Executive Director)
- Sponsor, Project and Data Management: UCR, Frida Kåver (Project Manager), Lars Wallentin (sponsor representative)
- Clinical Events Committee: UCR, Claes Held (Chair)
- Angiographic Core Lab: CRF, Ziad A. Ali (Director)
- IVUS-NIRS Core Lab: CRF, Akiko Maehara (Director)
- Programming, Biostatistics and Data Analysis: CRF, Aaron Crowley (Director)
- DSMB: Patrick W. Serruys (Chair)
- Funding support: Abbott Vascular, Infraredx Inc, The Medicines Company



PROSPECT ABSORB RCT

ClinicalTrials.gov Identifier NCT02171065

PROSPECT II
Troponin + ACS
Successful PCI
(N=902)

→

3 vessel IVUS
+ NIRS (blinded)
(N=898)*

→

≥1 non-flow-limiting NCL
with site-assessed
≥65% plaque burden
(n=182)

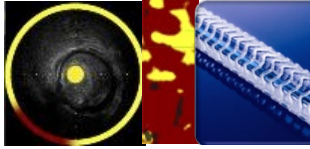
Excluded (n=716)

386 actively screened and did not meet all inclusion criteria or met one or more exclusion criteria (not mutually exclusive)

- 267 site-determined IVUS plaque burden <65%
- 43 visually estimated reference vessel diameter >4.0mm or <2.5mm
- 37 severe lesion calcification or vessel tortuosity
- 23 ostial lesion
- 16 randomized lesion was within 10 mm from a previously implanted stent or scaffold
- 15 bifurcation lesion with side branch >2.5mm or there is a lesion longer than 5mm from ostium
- 5 located in the left main coronary artery

330 not actively screened or unknown reasons

*Per protocol, 4 pts were not followed beyond 30 days because NCL imaging data was not acquired; these pts remained in the safety cohort



PROSPECT ABSORB RCT

ClinicalTrials.gov Identifier NCT02171065

≥1 non-flow-limiting NCL with site-assessed ≥65% plaque burden (n=182)

R 1:1

92 received allocated intervention
1 DES implanted instead of BVS
Analyzable IVUS (n=91)

ABSORB BVS + GDMT (N=93)

GDMT alone (N=89)

88 received allocated intervention
1 Absorb BVS implanted in error
Analyzable IVUS (n=88)

Routine angiography with 3V IVUS-NIRS FU at 25 months

ABSORB BVS + GDMT	GDMT alone
Clinical follow-up at 24 months (n=93)	Clinical follow-up at 24 months (n=88)
Follow-up angiography (n=87)	Follow-up angiography (n=80)
Qualifying follow-up IVUS (n=85)	Qualifying follow-up IVUS (n=77)
Analyzable follow-up IVUS (n=84)	Analyzable follow-up IVUS (n=72)
Analyzable baseline and follow-up IVUS (n=83)	Analyzable baseline and follow-up IVUS (n=72)

GDMT = guideline-directed medical therapy

2-year clinical FU 181 pts (99.5%); median clinical FU 4.1 years
25-mo angio FU 167 pts (91.8%); qualifying IVUS FU 156 pts (85.7%)

PROSPECT ABSORB
Hospitals and Principal Investigators

- **Denmark (132 randomized):** National Coordinating Investigator: Thomas Engström. Aarhus: Hans Erik Bøtker, Michael Maeng, Roskilde: Lars Kjöller-Hansen, Copenhagen: Thomas Engström, Odense: Lisette Okkels Jensen

- **Sweden (32 randomized):** National Coordinating Investigator: David Erlinge. Lund: David Erlinge, Örebro: Ole Fröbert, Danderyd Hospital, Stockholm: Jonas Persson, Uppsala: Stefan James, Södersjukhuset, Stockholm: Ulf Jensen, Falun: Iwar Sjögren, Kalmar: Jörg Carlsson

- **Norway (18 randomized):** National Coordinating Investigator: Jan Erik Nordrehaug. Trondheim: Rune Wiseth, Stavanger, Alf Inge Larsen, Bergen; Öyvind Bleie, Tromsö: Thor Trovik

Baseline Characteristics

- 182 patients and lesions randomized -

Baseline feature	BVS plus GDMT (N=93)	GDMT alone (N=89)
Age (years)	63.0 (56.0, 69.0)	65.0 (58.0, 72.0)
Sex (male)	86.0% (80/93)	78.7% (70/89)
Body mass index (kg/m^2)	27.2 (25.0, 29.6)	26.4 (24.6, 29.8)
Hypertension, medically treated	38.7% (36/93)	40.4% (36/89)
Dyslipidemia, medically treated	24.7% (23/93)	18.0% (16/89)
Diabetes mellitus	11.8% (11/93)	10.1% (9/89)
Recent tobacco use (within 1 month)	38.0% (35/92)	34.1% (30/88)
Prior PCI	12.9% (12/93)	10.1% (9/89)
Prior MI	7.5% (7/93)	9.0% (8/89)
Presentation with STEMI	33.3% (31/93)	25.8% (23/89)
Presentation with NSTEMI	66.7% (62/93)	74.2% (66/89)

There were no significant differences between groups

Baseline Characteristics

- 182 patients and lesions randomized -

Baseline feature	BVS plus GDMT (N=93)	GDMT alone (N=89)
LVEF <50%	38.2% (34/89)	22.6% (19/84)
Total cholesterol (mg/dL)	208.8 (166.3, 228.2)	197.2 (170.1, 235.9)
- HDL (mg/dL)	42.5 (36.7, 54.1)	42.5 (36.3, 54.1)
- LDL (mg/dL)	133.4 (104.4, 154.7)	127.6 (104.4, 162.4)
- TGs (mg/dL)	124.0 (86.8, 177.1)	115.1 (79.7, 177.1)
Serum creatinine (mg/dL)	0.84 (0.75, 0.96)	0.89 (0.75, 1.05)
High-sensitivity CRP (µg/mL)	3.6 (1.4, 8.1)	3.1 (1.7, 5.0)
Hemoglobin (g/dL)	14.5 (13.8, 15.1)	14.3 (13.2, 15.1)
White blood cell count (x10^9/L)	9.0 (7.4, 12.0)	8.2 (6.9, 11.1)
Platelet count (x10^9/L)	216 (194, 266)	233 (196, 277)

There were no significant differences between groups

Baseline QCA (Core Lab)

- 182 patients and lesions randomized -

Baseline feature	BVS plus GDMT (N=93)	GDMT alone (N=89)
Location: LAD	29.0% (27/93)	39.3% (35/89)
Location: LCX	34.4% (32/93)	34.8% (31/89)
Location: RCA	36.6% (34/93)	25.8% (23/89)
Location: Proximal	25.8% (24/93)	31.5% (28/89)
Location: Mid	44.1% (41/93)	36.0% (32/89)
Location: Distal	16.1% (15/93)	13.5% (12/89)
Location: Side-branch	14.0% (13/93)	19.1% (17/89)
TIMI flow = 3	97.8% (89/91)	97.6% (82/84)
Reference vessel diameter (mm)	2.85 (2.61, 3.24)	2.81 (2.45, 3.11)
Minimum luminal diameter (mm)	1.64 (1.43, 2.04)	1.60 (1.40, 1.84)
Diameter stenosis (%)*	41.0 (32.8, 49.4)	42.1 (36.1, 48.6)
Lesion length (mm)	13.4 (9.5, 17.4)	12.1 (8.7, 18.4)

*FFR or iFR was negative (FRR >0.80 or iFR >0.89) in 93/97 (95.9%) randomized lesions.
There were no significant differences between groups.

