



The Role of Polymer in DES

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Background

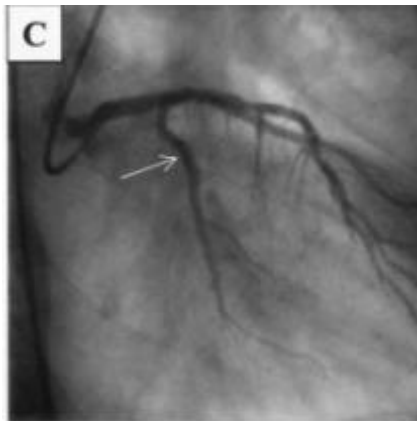


- ❖ Current polymeric DES have demonstrated excellent efficacy vs. BMS
- ❖ ACC/AHA/ESC guidelines recommend DAPT for duration (≥ 12 months) after DES
- ❖ Although rare, VLST still occur and be a catastrophic event

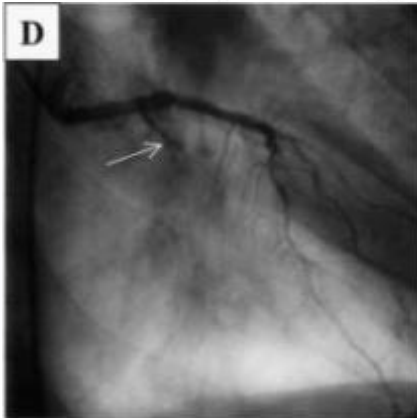
Localized Hypersensitivity and Late Coronary Thrombosis Secondary to a Sirolimus-Eluting Stent

Should We Be Cautious?

Renu Virmani, MD; Giulio Guagliumi, MD; Andrew Farb, MD; Giuseppe Musumeci, MD;
Niccolo Grieco, MD; Teresio Motta, MD; Laurian Mihalesik, MD; Maurizio Tespili, MD;
Orazio Valsecchi, MD; Frank D. Kolodgie, PhD



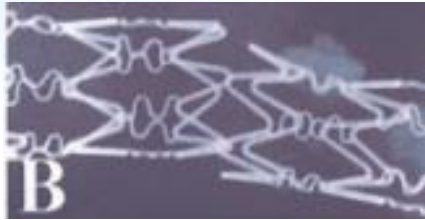
Follow-up (8 Months)



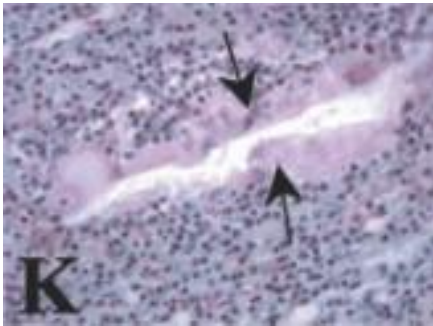
Follow-up (18 Months)

- ❖ M/58
- ❖ uAP (2001')
- ❖ Enrolled in the E-SIRUS trial
Randomized to SES
- ❖ SES 3.0x18 + 2.5x18 mm at the LCX
- ❖ 1yr f/u : negative isotope stress test
- ❖ At 18 mo : chest pain with syncope
- ❖ CAG 8 days after the onset of chest pain
- ❖ He died of cardiac rupture

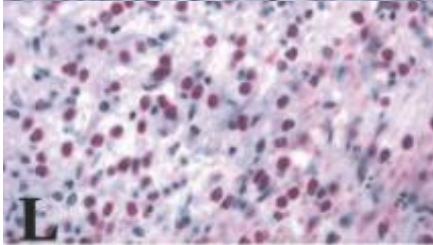
Localized Hypersensitivity Vasculitis



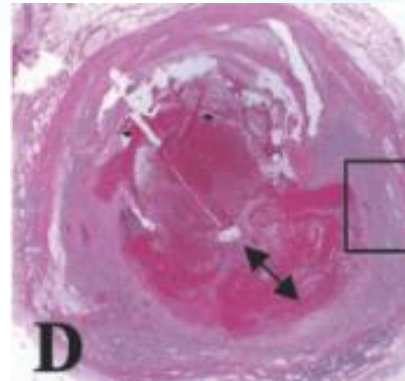
Stent Fracture



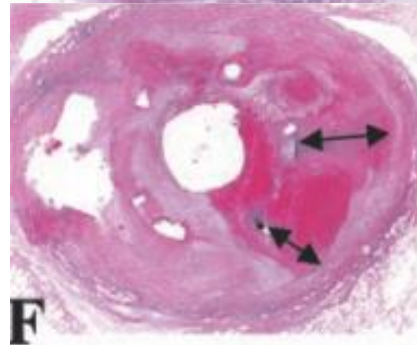
Giant cells (arrow)
around a polymer
remnant



Luna Stain (K and L)



Occlusive luminal
thrombosis



Aneurysmal
dilatation (double
arrows)

Hypersensitivity to Metals

- molybdenum, nickel, chromium
- Associated with **restenosis** and not thrombosis

Hypersensitivity to Polymers

- Extensive **eosinophilic** infiltration
- Focal **giant cell reaction** surrounding a few polymer remnants

Do we need a polymer on DES?

The typical role of a polymer on DES

Protect

Assures stability of drug during the manufacturing processes and over time

Transport

Allows safe transport of the drug to the target lesion

Release

Controls drug release in a reliable and reproducible fashion

Should be biocompatible

Biodegradable Polymer



❖ Benefit

- Reduce chronic polymer effects

❖ Issues

- Degradation rates, inflammatory byproducts, more complex elution profiles

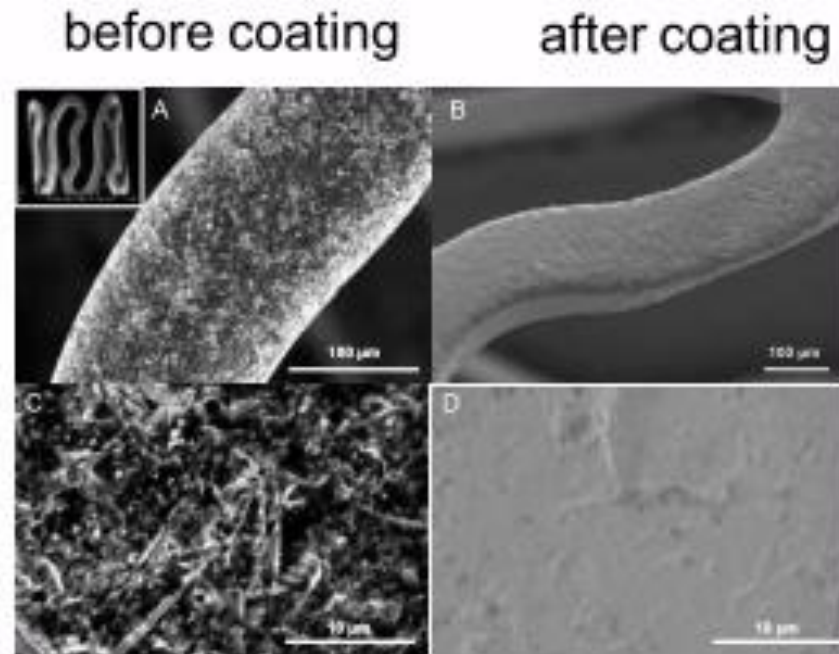
❖ Examples

- BioMatrix (Biosensors®)
- Nobori(Terumo®)
- Nevo (Cordis®)
- Synergy (BSC®)

ISAR : Individualized Drug-Eluting Stent System to Abrogate Restenosis Project

Design, development and clinical implementation of novel microporous DES without permanent polymer

- ❖ ISAR Generation 1 (No polymer at all)
- ❖ ISAR Generation 2 (Biodegradable polymer)
- ❖ ISAR Generation 3 (Dual-drug, no polymer)



ISAR-TEST 4 Study

Intracoronary Stenting and Angiographic Results: Test Efficacy of 3 Limus-Eluting Stents - 4

2603 patients with *de novo* lesions

Biodegradable polymer DES

(BP-DES)

n=1299

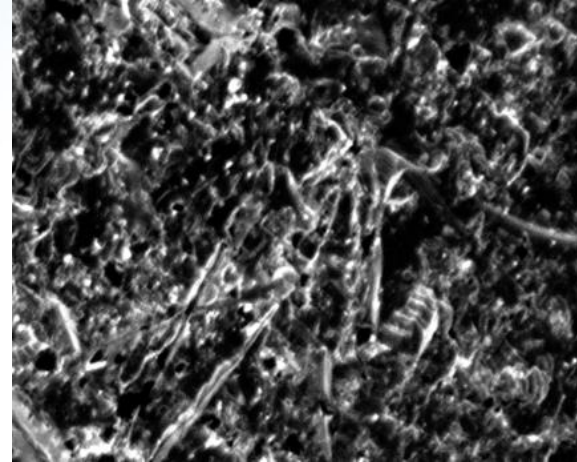
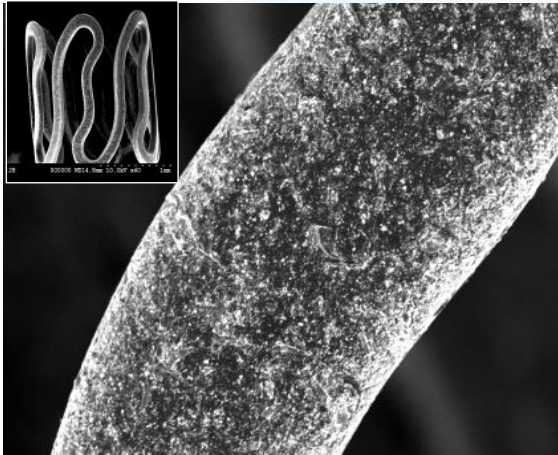
Permanent polymer DES
(PP-DES: **Xience** & **Cypher**)

