Coronary & Valve Theater, Level 1 - TCTAP Pre-workshop Course

BRS Thrombosis

Davide Capodanno, MD, PhD

Associate Professor of Cardiology
University of Catania, Italy

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

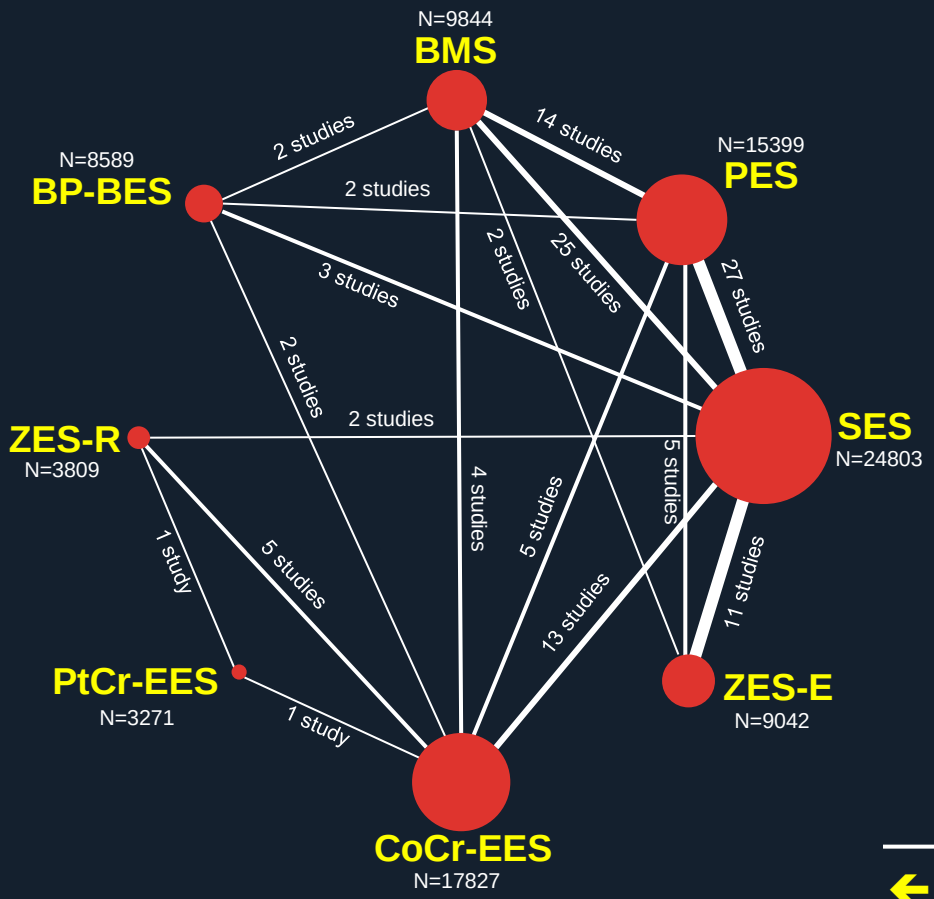
Disclosure of financial interest

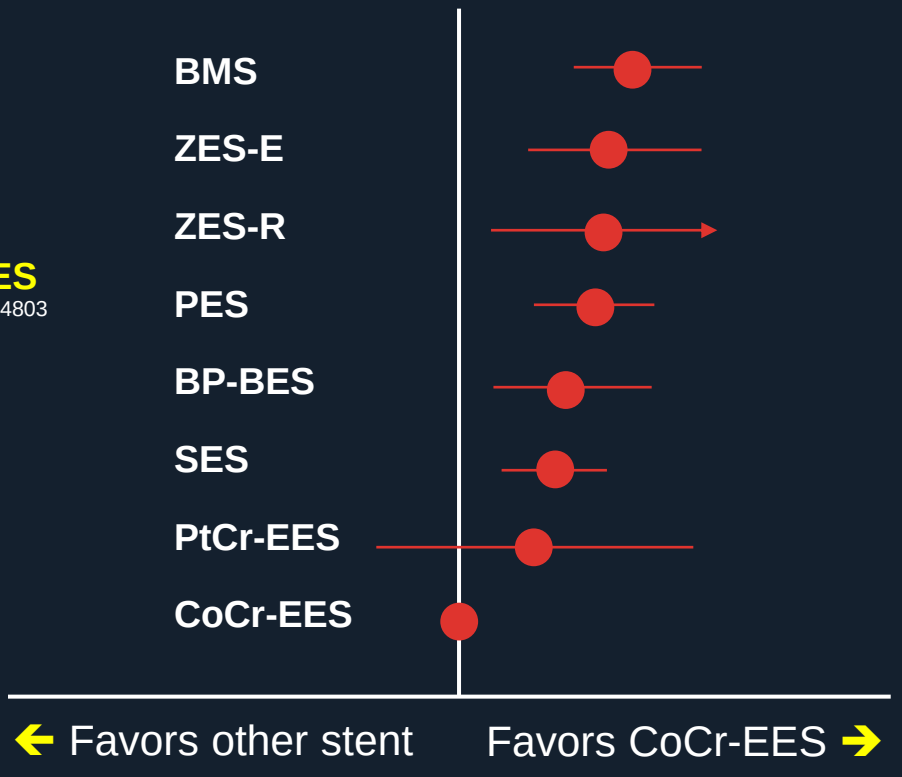
Within the past 12 months, I, **Davide Capodanno**, have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial relationship	Company
• **Speakers' honoraria**	Abbott Vascular, Aspen, AstraZeneca, Bayer, Cordis, Daiichi Sankyo, Eli-Lilly
• **Consulting**	Abbott Vascular, Stentys
• **Advisory Board**	AstraZeneca