Baseline NIRS-IVUS (Core Lab)

- 182 patients and lesions randomized -

Baseline feature	BVS plus GDMT (N=93)	GDMT alone (N=89)
IVUS findings		
Maximum plaque burden (%)	73.8 (70.0, 77.6)	73.7 (70.2, 76.8)
Measures at the MLA site		
- Minimal luminal area (mm^2)	3.0 (2.4, 3.9)	2.9 (2.5, 3.6)
- Distance from ostium (mm)	32.8 (17.1, 53.9)	29.2 (16.8, 40.3)
- Disease arc (°)	270 (180, 360)	240 (180, 360)
- Remodeling index	0.89 (0.78, 1.00)	0.85 (0.72, 0.99)
- Vessel area (mm^2)	11.6 (8.8, 14.7)	11.0 (8.4, 13.3)
Lesion length (mm)	23.0 (15.5, 35.0)	23.0 (15.0, 34.5)
NIRS findings		
$MaxLCBI_{4mm}$	326.6 (207.2, 491.4)	337.2 (179.9, 469.6)

There were no significant differences between groups

Baseline Core Lab Imaging

- 182 patients and lesions randomized -

Baseline feature	BVS plus GDMT (N=93)	GDMT alone (N=89)
High-risk Plaque Morphology		
Lesions with plaque burden ≥70%	76.1% (70/92)	78.4% (69/88)
Lesions with $maxLCBI_{4mm}$ ≥324.7*	51.7% (46/89)	53.5% (46/86)
Lesions with MLA ≤4.0 mm^2	78.3% (72/92)	88.6% (78/88)
Lesions with ≥1 of 3 high-risk plaque characteristics†	93.3% (83/89)	97.7% (84/86)
Lesions with ≥2 of 3 high-risk plaque characteristics†	71.9% (64/89)	76.7% (66/86)
Lesions with 3 of 3 high-risk plaque characteristics†	40.4% (36/89)	45.3% (39/86)

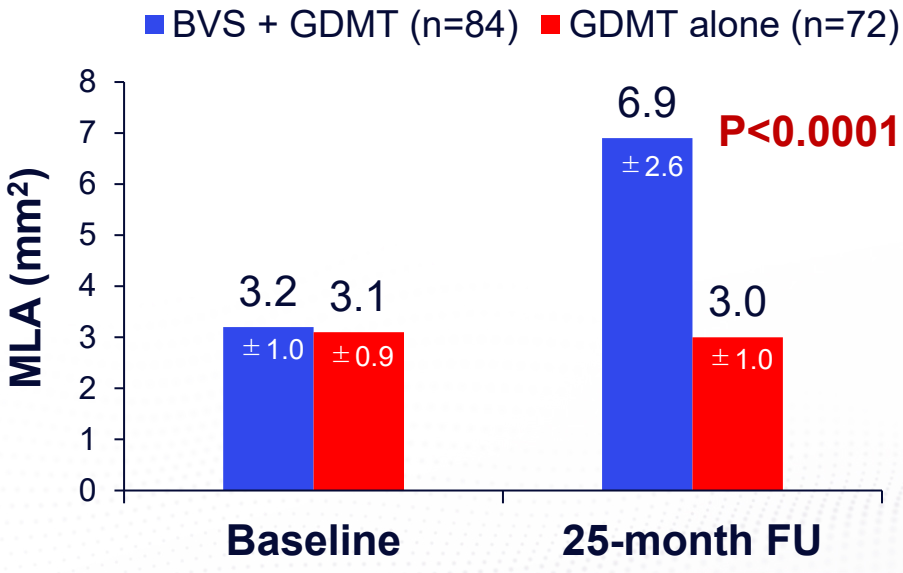
*$MaxLCBI_{4mm}$ denotes the highest lipid content over any 4 mm segment in the lesion, scored on a scale of 0 to 1000 which signifies 0% to 100% lipid content. 324.7 represents the upper quartile cutoff of all untreated imaged non-culprit lesions in the PROSPECT II study, the pre-specified definition of a high-risk plaque by near-infrared spectroscopy criteria. †Pre-specified high-risk plaque characteristics include $maxLCBI_{4mm}$ ≥324.7, maximum plaque burden ≥70%, and MLA≤ 4.0 mm^2.

There were no significant differences between groups

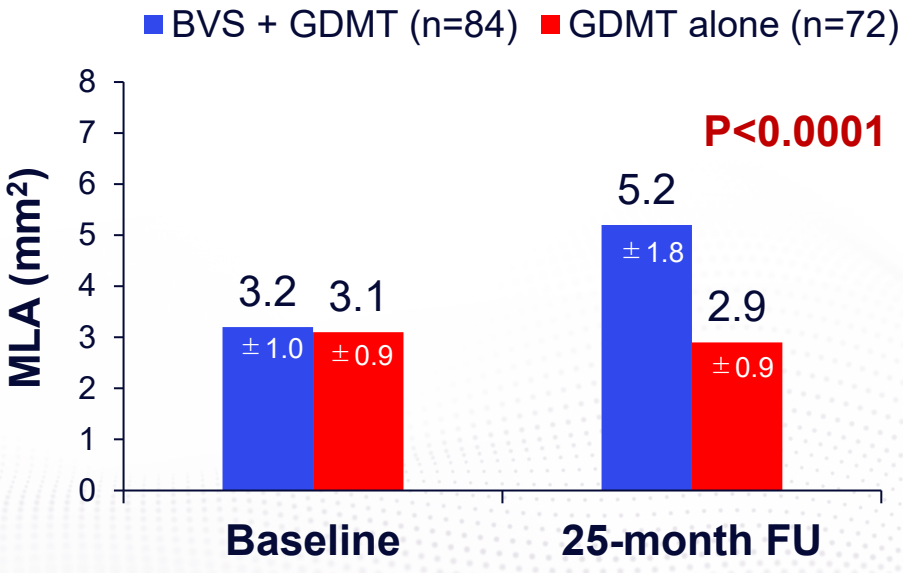
25-Month Follow-up IVUS MLA

Primary Powered Endpoint

At the original MLA site (primary analysis)



Across the entire lesion (includes 5 mm margins)



25-Month FU NIRS-IVUS (Core Lab)

	BVS plus GDMT (N=84)	GDMT alone (N=72)	P value
IVUS findings			
At the original MLA site			
- Follow-up MLA (mm^2) – primary endpoint	6.9 ± 2.6	3.0 ± 1.0	<0.0001
- Baseline MLA (mm^2), paired	3.2 ± 1.0	3.1 ± 0.9	-
- Change from baseline to follow-up (mm^2)	3.7 ± 2.5	-0.1 ± 0.5	<0.0001
- Follow-up vessel area	15.9 (12.5, 20.1)	10.2 (7.8, 12.4)	<0.0001
Across the entire lesion and 5 mm margins			
- Follow-up MLA (mm^2) – secondary endpoint	5.2 ± 1.8	2.9 ± 0.9	<0.0001
- Baseline MLA (mm^2), paired	3.2 ± 1.0	3.1 ± 0.9	-
- Change from baseline to follow-up (mm^2)	2.0 ± 1.5	-0.2 ± 0.5	<0.0001
Neointimal hyperplasia (μm) - ”neocap”	210 (180, 240)	-	-
Strut discontinuities or malapposition	1 (1.2%)*	-	-
NIRS findings			
$MaxLCBI_{4mm}$	62.0 (0.0, 213.8)	268.8 (157.2, 396.7)	<0.0001

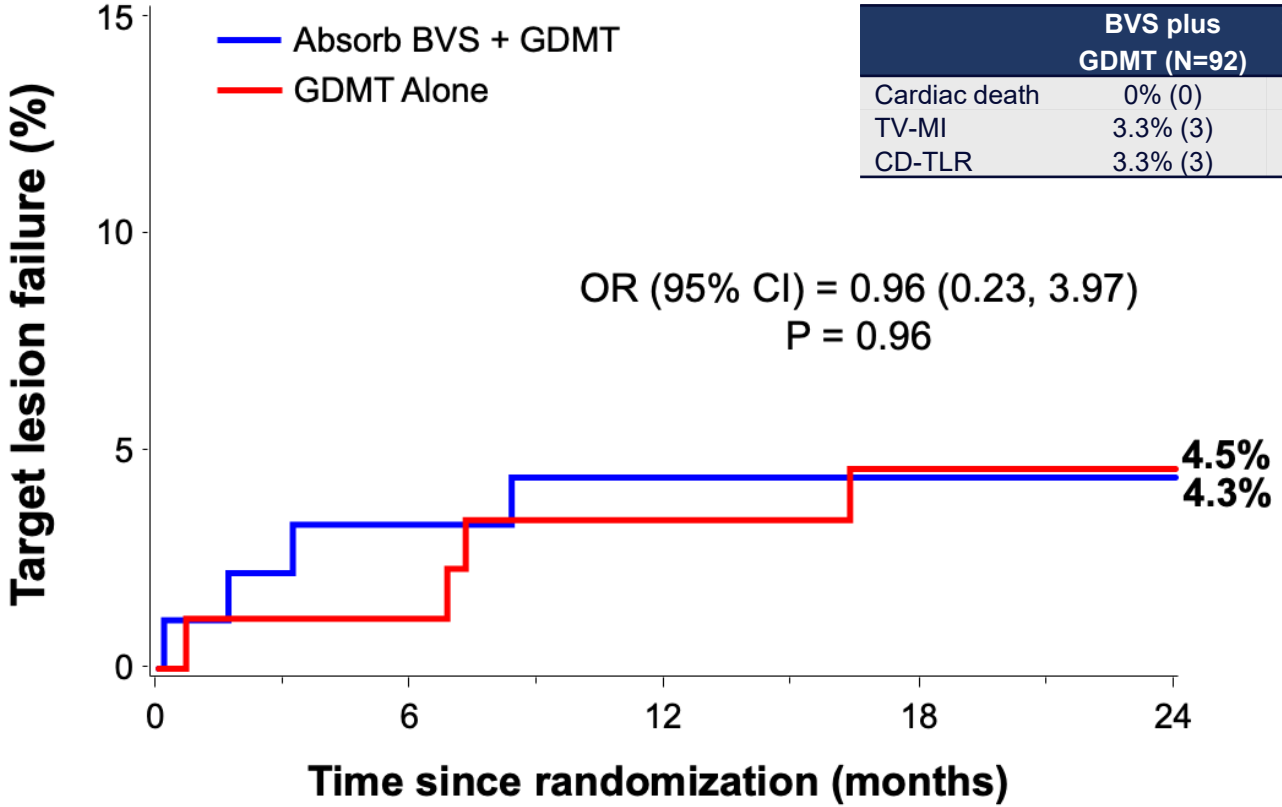
*Pt remained asymptomatic and MACE-free during 3.6-year FU