n=1304

6-8 month & 2 year FU angiography

36-month clinical follow-up

Biodegradable Polymer Stent

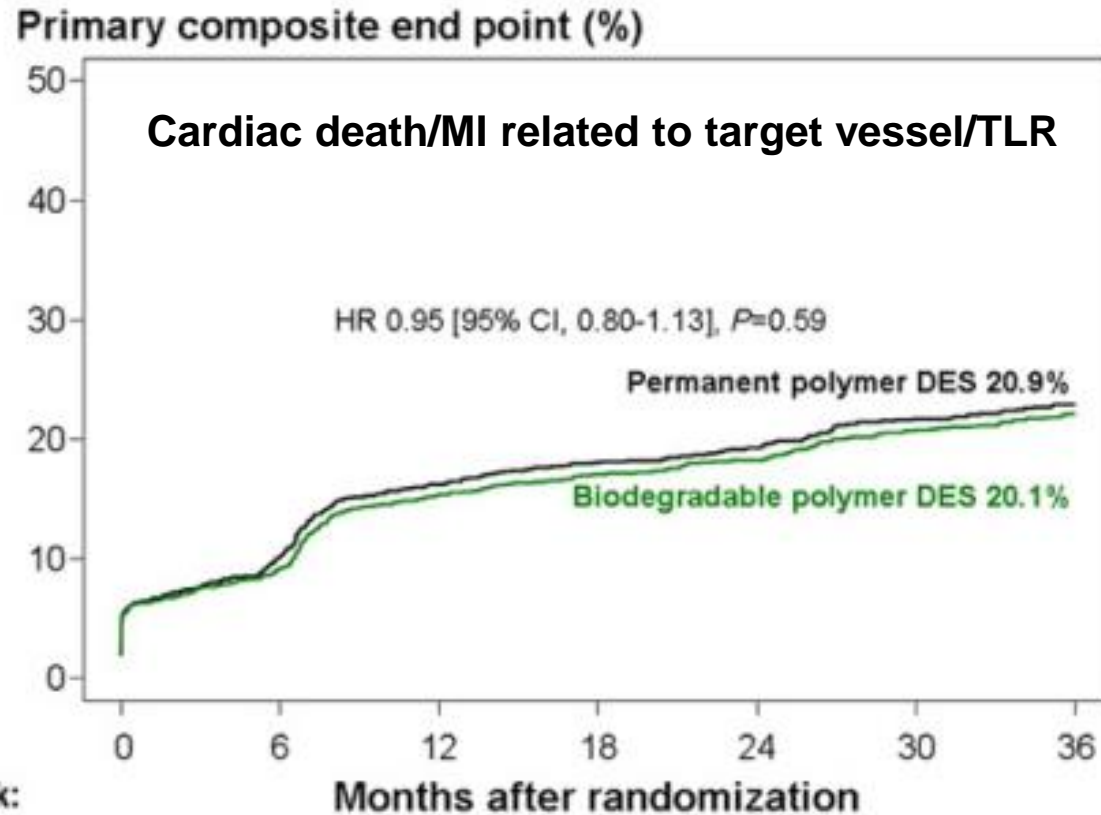


❖ Stent platform

- Sand-blasted
- 316L stainless steel microporous stent
- Coated on site with a mixture of rapamycin, biodegradable polymer, shellac resin
- The BP matrix is completely **resorbed within ~6-9 weeks**
- **Yucon Choice PC stent** (Trnaslumina Therapeutics®)

Biodegradable vs. Permanent Polymer

A



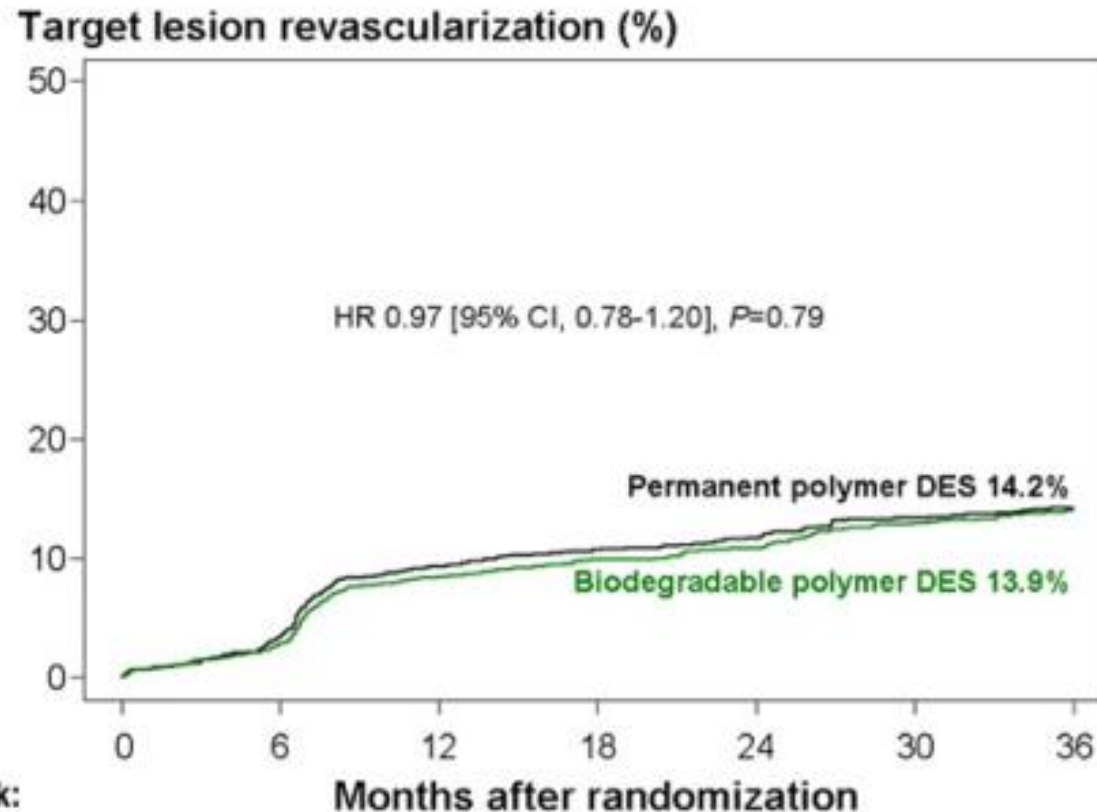
Patients at risk:

Permanent polymer DES	1304	1168	1077	1039	1001	944	791
Biodegradable polymer DES	1299	1178	1087	1038	1007	951	801

Not significantly different

Biodegradable vs. Permanent Polymer

B



Patients at risk:

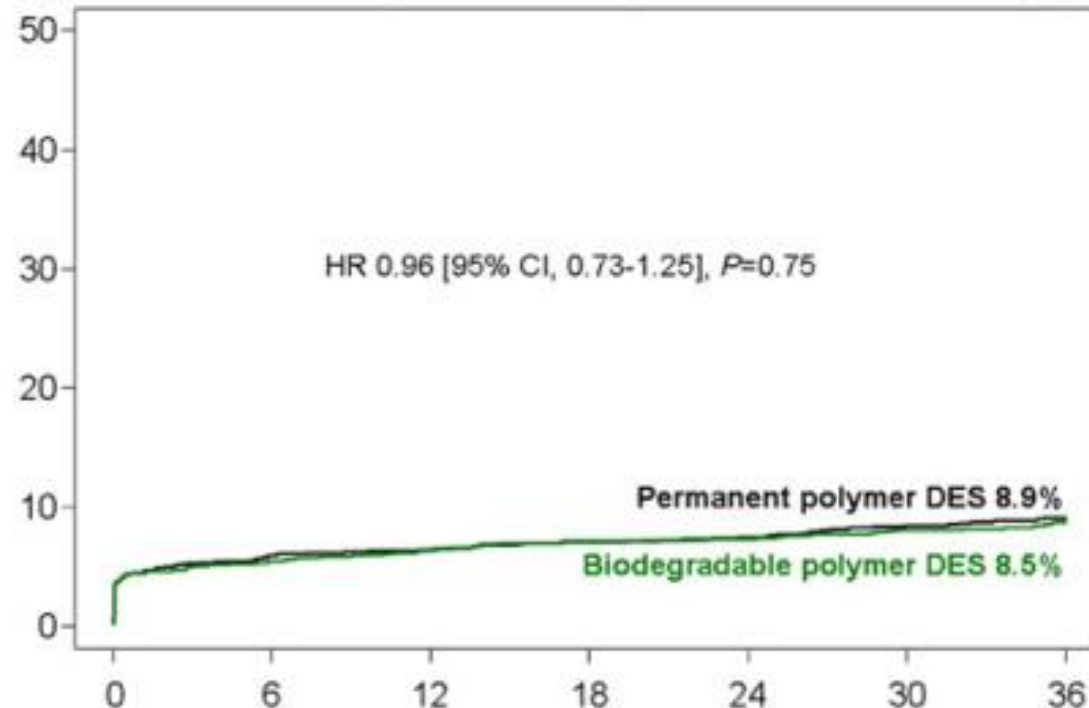
Permanent polymer DES	1304	1200	1108	1069	1028	973	817
Biodegradable polymer DES	1299	1210	1114	1065	1033	977	824

Similar in antirestenotic efficacy

Biodegradable vs. Permanent Polymer

C

Cardiac death or target vessel myocardial infarction (%)



