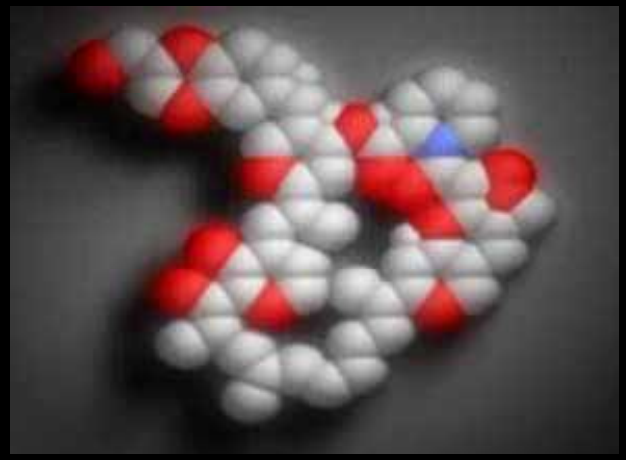
Promus-Element Stent

Alan C. Yeung, MD
Stanford University School of Medicine

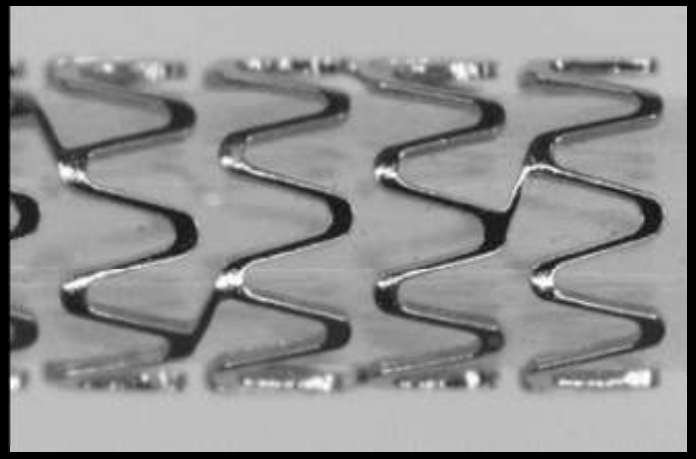
Elements of DES Design

DES design affects procedural success and clinical outcomes

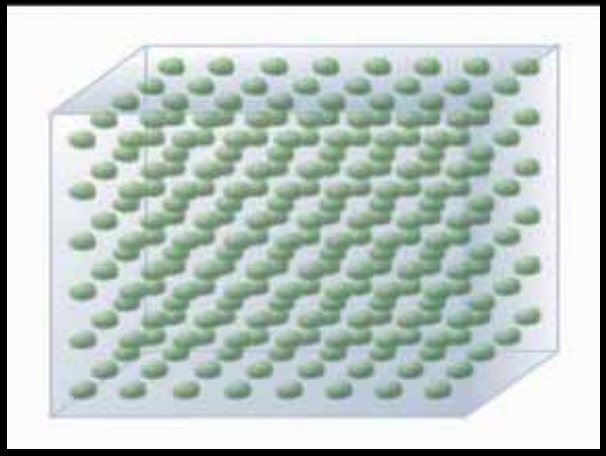
Drug



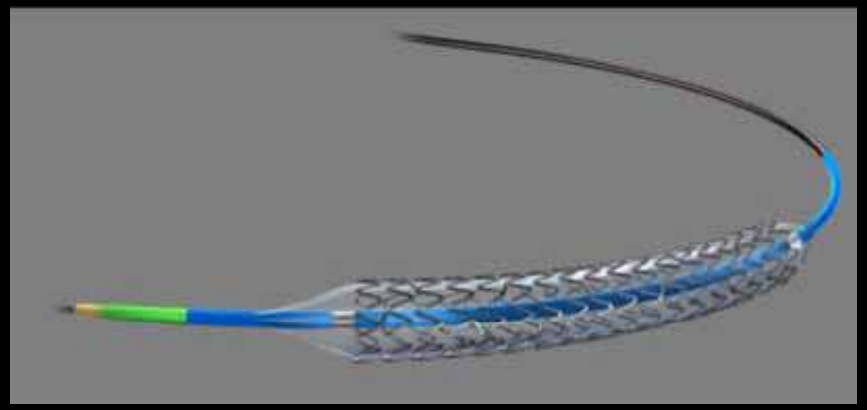
Scaffold



Polymer

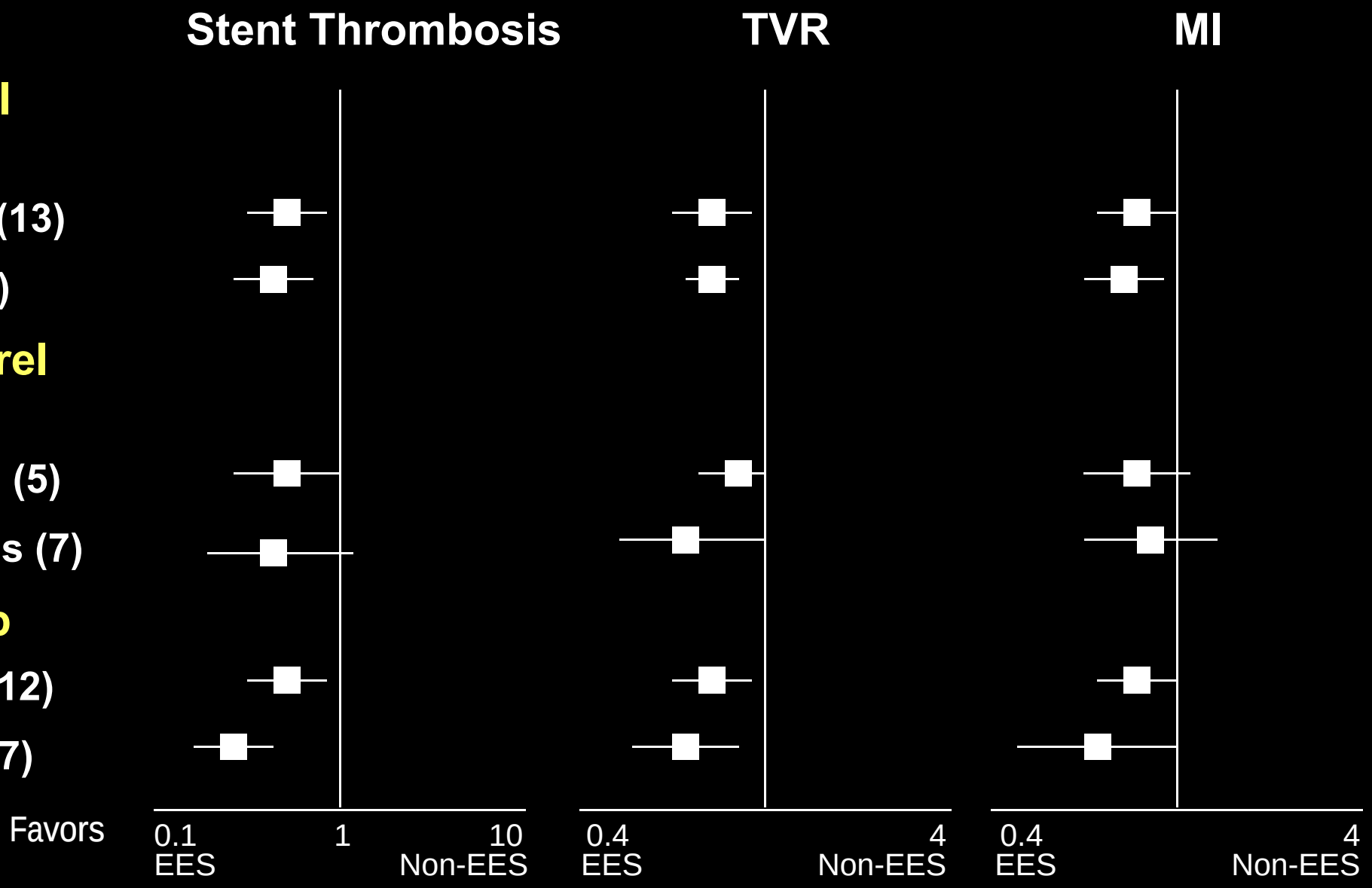


Delivery System



Clinical Outcomes with EES vs. non-EES DES

Meta Analysis of 13 RCCT Involving 17,097 Patients



Baber et al. JACC 2011;58:1569-77

Everolimus-Eluting Stents
Xience V™ and PROMUS Element™

Same Drug and Polymer

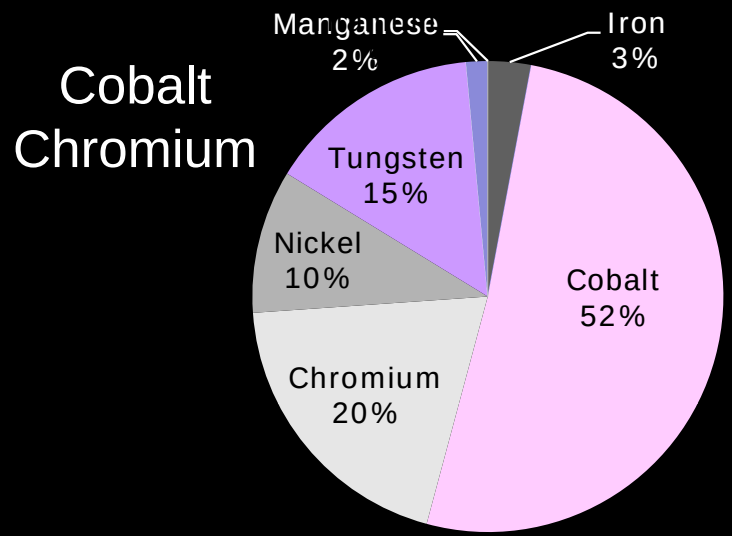
Everolimus concentration: 100 ug/cm^2

Polymer: PVDF-HFP

Polymer Thickness: 8 μm

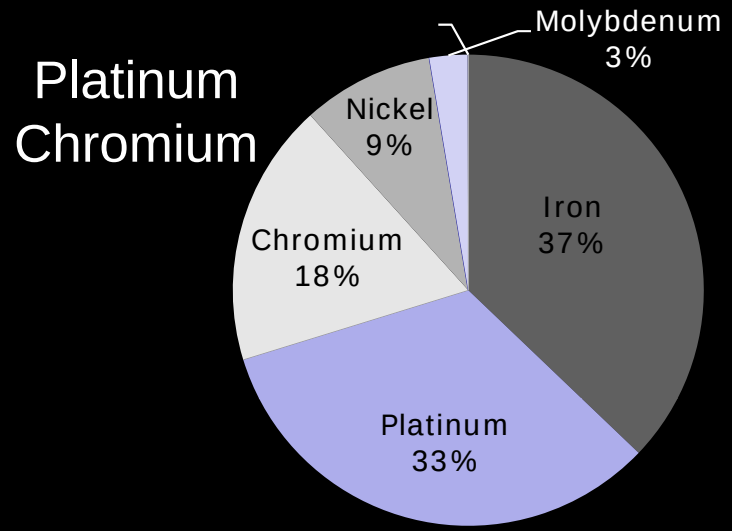
Xience V™ CoCr Stent

Strut Thickness: 81 μm



PROMUS Element™ PtCr Stent

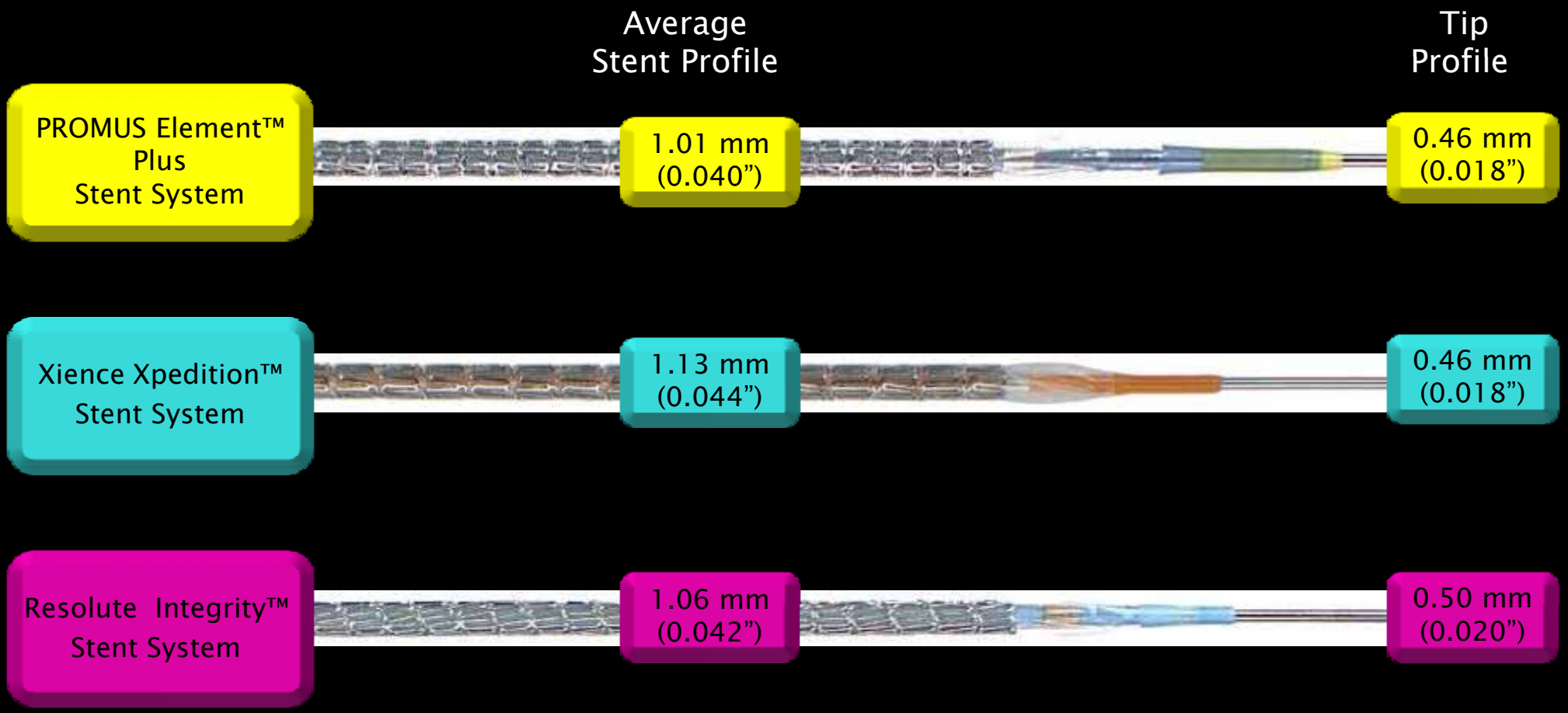
Strut Thickness: 81 μm



Metal composition source: Menown et al, Adv Ther, 2010

Profile and Deliverability

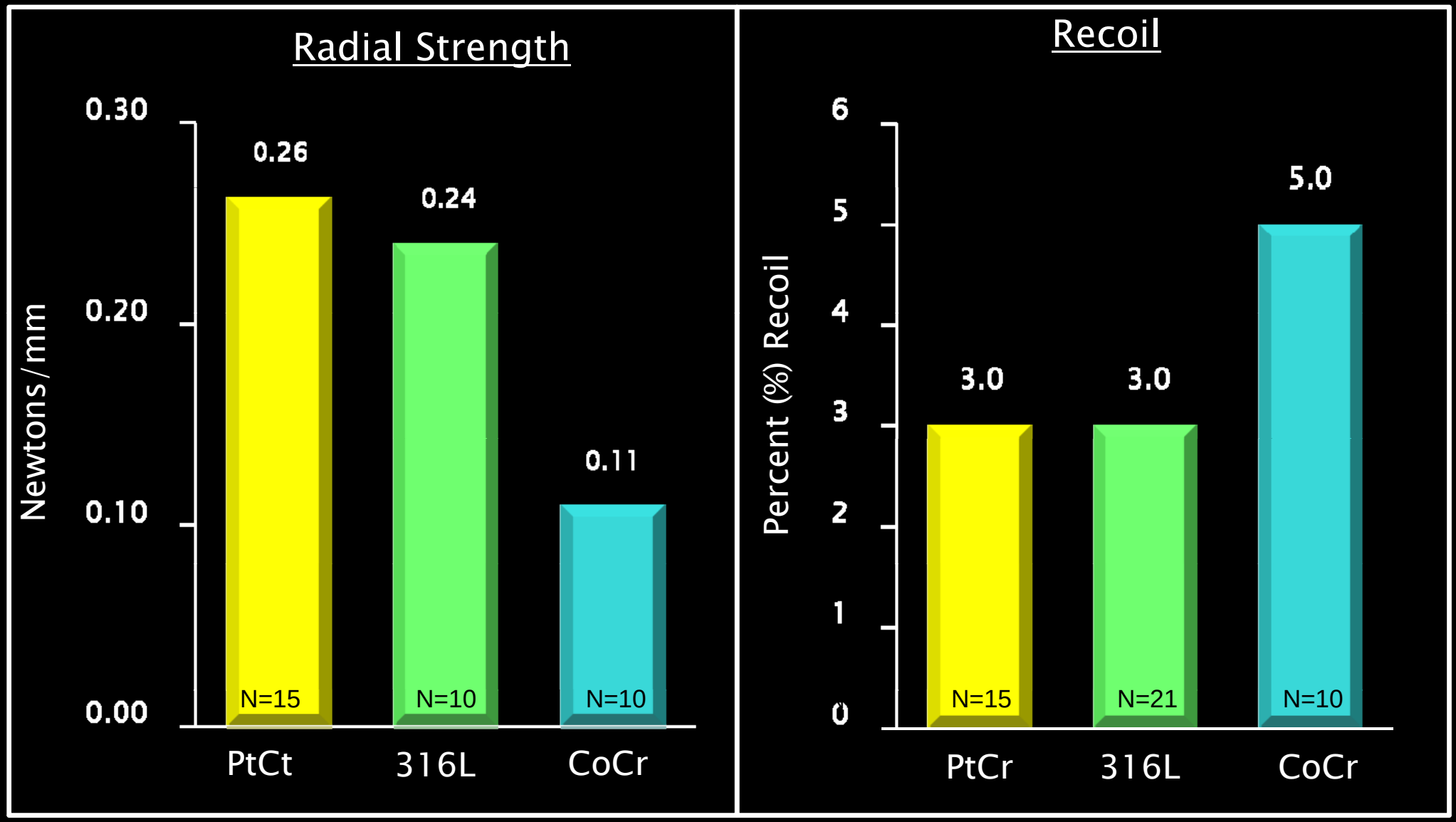
Achieved via thin struts and stent delivery system