Stent Thrombosis in the pre-BRS era

Network meta-analysis of 77 RCTs and 73,255 patients





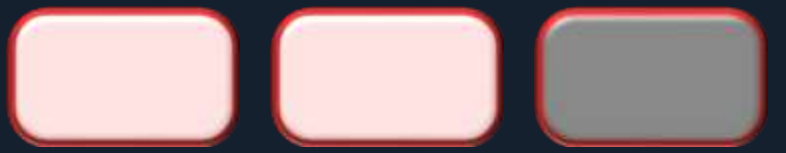
Kang SH, et al. Eur Heart J. 2014;35:1147-58

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

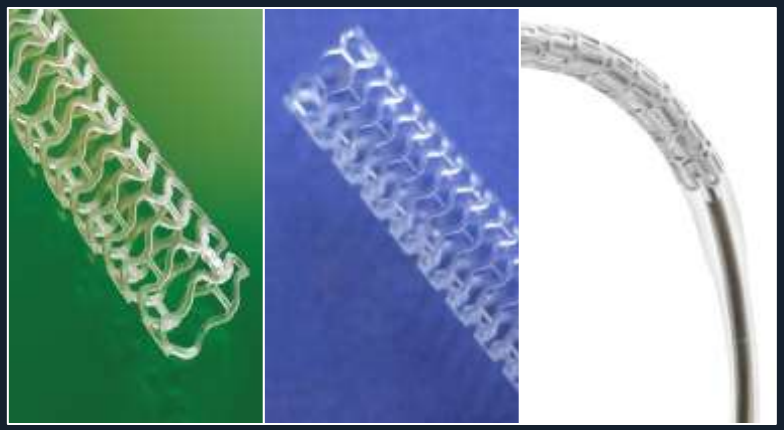
How do BRS compare with best-in-class DES?

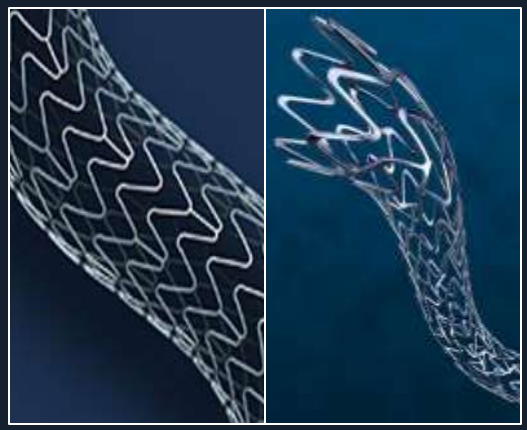
Fully resorbable scaffolds

CoCr/PtCr EES



BVS	DESolve	DREAMS 2G		Xience Xpedition	Promus Premier
150 μm	150 μm	150 μm	**Strut thickness**	81 μm	81 μm
3 μm / side	<3 μm / side	8 μm / side	**Coat thickness**	8 μm / side	8 μm / side





UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

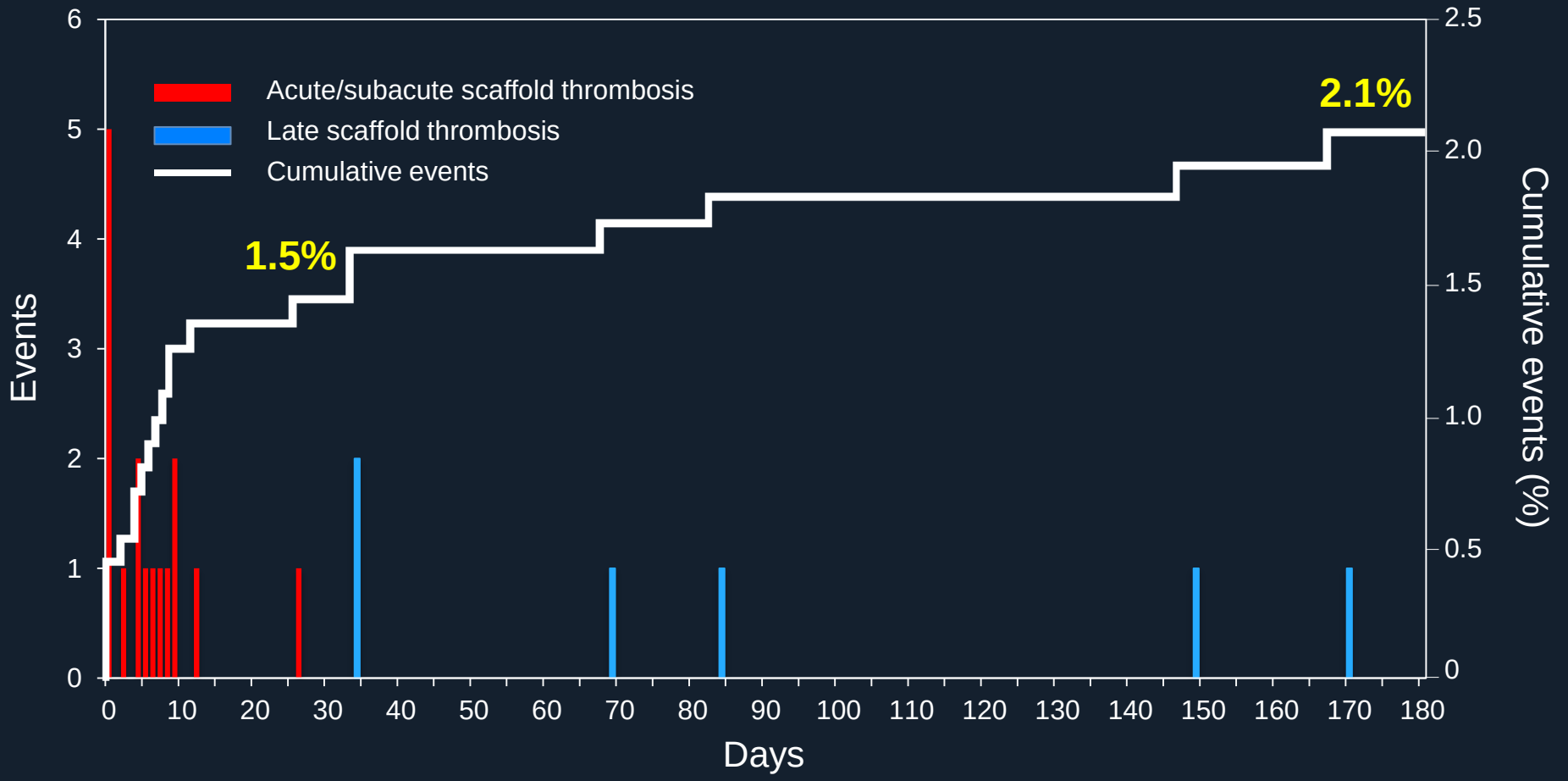
Capodanno D. Personal Communication

Scaffold thrombosis

INCIDENCE

BRS Thrombosis: "A non-negligible rate…"

GHOST-EU: 1,189 patients, 1,731 Absorb BVS from 10 centers



UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

Capodanno D, et al. EuroIntervention. 2015;10:1144-53

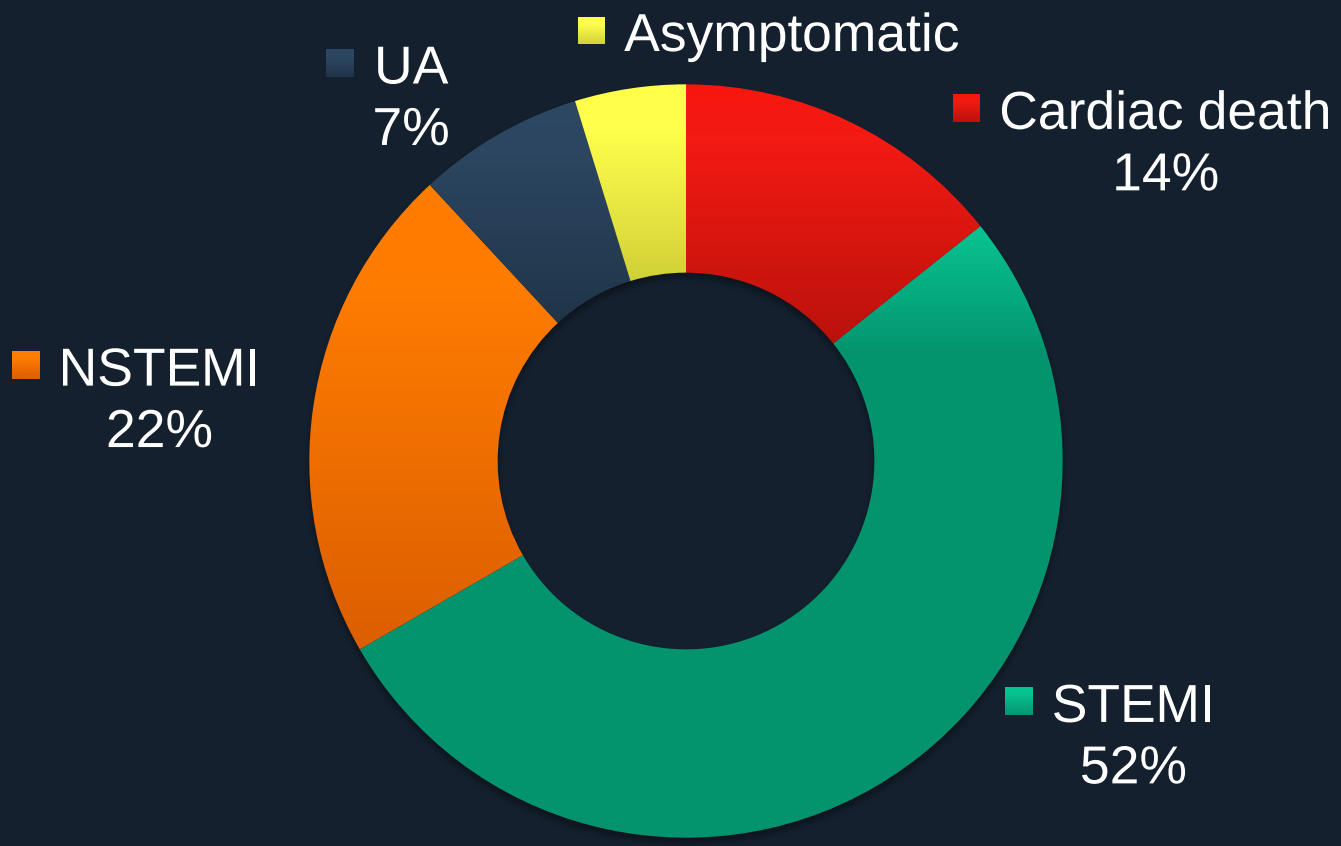
Timing of BRS Thrombosis is Evenly Distributed from Acute to Very Late

