A Prospective, Randomized Investigation of a Novel Platinum Chromium Everolimus-Eluting Coronary Stent: The PLATINUM Trial

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Disclosures

Scientific advisory boards for and honoraria from Boston Scientific and Abbott Vascular, and consultant to Medtronic

Background

- Advances in stent technology have continued to improve the clinical outcomes for patients undergoing PCI
- The cobalt chromium everolimus-eluting stent (CoCr-EES; XIENCE V / PROMUS) has established a new standard for clinical safety and efficacy, with numerous randomized trials demonstrating low rates of restenosis and stent thrombosis

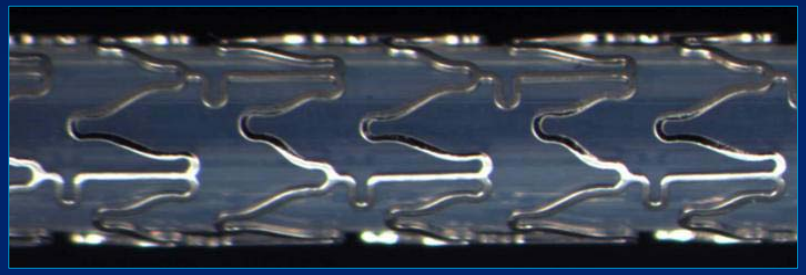
Background

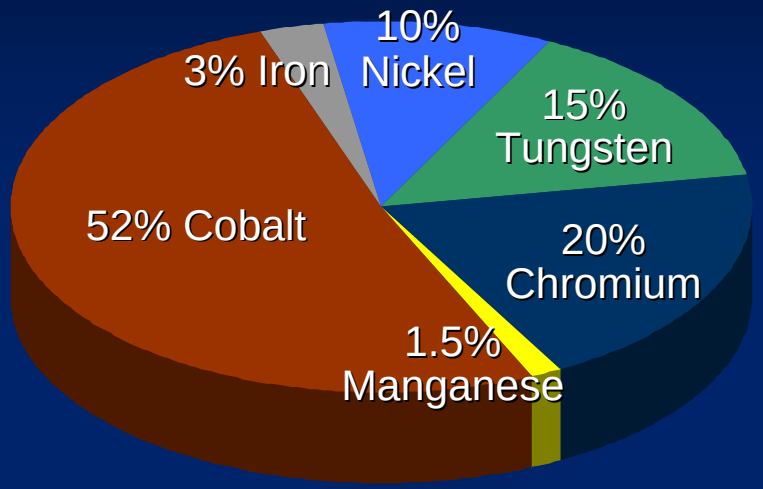
- A novel stent based on a new metal alloy has been developed, the platinum chromium EES (PtCr-EES; PROMUS Element), which uses the same durable, biocompatible, inert fluorocopolymer and antiproliferative agent as the predicate CoCr-EES, but with a modified scaffold designed for improved deliverability, vessel conformability, side-branch access, radiopacity, radial strength and fracture resistance

Everolimus-Eluting Stents

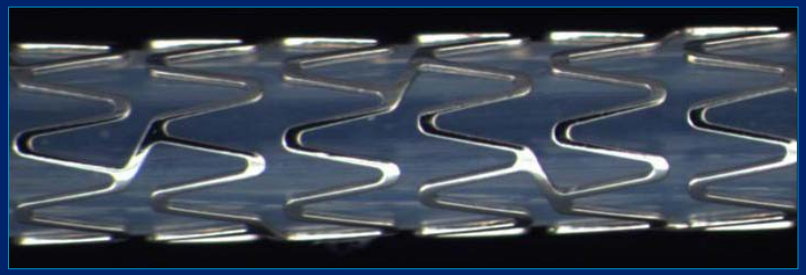
Everolimus concentration: 100 ug/cm^2
Polymer: PBMA & PVDF−HFP (7μm thickness)

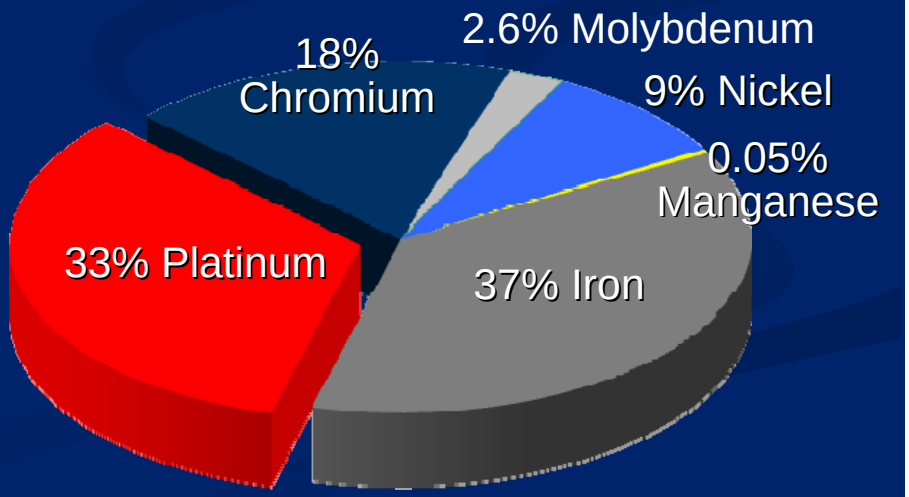
XIENCE V / PROMUS (CoCr-EES)





PROMUS Element (PtCr-EES)



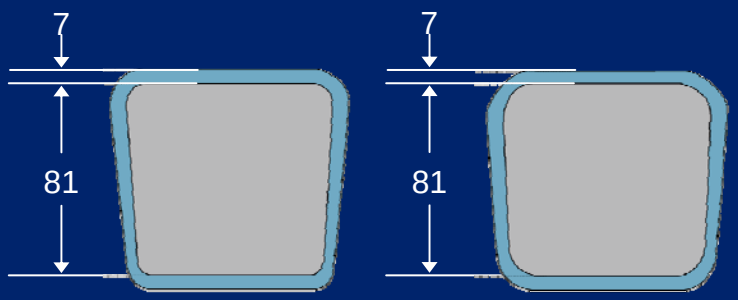


PBMA=poly (n−butyl methacrylate) (primer layer); PVDF-HFP=poly (vinylidene fluoride−co−hexafluoropropylene) (drug matrix layer)

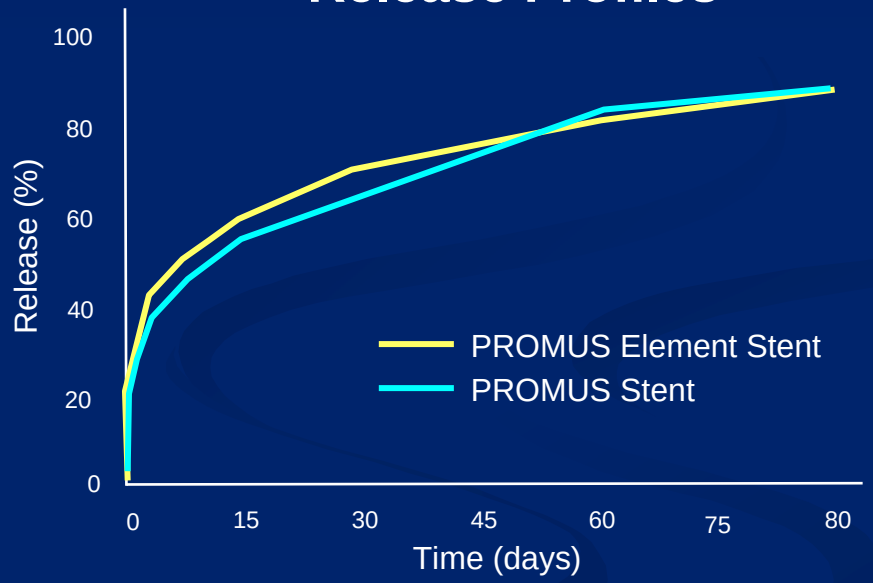
PROMUS Element and PROMUS Stents:

Equivalent Polymer Thickness and Drug Release Profiles

Same Polymer and Strut Thickness (µm)



