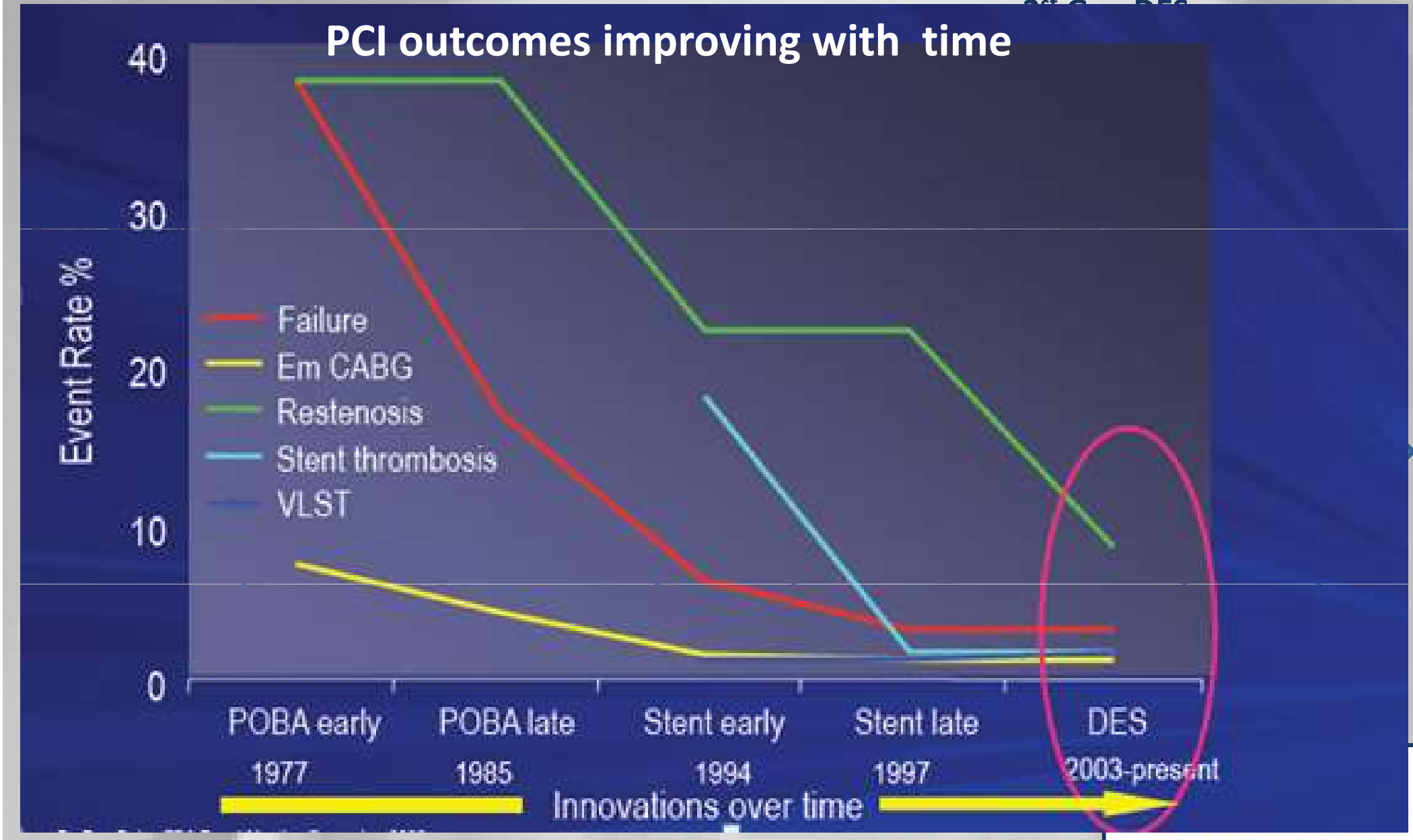
Η εξέλιξη των ενδοστεφανιαίων προθέσεων (stents) και η επίπτωση της στην φυσική ιστορία της νόσου και της χορηγούμενης αντιαιμοπεταλιακής αγωγής

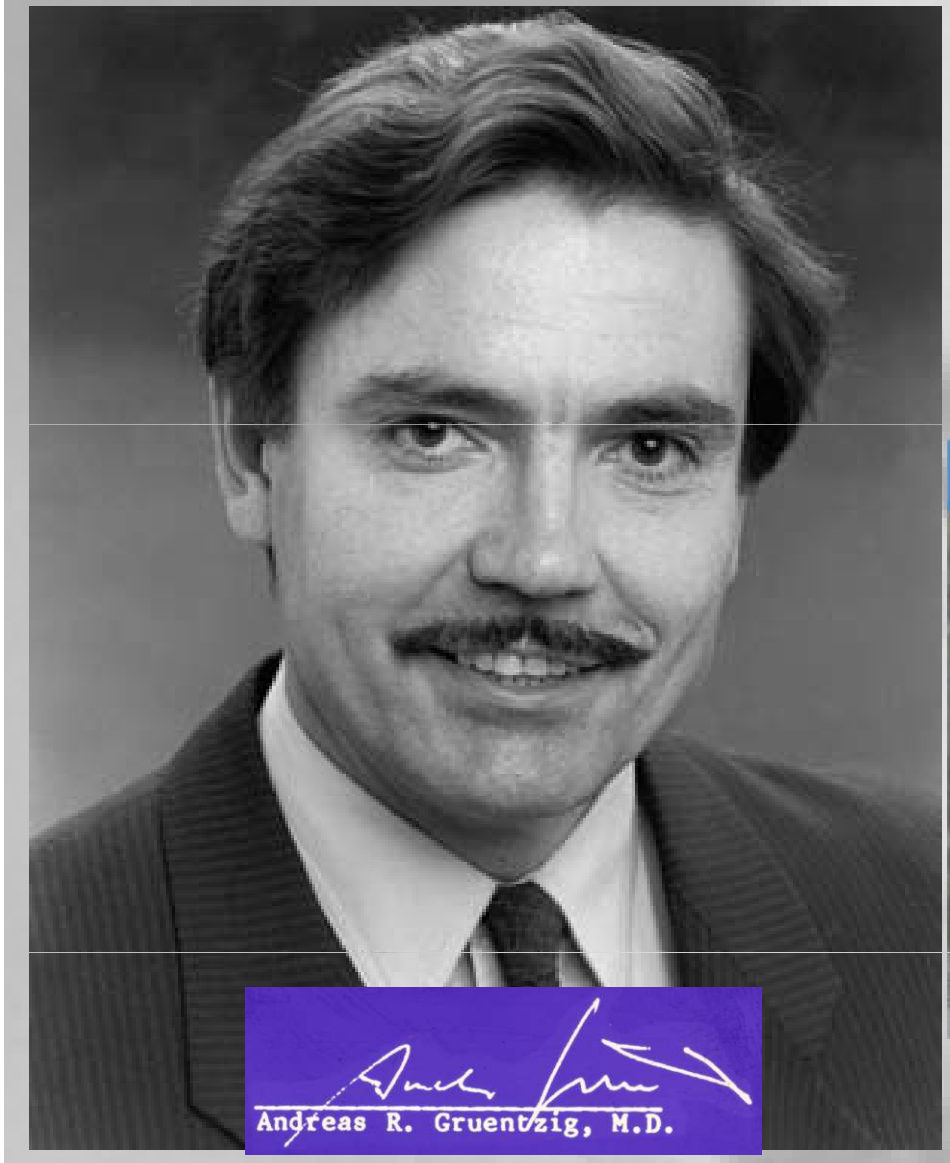
ΓΡΑΪΔΗΣ ΧΡΗΣΤΟΣ
Επεμβατικός Καρδιολόγος, FSCAI
Euromedica-Κυανούς Σταυρός

31 Ιανουαρίου-1 Φεβρουαρίου 2013
Ξενοδοχείο Αιγές, Βέροια

Hellenic Institute of Cardiovascular Diseases
www.e-Cardio.gr

History of PCI and Antiplatelet Therapy



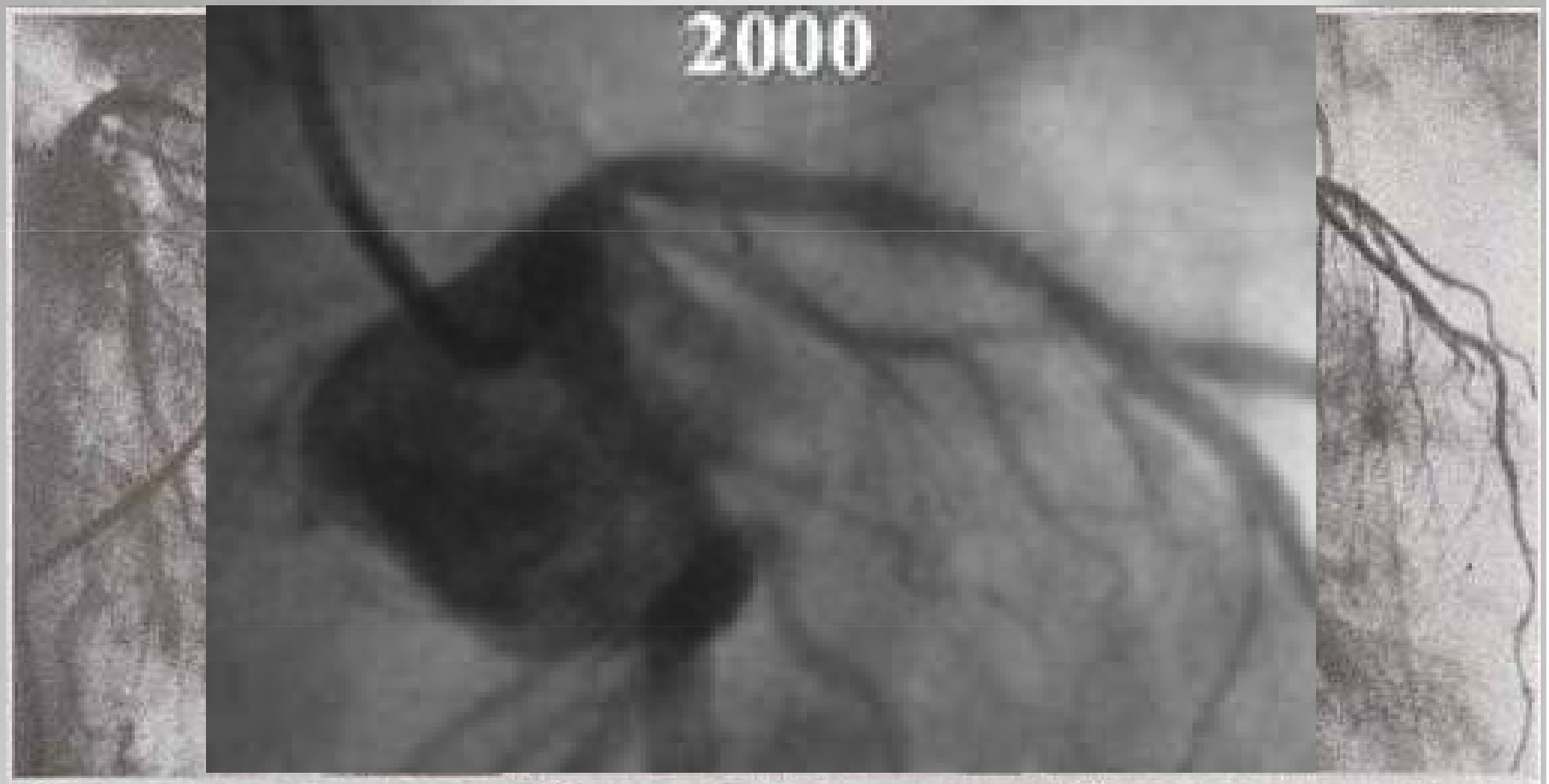


Andreas Roland Grüntzig

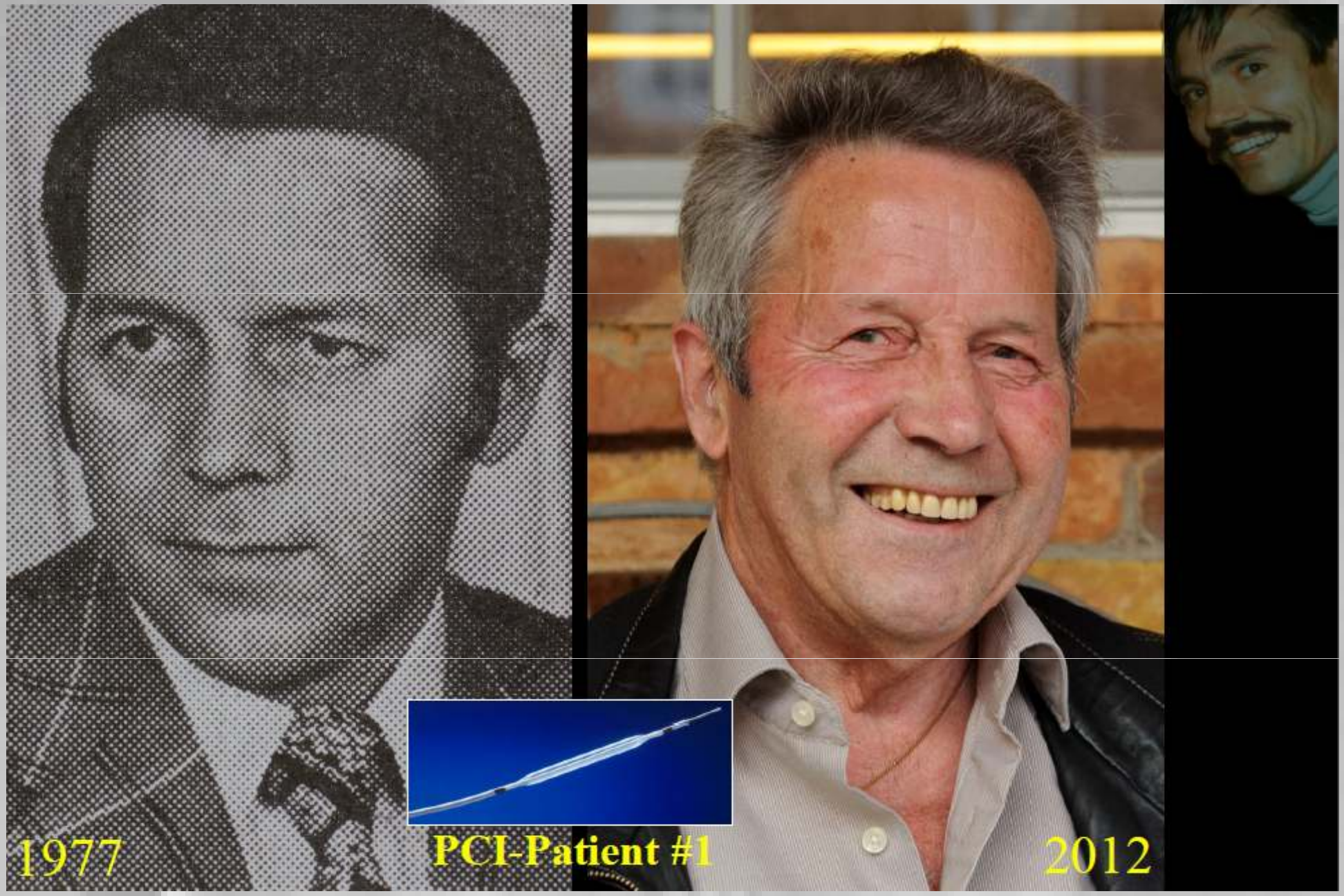
Zurich, 1977 September 16th

First coronary angioplasty in man

Born June 25, 1939 Dresden
Died October 27, 1985 Atlanta in a plane crash



(A) 9–14–77 (B) 9–16–77 (C) 10–20–77


1977
PCI-Patient #1
2012

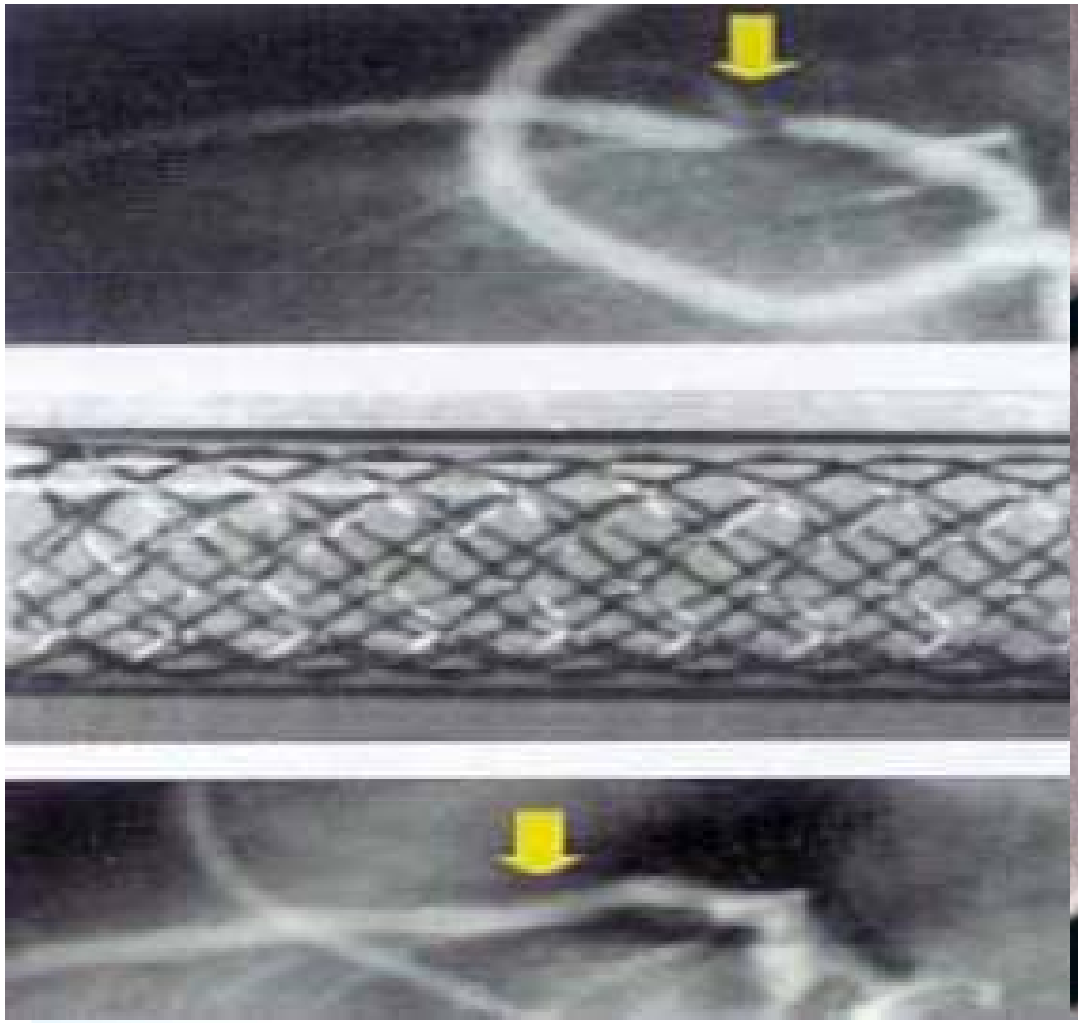
In the first 50 patients who underwent percutaneous transluminal coronary angioplasty (PTCA),

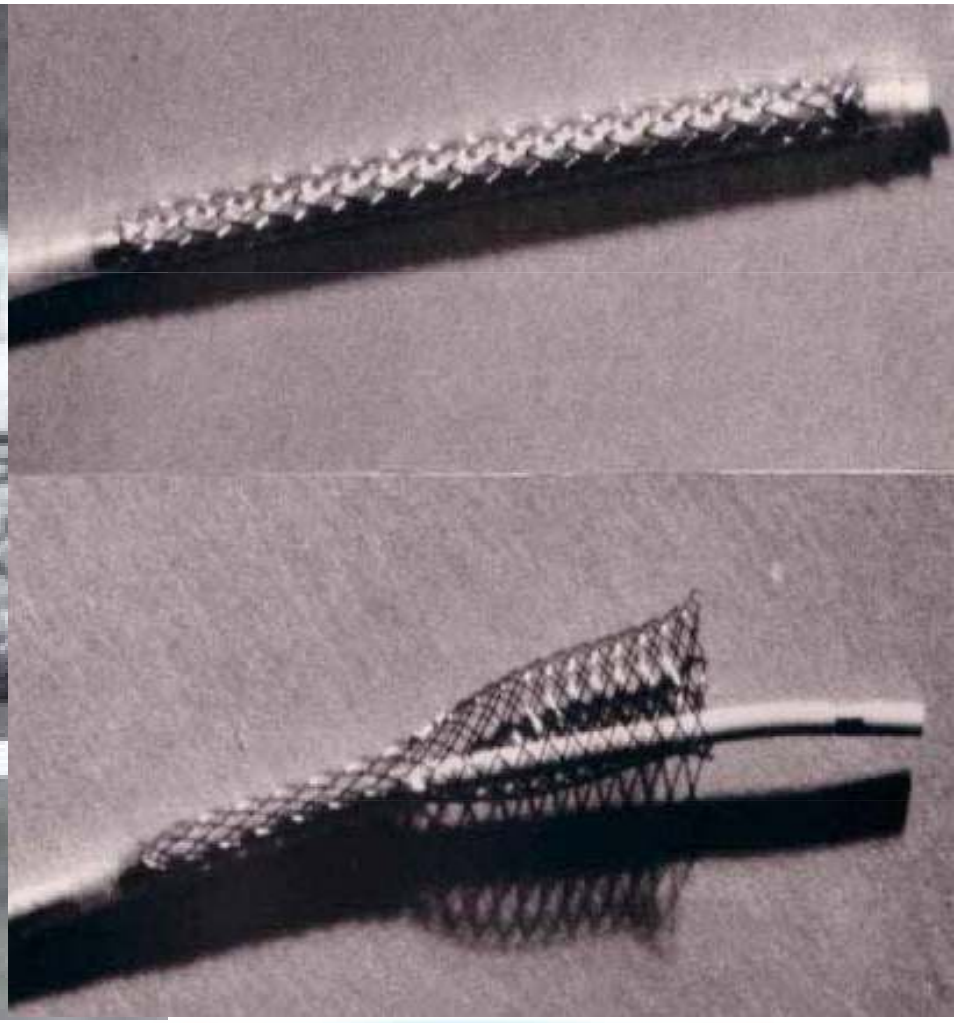
- the primary success rate was only 64% and
- emergency CABG was required in 14%, with
- a periprocedural myocardial infarction (MI) rate of 6%.

As experience with PTCA grew, its success rate increased to approximately 90%.

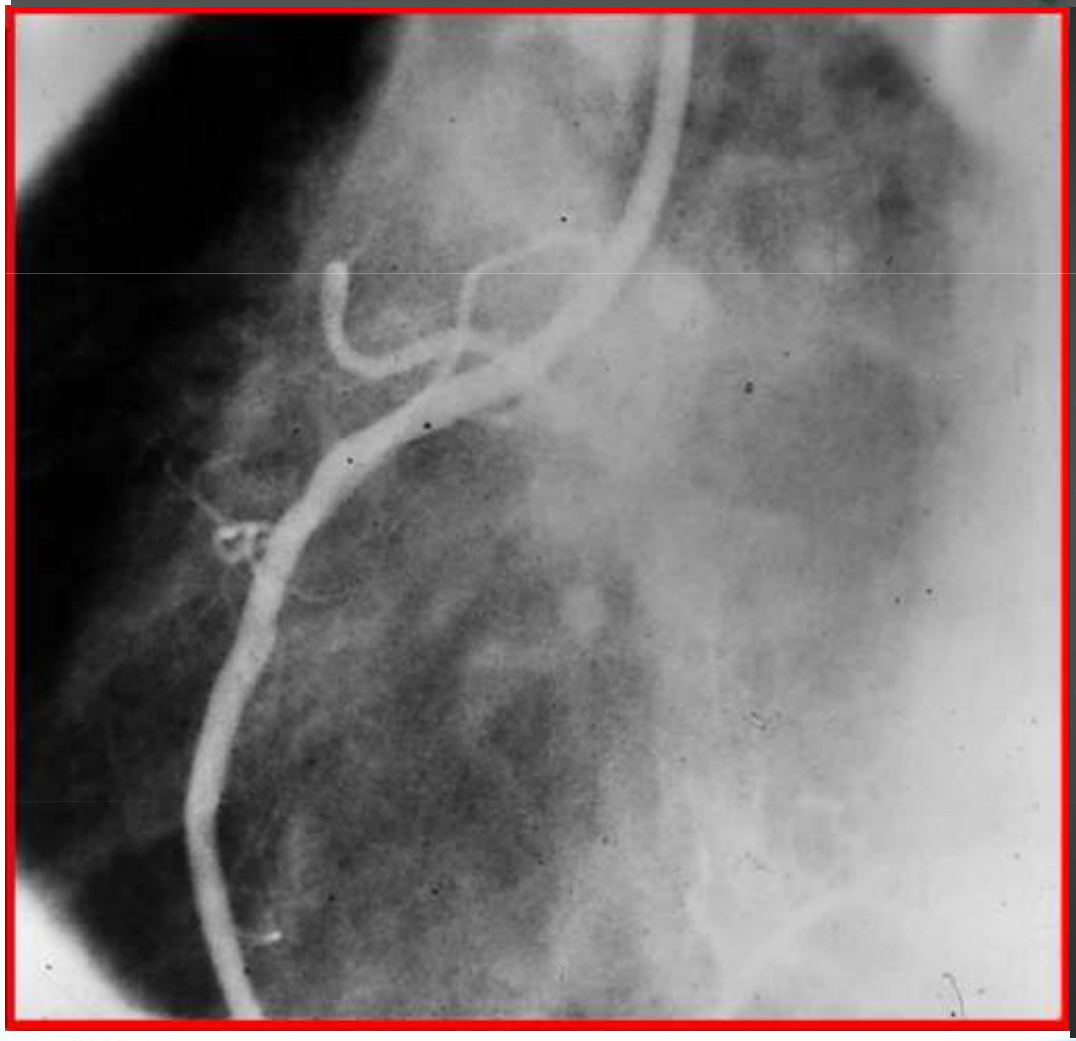
- abrupt closure after balloon dilation remained in the range of 4%–8%
- the overall mortality rate was 4.9%
- more than 20% of patients requiring emergency CABG
- **Restenosis rate 30-50%** (neointima hyperplasia)

First stent implantation in man (Puel/Sigwart, March 1986)





First Palmaz-Schatz Stent in Human
December 31st, 1987



O paciente:

Jorge Cassiano Jr.

