LEADERS

*L*imus *E*luted From *A* *D*urable vs *ER*odable *S*tent Coating

LEADERS - TAKING THE LEAD IN DES CLINICAL EXCELLENCE

12 MONTHS RESULTS

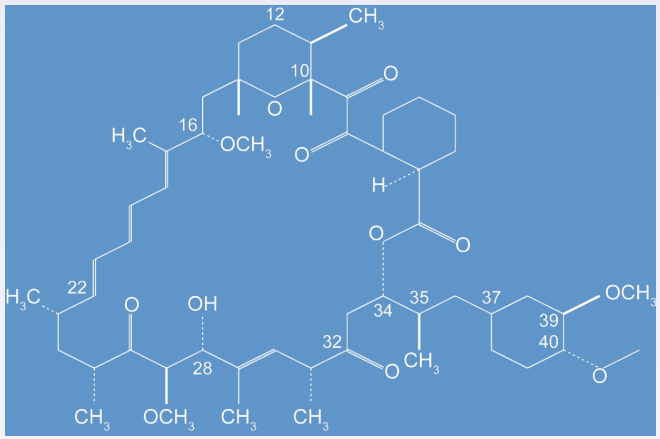
Patrick W. Serruys

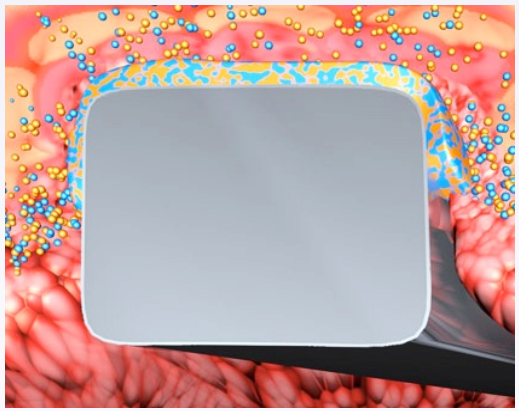
Rotterdam

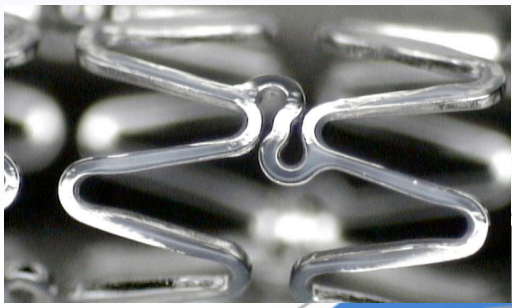
Funded by Biosensors

BIOLIMUS-A9™ ELUTING STENT

- Biolimus is a semi-synthetic sirolimus analogue with 10x higher lipophilicity and similar potency to sirolimus.
- Biolimus is immersed at a concentration of 15.6 μg/mm into a biodegradable polymer, polylactic acid, and applied solely to the abluminal stent surface by a fully automated process.
- Polylactic acid is co-released with biolimus and completely dissolves into carbon dioxide and water during a 6-9 months period.
- The stainless steel stent platform has a strut thickness of 112 μm with a quadrature link design.







LEADERS Trial (PI: S. Windecker, Co-PI: P. Serruys)

Limus **E**luted from **A** **D**urable versus **ER**odable **S**tent Coating

Randomized (1:1), Single-Blind, Multi-Center Study

"Real World": SVG, De Novo or Restenotic Coronary Artery Lesions
Chronic Stable Angina, Silent Ischemia, Acute Coronary Syndromes

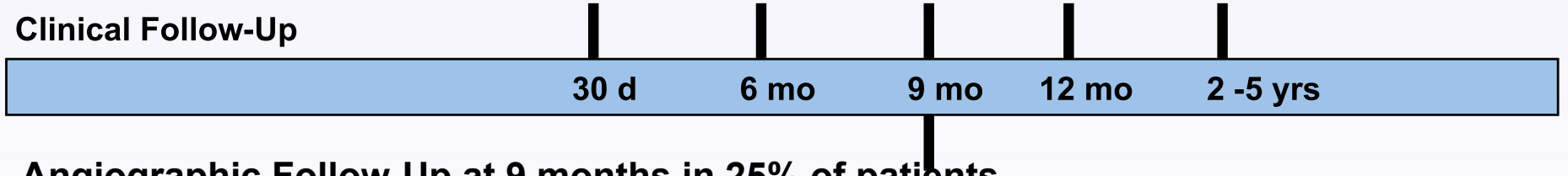
Vessel Diameters:	≥2.25 – ≤3.5 mm
Stent Diameters:	2.25 – 3.5 mm
Lesion Length:	No limititation
Stent Lengths:	8 - 28 mm

Pre-Dilatation and Post-Dilatation @ Physicians Discretion

BioMatrix Flex™ n= ~850

CYPHER SELECT™ n= ~850

Sites: Europe (10)



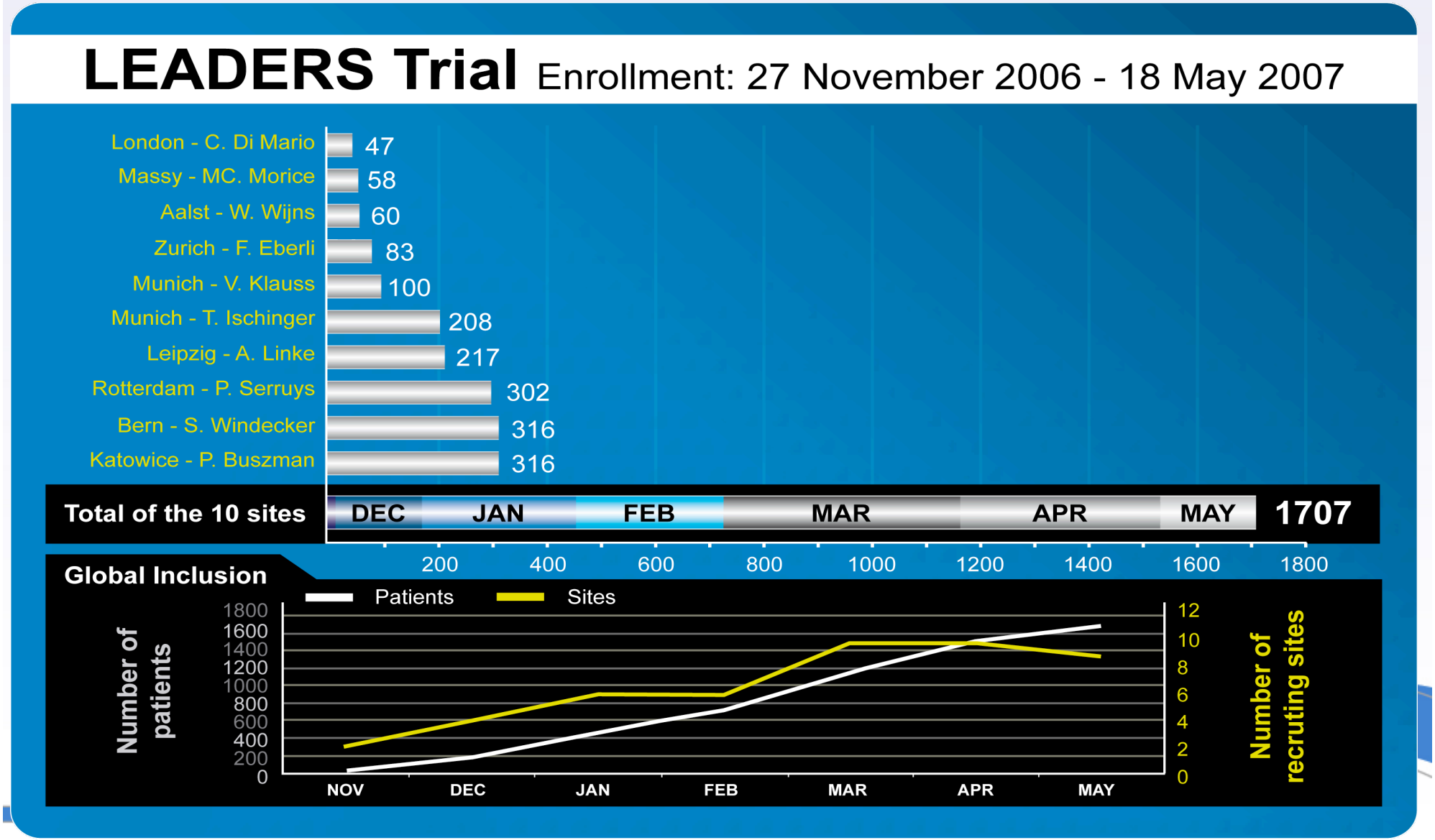
Angiographic Follow-Up at 9 months in 25% of patients