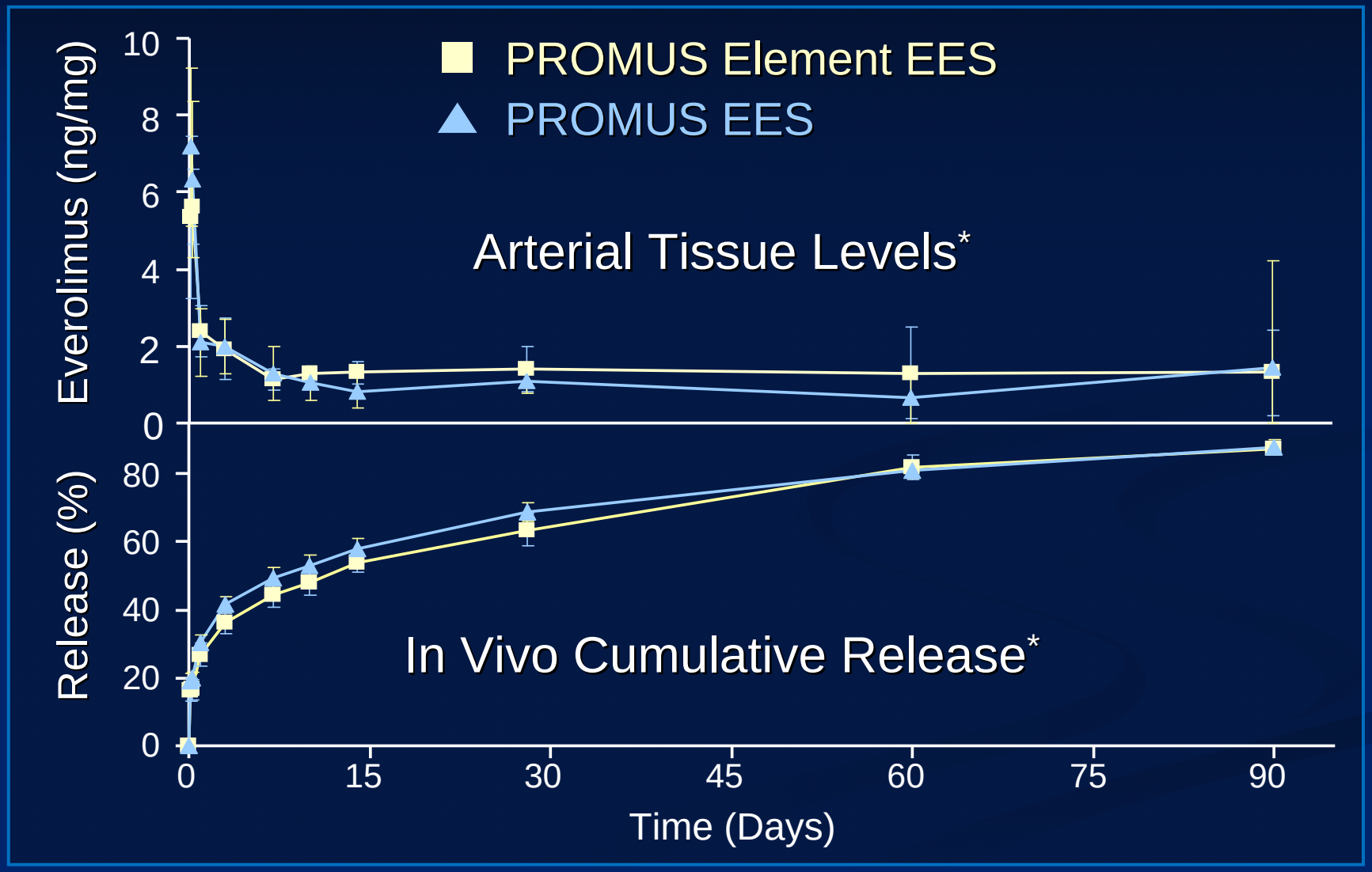
Comparable Kinetic Drug Release Profiles



BSC Data on file, average over all sizes, PROMUS Stent 2.5mm x 8mm N=12, 3.0mm x 16mm N=6, 4.0mm x 28mm N=6, PROMUS Element Stent 2.5mm x 8mm N=12, 3.0mm x 15mm N=6, 4.0mm x 28mm N=6.

Drug Release Kinetics In Vivo

Noninjured Porcine Model

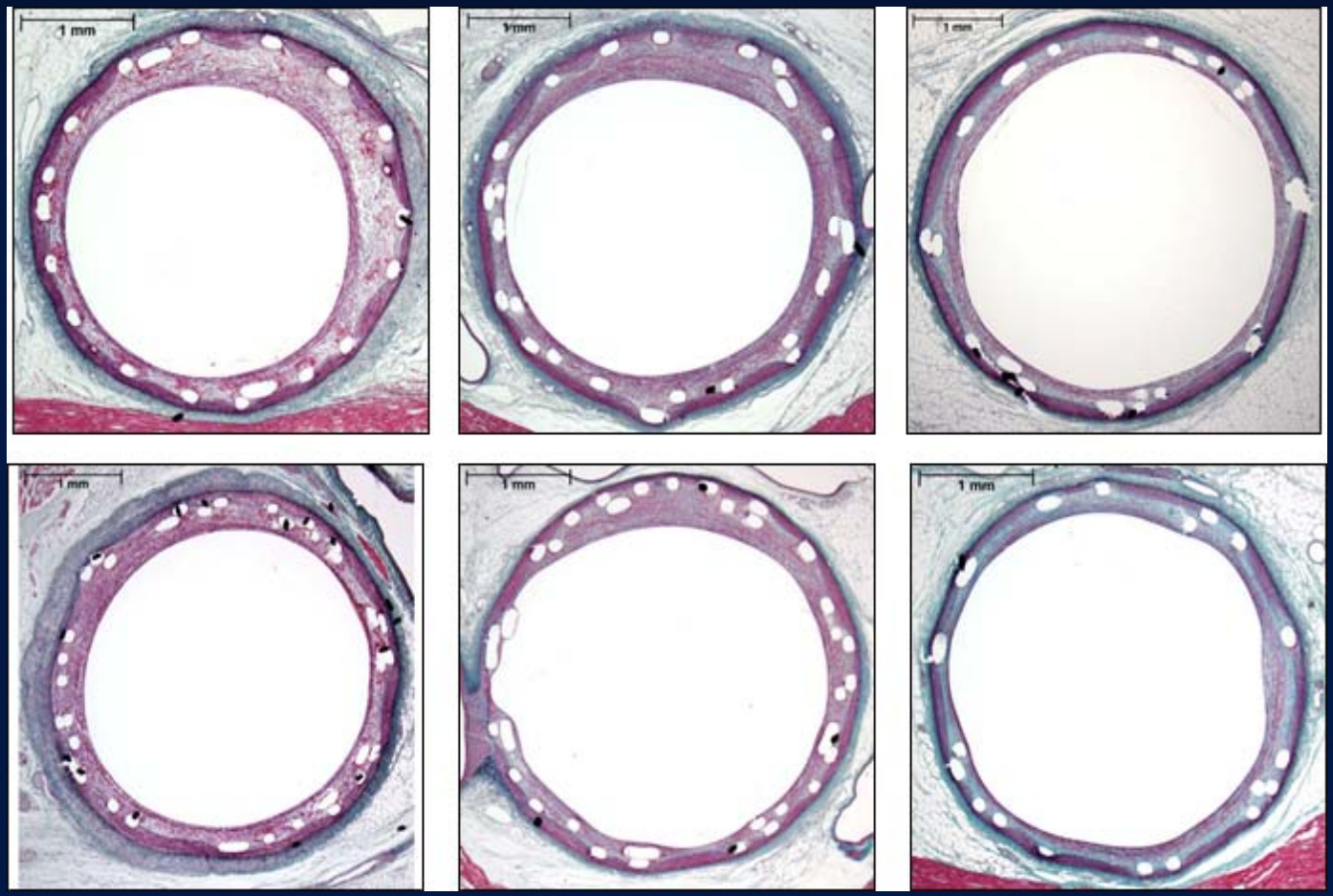


* Boston Scientific Corporation in-house testing; N=9-12 stents per time point; data are mean±SD; EES=everolimus-eluting stent

Representative Histology: Porcine Model

Stent Overlap Areas @ 30, 90 & 270 Days

PROMUS PLATINUM



PROMUS Element

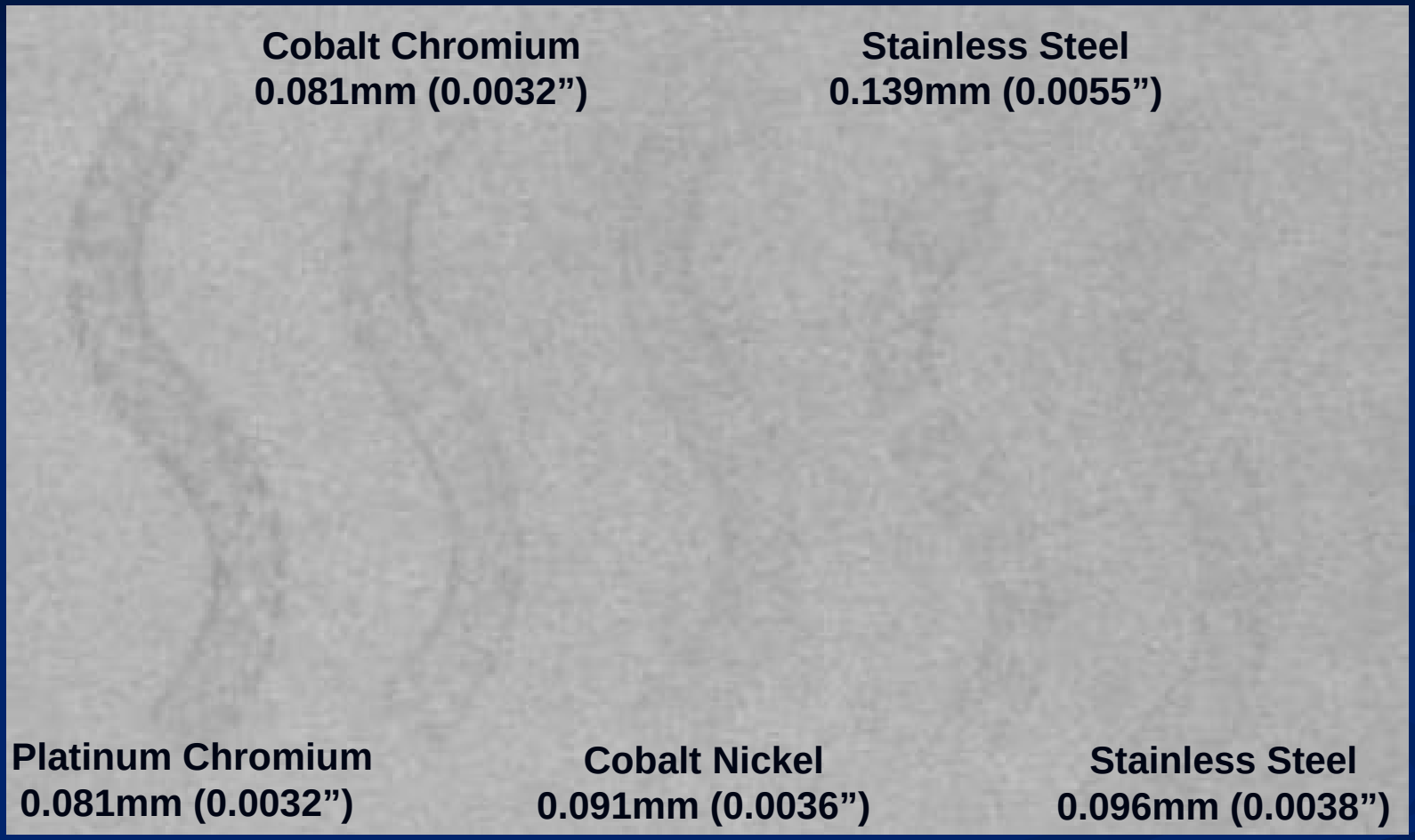
PROMUS (XIENCE V)

