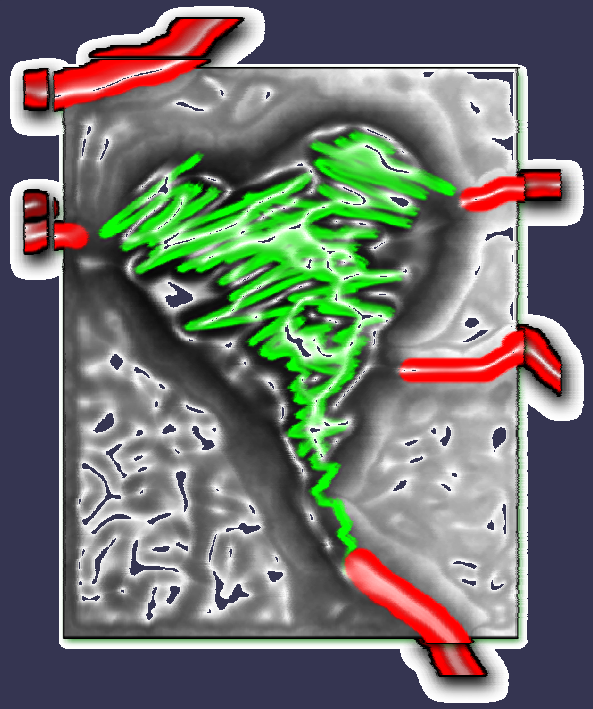
TCT Asia Pacific 08



Use of DES in STEMI

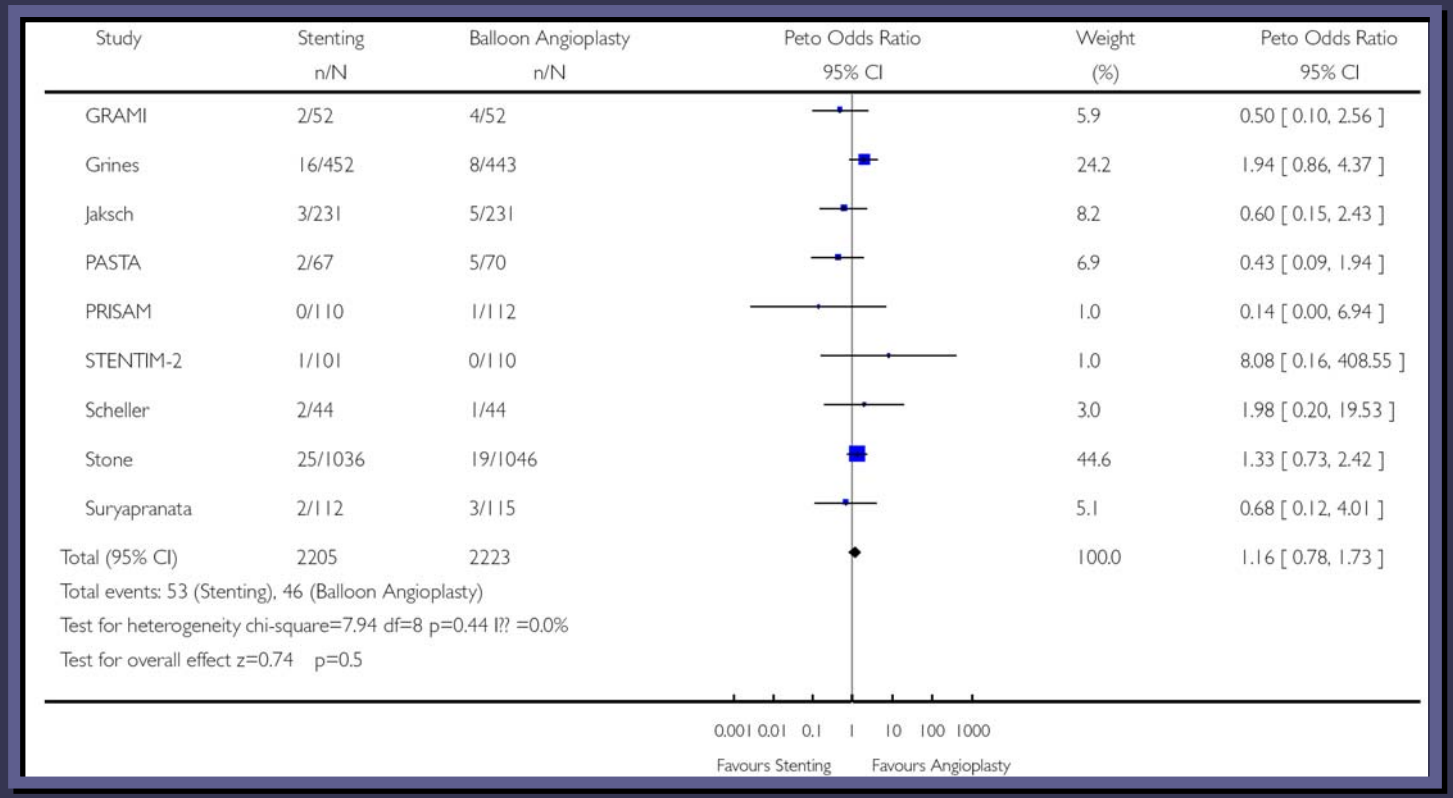
M. Valgimigli, MD, PhD
Ferrara, Italy

Background

- Primary angioplasty is the current preferred therapeutic option for patients with ST-segment elevation myocardial infarction (STEMI).
- Routine coronary stent implantation in patients with STEMI decreases the need for target vessel revascularization (TVR).

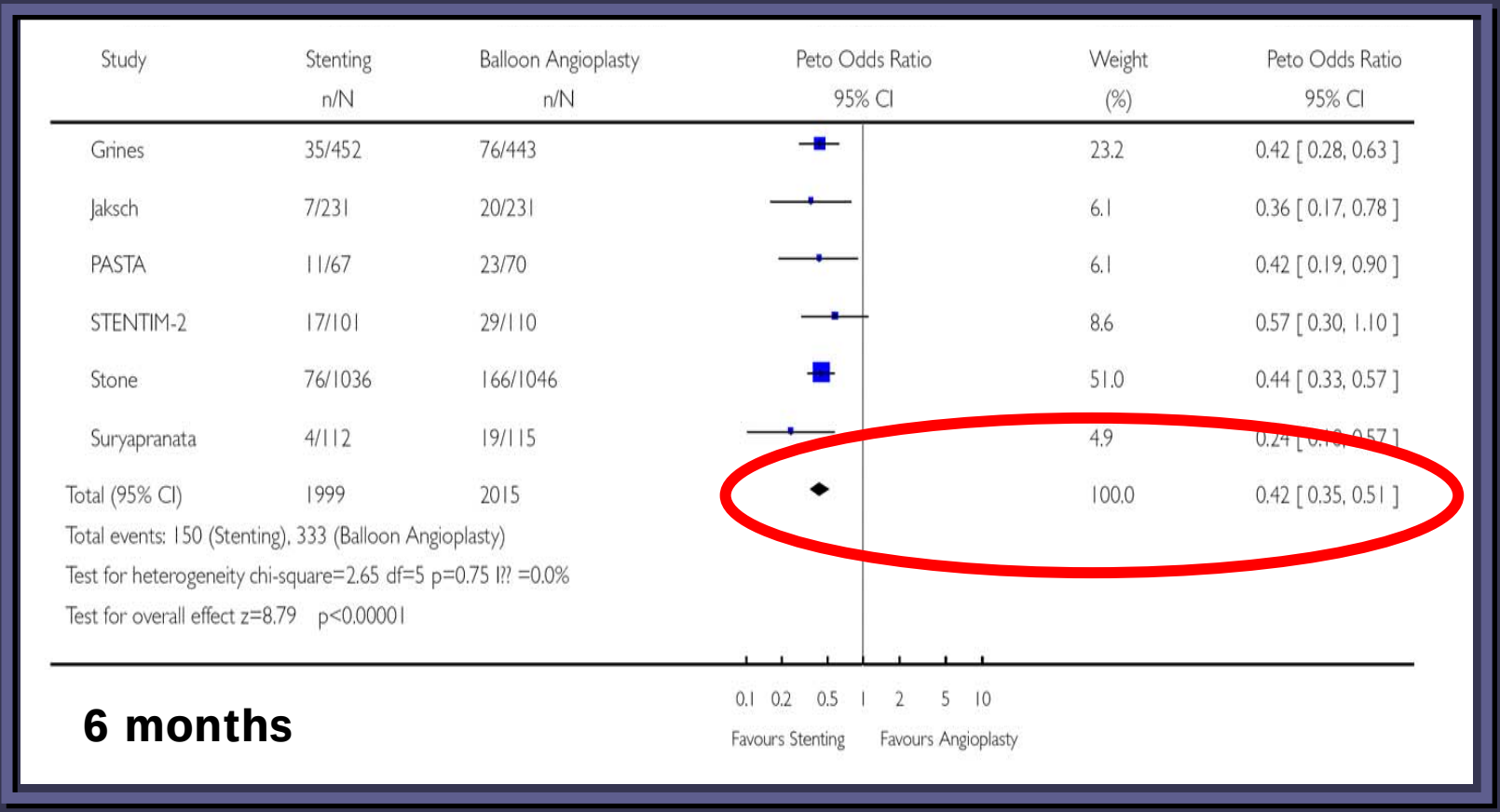
Grines CL, et al. N Engl J Med 1999; 341: 1949
Stone G, et al. N Engl J Med 2002; 346: 957

STEMI: Stent and Mortality



Cochrane Database of Systematic Reviews 2005, Issue 2. Art. No.: CD005313.

STEMI: Stent and Reintervention

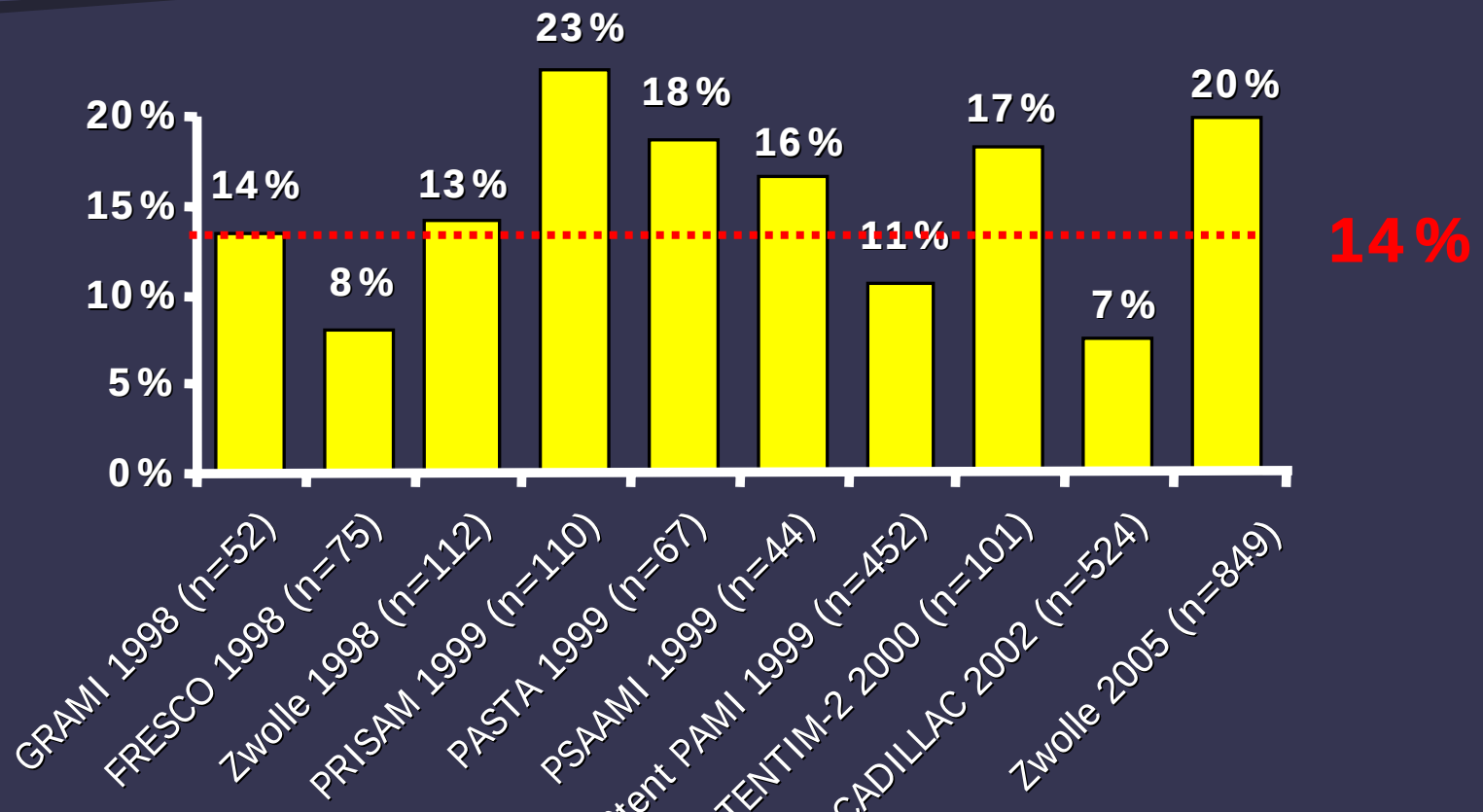


6 months

Cochrane Database of Systematic Reviews 2005, Issue 2. Art. No.: CD005313.