Cardiology team:

Amanda Sousa

J. Eduardo Sousa

Fausto Feres

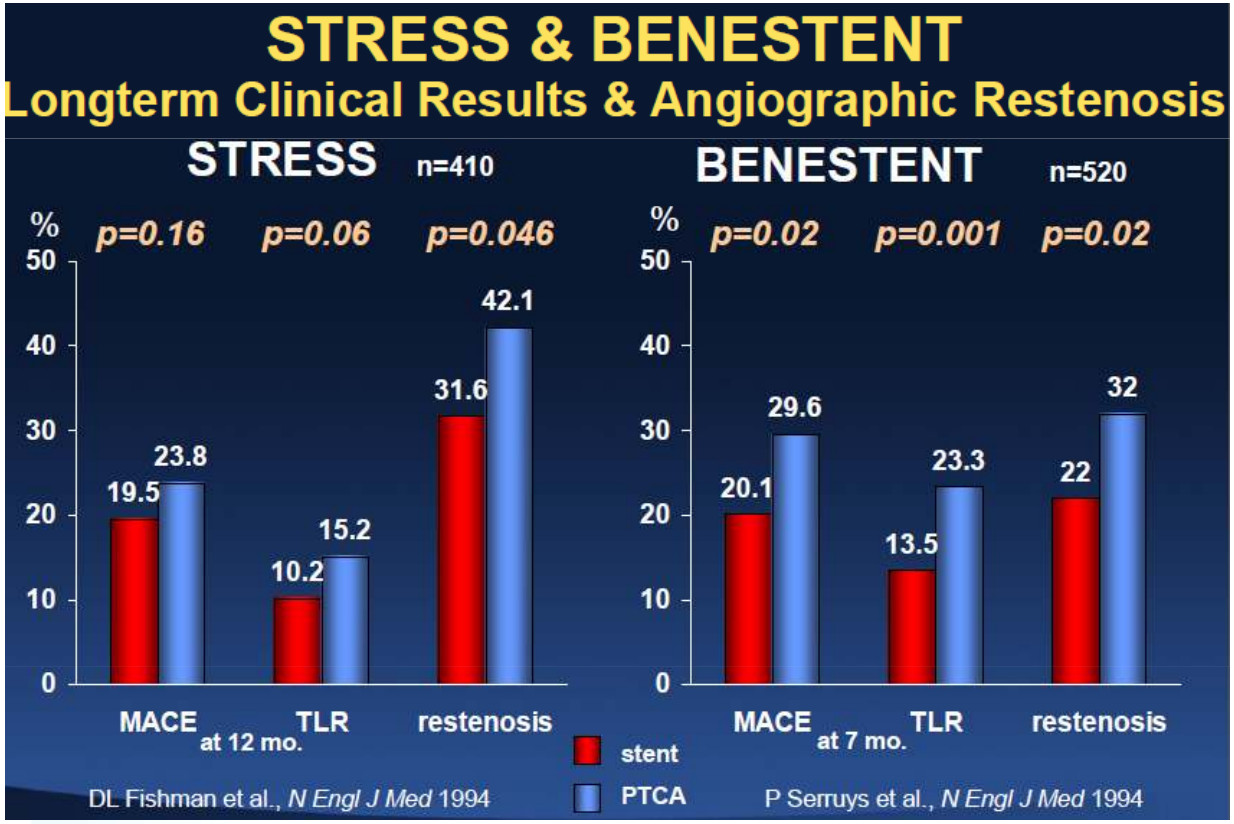
Julio Palmaz

Ibraim Pinto

Richard Schatz

Celia Benette

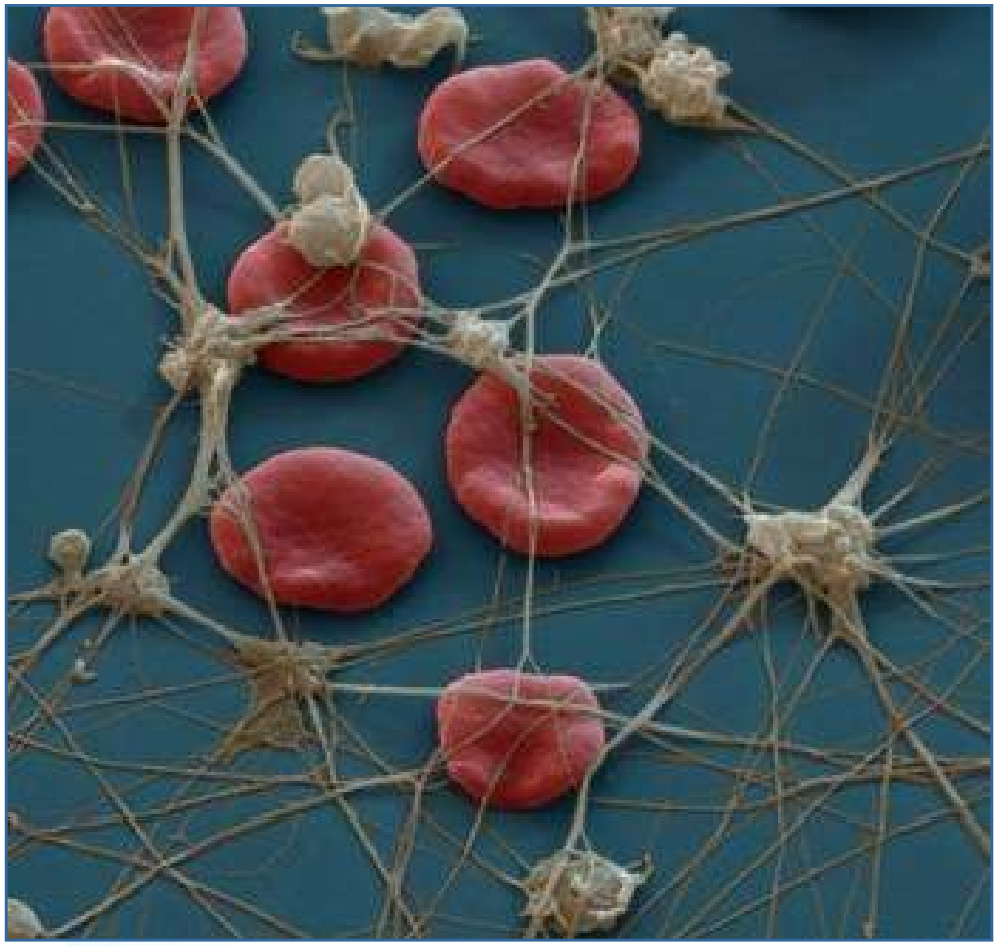
In 1993, two landmark trials, the Belgium Netherlands Stent Arterial Revascularization Therapies Study (BENESTENT) and the North American Stent Restenosis Study (STRESS) , confirmed coronary stenting significantly improved angiographic and clinical outcomes, thus establishing elective coronary stent implantation as an accepted standard of care.



➢Restenosis decreased from 42% to 32% (*P 0.04) in the STRESS trial and from 32% to 22% (P 0.02) in the BENESTENT trial.*

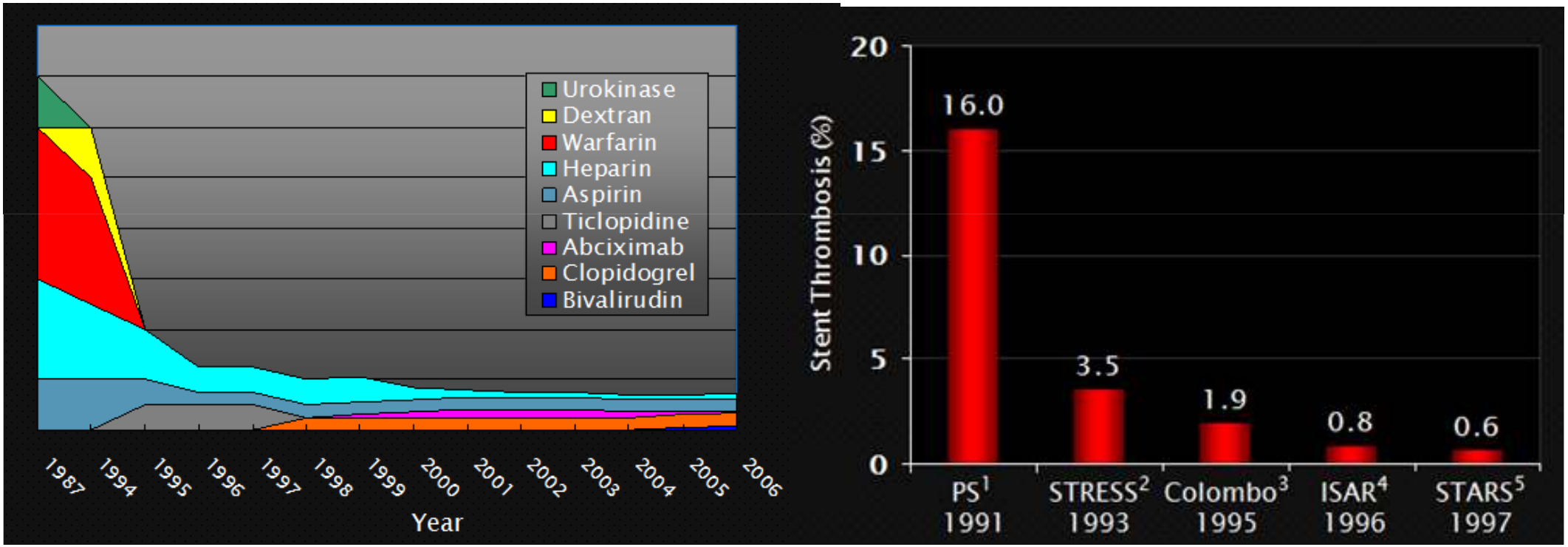
By 1999, 84.2% of all interventions involved stent insertion

The Platelet, the enemy of the interventionist…



Thrombosis had long been recognized as a serious complication of stent implantation in both animal and early clinical studies.

Intra-coronary stents
Anticoagulant & Antiplatelet therapy



The BENESTENT and STRESS studies reported **subacute stent thrombosis rates of 3.5% and 3.4%**, respectively, despite the use of a complex anticoagulation regimen consisting of dextran, aspirin, dipyridamole, heparin, and warfarin.

Two practices led to a dramatic reduction in the incidence of stent thrombosis in BMS:

(1) the use of intravascular ultrasound and high balloon pressures to optimize apposition of the stent struts to the vessel wall, and

(2) ***the replacement of anticoagulation with dual-antiplatelet therapy***

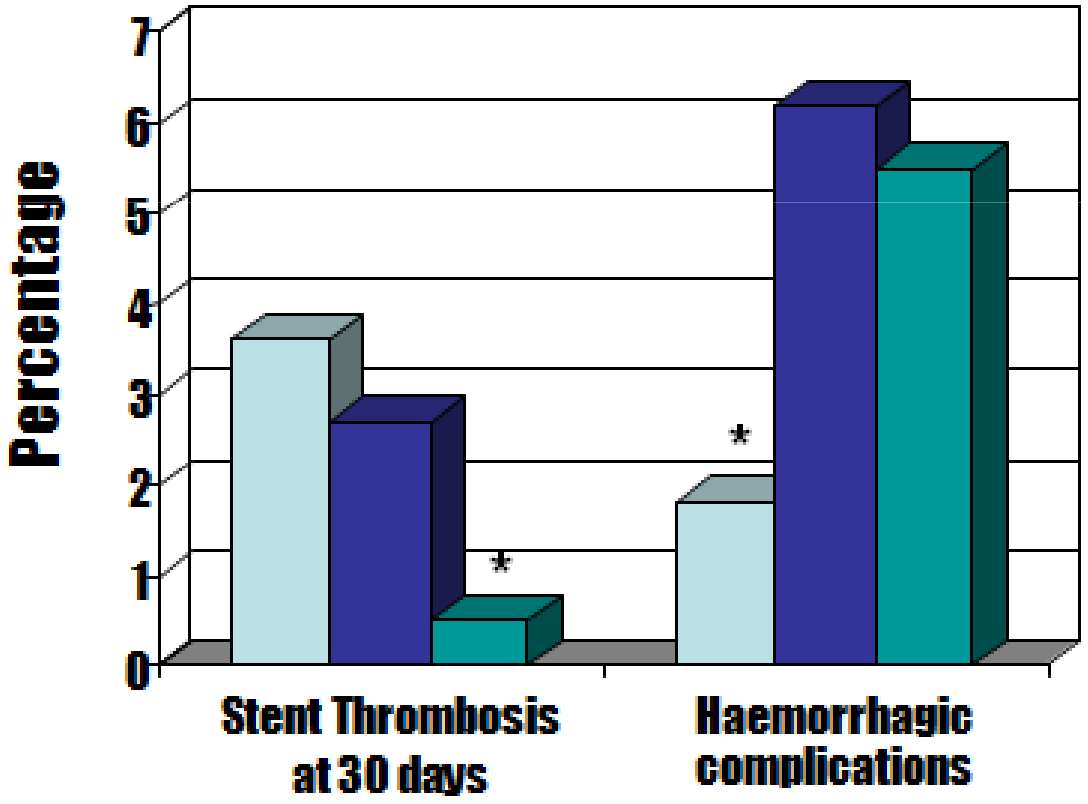
The combination of a thienopyridine with aspirin became the cornerstone of antithrombotic prophylaxis.

- **Their combined effects resulted in superior antithrombotic activity when compared to conventional anticoagulation in initial studies.**

Initially, ticlopidine was prescribed with aspirin

- Irreversibly inhibits platelet aggregation when bound to the P2Y12 portion of ADP-receptors
- Usual dose: 250 mg po BID
- Pharmacokinetics:
  - Well absorbed, peak levels @ 2 hrs,
  - Max effect @ 8-11 days
  - Metabolized via CYP 3A4
  - No active metabolites
- Hold 10-14 days prior to surgery

The STARS Trial



1965 patients
50 centres
84% angio. success

- Aspirin
- Aspirin+Warfarin
- Aspirin +Ticlopidine

* p<0.001 vs. others

Leon MB et al, NEJM 1998;339:1702-4

Adverse effects make this agent problematic

- Agranulocytosis
- Thrombotic Thrombocytopenia Purpura (TTP)
- Aplastic Anemia

Requires CBC baseline and every 2 weeks for the first 3 months of therapy

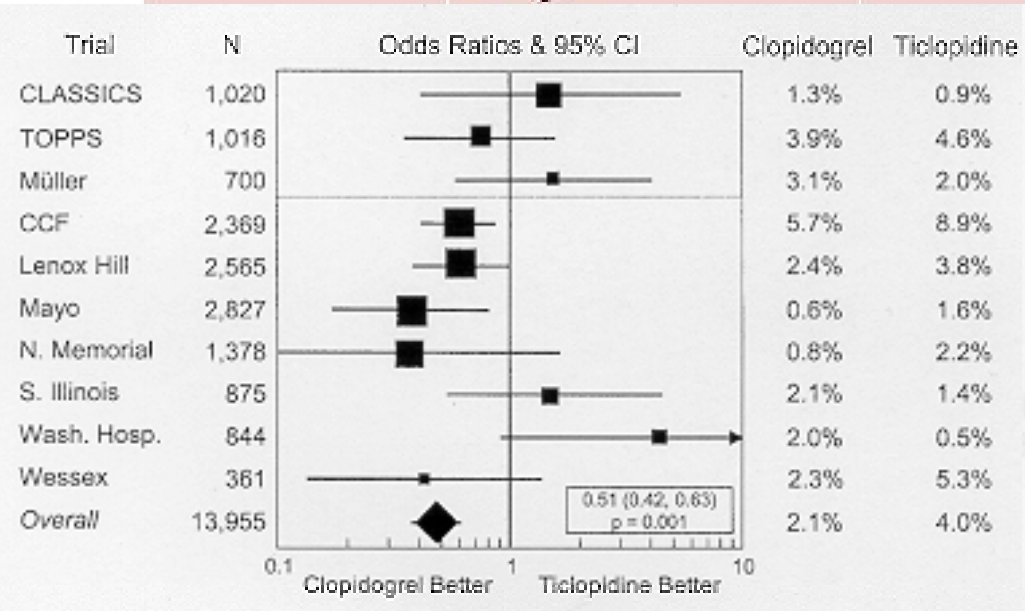
Clopidogrel later replaced ticlopidine owing to its better safety profile

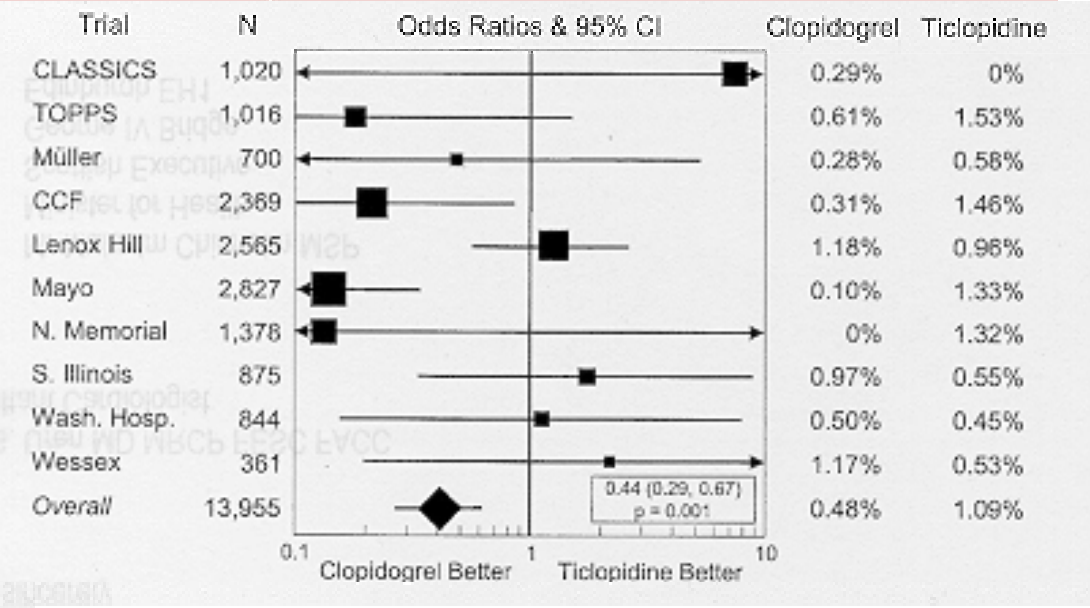
Less frequent incidences of rash, neutropenia, and thrombotic thrombocytopenic purpura.

Clopidogrel vs. Ticlopidine Post-PCI

- **No one trial large enough to demonstrate comparability**

CLASSICS Trial[18] 2000	Clopidogrel 300mg load followed by 75mg daily	Ticlopidine 250 mg BID OR Clopidogrel 75 mg daily	- Less bleeding, thrombocytopenia, and leukopenia with clopidogrel - No difference in MACE

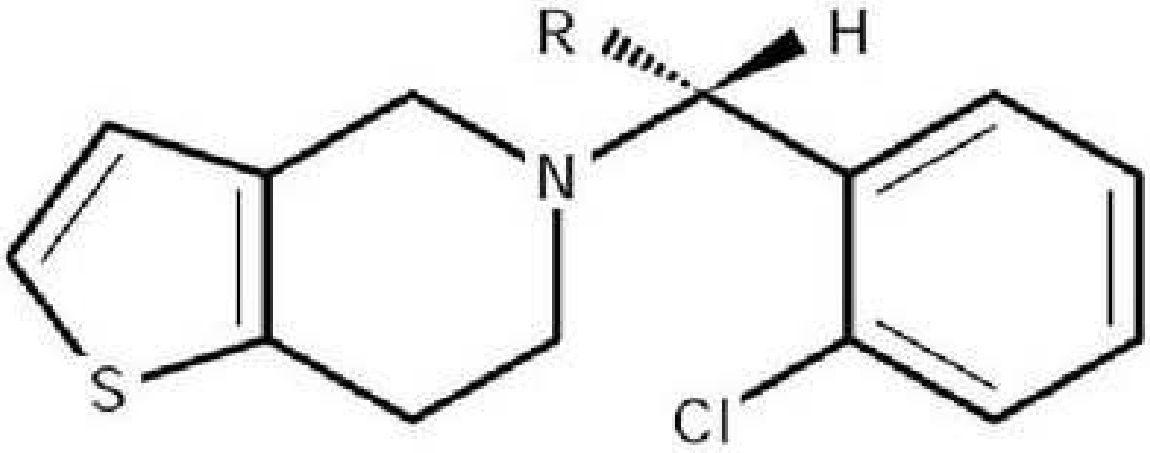




- **n=13,995 meta-analysis**
- **1° endpoint of MACE at 30 days after stenting**
- **MACE $_{clopidogrel}$ = 2.1% vs MACE $_{ticlopidine}$ = 4.0%**
- **Death $_{clopidogrel}$ = 0.48% vs death $_{ticlopidine}$ = 1.1%**

Bhatt DI et al
JACC 2002;39:9-14

The stent survived, thanks to...



R = CO_2CH_3 Clopidogrel

BMS AND IN-STENT RESTENOSIS

BMS are associated with a 20%–25% restenosis rate within 6 mo of implantation.

Lesion complexities (long lesions,calcification etc), comorbidities (diabetes, renal insufficiency) increase this incidence, and restenosis rates approaching 80% have been observed in these subgroups

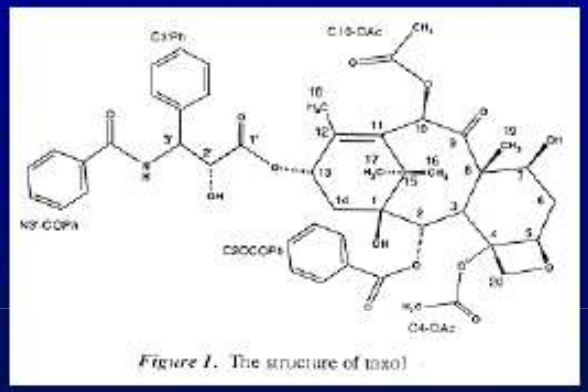
In-stent restenosis incidence peaks at 3 mo, reaches a plateau between 3 and 6 mo, but can persist beyond 1 yr after stent deployment

Drug eluting stents-DES

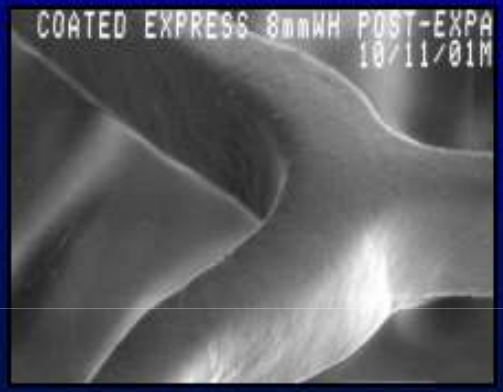
The combination of stent properties to inhibit recoil and negative remodeling with drugs that inhibit neointimal proliferation, utilizing the stent as a local delivery platform, have emerged as a highly promising alternative to reduce instent restenosis.

Drug-eluting Stents: 1st Generation

TAXUS



Paclitaxel

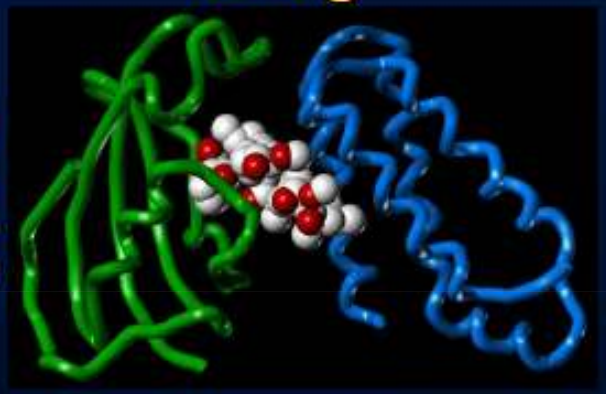


Polyolefin derivative

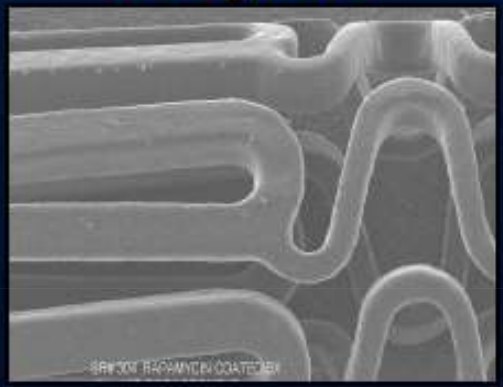
Liberté

Drug | Polymer | Stent

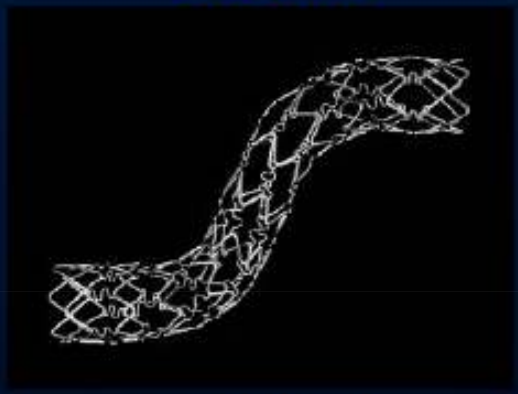
Cypher



Sirolimus



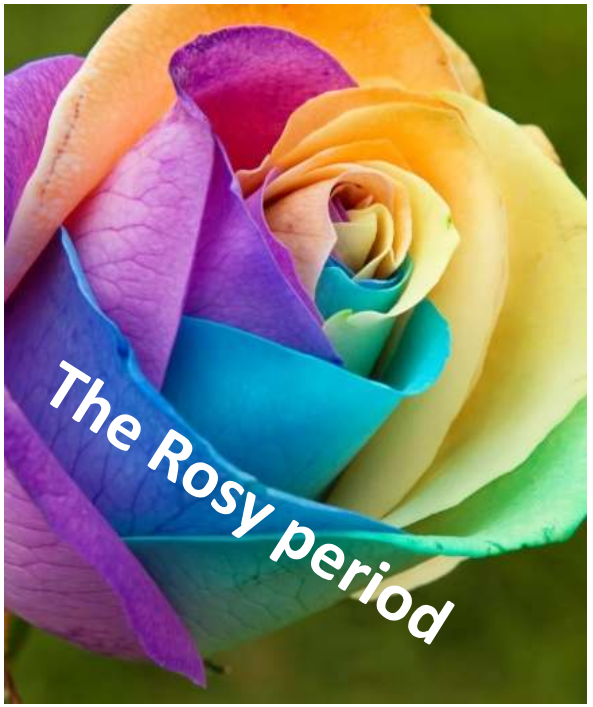
PEVA + PBMA blend



BX Velocity

First-In-Man study with CYPHER:
Sao Paulo, FU completed

FIM: FIRST IN MAN



Rapamycin experience:

15 patients (Sao Paulo, E. Sousa) ; fast release

- **4 months follow-up No restenosis, no TVR**

15 patients (Sao Paulo, E. Sousa) ; slow release

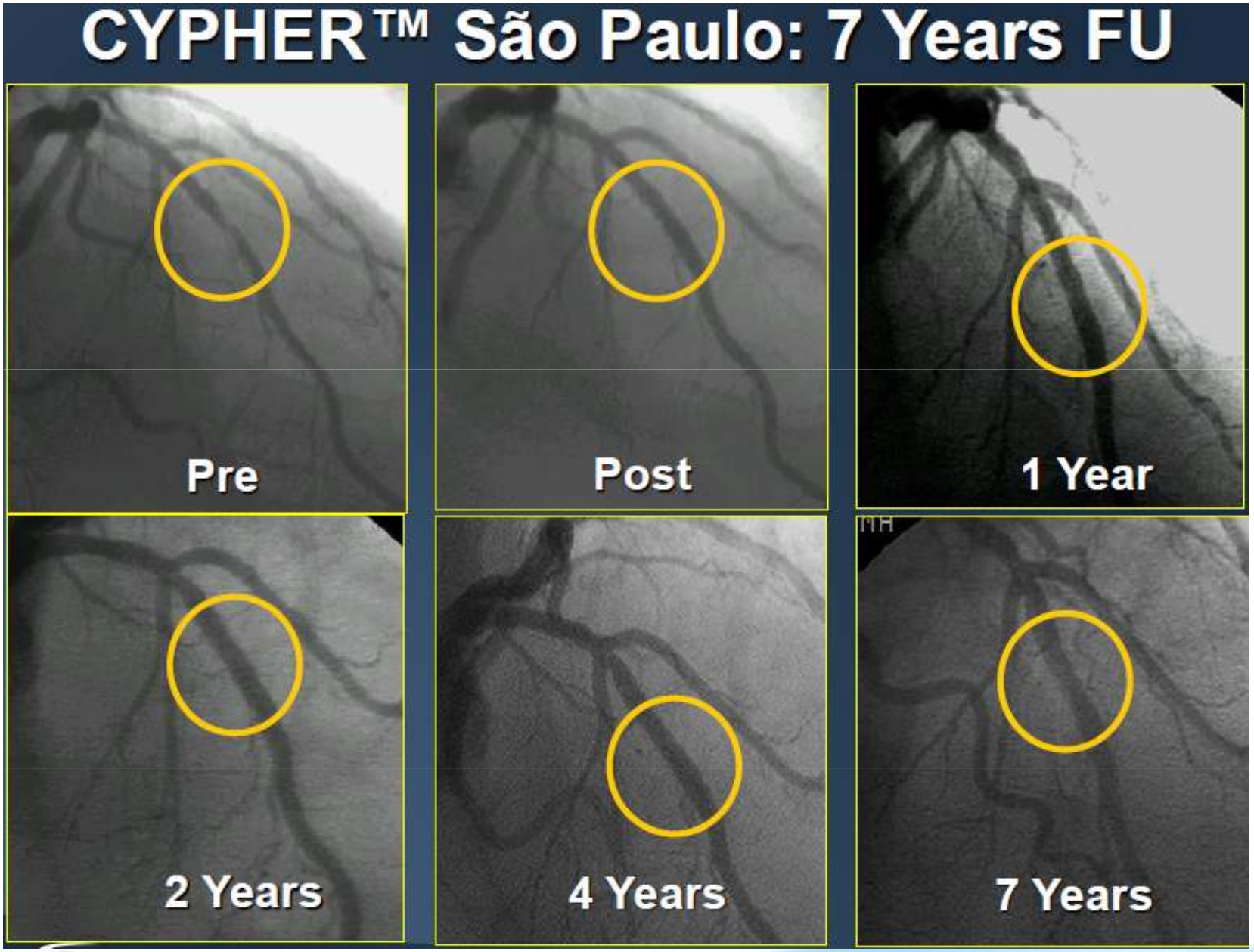
- **6 months follow-up No restenosis, no TVR**