30 Days | 90 Days | 270 Days

Wilson GJ, et al. EuroIntervention 2010;6, Supplement H:H38

Platinum Chromium Visibility

PROMUS PLATINUM



Radiopacity of a 0.081mm (0.0032”) PtCr stent compared to Cobalt Nickel, Cobalt Chromium and Stainless Steel stents.

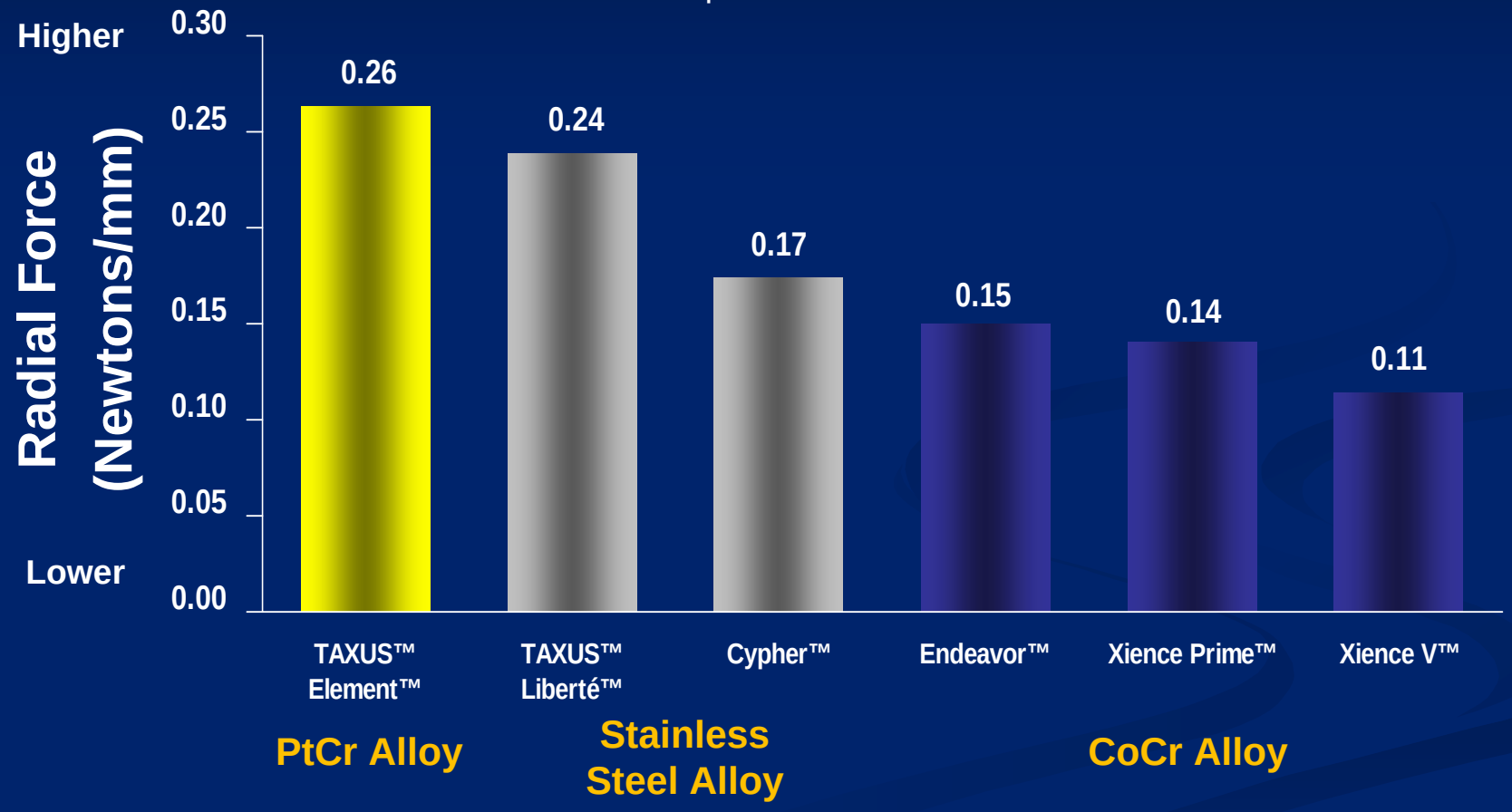
Data on file Boston Scientific.

PtCr Stent Platform

Radial Strength Bench Test Data

PROMUS PLATINUM

Amount of compression force the stent resists



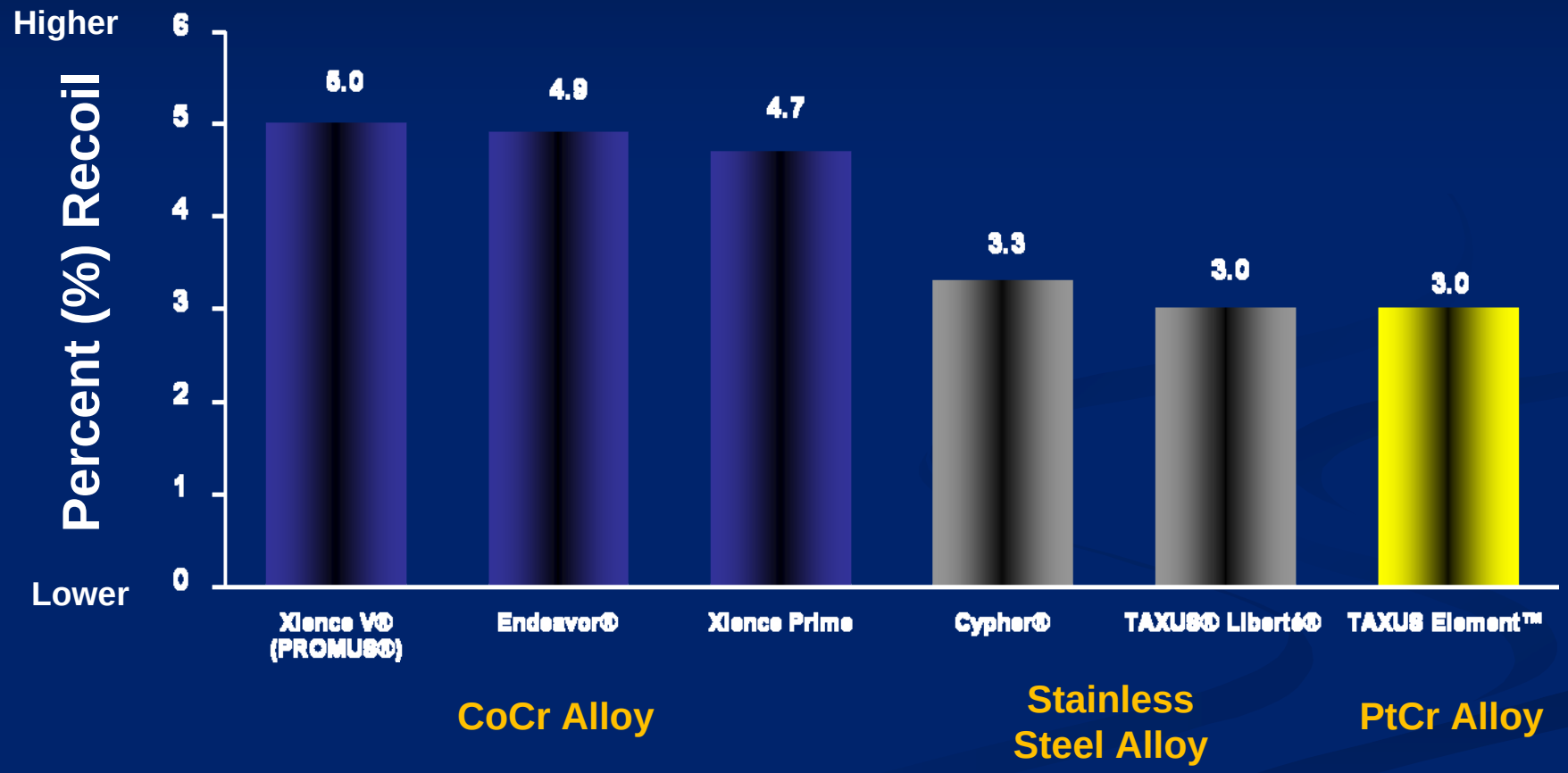
Data on File Boston Scientific. 2.50mm Stents. TAXUS Element n=15. TAXUS Liberté n=10. Cypher n=3. Xience Prime n=5. Endeavor n=7. Xience V n=10.

