How Much Promising BRS in Real-World PCI?

Updated Real-World Experience and Registry Data

Duk-Woo Park, MD, PhD
Heart Institute, University of Ulsan College of Medicine,
Asan Medical, Seoul, Korea

Evolution of DES Technology

First Gen

Durable Polymer Stents

	Cypher	TAXUS Express	TAXUS Liberte
Strut Thickness	140 µm	132 µm	96 µm
Coat Thickness	7µm / side	16µm/side	14µm/side

Bioabsorbable Polymer Stents

	Biomatrix	Nobori
Strut Thickness	120 µm	125 µm
Coat Thickness	10 µm	20 µm

Second Gen

	Resolute Integrity	Xience Xpedition	Promus PREMIER
Strut Thickness	89 µm	81 µm	81 µm
Coat Thickness	6µm / side	8µm / side	8µm / side

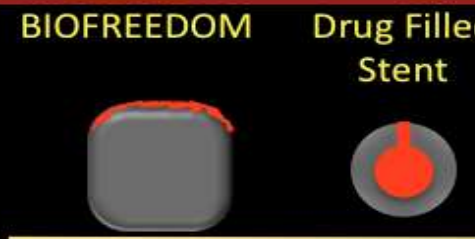
	Firehawk	Synergy	Ultimaster
Strut Thickness	86µm	74µm	80µm
Coat Thickness	10 µm	4 µm	14 µm

First Generation Future Technologies

Fully Bioresorbable Stents

	BVS	ELIXIR DESolve	DREAMS II
Strut Thickness	150 µm	150 µm	150 µm
Coat Thickness	3 µm / side	<3 µm / side	8 µm / side

Polymer Free Stents



	BIOFREEDOM	Drug Filled Stent
Strut Thickness	112	86
Coat Thickness	NA	NA

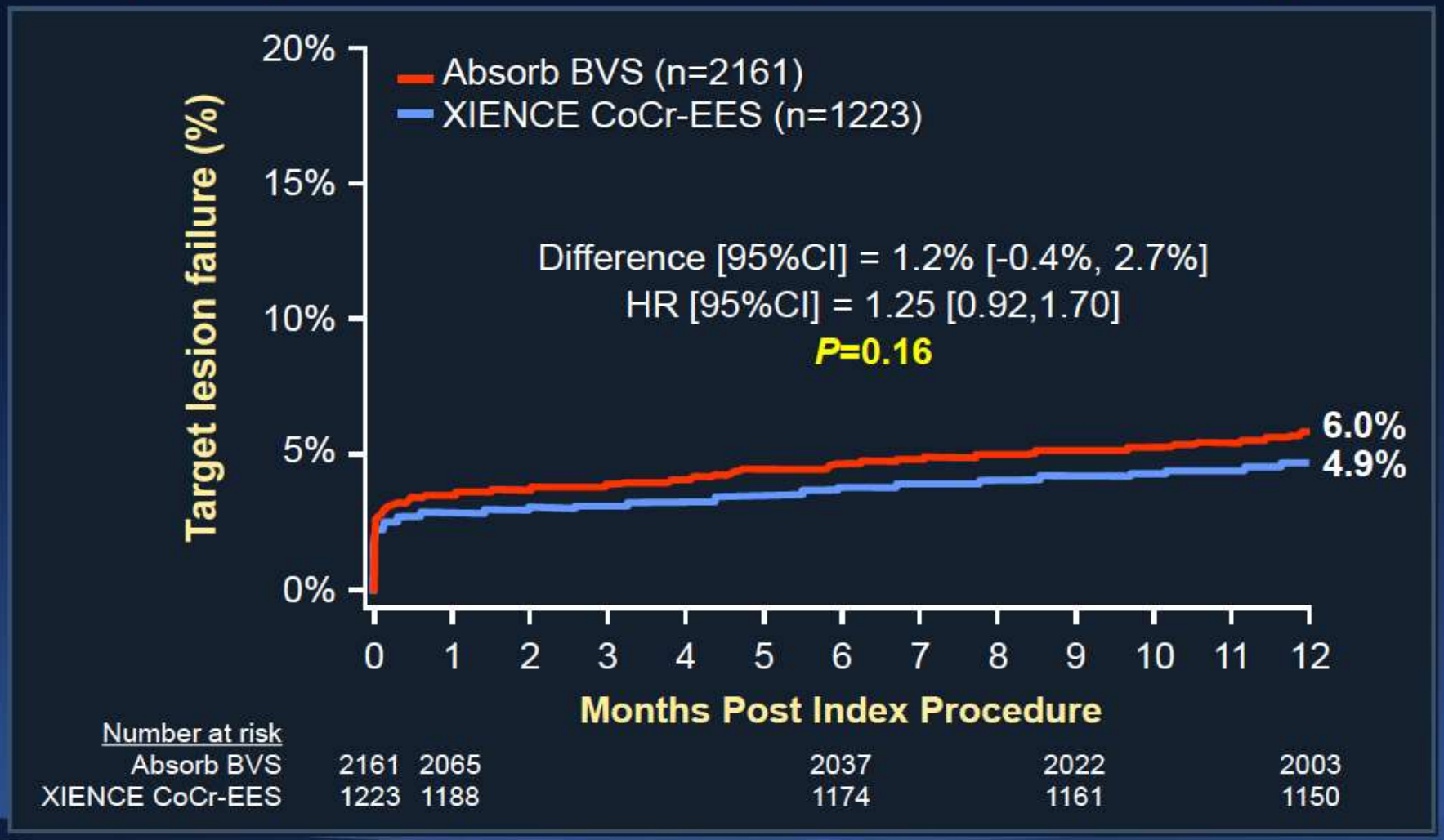
Potential Advantages of BRS

- Provides *transient* vessel scaffolding when needed, “leaving nothing behind”
- Local drug release inhibits restenosis
- Restores vessel to natural state with normal function and healing responses
- Reduces need for long term DAPT
- Eliminates source of inflammation/ irritation
- Reduces late events (esp. SAT)
- Vessel free for future interventions; CABG

ABSORB 1-Year Meta-analysis

ABSORB II, ABSORB III, ABSORB Japan, ABSORB China

DoCE (TLF): Cardiac Death, MI or ID-TLR (pooled)

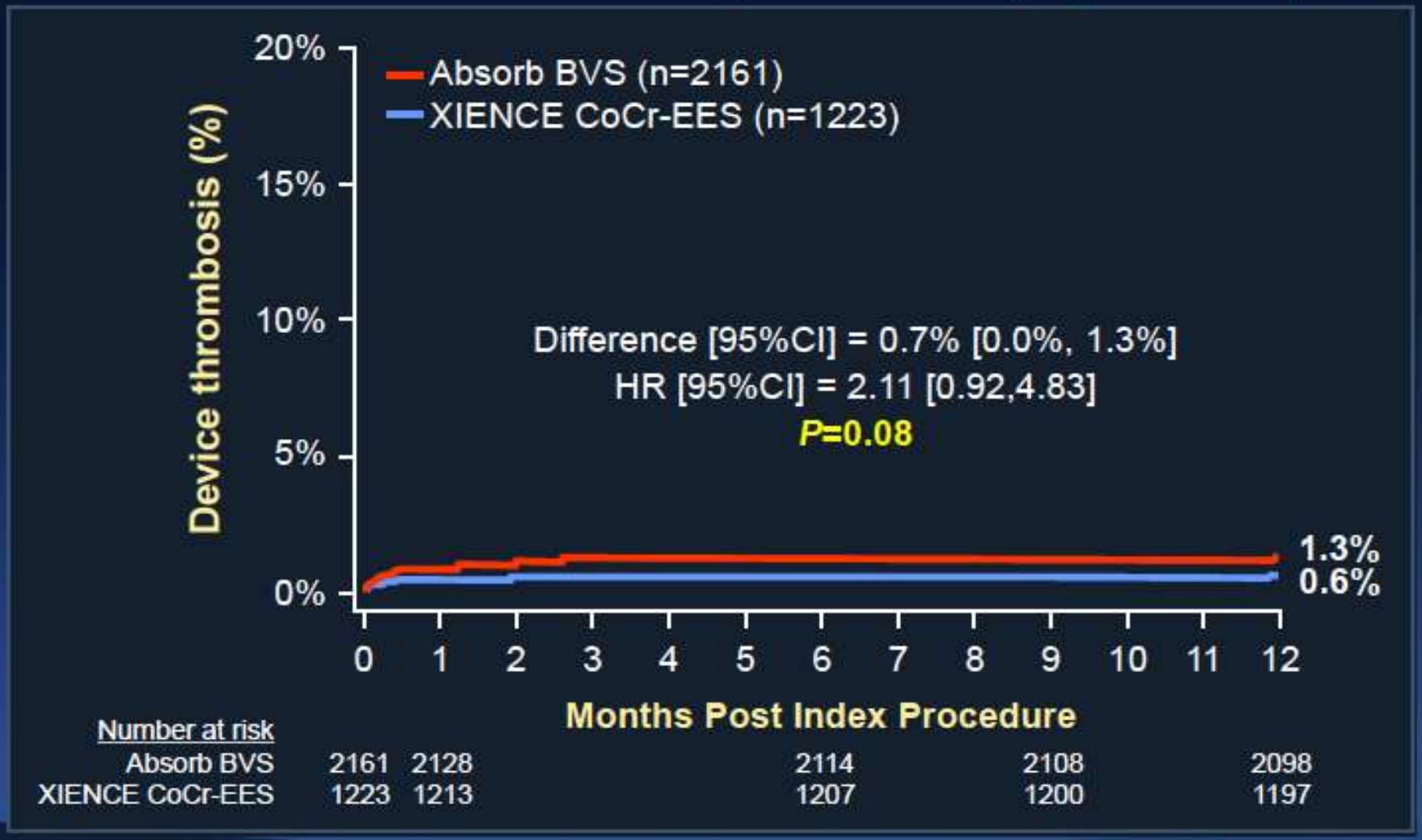


Lancet. 2016 Jan 25

ABSORB 1-Year Meta-analysis

ABSORB II, ABSORB III, ABSORB Japan, ABSORB China

Device Thrombosis (Def/Prob) (pooled)