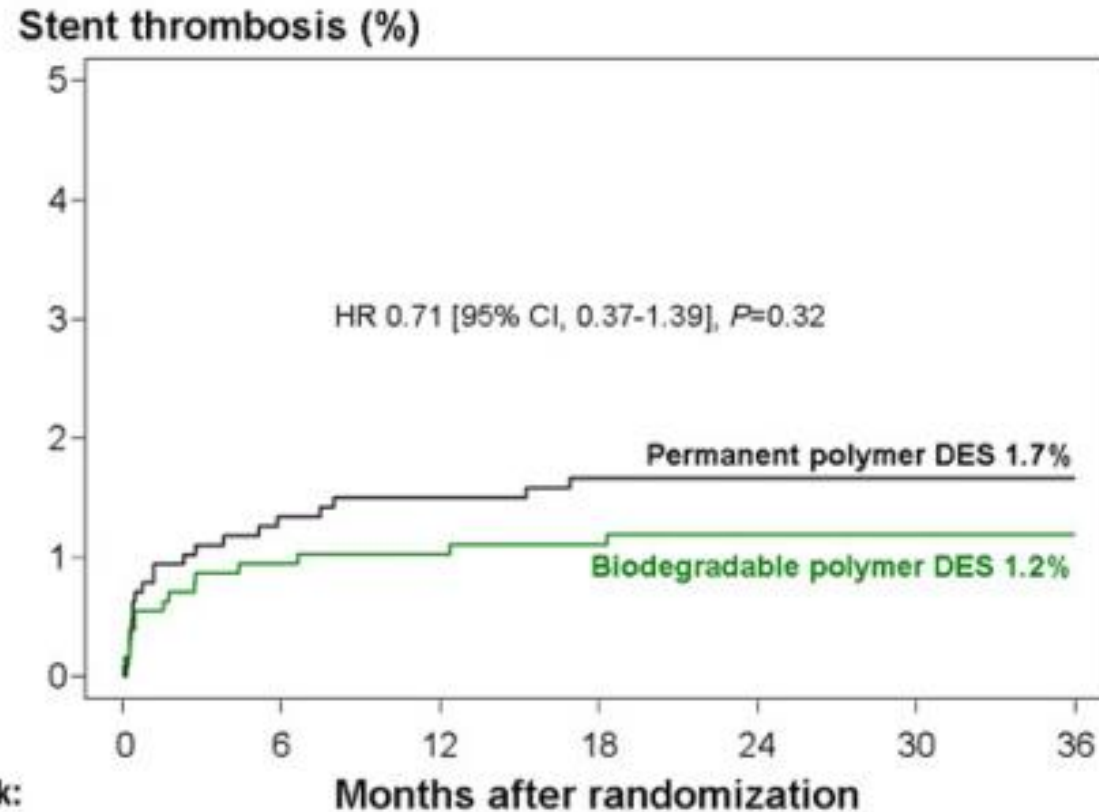
Patients at risk:

	0	6	12	18	24	30	36
Permanent polymer DES	1304	1200	1178	1152	1125	1083	913
Biodegradable polymer DES	1299	1204	1177	1142	1117	1081	911

With regard to safety outcomes, the incidence was low across the treatment groups

Biodegradable vs. Permanent Polymer

D



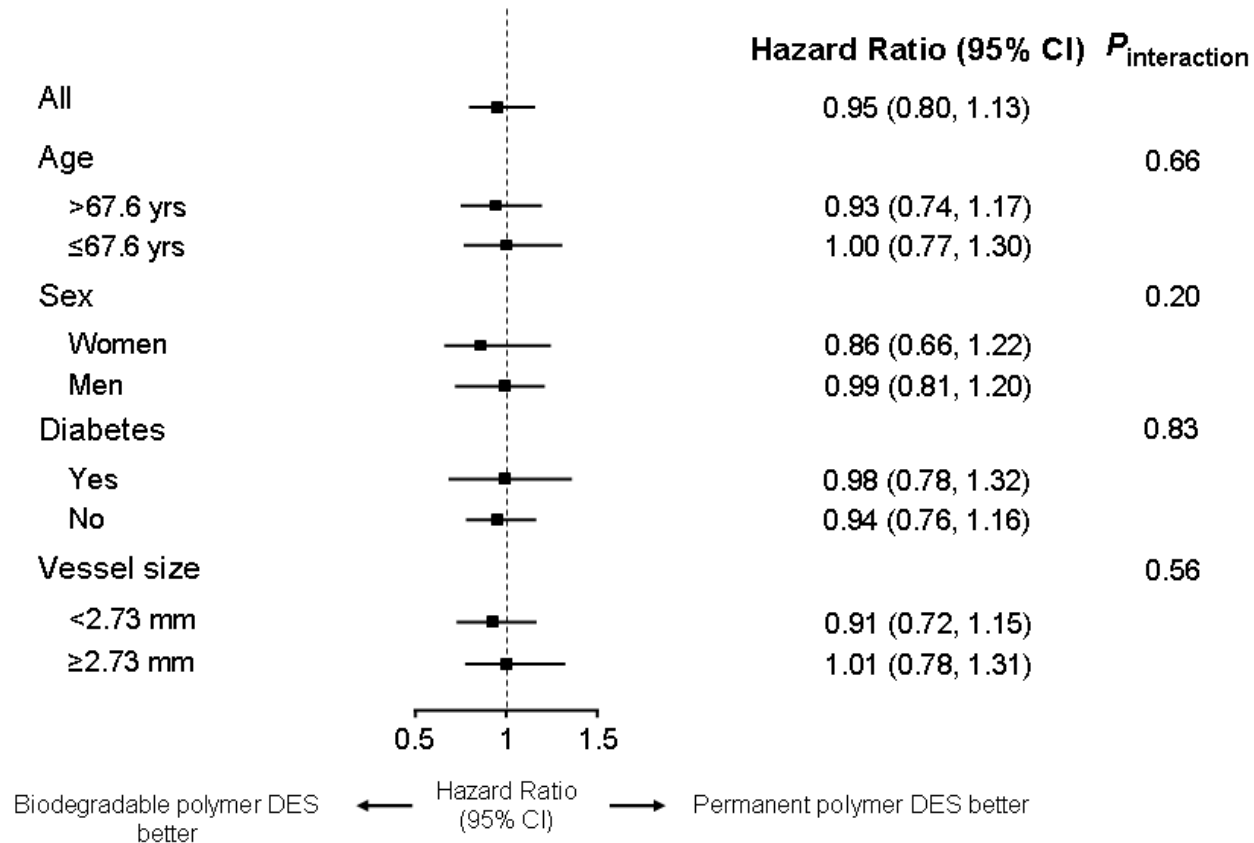
Patients at risk:

Permanent polymer DES	1304	1232	1209	1183	1154	1115	943
Biodegradable polymer DES	1299	1237	1209	1175	1149	1113	938