PtCr Stent Platform

Recoil Bench Test Data

PROMUS PLATINUM

Percentage stent diameter decreases after balloon deflation



Data on File Boston Scientific. 2.50mm Stents. TAXUS Element n=21. TAXUS Liberté n=6. Cypher n=3. Xience Prime n=5. Endeavor n=7.

PtCr Stent Platform

Conformability Bench Test Data

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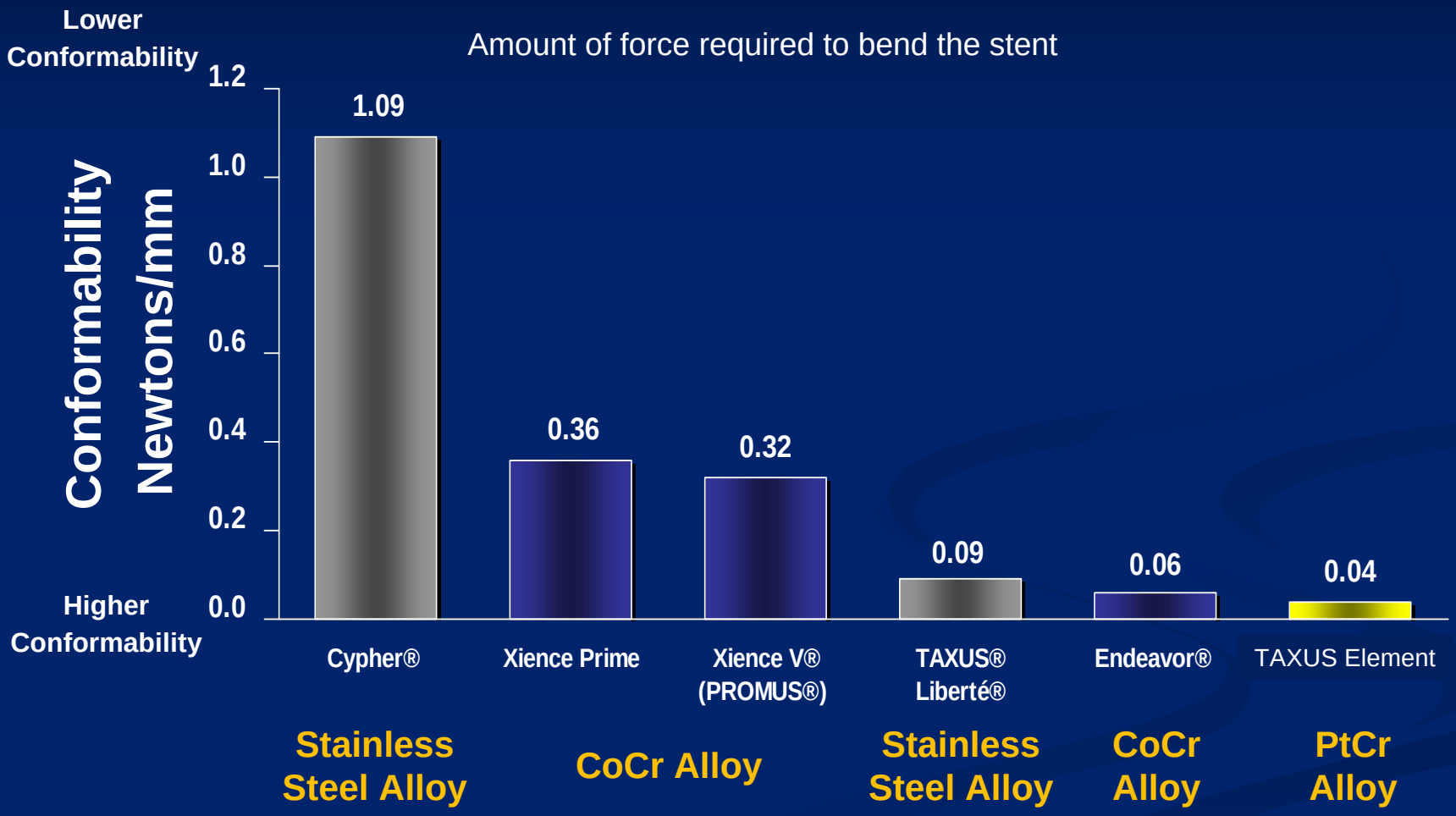

Data on File Boston Scientific. 2.50mm Stents. TAXUS Element n=15. TAXUS Liberté n=15. Cypher n=6. Xience Prime n=5. Endeavor n=7. Xience V n=10.

CoCr & PtCr Everolimus-Eluting Stents

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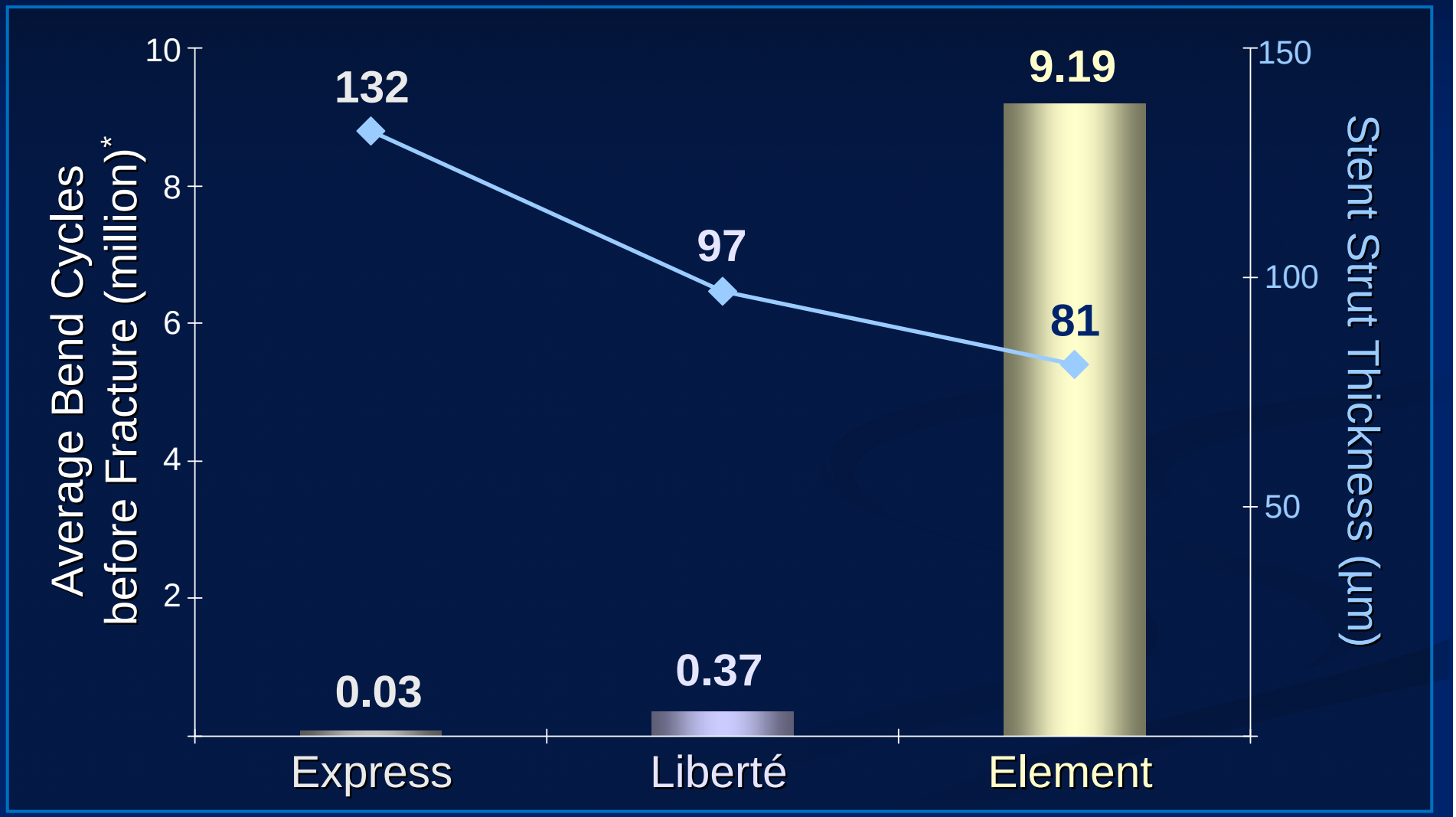
Parameter (3.0 mm stents)	CoCr-EES (n=10)	PtCr-EES (n=15)
Strut width (μm)	91	86
Strut thickness (μm)	81	81
Radial strength (N/mm)	0.14	0.23
Stent recoil (%)	4.6	3.6
Conformability (N·mm)†	0.30	0.09
Radiopacity/density (g/cm^3)	9.1	9.9
Trackability (gr· cm cath.)‡	158	133