Lancet. 2016 Jan 25

Study-level Meta-Analysis of 6 RCT

ABSORB Series and EVERBIO II and TROFI II

A Target lesion revascularisation

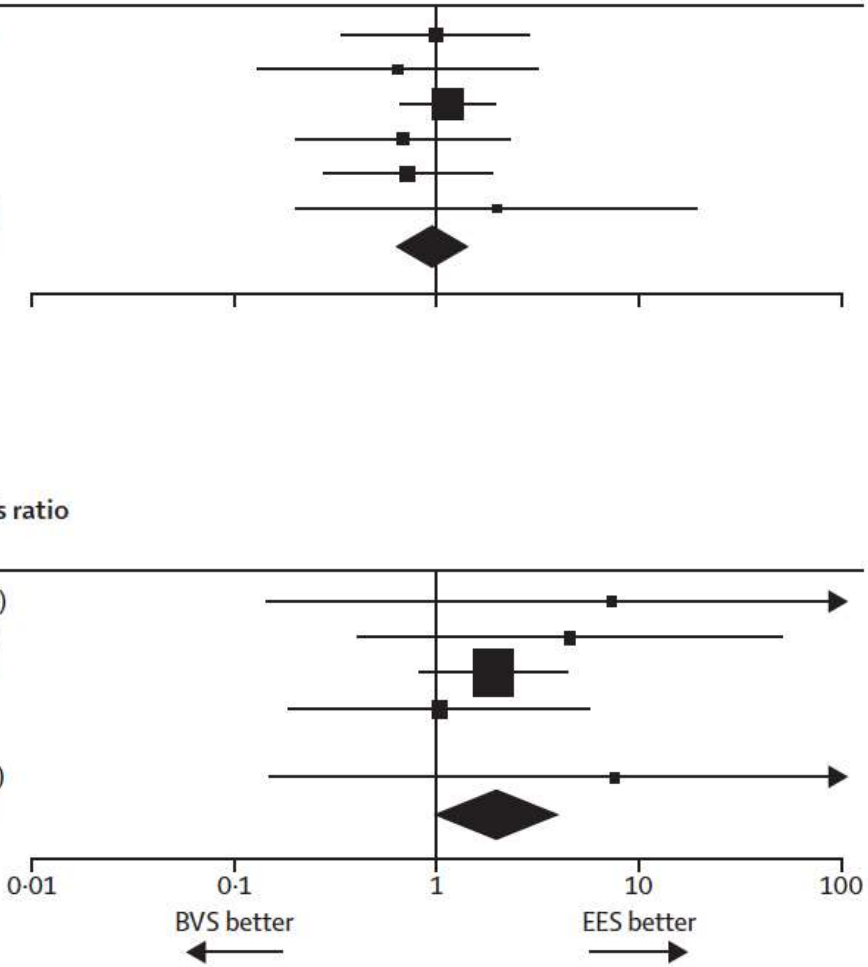
	BVS Events	BVS Total	EES Events	EES Total	Weight (%)	Fixed-effects odds ratio (95% CI)
ABSORB China	7	238	7	237	13·2	1·00 (0·34–2·88)
ABSORB II	4	335	3	166	5·9	0·64 (0·13–3·12)
ABSORB III	42	1313	19	677	51·6	1·14 (0·67–1·95)
ABSORB Japan	7	265	5	133	10·1	0·68 (0·20–2·31)
EVERBIO II	8	78	11	80	16·3	0·72 (0·28–1·87)
TROFI II	2	95	1	96	2·9	1·98 (0·20–19·29)
Overall	**70**	**2324**	**46**	**1389**	**100**	**0·97 (0·66–1·43)**

Heterogeneity: χ^2=1·69, df=5; p=0·89; I^2=0%
Test for overall effect: Z=0·16; p=0·87
Random-effects odds ratio 0·97 (95% CI 0·66–1·43)

B Definite or probable stent thrombosis

	BVS Events	BVS Total	EES Events	EES Total	Weight (%)	Fixed-effects odds ratio (95% CI)
ABSORB China	1	238	0	232	3·1	7·21 (0·14–363·23)
ABSORB II	3	335	0	166	8·2	4·49 (0·04–49·92)
ABSORB III	20	1301	5	675	69·1	1·89 (0·82–4·34)
ABSORB Japan	4	262	2	133	16·5	1·02 (0·18–5·58)
EVERBIO II	0	78	0	80		Not estimable
TROFI II	1	95	0	96	3·1	7·47 (0·15–376·35)
Overall	**29**	**2309**	**7**	**1382**	**100**	**1·99 (1·00–3·98)**

Heterogeneity: χ^2=1·90, df=4; p=0·75; I^2=0%
Test for overall effect: Z=1·96; p=0·05
Random-effects odds ratio 1·99 (95% CI 1·00–3·98)



Lancet 2016; 387: 537–44

A Target lesion failure

	BVS Events	BVS Total	EES Events	EES Total	Weight (%)	Fixed-effects odds ratio (95% CI)
ABSORB China	8	238	10	237	9·3	0·79 (0·31–2·03)
ABSORB II	16	335	5	166	9·6	1·55 (0·61–3·92)
ABSORB III	102	1313	41	677	63·9	1·29 (0·09–1·85)
ABSORB Japan	11	265	5	133	7·3	1·11 (0·38–3·19)
EVERBIO II	9	78	11	80	9·4	0·82 (0·32–2·09)
TROFI II	1	95	0	96	0·5	7·47 (0·15–376·35)
Overall	**147**	**2324**	**72**	**1389**	**100**	**1·20 (0·90–1·60)**

Heterogeneity: χ^2=2·71, df=5; p=0·74; I^2=0%
Test for overall effect: Z=1·25; p=0·21
Random-effects odds ratio 1·20 (95% CI 0·90–1·60)

B Myocardial infarction

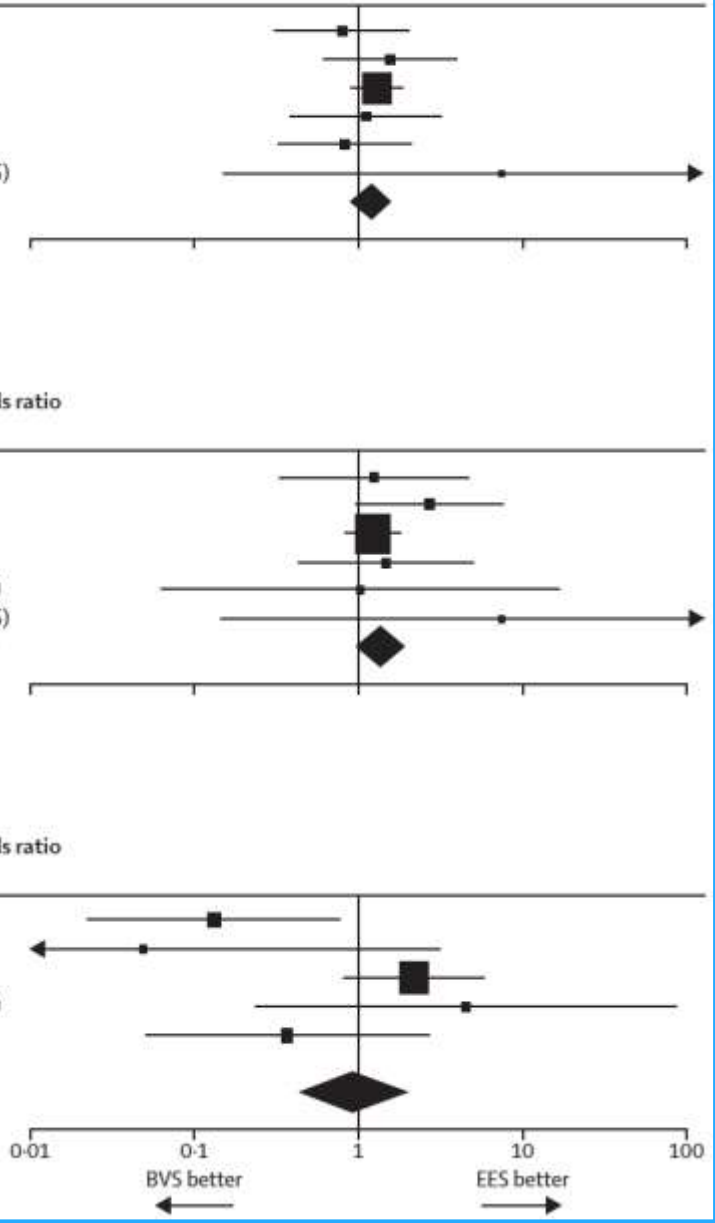
	BVS Events	BVS Total	EES Events	EES Total	Weight (%)	Fixed-effects odds ratio (95% CI)
ABSORB China	5	238	4	237	6·1	1·25 (0·33–4·66)
ABSORB II	15	335	2	166	10·1	2·71 (0·97–7·56)
ABSORB III	90	1313	38	677	74·5	1·23 (0·84–1·79)
ABSORB Japan	9	265	3	133	7·2	1·48 (0·44–4·98)
EVERBIO II	1	78	1	80	1·4	1·03 (0·06–16·55)
TROFI II	1	95	0	96	0·7	7·47 (0·15–376·35)
Overall	**121**	**2324**	**48**	**1389**	**100**	**1·36 (0·98–1·89)**

