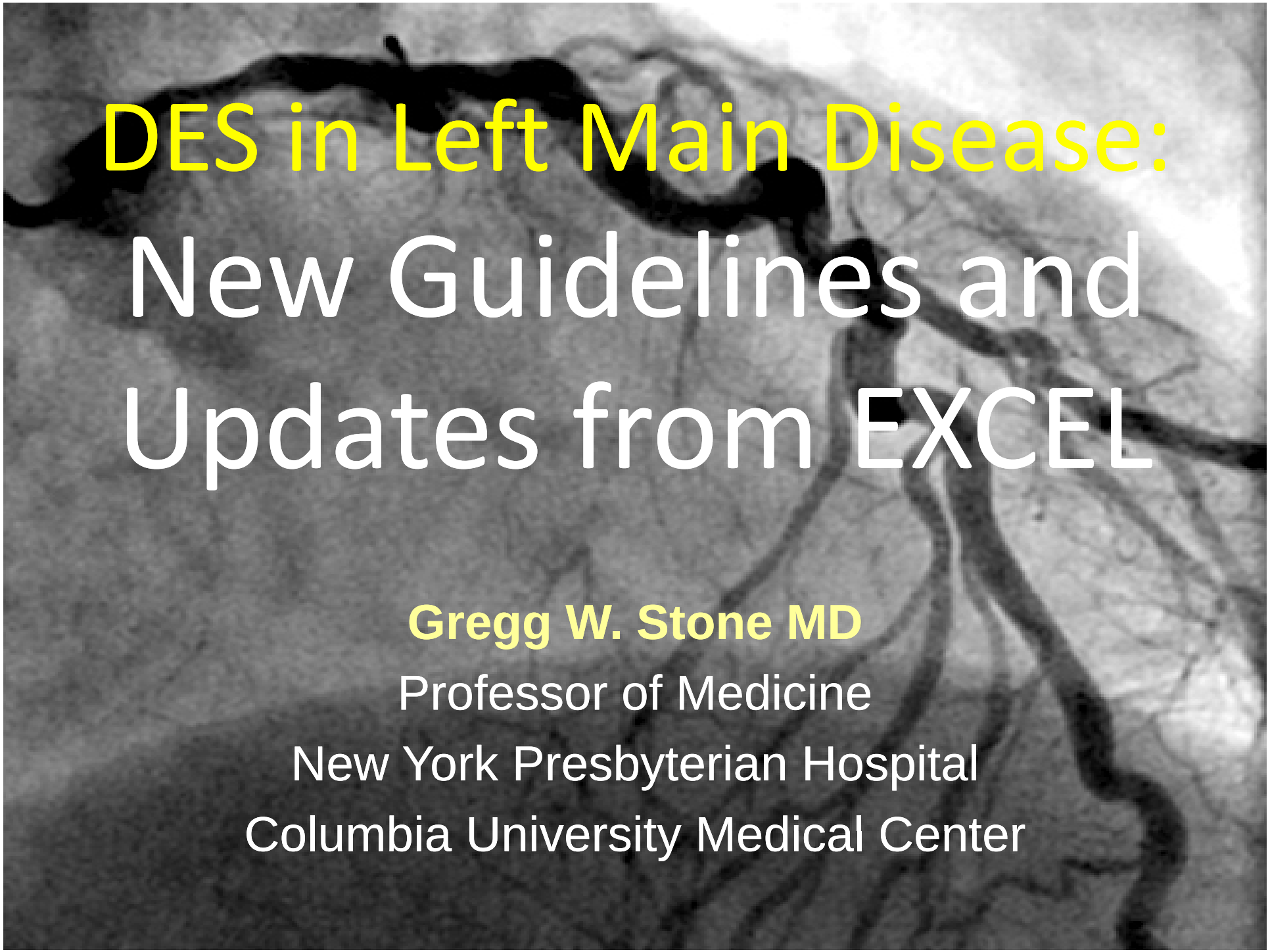


DES in Left Main Disease: New Guidelines and Updates from EXCEL

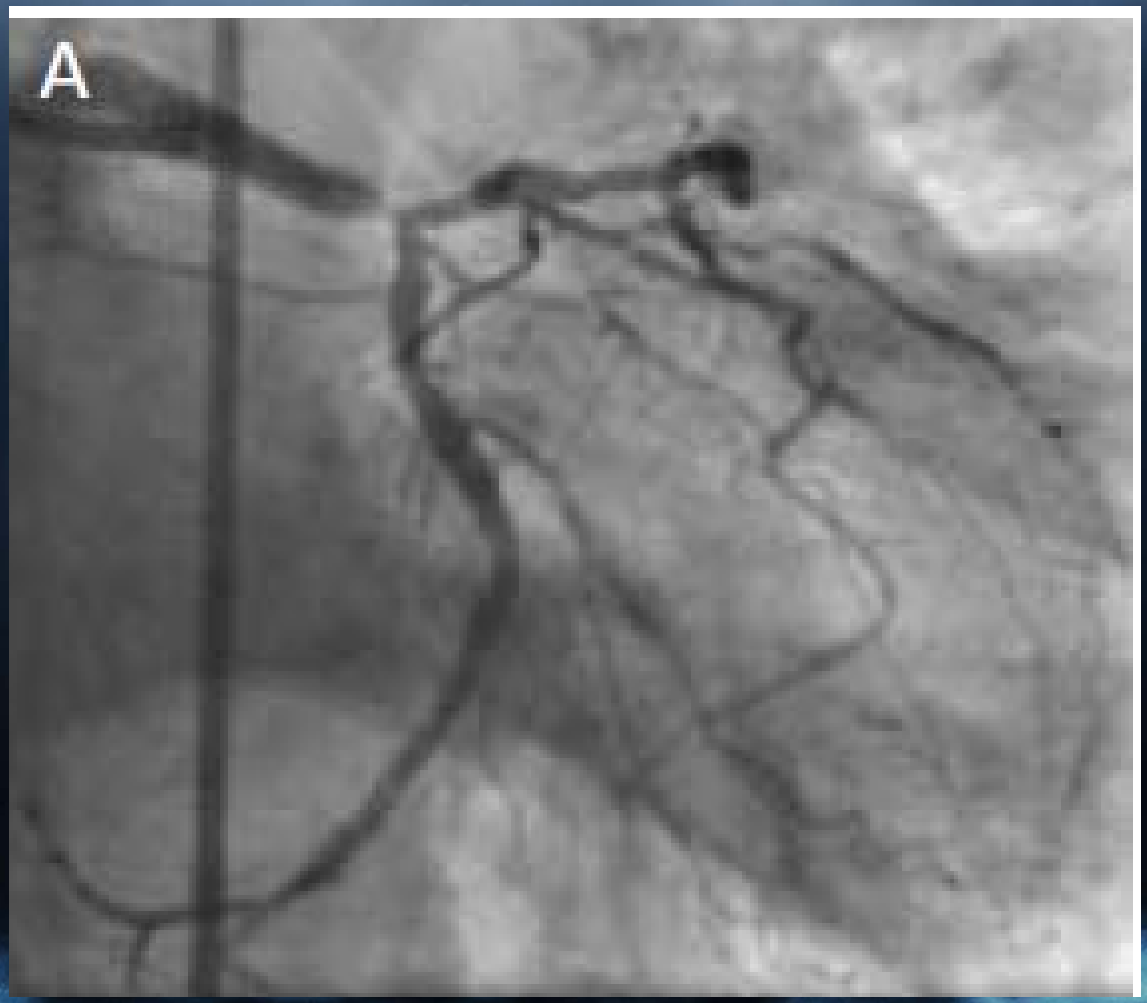
Gregg W. Stone MD
Professor of Medicine
New York Presbyterian Hospital
Columbia University Medical Center

