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Potential conflicts of interest

Speaker's name: Pieter C. Smits

I have the following potential conflicts of interest to report:

X Research contracts: Abbott Vascular, Terumo, St. Jude
☐ Consulting: none
☐ Employment in industry; none
☐ Stockholder of a healthcare company; none
☐ Owner of a healthcare company; none
X Other(s): travel and speaking fees from Abbott Vascular

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COMPARE II trial
3 year follow-up data

Pieter Smits

On behalf of all principal COMPARE II investigators:

Sjoerd Hofma, Jean-Jaques Goy, Peter den Heyer, Antonio Serra, Ton Slagboom, Mario Togni, Ramiro Trillo Nouche, Mariano Valdés, Andre Vuillomenet, Jose Vázquez, Vassilis Voudris

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COMPARE II trial

Is a large scale, multicenter, prospective randomised comparison between the durable polymer everolimus-eluting stent and the abluminal biodegradable polymer biolimus-eluting stent in a real life setting

ClinicalTrials.gov Identifier: NCT01233453

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Introduction

First generation drug eluting stents (DES) have shown to be superior in preventing re-stenosis compared to bare metal stents, however, at an increased risk of late stent thrombosis due to delayed re-endothelialisation and healing, specifically when used in a real life /off-label setting.

In an attempt to overcome these unwanted late effects of DES, new generation DES with other limus analogues and more biocompatible durable polymers or biodegradable polymers have been developed.

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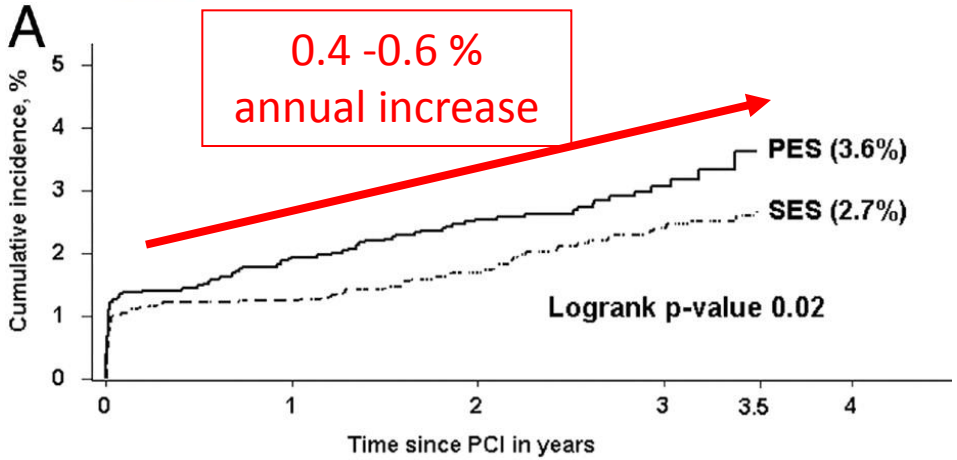
Incidence of ST with 1e gen DES



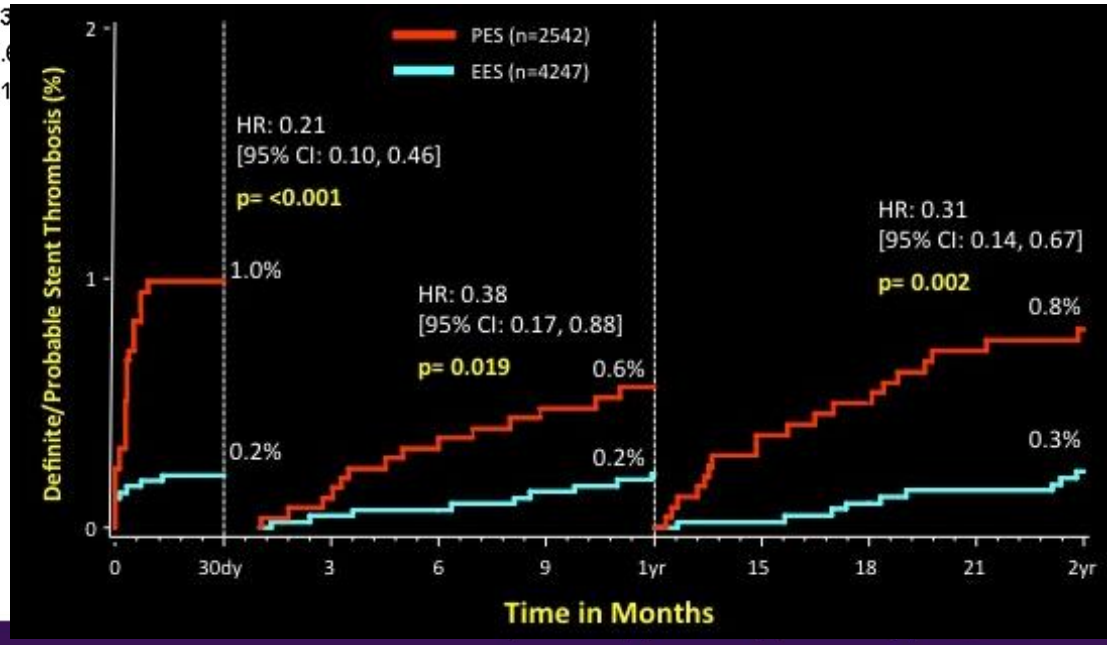
Months	1	12	24	36	42
Cumulative incidence SES, %	1.0	1.2	1.7	2.4	2.7
Patients at risk SES	3645	3519	2512	1736	13
Cumulative incidence PES, %	1.3	1.9	2.5	3.1	3.
Patients at risk PES	3892	3690	2645	1011	21

Bern-Rotterdam registry
8146 pts. Def. ST

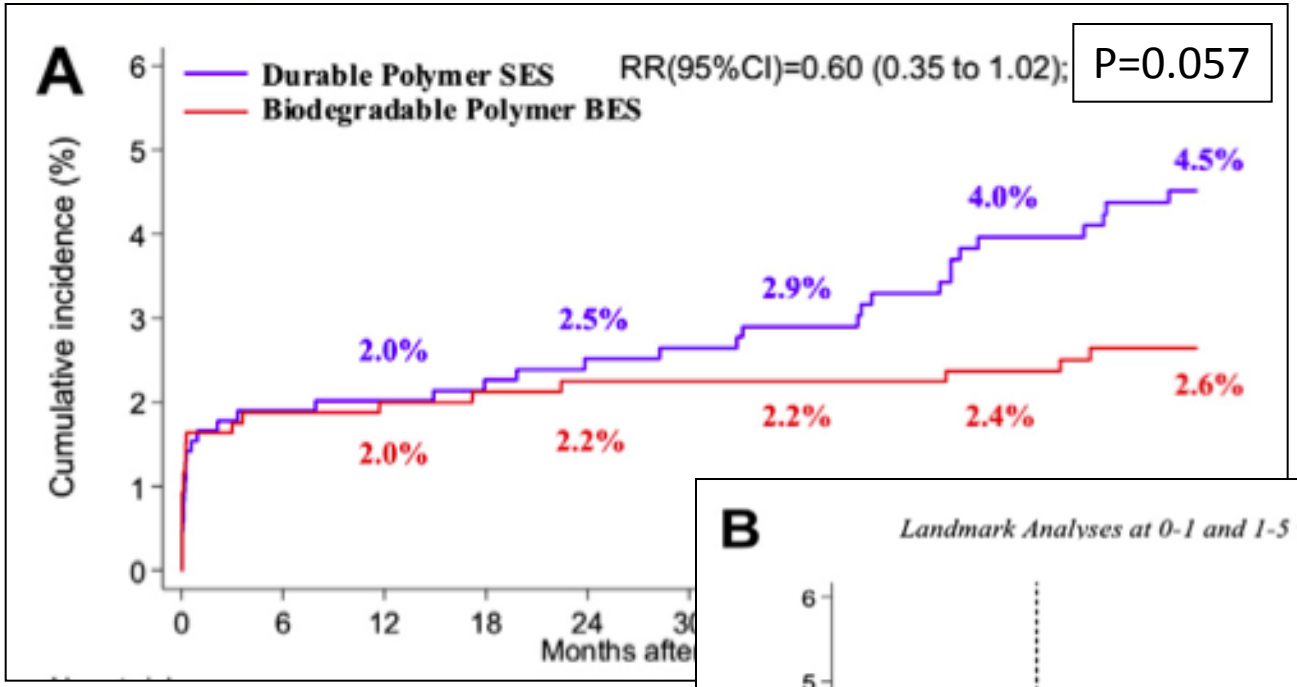
Wenaweser, P. et al. J ACC 2008;52:1134-1140

