The Efficacy and Safety of Everolimus-Eluting Stent in "Real World" Patients

Preliminary data From AMC registry

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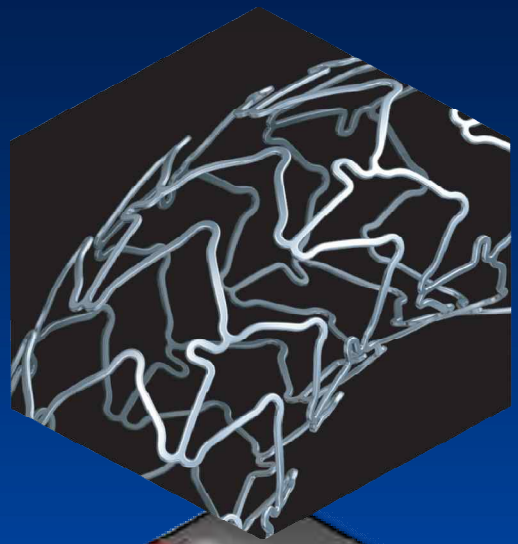
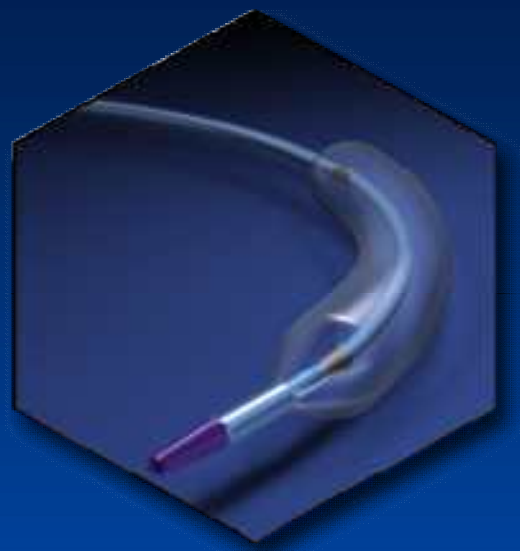
What's New ?

Xience V

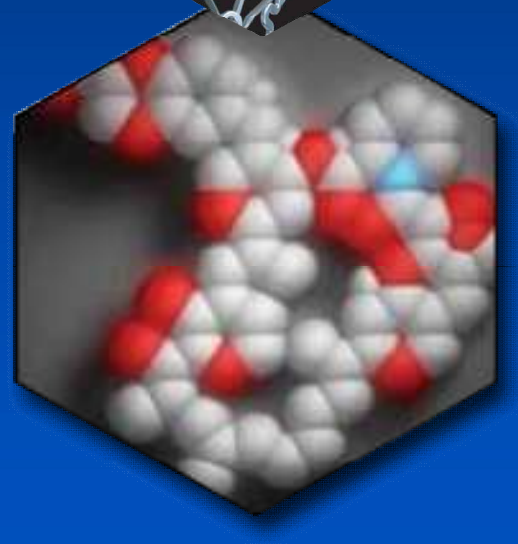
Cobalt Chromium Thinner Strut

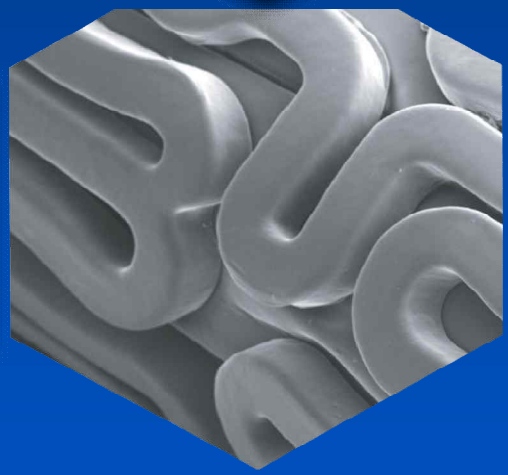




Low System Profile

Everolimus





Fluorinated Copolymer

Background

- Everolimus-eluting stent (EES) is a second-generation drug-eluting stent comprising 3 components: (1) a low-profile, flexible cobalt chromium stent; (2) a biocompatible fluoropolymer; and (3) everolimus, an antiproliferative drug.

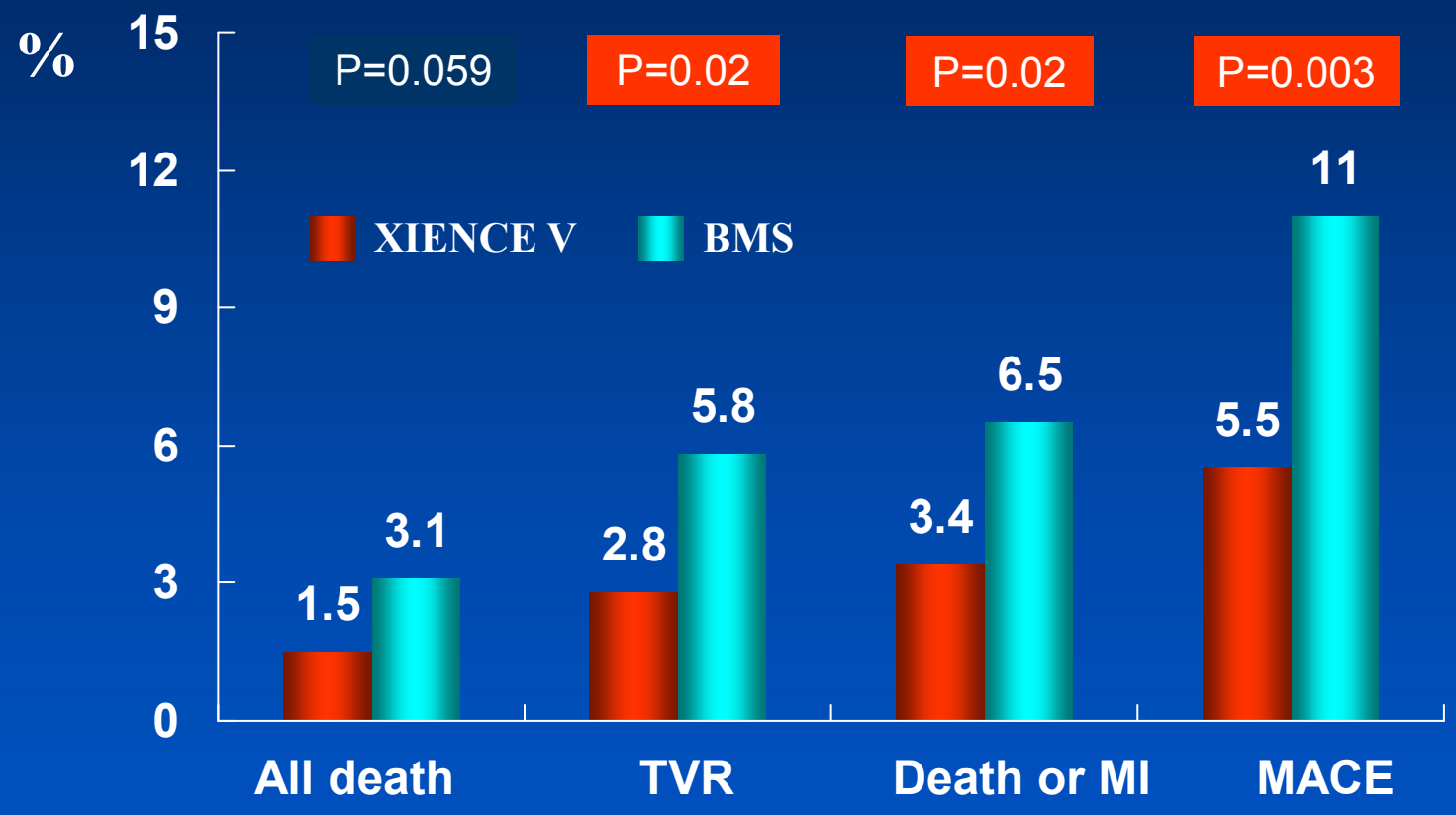
- EES have been shown to be effective in randomized trials with selected patients such as SPIRIT II, III, IV trials

Xience vs. BMS
vs. TAXUS
vs. Endeavor
vs. Cypher

X-SEARCH

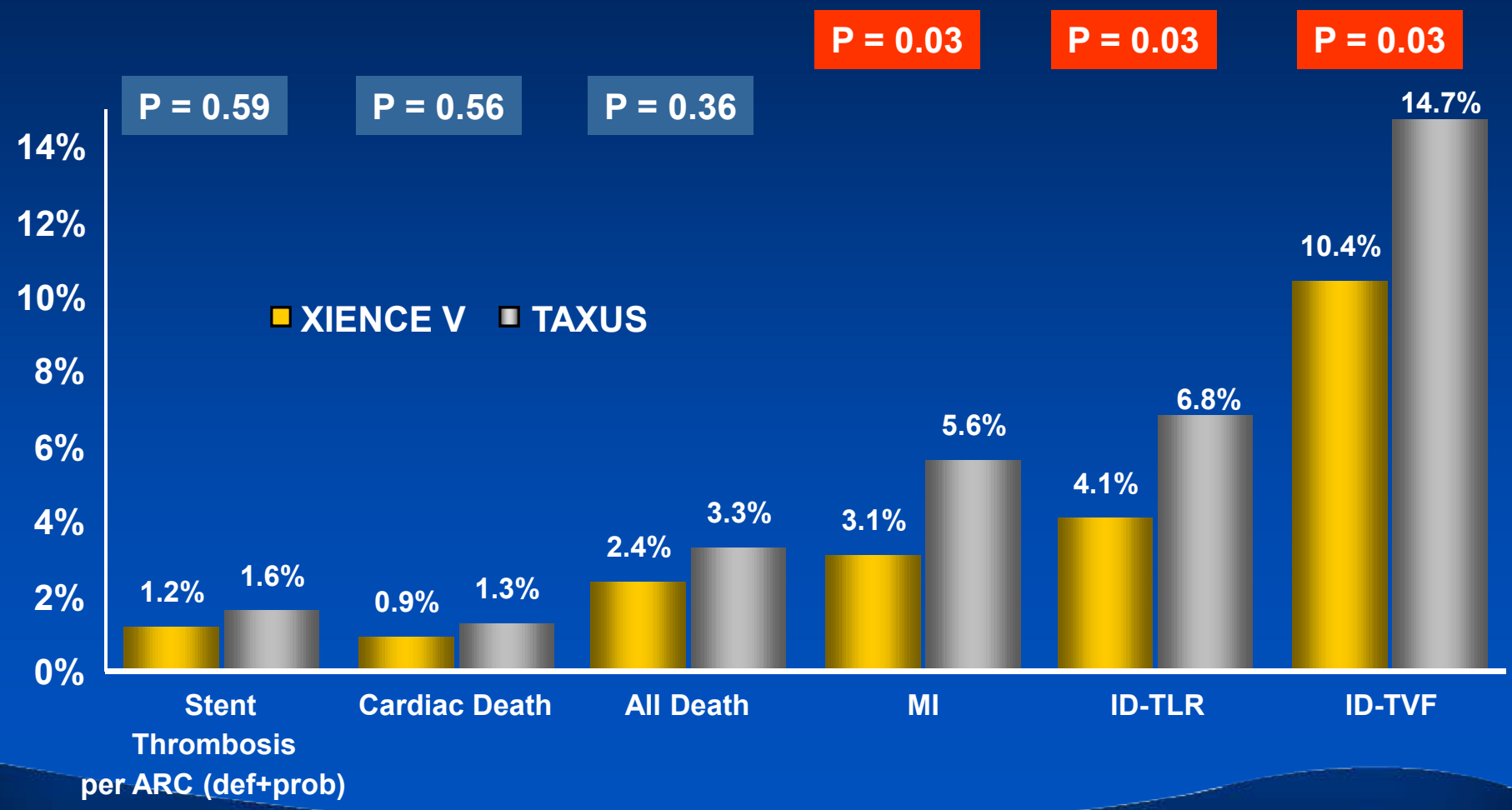
6-month Clinical Outcomes

EES (n=649) vs. BMS (n=450)



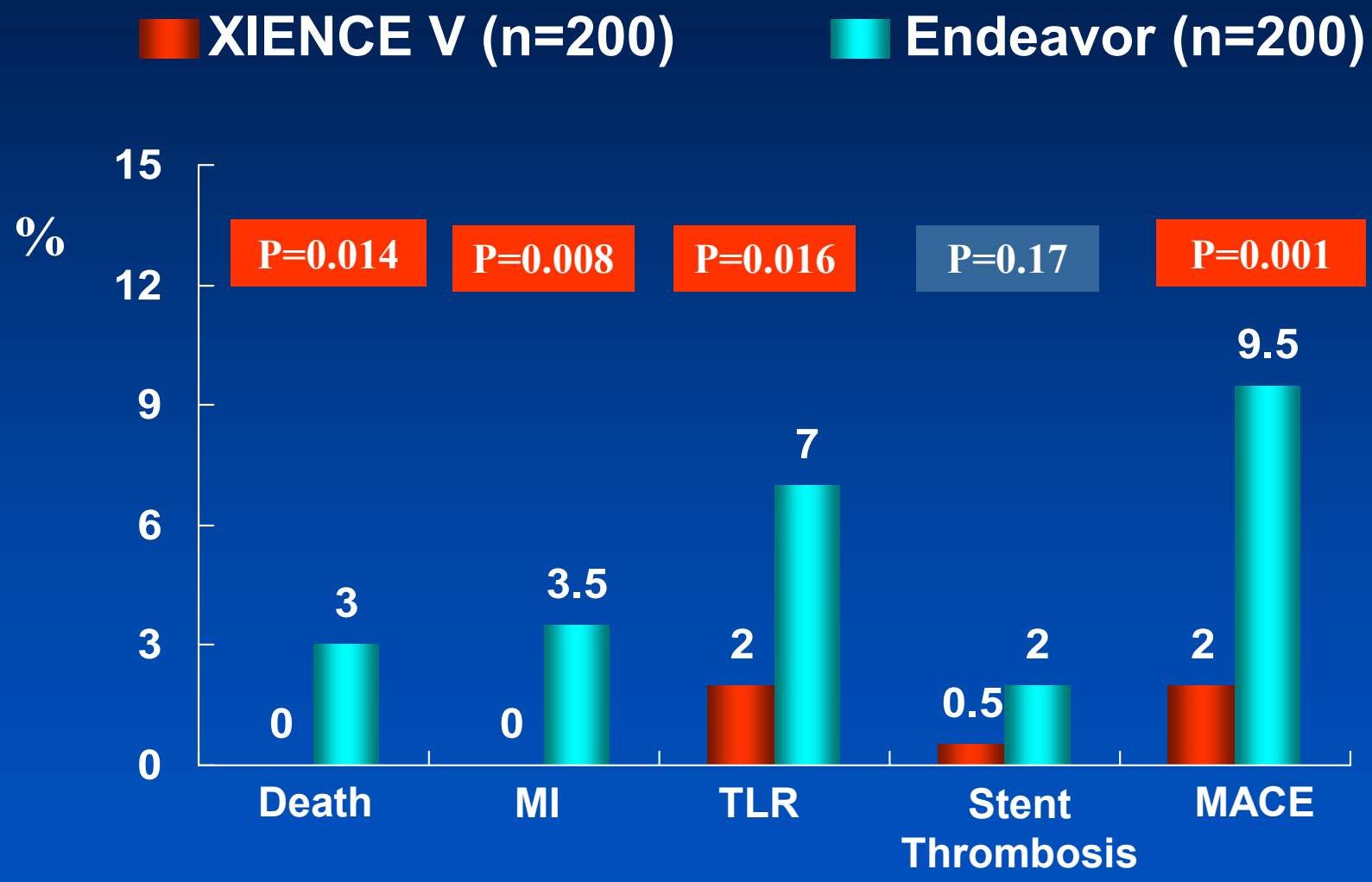
Onuma Y, et al. J Am Coll Cardiol 2009;54:269-76

SPIRIT II & III Meta-Analysis
Clinical Events Through 2 Years



Clinical Outcomes through 1 year

Prospective Registry data



MACE: all death, MI, TLR

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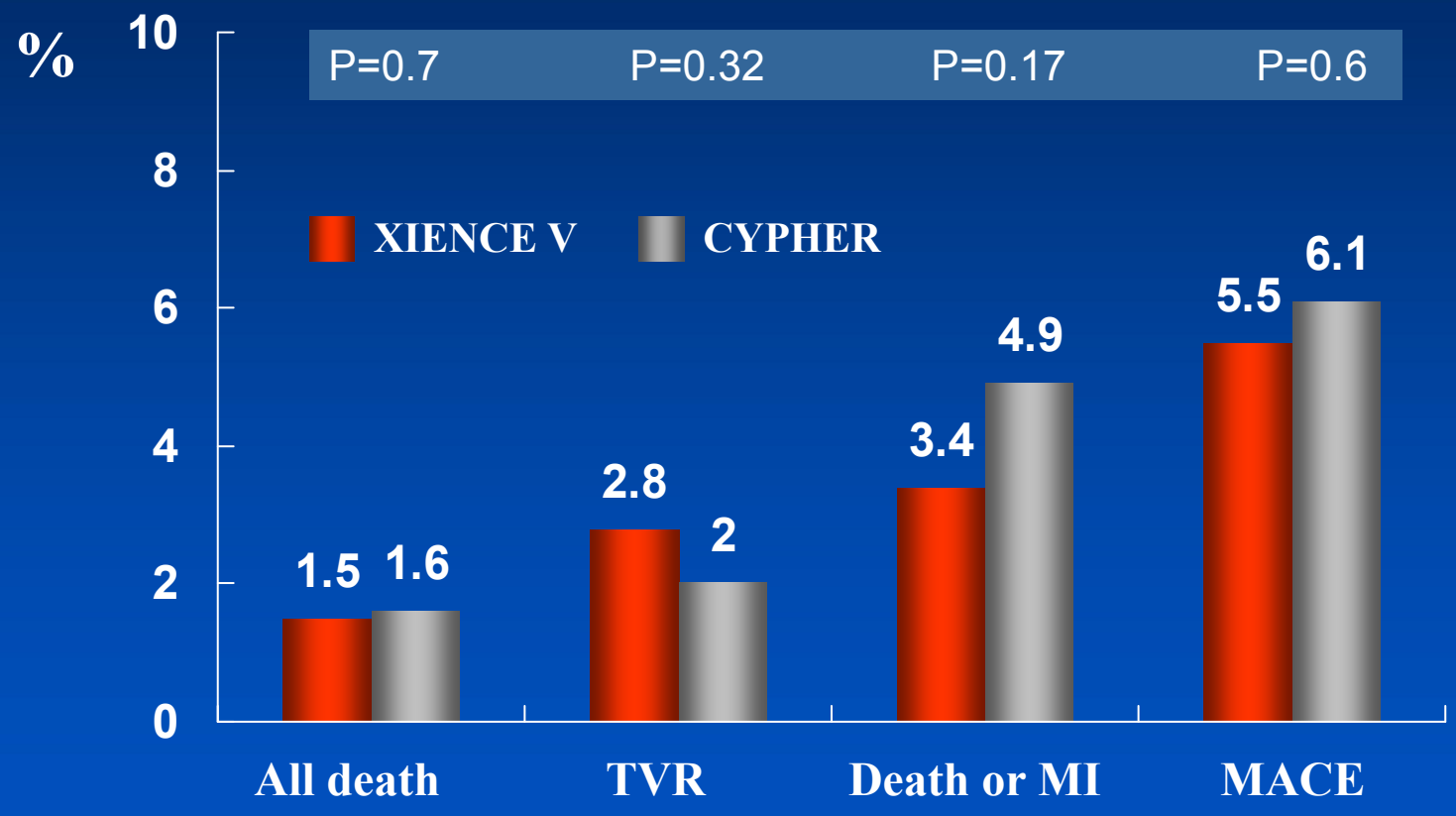
X-SEARCH

6-month Clinical Outcomes

EES (n=649) vs. SES (n=508)



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Xience V stent,

Better performance than Endeavor and Taxus. Similar performance with Cypher.

Which one is the Best stent ?

