Part I: PCI Controversies

With GHOST-EU Registry, Bioresorbable Scaffold (BRS) – For Simple Lesion Only?

Corrado Tamburino, MD, PhD

Ferrarotto Hospital, University of Catania, Catania Italy

Potential conflicts of interest

Speaker's name: Corrado Tamburino

✓ **I have the following** potential conflicts of interest to report:

Research contracts
☑ Consulting Medtronic, Abbott v, Edwards, Boston Sc.
Employment in industry
Stockholder of a healthcare company
Owner of a healthcare company
Other(s)

I do not have any potential conflict of interest

BRS: Predicated Benefits

Vascular restoration therapy (VRT)

▪ Superior conformability and flexibility	→	Improved distribution of the tissue biomechanics and preserved vessel geometry
▪ "Liberation of vessel from a metallic cage"	→	Restoration of physiological vasomotion, adaptive shear stress, late luminal gain, and late expansive remodelling
▪ Absence of any residual foreign material ▪ Restoration of functional endothelial coverage	→	Resolution of malapposition and stent fracture; Reduced inflammation and neoatherosclerosis
▪ Plaque sealing	→	Reduced neoatherosclerosis Passivation of vulnerable plaques
▪ Additional technical benefits	→	No 'jailing' of the side branches; No overhang at ostial lesions; No inability to graft the stented segment; Reduced distal embolization

Expected clinical implications of BRS biological effects

1. Reduction of angina

1. **Prevention of late thrombotic events**

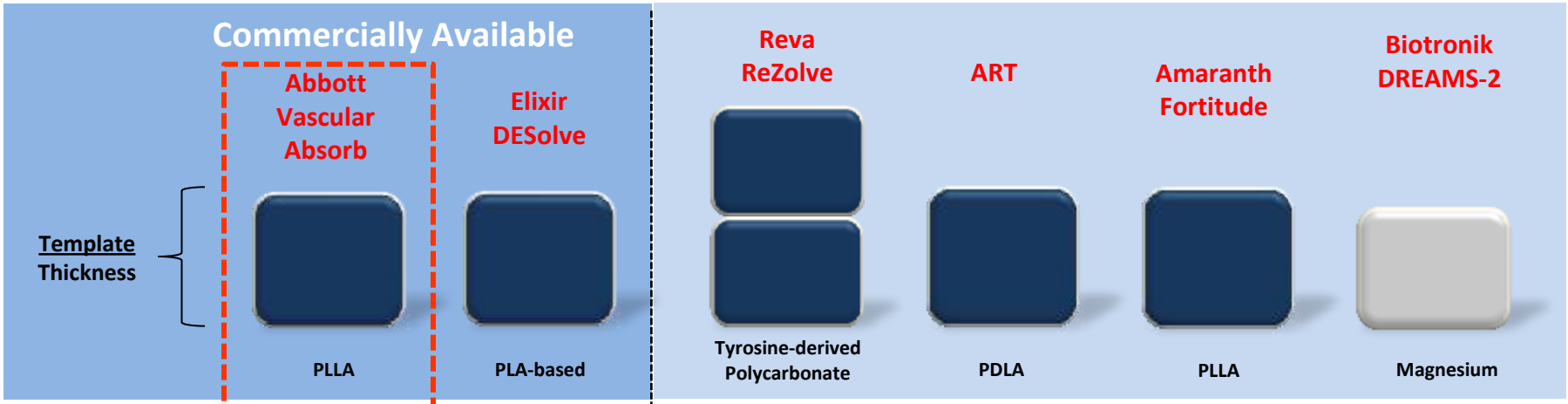
Challenges of BRS

▪ Deliverability and crossing profile	Radial strength versus crossing profile (thick struts: **challenging use in complex lesions and higher thrombogenicity**
▪ Stretchability and strut fracture	Limitations of expansion (risk of malapposition, underexpansion) and potential for breaks with over-dilatation.
▪ Side branch occlusion	Periprocedural myocardial infarctions? Issues with accessibility of side branches
▪ Duration of antiplatelet therapy	Concerns over early discontinuation, further studies are warranted
▪ Use in ACS and complex lesions	Safety and efficacy data in complex lesions not widely available

Weighting BRS biological effects vs. clinical performance of BRS

1. Based on biological effects of BRS, potentially, all CAD spectrum would benefit from VRT.
2. Complex lesions (AMI, long-lesions, diffuse or small vessel disease, bifurcations), in which mechanisms underlying late thrombotic events are more pronounced, would benefit the most from VRT with BRS.
3. BRS have specific mechanical properties impacting on feasibility, safety and efficacy, especially in more complex PCI.

Absorb BVS versus Other BRS



	Abbott Vascular Absorb	Elixir DESolve	Reva ReZolve	ART	Amaranth Fortitude	Biotronik DREAMS-2
Template Thickness	~150 μm	~150 μm	~122 μm X 2	~160 μm	~150 μm	~125 μm
Support Time	6 months	3 – < 6 months	~6 months	≤ 3 months	3 – 6 months	≤ 3 months
Degradation Products	H_2O & CO_2	H_2O & CO_2	I_2DAT, I_2DT, PCL, Tyrosine	H_2O & CO_2	H_2O & CO_2	Soft Hydroxyapatite
Resorption Time	< 36 months (*slow*)	18 – 24 months (*fast*)	~ 36 months (*slow*)	~18 months (very *fast*)	> 48 months (*very slow*)	9 – 12 months (*very fast*)

•cvPipeline and company presentations

ABSORB experience current status

- According to the IFU, ABSORB is indicated for "de novo native coronary artery lesions". The treated lesion length should be less than the nominal scaffolding length (12 mm,18 mm, 28 mm) with reference vessel diameters ≥ 2.0 mm and ≤ 3.8 mm".
- Current ABSORB experience: moving from simple to complex lesions

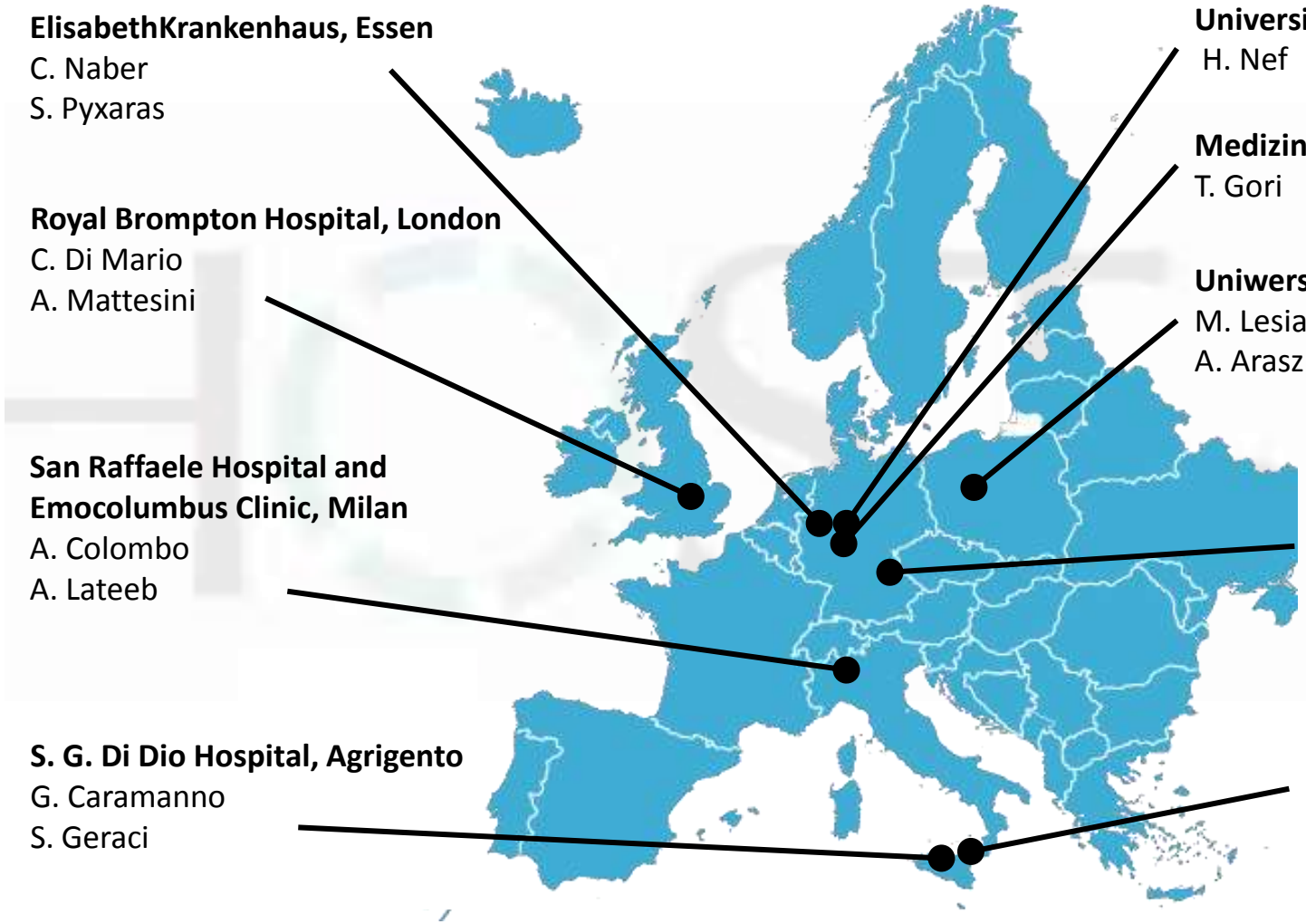
GHOST-EU: Participating centers

ElisabethKrankenhaus, Essen
C. Naber
S. Pyxaras

Royal Brompton Hospital, London
C. Di Mario
A. Mattesini

San Raffaele Hospital and Emocolumbus Clinic, Milan
A. Colombo
A. Lateeb

S. G. Di Dio Hospital, Agrigento
G. Caramanno
S. Geraci



University of Giessen, Giessen
H. Nef

Medizinische Klinik, Mainz
T. Gori

Uniwersytet Medyczny, Poznan
M. Lesiak
A. Araszkiewicz

Klinikum Großhadern, Munich
J. Mehilli

Ferrarotto Hospital, Catania
C. Tamburino (PI)
D. Capodanno (co-PI)
P. Capranzano

GHOST-EU Extended Use* 1.189 patients

Clinical

Angiographic

NSTEMI/STEMI, N=406/1,189(34.1%)

LVEF<30%, N=32/980 (3.3%)

CKD (eGFR<60), N=111/743 (14.9%)

ISR, N=49/1,440 (3.4%)

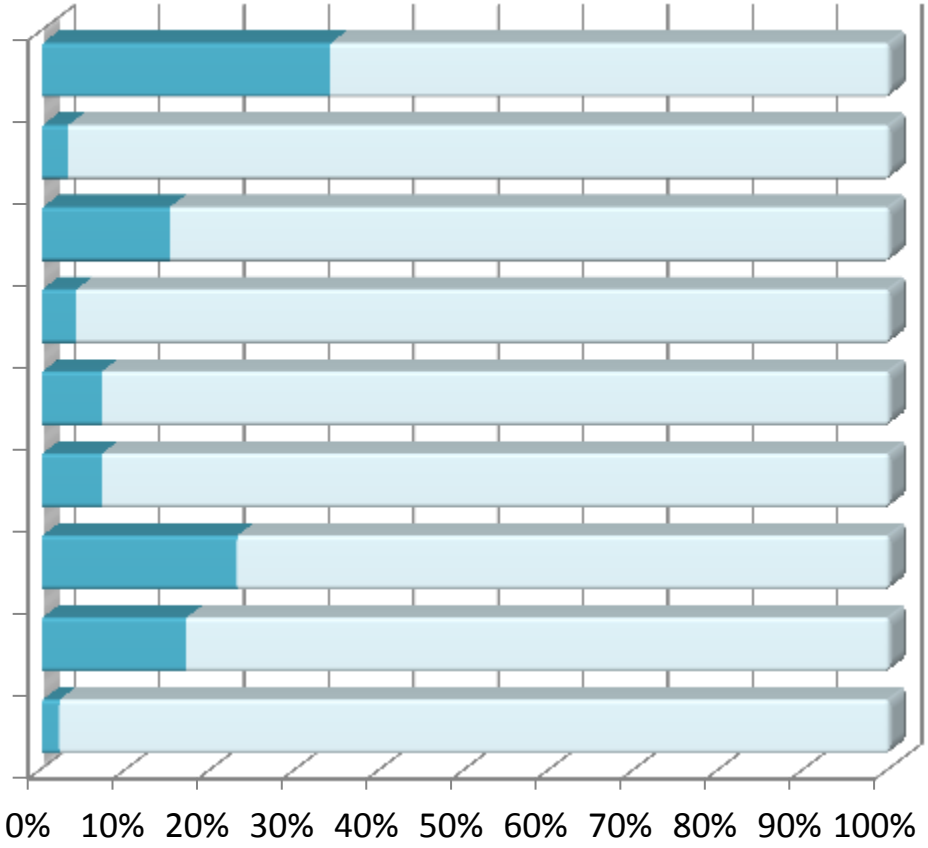
Ostial, N=90/1,282 (7.0%)

CTO, N=96/1,440(6.7%)

Bifurcations, N=333/1,440(23.1%)

Thrombus, N=242/1,440(16.8%)

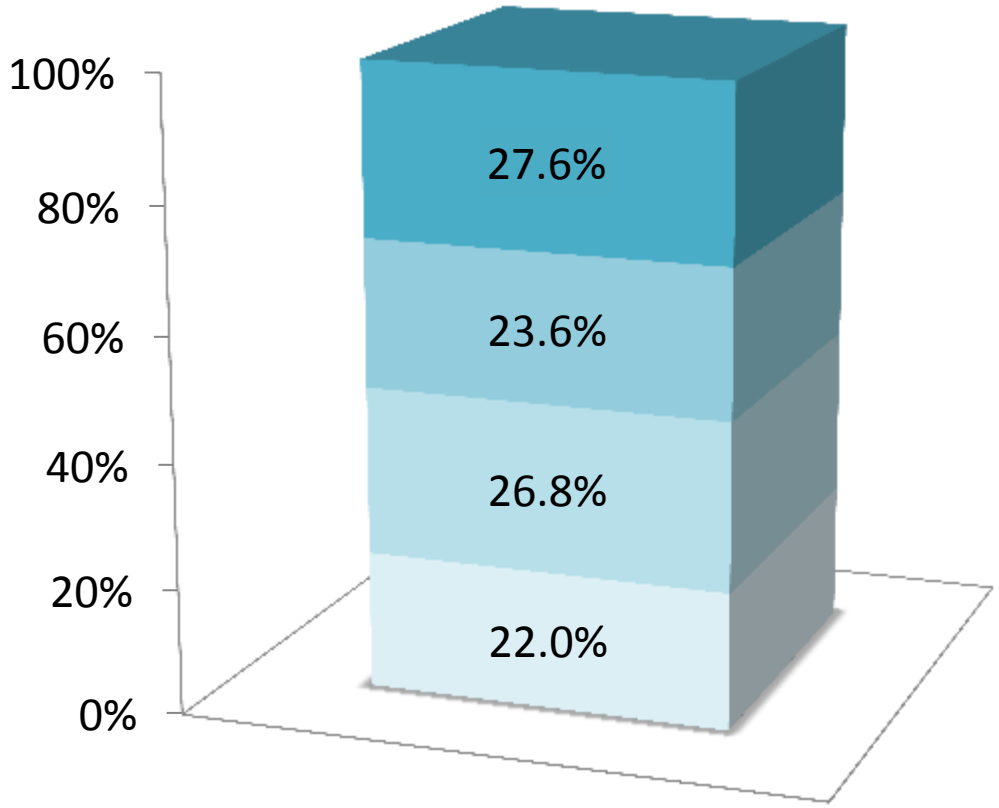
Left main, N=17/1,427(1.2%)