Primary Endpoint:	MACE at 9 months
Key Secondary Endpoints:	MACE at 30 days, 6 months, 12 months
	Clinically driven TLR, TVR, & TVF at 6 and 9 months
	Device, Lesion and Procedure Success
	MLD, Binary Restenosis and Late Loss at 9 months

Anti-Platelet Therapy for a minimum of 12 months

STUDY SITES AND INVESTIGATORS

PI: S. Windecker; Co-PI: P. Serruys



Primary Clinical Endpoint

- Cardiac death, MI, or clinically-indicated TVR @ 9 months
  - Diameter stenosis ≥50% with ischemic signs or symptoms
  - Diameter stenosis ≥70% in the absence of symptoms
- Assumed event rate @ 9 months: 8% in both arms (based on BASKET and SIRTAX)
- Non-inferiority margin = 4%, one sided α = 0.05
- 1700 patients ⟶ 90% power

Principal Angiographic Endpoint

- In-stent percent diameter stenosis @ 9 months
- Assumed % DS = 23 ± 16% in both arms (REALITY trial)
- Non-inferiority margin = 5%, average number of 1.5 lesions, 30% of allocated patients without analysable angiogram, one sided α = 0.05
- 1:3 random sample of 425 patients ⟶ 90% power

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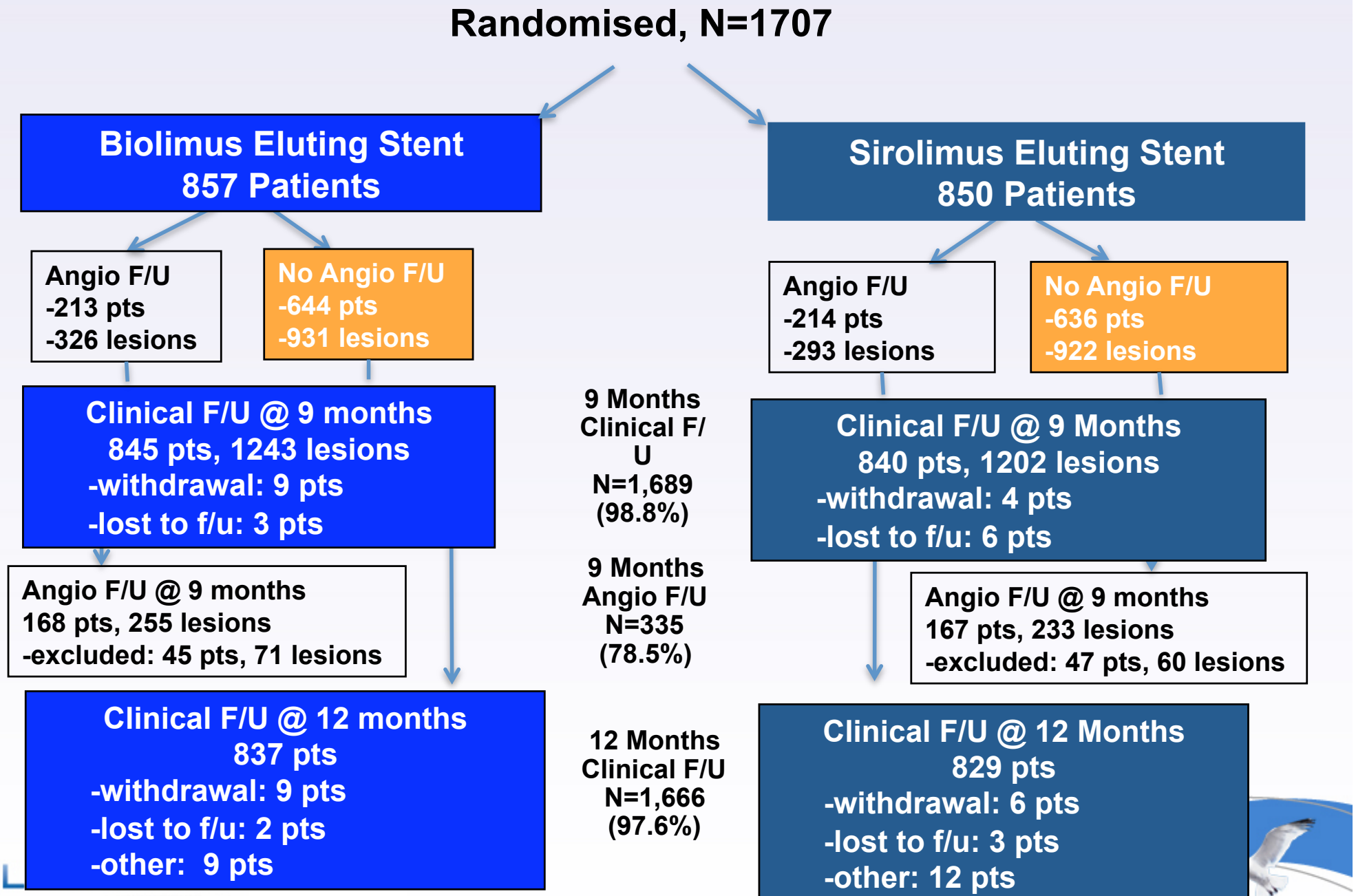
FLOW OF PATIENTS



PATIENT DEMOGRAPHICS

	Sirolimus Stent	Biolimus Stent 857 Patients 850
Patients		
Age in years	65 ± 11	65 ± 11
Male gender	75%	75%
Arterial hypertension	74%	73%
Diabetes mellitus	26%	23%
- insulin-dependent	10%	9%
Hypercholesterolemia	65%	68%
Family history	40%	44%
Smoking	24%	25%
Previous MI	32%	33%
Previous PCI	36%	37%
- with drug-eluting stent	12%	14%
Previous CABG	11%	13%
Chronic stable angina	45%	44%

PATIENT CHARACTERISTICS

Biolimus Stent	Sirolimus Stent	
	857 Patients	850
Patients		
Acute coronary syndrome	55%	56%
- Unstable angina	22%20%	
- Non-ST-elevation MI	18%19%	
- ST-elevation MI	16%17%	
Left ventricular ejection fraction	56 ± 11%	55 ± 12%
Number of lesions per patient	1.5 ± 0.7 1.4 ± 0.7	
Lesions per patient		
- 1 lesion	63%69%	
- 2 lesions	29%22%	
- 3 lesions	7%8%	
- > 4 lesions	1%2%	
De novo lesions	92%91%	
Long lesions (>20 mm)	31%27%	
Small vessels (RVD ≤2.75 mm)	68%69%	
Off label use	81%78%	

PROCEDURAL CHARACTERISTICS

	Biolimus Stent 1257 Lesions	Sirolimus Stent 1215 Lesion	*P*
# stents per lesion	1.3 ± 0.7	1.3 ± 0.7	0.36
Maximal stent diameter (mm)	3.0 ± 0.4	3.0 ± 0.4	0.96
Stent length per lesion (mm)	24.7 ± 15.5	24.6 ± 14.8	0.95
Direct stenting (%)	40.4%	39.9%	0.76
Implantation of study stent (%)	97.5%	95.7%	0.05
Device success (%)	95.8%	94.2%	0.11
Lesion success (%)	98.6%	97.8%	0.15