"Best stent" shows good performance at complex patient and lesion subsets in real world practice

AMC Stent Registry

Inclusion Period and Patients

All comers in Real Life

including STEMI, LMCA disease, in-stent restenosis lesion, and severe LV dysfunction

Clinical & Angiographic Follow-up

702 patients
(1057 lesions, 1717 stents)

From 1 June 2008 to 31 December 2009

Follow-up

702 patients
(1057 lesions, 1717 stents)

Clinical Follow-up

- Median follow up duration : 10.1(0, 23.9) months

Angiographic Follow-up : 255 patients

- Median follow up duration : 8.8 (0, 21.7) months

Primary Study Endpoint

- The composite clinical outcome of
  - Death from any cause
  - Myocardial infarction (MI)
  - Target Vessel Revascularization (TVR)
- Other clinical outcomes were considered as secondary

Antiplatelet Regimen

Pre-Procedure

- Aspirin (≥ 100mg)
- Clopidogrel (loading dose) : 300 or 600 mg

During Procedure

- Heparin: IV bolus + boluses to maintain ACT > 250 s
- GP IIb/IIIa inhibitors: at physician's discretion

After Discharge

- Aspirin: 100-325 mg /day indefinitely
- Clopidogrel: 75 mg once daily for ≥ at least 12 months

Results

Baseline Characteristics

Variables	EES (n=702)
Age	62.6 ± 9.8
Male	509 (72.5)
DM	286 (40.7)
HTN	435 (62.0)
Hyperlipidemia	520 (74.1)
Current smoker	162 (23.1)
Family Hx of CAD	20 (2.8)
Previous PCI	176 (25.1)

Baseline Characteristics

Variables	EES (n=702)
Previous CABG	33 (4.7)
Previous MI	36 (5.1)
Cerebrovascular disease	42 (6.0)
Renal insufficiency	14 (2.0)
Vascular extent	
One vessel disease	267 (38.0)
Two vessel disease	250 (35.6)
Three vessel disease	185 (26.3)
Ejection fraction, %	58.2 ±7.2

Baseline Characteristics

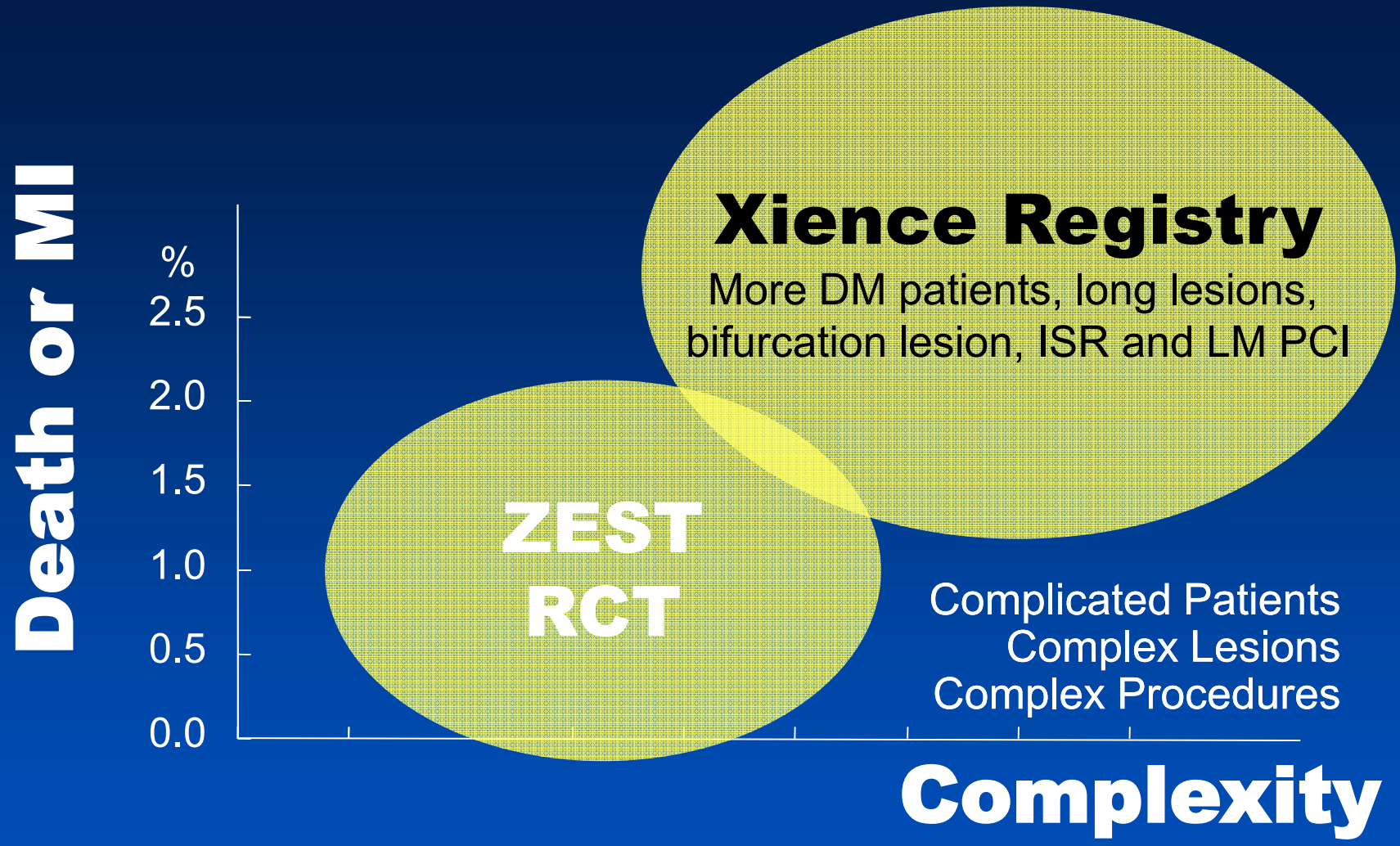
Variables	EES (n=702)
Clinical indication	
Silent ischemia	57 (8.1)
Chronic stable angina	437 (62.3)
Unstable angina	156 (22.2)
NSTEMI	29 (4.1)
STEMI	23 (3.3)
Electrocardiographic findings	
Sinus rhythm	675 (96.2)
AF	14 (2.0)
Others	13 (1.9)

Lesion Characteristics

Variables	EES (n=702)
Location	
LM	111 (15.8)
LAD	396 (56.4)
RCA	169 (24.1)
LCX	80 (11.4)
Coronary graft	8 (1.1)
CTO lesion	55 (7.8)
Bifurcation lesion	31 (4.4)
Ostial lesion	41 (5.8)
Infarct related artery	19 (2.7)
Restenotic lesion	81 (11.5)
DES/BMS	52/31

Procedural Characteristics

Variables	EES (n=702)
No. of stents per lesion	1.6 ± 0.7
No. of stents per patient	2.6 ± 1.7
Maximal stent diameter	3.5 ± 0.4
Stent length per lesion	40.0 ± 19.4
Stent length per patient	63.4 ± 43.6
Maximal pressure	16.8 ± 6.9
Direct stenting	148 (21.1)
Use of IABP	21 (3.0)
Procedure success	99.5%

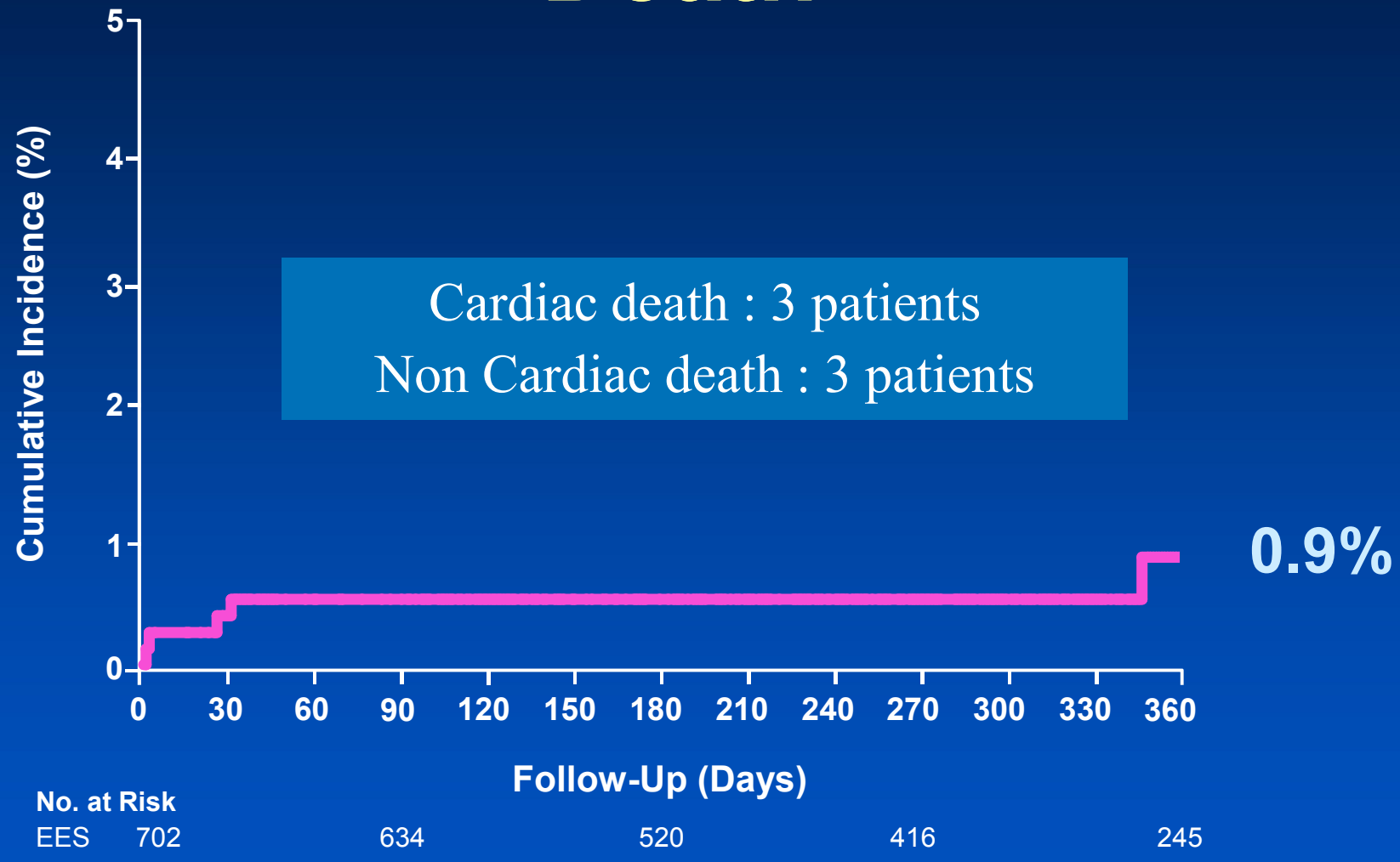

Death or MI
%
2.5
2.0
1.5
1.0
0.5
0.0
Xience Registry
More DM patients, long lesions, bifurcation lesion, ISR and LM PCI
ZEST RCT
Complicated Patients
Complex Lesions
Complex Procedures
Complexity

Clinical Events During 12 Months of Follow-Up

Clinical Outcomes during follow-up

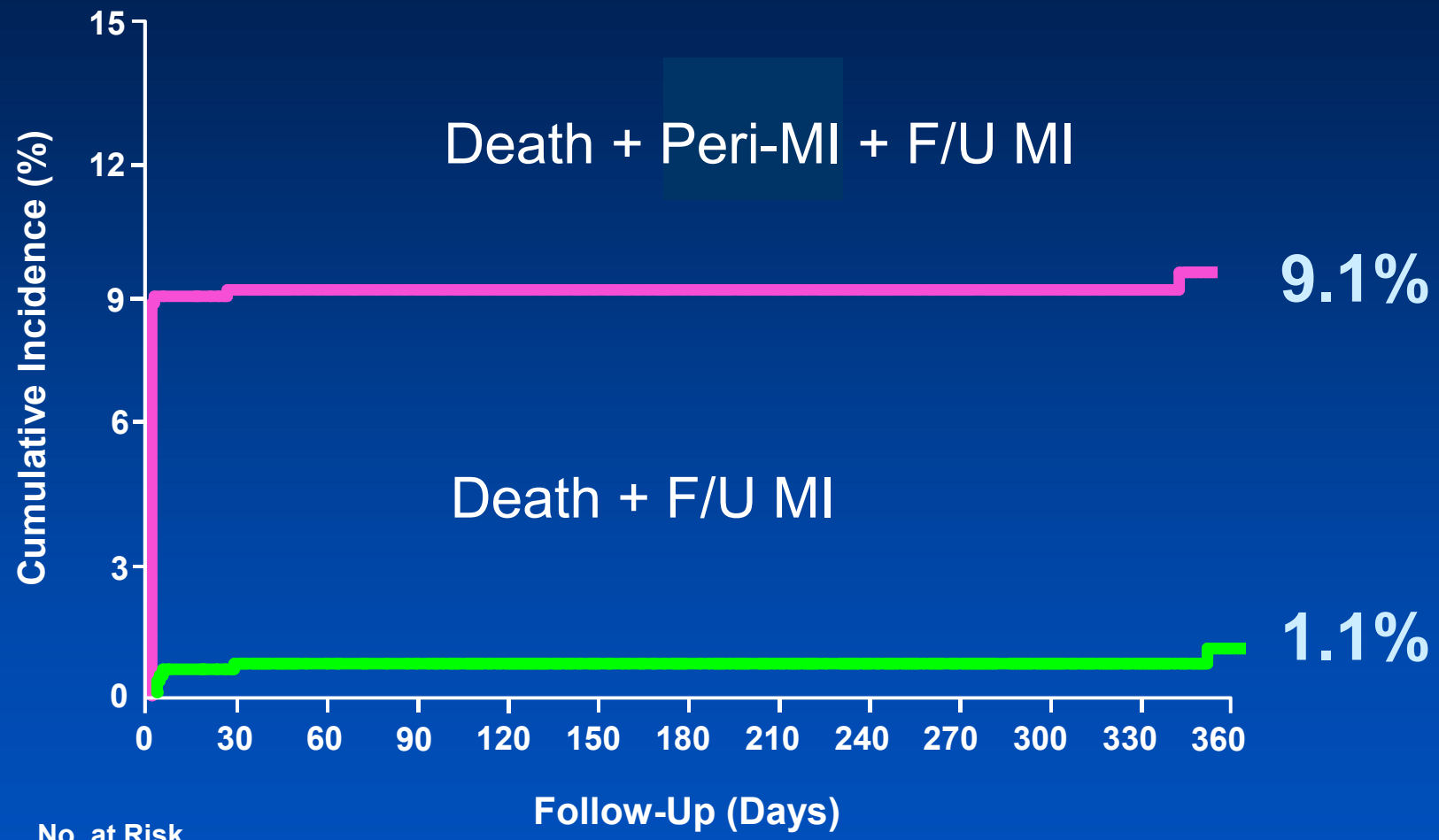
	EES (n=702)
Death	6 (0.9)
Cardiac	3 (0.5)
Non-cardiac	3 (0.5)
Myocardial infarction	
Peri-procedure	74 (10.6)
During follow-up	1 (0.1)
Stent thrombosis	
Acute	0
Subacute	1 (0.1)
Late	0
Target lesion revascularization	21 (4.2)
Target vessel revascularization	21 (4.2)

Death



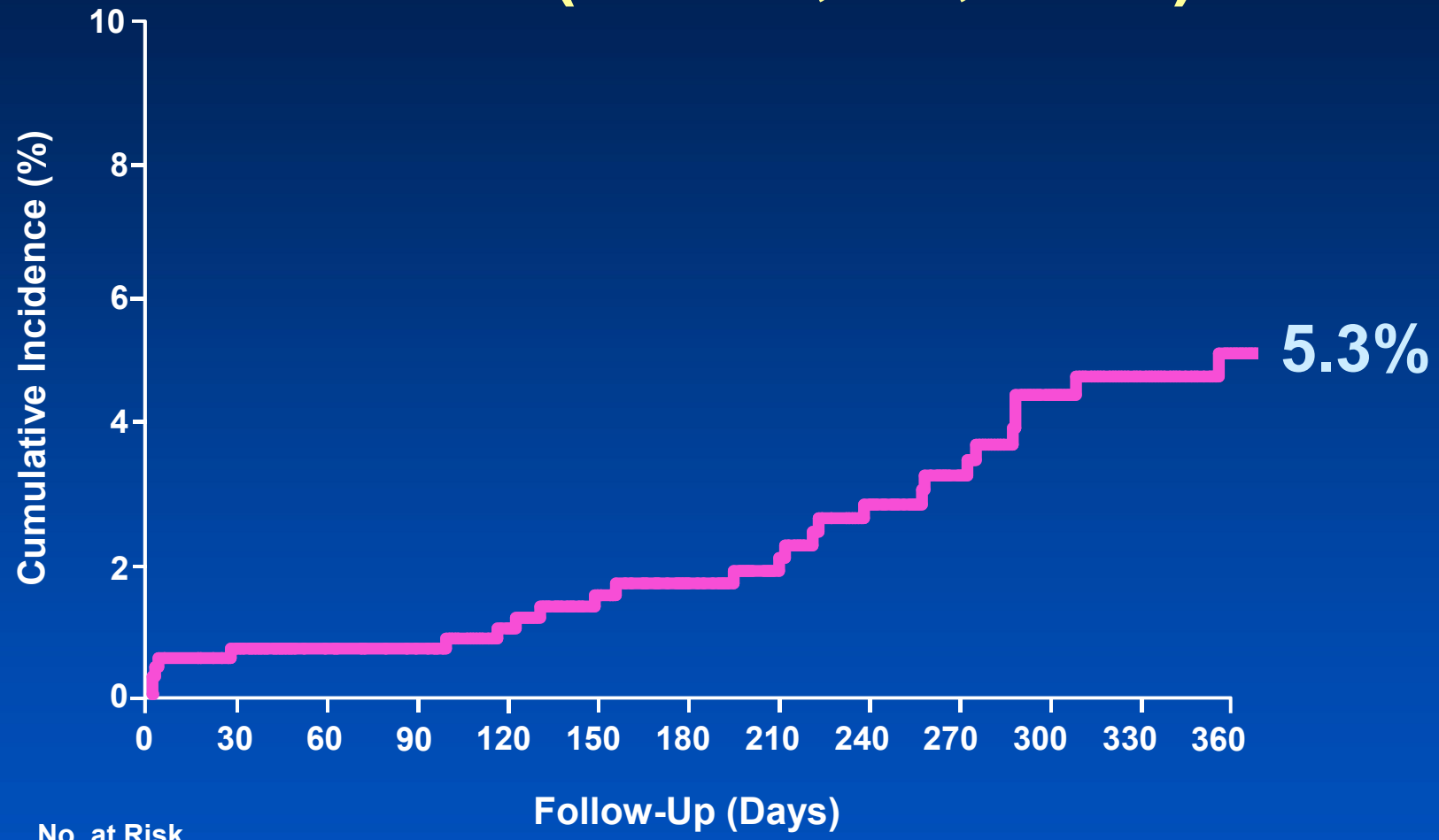
Cardiac death : 3 patients
Non Cardiac death : 3 patients