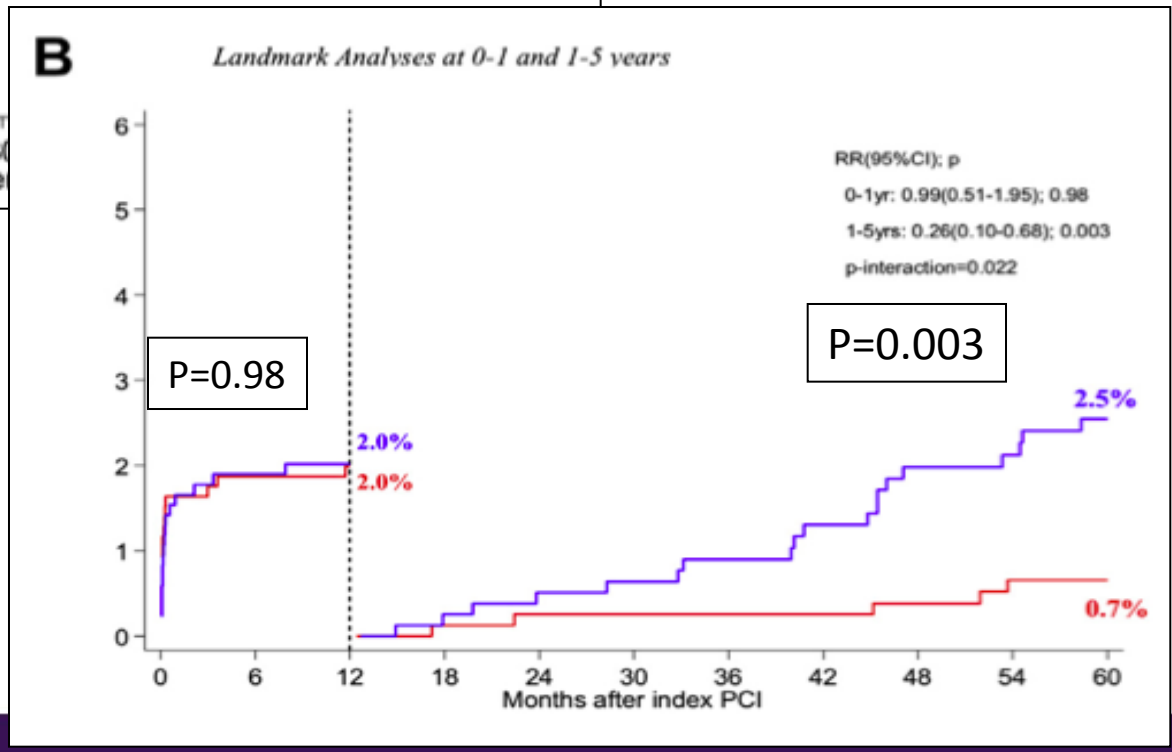
Pooled SPIRIT II, II, IV & COMPARE
6788 pts, def/prob ST

Planer/Smits et al. JACC. Int 2011



LEADERS 5 year def. ST





Serruys et al.
JACC INTERV 2013

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Purpose

The main objective of the COMPARE II trial is

a head to head comparison of

the everolimus eluting XIENCE-V/PRIME/ PROMUS®(EES)

with

the biolimus eluting NOBORI® stent (BES)

to assess:

whether there is a difference in clinical outcome between the two different stent types in a real life situation at short (1 year) and long term (3 & 5 year) follow-up

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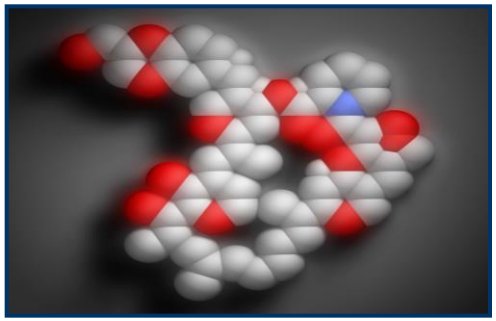
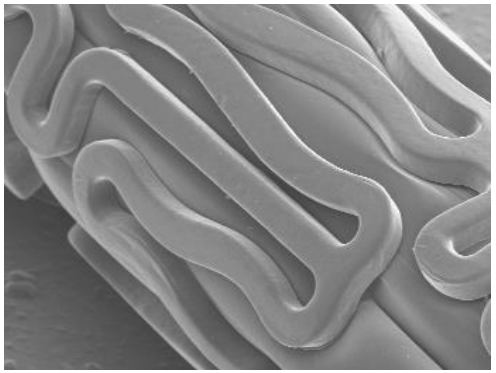
Xience / Promus



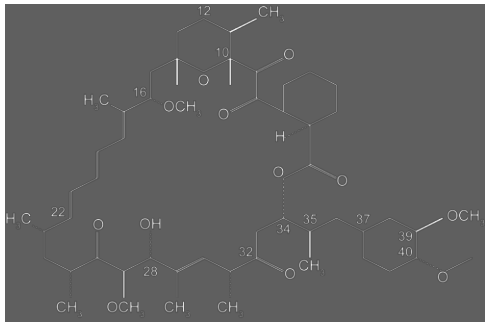
Everolimus 1.0 $\mu g/mm^2$



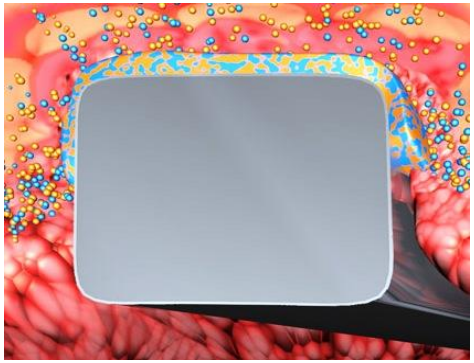
Fluoropolymer

Vision multilink™
CoCr, strut 81 μm

Nobori



Biolimus 15,6 $\mu g/mm$

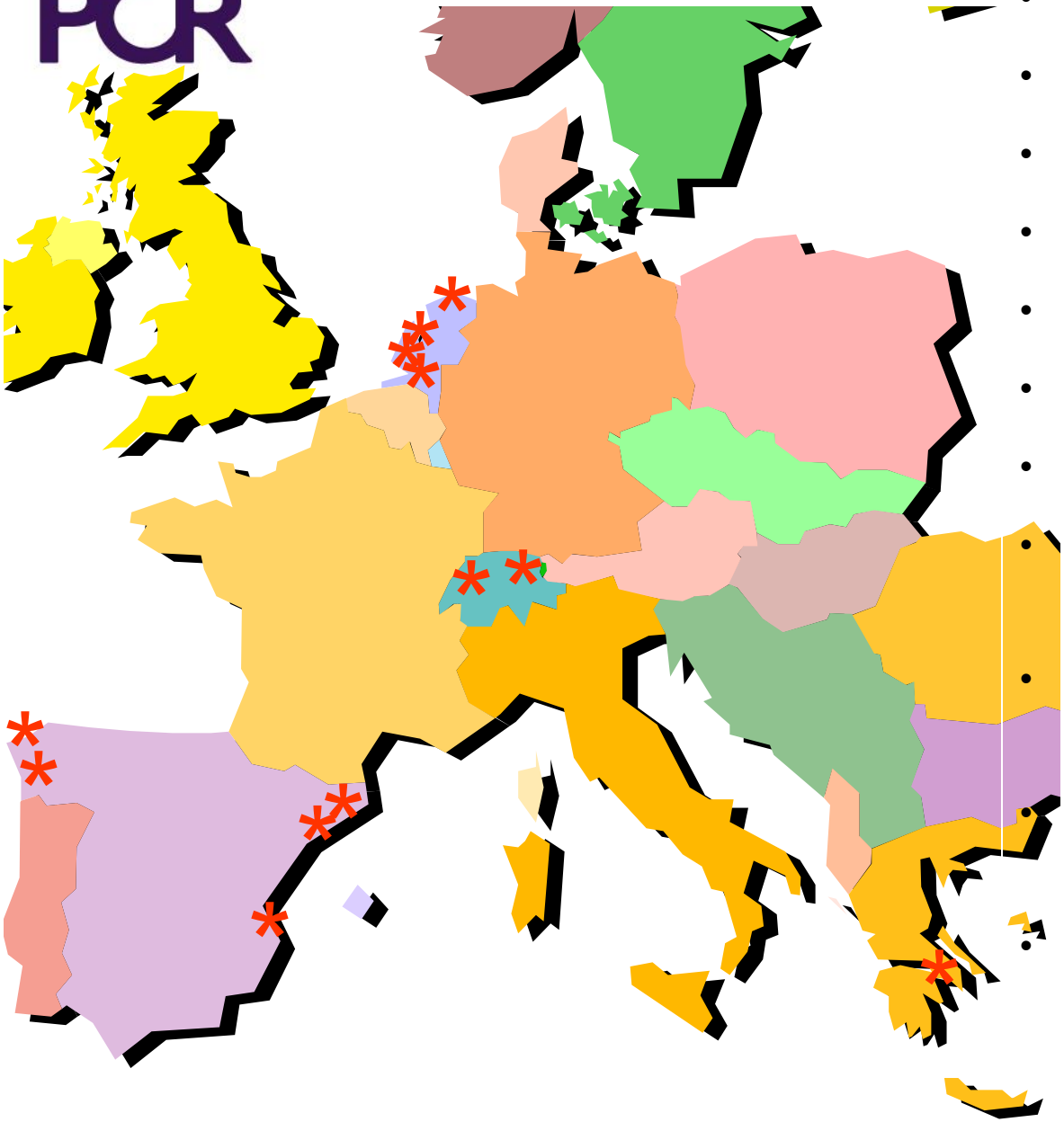


Poly-lactic acid

S-Stent™
Stainless Steel, 120 μm

Methodology

- Patients eligible for PCI were prospectively randomized (1:2) between EES or BES in 12 sites across Europe