BMS in AMI

6/12-month TVR in the stent arms of randomized trials



BMS in AMI

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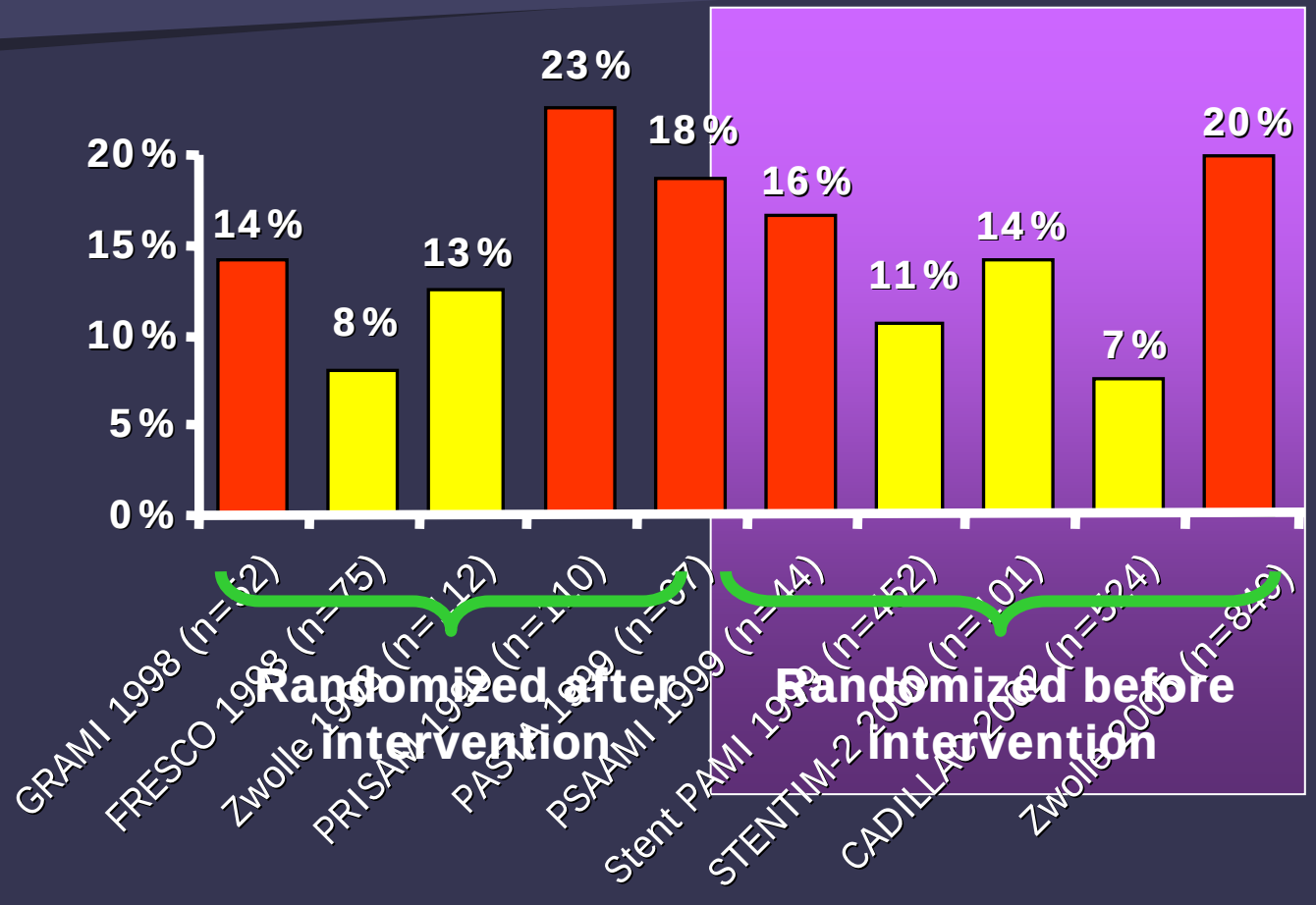
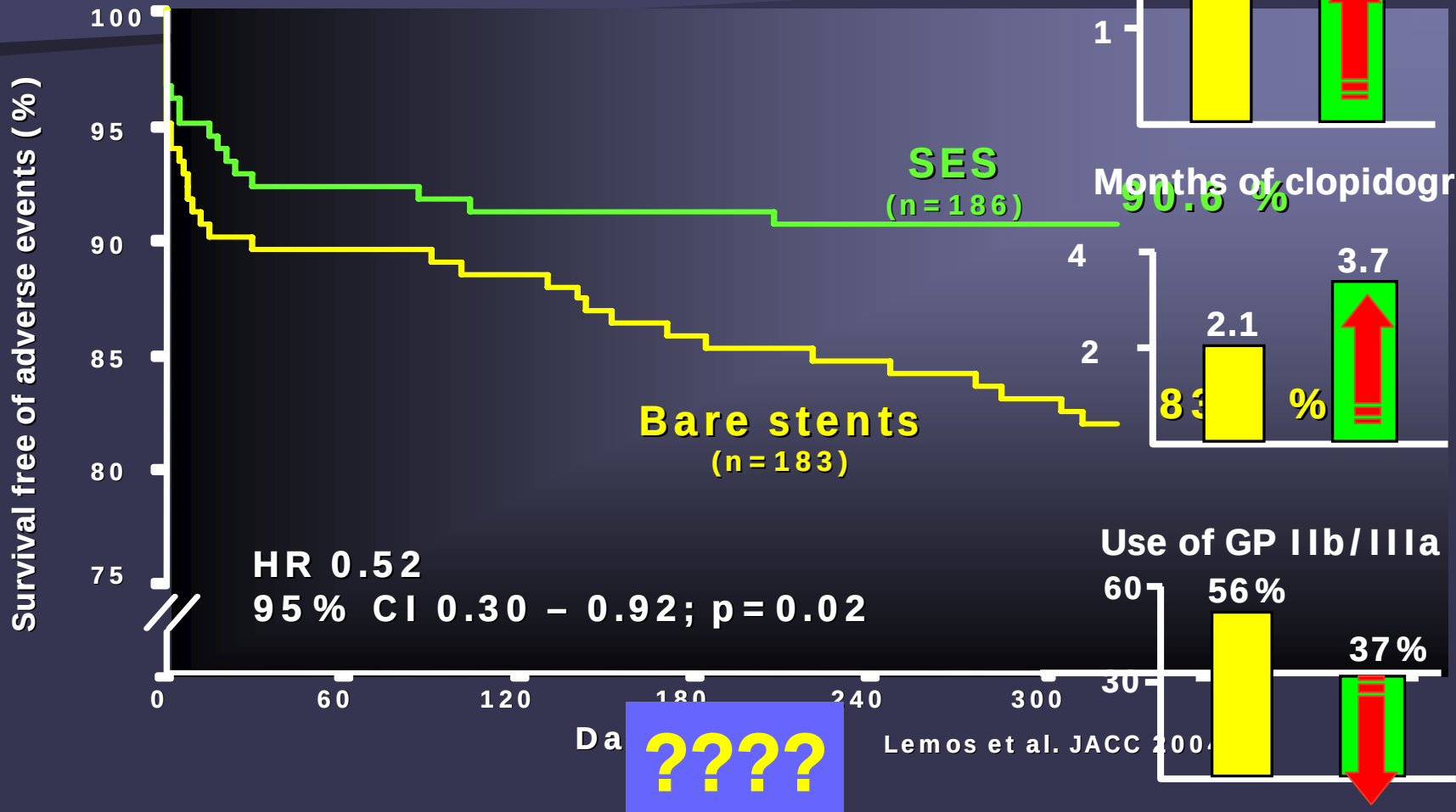


RESEARCH registry - AMI

MACE free Survival



Competition on the basis of their high costs

Objectives

- To test the safety and efficacy of SES when implanted in STEMI patients in RCT

- To investigate a new strategy of treatment, which incorporates SES but results in no increase in medical expenditure

Valgimigli et al. Cardiovasc Drugs Ther 04; 18: 225-30

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ISSN 0735-1097/03/$30.00
doi:10.1016/j.jacc.2003.07.017

CLINICAL RESEARCH **Clinical Trials**

A Randomized Trial Comparing Primary Infarct Artery Stenting With or Without Abciximab in Acute Myocardial Infarction

David Antoniucci, MD,* Alfredo Rodriguez, MD,† Albrecht Hempel, MD,‡ Renato Valenti, MD,* Angela Migliorini, MD,* Federico Vigo, MD,† Guido Parodi, MD,* Carlos Fernandez-Pereira, MD,† Guia Moschi, MD,* Antonio Bartorelli, MD,§ Giovanni Maria Santoro, MD,* Leonardo Bolognese, MD,* Antonio Colombo, MD‖

Florence and Milan, Italy; Buenos Aires, Argentina; and Bernau, Germany

OBJECTIVES We sought to evaluate the efficacy of abciximab as adjunctive therapy to routine infarct-related artery (IRA) stenting.

BACKGROUND The impact of abciximab on the efficacy of myocardial reperfusion and the outcome of patients with acute myocardial infarction (AMI) undergoing IRA stenting have not yet been defined.

METHODS In a randomized trial, we assigned 400 patients with AMI to undergo IRA stenting alone or stenting plus abciximab. The primary end point was a composite of death, reinfarction, target vessel revascularization (TVR), and stroke at one month.

RESULTS The incidence of the primary end point was lower in the abciximab group than in the stent only group (4.5% and 10.5%, respectively; $p = 0.023$), and randomization to abciximab was independently related to the risk of the primary end point (odds ratio 0.41, 95% confidence interval 0.17 to 0.97; $p = 0.041$). Early ST-segment resolution was more frequent in the abciximab group (85% vs. 68%, $p < 0.001$). Infarct size, as assessed by one-month technetium-99m sestamibi scintigraphy, revealed smaller infarcts in the abciximab group. At six months, the cumulative difference in mortality between the groups increased (4.5% vs. 8%), and the incidence of the composite of six-month death and reinfarction was lower in the abciximab group than in the stent only group (5.5% and 13.5%, respectively; $p = 0.006$). Six-month repeat TVR and restenosis rates were similar in the two groups.

CONCLUSIONS Abciximab plus IRA stenting should be considered the routine reperfusion strategy in patients with AMI undergoing primary percutaneous mechanical revascularization, especially in high-risk patients. (J Am Coll Cardiol 2003;42:1879–85) © 2003 by the American College of Cardiology Foundation

STRATEGY

BMS and abciximab display a synergistic role in primary PCI setting and...

"should be currently regarded as the gold standard for STEMI"

Journal of the American College of Cardiology
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EDITORIAL COMMENT

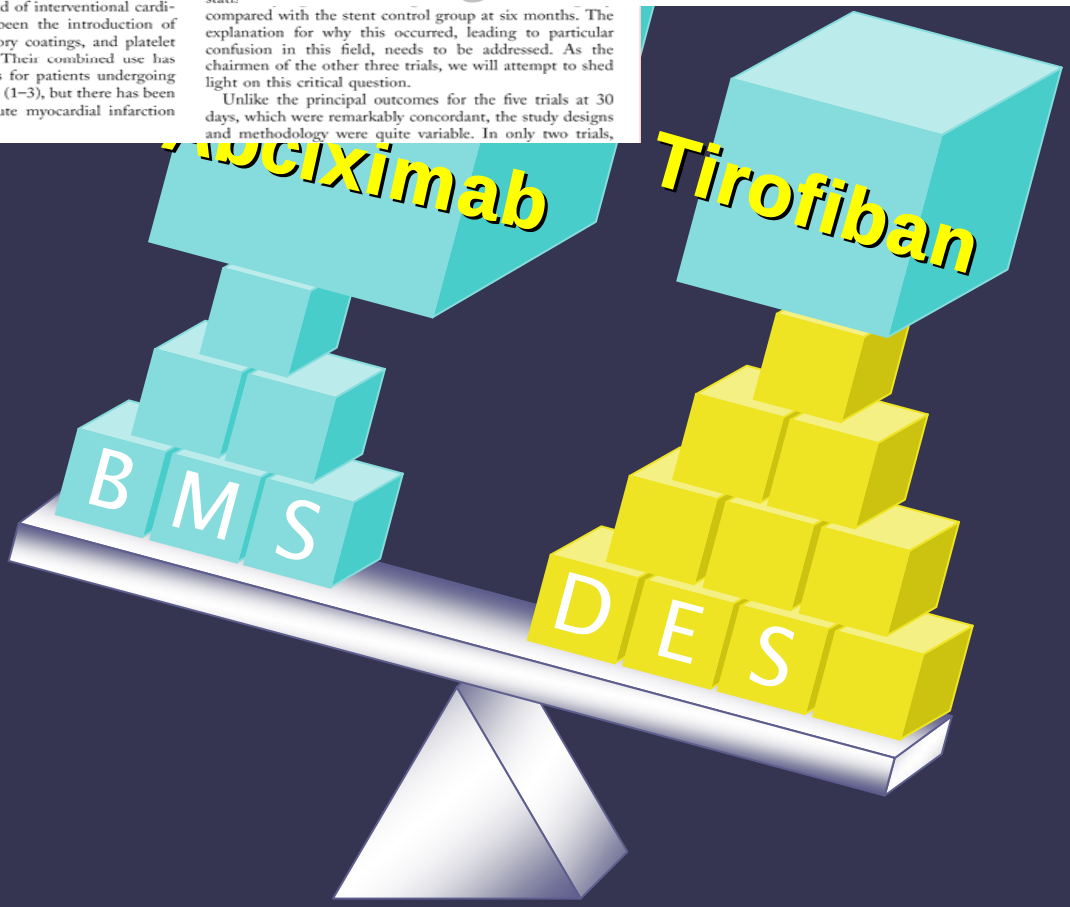
A Preferred Reperfusion Strategy for Acute Myocardial Infarction*

Eric J. Topol, MD, FACC, FESC,†
Franz-Josef Neumann, MD, FACC, FESC,‡
Gilles Montalescot, MD, PHD§
Cleveland, Ohio; Bad Krozingen, Germany; and Paris, France

The major innovations in the field of interventional cardiology in the past decade have been the introduction of stents, now with anti-inflammatory coatings, and platelet glycoprotein IIb/IIIa inhibitors. Their combined use has been validated in dedicated trials for patients undergoing elective coronary revascularization (1–3), but there has been controversy in the setting of acute myocardial infarction (MI).

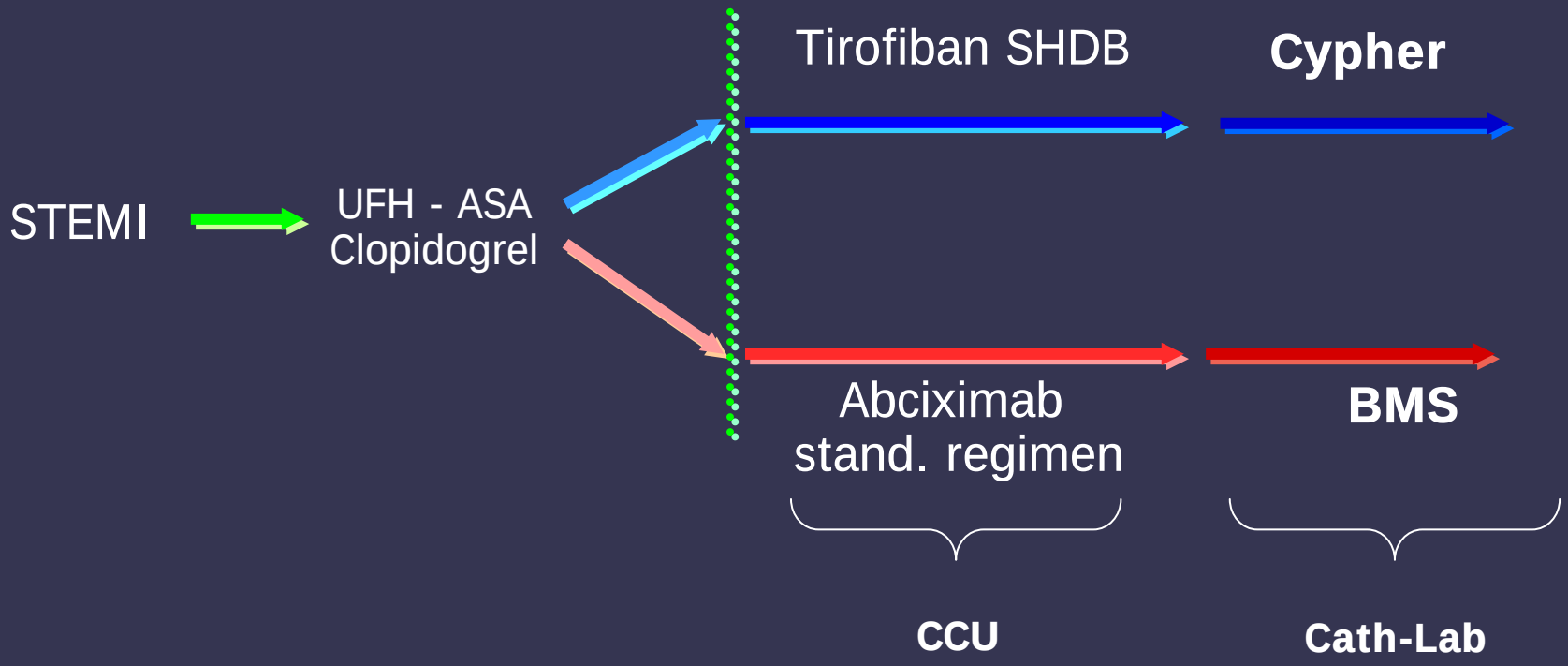
compared with the stent control group at six months. The explanation for why this occurred, leading to particular confusion in this field, needs to be addressed. As the chairmen of the other three trials, we will attempt to shed light on this critical question.

