

Comparative Outcomes of Contemporary DES: Are there Major Difference?

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Disclosure Statement of Financial Interest

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

Affiliation/Financial Relationship

- Grant/Research Support
- Scientific Advisory Board
- Executive Physician Council

Company

- Abbott Vascular, Medtronic
- Medtronic, Abbott Vascular
- Boston Scientific Corp

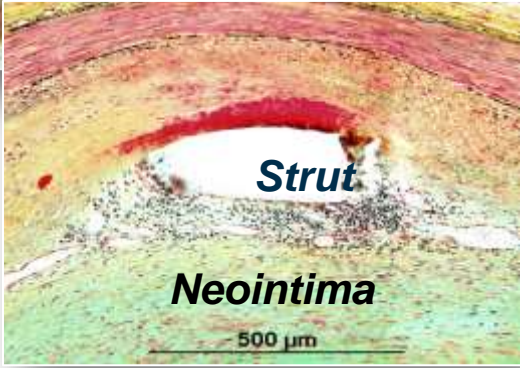
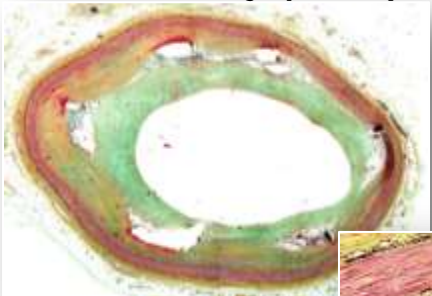


ALL DES ARE THE SAME?

- **No !**
 - **First Gen not as good as Second Gen....**
 - **May require greater than 1 year of DAPT**
- **Yes !**
 - **Second Gen similar in TLF (composite and individual endpoints) in the short to medium term**
 - **Deliverability**
- **May be not the same?**
 - **Bioabsorbable Polymer vs Durable Polymer**
 - **Duration of DAPT**

Delayed Arterial Healing in 1st Generation DES

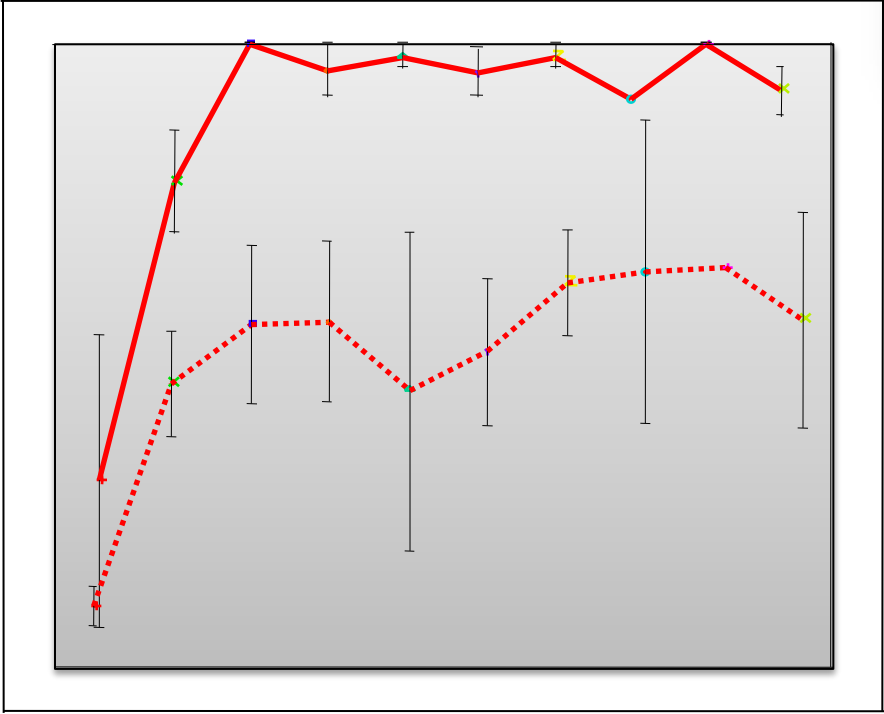
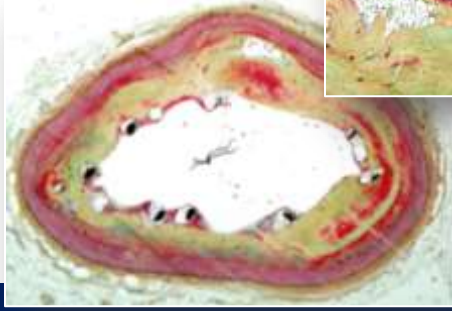
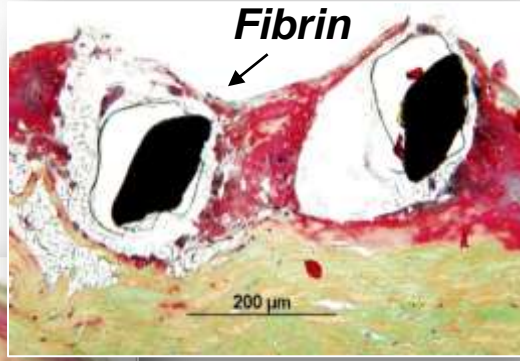
BxVelocity (BMS)



— **BMS**

... **DES**

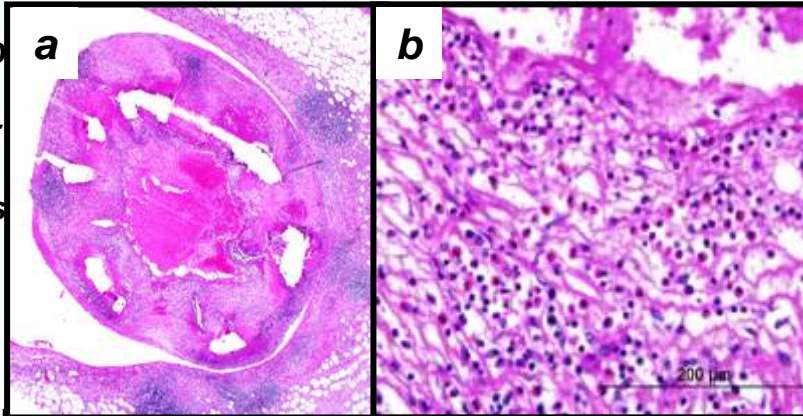
Cypher (DES)



Mean % Endothelialization

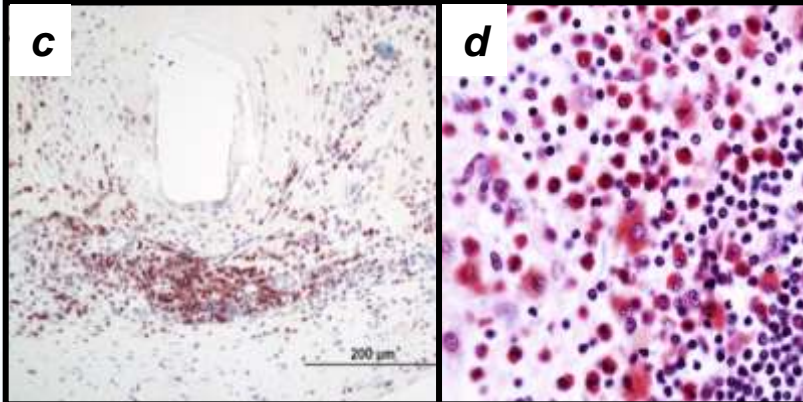
Hypersensitivity Reaction to SES

40F with 2 SES in LAD and RCA, died suddenly 4 days after surgical removal of melanoma. DAPT was discontinued 5 days before surgery.



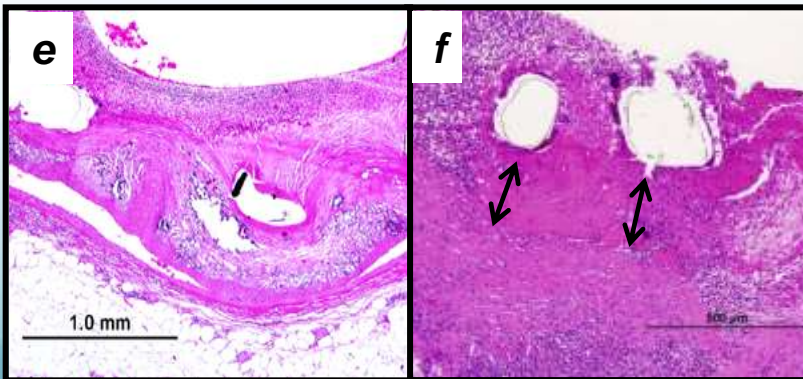
(a)-(d)

LAD: SES
17months

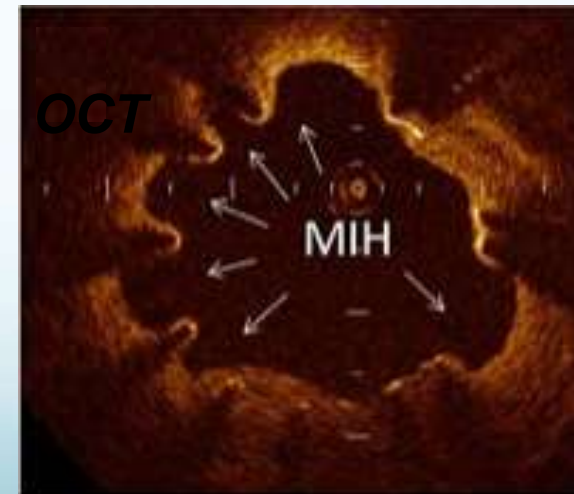
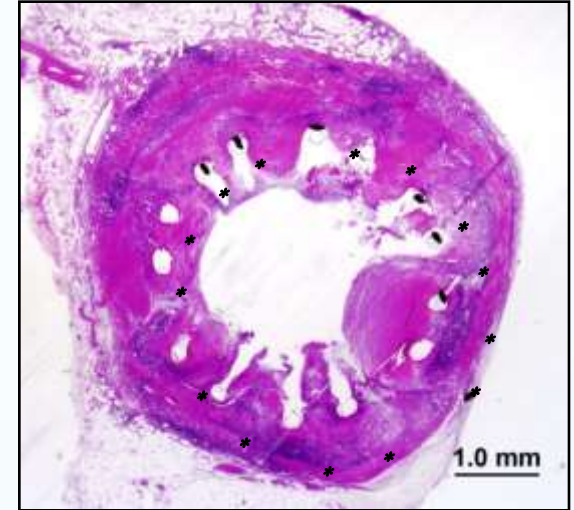


(e), (f)

RCA: SES
17months



39F SES in LMCA for 5 yrs.
The patient recently stopped taking medication due to lack of insurance.

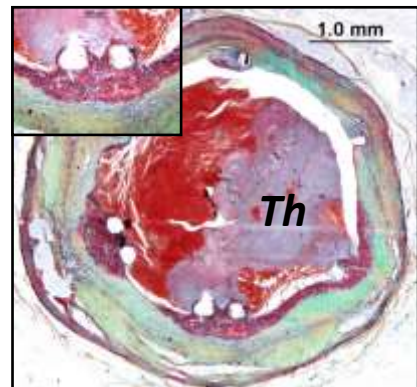


MIH = Multiple interstrut hollow

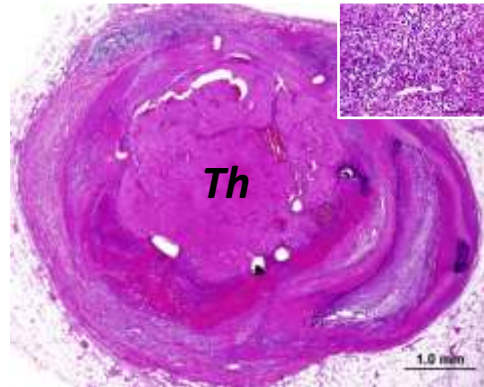
Pathology of 1st-Generation DES: High Efficacy, Incomplete Healing

- **Thick struts**
- **Thick, durable coating (~15 μm)**
- **High drug dose**
- **High polymer load**

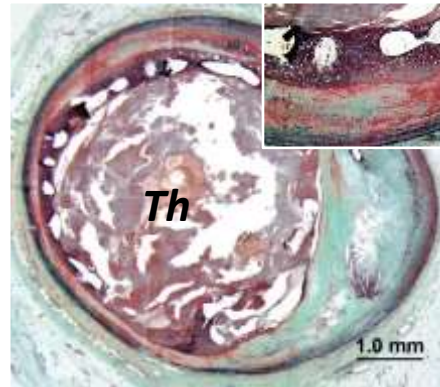
- ✓ **Uncovered struts**
- ✓ **Hypersensitivity**
- ✓ **Malapposition**
- ✓ **Late stent thrombosis**
- ✓ **Neoatherosclerosis**



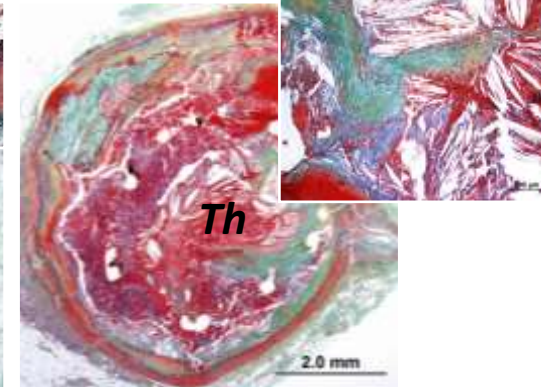
Uncovered struts



Hypersensitivity reaction



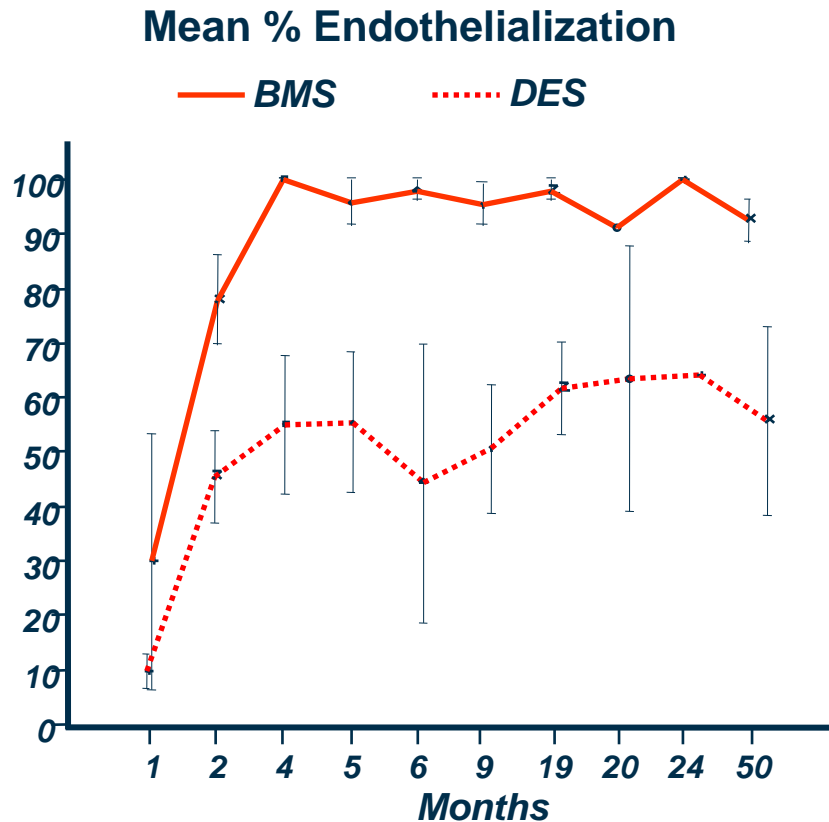
**Malapposition from
excessive fibrin deposition**