- MC Leeuwarden, NL
- Maasstad Rotterdam, NL
- OLVG Amsterdam, NL
- Amphia Breda, NL
- Kantonsspital Aarau, Aarau, Sw
- HFR Hospital, Fribourg, Sw
- University Hospital, Coruna, Sp
- University Hospital, Santiago de Compostella, Sp
- Hospital del Mar & San Pau, Barcelona, Sp
- University Hospital, Virgin de la Arrixaca, Murcia, Sp
- Onassis Cardiac Surgery Center, Athens, Gr

Methodology

- Patients eligible for PCI were prospectively randomized (1:2) between EES or BES in 12 sites across Europe
- There were minimal in- and exclusion criteria

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Study Outline

Inclusion criteria

- All patients eligible for PCI > 18 years old
- Life expectancy of > 5 years
- Ref. lumen diameter 2.0 – 4.0 mm

Exclusion criteria

- No dual antiplatelet therapy for 12 months
- Cardiogenic shock at presentation (Killip class IV)
- Expected planned major surgery within 1 month
- PCI with DES in the previous year
- Participation in investigative stent study
- No informed consent or expected loss follow-up

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Methodology

- Patients eligible for PCI were prospectively randomized (1:2) between EES or BES in 12 sites across Europe
- There were minimal in- and exclusion criteria
- The trial was physician initiated
- All sites independently monitored
- All events independently adjudicated
- Primary analysis: non inferiority @ 1 year

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Endpoints

Primary endpoint

Composite of cardiac death, non-fatal myocardial infarction and target vessel revascularization

Major secondary endpoints

- Composite of cardiac death, non-fatal myocardial infarction and clinically indicated target lesion revascularization
- Stent thrombosis (def/prob) according to ARC

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N=2707
Enrolled patients

1:2 randomisation

Xience / Promus
N=912
1387 lesions

Nobori
N=1795
2638 lesions

Lost to follow-up n=7
Withdrew consent n=1

Lost to follow-up n=4
Withdrew consent n=2

Xience / Promus
(N=904)

1-year Follow-up
(N= 2693; 99.5%)

Nobori
(N=1789)

Lost to follow-up n=0
Withdrew consent n=1

Lost to follow-up n=3
Withdrew consent n=6

Xience / Promus
(N=903)

3-year Follow-up
(N= 2683; 99.1%)

Nobori
(N=1780)

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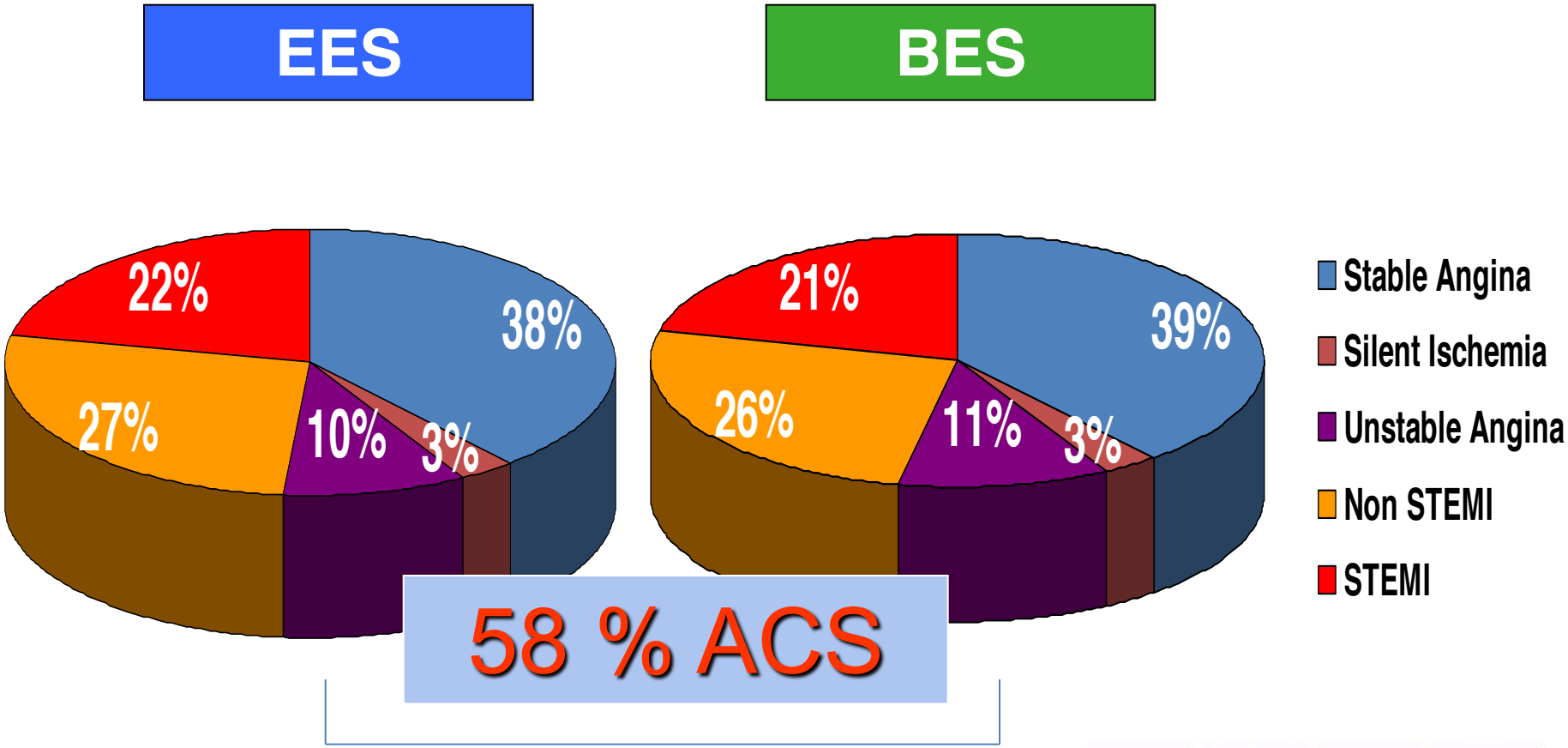
Baseline Characteristics
Clinical presentation 2707 pts.

	EES 912 pts	BES 1795 pts	p
Age	62.7	63.0	0.37
Male	74 %	74 %	0.96
• Previous AMI	19 %	20 %	0.36
• Previous PCI	17 %	18 %	0.63
• Previous CABG	5.7 %	5.9 %	0.93
• Previous CVA	5.3 %	5.3 %	1.00
• Peripheral artery disease	5.6 %	7.6 %	0.06
Diabetes	22 %	22 %	0.92
Smoking (active)	27 %	31 %	0.07
Smoking (past)	37 %	36 %	0.61
Hypertension	56 %	55 %	0.49

Clinical Presentation
2707 pts.