The rate of definite/probable stent thrombosis was low in both groups

Biodegradable vs. Permanent Polymer

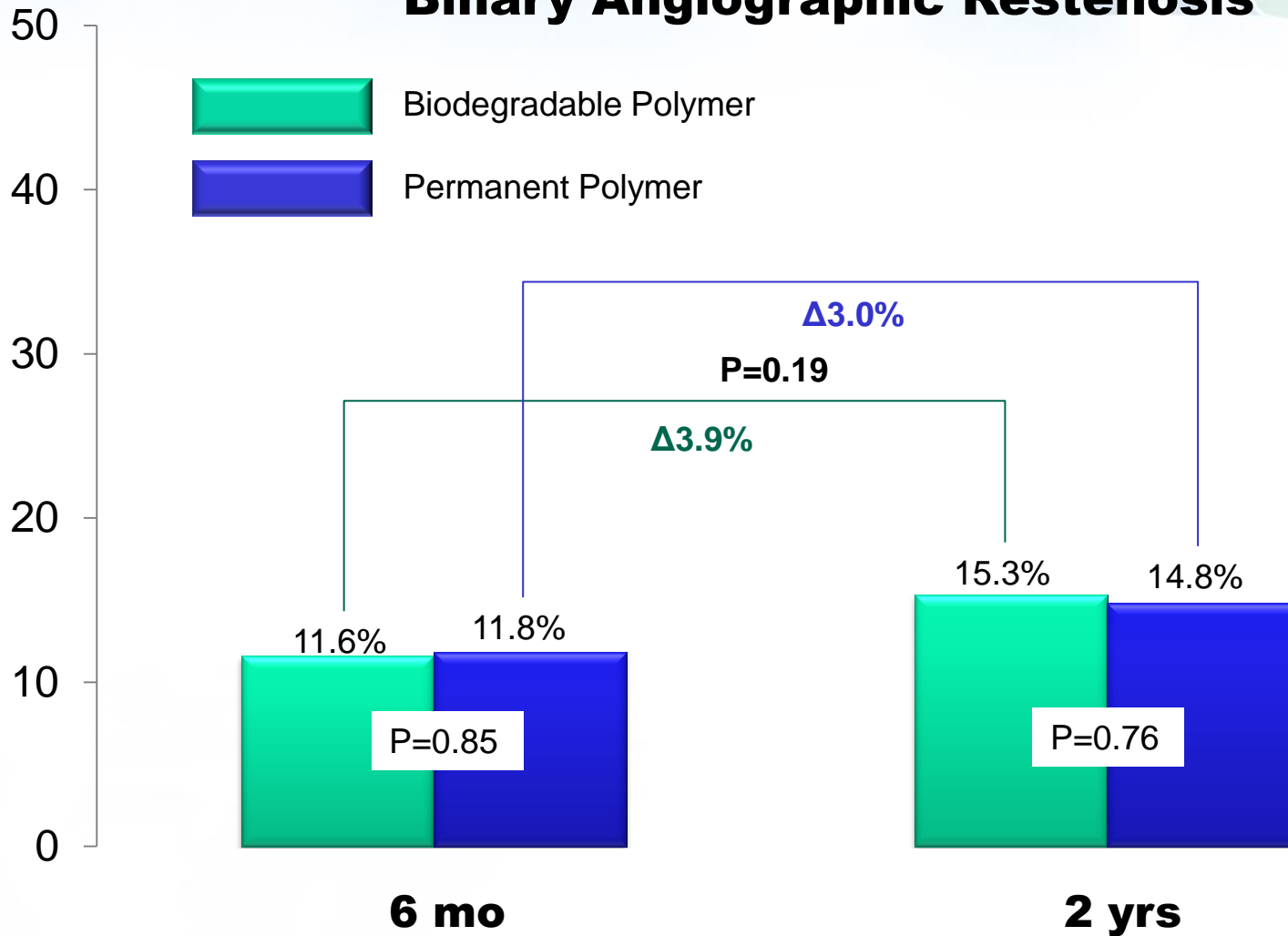
According to Pre-specified Subgroups



The results were consistent across all pre-specified subgroups

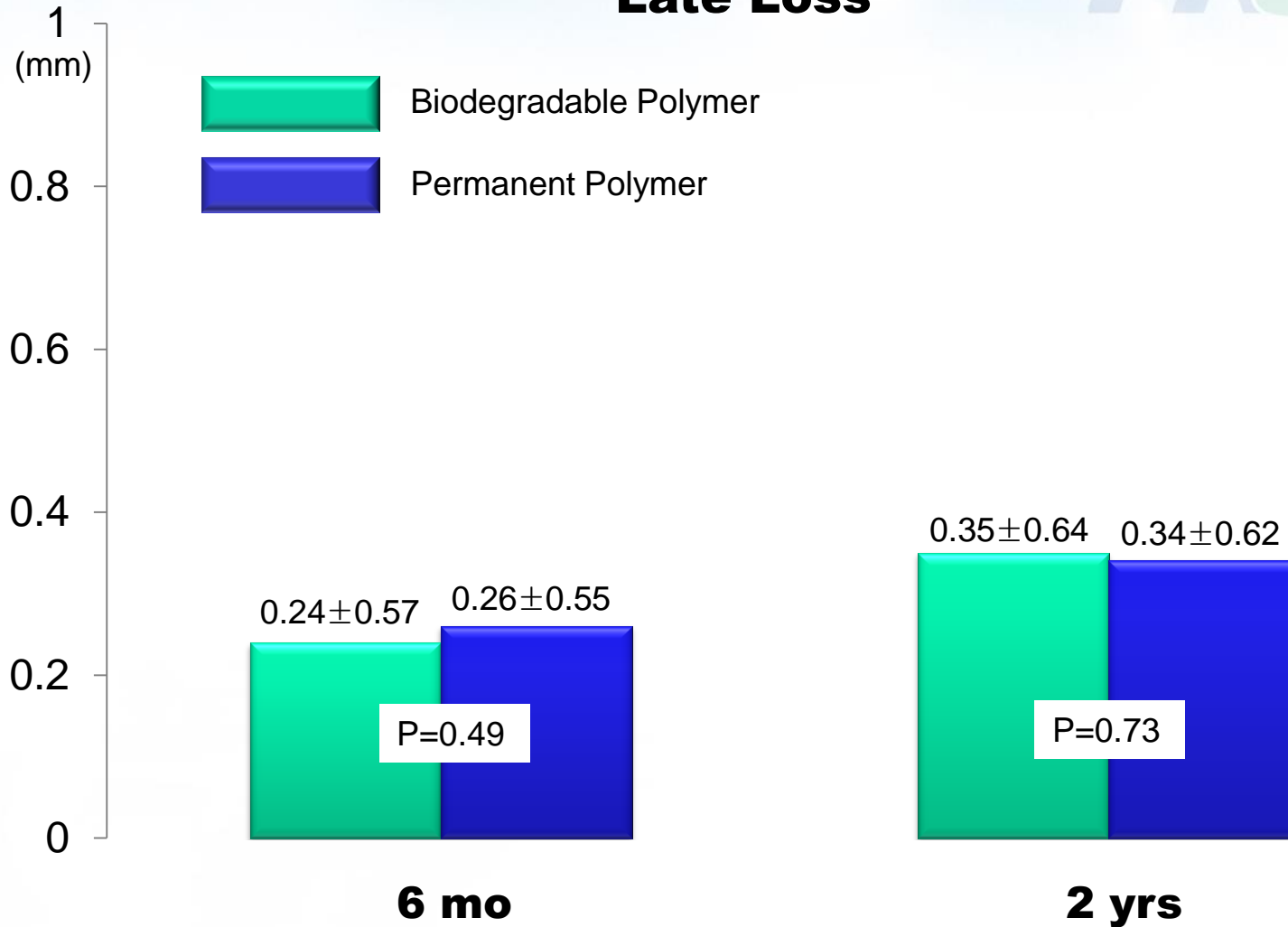
Biodegradable vs. Permanent Polymer

Binary Angiographic Restenosis

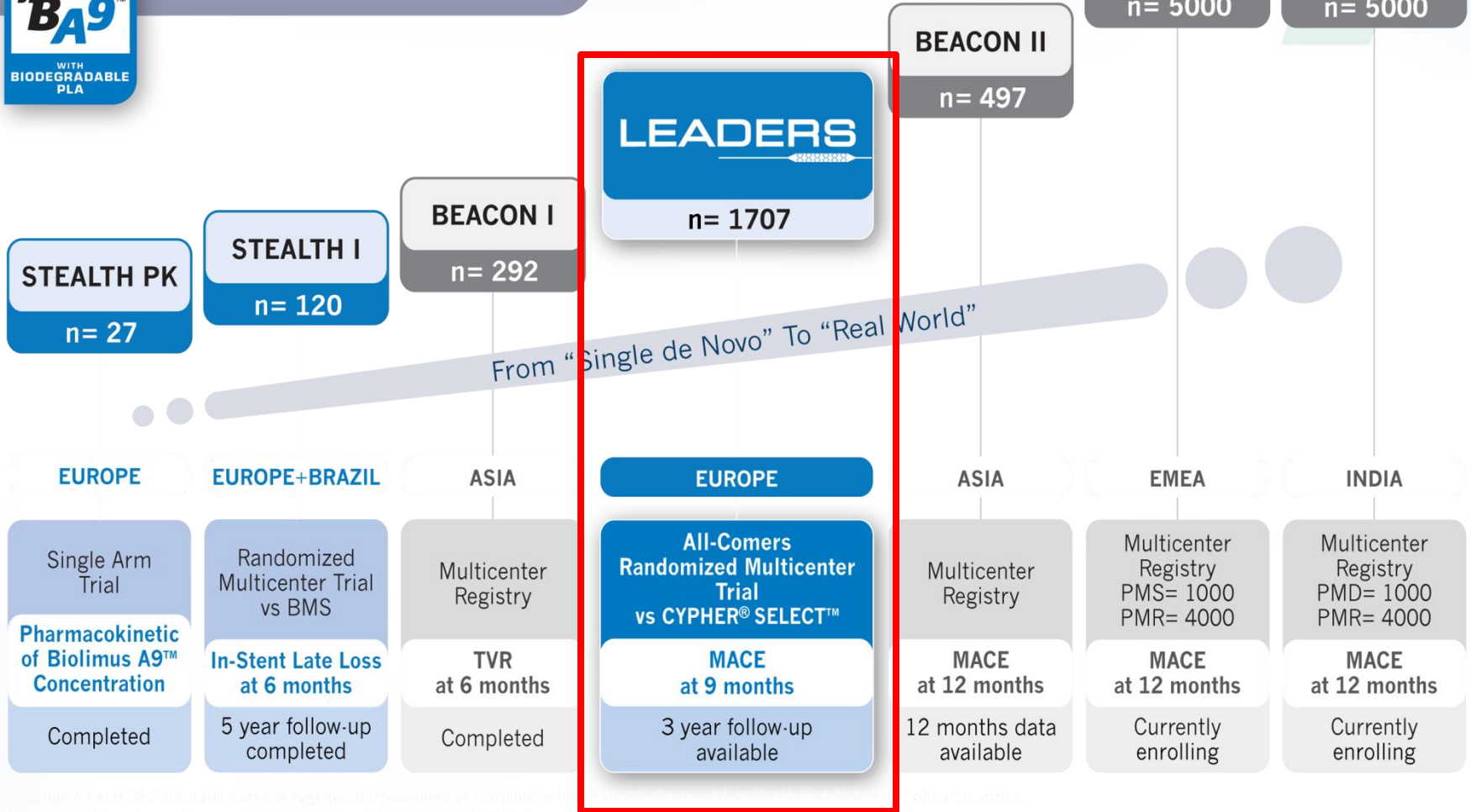


Biodegradable vs. Permanent Polymer

Late Loss



Biolimus A9™ / Abluminal Biodegradable Polymer DES Clinical Trial Program

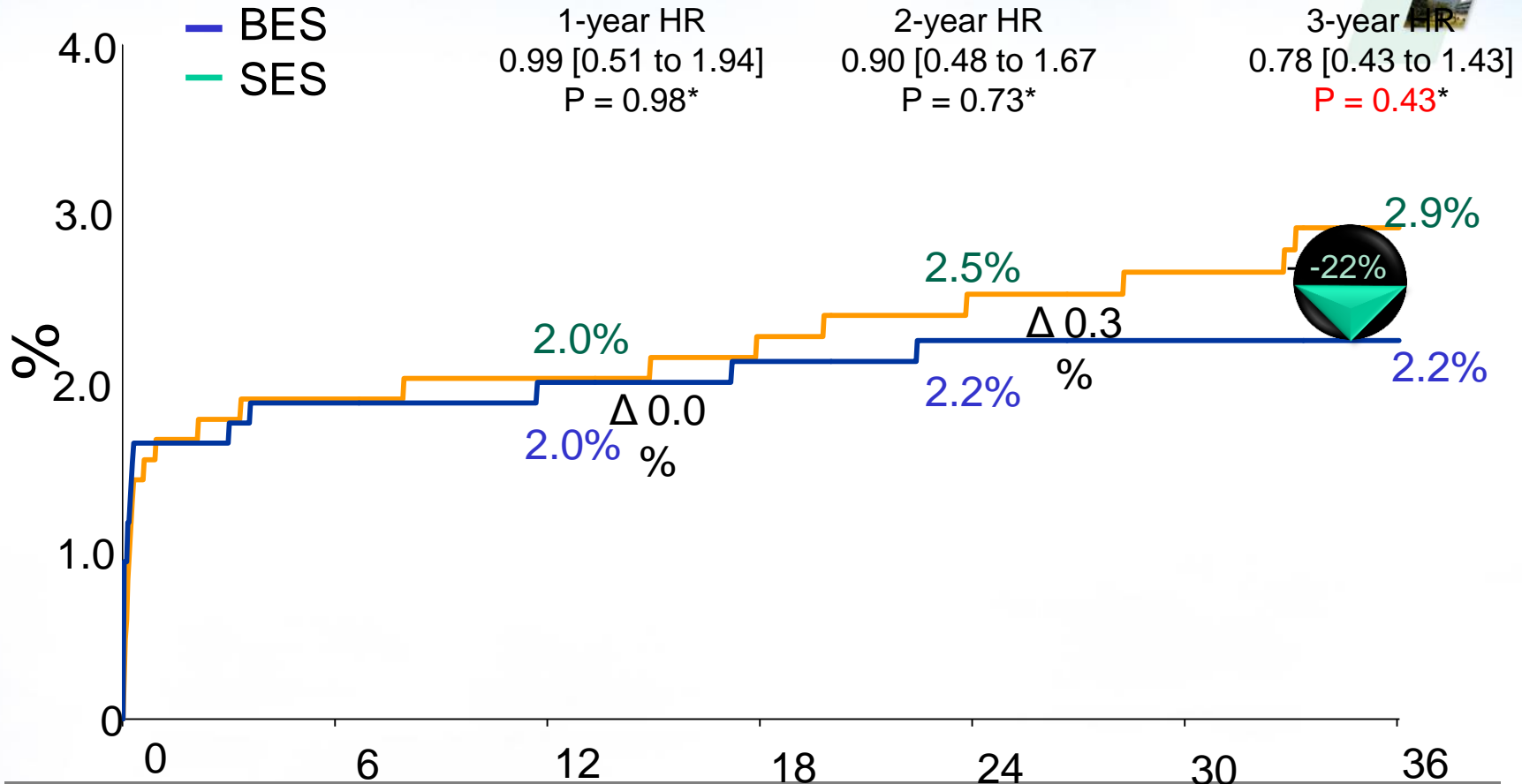


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PMS = Post Market Surveillance
