PROMUS PLATINUM

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

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for the PLATINUM Trial Investigators

Disclosures

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GW Stone:	Scientific advisory boards for and honoraria from Boston Scientific and Abbott Vascular, and consultant to Medtronic
IT Meredith:	Scientific advisory board for and honoraria from Boston Scientific
PS Teirstein:	Research grants, honoraria, and consulting fees from Boston Scientific, Abbott, Cordis and Medtronic
B Farah:	Honoraria from Boston Scientific and Abbott Vascular
CL Dubois:	Honoraria from Boston Scientific and Abbott Vascular
TL Feldman:	Scientific advisory board for and honoraria from Boston Scientific
J Dens:	None
N Hagiwara:	None
DJ Allocco:	Full-time employee and stockholder of Boston Scientific
KD Dawkins:	Full-time employee and stockholder of Boston Scientific

Background

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- 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

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- 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)

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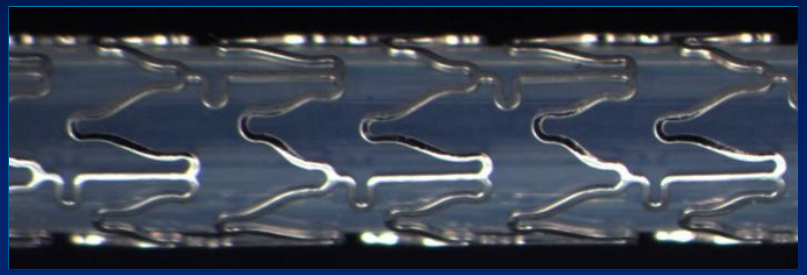
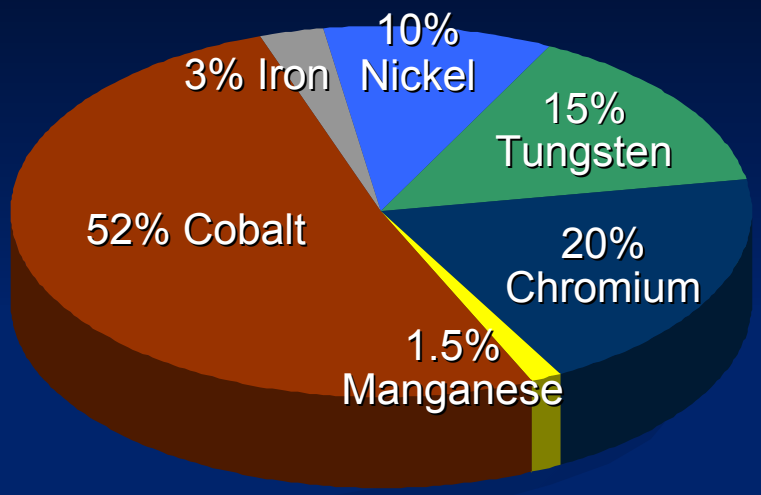
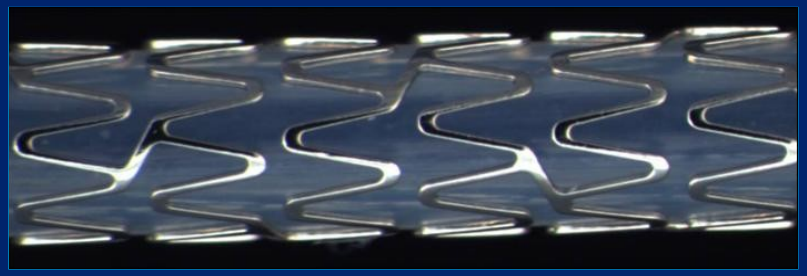
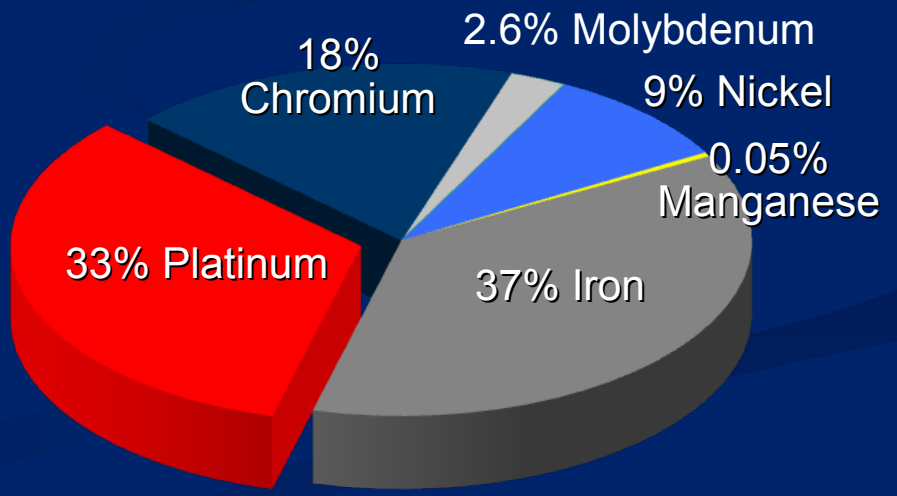
XIENCE V / PROMUS (CoCr-EES)