Disclosures

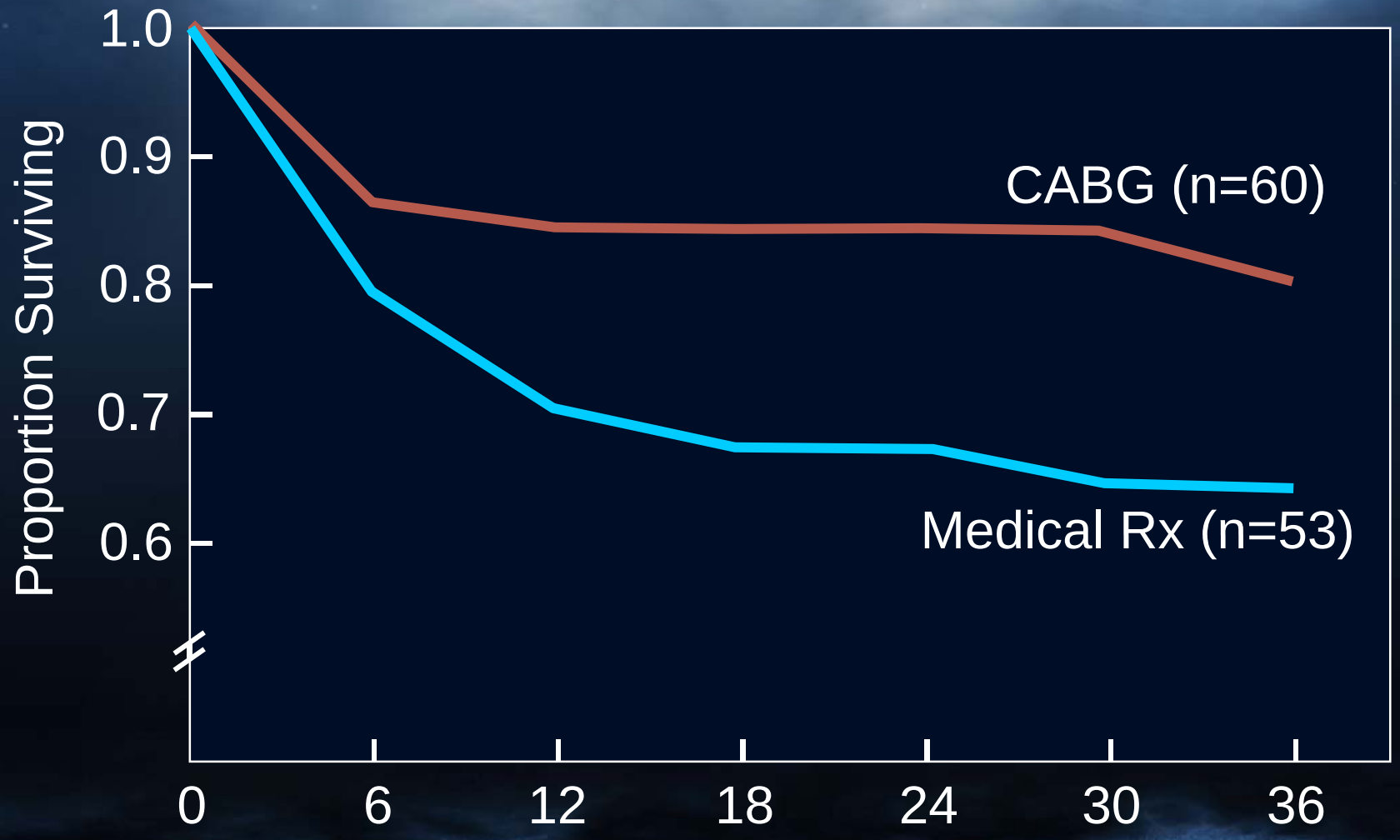
Scientific advisory boards for and honoraria from Abbott Vascular and Boston Scientific

Consultant to Medtronic

The Problem: Left Main Coronary Artery Disease



VA Randomized Trial (n=113)
LM Stenosis



Death

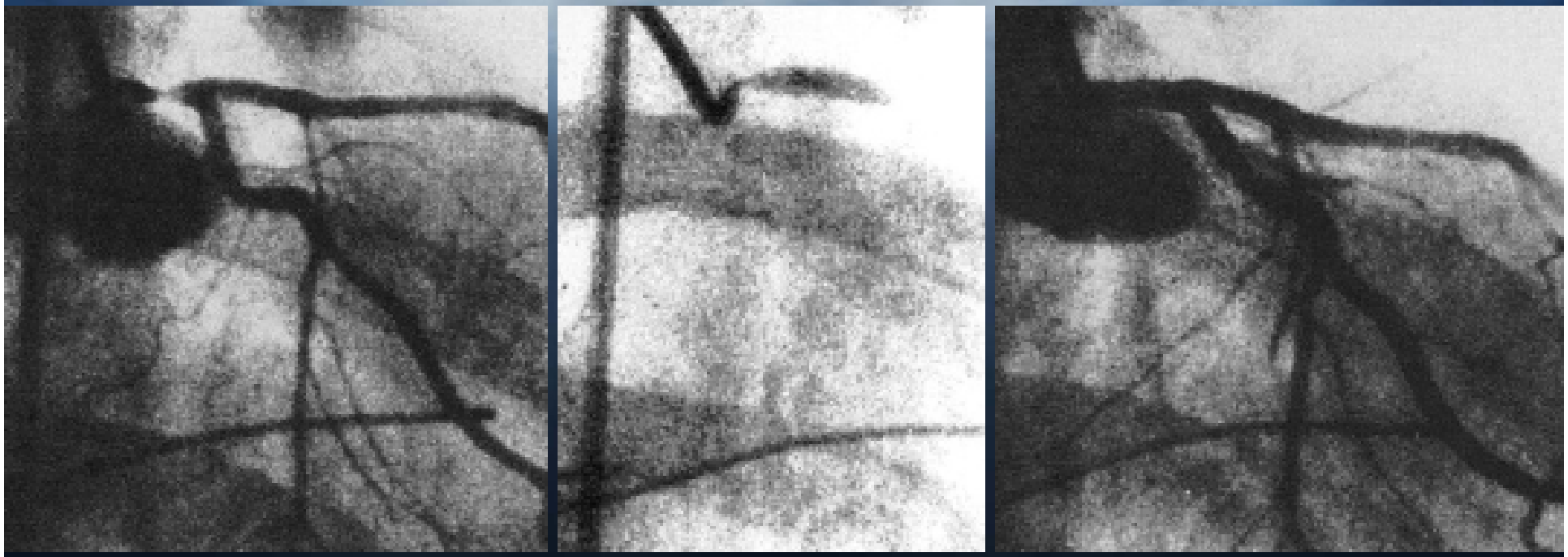
20%

36%

P=0.06

Takaro T et al: Circulation 1976;54(6 Suppl):III107-17.

Gruntzig's 3rd PTCA

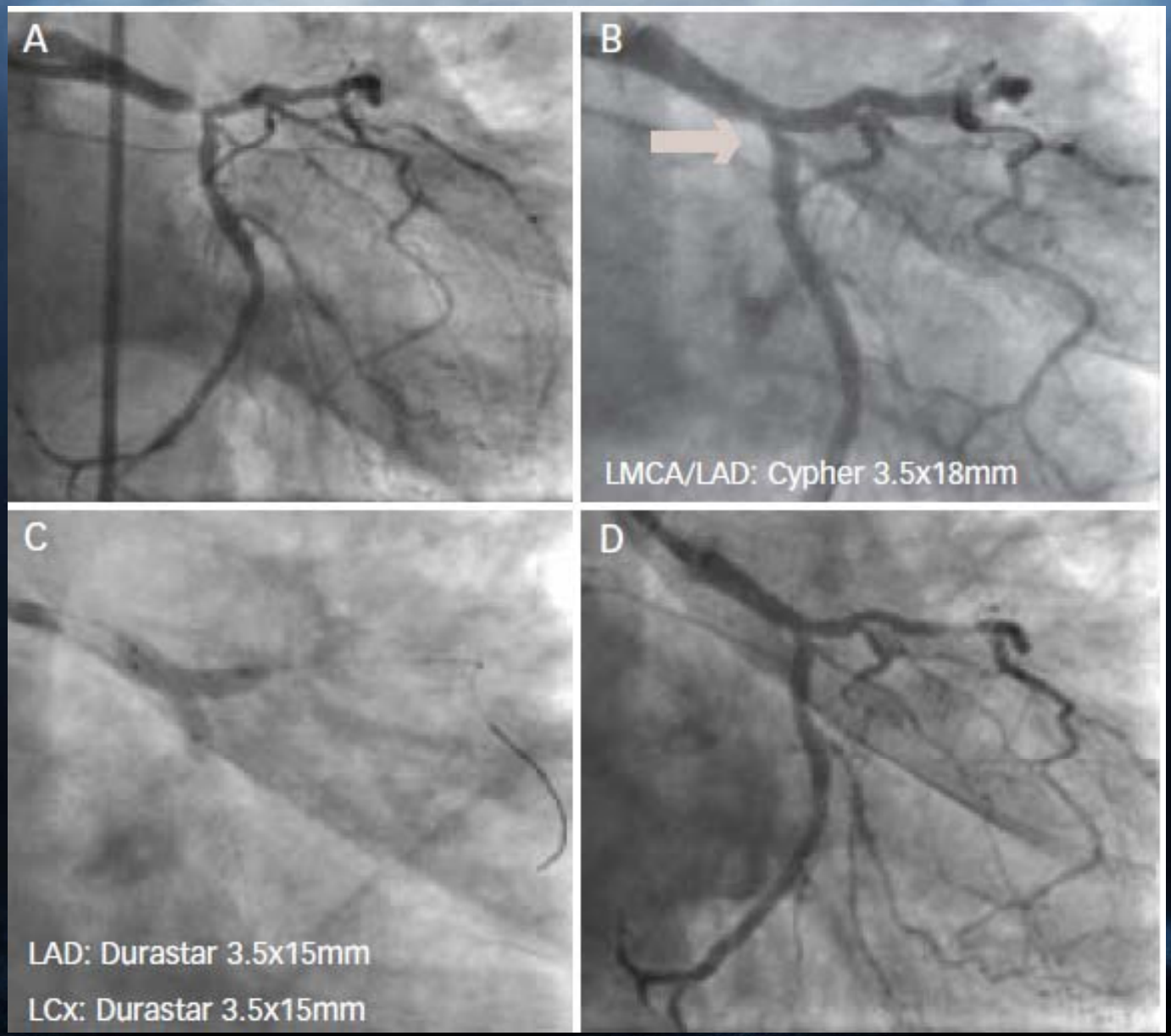


"Third PCI patient ever treated. Forty-three year old man with severe angina pectoris since September, 1977. First angiogram (November 11) revealed severe stenosis of the main L.C.A. . ."