Unlike the principal outcomes for the five trials at 30 days, which were remarkably concordant, the study designs and methodology were quite variable. In only two trials,



Study design

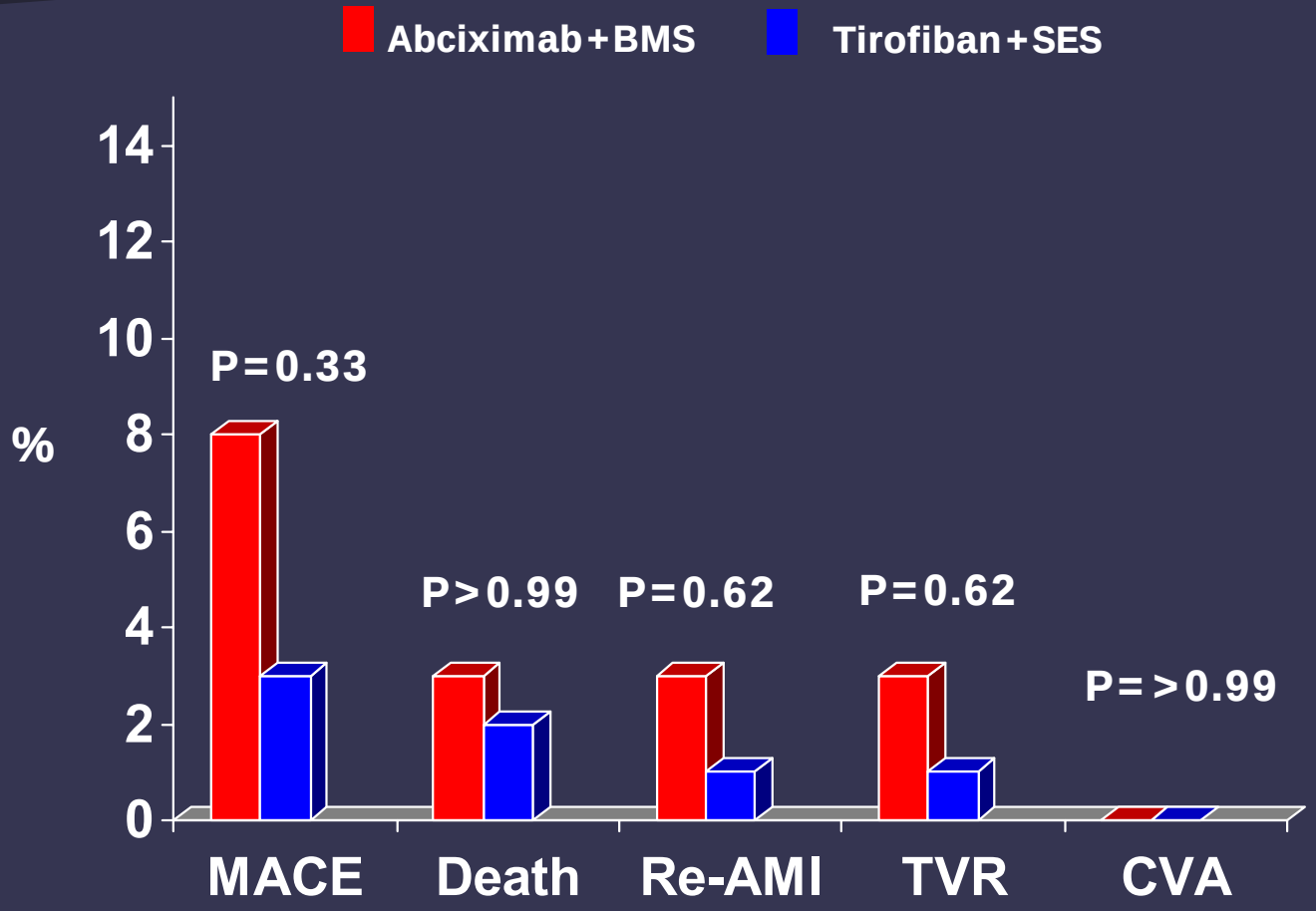
- **Inclusion Criteria**: STEMI all comers: shock, elderly included
- **Exclusion Criteria**: Contraindications to Gp IIb/IIIa



Valgimigli et al. Cardiovasc Drugs Ther 04; 18: 225-30

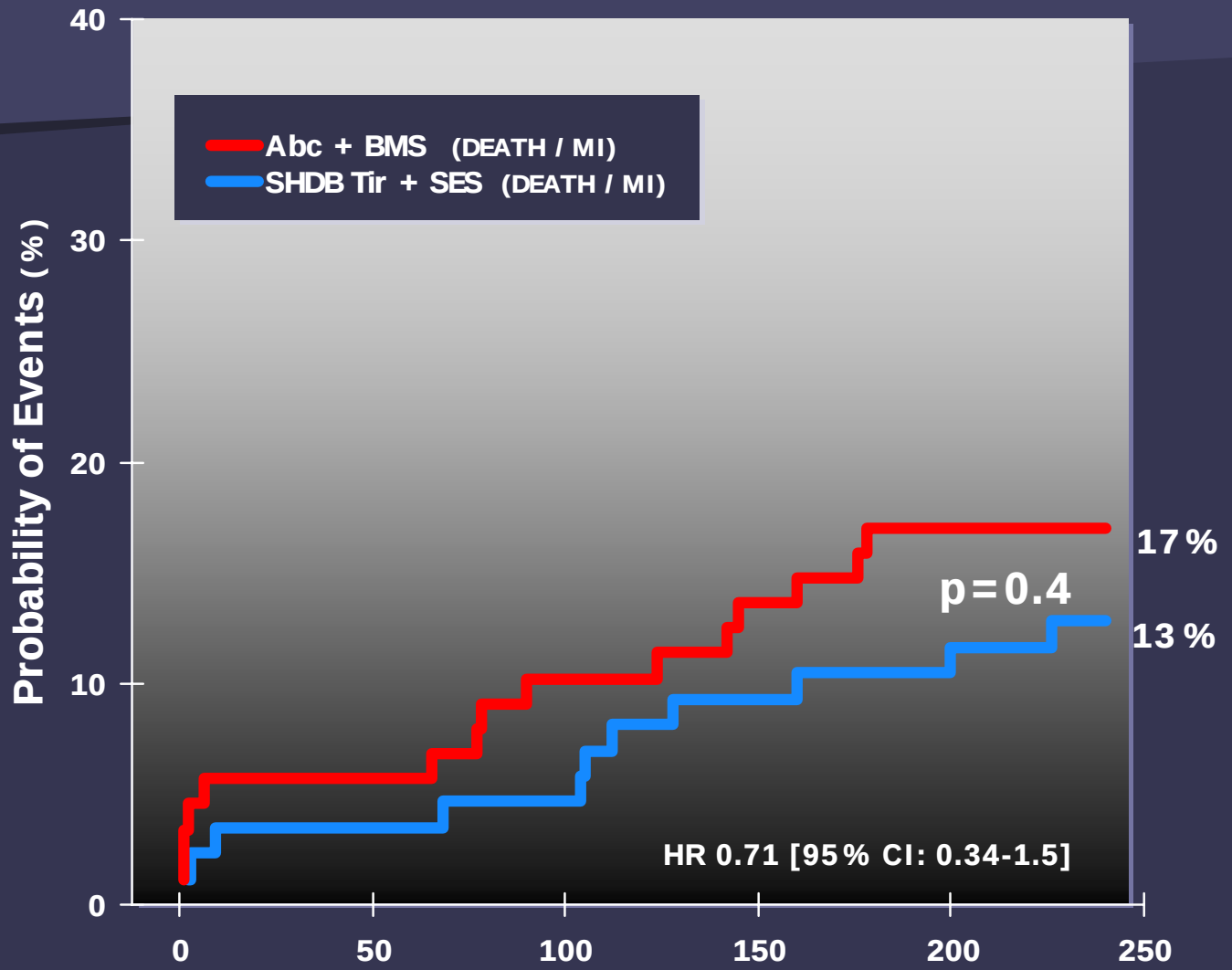
30-Day Outcome

n=175



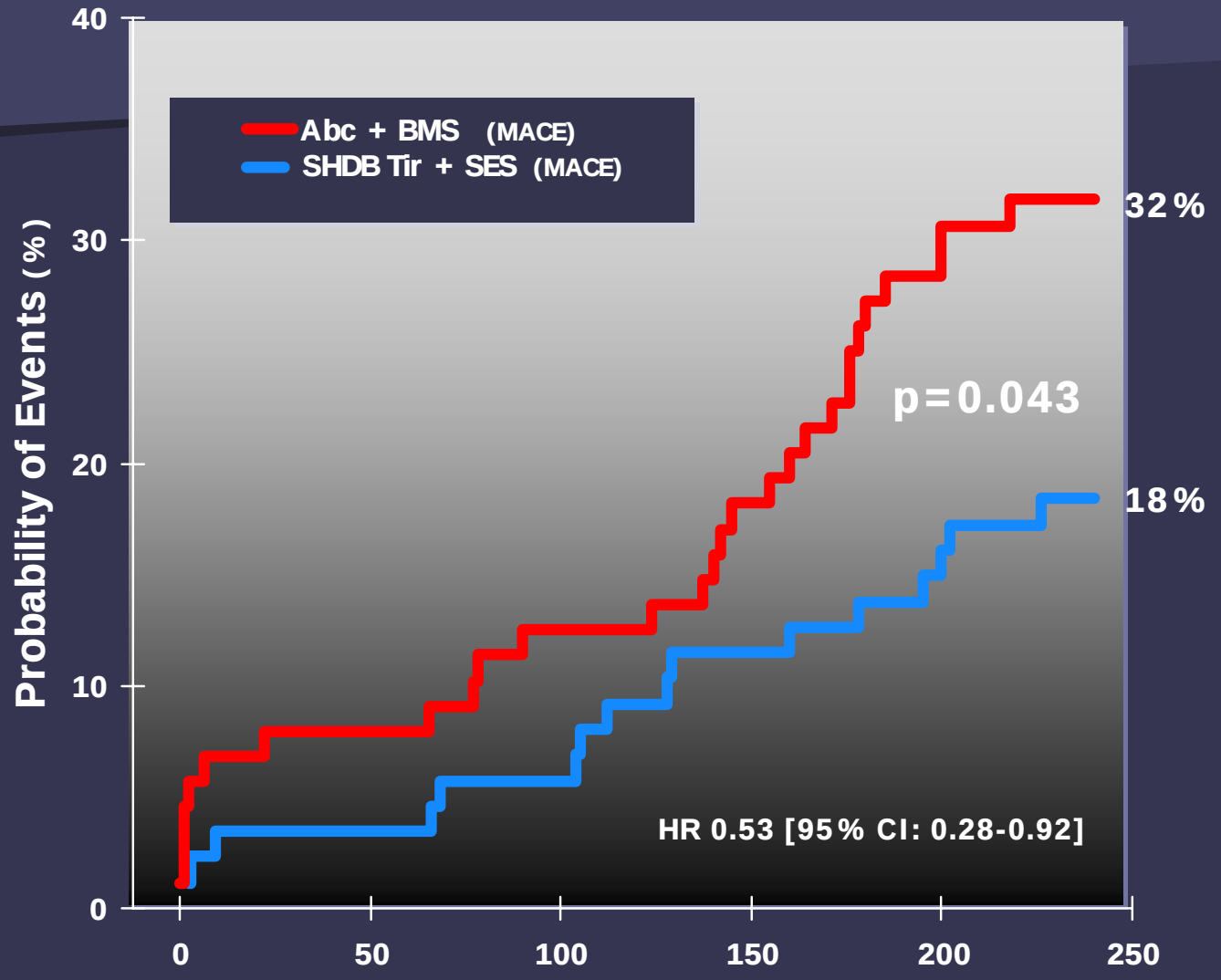
Valgimigli et al. *JAMA* 2005; 293: 2109-2117