Death, MI



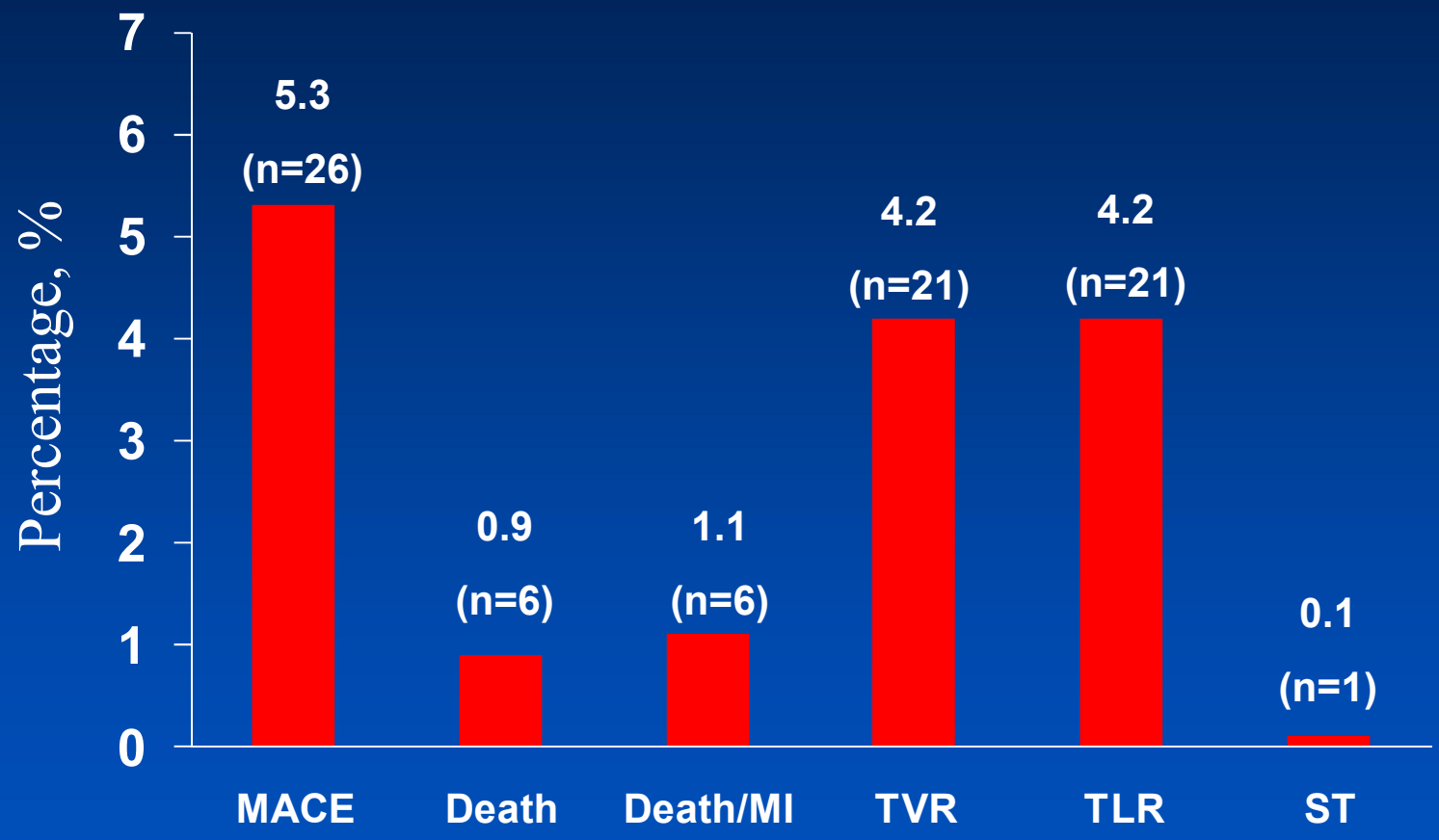
No. at Risk					
EES	702	580	467	375	217
EES	702	634	520	416	245

MACE (Death, MI, TVR)



No. at Risk					
EES	702	637	516	404	237

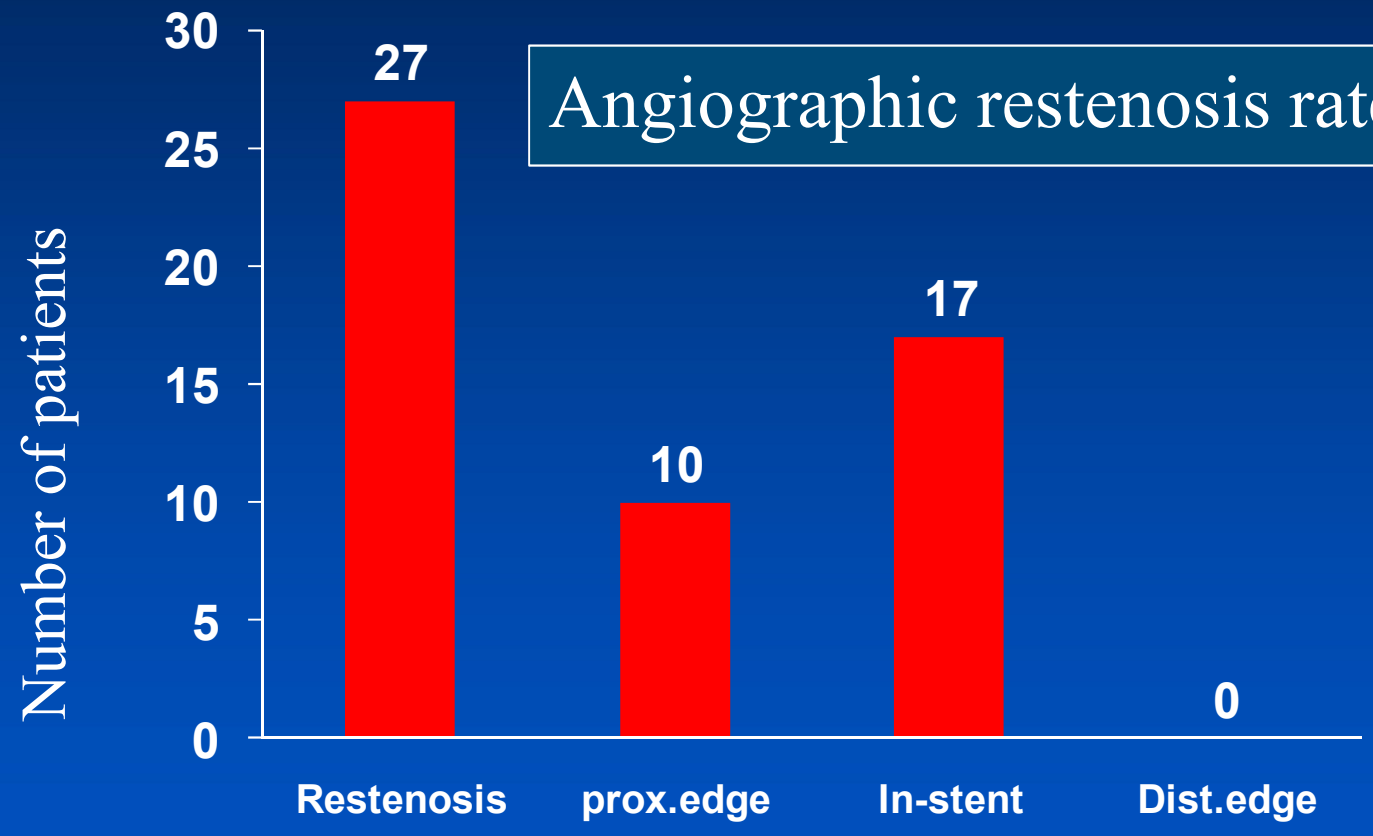
Major Clinical Events at 12 Months



* Event rates derived from K-M Curve

Angiographic In-Stent Restenosis

Angiographic follow-up : 255 patients



Angiographic restenosis rate : 10.6%

Follow-Up Duration : 8.8 (0, 21.7) months

Predictors of MACE at 12months

Variables	OR	p value
Restenotic lesion	4.42 (1.96, 9.97)	<0.01
Left main CAD	2.38 (0.99, 5.71)	0.051
Renal failure	3.90 (0.90, 16.82)	0.068

* MACE : Death, MI, TVR

In the comparison with ZES, PES & SES from **ZEST trial**

ZEST Trial

All Comer requiring PCI with DES for coronary lesions
in 19 Centers of Korea
(Total 2,640 patients)

Randomize 1:1:1
stratified by 1) Sites, 2) Diabetes, 3) Long lesions (≥ 28 mm)

ENDEAVOR®
(N=880)

CYPER®
(N=880)

TAXUS Liberte™
(N=880)

Clinical follow-up at 12 months
Angiographic follow-up at 9 months

Major Inclusion Criteria

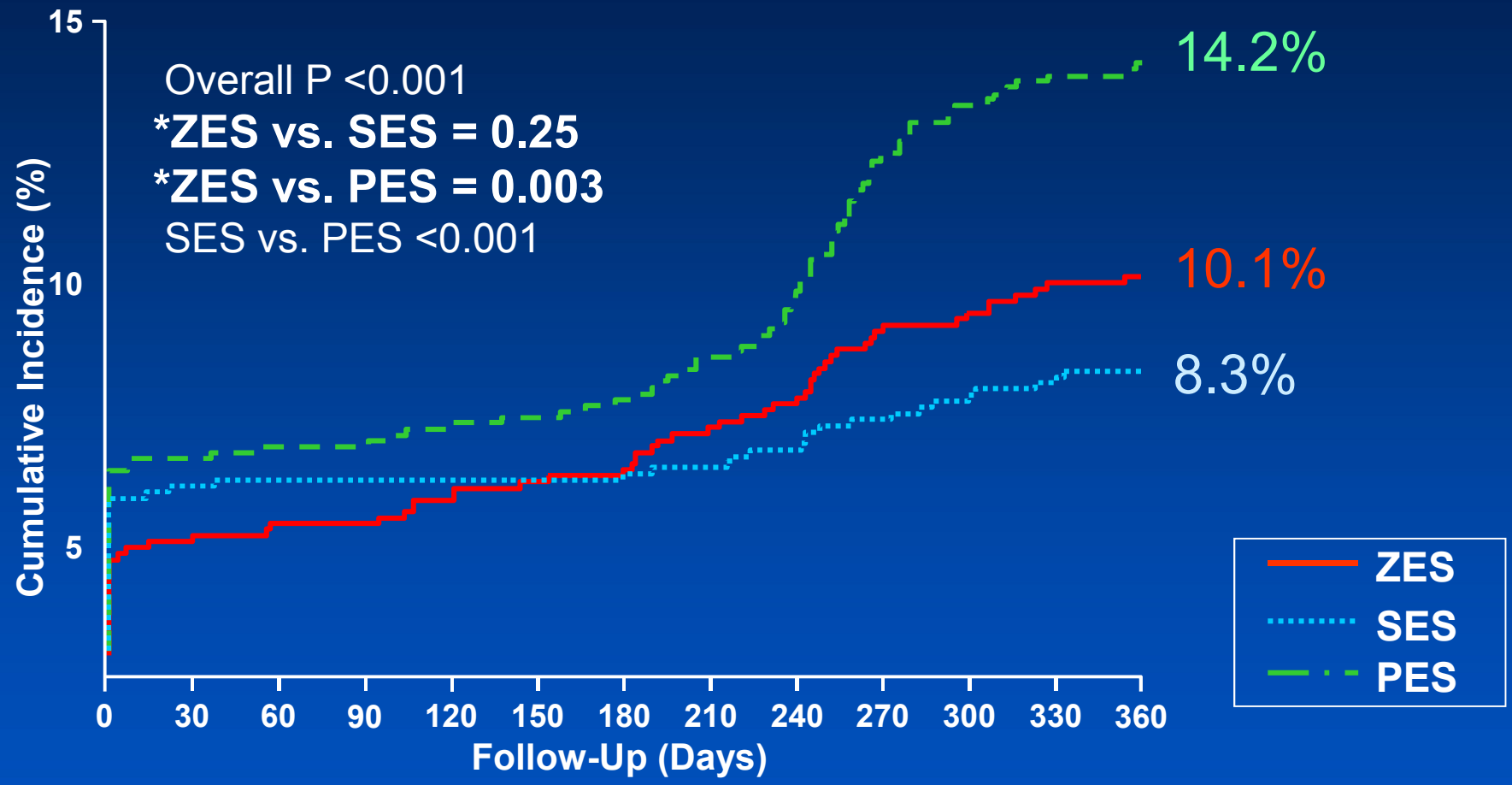
- Significant CAD (≥ 50% stenosis), amenable to stent-assisted PCI
- Silent ischemia, stable angina, and ACS (unstable angina, NSTEMI)

Major Exclusion Criteria

- Severe LV dysfunction (EF < 25%)
  or Cardiogenic Shock
- STEMI requiring primary PCI
- Creatinine ≥ 3.0 mg/dl or LFT > 3times
- Left Main Disease
- In-stent restenosis of DES
- Limited life expectancy < 1 year

Primary End Point at 12 month

: Death, MI, Ischemia-driven TVR



No. at Risk					
ZES	883	827	816	790	782
SES	878	816	813	802	792
PES	884	821	808	763	745

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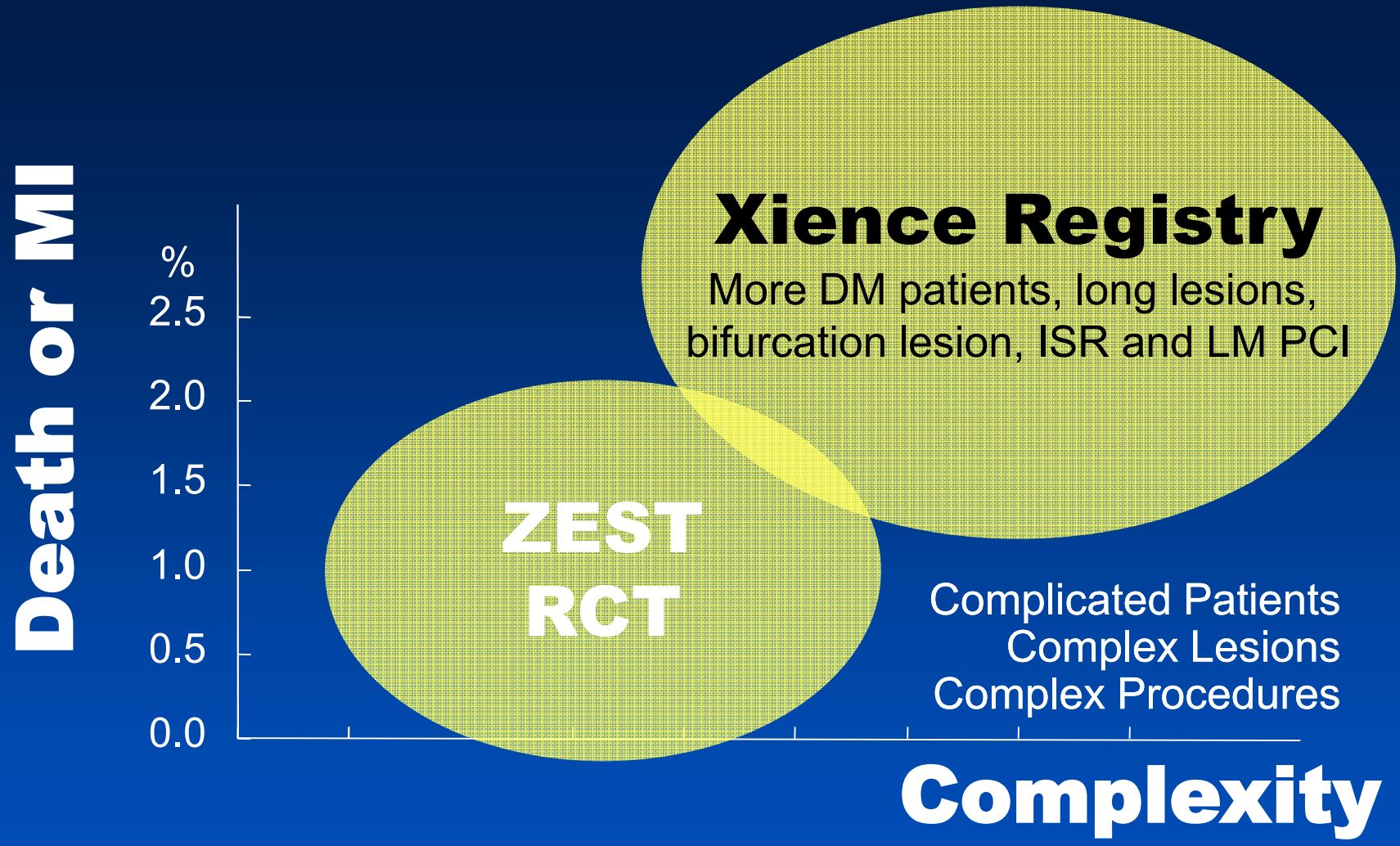

Death or MI
%
2.5
2.0
1.5
1.0
0.5
0.0
Xience Registry
More DM patients, long lesions, bifurcation lesion, ISR and LM PCI
ZEST RCT
Complicated Patients
Complex Lesions
Complex Procedures
Complexity

Flowchart of patients selection EES treated patients

1 June 2008 – 31 December 2009
702 patients
(1057 lesions, 1717 stents)

Excluded

LM 111 pts

STEMI 23 pts

DES-ISR 52 pts

527 patients
(770 lesions, 1003 stents)

Results

Baseline Characteristics

Patients	EES (n=527)	ZES (n=883)	SES (n=878)	PES (n=884)	P value
Age (yr)	63±9	62±9	62±10	62±10	0.49
Male sex	374 (71)	586 (66)	591 (67)	582 (66)	0.20
Diabetes mellitus					
Any diabetes	211 (40)	268 (30)	247 (28)	245 (28)	<0.01
Requiring insulin	20 (4)	32 (4)	33 (4)	36 (4)	0.88
Hypertension	333 (63)	552 (63)	517 (59)	540 (61)	0.25
Hyperlipidemia	387 (73)	466 (53)	451 (51)	446 (51)	<0.01
Current smoker	122 (23)	236 (27)	256 (29)	243 (28)	0.10
Family history of CAD	17 (3)	48 (5)	44 (5)	52 (6)	0.09

n (%)

Baseline Characteristics

Patients	EES (n=527)	ZES (n=883)	SES (n=878)	PES (n=884)	P value
Previous PCI	105 (20)	75 (9)	82 (9)	83 (9)	<0.01
Previous CABG	22 (4)	6 (1)	6 (1)	5 (1)	<0.01
Previous MI	23 (4)	30 (3)	39 (4)	41 (5)	0.53
Previous CHF	10 (2)	9 (1)	4 (1)	7 (1)	0.39
Cerebrovascular disease	28 (5.3)	65 (7)	55 (6)	53 (6)	0.12
Renal insufficiency	14 (3)	7 (1)	7 (1)	6 (1)	<0.01
Multi-vessel disease	316 (60)	414 (47)	430 (49)	410 (46)	0.01
Ejection fraction (%)	59±7	61±8	61±8	61±8	<0.01

n (%)

Baseline Characteristics

Patients	EES (n=527)	ZES (n=883)	SES (n=878)	PES (n=884)	P value
Clinical indication (%)					<0.01
Silent ischemia	36 (7)	48 (5)	44 (5)	56 (6)	
Chronic stable angina	314 (63)	348 (39)	343 (39)	343 (39)	
Unstable angina	129 (25)	410 (46)	424 (48)	403 (46)	
NSTEMI	23 (5)	77 (9)	67 (8)	82 (9)	
Electrocardiographic findings					0.45
Sinus rhythm	503 (95)	850 (96)	849 (97)	854 (97)	
Atrial fibrillation	14 (3)	21 (2)	18 (2)	17 (2)	
Other	10 (2)	12 (1)	11 (1)	13 (1)	
n (%)					

Lesion Characteristics

Lesions	EES (n=770)	ZES (n=1190)	SES (n=1218)	PES (n=1205)	P alue
Location					<0.01
LAD	347 (45)	622 (52)	645 (53)	611 (51)	
LCX	146 (19)	252 (21)	225 (19)	253 (21)	
RCA	262 (34)	316 (27)	348 (29)	340 (28)	
Graft vessel	15 (2)	0	0	1 (0.1)	
Total occlusion	56 (7)	68 (6)	76 (6)	96 (8)	0.12
Thrombus-containing	17 (2)	32 (3)	37 (3)	38 (3)	0.61
Bifurcation lesion	148 (19)	181 (15)	151 (12)	168 (14)	<0.01
Ostial lesion	38 (5)	85 (7)	72 (6)	82 (7)	0.21
Infarct related artery	16 (2)	44 (4)	38 (3)	43 (4)	0.20

n (%)

Lesion Characteristics

Lesions	EES (n=770)	ZES (n=1190)	SES (n=1218)	PES (n=1205)	P value
Calcification					<0.01
None or mild	700 (91)	1129 (95)	1145 (94)	1132 (94)	
Moderate	36 (5)	40 (3)	43 (4)	46 (4)	
Severe	34 (4)	21 (2)	30 (3)	27 (2)	
Lesion length					<0.01
<10 mm	21 (3)	73 (6)	71 (6)	61 (5)	
10-20 mm	112 (15)	466 (39)	444 (37)	504 (42)	
>20 mm	637 (83)	651 (55)	703 (58)	640 (53)	

n (%)