25-Month FU QCA (Core Lab)

	BVS plus GDMT (N=86)	GDMT alone (N=80)	P value
TIMI flow 3	94.0% (78/83)	98.7% (77/78)	0.21
Reference vessel diameter (mm)	2.84 ± 0.40	2.73 ± 0.51	0.048
In-scaffold measures			
- Minimum luminal diameter (mm)	2.29 ± 0.46	-	-
- Late loss (mm)	0.37 ± 0.40	-	-
- Diameter stenosis (%)	20.6 ±13.1	-	-
- Diameter stenosis ≥50%	3.5% (3/86)	-	-
In-lesion measures (includes 5 mm margins)			
- Minimum luminal diameter (mm)	2.15 ± 0.44	1.66 ± 0.40	<0.0001
- Late loss (mm)	0.27 ± 0.36	0.00 ± 0.45	<0.0001
- Diameter stenosis (%)	23.8 ± 14.3	38.6 ± 13.8	<0.0001
- Diameter stenosis ≥50%	4.7% (4/86)	15.0% (12/80)	0.02

Target Lesion Failure, 24 Months

	BVS plus GDMT (N=92)	GDMT alone (N=89)
Cardiac death	0% (0)	0% (0)
TV-MI	3.3% (3)	1.1% (1)
CD-TLR	3.3% (3)	3.4% (3)

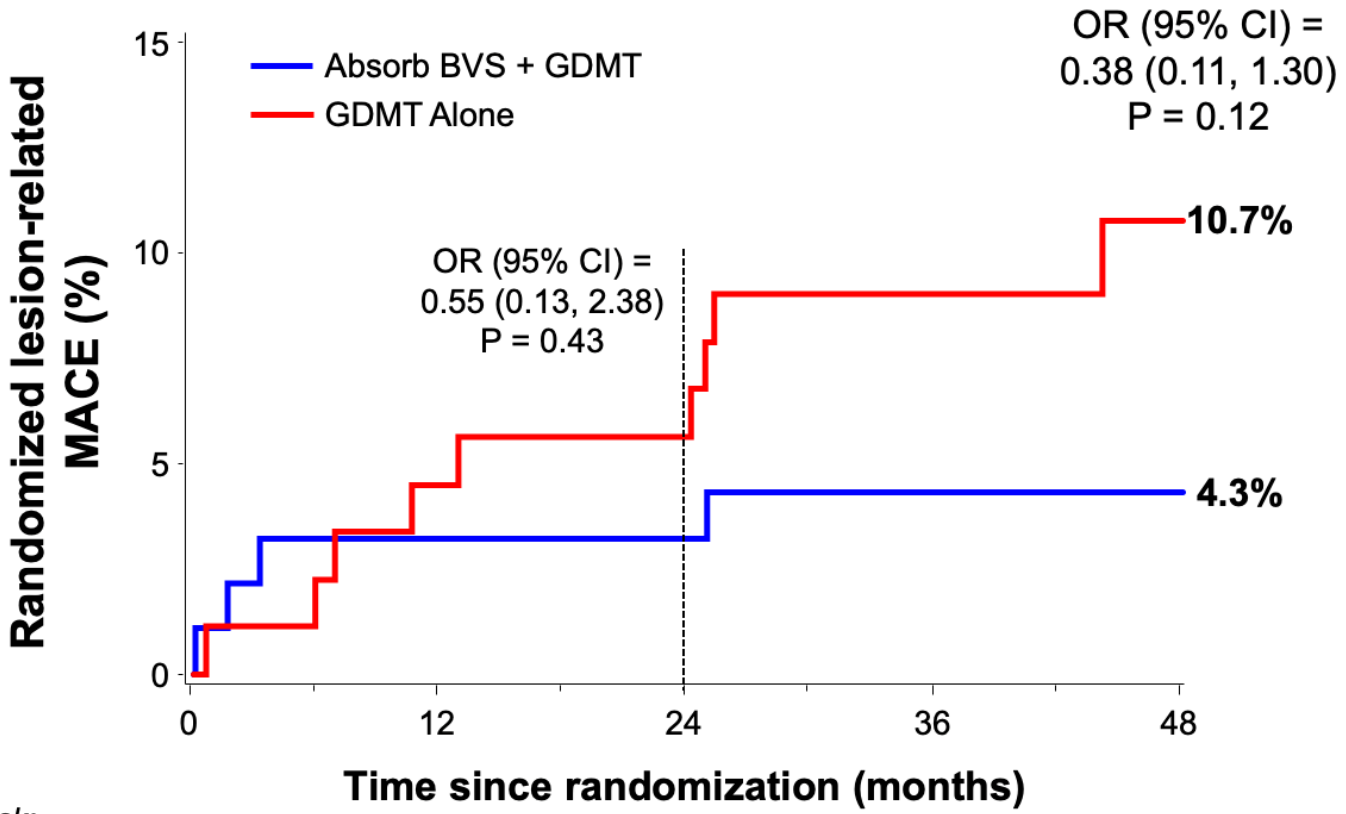


BVS-implanted per protocol safety cohort

Number at risk:

Absorb BVS + GDMT	92	89	88	88	88
GDMT Alone	89	88	86	84	84

Randomized Lesion-Related MACE



ITT population

Number at risk:

Absorb BVS + GDMT	93	90	90	78	45
GDMT Alone	89	85	83	68	42

Randomized Lesion-Related MACE

Event rate, entire study	BVS plus GDMT (N=93)	GDMT alone (N=89)	P value
MACE	4.3% (4)	10.7% (9)	0.12
- Cardiac death	0% (0)	0% (0)	-
- Myocardial infarction	2.2% (2)	1.7% (1)	-
- Procedural	0% (0)	0% (0)	-
- Non-procedural	2.2% (2)	1.7% (1)	-
- Unstable angina	1.1% (1)	0% (0)	-
- Progressive angina	1.1% (1)	9.0% (8)	-
- Requiring revascularization	1.1% (1)	6.8% (6)	-
- With ACL-confirmed rapid lesion progression	0% (0)	2.2% (2)	-
Clinically-driven revascularization	4.3% (4)	8.5% (7)	-
- PCI	4.3% (4)	8.5% (7)	-
- CABG	0% (0)	0% (0)	-
Scaffold thrombosis*	1.1% (1)	-	-

*Thrombosis at day 50 of a Dg side-branch pinched by LAD BVS struts, w/o scaffold thrombosis