PMR = Post Market Registry
PMD = Post Market Registry Diabetics

BEACON II: MACE defined as Cardiac Death, Ischemic Driven MI (Q-wave and NQ-wave) and clinically indicated TLR (PTCA and CABG)
e-BioMatrix / e-BioMatrix India: MACE defined as Cardiac Death, MI (Q-wave and NQ-wave), or clinically indicated TVR
LEADERS: MACE defined as Cardiac Death, MI (Q-wave and NQ-wave), or clinically indicated TVR

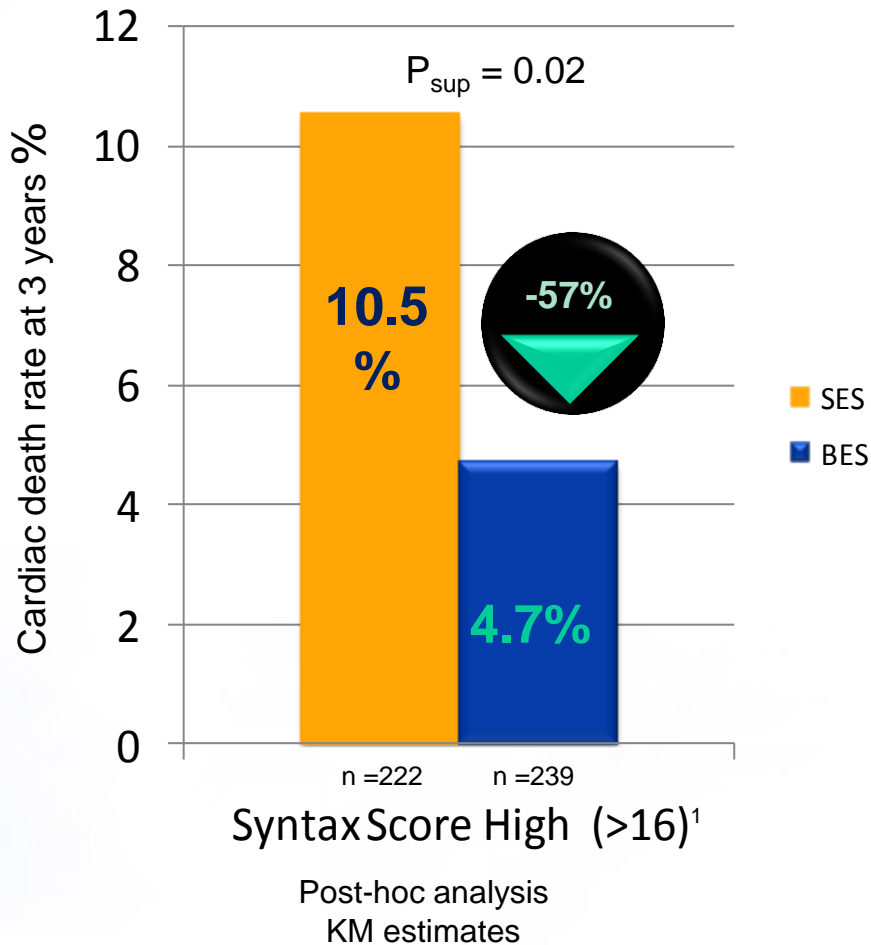
Definite ST through 3 years



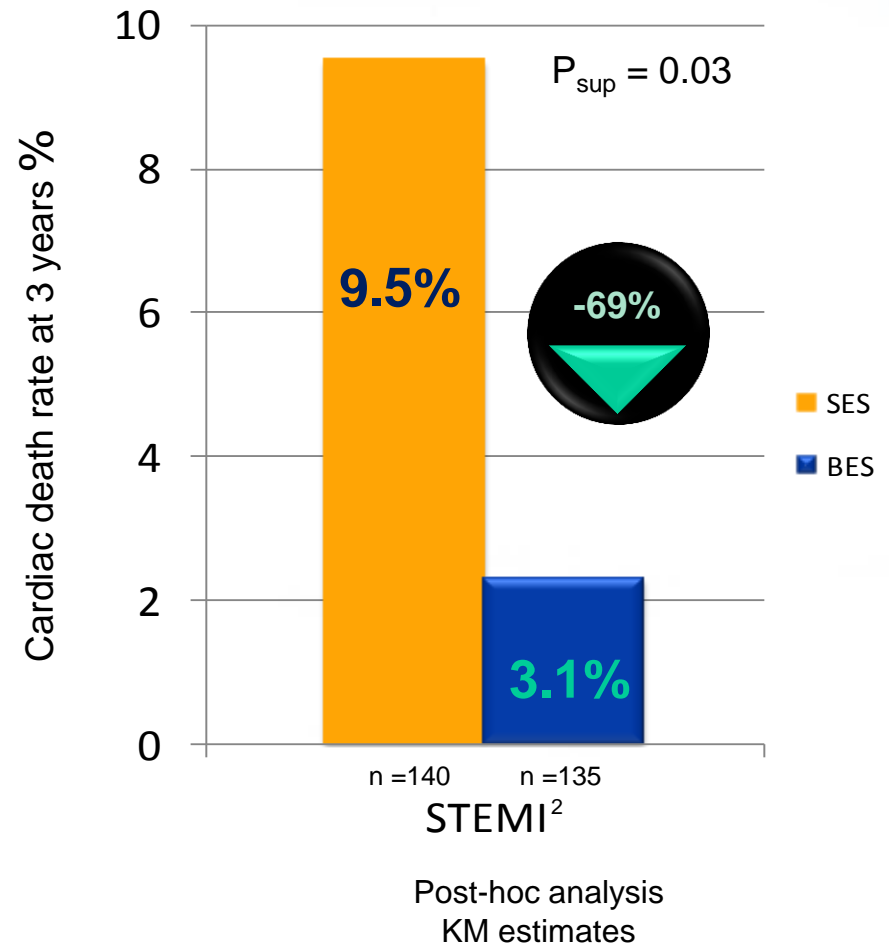
Number at risk		0	6	12	18	24	30	36
BES	857	846	808	797	787	774	732	
SES	850	841	801	792	779	758	715	