Note: The patient expired suddenly about 4 months after this procedure.

Gruntzig A. Lancet 1978;1:263.

34 Years After Gruentzig



SYNTAX Eligible Patients

De novo disease (n=1800)

Limited Exclusion Criteria

- Previous interventions
- Acute MI with CPK>2x
- Concomitant cardiac surgery

Left Main Disease (isolated, +1, +2 or +3 vessels)	3 Vessel Disease (revasc all 3 vascular territories)
N=705	**N=1095**

Primary endpoint = death/MI/stroke/repeat revasc at 1 year

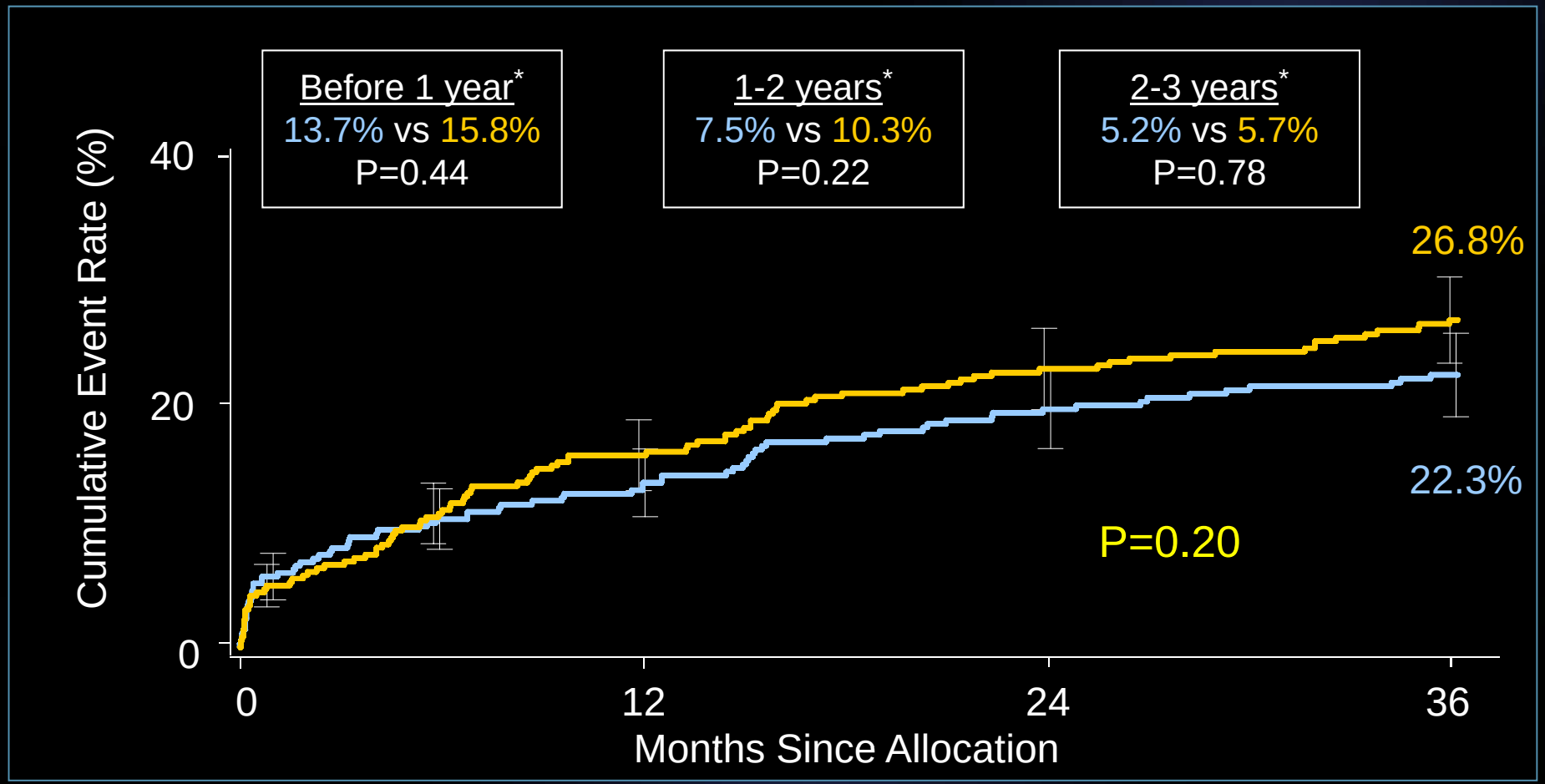
Serruys PW et al. NEJM 2009;360:961-72

MACCE to 3 Years

Left Main Subset

SYNTAX

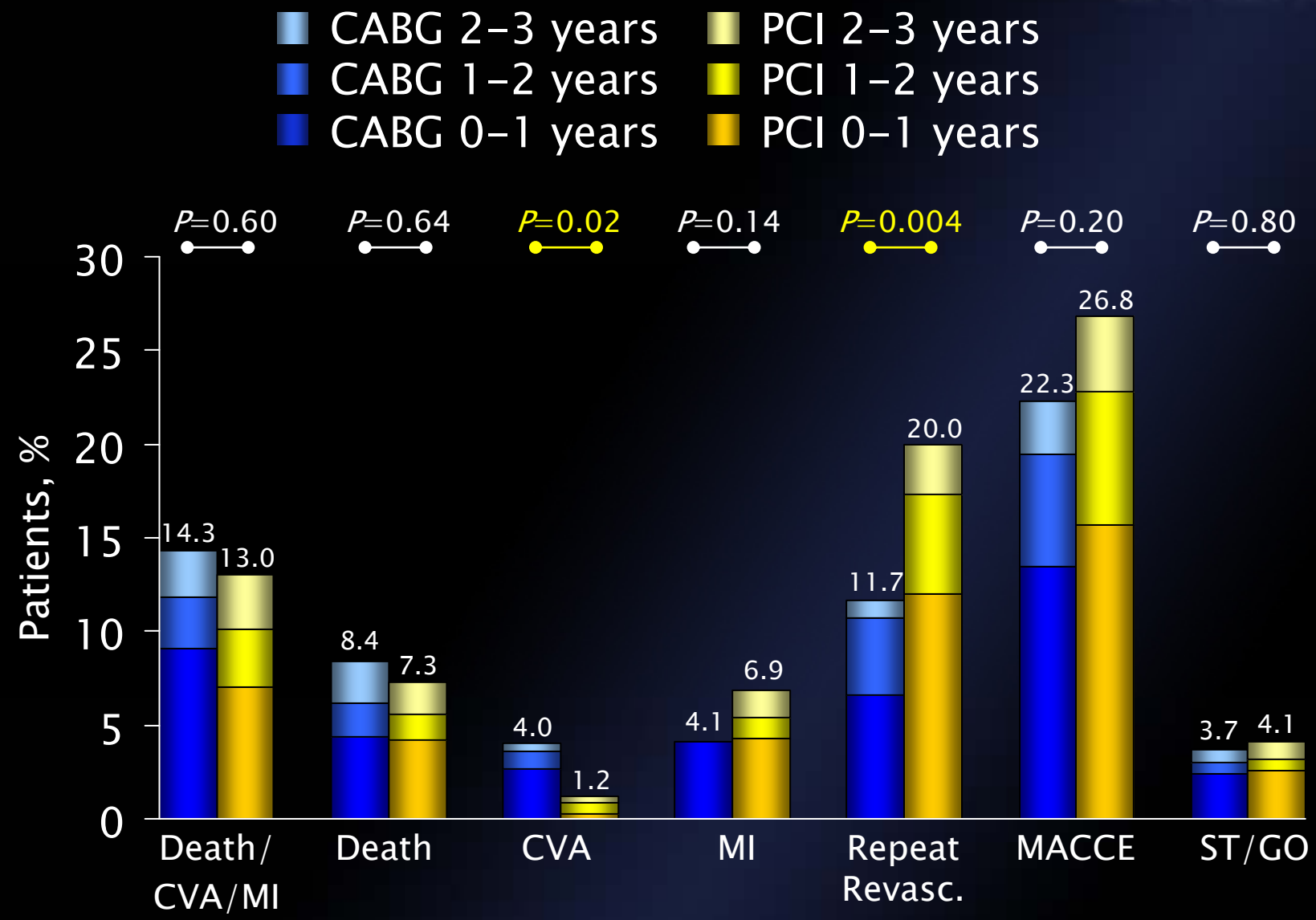
CABG (N=348) TAXUS (N=357)