***Compared to ABSORB II eligibility (Diletti et al. Am Heart J. 2012;164:654-63)**

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

ACC/AHA Lesion Complexity

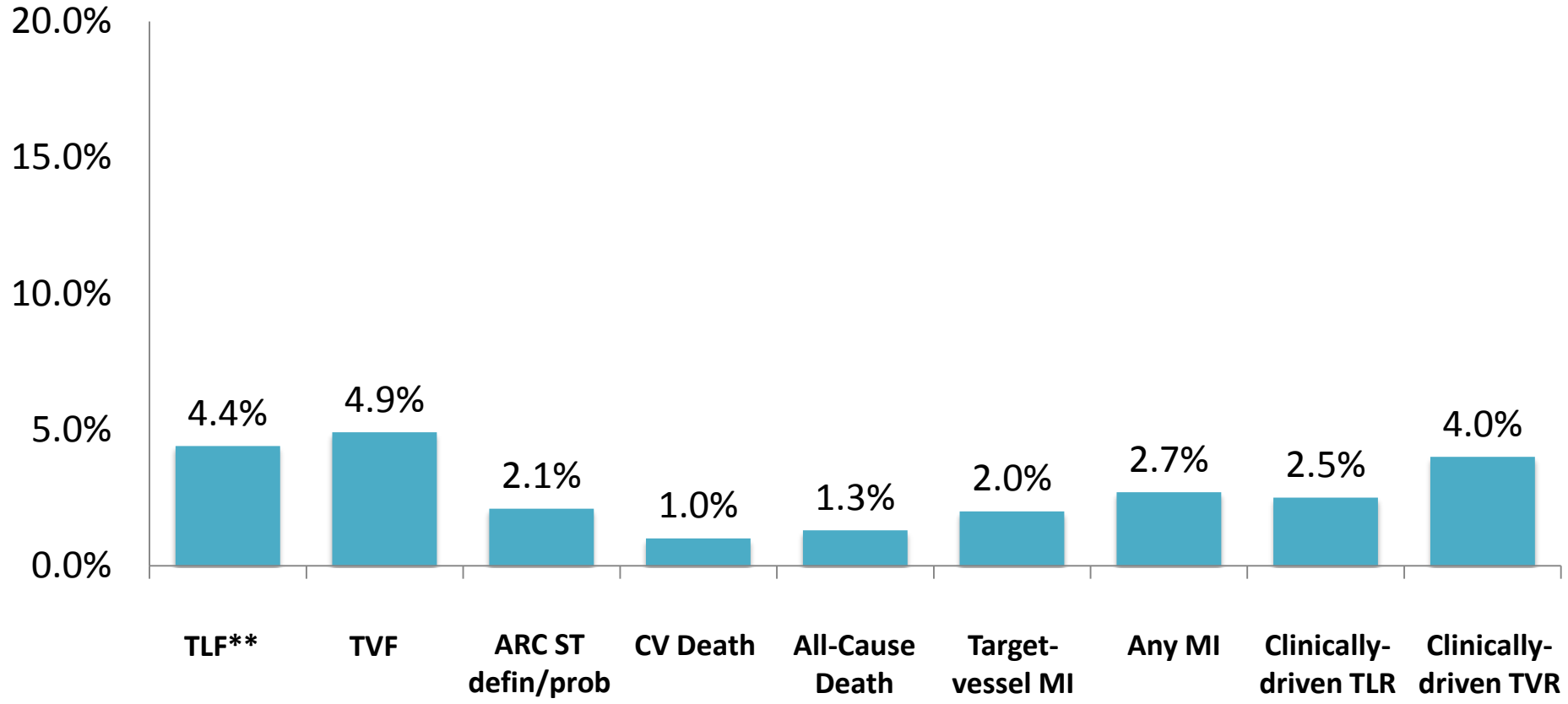


ACC/AHA B2/C
N= 687/1,343 (51.2%)*

- ACC/AHA type C (N=370)
- ACC/AHA type B2 (N=317)
- ACC/AHA type B1 (N=360)
- ACC/AHA type A (N=296)

*Vs. 40% in the ABSORB EXTEND
Whitbourn et al. – TCT 2013

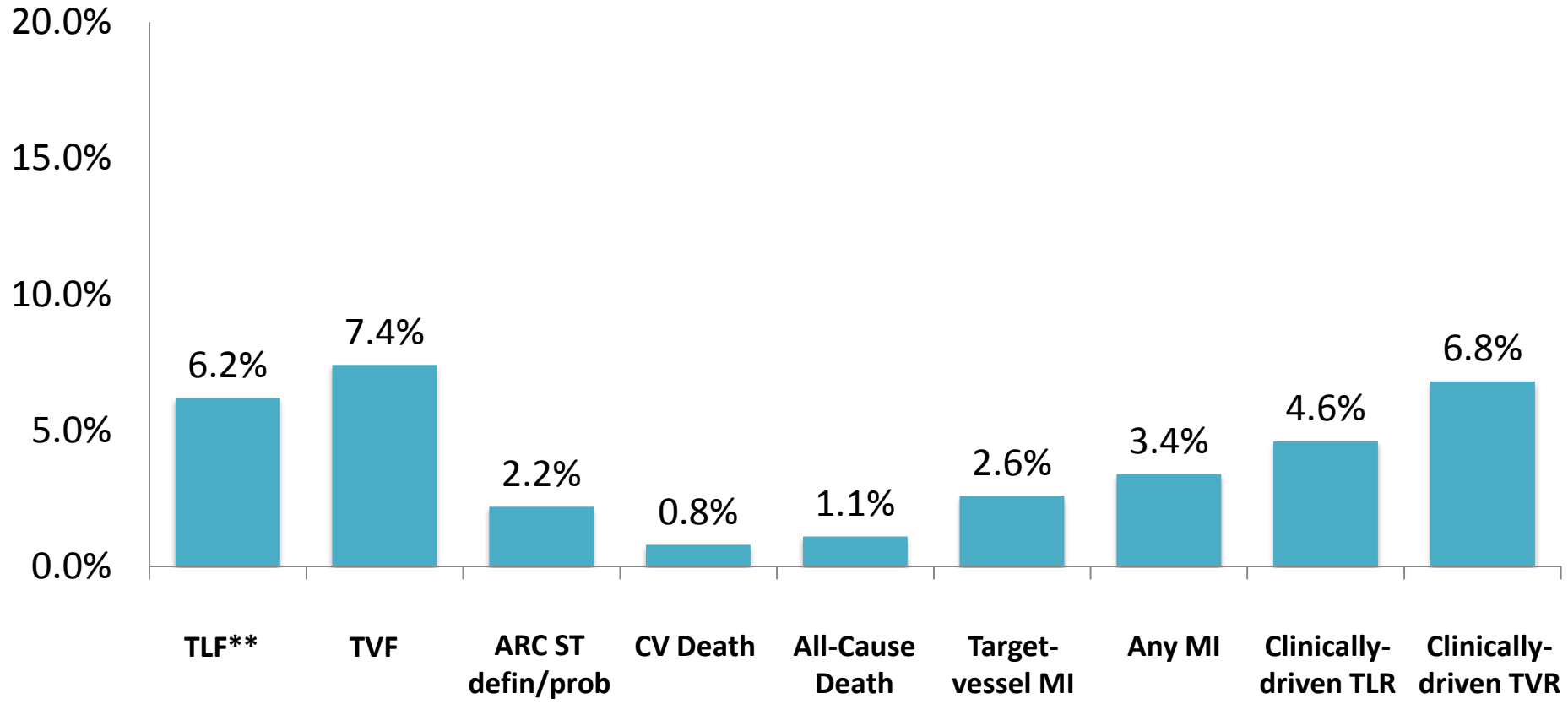
6-Month Outcomes* 1189 patients
6-month follow-up available in 76%



*Event rates are expressed as Kaplan Meier estimates
** Device-Oriented composite primiry endpoint

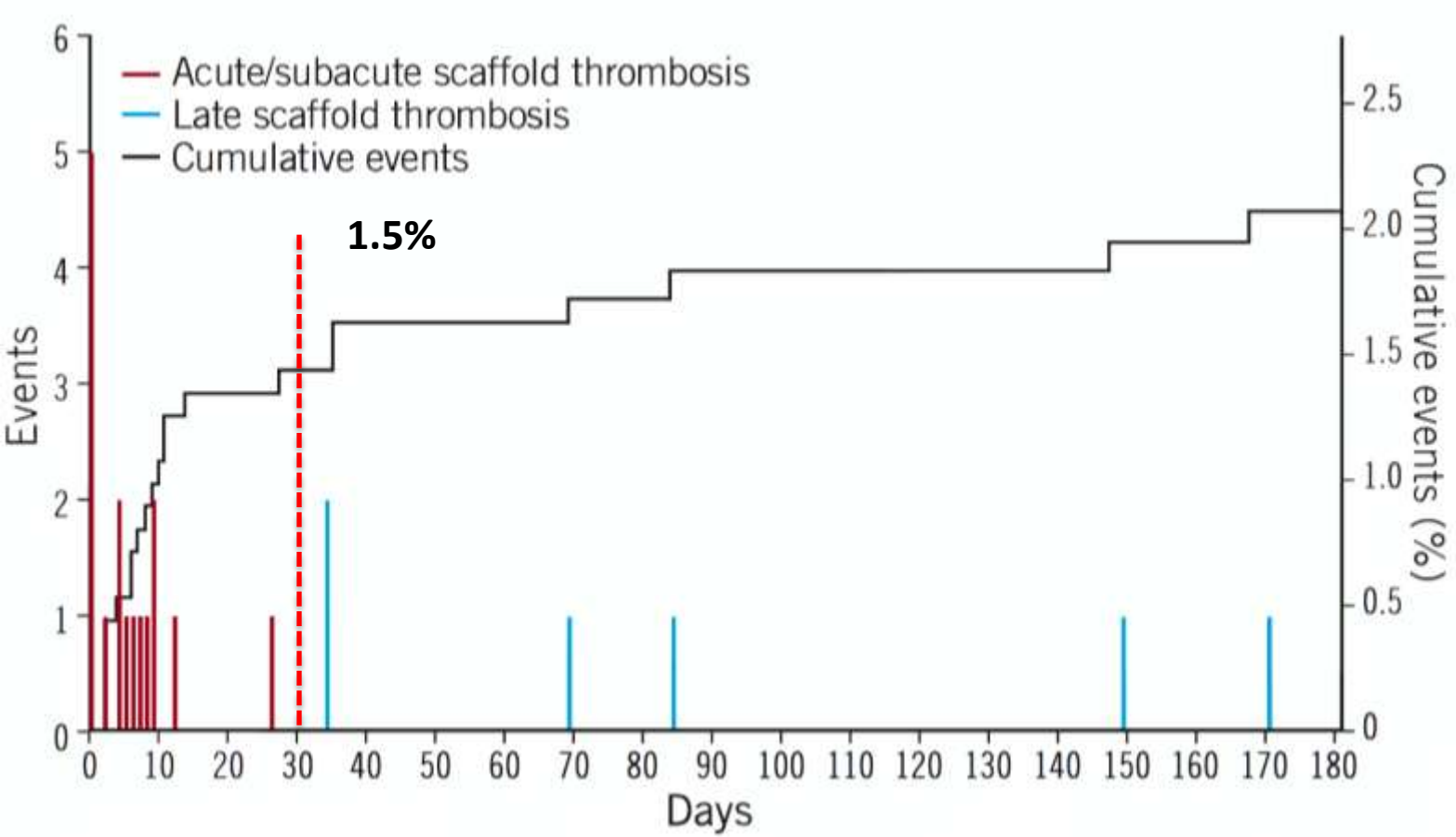
Capodanno D et at. EuroIntervention 2015;10:1144-53.

1-Year Outcomes* 1189 patients
1-year follow-up available in 86%



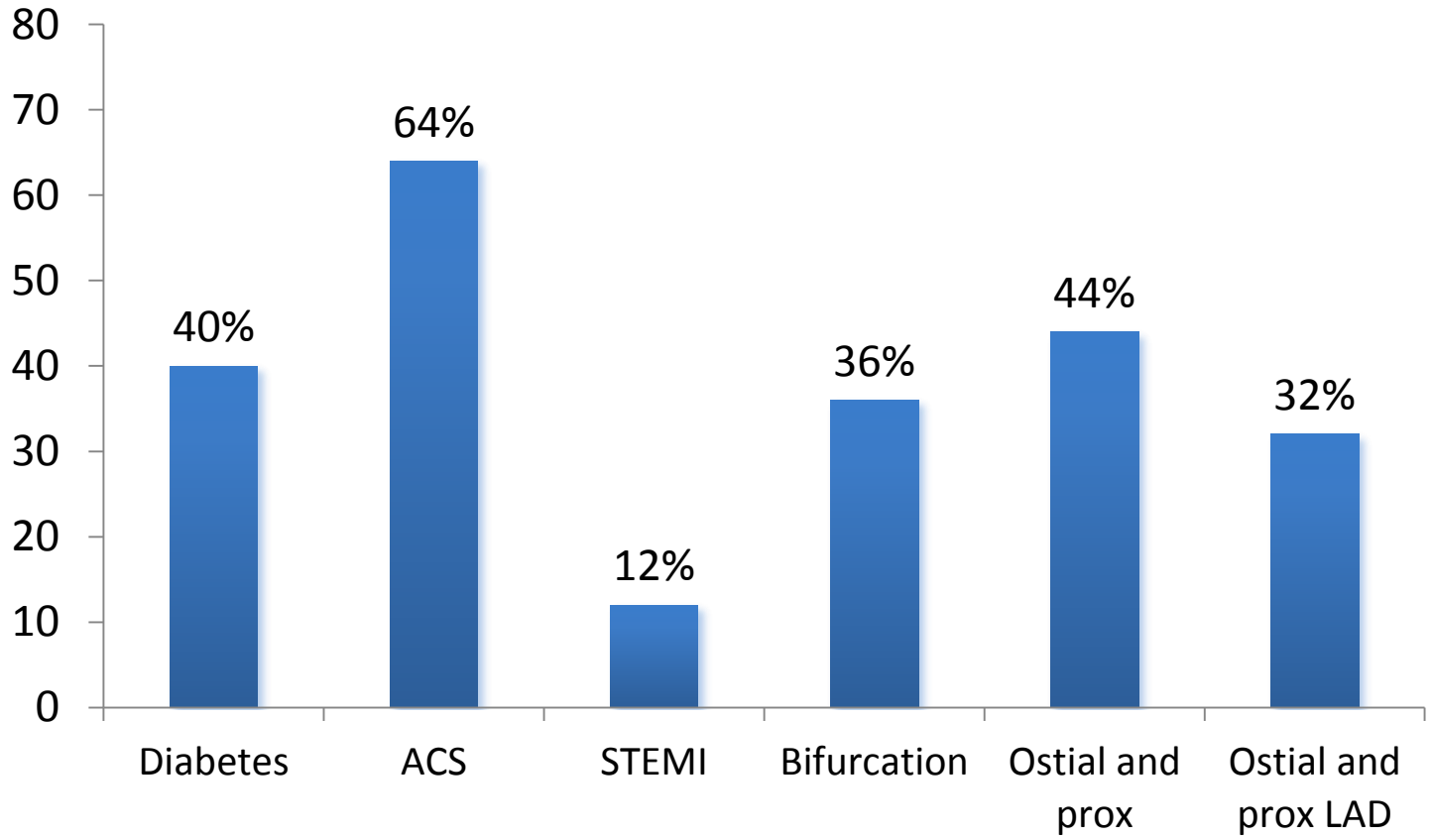
*Event rates are expressed as Kaplan Meier estimates
** Device-Oriented composite primary endpoint

GHOST-EU Scaffold Thrombosis : 1189 patients



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

Prevalence of clinical and angiographic factors among 25 patients with scaffold thrombosis



Scaffold Thrombosis GHOST-EU: 1189 patients

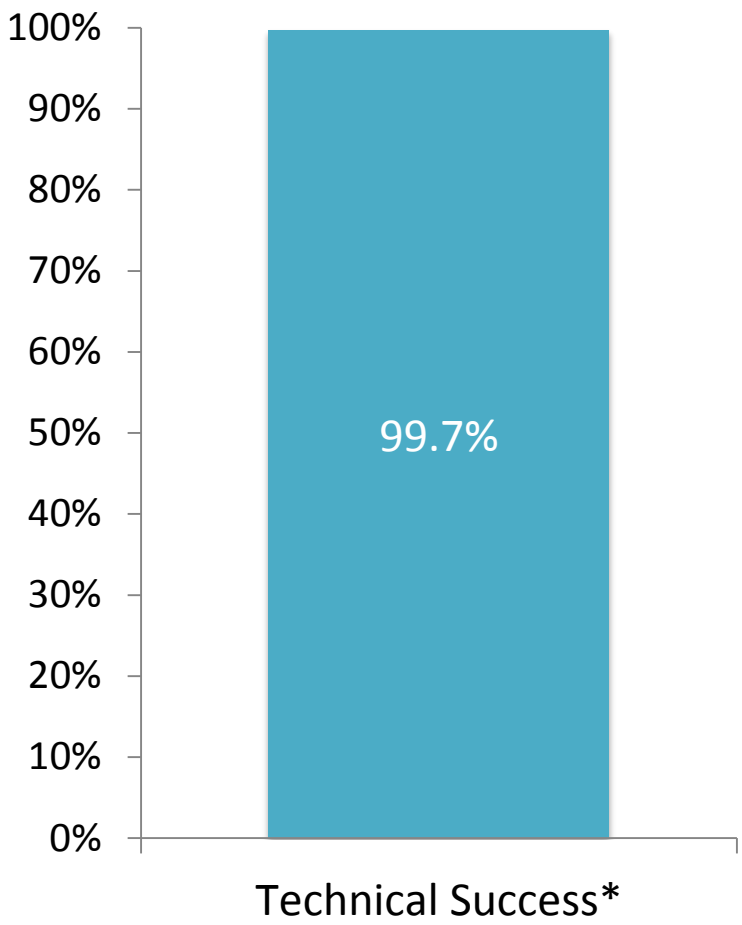
- There were 20 cases of angiographically confirmed ST and three of probable ST.
- 70% occurred in the first month after PCI, **at a median of 5 days,** suggesting the need for scrupulous lesion selection and PCI techniques when using BVS.
- Intravascular imaging was performed in only 4 of 23 patients who experienced ST, of whom 2 discontinued DAPT.
- 18 of 23 were on clopidogrel.
- 20 of 23 patients were on DAPT at the time of ST.