15 patients (Rotterdam, PW. Serruys); slow release

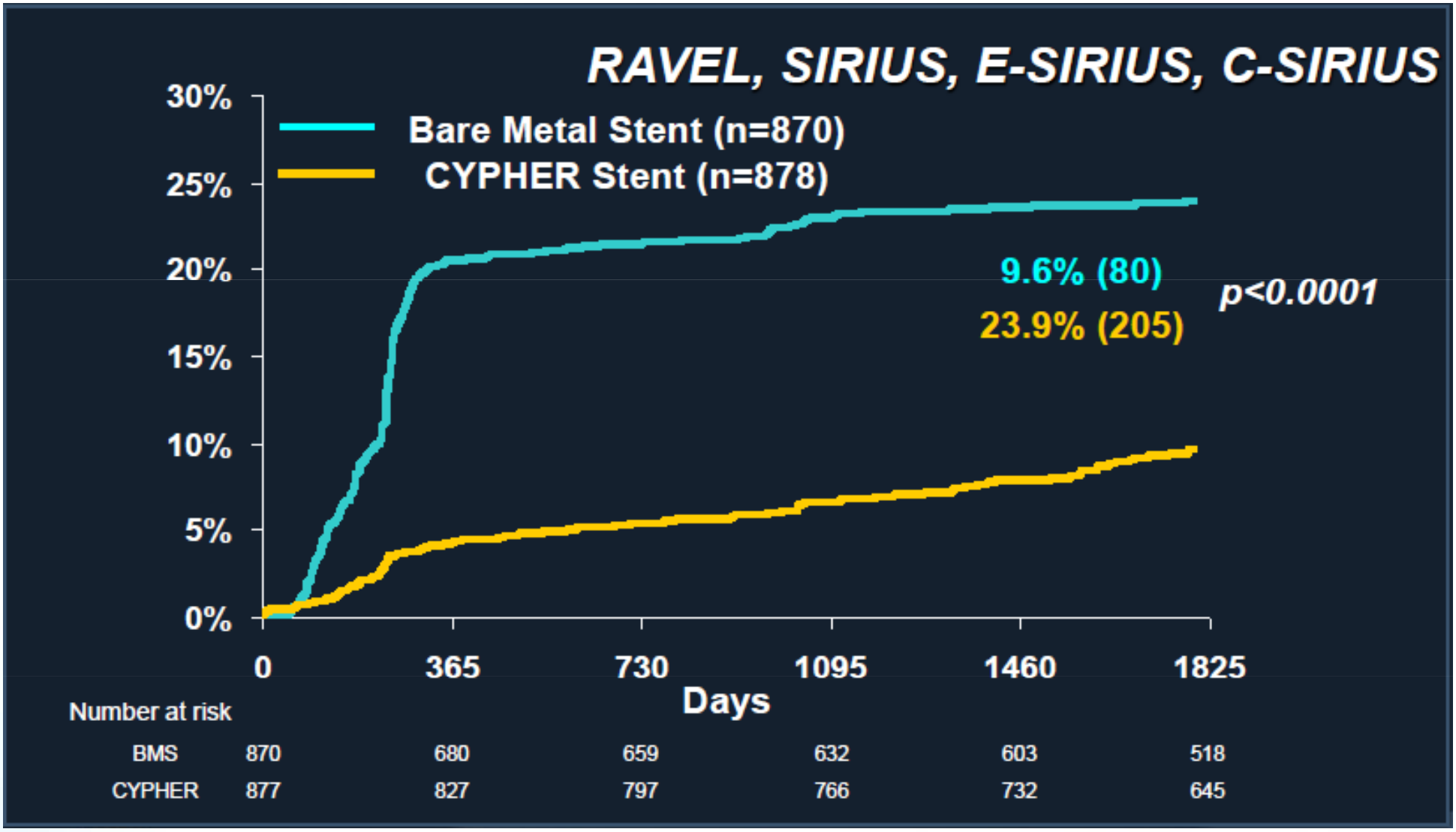
- **4 months follow-up No restenosis, no TVR**

Don't wake me up, don't pinch me, let me keep dreaming

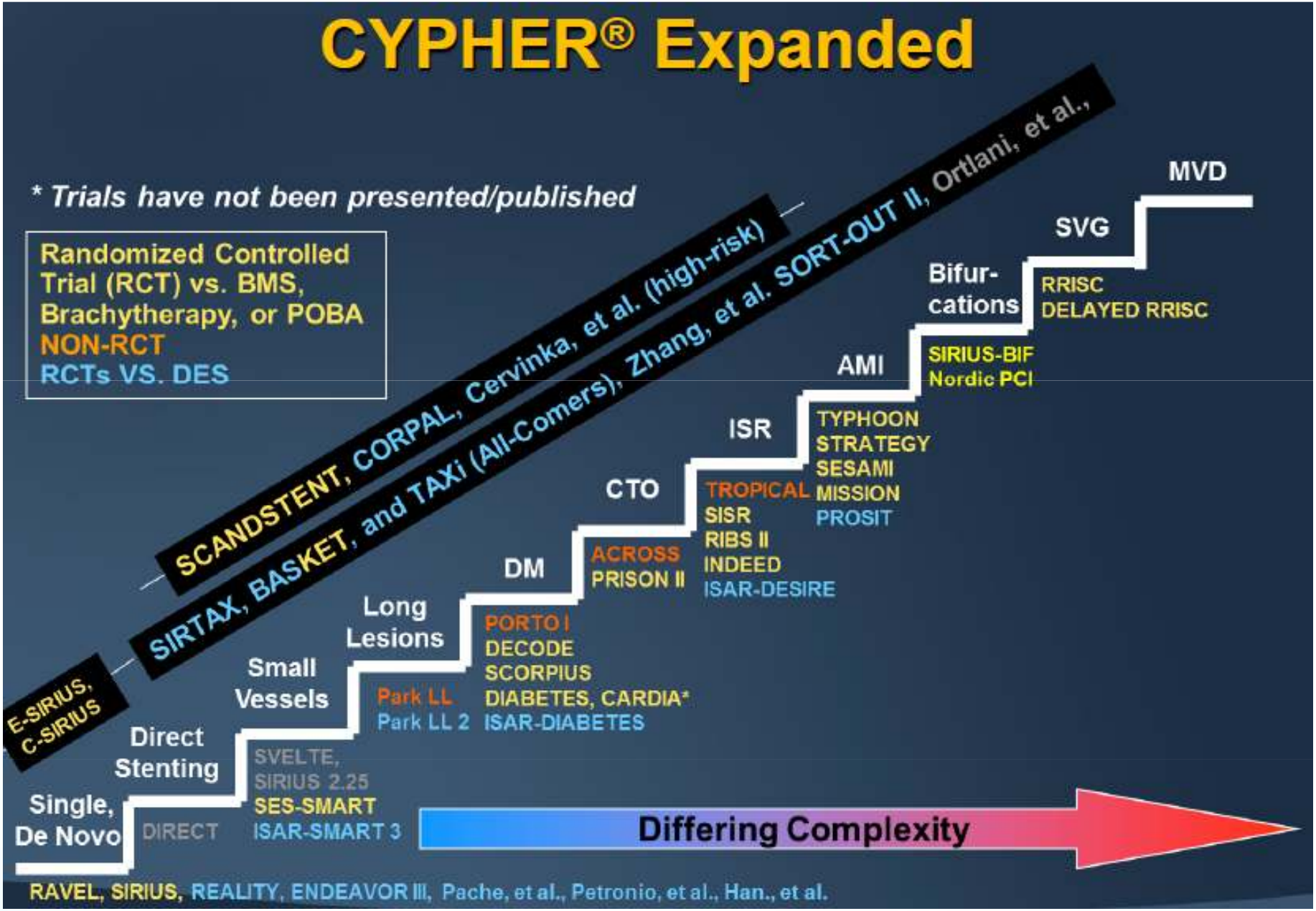
CYPHER™ São Paulo: 7 Years FU

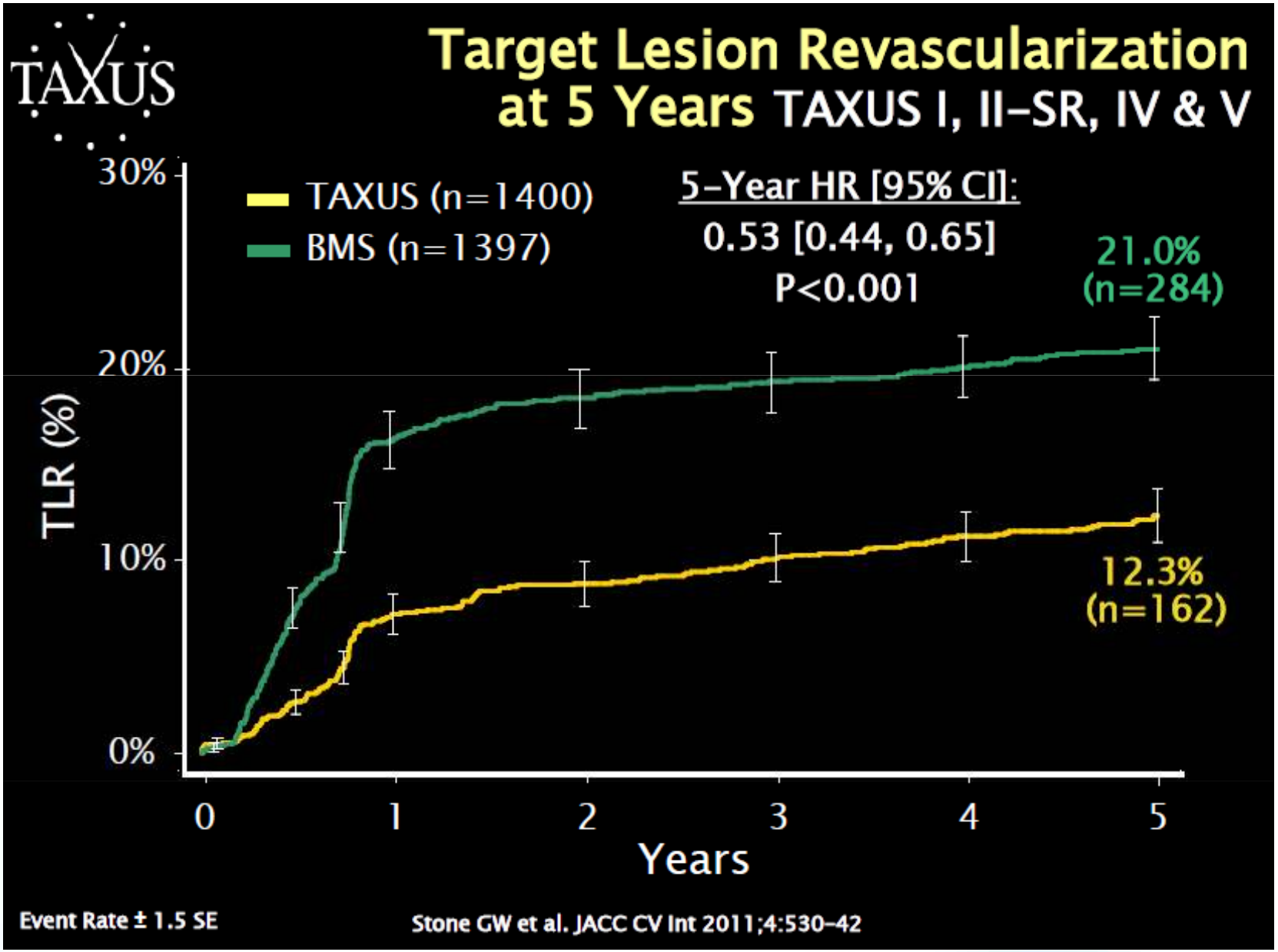


CYPHER vs. BMS: TLR *Pooled Analyses of 4 RCTs*

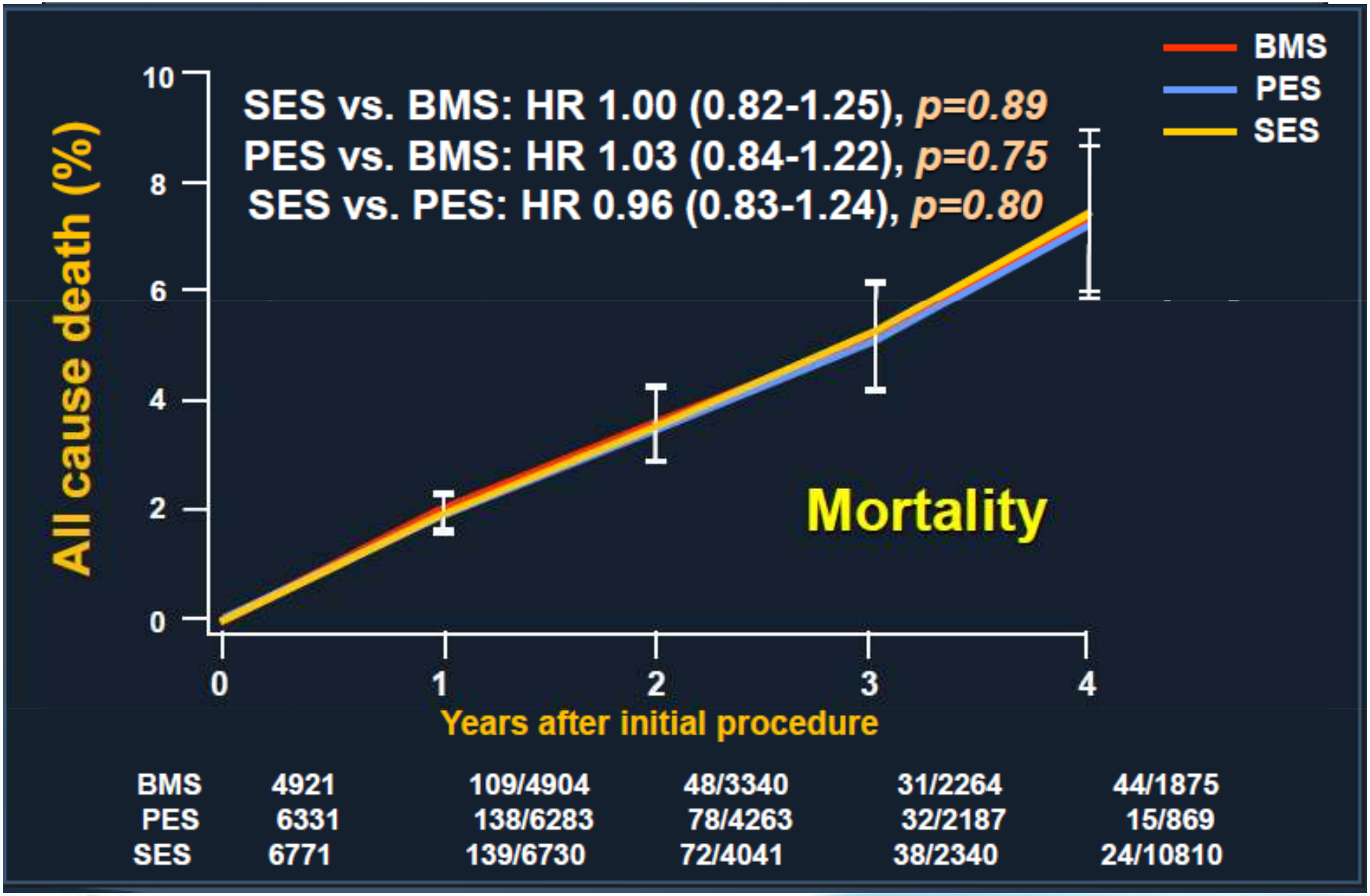


Kirtane A. TCT 2007. Adapted from Stone GW et al. *NEJM 2007;356:998–1008*


CYPHER® Expanded
* Trials have not been presented/published
Randomized Controlled Trial (RCT) vs. BMS, Brachytherapy, or POBA
NON-RCT
RCTs VS. DES
SCANDSTENT, CORPAL, Cervinka, et al. (high-risk)
SIRTAX, BASKET, and TAXi (All-Comers), Zhang, et al. SORT-OUT II, Ortlani, et al.,
E-SIRIUS, C-SIRIUS
Single, De Novo
Direct Stenting
DIRECT
Small Vessels
SVELTE, SIRIUS 2.25
SES-SMART
ISAR-SMART 3
Long Lesions
Park LL
Park LL 2
DM
PORTO I
DECODE
SCORPIUS
DIABETES, CARDIA*
ISAR-DIABETES
CTO
ACROSS
PRISON II
ISR
TROPICAL
SISR
RIBS II
INDEED
ISAR-DESIRE
AMI
TYPHOON
STRATEGY
SESAMI
MISSION
PROSIT
Bifur-cations
SIRIUS-BIF
Nordic PCI
SVG
RRISC
DELAYED RRISC
MVD
Differing Complexity
RAVEL, SIRIUS, REALITY, ENDEAVOR III, Pache, et al., Petronio, et al., Han., et al.


TAXUS
Target Lesion Revascularization
at 5 Years TAXUS I, II–SR, IV & V
TAXUS (n=1400)
BMS (n=1397)
5-Year HR [95% CI]:
0.53 [0.44, 0.65]
P<0.001
21.0%
(n=284)
12.3%
(n=162)
30%
20%
10%
0%
TLR (%)
0
1
2
3
4
5
Years
Event Rate ± 1.5 SE
Stone GW et al. JACC CV Int 2011;4:530–42

Network Meta-analysis: 38 trials, 18,023 pts



Stettler C et al. Lancet 2007;370:937- 48

The DES journey from the rosy period to harsh reality

TUESDAY

ESC Congress News

World Congress of Cardiology 2006

The unique meeting of the European Society of Cardiology Congress 2006 and the World Heart Federation's XVth World Congress of Cardiology

"Our Black Tuesday"

Do drug-eluting stents increase deaths?

TWO SEPARATE, independent meta-analyses, presented in Hot Line session I, suggest drug-eluting stents (DES) may increase death, Q-wave myocardial infarction (clinical surrogates of in-stent thrombosis) and cancer deaths, bringing the long-term safety of DES firmly into the spotlight. Discussant Salim Yusuf (McMaster University, Canada) hailed the data as one of the most important presentations to come out of this year's meeting.

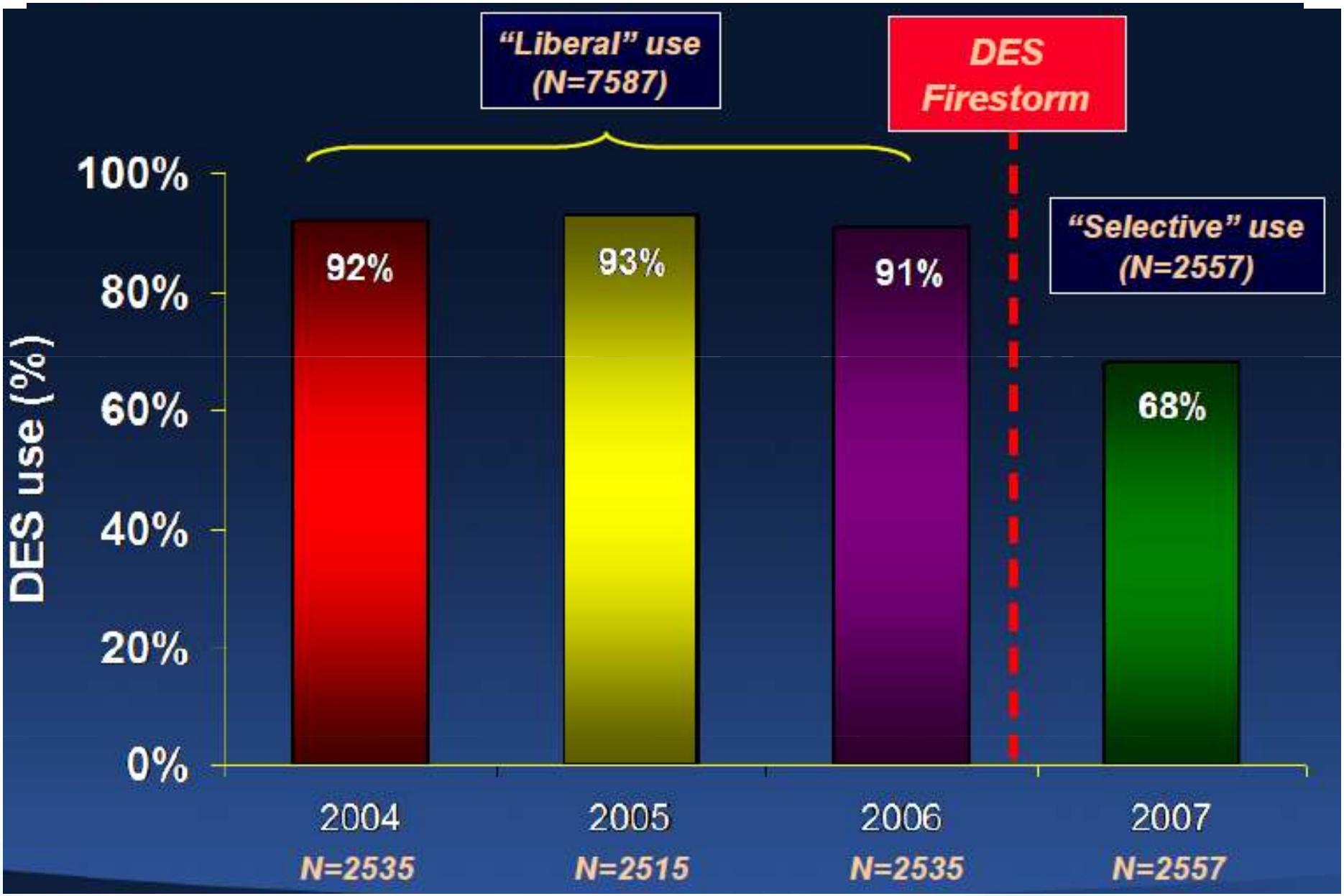
"Six million people in the world have been implanted with DES, yet their long-term safety and efficacy is unknown," said Yusuf. "I've a feeling the data we're seeing today is only the tip of the iceberg. We need to encourage more

obtain this data from the manufacturer," said Nordmann. He speculated that the increase in cancer might be due to a rapid impairment of the immune system.

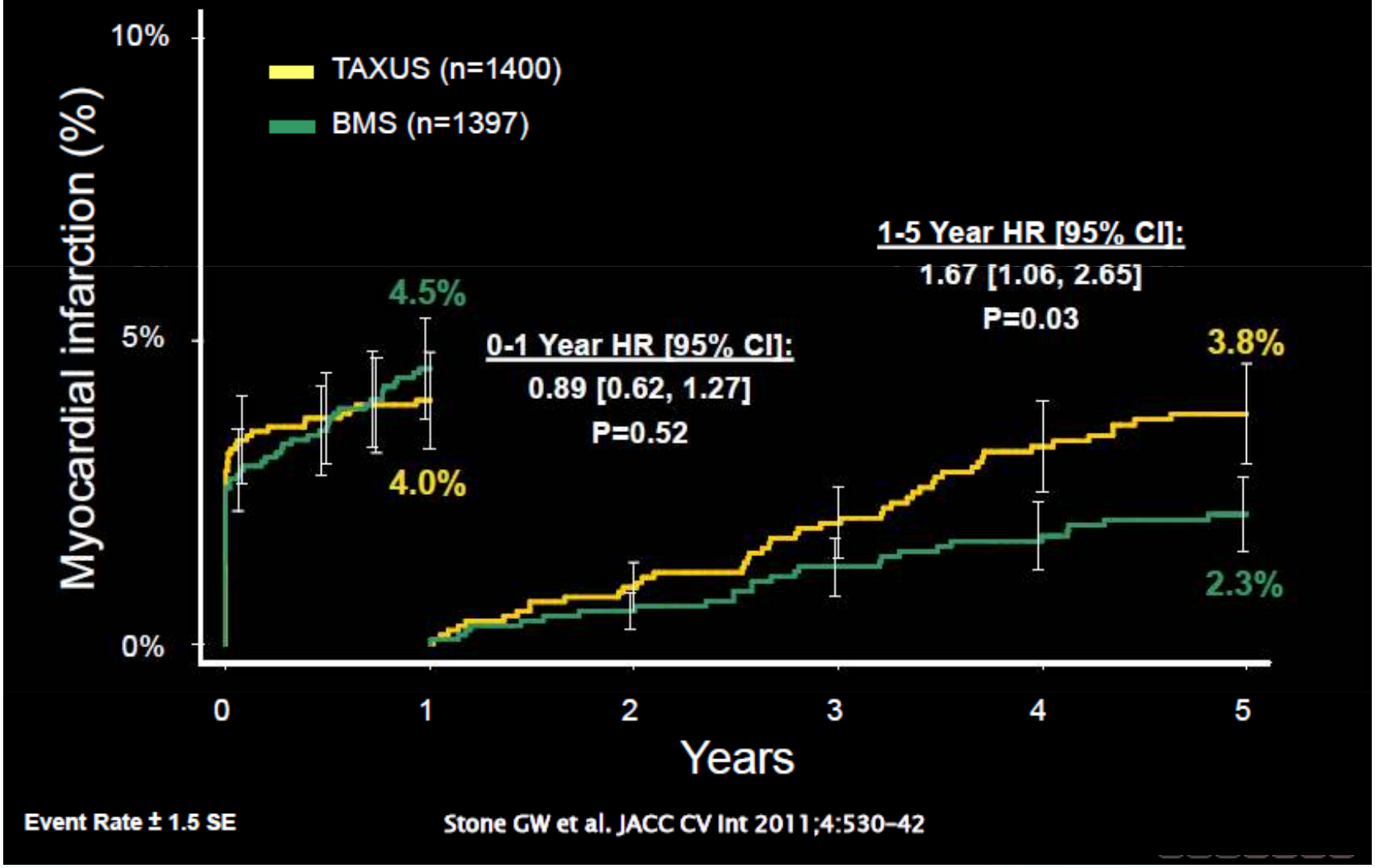
Yusuf widened the debate to include percutaneous coronary intervention (PCI). "The overuse of PCI is an insidious change in the culture of cardiology that needs to be reversed," he said. The use of PCI was established in MI, [illegible] unstable angina and cardiogenic [illegible] however its use in stable disease was a total[illegible]erent [illegible]tion.