Procedure Characteristics

Lesions	EES (n=770)	ZES (n=1190)	SES (n=1218)	PES (n=1205)	P value
No. of stents/lesion	1.6±0.7	1.2±0.4	1.2±0.4	1.2±0.4	<0.01
No. of stents/patient	2.4±1.4	1.6±0.9	1.6±0.9	1.6±0.9	<0.01
Length of stents/lesion	39.1±19.6	27.9±13.1	28.9±13.5	28.9±14.3	<0.01
Length of stents/patients	59.4±24.8	39.7±26.8	38.3±24.3	38.9±25.2	<0.01
Maximal stent diameter	3.7±0.5	3.4±0.7	3.4±0.7	3.5±0.6	0.07
Maximal pressure	16.5±4.5	16.3±4.2	16.3±4.1	16.2±4.2	0.45
Direct stenting	123 (16)	84 (7)	109 (9)	89 (7)	<0.01
n (%)					

Discharge Medication

Patients	EES (n=527)	ZES (n=883)	SES (n=878)	PES (n=884)	P value
Aspirin	526 (99.8)	882 (99.9)	873 (99.4)	880 (99.5)	0.36
Clopidogrel	526 (99.8)	876 (99.2)	874 (99.5)	881 (99.7)	0.37
Cilostazol	53 (10.1)	251 (28.4)	230 (26.2)	244 (27.6)	<0.01
Warfarin	4 (0.8)	3 (0.3)	7 (0.8)	6 (0.7)	0.61
Statin	456 (86.5)	698 (79.0)	720 (82.0)	715 (80.9)	<0.01
ACEi	170 (32.3)	343 (38.8)	312 (35.5)	315 (35.6)	0.09
ß-blocker	361 (68.5)	581 (65.8)	562 (64.0)	594 (67.2)	0.26
CCB	442 (83.9)	460 (52.1)	481 (54.8)	439 (49.7)	<0.01

n (%)

Clinical Events
During 12 Months of Follow-Up

Extreme

in lesion and patient subsets

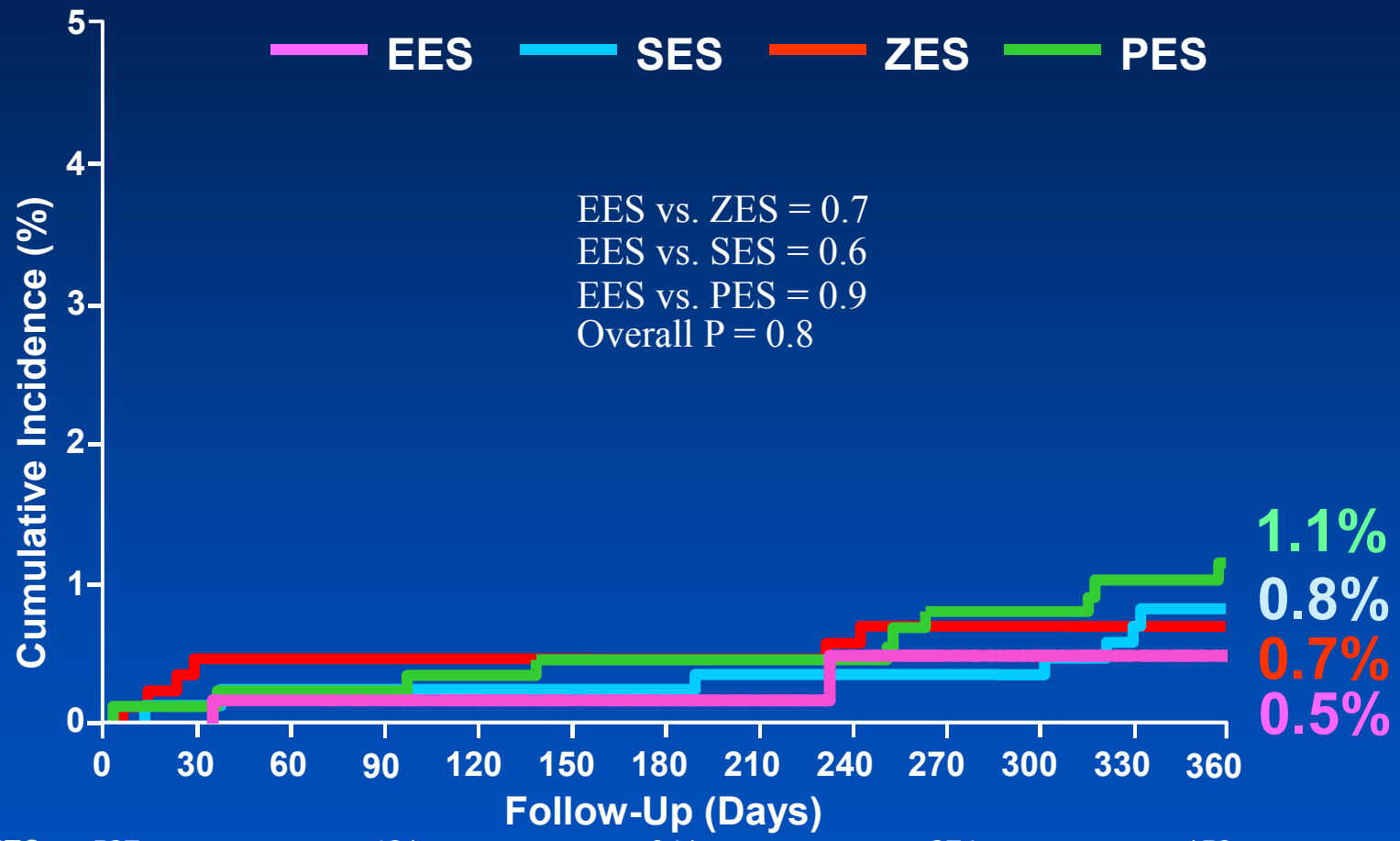
Major Clinical Events at 12 Months

	EES (n=527)	ZES (n=883)	SES (n=878)	PES (n=884)	P
Death	4 (0.5)*	6 (0.7)	7 (0.8)	10 (1.1)	0.8
Cardiac	2 (0.2)	5 (0.6)	3 (0.3)	5 (0.6)	
Noncardiac	2 (0.2)	1 (0.1)	4 (0.5)	5 (0.6)	
Death or MI	48 (9.1)	51 (5.8)	61 (6.9)	67 (7.6)	0.02
TLR	10 (2.6)	43 (4.9)	12 (1.4)	66 (7.5)	<0.01
TVR	10 (2.6)	46 (5.2)	16 (1.8)	67 (7.6)	<0.01
Stent thrombosis	1 (0.1)	7 (0.8)	1 (0.1)	9 (1.0)	0.06
Primary end point	61(12.0)	90 (10.2)	73 (8.3)	125 (14.1)	<0.01

Primary end point: composite of death, MI, or TVR

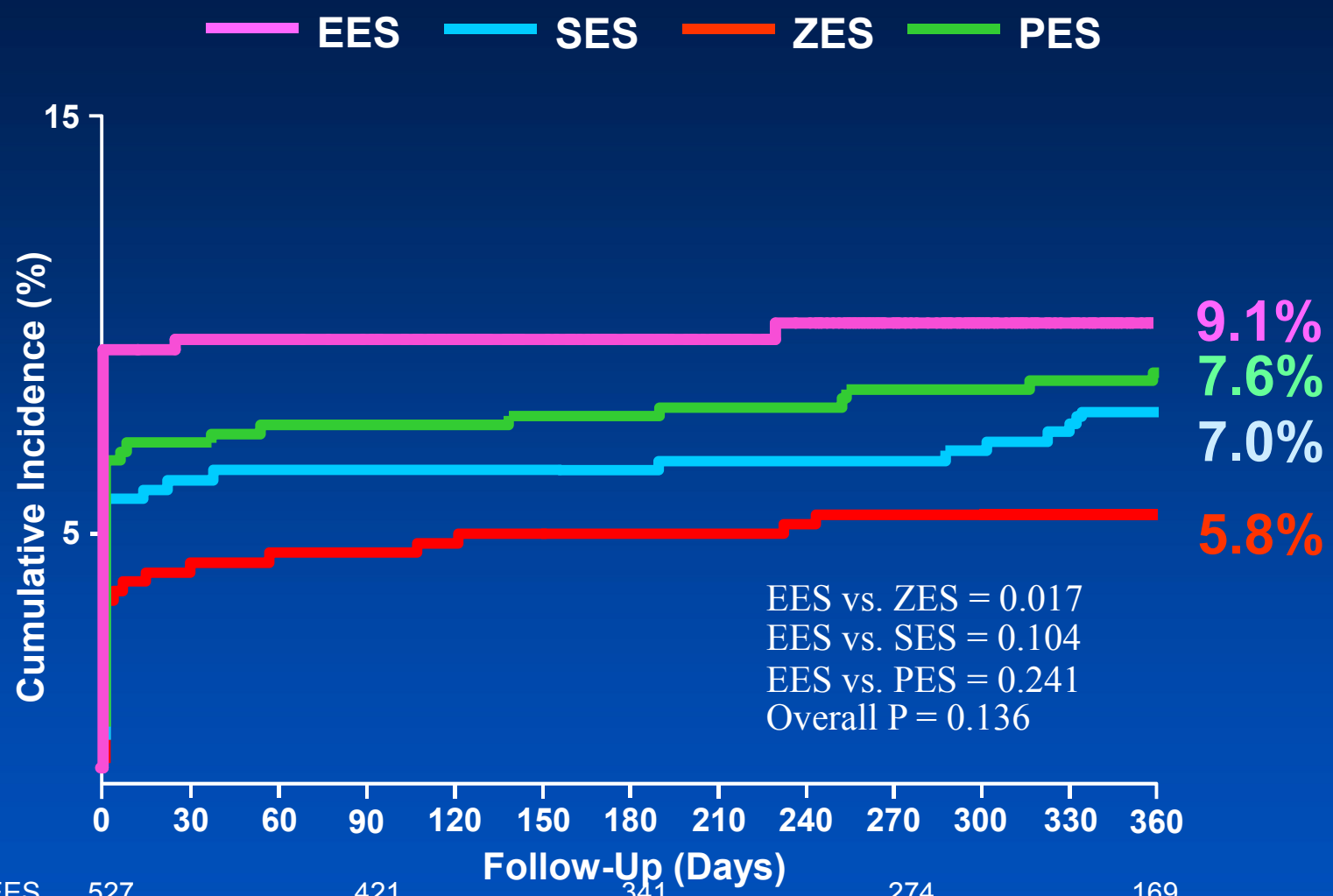
* Event rates were derived from K-M curve

Death



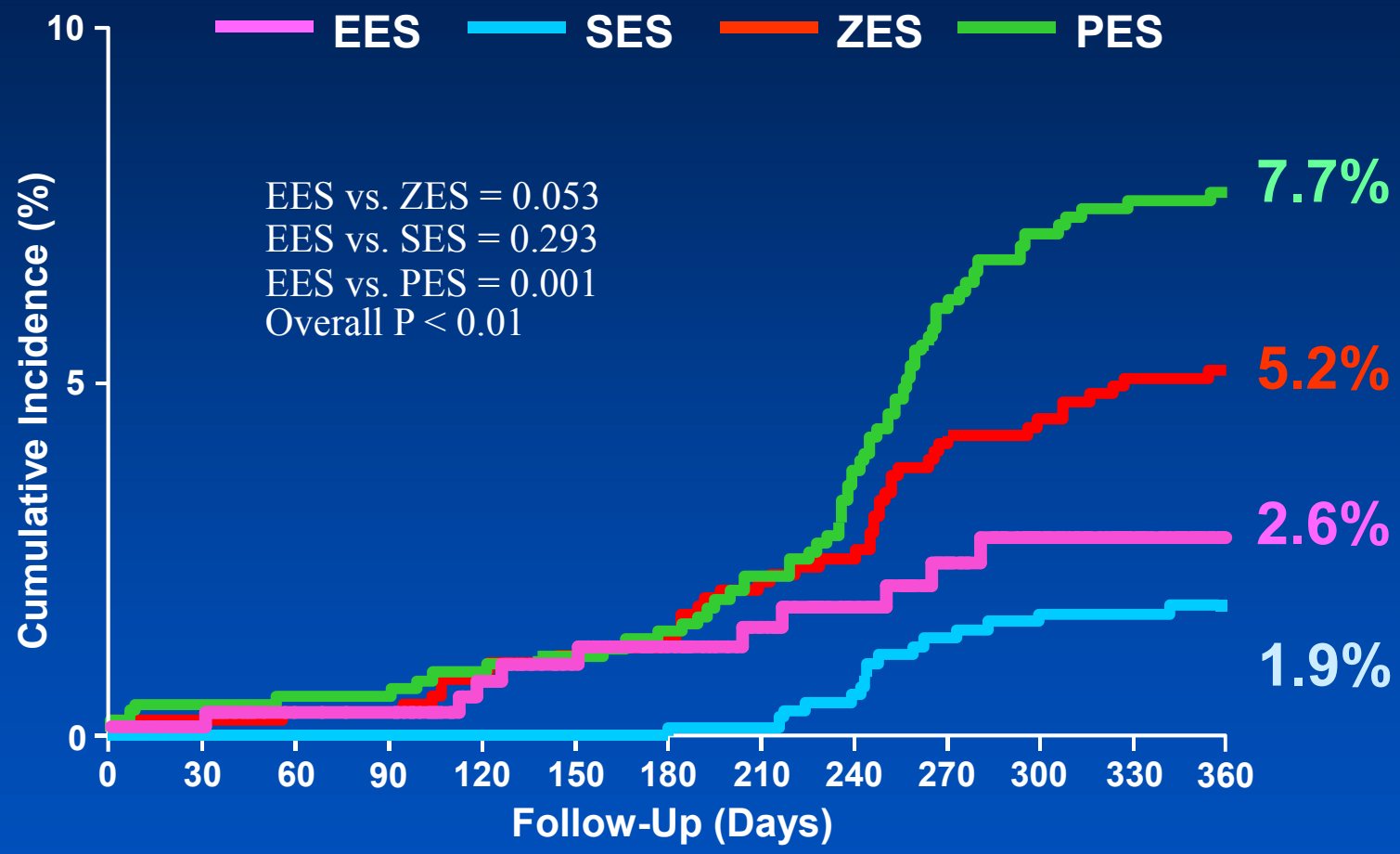
EES	527	421	341	274	158
ZES	883	871	869	864	864
SES	878	869	867	863	857
PES	884	880	873	865	859

Death or MI



EES	527	421	341	274	169
ZES	883	828	824	820	820
SES	878	817	814	811	804
PES	884	821	815	808	803

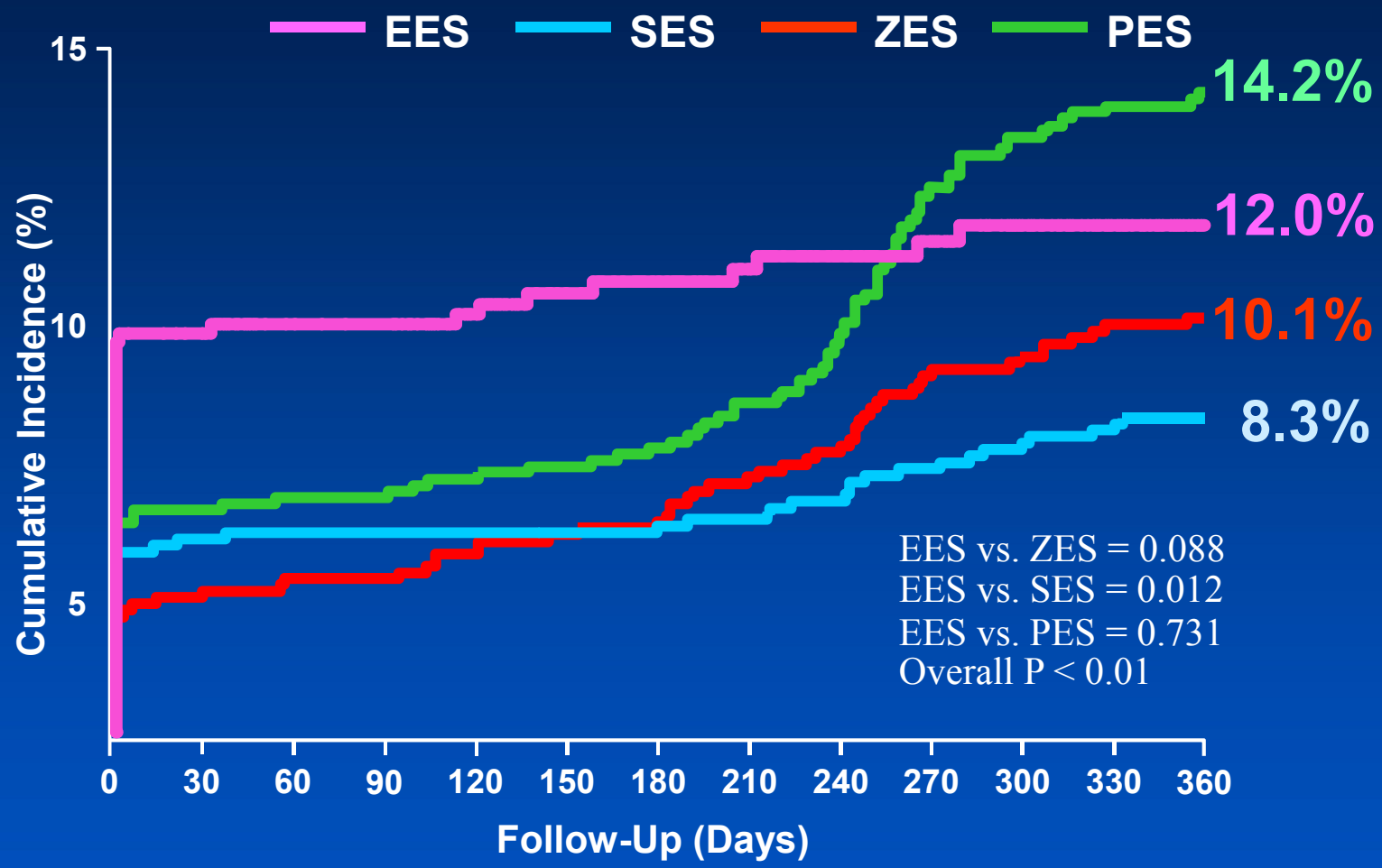
Target Vessel Revascularization



EES	527	462	377	300	191
ZES	883	868	857	827	819
SES	878	869	866	851	841
PES	884	875	861	812	793

Death, MI, TVR

Primary End Point at 12 month



EES	527	421	338	267	165
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SES	878	816	813	802	792
PES	884	821	808	763	745