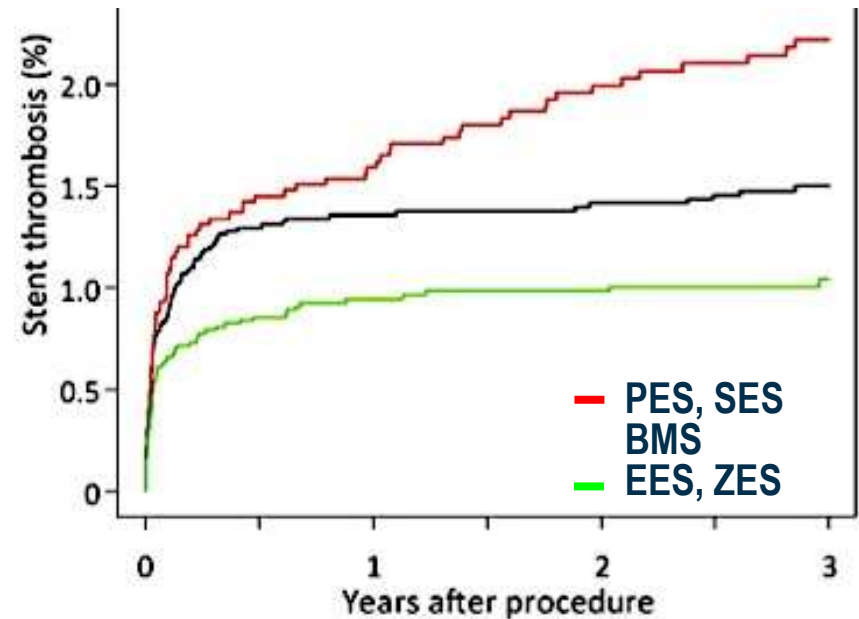
Neoatherosclerosis

Late and Very Late Stent Thrombosis (LST/VLST) Following 1st-generation DES

Registry of 18 334 patients



Joner M & Finn AV. J Am Coll Cardiol. 2006;48:193-202.

















Tada et al. JACC INTV 2013; 6:1267-74

Annual Rate of LST/VLST

- ✓ 0.4-0.6%/year up to 4 years (Bern/Rotterdam registries: SES and PES)
- ✓ 0.26%/year up to 5 years (j-Cypher: SES)

Consistency of Treatment Effect MACCE (12-30 Months)

Factor	N		HR and 95% CI	Interaction P
< 75 Years	N=8929		0.69 (0.57,0.83)	0.22
>= 75 Years	N=1032		0.95 (0.59,1.52)	
Male	N=7435		0.69 (0.56,0.85)	0.46
Female	N=2526		0.81 (0.56,1.17)	
No diabetes	N=6924		0.59 (0.46,0.74)	0.01
Diabetes	N=3037		0.95 (0.72,1.25)	
No Risk Factors for ST	N=5162		0.78 (0.60,1.03)	0.41
Risk Factors for ST	N=4799		0.67 (0.53,0.86)	
Clopidogrel	N=6500		0.80 (0.64,1.01)	0.03
Prasugrel	N=3461		0.52 (0.38,0.71)	
Sirolimus	N=1118		0.54 (0.31,0.93)	0.048
Zotarolimus	N=1264		0.76 (0.44,1.30)	
Paclitaxel	N=2666		0.52 (0.37,0.71)	
Everolimus	N=4703		0.89 (0.67,1.18)	



TWENTE Trial

- 1391 pts with stable angina or non-ST-elevation ACS requiring DES
- No limit of number of lesions or vessels treated
- No limit of RVD or lesion length
- Exclusions: STEMI <48°, hemodialysis, staged PCI

Zotarolimus-eluting
Resolute
n = 697

1:1 Randomization

Everolimus-eluting
Xience V
n = 694

30 d

1 yr

2 yrs

Control angiography only if clinically indicated

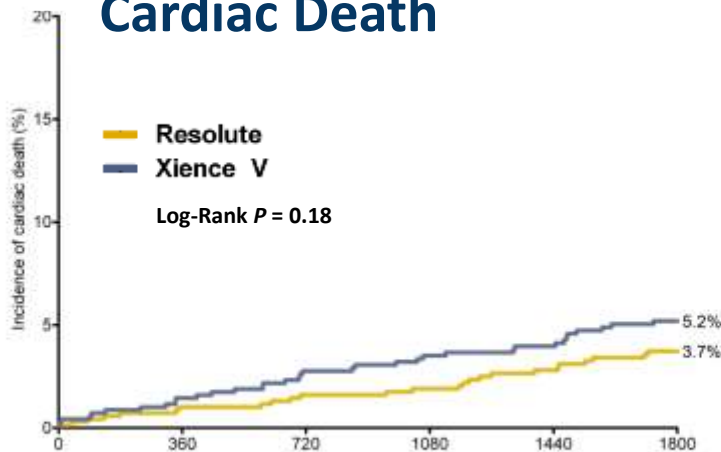
Primary endpoint Target vessel failure at one year

Secondary endpoints Components of primary endpoint; stent thrombosis; patient oriented composite endpoint



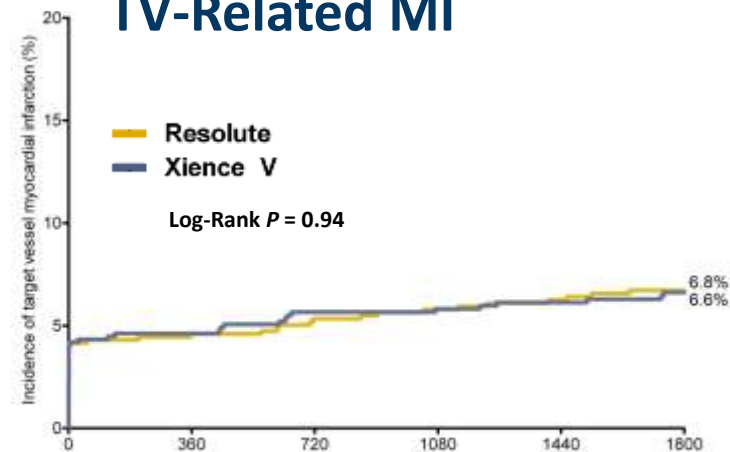
TWENTE 5-Years: CD, TV-MI, CI-TVR, TVF

Cardiac Death



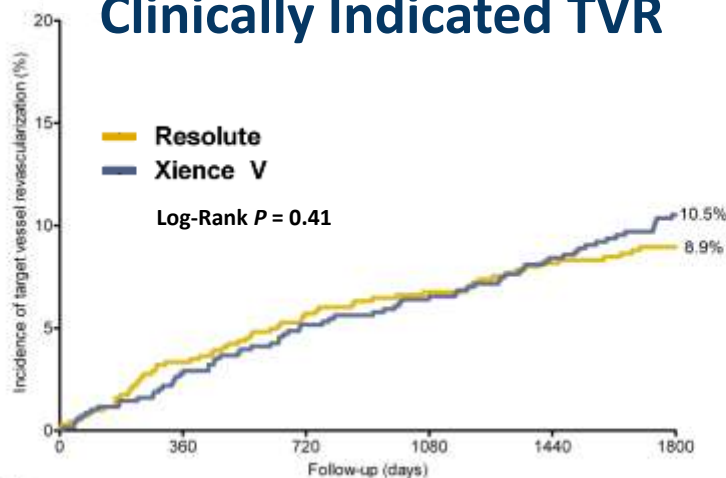
Number at risk		0	360	720	1080	1440	1800
Resolute	697	680	666	657	639	621	
Xience V	694	678	659	645	628	607	

TV-Related MI



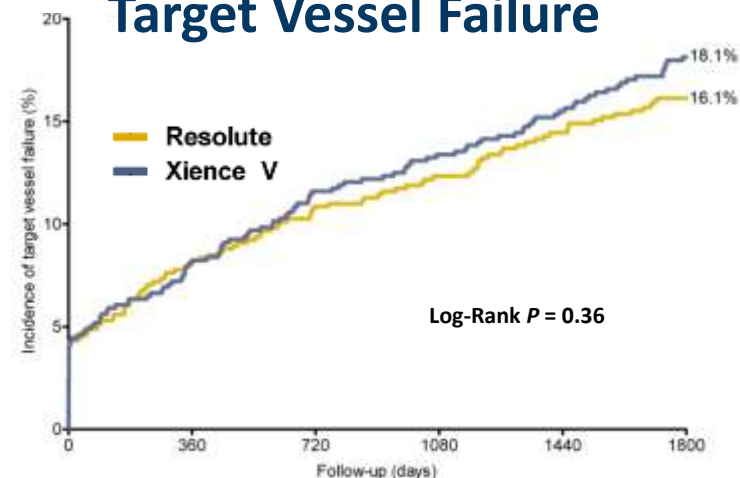
Number at risk		0	360	720	1080	1440	1800
Resolute	697	649	632	621	601	582	
Xience V	694	650	626	611	593	570	

Clinically Indicated TVR



Number at risk		0	360	720	1080	1440	1800
Resolute	697	657	629	614	589	567	
Xience V	694	659	626	605	578	548	

Target Vessel Failure



Number at risk		0	360	720	1080	1440	1800
Resolute	697	631	603	588	563	541	
Xience V	694	632	600	579	553	523	

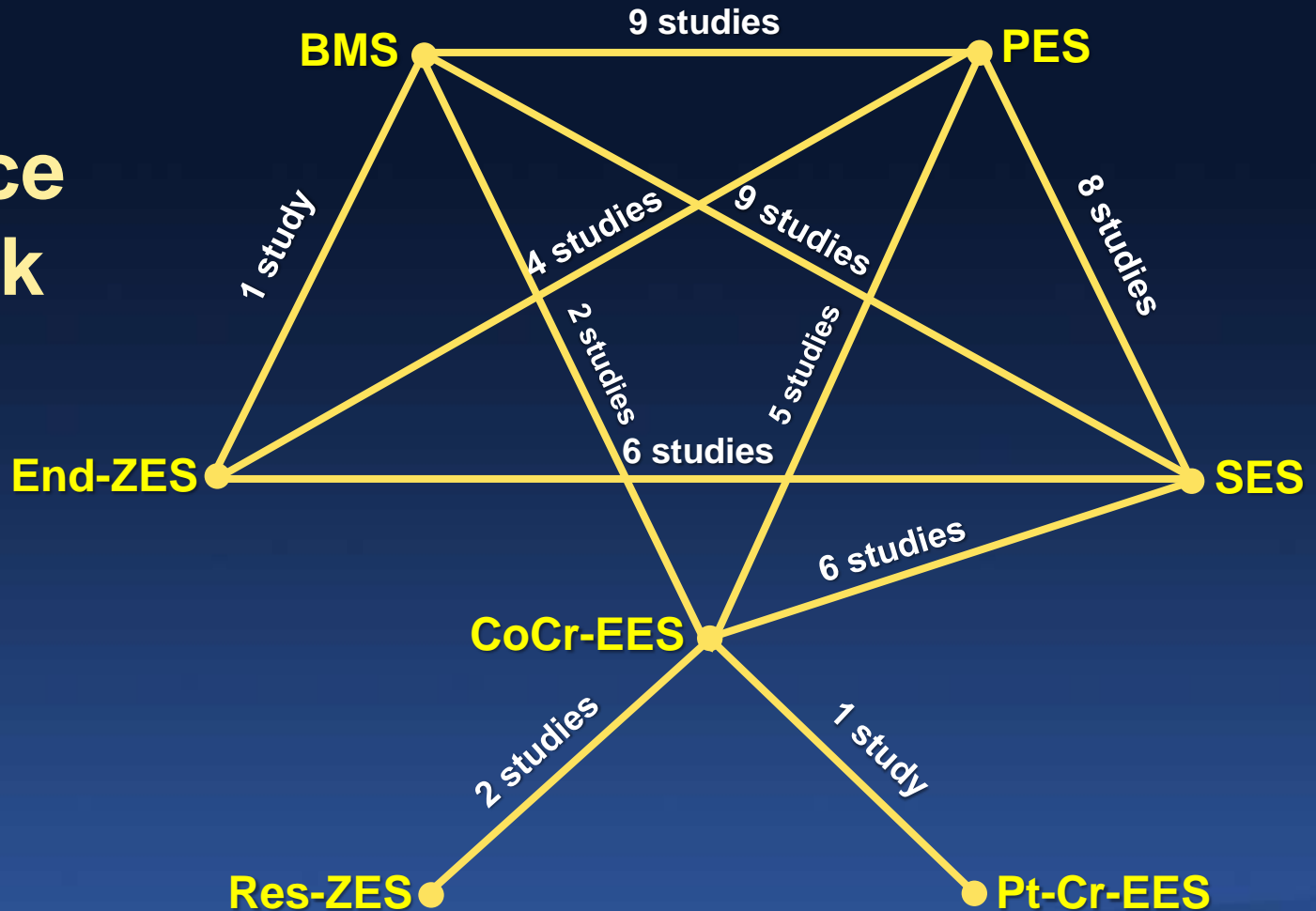
MI = myocardial infarction; TV = target vessel; TVF = target vessel failure; TVR = target vessel revascularization

Stent Thrombosis Network Meta-analysis

Primary EP: ARC Definite ST (FU through 2 years)