Heterogeneity: χ^2=2·80, df=5; p=0·73; I^2=0%
Test for overall effect: Z=1·86; p=0·06
Random-effects odds ratio 1·36 (95% CI 0·98–1·89)

C Death

	BVS Events	BVS Total	EES Events	EES Total	Weight (%)	Fixed-effects odds ratio (95% CI)
ABSORB China	0	238	5	237	18·0	0·13 (0·02–0·77)
ABSORB II	0	335	1	166	3·2	0·05 (0·00–3·15)
ABSORB III	15	1313	3	677	58·1	2·18 (0·82–5·81)
ABSORB Japan	2	265	0	133	6·4	4·51 (0·24–85·41)
EVERBIO II	1	78	3	80	14·2	0·37 (0·05–2·68)
TROFI II	0	95	0	96		Not estimable
Overall	**18**	**2324**	**12**	**1389**	**100**	**0·95 (0·45–2·00)**

Heterogeneity: χ^2=11·47, df=4; p=0·02; I^2=65%
Test for overall effect: Z=0·14; p=0·89
Random-effects odds ratio 0·59 (95% CI 0·12–2·74)



Lancet 2016; 387: 537–44

Study-level Meta-Analysis of 6 RCT

ABSORB Series and EVERBIO II and TROFI II

A In-device late lumen loss

	BVS Mean	(SD)	Total	EES Mean	(SD)	Total	Weight (%)	Mean difference (95% CI)
ABSORB China	0·24	(0·39)	240	0·10	(0·32)	246	33·3	0·14 (0·08 to 0·20)
ABSORB Japan	0·19	(0·31)	272	0·16	(0·33)	137	30·4	0·03 (–0·04 to 0·10)
EVERBIO II	0·28	(0·39)	75	0·24	(0·32)	103	11·6	0·04 (–0·07 to 0·15)
TROFI II	0·17	(0·24)	94	0·08	(0·28)	98	24·7	0·09 (0·02 to 0·16)
Overall			**681**			**584**	**100**	**0·08 (0·05–0·12)**

Heterogeneity: χ^2=6·19, df=3; p=0·10; I^2=52%

Test for overall effect: Z=4·42; p<0·0001

Random-effects mean difference 0·08 (95% CI 0·03–0·13)

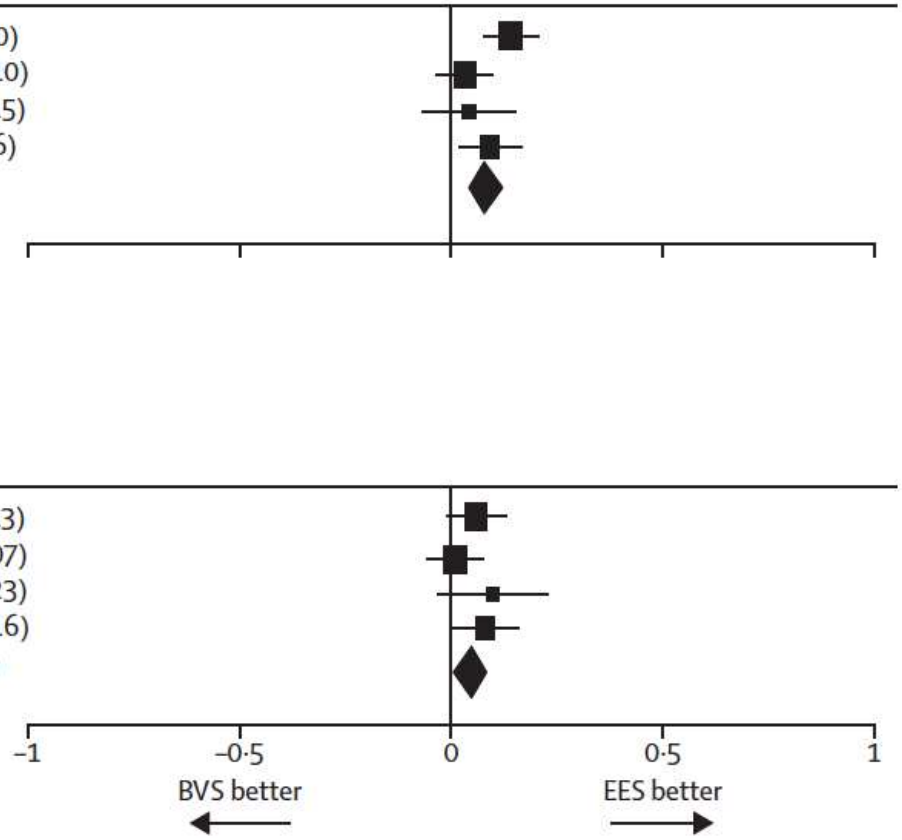
B In-segment late lumen loss

	BVS Mean	(SD)	Total	EES Mean	(SD)	Total	Weight (%)	Mean difference (95% CI)
ABSORB China	0·19	(0·40)	240	0·13	(0·37)	246	31·9	0·06 (–0·01 to 0·13)
ABSORB Japan	0·13	(0·30)	272	0·12	(0·32)	137	36·2	0·01 (–0·05 to 0·07)
EVERBIO II	0·30	(0·44)	75	0·20	(0·43)	103	8·9	0·10 (–0·03 to 0·23)
TROFI II	0·14	(0·28)	94	0·06	(0·29)	98	23·0	0·08 (–0·00 to 0·16)
Overall			**681**			**584**	**100**	**0·05 (0·01–0·09)**

Heterogeneity: χ^2=2·67, df=3; p=0·45; I^2=0%

Test for overall effect: Z=2·54; p=0·01

Random-effects mean difference 0·05 (95% CI 0·01–0·09)



Lancet 2016; 387: 537–44

Limitations of BVS Platforms

Strut and Coating Thickness In Perspective

Durable Polymer Coated Stents		Bioabsorbable Polymer Coated Stents			Bioabsorbable Stent
Xience CoCr-EES Promus PtCr-EES	Resolute CoNi-ZES	Biomatrix 316L-BES	Nobori 316L-BES	SYNERGY PtCr-EES	BVS PLLA-EES

Strut Thickness					
81µm	89µm	120µm	125µm	74µm	150µm
Polymer Coating					
Conformable 7-8µm / side	Conformable 6µm / side	Abluminal 11µm	Abluminal 20µm	Abluminal 4µm	Conformable 3µm / side

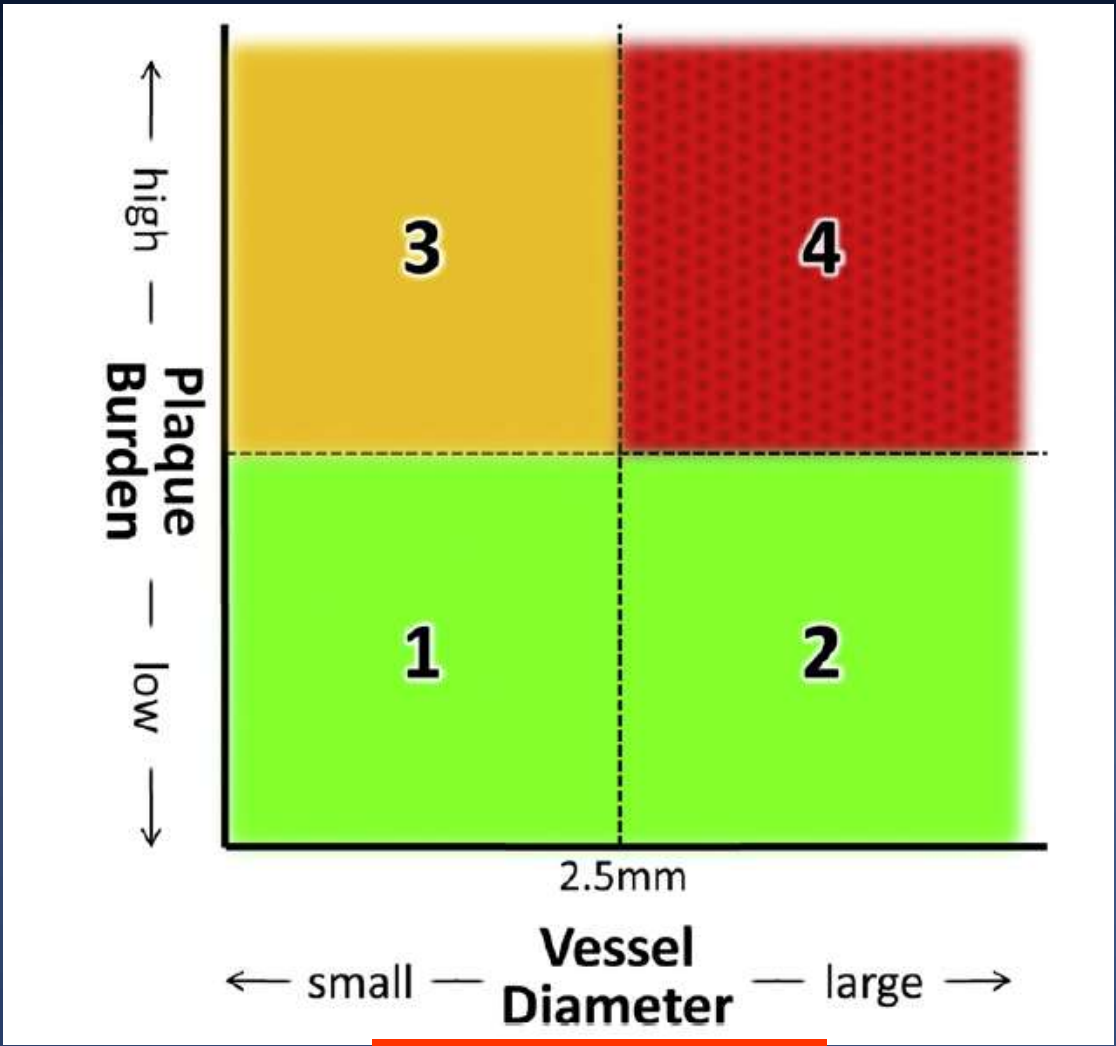
Unresolved Limitations of BVS

- High profile; type A lesions
- Complex lesions; Calcified or tortuous, LM, long, bifurcation
- Stretchability and fracture
- Overlapping
- Side branch
- Relatively high late loss

