Two-Year Results of the PLATINUM Randomized Trial Comparing Platinum Chromium PROMUS Element and Cobalt Chromium PROMUS/XIENCE V Everolimus-Eluting Stents in De Novo Coronary Artery Lesions

Gregg W. Stone MD

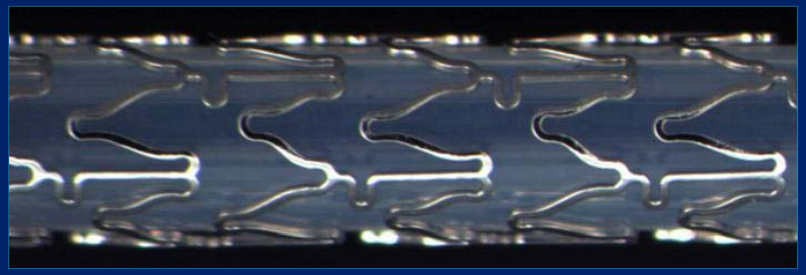
Paul S. Teirstein MD, Ian T. Meredith MBBS, PhD,
Alain Bouchard MD, Didier Carrié MD, Helge Möllmann MD,
Keith Oldroyd MD, Jack Hall MD, Dominic J. Allocco MD,
Keith D. Dawkins MD

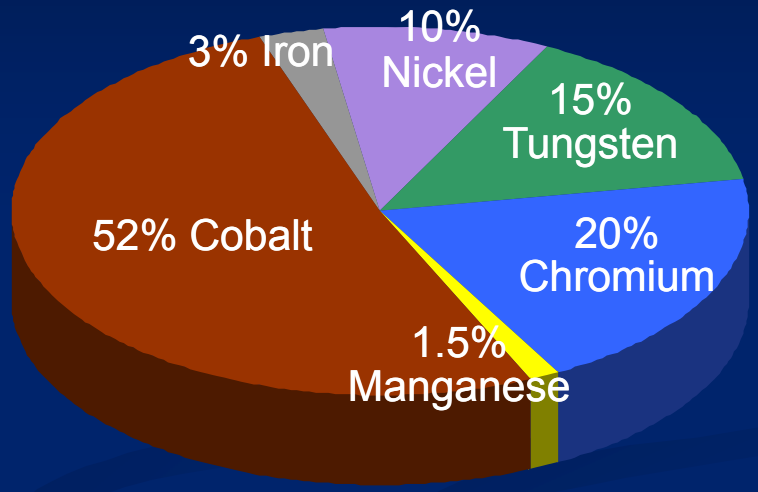
Everolimus-Eluting Stents

PROMUS PLATINUM

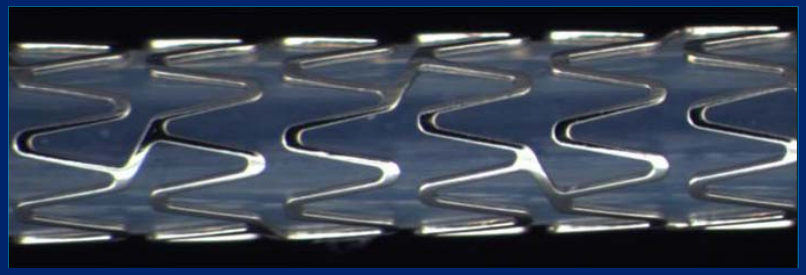
Everolimus concentration: 100 ug/cm^2
Polymer: PBMA & PVDF-HFP (7μm thickness)

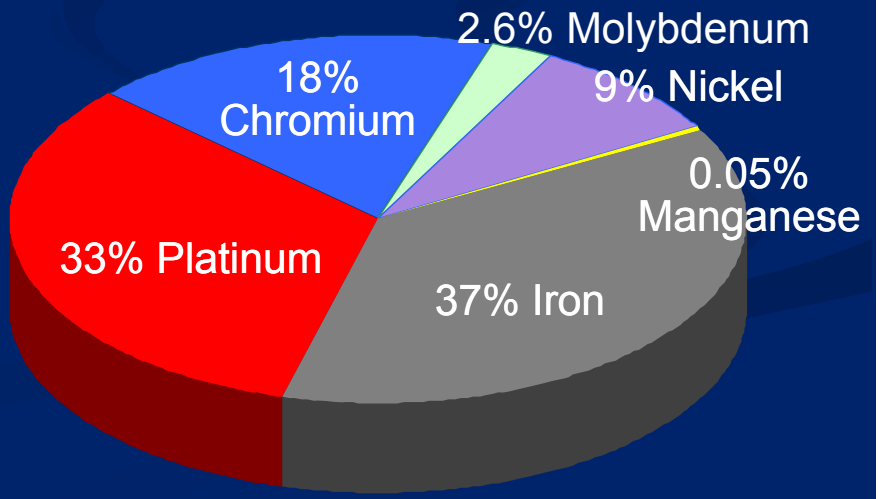
XIENCE V / PROMUS (CoCr-EES)





PROMUS Element (PtCr-EES)





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

Objective

PROMUS PLATINUM

- In the prospective, multicenter, randomized PLATINUM trial, the platinum chromium PROMUS Element Everolimus Eluting Stent (PtCr-EES) was non-inferior to the predicate cobalt chromium PROMUS/XIENCE V EES (CoCr-EES) for the 12-month primary endpoint of target lesion failure (TLF).
- Objective: To report 2-year outcomes of the PLATINUM randomized controlled trial.

PLATINUM Study Algorithm

PROMUS PLATINUM

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 2-Year Analysis

PROMUS PLATINUM

1530 patients randomized at 132 clinical sites in Asia/Pacific (N=56), European Union (N=562), Japan (N=124), & United States (N=788)

CoCr-EES (N=762)

- No 2-yr f/u (N=25)
  - Withdrew consent: 6
  - Missed 2-yr visit: 19
- No Study Stent Implanted* (N=13)

2-Year Follow-up
96.7% (724/749)

PtCr-EES (N=768)

- No 2-yr f/u (N=22)
  - Withdrew consent: 1
  - Missed 2-yr visit: 20
  - Other: 1
- No Study Stent Implanted* (N=10)

2-Year Follow-up
97.1% (736/758)

* Patients who did not receive a study stent were only followed through 1 year

Baseline Demographics

PROMUS PLATINUM

	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)