PRE- AND POST PROCEDURAL QCA

Pre-procedure	Biolimus Stent 1257 lesions	Sirolimus Stent 1215 lesions	*P*
RVD (mm)	2.60 ± 0.61	2.60 ± 0.57	
MLD (mm)	0.91 ± 0.50	0.95 ± 0.52	
% DS	64.6 ± 17.9	63.3 ± 18.2	
Lesion length (mm)	12.7 ± 8.1	12.4 ± 8.5	
Acute gain (mm)			
In-segment	1.11 ± 0.58	1.10 ± 0.56	0.41
In-stent	1.41 ± 0.57	1.37 ± 0.54	0.07
MLD (mm)			
In-segment	2.03 ± 0.53	2.05 ± 0.52	0.60
In-stent	2.33 ± 0.52	2.33 ± 0.50	0.78
% Diameter Stenosis			
In-segment	23.3 ±10.9	22.9 ± 11.3	0.41
In-stent	15.1 ± 9.8	15.1 ± 10.2	0.91

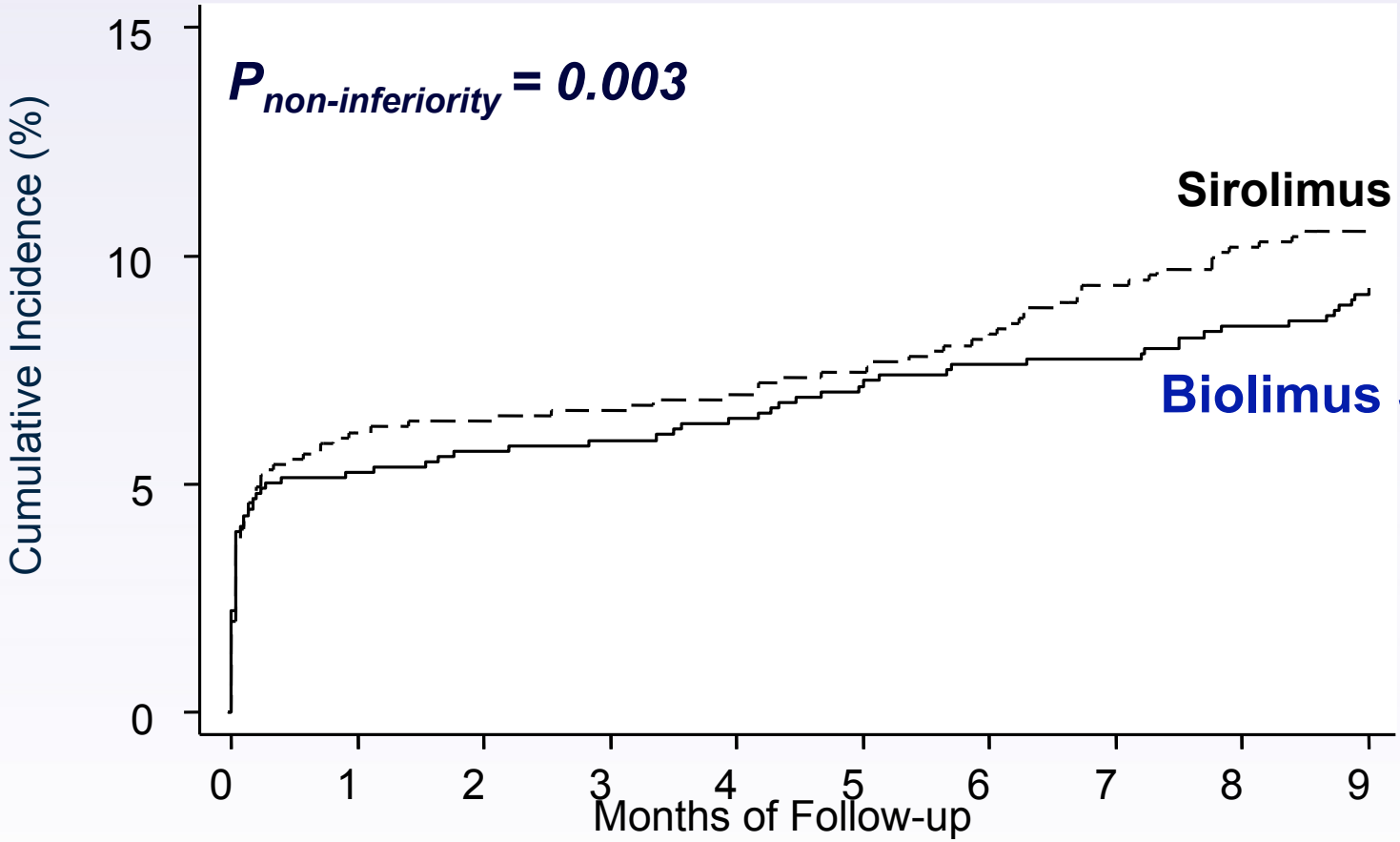
Angiographic Follow-up Results

	Biolimus Stent 255 lesions	Sirolimus Stent 233 lesions	P*
MLD			
in-stent (mm)	2.23 ± 0.64	2.11 ± 0.70	0.08
in-segment (mm)	2.01 ± 0.59	1.87 ± 0.64	0.03
Diameter stenosis			
in-stent (%)	20.9 ± 17.5	23.3 ± 19.6	0.26
in-segment (%)	27.1 ± 16.4	29.9 ± 18.5	0.14
Late lumen loss			
in-stent (mm)	0.13 ± 0.46	0.19 ± 0.50	0.34
in-segment (mm)	0.08 ± 0.45	0.15 ± 0.46	0.12
Binary restenosis			
in-stent (%)	5.5	8.7	0.20
in-segment (%)	6.7	10.8	0.15

* P values for superiority

PRIMARY ENDPOINT

CARDIAC DEATH, MI, OR TVR @ 9 MONTHS



No. at risk

BES	857	806	798	796	792	784	779	777	771	761
SES	850	791	786	784	781	777	771	758	751	746

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Biolimus-eluting stent with biodegradable polymer versus sirolimus-eluting stent with durable polymer for coronary revascularisation: a randomised non-inferiority trial

Stephan Windecker, Patrick W Serruys, Simon Wandel, Pawel Buszman, Stanislaw Trznadel, Axel Linke, Karsten Lenk, Thomas Ischinger, Volker Klauss, Franz Eberli, Roberto Corti, William Wijns, Marie-Claude Morice, Carlo di Mario, Simon Davies, Robert-Jan van Geuns, Pedro Eerdmans, Gerrit-Anne van Es, Bernhard Meier, Peter Jüni

Summary

Background A novel stent platform eluting biolimus, a sirolimus analogue, from a biodegradable polymer showed promising results in preliminary studies. We compared the safety and efficacy of a biolimus-eluting stent (with biodegradable polymer) with a sirolimus-eluting stent (with durable polymer).

Methods We undertook a multicentre, assessor-blind, non-inferiority study in ten European centres. 1707 patients aged 18 years or older with chronic stable coronary artery disease or acute coronary syndromes were centrally randomised by a computer-generated allocation sequence to treatment with either biolimus-eluting (n=857) or sirolimus-eluting stents (n=850). The primary endpoint was a composite of cardiac death, myocardial infarction, or clinically-indicated target vessel revascularisation within 9 months. Analysis was by intention to treat. 427 patients were randomly allocated to angiographic follow-up, with in-stent percentage diameter stenosis as principal outcome measure at 9 months. The trial is registered with ClinicalTrials.gov, number NCT00389220.