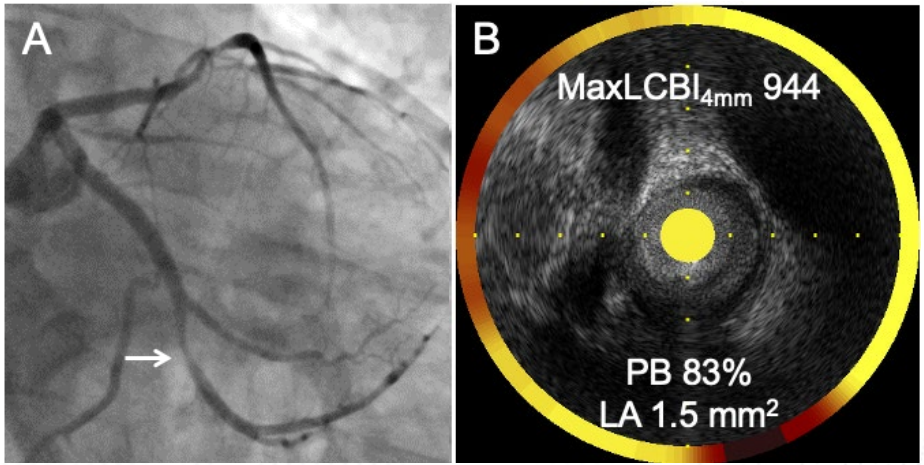
Randomized Lesion-related MACE at Last FU According to Pre-specified HRP Characteristics

High-risk plaque characteristics	Absorb BVS + GDMT (n=93)		GDMT Alone (n=89)			
	N lsns	KM % (n)	N lsns	KM % (n)	OR (95% CI)	P_{int}
Lesion with $MaxLCBI_{4mm}$ ≥324.7						
No	43	4.7% (2)	40	7.5% (3)	0.59 (0.09, 3.72)	0.56
Yes	46	4.3% (2)	46	13.8% (6)	0.28 (0.05, 1.48)	
Lesion with plaque burden ≥70%						
No	22	0.0% (0)	19	5.3% (1)	-	0.98
Yes	70	5.7% (4)	69	12.4% (8)	0.42 (0.12, 1.49)	
Lesion with MLA ≤4.0 mm^2						
No	20	0.0% (0)	10	10.0% (1)	-	0.98
Yes	72	5.6% (4)	78	11.0% (8)	0.48 (0.14, 1.67)	
Number of high-risk features, any						
0/1	25	0.0% (0)	20	5.0% (1)	-	0.98
2/3	64	6.3% (4)	66	12.9% (8)	0.45 (0.13, 1.57)	

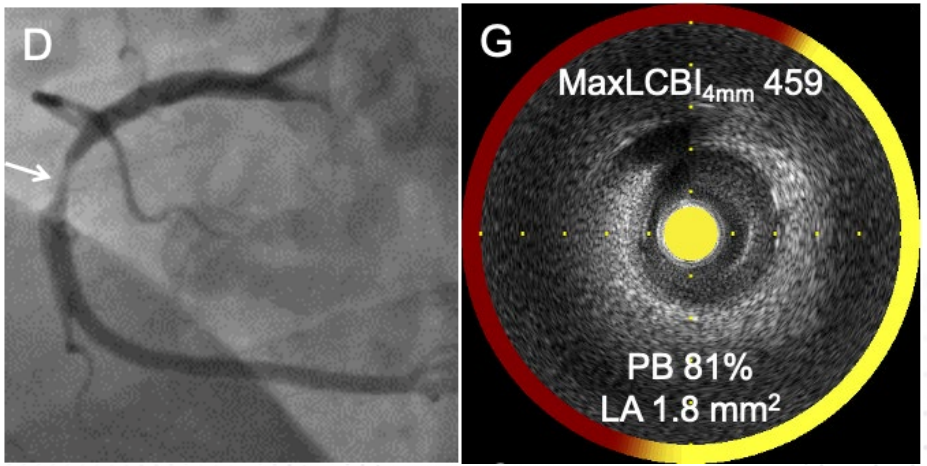
Illustrative Case

57-yo man w/NSTEMI due LAD stenosis, treated successfully. 3-vessel NIRS-IVUS imaging was performed. Operator considered two possible lesions with PB ≥65% for randomization, LCX-OM and mid RCA. Both were angiographically moderate but were negative by FFR (0.90 in both).

LCX-OM



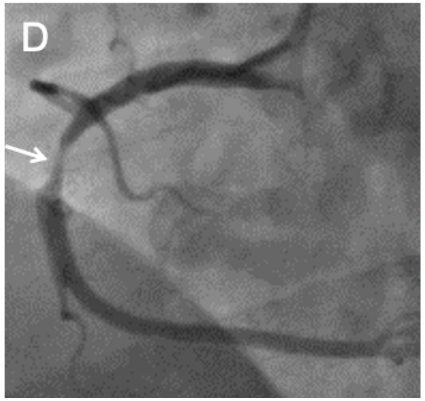
Mid RCA

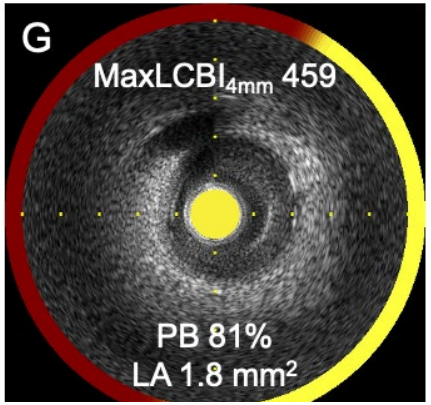


Illustrative Case

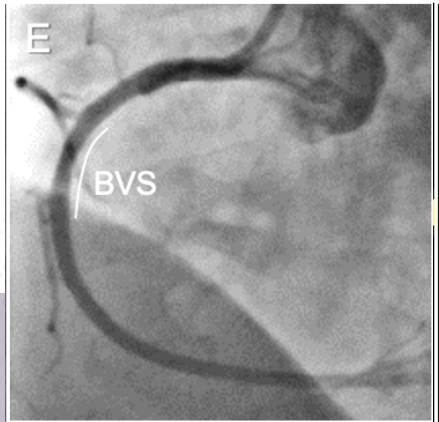
Mid RCA was treated - a 3.5 x 23 mm BVS was implanted at 16 atm and post-dilated with a 4.0 mm non-compliant balloon at 18 atm. The LCX-OM was not treated.

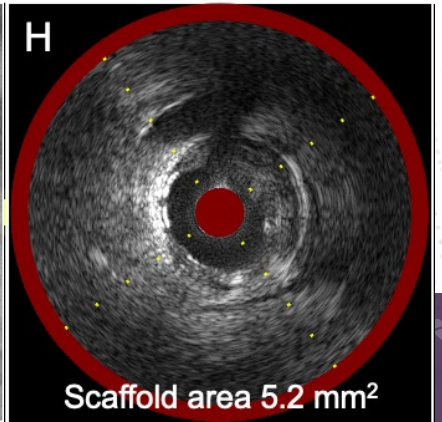
Mid RCA Pre





Mid RCA Post BVS

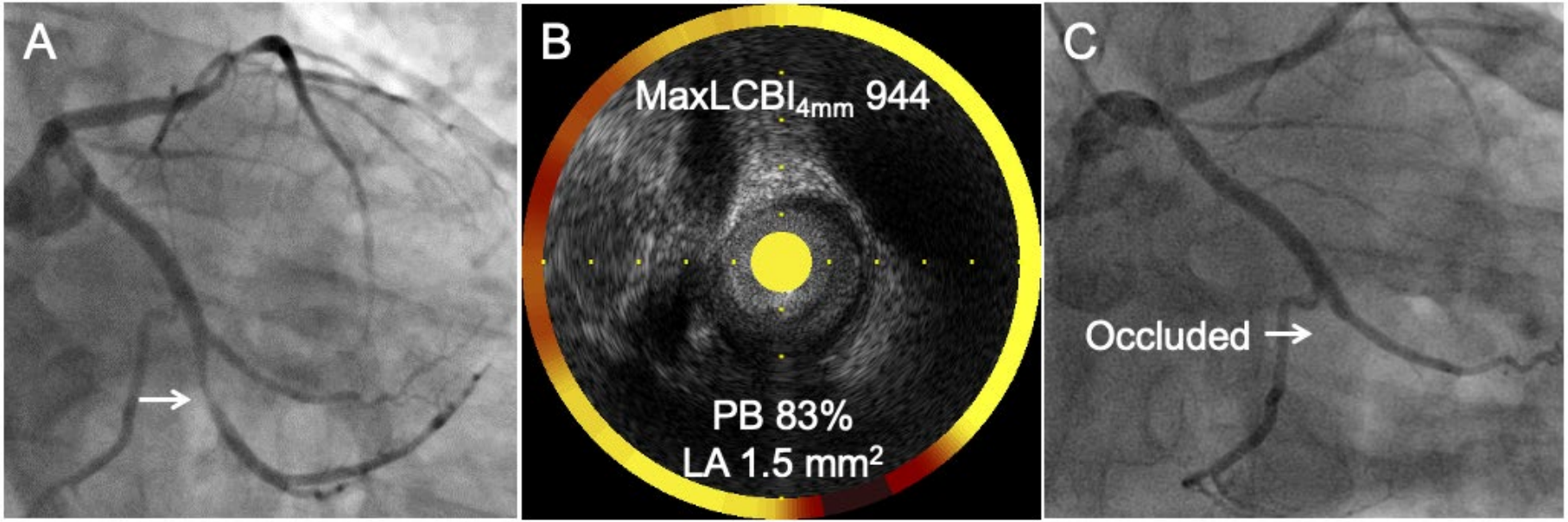




Illustrative Case

The patient was initially asymptomatic but presented 9 months later with severe progressive angina. Repeat angiography demonstrated a patent RCA (not shown) and a thrombotically occluded OM branch of the LCX adjacent to the site of the original high-risk lesion (despite ongoing high-dose statin therapy and other GDMT) (panel C). The operator chose to treat the LCX conservatively.