PROMUS Element (PtCr-EES)





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

PLATINUM Study Algorithm

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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

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- 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

Sample Size & Power Calculation

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Primary Endpoint: 12-Month Target Lesion Failure

xpected CoCr-EES (control) rate = 5.5%*

xpected PtCr-EES (test) rate = 5.5%

on-inferiority margin (Δ) = 3.5%

est significance level (α) = 0.05 (1-sided)

ower (1–β) = approximately 0.89

xpected rate of attrition = 5%

If the *P* value from the one-sided Farrington-Manning test is <0.05, it will be concluded that PtCr-EES is non-inferior to CoCr-EES

* From SPIRIT II & SPIRIT III

PLATINUM Study Organization

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Principal Investigator	Gregg W. Stone, MD, Columbia University, NY, NY	
Co-Principal Investigators	Paul S. Teirstein, MD, Scripps Foundation, La Jolla, CA Ian T. Meredith, MBBS, PhD, Monash Medical Centre Melbourne, Australia	
Core Angiographic Laboratory	Jeffrey J. Popma, MD (Director) Beth Israel Deaconess Medical Center, Boston, MA	
Clinical Events Committee	David G. Hurrell, MD (Chair) Jeffrey Chambers, MD David D. Laxon, MD	Yale Wang, MD Robert F. Wilson, MD
Data Safety and Monitoring Committee	W. Douglas Weaver, MD (Chair) David P. Faxon, MD Steven R. Bailey, MD	David J. Moliterno, MD Jan G. P. Tijssen, PhD Adam Greenbaum, MD
Data Management, Biostats Analysis, Safety Monitoring	Boston Scientific Corporation, Natick, MA	