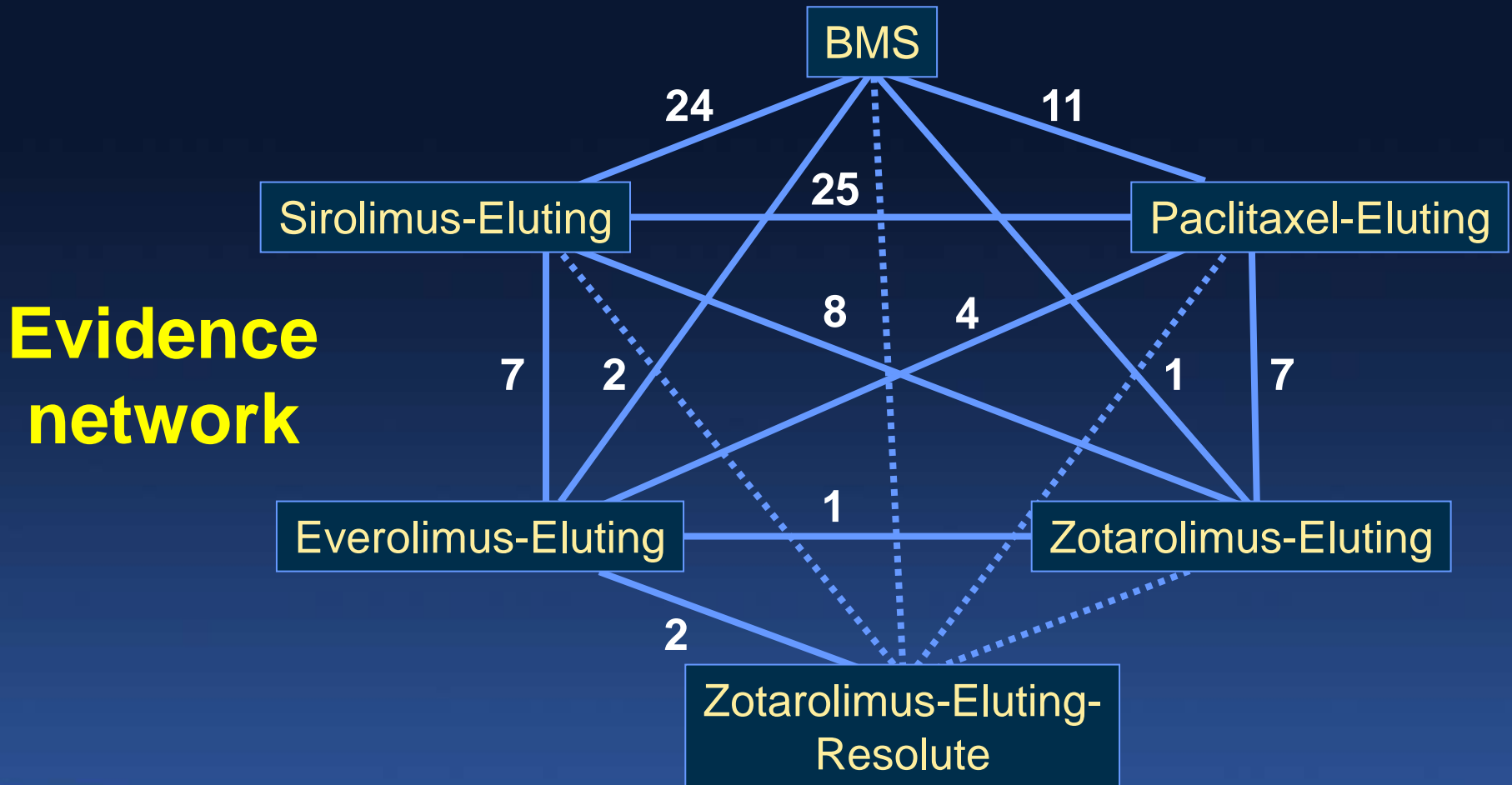
49 RCTs, 50,844 pts

Evidence
network



Network Meta-analysis

Endpoints: Death, MI, ST, TVR early (<1 yr) and late
77 RCTs, 57,138 pts, 117,762 pt-yrs of FU



Network Meta-analysis: Median Long-term Event Rates (per 1,000 Pt-Years of Follow-Up)

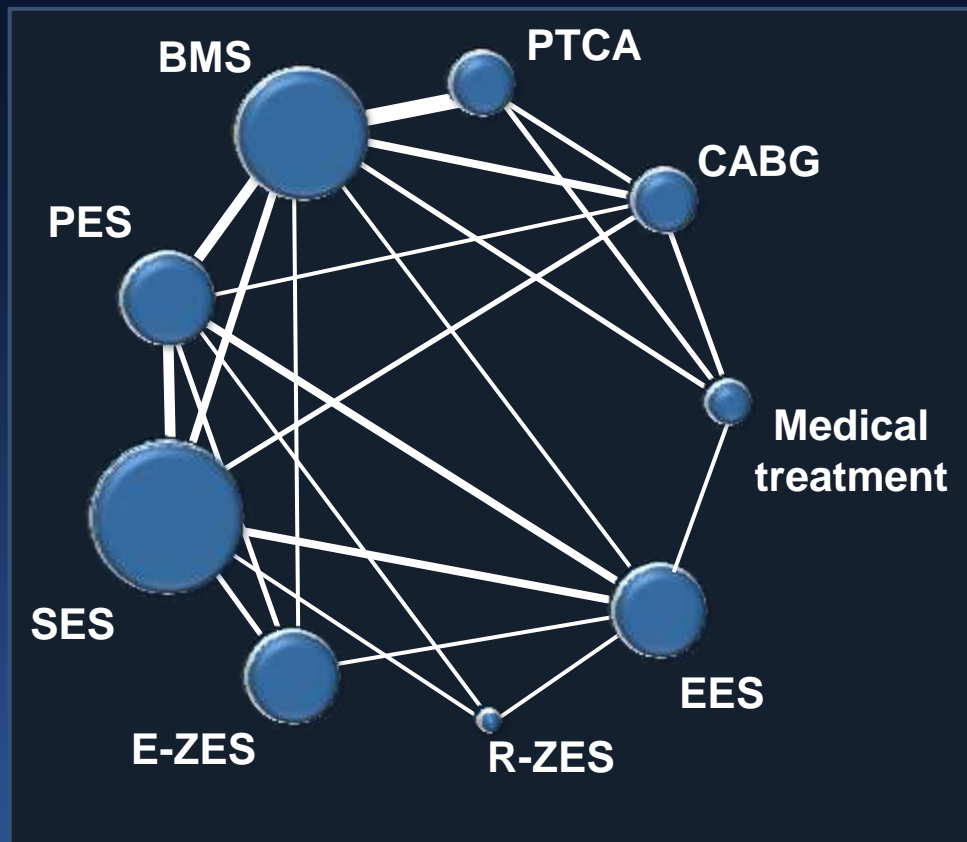
77 RCTs, 57,138 pts, 117,762 pt-yrs of FU

Stent type	Death rate (95% CrI)	Prob of Being Best, %	MI Rate (95% CrI)	Prob of Being Best, %	Rate of Def/Prob ST (95% CrI)	Prob of Being Best, %	TVR Rate (95% CrI)	Prob of Being Best, %
Bare metal	16.60 (12.87-21.59)	0.25	26.51 (23.4-29.79)	0.00	7.17 (5.54-8.96)	0.03	89.42 (82.88-96)	0.00
SES	15.05 (11.52-19.74)	1.58	21.78 (18.92-24.86)	0.08	5.75 (4.28-7.63)	0.11	35.15 (30.71-39.84)	35.22
PES	14.99 (11.48-19.65)	8.87	27.32 (23.59-31.56)	0.00	7.95 (5.84-10.69)	0.00	54.30 (46.92-62.09)	0.00
EES	13.18 (9.54-18.05)	17.17	16.75 (13.55-21.08)	46.90	3.27 (2.15-4.98)	73.33	34.40 (27.49-42.38)	42.07
E-ZES	15.74 (11.19-21.86)	3.65	18.23 (13.77-23.56)	26.66	4.95 (2.73-8.87)	9.51	54.54 (42.86-68.71)	0.01
R-ZES	11.55 (5.02-19.55)	68.48	18.22 (12.15-27.04)	26.36	4.47 (1.98-10.07)	17.02	39.00 (24.53-61.43)	22.70

Revascularization vs. Medical Rx: Impact of new DES

100 trials in 93,553 pts with 262,090 pt-yrs follow-up

Network of Trials

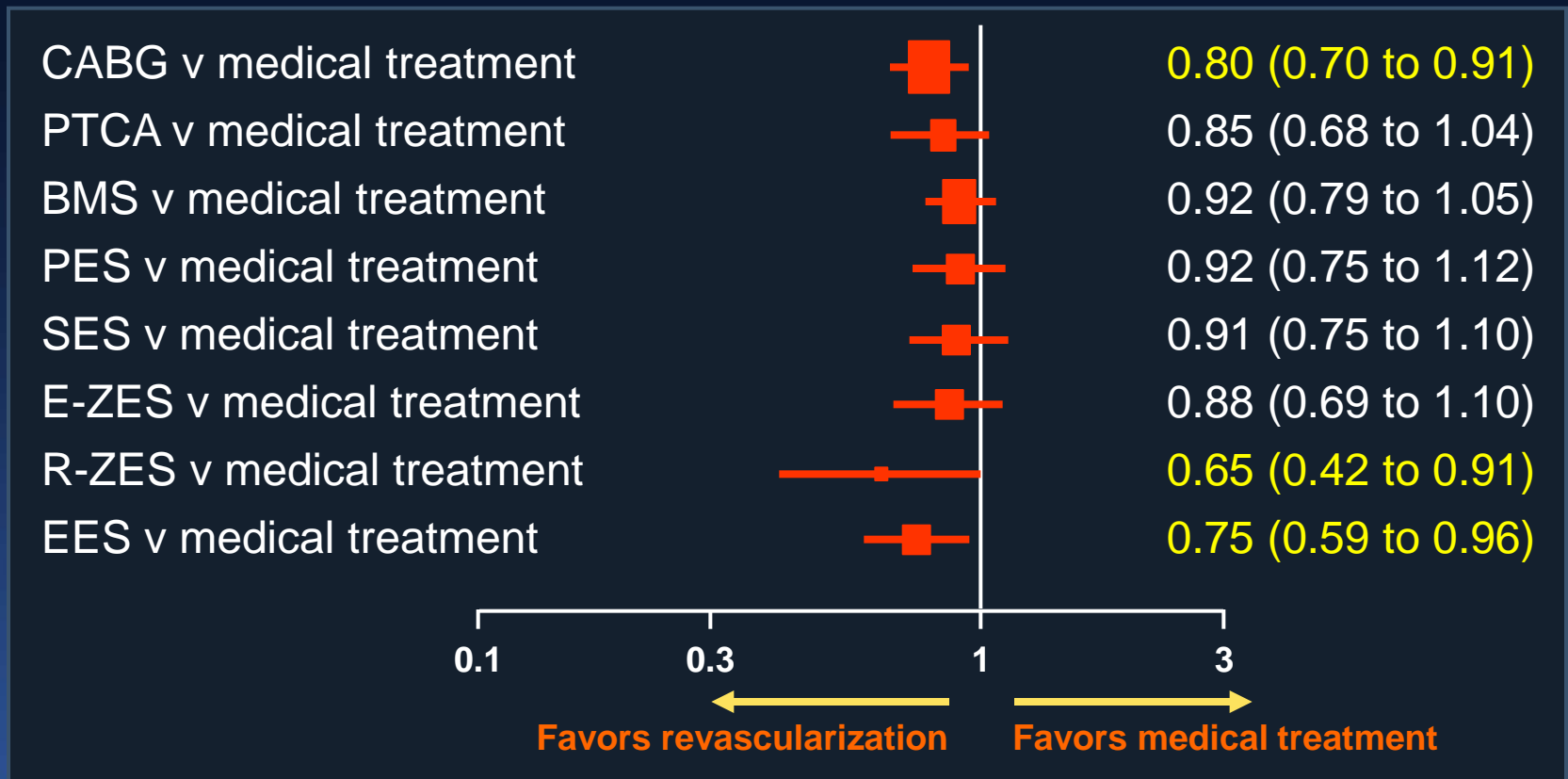


Treatment	Follow-up (Patient-Years)*
Medical	30,628
CABG	38,709
PTCA	17,678
BMS	45,467
PES	27,592
SES	45,879
E-ZES	27,134
R-ZES	3,384
EES	23,619

Revascularization vs. Medical Rx: Impact of new DES

100 trials in 93,553 pts with 262,090 pt-yrs follow-up

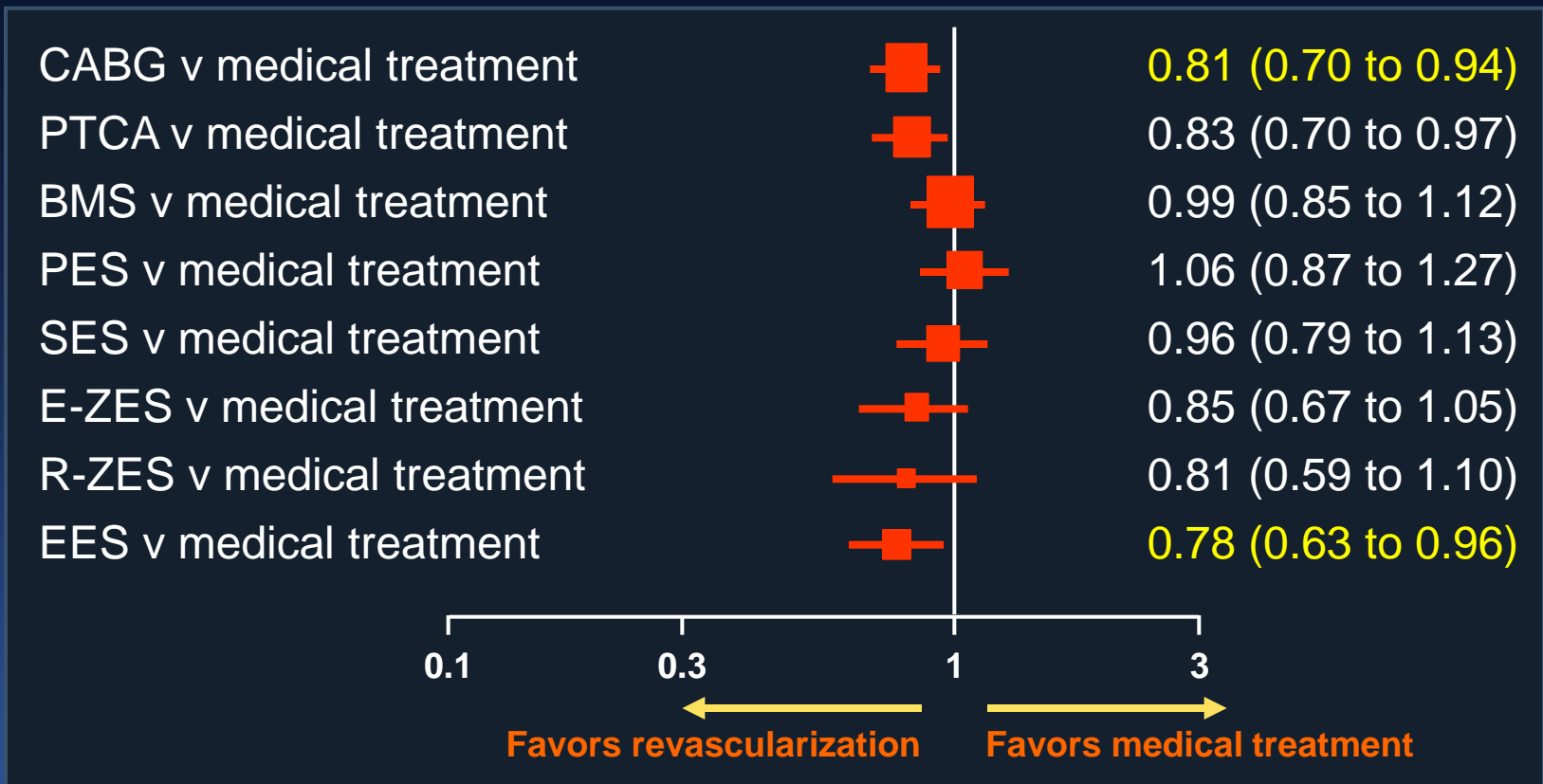
All-cause mortality (95 trials, 93,533 pts)