Capodanno D et al. Eurointervention 2014. In press

GHOST-EU Procedural Details :1189 patients

Lesion-based	
Pre-Dilatation	1,405/1,440 (98%)
Post-Dilatation	712/1,1440 (49%)

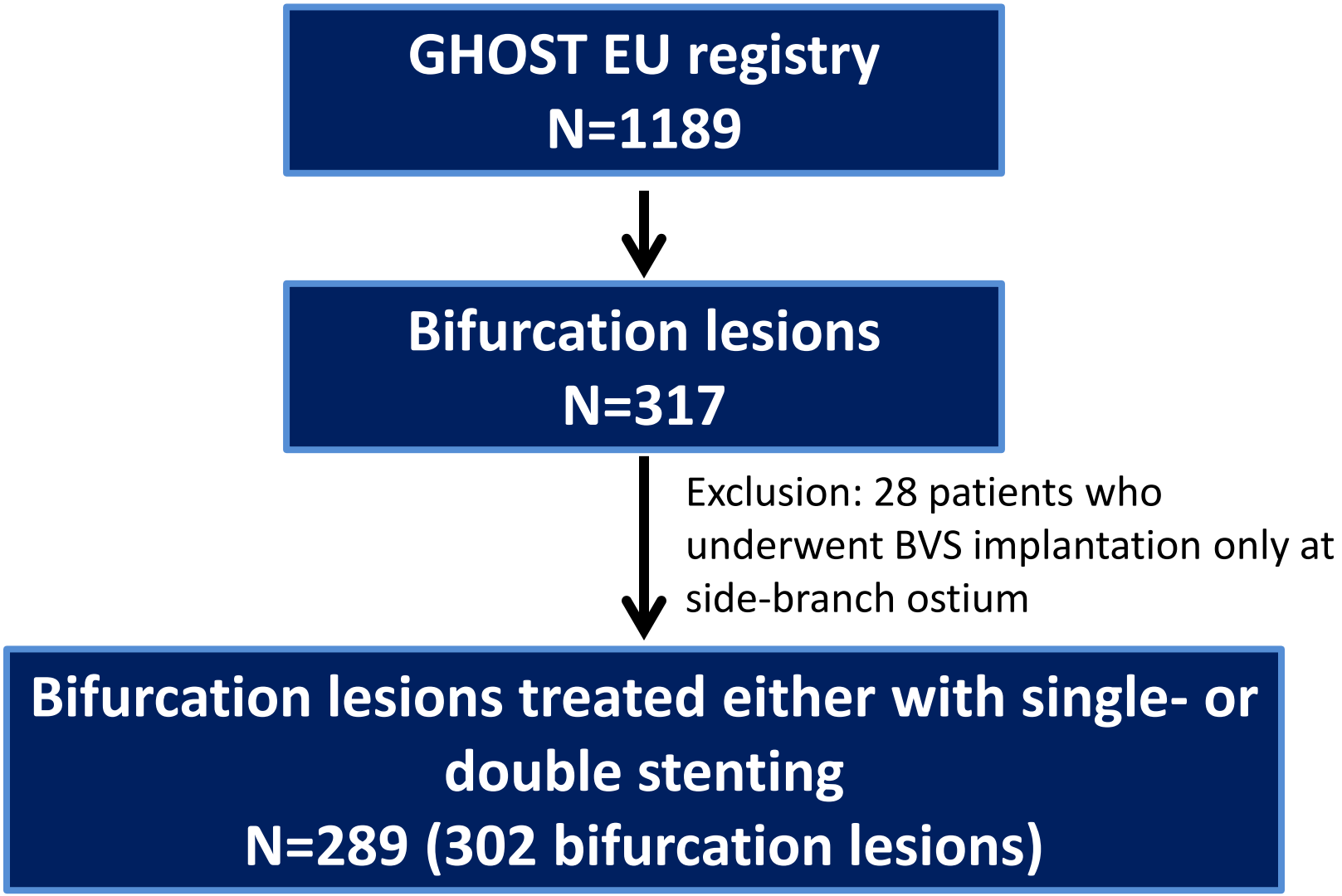
Patient-based	
No. Target Lesion/Pt	1.2±0.5
Multivessel Disease	485/1,186 (40.9%)
SYNTAX Score	11.3±7.9 (820)
Hybrid (BVS plus non-BVS)	219/1,189 (18.4%)
IVUS-guided	171/1,184 (14.4%)
OCT-guided	163/1,184 (13.8%)
Tot. Scaffold Length (mm)	32.6±23.0 (1,189)
Aver. Scaffold Diameter (mm)	3.0±0.5 (1,189)
Tot. Scaffold Implanted (n)	1731



*** Residual in-scaffold diameter stenosis < 30%**

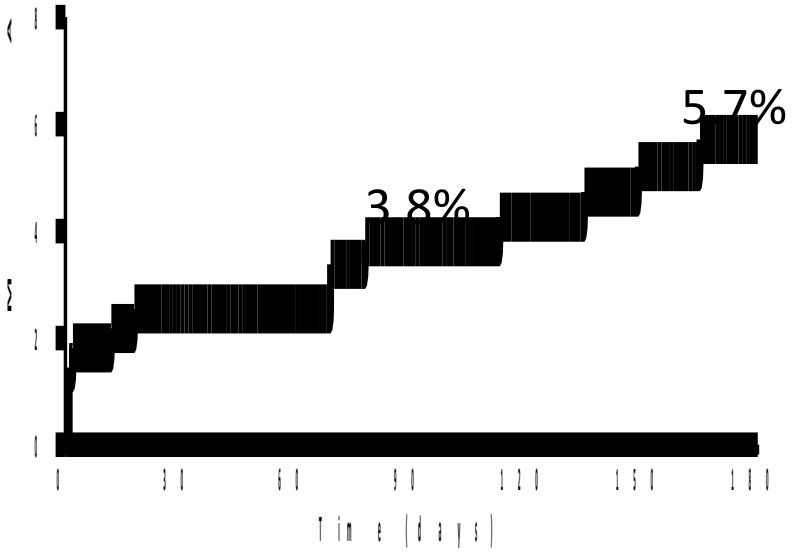
No information on predilatation strategy

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



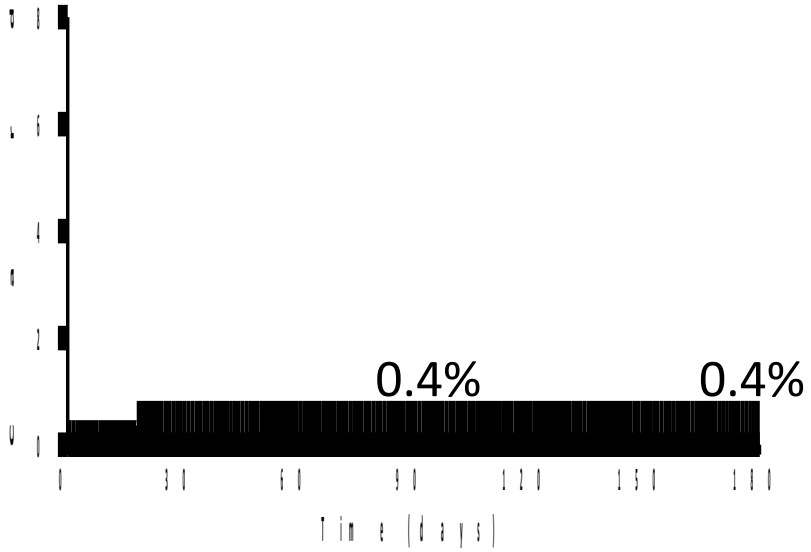
Naganuma T, Latib A, et al. GHOST-EU Investigators

Clinical Outcomes



Number at risk

289 262 240 221 207 200 170

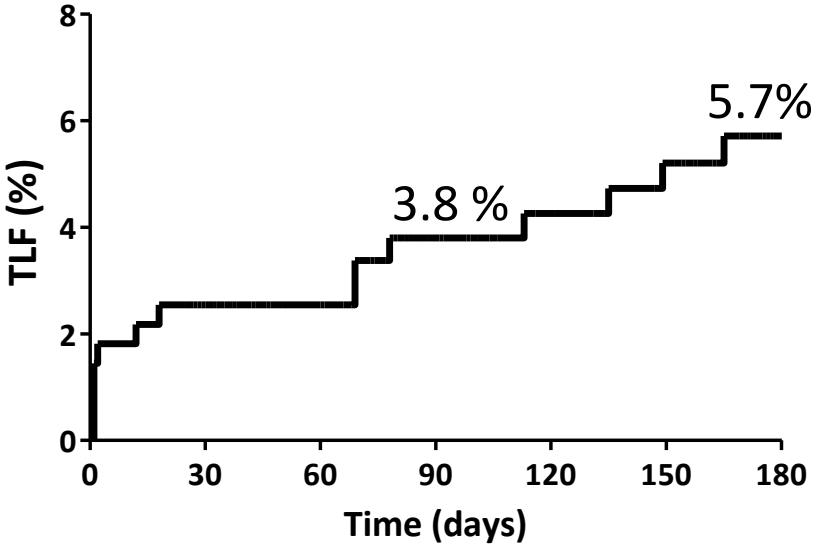


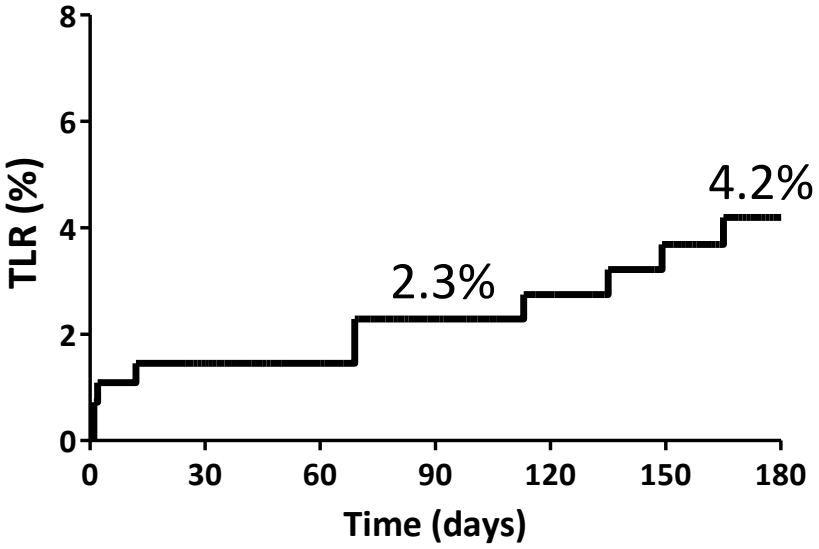
Number at risk

289 268 246 230 217 211 181

MACE includes all-cause death, MI and TVR

Clinical Outcomes





Number at risk

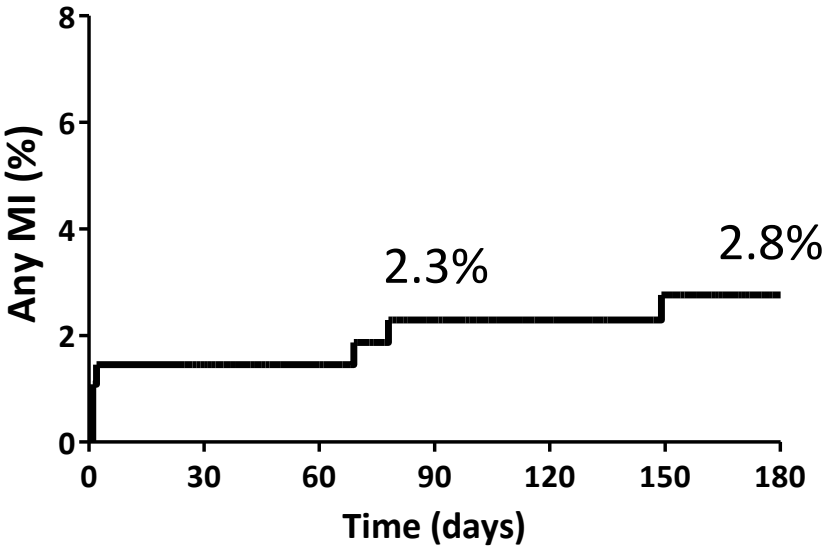
289	262	240	221	207	200	170

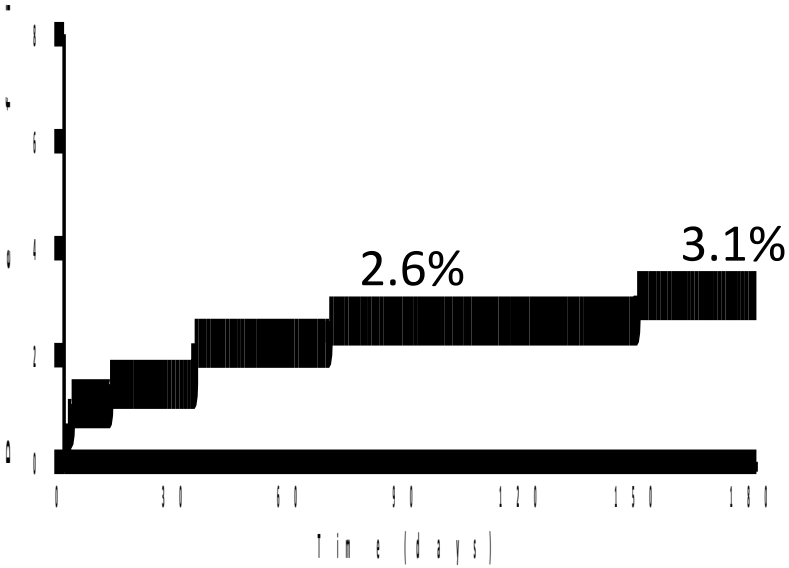
Number at risk

289	265	243	225	211	204	174

TLF includes cardiac death, target vessel MI and clinically driven TLR

Clinical Outcomes





Number at risk

265 243 225 212 206 175

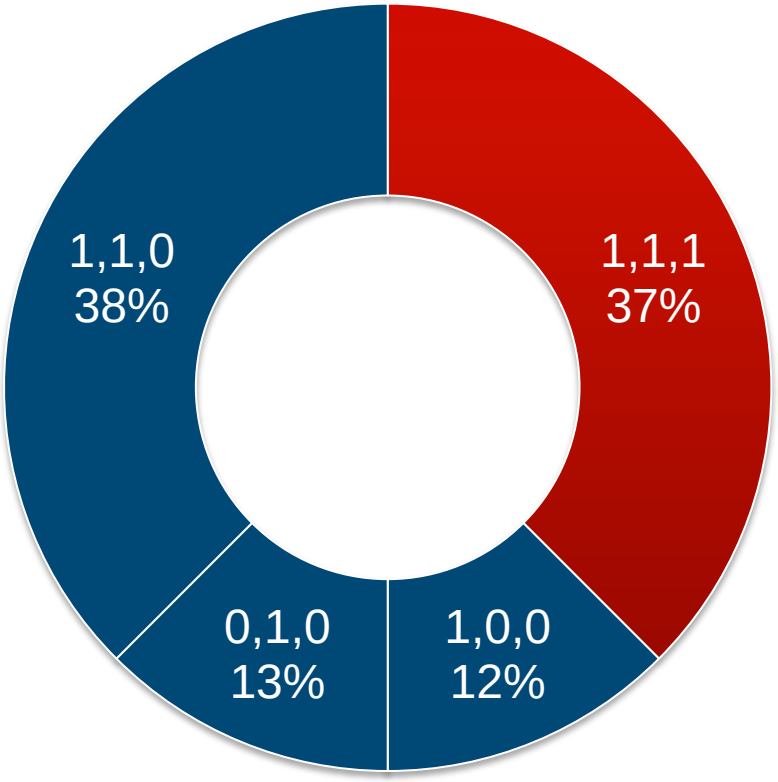
Number at risk

289 264 240 223 210 204 173

Prasugrel or ticagrelor was used in 55 (19.0%) patients.