Data on file. at Boston Scientific. 2.50 mm stent systems.
The Synergy Stent is an investigational device in the US and Japan and not for sale.

Radial Strength and Recoil

Bench Test Data

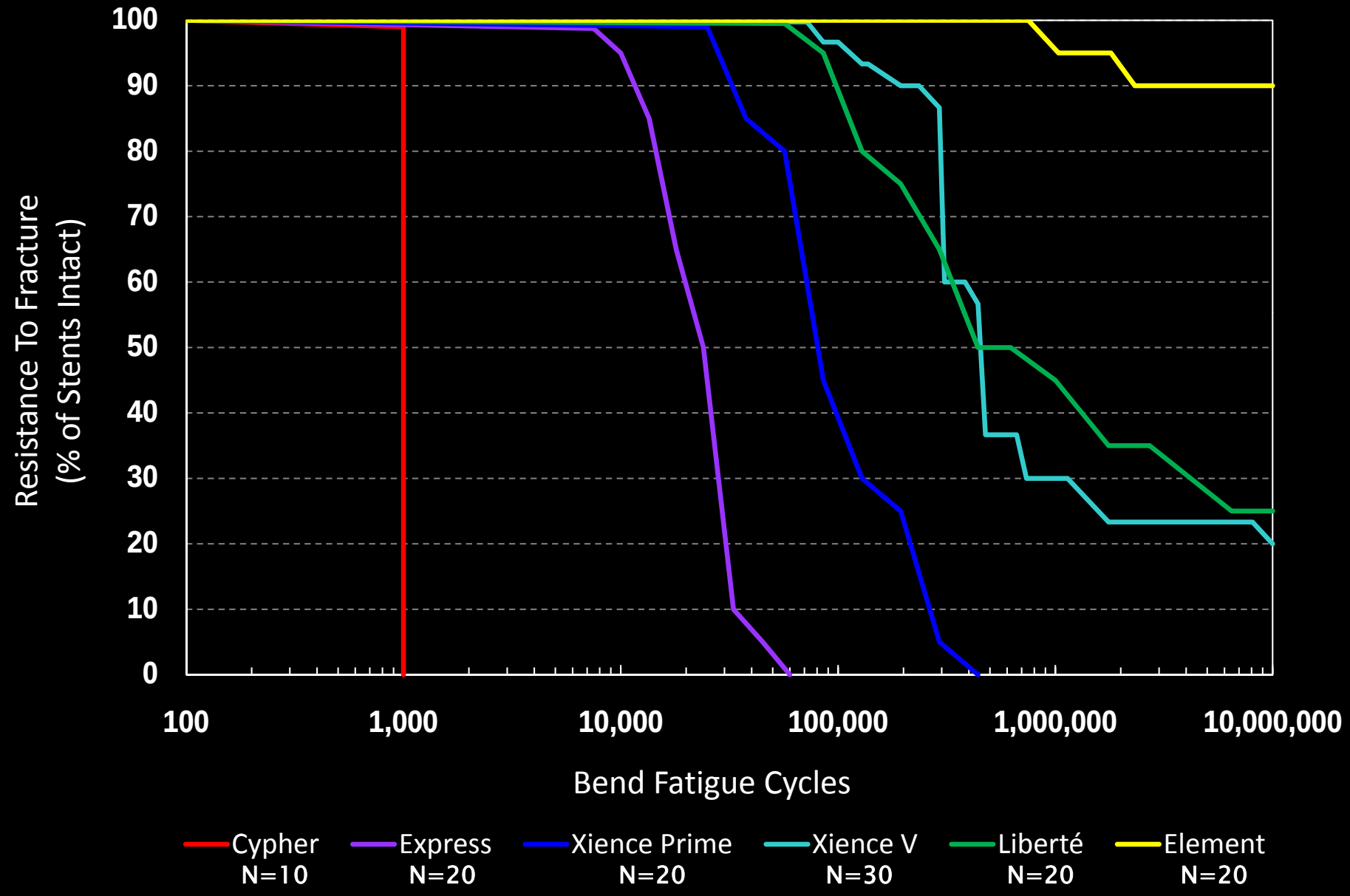


PROMUS Element™ Stent TAXUS Liberte™ Stent Xience V™ Stent

Data on file at Boston Scientific. 2.5mm diameter stents. Bench test results may not be indicative of clinical performance.

Increased Fracture Resistance with Flexibility

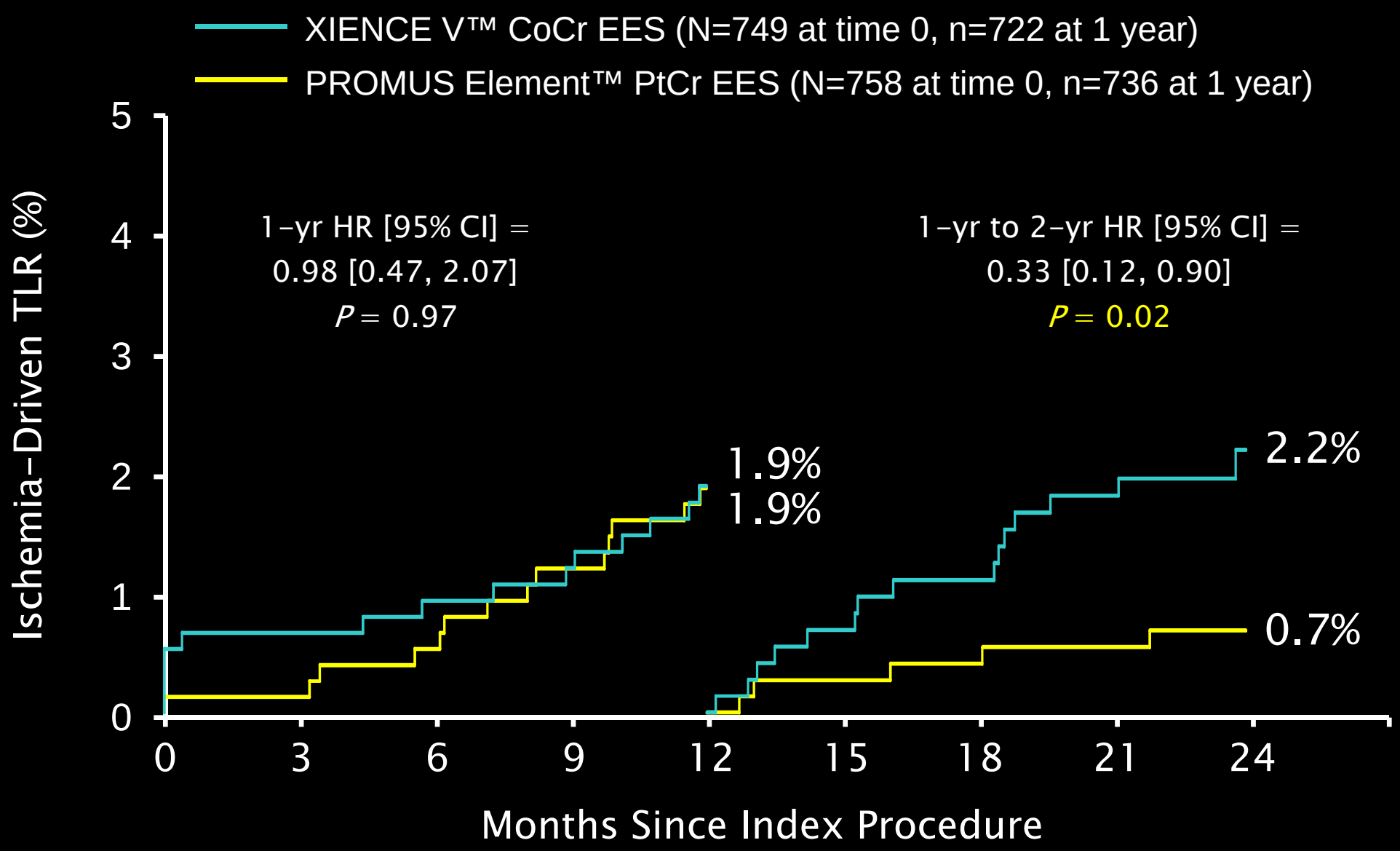
Bend Fatigue Bench Test



Data on file at Boston Scientific. 3.0mm diameter stents, 5mm test length. Bench test results not necessarily indicative of clinical performance.

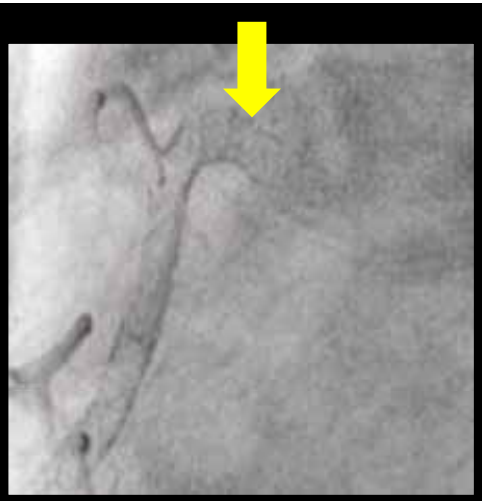
PLATINUM Workhorse

2-Year Landmark Analysis Ischemia-Driven TLR



Presented by Gregg W. Stone, MD at ACC 2012.

Platform Differences May Impact Clinical Outcomes



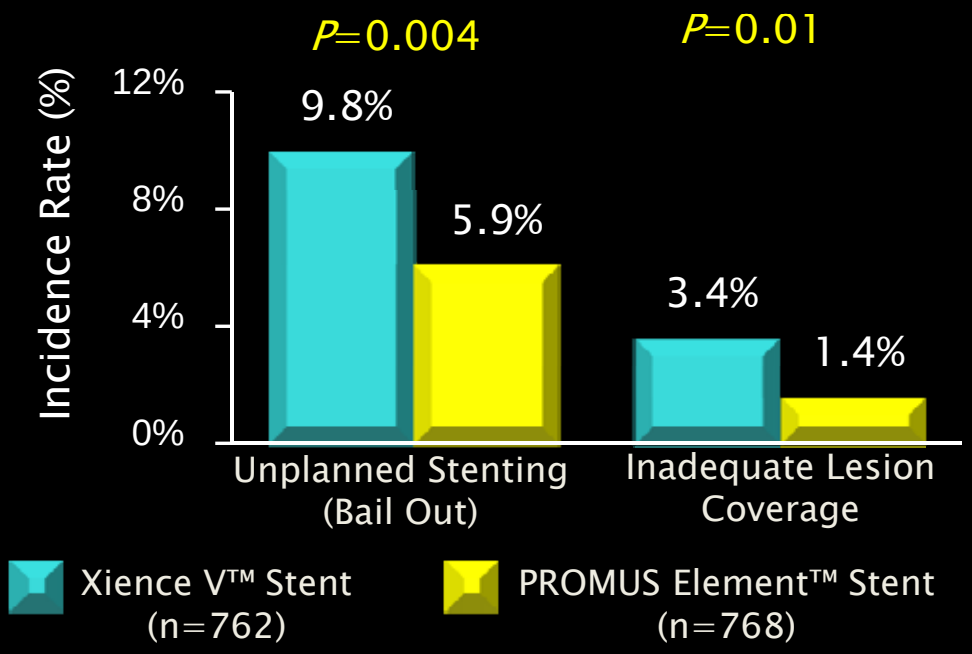
PROMUS Element™ Stent

Platform Flexibility and Conformability:

- Reduces vessel straightening
- Affects shear stress and flow velocity
- Influences fracture resistance
- Impacts ID-TLR / Restenosis