*P values for superiority

The Biolimus A9™ eluting stent shows a significant **cardiac mortality benefit**



¹Serruys, P., oral presentation, TCT 2010



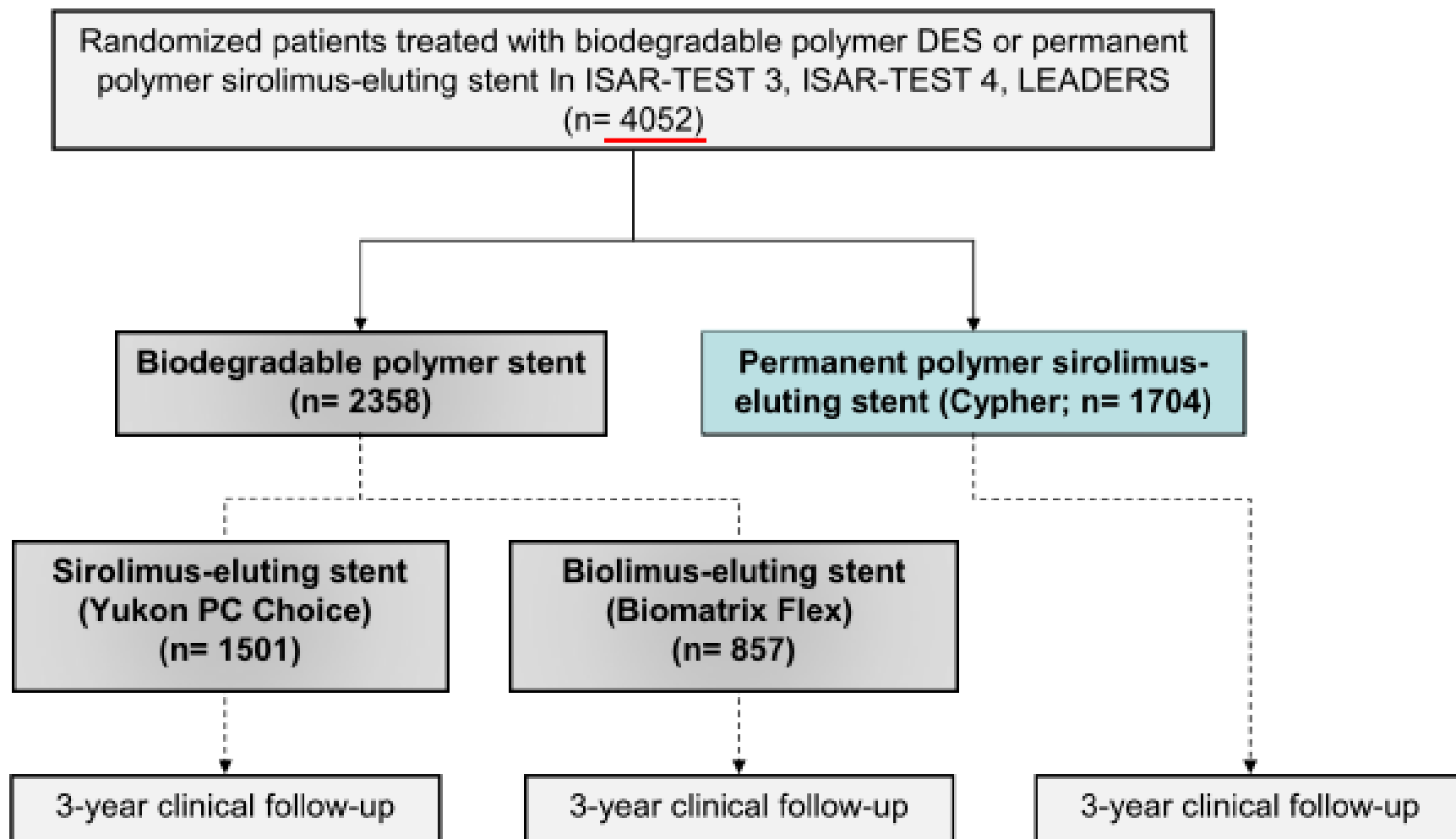
² Windecker, S., oral presentation, TCT 2010

Biodegradable Polymer Versus Durable Polymer Drug-Eluting Stents for Patients With Coronary Artery Disease:

**3-year Pooled Analysis of Individual Patient Data
from ISAR-TEST 3, ISAR-TEST 4, and LEADERS
Randomized Trials**

**Robert A. Byrne, Giulio Stefanini, Julinda Mehilli,
Bernhard Meier, Steffen Massberg, Patrick W. Serruys,
Peter Jüni, Albert Schömig, Stephan Windecker,
Adnan Kastrati**