Revascularization vs. Medical Rx: Impact of new DES

100 trials in 93,553 pts with 262,090 pt-yrs follow-up

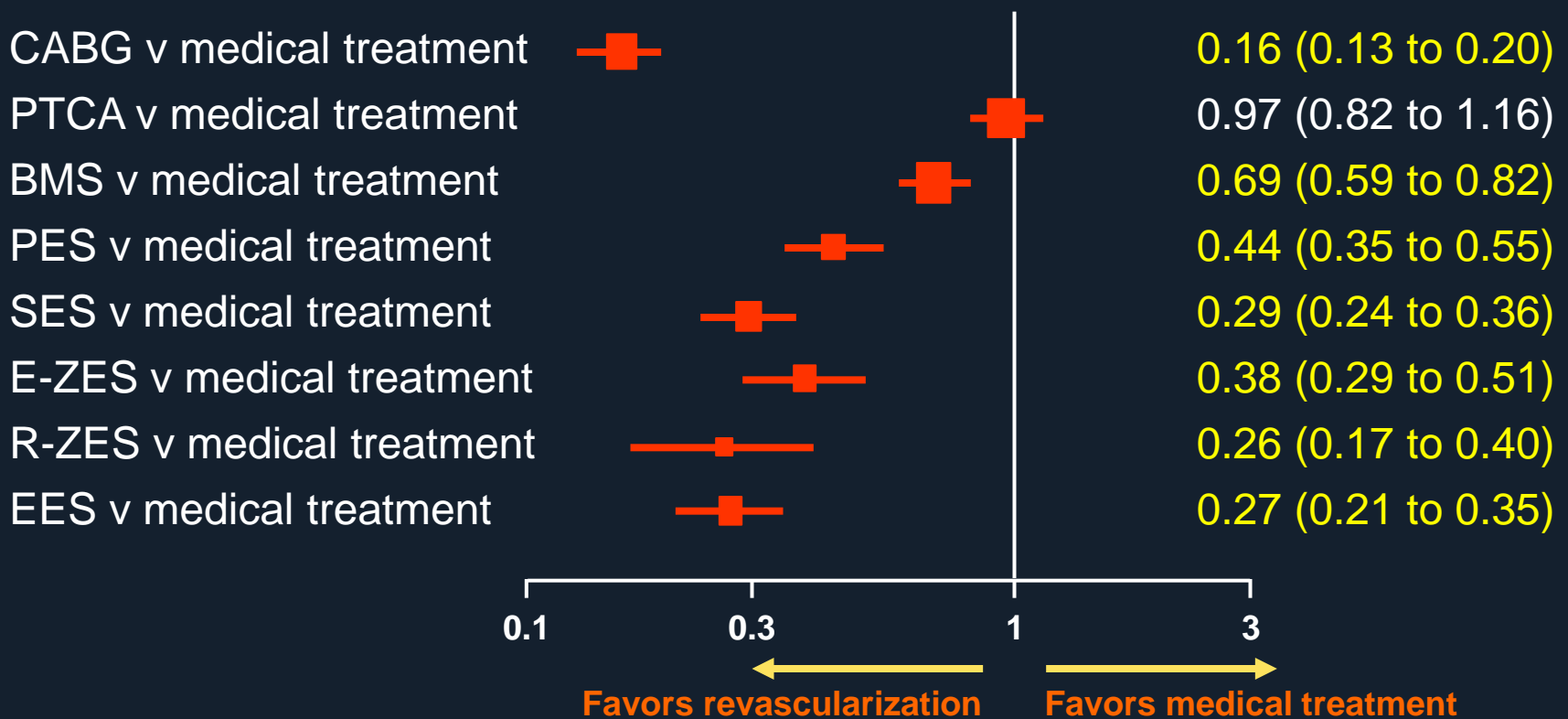
Death or MI (88 trials, 89,373 pts)



Revascularization vs. Medical Rx: Impact of new DES

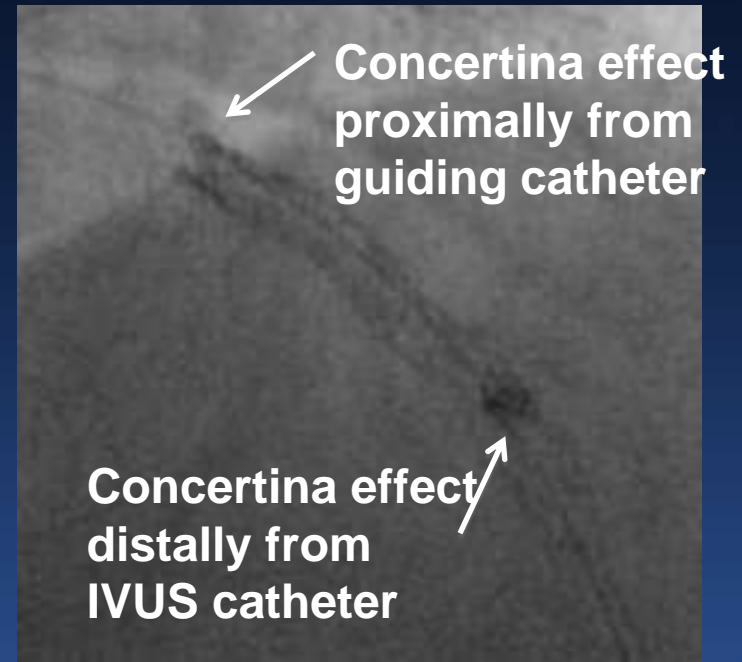
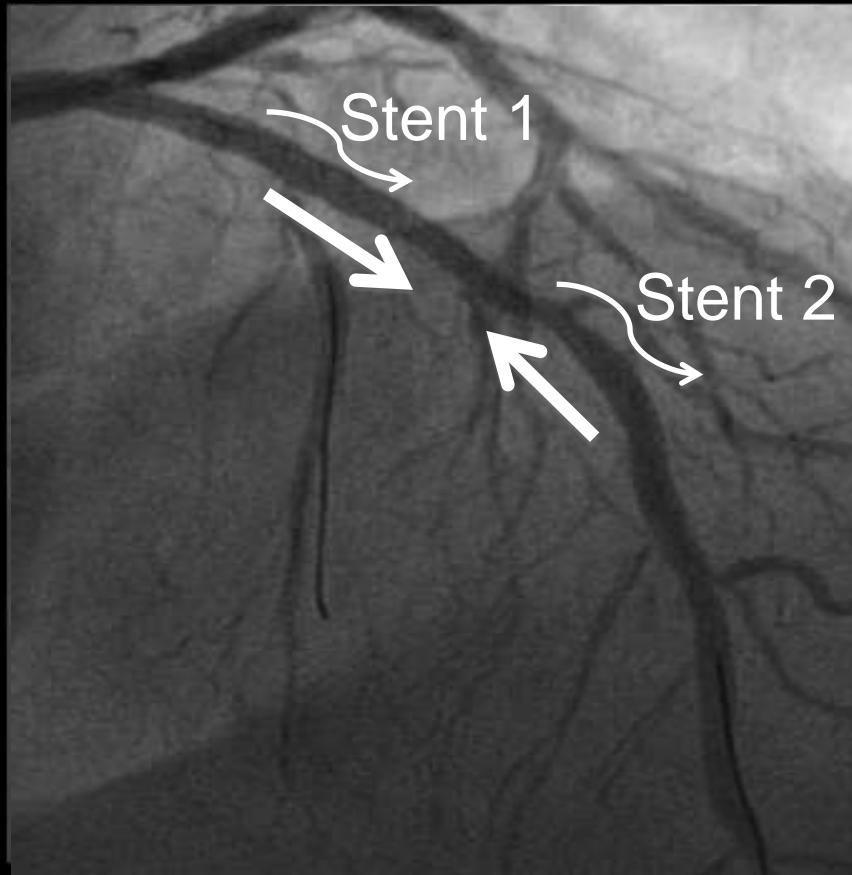
100 trials in 93,553 pts with 262,090 pt-yrs follow-up

Revascularization (94 trials, 90,282 pts)

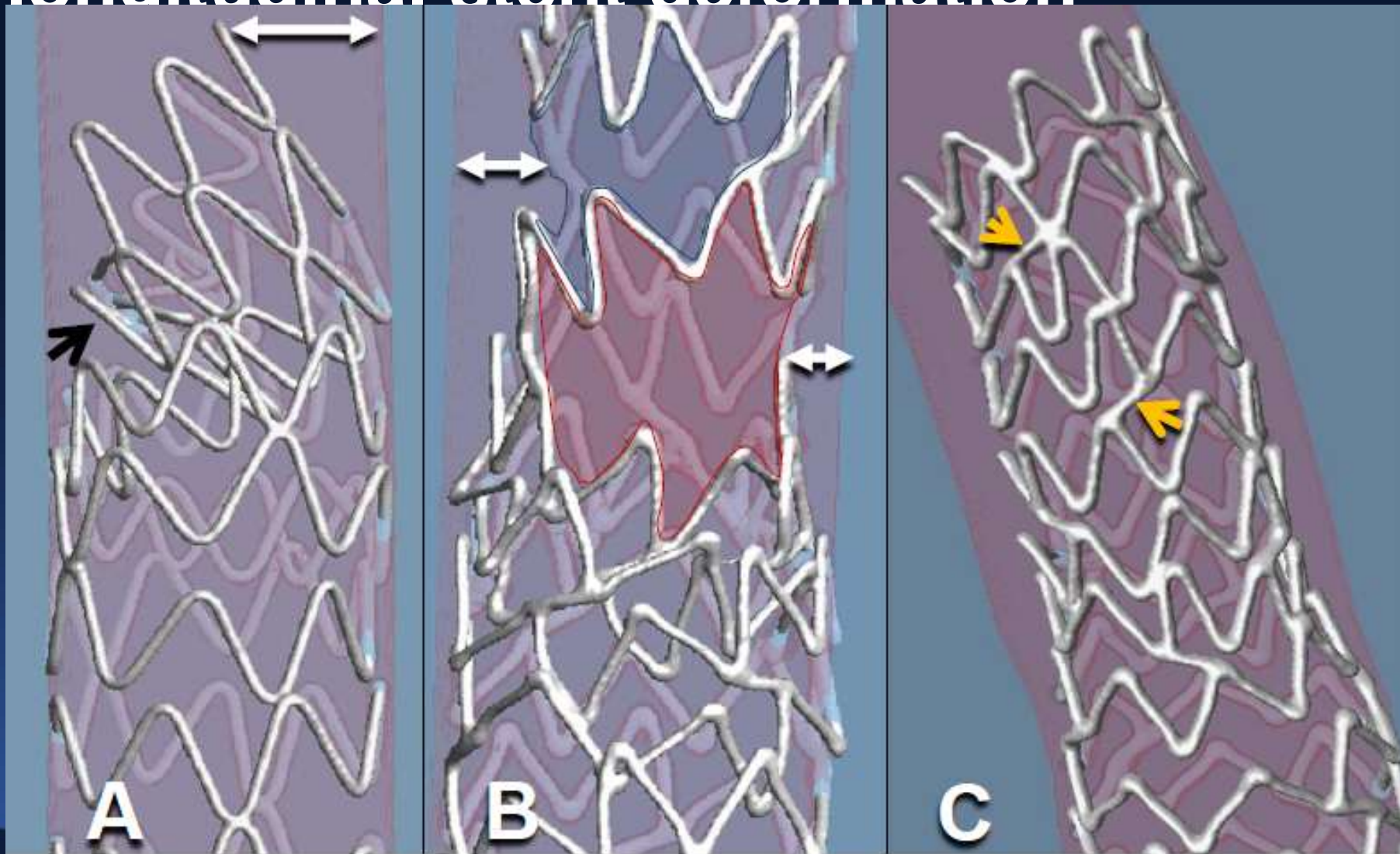


Pulled hard- IVUS removed









Both stents severely shortened with 'double layer' visible proximally and distally indicating crushing/concertina effect



MicroCT examples of longitudinal stent deformation



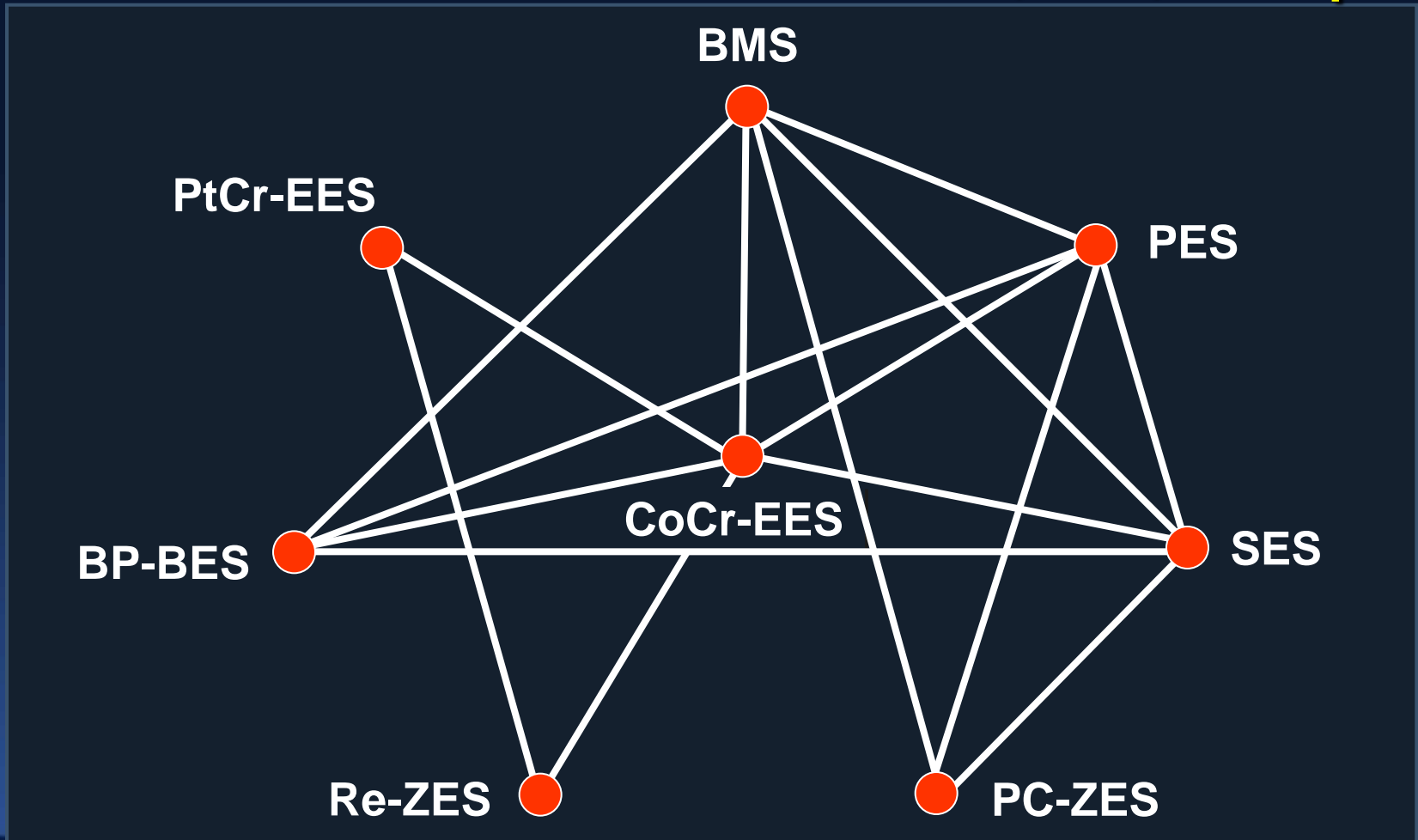
Contemporary DES : Strut Thickness/Coating

	Durable Polymer Coated		Bioabsorbable Polymer Coated					
	Xience CoCr-EES	Resolute	Biomatrix	Nobori	SYNERGY	BioMime	MiStent	Orsiro
	Promus PtCr-EES	CoNi-ZES	316L-BES	316L-BES	PtCr-EES	CoCr-SES	CoCr-SES	CoCr-SES
								