Karanasos et al.
Circ Cardiovasc Interv 2016 [In press]
14 ScT (definite)
733 patients

Puricel et al.
J Am Coll Cardiol. 2016;67:921-31
42 ScT (any)
1,305 patients

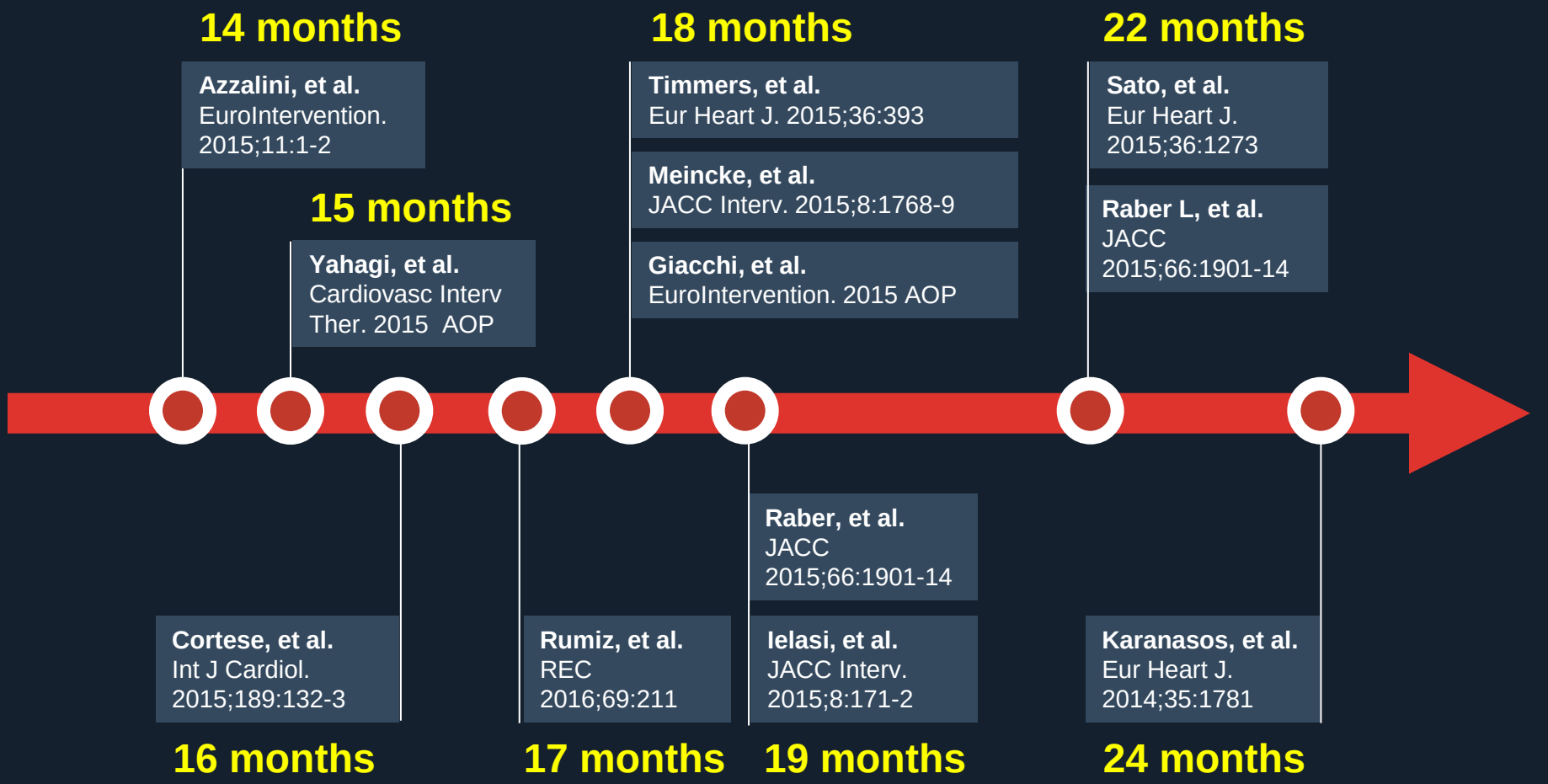
Consequences of BRS Thrombosis

42 ScT in 1,305 patients from 4 German and Swiss centers

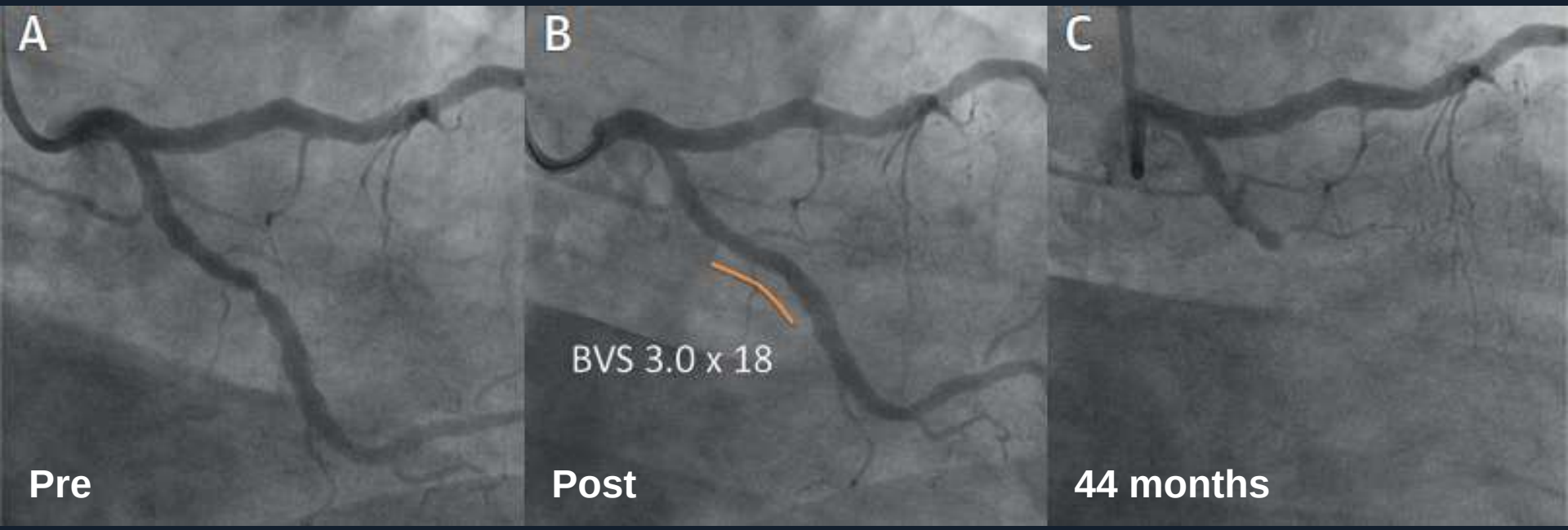


Puricel S, et al. J Am Coll Cardiol. 2016;67:921-31

Very Late BRS Thrombosis



Latest BRS Thrombosis Ever Reported



Scaffold remnants detected in 94% of analyzed frames at OCT

Inclusion of scaffold remnants in the thrombus aspirate

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

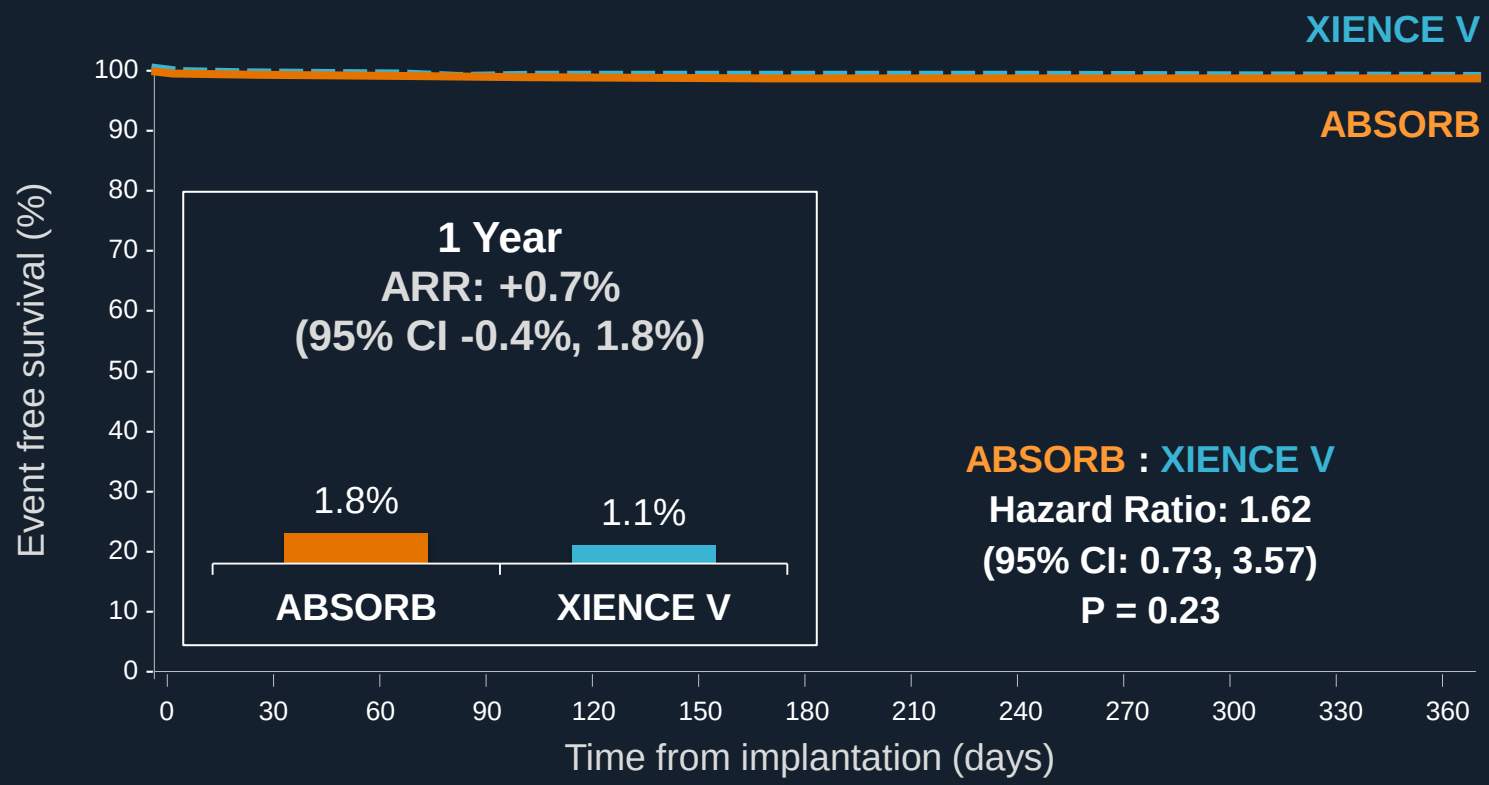
Raber L, et al. J Am Coll Cardiol. 2015;66:1901-14

Scaffold thrombosis

BVS vs. EES

1-Year definite or probable ScT

905 matched pairs from GHOST-EU and XIENCE V USA



# at risk	30 Days	6 Months	12 Months
ABSORB	880	831	760
XIENCE V	888	859	825

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

Tamburino C, et al. JACC Cardiovasc Interv. 2016;9:440-9

ABSORB III: Device Thrombosis to 1 Year

	Absorb (N=1322)	Xience (N=686)	p-value