Lancet 2008; 372:

Department of Cardiology, Bern University Hospital, Bern, Switzerland (Prof S Windecker MD, Prof B Meier MD); **CTU Bern, Bern University Hospital, Bern, Switzerland** (S Windecker, S Wandel MSc, P Jüni MD); **Thoraxcentre, Erasmus University, Rotterdam, Netherlands** (Prof P W Serruys MD, R-J van Geuns MD); **Institute of**

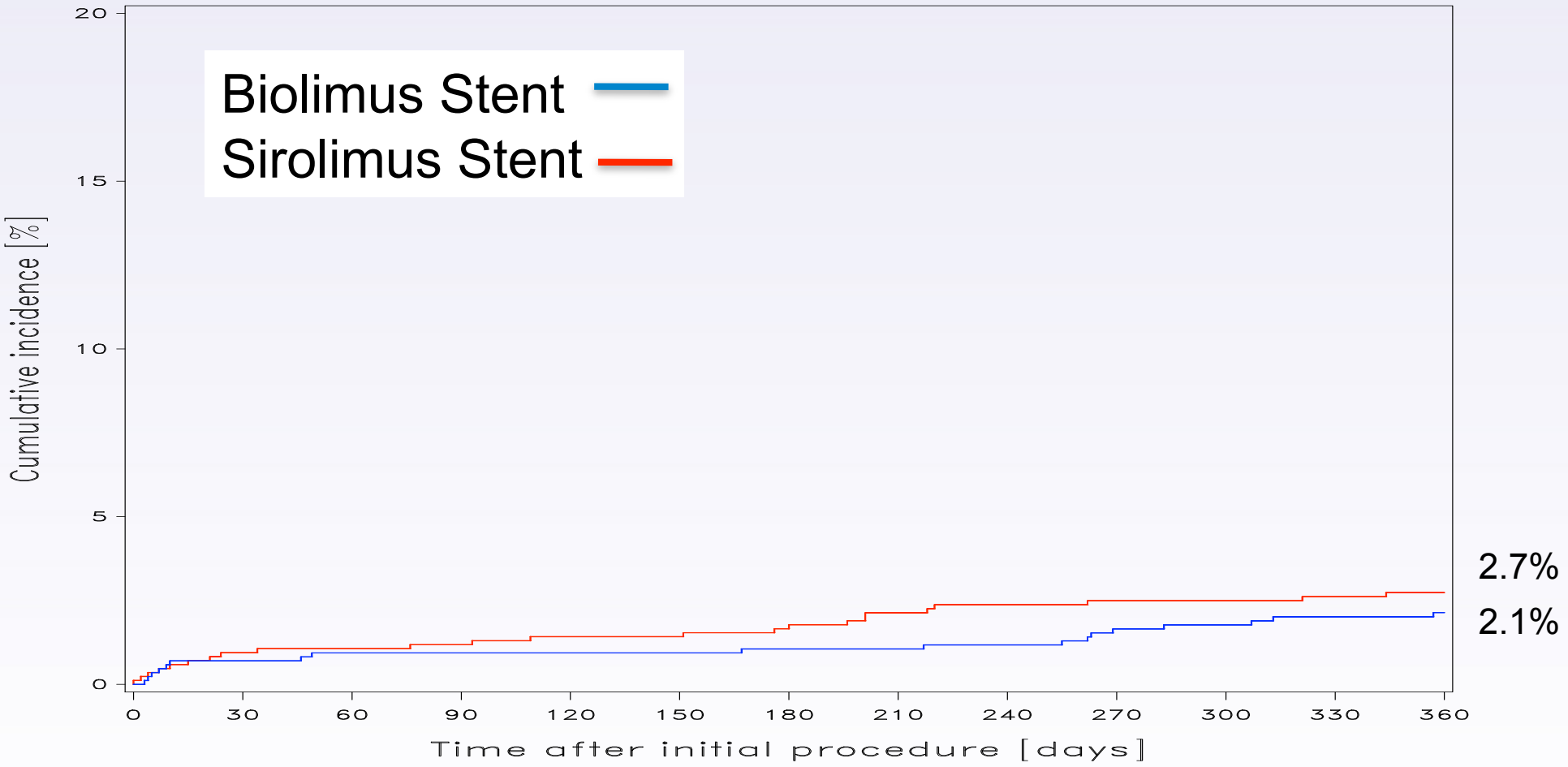
CONCLUSION 9 MONTHS RESULTS

- Biosensors‘ biolimus eluting stent with abluminal biodegradable polymer achieved its primary endpoint and resulted in non-inferior safety, efficacy and angiographic outcome at 9 months.
- The findings of the present study provide a high level of generalisability to routine clinical practice.
- LEADERS study 9 months results have been published in The Lancet (2008; 372:1163-1173).
- Longer term follow-up will be necessary to determine potential differences in late stent thrombosis related to biodegradable as opposed to durable polymer for drug release.

12 MONTHS RESULTS

SAFETY ENDPOINT

Cardiac death



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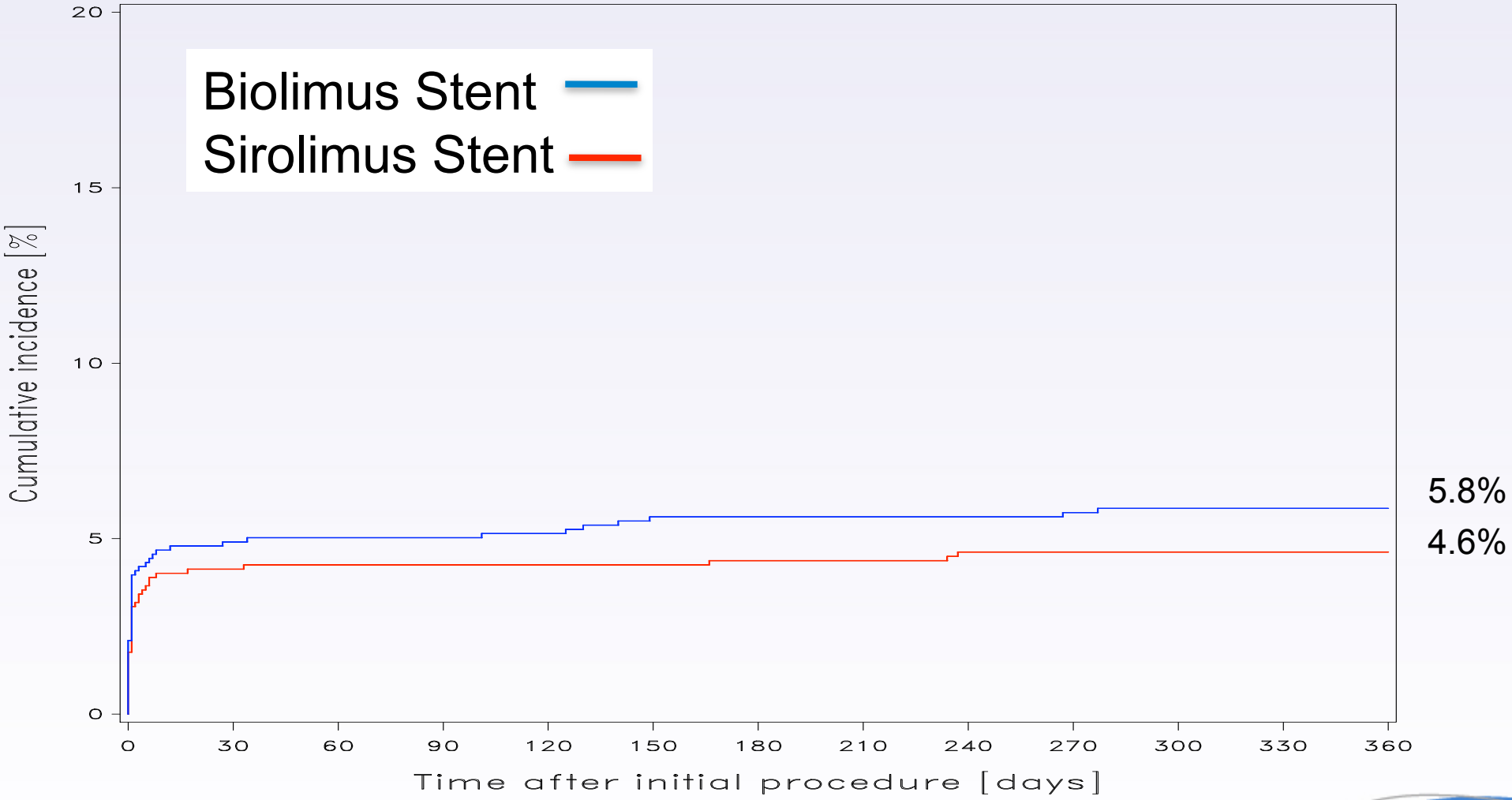
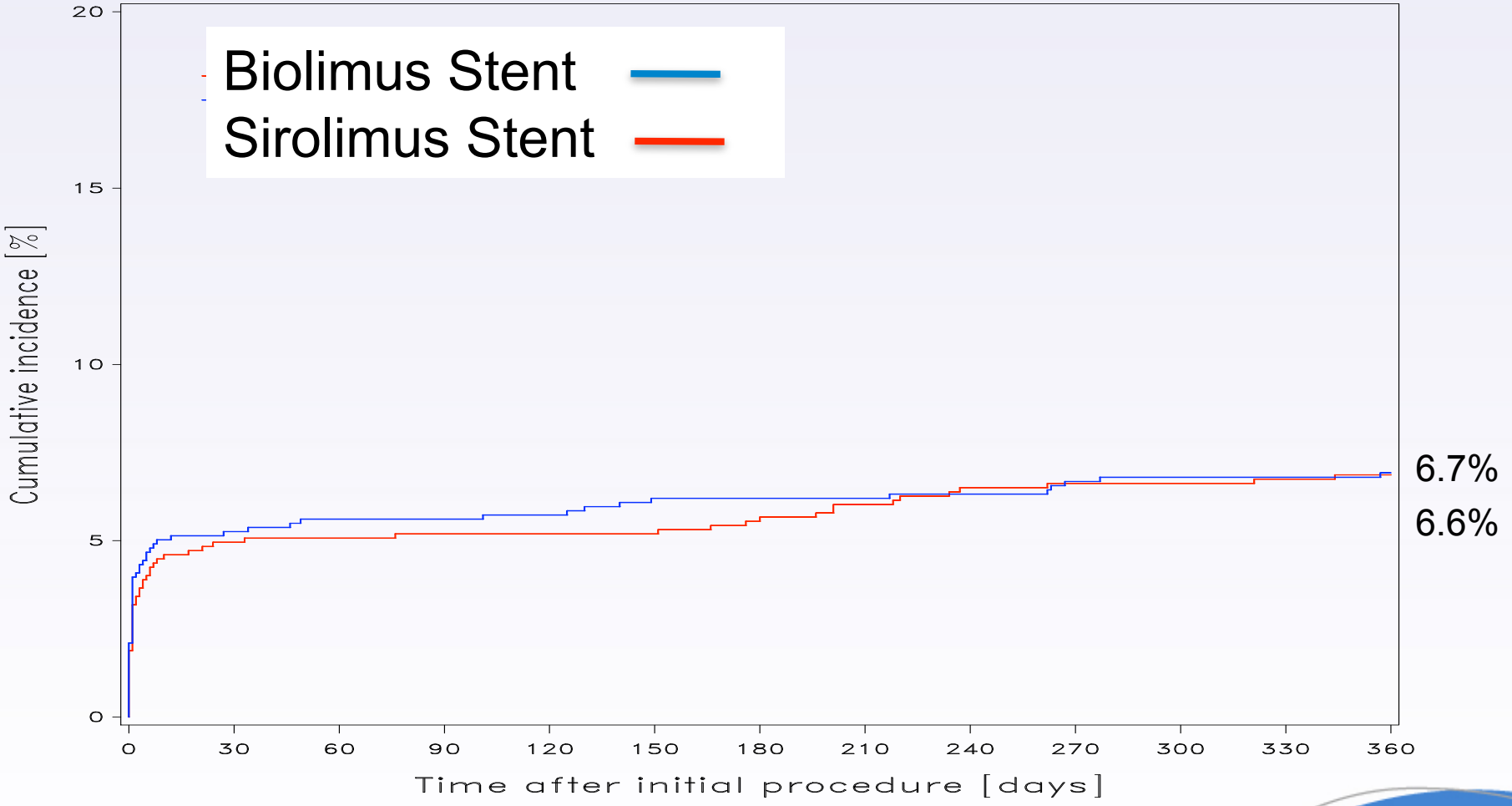
SAFETY ENDPOINT