p = ns

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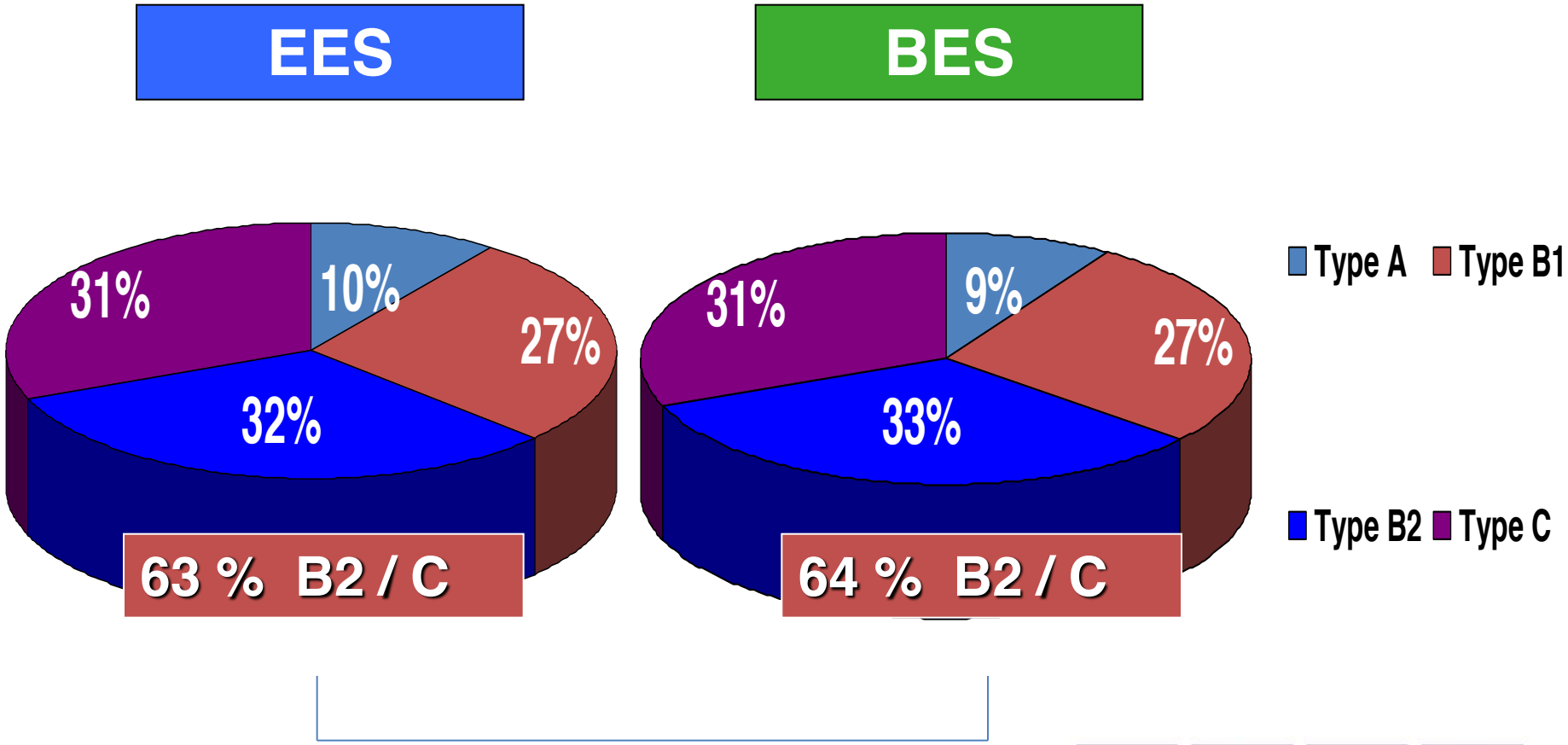
Baseline Characteristics
2707 patients / 4025 lesions

	EES	BES	p
Lesions	**1387**	**2638**	
• LM	1.2 %	1.6 %	0.35
• LAD	39.7 %	40.9 %	
• RCX	25.7 %	22.8 %	
• RCA	32.3 %	33.4 %	
• Grafts	1.3 %	1.2 %	
Lesion per patient	1.52	1.47	0.36
Bifurcation treatment	6.5 %	6.4 %	0.95
Stent per lesion	1.43	1.44	0.98
GP 2b3a blockers	20 %	20 %	0.71

Lesion Characteristics
2707 patients / 4025 lesions



COMPARE II TRIAL

STEMI 21 %

Ostial 14 %

Chronic renal failure 4 %

Bifurcation 6 %

Calcification 31 %

Diabetes 22 %

Direct stenting 39 %

"REAL WORLD"