Death / MI at 8 Months



JAMA 2005; 293: 2109-2117

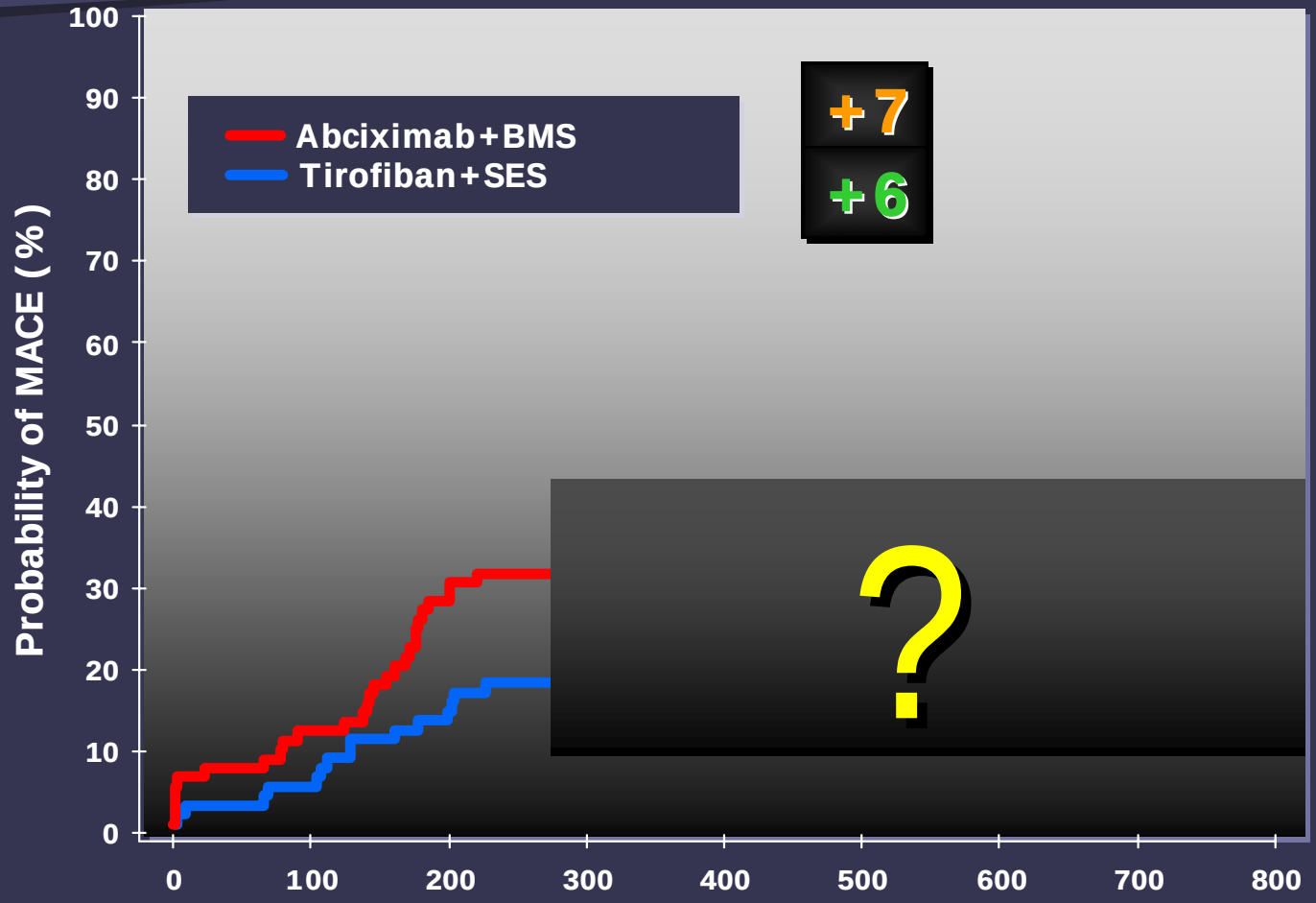
Death / MI / TVR at 8 Months



JAMA 2005; 293: 2109-2117

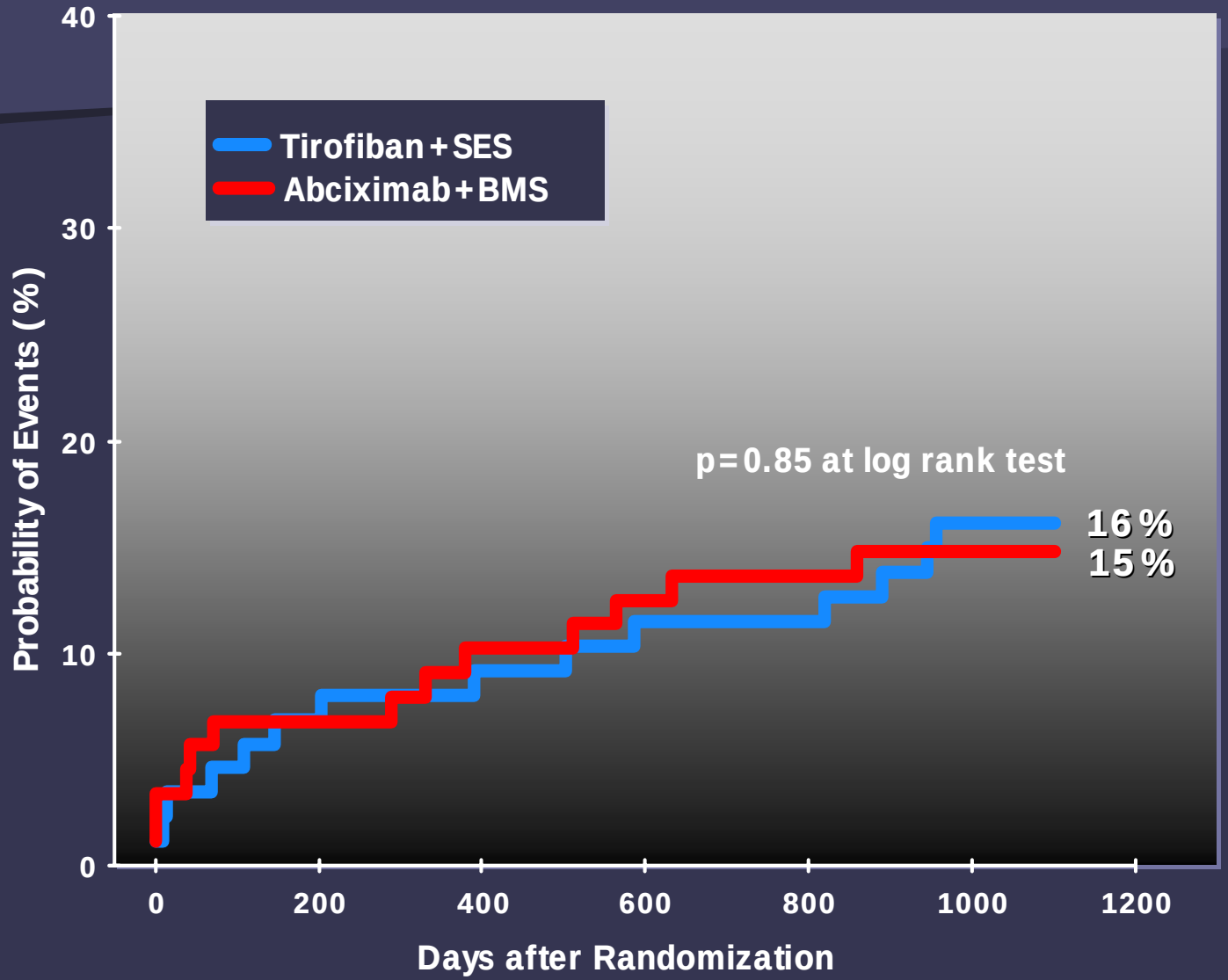
2-year Follow-up

The Benefit is mainly carried over



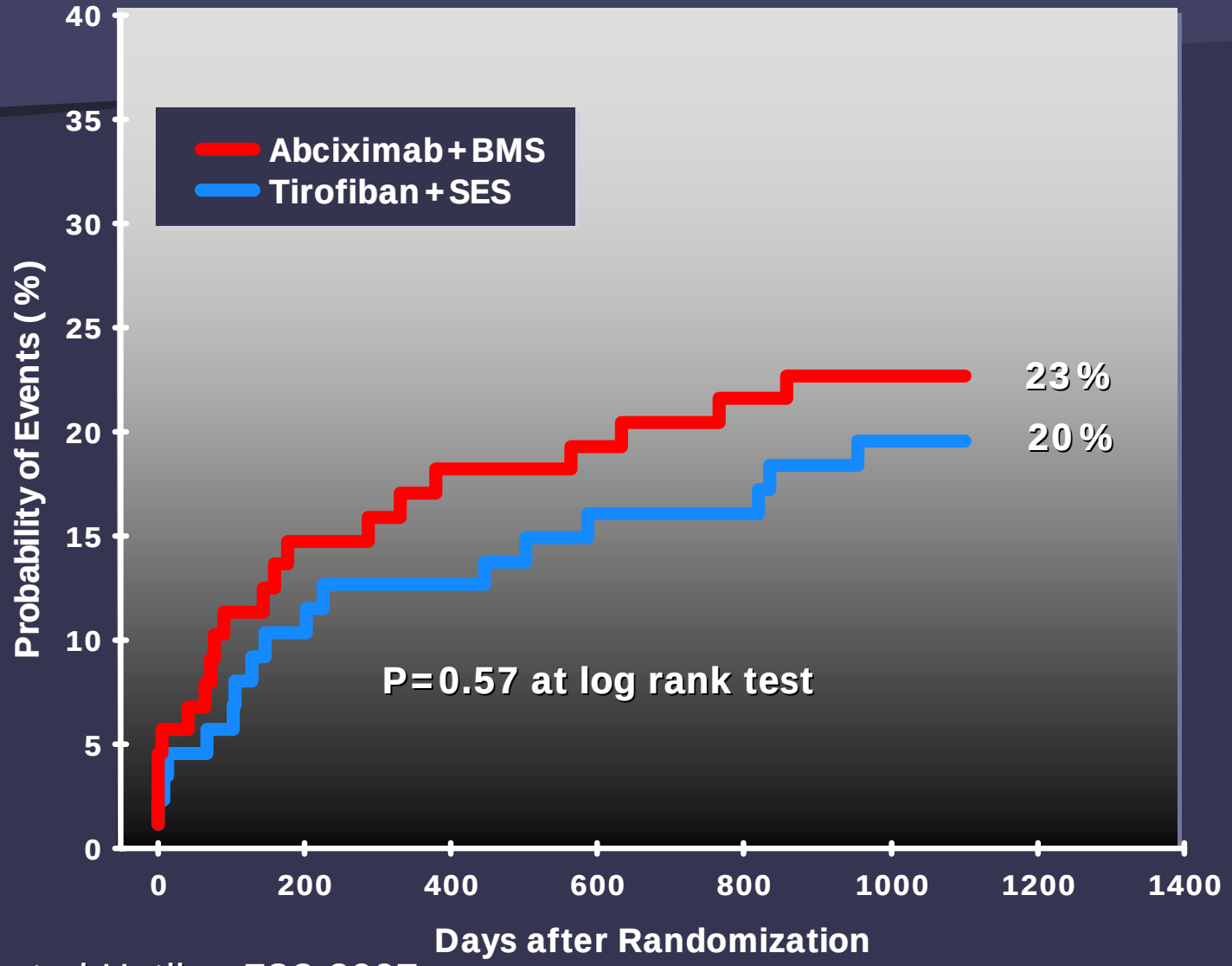
Valgimigli et al, JACC 07

All cause mortality at 3 years



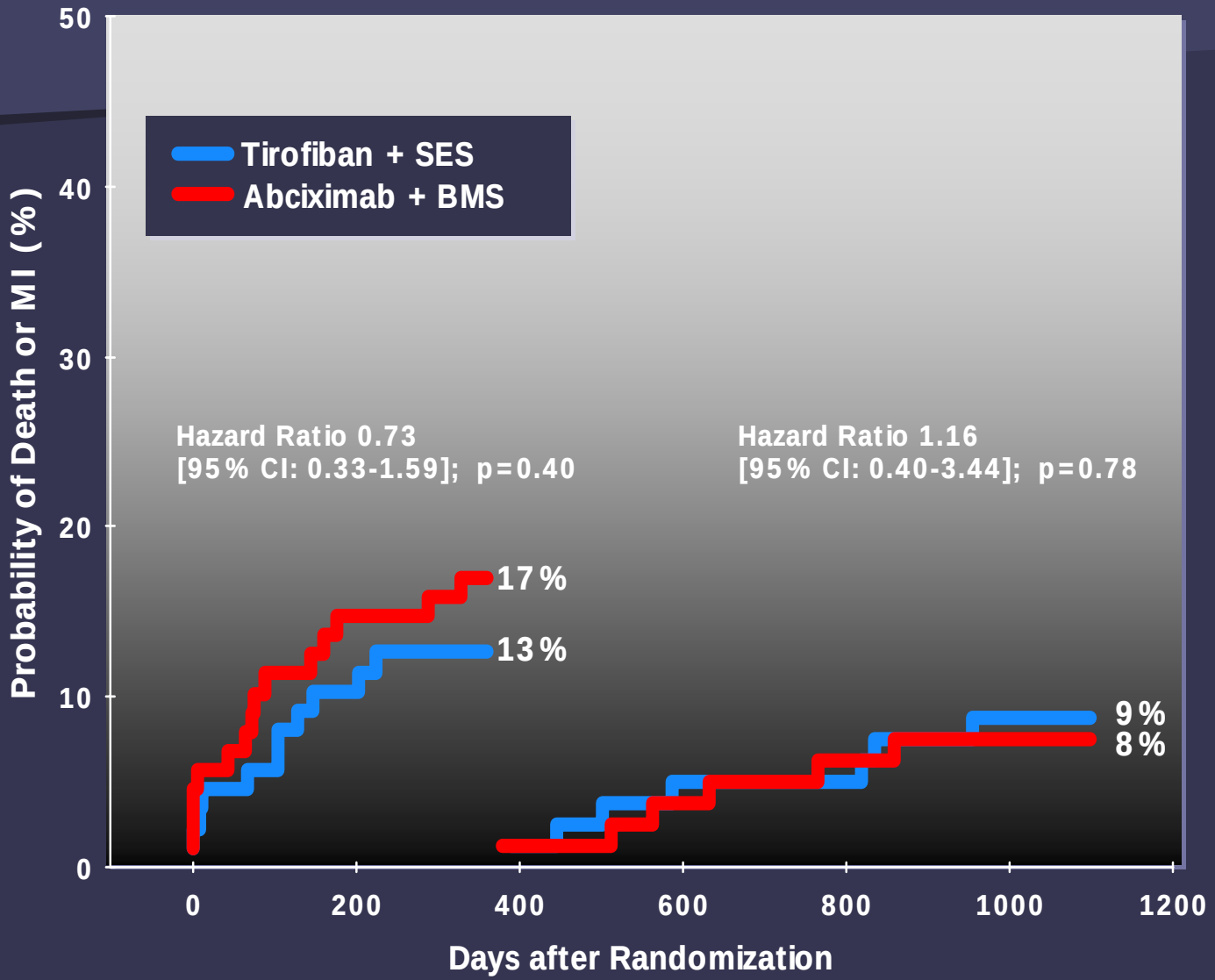
Valgimigli et al Hotline ESC 2007

Death / MI at 3 years



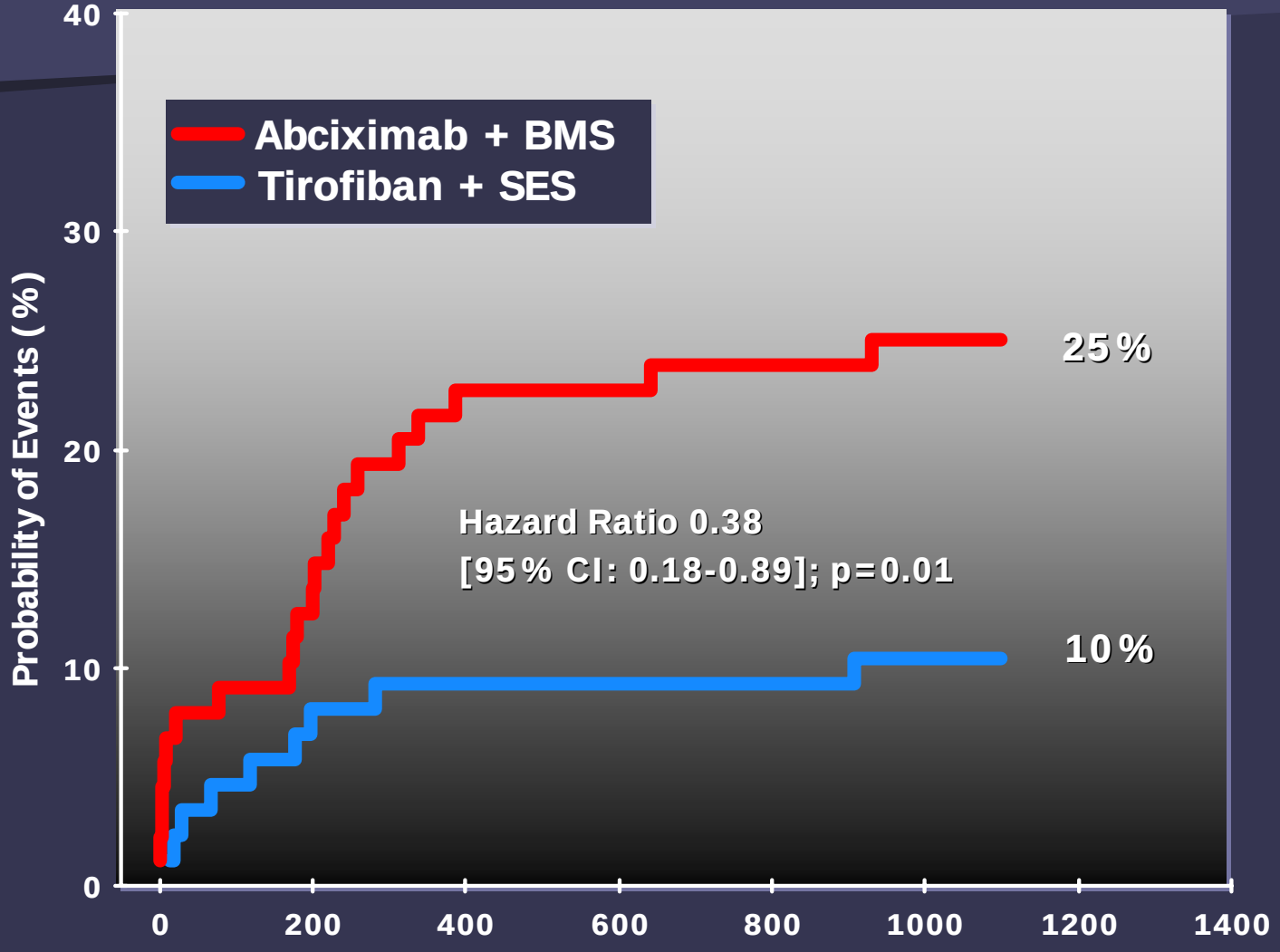
Valgimigli et al Hotline ESC 2007

Death/MI Landmark Analysis



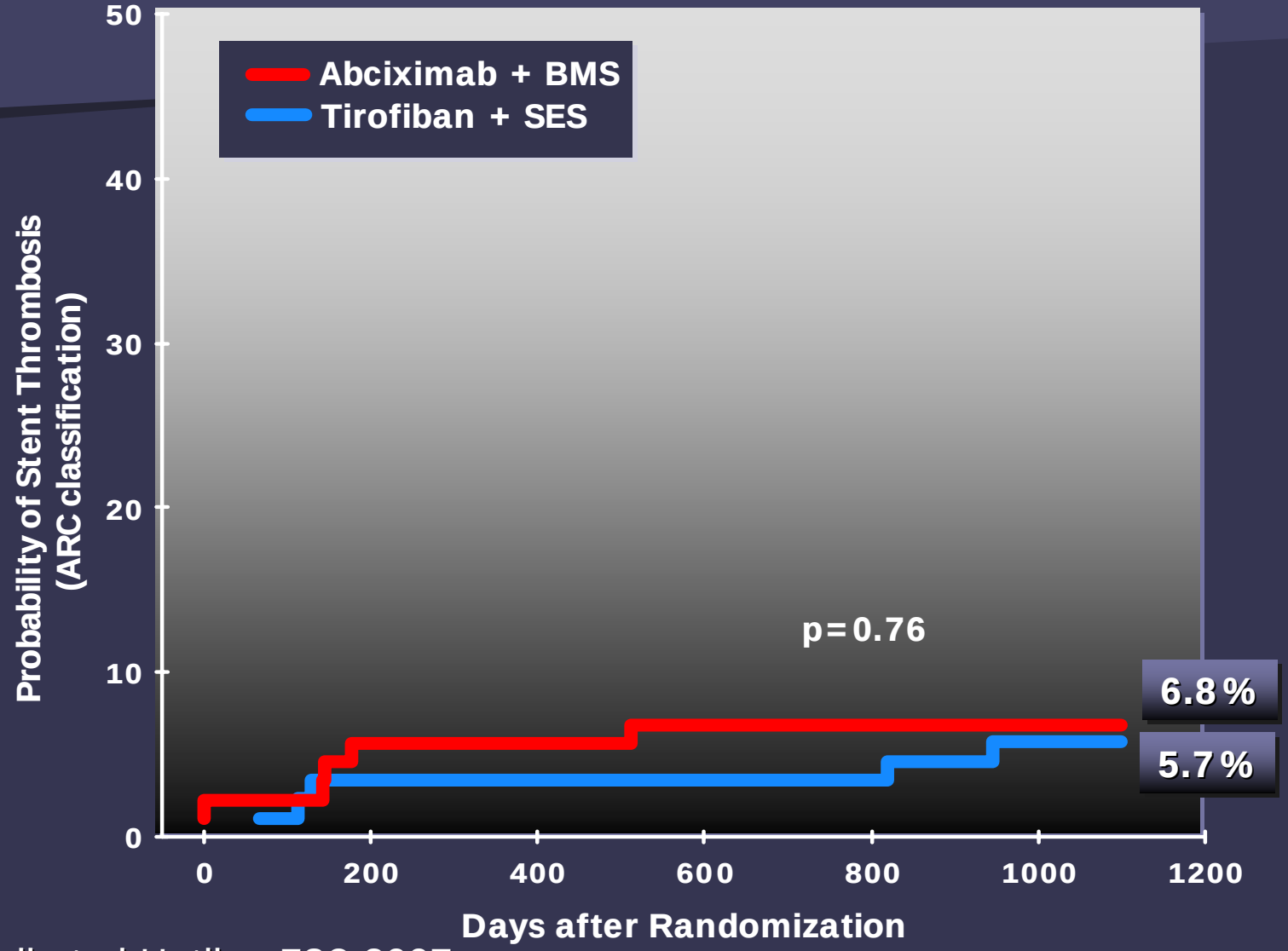
Valgimigli et al Hotline ESC 2007

TVR at 3 years



Valgimigli et al Hotline ESC 2007

Stent Thrombosis at 3 years



Valgimigli et al Hotline ESC 2007

Study Limitations

- Single center
- Systematic angiographic follow-up
- Surrogate endpoints with small sample size
- Two “rigid” combinations between stents and GP IIb/IIIa inhibitors were compared