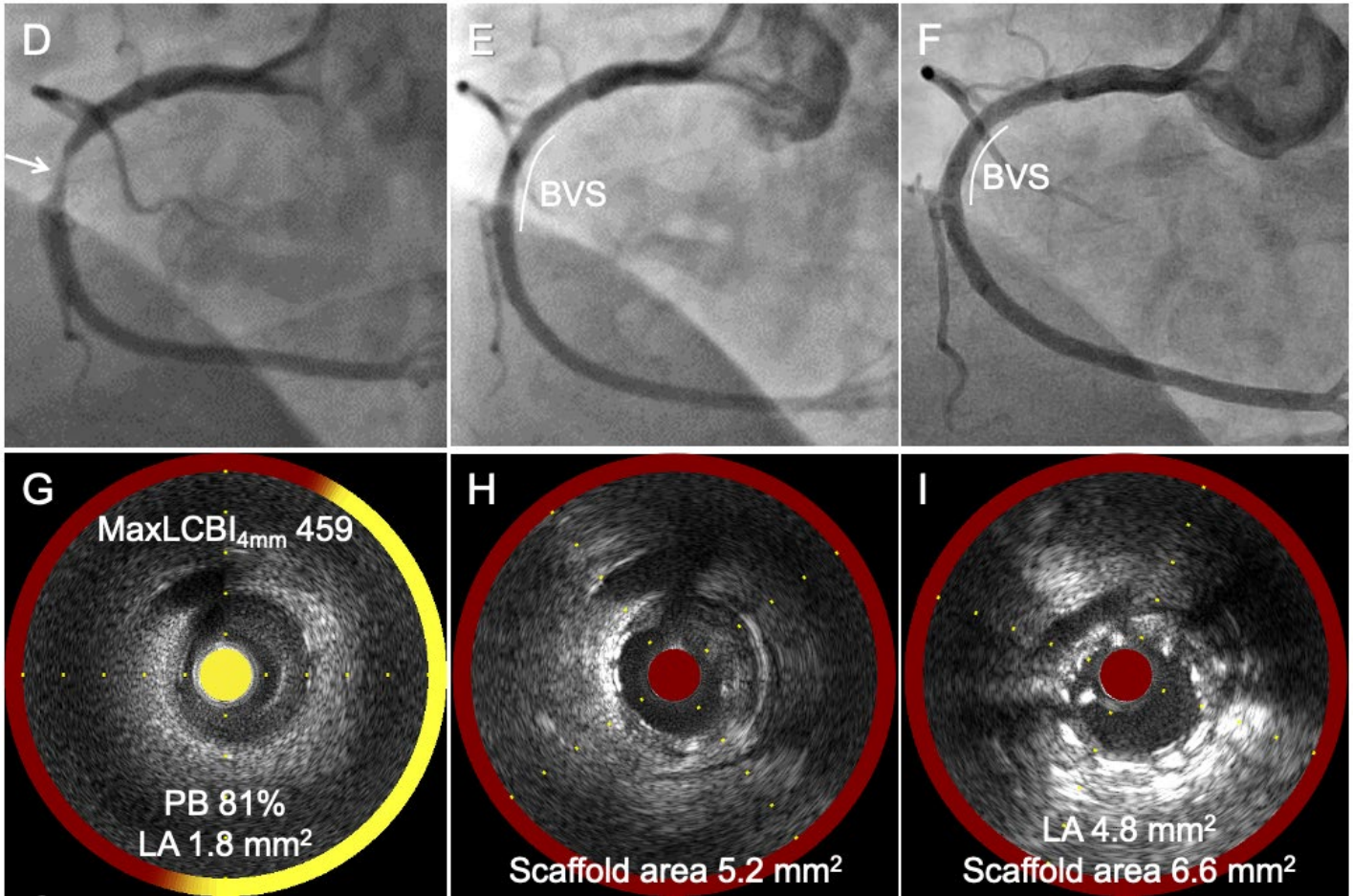
LCX-OM at 9 mos



Illustrative Case

RCA at 25 mos

The pt remained stable but with mild angina. At 25 mos protocol-driven routine FU angiography and imaging were performed. The LCX OM remained occluded (not shown). The RCA was widely patent with a scaffold area of 6.6 mm^2 and MLA of 4.8 mm^2 (panel I), the difference representing neointimal hyperplasia, functionally a thickened "neocap" covering the prior fibroatheroma.



Limitations

- Trial was not powered for clinical outcomes
- IVUS lacks sufficient resolution to detect all cases of malapposition and scaffold discontinuities, but severe cases would likely be identified
- The mechanisms underlying the reduction in randomized lesion lipid content from baseline to 25-month follow-up after BVS-treatment are uncertain
- Median follow-up was only 4.1 years, but even in more complex lesions BVS treatment results in few TLF and thrombosis events after 3 years*
- The present PCI results apply to the first generation everolimus-eluting Absorb BVS; whether the results would be superior with a thinner-strut BVS or a contemporary metallic DES is unknown

*Stone GW et al. JAMA Cardiol. 2019;4:1261-9

Conclusions

- In the present RCT BVS implantation in angiographically mild non–flow-limiting lesions with large PB, small lumen areas and high lipid content was safe and substantially enlarged luminal dimensions during FU
- The favorable randomized lesion-related MACE rates observed after BVS treatment compared with GDMT alone warrants the performance of an adequately powered randomized trial to determine whether PCI treatment of focal vulnerable plaques improves patient outcomes

JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

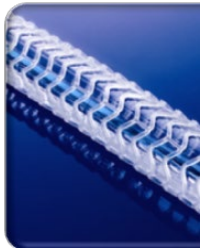
Percutaneous Coronary Intervention for Vulnerable Coronary Atherosclerotic Plaque

Gregg W. Stone, MD,[a,b] Akiko Maehara, MD,[b,c] Ziad A. Ali, MD, DPhil,[b,c] Claes Held, MD, PhD,[d] Mitsuaki Matsumura, BS,[b] Lars Kjøller-Hansen, MD, DMSc,[e] Hans Erik Bøtker, MD, PhD, DMSc,[f] Michael Maeng, MD, PhD,[f] Thomas Engstrøm, MD, PhD,[g] Rune Wiseth, MD, PhD,[h] Jonas Persson, MD, PhD,[i] Thor Trovik, MD, PhD,[j] Ulf Jensen, MD, PhD,[k] Stefan K. James, MD, PhD,[d] Gary S. Mintz, MD,[b] Ovidiu Dressler, MD,[b] Aaron Crowley, MA,[b] Ori Ben-Yehuda, MD,[b,l] David Erlinge, MD, PhD,[m] for the PROSPECT ABSORB Investigators

J Am Coll Cardiol 2020:on-line

Back-up Slides

BVS Implantation



- BVS were chosen for this study rather than metallic DES given their potential to thicken the fibrous cap and normalize wall stress, their acceptable mechanical properties in non-obstructive lipid-rich non-calcific plaques, and their non-permanence
- Implantation technique - The protocol recommended:
  - Appropriate pre-dilatation of the target lesion with a NC balloon with diameter selected by IVUS to match the RVD;
  - Appropriate scaffold sizing after intracoronary TNG based on imaging with standard BVS deployment technique; and
  - Mandatory post-dilatation at high pressure (>16 atm.) with an NC balloon diameter ≤0.5 mm larger than the nominal scaffold diameter, assuring <10% final residual stenosis and complete apposition of the scaffold by IVUS

Bourantas CV et al. EuroIntervention. 2015;11:746-56
Bourantas CV et al. AHJ. 2013;165:869-81
Gomez-Lara J et al. JACC CV Interv. 2011;4:1271-80
Bourantas CV et al. JACC CV Interv. 2014;7:315-24