Device Thrombosis (def*/prob)	1.54%	0.74%	0.13
- Early (0 to 30 days)	1.06%	0.73%	0.46
- Late (> 30 to 1 year)	0.46%	0.00%	0.10
- Definite* (1 year)	1.38%	0.74%	0.21
- Probable (1 year)	0.15%	0.00%	0.55

*One “definite ST” in the Absorb arm by ITT was in a pt that was treated with Xience

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

Ellis SG, et al. N Engl J Med. 2015;373:1905-15

Meta-analyses of BRS vs EES

	Cassese et al.	Lipinski et al.	Stone et al.
Publication date	2016	2016	2016
Journal	Lancet	JACC: Card Interv	Lancet
Type	Study level	Study level	Patient-level
Search date	October 2015	July 2015	October 2015
Screened studies	171	449	NA
Pooled patients	3,691	4,098	3,389
Model	Fixed-effects	Random-effects	Fixed-effects
Summary measure	OR (95% CI)	OR (95% CI)	RR (95% CI)
Studies included	6 RCTs	2 RCTs, 7 OSs	4 RCTs
BRS studies	6 RCTs	2 RCTs, 7 OSs	4 RCTs
Follow up	1 year (median)	6 months (mean)	1 year
Effect size (BRS:EES)			
Definite or probable	**1.99 (1.00–3.98)**	**2.06 (1.07-3.98)**	2.09 (0.92–4.75)
Early	NA	2.02 (0.69-5.93)	1.76 (0.72–4.34)
Acute	0.36 (0.07-1.71)	NA	NA
Subacute	**3.11 (1.24-7.82)**	NA	NA
Late	NA	NA	4.10 (0.52–32.56)
Definite	1.98 (0.94-4.16)	1.91 (0.82-4.46)	2.06 (0.85–5.03)
Probable	NA	NA	2.28 (0.28–18.51)

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

Capodanno D. J Thorac Dis 2019 [In press]

Scaffold thrombosis

FACTORS

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

BRS Thrombosis: Putative Factors

Patient-related factors 	Smoking	DAPT discontinuation
	Diabetes mellitus	Resistance to antiplatelets
	Renal failure	Thrombocytosis
	Poor ventricular function	Malignancy
	Acute coronary syndrome	Surgical procedures
Anatomy-related factors 	Diffuse disease	Saphenous vein graft
	Small vessel disease	Thrombus containing lesion
	Bifurcation lesion	Inflow or outflow tandem lesions
	Chronic total occlusion	Stasis
Procedure-related factors 	Inadequate expansion or sizing	Deployment in necrotic core
	Incomplete apposition	Residual edge dissection
Device-related factors 	Hypersensitivity or inflammation	Late-acquired malapposition
	Delayed or incomplete healing	Aneurysm formation
	Thick-strut design	Neoatherosclerosis