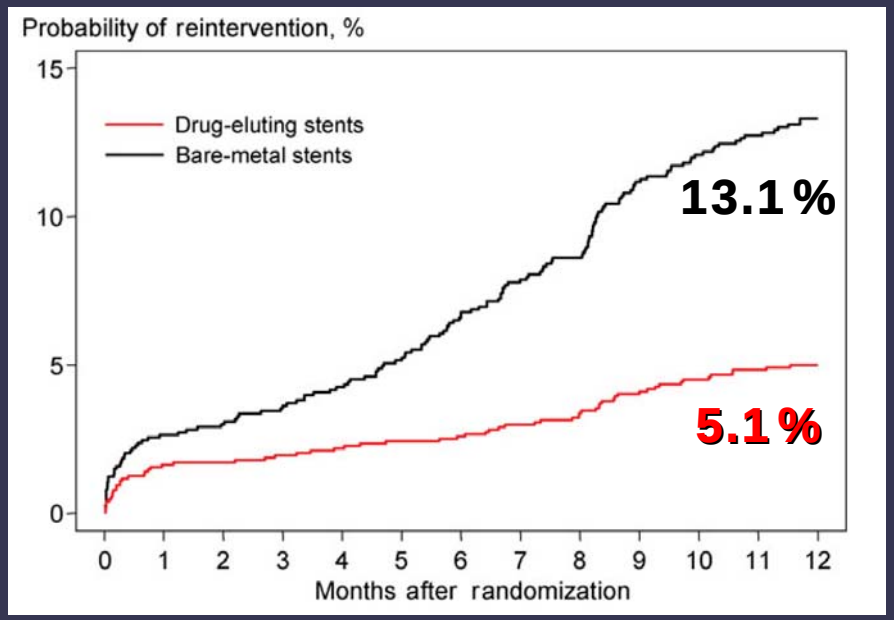
Overview of available RCTs on DES in STEMI

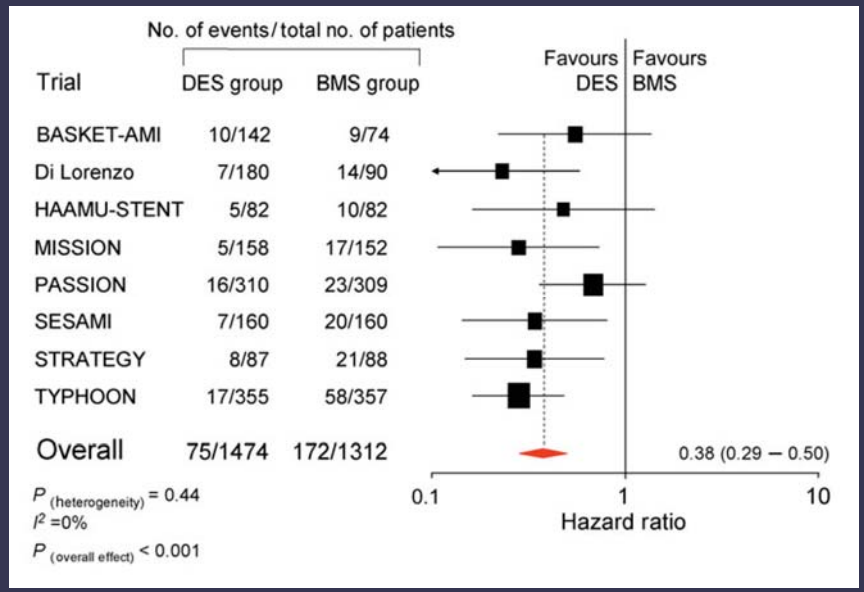
Study	No. of Patients	No. of Patients With Diabetes	Mean Age (years)	Type of DES	Availability of Individual Patient Data	Primary End Point	Length of thienopyridine therapy (months)	Mean Length of Follow-Up (months)
HAAMU-STENT	164	24	63.0	PES	Yes	Angiographic late lumen loss	12	16.7
MISSION	310	30	59.2	SES	No	Angiographic late lumen loss	12	12.0
PASSION	619	68	[illegible]	PES	[illegible]	Cardiac death, MI, or TVR	6	12.0
SESAMI	320	65	61.6	[illegible]	[illegible]	[illegible]inary [illegible]	12	12.3
STRATEGY	175	26	62	[illegible]	[illegible]	[illegible]MI, [illegible] or [illegible] stenosis	3	24.2
TYPHOON	712	116	59.3	[illegible]	[illegible]	[illegible]ac death, [illegible] or TVR	6	12.1
BASKET-AMI	216	[illegible]	62.2	SES/PE[illegible]	Yes	Cardiac death, MI, or TVR	6	18
Di Lorenzo et al	270	[illegible]	64	SES/PES	Yes	Death, MI, or TVR	6	12

2476

Meta-analysis of randomized trials on drug-eluting stents vs. bare-metal stents in patients with acute myocardial infarction

REINTERVENTION





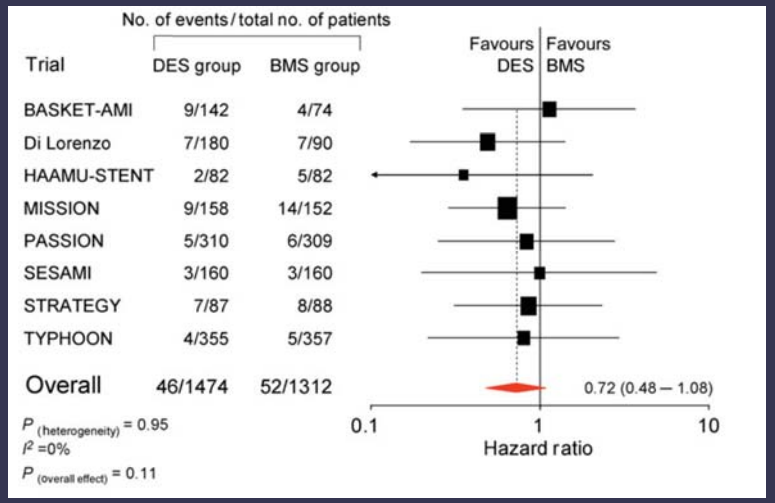
RRR: 62%

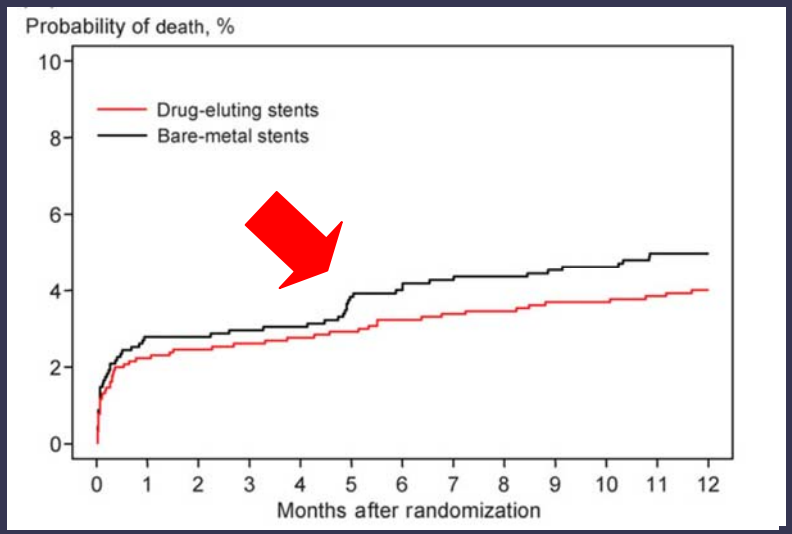
NNT: 13

Kastrati et al. EHJ (2007) 28, 2706–2713

Meta-analysis of randomized trials on drug-eluting stents vs. bare-metal stents in patients with acute myocardial infarction

Death rction

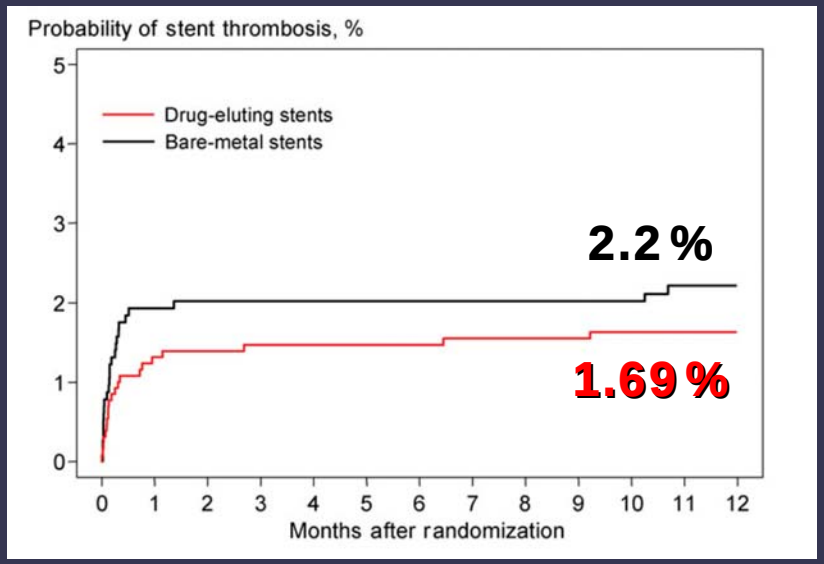


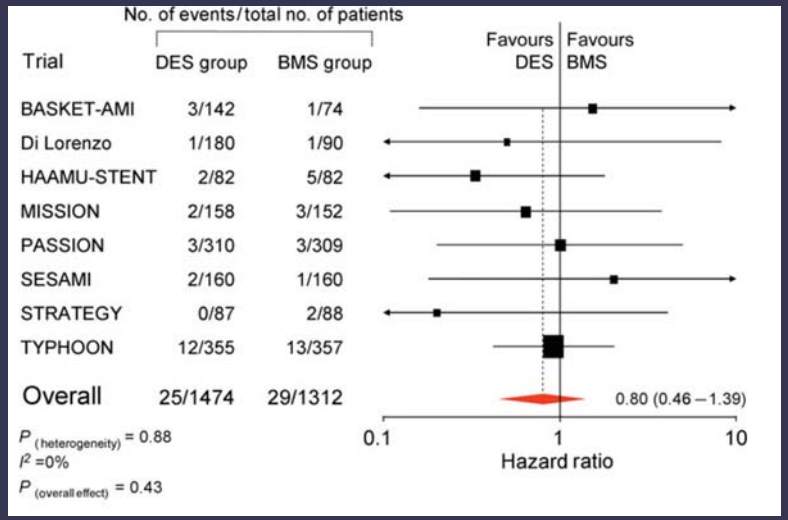


Kastrati et al. EHJ (2007) 28, 2706–2713

Meta-analysis of randomized trials on drug-eluting stents vs. bare-metal stents in patients with acute myocardial infarction