Saphenous graft 1.2 %

Overlapping 30 %

Multivessel 25 %

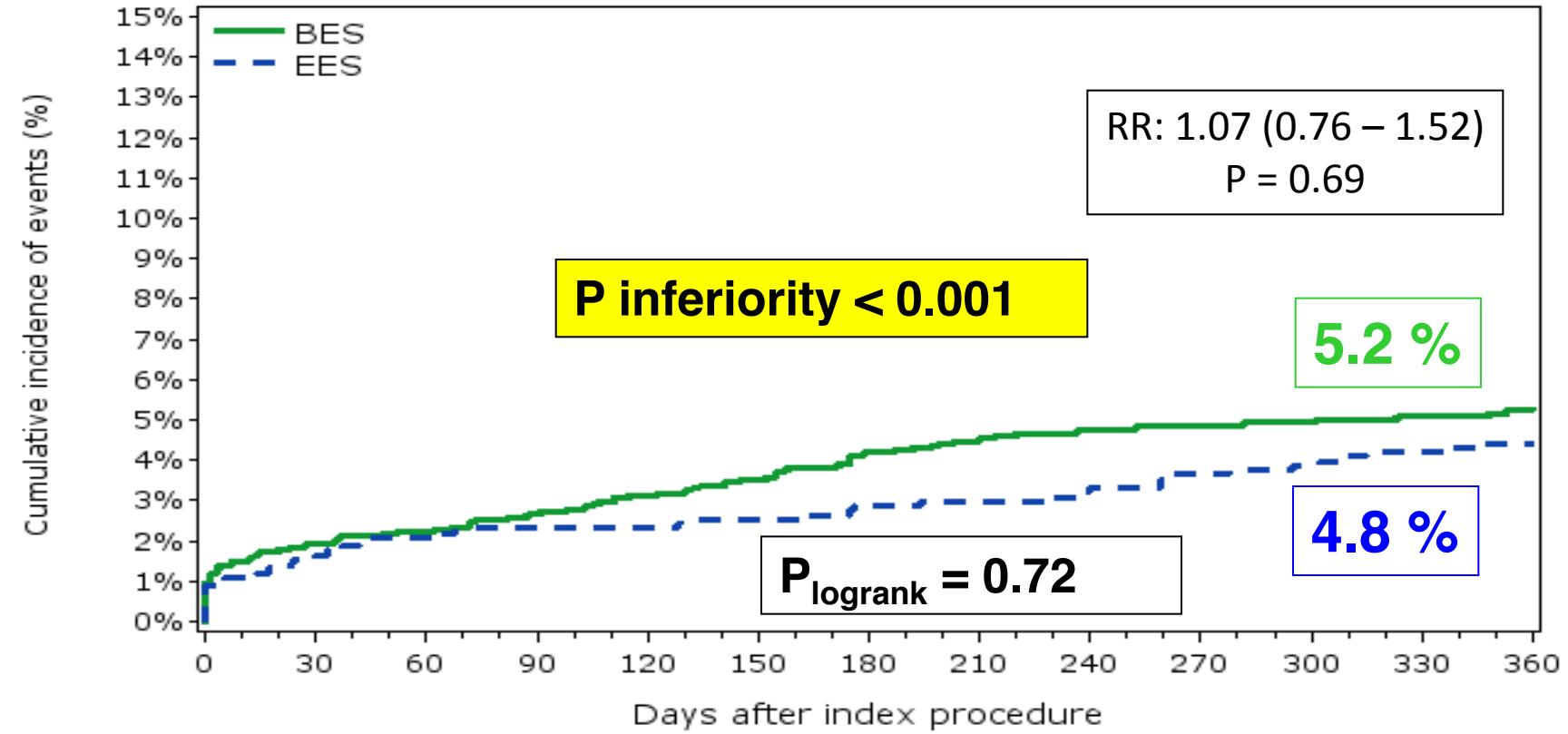
Left Main 1.4 %

NSTEMI 26 %

Thrombus 21 %

CTO 3 %

Primary endpoint @ 1 year
C-Death, MI, CI-TVR



Number at Risk

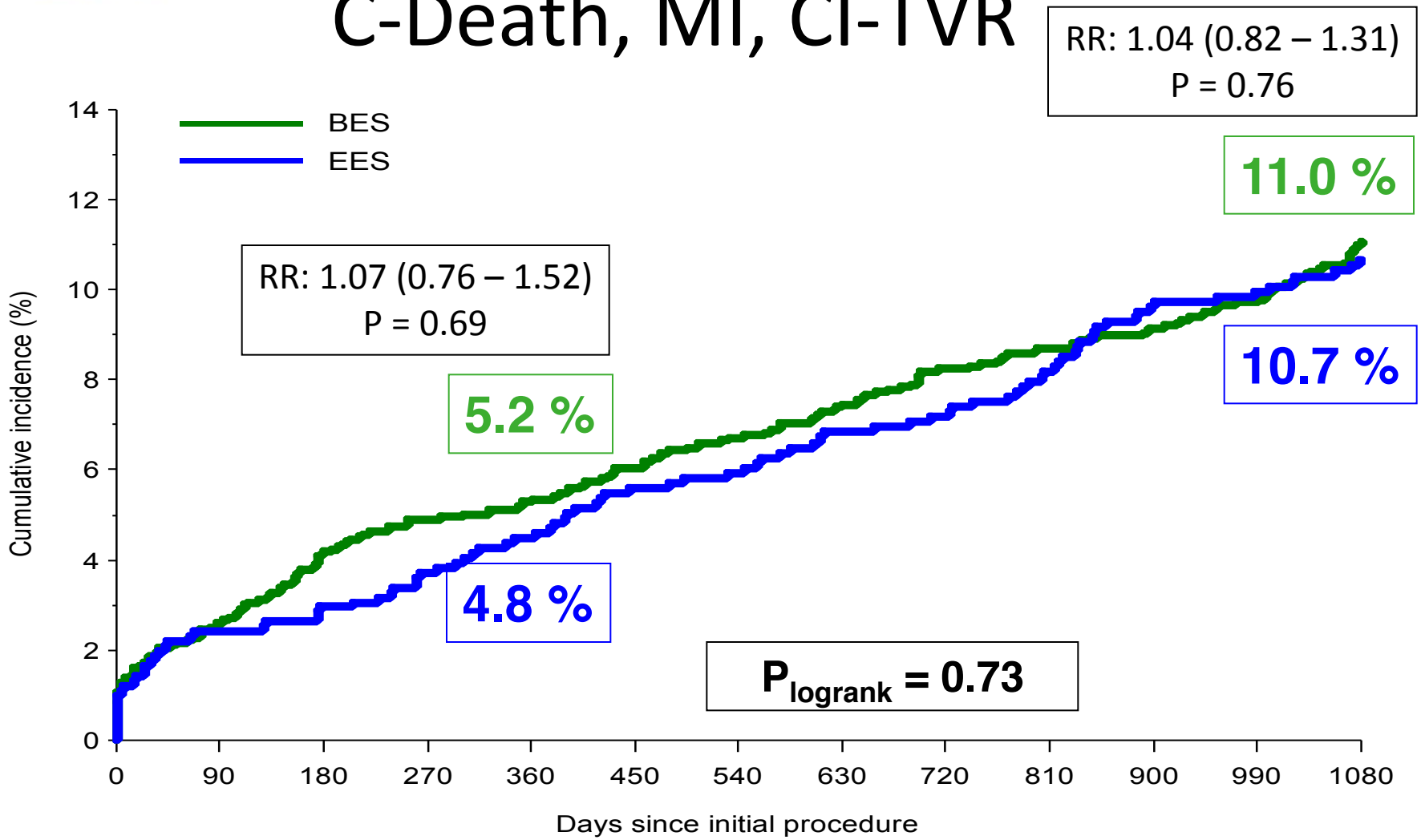
BES	1795	1753	1743	1734	1726	1719	1707	1702	1697	1695	1694	1691	1688