PROMUS PLATINUM

	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

PROMUS PLATINUM

	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

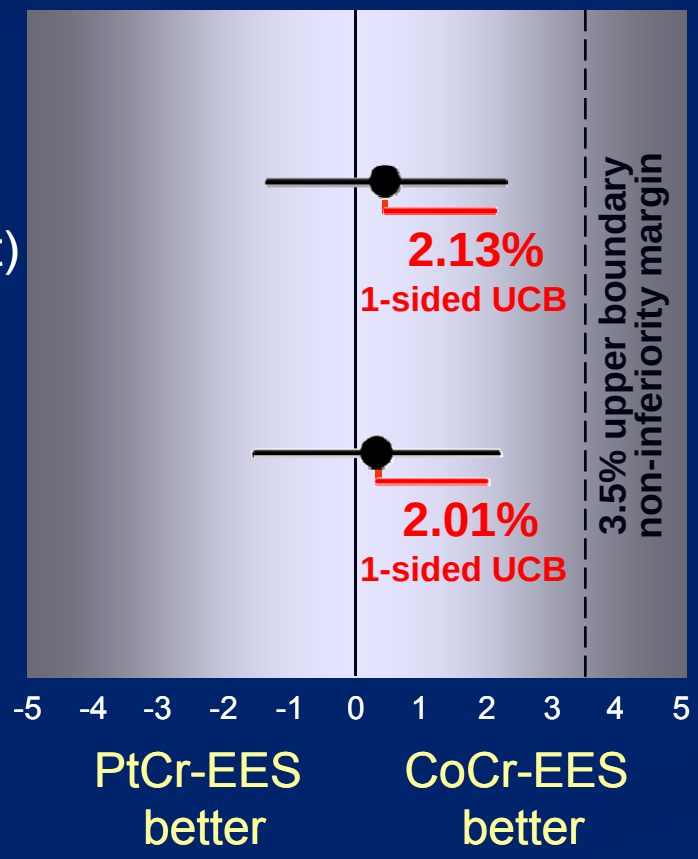
Antiplatelet Medication Usage

PROMUS PLATINUM

Medication	CoCr-EES (N=749)	PtCr-EES (N=758)	*P* value
	Discharge		
Aspirin	99.6%	98.9%	0.14
Thienopyridine	99.2%	98.9%	0.61
Aspirin + Thienopyridine	98.9%	98.0%	0.15
	1 Year		
Aspirin	93.7%	94.7%	0.41
Thienopyridine	82.7%	84.8%	0.29
Aspirin + Thienopyridine	80.5%	83.4%	0.13
	2 Years		
Aspirin	92.7%	94.8%	0.09
Thienopyridine	50.8%	53.7%	0.25
Aspirin + Thienopyridine	48.0%	51.4%	0.19

Primary Endpoint

Target Lesion Failure at 12 Months

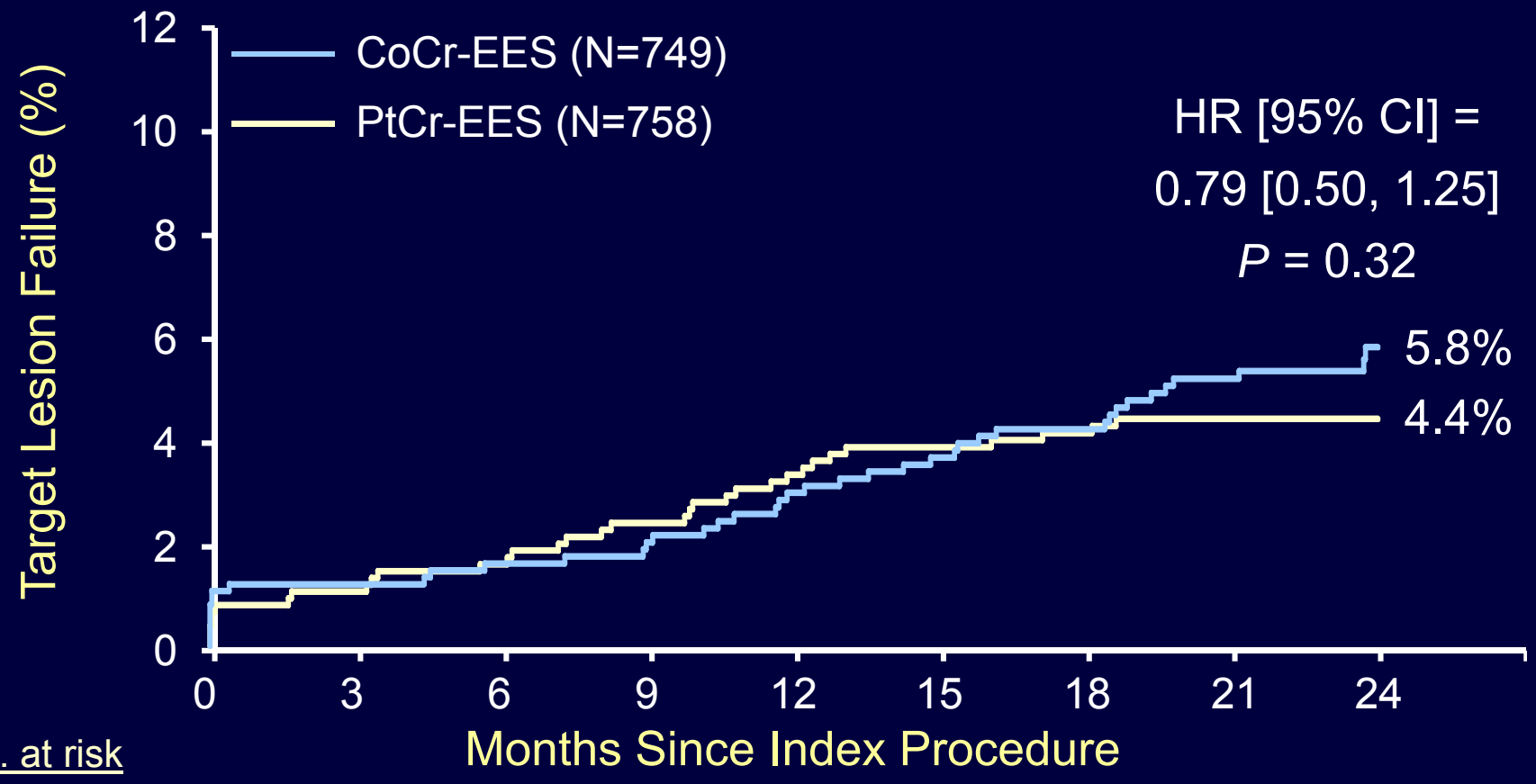


Population	Difference [2-sided 95% CI] (1-sided UCB)	CoCr-EES (N=762)	PtCr-EES (N=768)	Difference [2-sided 95% CI]	*P* Value (noninferiority) (superiority)
Per protocol (1° endpt)		2.9% (21/714)	3.4% (25/731)	0.5% [-1.3%, 2.3%]	0.001 0.60
Intent-to-treat		3.2% (23/727)	3.5% (26/742)	0.3% [-1.5%, 2.2%]	0.0009 0.72