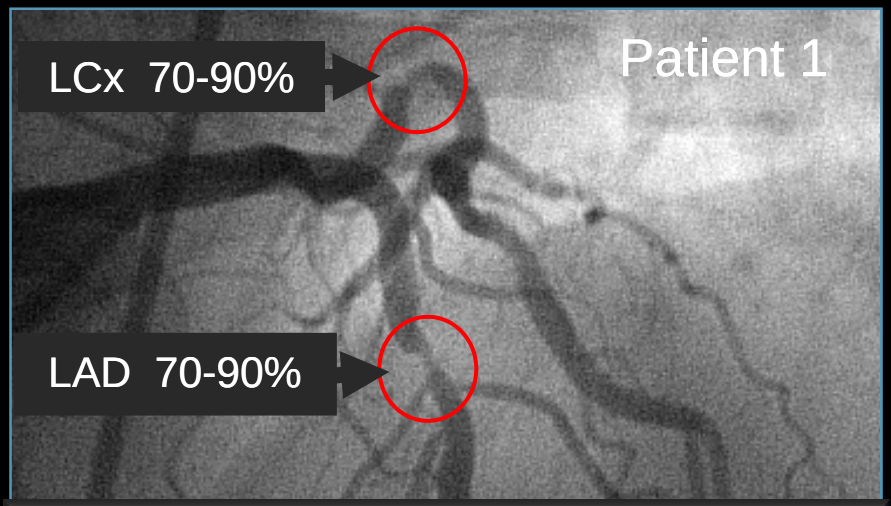
Cumulative KM Event Rate ± 1.5 SE; log-rank P value; *Binary rates