EES	912	893	886	884	882	880	877	876	874	870	868	865	863

C-Death = Cardiac Death

CI-TVR = Clinically Indicated TVR

Smits et al. Lancet 2013

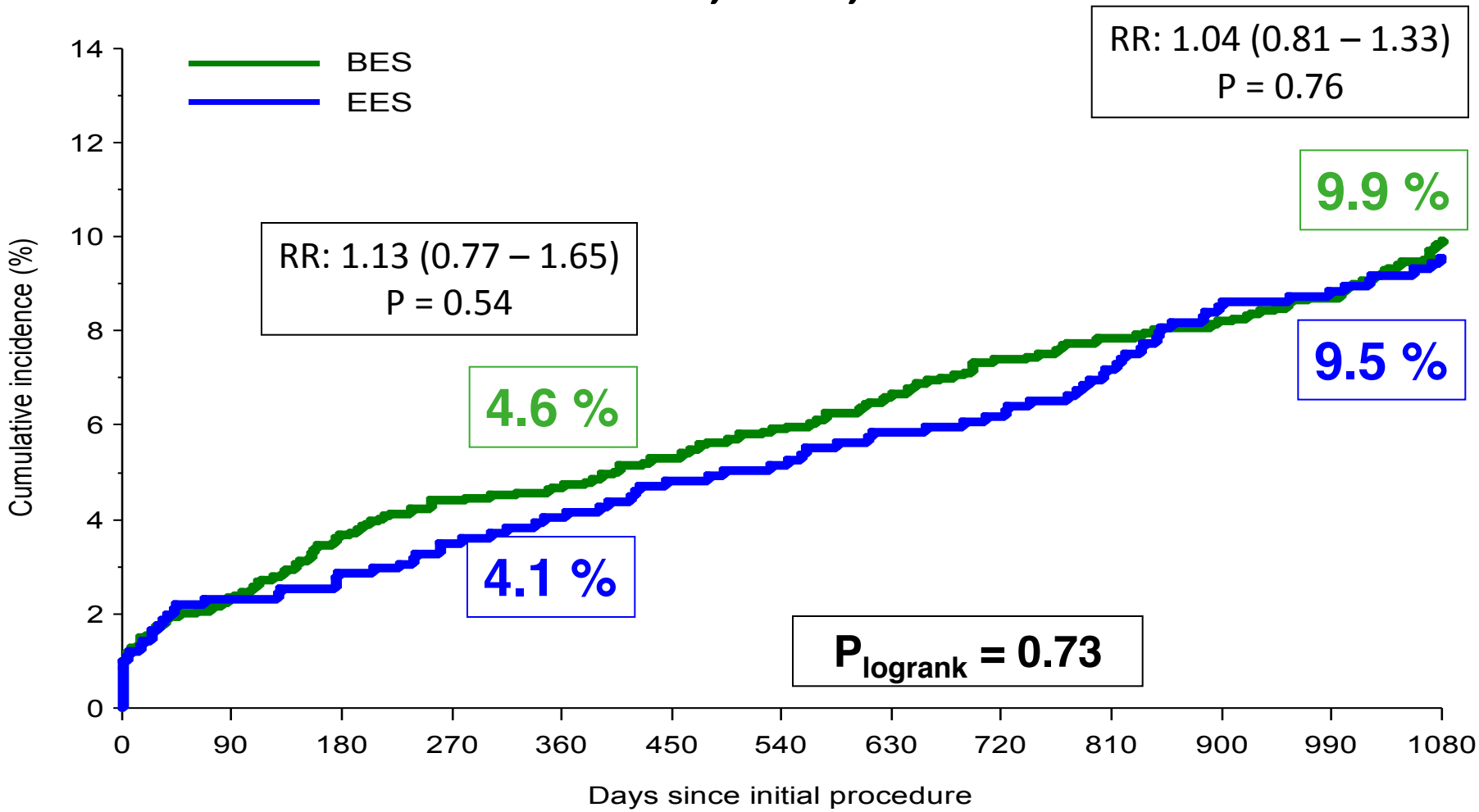
Primary endpoint @ 3 year
C-Death, MI, CI-TVR



C-Death = Cardiac Death

CI-TVR = Clinically Indicated TVR

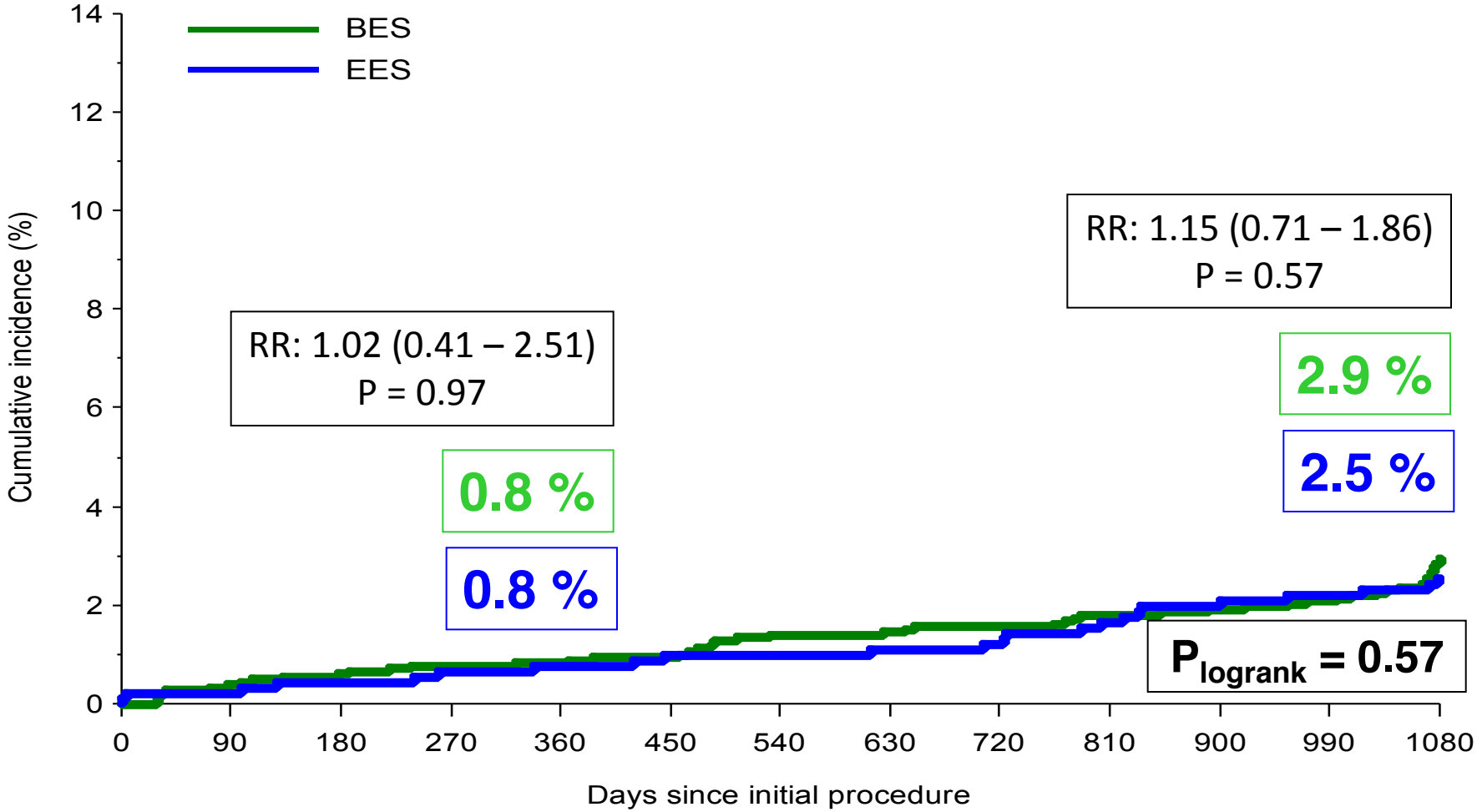
Secondary endpoint @ 3 year C-Death, MI, CI-TLR