GHOST-EU : 8/23 ST were in bifurcations

Kaplan-Meier 30-day and 6-mo ST in bifurcations: 1.5% and 3.1%, respectively

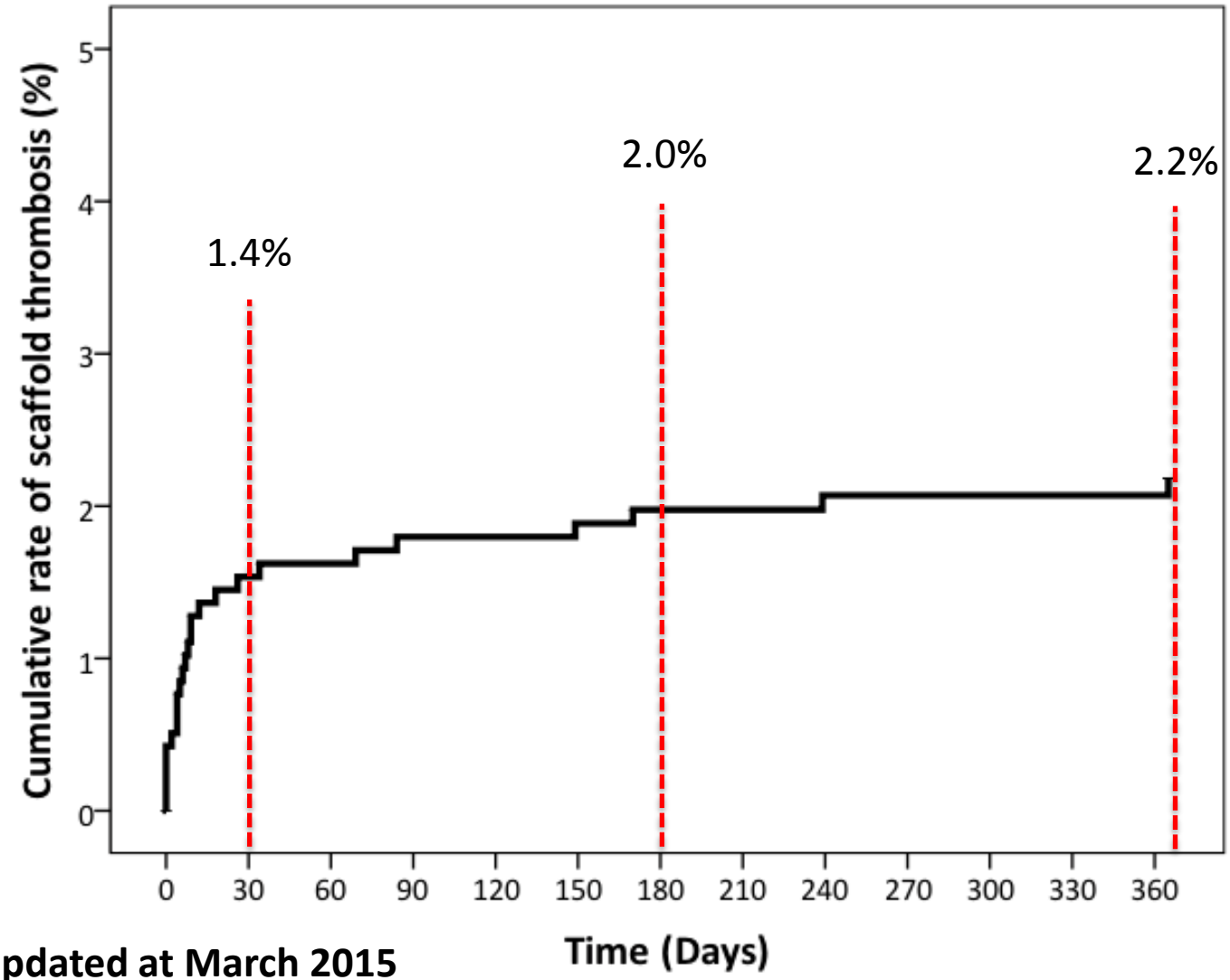


Medina classes in 8 bifurcations ST

Case	Days	ACS	Strategy	PD	KBI	IG	DAPT
#1	149	No	Single	Yes	No	Yes	No
#2	69	No	Single	No	No	No	Yes
#3	2	Yes	Single	No	No	Yes	Yes
#4	0	Yes	Single	No	No	No	Yes
#5	34	Yes	Single	No	No	No	Yes
#6	34	Yes	Double	Yes	No	No	No
#7	0	Yes	Single	No	No	No	Yes
#8	12	Yes	Single	No	No	No	Yes

ACS = acute coronary syndromes; PD = main branch post-dilatation;
IG = intravascular guidance; DAPT = on dual antiplatelet therapy

Scaffold Thrombosis GHOST-EU: 1189 patients



Follow-up updated at March 2015

GHOST | Ferrarotto Population

Patients enrolled N=319; lesions N = 406

From 1/3/2013 to 30/06/2014

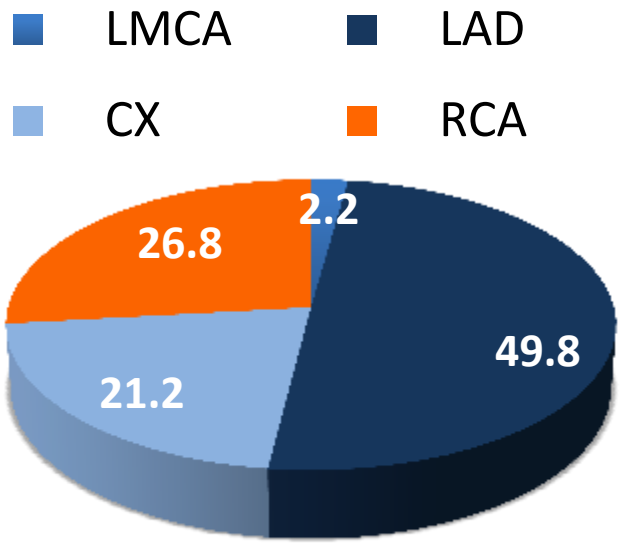
- **6-months FU in 305 patients (95.6%)**
- **1-year FU in 281 patients: 88.1% of overall population and 95% of those eligible (n=296)**

GHOST

Ferrarotto Population Clinical characteristics

Variable	Patient-based (N = 319)
Age, years±SD	60.7 ± 9.6
Male	272 (85.3%)
Diabetes mellitus	**79 (24.8%)**
On insulin	32 (10.0%)
Dyslipidemia	187 (58.6%)
Hypertension	221 (69.3%)
Smoker	117 (36.7%)
Previous PCI	102 (32.0%)
Prior CABG	10 (3.1%)
ACS	**158 (49.5%)**
NSTEMI	**46 (14.4%)**
STEMI	**58 (18.2%)**

Ferrarotto Population
Lesions and procedural characteristics



Lesions B2/C: 51.2%
Bifurcations: 16.7%
CTO: 8.4%

*per patient

Variable	Lesions (N = 406)
Lesion Lenght	21.2 ± 16.8
Lesion length >34 mm	55 (13.5%)
Reference vessel diameter (mm)	2.9 ± 0.5
Total scaffold length (mm)	32.8 ± 21.6
Average scaffold diameter (mm)	3.1 ± 0.4
Average of scaffolds implanted (n)	1.9 ± 1.2*
Post-dilatation	**289 (71.2%)**
Post-dilation balloon pressure, atm	**16.6±4.3**
Scaffold implantation pressure, atm	**13.5±3.4**
Overlapping	132 (32.5%)
Optical coherence tomography use	80 (25.1)*
Intravascular ultrasound use	37 (11.6)*

GHOST

Ferrarotto Population
1-year outcomes

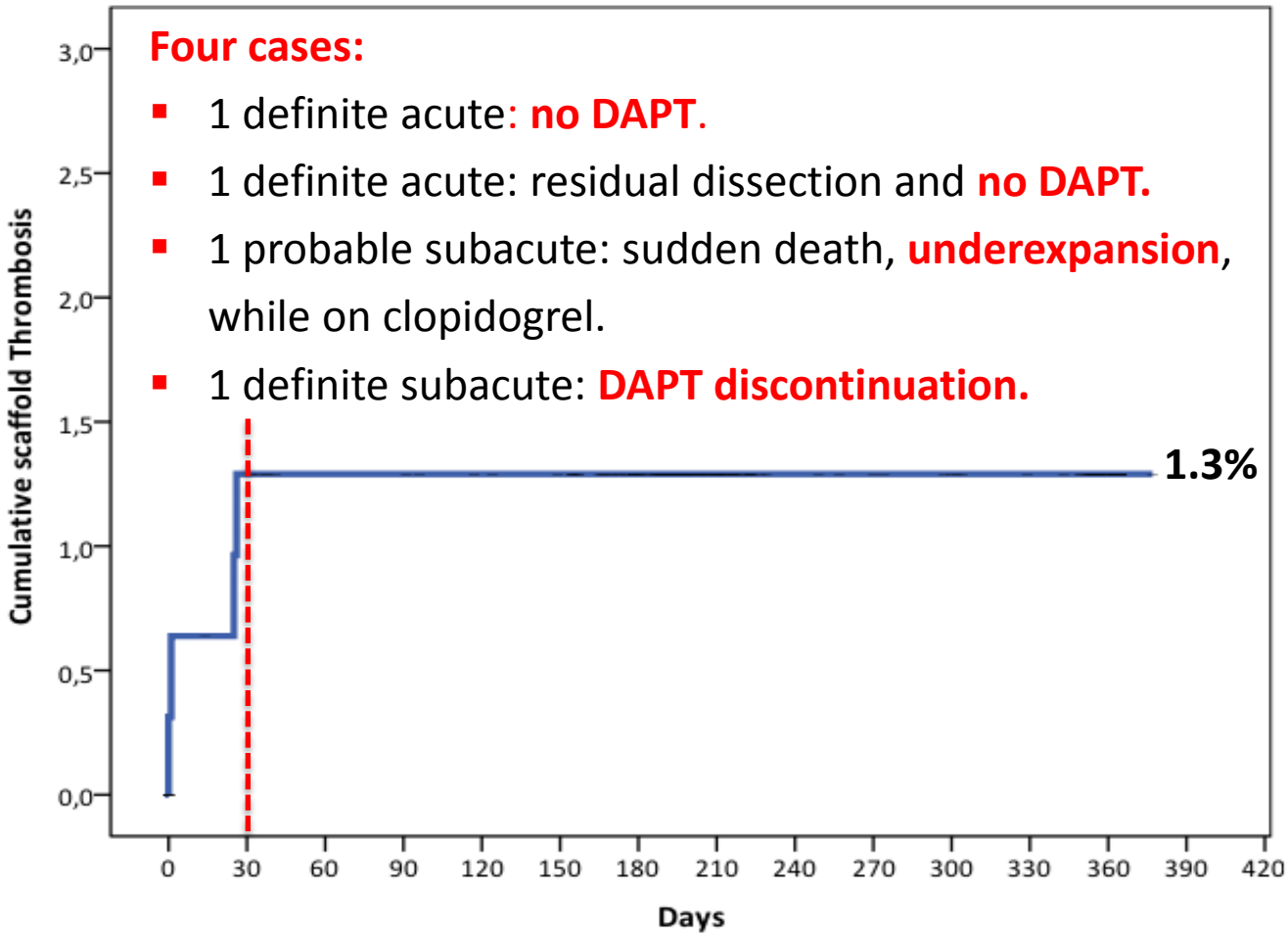
TLF (cardiac death, target-vessel MI, or clinically-driven TLR)	5.2%
TVF (cardiac death, target-vessel MI, or clinically-driven TVR)	5.6%
All Death	1.7%
Non-Cardiac Death	1.0%
Cardiac Death	0.3%
Any MI (all target vessel)	1.3%
TVR	5.3%
TLR	4.9%

Event rates are expressed as Kaplan Meier estimates.

Ferrarotto Population
1-year scaffold thrombosis

Four cases:

- 1 definite acute**: no DAPT**.
- 1 definite acute: residual dissection and **no DAPT.**
- 1 probable subacute: sudden death, **underexpansion**, while on clopidogrel.
- 1 definite subacute: **DAPT discontinuation.**



Ferrarotto Population
Lesions characteristics

Variable	Absorb II inclusion Patient N = 89 Lesions N = 110	Absorb II exclusion Patient N = 230 Lesions N = 296	P values
Lesion type			0.01
A	20.0%	11.8%	
B1	41.8%	32.1%	
B2	17.3%	22.6%	
C	20.9%	33.4%	
Bifurcation	**10.9%***	**18.9%**	0.07
CTO	**-**	**11.5%**	
Lesion Length	16.4 ± 7.9	22.9 ± 18.7	<0.0001
Lesion length >34 mm	**5.5%**	**16.6%**	**0.006**
Reference vessel diameter (mm)	2.9 ± 0.5	2.9 ± 0.5	0.32