Strut thickness	81µm 0.0032"	89µm 0.0035"	120µm 0.0046"	125µm 0.0047"	74µm 0.0029"	65µm 0.0026"	64µm 0.0025"	61µm 0.0024"
Polymer	PVDF	BioLINX	PLA	PLA	PLGA	PLLA + PLGA	PLGA	PLLA Probio*
Distribution / thickness	Conformal 7-8µm / side	Conformal 6µm / side	Abluminal 10µm	Abluminal 20µm	Abluminal 4µm	Conformal 2µ / 2µ	Conformal 5µm / 15µm	Conformal 3.5µm / 7.5µm

*silicon carbide

Bioabsorbable Polymer-based vs. Durable Polymer-based DES and BMS

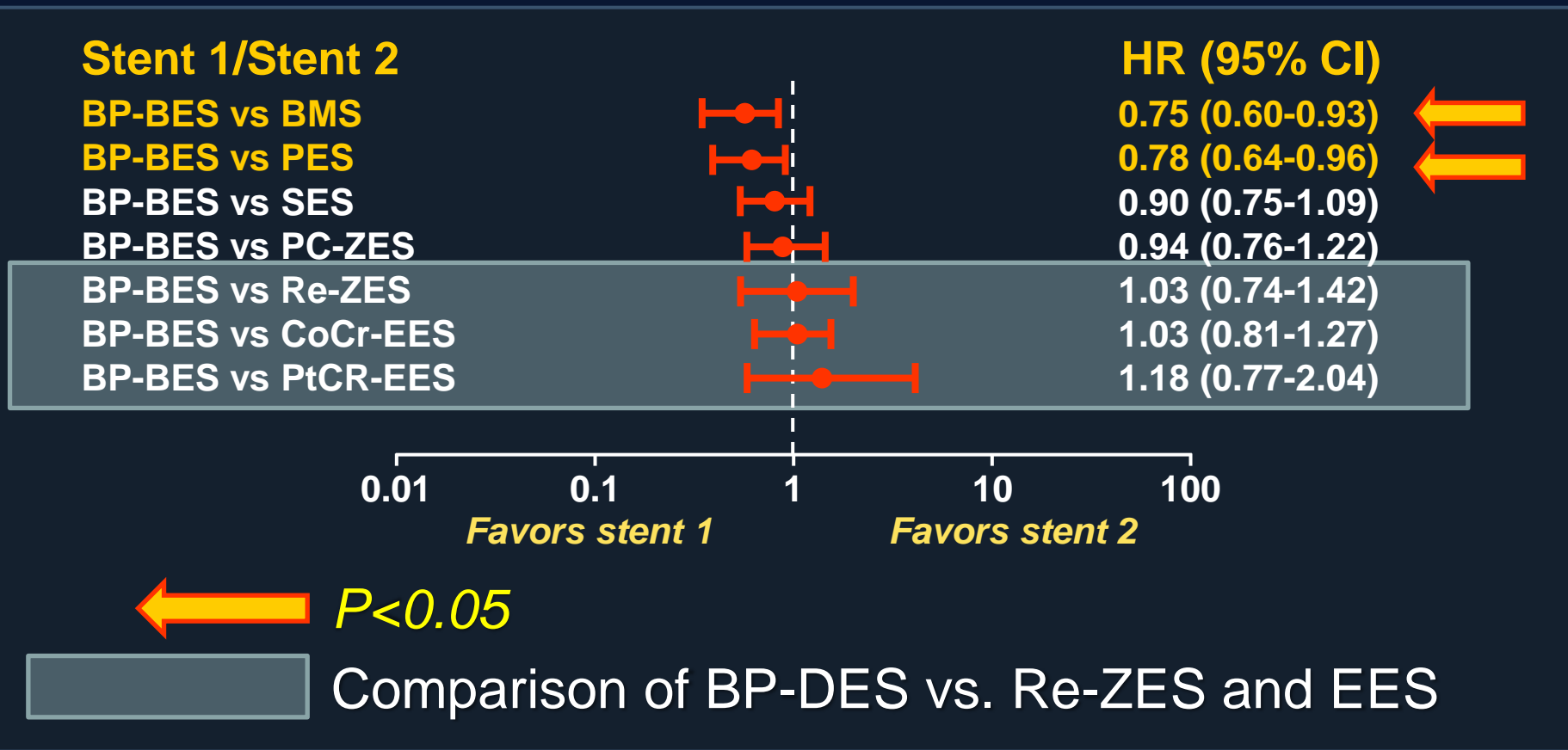
Evidence network: 89 RCTs, 85,490 pts



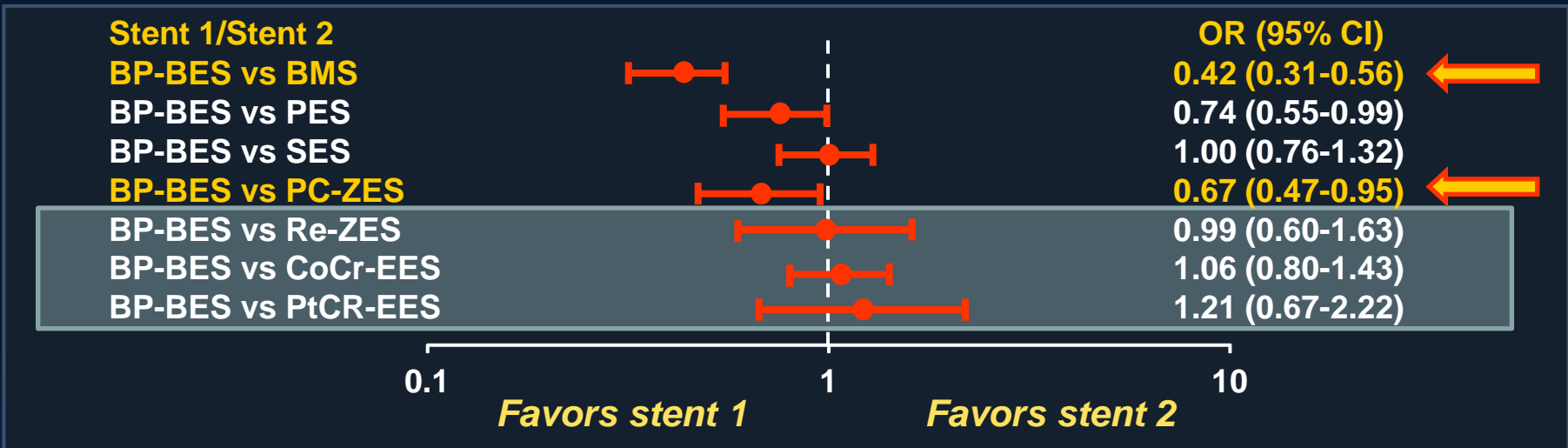
Bioabsorbable Polymer-based vs. Durable Polymer-based DES and BMS

Evidence network: 89 RCTs, 85,490 pts

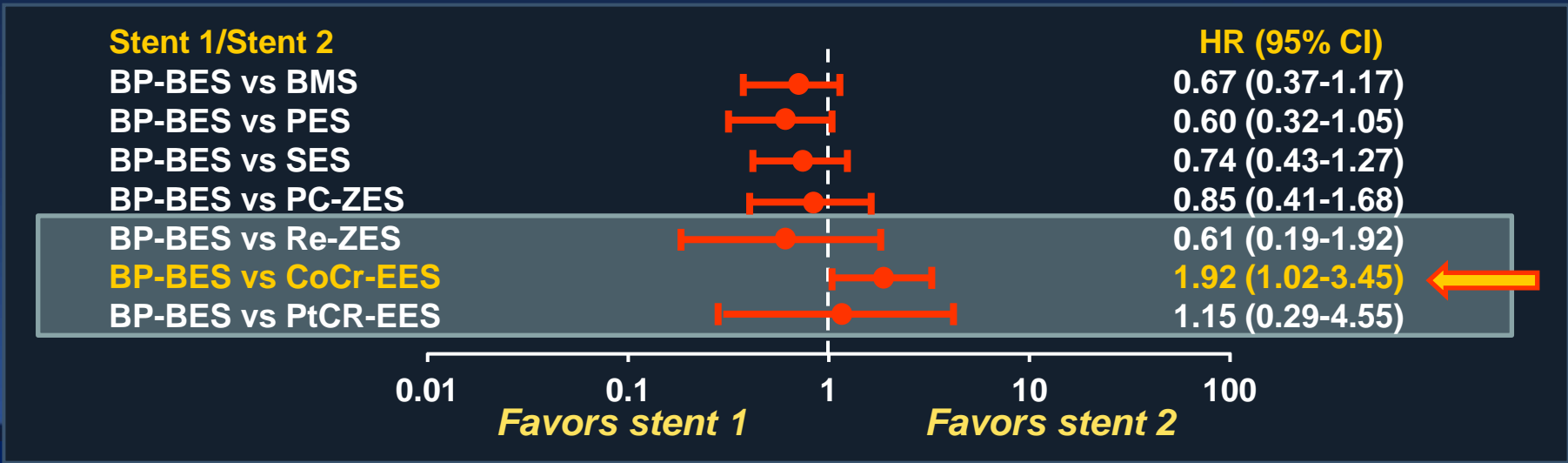
Long-term Cardiac Death or MI



Long-term TVR



Long-term Definite Stent Thrombosis



EVOLVE II Pivotal Trial Design

Patients with ≤ 3 native coronary artery lesions in ≤ 2 major epicardial vessels; lesion length ≤ 34 mm, RVD ≥ 2.25 mm ≤ 4.0 , %DS $\geq 50 < 100$
 (excluded LM disease, CTO, SVG, ISR or recent STEMI)

Randomized Cohort (RCT)

Up to 160 global sites

PROMUS Element Plus
 N=842

SYNERGY
 N=842

PK Substudy

SYNERGY
 N=21

Diabetes Substudy

SYNERGY
 N=203

RCT Design

Multicenter noninferiority trial

Pivotal, single-blind, 1:1 randomization

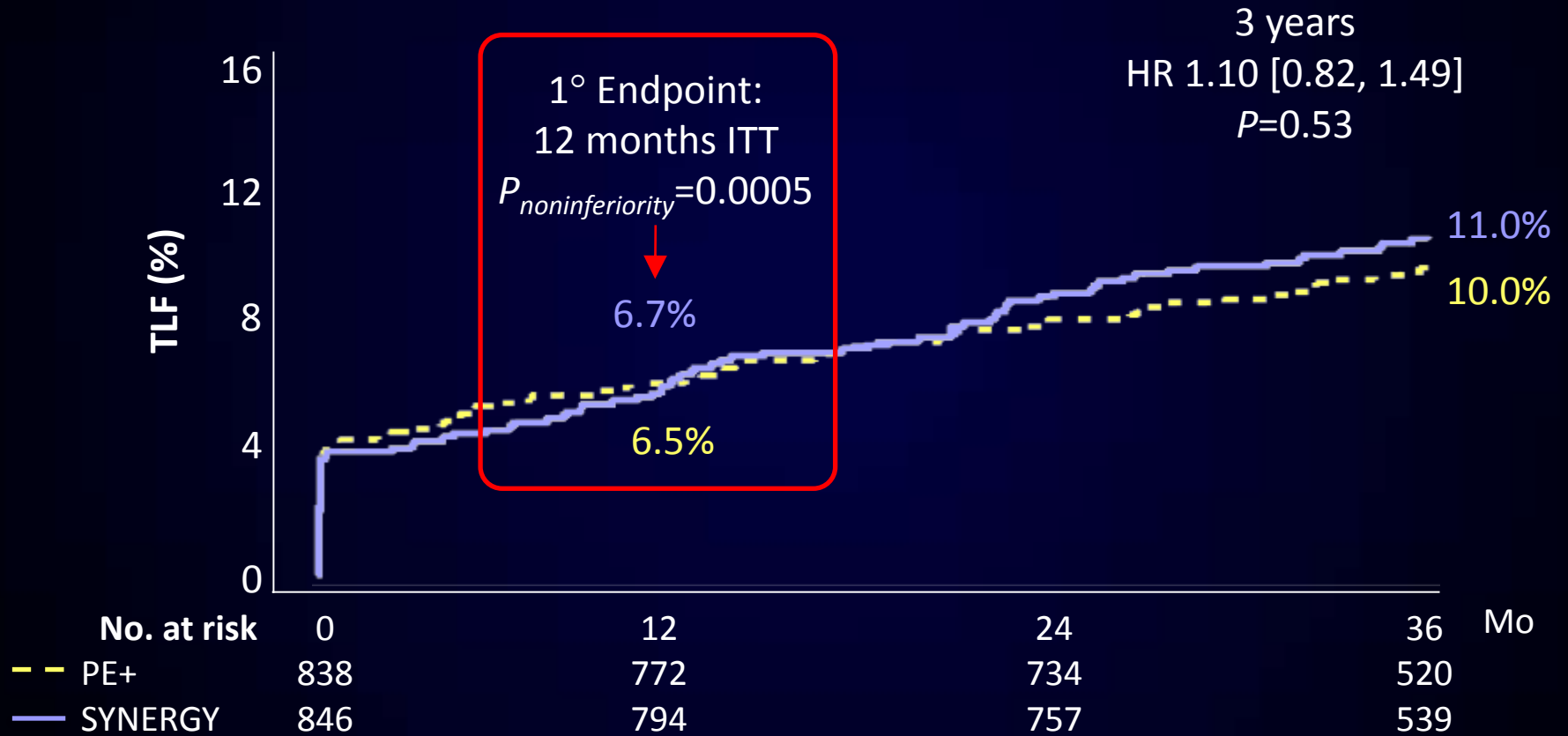
Primary Endpoint: TLF (CD, TV-MI, or TLR) at 12 mo

Follow-up through 5 years

DAPT (ASA + clopidogrel, ticlopidine, prasugrel, ticagrelor) ≥ 6 months or longer as tolerated