Relatively Complex Procedure for BVS

- Thicker Struts
- Greater Attention to Procedure
  - Strut fracture with overdilation
  - Early thrombosis with underexpansion
- More Techniques Necessary
  - Pre: More Aggressive Plaque Modification
  - Post: Routine NC Balloon
  - Routine Intravascular Imaging

BRS for Left Main Lesions



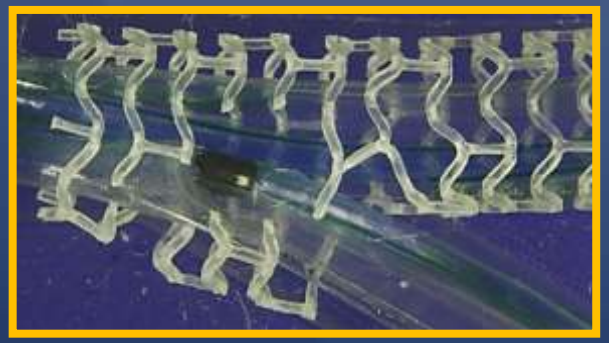
- Panel 1,2; BVS can be performed
- Panel 3; BVS should be decided on a case-by-case basis
- Panel 4; BVS should be avoided (SB big, large plaque)

Side-Branch

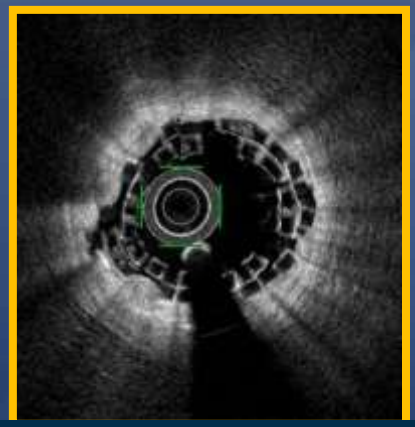
Colombo et al. Int J Cardiol. 2014;175(1):e11-3.

BRS for Bifurcation Lesions

- Potential limitations
  - Limited post-dilation and cell expansion affecting two BRS techniques and post-dilation optimization
  - Risk of fracture and distortion.
- Reports of increased BRS thrombosis in complex anatomy
  - Potential role of strut thickness, overlapping scaffolds, under-sizing and malapposition due to inadequate post-dilation driven by strut fracture fear



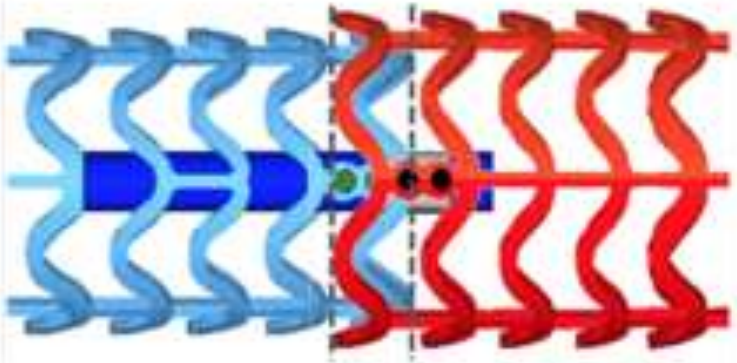
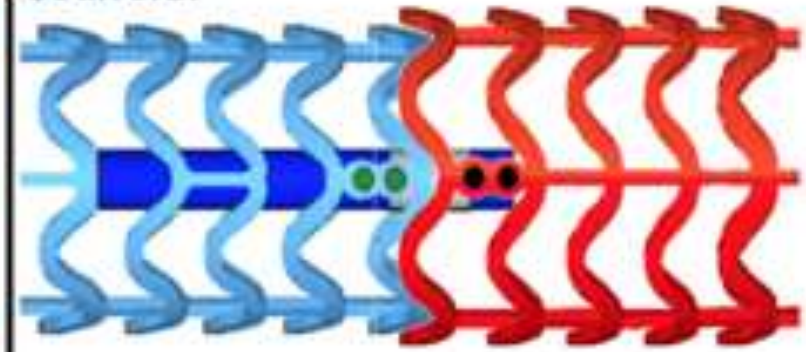
BVS fracture