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

Capodanno D, et al. EuroIntervention. 2015;11 Suppl V:V181-4

Predictors of 1-Year Device Thrombosis

Patient-level meta-analysis of 3,389 patients from the 4 ABSORB trials

1-Y ST or ScT (Definite/Probable)	RR (95% CI)	p-value
Diabetes	2.88 (1.49–5.60)	0.002
Any lesion with reference vessel diameter <median (2.65 mm)*	3.28 (1.50–7.20)	0.003
Any ACC/AHA class B2 or C lesion (vs class A or B1)*	2.91 (1.13–7.46)	0.03
BVS (vs CoCr-EES)	2.19 (0.96–4.98)	0.06

The following variables were entered into the model: diabetes, reference vessel diameter, lesion length, presentation with unstable angina or recent myocardial infarction, any ACC/AHA class B2/C lesion, BVS (vs CoCr-EES).
*Angiographic core laboratory determination.

Stone GW, et al. Lancet. 2016;387:1277-89

Predictors of 1-Year BVS Thrombosis

42 ScT in 1,305 patients from 4 German and Swiss centers

1-Y ScT (Definite/Probable/Possible)	HR (95% CI)	p-value
LVEF (5% increase)	0.82 (0.70–0.97)	0.019
Ostial lesion	2.59 (1.01–6.64)	0.049
MLD*	0.05 (0.01–0.28)	0.001
RVD*	0.13 (0.04–0.46)	0.002
Maximum footprint, %*	1.20 (1.08–1.33)	0.001
Scaled residual stenosis*	1,714 (20–146)	0.001

The following variables were entered into the model for device thrombosis: diabetes, LVEF (5% increase), number of vessels treated, total BVS surface, ticagrelor use, ostial lesions. *Adjusted data obtained from 1:2 matched patients with and without ScT. Scaled residual stenosis = MLD divided by the nominal BVS diameter. Maximum footprint = % of the vascular circumference occupied by struts at the level of the MLD

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

Puricel S, et al. J Am Coll Cardiol. 2016;67:921-31

Most Likely Reason for Very Late ScT

Azzalini et al.	EIJ 2015	14 months	Incomplete tissue coverage
Yahagi et al.	CIT 2015	15 months	DAPT discontinuation
Cortese et al.	IJC 2016	16 months	Scaffold recoil
Rumiz et al.	REC 2016	17 months	Incomplete tissue coverage
Timmers et al.	EHJ 2015	18 months	Incomplete tissue coverage
Meincke et al.	JACC Intv 2015	18 months	Incomplete tissue coverage
Giacchi et al.	EIJ 2015	18 months	Incomplete tissue coverage
Raber et al. #1	JACC 2015	19 months	Intraluminal scaffold dismantling
Raber et al. #2	JACC 2015	19 months	Intraluminal scaffold dismantling
Ielasi et al.	JACC Intv 2015	19 months	Intraluminal scaffold dismantling
Sato et al.	EHJ 2015	21 months	DAPT discontinuation
Raber et al.	JACC 2015	21 months	Incomplete tissue coverage
Karanasos et al.	EHJ 2015	24 months	DAPT discontinuation
Raber et al.	JACC 2015	44 months	Intraluminal scaffold dismantling