EVOLVE II TLF at 3 years

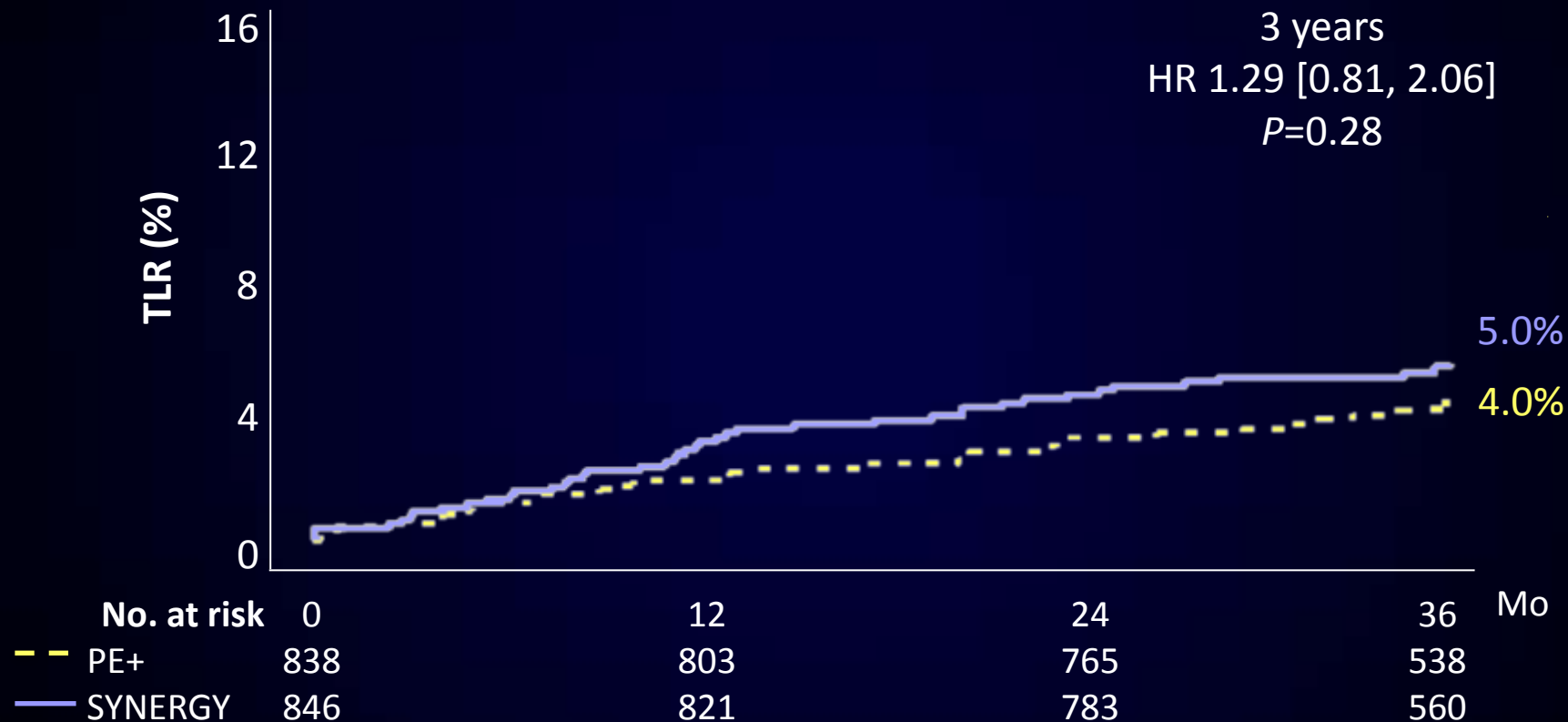
PROMUS Element Plus vs. SYNERGY



ITT; Patients who did not receive a study stent were censored at 1 year; KM Event Rate; log-rank P values

EVOLVE II TLR at 3 years

PROMUS Element Plus vs. SYNERGY

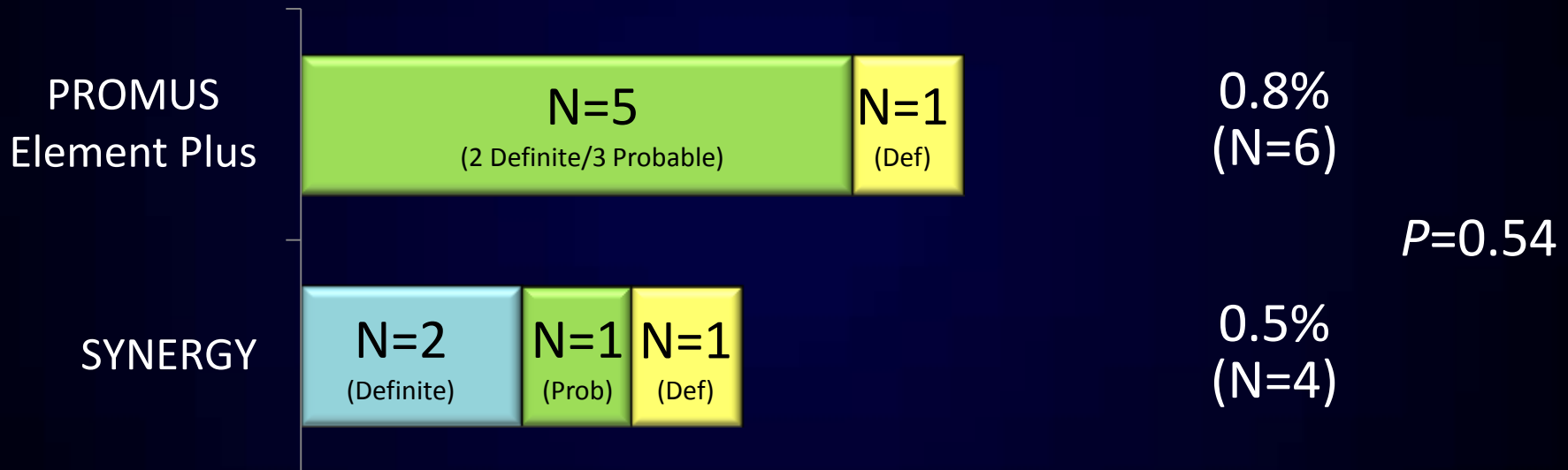


ITT; Patients who did not receive a study stent were censored at 1 year; KM Event Rate; log-rank P values

Stent Thrombosis at 3 years

Definite/Probable: ITT Population

■ Acute (≤ 1 d) ■ Subacute (2-30 d) ■ Late (30 d – 1 y) ■ Very Late (1 – 3 y)



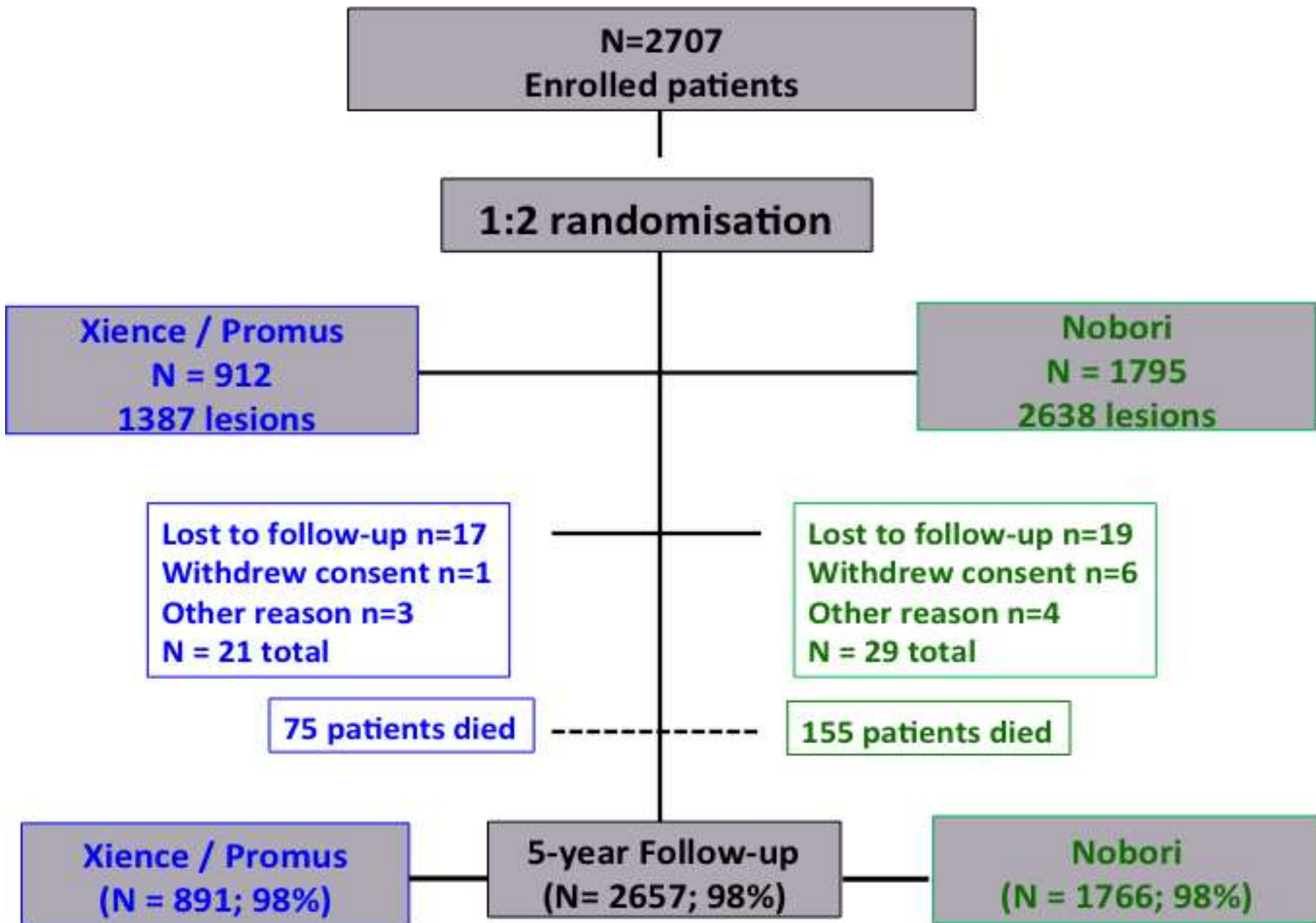
CEC confirmed MI/TLR/ST Day 901 in the *SYNERGY* arm

The Final 5 Year Results From The COMPARE II trial

The first real long-term results between
Biodegradable Polymer-BES and Durable Polymer-EES

Pieter C. Smits

on behalf of all the COMPARE II Investigators



BIO-RESORT (TWENTE III):

A prospective, randomized, three-arm trial comparing two different biodegradable polymer-based drug-eluting stents and a durable polymer-based drug-eluting stent in all-comers with coronary artery disease



Clemens von Birgelen, MD PhD

*Thoraxcentrum Twente, MST, Enschede, the Netherlands
on behalf of the BIO-RESORT Investigators*



BIO-RESORT: Study Devices



Durable Polymer DES

Resolute
Integrity
CoCr-ZES



Thickness (μm) of uncoated strut

91

Distribution, thickness (μm), and type of polymer

**Circumfer.
6/side
BioLinx™**

Biodegradable Polymer DES

Synergy
PtCr-EES



Orsiro
CoCr-SES



74*

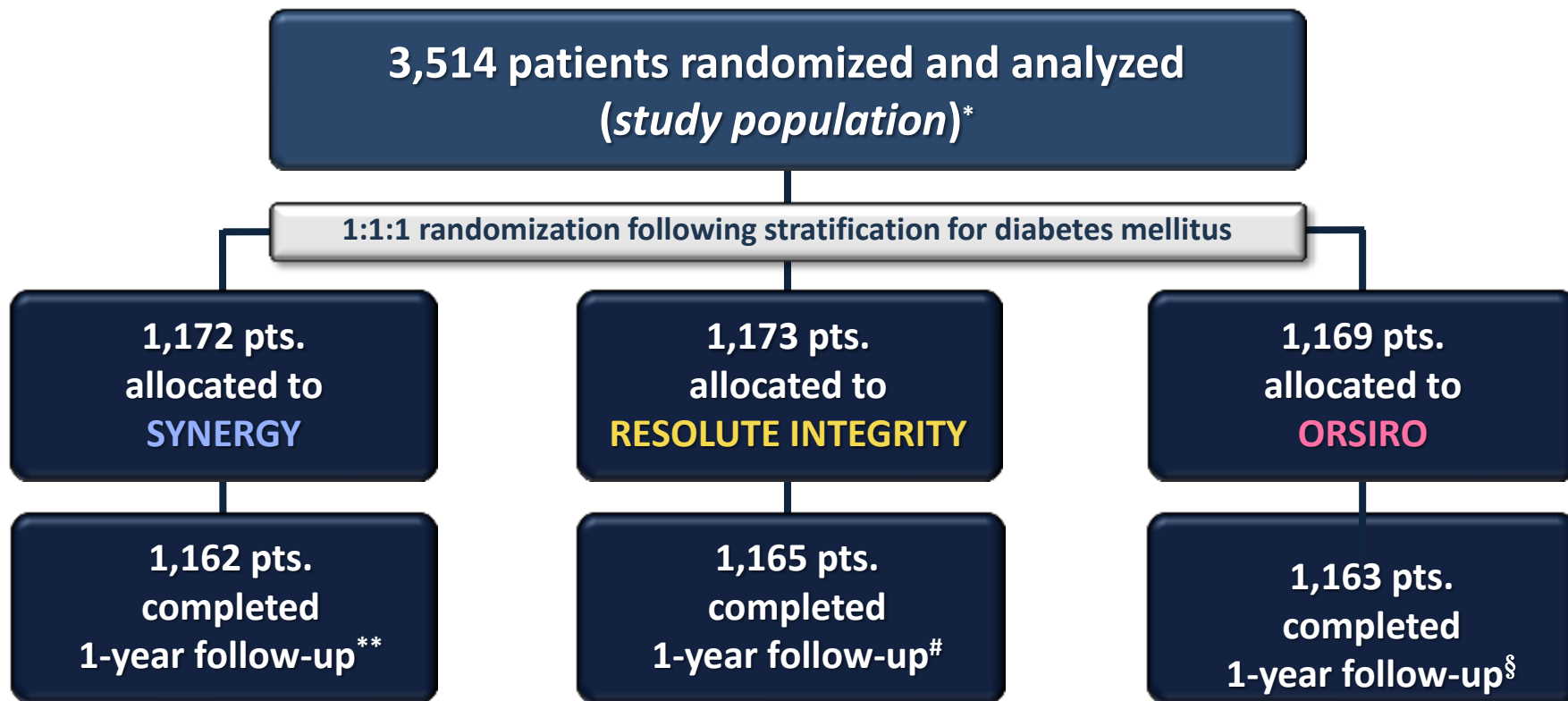
60**

**Abluminal
4
PLGA, PCL**

**Cicumfer.
4-7/side
PLLA****



Study Flow Diagram



• 1-year follow-up data were obtained from 99.3% of the study population, which represents 99.9% of the patients who still participated in the trial or had died.