Myocardial Infarction



SAFETY ENDPOINT

Cardiac Death & Myocardial Infarction



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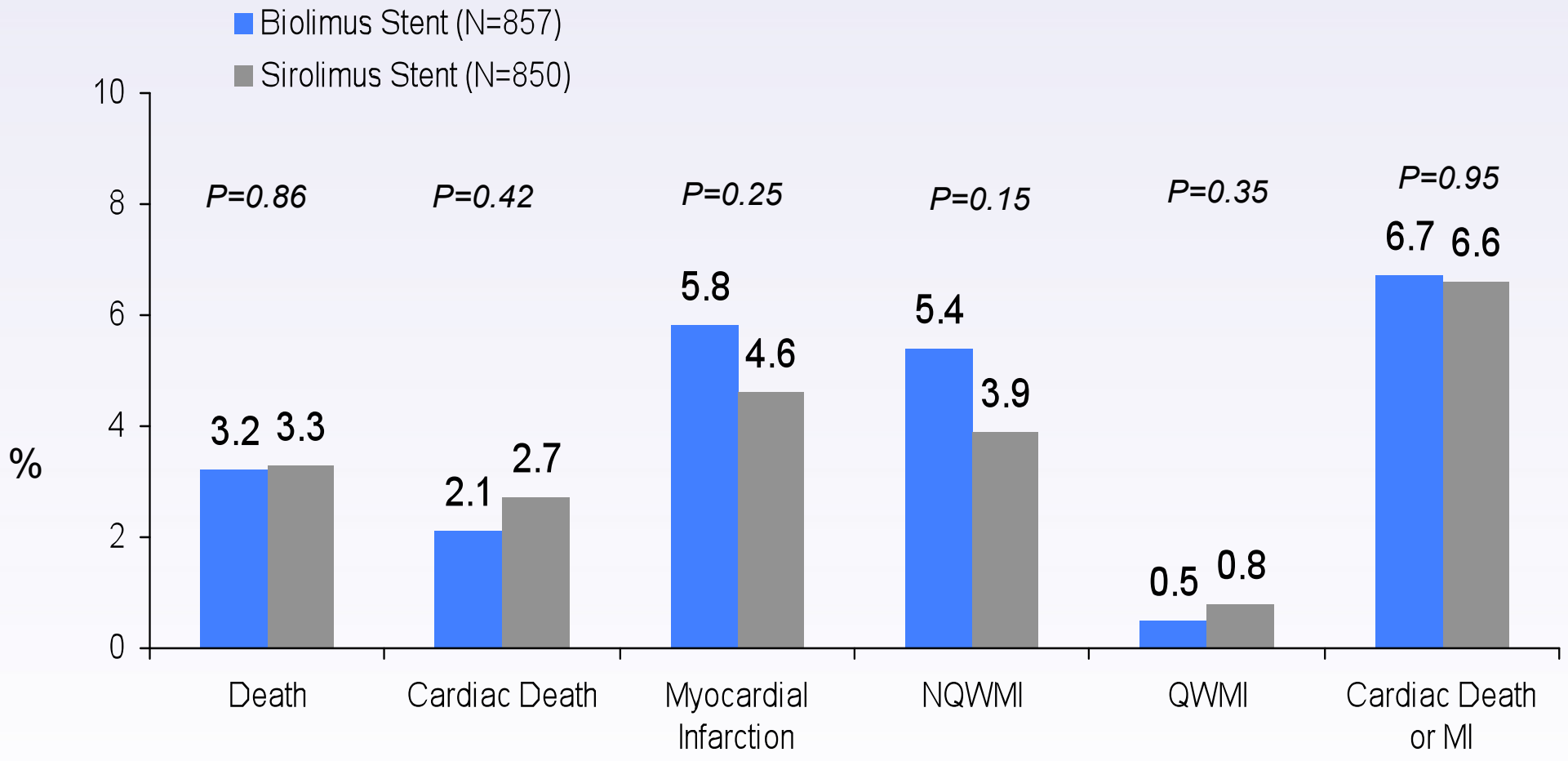
SAFETY ENDPOINTS @ 12 MONTHS