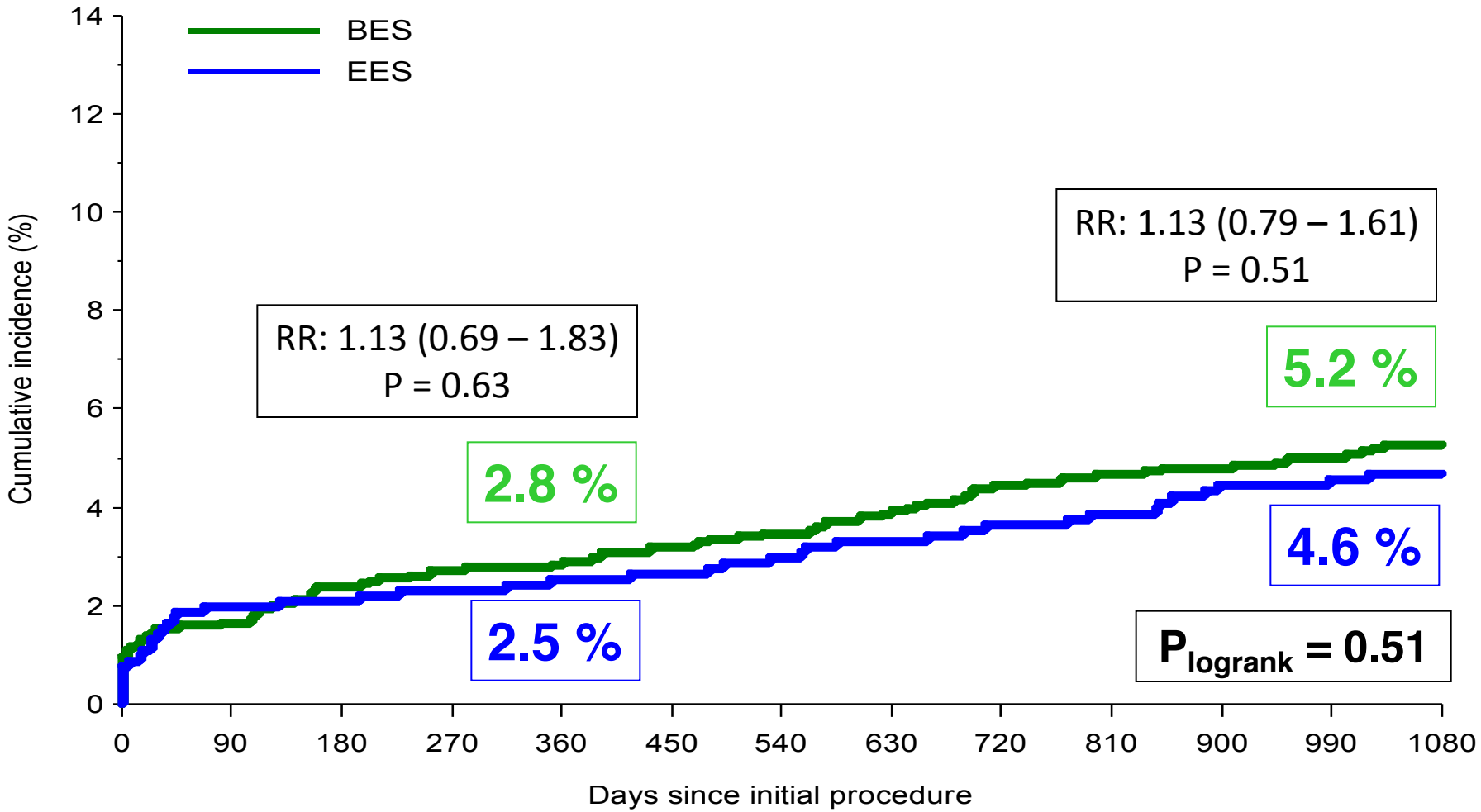
C-Death = Cardiac Death

CI-TLR = Clinically Indicated TLR

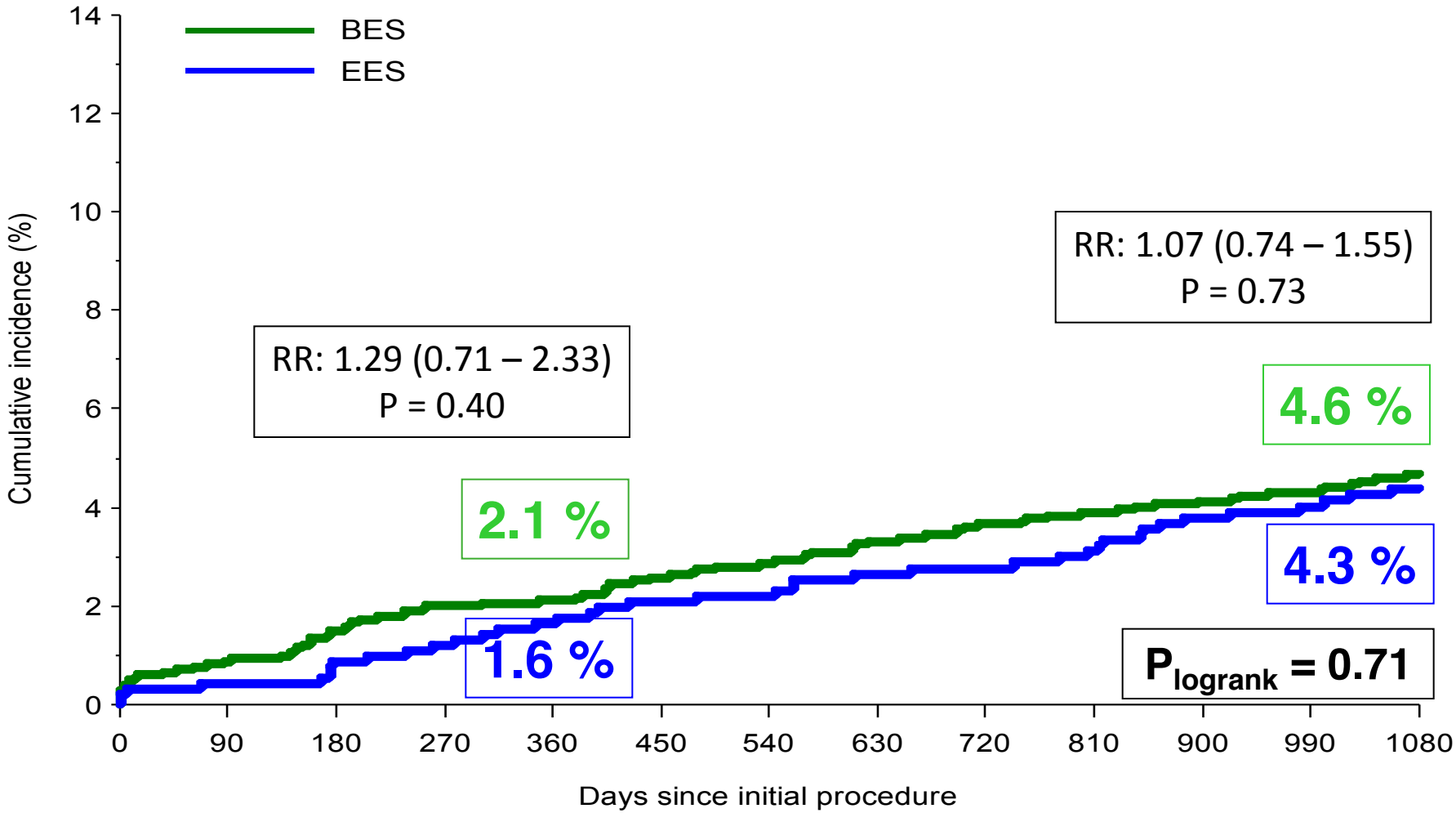
Cardiac Death @ 3 year



Myocardial Infarction @ 3 year

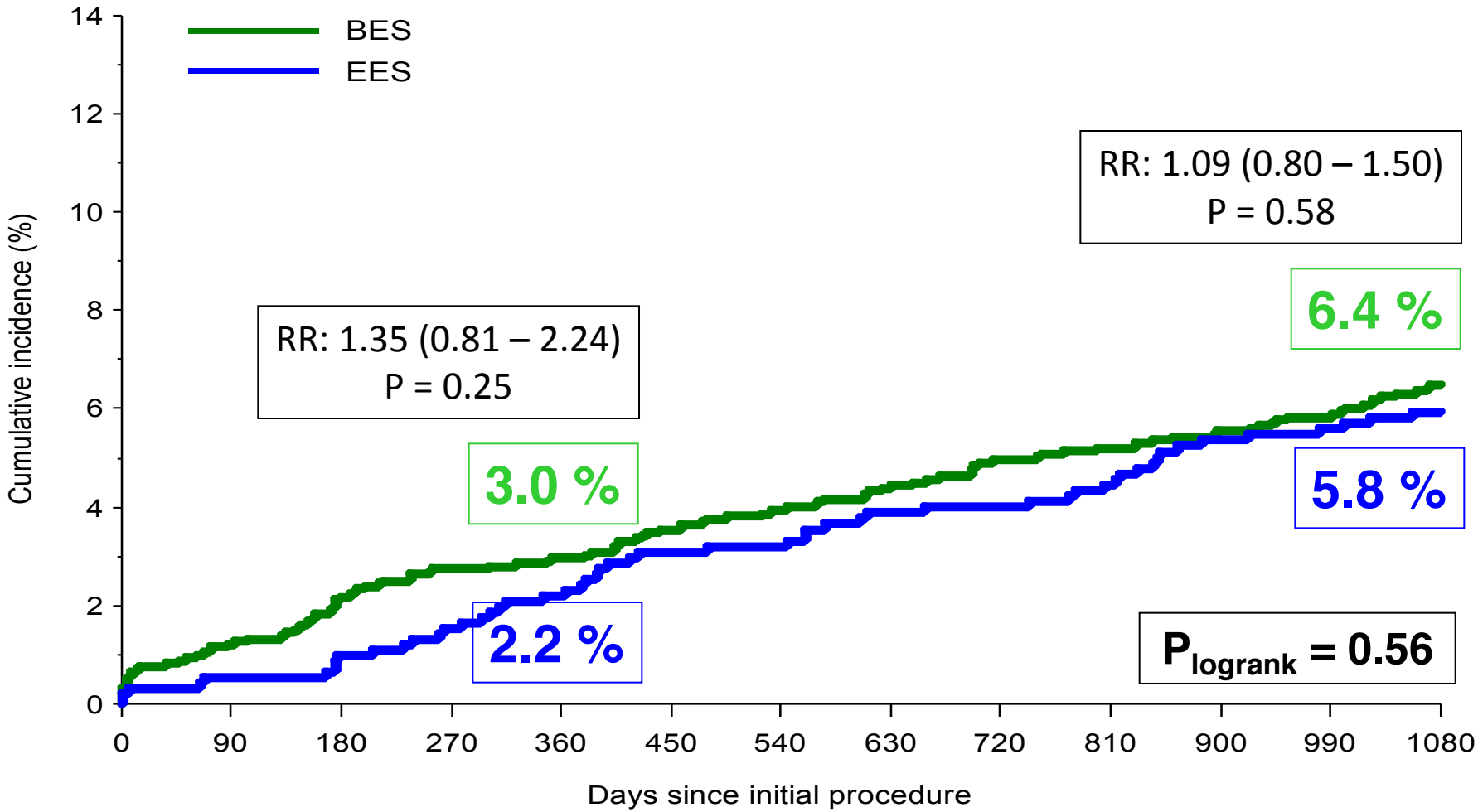


CI-TLR @ 3 year



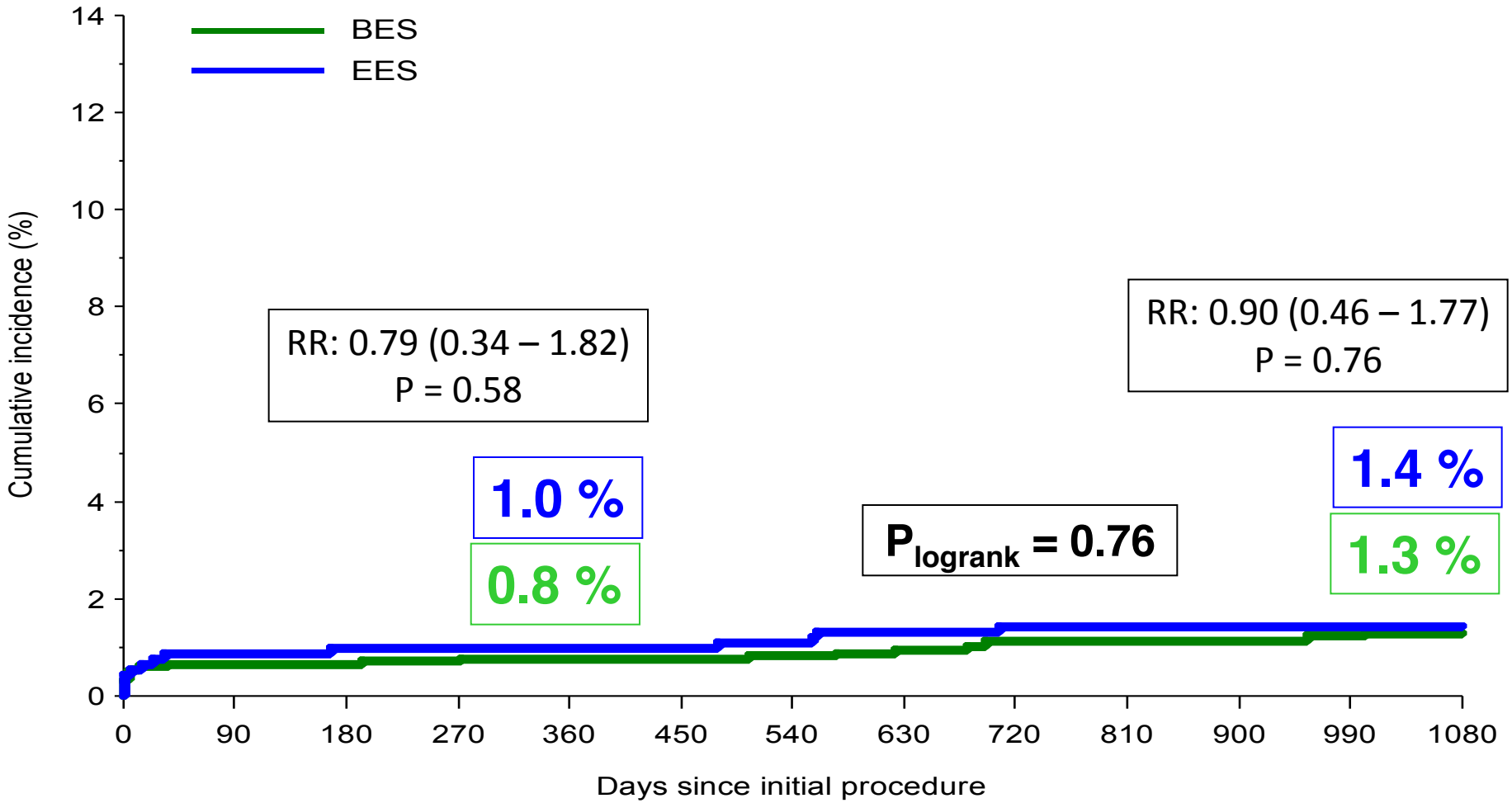
CI-TLR = Clinically Indicated Target Lesion revascularisation