Reduced Bailout & Inadequate Lesion Coverage

PLATINUM Workhorse Trial

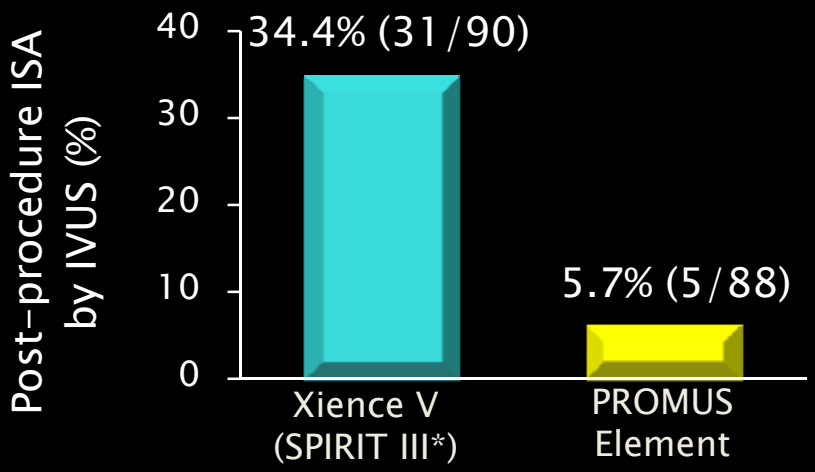


Stone et al. JACC. 2011;57:1700-1708

Incomplete Stent Apposition

PLATINUM QCA Trial

Pre-specified Efficacy Endpoint:
ISA Post-Procedure versus Historical Control*



Meredith et al. *EuroIntervention* 2011;7:84-90
*SPIRIT III Trial (Stone et al. *JAMA*. 2008;299:1903)

HOST
ASSURE

Randomized Comparison of PtCr-EES vs CoCr-ZES in All-Comers Receiving PCI

: The HOST-ASSURE Randomized Trial

Hyo-Soo Kim, MD/PhD

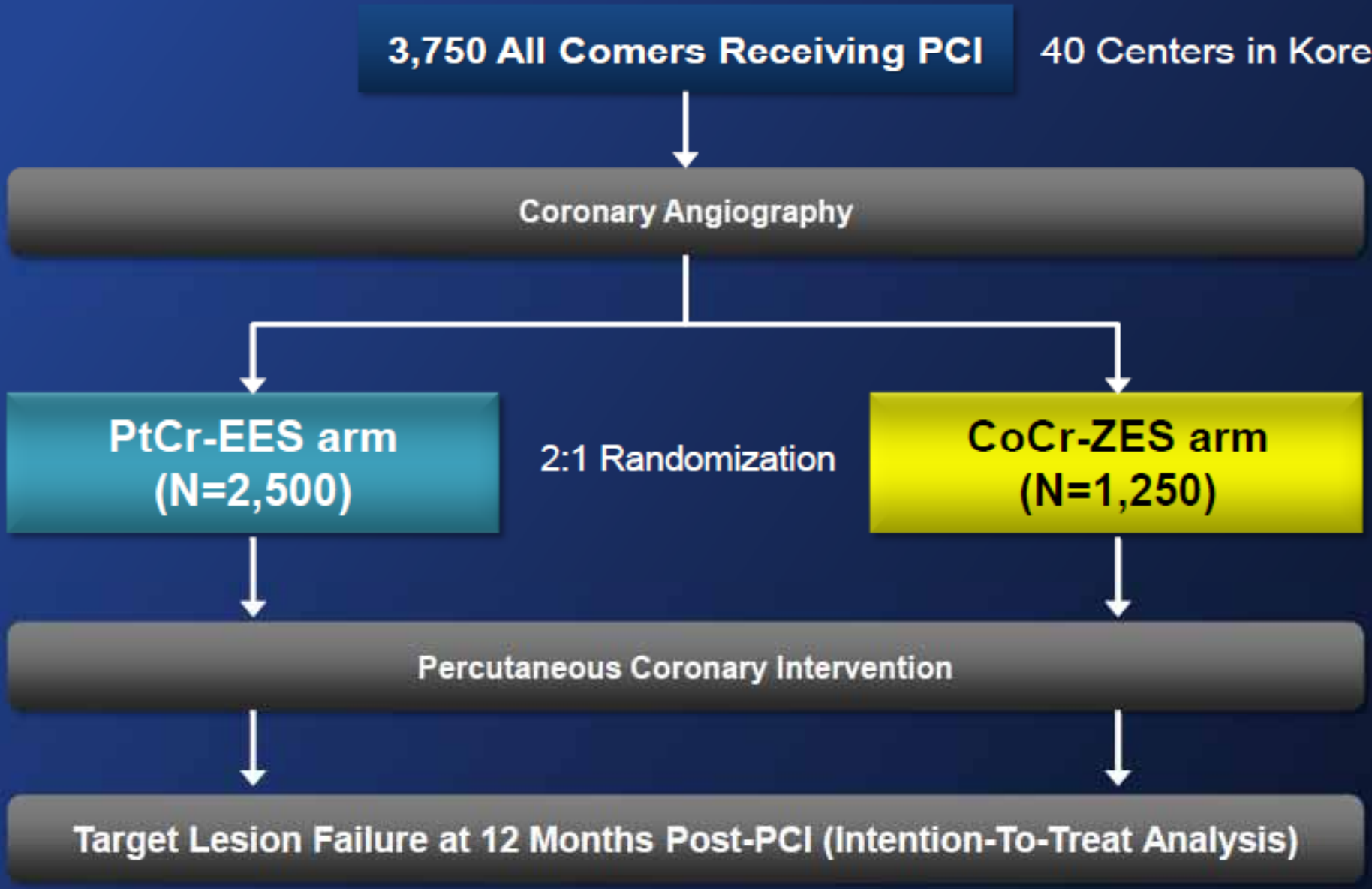
Kyung-Woo Park, Si-Hyuck Kang, Kwang-Soo Cha,
Byoung-Eun Park, Jay-Young Rhew, Hui-Kyung Jeon, In-Ho Chae
On Behalf of The HOST-ASSURE Trial Investigators

Seoul National University Hospital, Seoul, Korea

Study Design

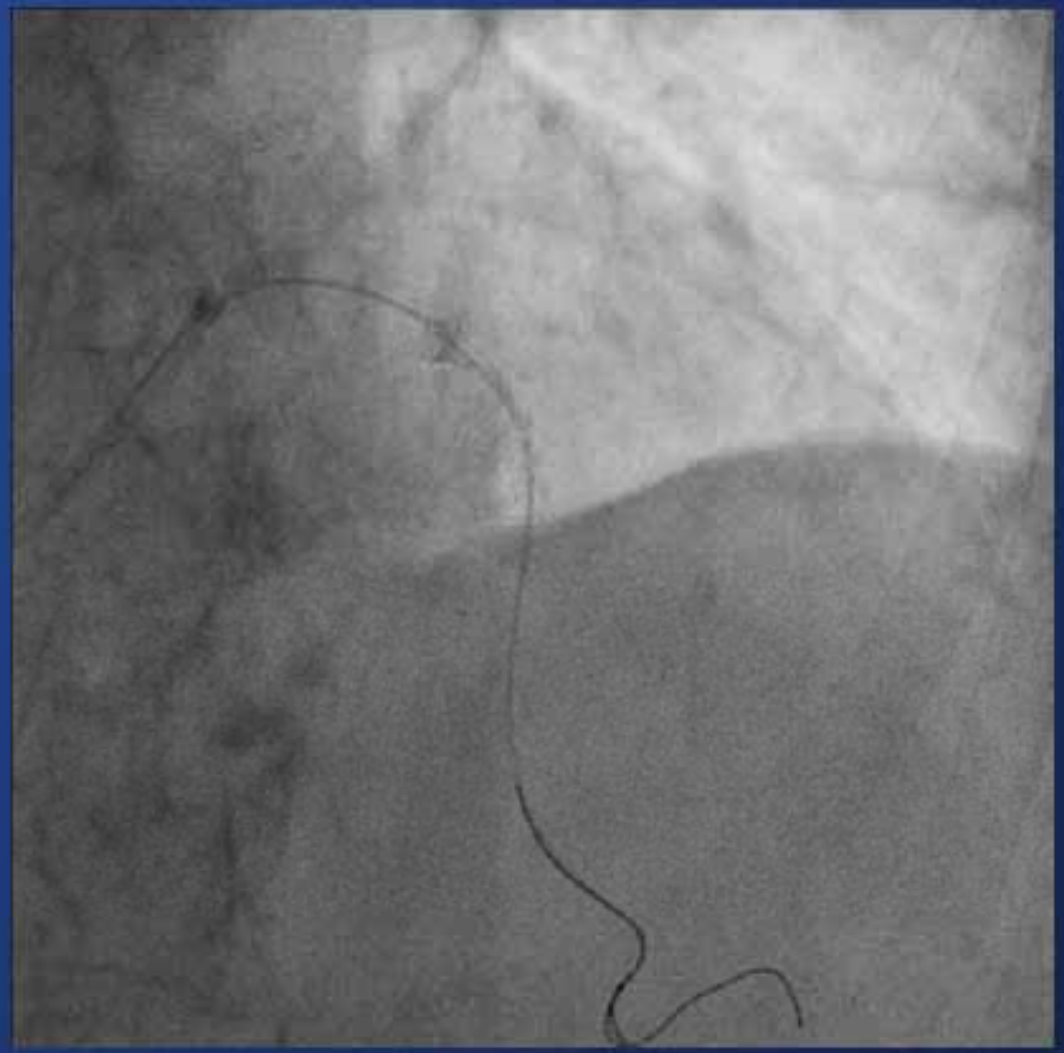
Prospective, single-blinded, randomized multi-center trial

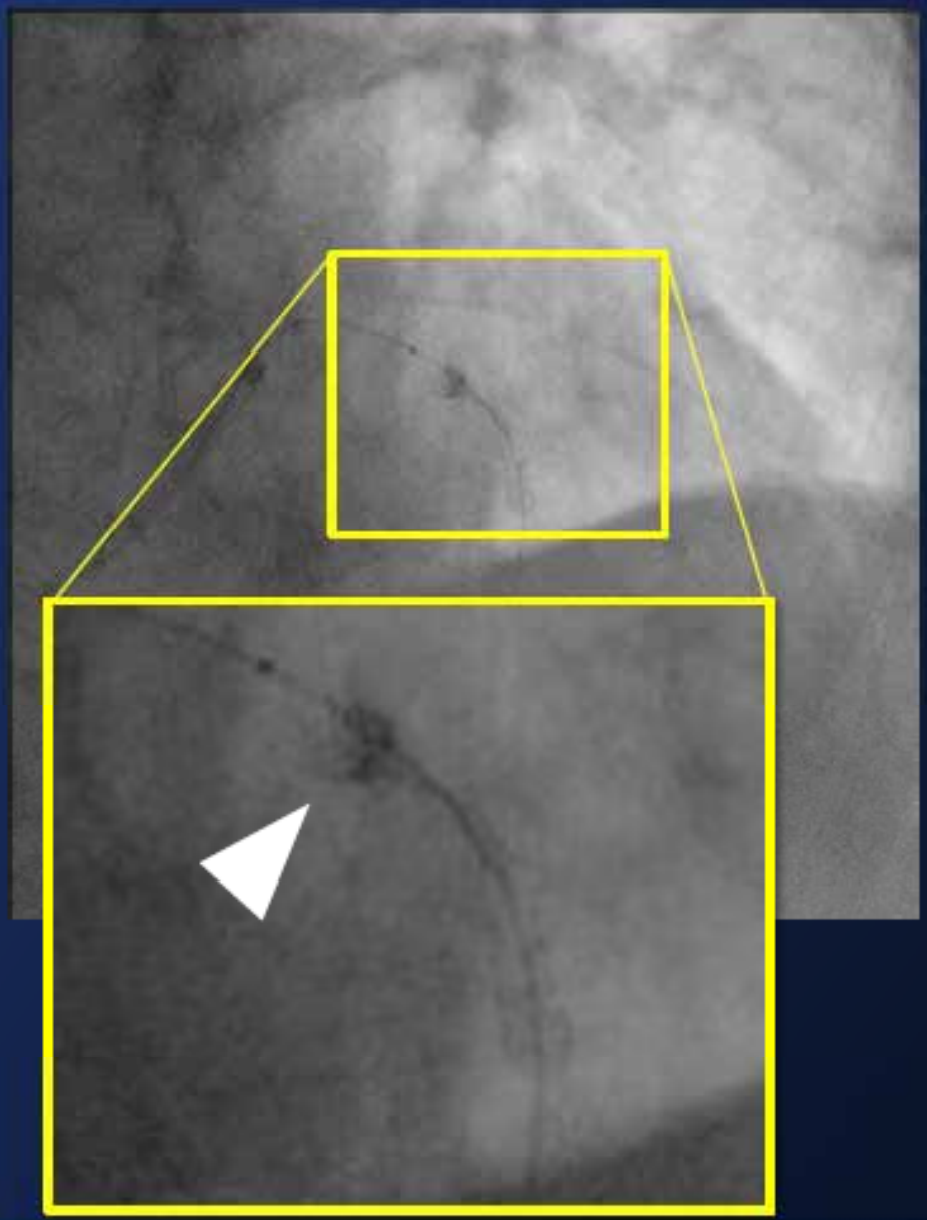
HOST ASSURE



Longitudinal Stent Deformation (LSD) : a trade-off of thin strut

How often does it happen?
Under what conditions does it occur?
How severe can it be?





Baseline Characteristics

HOST ASSURE

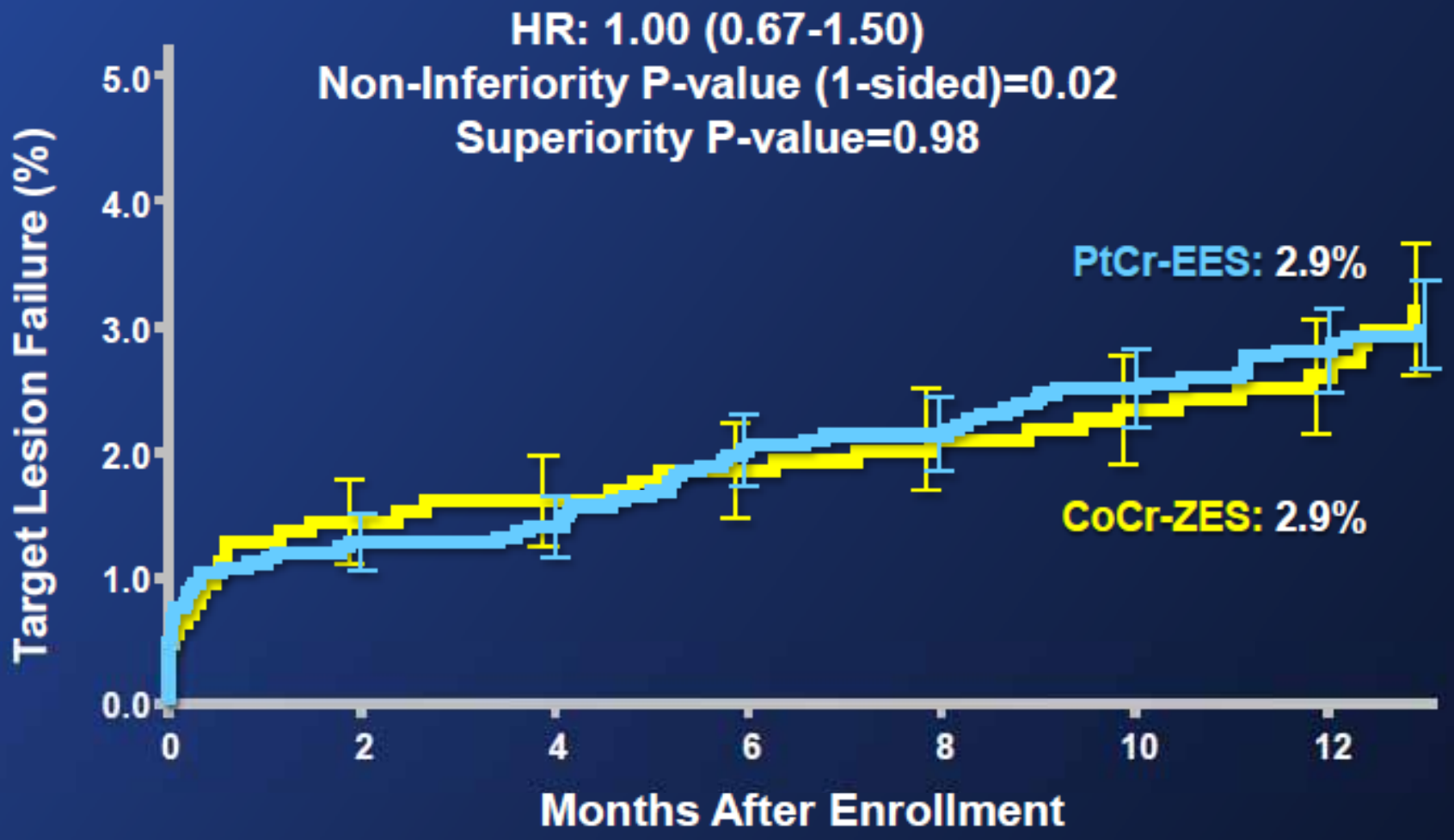
Characteristic	PtCr-EES (N=2,503)	CoCr-ZES (N=1,252)
Age	63.1±10.8	63.5±10.7
Men	1,746 (69.8)	820 (65.6)
Body mass index	24.6±3.2	24.7±3.2
Hypertension	1,706 (68.2)	852 (68.1)
Diabetes	795 (31.8)	401 (32.0)
Dyslipidemia	1,601 (64.0)	822 (65.7)
Current smoker	823 (32.9)	369 (29.5)
Chronic renal failure	59 (2.4)	36 (2.9)
Peripheral artery disease	41 (1.6)	27 (2.2)
Cerebrovascular disease	172 (6.9)	79 (6.3)
Previous PCI	247 (9.9)	120 (9.6)
Previous bypass surgery	16 (0.6)	10 (0.8)
Pervious MI	116 (4.6)	49 (3.9)
Previous CHF	41 (1.6)	13 (1.0)
Clinical diagnosis		
Slient ischemia	119 (4.8)	63 (5.0)
Stable angina	746 (29.8)	367 (29.3)
Unstable angina	903 (36.1)	476 (38.0)
NSTEMI	452 (18.1)	209 (16.7)
STEMI	283 (11.3)	137 (10.9)