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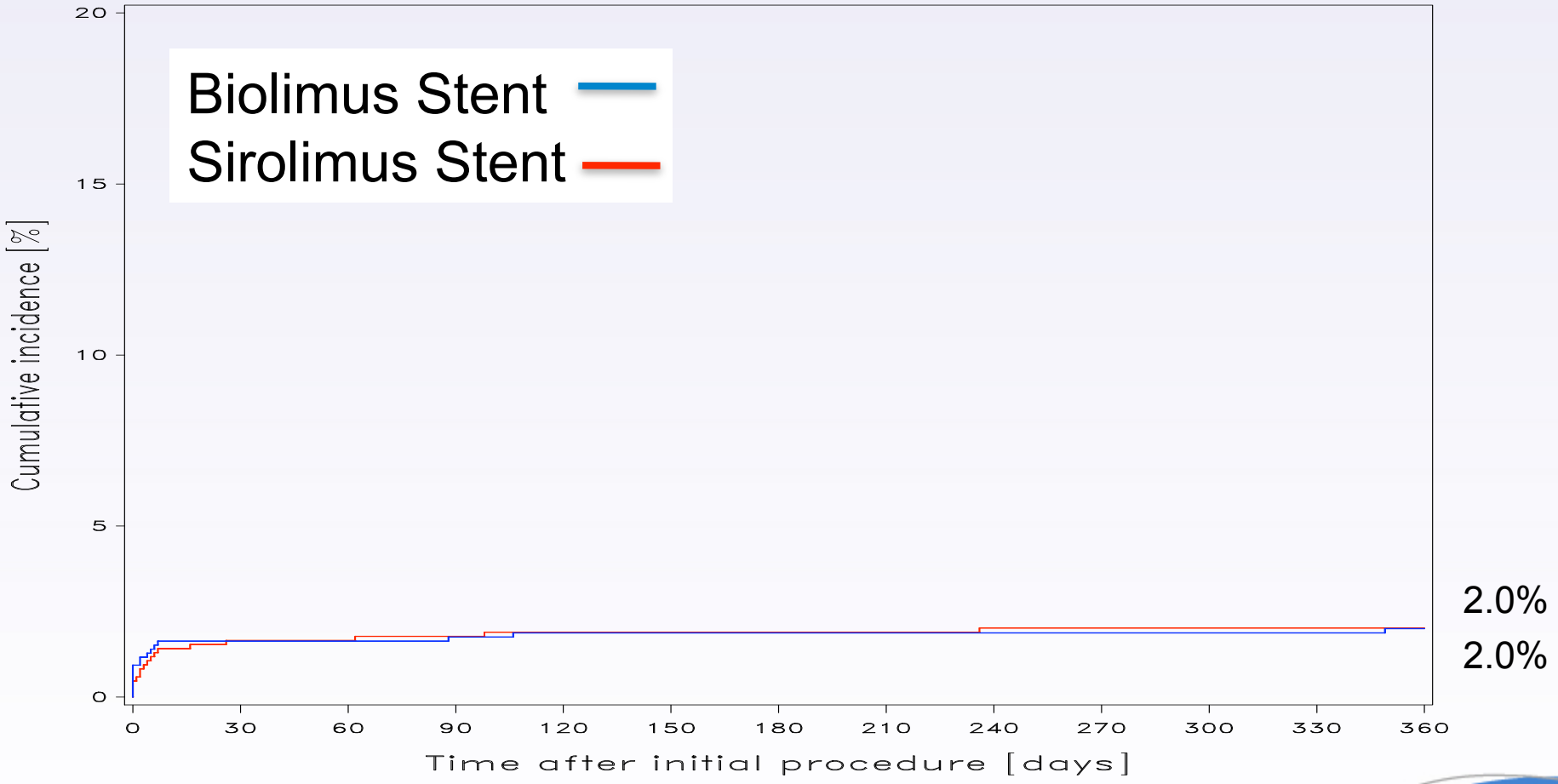
DEFINITE STENT THROMBOSIS



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STENT THROMBOSIS

	Biolimus Stent 857 Patients	Sirolimus Stent 850 Patients	*P*
Definite ST			
0-30 days	**1.6%**	**1.6%**	**0.99**
>30 days – 12 mo	**0.4%**	**0.5%**	**0.70**
0 days – 12 mo	**2.0%**	**2.0%***	**0.99**
Probable ST			
0-30 days	**0.6%**	**0.2%**	**0.28**
>30 days – 12 mo	**0.2%**	**0.0%**	**-**
0 days – 12 mo	**0.8%**	**0.2%**	**0.12**
Possible ST			
0-30 days	**0.0%**	**0.0%**	**-**
>30 days – 12 mo	**0.8%**	**1.1%**	**0.60**
0 days – 12 mo	**0.8%**	**1.1%**	**0.60**

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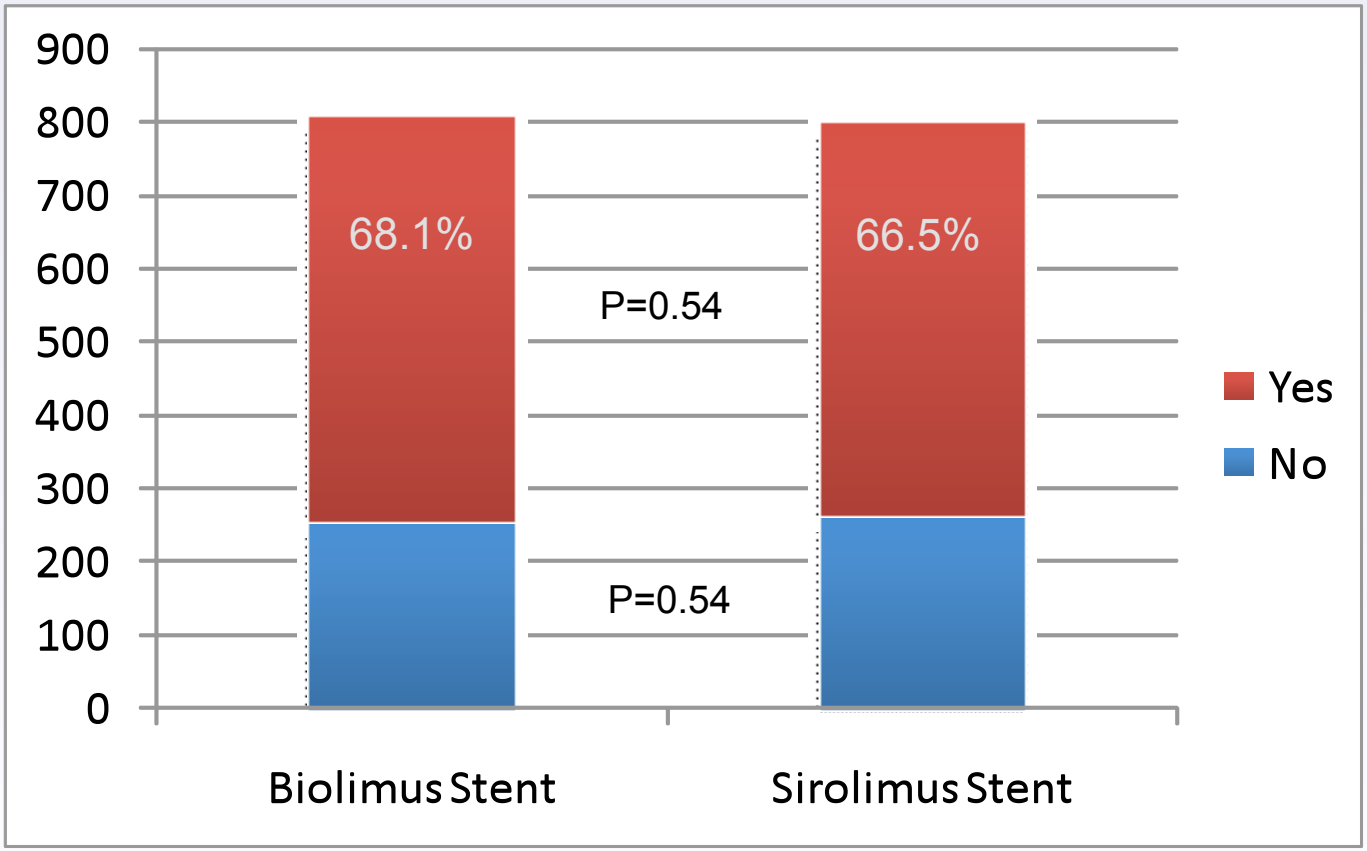
•Excludes one secondary, definite ST occurring at 60 days in a patient who had early ST at 3 days