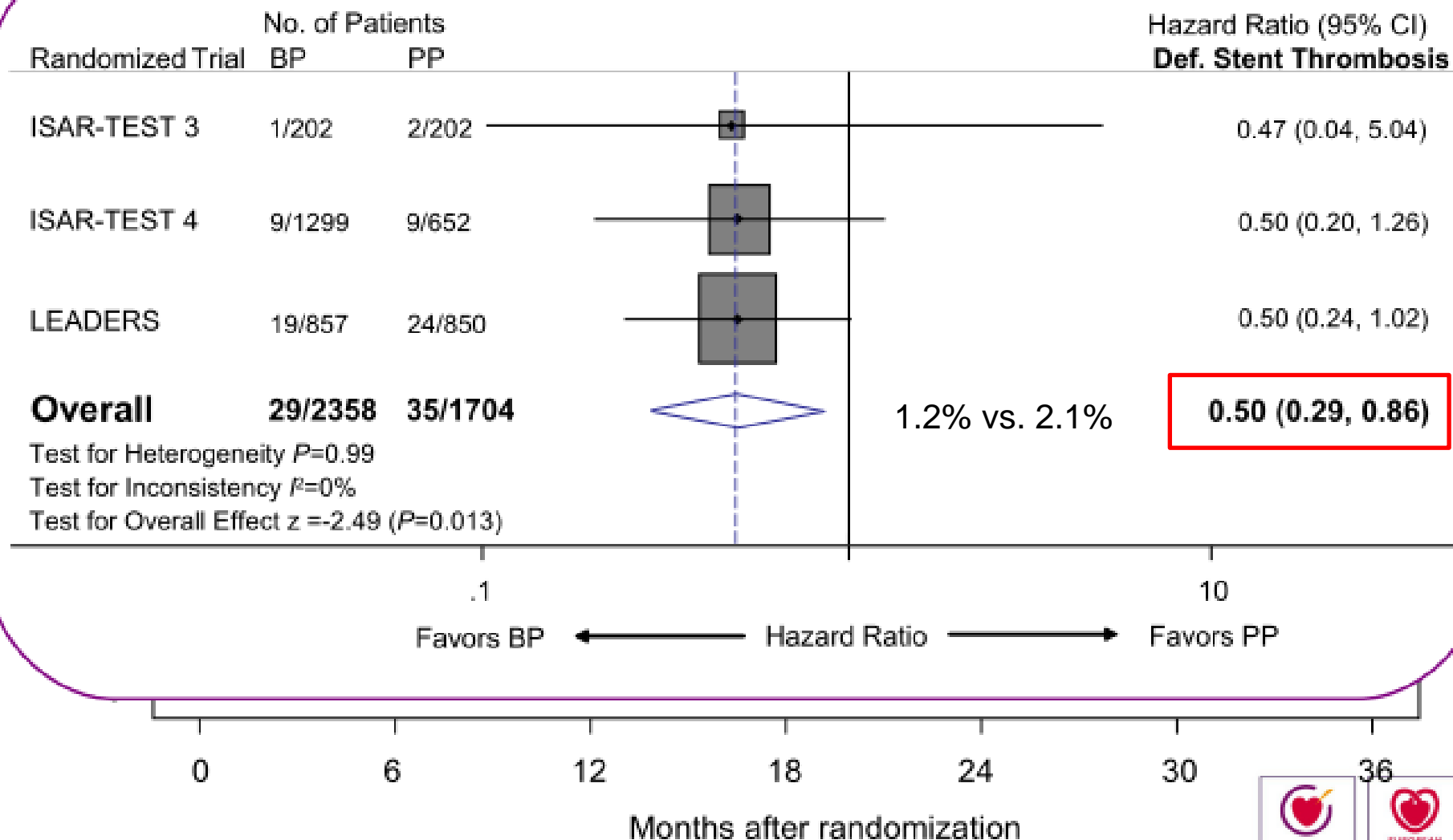
Study Flow



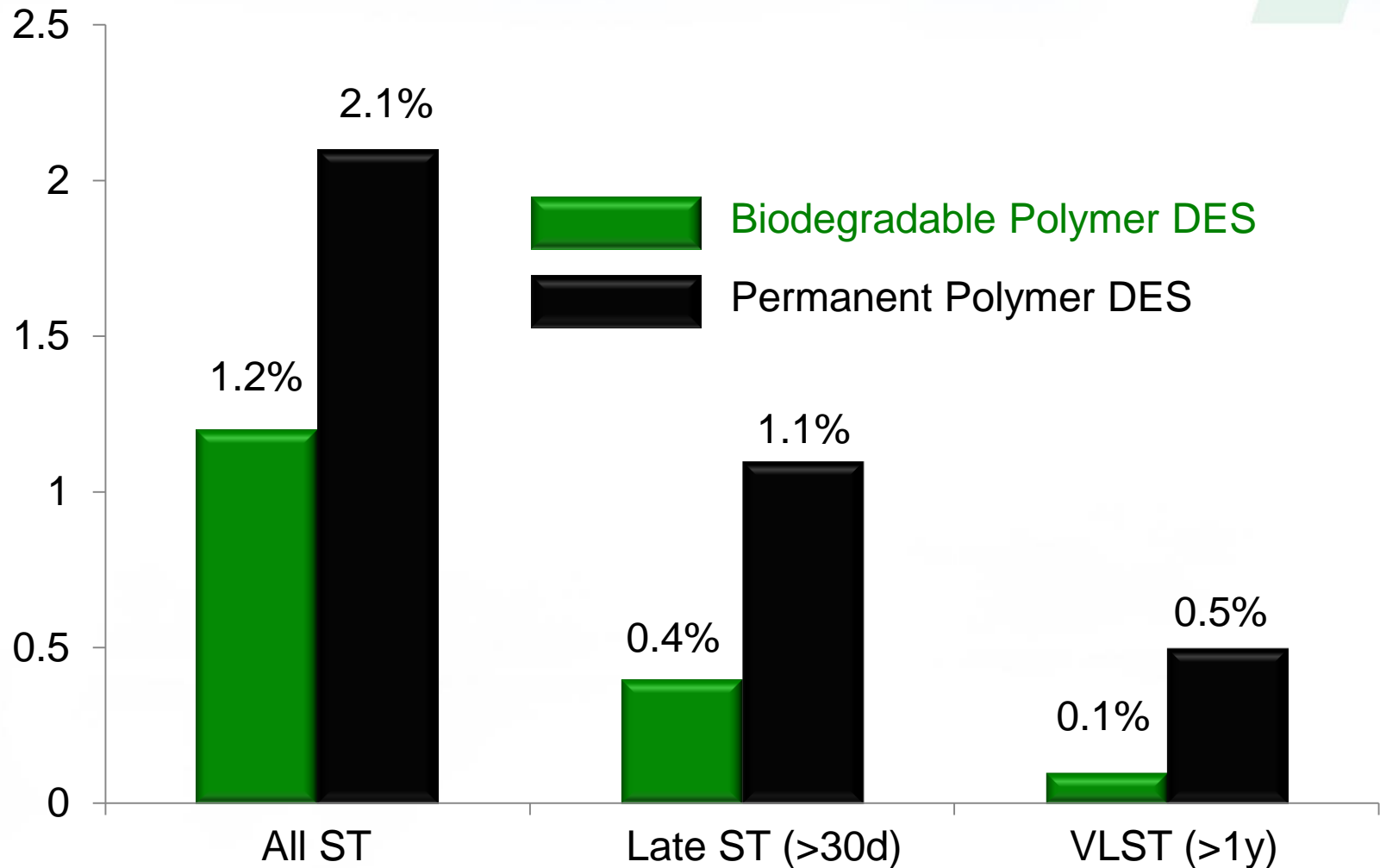
Trial Characteristics

Trials	ISAR-TEST 3	ISAR-TEST 4	LEADERS
Patients	605	2603	1707
Mean age	66.1 yrs	66.8 yrs	64.6 yrs
Diabetes	27%	29%	24%
Exclusion	LMS/Bypass/Reste nosis	LMS/Bypass/Reste nosis	None
Lesion/patients	1.2	1.3	1.5
Follow-Up	3 years	3 years	3 years

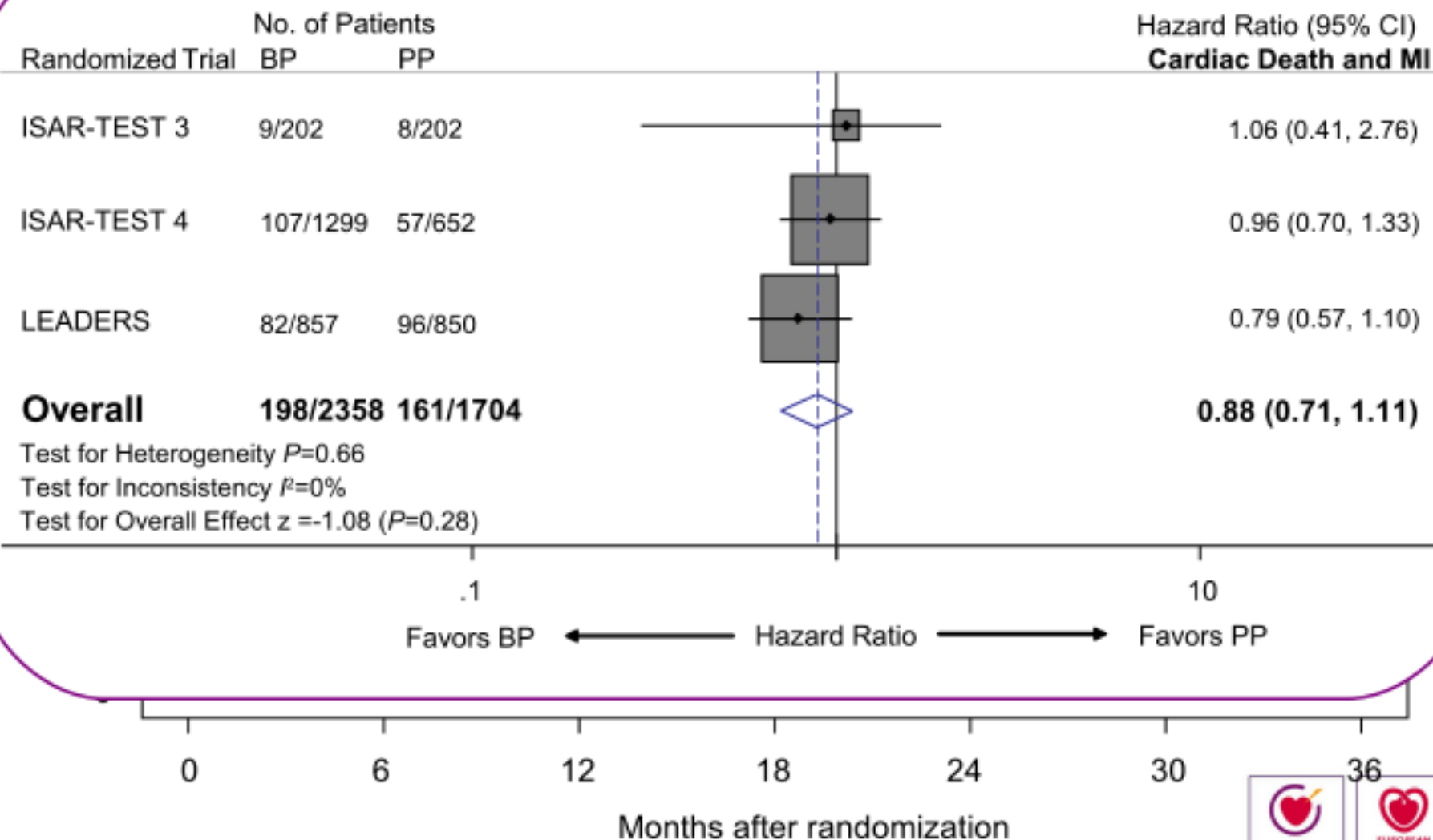
Definite Stent Thrombosis



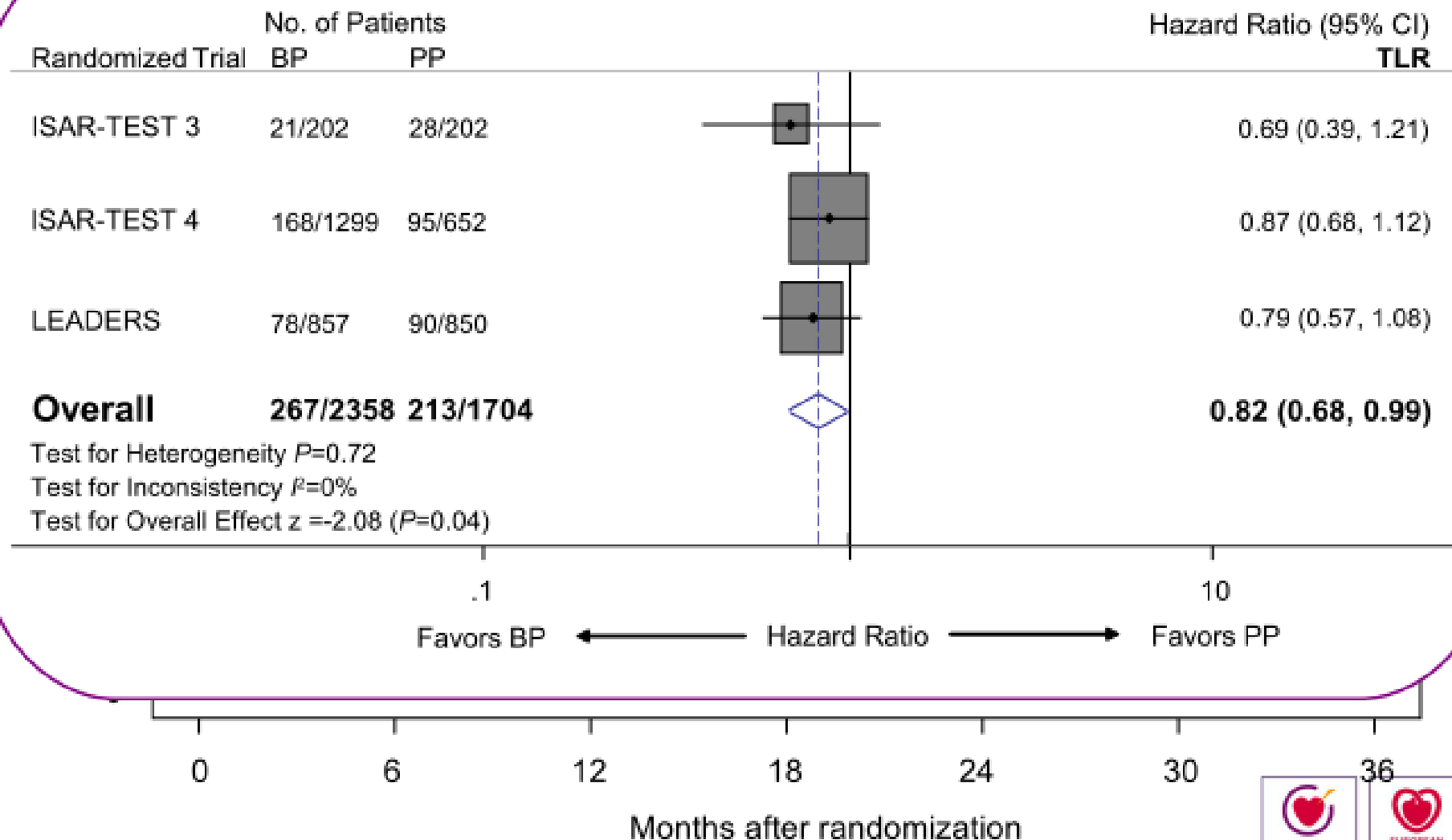
Definite Stent Thrombosis Landmark Analysis