*side branch <2 mm

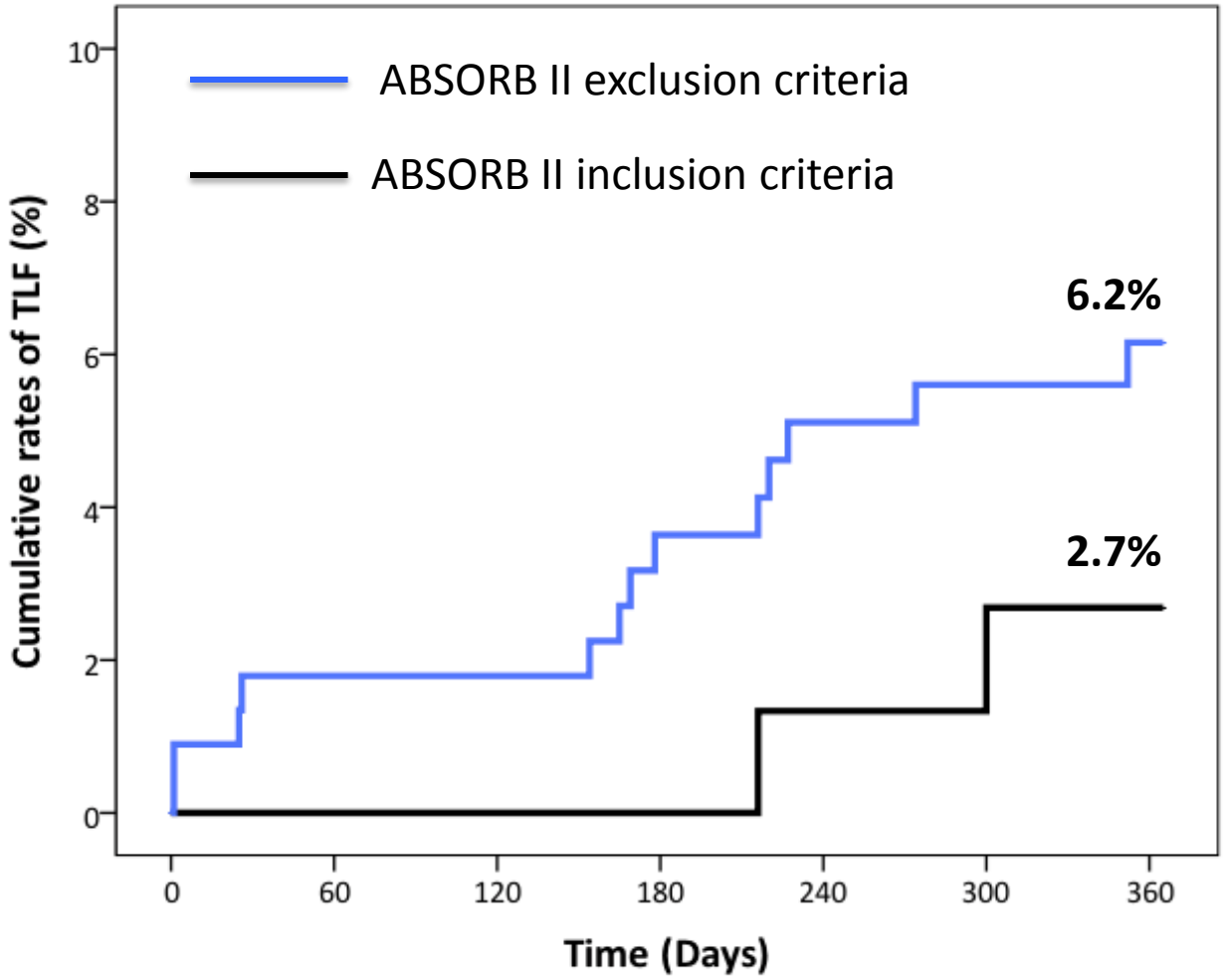
Ferrarotto Population
Procedural characteristics

Variable	Absorb II inclusion Patient N = 89 Lesions N = 110	Absorb II exclusion Patient N = 230 Lesions N = 296	P values
Total scaffold length (mm)	25.8 ± 11.5	35.3 ± 23.8	<0.001
Average scaffold diameter (mm)	3.1 ± 0.4	3.2 ± 0.4	0.11
Avarage of scaffolds implanted (n)	1.5 ± 0.7 *	2.0 ± 1.3*	<0.001
Post-dilatation	**59.1%**	**75.7%**	**0.002**
Overlapping	21.5%	36.5%	0.005
Optical coherence tomography use	9.0%*	31.3%*	<0.001
Intravascular ultrasound use	11.2%*	11.7%*	1.00

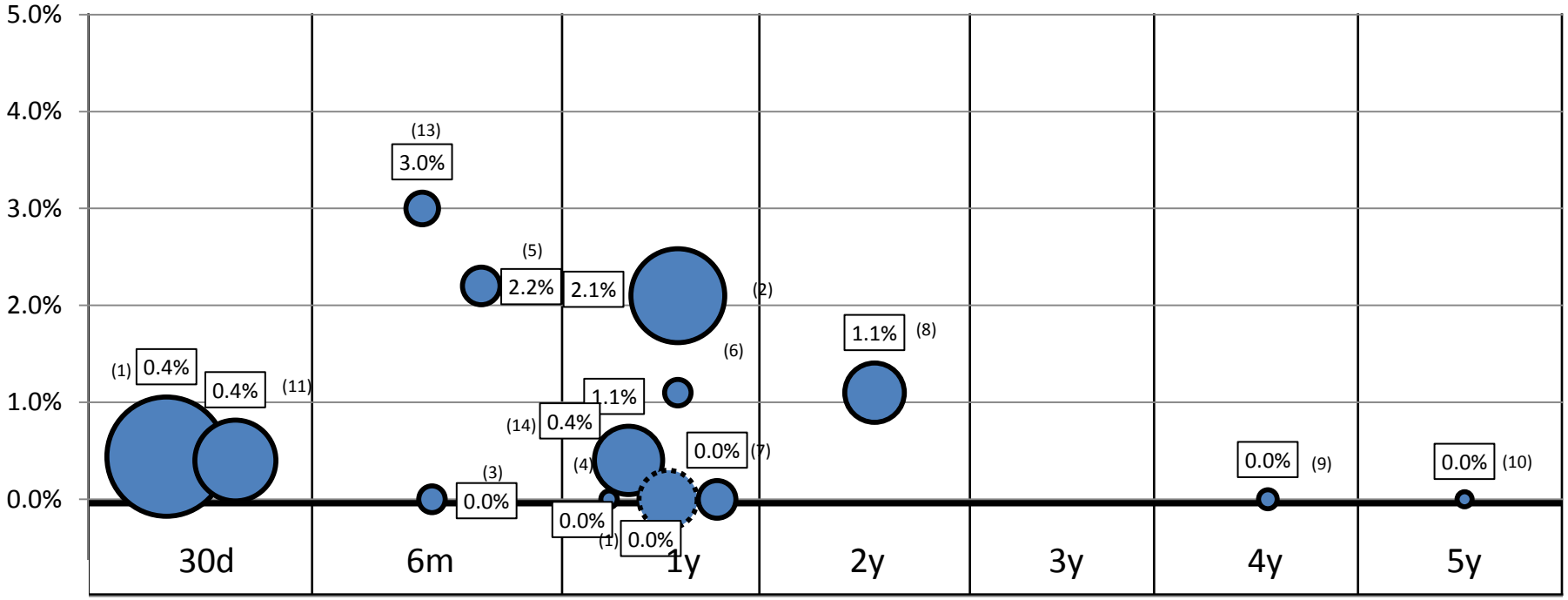
*per patient

GHOST

Ferrarotto Population
1-year TLF



ABSORB Data
Scaffold Thrombosis (Longest Available FU)



(1) ABSORB FIRST: **All Comers (@AsiaPCR2015)**

(2) GHOST-EU: **All Comers** (@JIM2015)

(3) Dr. Costopoulos on CCI: **All Comers (in CCI2014)**

(4) CTO (Dr. Serra): **CTO (on Eurointervention2014)**

(5) ABSORB EXPAND: **All Comers (@EuroPCR2014)**

(6) POLAR ACS: **ACS (@ EuroPC2014)**

(7) ASSURE: **All Comers (on Eurointervention2014)**

(8) ABSORB EXTEND: **selected (@ EuroPCR2014)**

(9) ABSORB Cohort B: **simple (@ EuroPCR2014)**

(10) ABSORB Cohort A: **simple @ EuroPCR2011)**

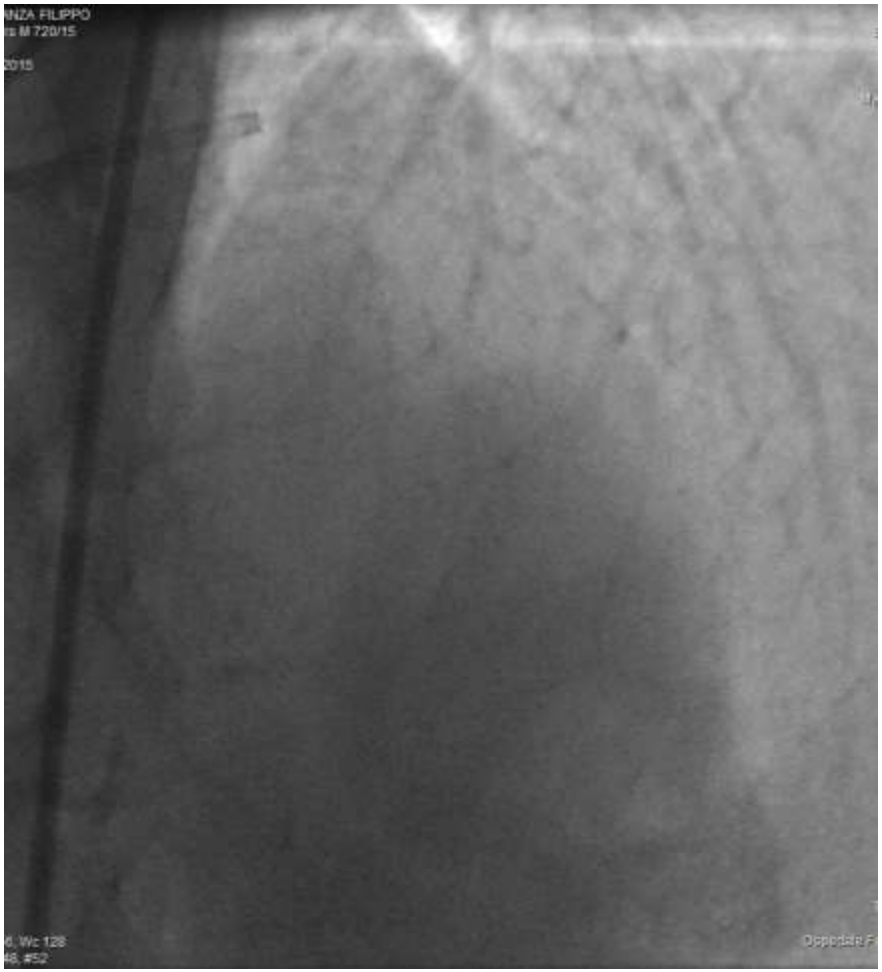
(11) GABI-R: **All Comers (@Germand congress2014)**

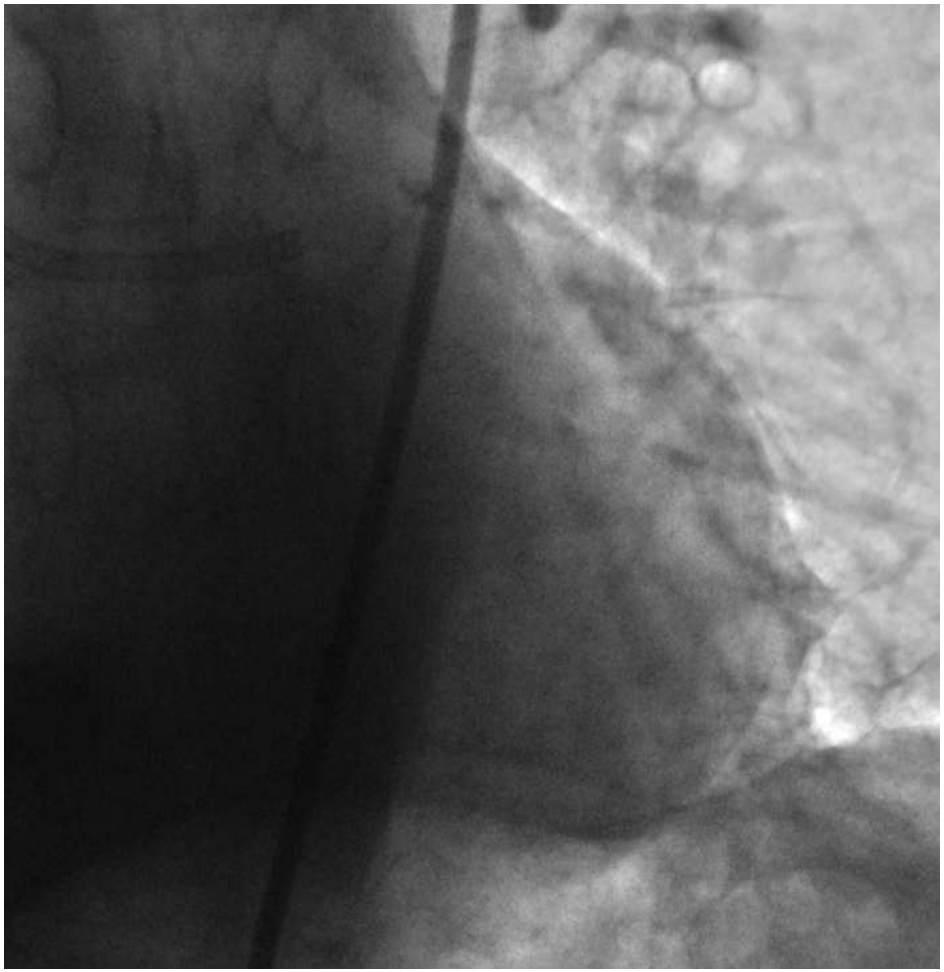
(12) ABSORB II**: selected (in Lancet 2014)**

(13) AMC Registry**: AC (in Eurointervention 2014)**

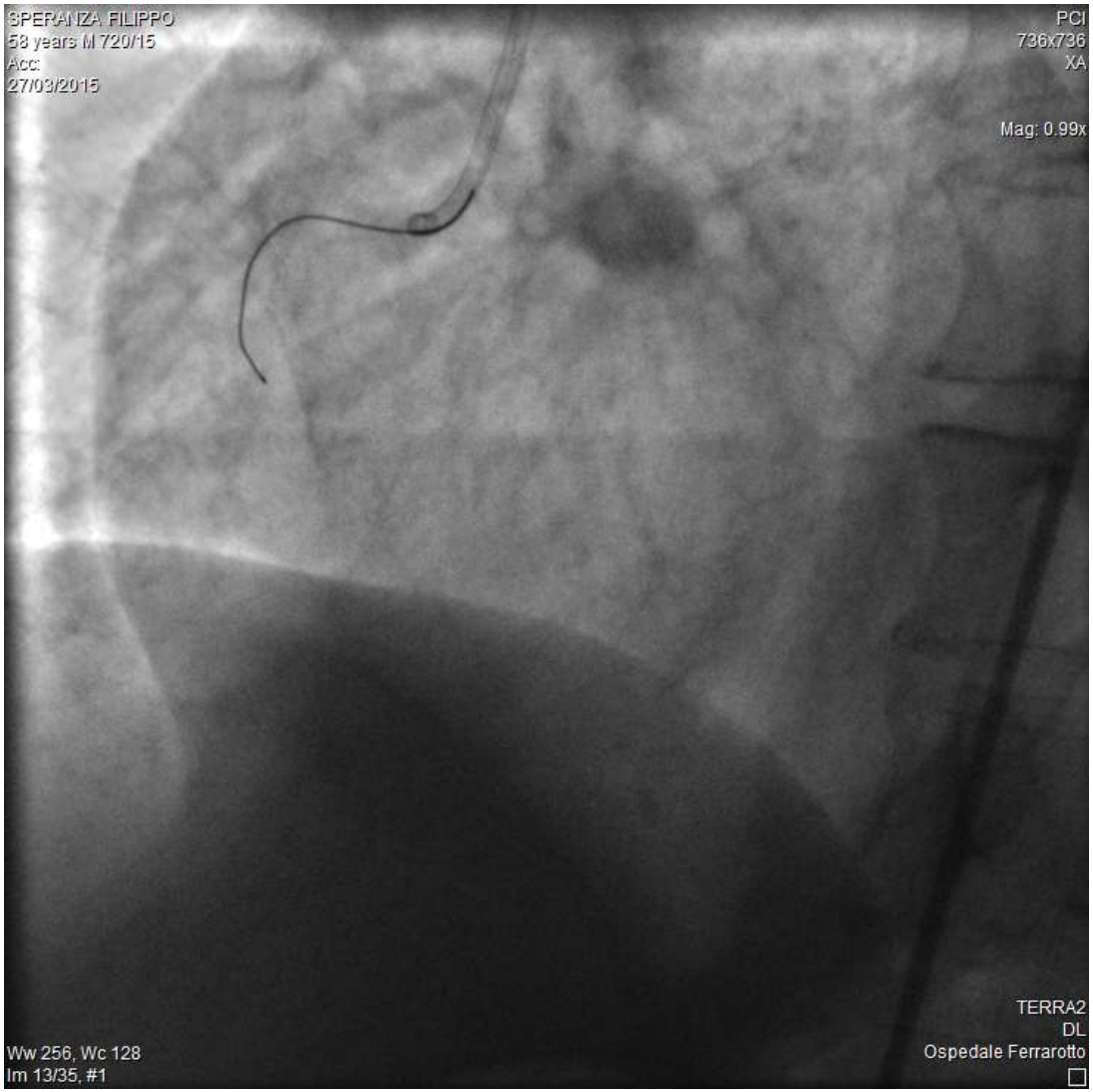
(14) Polish BVS registry: **all comers (@NFIC2014)**