"There's no beneficial influence on mortality – PCI does nothing to prevent heart attack. All we are doing is providing short-term relief of chest pain. It's not re-stenosis that kills but the

2006: The ESC "Firestorm"

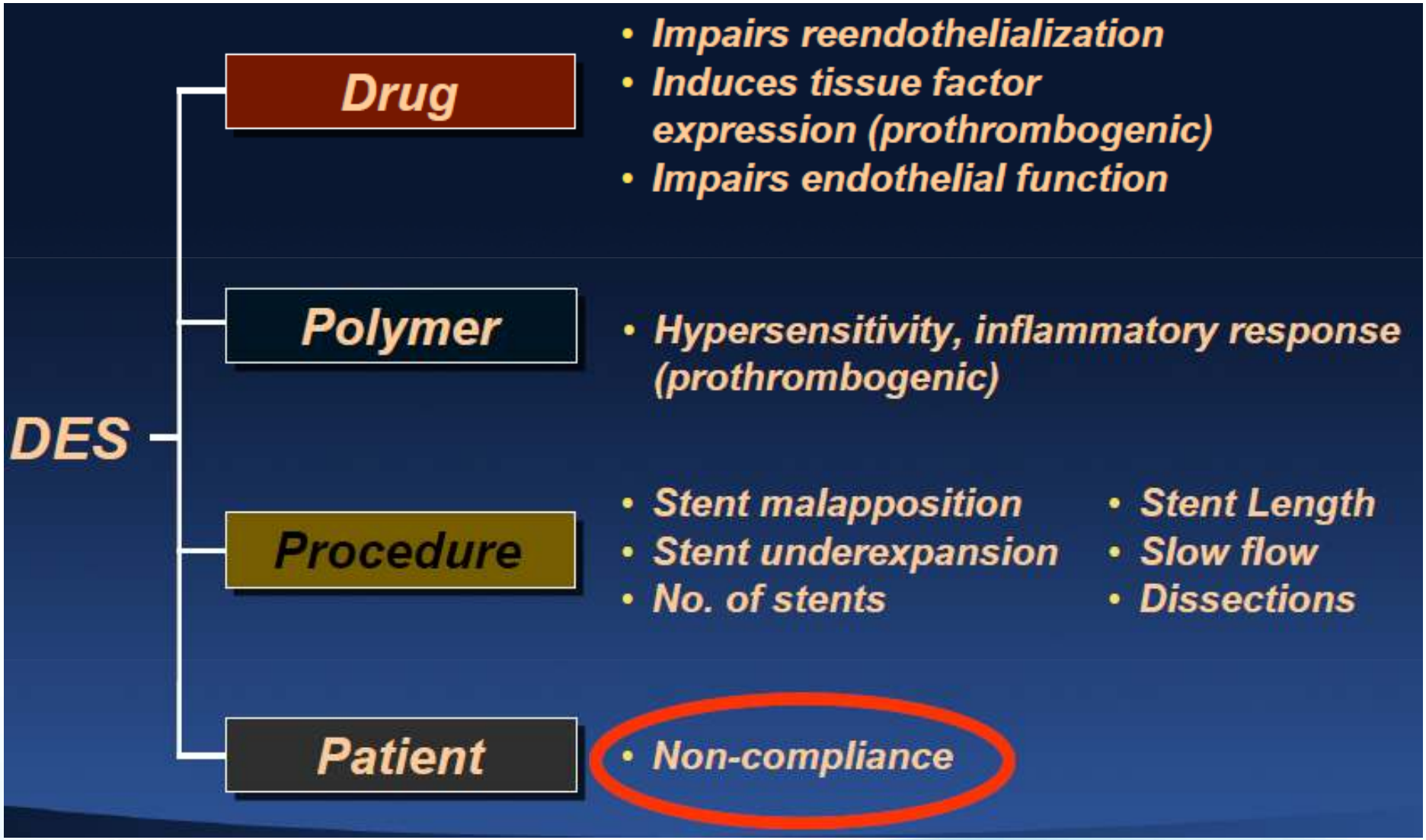

"Liberal" use
(N=7587)
DES
Firestorm
"Selective" use
(N=2557)
DES use (%)
100%
80%
60%
40%
20%
0%
92%
93%
91%
68%
2004
N=2535
2005
N=2515
2006
N=2535
2007
N=2557

Myocardial Infarction: Landmark Analysis TAXUS I, II–SR, IV & V (n=2,797)

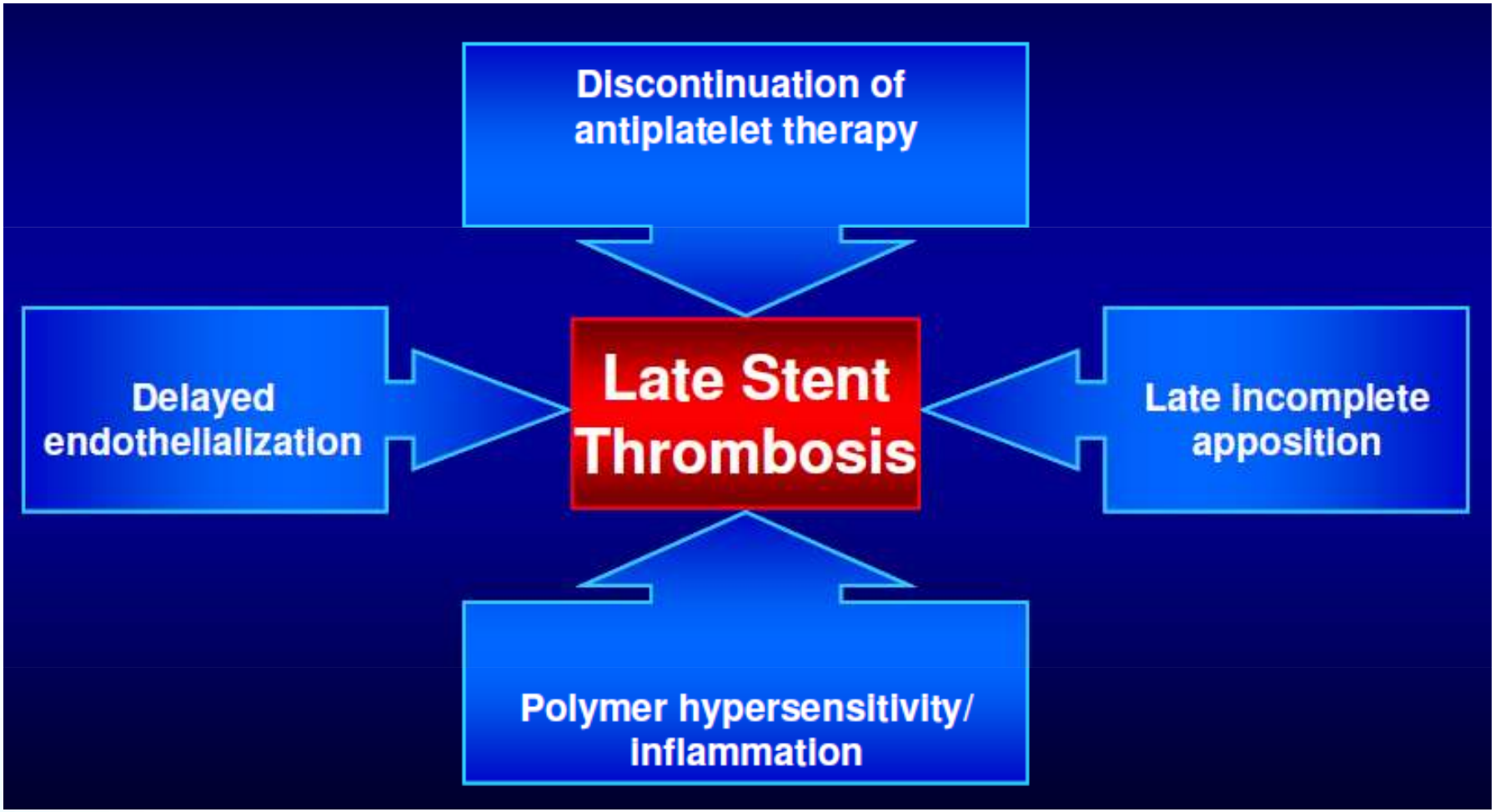


Stone GW et al. JACC CV Int 2011;4:530–42

Potential Problems with DES



DEStent Thrombosis: Late



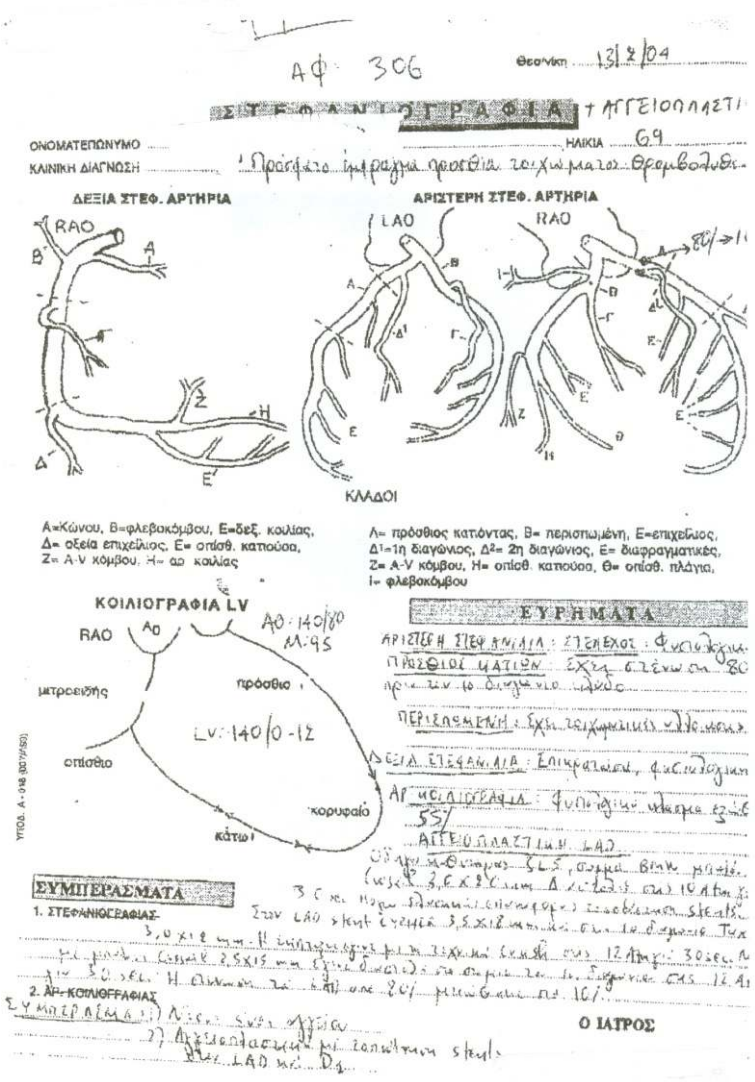
VERY LATE (67 MONTHS) DRUG-ELUTING STENT THROMBOSIS SOON AFTER DISCONTINUATION OF ANTIPLATELET THERAPY

C. Graidis, D. Dimitriadis, A. Ntatsios, A. D. Mavrogianni,
F. Economou, V. Psifos, I. Vogiatzis, G. Spiromitros,
K. Voloudakis, N. Chamouratidis.

Euromedica – Kyanous Stavros, Cardiology Department, Thessaloniki

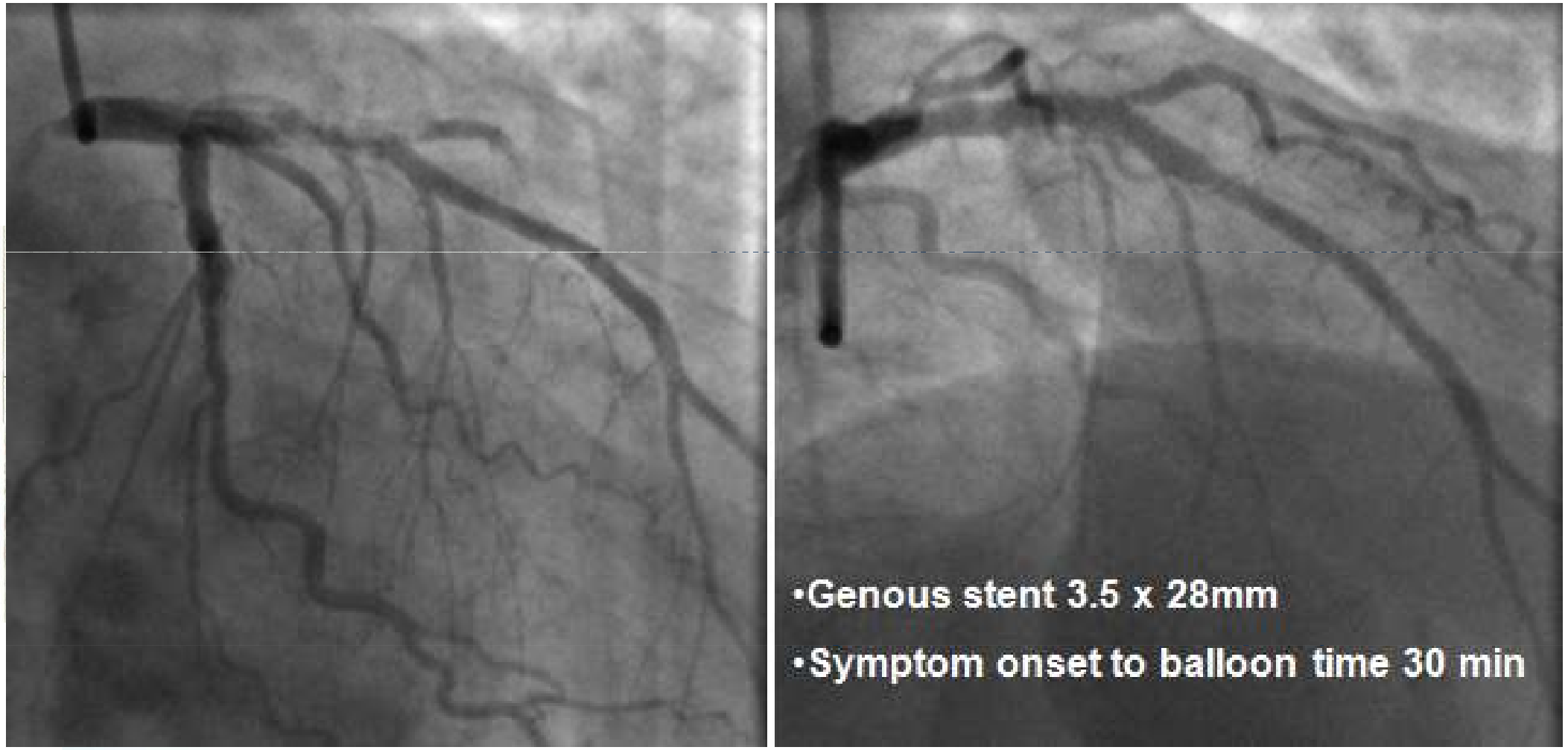
Interventional Cardiovascular Education 2009
Congress Hall 'Du Lac'
Ioannina, 3 – 5 December, 2009

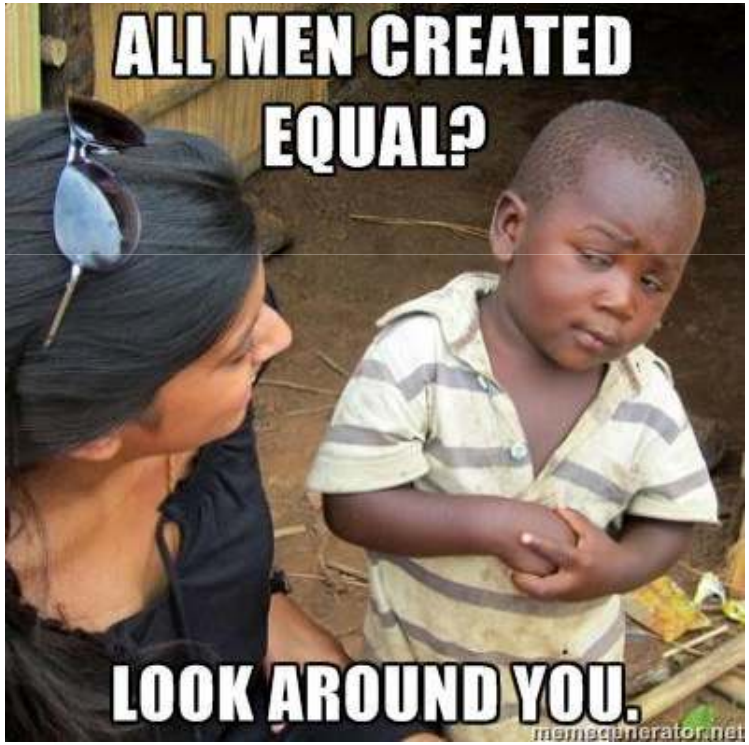
CASE REPORT

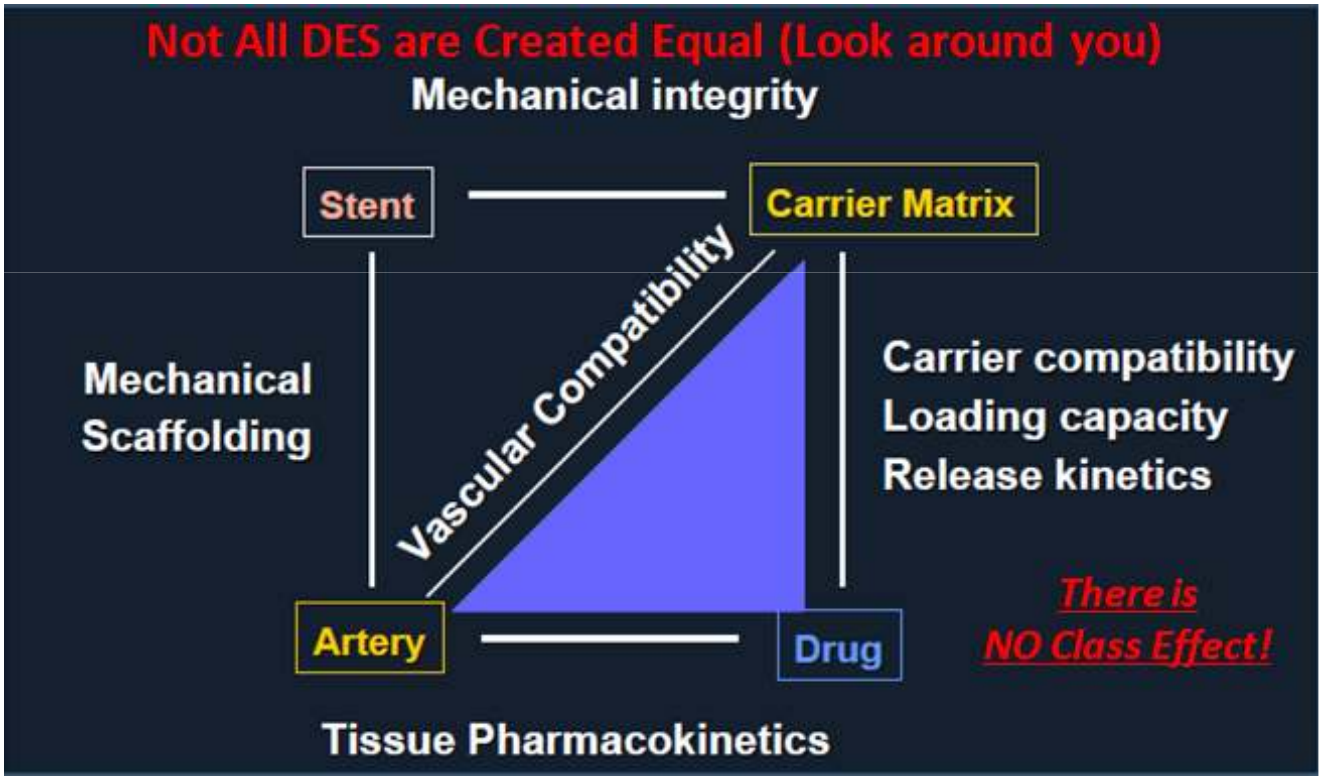


- 74 y.o. male.
- Risk factors for IHD: Hypertension, Dyslipidaemia, Ex-smoker.
- 13 Feb 2004: PCI for a bifurcation lesion LAD / D1 (Recent Anterior STEMI thrombolysed).
  - Crushing technique
    - LAD: Cypher 3.5 x 18mm
    - D1: Taxus 3 x 12mm
  - No final kissing balloon performed.

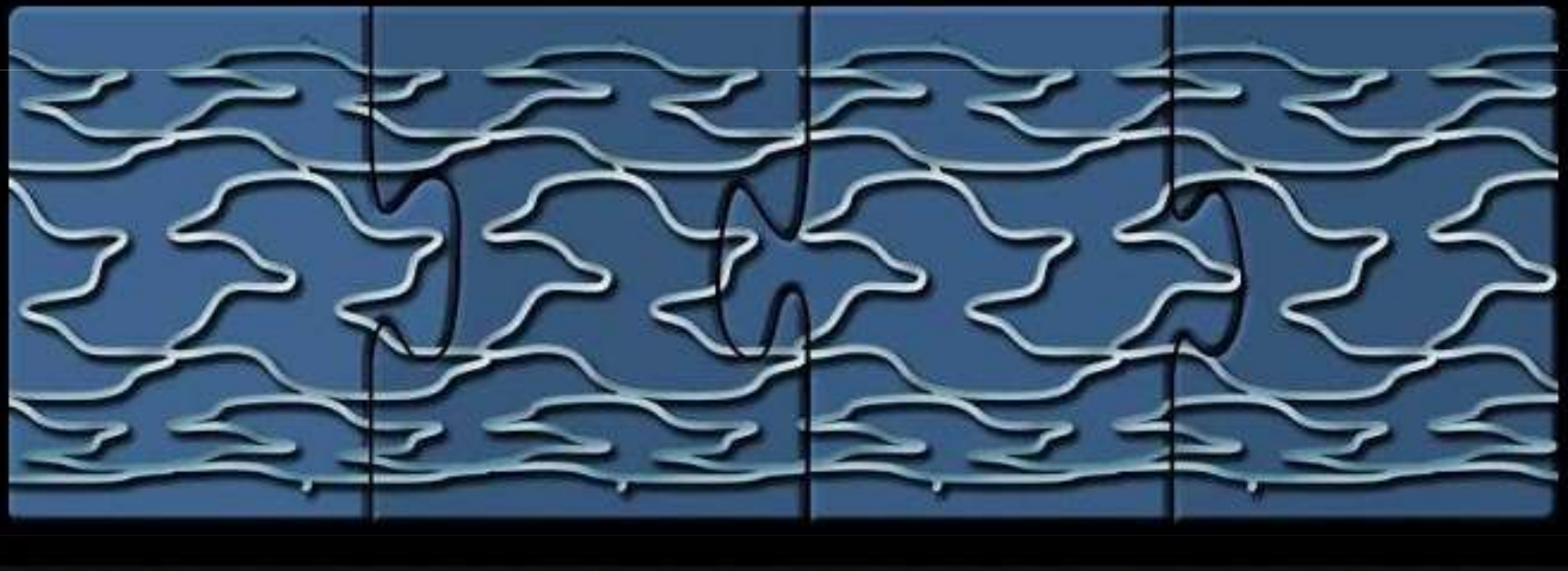
CASE REPORT




ALL MEN CREATED EQUAL?
LOOK AROUND YOU.
memegenerator.net


Not All DES are Created Equal (Look around you)
Mechanical integrity
Stent
Carrier Matrix
Vascular Compatibility
Mechanical
Scaffolding
Carrier compatibility
Loading capacity
Release kinetics
There is
NO Class Effect!
Artery
Drug
Tissue Pharmacokinetics