ACS 65.5%

Target Lesion Failure

Composite of C-death, TV-related MI, ischemia-driven TLR

HOST ASSURE

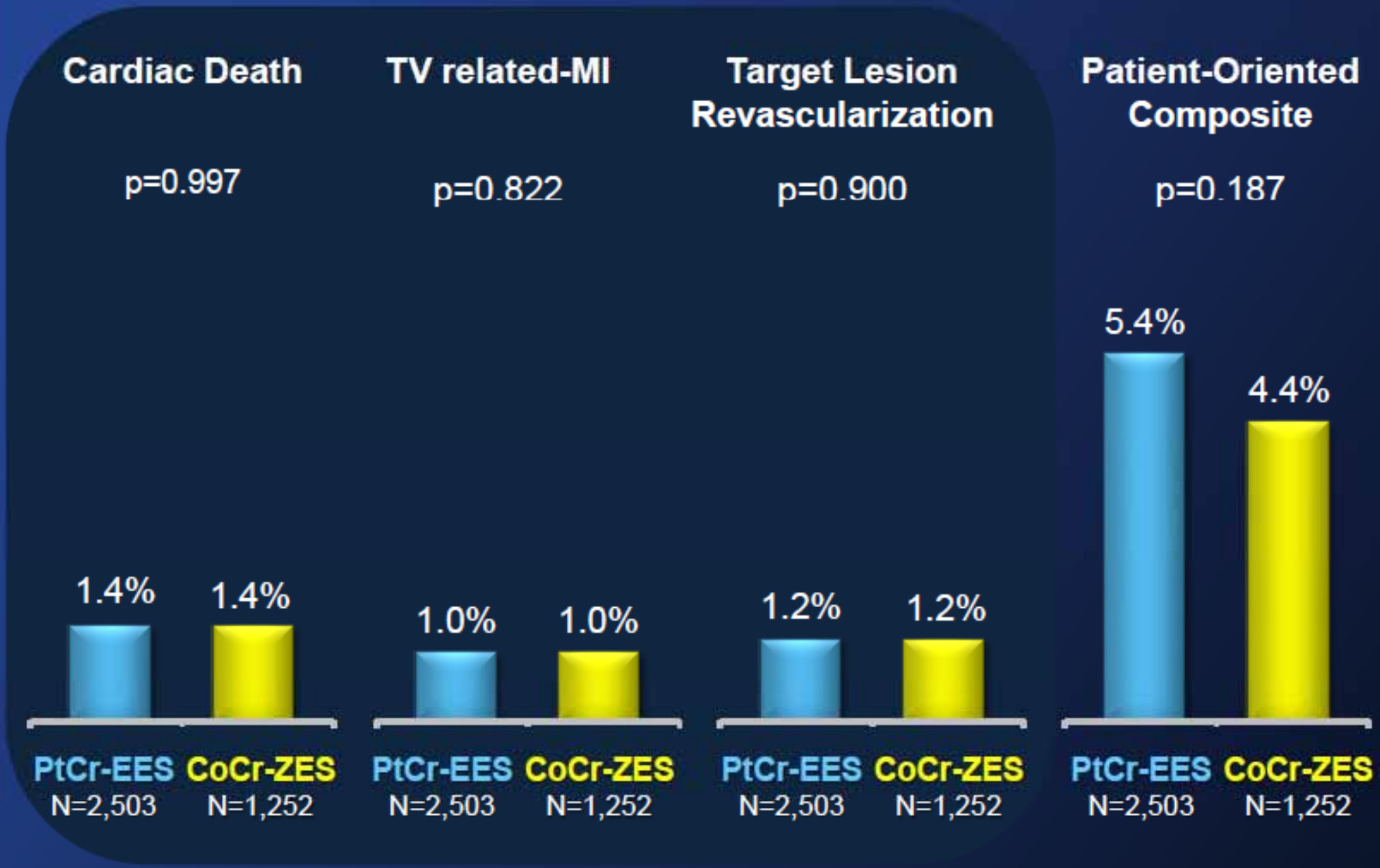


Patient Number At Risk

PtCr-EES	2,503	2,446	2,426	2,408	2,401	2,376	1,887
CoCr-ZES	1,252	1,222	1,213	1,209	1,205	1,198	952

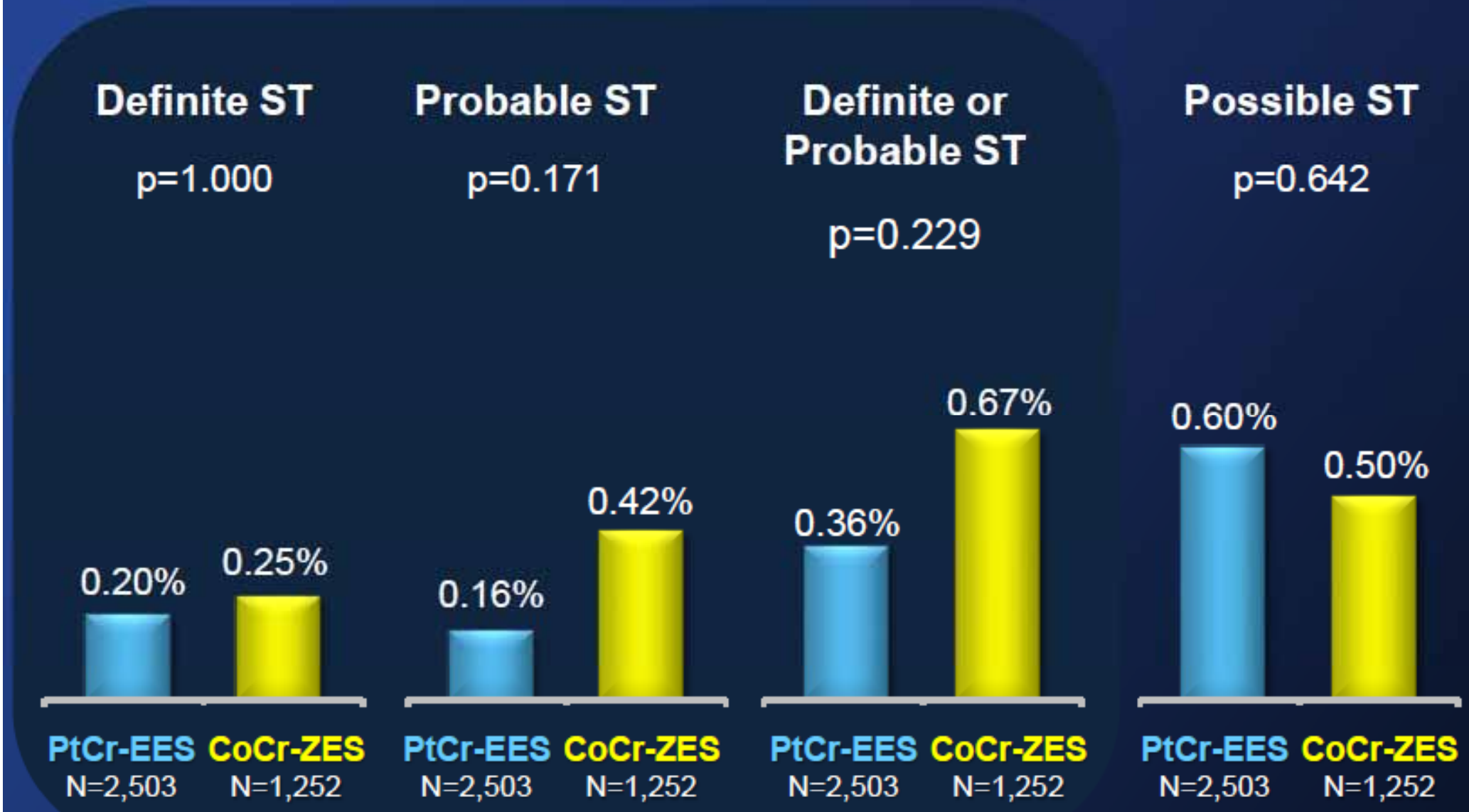
Clinical Events at 12 Months

HOST ASSURE

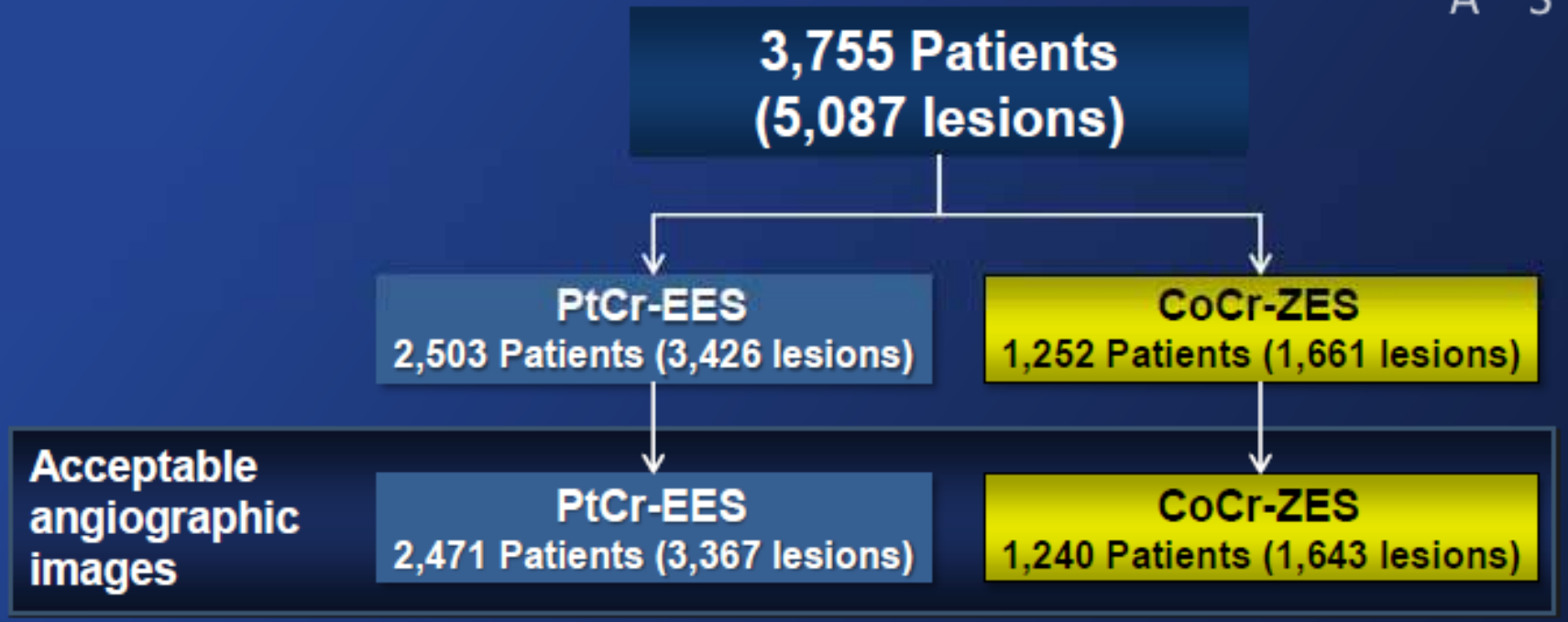


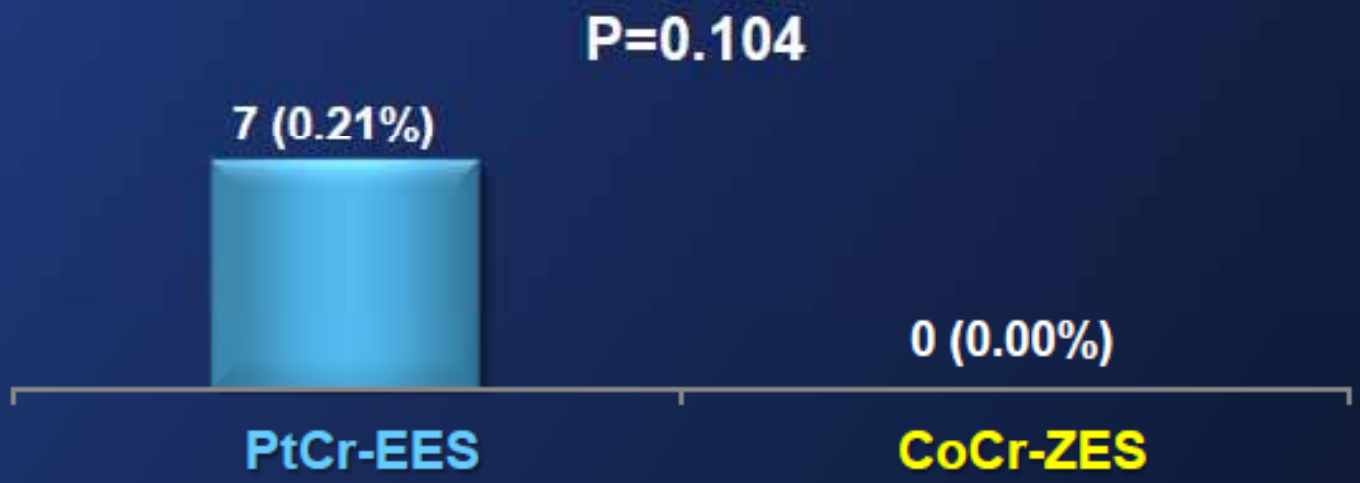
Stent Thrombosis

HOST ASSURE



Longitudinal Stent Deformation





Incidence: 2.1 (95% CI: 0.8-4.3) per 1,000 lesions treated with PtCr-EES

Details of 7 Patients with LSD

HOST ASSURE

Age /Sex	Lesion Loci	Stent Size (mm)	Precipitating Factor	Bifurcation	Ostial Lesion	Segment of Stent Involved	Additional Stenting Required	Future Clinical Events
61/M	LMCA	P-E 3.0x24	Deep engagement of guiding catheter (GC)	Yes	Yes	Proximal part	No	No
59/M	LMCA	P-E 3.0x28	Deep engagement of GC d/t trapped retrograde guidewire (CTO)	No	No	Proximal part	No	No
50/F	Mid LAD	P-E 4.0x28	Deep engagement of GC d/t trapped IVUS catheter	No	No	Proximal part	No	No
72/M	Proximal RCA	P-E 3.0x28	Deep engagement of GC d/t trapped stent	No	No	Proximal part	No	No
39/M	Proximal LAD	P-E 4.0x28	Advancing Adjunctive Balloon catheter	Yes	No	Proximal part	No	No
81/F	Mid LAD	P-E 3.0x20	Advancing Adjunctive Balloon catheter	Yes	No	Proximal part	Yes	No
68/M	Mid LAD	P-E 3.0x28	Advancing Adjunctive Balloon catheter	No	No	Proximal part	No	No

Conclusions

HOST ASSURE

1) PtCr-EES was **non-inferior** to CoCr-ZES at 1 year regarding TLF. Clinical outcomes were **very similar** between the two stents.