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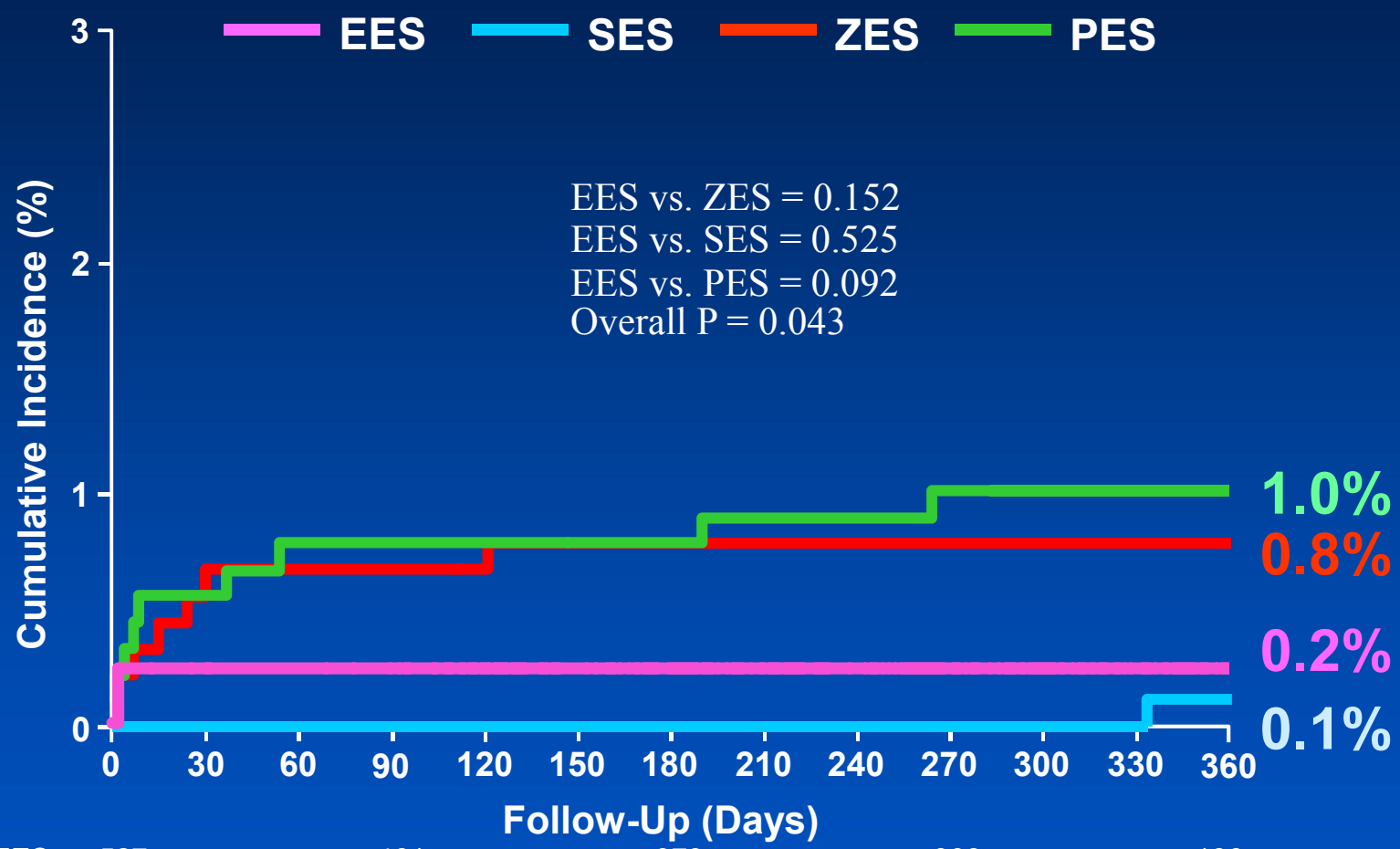
Stent Thrombosis

: ARC Any Criteria



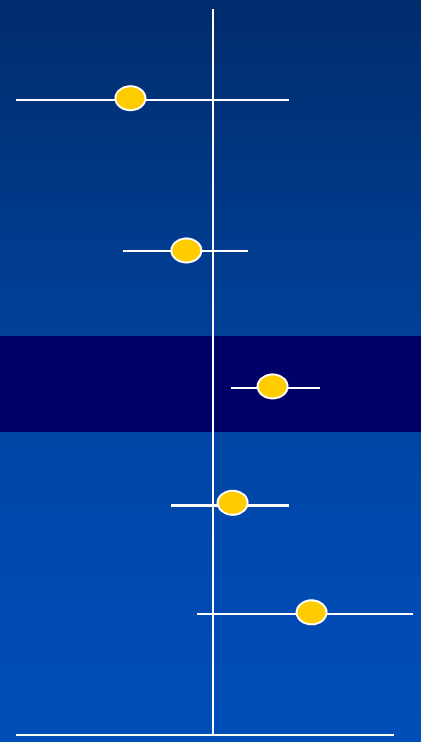
EES	527	461	373	308	186
ZES	883	869	866	861	861
SES	878	869	867	863	857
PES	884	875	868	859	853

Predictors of MACE at 12months in Overall cohort

Variables	HR	p value
Age	1.03 (1.02, 1.05)	<0.01
Stent No/Patient	1.30 (1.20, 1.40)	<0.01
Diabetes	1.34 (1.04, 1.71)	0.02

* MACE : Death, MI, TVR

Adjusted HR : EES vs. ZES



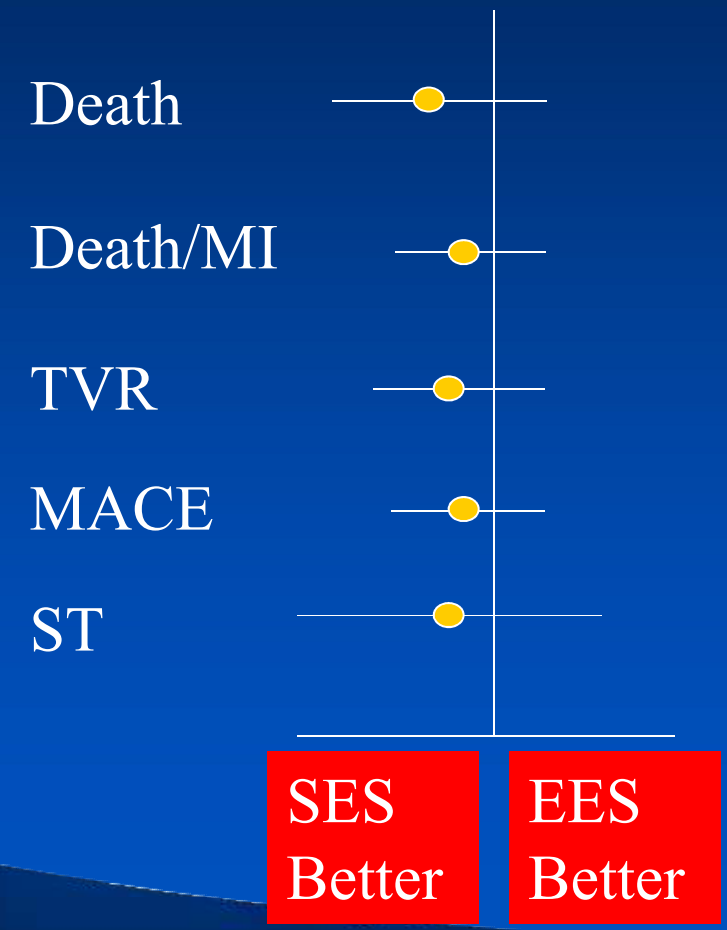
	HR	p value
Death	0.437 (0.119, 1.605)	0.212
Death/MI	0.931 (0.796, 1.089)	0.376
TVR	1.315 (1.014, 1.709)	0.039
MACE	1.004 (0.883, 1.142)	0.951
ST	1.773 (0.841, 3.731)	0.132

ZES Better

EES Better

* Adjusted by clinical and procedural characteristics

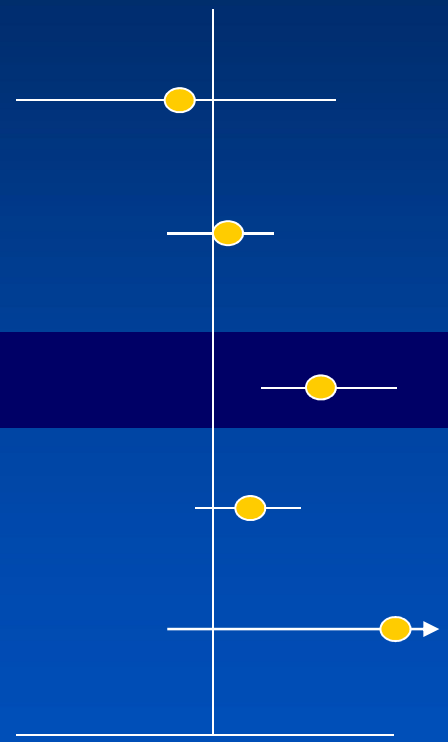
Adjusted HR : EES vs. SES



	HR	p value
Death	0.714 (0.352, 1.445)	0.349
Death/MI	0.971 (0.784, 1.203)	0.793
TVR	0.827 (0.529, 1.295)	0.407
MACE	0.899 (0.602, 1.344)	0.605
ST	0.807 (0.154, 4.237)	0.801

* Adjusted by clinical and procedural characteristics

Adjusted HR : EES vs. PES



	HR	p value
Death	0.610 (0.424, 7.042)	0.445
Death/MI	1.078 (0.711, 1.637)	0.721
TVR	3.378 (1.612, 7.042)	0.001
MACE	1.319 (0.938, 1.859)	0.111
ST	8.696 (0.913, 83.33)	0.060

PES Better

EES Better

* Adjusted by clinical and procedural characteristics

Summary

- Owing to higher lesion complexity, peri-procedural MI after EES is around 10%.
- During follow-up, rates of MI (0.1%), stent thrombosis (0.1%), or death (0.9%) are very low.
- Indirect comparison with SES, ZES, PES showed that EES appeared to be similarly effective as SES.

For the Extreme Cases
with Xience V

Left-Main Subgroup
N = 111

Baseline Characteristics

Variables	n = 111
Age	63.3±10.4
Male	80 (72.1)
DM	52 (46.8)
Renal failure	2 (1.8)
Previous PCI	26 (23.4)
Previous CABG	10 (9.0)
Previous MI	3 (2.7)
LVEF, %	57.8±8.0
Acute coronary syndrome	27 (24.3)
RCA stenting	21 (18.9)

Baseline Characteristics

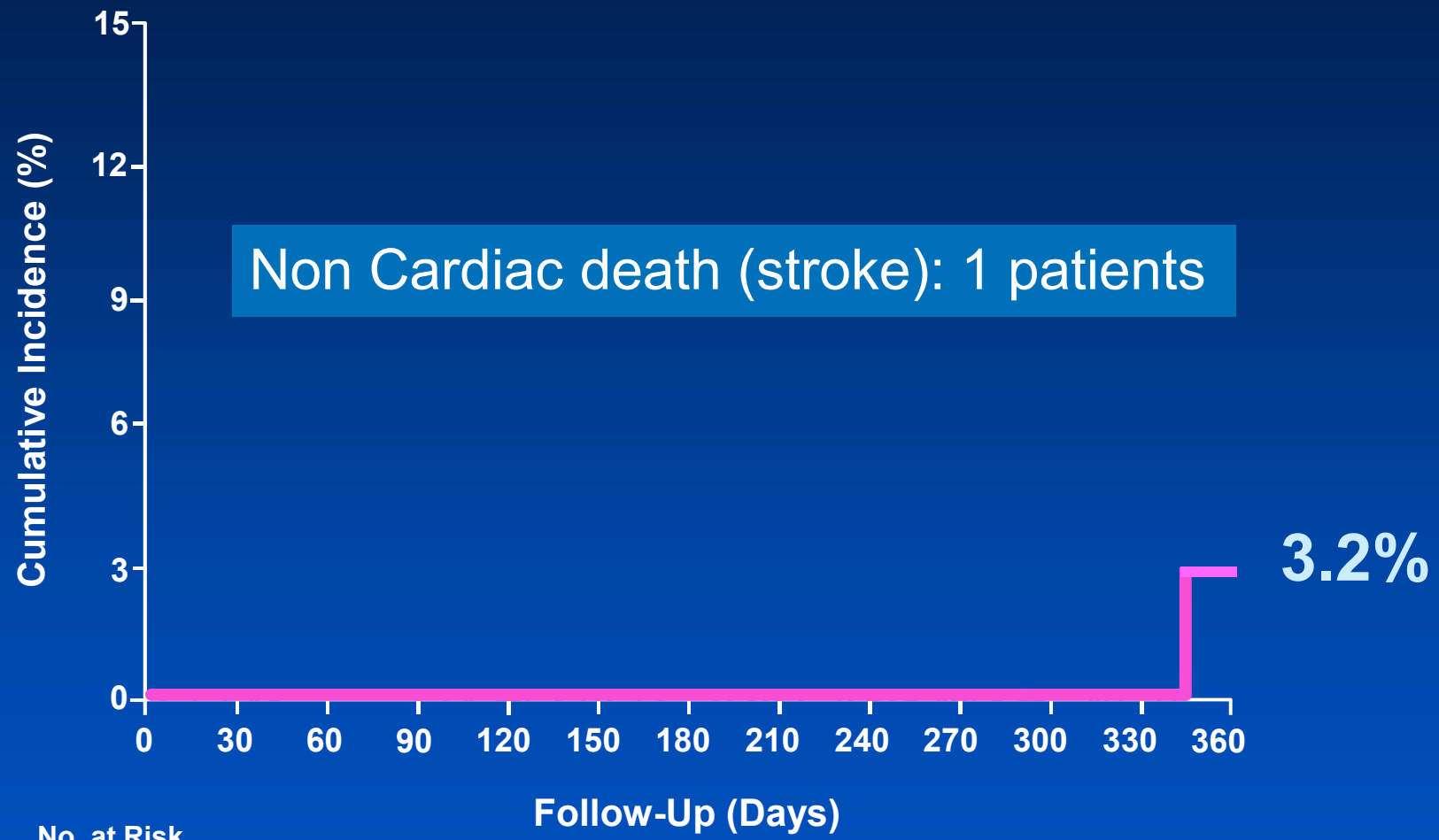
Variables	n = 111
Lesion location	
Ostial and shaft	17 (15.3)
Bifurcation	94 (84.7)
Number of stent at LM	2.7±1.1
Stent diameter at LM	3.8±0.3
Maximal balloon pressure	17.7±4.9
Bifurcation technique	
Crossover	46 (48.9)
Crushing	44 (46.8)
Kissing stenting	2 (2.1)
V stenting	2 (2.1)

Clinical Events During 12 Months of Follow-Up

Clinical Outcomes at 12 months

	EES (n=111)
Death	1 (3.2)
Cardiac	0
Non-cardiac	1 (3.2)
Myocardial infarction	
Peri-procedure	15 (13.6)
During follow-up	0
Stent thrombosis	
Acute	0
Subacute	0
Late	0
Target lesion revascularization	4 (8.1)
Target vessel revascularization	4 (8.1)

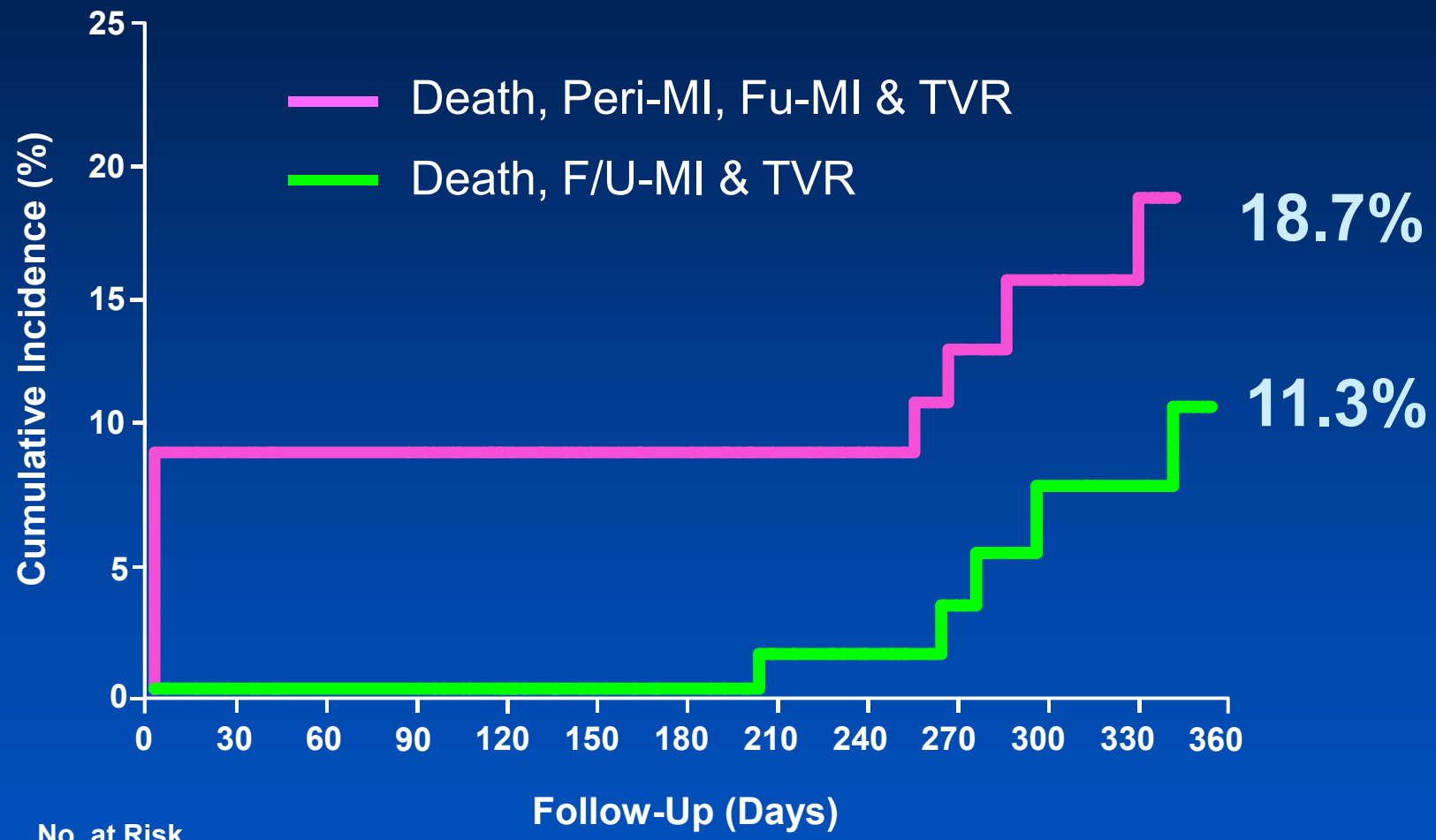
Death



No. at Risk

EES	111	102	79	54	23

MACE



No. at Risk					
EES	111	92	69	49	20
EES	111	102	78	52	22

Predictors of MACE at 12months

Variables	OR	p value
Stent No. at LM	1.89 (1.20, 2.99)	<0.01
Restenotic lesion	4.10 (1.09, 15.4)	0.036

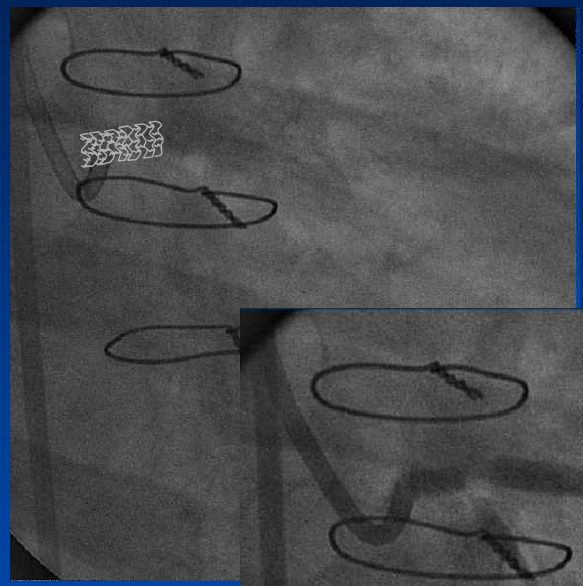
* MACE : Death, MI, TVR

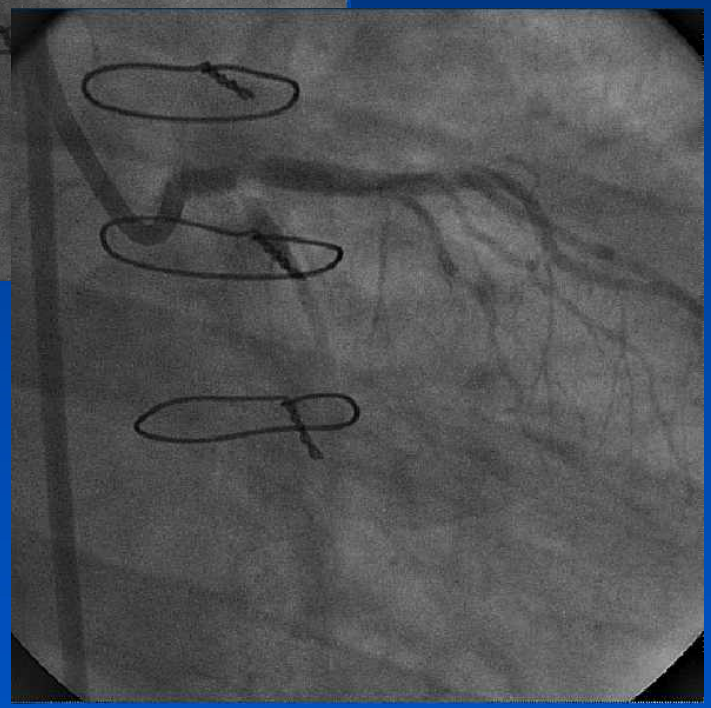
Extreme

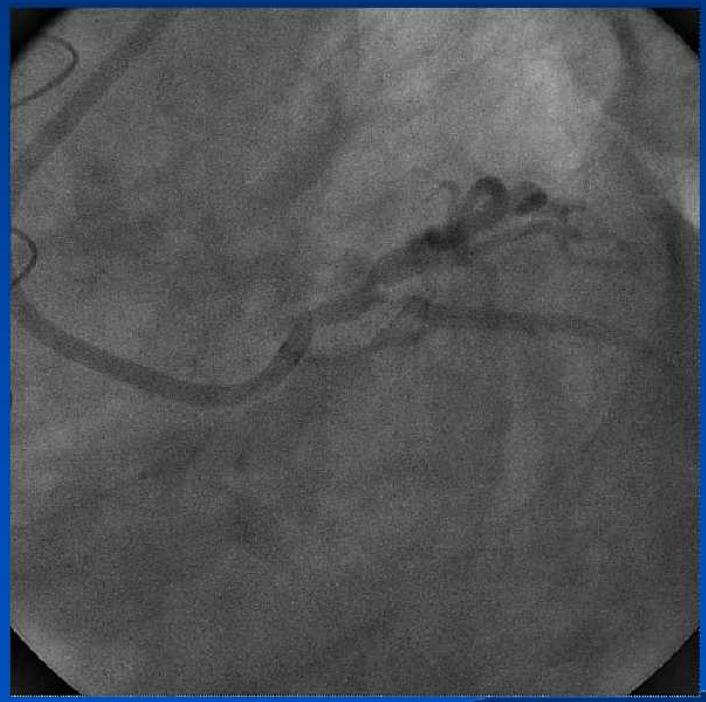
How do we treat the LM DES failure ?