UCB=upper confidence bound

Target Lesion Failure

2-Year Follow-up

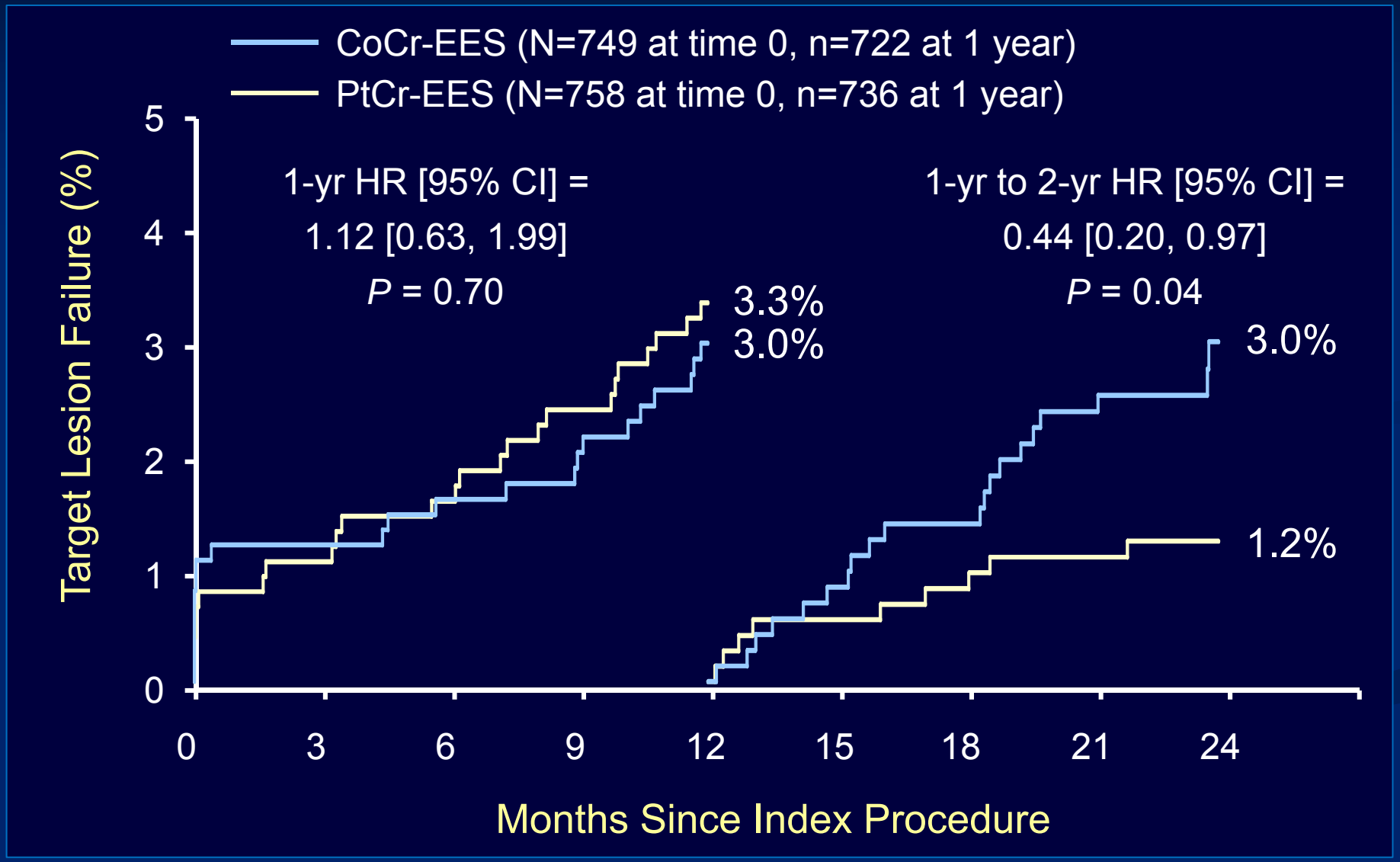


No. at risk							
CoCr-EES	749	738	737	729	717	703	685
PtCr-EES	758	747	742	739	727	718	700