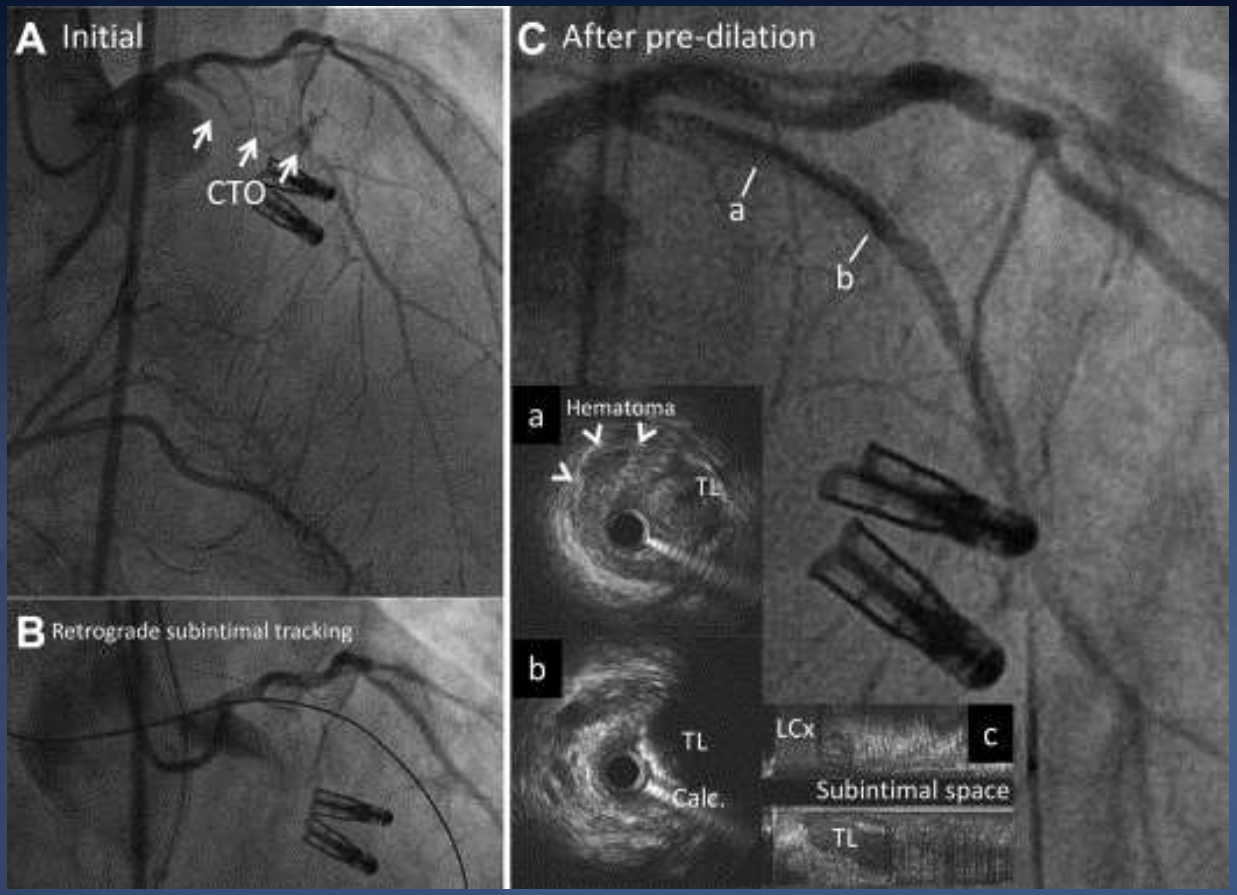
Two overlapped 2.5-mm BVS

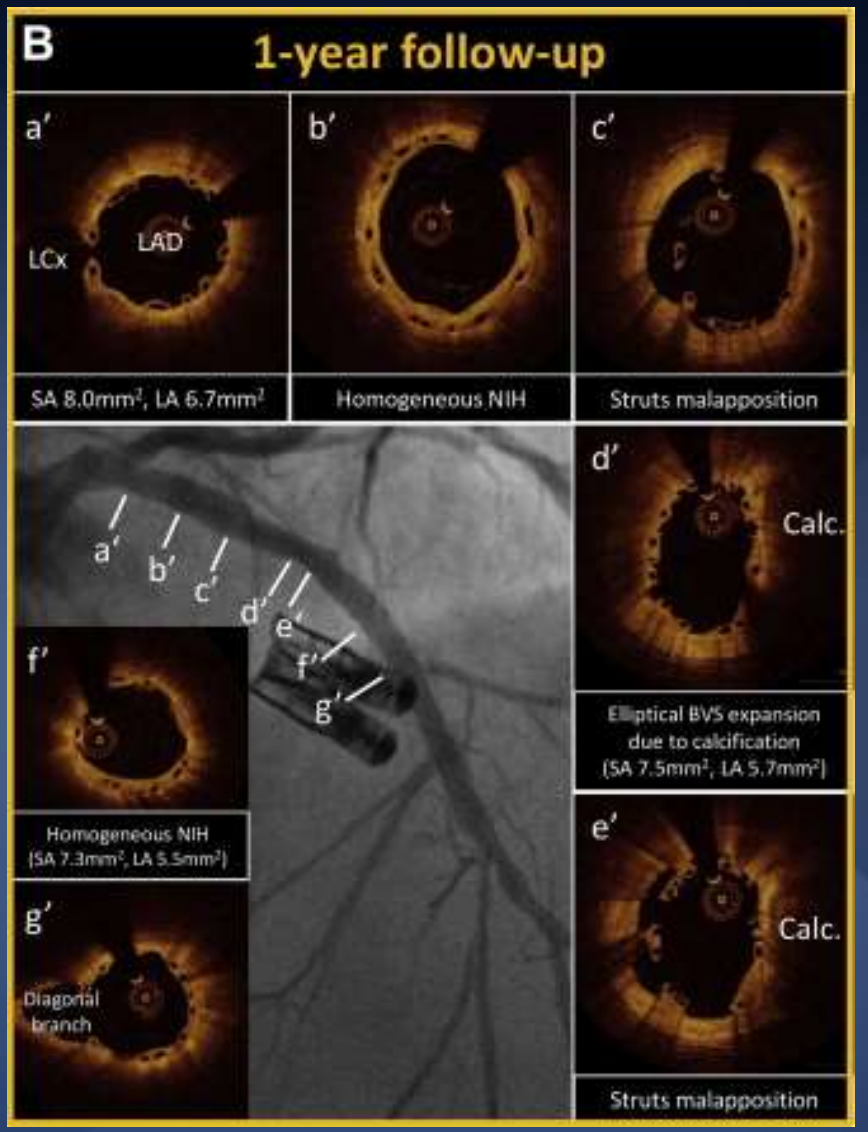
BRS for Long Coronary Lesions

Scaffold overlap considerations

Marker to Marker	Scaffold to Scaffold
Distal balloon marker aligned with the proximal marker beads of the implanted scaffold . *The markers of the second scaffold will be adjacent to the markers of the deployed scaffold.*	*Distal balloon marker proximal to the proximal marker beads of the implanted scaffold.* *There will be ~1 mm of space between the markers of the second scaffold and the markers of the deployed scaffold.*
	
= APPROX. 1 MM OVERLAP	NO or MINIMAL OVERLAP

BRS for CTO





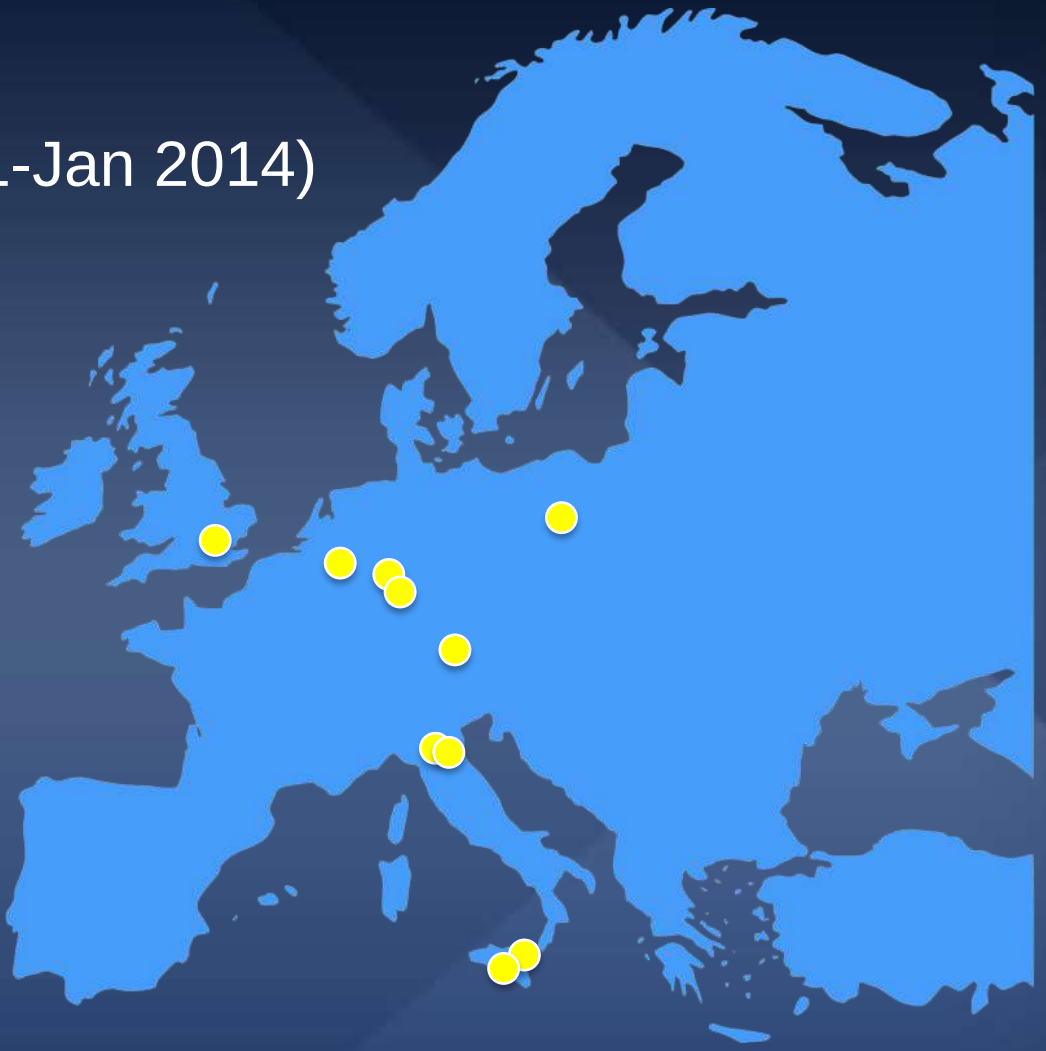
JACC: Cardiovascular Interventions 2014;7:e157–e159

BRS for STEMI

- Vessel preparation is mandatory
  - thrombus aspiration or balloon predilation
- Sizing of vessel may be difficult because of vasoconstriction and presence of thrombotic debris
- Imaging may be considered for optimal sizing
- Use potent P2Y12 platelet inhibitor

GHOST-EU (N=1,189)

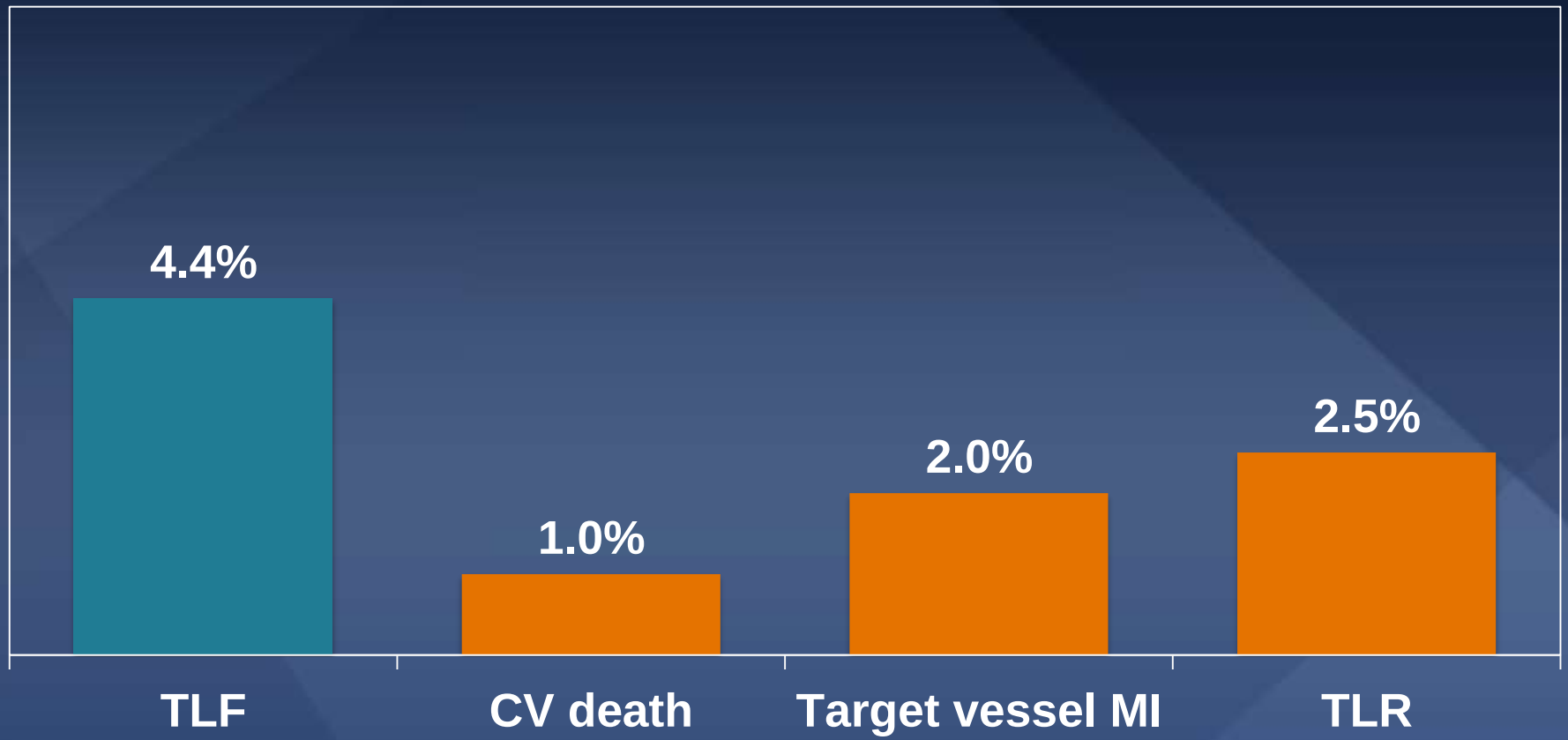
- Post-marketing (Nov 2011-Jan 2014)
- Investigator-initiated
- Retrospective
- Multicenter (N=10)
- Observational
- Single-arm
- No monitoring
- Site-reported events