PLATINUM Enrollment

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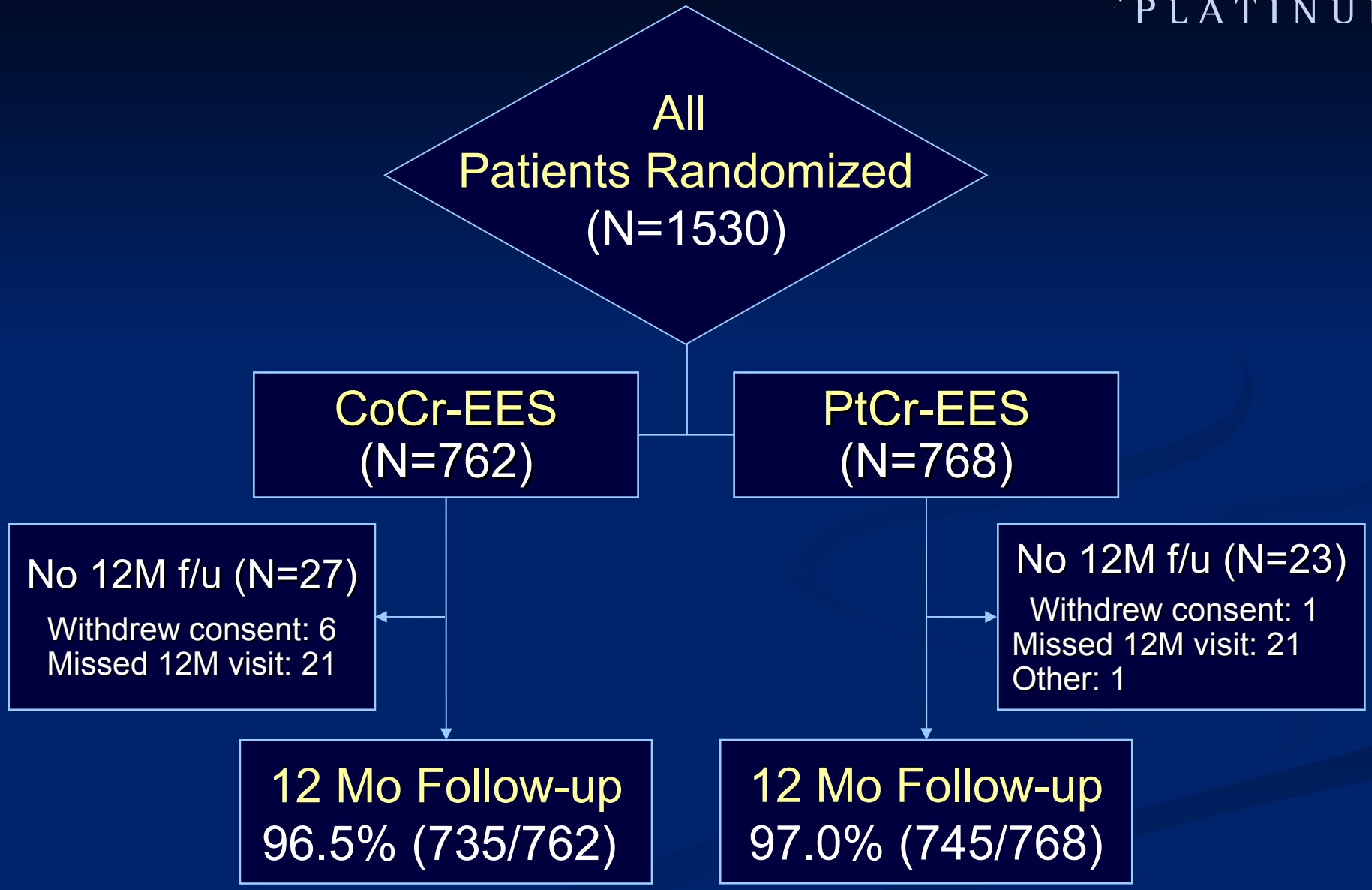
1530 pts enrolled between Jan. and Sept. 2009 at 132 centers

from the US (788), EU (562), Japan (124), and other Asia Pacific countries (56)

Top 12 Enrollers	Patients		Patients
Bruno Farah Clinique Pasteur, Toulouse, France	54	Helge Moellmann Kerckhoff Klinik, Bad Nauheim, Germany	35
Christophe Dubois University Hospital Leuven, Leuven, Belgium	51	Keith Oldroyd Golden Jubilee National Hospital, Clydebank, UK	33
Robert Feldman Mediquest Research Group, Inc. at Munroe Regional Medical Center, Ocala, FL, USA	41	Jack Hall St. Vincent's Hospital, Indianapolis, IN, USA	32
Joseph Dens Ziekenhuis Oost Limburg, Genk, Belgium	36	Nobuhisa Hagiwara Tokyo Women's Medical University Hospital, Tokyo, Japan	29
Alain Bouchard Baptist Medical Center Princeton, Birmingham, AL, USA	35	Robert Stoler Baylor Heart and Vascular Hospital, Dallas, TX, USA	29
Didier Carrié Centre Hôpital Universitaire Rangueil, Toulouse, France	35	Abram Rabinowitz TexSan Heart Hospital, San Antonio, TX, USA	28