47/M,
Stable angina,

Heart transplantation
Both edge restenosis after LM ostial stenting with Cypher 3.5x13 mm at 1 year F/U (June, 2008)







47/M,
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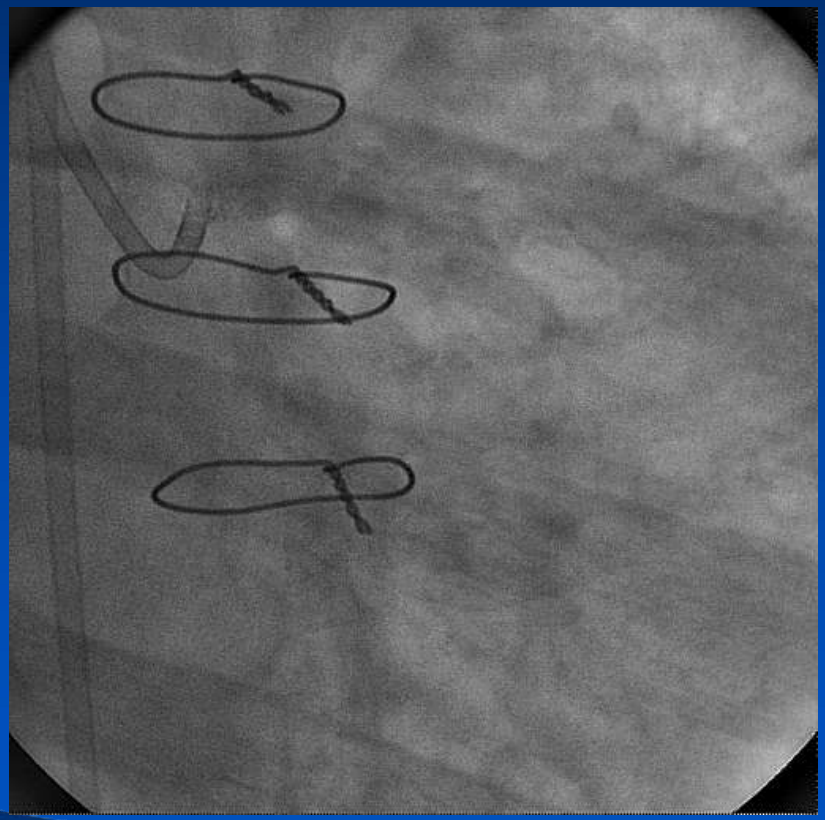
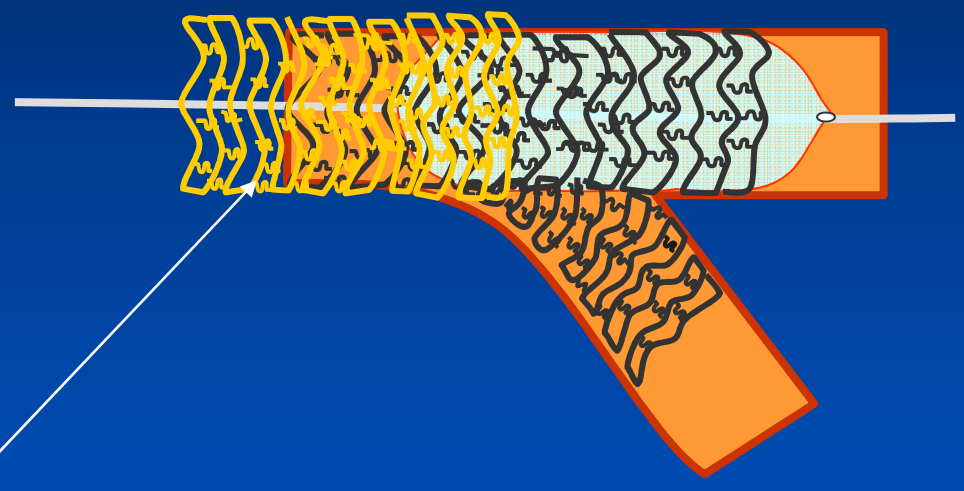
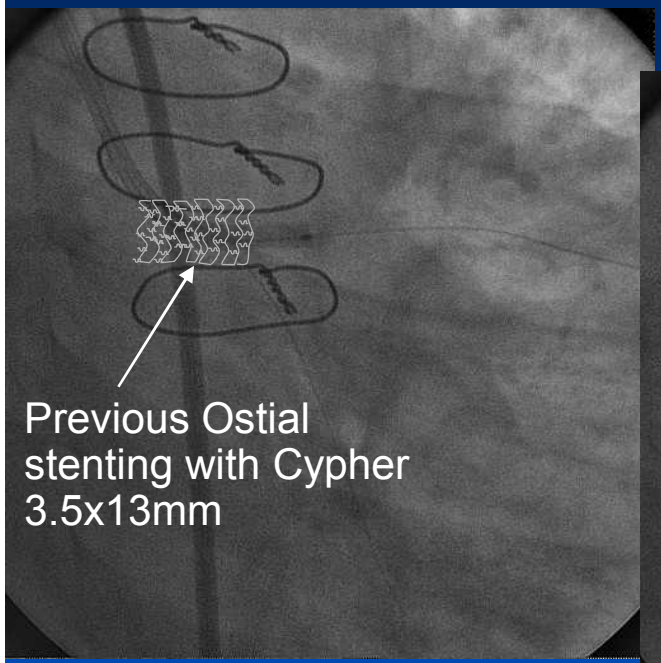


Stent crushing again
through the previous LM ostial stent

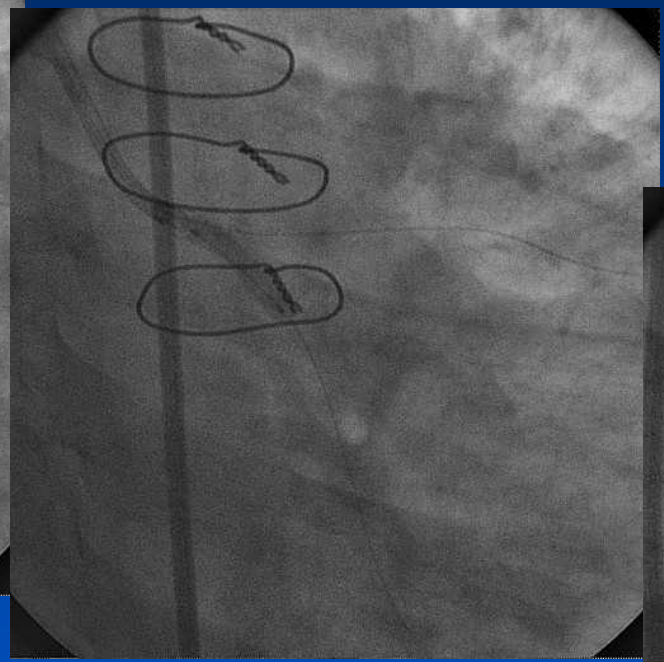


Previous stent,
Mainly Under-expansion

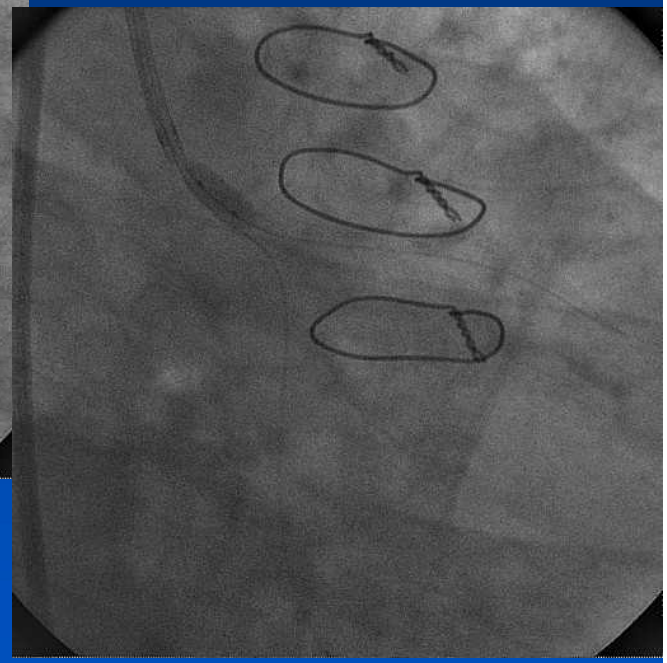
High pressure balloon dilation at LAD and LCX ostium and previous stent too.



Voyager 3.5x20mm

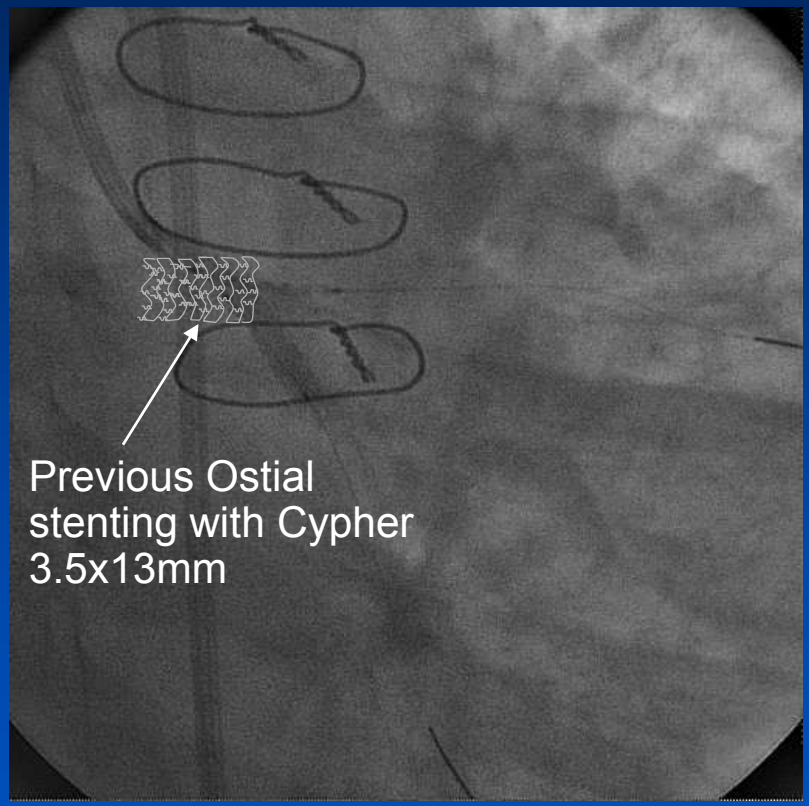


Voyager 3.5x20mm



Quantum 4.5x12mm

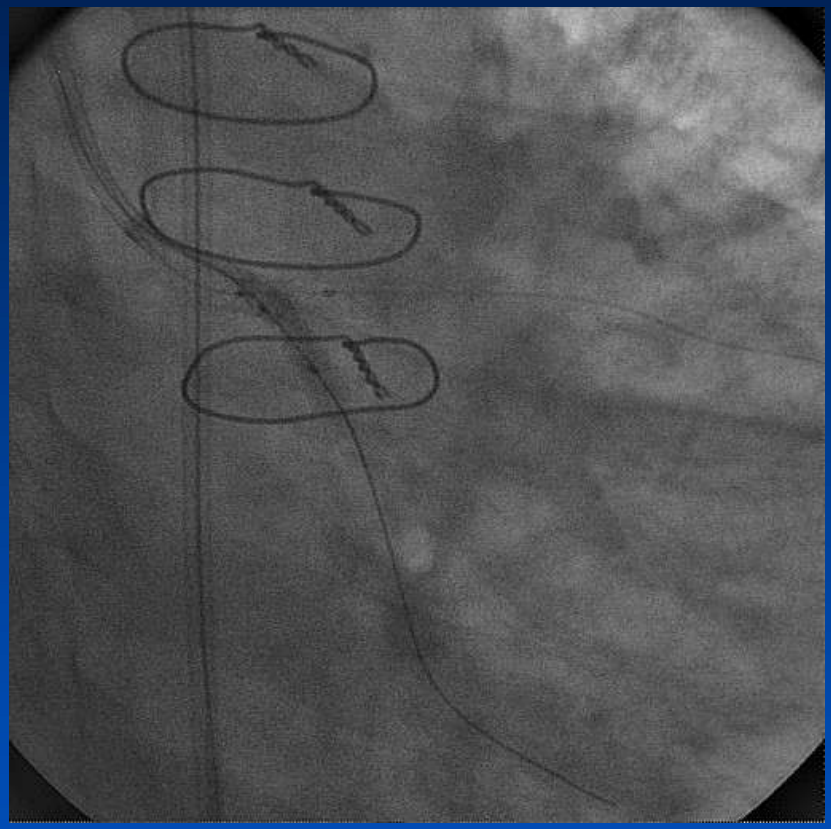
Stent crushing again
through the previous LM ostial stent



Xience V 3.5x18mm

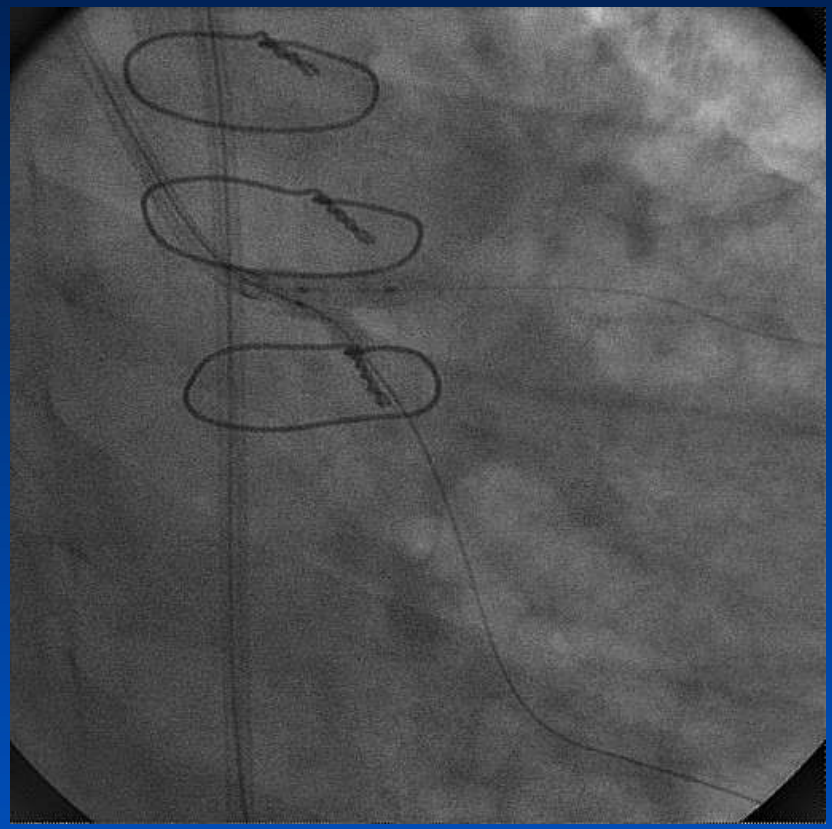
Xience V 3.5x18mm

High pressure inflation (25 atm) at LCX OS



LCX Os High-pressure Quantum 3.0x12mm, 25 atm through 2-4 layers(?) of stent struts