Statistical Analysis

- The primary effectiveness endpoint of MLA at 25-month follow-up is tested using analysis of covariance, adjusted for baseline MLA
- Assuming a standard deviation of 1.60 mm^2 in each group (based on data from PROSPECT), 140 evaluable lesions would provide 80% and 99% power to detect an absolute difference between groups of 0.75 mm^2 and 1.15 mm^2 respectively, tested at a 2-sided alpha of 0.05

Procedural Details

- 93 patients randomized to BVS -

Lesion pre-dilated	94.6% (88/93)	Overlapping scaffolds	9.8% (9/92)
- Balloon diameter (mm)	3.5 (3.0, 3.5)	Maximum scaffold length (mm)	18 (18, 23)
- Maximum pressure (atm)	14 (12, 16)	Total scaffold length (mm)	18 (18, 27)
Scaffold(s) implanted, any	98.9% (92/93)	Maximum scaffold diameter (mm)	3.5 (3.0, 3.5)
Number of scaffolds implanted	1.0 (1.0, 1.0)	Maximum scaffold pressure (atm)	16 (12, 16)
- Zero	1.1% (1/93)	Scaffold post-dilated	86.0% (80/93)
- One	86.0% (80/93)	- Max post-dil balloon dia (mm)	3.5 (3.5, 4.0)
- Two	12.9% (12/93)	- Max post-dil balloon press (atm)	18 (16, 20)
Reason(s) more than 1 scaffold implanted		- With a non-compliant balloon	79.6% (74/93)
- First scaffold too short to cover whole lesion	50.0% (6/12)	- With dia ≤0.5 mm >than scaffold	100.0% (73/73)
- Edge dissection after first scaffold	25.0% (3/12)	- Pressure (atm)	18 (16, 20)
- Dissection associated with pre-dilatation	8.3% (1/12)	- >16 atm	62.5% (45/72)
- Plaque shift	8.3% (1/12)	Per-protocol scaffold post-dilation*	49.5% (45/91)
- Different dia scaffolds needed (tapering lesn)	8.3% (1/12)	Any metallic DES implanted	2.2% (2/93)**

*Scaffold was post-dilated with a NC balloon with diameter ≤0.5 mm larger than the scaffold diameter at >16 atm. **A metallic DES was placed in 1 pt in whom after pre-dilatation the vessel diameter of the randomized lesion was felt to be too large (>4.0 mm) for a BVS. In a 2nd pt the randomized lesion was in the same vessel as the original culprit lesion causing the MI that had been treated with a metallic DES. After successful BVS implantation a small gap was present between the BVS and metallic DES which the operator elected to cover with an additional short metallic DES.

Post-PCI Imaging (Core Lab)

- 93 patients randomized to BVS -

QCA findings	n=91
TIMI flow	
- 0/1	0% (0/87)
- 2	1.1% (1/87)
- 3	98.9% (86/87)
Minimum lumen diameter (mm)	
- In-segment	2.40 (2.14, 2.69)
- In-scaffold	2.64 (2.39, 2.92)
Diameter stenosis (%)	
- In-segment	15.9 (12.2, 21.2)
- In-scaffold	11.2 (7.7, 15.2)
Acute gain (mm)	
- In-segment	0.79 (0.40, 1.02)
- In-scaffold	0.97 (0.71, 1.23)

IVUS findings	n=86
Minimal luminal area (mm^2)	5.4 (4.4, 6.6)
Minimum scaffold area (mm^2)	5.9 (4.7, 7.0)
Maximum plaque burden at the BVS edge (%)	51.4 (41.0, 58.5)
Major edge dissection (≥60º and ≥3 mm in length)	3.5% (3/86)
Major tissue protrusion (≥10% of scaffold area)	1.2% (1/86)
Malapposition	3.5% (3/86)
NIRS findings	**n=84**
$MaxLCBI_{4mm}$	86.9 (2.2, 232.9)
$MaxLCBI_{4mm}$ ≥324.7	19.0% (16/84)

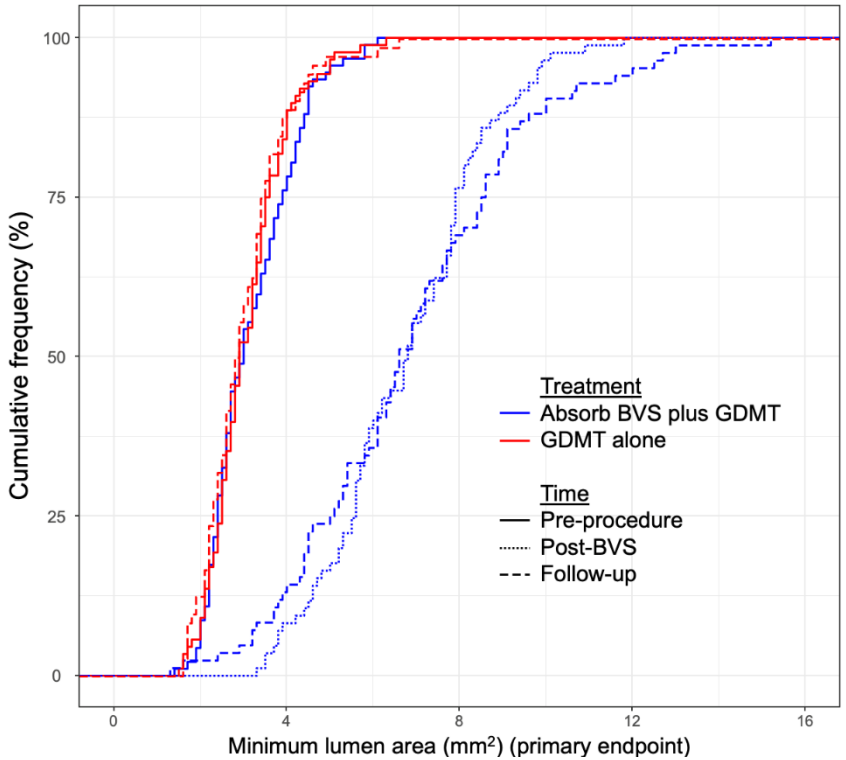
Selected Medication Use

Medication	Discharge		1 year		2 years	
	BVS + GDMT (n=93)	GDMT alone (n=89)	BVS + GDMT (n=93)	GDMT alone (n=87)	BVS + GDMT (n=93)	GDMT alone (n=88)
Aspirin or a P2Y12 inhibitor	100.0%	100.0%	97.8%	96.6%	95.7%	94.3%
- Aspirin	98.9%	96.6%	93.5%	92.0%	92.5%	88.6%
- P2Y12 inhibitor	100.0%	98.9%	32.3%	34.5%	10.8%	10.2%
- Clopidogrel or ticlopidine	7.5%	9.0%	7.5%	9.2%	7.5%	4.5%
- Prasugrel or ticagrelor	92.5%	89.9%	24.7%	25.3%	3.2%	5.7%
DAPT	98.9%	95.5%	28.0%	29.9%	7.5%	4.5%
Oral anticoagulant (VKA or DOAC)	5.4%	4.5%	4.3%	8.0%	6.5%	9.1%
ACEi, ARB or ARNI	53.8%	51.7%	55.9%	62.1%	55.9%	62.5%
Beta-blocker	80.6%	75.3%	74.2%	73.6%	71.0%	76.1%
Statin	98.9%	98.9%	95.7%	94.3%	94.6%	92.0%
- High-dose statin*	95.7%	88.8%	87.1%	82.8%	86.0%	81.8%
Ezetimibe	2.2%	1.1%	9.7%	6.9%	9.7%	6.8%
PCSK9 inhibitor	0.0%	1.1%	0.0%	1.1%	0.0%	1.1%