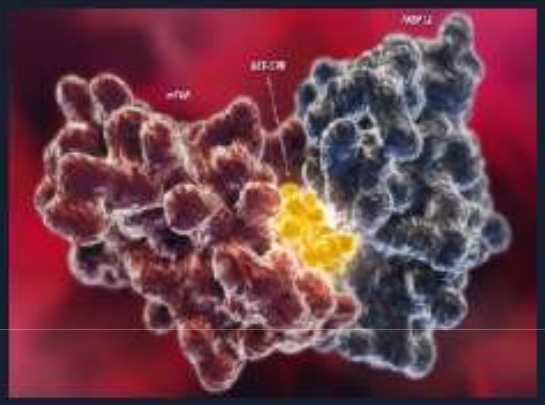
Requirements of the ideal DES



Efficacy Safety Deliverability Cost

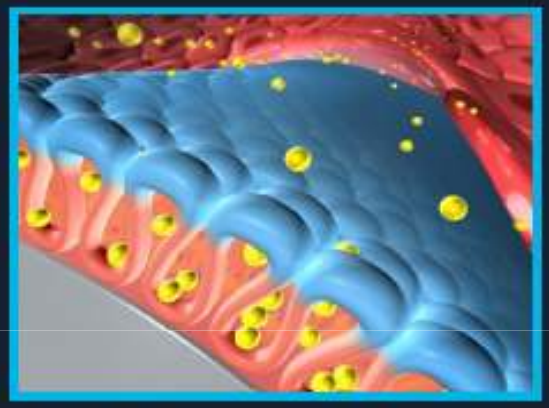
Second Generation DES

Resolute



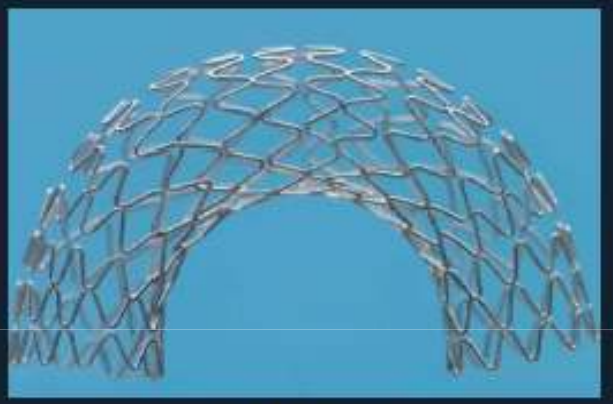
Zotarolimus

Drug



BioLinx copolymer

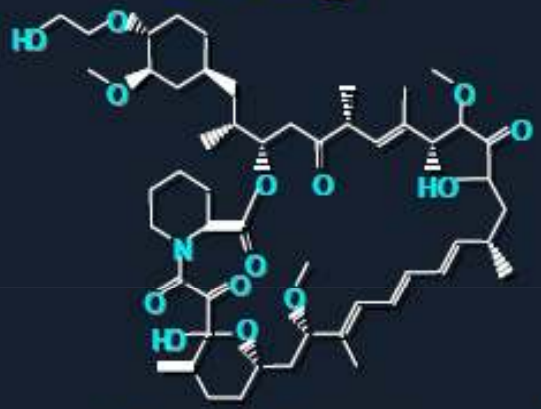
Polymer



Driver

Stent

Xience V*



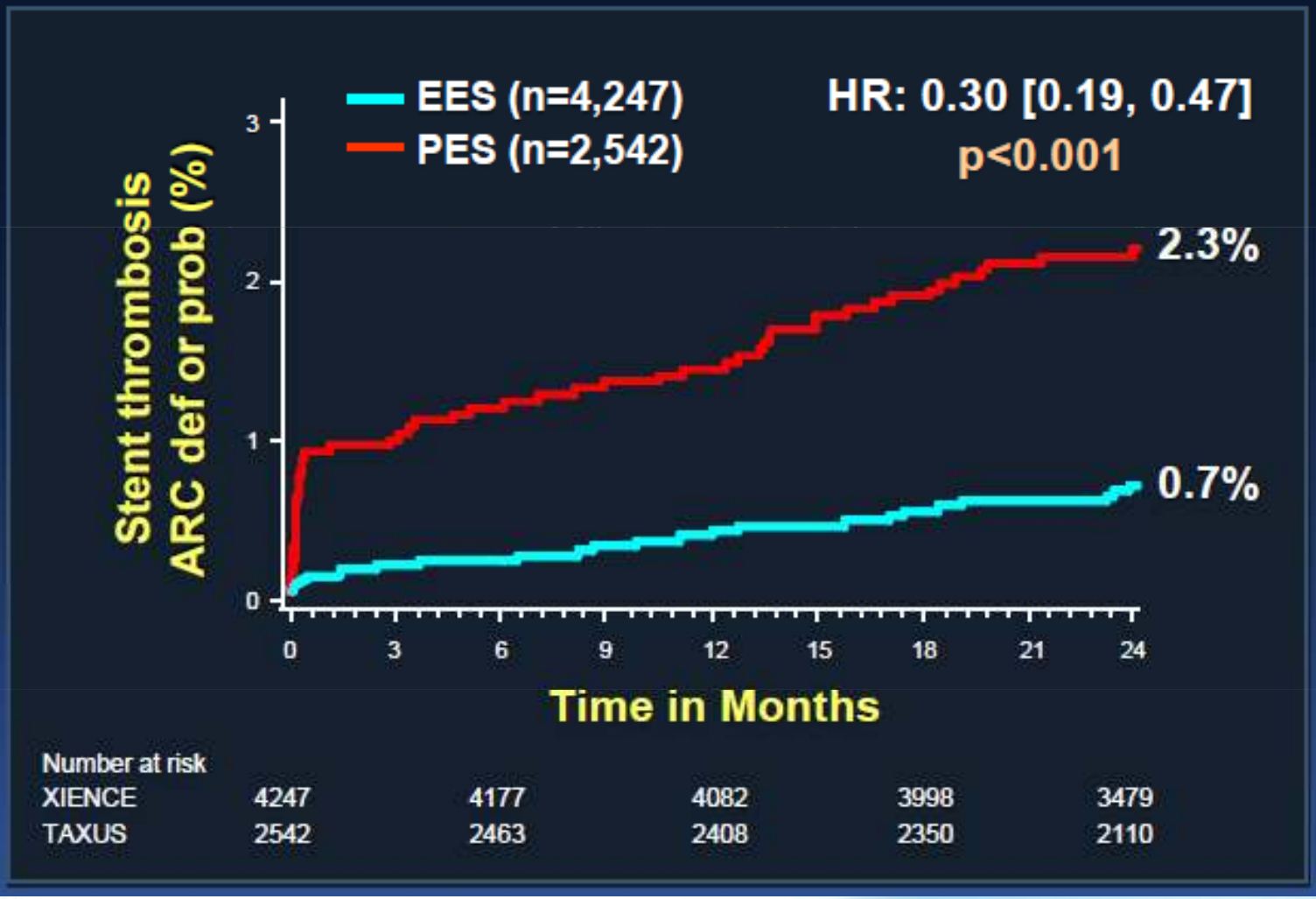
Everolimus

VDF + HFP copolymer

Vision

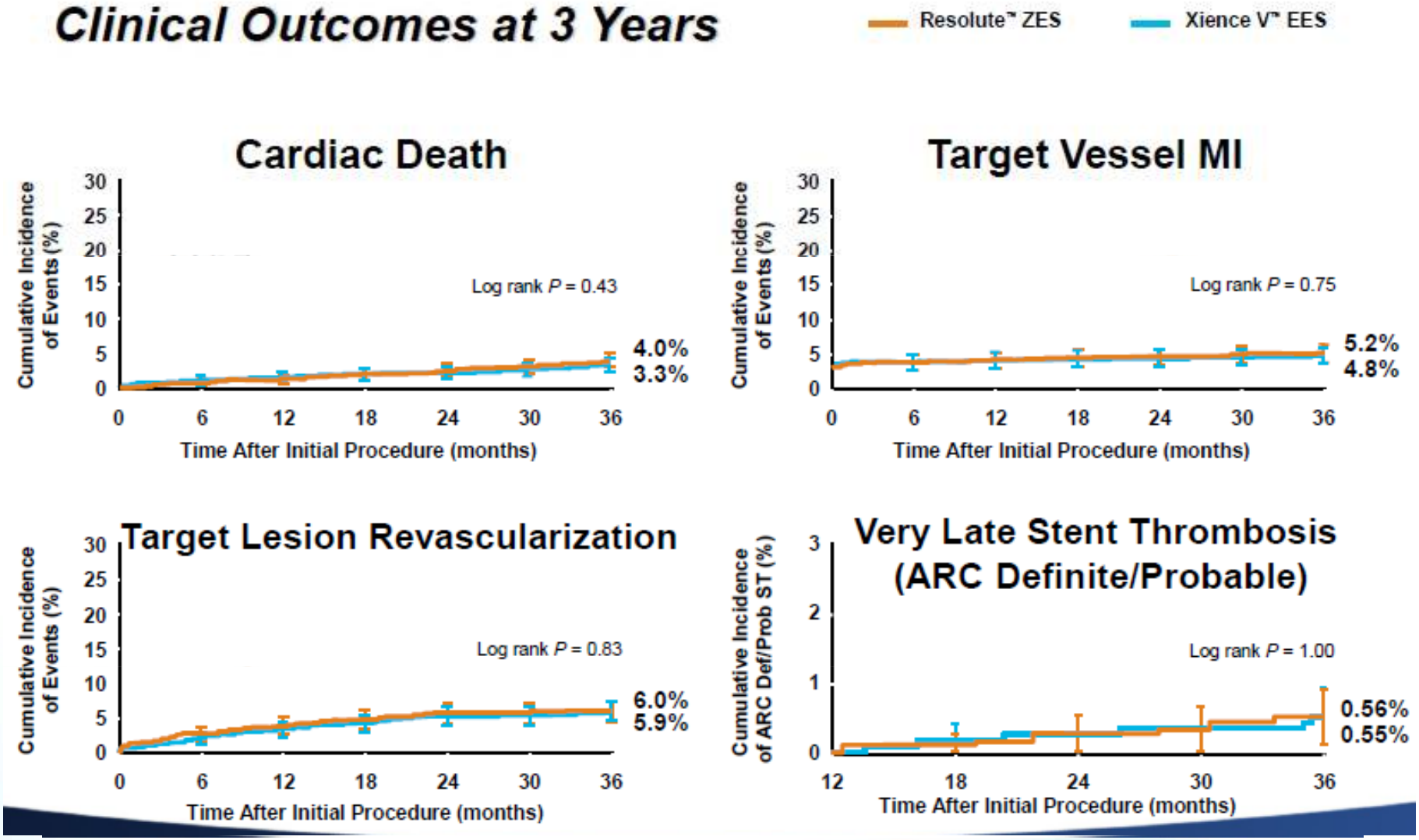
SPIRIT II, III, IV and COMPARE trials- Pooled database analysis (n=6,789)

MAC Stent thrombosis (ARC definite/probable)

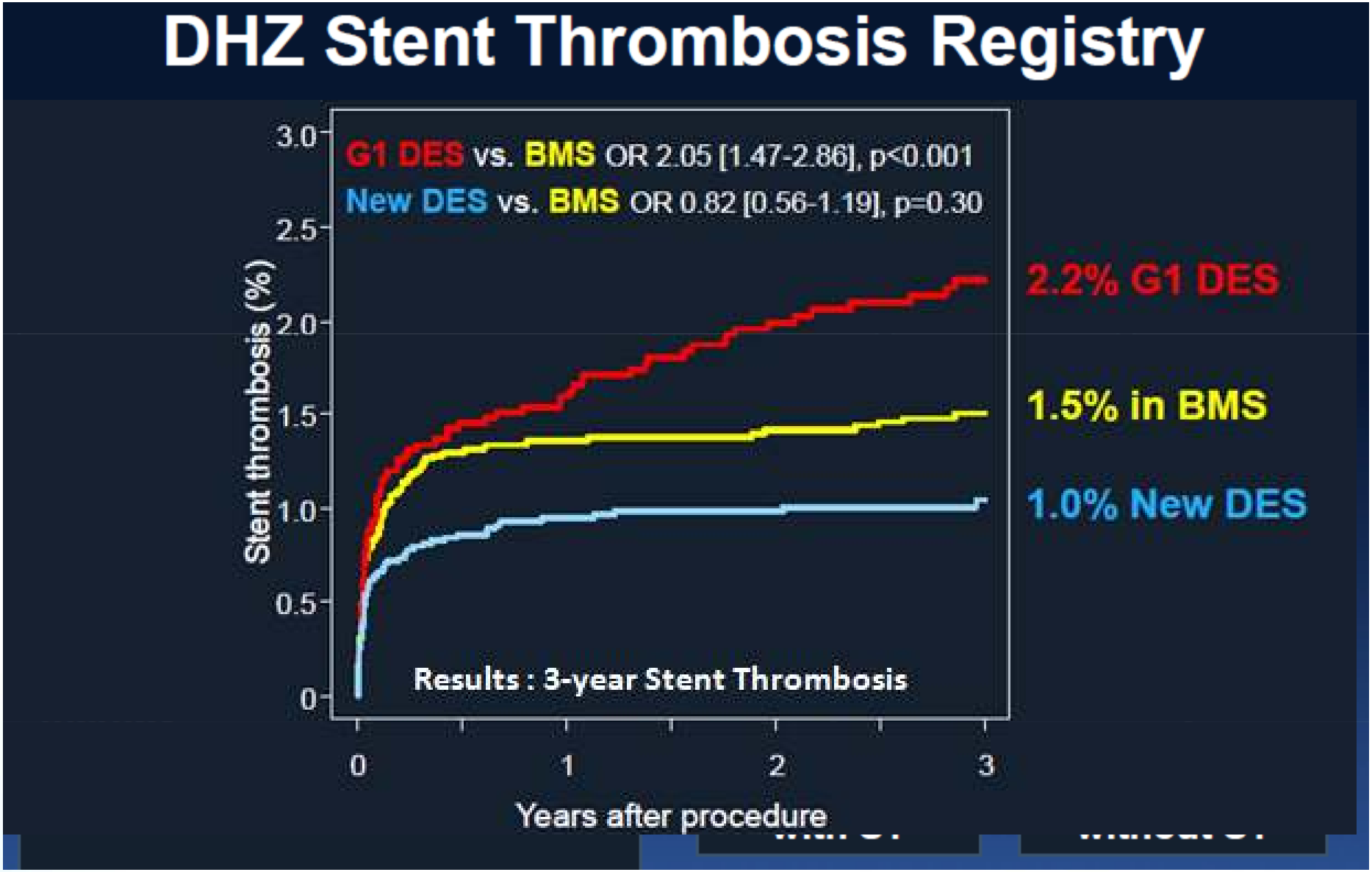


RESOLUTE All Comers

Clinical Outcomes at 3 Years



DHZ Stent Thrombosis Registry

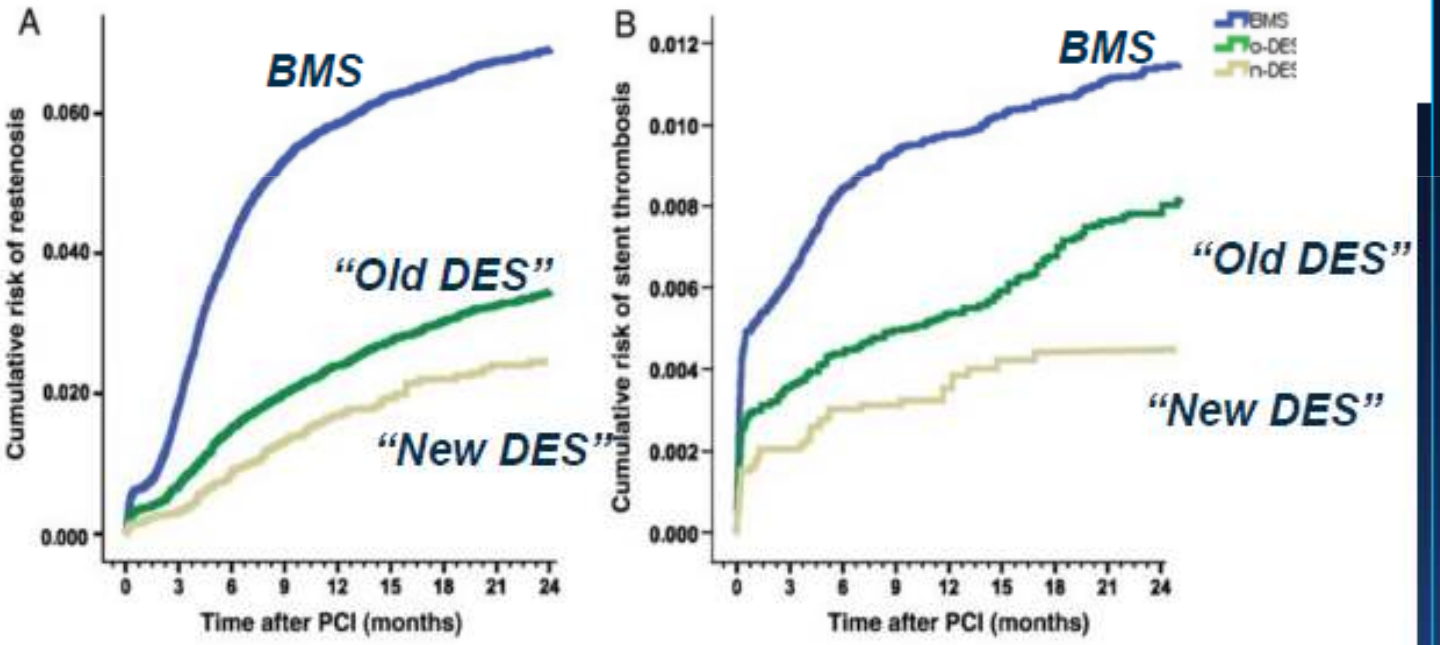


Tada et al. *J Am Coll Cardiol Interv Dec 2013 in press*

SCAAR Registry (94,384 pts)

Adjusted Risks of Adverse Events at 2 yrs

Restenosis ***Definite Stent Thrombosis***



n at risk	0 months	6 months	12 months	18 months	24 months
BMS	64631	56070	47968	40539	32698
o-DES	19202	17862	16014	13517	10533
n-DES	10551	8092	4188	2005	847

Sarno et al, Eur Heart J 2012

N=1050	1st Gen	2nd Gen	P value
Death	21 (4.51%)	17(3.06%)	0.2923
Cardiac Death	4 (0.86%)	6(1.08%)	0.9708
TVR	38(8.15%)	27(4.86%)	0.0437
MACE	59(12.6%)	44(7.93%)	0.01

In our study, patients treated with percutaneous coronary intervention (PCI) with second-generation drug-eluting stents (DES) had a lower risk of clinically driven TVR and MACE at long-term follow-up, compared with those treated with first-generation DES.

Second Generation DES

Newer generation DES combine improved efficacy with improved safety profile and constitute a new standard of care in patients undergoing percutaneous coronary intervention

Current Generation DES

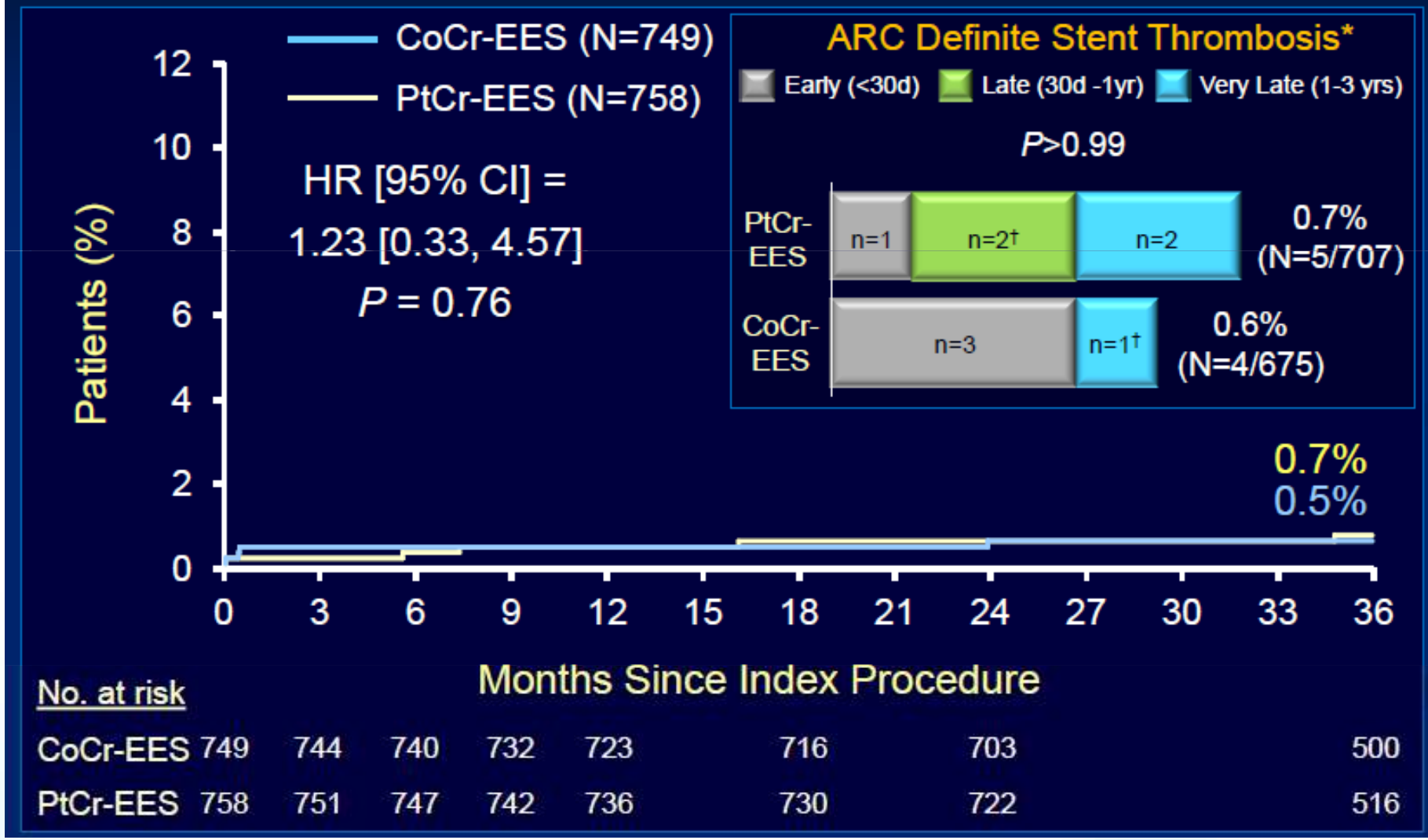
	 RESOLUTE INTEGRITY	 PROMUS ELEMENT
Polymer component	BioLinx®, a blend of hydrophobic C10 polymer, hydrophilic C19 polymer & poly-vinyl pyrrolidone	Fluoropolymer coating
Thickness of coating layer	5.6 µm	7 µm
Antiproliferative drug	Zotarolimus	Everolimus
Drug release period	180 days	120 days
Material of metal stent platform	Cobalt-chromium	Platinum-chromium
Strut thickness of metal stent platform	91 µm	81 µm
Stent manufacturer	Medtronic	Boston Scientific

DES vs. DES Comparisons

Stent Thrombosis - ARC Def/Prob

3-Year Follow-up

PROMUS PLATINUM

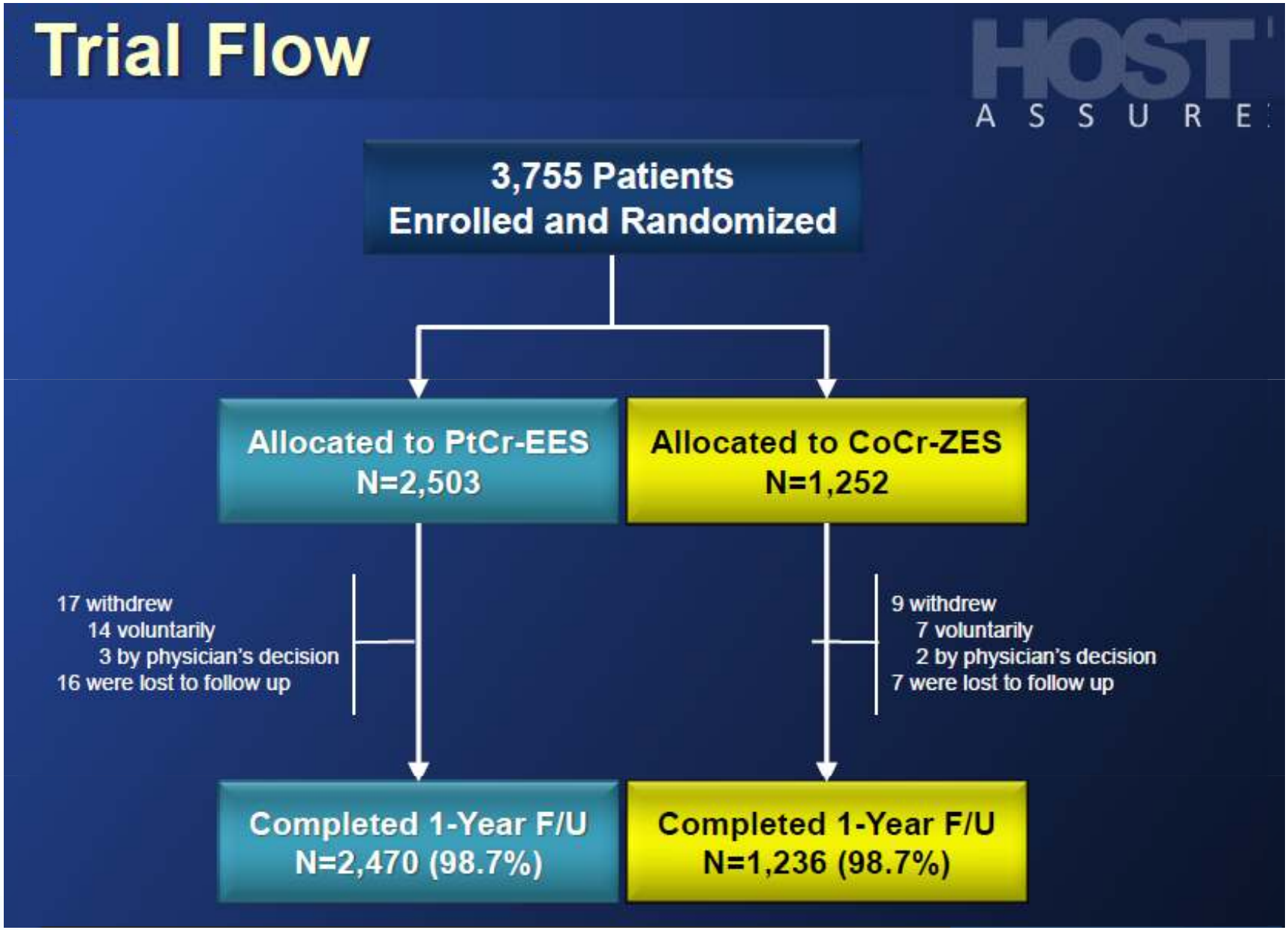


No. at risk

CoCr-EES	749	744	740	732	723	716	703	500
PtCr-EES	758	751	747	742	736	730	722	516

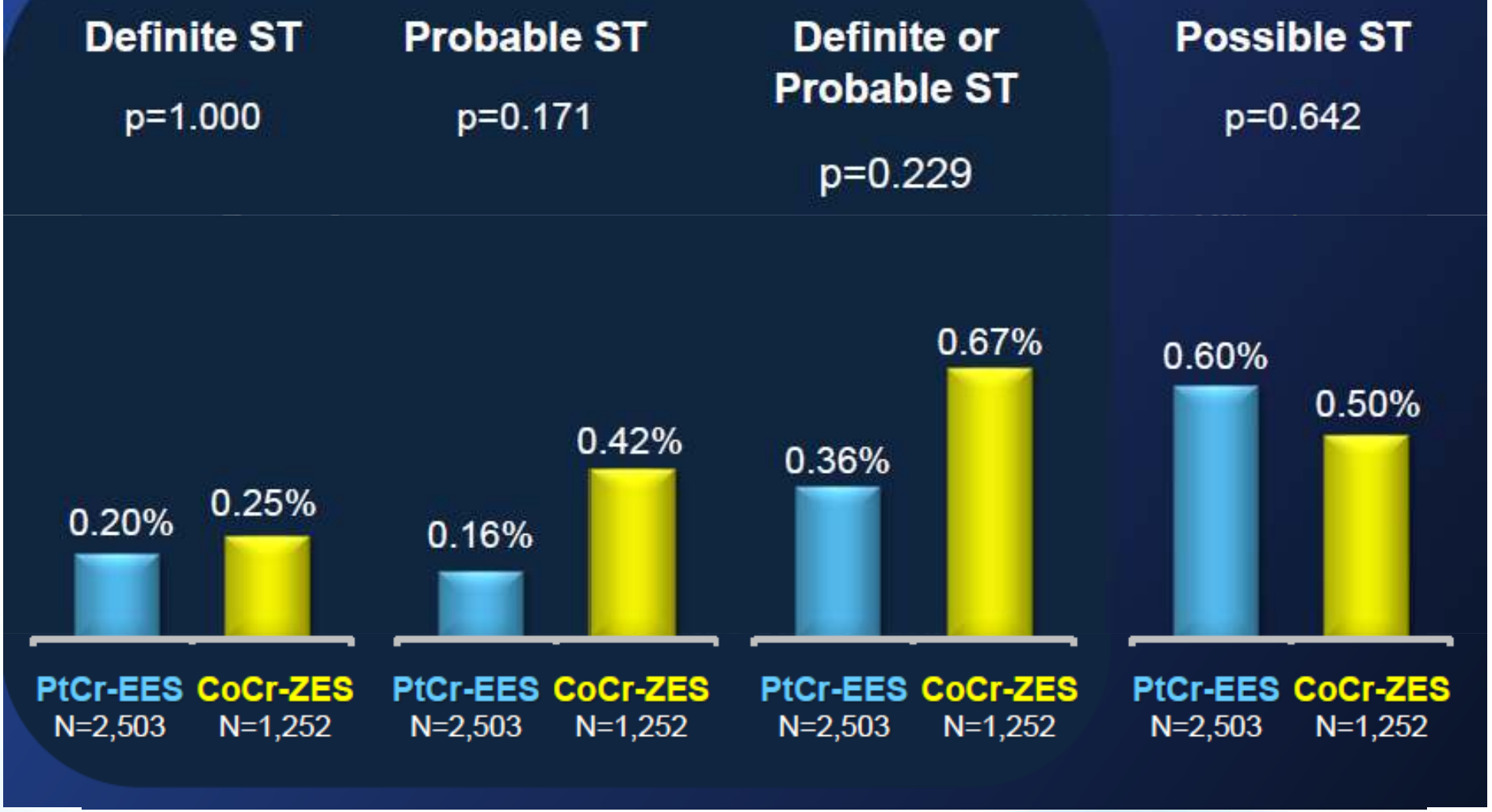
Stone GW et al. JACC 2013 (abstract)

Trial Flow

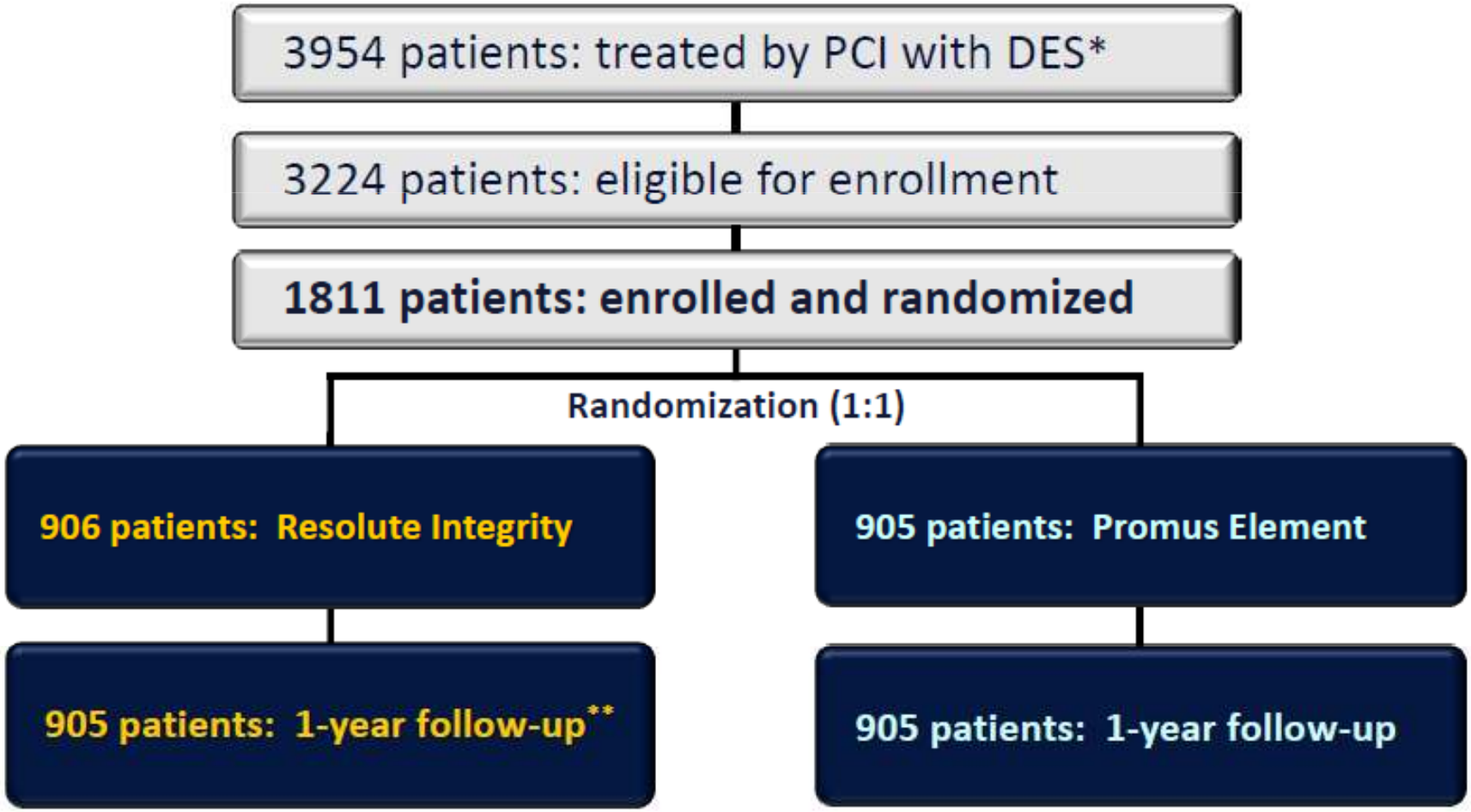

HOST ASSURE
3,755 Patients
Enrolled and Randomized
Allocated to PtCr-EES
N=2,503
Allocated to CoCr-ZES
N=1,252
17 withdrew
14 voluntarily
3 by physician's decision
16 were lost to follow up
9 withdrew
7 voluntarily
2 by physician's decision
7 were lost to follow up
Completed 1-Year F/U
N=2,470 (98.7%)
Completed 1-Year F/U
N=1,236 (98.7%)