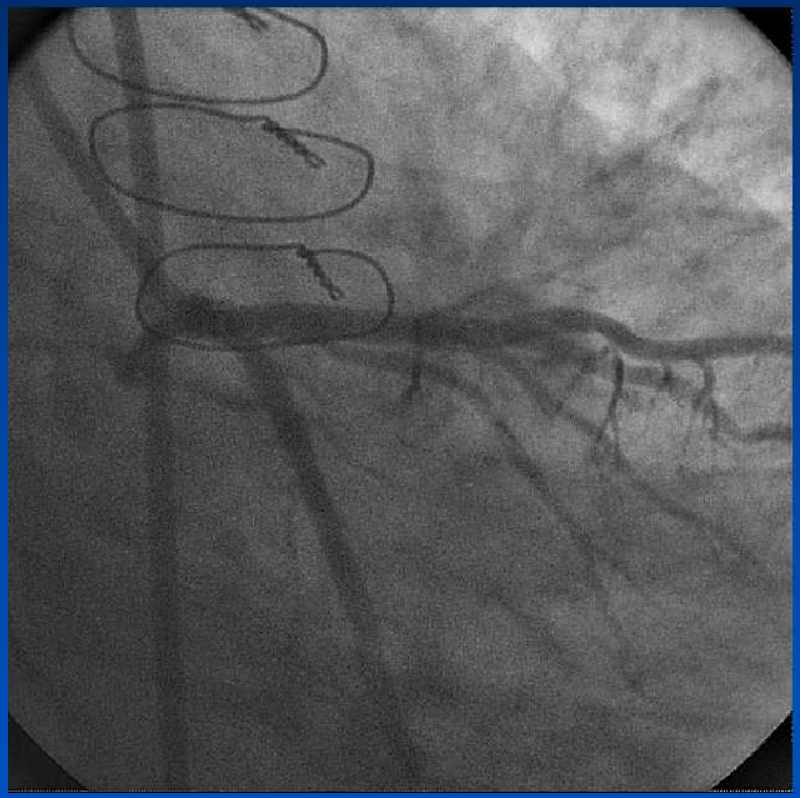
Final Kissing with big balloon

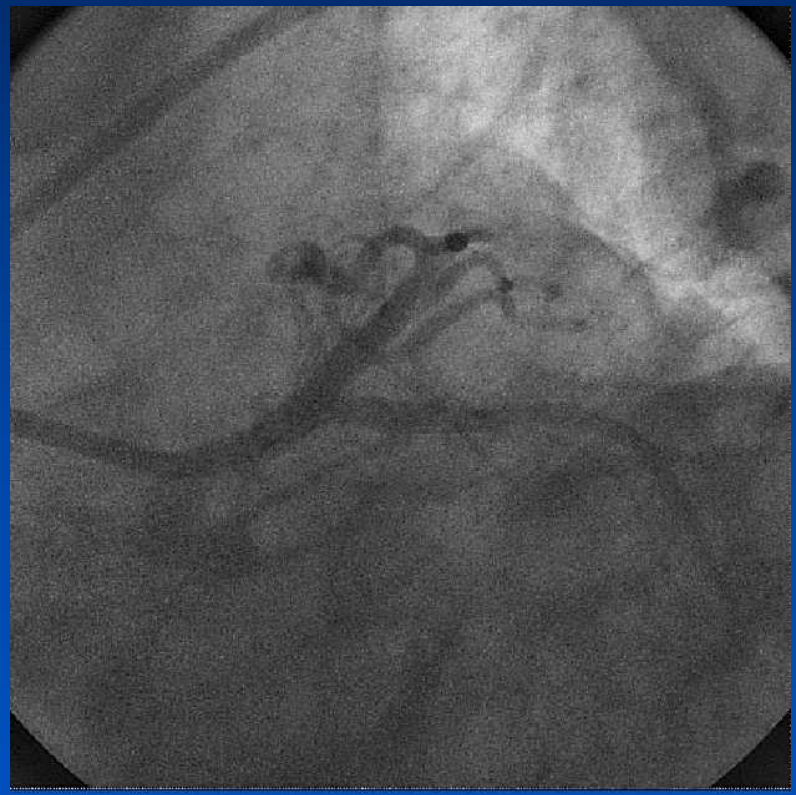


LAD: Quantum 4.5x12mm
LCX: Quantum 3.0x12mm

Final Results

Stent crushing again on the both edge restenosis

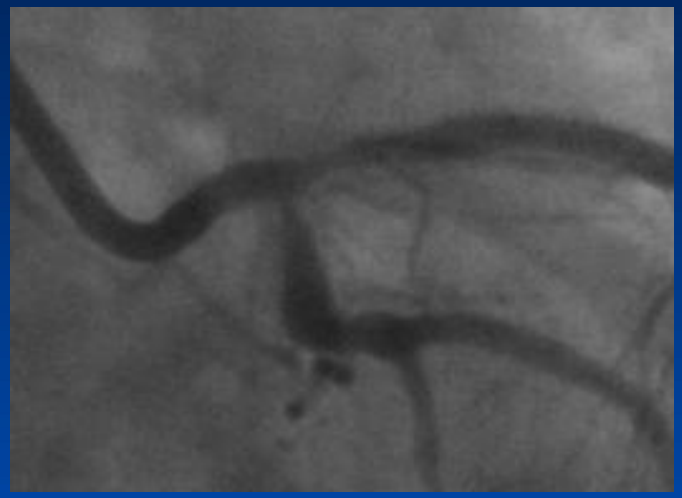


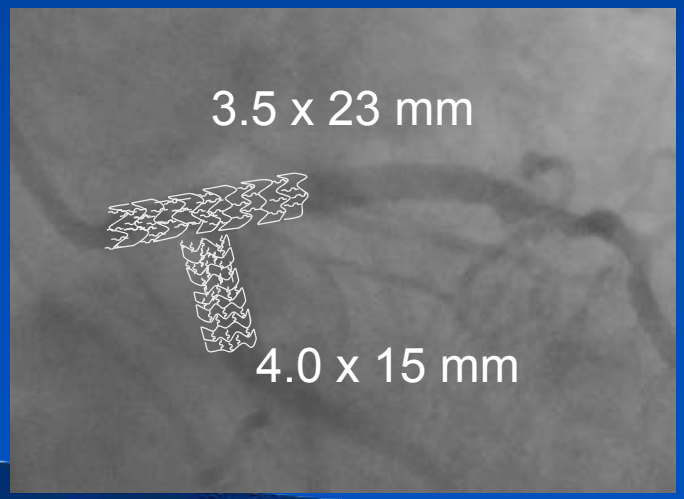


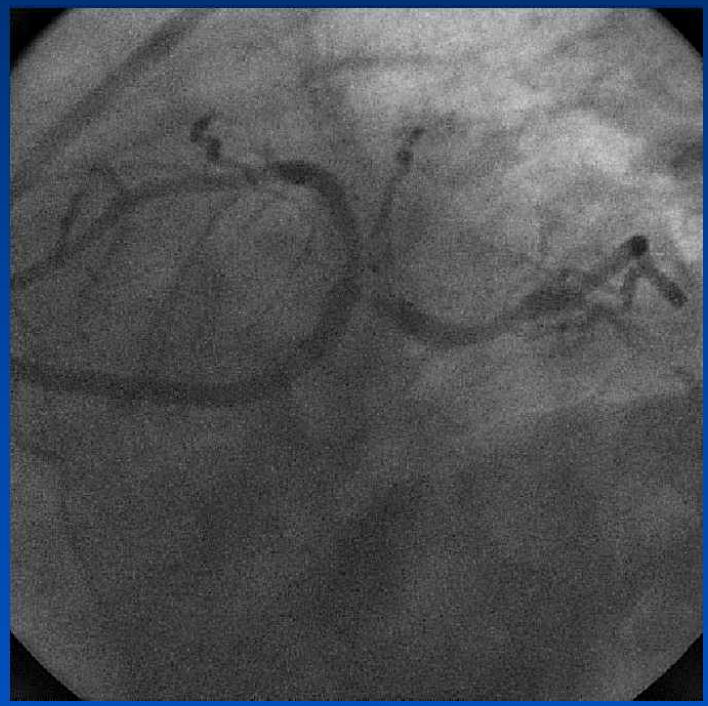
DES failure
after LM Bifurcation Stenting
(Classic T stent technique)

66/M,
Unstable angina,

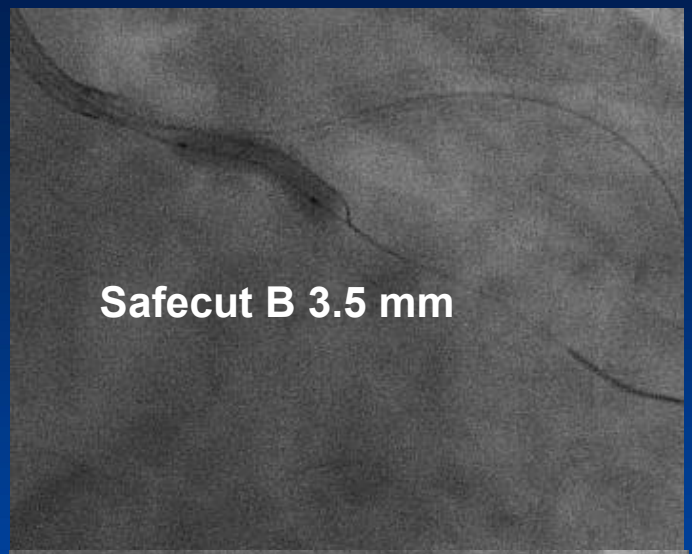
9 months after classic T stent - technique for distal LM disease
LM-LAD: Cypher 3.5x23 mm
LM-LCX: Cypher 4.0x15 mm

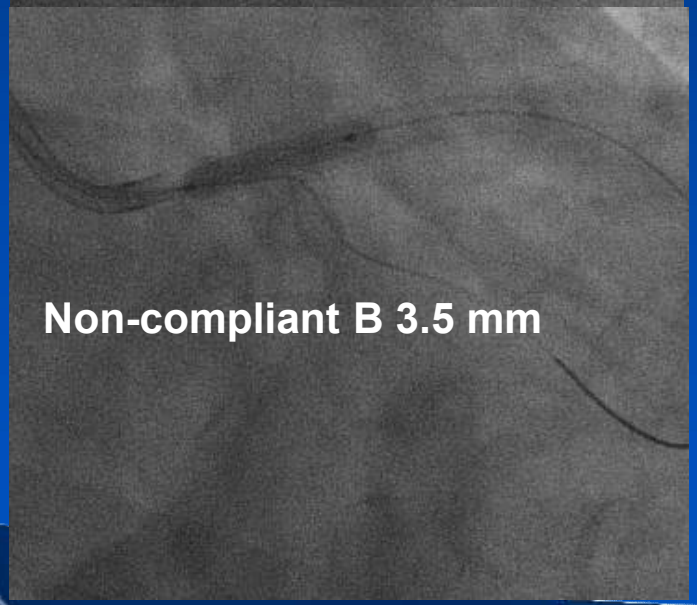


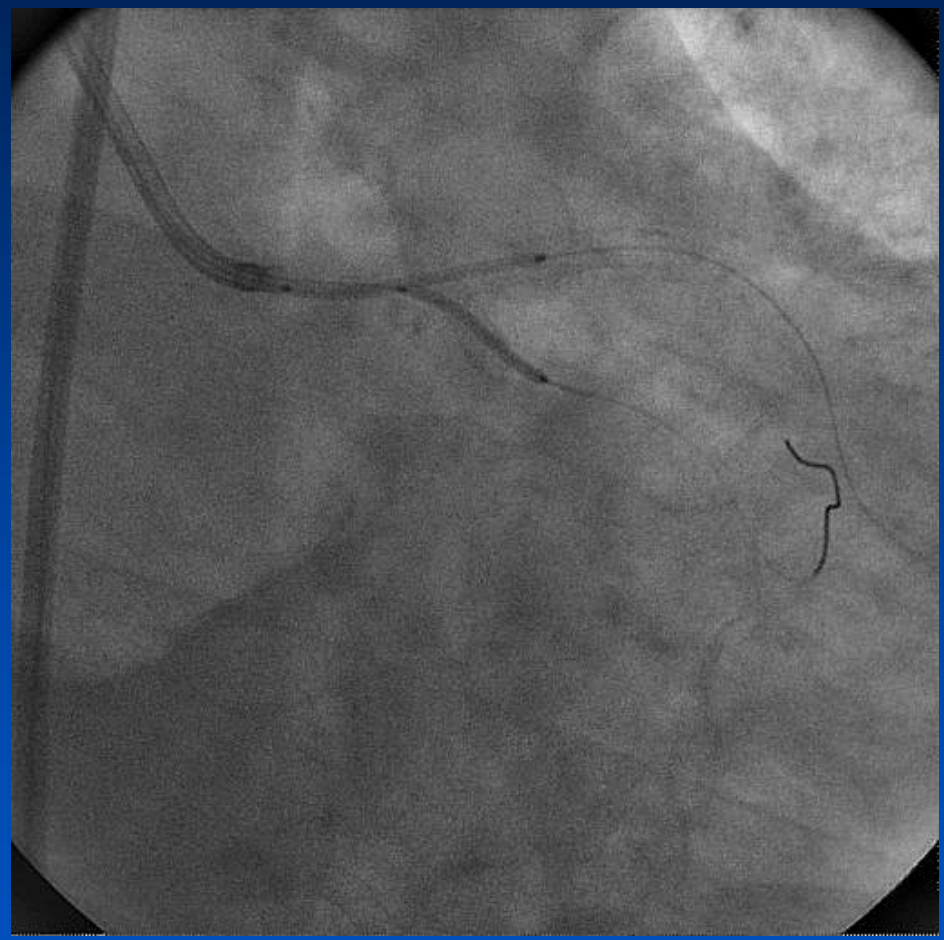




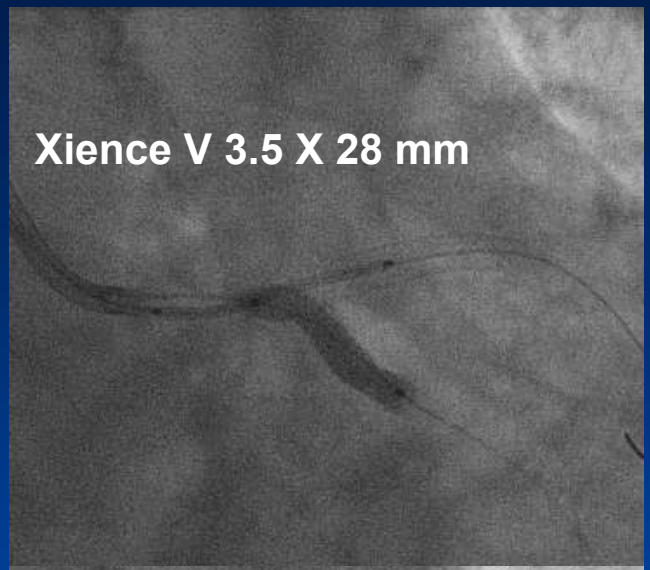
Mini-Crushing again with Xience V stents through the previous T stents

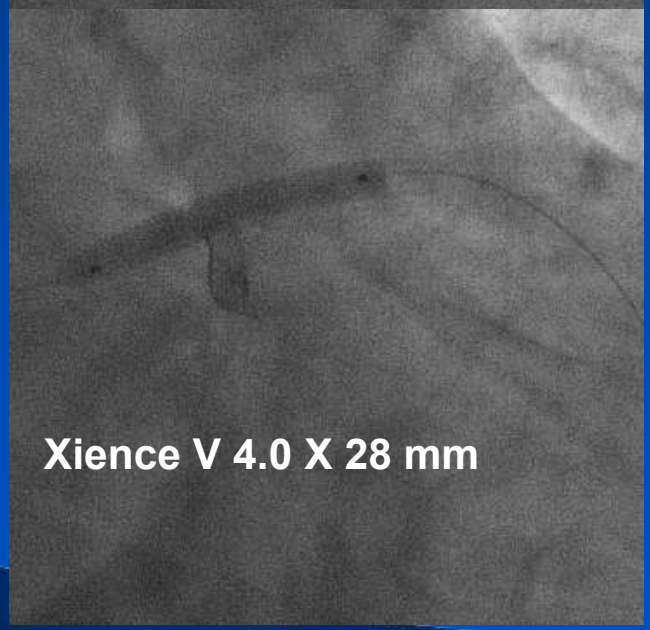




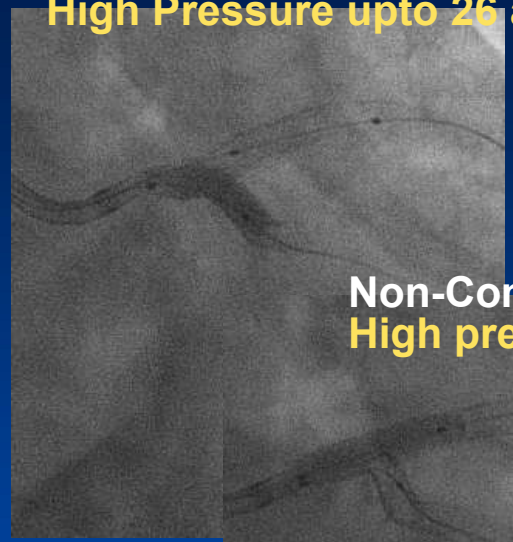


Stent Crushing again with Xience V

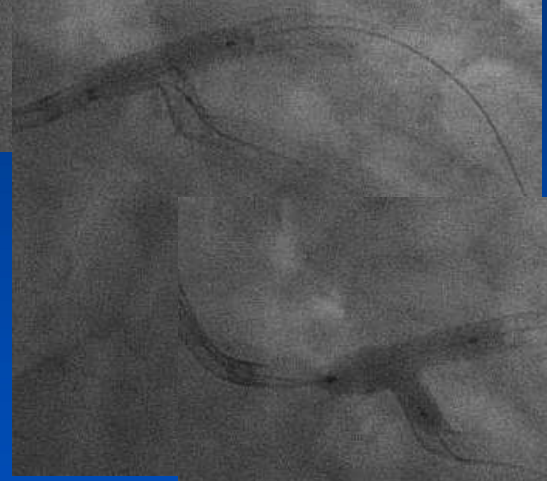


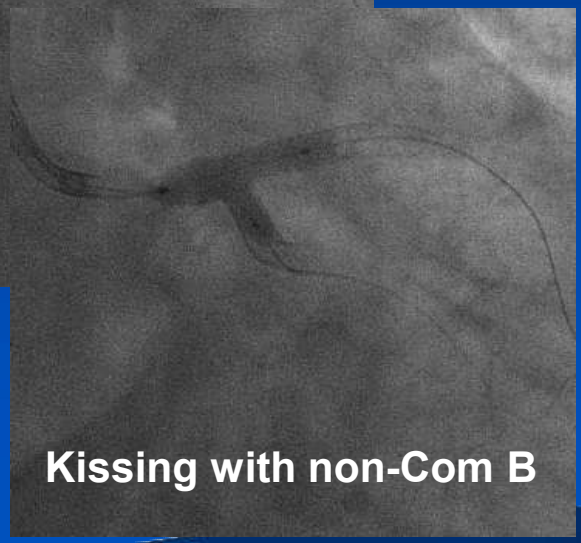


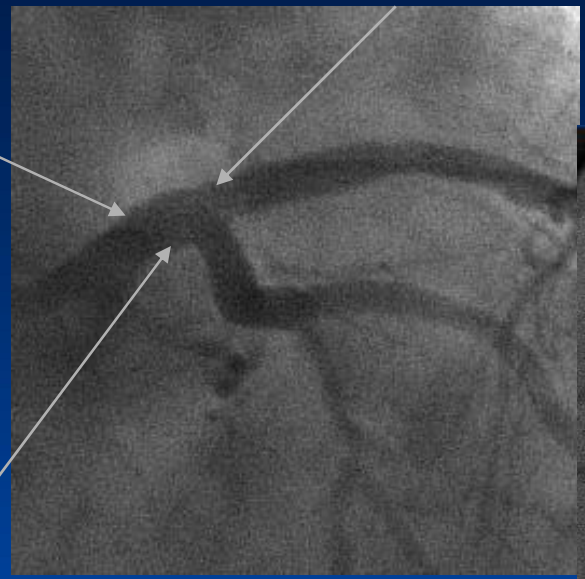
Non-Com B 3.5 X 18 mm
High Pressure upto 26 atm.

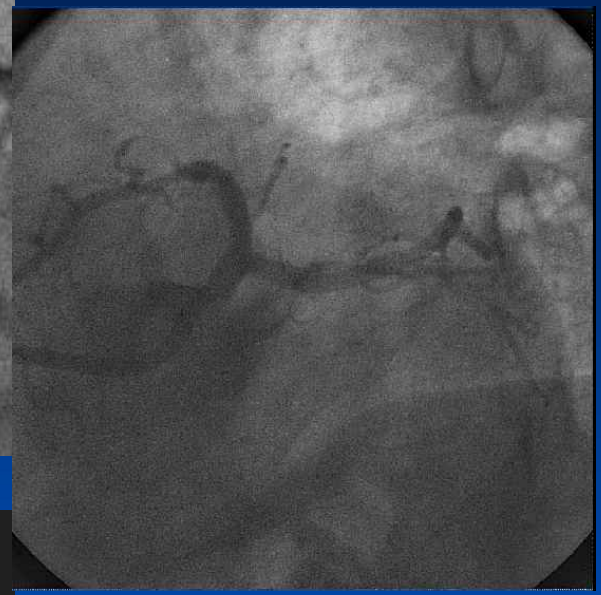


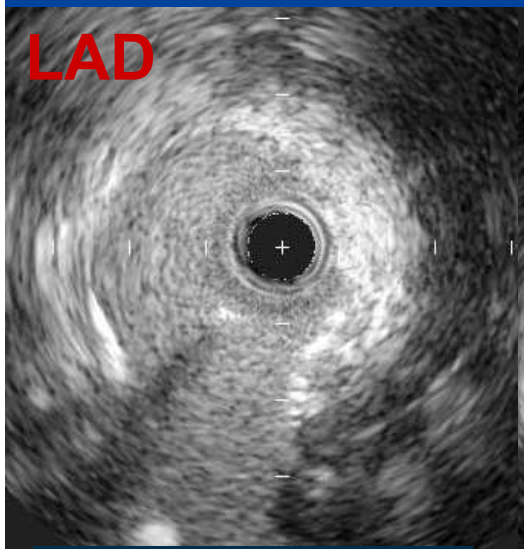
Non-Com B 4.0 X 18 mm
High pressure



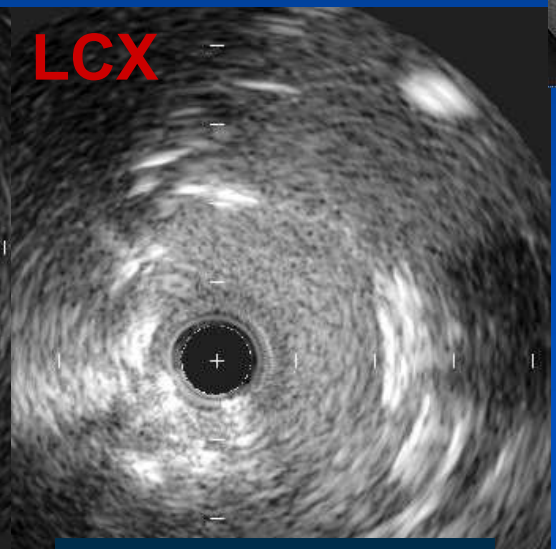








LAD os: 6.5 mm^2



LCX os: 5.2 mm^2

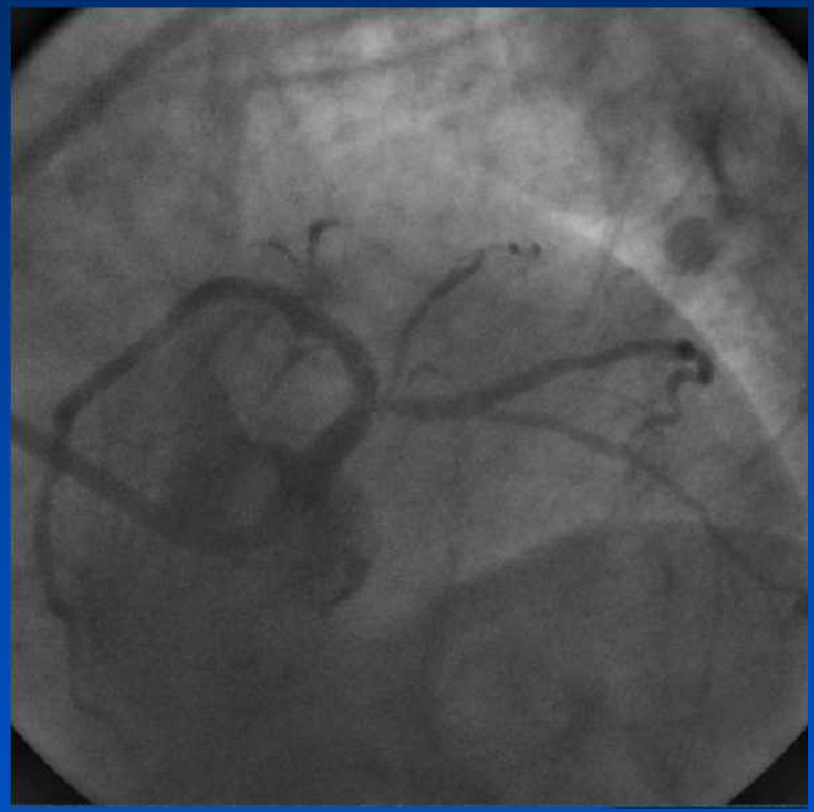
Stent Crushing again on the previous T stent technique