Left coronary angiography

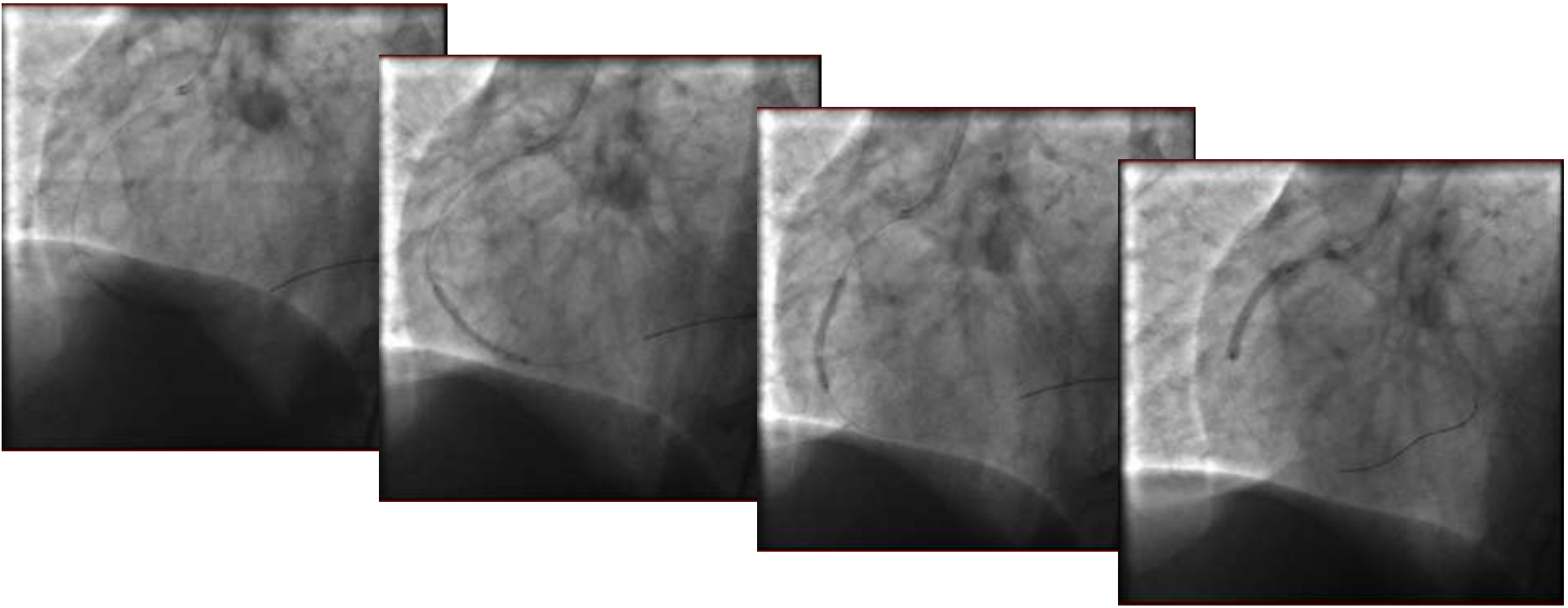




Right coronary angiography

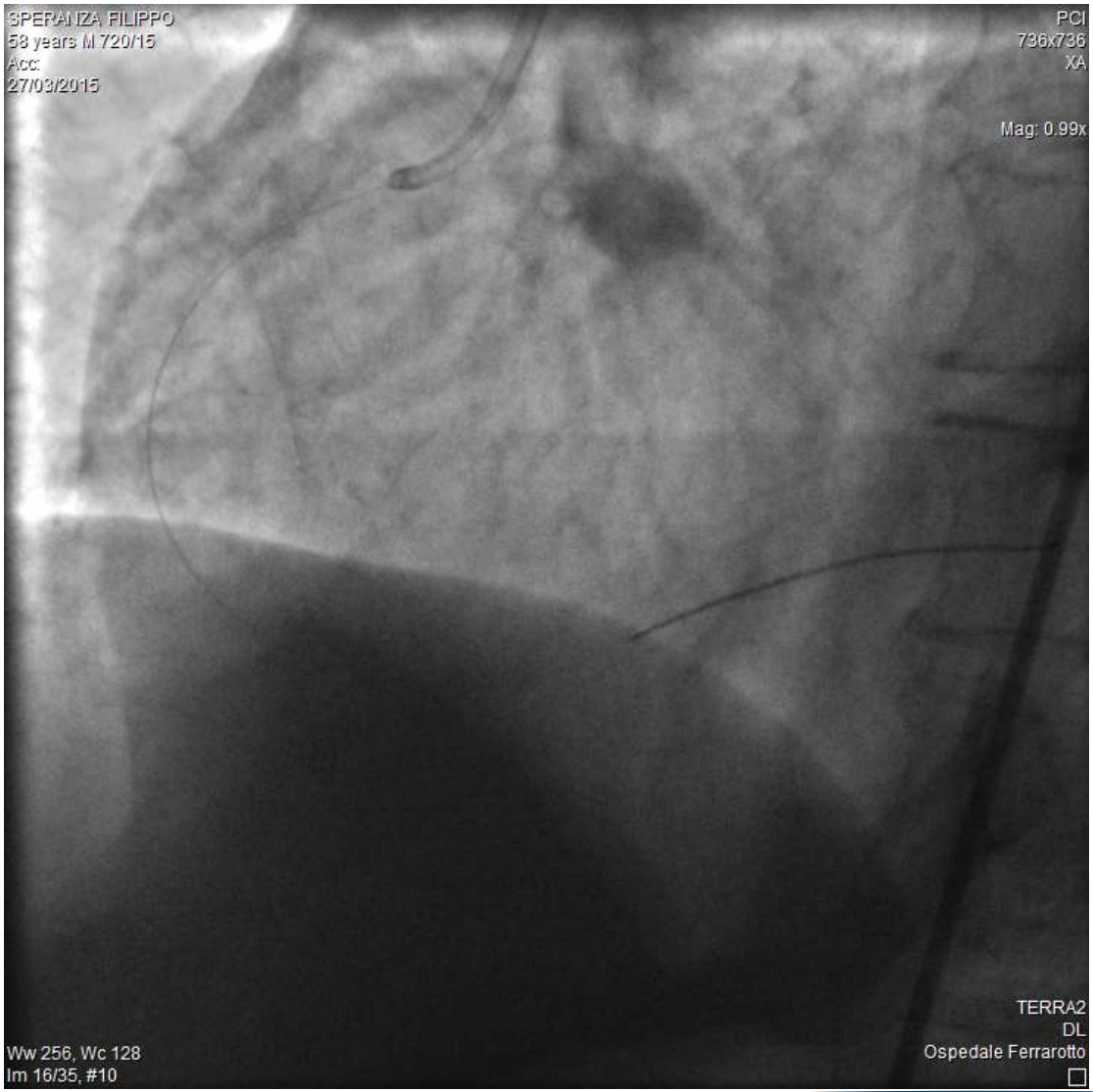


PCI on CDX: pre-dilatation



Pre-dilatation was performed using 2.75 s.c balloon and 3.0 N.C. balloon

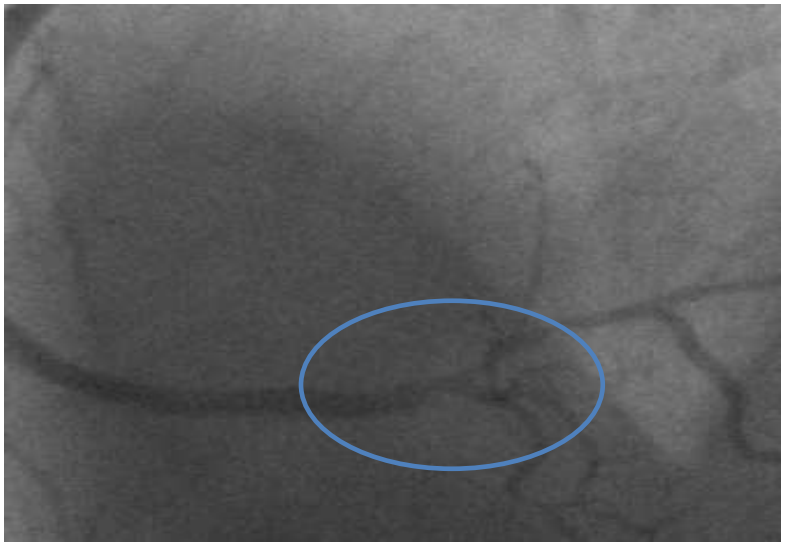
PCI on CDx after pre-dilatation

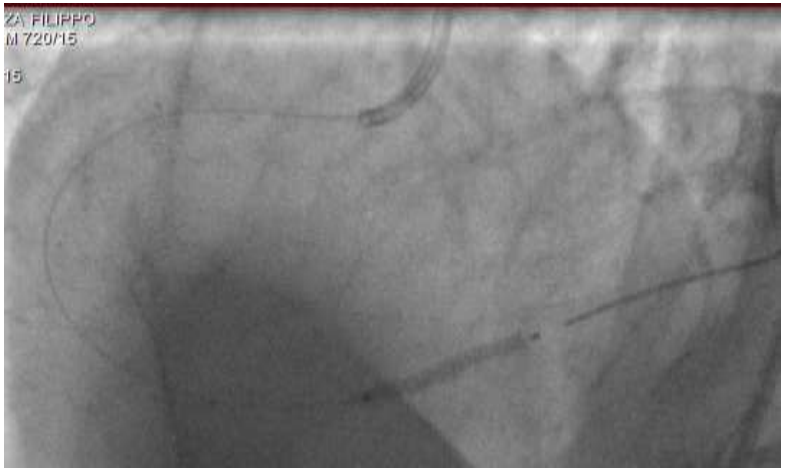


PCI on CDX: BVS implantation

PCI was performed with implantation of 4 BVS : distal to proximal were 2.5x28 mm, 3.0x28 mm, 3.5x28 mm and 3.5x12 mm. Post-dilatation was performed using 3.0/30 N.C balloon