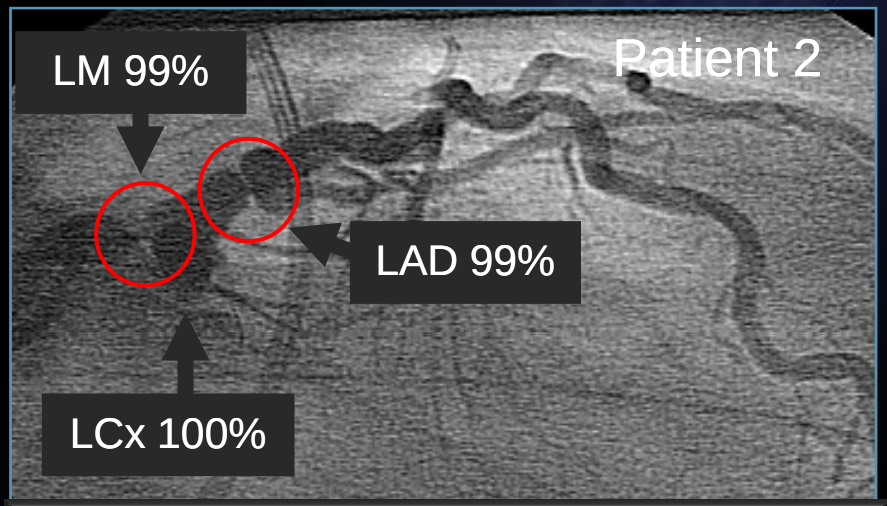
ITT population

3-Year Outcomes: *Left Main Subset*

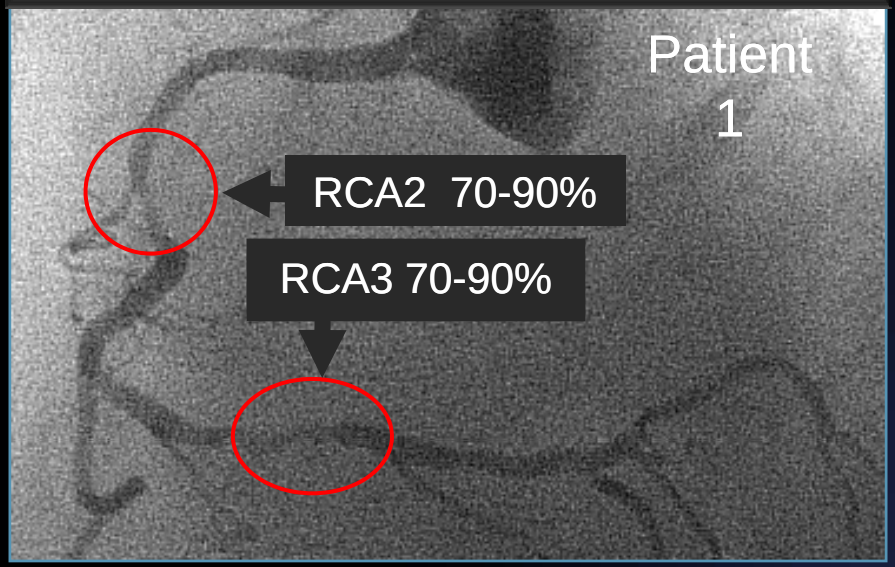


The SYNTAX Score

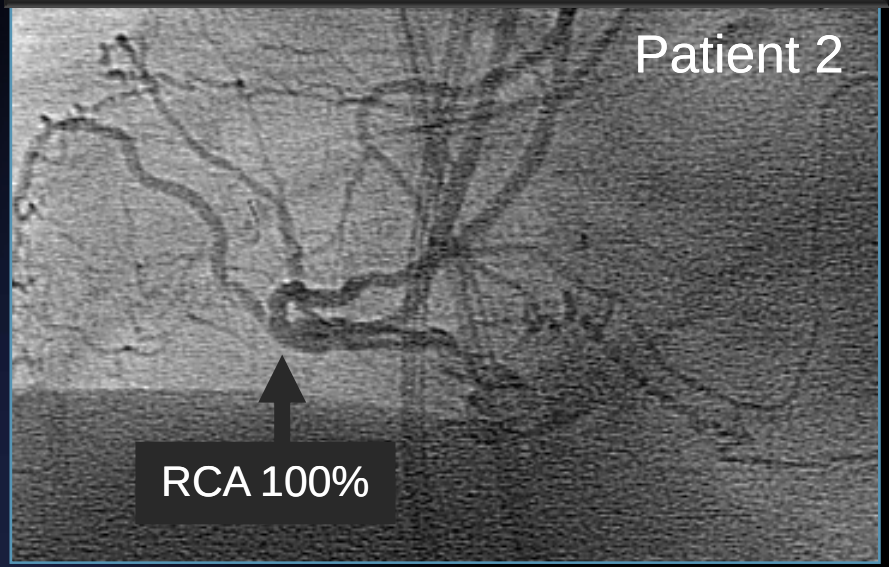




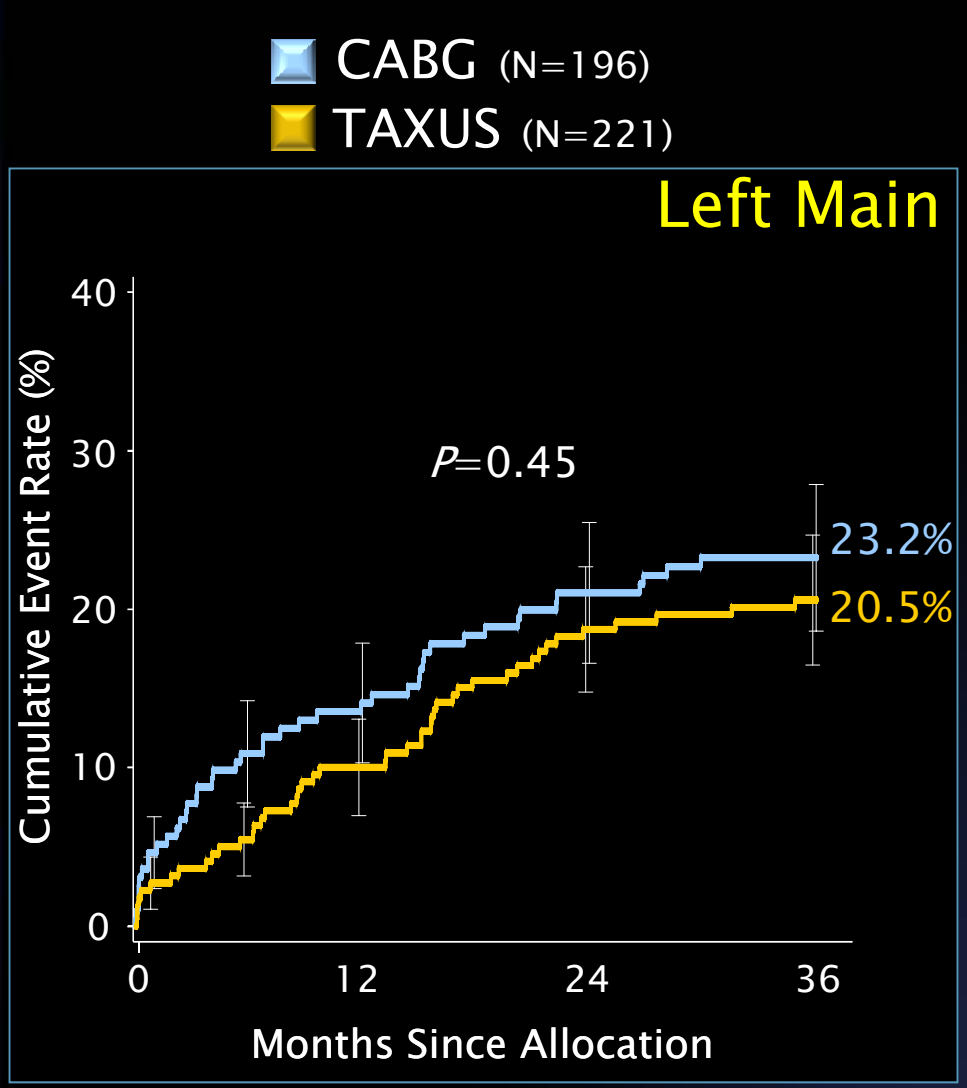
SYNTAX SCORE 21



SYNTAX SCORE 52



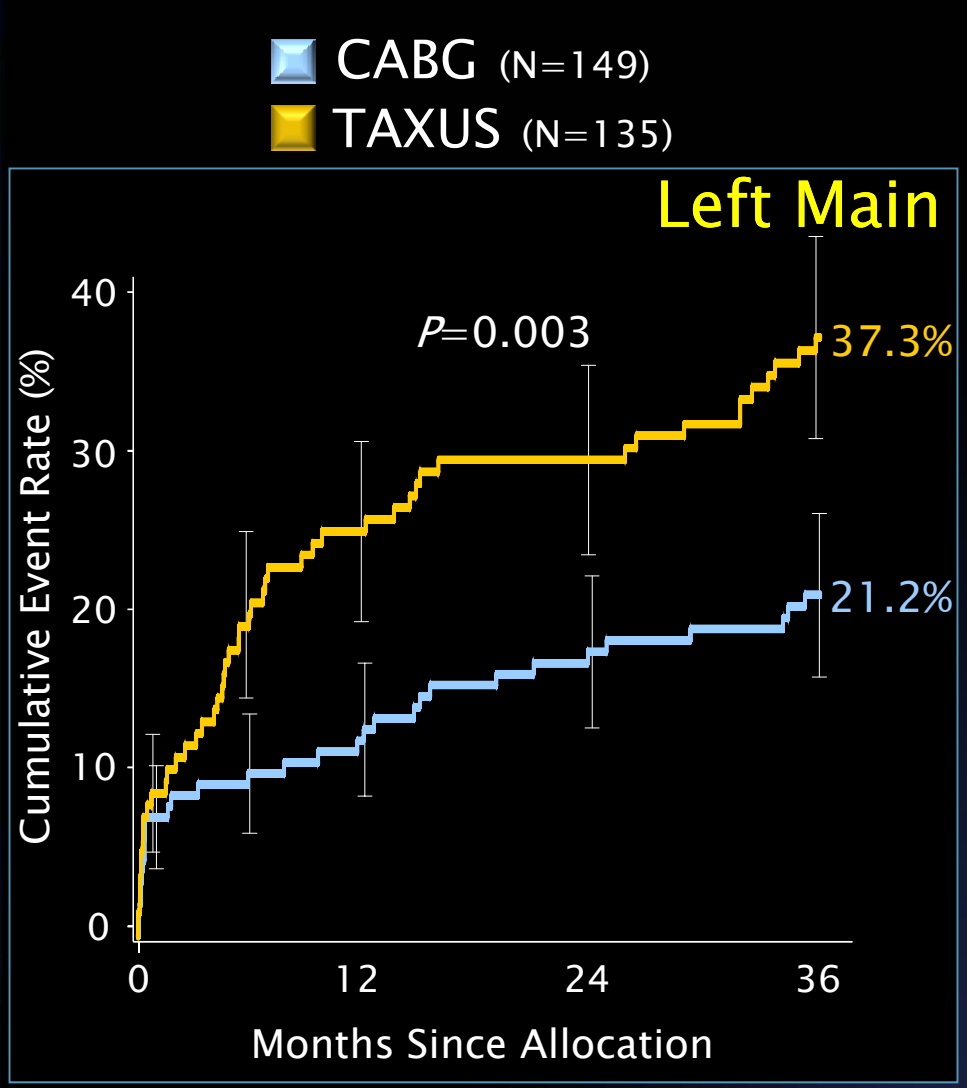
MACCE to 3 Years by SYNTAX Score Tercile *Low to Intermediate Scores (0–32)*



	CABG	PCI	*P* value
Death	9.0%	3.7%	**0.02**
CVA	3.3%	0.9%	0.09
MI	2.6%	4.6%	0.33
Death, CVA or MI	13.2%	8.7%	0.12
Revasc.	13.7%	15.7%	0.61

Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value

MACCE to 3 Years by SYNTAX Score Tercile *Left Main SYNTAX Score ≥33*



	CABG	PCI	*P* value
Death	7.6%	13.4%	0.10
CVA	4.9%	1.6%	0.13
MI	6.1%	10.9%	0.18
Death, CVA or MI	15.7%	20.1%	0.34
Revasc.	9.2%	27.7%	<0.001

Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value

ACC/AHA Guidelines Post SYNTAX

LMCA PCI is reasonable in pts with class III angina and >50% LM stenosis who are not eligible for CABG

Stenting of the LMCA as an alternative to CABG may be considered in pts with anatomic conditions that are associated with a low risk of PCI procedural complications and clinical conditions that predict an increased risk of adverse surgical outcomes

ACC/AHA 2009 Focused Updates for STEMI and PCI. Circulation 2009;120:2271–2306

ESC/EACTS Guidelines on Myocardial Revascularization

- Left main PCI: Isolated or 1-vessel ds. with LM ostium/shaft involvement

- Left main PCI: Isolated or 1-vessel ds. with LM distal bifurcation involvement
- Left main PCI: 2- or 3-vessel disease, SYNTAX score ≤32