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

Target Lesion Failure

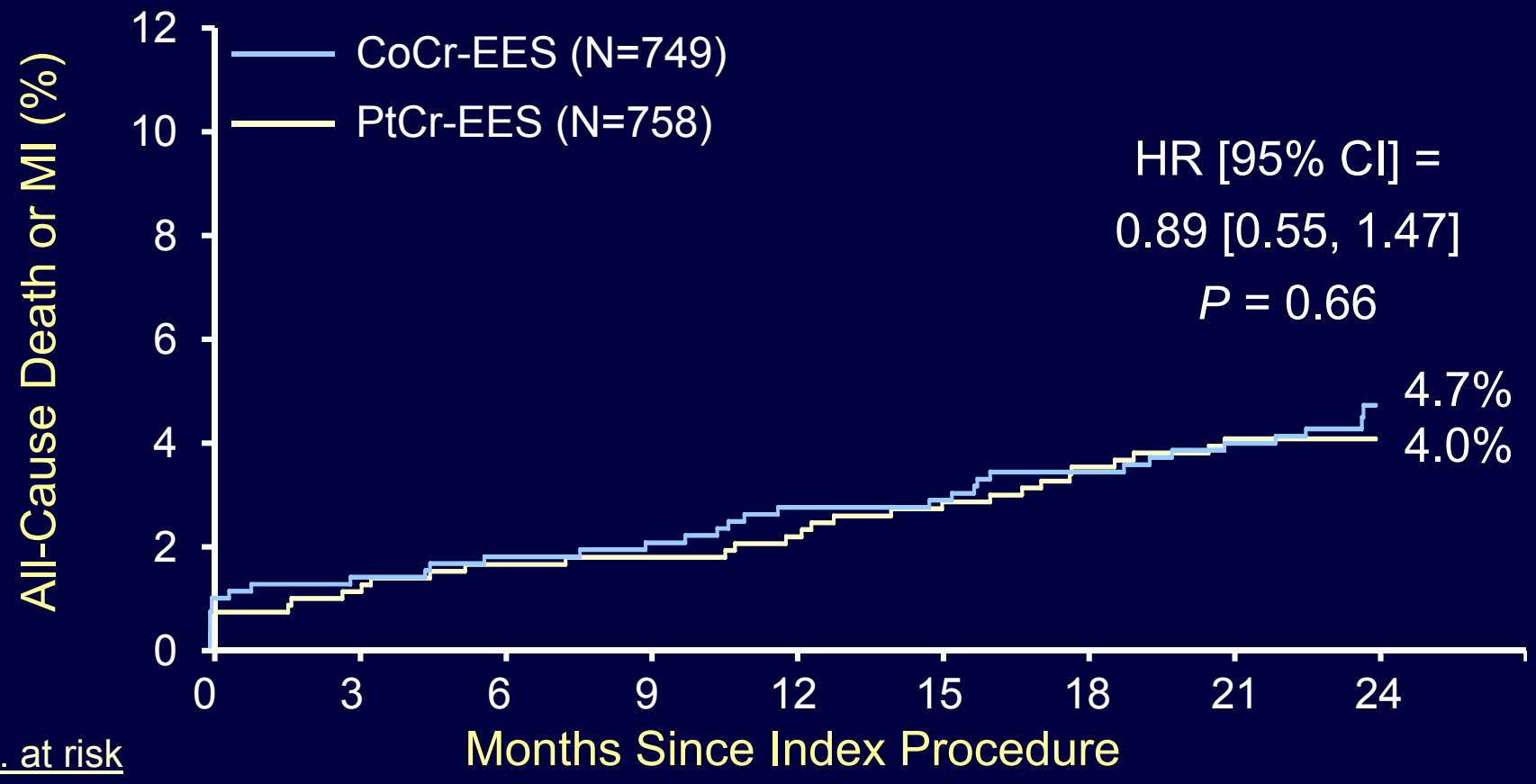
2-Year Landmark Analysis



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

All-Cause Death or MI

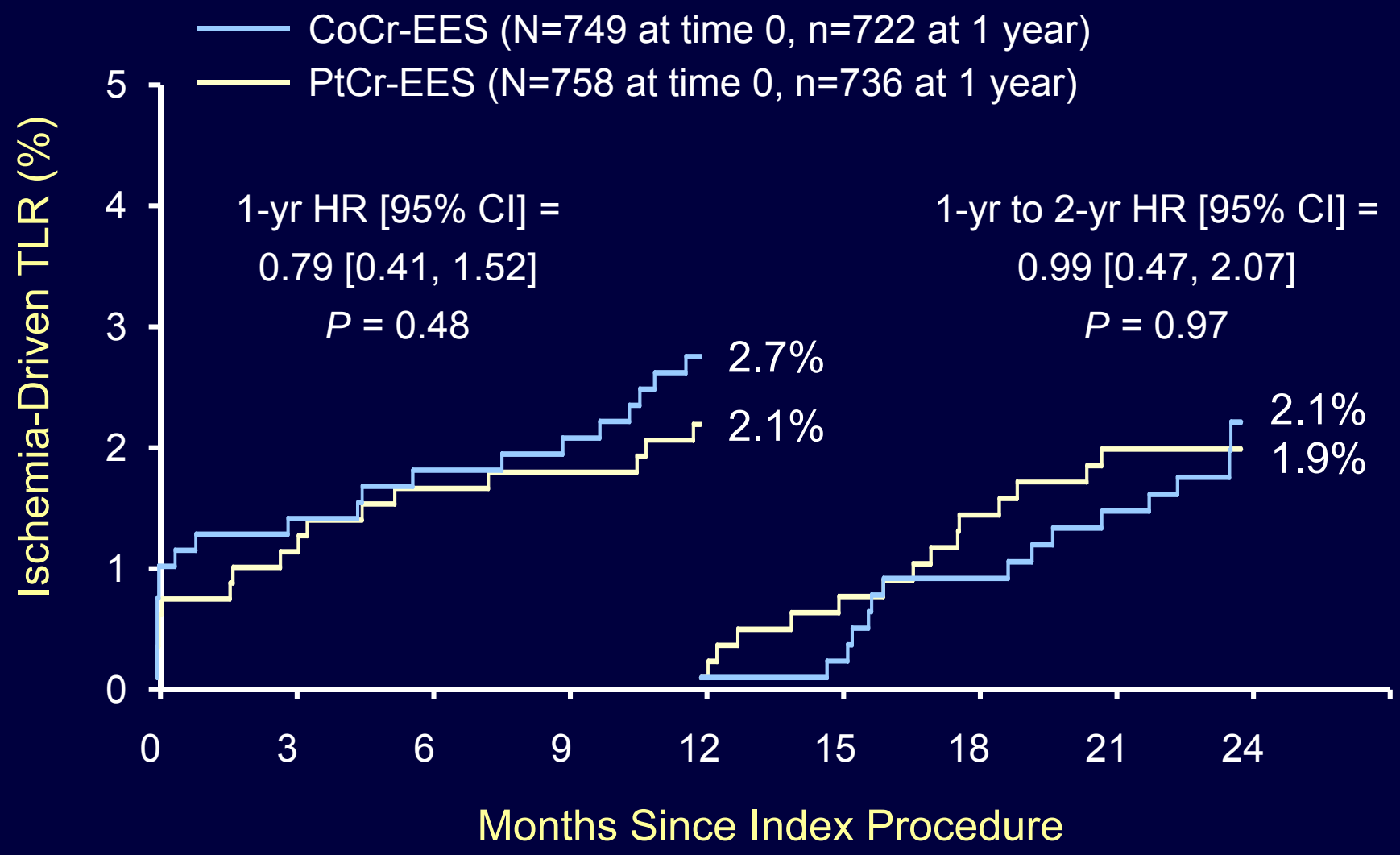
2-Year Follow-up



No. at risk							
CoCr-EES	749	739	738	731	720	711	700
PtCr-EES	758	748	745	741	733	729	713