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

GHOST-EU: 6-Mo Outcomes*

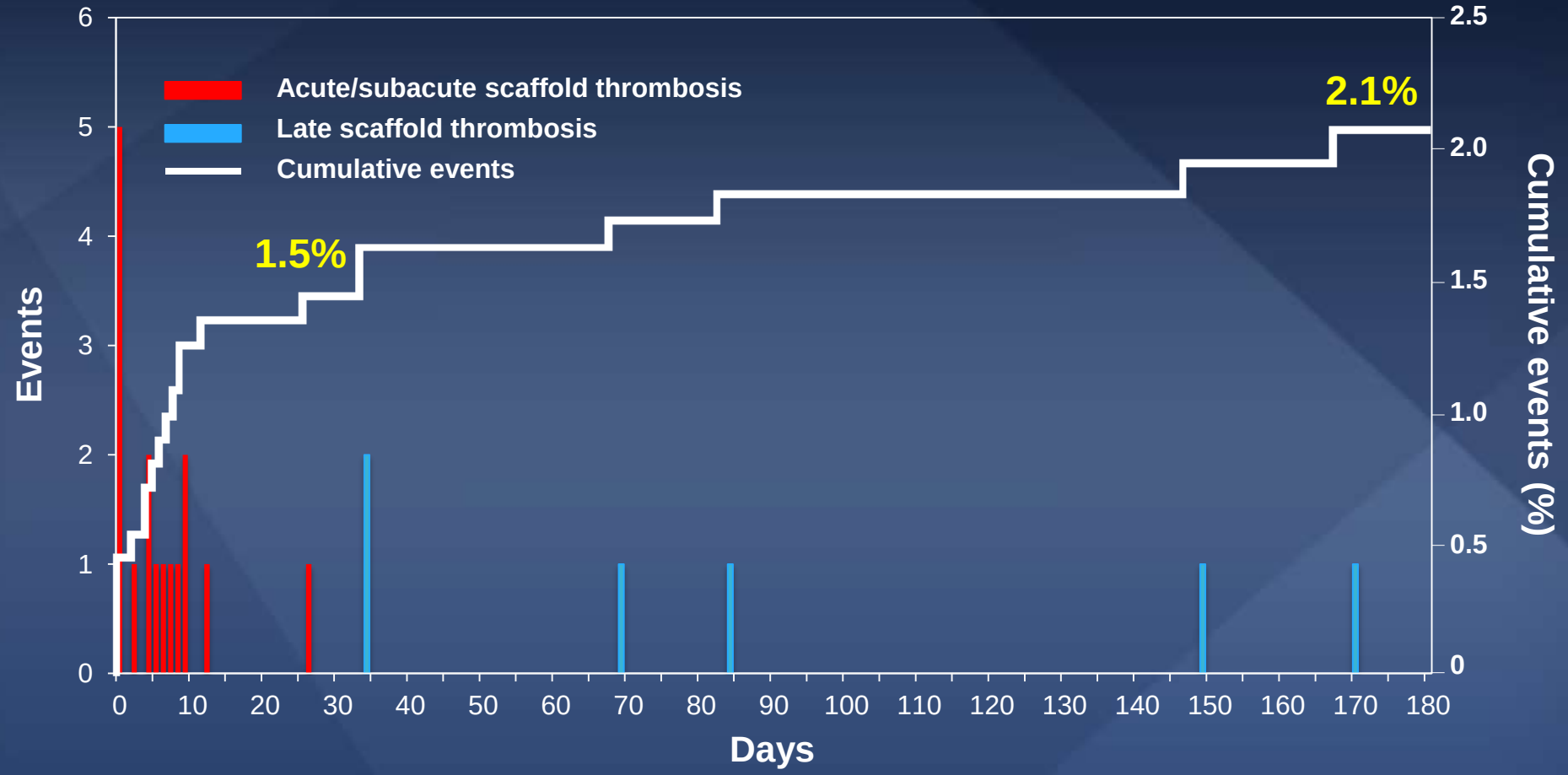
1,189 patients, 1,731 Absorb BVS



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

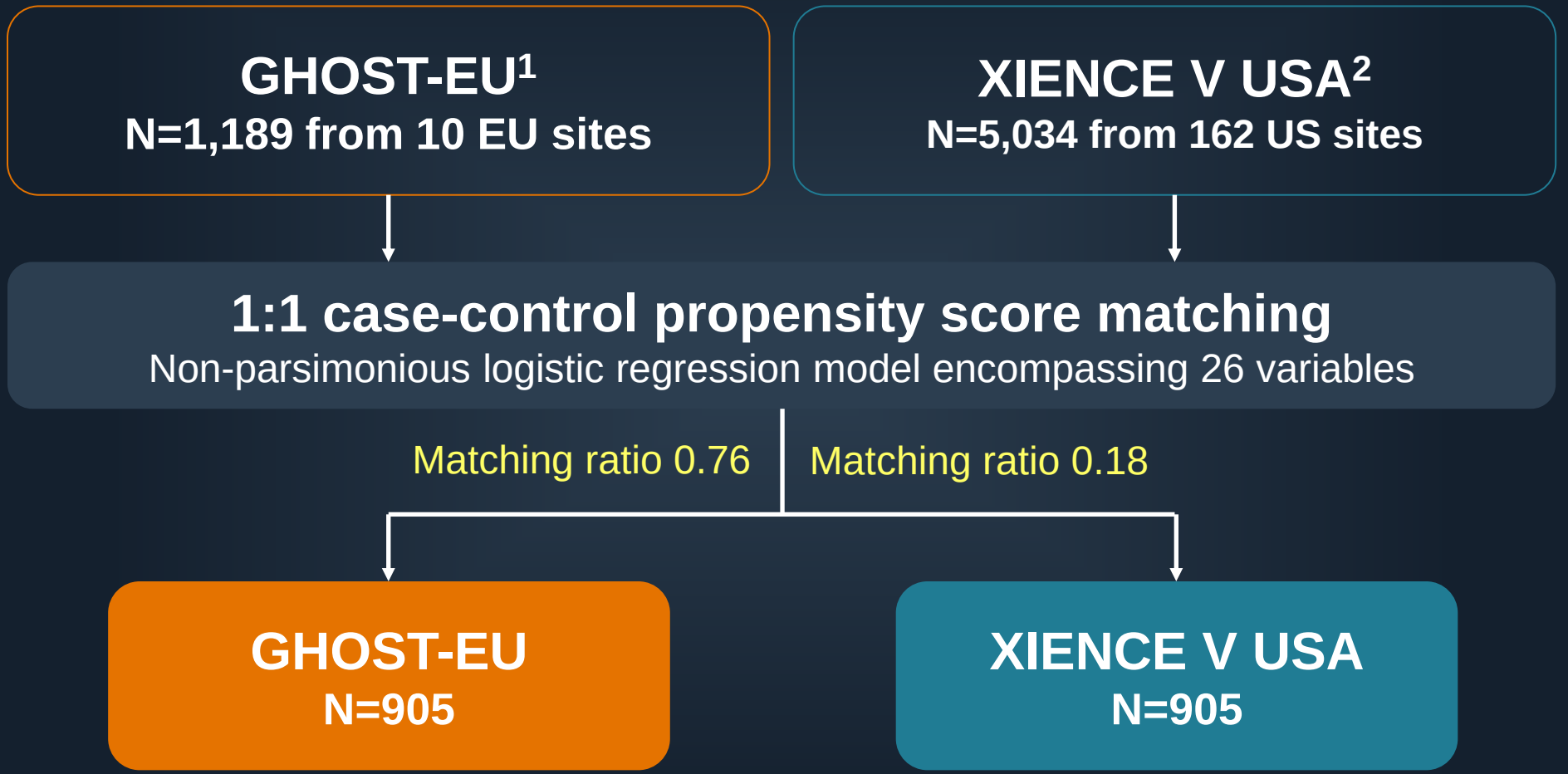
GHOST-EU: 6-Mo Outcomes*

1,189 patients, 1,731 Absorb BVS



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

Study Design



J Am Coll Cardiol Intv 2016;9:440–9

Patients Characteristics (matched)