- Left main PCI: 2- or 3-vessel disease, SYNTAX score ≥33

EHJ 2010:on-line

Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease

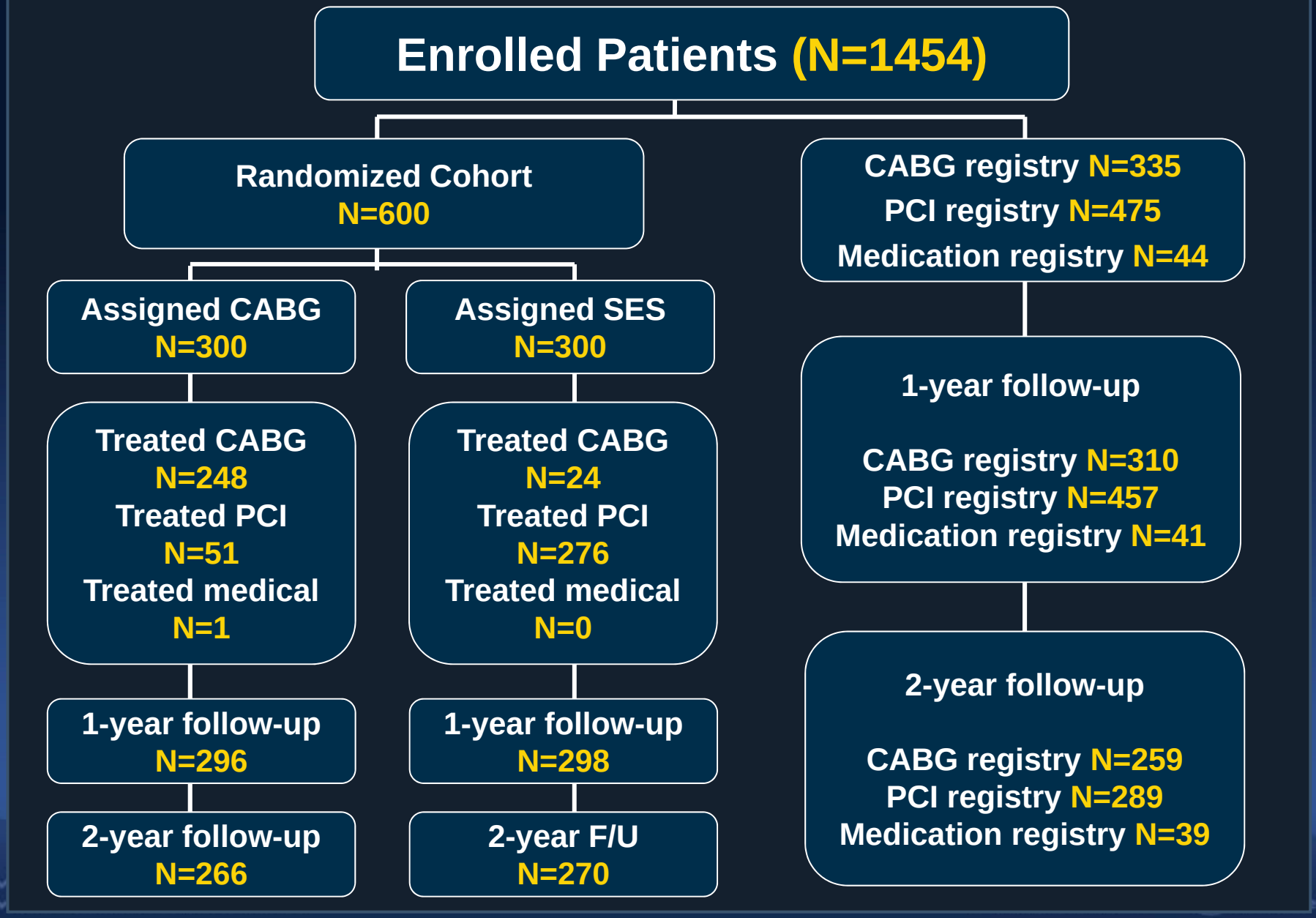
PRECOMBAT Trial

Seung-Jung Park, MD, PhD
On behalf of the PRECOMBAT Investigators

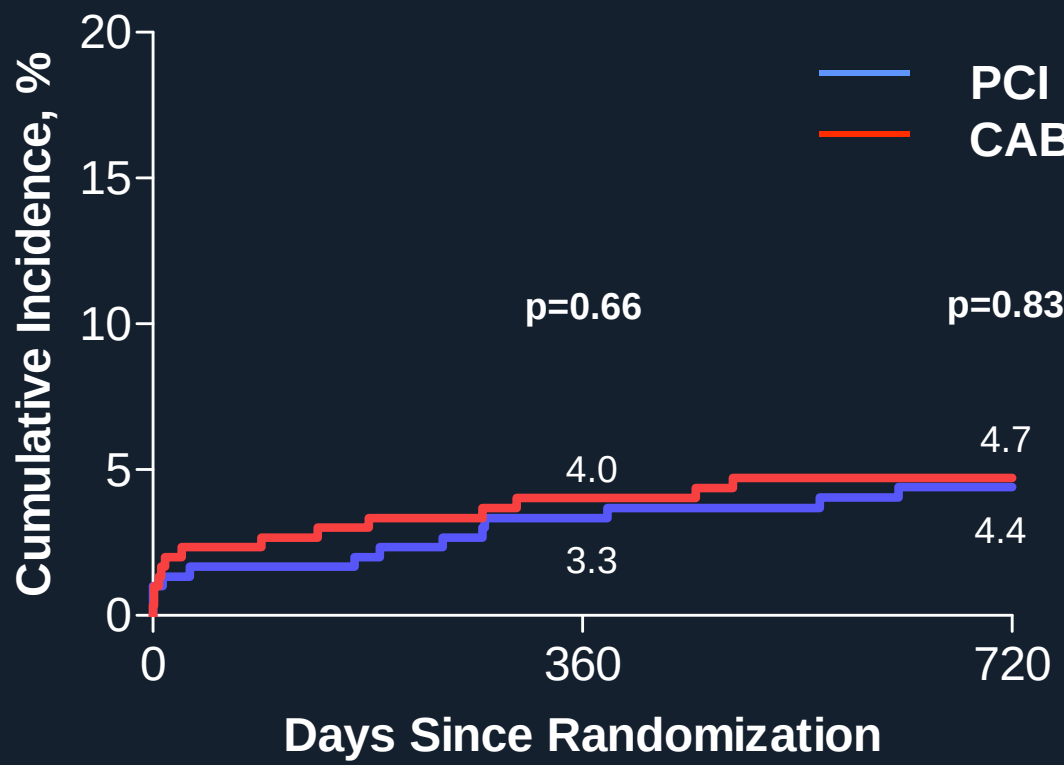
Professor of Medicine, University of Ulsan College of Medicine,
Heart Institute, Asan Medical Center, Seoul, Korea

ACC.11 60th Annual Scientific Session & Expo
i2 summit 2011 innovation in intervention ACC in partnership with CRF

Patient Flow

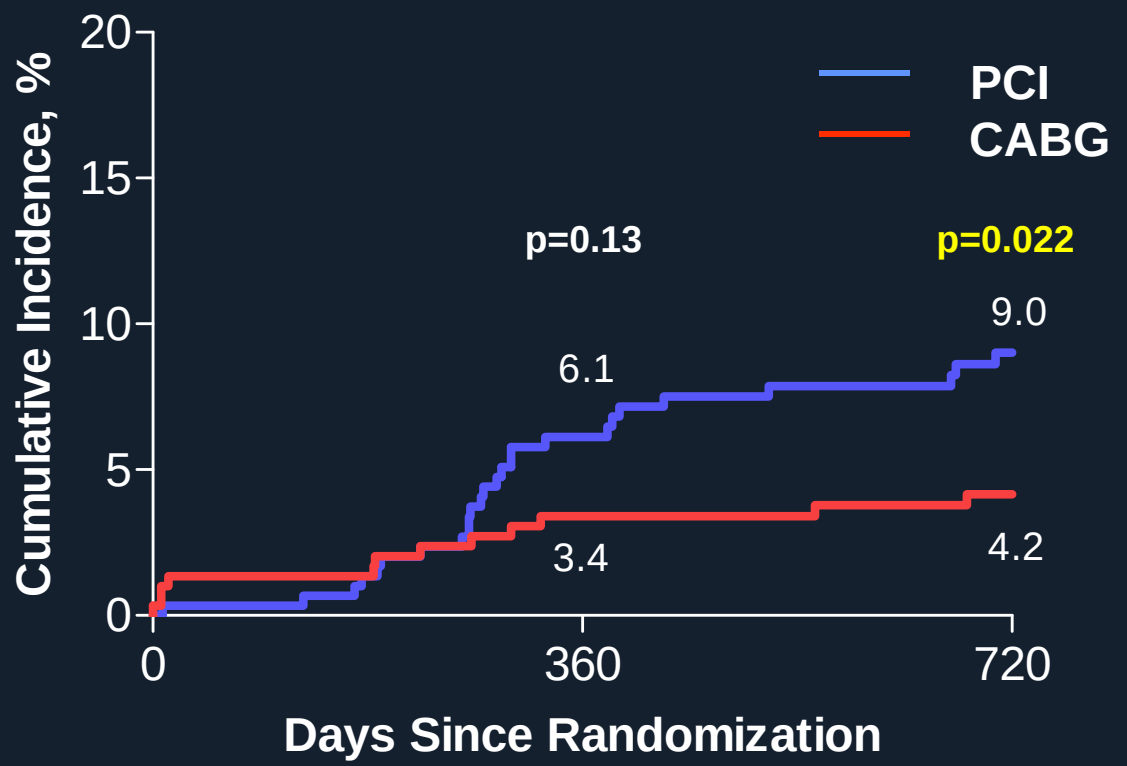


Death, MI or Stroke



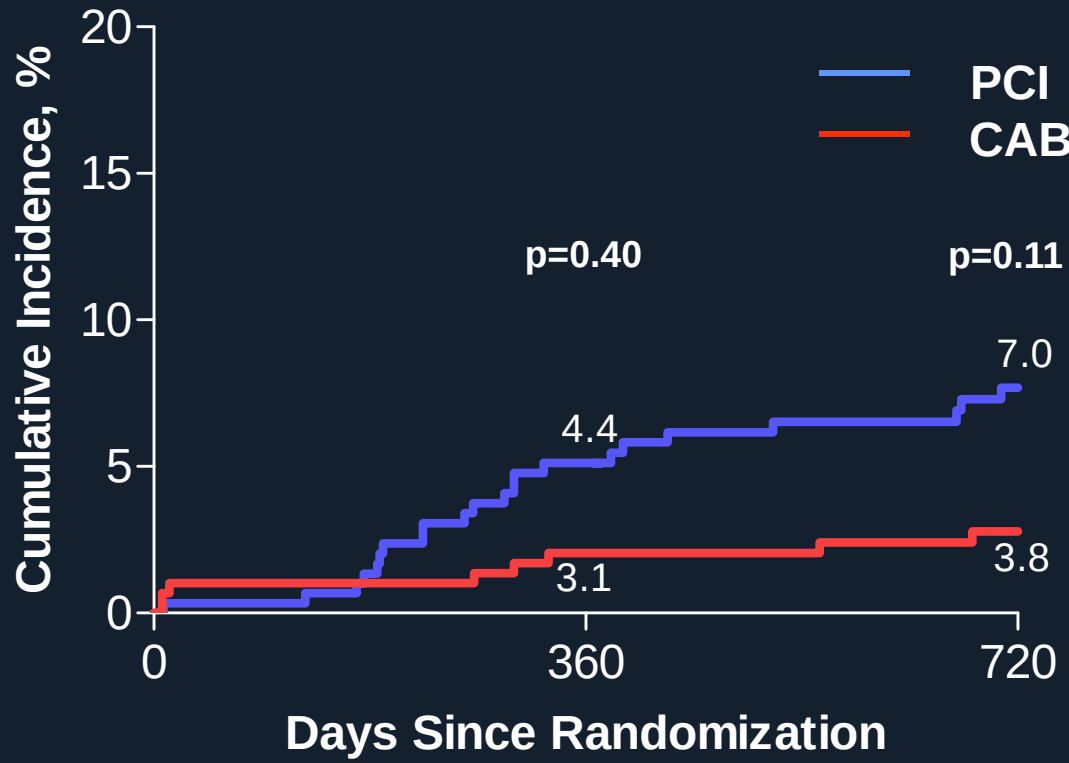
No. at Risk			
PCI	300	288	256
CABG	300	284	248