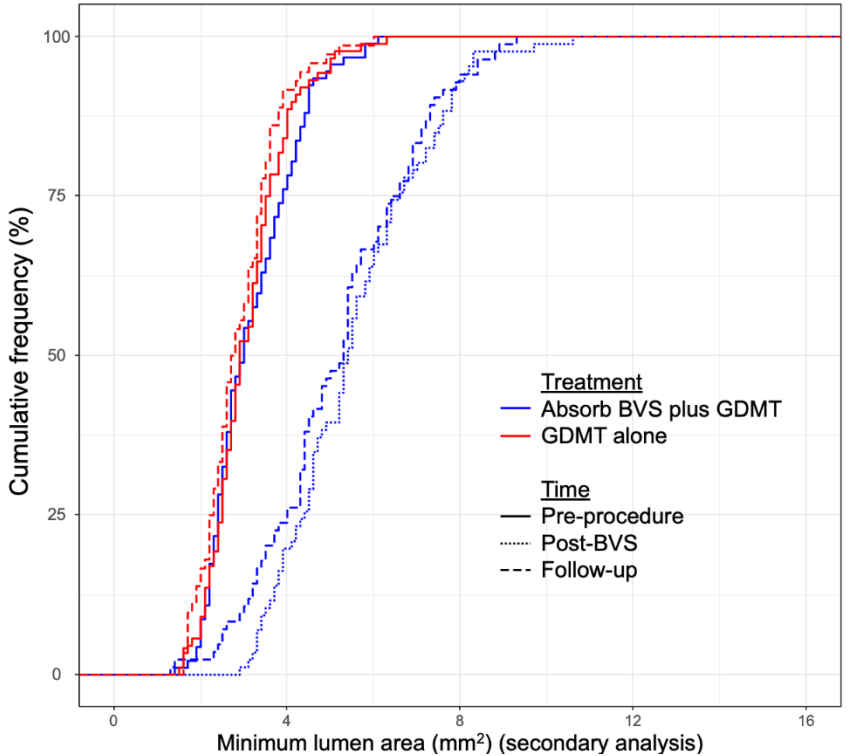
*Atorvastatin ≥40 mg/day or rosuvastatin ≥20 mg/day.
There were no significant differences between groups.

CFD Curves for IVUS MLA

At the original MLA site (primary outcome)

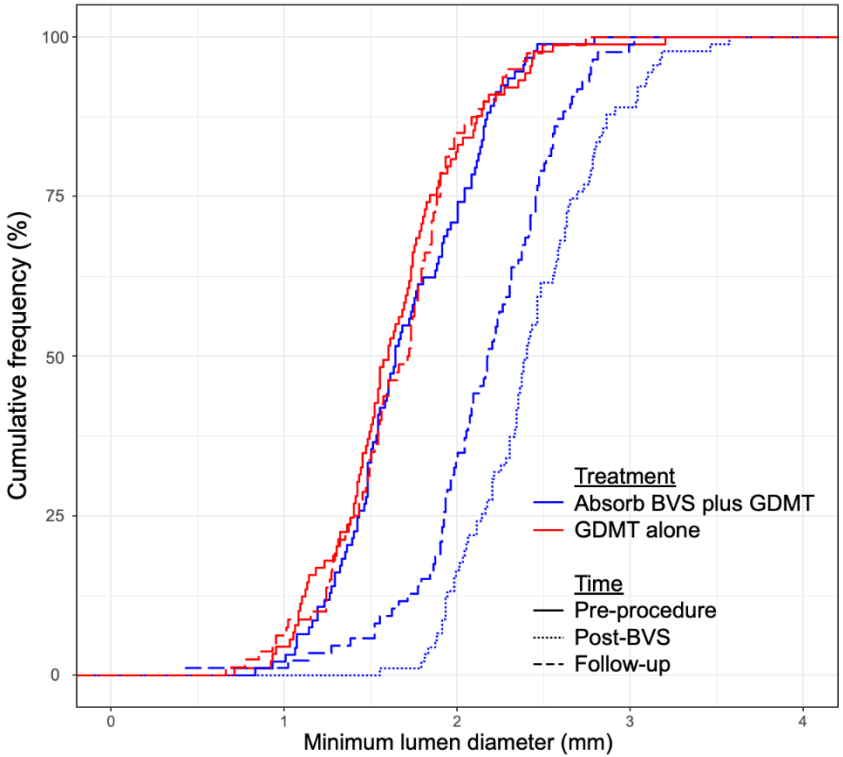


Across the entire lesion (includes 5 mm margins)