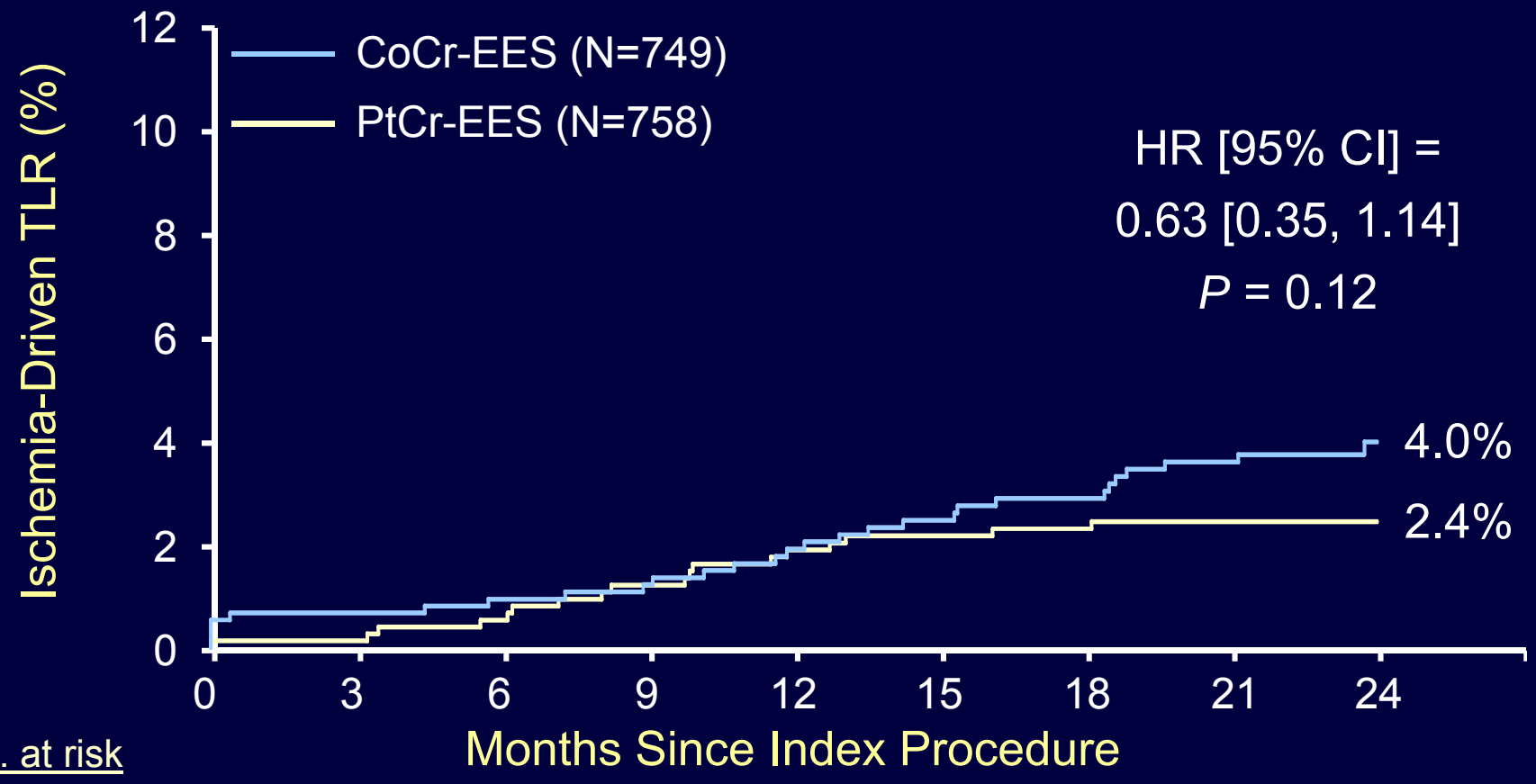
All-Cause Death or MI

2-Year Landmark Analysis



Ischemia-Driven TLR

2-Year Follow-up

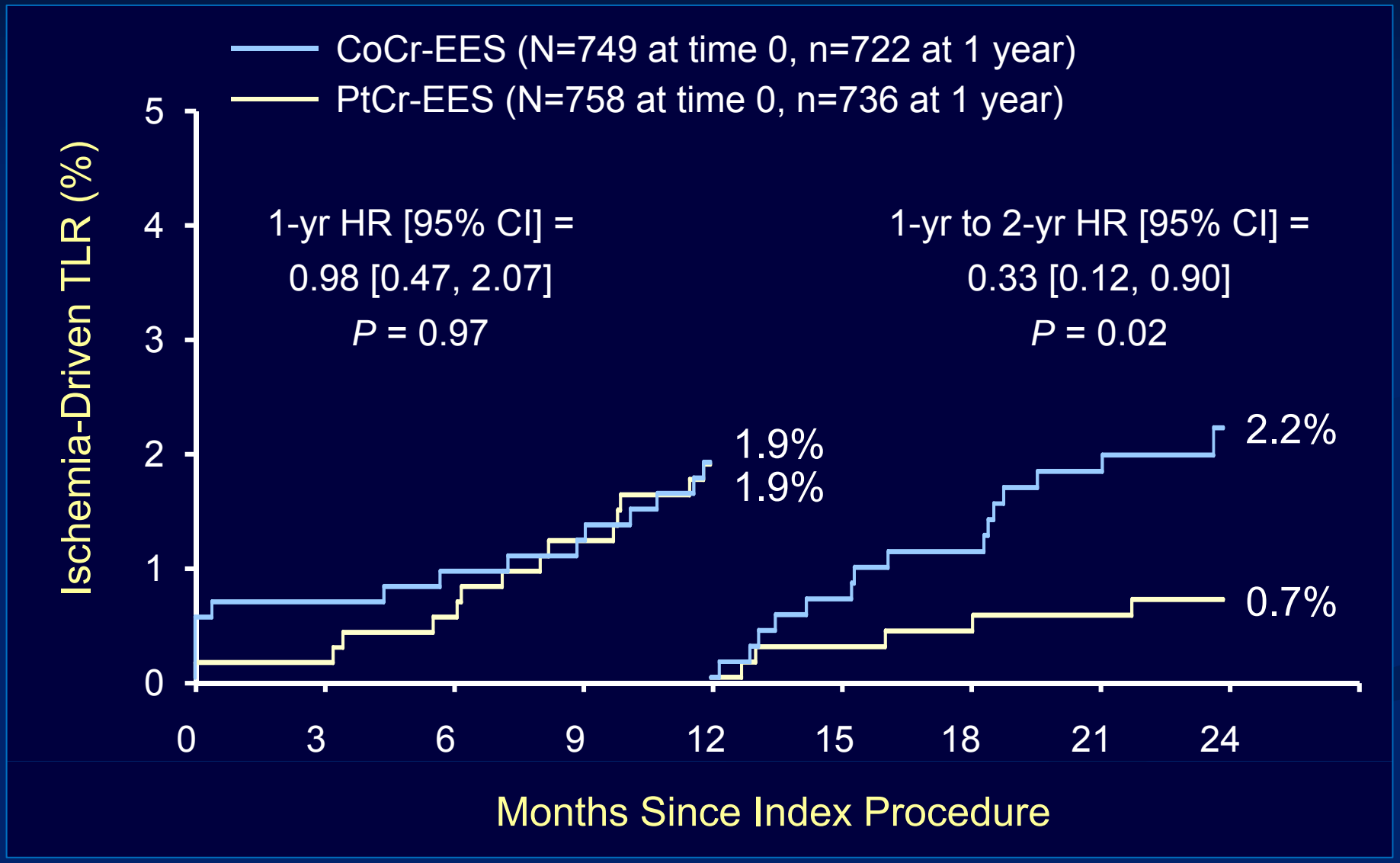


No. at risk							
CoCr-EES	749	742	741	733	721	708	690
PtCr-EES	758	751	746	743	732	723	708