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

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	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

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	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

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	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

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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

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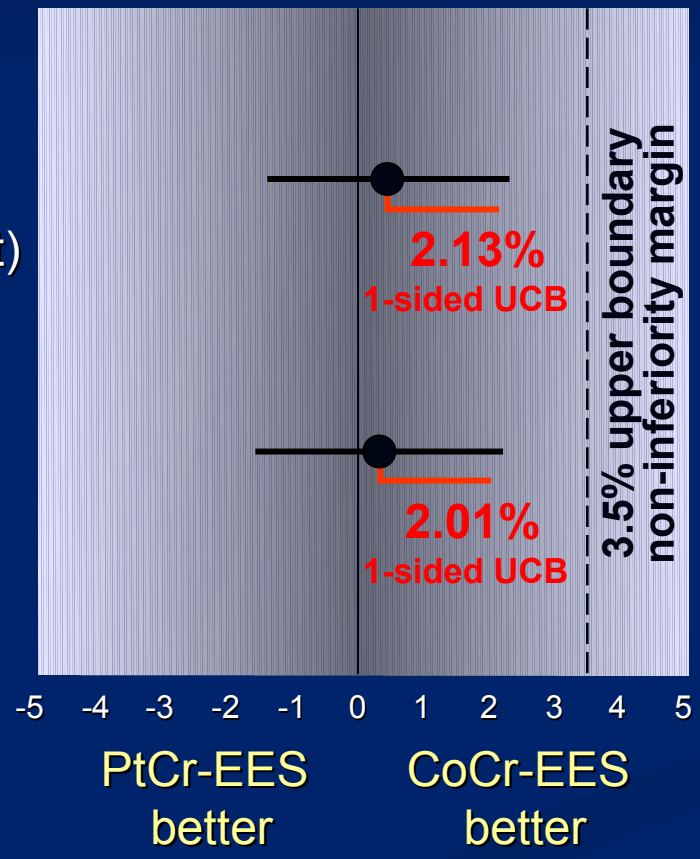
Population	Difference [2-sided 95% CI] (1-sided UCB)	CoCr-EES (N=762)	PtCr-EES (N=768)	Difference [2-sided 95% CI]	*P* Value (noninferiority) (superiority)