† Describes stent's ability to match natural vessel curvature without causing vessel straightening; a lower value reflects better conformability; ‡ Amount of work required to pass stent through a tortuous artery model; less work reflects better trackability; 16 mm PtCr-EES & 18 mm CoCr-EES, n=10 per group. N/mm=Newtons per millimeter; N·mm=Newton millimeters

Fracture Resistance & Strut Thickness

Element Stent Platform

PROMUS PLATINUM



* Boston Scientific Corporation in-house testing; N=20 per stent type

PLATINUM Clinical Trial Program

Study	Design	Primary Endpoint
Pharmacokinetics US, Japan N=22 (5 sites)	Multicenter; Single Arm PROMUS Element EES	Observational
PLATINUM QCA Asia Pacific N=100 (14 sites)	Multicenter; Single Arm PROMUS Element EES	Cardiac Death, MI, TLR, ST at 30 Days
Workhorse RCT US, EU, Japan, AP N=1,530 (132 sites)	Multicenter; 1:1 Randomization PROMUS Element EES; PROMUS EES	12-Month TLF
Small Vessel US, EU, Japan, AP N=94 (23 sites)	Multicenter; Single Arm PROMUS Element EES	12-Month TLF
Long Lesion US, EU, Japan, AP N=102 (30 sites)	Multicenter; Single Arm PROMUS Element EES	12-Month TLF

AP=Asia Pacific; MI=myocardial infarction; EES=everolimus-eluting stent; QCA=quantitative coronary angiography; RCT=randomized controlled trial; ST=stent thrombosis; TLF=target lesion failure; TLR=target lesion revascularization

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PLATINUM QCA
Pre-specified Efficacy Endpoint

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In-Stent Late Loss at 9 Months – Workhorse Lesions

Workhorse lesions: RVD ≥2.5–≤4.25 mm, lesion length ≤24 mm

* Mean ±SD; value of 0.17 with an upper confidence bound of 0.22 mm is significantly less (*P*<0.001) than performance goal based on historical TAXUS Express value (0.41 mm + delta [0.03 mm]).

Meredith I. TCT2010.

PLATINUM QCA: In-stent Late Loss

PROMUS Element & PROMUS

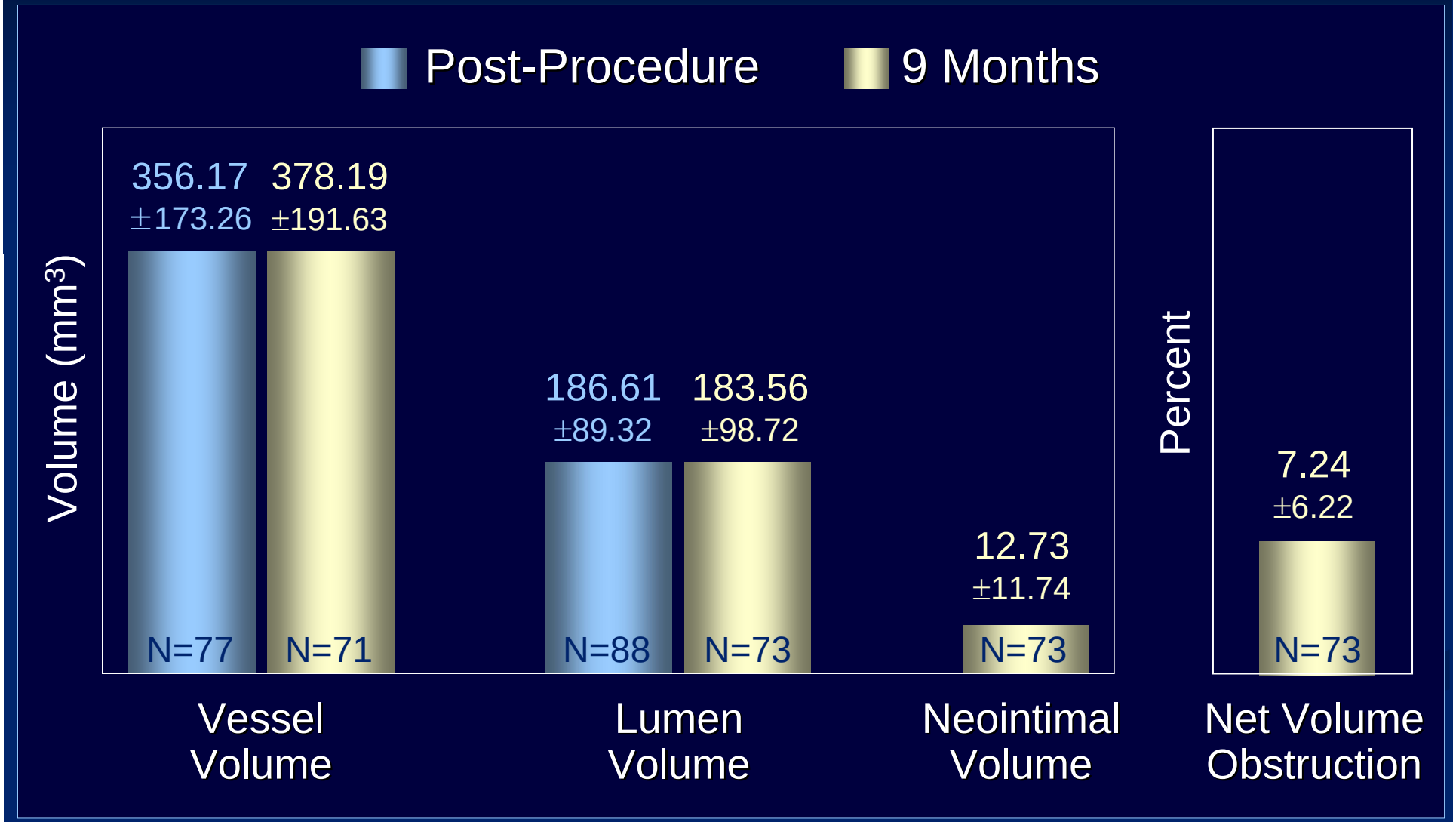
Study	In-Stent Late Loss (mm)	Time Point (months)
PLATINUM QCA (Workhorse lesions*)	0.17 ± 0.25 (n=73)	9
SPIRIT First†	0.10 ± 0.21 (n=23)	6
	0.24 ± 0.27 (n=20)	12
SPIRIT II‡	0.11 ± 0.27 (n=237)	6
SPIRIT III¶	0.16 ± 0.41 (n=301)	8

* Workhorse lesions: (RVD ≥2.5–≤4.25 mm, lesion length ≤24 mm; † Serruys, et al. *EuroIntervention* 2005;1:58 & Tsuchida, et al. *EuroIntervention* 2005;1:266; ‡Serruys, et al. *EuroIntervention* 2006;2:286; ¶Stone, et al. *JAMA* 2008;299:1903.

Meredith I. TCT2010.