Ischemia-Driven TVR



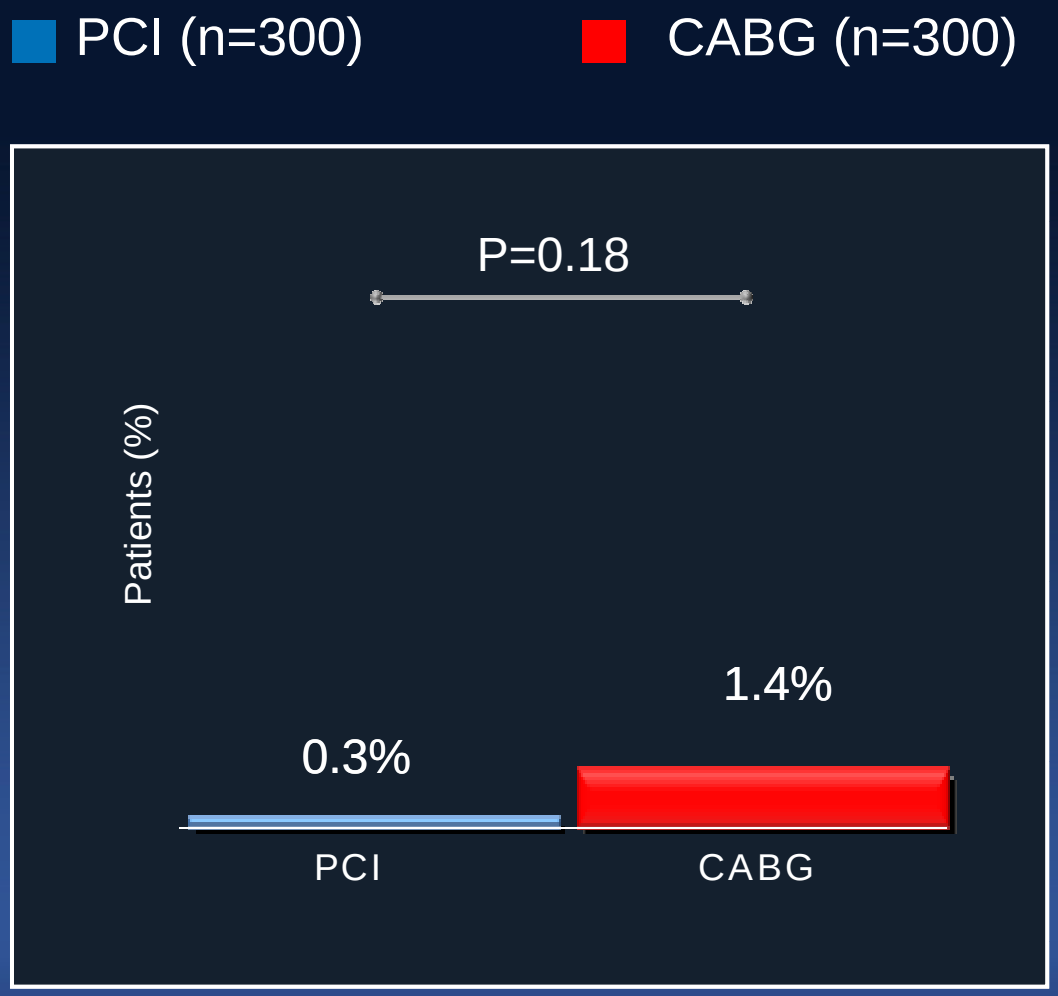
No. at Risk			
PCI	300	274	237
CABG	300	279	242

Clinical-driven TVR



No. at Risk			
PCI	300	279	243
CABG	300	280	246

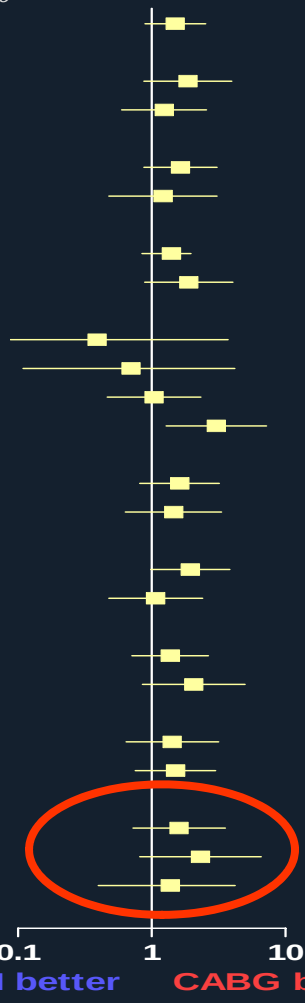
Symptomatic Graft Occlusion & Stent Thrombosis to 2 Years



Post-procedure; ITT population

Subgroup Analysis

Subgroup	MACCE		Hazard Ratio (95% CI)	P value	P value for Interaction
	PCI	CABG			
	Cumulative incidence, %				
Overall	12.2	8.1	1.50 (0.90, 2.52)	0.12	-
Age					0.44
≥65 yr	11.9	9.7	1.87 (0.88, 3.97)	0.10	
<65 yr	12.5	6.7	1.24 (0.60, 2.56)	0.57	
Sex					0.59
Male	11.7	7.0	1.65 (0.88, 3.07)	0.12	
Female	13.9	11.7	1.22 (0.48, 3.08)	0.68	
LM stenosis					0.63
>70 %	10.8	9.0	1.19 (0.57, 2.47)	0.64	
50-70 %	13.6	7.1	1.90 (0.89, 4.03)	0.10	
Vascular extent					0.14
LM only	3.8	8.8	0.39 (0.04, 3.72)	0.41	
LM with 1VD	4.1	5.8	0.70 (0.11, 4.16)	0.69	
LM with 2VD	13.0	12.2	1.04 (0.47, 2.32)	0.93	
LM with 3VD	16.8	5.8	3.05 (1.29, 7.21)	0.01	
Bifurcation involvement					0.83
Yes	13.2	9.1	1.62 (0.82, 3.20)	0.16	
No	11.8	7.3	1.46 (0.64, 3.32)	0.37	
RCA involvement					0.27
Yes	15.8	8.3	1.95 (0.99, 3.84)	0.05	
No	8.7	7.9	1.07 (0.48, 2.40)	0.86	
ACS					0.44
Yes	15.3	8.3	1.34 (0.70, 2.55)	0.38	
No	9.7	4.9	2.07 (0.85, 5.02)	0.11	
Diabetes					0.92
Yes	16.3	11.1	1.43 (0.65, 3.16)	0.37	
No	10.2	6.8	1.51 (0.76, 2.99)	0.24	
SYNTAX score					0.80
High risk	17.0	11.1	1.60 (0.73, 3.54)	0.24	
Intermediate risk	12.7	7.4	2.32 (0.82, 6.57)	0.11	
Low risk	8.2	4.9	1.38 (0.40, 4.21)	0.57	



What Does SYNTAX Not Tell Us?