Per protocol (1º endpt)	2.13% 1-sided UCB	2.9% (21/714)	3.4% (25/731)	0.5% [-1.3%, 2.3%]	0.001 0.60
Intent-to-treat	2.01% 1-sided UCB	3.2% (23/737)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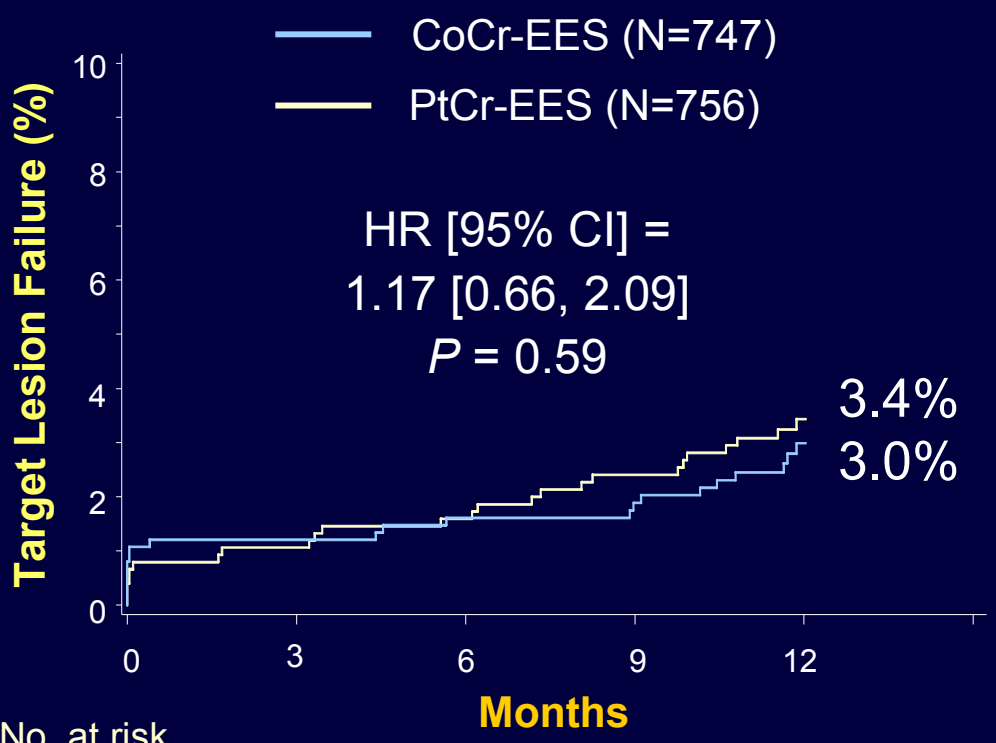
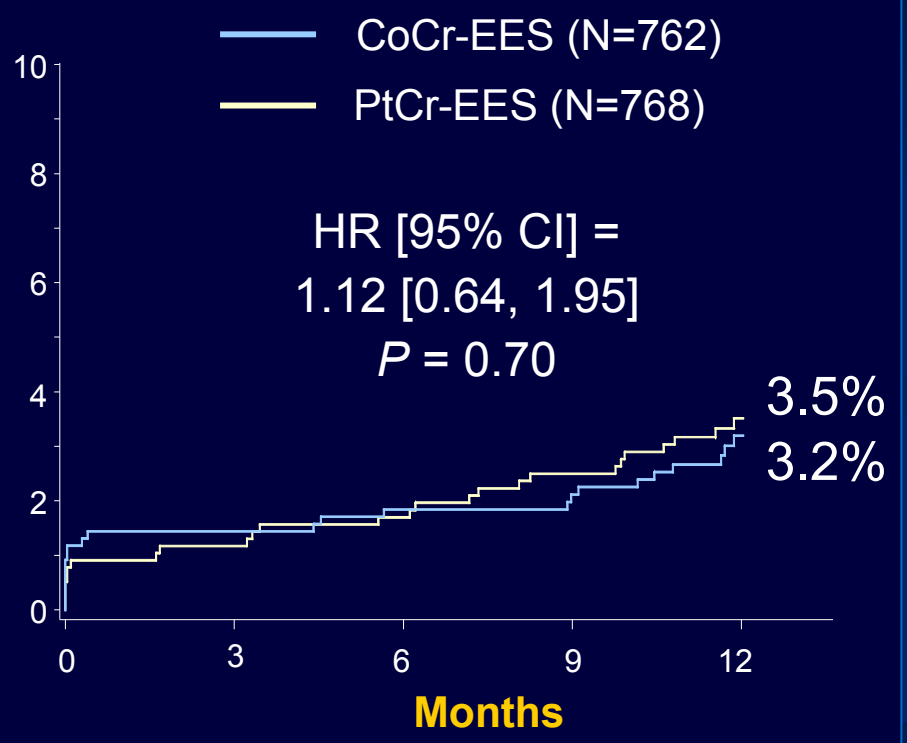
Per Protocol



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

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	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

12 Months – Intent-to-Treat

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	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