PLATINUM QCA: IVUS Outcomes

PLATINUM QCA Study



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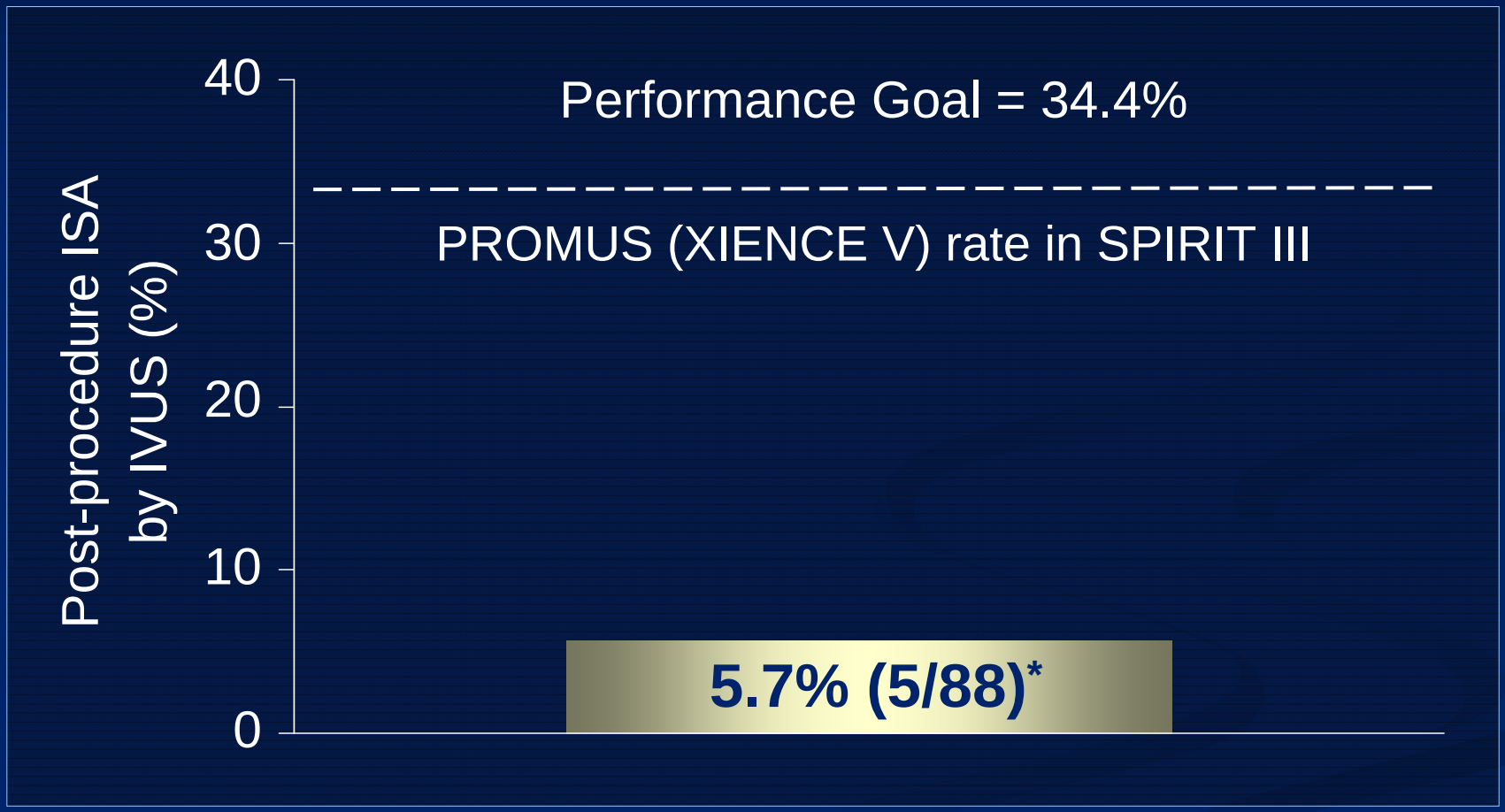
PLATINUM QCA
Pre-specified IVUS Efficacy Endpoint

Incomplete Stent Apposition Post Procedure



* 12 patients had unreadable post-procedure analyses; value of 5.7% with upper confidence bound of 11.6% is significantly below (*P*<0.001) the performance goal of 34.4% post-procedure ISA based on PROMUS (XIENCE V) data from SPIRIT III (Stone, et al. *JAMA*. 2008;299:1903)

ISA=incomplete stent apposition

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Incomplete Stent Apposition (IVUS)

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PLATINUM QCA Study

Event	Patients (N=69)* (Post-procedure & 9M)
Early (Post-Procedure)	5.8% (4)
Late (9-Month)	0.0% (0)
Resolved	5.8% (4)
Persistent	0.0% (0)
Late Acquired	0.0% (0)

* Patients with both post-procedure and 9-month assessments

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Clinical Outcomes through 9 Months

PLATINUM QCA (N=100)	30 Days	9 Months
All death, MI, TVR	1.0% (1)	1.0% (1)
All death	0.0% (0)	0.0% (0)
Myocardial infarction	0.0% (0)	0.0% (0)
Q-wave	0.0% (0)	0.0% (0)
Non–Q-wave	0.0% (0)	0.0% (0)
Target vessel revascularization	1.0% (1)	1.0% (1)
Target lesion revascularization	1.0% (1)	1.0% (1)
Target lesion failure*	1.0% (1)	1.0% (1)
Stent thrombosis (ARC def/prob)	1.0% (1)	1.0% (1)

* Ischemia-driven TLR, or MI/cardiac death related to the target vessel

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PLATINUM Trial Algorithm

Patients with 1 or 2 *de novo* native coronary artery target lesions

RVD ≥2.5 to ≤4.25; Lesion length ≤24 mm

Peri-proc: ASA ≥300 mg, clopidogrel ≥300 mg load unless on chronic Rx

Randomized 1:1

Stratified by diabetes, intention to treat 1 vs. 2 target lesions, & study site

Cobalt chromium everolimus-eluting stent

Platinum chromium everolimus-eluting stent

ASA indefinitely, thienopyridine ≥6 mos (≥12 mos if not high risk for bleeding)

Clinical f/u only: 1, 6, 12, 18 months then yearly for 2-5 years

PLATINUM Major Endpoints

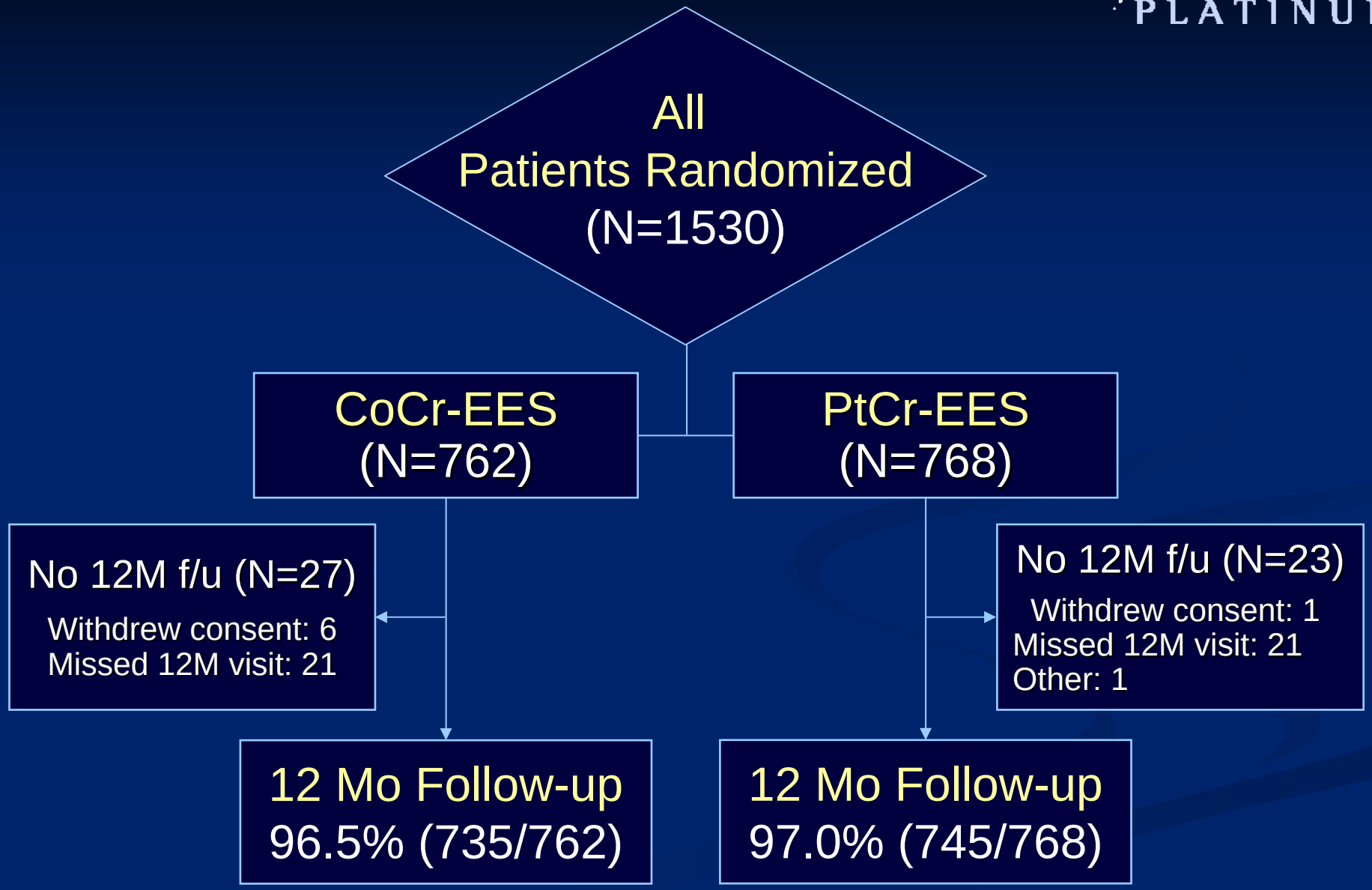
- Primary endpoint
  - Target lesion failure (TLF) at 12 months
    - Cardiac death related to the target vessel, or
    - MI related to the target vessel, or
    - Ischemia-driven target lesion revascularization
  - Per protocol population*
- Additional endpoints
  - Components of TLF
  - Stent thrombosis (ARC definite/probable)
  - Technical success†
  - Clinical procedural success‡

* Patients who received ≥1 assigned study stent

† Successful delivery & deployment of study stent to the target vessel, without balloon rupture or stent embolization

‡ Lesion DS<30% with visually assessed TIMI 3 flow and without the occurrence of in-hospital cardiac death, MI, or TVR