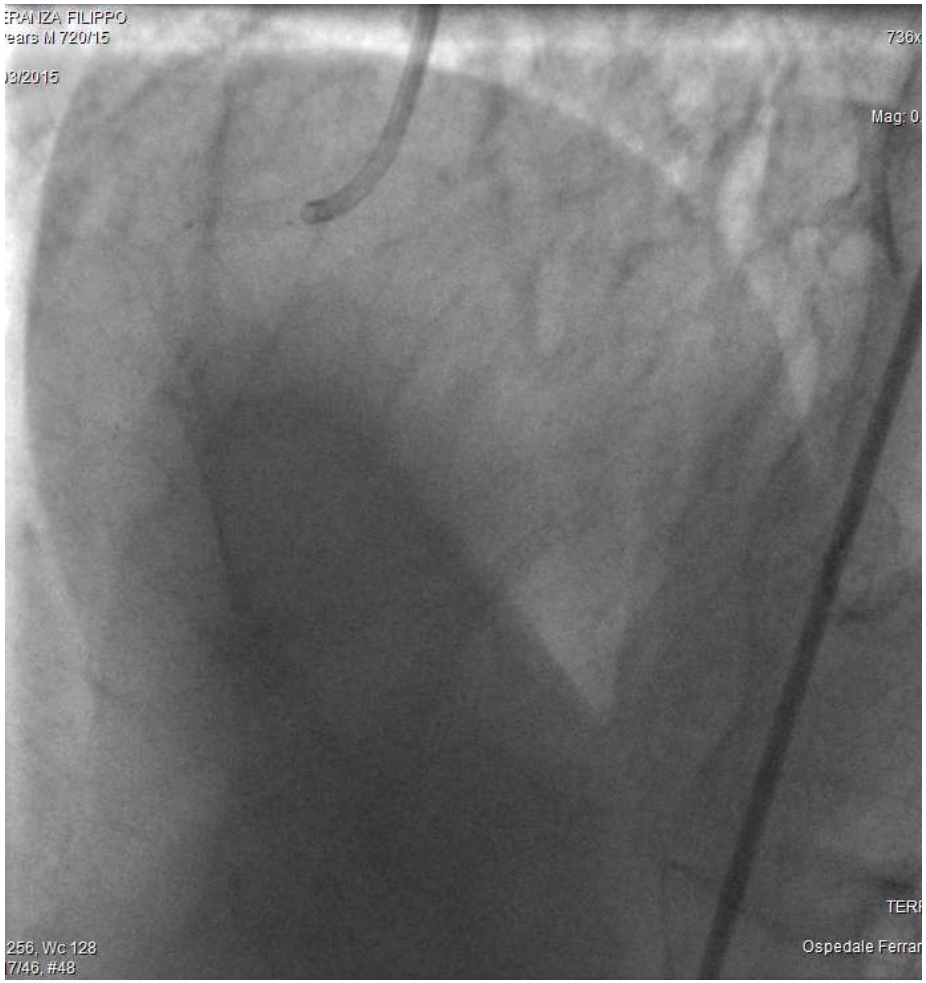
PCI on CDX: after BVS implantation

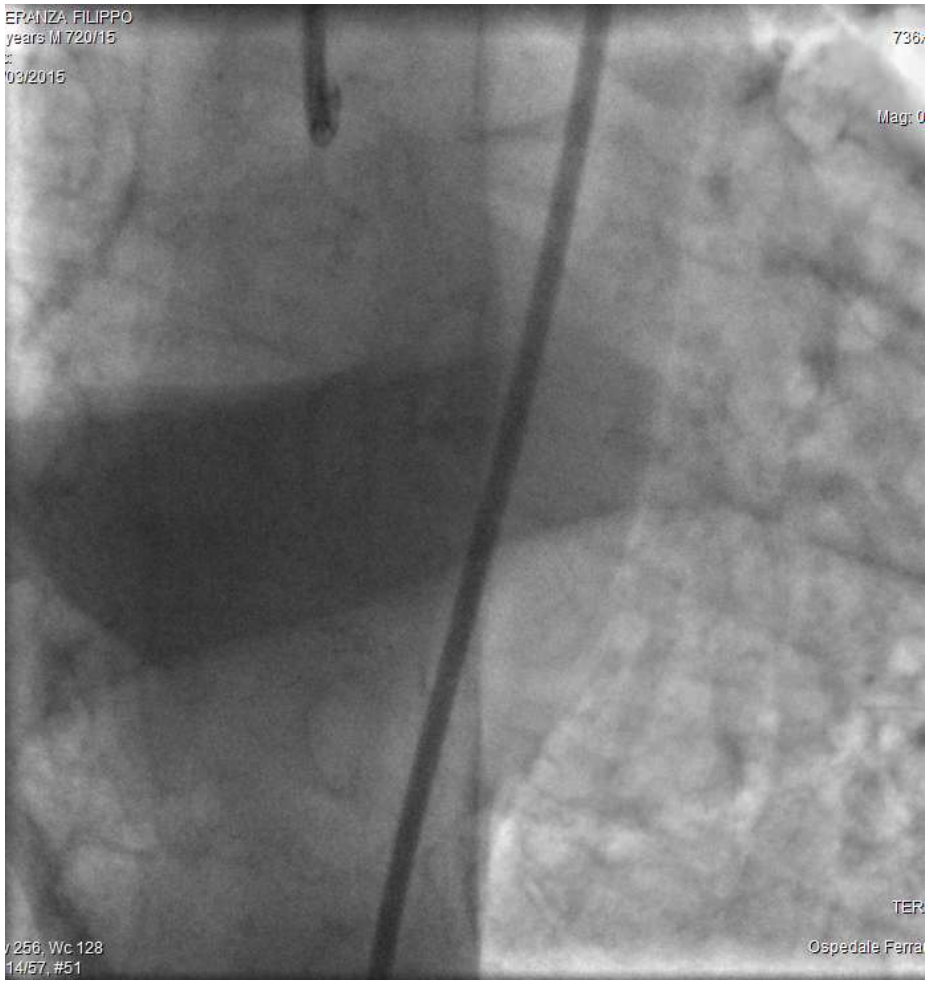




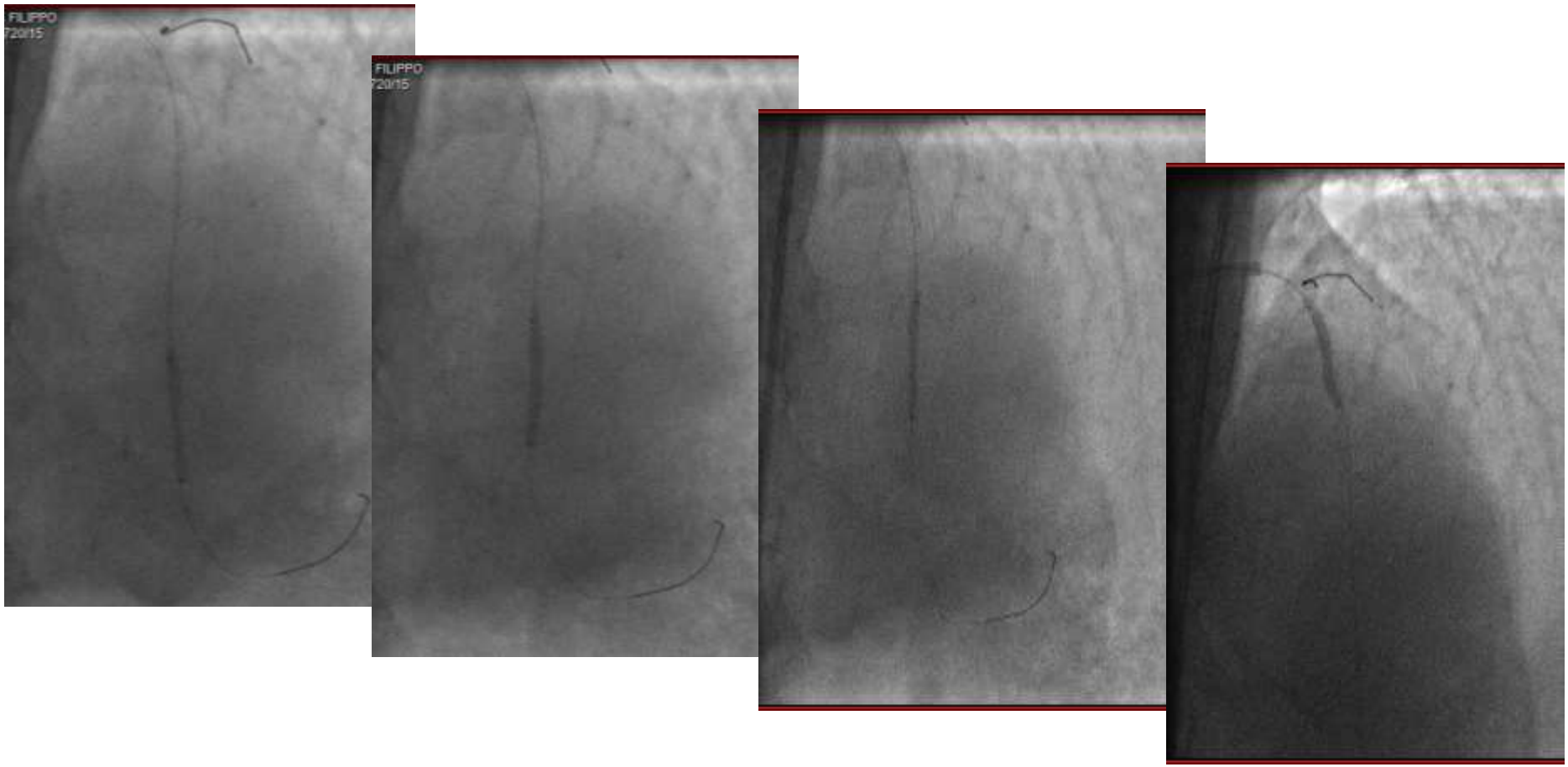
Presence of distal edge dissection treated with DES 2.5/18 mm

PCI on CDx: final result



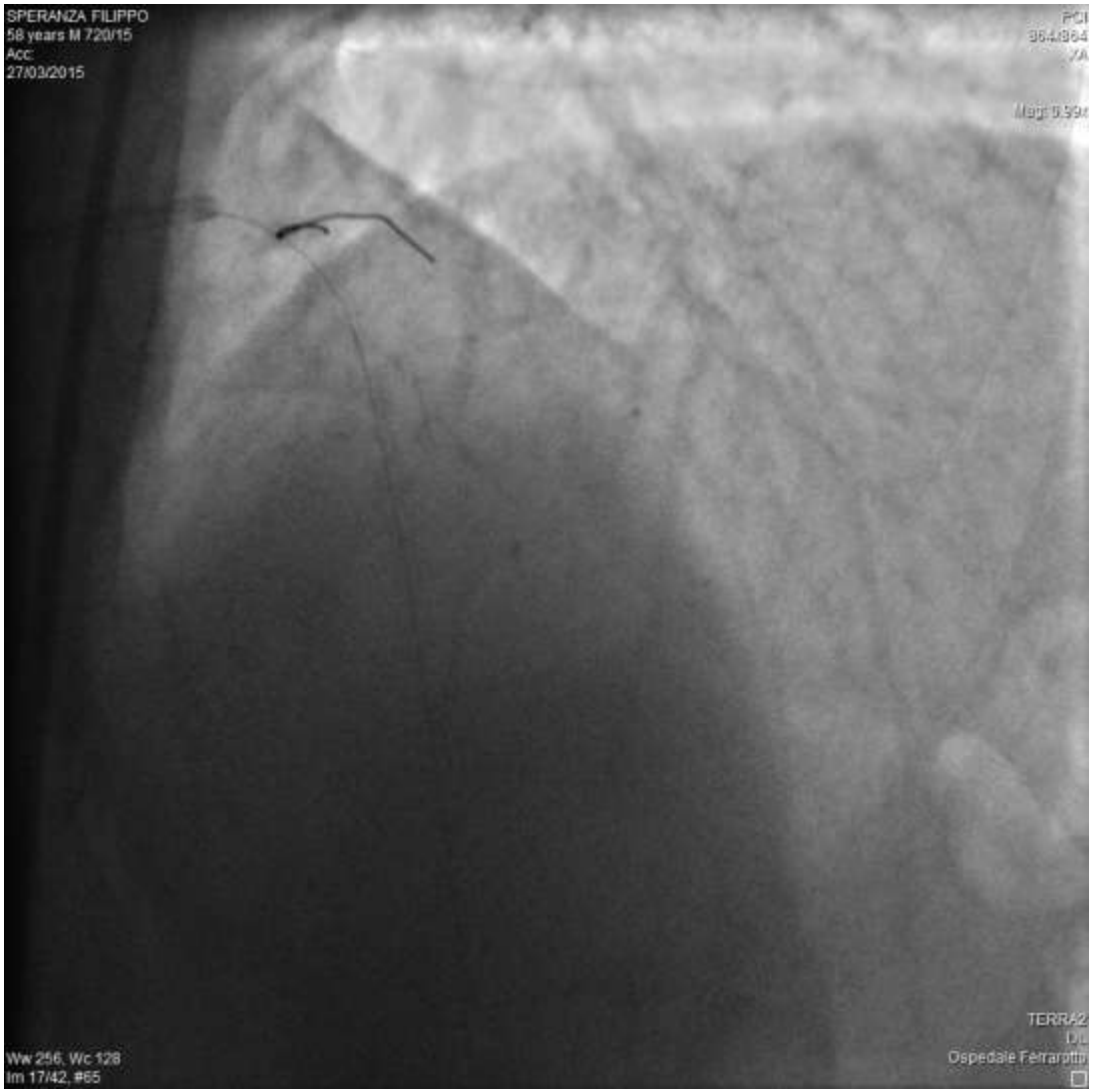


PCI on LAD: pre-dilatation



Pre-dilatation was performed using 2.75-2.25/25 mm conic balloon and 3.0/30 mm s.c. balloon

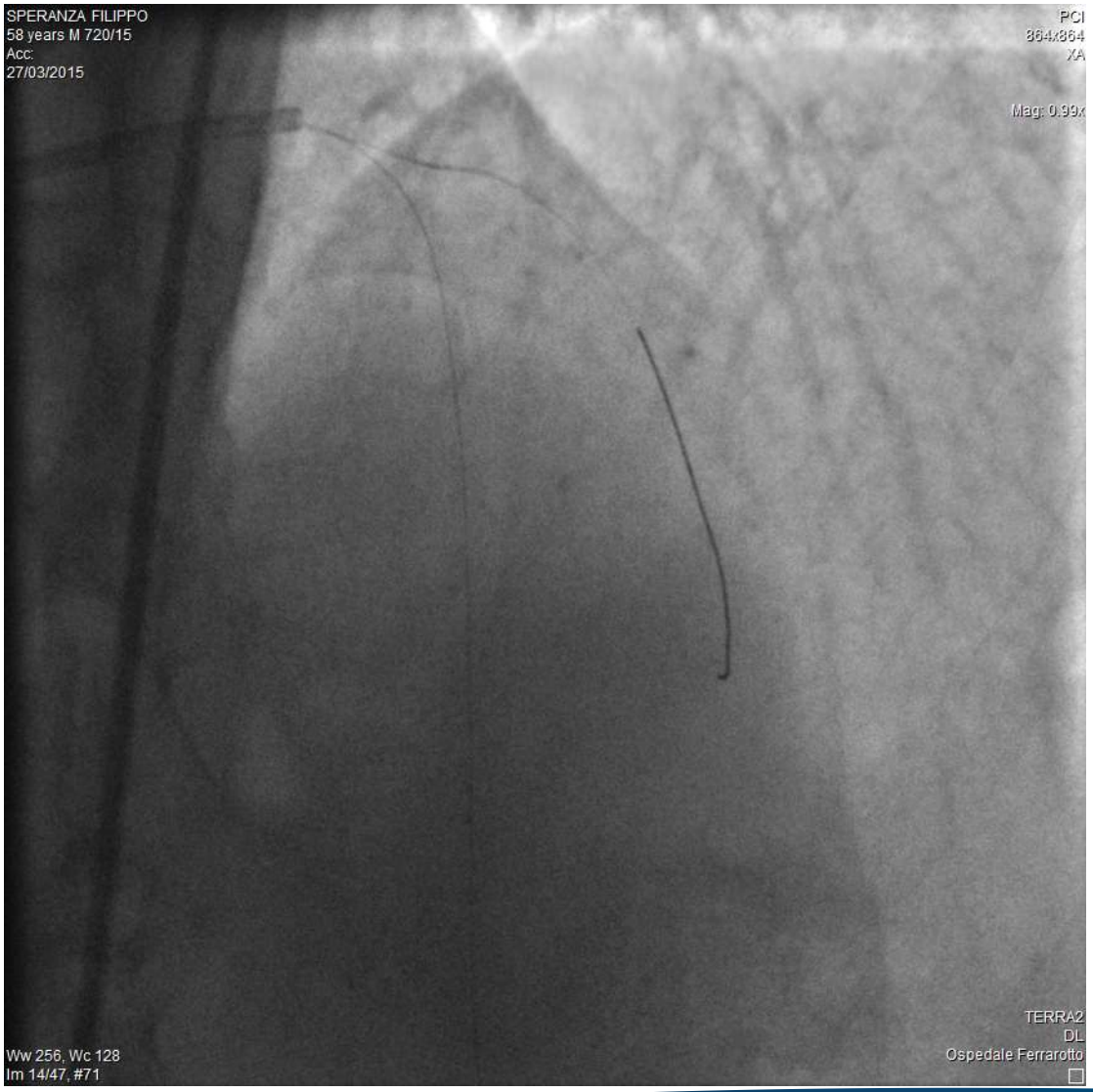
PCI on LAD after pre-dilatation



PCI on LAD: cutting balloon

Multiple dilatations with cutting balloon 2.5/15 mm

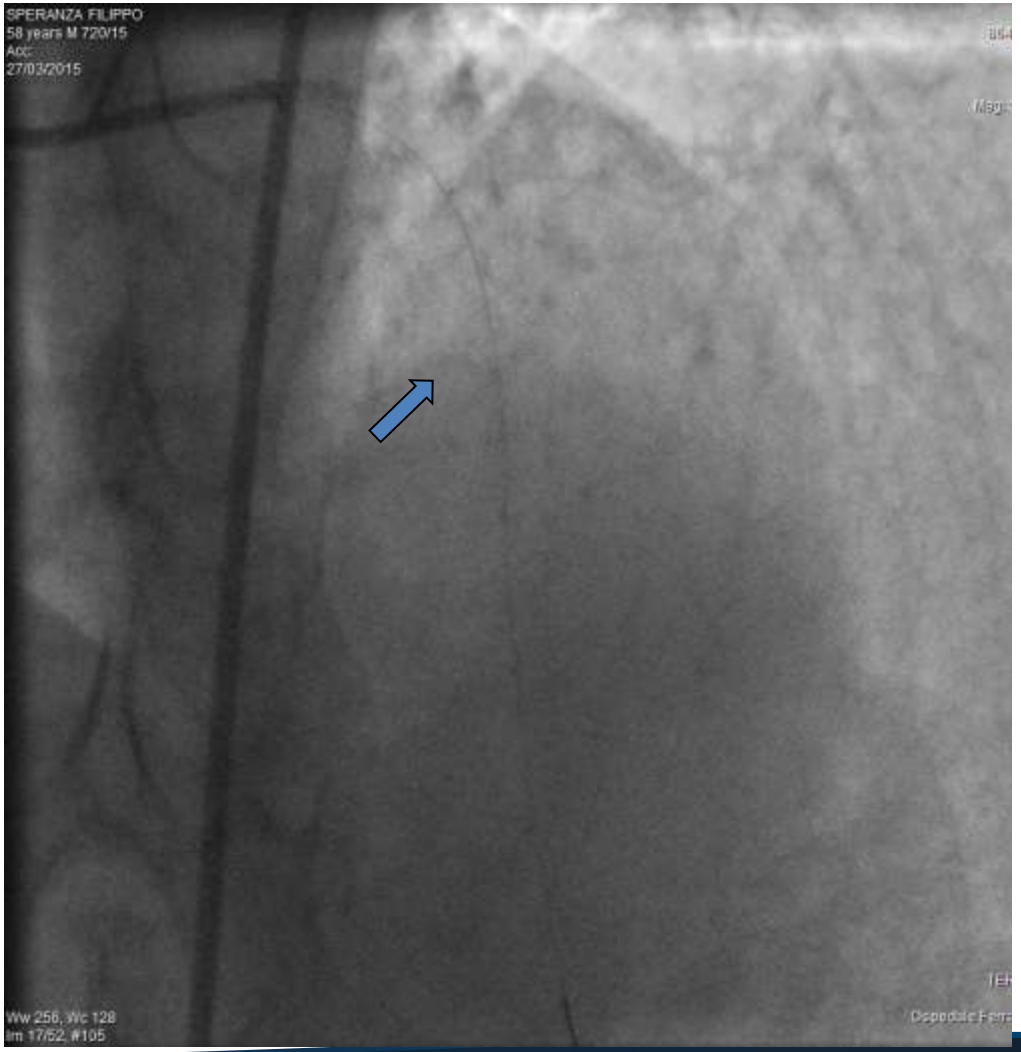
PCI on LAD: after cutting balloon



PCI on LAD: BVS implantation

BRS 2.5/28 - 2.5/28 - 3.0/28 at high pressure

After BVS, angiogram showed luminal irregularities suggestive of intramural hematoma