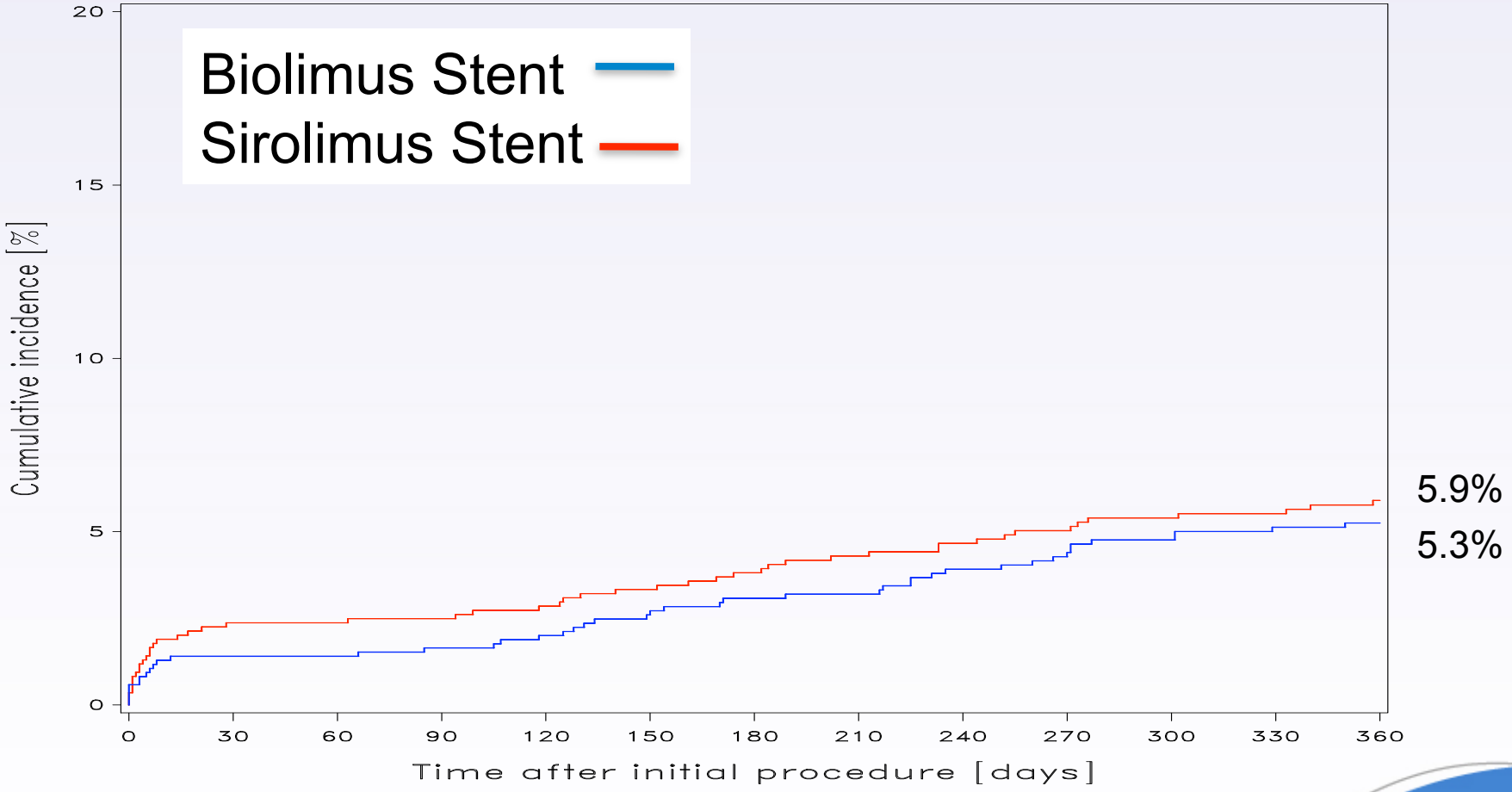
NB: a patient maybe counted under more than one eventtype

ANTI-PLATELET THERAPY COMPLIANCE @ 12 MONTHS



EFFICACY ENDPOINT

Clinically-Indicated Target Lesion Revascularization



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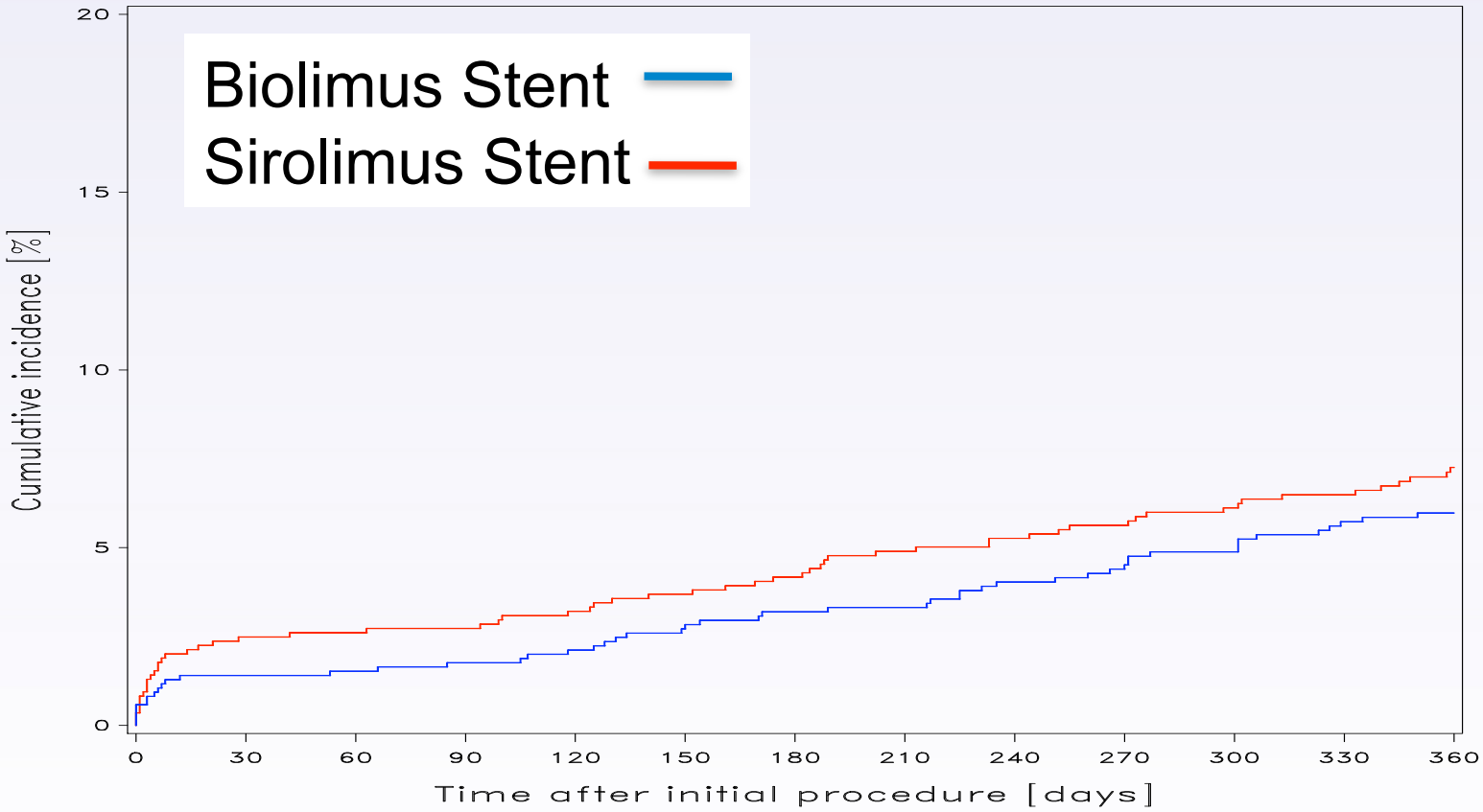
EFFICACY ENDPOINT