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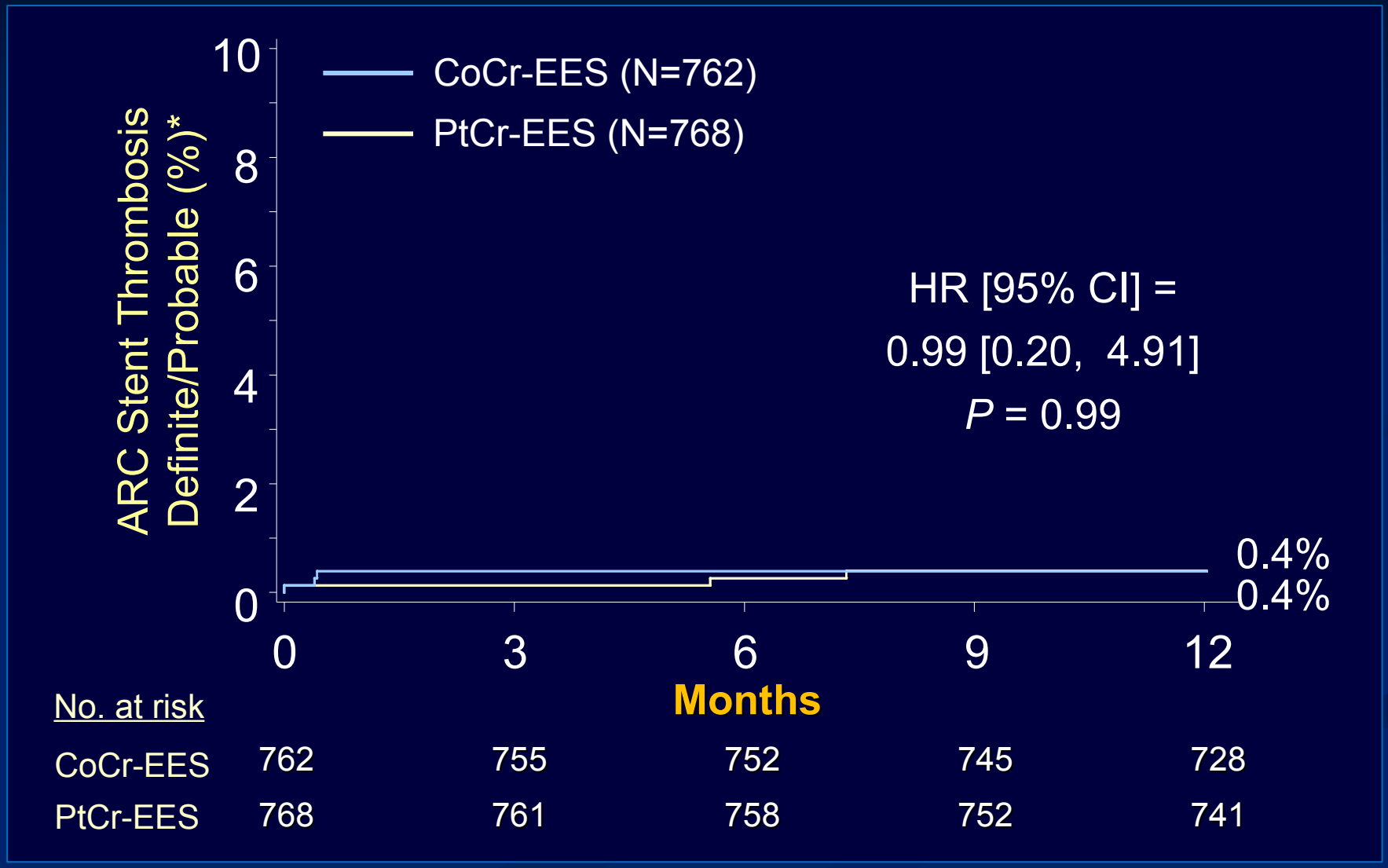

* All were definite ST

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