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

Capodanno D. Personal communication

Scaffold thrombosis

PREVENTION

BRS thrombosis: prevention rules

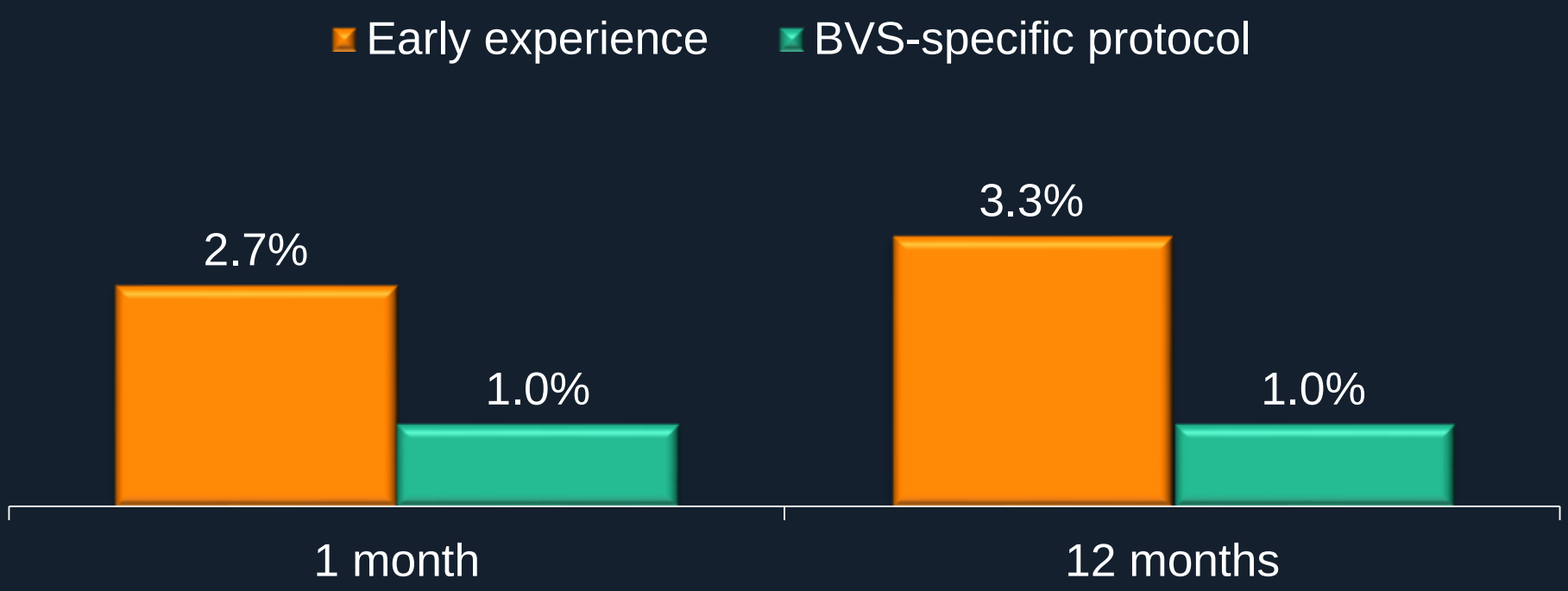
1. Avoid situations with pronounced mismatch between scaffold and artery size
2. Avoid BRS in patients at risk for DAPT cessation, consider platelet function testing
3. Respect the postdilatation limits
4. Minimize the overlap length
5. Ensure complete coverage of the lesion and injured segments, including angiographically apparent edge dissections after predilatation and thrombus in acute coronary syndromes
6. Avoid underexpansion and acute malapposition
7. Use invasive imaging guidance liberally

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

Capodanno D, et al. EuroIntervention. 2015;11 Suppl V:V181-4

Impact of a BRS-specific implantation protocol

42 ScT in 1,305 patients from 4 German and Swiss centers



Adj. HR for a BVS-specific implantation strategy introduced in 2014
0.26 (0.08-0.90), P=0.035

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy

Puricel S, et al. J Am Coll Cardiol. 2016;67:921-31

DAPT Duration in Clinical Guidelines

Population	ESC Guidelines	ACCF/AHA/SCAI 2016
Acute Coronary Syndrome (BMS or DES)	Maximum of 12 months (Class I-A) Shorter or longer durations may be considered (Class IIb-A)	At least 12 months (Class I-BR) Shorter (Class IIb-C-LD) or longer (Class IIb-A^{SR}) durations may be considered
Stable Ischemia and BMS	At least 1 month (Class I-A)	At least 1 month (Class I-A) >1 month if no HBR (Class IIb-A)
Stable Ischemia and DES	6 months (Class I-B)	At least 6 months (Class I-B-NR) >6 months if no HBR (Class IIb-A) HBR: 3 months (Class IIb-C-LD)
Secondary Prevention	Selected patients at high ischemic risk	Prior MI (1-3 yrs), no HBR: May be reasonable (Class IIb-A)

Roffi M, et al. 2015 ESC Guidelines for Management of ACS. EHJ 2015 (Online Aug 29, 2015). Windecker S, et al. 2014 ESC/EACTS Guidelines on Myocardial Revascularization. EHJ 2014;35:3541-619. Amsterdam EA, et al. 2014 AHA/ACC Guideline for Management of NSTE-ACS. JACC 2014;64:e139-228. Montalescot G, et al. 2013 ESC Guidelines on Management of Stable CAD. EHJ 2013;34:2949-3003. Levine GN, et al. 2011 ACCF/AHA/SCAI Guidelines for PCI. JACC 2011;58:e44-122. Smith SC Jr, et al. 2011 AHA/ACCF Secondary Prevention Guidelines. JACC 2011;58:2342-46. Levine GN, et al. 2016 ACC/AHA Guidelines for DAPT. JACC AOP

Minimum DAPT duration As Mandated By Study Protocol in ABSORB Trials

Closing remarks

- The first-generation Absorb BRS carries a 2-fold increased risk of 1-year ScT compared with CoCr-EES.
- The timing of ScT appears to be evenly distributed from acute to very late events.
  - Similar to DES, the leading morphological substrate of **acute and subacute BRS thrombosis** appears to be suboptimal implantation (ie, underexpansion, acute malapposition)
  - **Late and very late BRS thrombosis** has been observed in the presence of regional suboptimal flow conditions (i.e. persistent and acquired malapposition, strut discontinuity) and delayed healing, and may also be triggered by DAPT discontinuation.
- Prevention of ScT involves careful patient selection, best implantation practices and long-term DAPT.

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico–Vittorio Emanuele
Catania, Italy
dcapodanno@gmal.com