Stent thrombosis



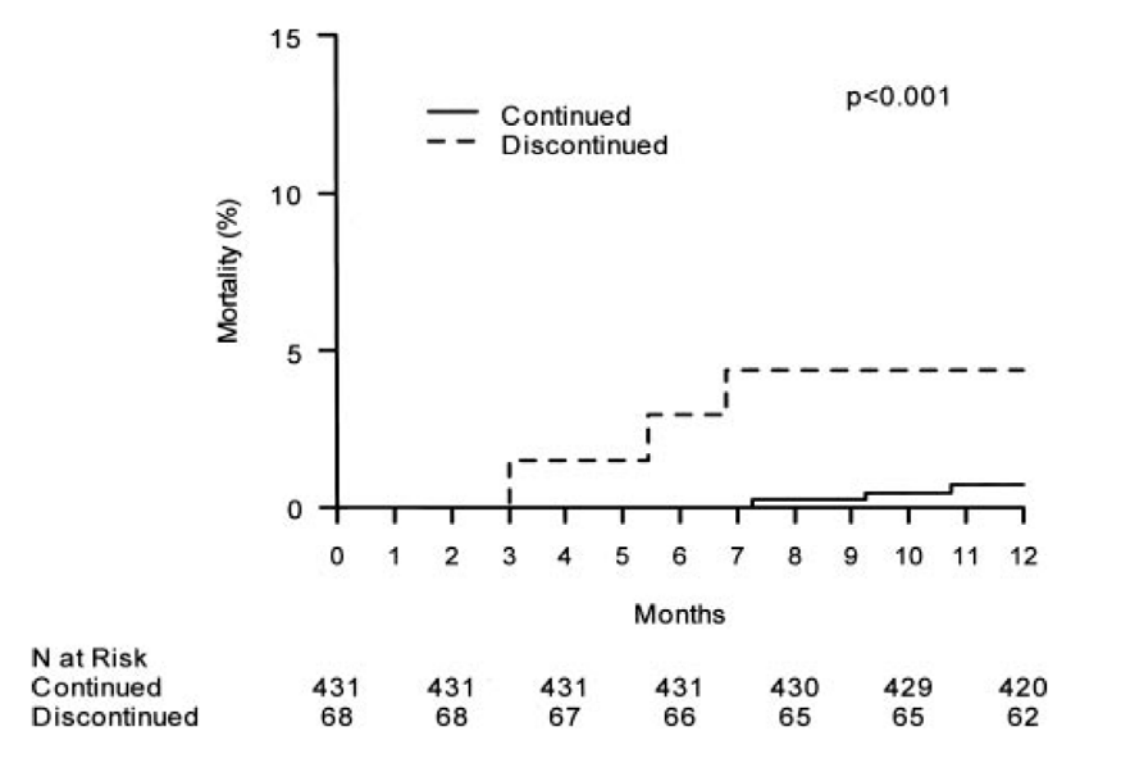


Kastrati et al. EHJ (2007) 28, 2706–2713

Contrasting data from Registries

PREMIER Registry

500 DES-treated MI patients who were discharged on thienopyridine



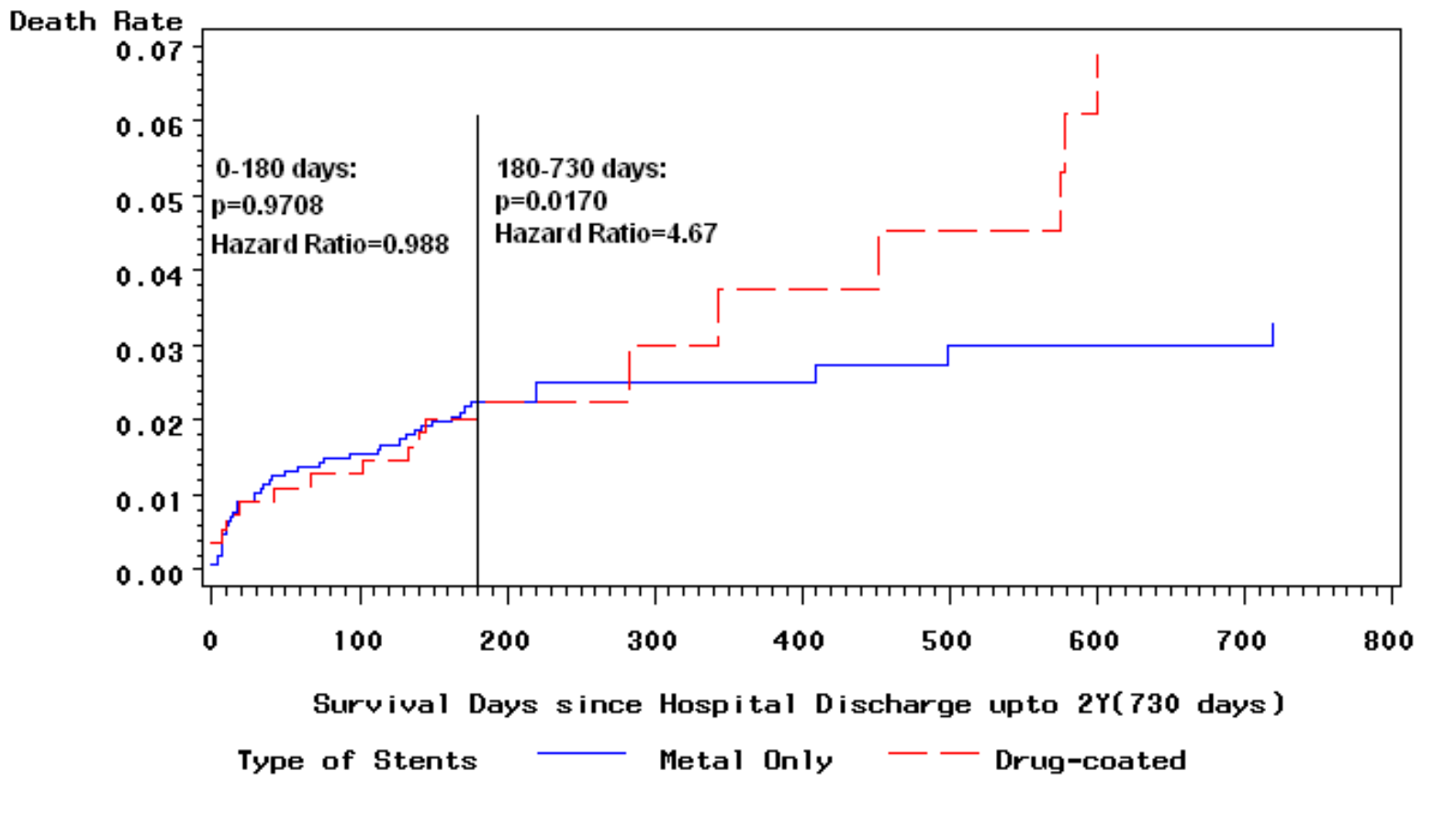
Circulation. 2006;113:2803-2809

Contrasting data from Registries

GRACE™ GLOBAL REGISTRY OF ACUTE CORONARY EVENTS

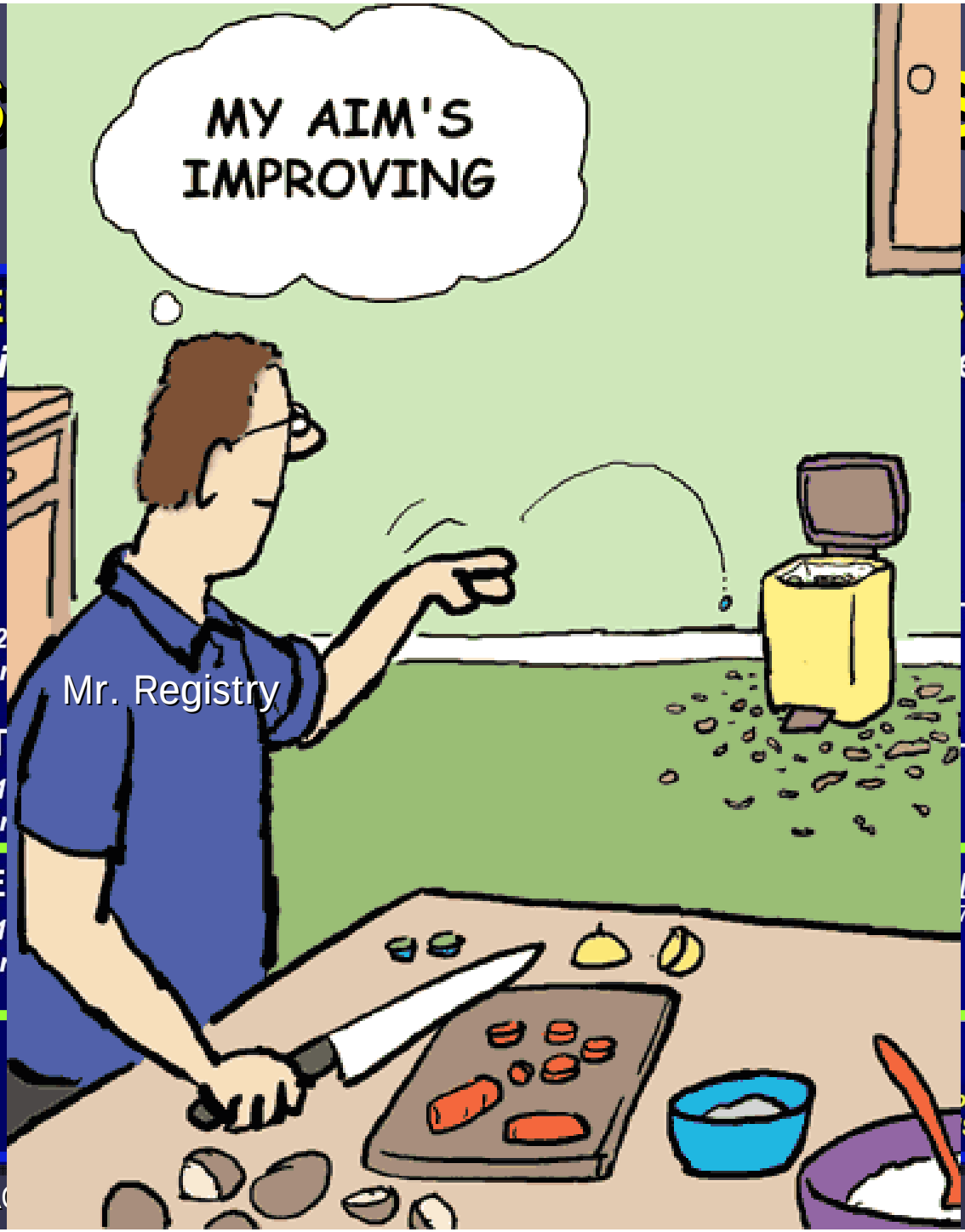
Courtesy of PG Steg

Landmark post-discharge survival analysis – STEMI



All patients died in hospital were excluded, as well as the patients without follow-up

DES … STEMI



Drug-E…
Risk Di…
MI
n=2…
pai…
NST…
n=1…
pai…
STE…
n=1…
pai…
…ears
-3.1%, 0.2%]
-5.0%, 0.3%]
[-3.7%, 0.5%]
6%
…ors
…S

Mauri L. SCAI2/A…

Overview of available RCTs on DES in STEMI

Study	No. of Patients	No. of Patients With Diabetes	Mean Age (years)	Type of DES	Availability of Individual Patient Data	Primary End Point	Length of thienopyridine therapy (months)	Mean Length of Follow-Up (months)
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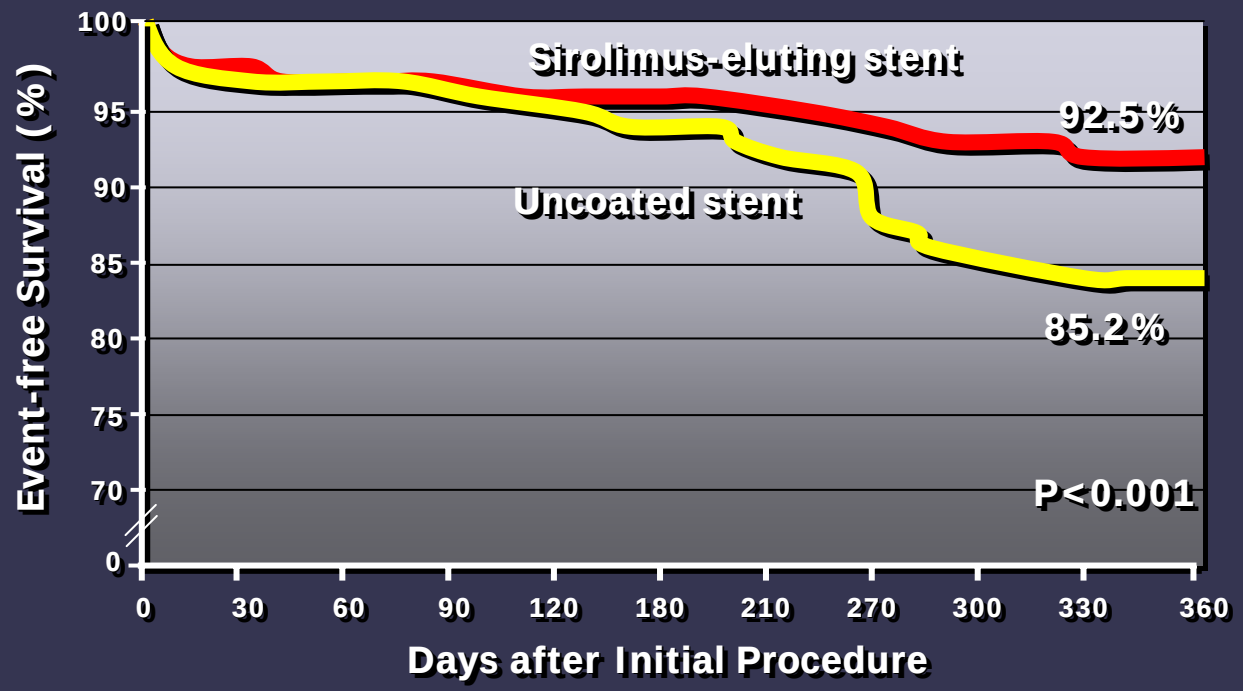
SESAMI	320	65	61.6	SES	Yes	Single centre !!	12	12.3
STRATEGY	175	26	62.6	SES	Ye	Death, MI Single centre !! restenosis	3	24.2
TYPHOON			3	SES	Yes	Cardiac death, MI, or TVR	6	12.1
BASKET-AMI	216		62.2	SES/PES	Ye	Single centre !!	6	18
Di Lorenzo et al	270		64	SES/PES	Ye	Single centre !!	6	12

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 14, 2006 VOL. 355 NO. 11

Sirolimus-Eluting versus Uncoated Stents in Acute Myocardial Infarction

Christian Spaulding, M.D., Patrick Henry, M.D., Ph.D., Emmanuel Teiger, M.D., Ph.D., Kevin Beatt, M.B., B.S., Ph.D., Ezio Bramucci, M.D., Didier Carrié, M.D., Michel S. Slama, M.D., Bela Merkely, M.D., Ph.D., Andrejs Erglis, M.D., Ph.D., Massimo Margheri, M.D., Olivier Varenne, M.D., Ph.D., Ana Cebrian, Ph.D., Hans-Peter Stoll, M.D., David B. Snead, Ph.D., and Christoph Bode, M.D., for the TYPHOON Investigators*

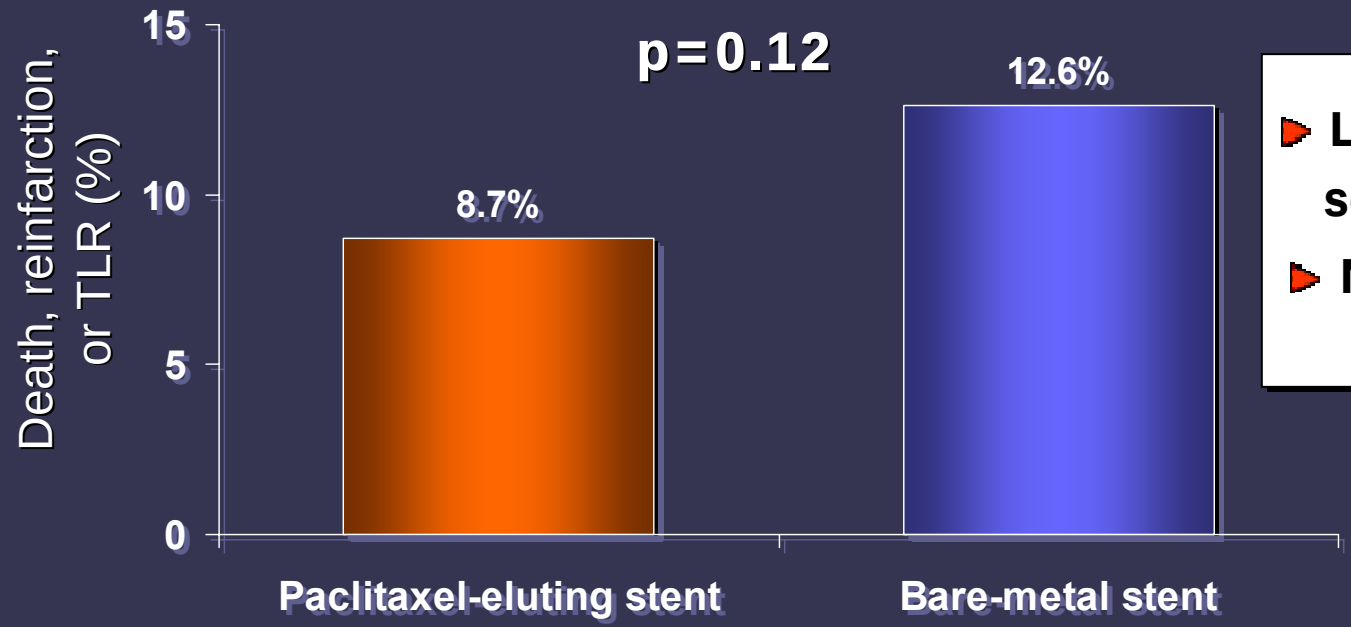


ORIGINAL ARTICLE

Paclitaxel-Eluting versus Uncoated Stents in Primary Percutaneous Coronary Intervention

Gerrit J. Laarman, M.D., Ph.D., Maarten J. Suttorp, M.D., Ph.D., Maurits T. Dirksen, M.D., Loek van Heerebeek, M.D., Ferdinand Kiemeneij, M.D., Ph.D., Ton Slagboom, M.D., L. Ron van der Wieken, M.D., Jan G.P. Tijssen, Ph.D., Benno J. Rensing, M.D., Ph.D., and Mark Patterson, M.R.C.P.

Composite endpoint of death, reinfarction, or TLR at one year (%)

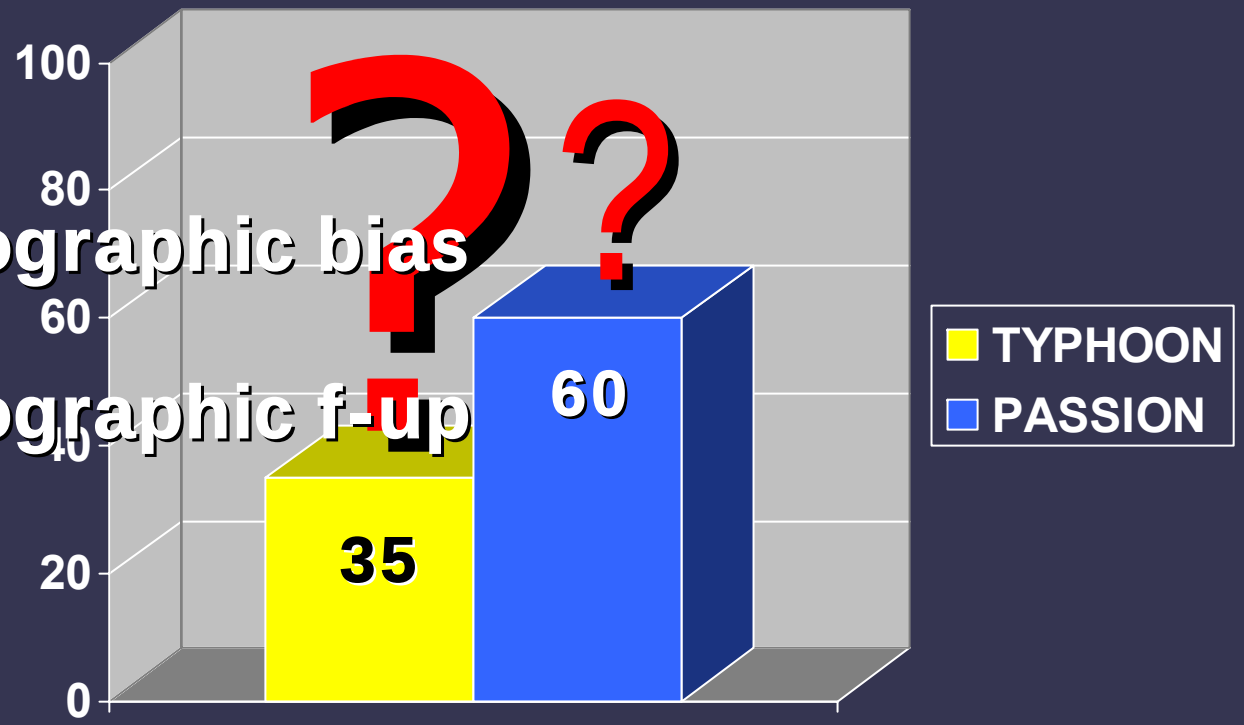


- Less Angiographic selection
- No Angio follow-up

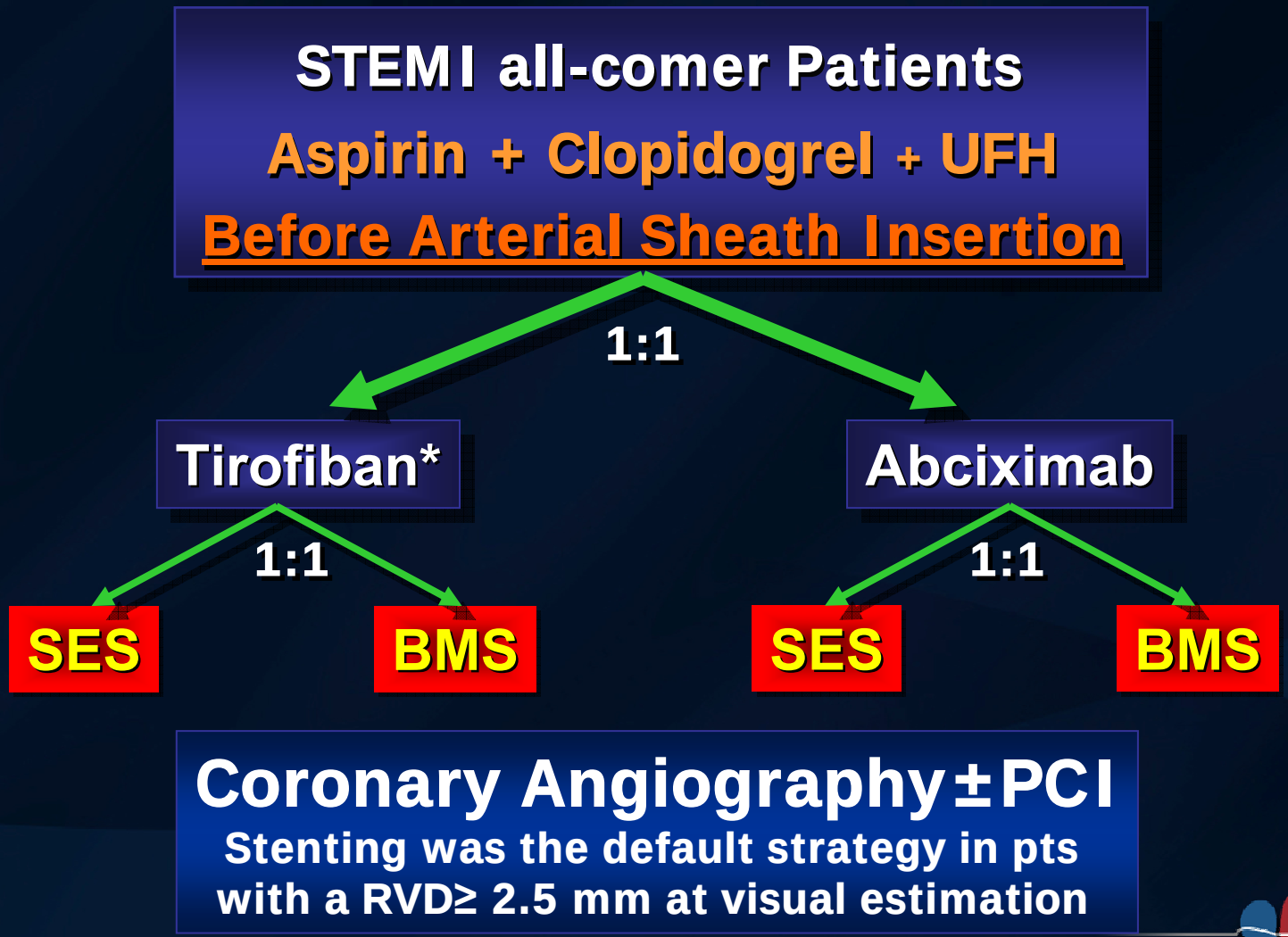
Enrolled/Screened Ratio

DES in STEMI in Multicenter studies

- No angiographic bias
- No angiographic f-up



Trial Design



*: given as a bolus of 25 μg/kg, followed by an 18-24 hour infusion at 0.15 μg/kg/min