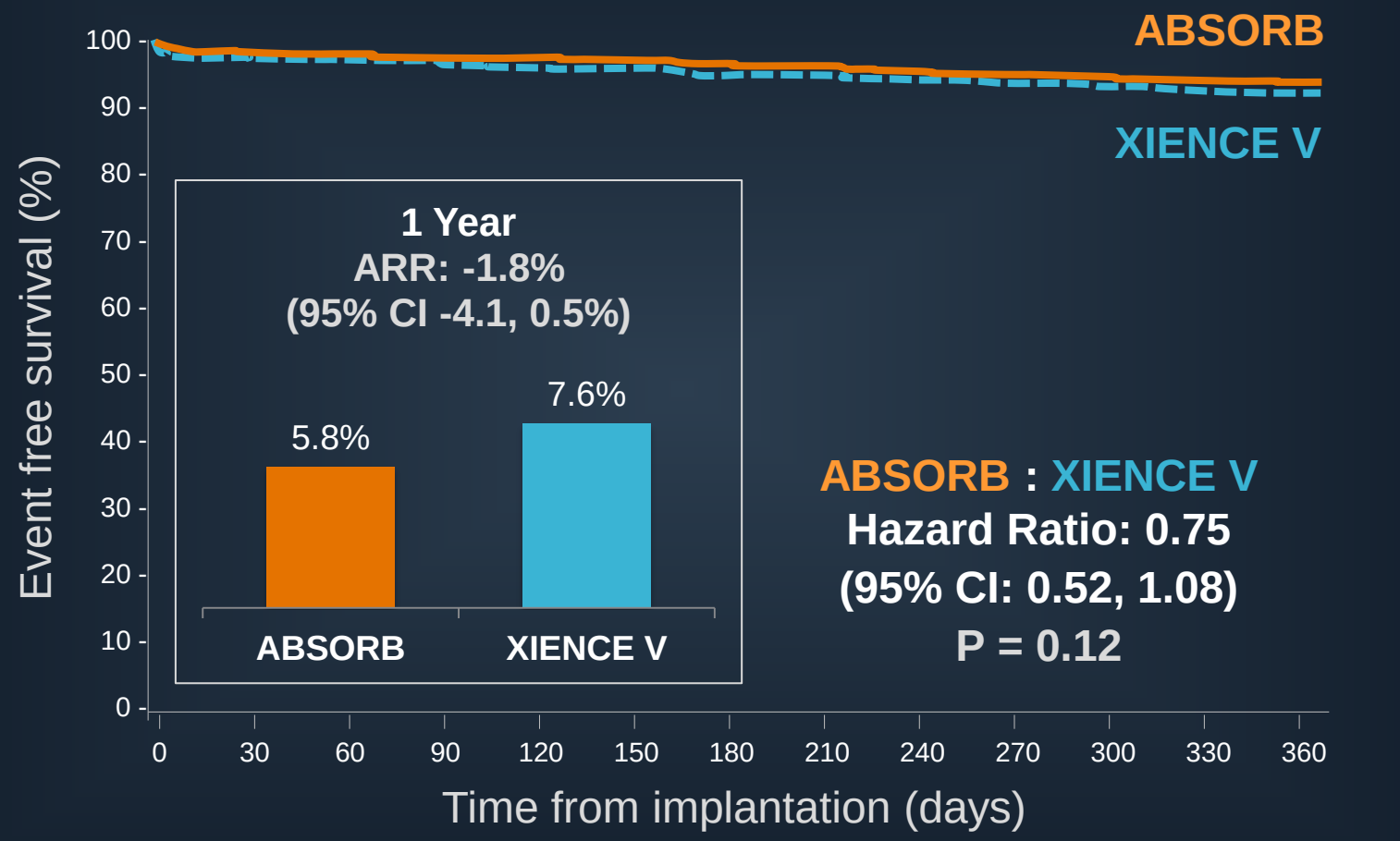
		ABSORB (n=905)	XIENCE V (n=905)	P value
Demographics	Age - mean ± SD, yrs	63 ± 11	63 ± 11	0.57
	Male sex - %	78	78	1.00
Risk factors	Diabetes - %	28	27	0.82
	Renal disease - %	16	19	0.10
Clinical presentation	Acute coronary syndrome - %	42	43	0.92
	Multivessel disease - %	58	60	0.41
Lesion characteristics	ACC/AHA B2/C lesions - %	55	55	0.96
	De novo - %	95	95	0.82
	Chronic total occlusion - %	8	8	0.86
	Ostial - %	8	11	0.06
	Bifurcation - %	22	23	0.79
	Lesion length – mean ± SD, mm	20 ± 15	20 ± 13	0.65
	RVD – mean ± SD, mm	3.0 ± 0.5	3.0 ± 0.5	0.49
	Diam. stenosis– mean ± SD, %	85 ± 13	85 ± 11	0.86
Procedure details	Post-dilatation - %	52	51	0.64