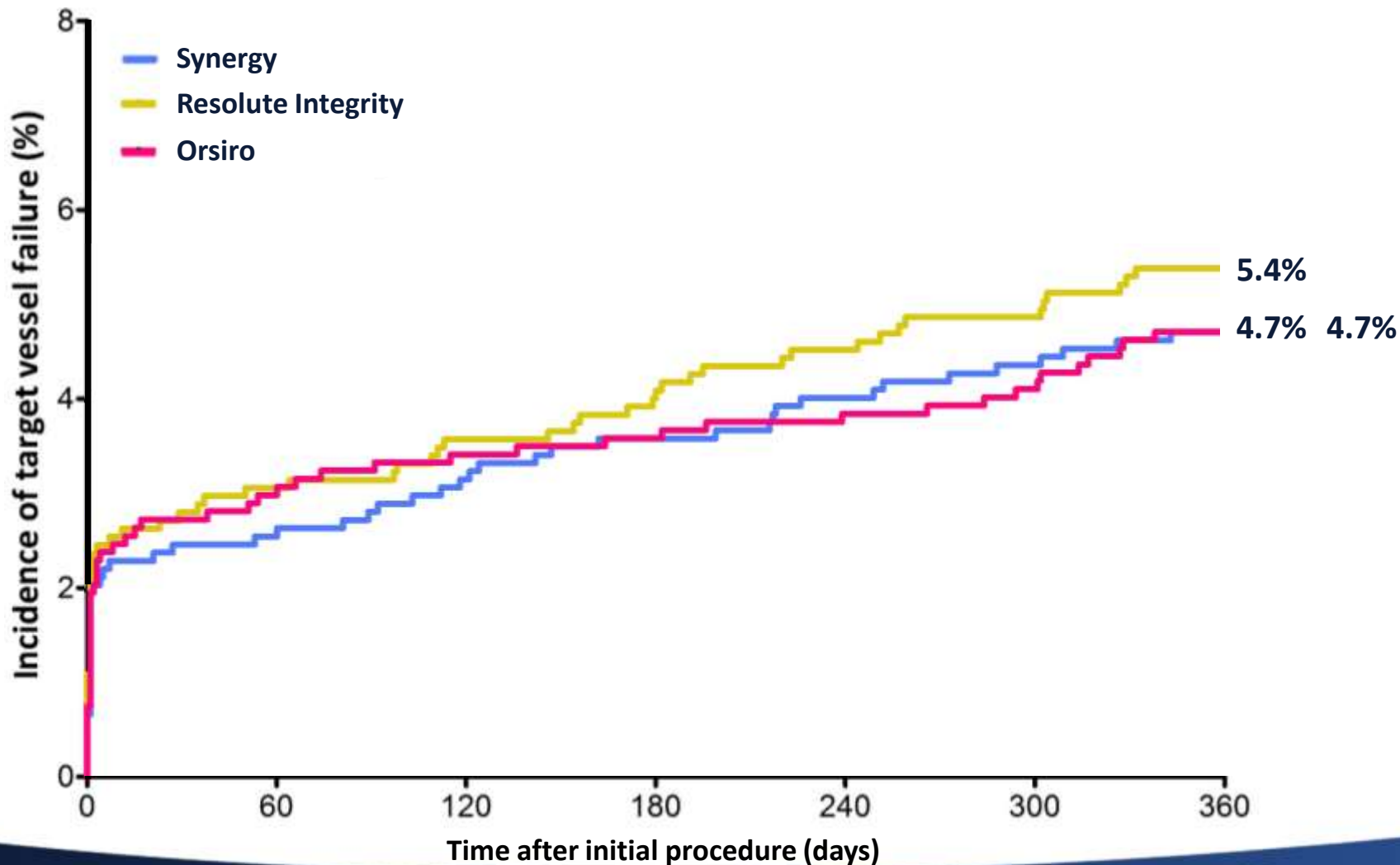
• During the first year of follow-up, 21 patients (0.6%) withdrew consent, while only 3 / 3,514 patients (< 1 %) were actually “lost” (i.e., could not be contacted).



Primary Endpoint

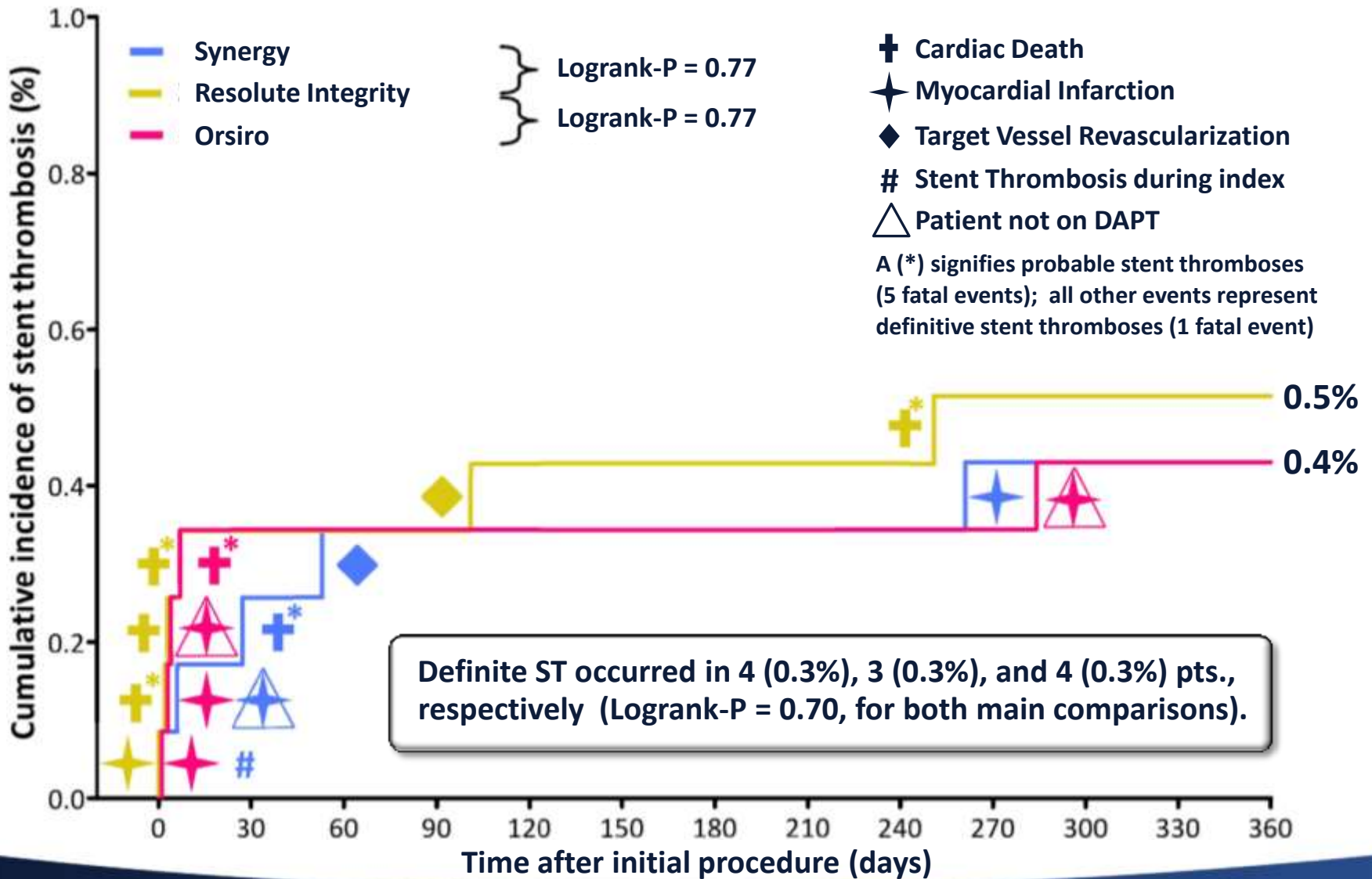


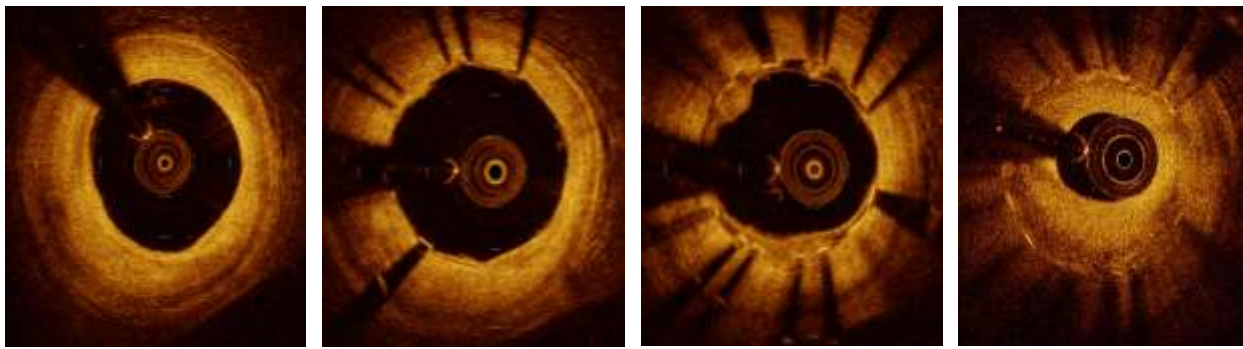
Target Vessel Failure at 1-Year Follow-Up





Definite or Probable Stent Thrombosis





TRANSFORM-OCT*: A Prospective, Randomized Trial Using OCT Imaging to Evaluate Strut Coverage at 3 Months and Neoatherosclerosis at 18 Months in Bioresorbable Polymer-Based and Durable Polymer-Based Drug-Eluting Stents

***TRiple Assessment of Neointima Stent Formation to Reabsorbable polyMer with OCT**

Giulio Guagliumi¹, Kunihiro Shimamura², Vasile Sirbu¹, Roberto Garbo³, Luigi Fiocca¹, Angelina Vassileva¹, Francesco Colombo³, Daisuke Nakamura⁴, Gabriel Tensor Rodriguez Pereira⁴, Guilherme F Attizzani⁴, Giuseppe Musumeci¹, Orazio Valsecchi¹, Irene Pescetelli¹, Leonardo De Luca⁶, Francesco Saia⁷, Davide Capodanno⁸

¹ ASST Papa Giovanni XXIII, Bergamo, Italy

² Wakayama Medical University, Wakayama, Japan

³ Ospedale San Giovanni Bosco, Torino, Italy

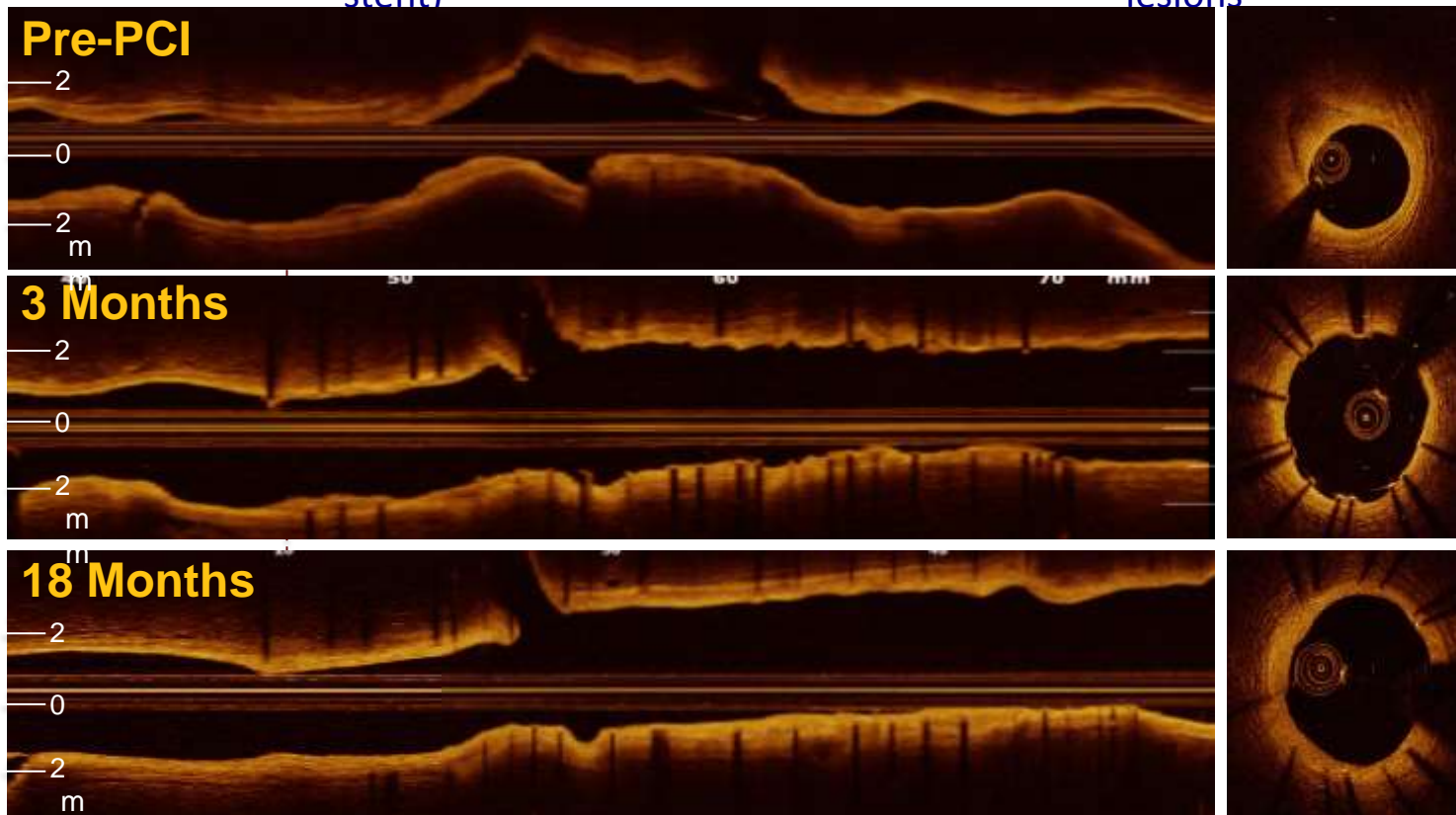
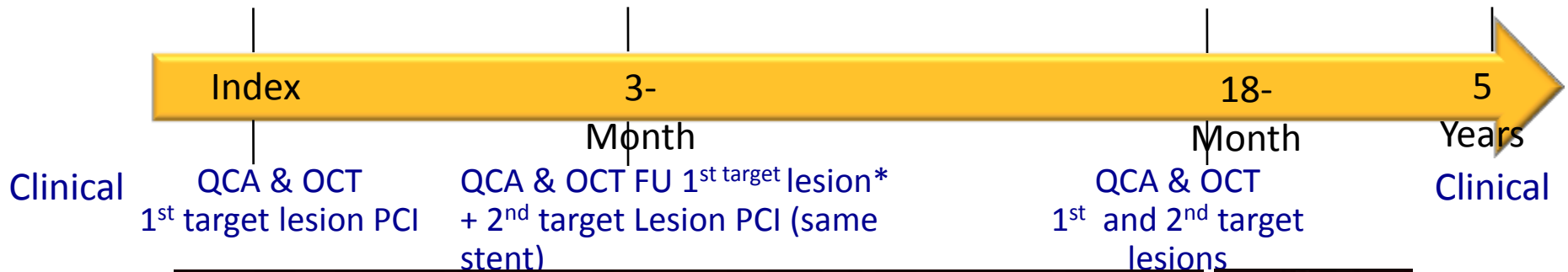
⁴ Cardiovascular Imaging Core Laboratory, Cleveland, OH, US

⁶ Ospedale S. Giovanni Evangelista, Tivoli, Italy

⁷ Cardiothoracic Vascular Department, University Hospital, Bologna, Italy

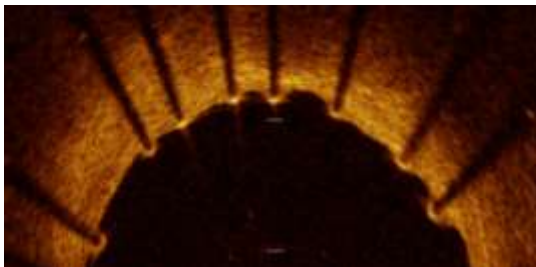
⁸ Ferrarotto Hospital, University of Catania, Catania, Italy