Cardiac Death/Myocardial Infarction

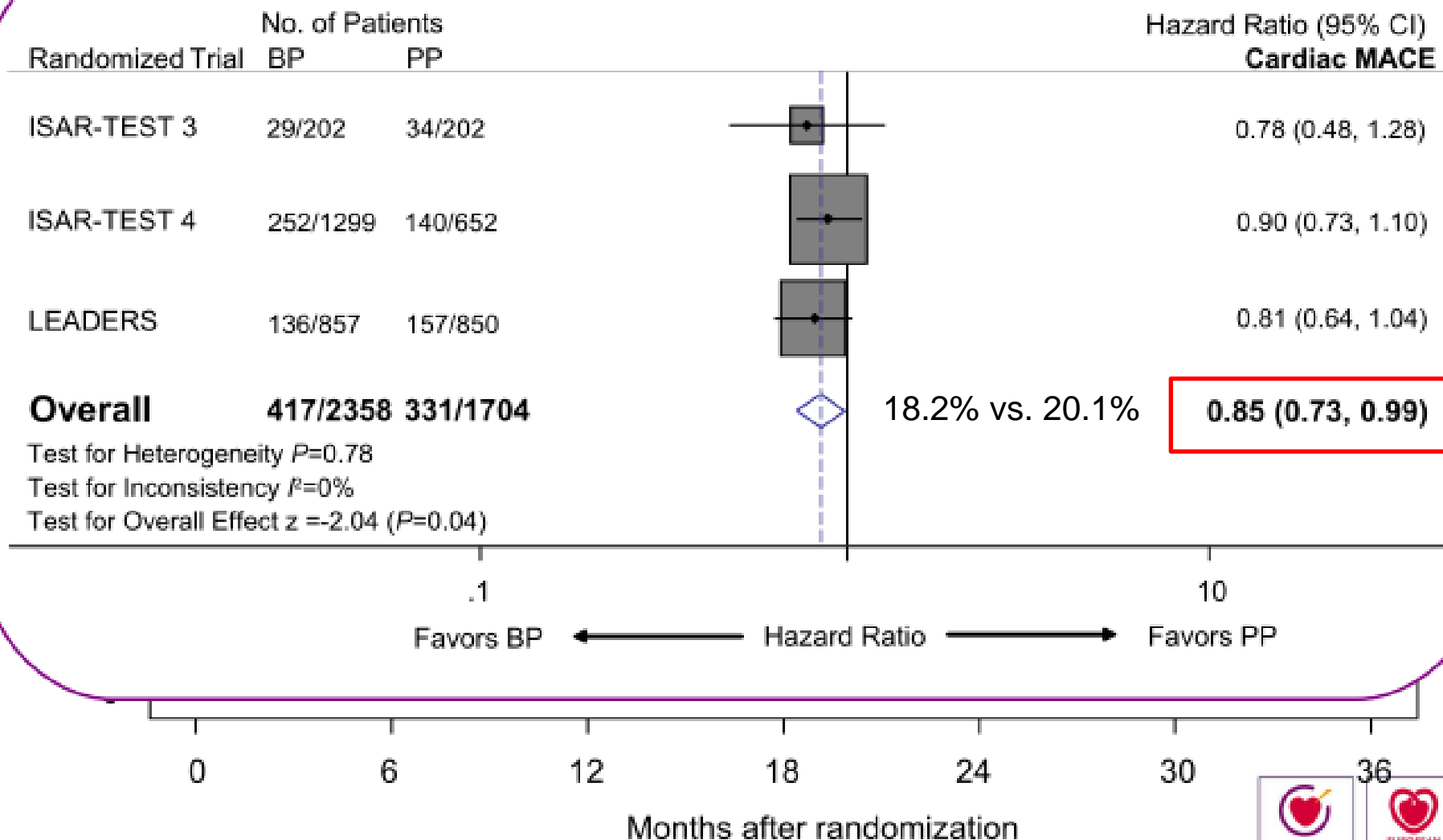


Target Lesion Revascularization



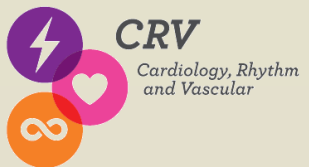
Primary Composite Endpoint

Cardiac death/MI/TLR

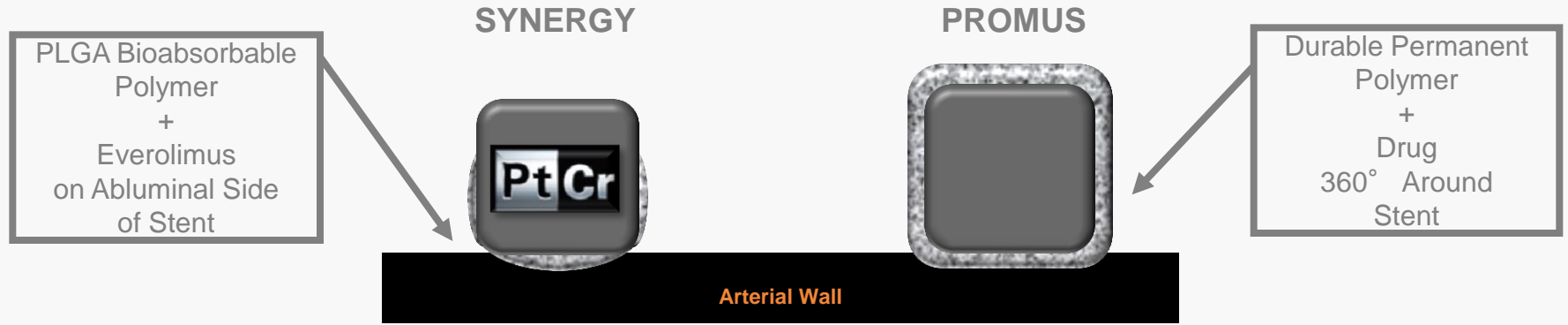
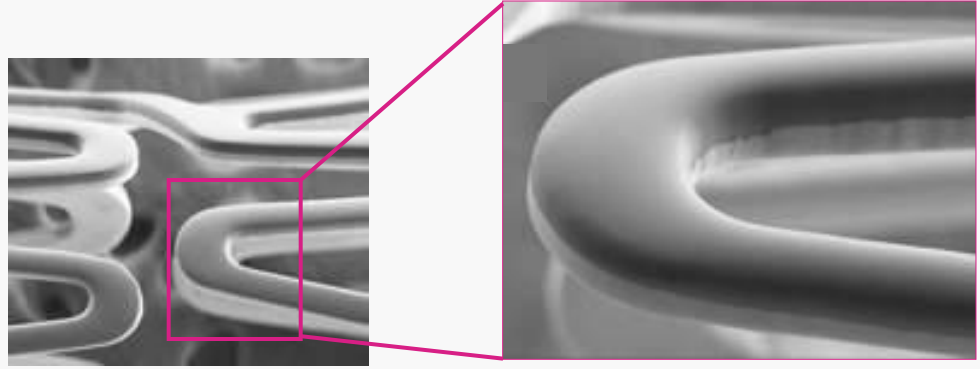


SYNERGY

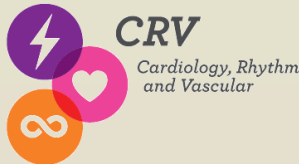
Bioabsorbable Polymer Everolimus-Eluting PtCr Stent



- Ultra-thin bioabsorbable polymer (PLGA) is only applied to the abluminal surface and is fully absorbed within 4 months
- Everolimus drug: Similar release kinetics to PROMUS Element™
- Enhanced Element Stent Design
- Strut Thickness: 74µm
- New Stent Delivery System
- Lowest polymer coating weight of any DES currently on the market



Thin Stent Strut Profiles on New Stent Platforms



	1 st Generation		2 nd Generation			3 rd Generation	4 th Generation	
DES Platform	Cypher™ Stent	TAXUS™ Express Stent	Endeavor™ Stent	XIENCE V™ Stent	TAXUS™ Liberté™ Stent	XIENCE™ Prime™ Stent	Element™ Stent Series	SYNERGY™ Stent
BMS Platform	Bx Velocity™ Stent 0.140 mm (0.0055") Stainless Steel	Express™ Stent 0.132 mm (0.0052") Stainless Steel	Driver™ Stent 0.091 mm (0.0036") Cobalt Chromium	Multi-Link Vision™ Stent 0.081 mm (0.0032") Cobalt Chromium	Liberté™ Stent 0.096 mm (0.0038") Stainless Steel	XIENCE Prime™ Stent 0.081 mm (0.0032") Cobalt Chromium	Element™ Stent 0.081 mm (0.0032") Platinum Chromium	Synergy™ Stent 0.074 mm (0.0029") Platinum Chromium

Bioabsorbable and Polymer-Free Stents

Clinical and Regulatory Status

Status	Primary Clinical Data Presented	Patients	Global Launch Planned
FIM	EVOLVE*	291	YES
CE Mark	LEADERS	1700	NO
CE Mark	NOBORI-I	243	NO
FIM+CE Mark	DESSOLVE-I+II	30+230	NO
CE Mark	FIM-II+EXCELLA-II	9+145	NO
CE Mark	BIOFLOW-I	30	NO
CE Mark	ISAR-TEST	450	NO
CE Mark	NEXT	323	NO
CE Mark	ABSORB A/B	131	YES
FIM	DESolve I	15	NO

Synergy™
(Boston Scientific)

BioMatrix Flex™
(Biosensors)

Nobori™
(Terumo)

MiStent™
(Micell)

DESyne™
(Elixir)

Orsiro™
(Biotronik)

Yukon Choice™
(Translumina)

CRE8™
(CID)

BVS™
(Abbott)

DESolve™ Nx
(Flivir)

 Bioabsorbable Abluminal Polymer

 Polymer Free

 Bioabsorbable Conformal Polymer

 Fully Bioresorbable

Conclusion



- ❖ Newer generation DES appear to be associated with fewer LST and VLST events
- ❖ Whether this is consequent upon DES design, drug and polymer improvements or in part coincident with technical and procedural improvements is unclear
- ❖ There is an almost universal move to minimize drug and polymer load

Thank You