2) Both stents demonstrated **outstanding safety** as well as **efficacy.** : ST <1%; TLF <3% in PCI population of ***"all-comers"***

3) **LSD** was very rare, observed only in a few cases of PtCr-EES, and was **not associated with future adverse clinical events.** There was **not a serious systematic shortening** of either stent platform.

Promus PREMIER™ Stent

Next generation durable polymer stent technology

Design Goals

Customized PtCr Stent Architecture

Balance of strength and flexibility

Everolimus Drug & PVDF-HFP Polymer

Outstanding safety and efficacy

Enhanced Stent Delivery System

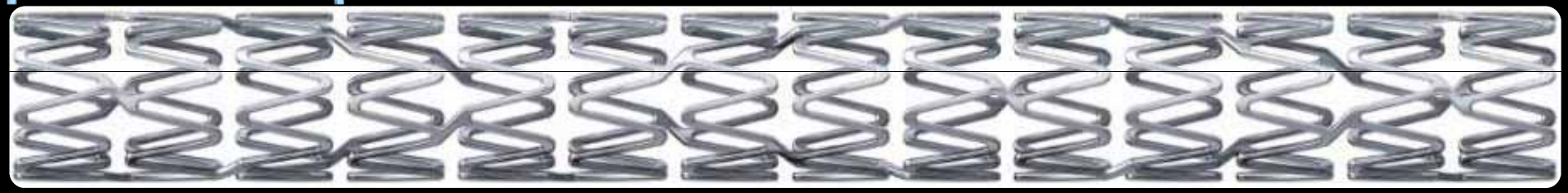
Improved deliverability

*Data on file–Boston Scientific. Promus PREMIER is an investigational device in the US and not for sale.

Promus PREMIER™ Stent

Customized Architecture for Strength and Flexibility

4 connectors on proximal end → Proximal end more robust and resistant to axial length change (ALC)



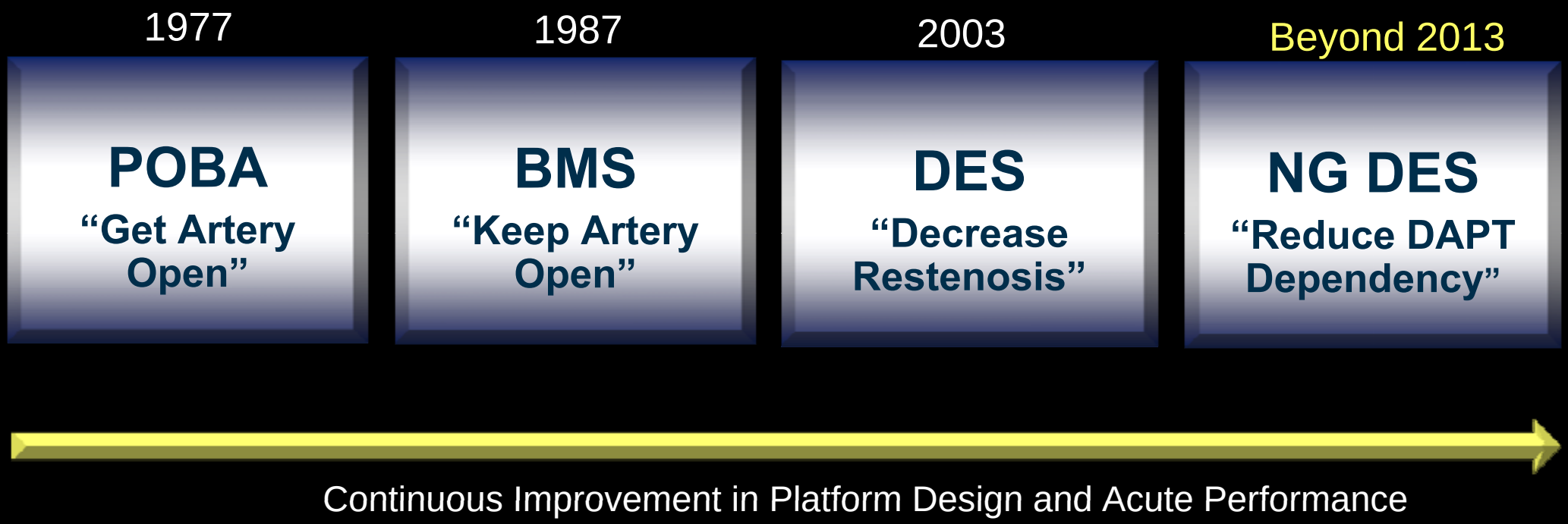
*ALC occurs most frequently on proximal end

2 connectors throughout body

Maintain flexibility, conformability, and fracture resistance

Data on file–Boston Scientific. Promus PREMIER is an investigational device in the US and not for sale.

Evolution of PCI



SYNERGY™ Everolimus-Eluting Stent with Synchrony™ Bioabsorbable Coating

Polymer and drug applied as ultra-thin abluminal coating

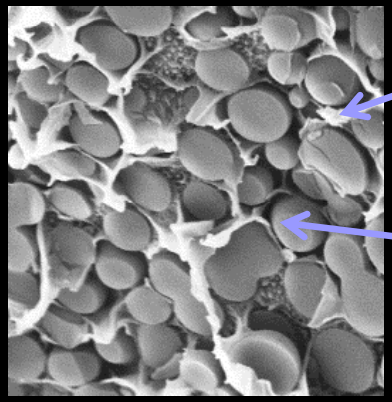
Synchronized drug release and polymer absorption

Polymer gone shortly after completion of drug elution at 3 months

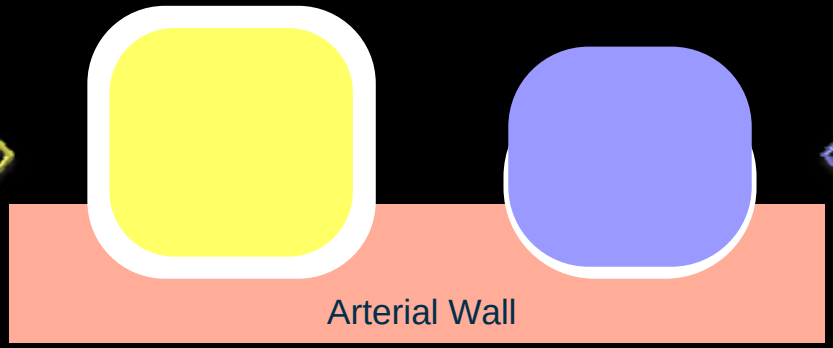
SYNERGY Stent

Abluminal Coating

Coating Microstructure



Stent Strut Cross Sections



PROMUS Element

PVDF durable polymer 360° around stent strut

SYNERGY

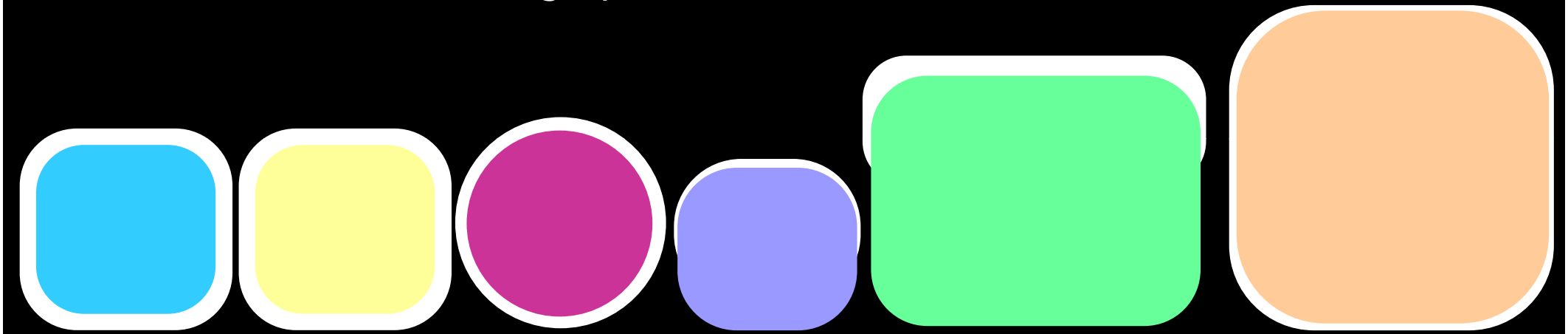
PLGA bioabsorbable polymer only on abluminal surface

The SYNERGY™ stent is an investigational device in the US and Japan and not for sale.

SYNERGY™ Stent Platform

Strut and Coating Thickness In Perspective

Durable Polymer Coated Stents			Bioabsorbable Polymer Coated Stents		Bioabsorbable Stent
Xience V™	PROMUS Element™	Resolute Integrity™	SYNERGY™	BioMatrix Flex™	BVS



Strut Thickness					
81 µm (0.0032”)	81 µm (0.0032”)	89 µm (0.0035”)	74 µm (0.0029”)	120 µm (0.0047”)	150 µm (0.0059”)
Coating Thickness					
Conformal 8µm / side	Conformal 8µm / side	Conformal 6µm / side	Abluminal 4µm	Abluminal 10µm	Conformal 3µm / side

The SYNERGY™ stent is an investigational device in the US and Japan and not for sale.

EVOLVE II Study Design
SYNERGY™ Stent Pivotal Trial

1,954-2,006 patients with atherosclerotic native coronary lesions

≤ 34 mm in length, RVD ≥2.25 mm ≤ 4.0, %DS ≥ 50

Up to 3 lesions in 2 vessels

(excludes LM disease, CTO, ISR, STEMI)

Randomized Cohort (RCT)

Up to 160 global sites

- **PROMUS Element™ Plus N=842**
- **SYNERGY™ N=842**

PK Substudy

SYNERGY™ N=20-30

Diabetes Substudy

SYNERGY™ N=250-292

RCT Design

Mulitcenter noninferiority trial

Single-blind, 1:1 randomization

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

Follow-up: 30d, 6m, 12m, 18m and annual 2-5 yrs

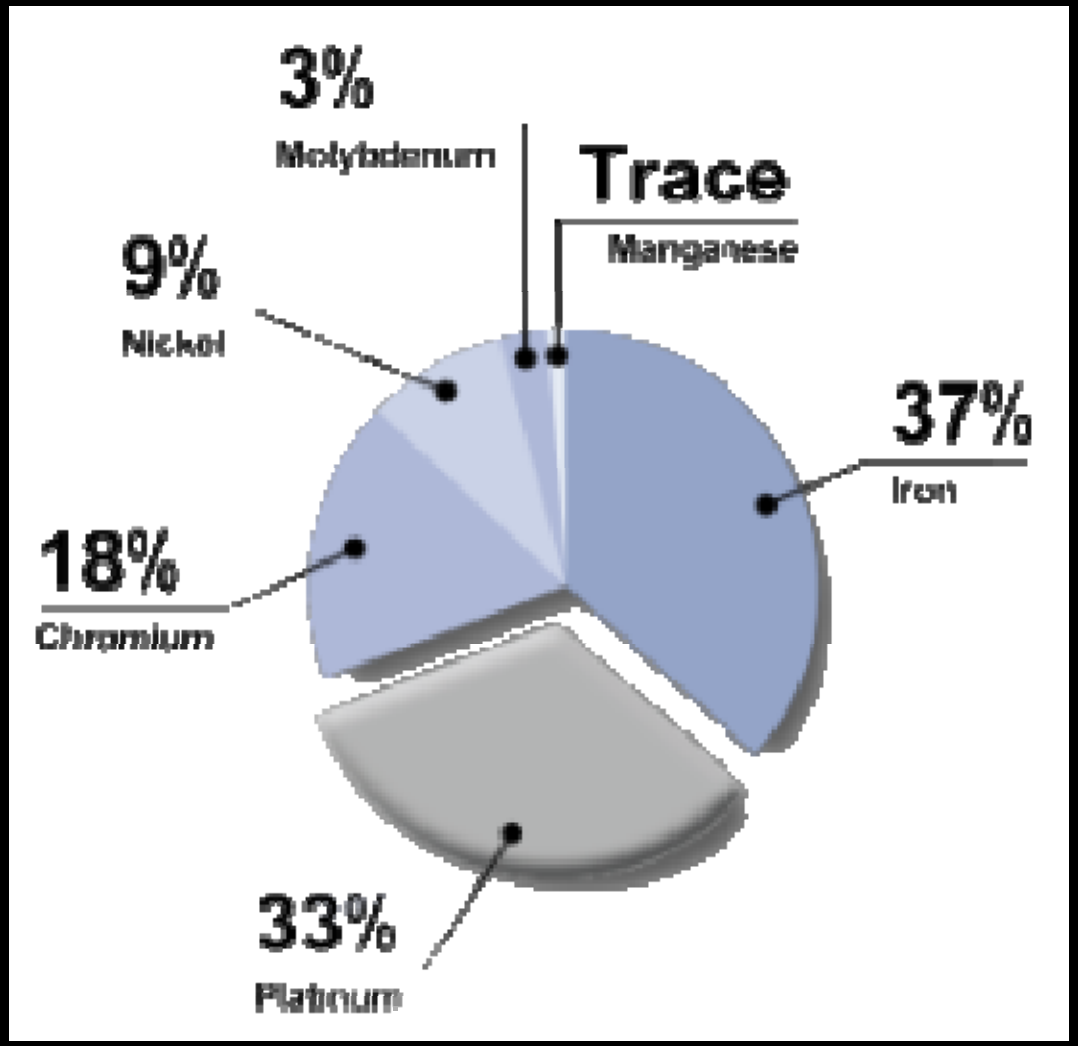
The SYNERGY™ stent is an investigational device in the US and Japan and not for sale.