Study Flow



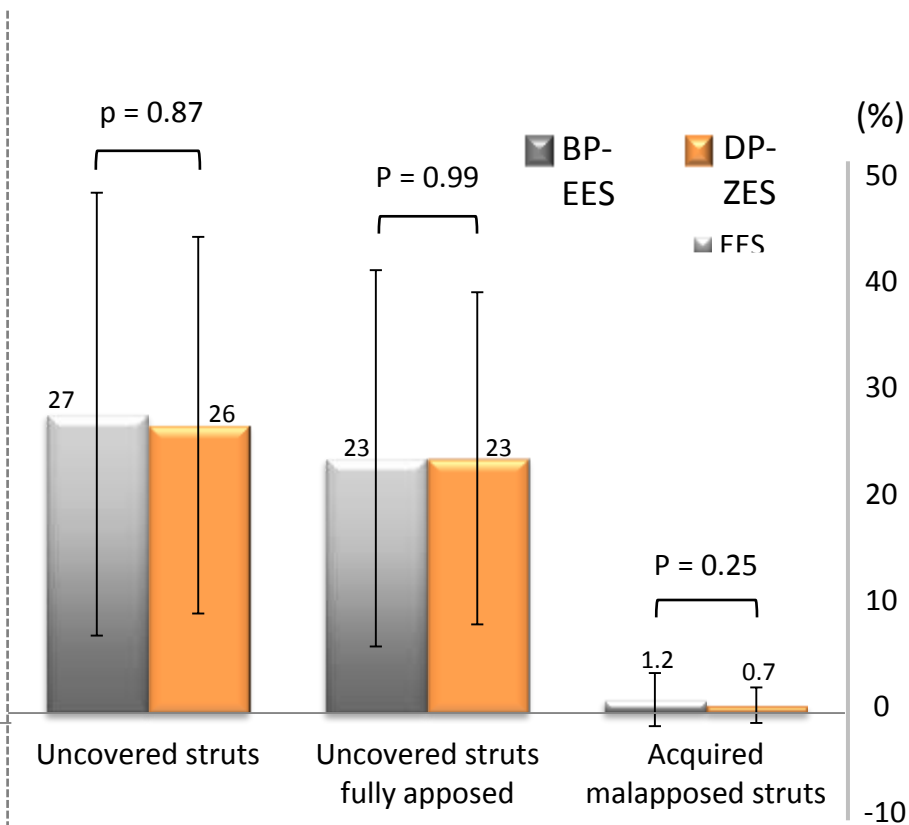
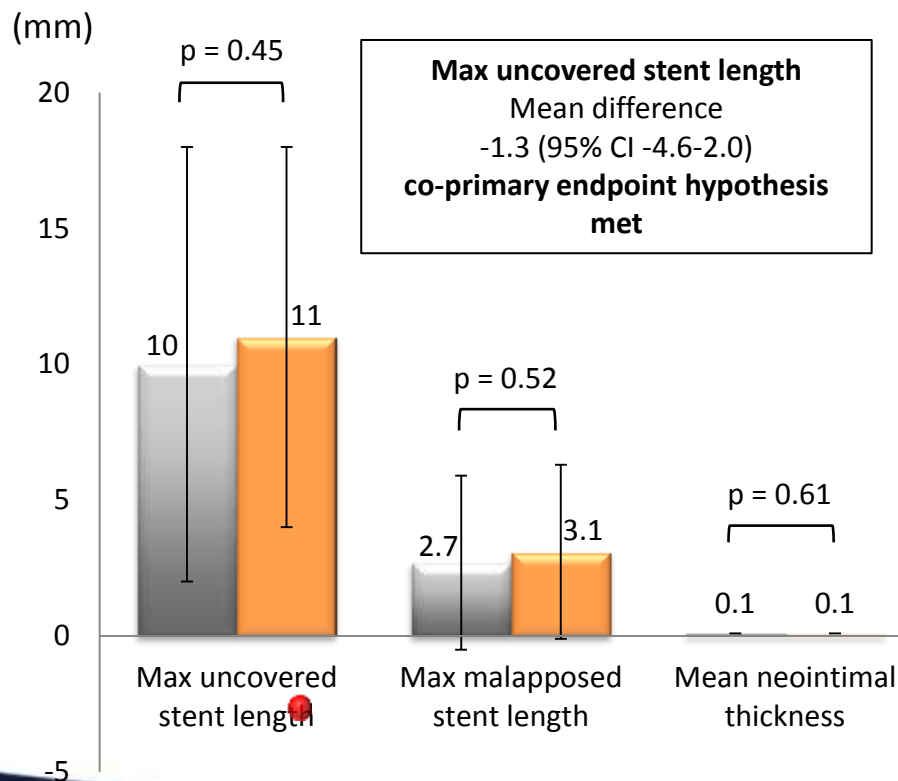
Quantitative OCT Analysis- 3 Months

90 patients - 100% OCT FU - 43.607 struts



Primary end point: intra-class correlation for 2 readers			
CCC	Standard Error	Lower CL	Upper CL
0.9971	0.0021	0.9878	0.9993

● Co-primary end point



Primary Endpoint: In-stent NA by OCT at 18 months

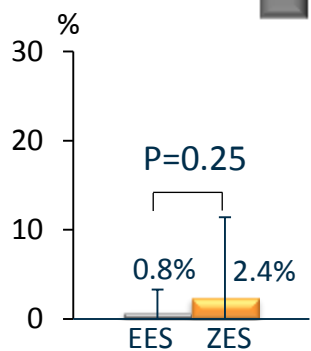
87/88 patients (98.9% of all the eligible), 42.262 struts

% of frames with neoatherosclerosis

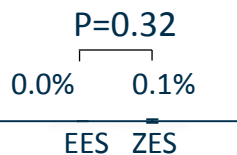
546 ± 52 days

BP-EES **1.1 ± 3.1** vs **2.5 ± 9.1** DP-ZES

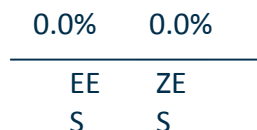
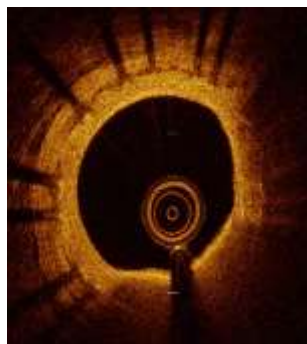
p= 0.33



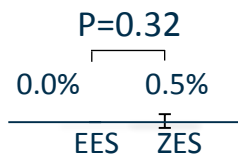
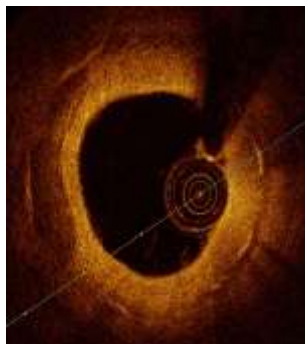
Lipid laden neointima



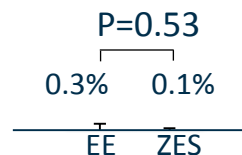
Macrophages



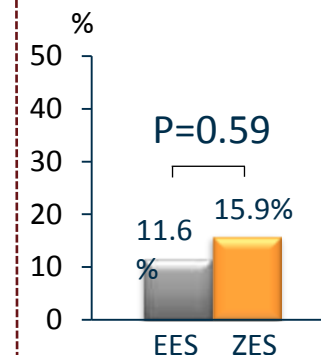
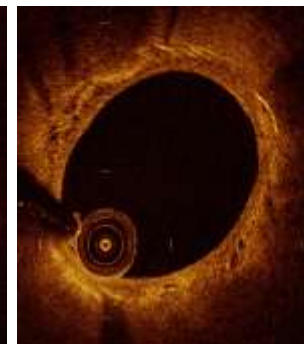
Calcification



TCFA



Neovessels

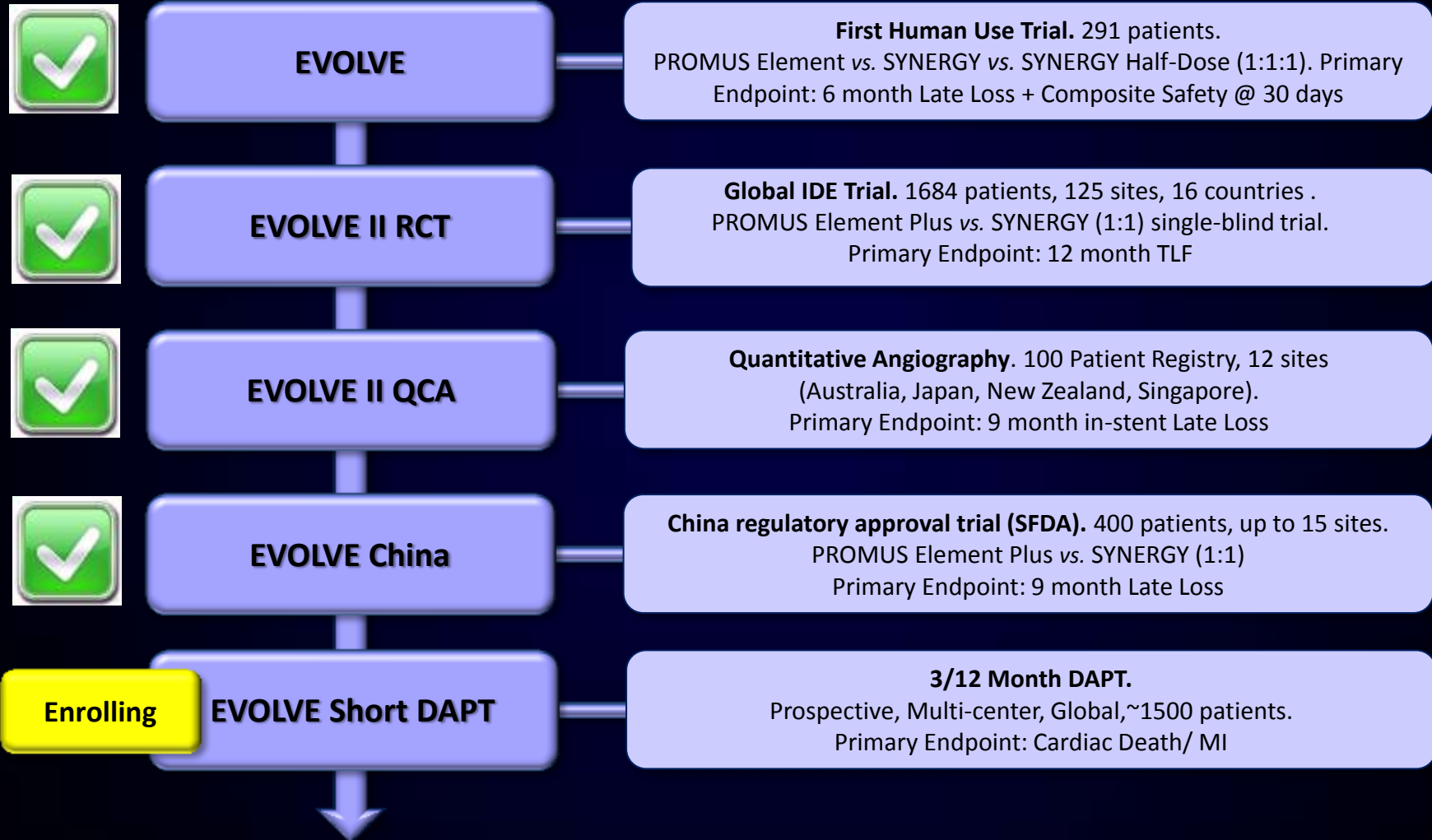


N= 5/43 7/44

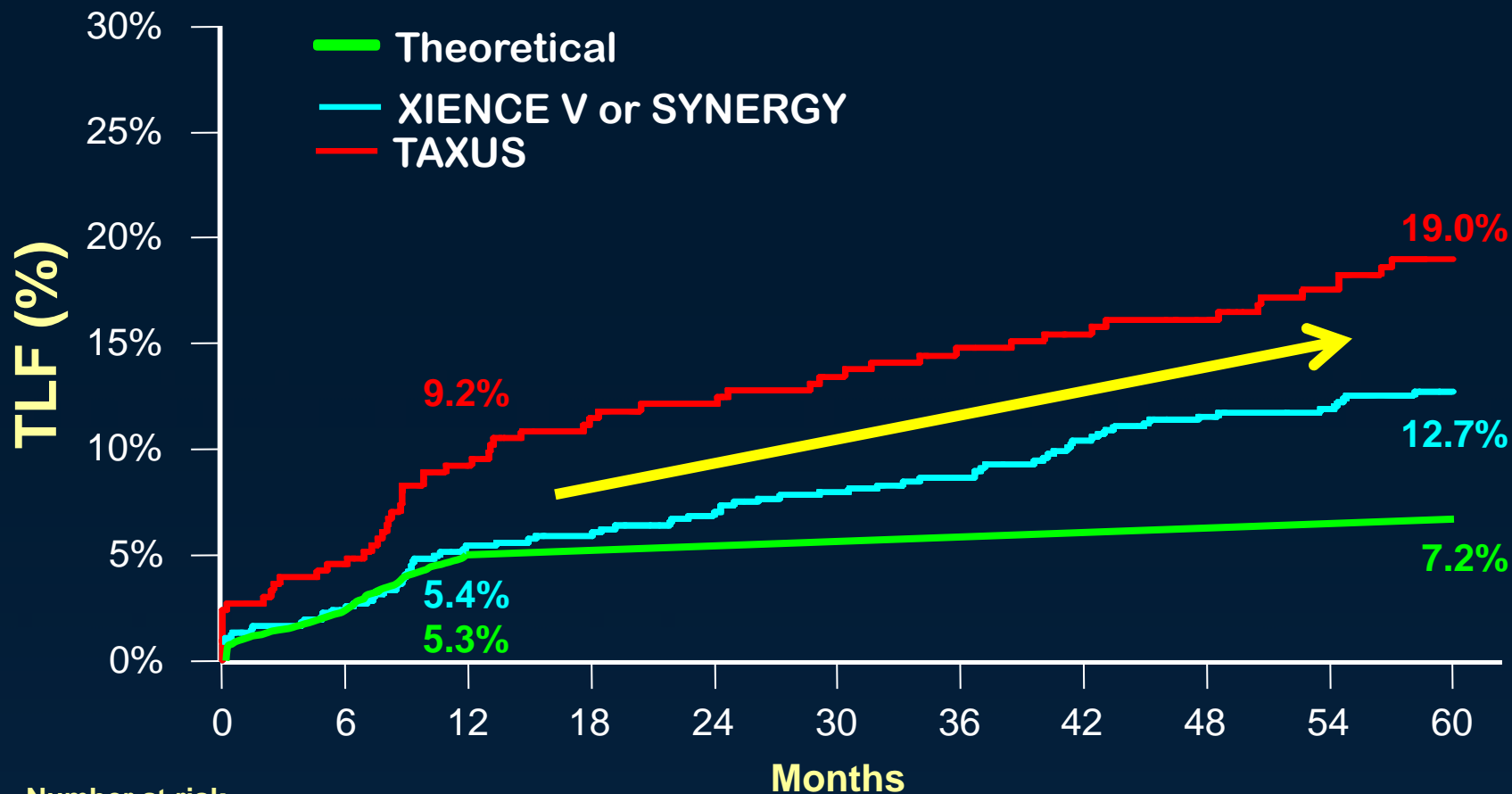
% Patients with frames of neoatherosclerosis



SYNERGY: BSC Clinical Trials



From TAXUS to XIENCE to Ideal



Number at risk

XIENCE V	669	646	616	601	582	571	565	548	537	529	521
TAXUS	332	310	288	274	269	262	255	248	243	231	223

TLF = cardiac death, target vessel MI, or ischemic-driven TLR