Stent Thrombosis

HOST ASSURE

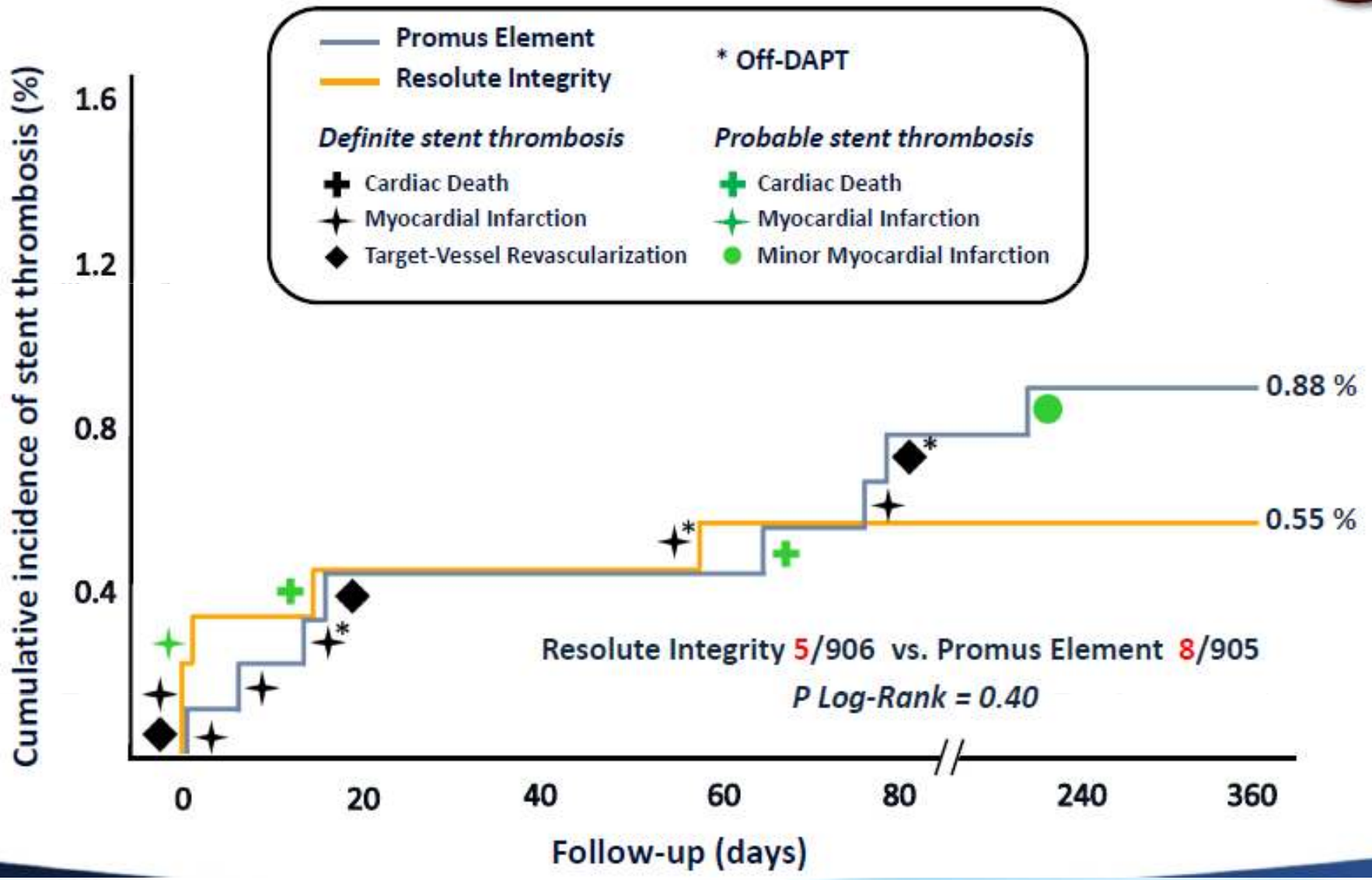


Study Flow Diagram



- 56% of eligible patients enrolled
- Follow-up data obtained in 99.9% of patients

Stent Thrombosis at 1-Year



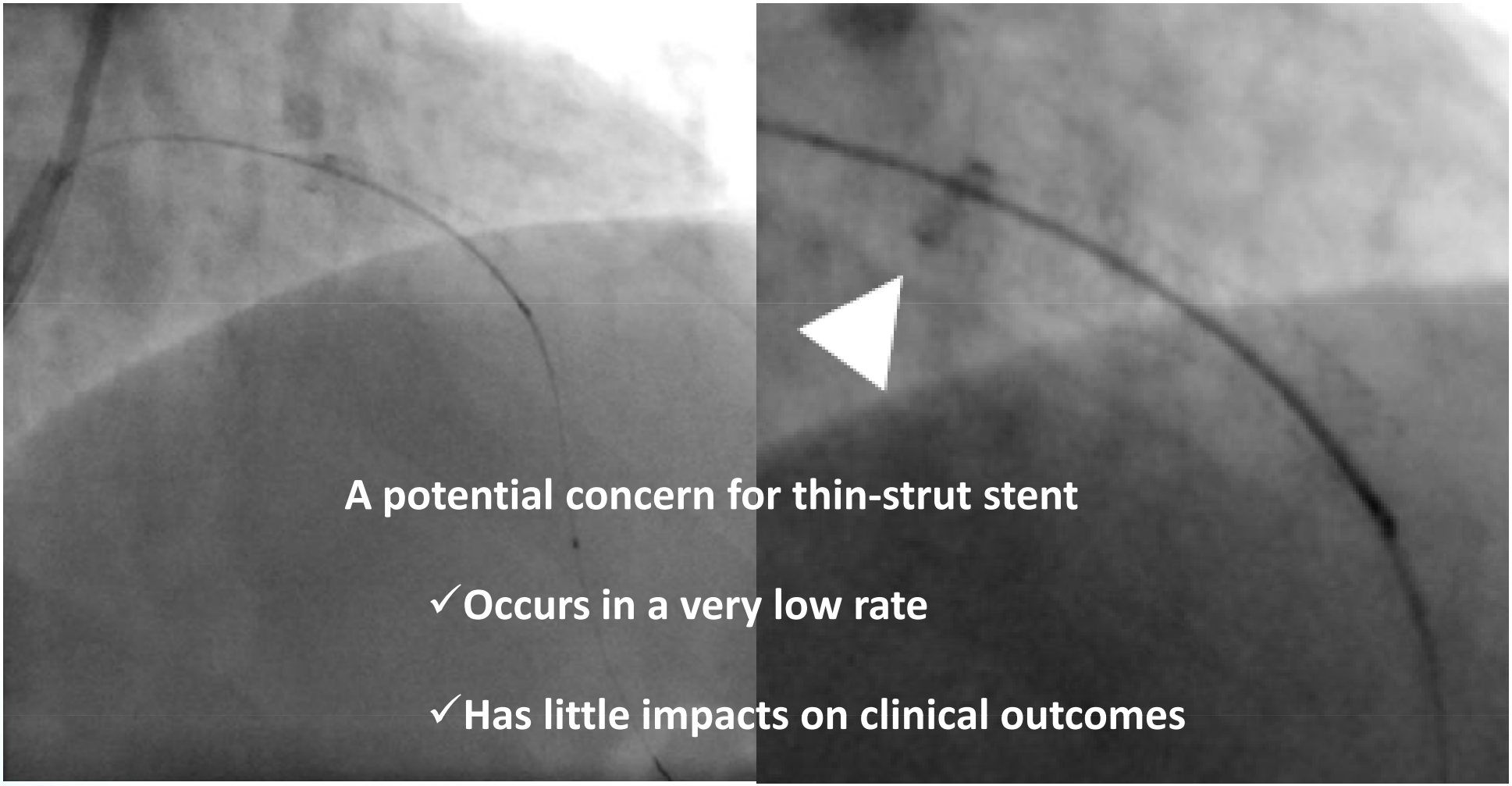
Clinical Outcomes At Mid Term FU (9.3± 3.2months) N=234	
All -cause death, MI, TVR	10 (4.3%)
All -cause death	7 (3%)
cardiac	4 (1.7%)
Related to the TV	3 (1.3%)
Not related to the TV	1 (0.4%)
non-cardiac	3 (1.3%)
Myocardial infarction	0 (0%)
Target vessel revascularization (TVR)	3 (1.3%)
Target lesion revascularization (TLR)	2 (0.9%)
TLR, PCI	1 (0.4%)
TLR, CABG	1 (0.4%)
Non-TLR TVR, overall	1 (0.4%)
Stent thrombosis (ARC def/prob)	1 (0.4%)
Target lesion failure	6 (2.6%)

Current DES generation - Are Patient Outcomes Improving ?

Advanced stent platforms with excellent deliverability, less arterial injury and improved biocompatibility resulted in excellent clinical outcomes

- **The risk of repeat revascularization is further reduced**
- **The risk of ST is exceedingly low**
- **Stenting of ischemic lesions improves outcomes**

Longitudinal deformation, a trade-off of thin strut?



A potential concern for thin-strut stent

- ✓Occurs in a very low rate
- ✓Has little impacts on clinical outcomes

Longitudinal Stent Deformation

- Angiograms of all patients were reviewed for stent deformation (LSD).
- LSD was defined as distortion or shortening of an implanted stent in the longitudinal axis following successful initial deployment.
- LSD was noted on angiograms of 9 patients of the Promus Element group and none of the Resolute Integrity group (9/905 vs. 0/906; p=0.002).
- In the Promus Element group, LSD was seen in 1/100 patients treated (1%) and in 0.6/100 Promus Element stents implanted (0.6%).
- LSD often triggered postdilation and implantation of additional stents, but was not associated with any adverse events.

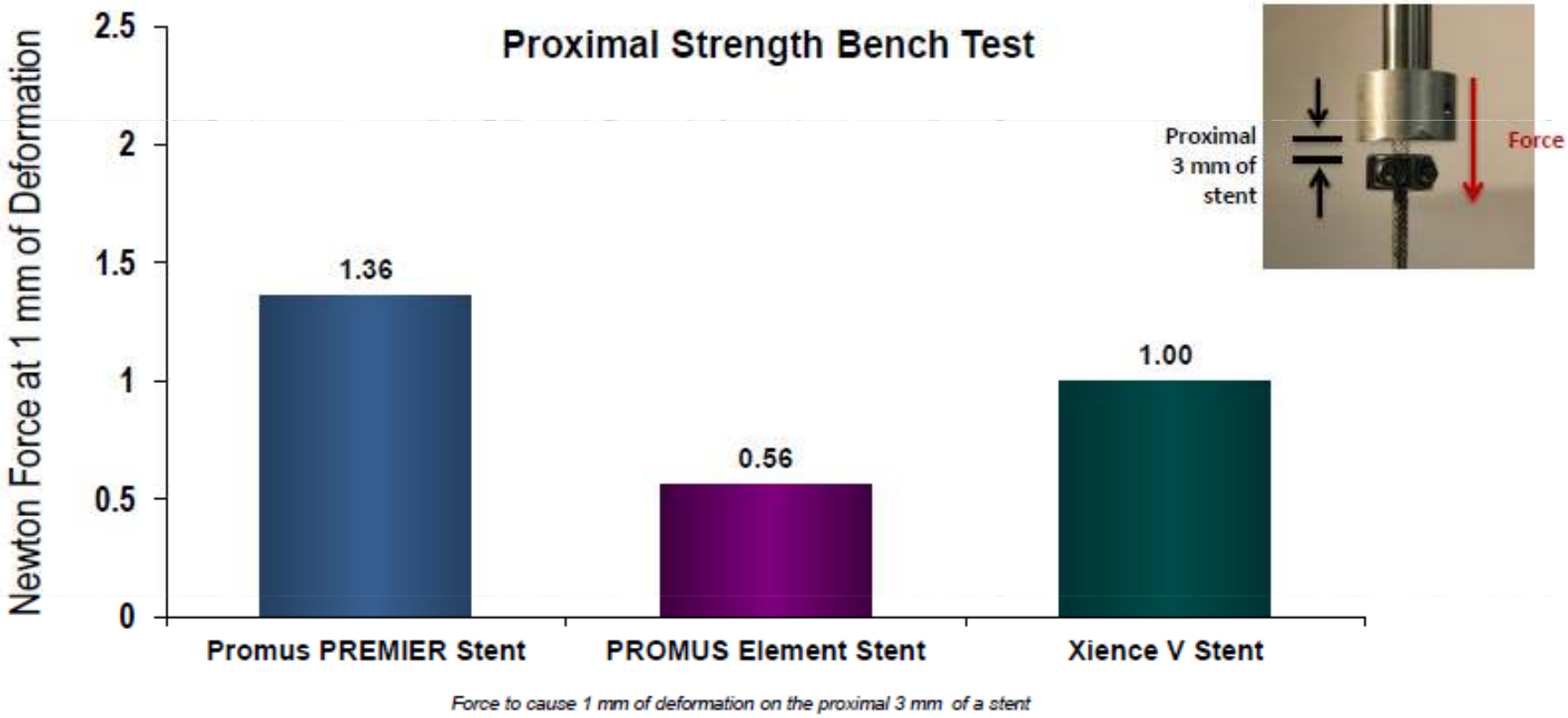
Case	PDSL	Stent type	Diameter	Vessel	Lesion	Characteristics	Post-dilation	Additional prox. stent	Association with clinical event
Following attempts to re-cross stent									
1	0.94	Pr. Element	3.0 mm	LAD	C	bifurcation	+	+	none
2	0.83	Pr. Element	2.5 mm	RCA	C	severe calcification	+	+	none
3	0.74	Pr. Element	3.5 mm	LAD	C	bifurcation	+	+	none
4	0.79	Pr. Element	2.25 mm	LAD	C	bifurcation	–	+	none
Following very oversized postdilatation									
5	0.94	Pr. Element	2.25 mm	LAD	C	severe calcification	+	+	none
6	0.87	Pr. Element	3.5 mm	Left main	B2	bifurcation	+	–	none
Following contact with guiding or balloon catheter									
7	0.81	Pr. Element	2.5 mm	RCA	C	bifurcation	+	+	none
8	0.91	Pr. Element	3.0 mm	LAD	C	moderate calcification	+	+	none
9	0.84	Pr. Element	3.0 mm	RCA	C	severe calcification	+	–	none

Results

- The rate of stent deformation varied from 0% in several stent types to 0.55% in the case of the Promus Element stent.

Concentric Compression Test
Difference in Promus Premier stent

Promus PREMIER Stent is 2.4x stronger than the PROMUS Element™ Stent and 1.4x stronger than the Xience V™ Stent following deformation



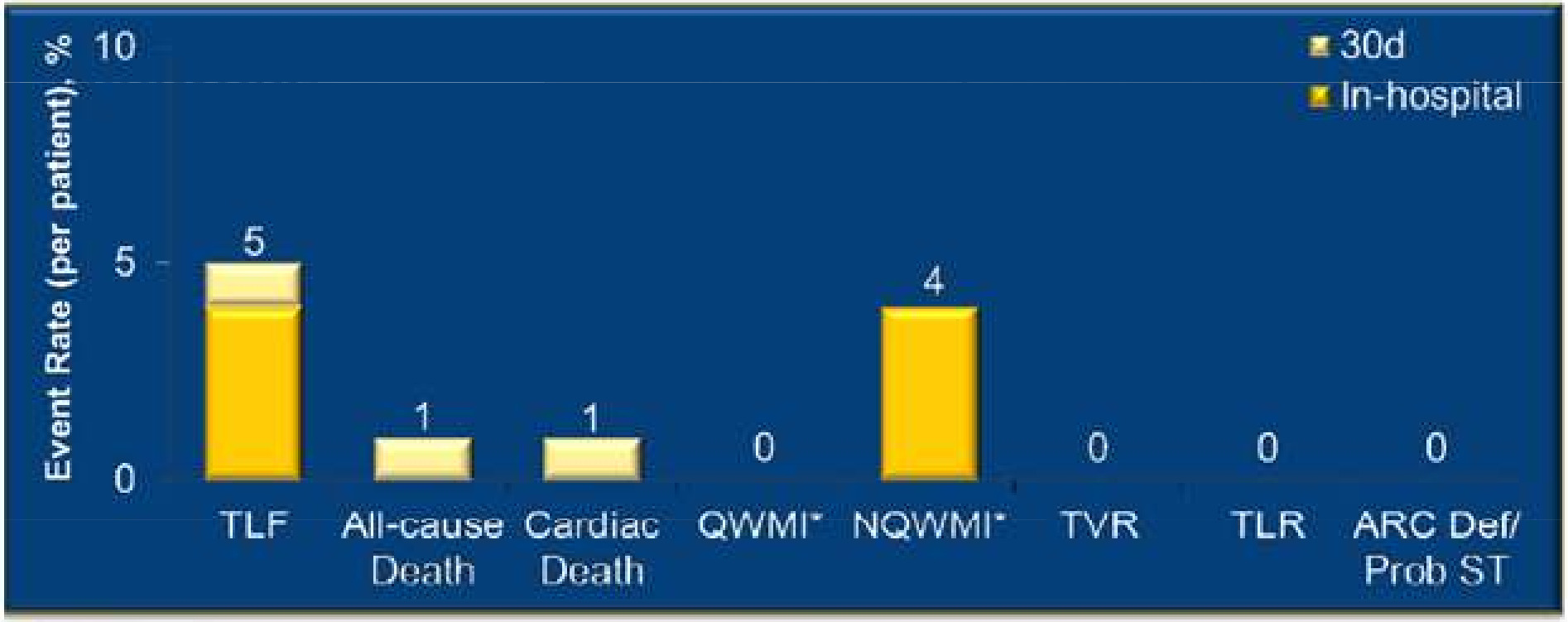
Force to cause 1 mm of deformation on the proximal 3 mm of a stent

2.5±0.5mm	2.4±0.8mm	1.3±0.1mm	4.1 ± 0.1mm	2.8±0.3mm	2.2 ±0.7mm

NG PROMUS Trial

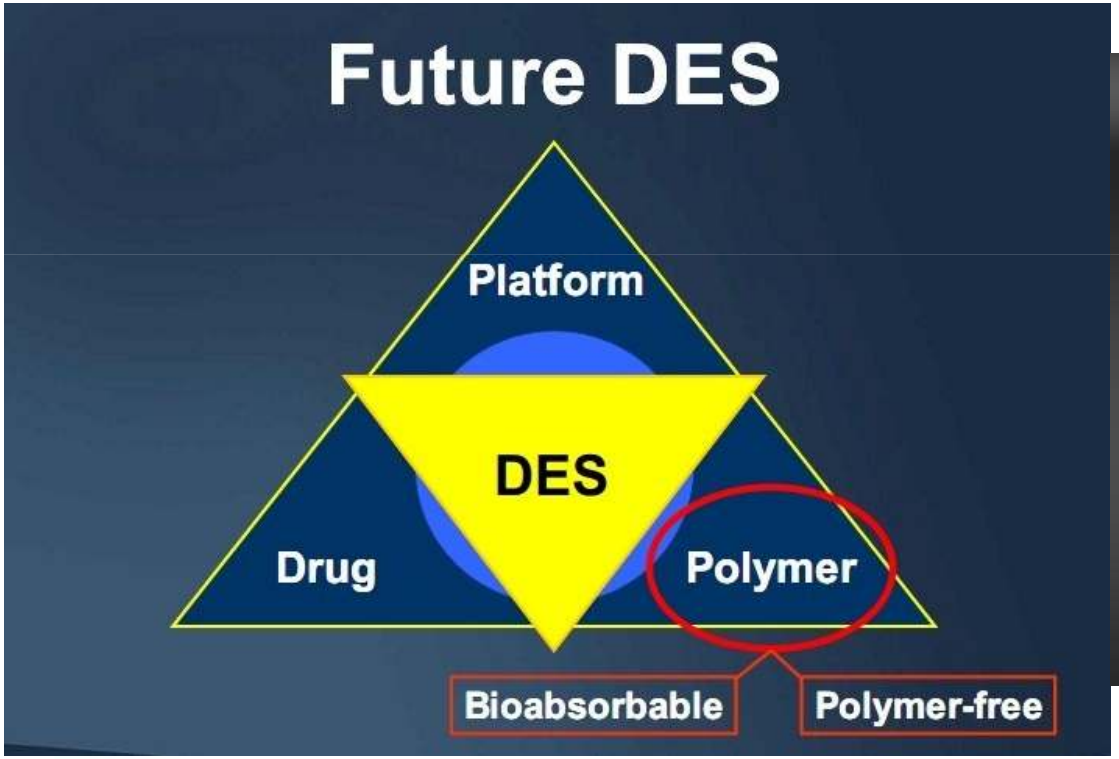
euro PCR 2013

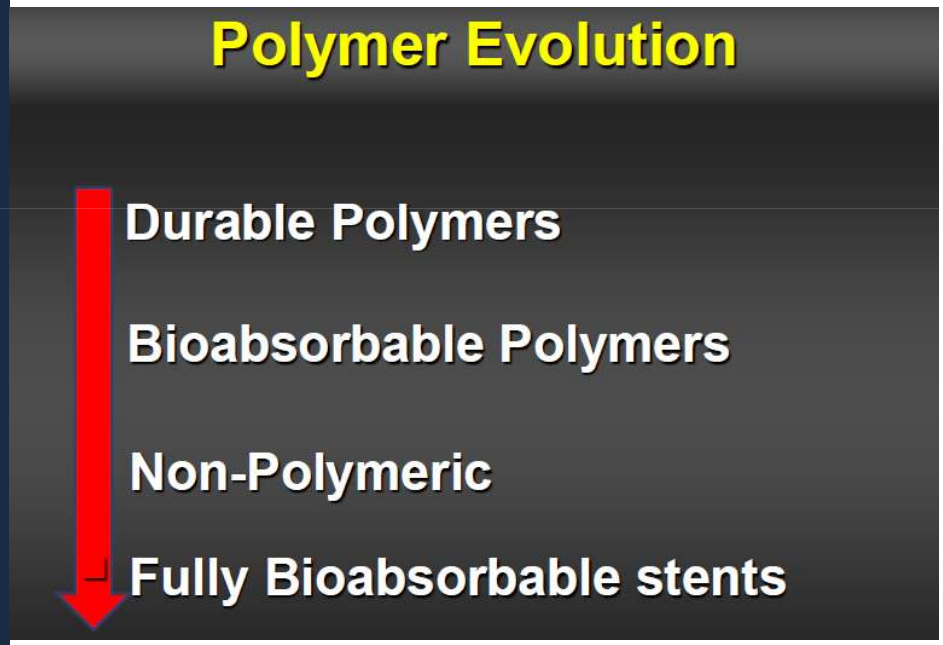
Clinical Outcomes (30 days)



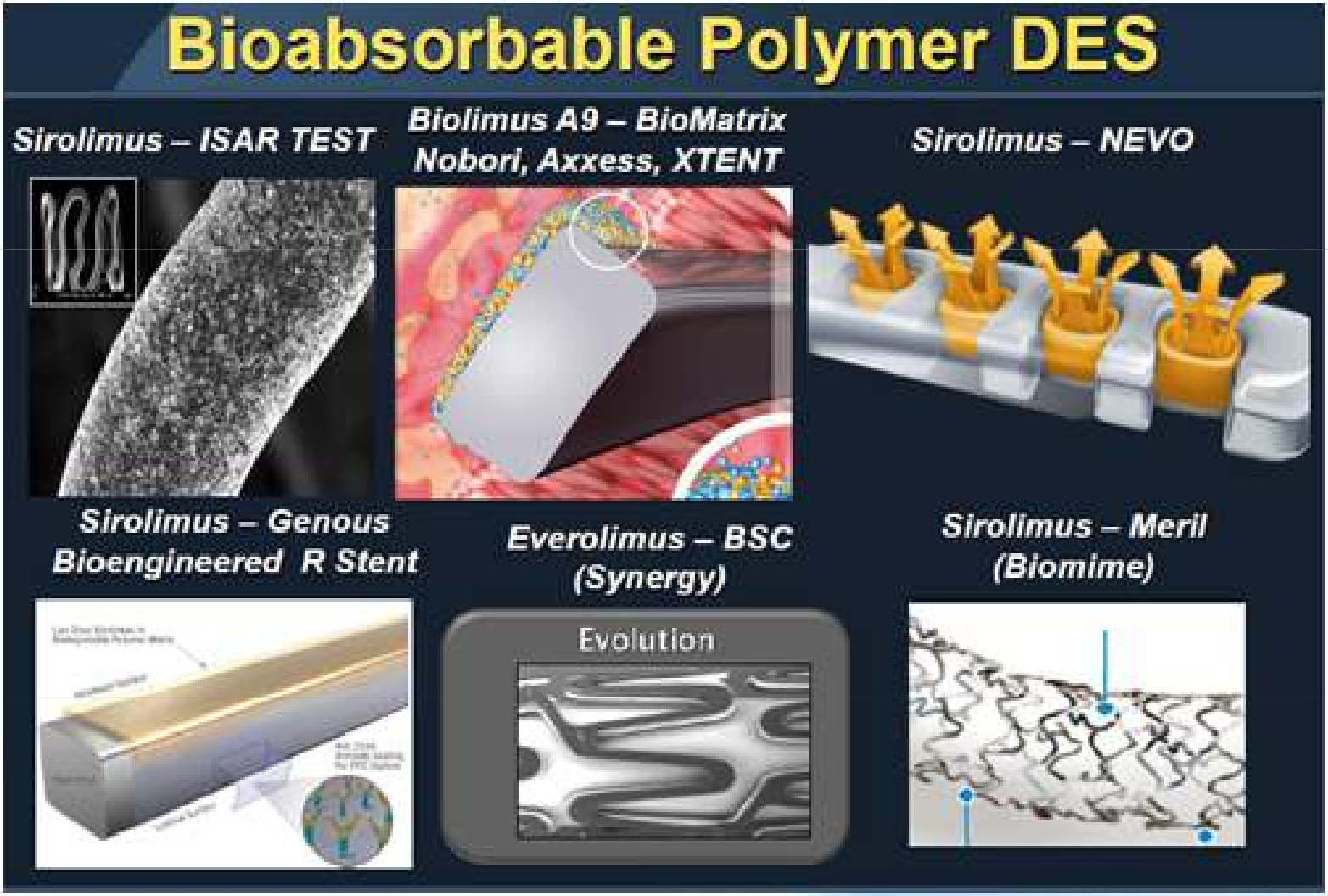

PROBLEM
SOLVED!

An important factor of uncertainty about the efficacy of drug-eluting stents is the use of polymers.