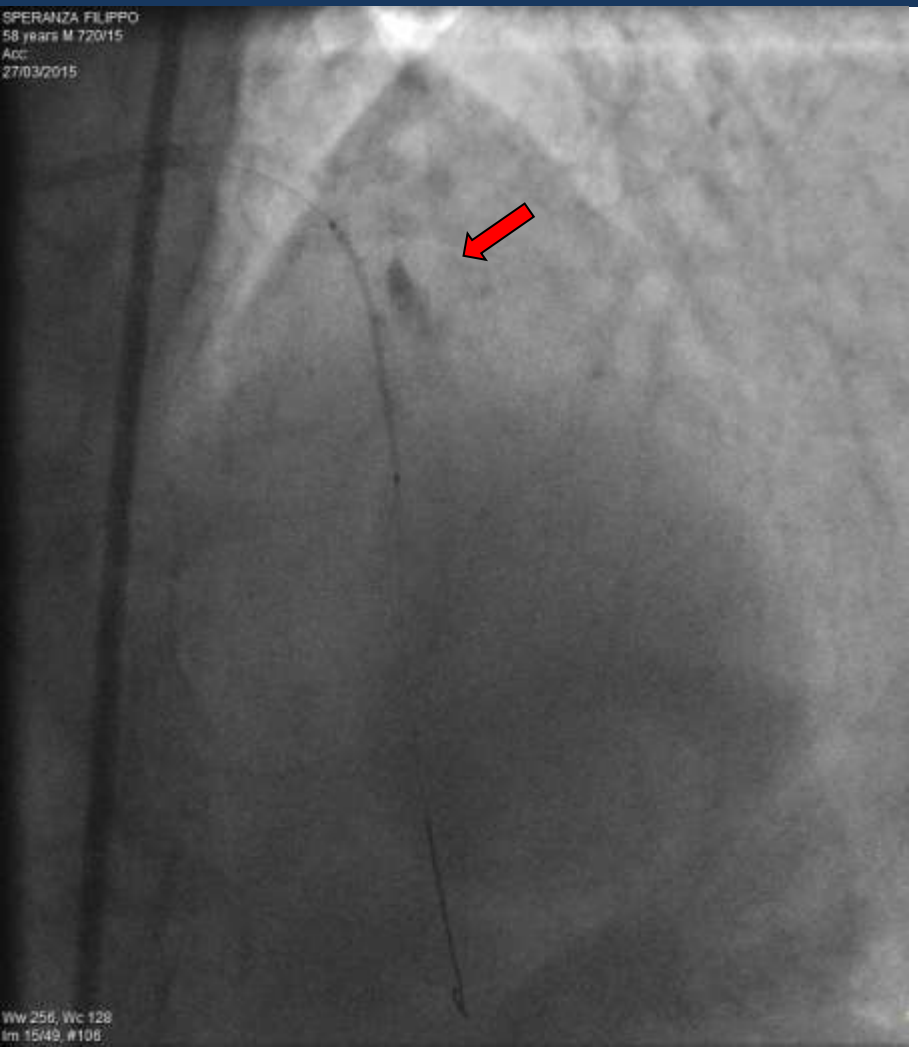


PCI on LM

Pre-dilatation with s.c. balloon 3.5/12 mm

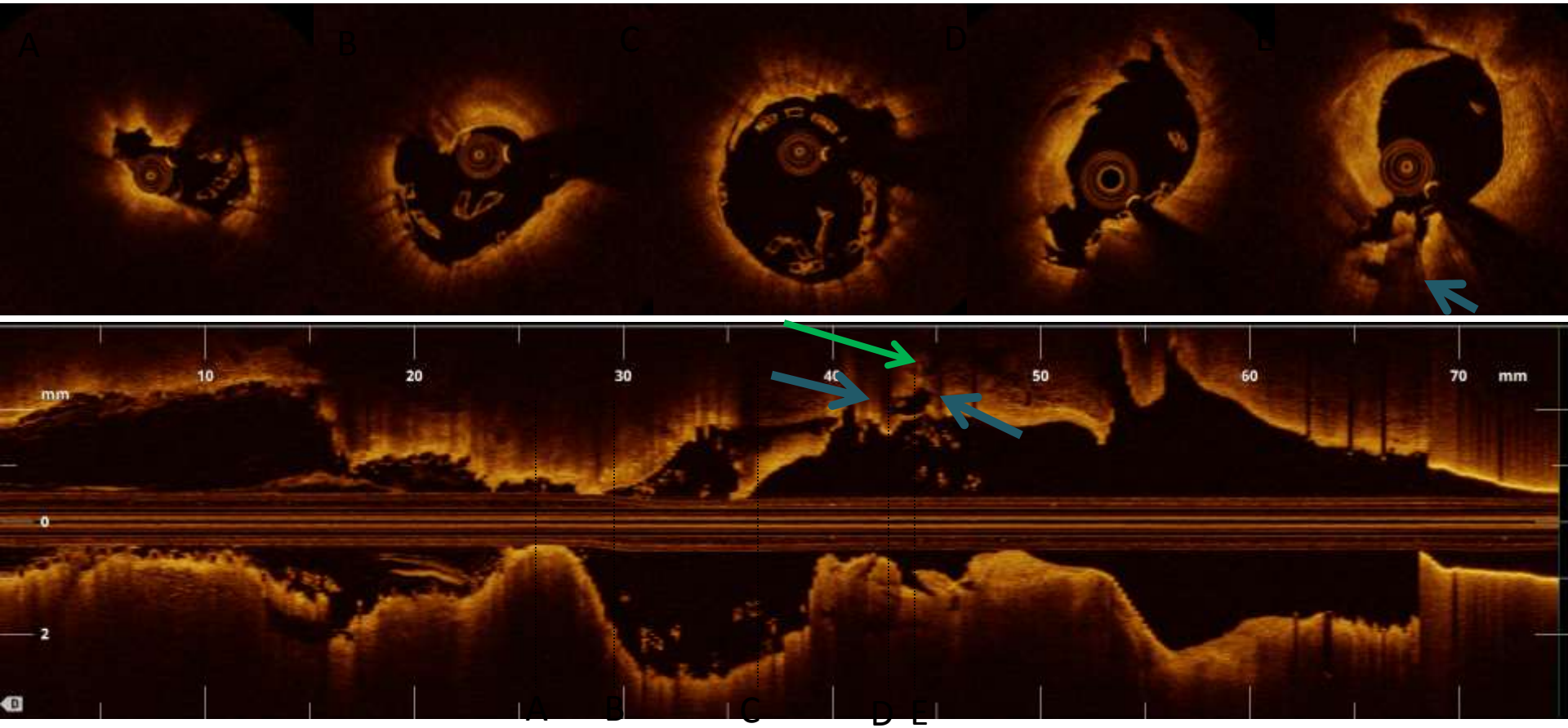
DES 4.0/12 mm

PCI on LM: result

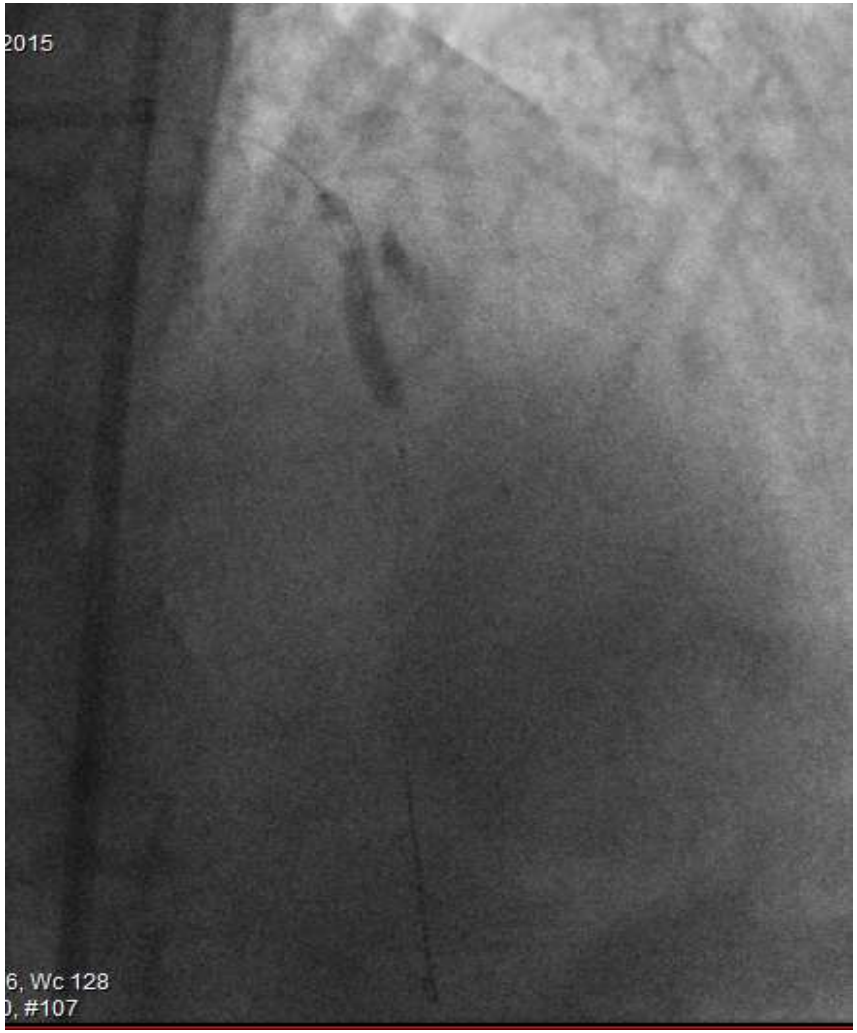


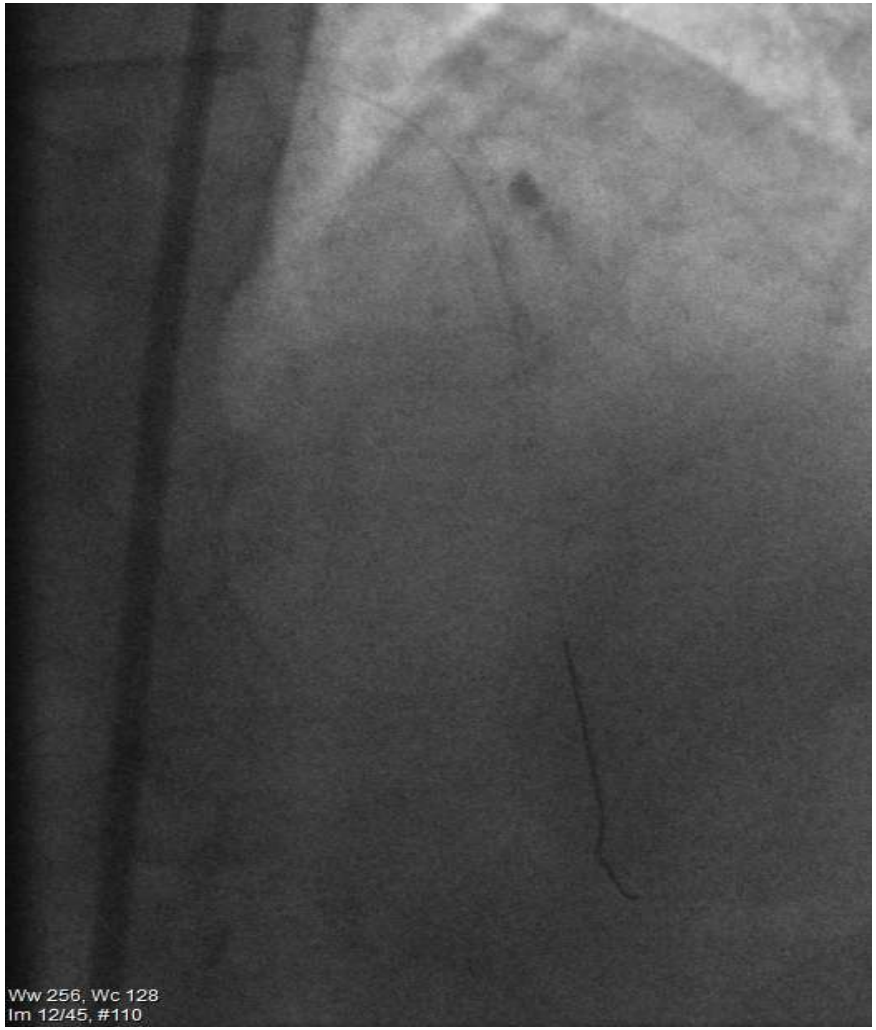
Angiogram showed contrast extravascular effusion suggestive of coronary perforation

OCT after 4 BVS impantation 2.5-3.0-3.5



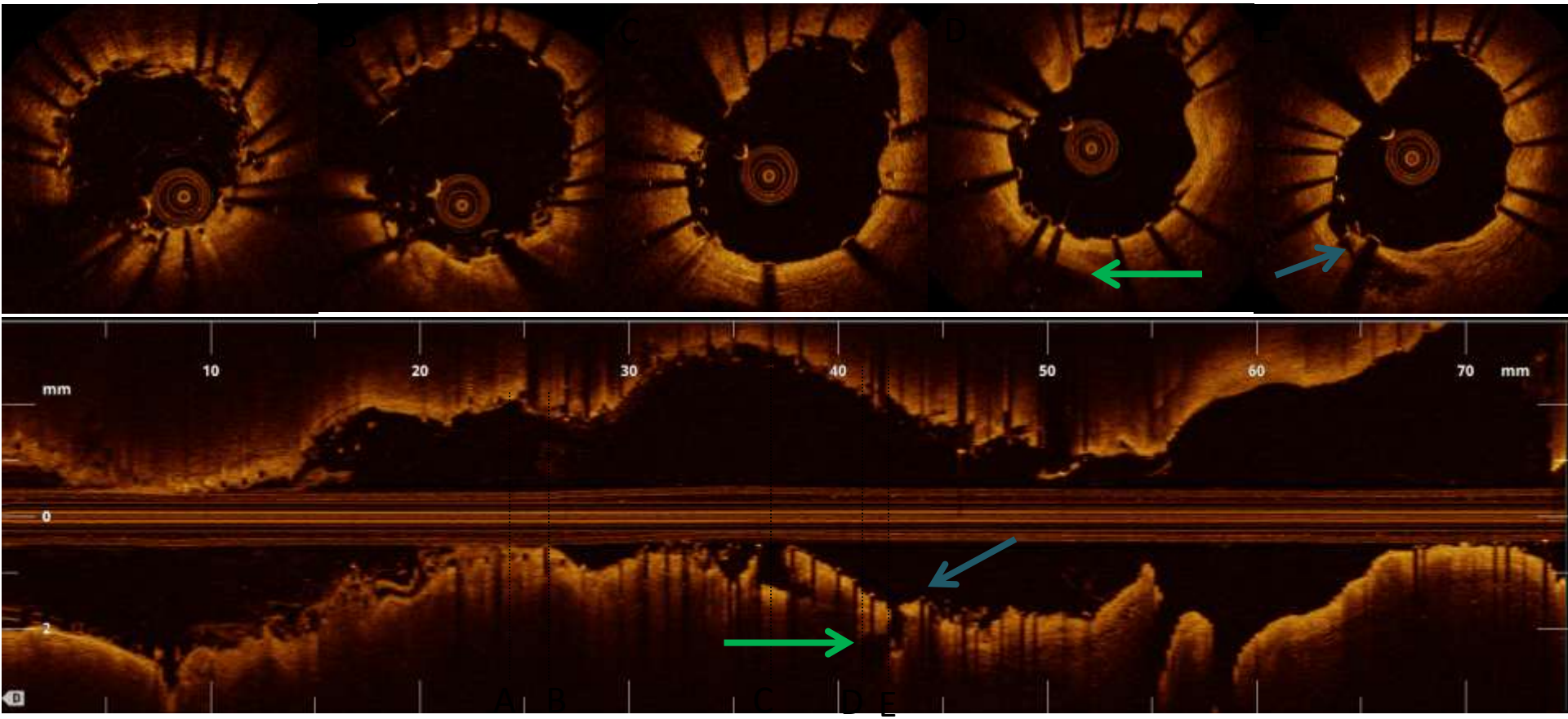
DES on LAD





OCT showed that perforation was due to huge dissection, so we decided to use a normal DES (and not a covered stent) in order to close the «dissection tunnel».

OCT after DES implantation



Conclusions

- Complex lesions can benefit the most from BRS.
- The GHOST-EU 1-year results showed good efficacy results.
- In the GHOST-EU there was an increase in 6-month ST, suggesting the impact of lesion selection and suboptimal implantation technique.
- The key message from the GHOST-EU is that an optimal implantation technique is of importance for BRS safety, especially when treating complex lesions.
- There are “complex” and “complex” lesions. It is important to define who is the best candidate for BRS and who should not be treated with BRS. Severely calcified lesions could not be godd candidate for BRS
- More data are needed to better define the safety of BRS on complex settings treated with standardized technique.