DES failure
after LM Bifurcation Stenting
(TAP technique)

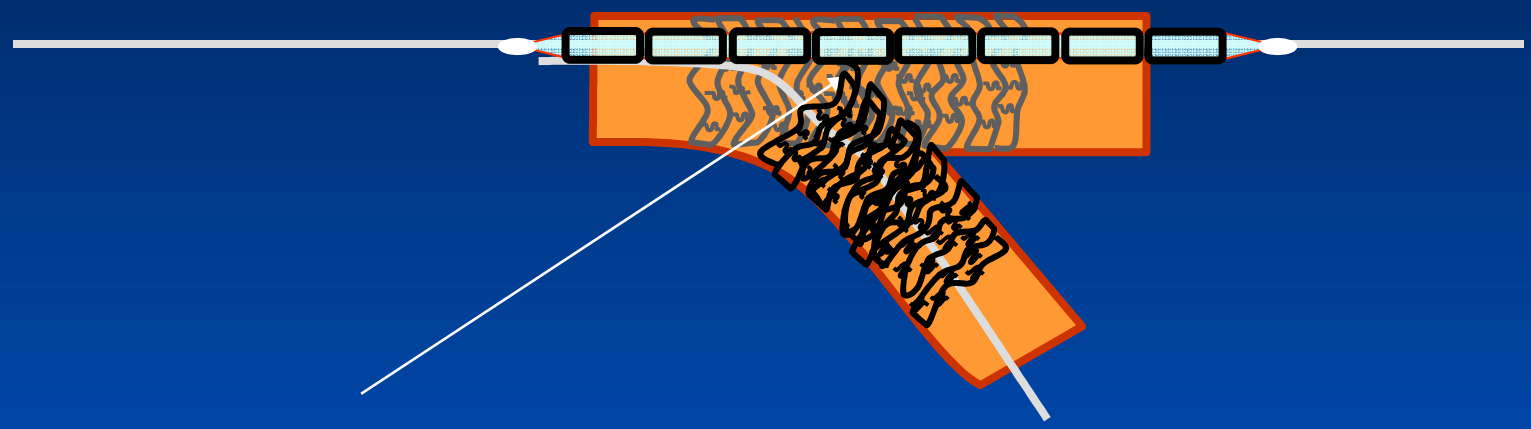
60/M,
Unstable angina,

One-year after TAP technique for distal LM disease

LM-LAD: Cypher 3.5x23, 3.0x33
LM-LCX: Cypher 2.75x18

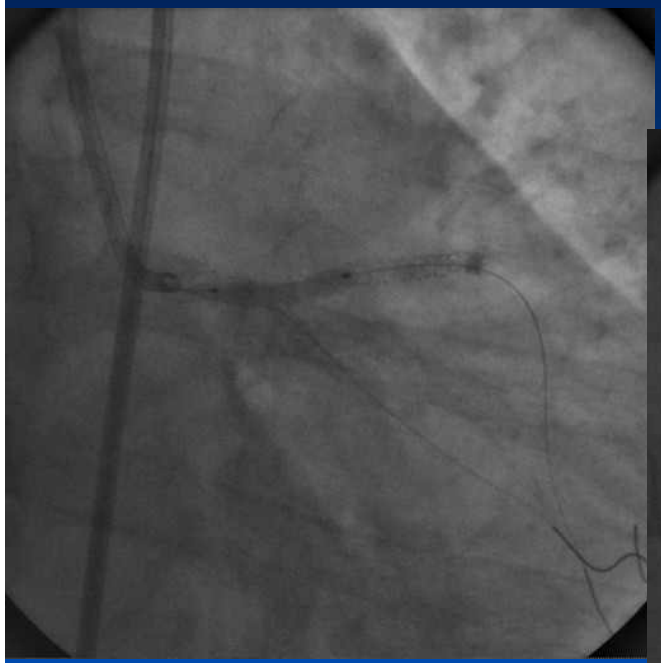


Second Stent Crossover again

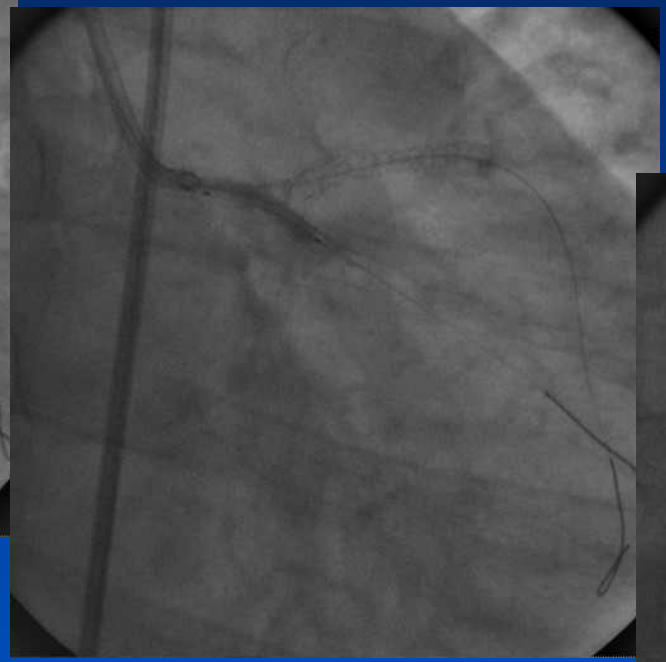


Small protrusion of previous stent

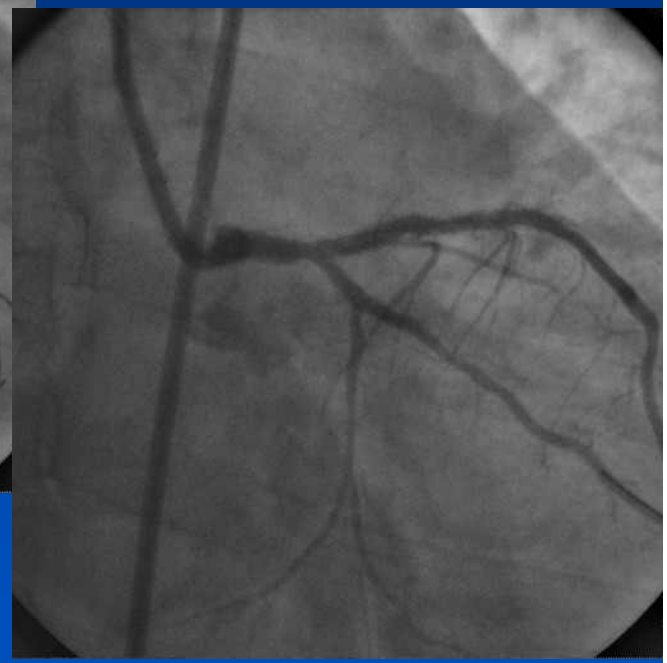
Safe-cut dilation as a pre-modification of ISR (DES failure)



Safecut 2.5x20mm

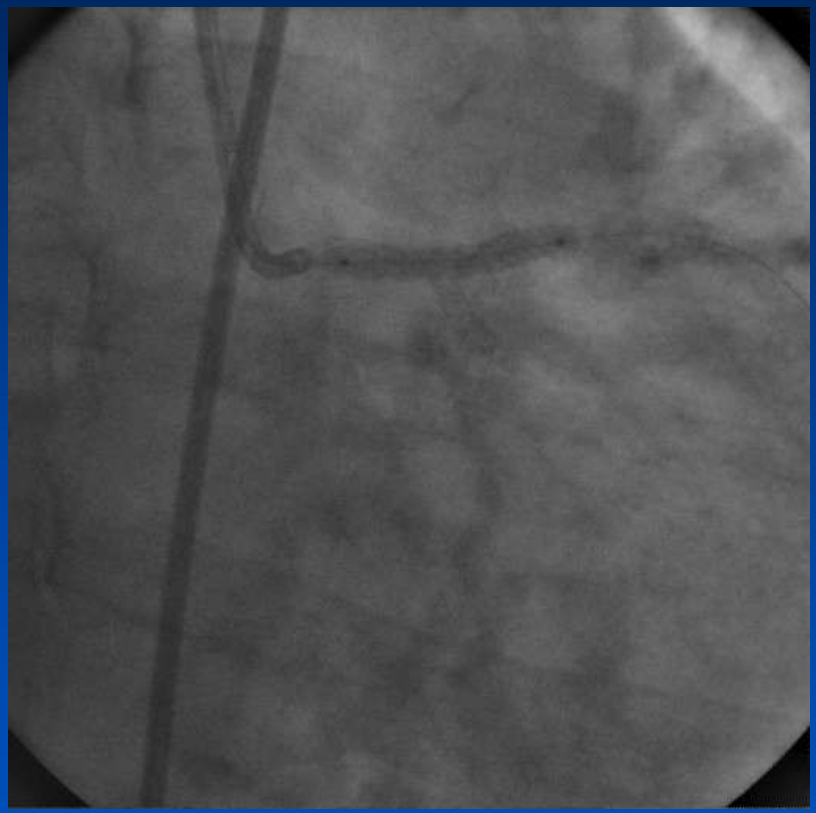


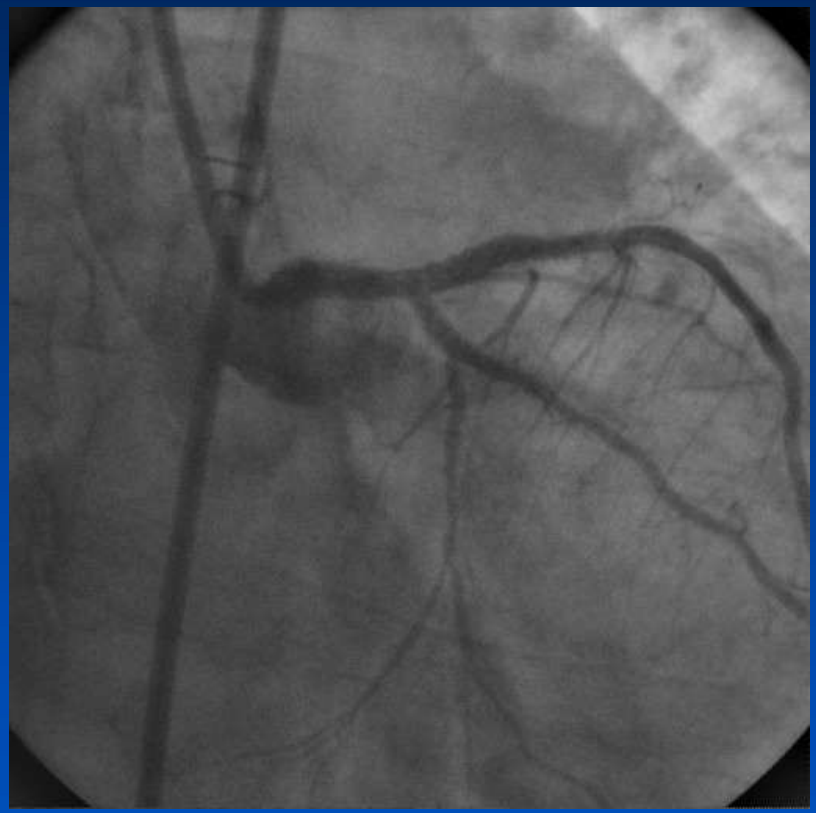
Safecut 2.5x20mm



After safecut

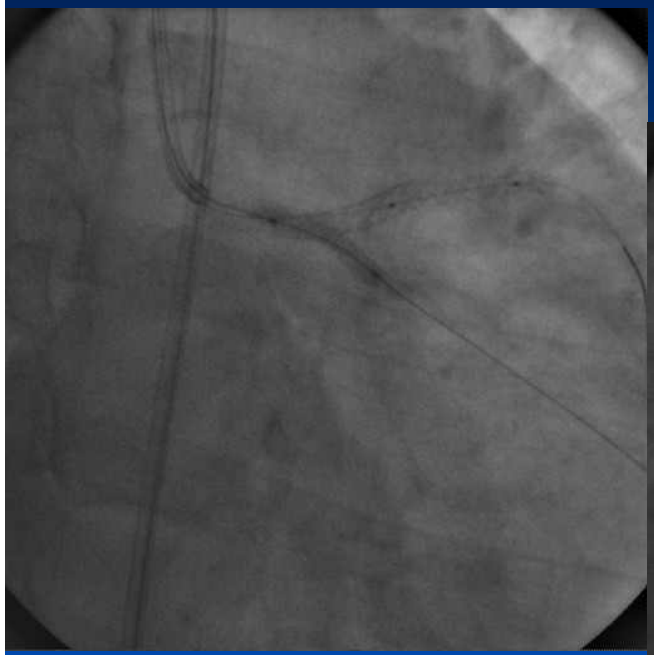
Second Stent Crossover again





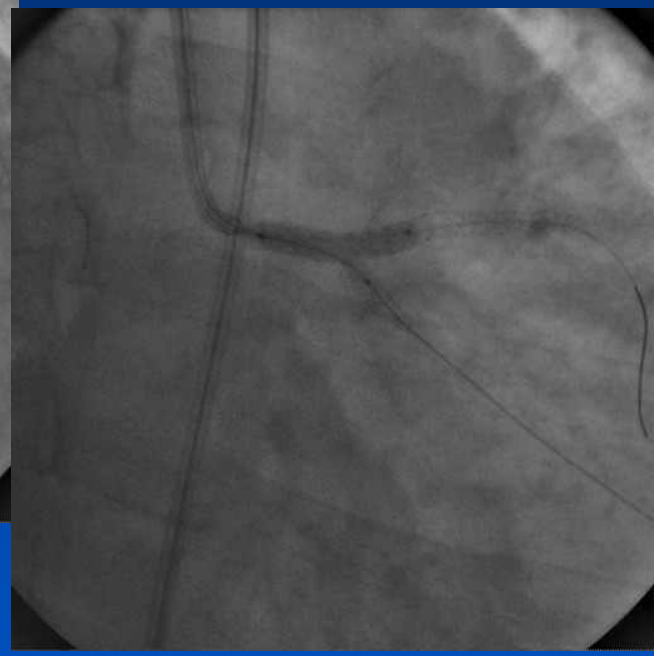
Xience V 3.5x28mm

High pressure inflation at LCX ostium (25atm) and final kissing with big balloon



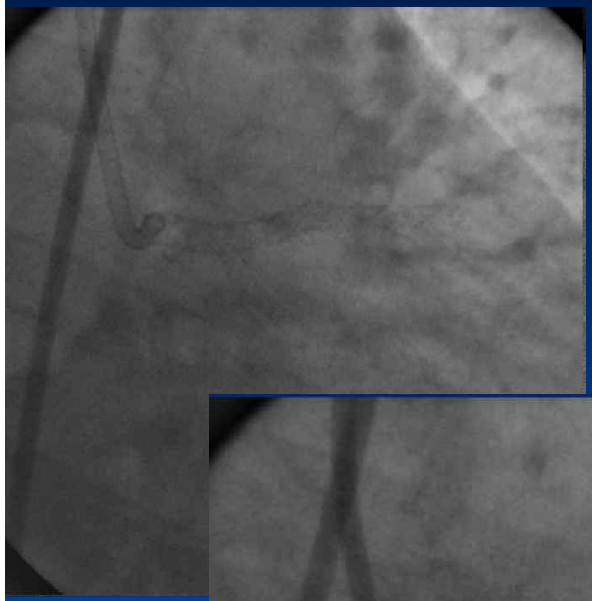
Fortis 3.0x20mm
25 atm

LM High-pressure
Fortis 4.0x13mm

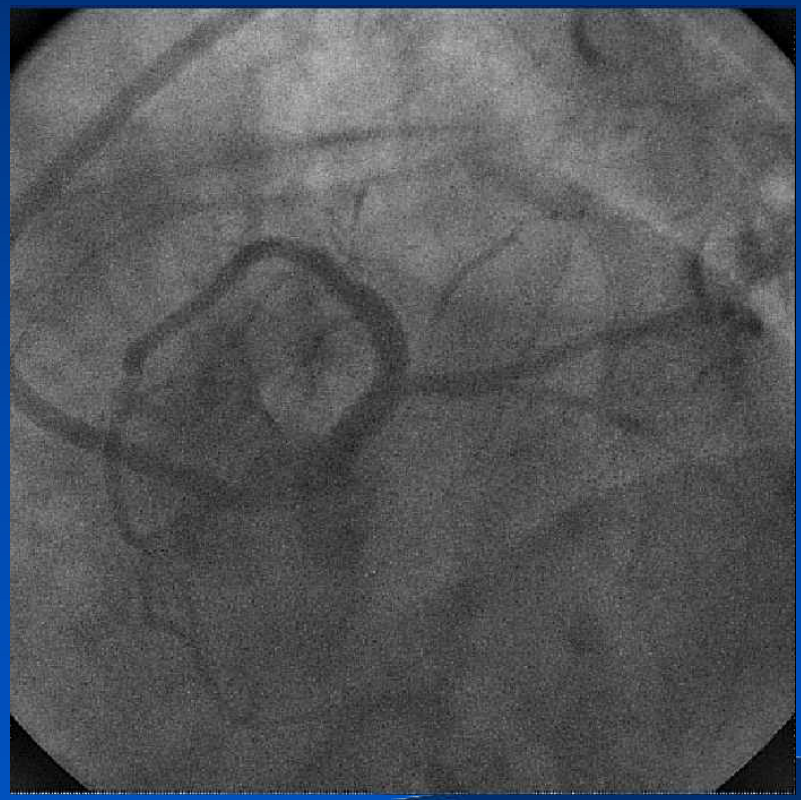


LAD: Amadeus 4.0x20mm LC
Runner 3.0x20mm

Final Results



Stenting cross over again
on the previous TAP technique



How do we treat the LM DES failure ?

High pressure stent crushing again using thinner strut DES (Xience V) and /or non-compliant large balloon crushing with high pressure alone under the IVUS guidance may be effective alternative in some cases

Xience V stent would be the only choice for extreme cases like LM and LM DES failure due to thinner stent strut.

Xience V stent - New Paradigm

Better performance than Endeavor and Taxus. Similar performance with Cypher. Only for extreme.

Thank You !!

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