Patient Flow



Baseline Demographics

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	CoCr-EES (N=762)	PtCr-EES (N=768)	*P* value
Age, years	63.1 ± 10.3	64.0 ± 10.3	0.09
Male	71.1%	71.6%	0.83
Hypertension	73.2%	70.9%	0.32
Hyperlipidemia	76.2%	78.2%	0.36
Diabetes	25.1%	22.0%	0.16
- Insulin treated	6.3%	7.7%	0.29
Current smoker	17.7%	21.0%	0.10
Prior MI	21.1%	21.0%	0.99
Unstable angina	24.7%	24.1%	0.80

Baseline Lesion Characteristics (QCA)

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	CoCr-EES (N=762 Patients) (N=841 Lesions)	PtCr-EES (N=768 Patients) (N=853 Lesions)	*P* value
Target lesions	1.10 ± 0.31	1.11 ± 0.31	0.66
- 2 lesions treated	10.1%	11.1%	0.54
RVD, mm	2.63 ± 0.49	2.67 ± 0.49	0.09
MLD, mm	0.74 ± 0.34	0.75 ± 0.35	0.40
DS, %	71.9 ± 11.5	71.8 ± 11.5	0.87
Lesion length, mm	12.5 ± 5.5	13.0 ± 5.7	0.10

Procedural Characteristics

PROMUS PLATINUM

	CoCr-EES (N=762 Patients) (N=841 Lesions)	PtCr-EES (N=768 Patients) (N=853 Lesions)	*P* value
Stents per patient	1.20 ± 0.48	1.16 ± 0.44	0.16
Stents per target lesion	1.08 ± 0.35	1.05 ± 0.26	0.01
Max stent diam. per lesion (mm)	3.05 ± 0.44	3.09 ± 0.45	0.07
Stent length per lesion (mm)	19.7 ± 8.9	20.5 ± 7.0	0.06
Post-dilatation	49.3%	49.8%	0.84
Max pressure overall (atm)	15.9 ± 3.2	16.3 ± 3.1	0.002
Fluoroscopy time (min)	11.3 ± 10.1	12.2 ± 11.8	0.10

Technical & Procedural Success

	CoCr-EES (N=762)	PtCr-EES (N=768)	*P* value
Technical success[a]	98.8%	99.4%	0.14
Clinical procedural success[b]	98.2%	98.3%	0.83
Unplanned (bail-out) stenting[c]	9.8%	5.9%	0.004
- Procedural complications	4.7%	3.8%	0.36
- Inadequate lesion coverage	3.4%	1.4%	0.01
- Other reasons	1.7%	0.7%	0.06

a: Successful delivery & deployment of study stent to the target vessel, without balloon rupture or stent embolization (per stent)
b: Mean lesion diameter stenosis <30% with visually assessed TIMI 3 flow and without the occurrence of in-hospital cardiac death, MI, or TVR
c: Study or non-study stents

Post-Procedure Angiographic Outcomes

PROMUS PLATINUM

	CoCr-EES (N=762 Patients) (N=841 Lesions)	PtCr-EES (N=768 Patients) (N=853 Lesions)	*P* value
RVD, mm	2.67 ± 0.50	2.70 ± 0.49	0.27
MLD, in-stent, mm	2.54 ± 0.44	2.57 ± 0.42	0.25
MLD, in-segment, mm	2.16 ± 0.47	2.19 ± 0.47	0.15
DS, in-stent, %	4.3 ± 8.7	4.3 ± 9.1	0.95
DS, in-segment, %	19.2 ± 9.0	18.8 ± 8.6	0.43
Acute gain, in-stent, mm	1.80 ± 0.45	1.81 ± 0.43	0.73
Acute gain, in-segment, mm	1.42 ± 0.47	1.44 ± 0.46	0.45

Antiplatelet Medication Usage

PROMUS PLATINUM

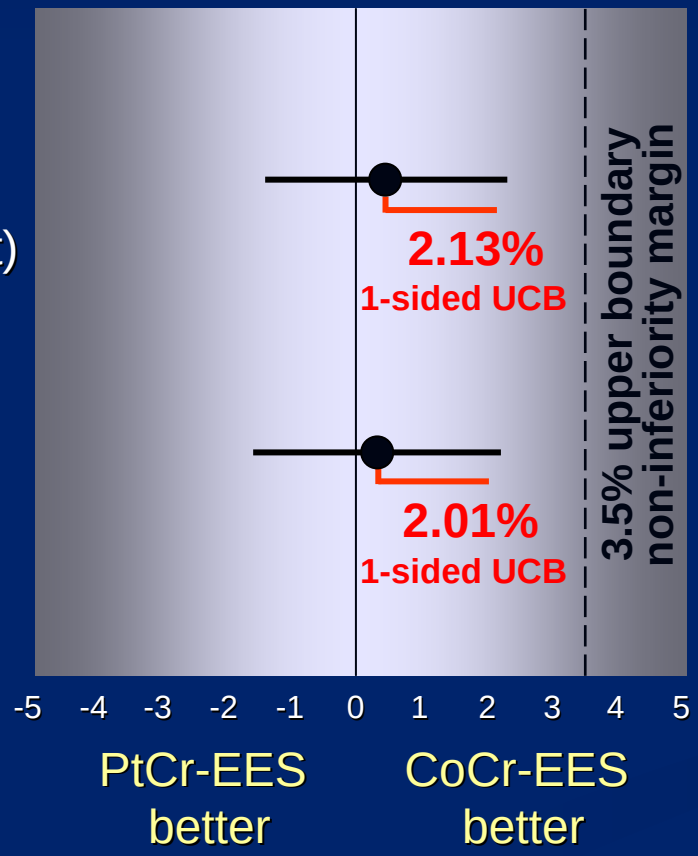
Medication	CoCr-EES (N=762)	PtCr-EES (N=768)	*P* value
	Pre-PCI*		
Aspirin	99.6%	99.3%	0.73
Thienopyridine	98.6%	99.0%	0.48
Aspirin + Thienopyridine	98.3%	98.3%	0.98
	Discharge		
Aspirin	99.6%	98.7%	0.053
Thienopyridine	99.1%	98.8%	0.63
Aspirin + Thienopyridine	98.8%	97.7%	0.08
	12 Months		
Aspirin	97.4%	97.6%	0.84
Thienopyridine	89.4%	90.9%	0.34
Aspirin + Thienopyridine	87.3%	89.3%	0.26

*Per-protocol, thienopyridine could be given up to 2 hours after the procedure

Primary Endpoint

Target Lesion Failure at 12 Months

Population	Difference [2-sided 95% CI] (1-sided UCB)	CoCr-EES (N=762)	PtCr-EES (N=768)	Difference [2-sided 95% CI]	*P* Value (noninferiority) (superiority)
Per protocol (1º endpt)	2.13% 1-sided UCB	2.9% (21/714)	3.4% (25/731)	0.5% [-1.3%, 2.3%]	0.001 0.60
Intent-to-treat	2.01% 1-sided UCB	3.2% (23/737)	3.5% (26/742)	0.3% [-1.5%, 2.2%]	0.0009 0.72