Current Status of Coronary Stenting:
Summary

- All DES are not created equal; EES consistently reduce stent thrombosis, TVR; MI vs. non-EES DES.
- Among EES, late outcomes (TLF, ID-TLR) beyond 1 year may be influenced by differences in metal platform characteristics.
- Platform flexibility and conformability impacts vessel angulation, shear stress, flow velocity, and fracture resistance, which influence ID-TLR and restenosis.
- A stent platform with a customized design to increase axial robustness while maintaining flexibility and conformability may further optimize clinical performance.
- Bioabsorbable polymer DES may improve late outcomes (reduce late / very late ST), minimize DAPT dependency, and enhance healing vs. durable polymer DES. This will be established in further trials.

Back Up

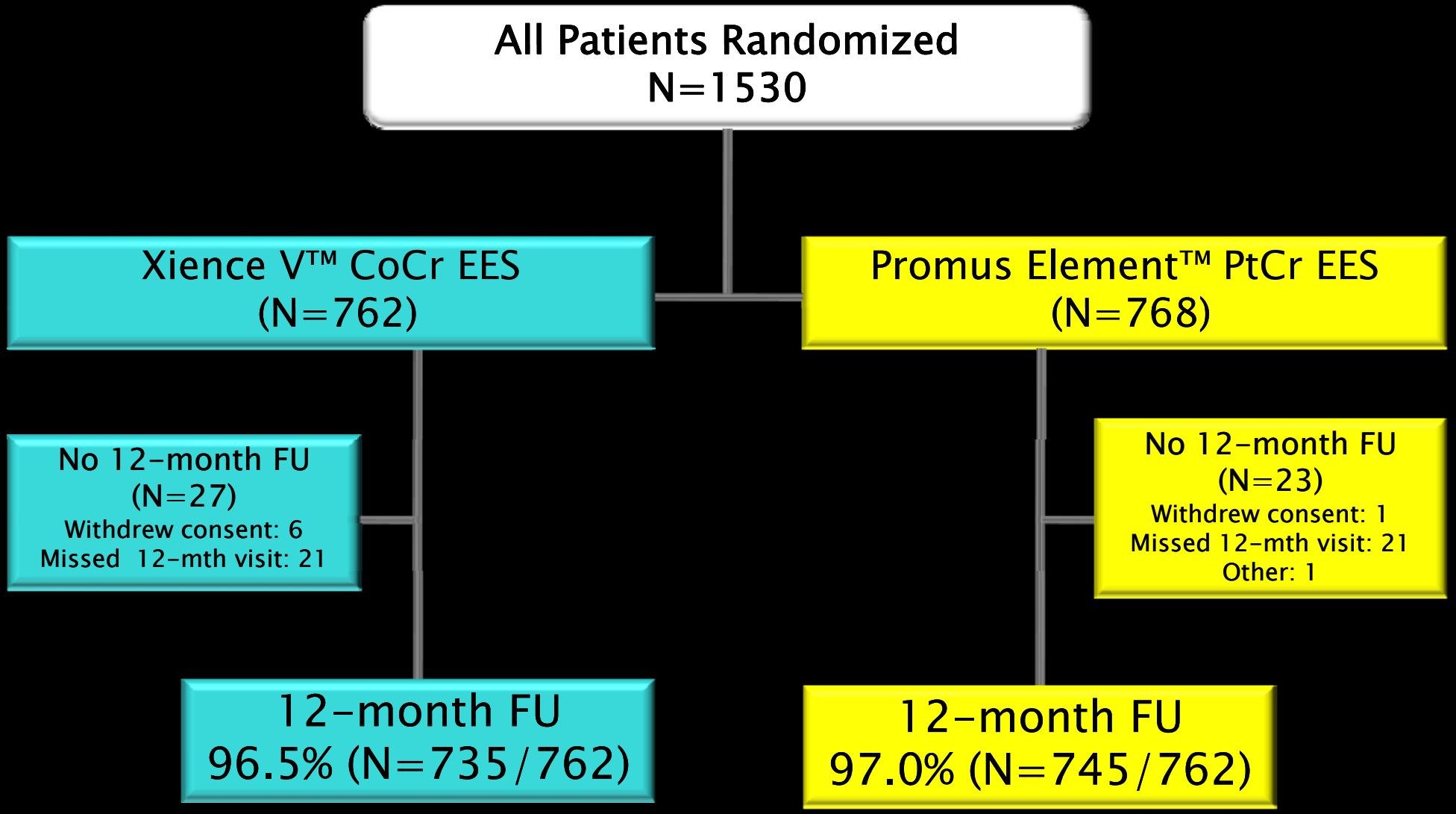
Platinum Chromium (PtCr) Alloy



- Platinum has over twice the density of Iron or Cobalt (improved radiopacity)
- Platinum provides increased strength when alloyed with stainless steel
- Specifically developed for coronary stents
- Biocompatible

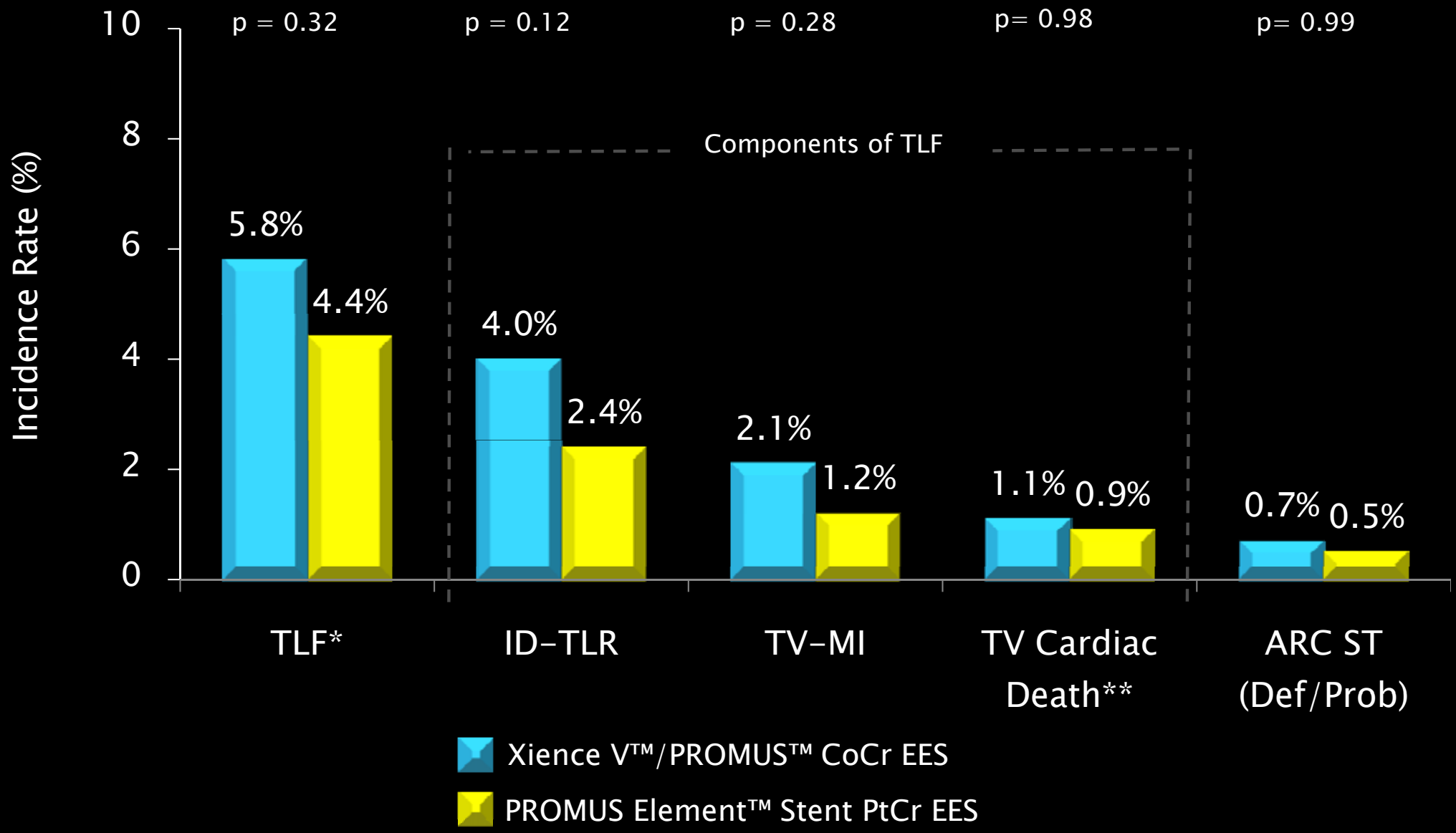
PLATINUM Workhorse Patient Flow

Prospective, Randomized, Single-blind, Multicenter Trial



PLATINUM Workhorse

2-Year Clinical Results



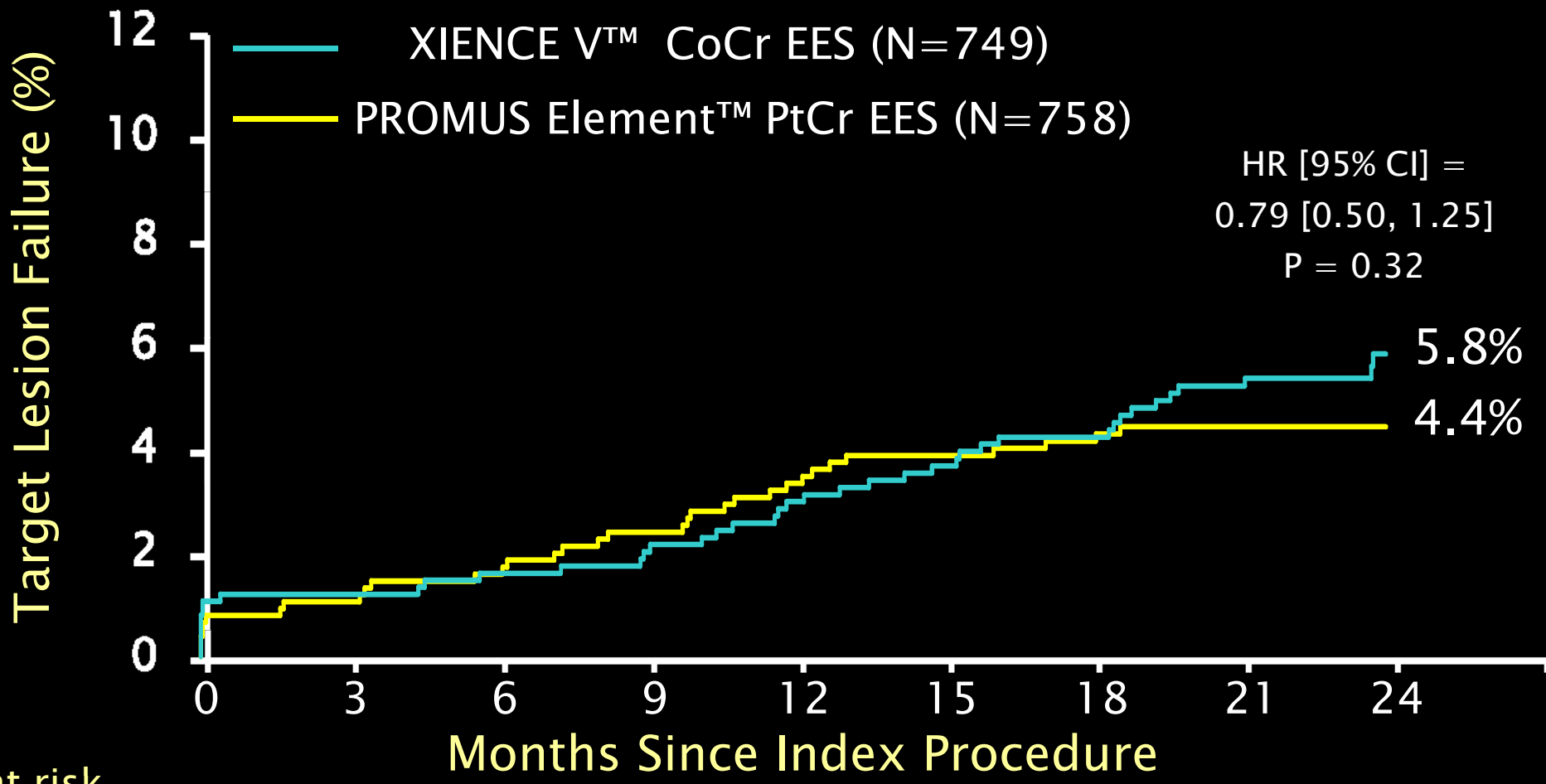
Presented by Gregg W. Stone, MD at ACC 2012.

Primary endpoint was TLF at 1-year; *TLF=Ischemia-driven (ID) target lesion revascularization (TLR), cardiac death related to the target vessel (TV) or myocardial infarction (MI) related to the TV. **Not presented, BSC internal data.

PROMUS is a private-labeled Xience V everolimus-eluting coronary stent system manufactured by Abbott and distributed by Boston Scientific.

PLATINUM Workhorse

2-Year TLF Follow-up



No. at risk

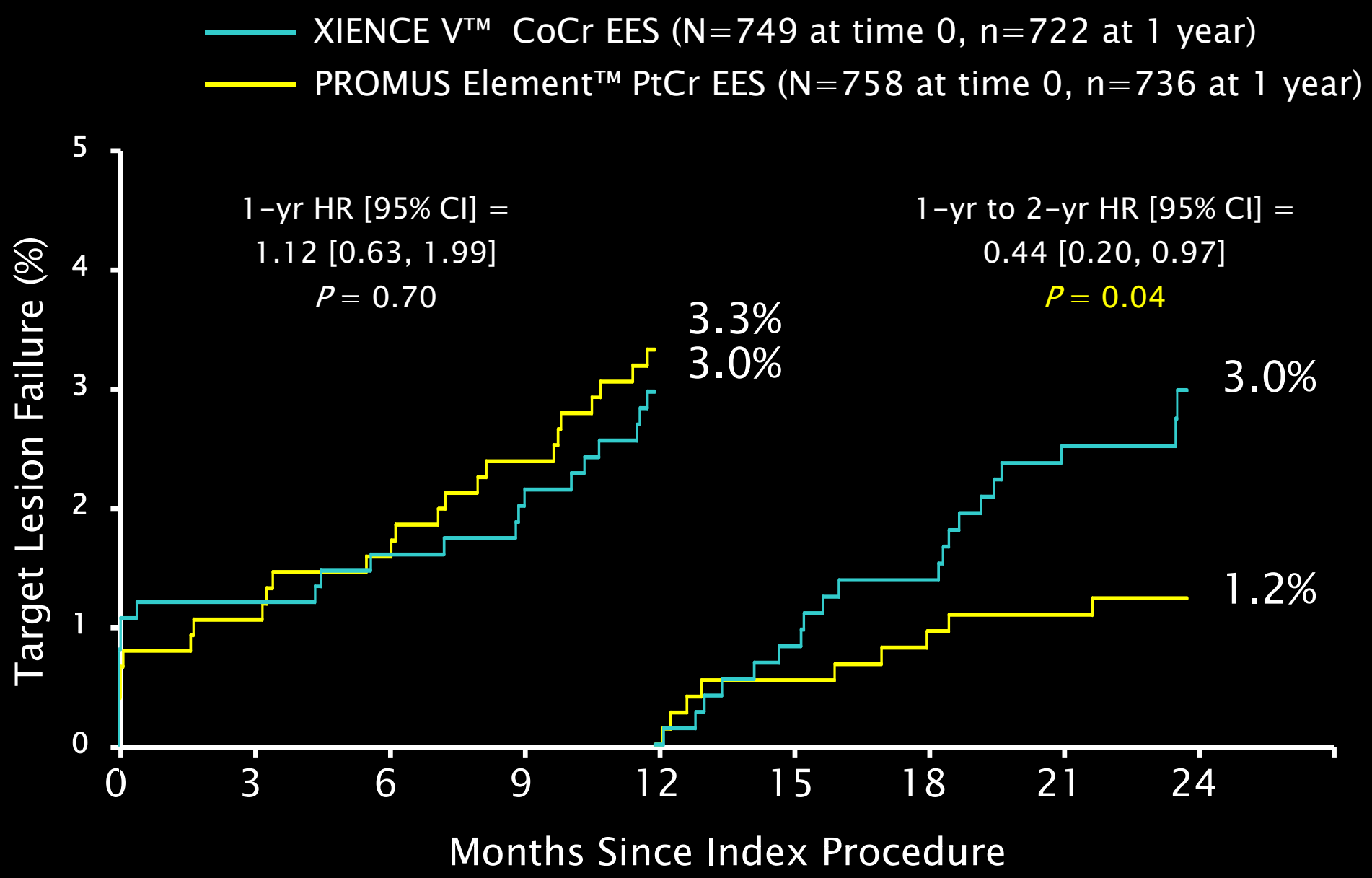
XIENCE V/PROMUS	749	738	737	729	717	703	685
PROMUS Element	758	747	742	739	727	718	700