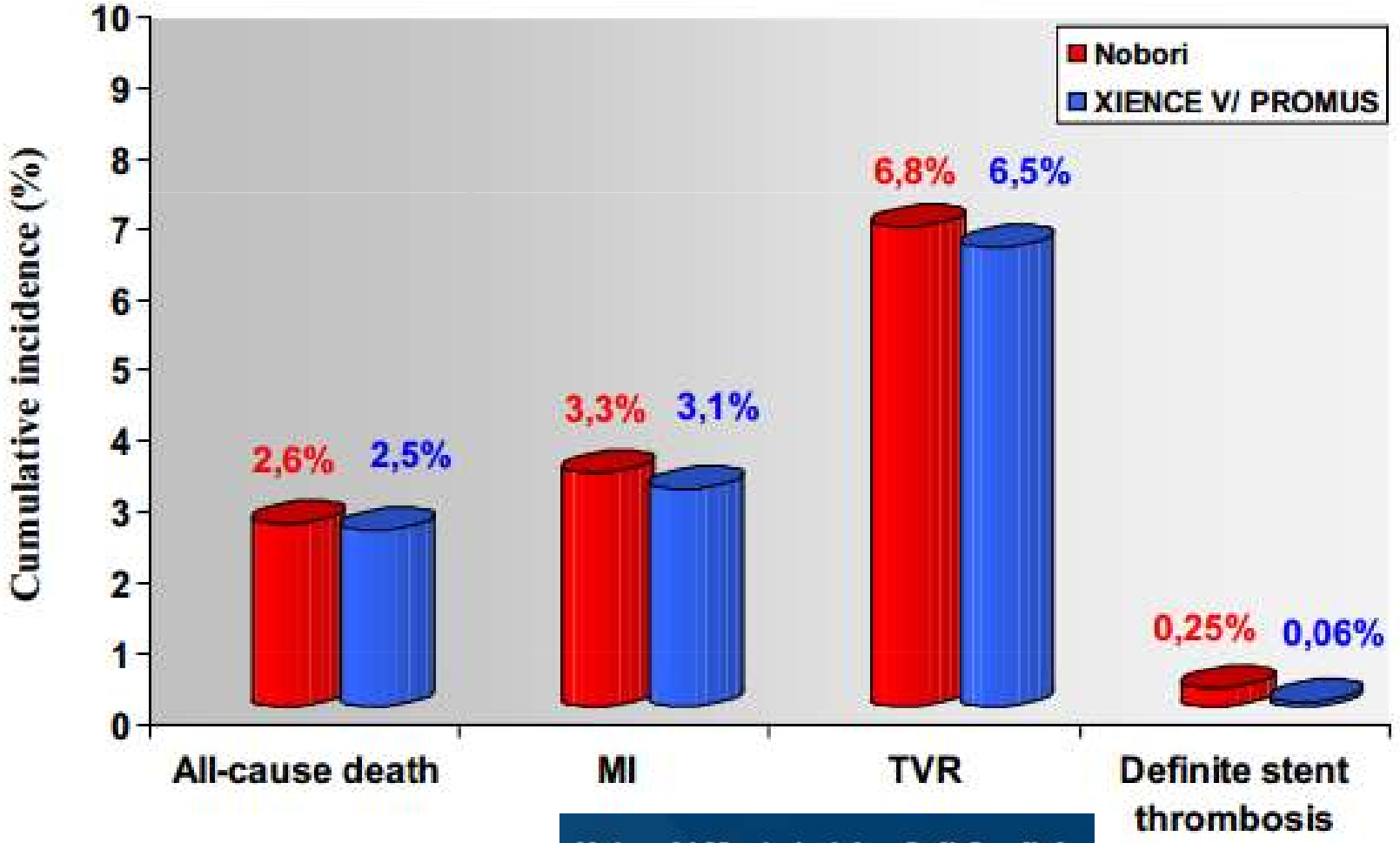


Are biodegradable polymer DES safer and\or perform better than durable polymer DES on the short and long-term run?



NEXT Trial

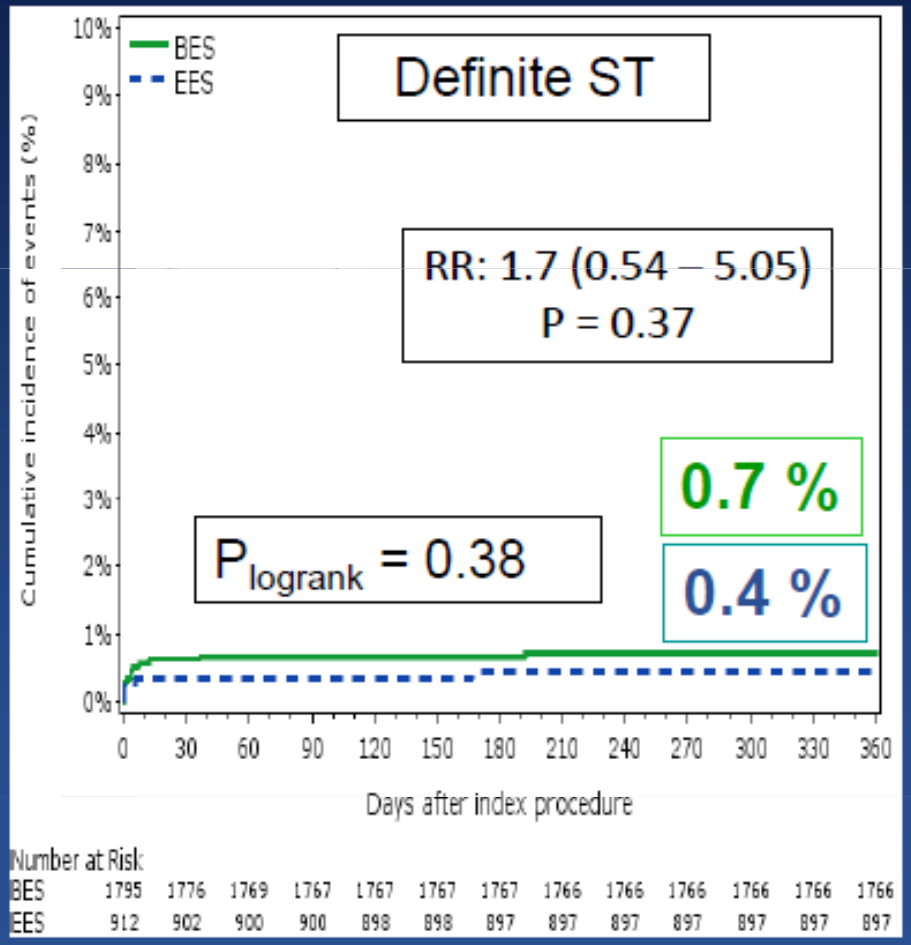
Primary Safety Endpoint: All-cause death, MI, TVR, Definite Stent Thrombosis at 1 Year

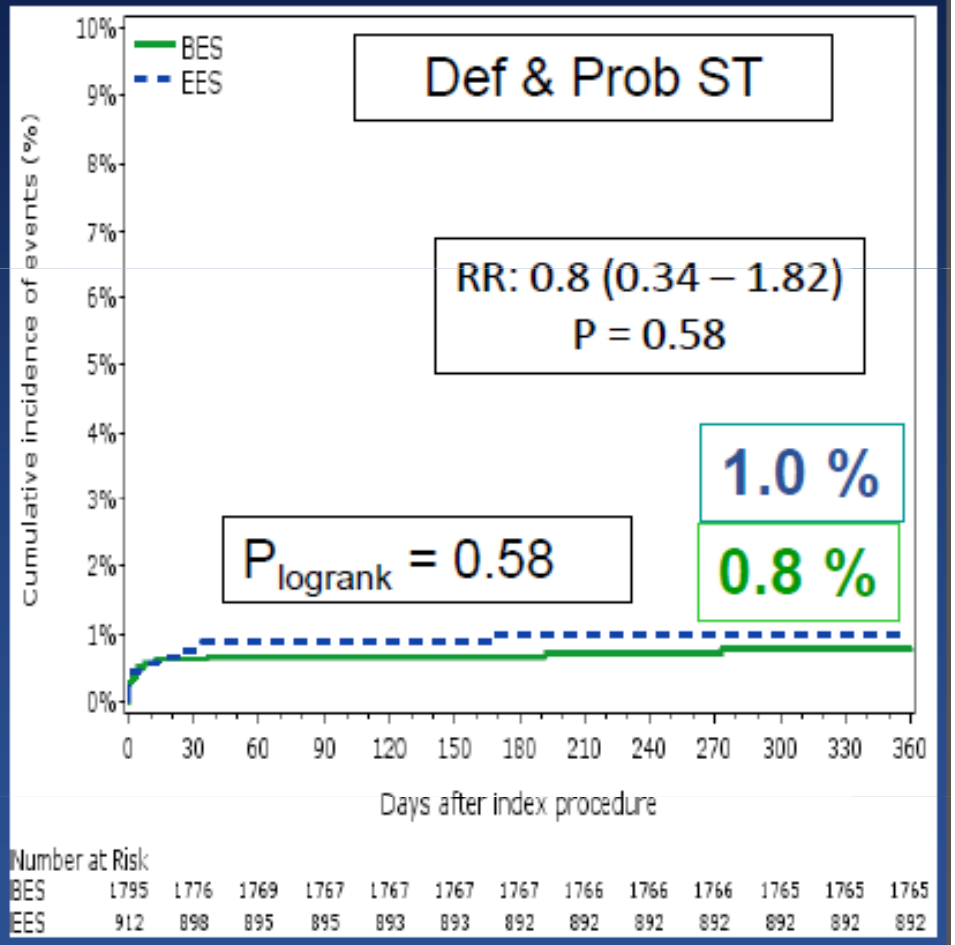


Natsuaki M, et al. *J Am Coll Cardiol.* 2013;Epub ahead of print.

COMPARE II trial

Stent Thrombosis (ARC)





Death/MI/TVR
2-year Follow-up

EVOLVE

PE vs SYNERGY HR 0.84 [0.33, 2.14] *P*=0.72
PE vs SYNERGY ½ HR 1.03 [0.43, 2.48] *P*=0.94

Numbers at risk	0	6	12	24 Months
PE	98	98	89	66
SYNERGY	92	91	87	63
SYNERGY ½ Dose	99	94	88	61

Safety Population; KM Event Rate; log-rank *P* values

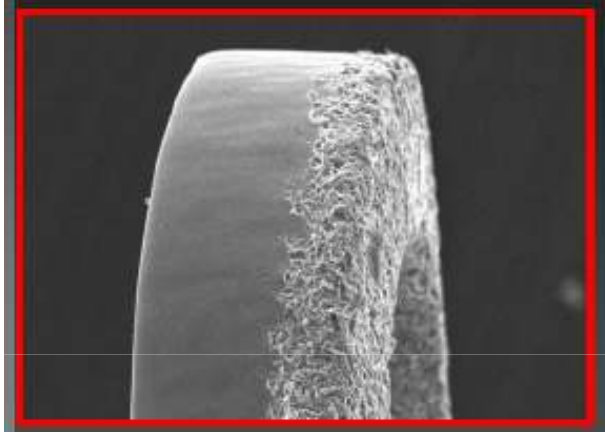
DES with biodegradable polymers have been associated as compared to 1° gen DES with durable polymer with improved efficacy and safety.

✓**Biodegradable polymer BES demonstrated a 74% relative risk reduction in very late definite stent thrombosis (VLST)**

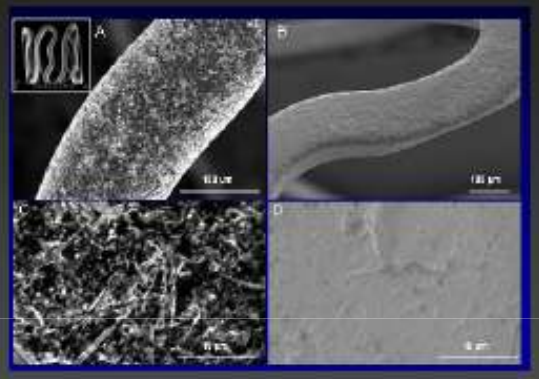
Although the concept behind biodegradable polymer DES is intuitively attractive, the hypothesized advantage of these devices *remains unproven comparing to 2o Gen DES*

✓**Primary and secondary endpoints in this real-life population did not significantly differ when comparing both stent groups, with similarly low cardiac death and stent thrombosis rates.**

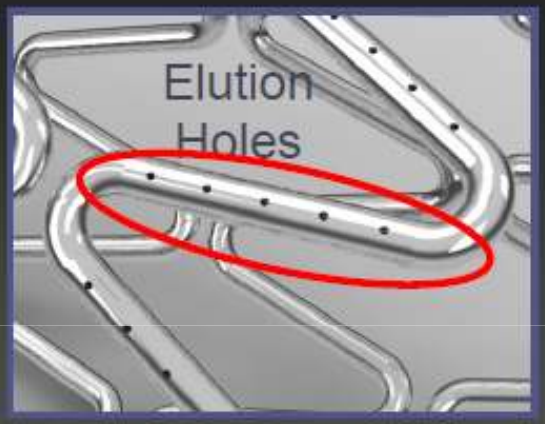
Polymer-Free Platforms



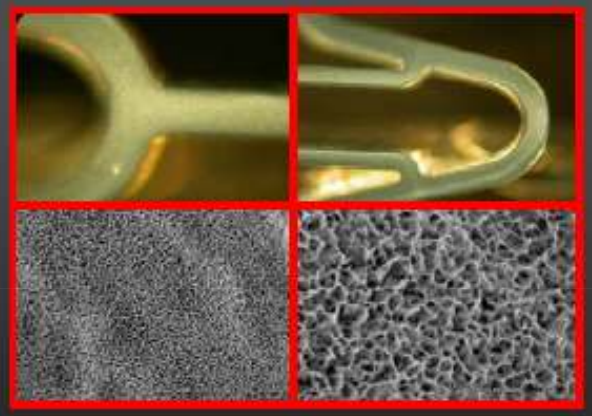
BioFreedom



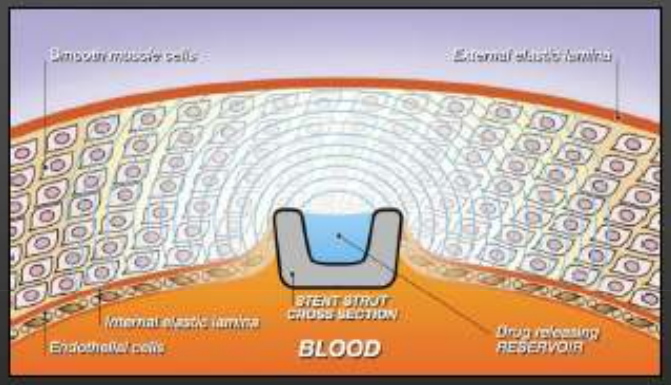
Translumina



Drug Filled Stent Concept



Hydroxyhepatite coating



Reservoir technology with Carbofilm

MeriT – I

primary safety and efficacy of biomime

MeriT – I is a prospective, single center primary safety and efficacy trial for BioMime™ Sirolimus Eluting Coronary Stent System.

- **Design:** Phase IV, prospective, single arm, single centre study. N = 30
- **Inclusion Criteria:** Single, Discrete, De novo lesions, Mean Vessel Lumen Diameter 2.5, 3.0 and 3.5mm. Stent lengths 19 to 24mm
- **Exclusion Criteria:** CTO's, Bifurcations, SVG's, AMI's, LM disease, LVEF <30 %

- **Late Loss (mm)**
  - In-segment 0.18 [0.06, 0.35]
  - In-stent 0.15 [0.09, 0.33]
- **Binary Restenosis** 0%

MeriT – II

biomime in real world scenario

MeriT – II is a prospective, multi-centric, non-randomized, all-comers study to asses safety and efficacy of BioMime™ Sirolimus Eluting Coronary Stent System.

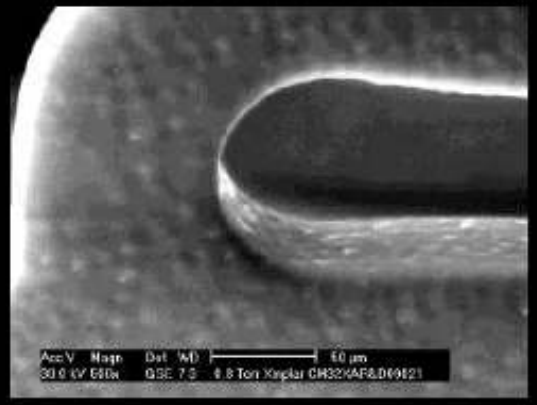
- Design : Prospective, Non-Randomized, Multi- Centre, Complex, Real world study involving 250 patients

- **Binary Restenosis**
  - In-segment 6 / 132 (4.6%)
  - In-stent 1/ 132 (0.8%)

Nanotech

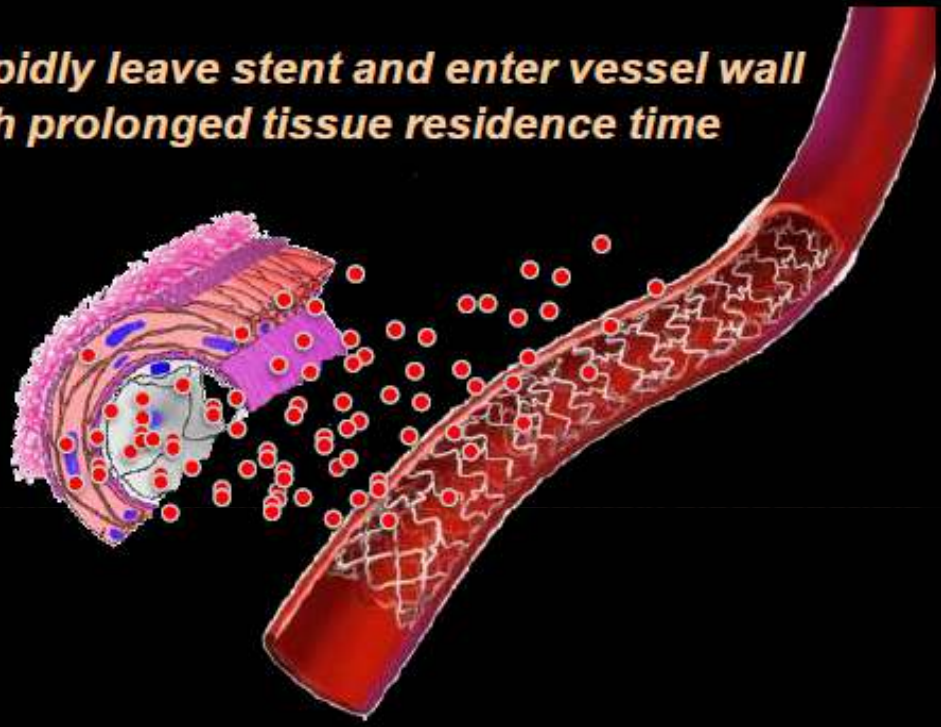
The Polymer-Free Formulation

Unique Formulation - Solid lipid nano-spheres (SLN) consisting of Merilimus + lipid (<300 nm)

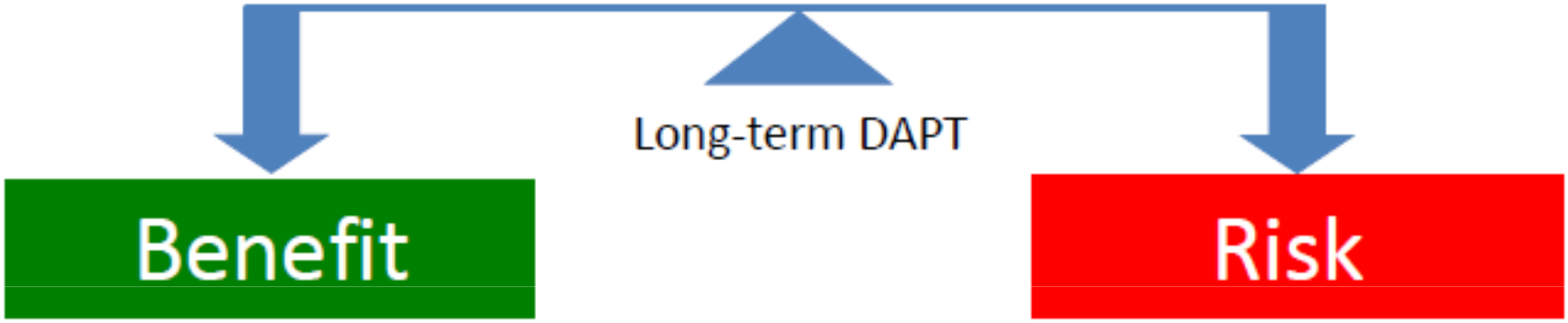


SEM picture of struts coated with nano-formulation

SLN rapidly leave stent and enter vessel wall with prolonged tissue residence time



THE OPTIMAL DURATION OF DAPT

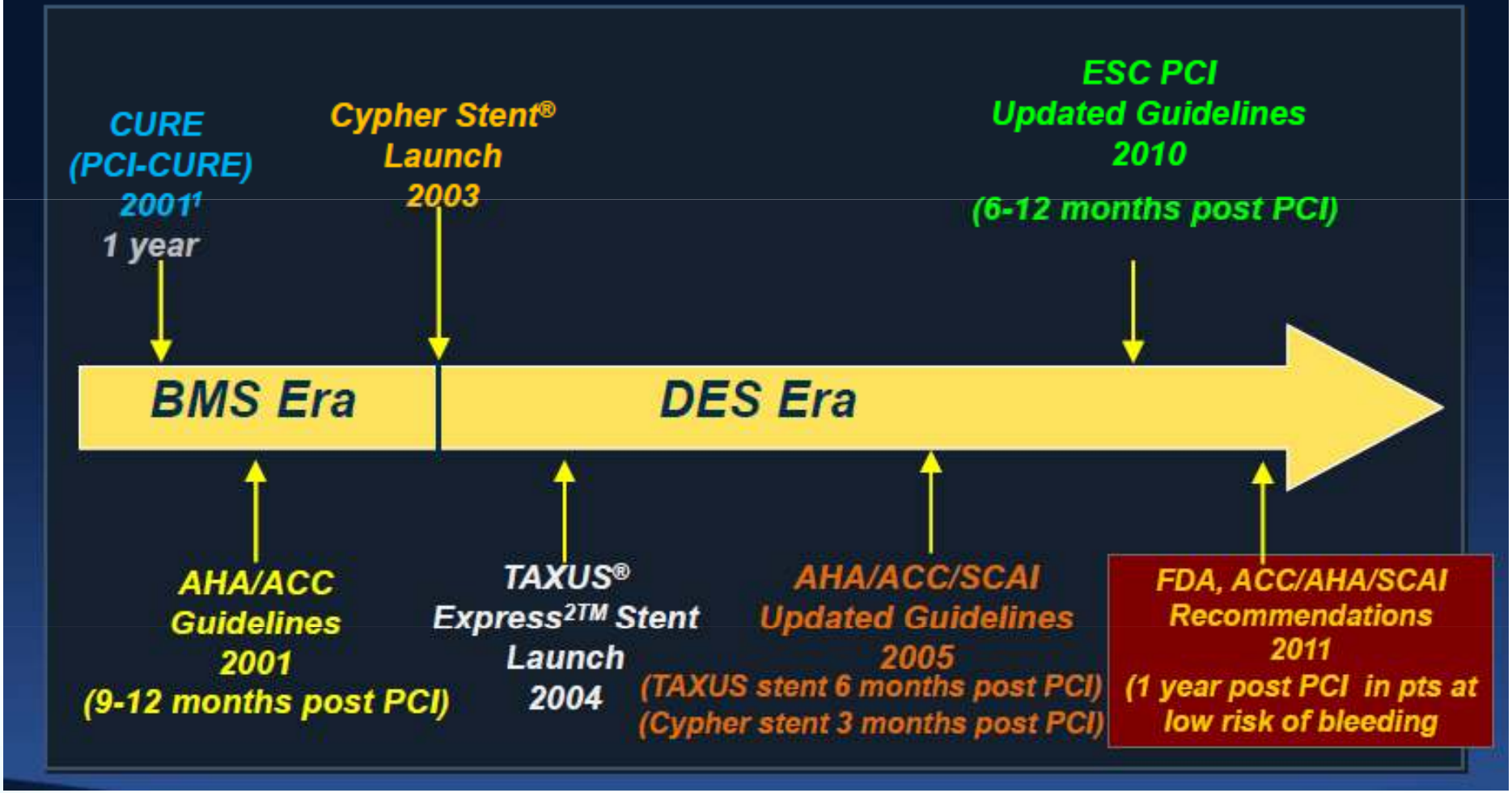


- Prevention of late stent thrombosis
- Secondary preventive effect

- Increased bleeding risk
- Excess cost
- Delayed procedures impacting QOL

Insufficient evidence to adjudicate optimal duration of dual antiplatelet therapy

Optimal Duration of Anti-platelet Therapy Post DES Still Unclear



2010 ESC/EACTS Revascularisation Guidelines

Duration of $P2Y_{12}$ Inhibitor Treatment Post-PCI

Dual Antiplatelet Therapy Post-PCI

- 1 month after BMS implantation in stable angina
- 6–12 months after DES in all patients
- 12 months in all patients after ACS, irrespective of revascularisation

Recent data suggest that DAPT for 6 months may be sufficient because late and very late stent thrombosis correlate poorly with discontinuation of DAPT

ESC, European Society of Cardiology; EACTS, European Association for Cardio-Thoracic Surgery.
Wijns W, et al. *Eur Heart J.* 2010;31:2501–55.

ESC/EACTS Guidelines on Myocardial Revascularisation

The optimal duration of DAPT after DES implantation is not known. Convincing data exist only for continuation up to 6 months.[237] Possibly, under some circumstances or with some DES, DAPT for 3 months could be sufficient but the evidence is not robust.[219] Recent evidence shows that (very) late stent thrombosis results from delayed hypersensitivity to components of the drug–polymer–device combination that causes necrotizing vasculitis and late malapposition.[238] Diabetics may require a longer duration of DAPT.