MULTISTRATEGY

MULTISTRATEGY P.I.s and Sites

G Campo Ferrara

G Percoco Lagosanto

M Anselmi Verona

L Bolognese Arezzo

S Colangelo Torino

N de Cesare Zingonia

A Rodriguez B. Aires

M Ferrario Pavia

R Moreno Madrid

T Piva Ancona

I Sheiban Torino

G Pasquetto Mirano

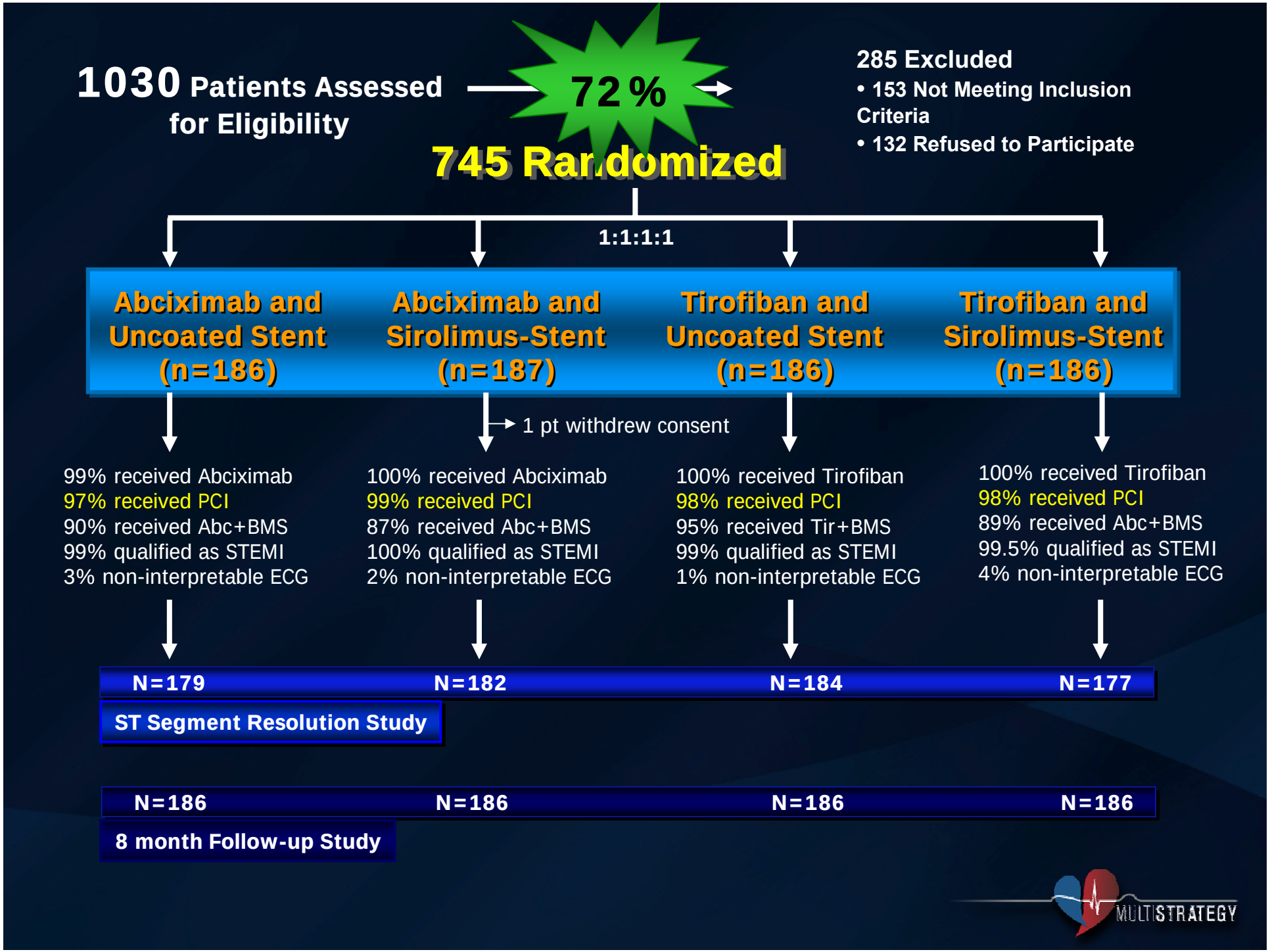
F Prati Rome

M Nazzaro Rome

J Fernández Huelva

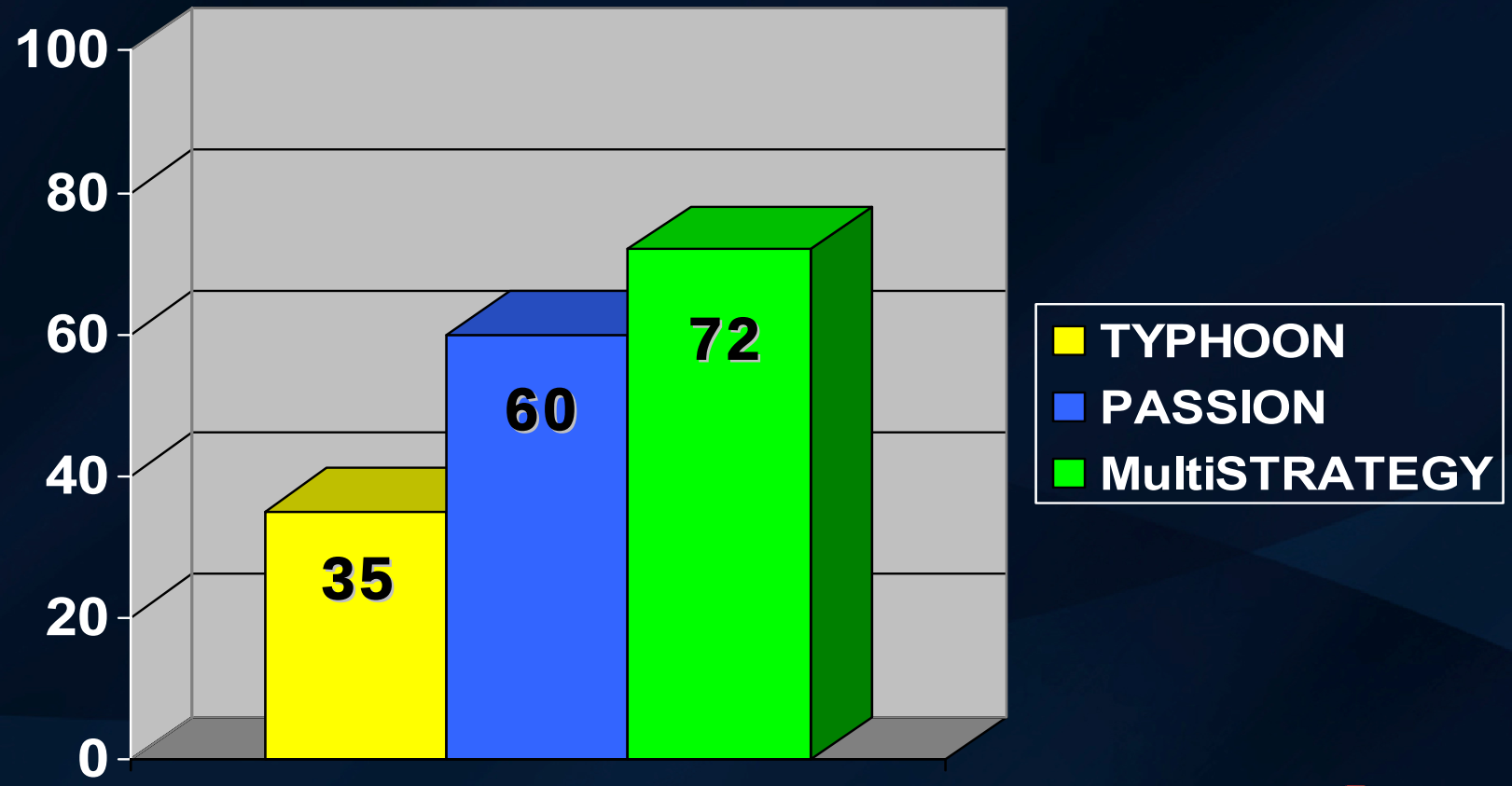
J Mieres B Aires

MULTISTRATEGY


1030 Patients Assessed for Eligibility
72 %
745 Randomized
285 Excluded
• 153 Not Meeting Inclusion Criteria
• 132 Refused to Participate
1:1:1:1
Abciximab and Uncoated Stent (n=186)
Abciximab and Sirolimus-Stent (n=187)
Tirofiban and Uncoated Stent (n=186)
Tirofiban and Sirolimus-Stent (n=186)
1 pt withdrew consent
99% received Abciximab
97% received PCI
90% received Abc+BMS
99% qualified as STEMI
3% non-interpretable ECG
100% received Abciximab
99% received PCI
87% received Abc+BMS
100% qualified as STEMI
2% non-interpretable ECG
100% received Tirofiban
98% received PCI
95% received Tir+BMS
99% qualified as STEMI
1% non-interpretable ECG
100% received Tirofiban
98% received PCI
89% received Abc+BMS
99.5% qualified as STEMI
4% non-interpretable ECG
N=179
N=182
N=184
N=177
ST Segment Resolution Study
N=186
N=186
N=186
N=186
8 month Follow-up Study
MULTISTRATEGY

Enrolled/Screened Ratio

DES in STEMI in Multicenter studies



MULTISTRATEGY

Baseline Characteristics

	Abciximab			P
	BMS	SES		
1-VD	40.3	45.7	45.2	
2-VD	36.6	34.9	32.8	
3-VD	20.4	18.3	21.5	
LAD-culprit	43.4	45.9	41.8	
RCA-culprit	35.1	39.3	42.9	
LMCA-culprit	1.6	1.6		0.14
SVG-culprit				0.13
Interventions				
De Novo culpri				
No. Stents	1	1		0.47
Stent Length	20	23		0.18
Max Stent Size	3.07±0.4	3.05±0.4		0.06
Stent post-dil	18.9	21.6	20.3	
Max Pressure	14.1±4.3	14.6±3.6		0.039
GP2b/3a infusion	12 (12-12)	12 (12-12)		<0.001
ACT at peak	225 (191-307)	250 (250-303)	(19	0.87

96% of the BMS implanted had <0.10 mm strut thickness

MULTISTRATEGY

QCA Analysis

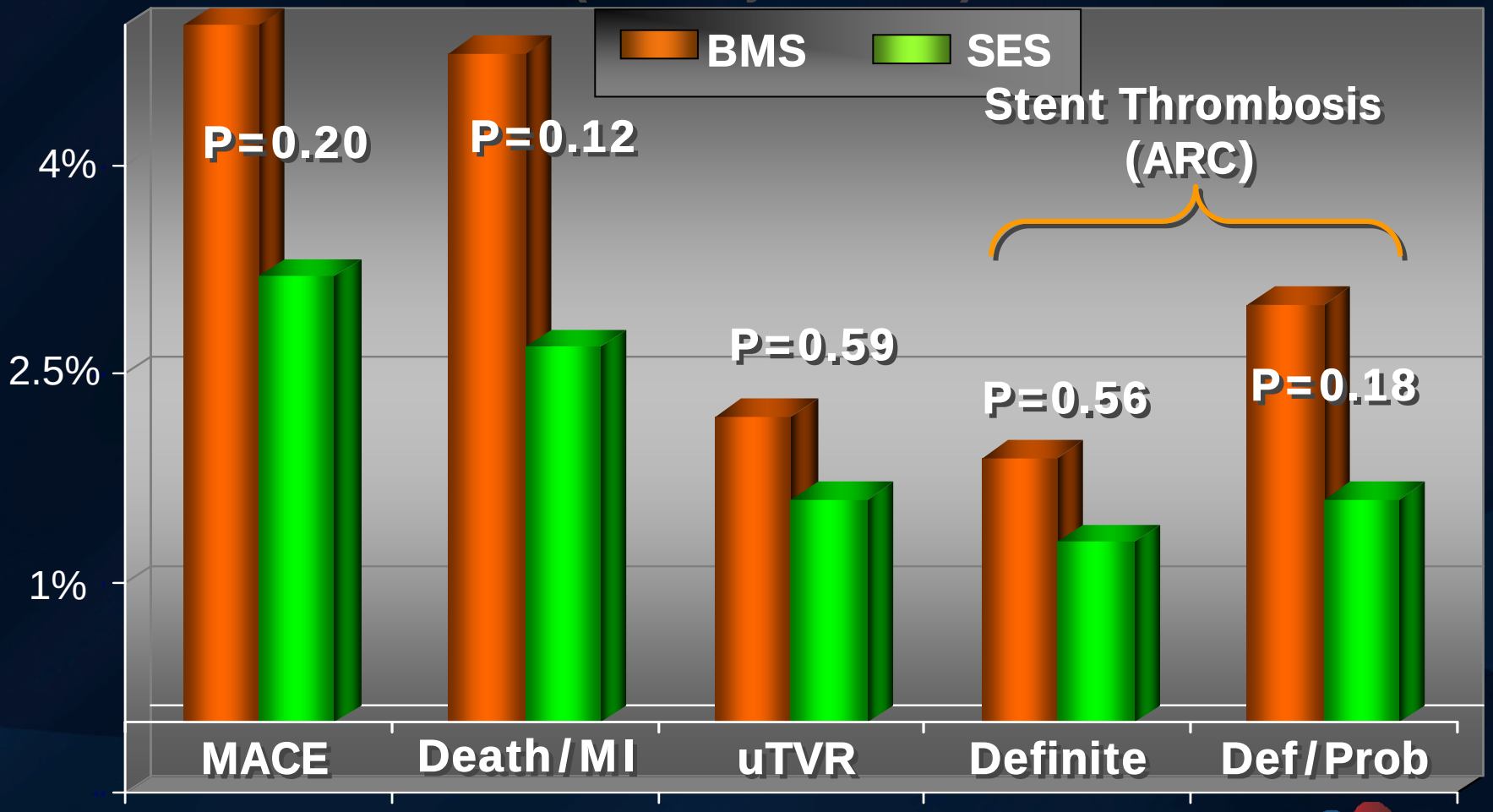
	Abciximab		Tirofiban		P
	BMS	SES	BMS	SES	
RVD (mm)					
before PCI	2.81	2.88	2.90	2.85	0.43
	2.52-3.16	2.55-3.14	2.58-3.23	2.61-3.06	
after PCI	2.87	2.91	2.90	2.86	0.79
	2.57-3.24	2.62-3.17	2.58-3.26	2.61-3.14	
MLD (mm)					
before PCI	0	0	0	0	0.34
	0-0.77	0-0.56	0-0.73	0-1.00	
after PCI	2.68	2.66	2.65	2.61	0.64
	2.34-2.96	2.42-2.91	2.41-3.00	2.42-2.91	
% stenosis					
before PCI	100	100	100	100	0.57
	71-100	79-100	76.5-100	70-100	
after PCI	6.5	7	6	8	0.89
	2-13	2-13	1-13	2-13.5	