TLF = cardiac death or MI related to the target vessel or ischemia-driven TLR

Presented by Gregg W. Stone, MD at ACC 2012

PLATINUM Workhorse

2-Year TLF Landmark Analysis

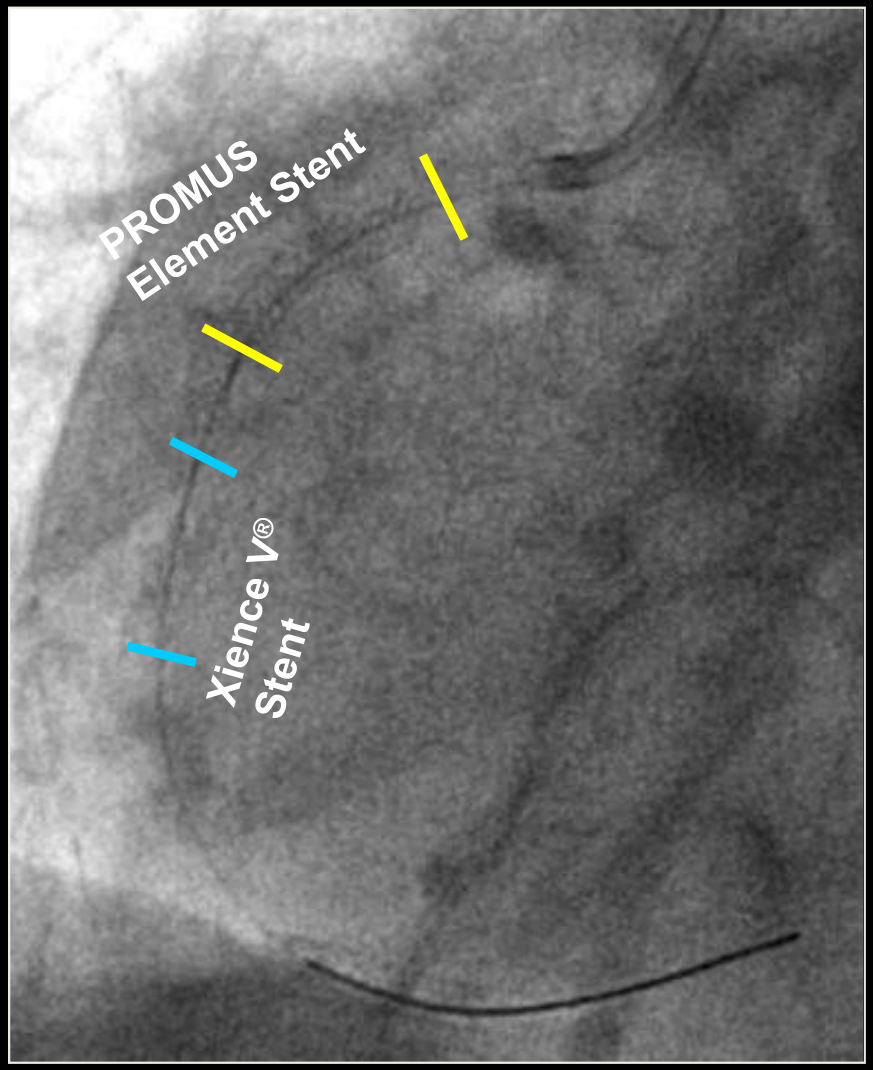


Presented by Gregg W. Stone, MD at ACC 2012.

TLF = cardiac death or MI related to the target vessel or ischemia-driven TLR; Patients with Study Stents.

PtCr Element™ Platform

Improved Visibility

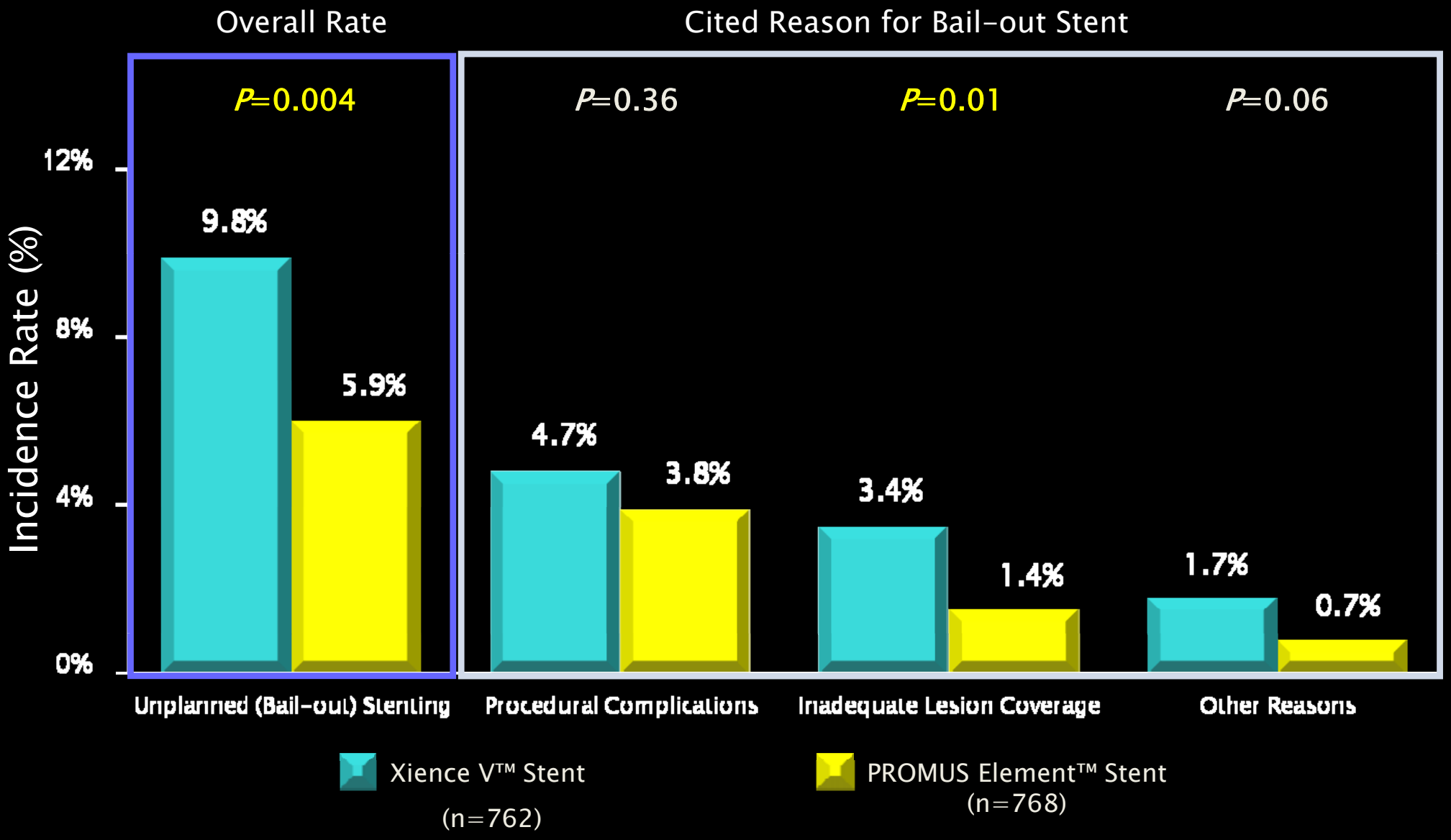


Images courtesy of Warwick Jaffe, MD. New Zealand.

Results from case studies are not predictive of results in other cases. Results in other cases may vary. Xience V Stent placed in prior procedure.

PLATINUM Workhorse

Less bail-out stenting driven by improved lesion coverage with PROMUS Element™ Stent

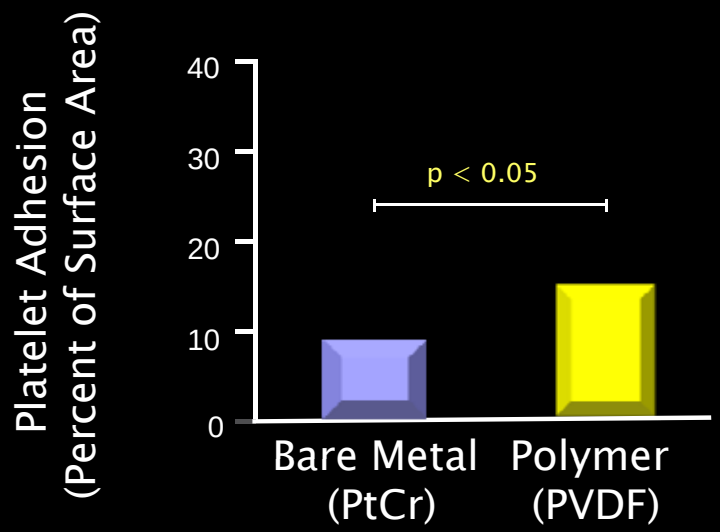


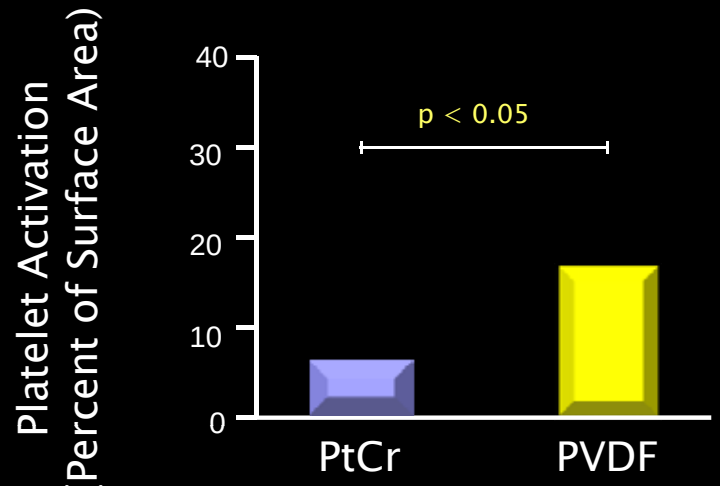
Stone et al. JACC. 2011;57:1700-1708

Cellular Response to Bare PtCr vs. Polymer Surface

Bare PtCr surface favorable to 'best in class' durable PVDF polymer for thromboresistance, strut coverage, and endothelial cell (EC) functionc

Thrombotic Potential for Stent Materials

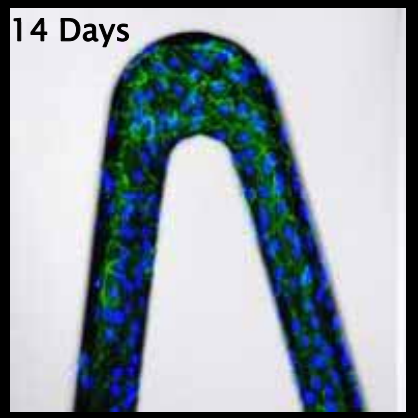


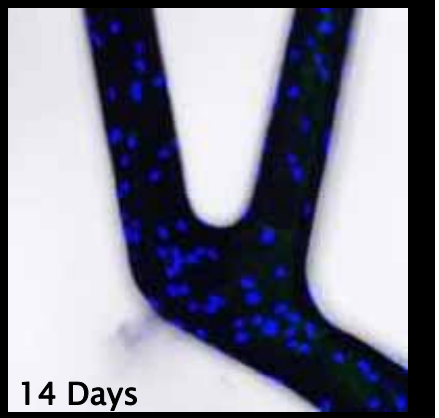


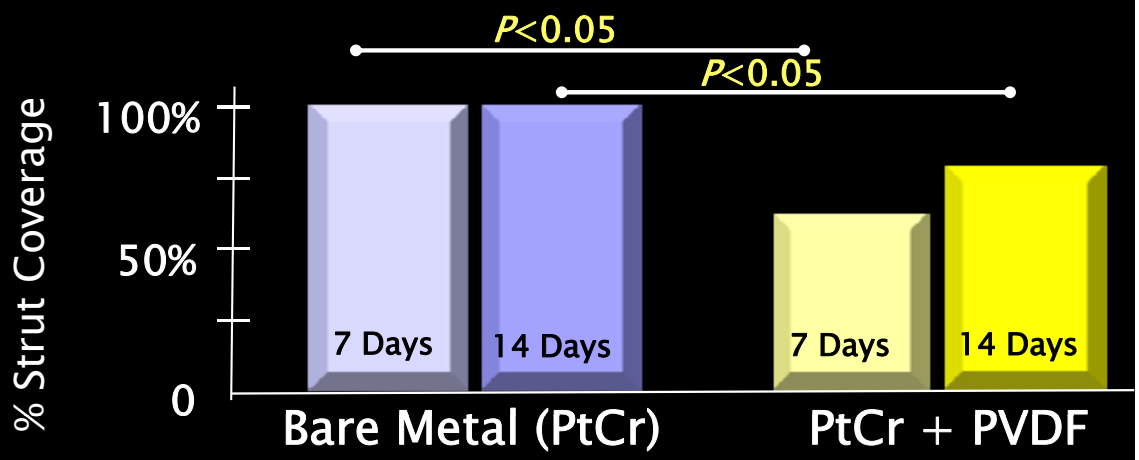
Endothelial Growth and Function on Stent Surfaces