TLR = target lesion revascularization

Ischemia-Driven TLR

2-Year Landmark Analysis



TLR = target lesion revascularization

Two-Year Safety Outcomes

PROMUS PLATINUM

Death and Myocardial Infarction	CoCr-EES (N=749)	PtCr-EES (N=758)	HR [95% CI]	*P* Value
All-cause death	2.8% (20)	2.4% (18)	0.89 [0.47-1.68]	0.71
- Cardiac	1.6% (11)	0.9% (7)	0.63 [0.24-1.62]	0.33
- Non-cardiac	1.2% (9)	1.5% (11)	1.20 [0.50-2.90]	0.68
Any MI	2.2% (15)	1.6% (12)	0.79 [0.37-1.68]	0.54
- TV-related	2.1% (14)	1.2% (9)	0.63 [0.27-1.46]	0.28
- Non-TV-related	0.1% (1)	0.4% (3)	2.97 [0.31-28.53]	0.32
- Q-wave	1.0% (6)	0.3% (2)	0.33 [0.07-1.63]	0.15
- Non-Q-wave	1.5% (11)	1.3% (10)	0.90 [0.38-2.11]	0.80

TV = Target Vessel

Two-Year Efficacy Outcomes

PROMUS PLATINUM

Ischemia-driven Revascularization	CoCr-EES (N=749)	PtCr-EES (N=758)	HR [95% CI]	*P* Value
Target Vessel	5.6% (39)	4.2% (31)	0.78 [0.49-1.25]	0.30
- PCI	4.8% (34)	3.5% (26)	0.75 [0.45-1.25]	0.27
- CABG	0.8% (5)	0.8% (6)	1.19 [0.36-3.89]	0.78
Target Lesion	4.0% (28)	2.4% (18)	0.63 [0.35-1.14]	0.12
- PCI	3.5% (25)	1.9% (14)	0.55 [0.29-1.06]	0.07
- CABG	0.4% (3)	0.5% (4)	1.31 [0.29-5.87]	0.72
TVR, non-TLR	1.9% (13)	2.0% (15)	1.14 [0.54-2.39]	0.73

TVR=target vessel revascularization; TLR=target lesion revascularization

One-Year to Two-Year Landmark

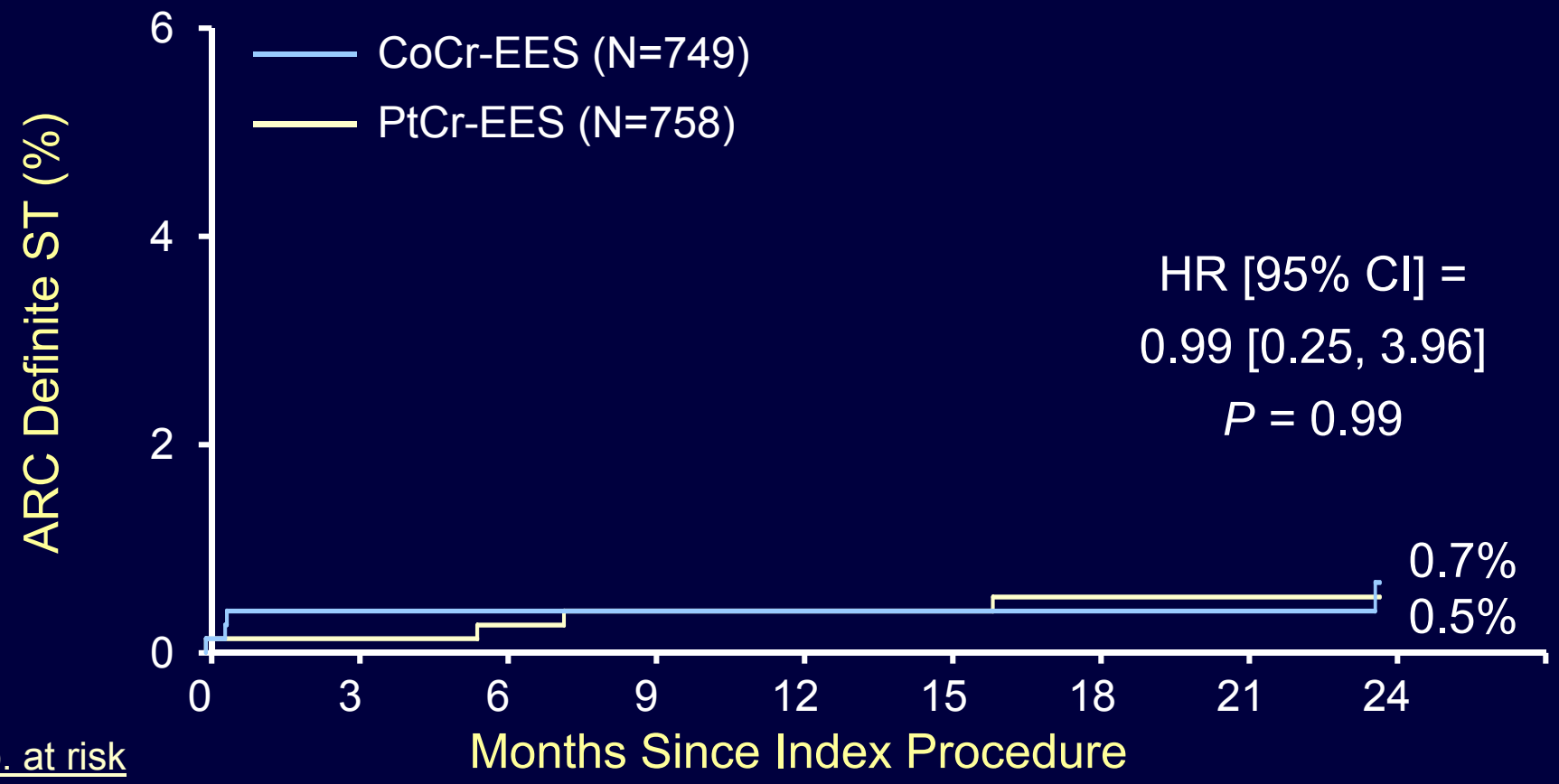
PROMUS PLATINUM

	CoCr-EES (N=722)	PtCr-EES (N=736)	HR [95% CI]	*P* Value
Death	1.6% (11)	1.2% (9)	0.80 [0.33-1.94]	0.63
- Cardiac	0.9% (6)	0.1% (1)	0.16 [0.02-1.36]	0.06
MI	0.9% (5)	0.7% (5)	0.99 [0.29-3.41]	0.98
Death or MI	2.1% (14)	1.9% (14)	0.99 [0.47-2.07]	0.97
TLR	2.2% (15)	0.7% (5)	0.33 [0.12-0.90]	0.02
TVR	2.8% (19)	1.7% (12)	0.62 [0.30-1.28]	0.19
TLF	3.0% (20)	1.2% (9)	0.44 [0.20-0.97]	0.04
Death, MI or TVR	4.6% (31)	3.3% (24)	0.76 [0.45-1.30]	0.31