UCB=upper confidence bound

Target Lesion Failure

Time-to-event analysis

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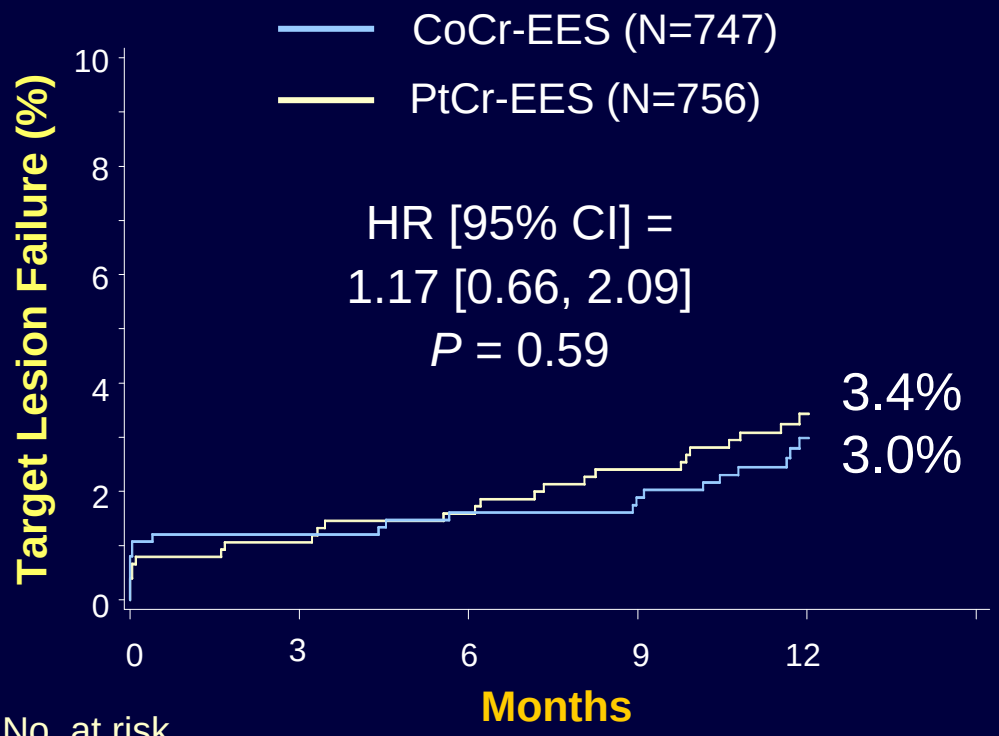
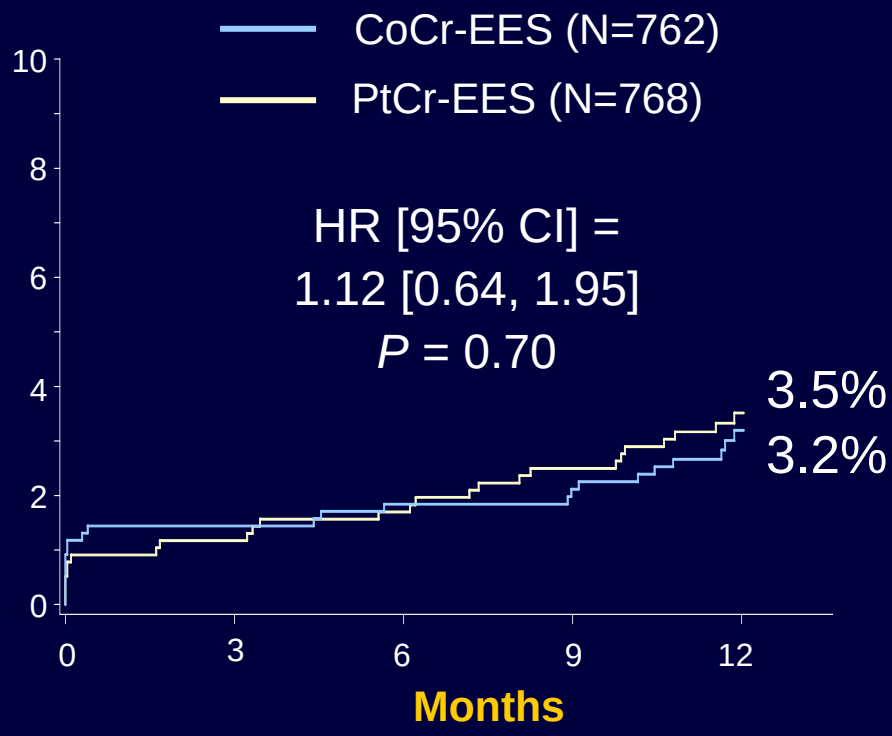
Per Protocol



Intention-to-Treat



No. at risk

CoCr EES	747	735	731	723	707	762	747	743	735	718
PtCr EES	756	745	740	734	719	768	756	751	745	730

Target Lesion Failure Components

12 Months

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	Per Protocol			Intention-to-Treat		
	CoCr-EES (N=747)	PtCr-EES (N=756)	*P* value	CoCr-EES (N=762)	PtCr-EES (N=768)	*P* value
TLF	2.9%	3.4%	0.60	3.2%	3.5%	0.72
Cardiac death-TV	0.4%	0.8%	0.51	0.4%	0.8%	0.51
MI-TV	1.4%	0.7%	0.18	1.6%	0.8%	0.14
ID-TLR	1.8%	1.9%	0.89	1.9%	1.9%	0.96

Death and Myocardial Infarction

12 Months – Intent-to-Treat

	CoCr-EES (N=762)	PtCr-EES (N=768)	*P* value
All-cause death or MI	3.0%	2.4%	0.49
All-cause death	1.2%	1.3%	0.85
Cardiac	0.7%	0.9%	0.58
Non-cardiac	0.5%	0.4%	0.72
Myocardial Infarction	1.8%	1.1%	0.25
Q-wave	0.7%	0.1%	0.12
Non-Q-wave	1.2%	0.9%	0.59
Cardiac death or MI	2.5%	2.0%	0.56

Revascularization, Ischemia-driven

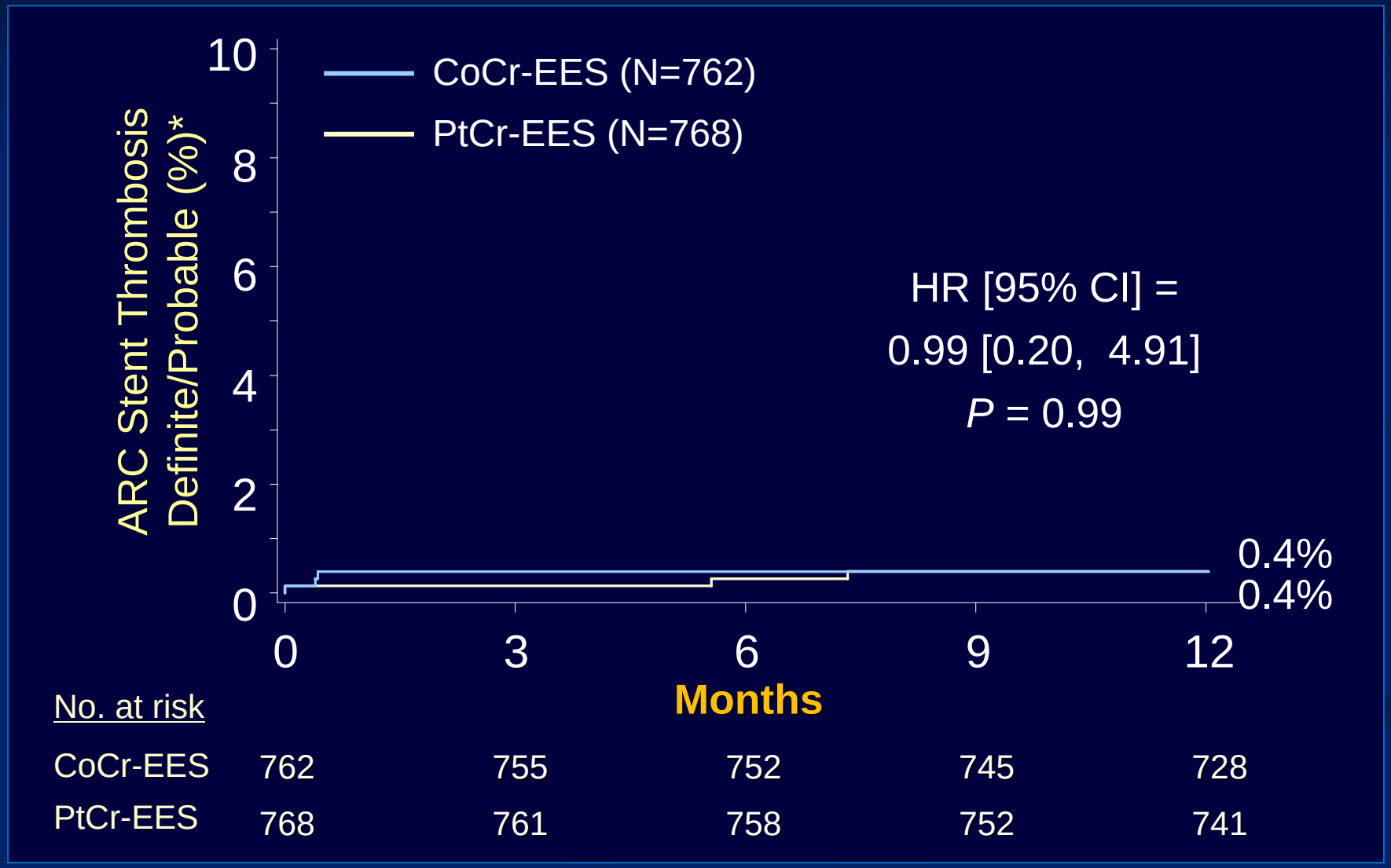
PROMUS PLATINUM

12 Months – Intent-to-Treat

	CoCr-EES (N=762)	PtCr-EES (N=768)	*P* value
TVR	2.9%	2.7%	0.83
TLR	1.9%	1.9%	0.96
TLR, PCI	1.6%	1.3%	0.64
TLR, CABG	0.3%	0.5%	0.69
TVR non-TLR	1.1%	0.9%	0.77

Stent Thrombosis – ARC Def/Prob

12 Months – Intent-to-Treat



* All were definite ST

Limitations

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- Patients with AMI, CTO, bifurcation, LMCA lesion, SVG lesion, ostial lesions or lesions with thrombus or excessive tortuosity or calcification were excluded
- Event rates were lower than expected; non-inferiority based on a delta of 3.5% was demonstrated, but small differences between PtCr-EES and CoCr-EES cannot be excluded
- Trial was not designed to assess differences in deliverability, acute performance or ease of use

Conclusions

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- A novel PtCr-EES has been developed which has been shown to be noninferior to the predicate CoCr-EES for TLF, with non-significant differences in measures of safety and efficacy demonstrated through 12-month follow-up after PCI

The PLATINUM Trial

PROMUS PLATINUM

EXPEDITED PUBLICATION

A Prospective, Randomized Evaluation of a Novel Everolimus-Eluting Coronary Stent

The PLATINUM (A Prospective, Randomized, Multicenter Trial to Assess an Everolimus-Eluting Coronary Stent System [PROMUS Element] for the Treatment of up to Two De Novo Coronary Artery Lesions) Trial

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Stone GW et al. J Am Coll Cardiol 2011;57:1700-8.