W Wijns et al. EHJ 2010; 31:2501-55, page 2536

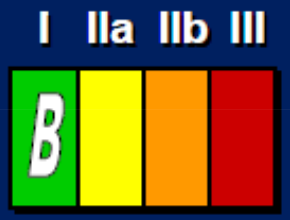
2011 ACC/AHA/SCAI Guideline for PCI

DURATION

The **duration of P2Y12 inhibitor therapy** should generally be as follows:

a. **In patients receiving a stent (BMS or DES) during PCI for ACS, P2Y12 inhibitor therapy should be given for at least 12 months. Options include clopidogrel** 75 mg daily,**prasugrel** 10 mg daily or **ticagrelor** 90mg twice daily

b. In patients receiving **DES for non-ACS indication, clopidogrel should be given for at least 12 months** if patients are not at high risk for bleeding.



c. In patients receiving **BMS for a non-ACS indication, clopidogrel should be given for a minimum of 1 month and ideally up to 12 months** (***unless patient is at increased risk for bleeding;then it should be given for a minimum of 2 weeks***)

Circulation 2011;124:e574-651

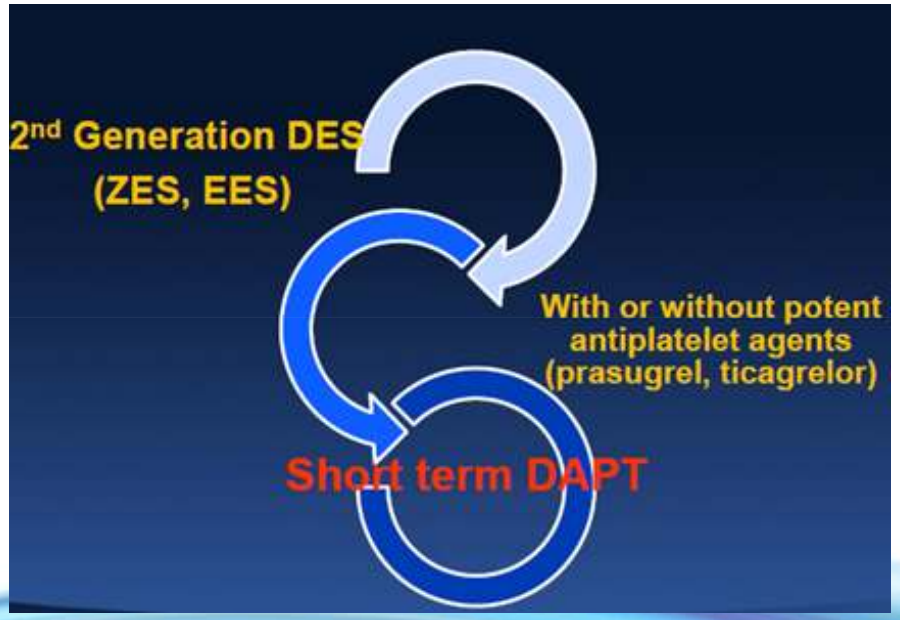
A “magic optimal duration of DAPT” after DES does *not exist because DES-types differ*

(“All DES not created equal”) :

Stent platforms differ with respect to risk for early , late and/or very late stent thrombosis events

Pro-thrombotic risk is determined by DES-type and thus DAPT-duration has to be adapted according to both DES potency profile and DES healings characteristics

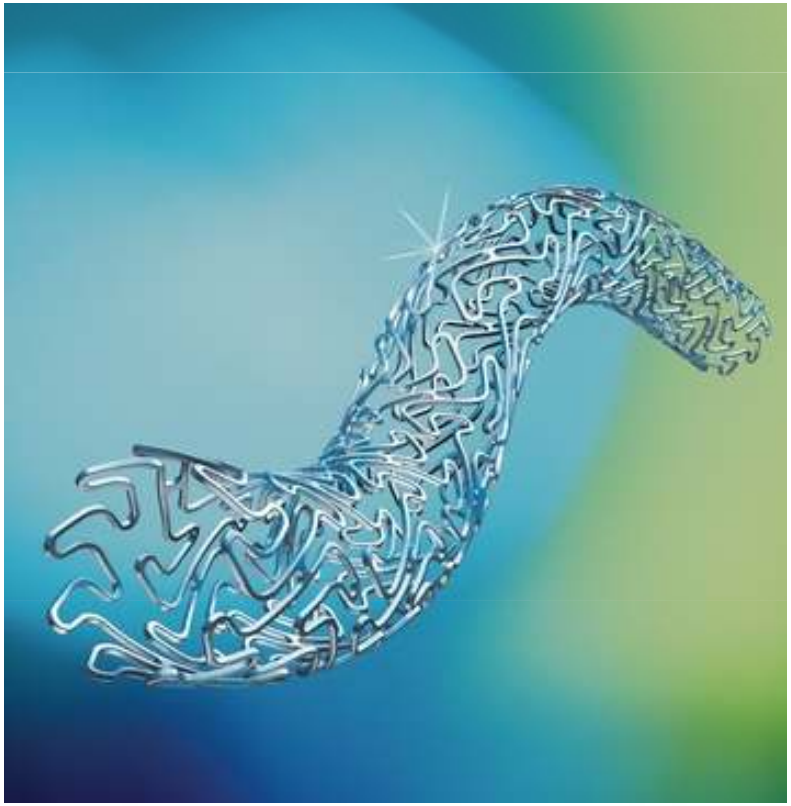
As safety improves with DES, duration of DAPT comes into question and needs further study



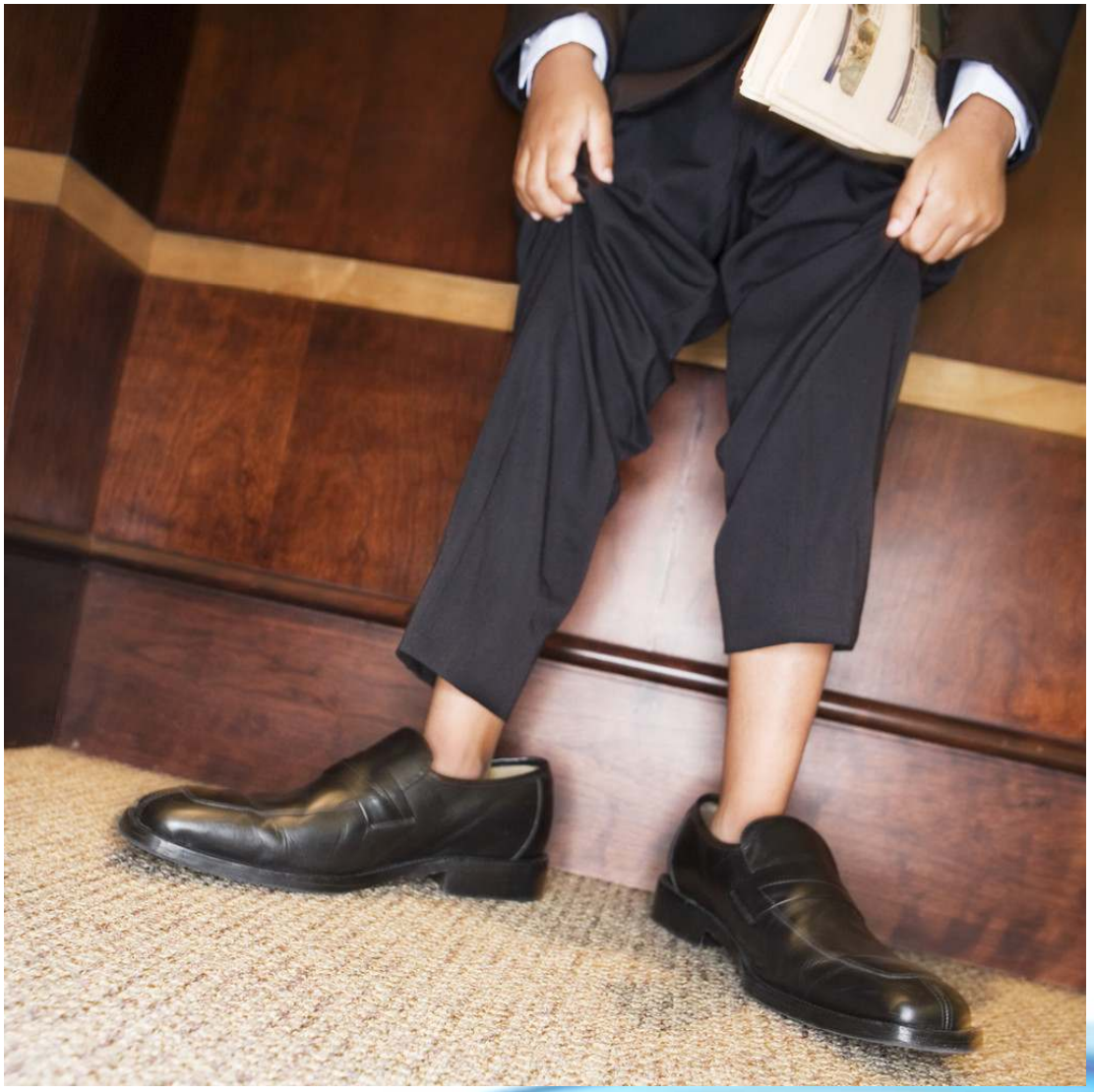
What are we treating?

The patient?

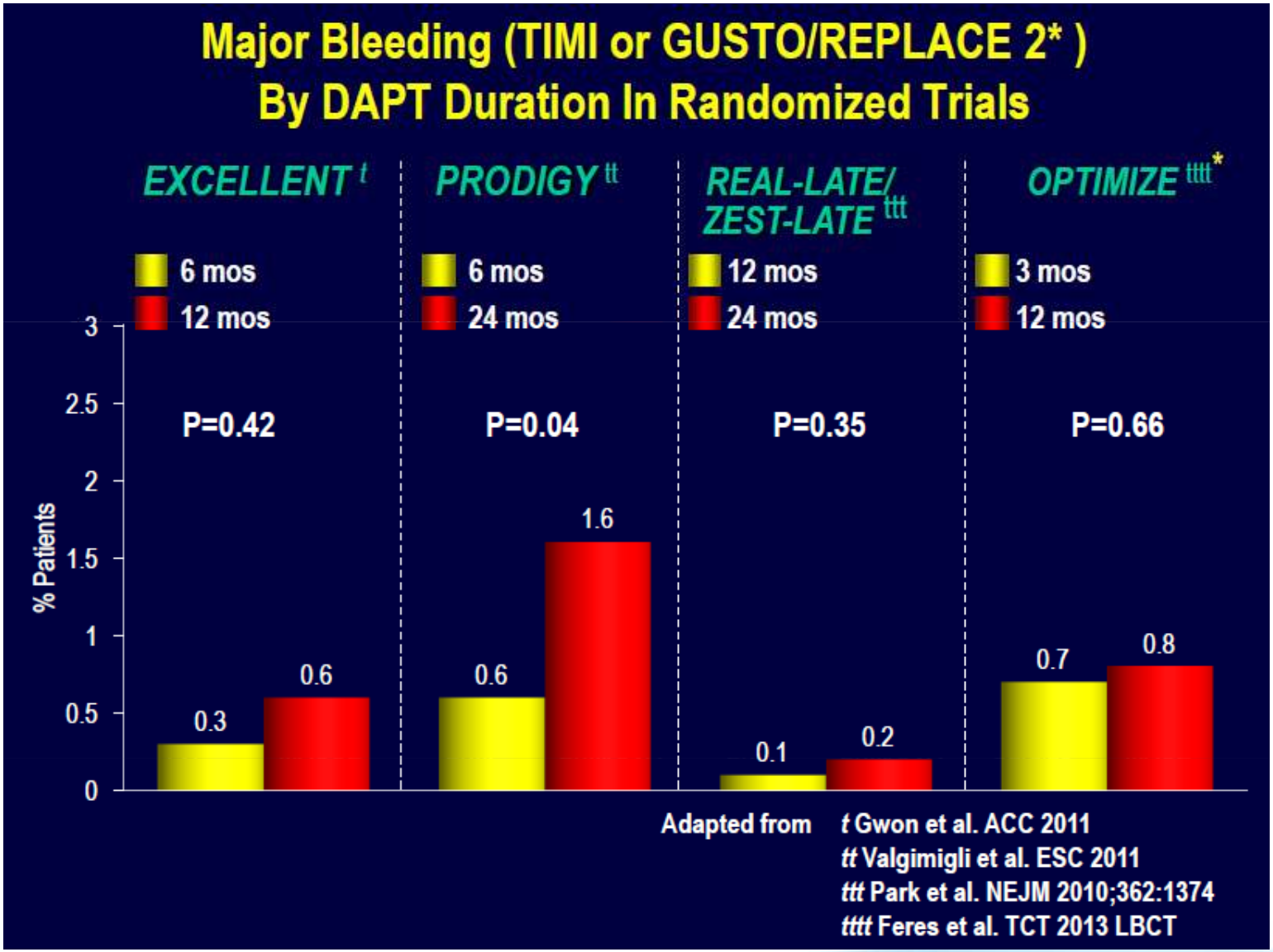
The stent?



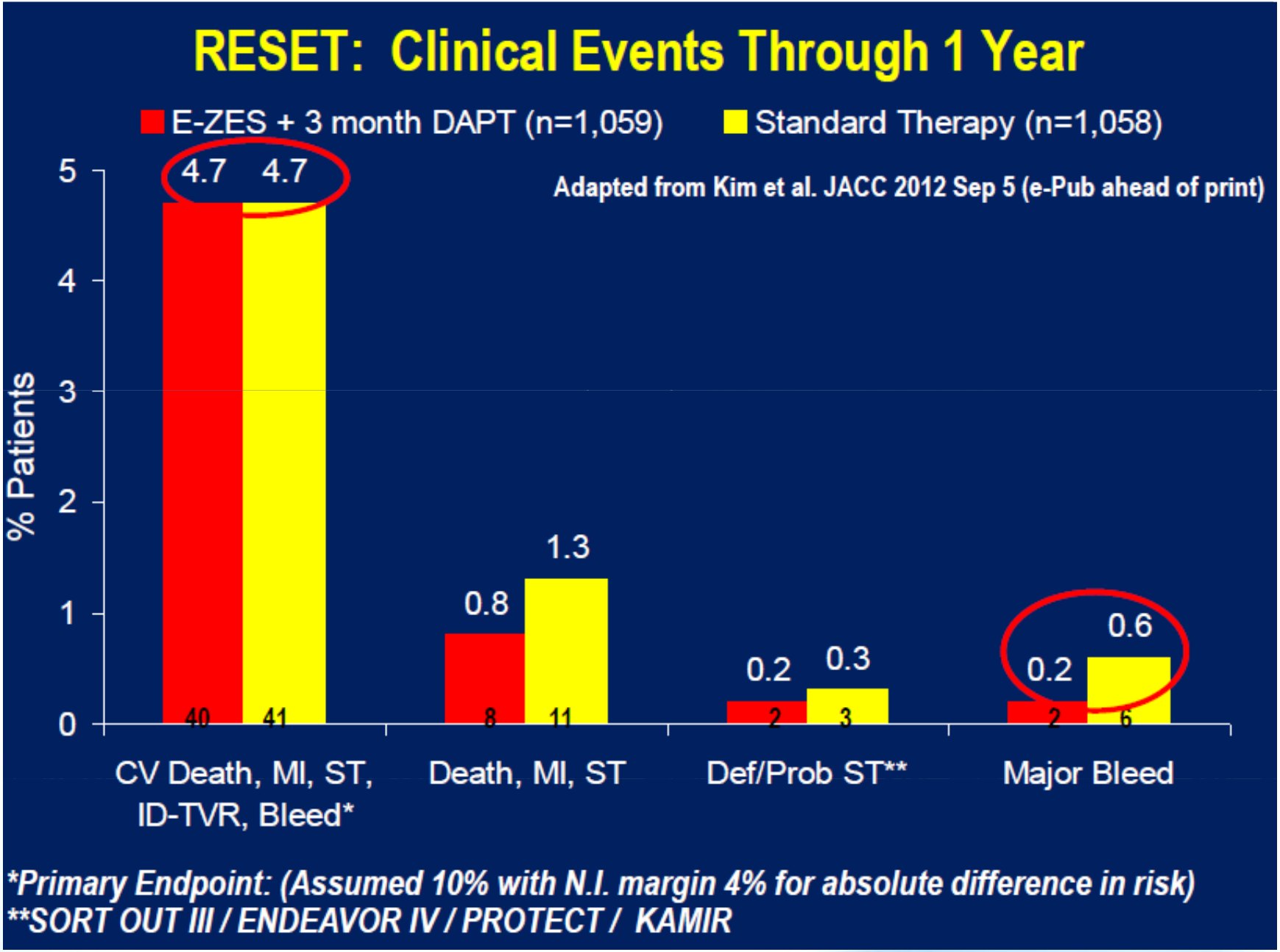
“One size shoe” approach for DAPT duration is unlikely to fit all patients



What is the current evidence for shorter DAPT?

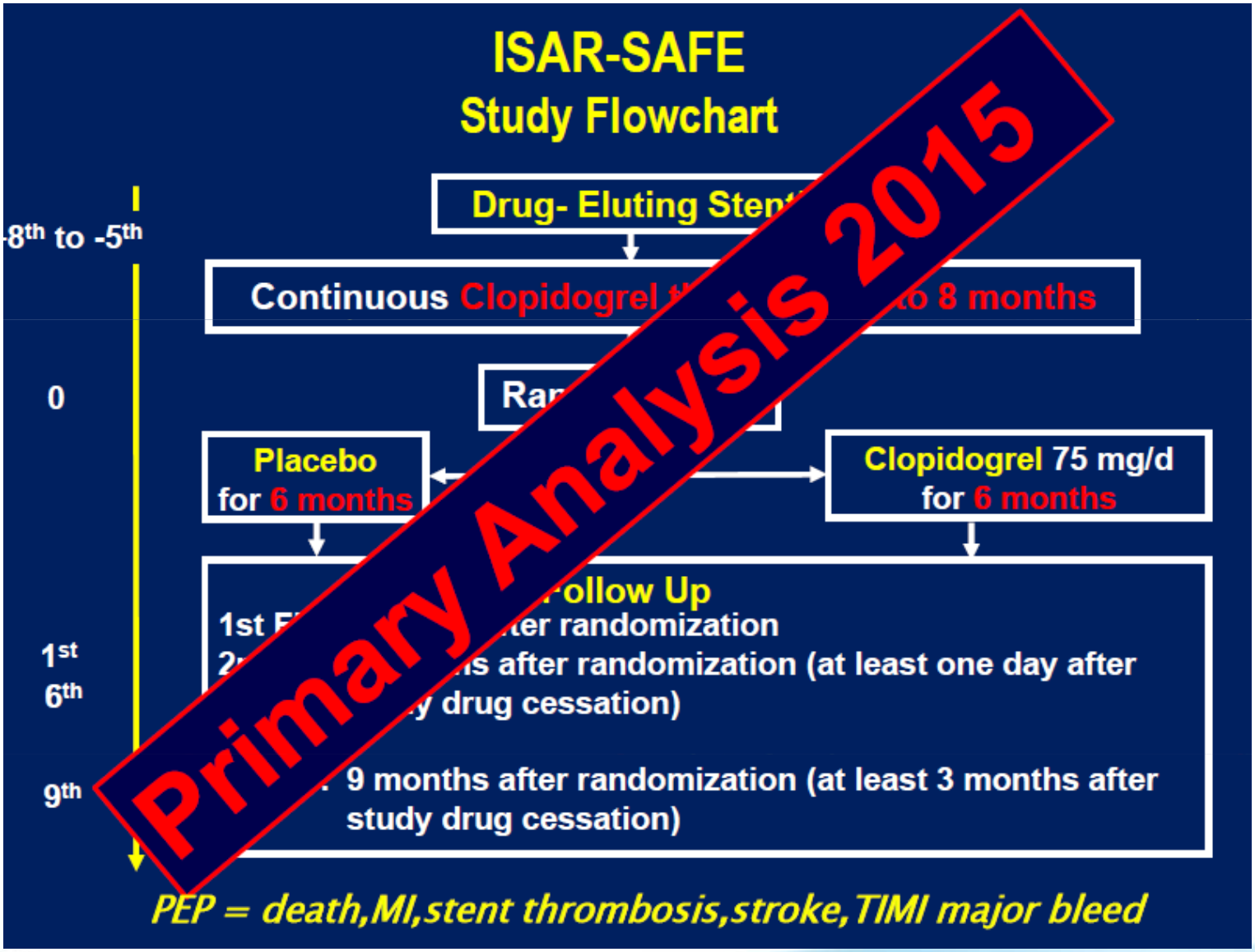


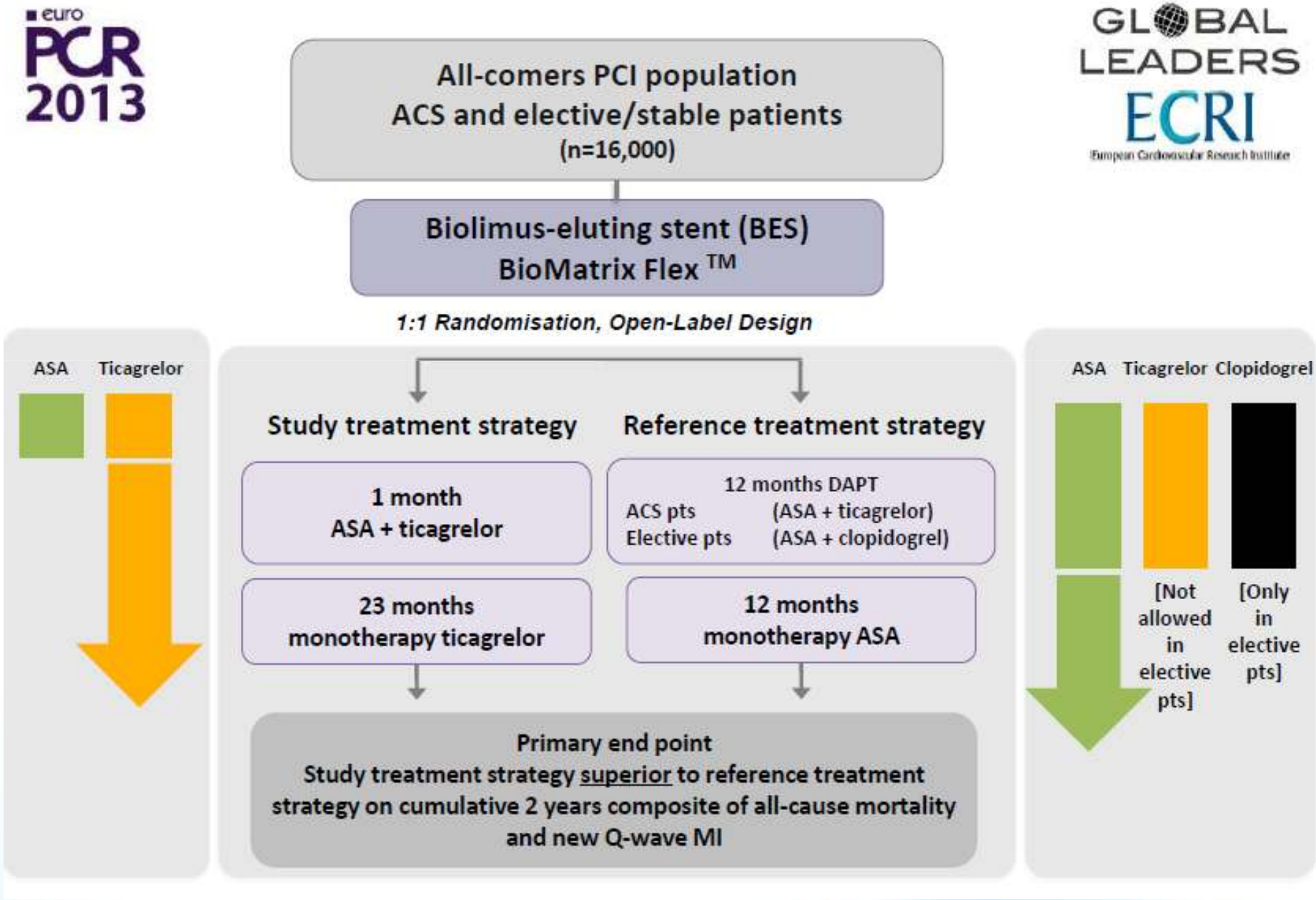
RESET: Clinical Events Through 1 Year



*Primary Endpoint: (Assumed 10% with N.I. margin 4% for absolute difference in risk)
**SORT OUT III / ENDEAVOR IV / PROTECT / KAMIR

Several large ongoing studies may resolve the uncertainties regarding optimal duration of DAPT



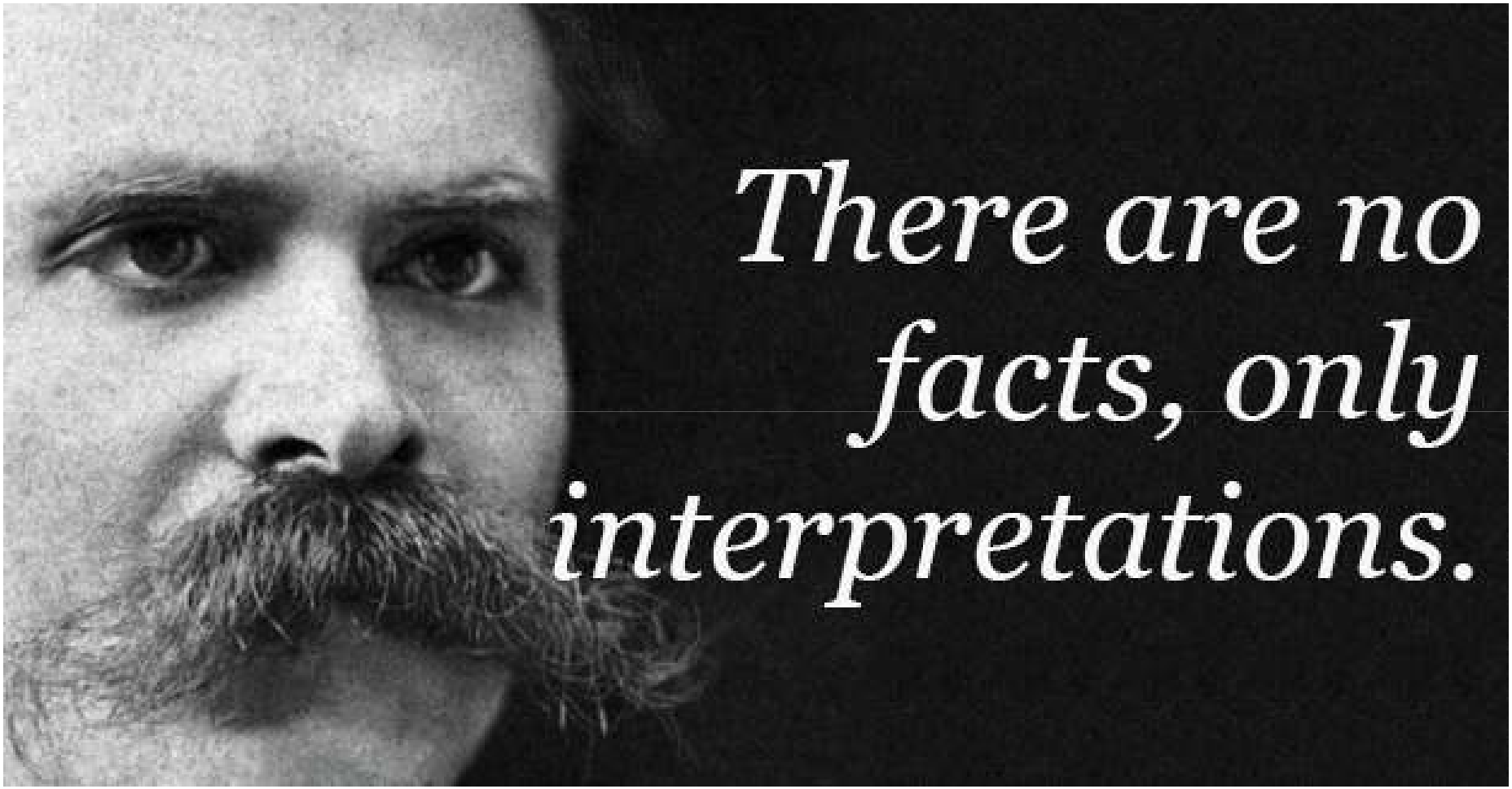

euro PCR 2013
GLOBAL LEADERS
ECRI
European Cardiovascular Research Institute
All-comers PCI population
ACS and elective/stable patients
(n=16,000)
Biolimus-eluting stent (BES)
BioMatrix Flex ™
1:1 Randomisation, Open-Label Design
ASA
Ticagrelor
Study treatment strategy
Reference treatment strategy
1 month
ASA + ticagrelor
12 months DAPT
ACS pts (ASA + ticagrelor)
Elective pts (ASA + clopidogrel)
23 months
monotherapy ticagrelor
12 months
monotherapy ASA
Primary end point
Study treatment strategy superior to reference treatment strategy on cumulative 2 years composite of all-cause mortality and new Q-wave MI
ASA
Ticagrelor
Clopidogrel
[Not allowed in elective pts]
[Only in elective pts]

✓Until we have more evidence, it is too early to say that 6-12m of DAPT is enough for all patients post-PCI

✓Customized approach would be ideal

✓Long-term might be preferable in targeting

- ➢High risk patients with previous ST,MI,DM
- ➢Complex intervention (LM disease, bifurcation, MVD etc.)



Thank you for your attention!
Questions and comments are welcome!

"Always remember that a medical device is the replacement of one disease with another…hopefully, a less severe one."

—William C. Roberts, MD


The next step in evolution……

Bioabsorbable Coronary Scaffold

Potential Benefits

- Minimize Neoatherosclerosis -> Less late stent thrombosis
- Restore normal vasomotor responses -> Less low shear distally -> less atherosclerosis; better peak exercise capacity
- Doesn't block CABG (esp LIMA to LAD)
- Allows better non-invasive CT evaluation

Challenges with Bioabsorbable Stents

- Time of degradation
- Scaffolding and radial force
- Rate of degradation
- Biocompatability
- Recoil early and late
- Biodegradable products
- Remaining polymer
- Elution of the drug from a biodegradable stents
- Radioopacity of the stents
- Deployments delivery system

The goal will be to prove what logically seems correct

In Science, Logic is not always right


Welcome To
The Future