EC nuclei

VE-Cadherin Junctional Protein forming EC blood barrier

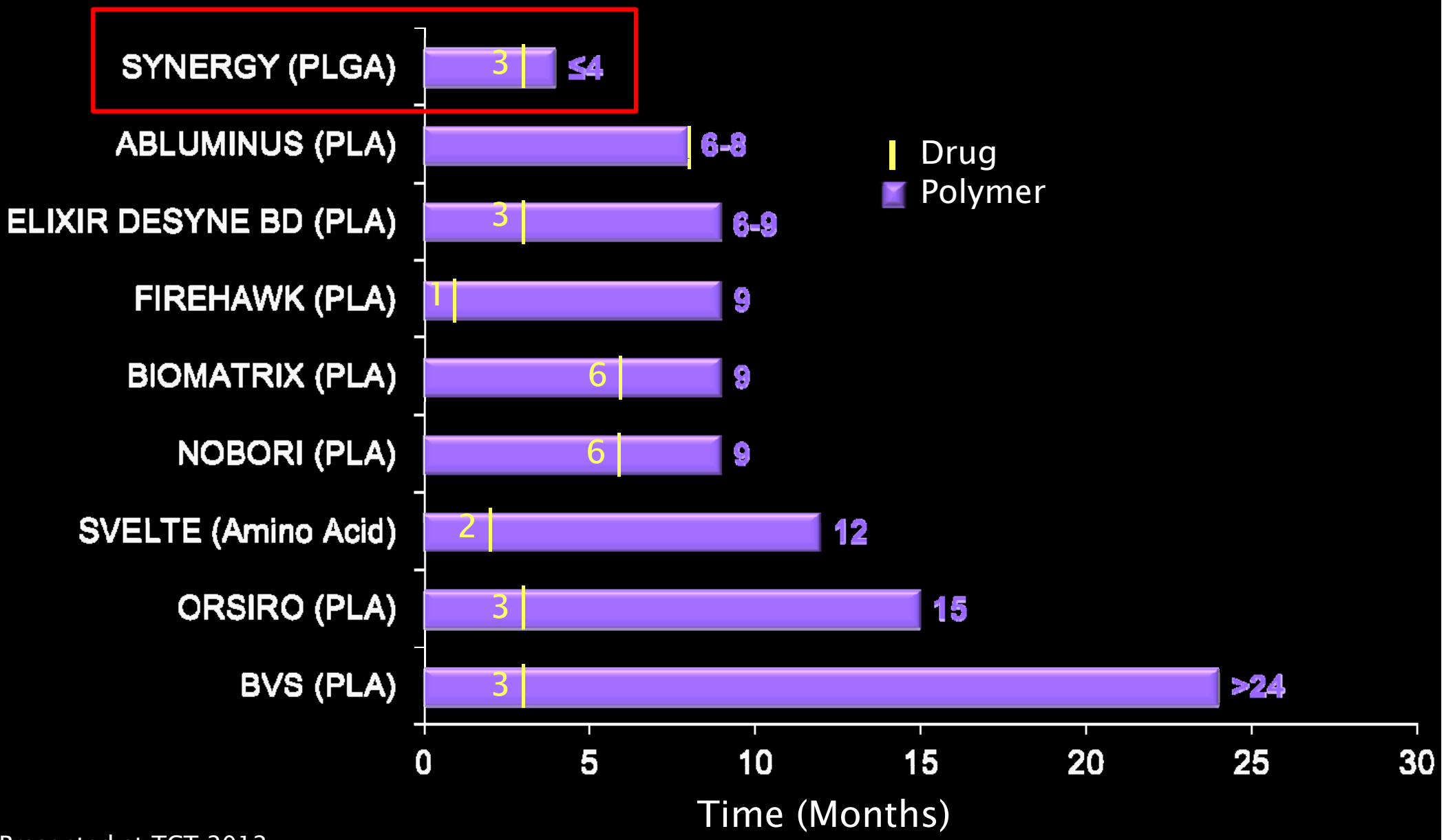






Presented by Jeff Garanich, PhD at TCT 2011 and data on file at Boston Scientific

Time Course For Polymer Bioabsorption

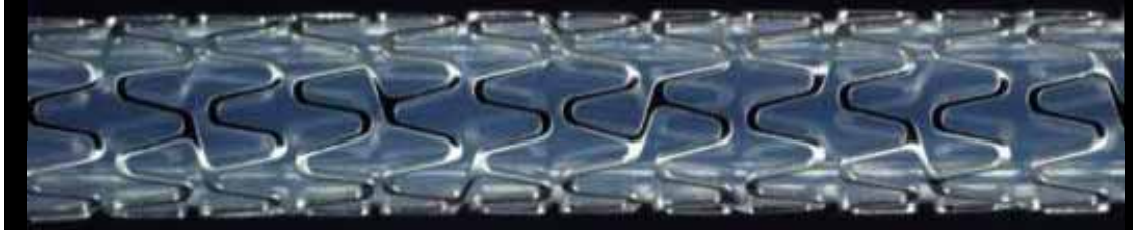


Presented at TCT 2012

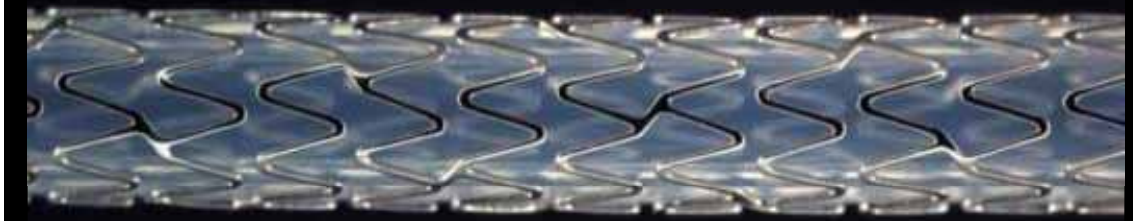
The SYNERGY™ stent is an investigational device in the US and Japan and not for sale.

SYNERGY™ Stent Platform

Stent Architecture

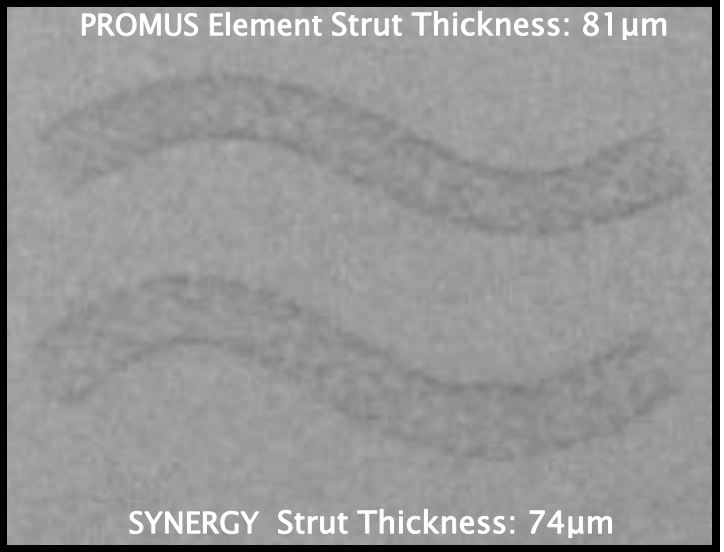


PROMUS Element™ Stent



SYNERGY™ Stent

Visibility



PROMUS Element and SYNERGY Stent Designs

Similarities

Platinum Chromium (PtCr) Alloy → Similar radial strength and visibility

SYNERGY Design Modifications

Strut Thickness
Connector Angle
Peak Radius
Additional End Connectors

→ Improve →

Crimping Profile
Flexibility
Conformability
Longitudinal Robustness

Data on file at Boston Scientific. 6.0 mm copper phantom to simulate body mass. Bench test results may not necessarily be indicative of clinical performance.
The SYNERGY™ stent is an investigational device in the US and Japan and not for sale.

EVOLVE Trial Design

Patients with *de novo* native coronary lesions
≤28 mm in length, RVD ≥2.25 mm ≤3.5, %DS>50
(excluded LM disease, CTO, AMI or recent MI)

↓

Randomized 1:1:1 at 29 sites
(EU, Australia, New Zealand)

PROMUS Element™	SYNERGY™	SYNERGY™
N=98	N=94	½ Dose
		N=99

Single-blind, noninferiority design
Primary Clinical Endpoint: TLF (TV-CD, TV-MI, or TLR) at 30 days
Primary Angiographic Endpoint: In-stent late loss at 6 months

Meredith et al. *J Am Coll Cardiol.* 2012; 59 (15): 1362.

The SYNERGY™ stent is an investigational device in the US and Japan and not for sale.

FDA Approved Product Labeling

PROMUS Element™ Stent System

PRESCRIPTIVE INFORMATION
Prior to use, please see the complete "Directions For Use" at www.bostonscientific.com for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events and Operator's Instructions.

INDICATIONS FOR USE
The PROMUS Element™ Plus Everolimus-Eluting Platinum Chromium Coronary Stent System is indicated for improving luminal diameter in patients with symptomatic heart disease or documented silent ischemia due to de novo lesions in native coronary arteries ≥2.25 mm to ≤4.00 mm in diameter in lesions ≤34 mm in length.

CONTRAINDICATIONS
Use of the PROMUS Element Plus Everolimus-Eluting Platinum Chromium Coronary Stent System is contraindicated in patients with known hypersensitivity to: 316L stainless steel or platinum • everolimus or structurally-related compounds • polymers or their individual components (see Section 2.2.2, Primer Polymer and Drug Matrix Copolymer Carrier).
Coronary Artery Stenting is contraindicated for use in: Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy (see Section 6.2, Pre- and Post-Procedure Antiplatelet Regimen for more information). • Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or delivery device.
Warnings: The use of this product carries the risks associated with coronary artery stenting, including stent thrombosis, vascular complications, and/or bleeding events. This product should not be used in patients who are not likely to comply with recommended antiplatelet therapy.

GENERAL PRECAUTIONS
Only physicians who have received adequate training should perform implantation of a stent. • Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed. • Subsequent stent blockage may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized stents is not well characterized. • Consideration should be given to the risks and benefits of use in patients with history of severe reaction to contrast agents. • Care should be taken to control the position of the guide catheter tip during stent delivery, deployment and balloon withdrawal. Before withdrawing the stent delivery system, visually confirm complete balloon deflation by fluoroscopy to avoid guiding catheter movement into the vessel and subsequent arterial damage. • Stent thrombosis is a low-frequency event that current drug-eluting stent (DES) clinical trials are not adequately powered to fully characterize. Stent thrombosis is frequently associated with myocardial infarction (MI) or death. In the clinical trials analyzed to date, differences in the incidence of stent thrombosis have not been associated with an increased risk of cardiac death, MI, or all-cause mortality. Additional data from longer-term follow-up of the PLATINUM clinical trials and analyses of stent thrombosis related to DES are expected and should be considered in making treatment decisions as data become available. • When DES are used outside the specified Indications for Use, patient outcomes may differ from the results observed in the PLATINUM pivotal clinical trials. • Compared to use within the specified Indications for Use, the use of DES in patients and lesions outside of the labeled indications may have an increased risk of adverse events, including stent thrombosis, stent embolization, MI or death. Oral Antiplatelet Therapy: Premature discontinuation of prescribed antiplatelet medication could result in a higher risk of thrombosis, MI or death. Prior to PCI, if a surgical or dental procedure is anticipated that requires early discontinuation of antiplatelet therapy, the interventional cardiologist and patient should carefully consider whether a DES and its associated recommended antiplatelet therapy is the appropriate PCI choice. Following PCI, should a surgical or dental procedure be recommended that requires suspension of antiplatelet therapy, the risks and benefits of the procedure should be weighed against the possible risk associated with premature discontinuation of antiplatelet therapy. Generally, it is recommended to postpone elective surgery for one year and among those patients for whom surgery cannot be deferred. ASA should be considered during the perioperative period in high risk DES patients.

The safety and effectiveness of the PROMUS Element stent have not been established in the cerebral, carotid, or peripheral vasculature or in the following patient populations: Pediatric patients • Patients with vessel thrombus at the lesion site. • Patients with coronary artery reference vessel diameters <2.25 or >4.0 mm. • Patients with coronary artery lesions longer than 34 mm or requiring more than one PROMUS Element stent. • Patients with lesions located in the saphenous vein grafts, in the left main coronary artery, ostial lesions, or lesions located at a bifurcation. • Patients with diffuse disease or poor flow distal to the identified lesions. • Patients with tortuous vessels (>60 degrees) in the region of the obstruction or proximal to the lesion. • Patients with a recent acute myocardial infarction where there is evidence of thrombus or poor flow. • Patients with in-stent restenosis. • Patients with moderate or severe calcification in the lesion or a chronic total occlusion. • Patients with 3 vessel disease.

POTENTIAL ADVERSE EVENTS
Potential adverse events (in alphabetical order) which may be associated with the use of a coronary stent in native coronary arteries include but are not limited to: Abrupt stent closure • Acute myocardial infarction • Allergic reaction to anti-coagulant and/or antiplatelet therapy, contrast medium, or stent materials • Angina • Arrhythmias, including ventricular fibrillation and ventricular tachycardia • Arteriovenous fistula • Bleeding • Cardiac tamponade • Cardiogenic shock/pulmonary edema • Coronary aneurysm • Death • Dissection • Emboli, distal (air, tissue or thrombotic material or material from devices(s) used in the procedure) • Heart failure • Hematoma • Hemorrhage, which may require transfusion • Hypotension/hypertension • Infection, local or systemic • Ischemia, myocardial • Pain, access site • Perforation or rupture of coronary artery • Pericardial effusion • Pseudoaneurysm, femoral • Renal insufficiency or failure • Respiratory failure • Restenosis of stented segment • Stent embolization or migration • Stent fracture • Stent thrombosis/occlusion • Stroke/cerebrovascular accident/transient ischemic attack • Total occlusion of coronary artery • Vessel spasm • Vessel trauma requiring surgical repair or reintervention.
The amount of drug that circulates in the bloodstream following implantation of a PROMUS Element stent is several folds lower than that obtained with oral doses (1.5 mg to 20 mg/day, see section 7.2, Pharmacokinetics). Adverse events associated with daily oral administration of everolimus to organ transplant patients include but are not limited to: Abdominal pain • Anemia • Angioedema • Anorexia • Asthenia • Constipation • Cough • Delayed would healing/fluid accumulation • Diarrhea • Dyslipidemia (including hyperlipidemia and hypercholesterolemia) • Dysgeusia • Dyspnea • Dysuria • Dry skin • Edema • Epistaxis • Fatigue • Headache • Hematuria • Hyperglycemia (may include new onset of diabetes) • Hyperkalemia • Hyperlipidemia • Hypertension • Hypokalemia • Hypomagnesemia • Hypophosphatemia • Increased serum creatinine • Infections and serious infections: bacterial, viral, fungal and protozoal infections (may Include herpes virus infection, polyoma virus infection which may be associated with BK virus associated nephropathy, and/or other opportunistic infections) • Insomnia • Interaction with strong inhibitors and inducers of CY3PA4 • Leukopenia • Lymphoma and other malignancies (including skin cancer) • Male infertility (azospermia and/or oligospermia) • Mucosal inflammation (including oral ulceration and oral mucositis) • Nausea • Neutropenia • Non-Infectious pneumonitis • Pain: extremity, incision site and procedural, back, chest, musculoskeletal • Proteinuria • Pyrexia • Rash • Stomatitis • Thrombocytopenia • Thrombotic microangiopathy (TMA/Thrombotic thombocytopenic purpua (TTP)/Hemolytic uremic syndrome (HUS) • Tremor • Upper respiratory tract infection • Urinary tract infection • Vomiting.
Live vaccinations should be avoided and close contact with those that have had live vaccines should be avoided. Fetal harm can occur when administered to a pregnant woman.
There may be other potential adverse events that are unforeseen at this time.

CAUTION
Federal Law (USA) restricts this device to sale by or on the order of a physician.

Promus Element is an unregistered trademark of Boston Scientific Corporation.

Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.
Information for the use only in countries with applicable health authority product registrations