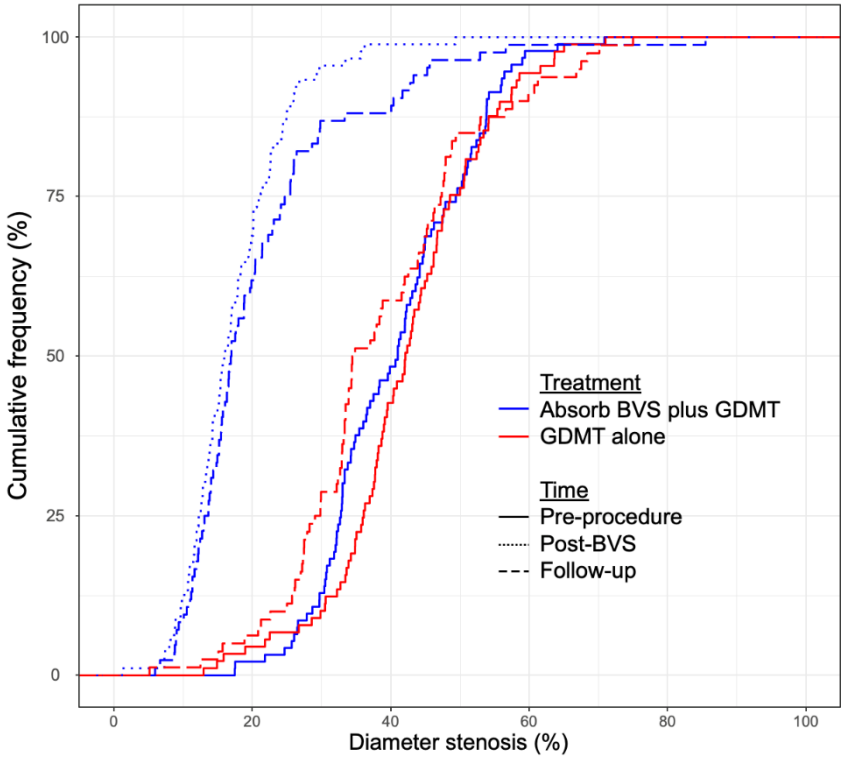


CFD Curves for IVUS QCA

Minimal luminal diameter

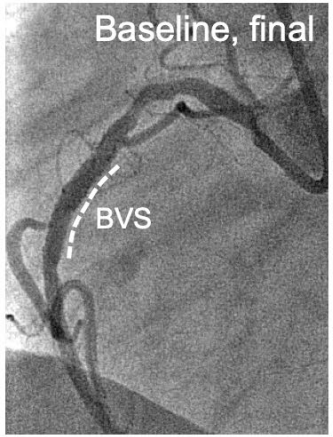


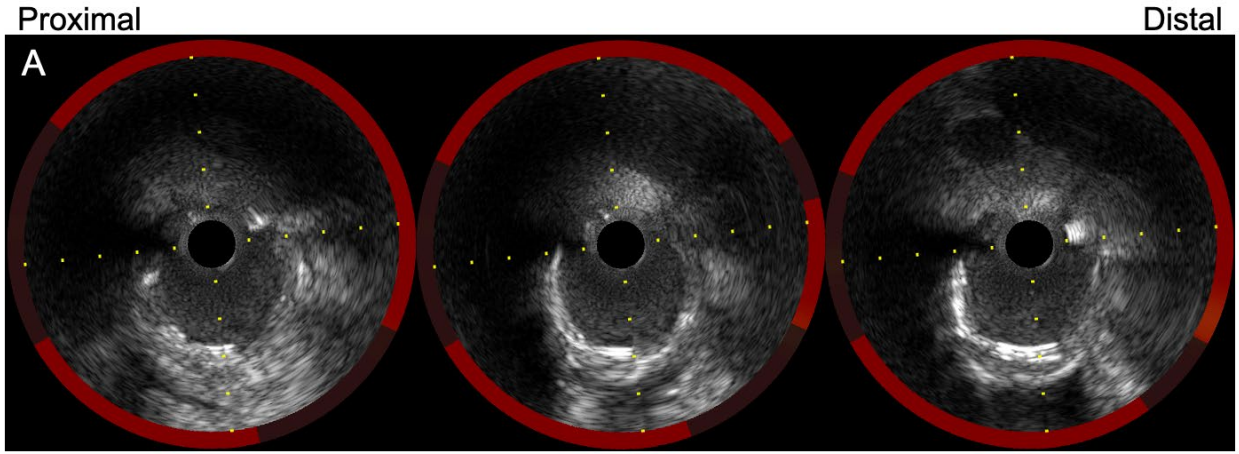
Diameter stenosis



Single Case of Late Acquired Malapposition and Intraluminal Scaffold Dismantling

A 3.5 mm BVS was implanted in the mRCA of a 71-yo woman

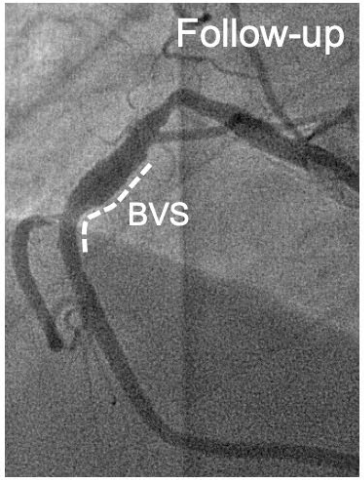




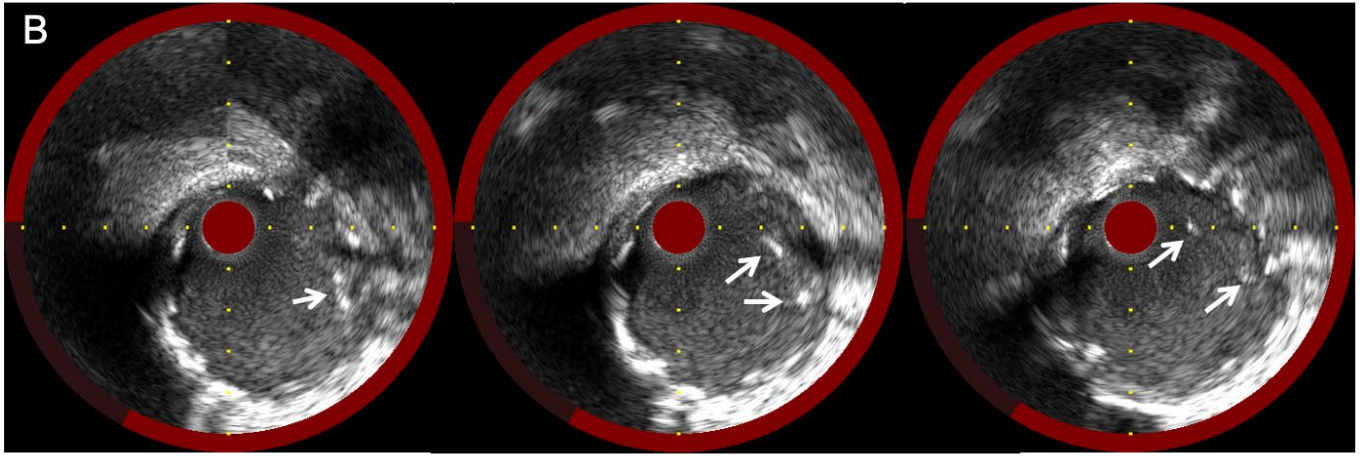
All scaffold struts were apposed to the vessel wall; the vessel area was 17.3 mm^2 and the MLA was 8.9 mm^2

Single Case of Late Acquired Malapposition and Intraluminal Scaffold Dismantling

The patient remained asymptomatic and underwent protocol-directed routine angiographic follow-up at 25 months



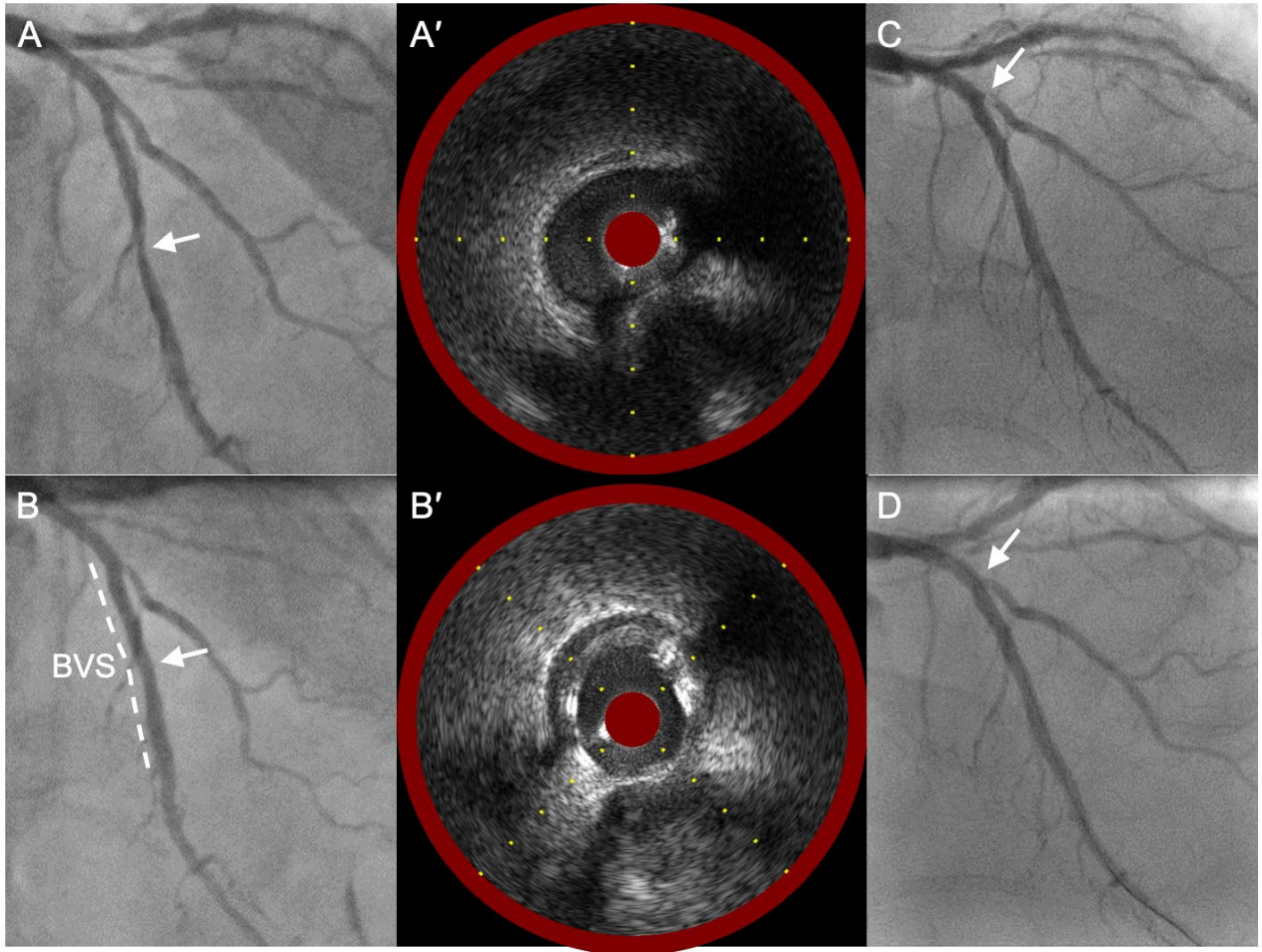
Borderline aneurysmal dilatation



Minimal neointimal hyperplasia; vessel area had increased to 26.2 mm^2 (positive remodeling) and MLA had increased to 13.8 mm^2. Several struts in the mid body of the BVS were malapposed (late acquired malapposition). The total malapposition length was 1.4 mm and the malapposition area was 1.3 mm^2. Several struts were also noted to be overlapping each other and displaced in the lumen (white arrows), representing a relatively mild case of intraluminal scaffold dismantling. PCI was not performed. The patient remained asymptomatic during follow-up of 3.6 years, presumably past the point of complete scaffold bioresorption.

PROSPECT II
PROSPECT ABSORB

Single Case of BVS Thrombosis



A 69-yo man presented with NSTEMI due to occluded dRCA. After PCI 3-vessel NIRS-IVUS was performed. A mild-mod mLAD stenosis was present (A) and was randomized to BVS. MLA measured 2.8 mm^2 and plaque burden was 66.2% (A′). A 3.5 mm × 28 mm scaffold distally and a 2^{nd} 3.5 mm × 12 mm scaffold proximally were implanted followed by NC high pressure (18 atm) post-dilatation (B). Final IVUS showed MLA 5.7 mm^2 (B′). Note that the scaffold crossed the ostium of diagonal branch which was angiographically narrowed but not treated. At 50 days, the patient presented with an acute MI. Emergent angiography showed a thrombus at the origin of the jailed diagonal branch (white arrow in C) without involvement of the LAD scaffolds. The pt underwent successful PTCA of the diagonal branch (D).

Conceptual Framework for the *In Vivo* Detection and Focal Passivation of Vulnerable Plaques