GHOST-EU

J Am Coll Cardiol Intv 2016;9:440–9

Target lesion failure

Cardiac death, MI, TLR

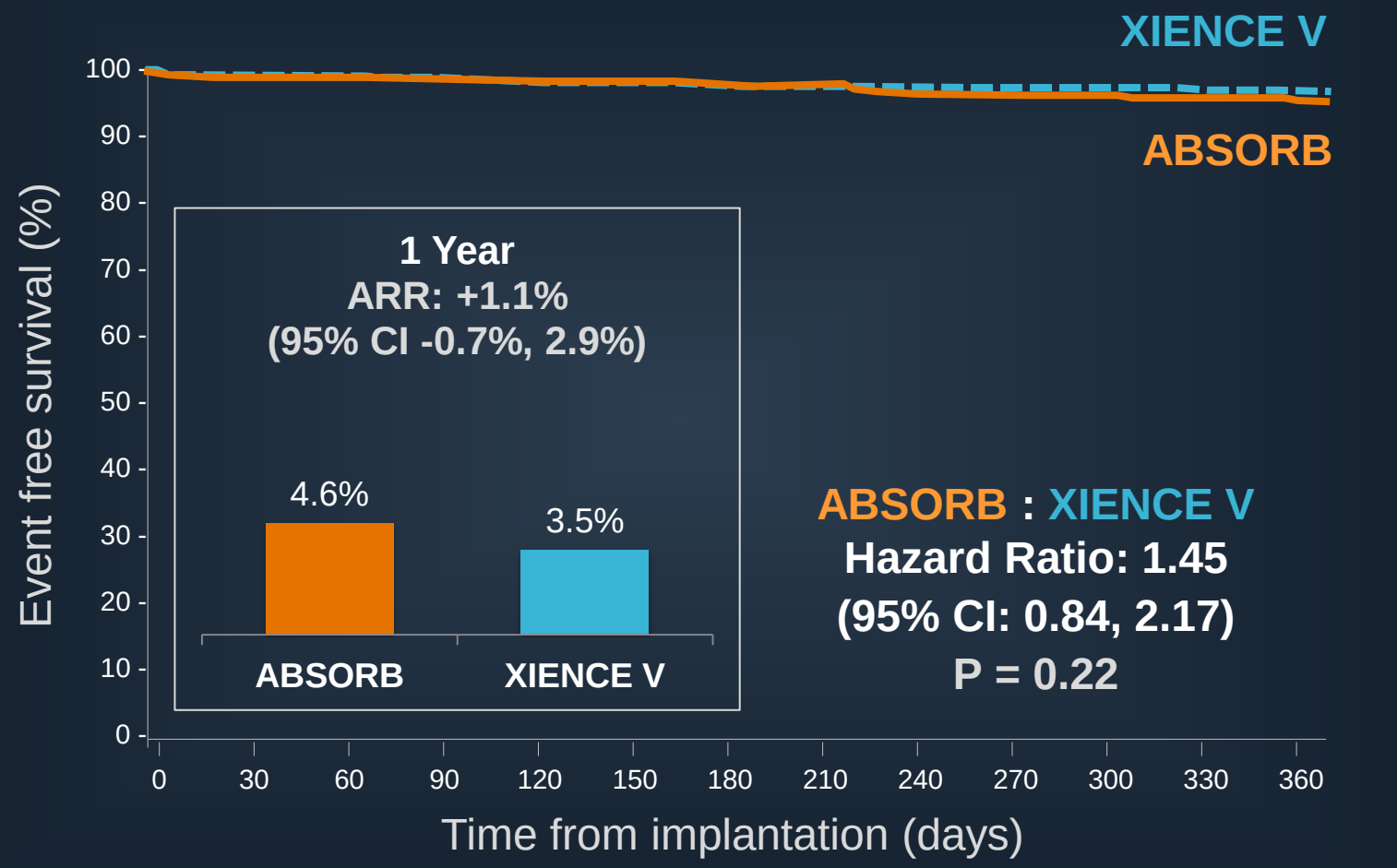


# at risk	30 Days	6 Months	12 Months
ABSORB	880	823	741
XIENCE V	876	834	785

GHOST-EU

J Am Coll Cardiol Intv 2016;9:440–9

Target Lesion Revascularization



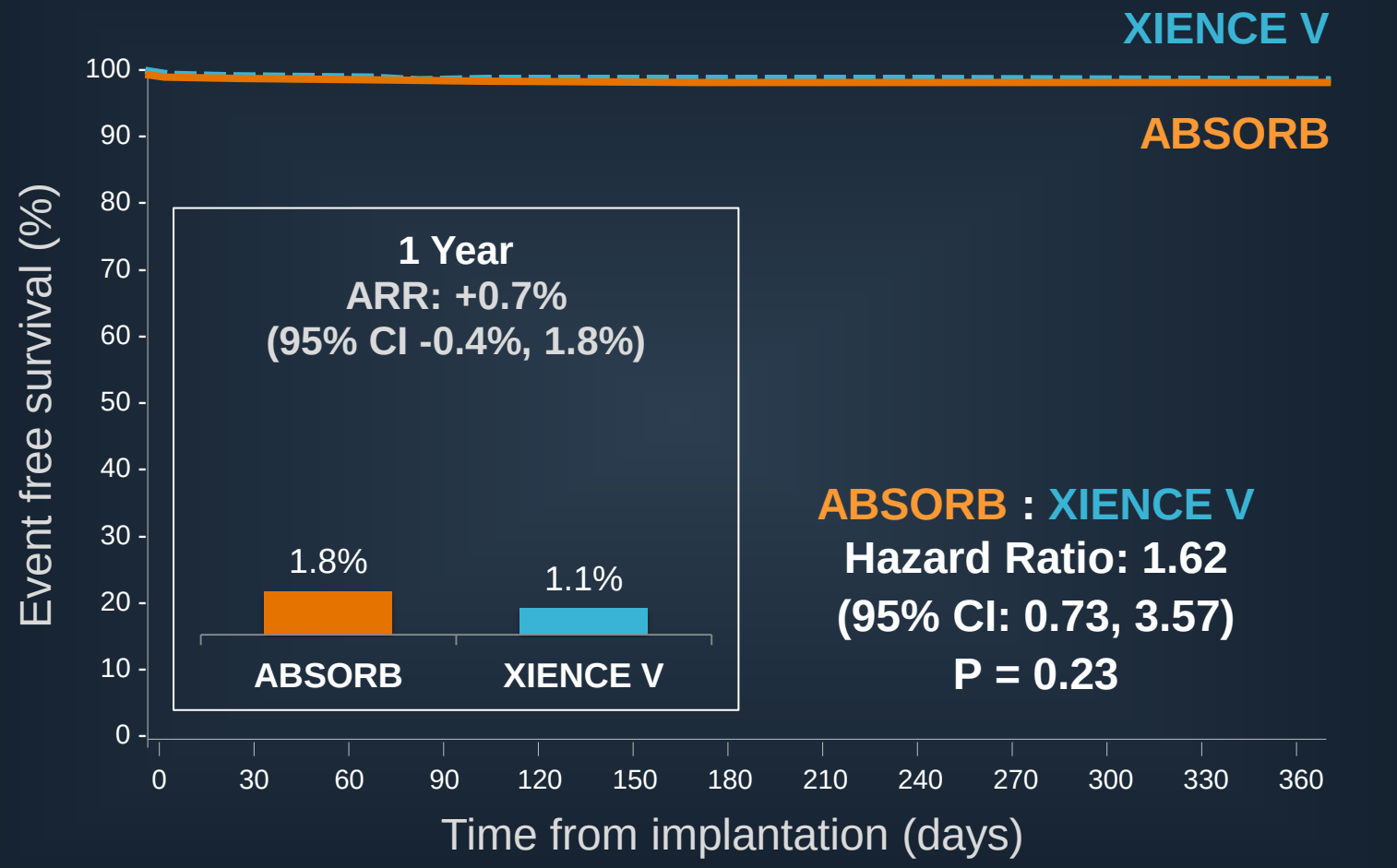
# at risk	30 Days	6 Months	12 Months
ABSORB	881	823	740
XIENCE V	887	846	802

GHOST-EU

J Am Coll Cardiol Intv 2016;9:440–9

Definite or Probable Device Thrombosis

ARC definition



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

GHOST-EU

J Am Coll Cardiol Intv 2016;9:440–9

ISAR-ABSORB Registry

- 419 patients from 2 high-volume centers in Munich.
- Routine angiographic surveillance 6–8 months.

	Patients
	419
Age (years)	66.6 ± 10.9
Male sex	321 (76.6)
Diabetes	132 (31.5)
Diabetes (insulin-treated)	43 (10.3)
Hypertension	361 (86.2)
Hypercholesterolemia	281 (67.1)
Current smoker	90 (21.5)
Glomerular filtration rate < 60 mL/min	98 (23.8)
Body mass index (kg/m^2)	27.8 ± 4.8
Left ventricular ejection fraction (%)	55.2 ± 9.4[a]
Previous MI	109 (26.0)
History of coronary bypass surgery	18 (4.3)
Multivessel disease	319 (76.1)
Clinical presentation	
Stable coronary artery disease	256 (61.1)
Unstable angina	48 (11.5)
Non-ST-elevation MI	80 (19.1)
ST-elevation MI	35 (8.4)

	Lesions
	527
Target vessel	
Left main stem	0 (0.0)
Left anterior descending	237 (45.0)
Left circumflex	110 (20.9)
Right coronary artery	176 (33.4)
Venous bypass graft	4 (0.8)
Lesion type	
Complex lesion morphology	258 (49.0)
Bifurcation lesion	69 (13.1)
Chronic occlusion	7 (1.3)
Lesion characteristics before intervention	
Reference vessel diameter (mm)	2.89 ± 0.46
Minimal lumen diameter (mm)	0.91 ± 0.47
Diameter stenosis (%)	68.6 ± 15.3
Lesion length (mm)	15.8± 9.5

CCI 2016;87:822-829

ISAR-ABSORB; Angiographic Outcomes

	Lesions 360
Reference vessel diameter (mm)	2.95 ± 0.46
Angiographic characteristics (in-stent)	
Minimal lumen diameter (mm)	2.33 ± 0.63
Diameter stenosis (%)	21.0 ± 17.4
Late lumen loss (mm)	0.26 ± 0.51
Angiographic characteristics (in-segment)	
Minimal lumen diameter (mm)	2.15 ± 0.60
Diameter stenosis (%)	27.5 ± 16.1
Late lumen loss (mm)	0.21 ± 0.50
Restenosis rate	27 (7.5)

CCI 2016;87:822-829

ISAR-ABSORB; Clinical Outcomes

	Patients		
	419	6-month rate	12-month rate
Death	15	2.7	4.0
Cardiac death	9	1.7	2.4
MI	11	2.4	2.7
Death or MI	24	4.9	6.2
Definite stent thrombosis	10	2.0	2.6
Definite or probable stent thrombosis	12	2.4	3.1
Target lesion revascularization	33	4.2	9.1
Composite of death, MI, target lesion revascularization	49	7.3	13.1

CCI 2016;87:822-829

BRS in Real-World PCI

- Theoretically, BRS has a unique safety and efficacy advantage beyond contemporary metallic DES.
- Despite conceptual advantages with BRS, current BRS platforms have mechanical limitations and require complicated preparation compared to current metallic DES.

BRS in Real-World PCI

- Next-generation BRS with thinner struts and more durable platform could be more widely applicable for real-world patients with diverse clinical and angiographic characteristics.
- In addition, long-term safety and efficacy should be continuously addressed in the real-world practice.

IRIS-DES Registry

Design

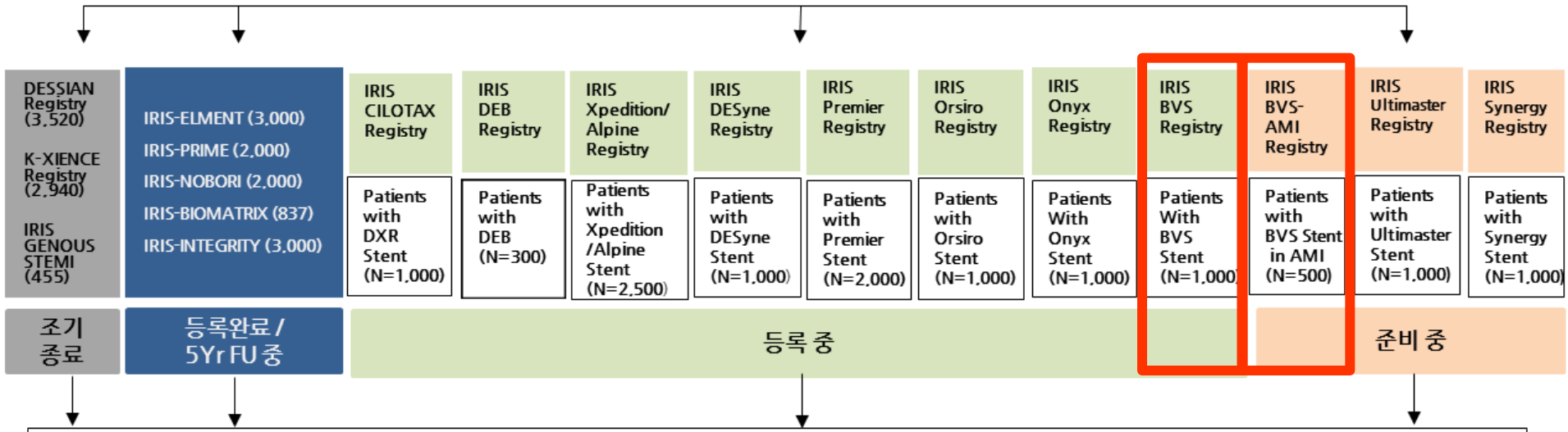
- DESIGN: An unrestricted, multicenter, prospective cohort
- OBJECTIVE: To compare the safety and efficacy of the second- or newer-generation DES and the first-generation DES in everyday clinical practice,
- PRINCIPAL INVESTIGATOR
  Seung-Jung Park, MD, PhD, Asan Medical Center, Seoul, Korea

Evaluation of Effectiveness and Safety of the First, Second, and New Drug-Eluting Stents in Routine Clinical Practice;

IRIS-DES Registry

Consecutive PCI patients receiving New DES without a mixture of other DES

Prospective Enrollment



Clinical follow-up at 1-, 6-, and 12-months, and annually up to 5 years

***Primary end point: Composite of Death, MI, and TVR at 12-months**

Comparative Effectiveness Research (CER) of Various Coronary Stents

- Enrollment and at least 2-year clinical follow-up was completed for Cypher, Xience, Genous, Promus element, Xience prime, Nobori, Biomatrix, and Resolute intergrity; analysis results are expected in the summer of 2016.
- The IRIS-BVS and IRIS-BVS AMI registries are actively ongoing, and comparative data will be available in the near future.