TVR = target vessel revascularization; TLR = target lesion revascularization; TLF = target lesion failure

Stent Thrombosis - ARC Definite

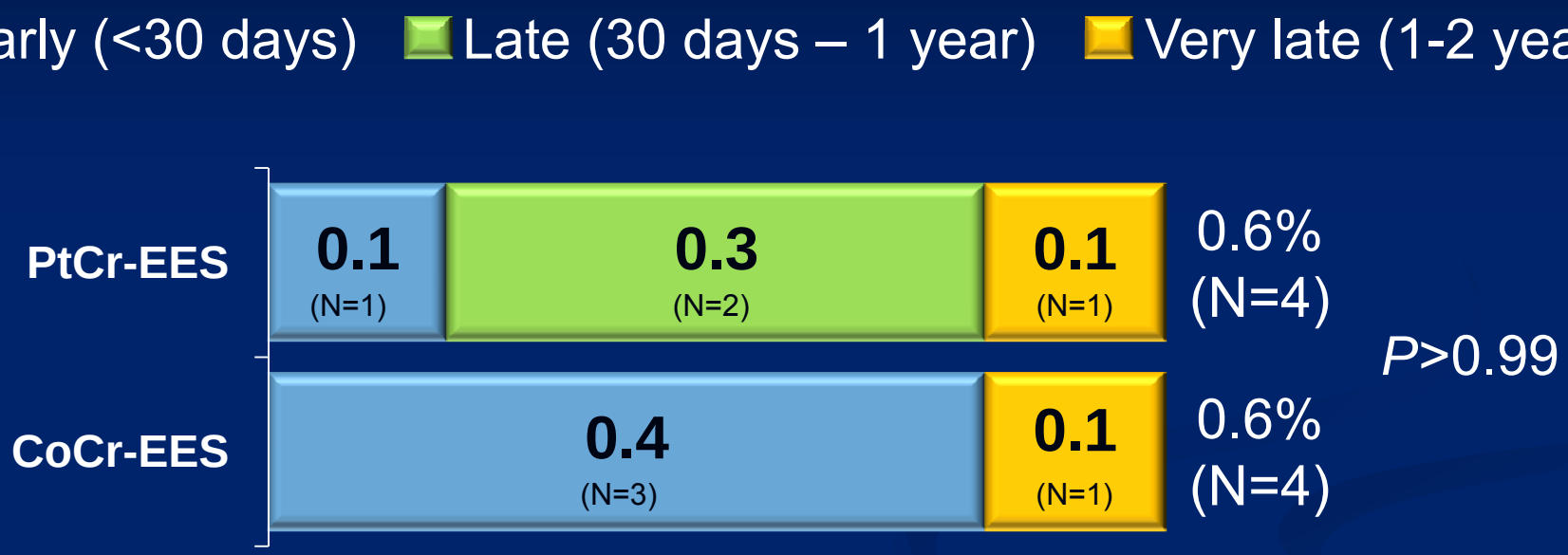
2-Year Follow-up



No. at risk							
CoCr-EES	749	744	743	737	726	719	708
PtCr-EES	758	751	748	745	737	733	720

Note: There were no adjudicated ARC probable ST events through 2 year follow-up

ARC Definite Stent Thrombosis



There were no adjudicated ARC probable ST events through 2-year follow-up

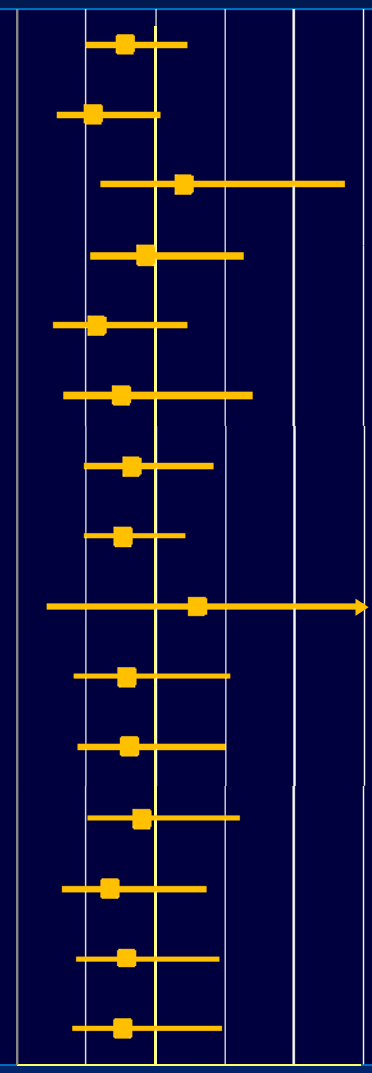
Binary Rates
ARC=Academic Research Consortium

PLATINUM Subgroup Analyses

PROMUS PLATINUM

TLF at 2 Years

	CoCr (%)	PtCr (%)	Relative Risk (95% CI)	*P* Interaction
All randomized (n=1507)	5.8%	4.6%	0.78 (0.50-1.22)	0.28
Age < 65.0 yrs (n=779)	7.0%	3.9%	0.55 (0.29-1.03)	0.10
Age ≥ 65.0 yrs (n=728)	4.4%	5.3%	1.20 (0.61-2.36)	
Male (n=1074)	4.8%	4.5%	0.93 (0.53-1.63)	0.30
Female (n=433)	8.4%	4.8%	0.57 (0.27-1.22)	
Diabetic (n=351)	7.9%	5.9%	0.75 (0.34-1.69)	0.86
Nondiabetic (n=1156)	5.1%	4.2%	0.82 (0.48-1.40)	
Single vessel Tx (n=1399)	6.0%	4.5%	0.76 (0.48-1.20)	0.56
Dual vessel Tx (n=108)	4.1%	5.3%	1.29 (0.22-7.41)	
BMI < 30 kg/m^2 (n=842)	4.8%	3.8%	0.79 (0.41-1.53)	0.96
BMI ≥ 30 kg/m^2 (n=663)	7.0%	5.7%	0.81 (0.44-1.49)	
RVD ≤ 2.62 mm (n=778)	6.3%	5.6%	0.90 (0.51-1.60)	0.52
RVD > 2.62 mm (n=728)	5.3%	3.6%	0.67 (0.33-1.35)	
Lesion ≤ 13.0 mm (n=870)	5.3%	4.2%	0.79 (0.43-1.45)	0.94
Lesion > 13.0 mm (n=636)	6.6%	5.0%	0.76 (0.40-1.47)	



Binary Rates

Conclusions (1)

PROMUS PLATINUM

- In the prospective, multicenter, randomized PLATINUM trial, the PtCr-EES was non-inferior to the predicate CoCr-EES for the primary endpoint of TLF at 12-months.
- Through 2-year follow-up, the safety and efficacy outcomes between the PtCr-EES and the CoCr-EES remain comparable, with no significant differences in the rates of death, MI, stent thrombosis, or ischemia-driven repeat revascularization.