MULTISTRATEGY

30-Day Outcomes

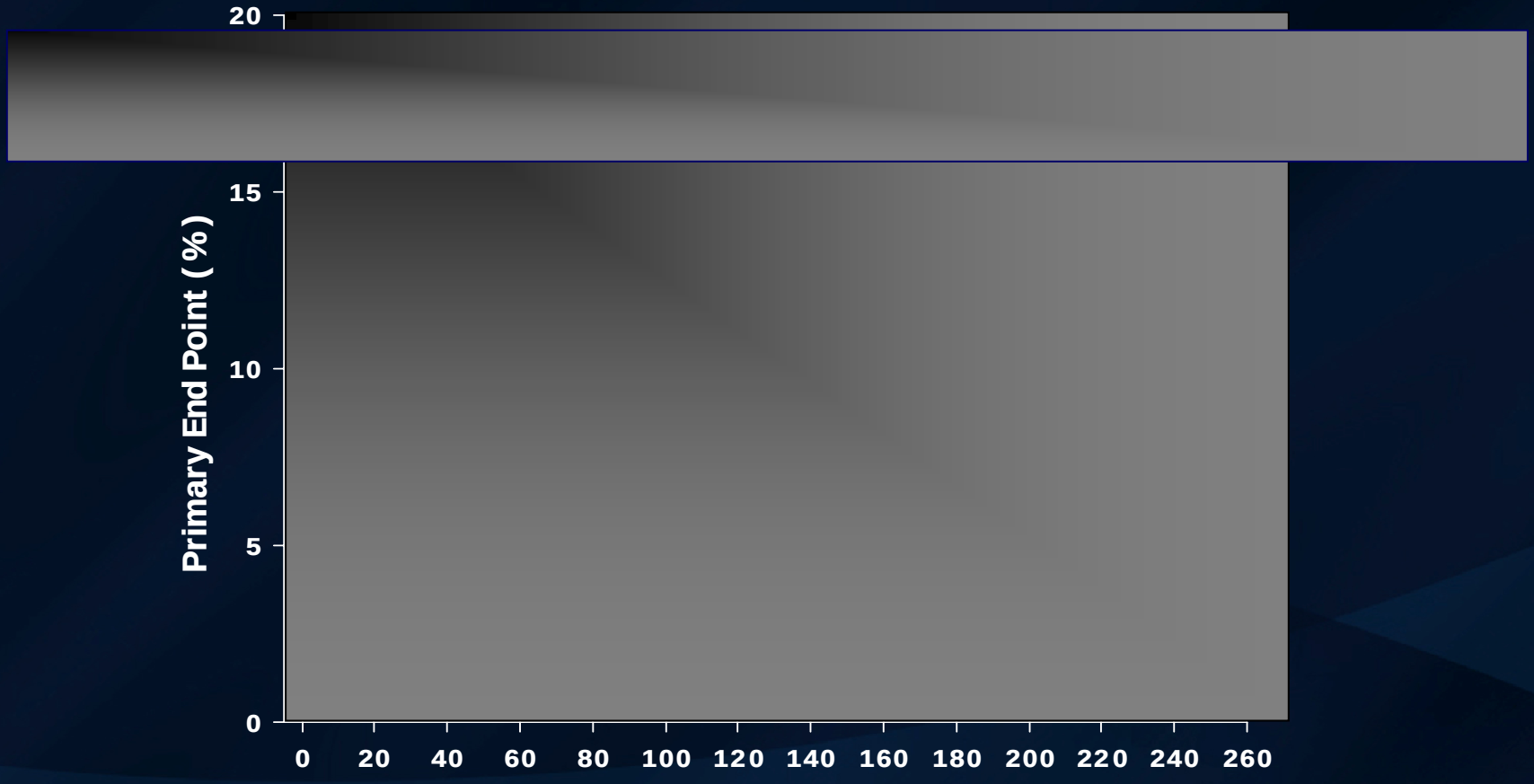
Efficacy Endpoints

(CEC adjudicated)



MULTISTRATEGY

Primary Endpoint
8-month MACE
(CEC adjudicated)



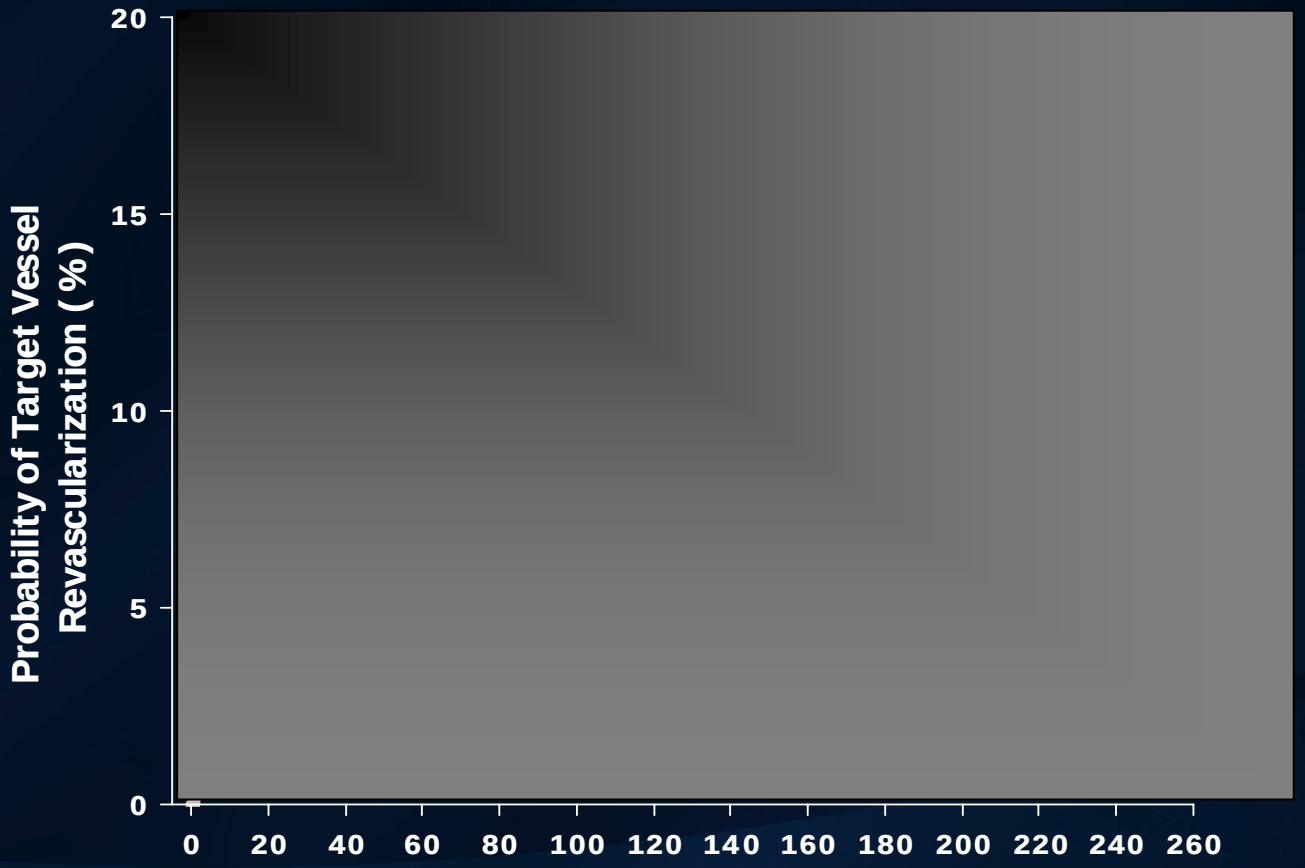
No. at Risk					
Uncoated Stent	372	351	342	326	318
Sirolimus-Stent	372	355	351	347	343

MULTISTRATEGY

8 Month Outcomes

Target Vessel Revascularization

(CEC adjudicated)



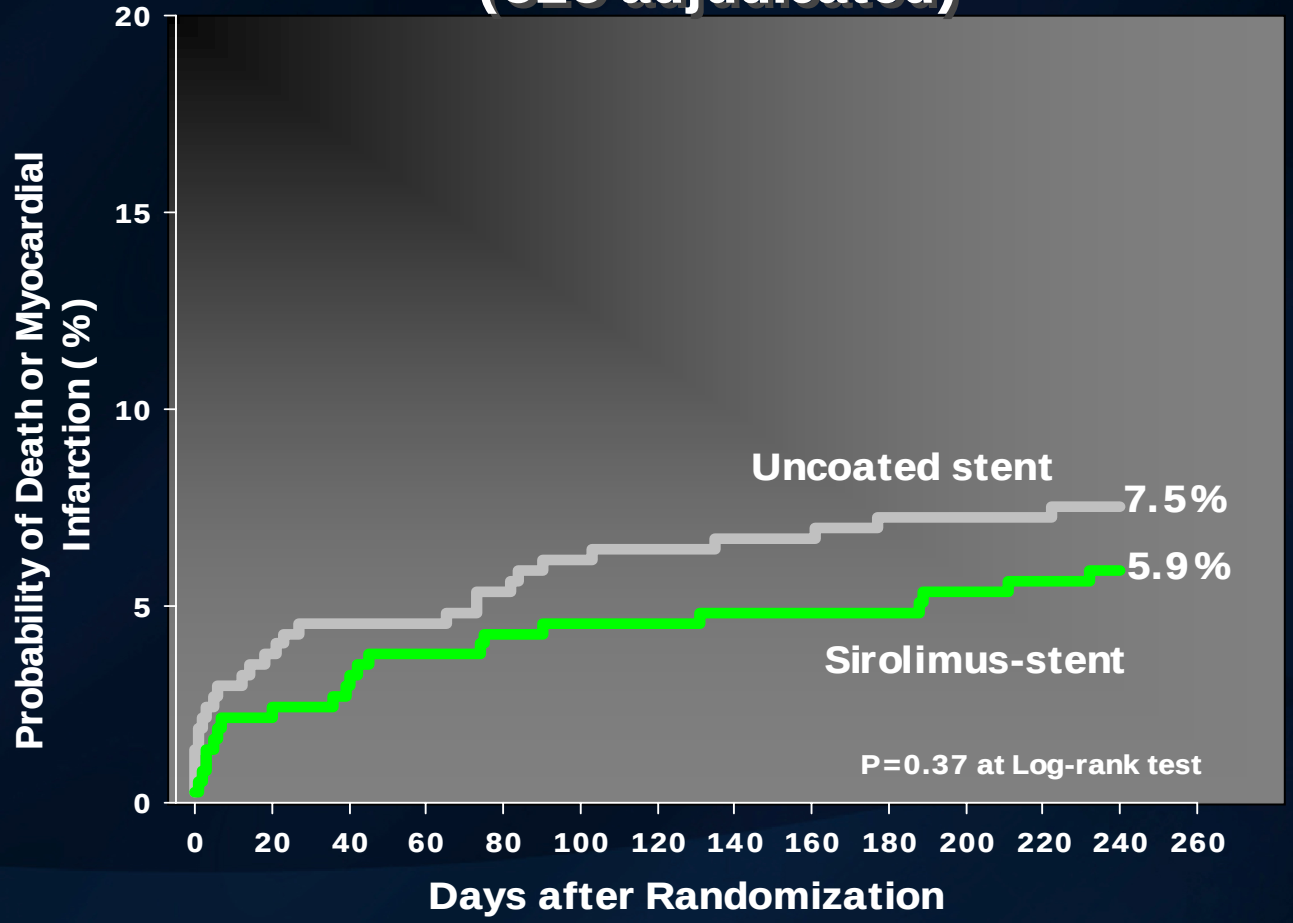
No. at Risk					
Uncoated Stent	372	355	347	331	322
Sirolimus-Stent	372	357	355	351	350

MULTISTRATEGY

8 Month Outcomes

Death/MI

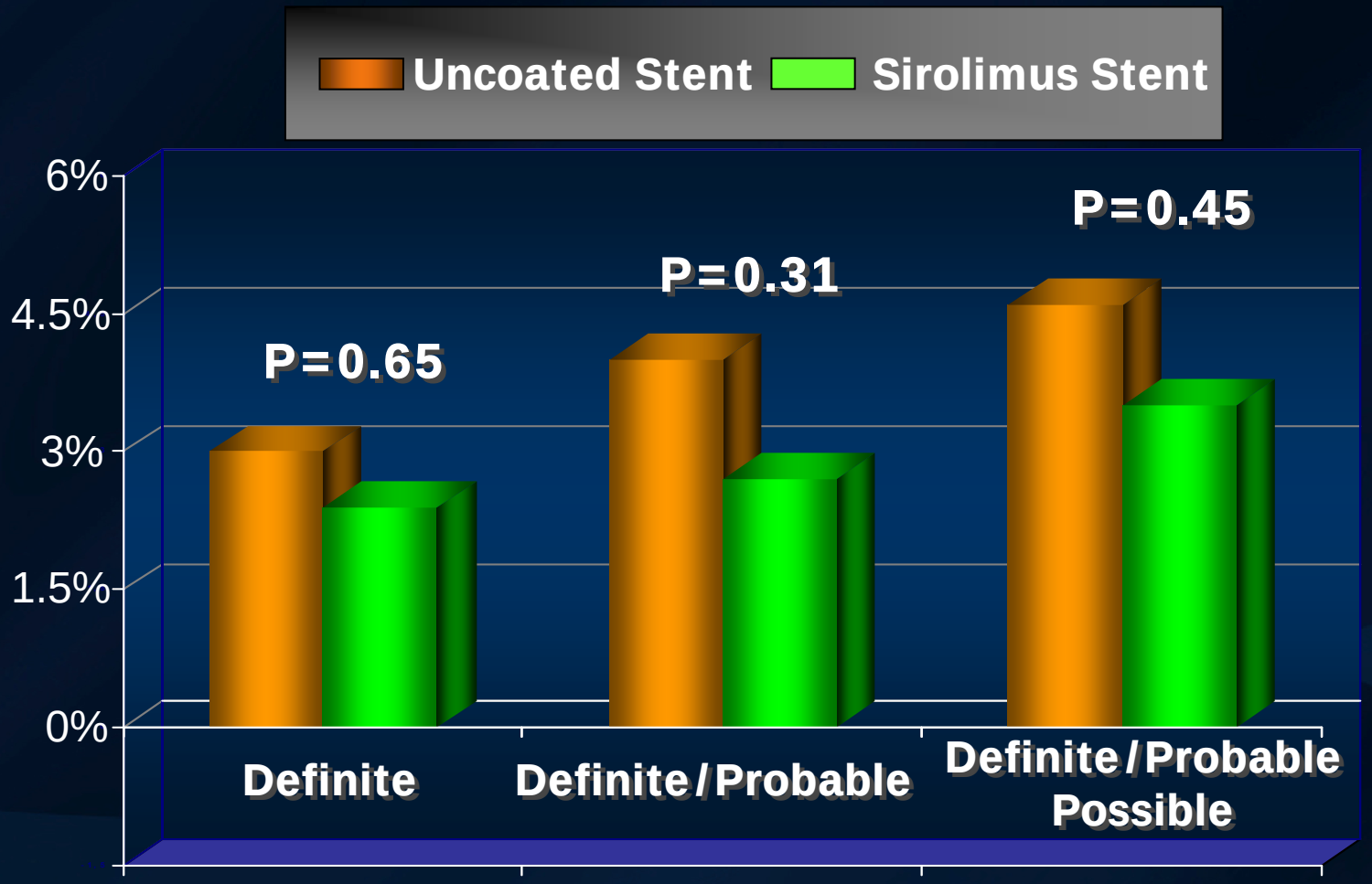
(CEC adjudicated)



MULTISTRATEGY

ARC Stent Thrombosis

(CEC adjudicated)



MULTISTRATEGY

Summary

- *While awaiting for Horizon Study and long term F-UP of all RCTs:*

  - **Routine DES implantation in STEMI is probably still not justifiable**
  - **Yet, in patients judged to be at high-risk for ISR after BMS based on clinical and/or angiographic findings the threshold to prefer a DES over a BMS should be low**
  - **SES is the most extensively studied DES in STEMI and likely the preferable option**

MULTISTRATEGY