CI-TVR @ 3 year

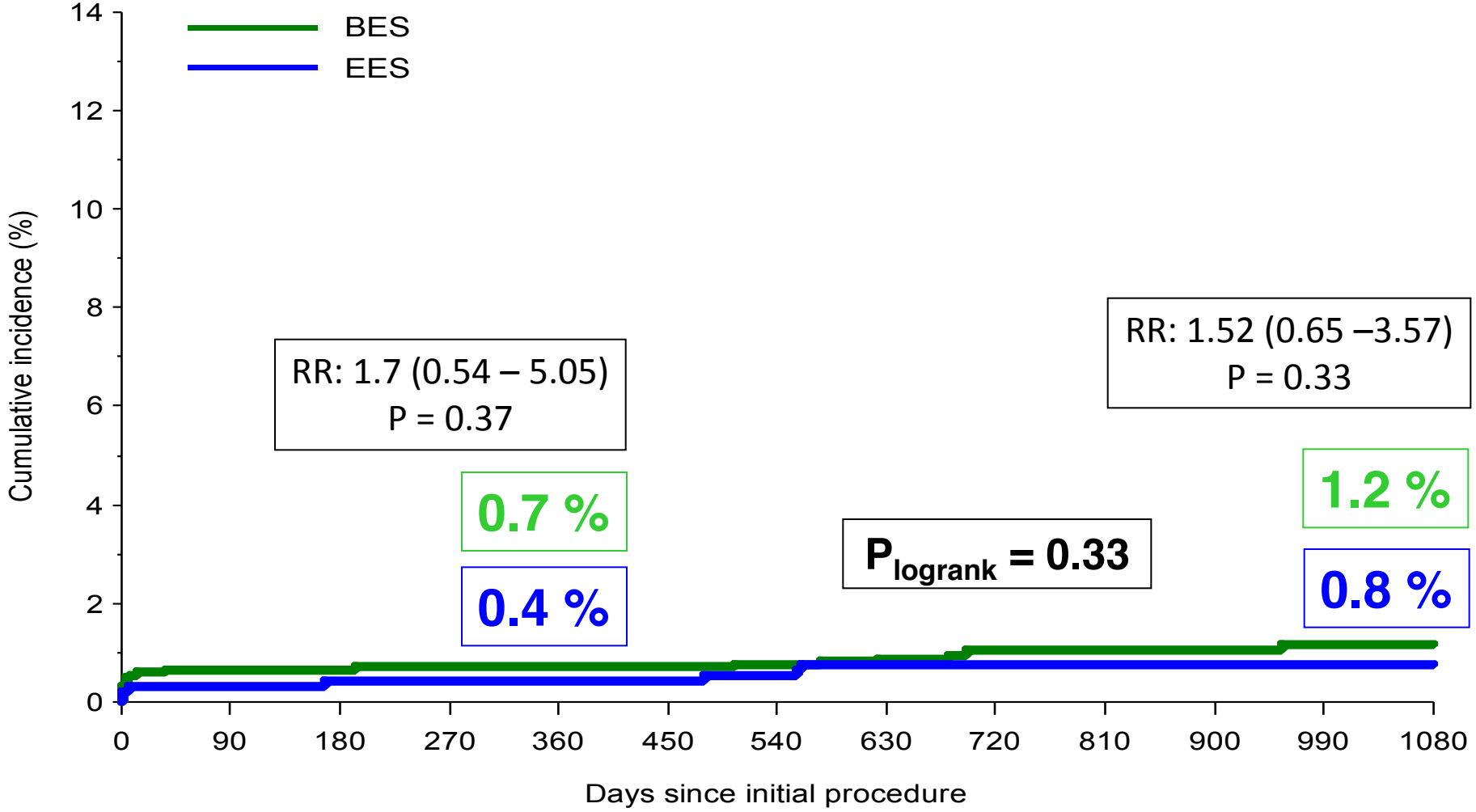


CI-TVR = Clinically Indicated Target Vessel Revascularisation

Def. & Prob. ST @ 3 year

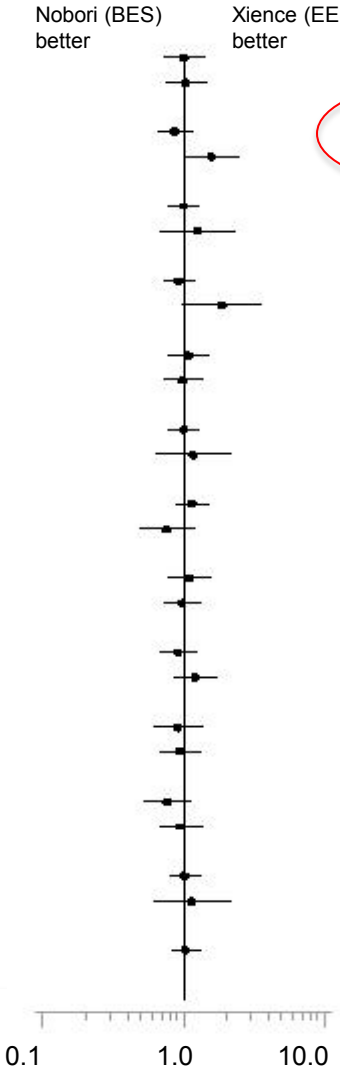


Definite ST @ 3 year



MACE @ 3 year in pre-specified subgroups

	Xience™ EES	Nobori BES	p-value	Relative Risk and 95% confidence interval	p-value for interaction
Age > 65 y	47/362 (13%)	99/749 (13%)	0.914	1.02 (0.74-1.41)	0.9290
Age ≤ 65 y	49/550 (9%)	97/1046 (9%)	0.810	1.04 (0.75-1.44)	
No Diabetes	74/715 (10%)	127/1404 (9%)	0.333	0.87 (0.67-1.15)	0.0378
Diabetes	22/197 (11%)	69/391 (18%)	0.040	1.58 (1.01-2.47)	
No IDDM	85/857 (10%)	167/1680 (10%)	0.986	1.00 (0.78-1.28)	0.5440
IDDM	11/55 (20%)	29/115 (25%)	0.453	1.26 (0.68-2.33)	
No NIDDM	85/770 (11%)	156/1520 (10%)	0.568	0.93 (0.72-1.19)	0.0549
NIDDM	11/142 (8%)	40/275 (15%)	0.045	1.88 (0.99-3.55)	
No ACS	44/385 (11%)	94/755 (12%)	0.617	1.09 (0.78-1.52)	0.7136
ACS	52/527 (10%)	102/1040 (10%)	0.970	0.99 (0.72-1.36)	
No STEMI	82/715 (11%)	165/1423 (12%)	0.931	1.01 (0.79-1.30)	0.6712
STEMI	14/197 (7%)	31/372 (8%)	0.606	1.17 (0.64-2.15)	
No Proximal LAD	65/645 (10%)	152/1301 (12%)	0.289	1.16 (0.88-1.53)	0.1366
Proximal LAD	31/267 (12%)	44/494 (9%)	0.232	0.77 (0.50-1.18)	
Single Vessel Disease	42/540 (8%)	91/1060 (9%)	0.580	1.10 (0.78-1.57)	0.6472
Multi Vessel Disease	54/372 (15%)	105/735 (14%)	0.918	0.98 (0.73-1.33)	
No Type C Lesion	56/567 (10%)	103/1134 (9%)	0.596	0.92 (0.67-1.25)	0.2705
At least one Type C Lesion	40/345 (12%)	93/661 (14%)	0.271	1.21 (0.86-1.72)	
No Long Lesions	33/337 (10%)	66/738 (9%)	0.655	0.91 (0.61-1.36)	0.8984
At least one Long Lesion	46/331 (14%)	80/608 (13%)	0.751	0.95 (0.68-1.33)	
No Small Vessels	39/390 (10%)	59/764 (8%)	0.189	0.77 (0.53-1.14)	0.4404
At least one Small Vessel	41/273 (15%)	81/562 (14%)	0.816	0.96 (0.68-1.36)	
No bifurcation	84/827 (10%)	169/1629 (10%)	0.867	1.02 (0.80-1.31)	0.7460
Bifurcation	12/85 (14%)	27/166 (16%)	0.657	1.15 (0.61-2.16)	
Overall	96/912 (11%)	196/1795 (11%)	0.755	1.04 (0.82-1.31)	



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Conclusions COMPARE II

- At 3-year follow-up the biodegradable polymer-coated BES is equivalent in outcome compared to the durable polymer-coated EES
- The results do not indicate any benefit towards reduction of very late adverse events with biodegradable polymer compared to durable polymer 2e gen. DES
- Moreover, EES might be superior over BES in diabetic patients.

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<u>DSMB</u>

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Patrick Serruys

<u>CEC</u>

Hector Gracia

Eugene McFadden

Benno Rensing

Pascal Vranckx (chairman)

<u>Sponsor</u>

Terumo

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