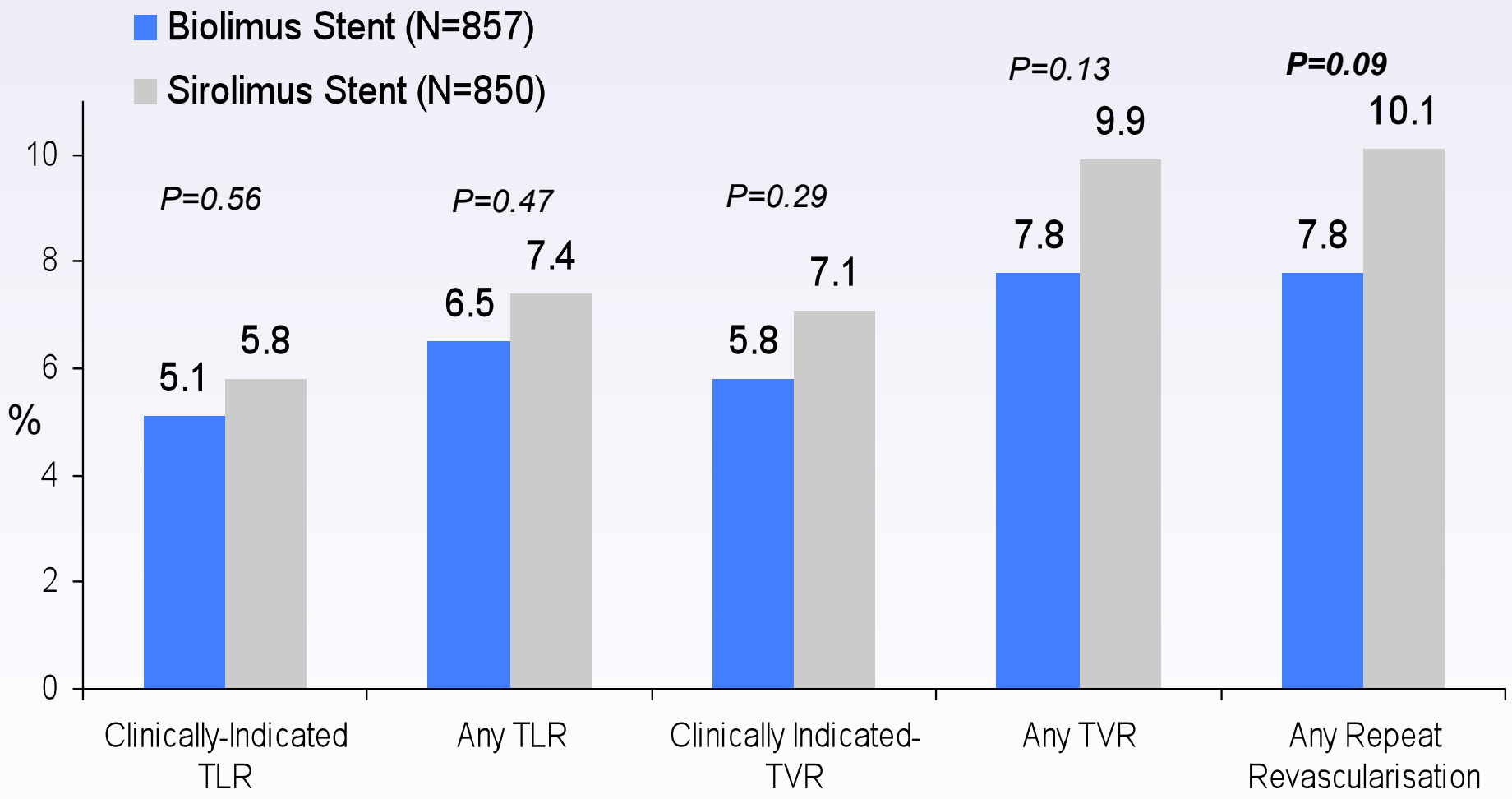
Clinically-Indicated Target Vessel Revascularization



7.3%

6.0%

EFFICACY ENDPOINTS @ 12 MONTHS



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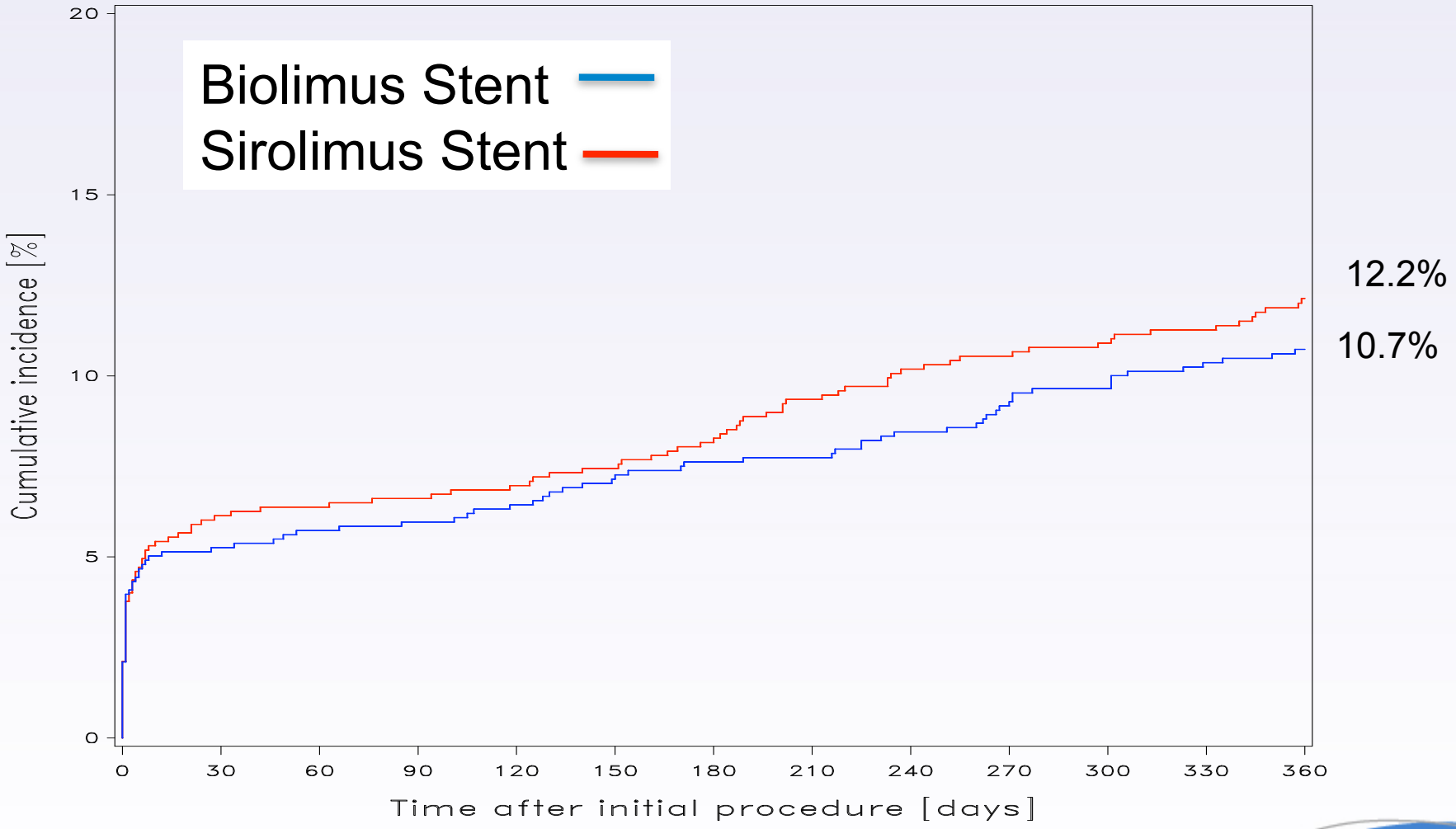
CARDIAC DEATH, MI, OR TVR @ 12 MONTHS



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12 MONTHS CONCLUSIONS

- LEADERS follow-up at 12 months in 97.6% of the patients has confirmed that the 9 months results are durable, with continuing safety and efficacy.
- Sustained but non-signifcant positive trends for reduced cardiac death, Q-Wave MI, angina, and TVR when implanting the biolimus eluting stent.
- A similar of compliance with dual antiplatelet therapy (68.1 vs 66.5%) was observed in both groups in this study of relatively high risk patients.
- The two year data for LEADERS provide some initial insights into whether the biodegradable polymer coating can confer a lower level of Very Late Stent thrombosis as compared to durable polymer coating in an all comers patient population. The data will be presented at an upcoming meeting during 2009.

THANK YOU!