Conclusions (2)

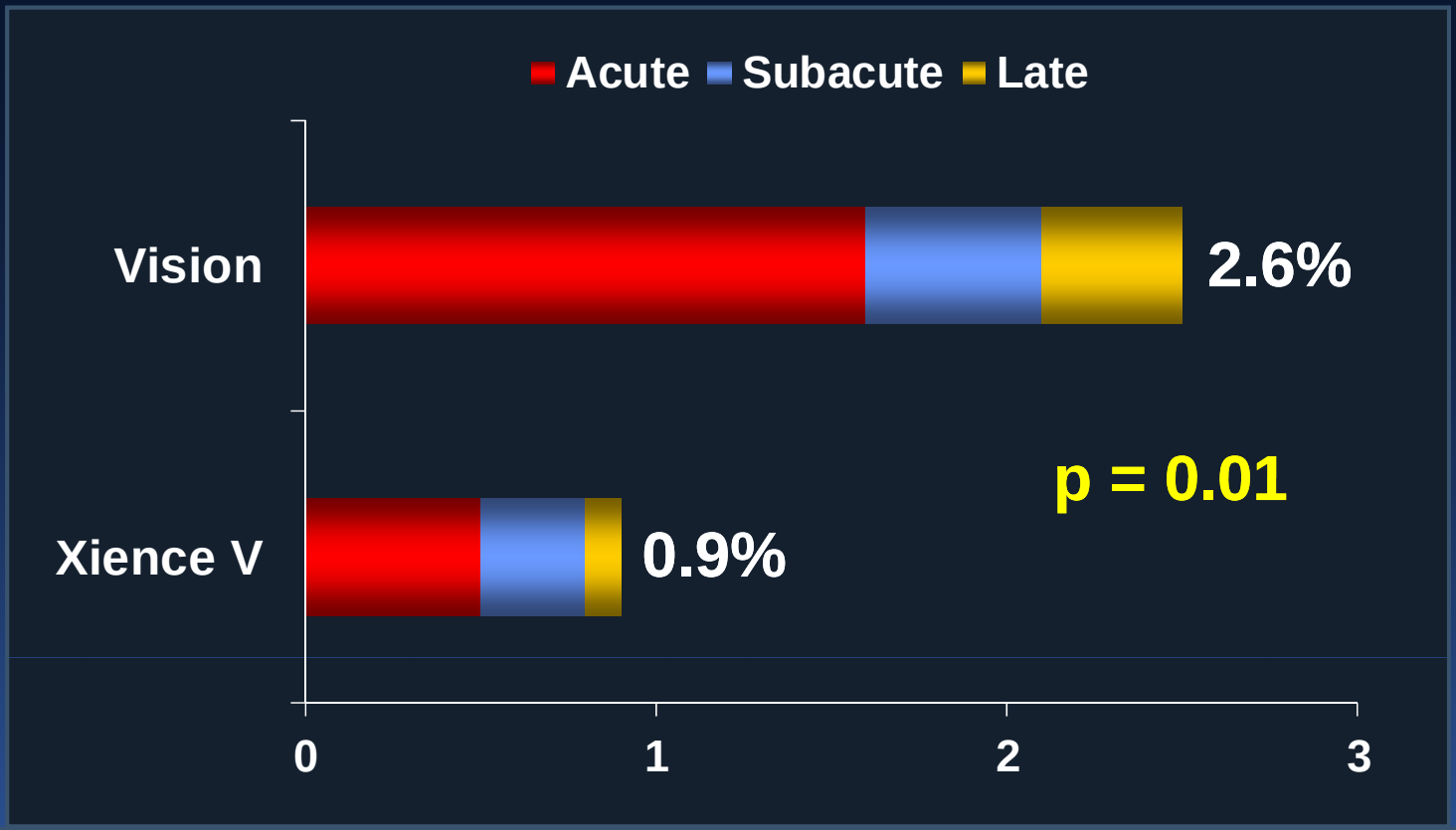
PROMUS PLATINUM

- Of note, a significant reduction in ischemia-driven repeat target lesion revascularization was present between the first and second year of follow-up with the PtCr-EES compared to the CoCr-EES.
- This finding, while potentially important, must be confirmed by longer-term follow-up.

EXAMINATION Trial

1504 pts with STEMI undergoing PCI within 48° (85% primary PCI within 12°) were randomized to Promus EES vs. Vision BMS

Stent thrombosis (Def/prob) within 1 year



Definite ST was reduced with Xience V from 1.9% to 0.5%, p=0.01

Sabate M. ESC 2011

HORIZONS-AMI II

Harmonizing Outcomes with Revascularization and Stents in AMI II

7,000 – 10,000 pts with STEMI

Aspirin | Prasugrel (open-label)

Primary PCI with bivalirudin anticoagulation

Stent randomization eligible — R 1:1

- Promus Element DES
- Omega BMS

Follow-up at 30 days

Pts without MACE or bleeding — R 1:1 — Double-blind

- Prasugrel
- Clopidogrel

Clinical FU: **All pts: 30 d, 6 mo, 1 yr, 2 yr, 3 yr**
Pharmacology rand only: 15 mo

HORIZONS AMI

HORIZONS-AMI II

Harmonizing Outcomes with Revascularization and Stents in AMI II

Powered endpoints

Stent randomization:

Death, MI or TLR at 12 months (superiority)
Stent thrombosis at 12 months (superiority)

Pharmacology randomization:

NACE: Death, MI, stroke, definite/probable stent thrombosis, or TIMI major/minor bleeding (noninferiority between 1 and 15 months)

Sponsors: Boston Scientific and The Medicines Co.
ARO partner: The Cardiovascular Research Foundation

HORIZONSAMI