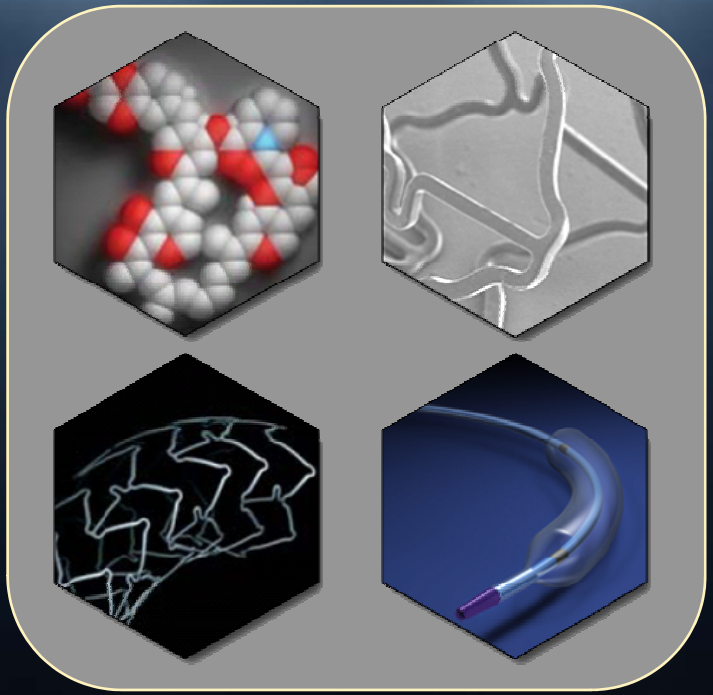
- **Can PCI outcomes be improved by…..?**
  - Use of better DES? (e.g. XIENCE V)
  - Use of better pharmacotherapy (e.g. bivalirudin)
  - IVUS/FFR? (used in <10% in SYNTAX)
  - More frequent staging? (14% in SYNTAX)
  - Avoidance of routine angiographic FU*?
- **Can CABG outcomes be further improved?**
- **Is PCI really non-inferior or superior to CABG in SYNTAX <33 patients with LM ds.?**

*Currently not recommended by the ACC/AHA Guidelines. Circulation 2009;120:2271–2306

XIENCE V / PROMUS
Everolimus-eluting Stent

Everolimus

ML VISION®
Stent Platform

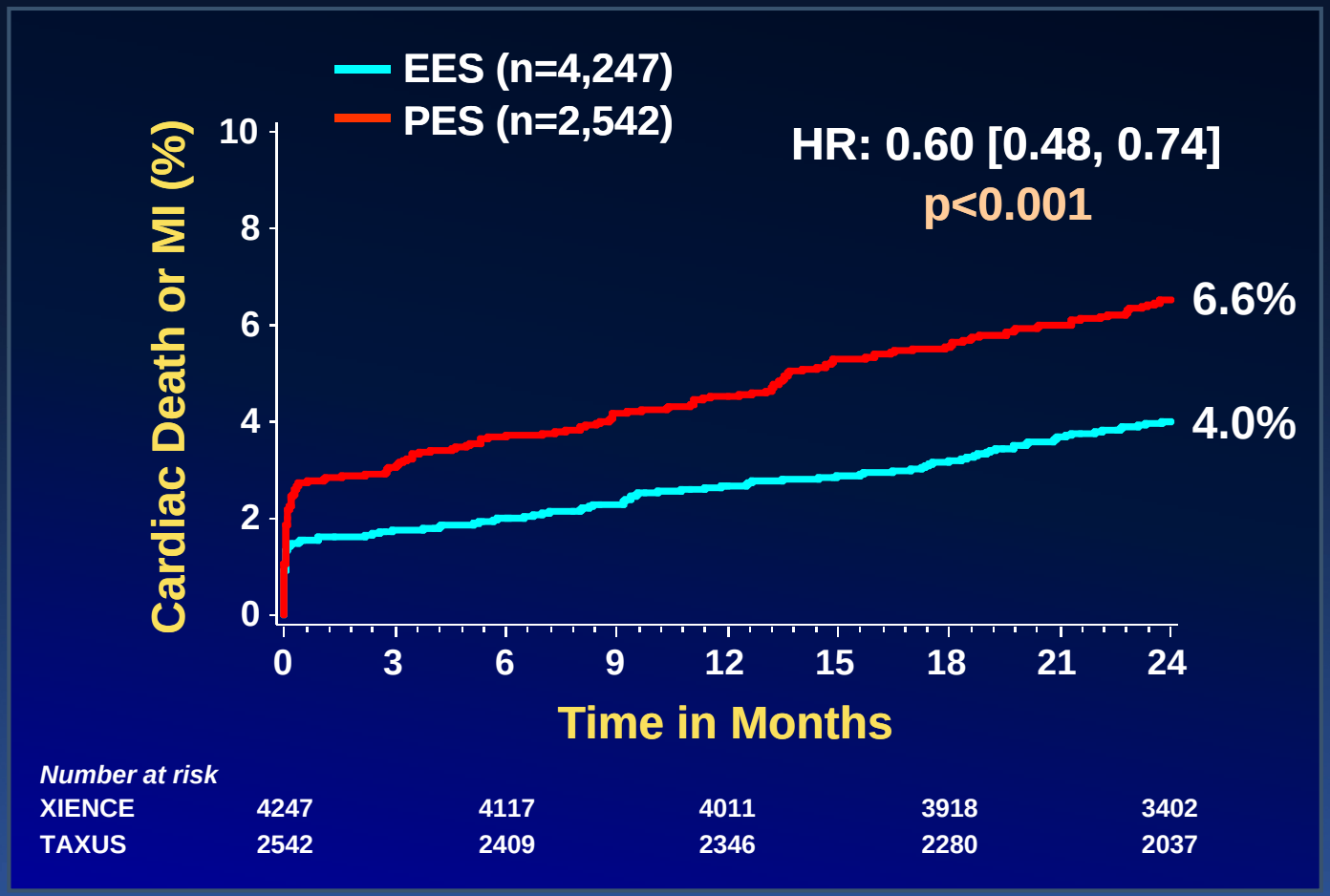


Durable
Fluorinated
Copolymer

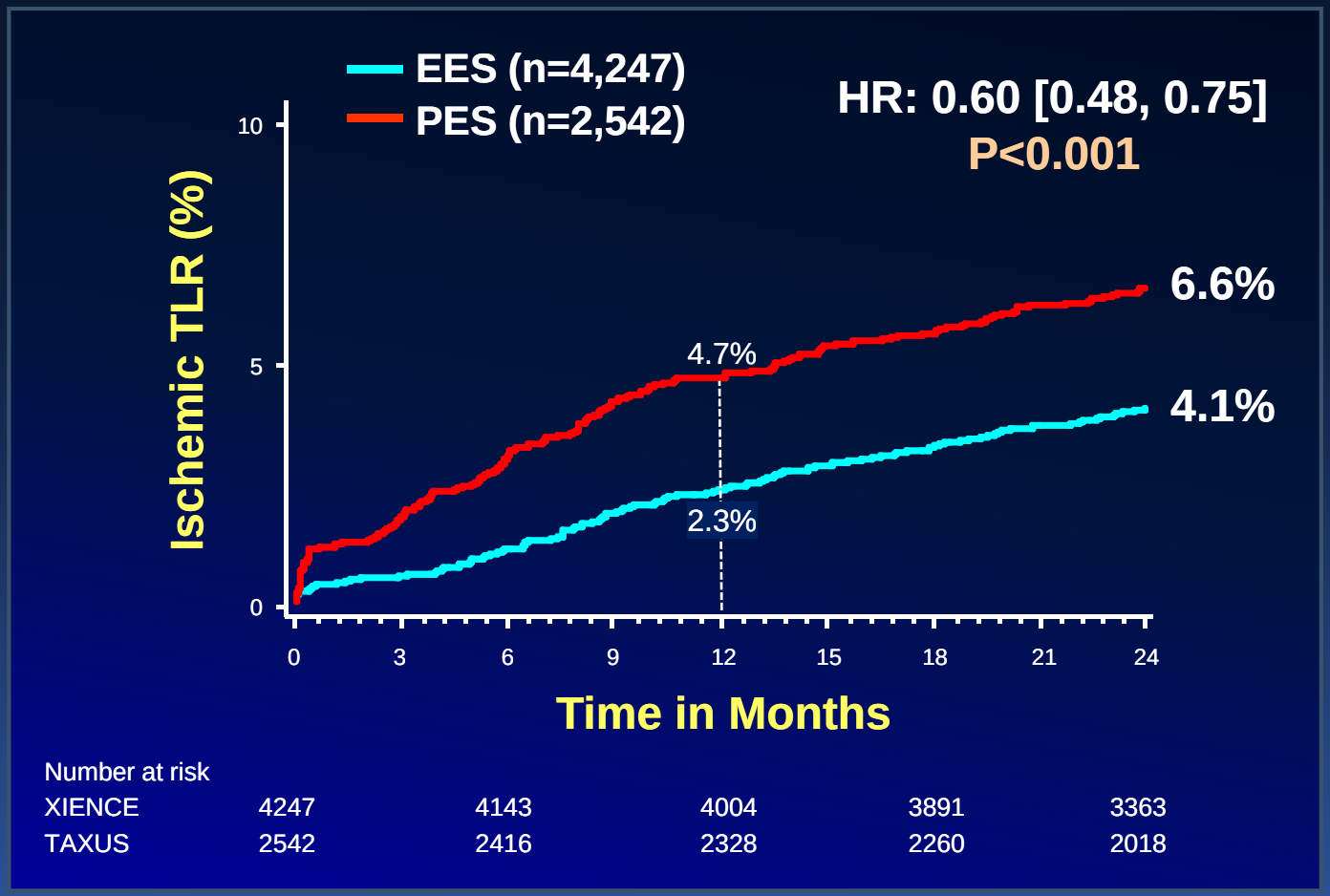
ML VISION
Stent Delivery
System

EES vs. PES
SPIRIT and COMPARE
Clinical Trials

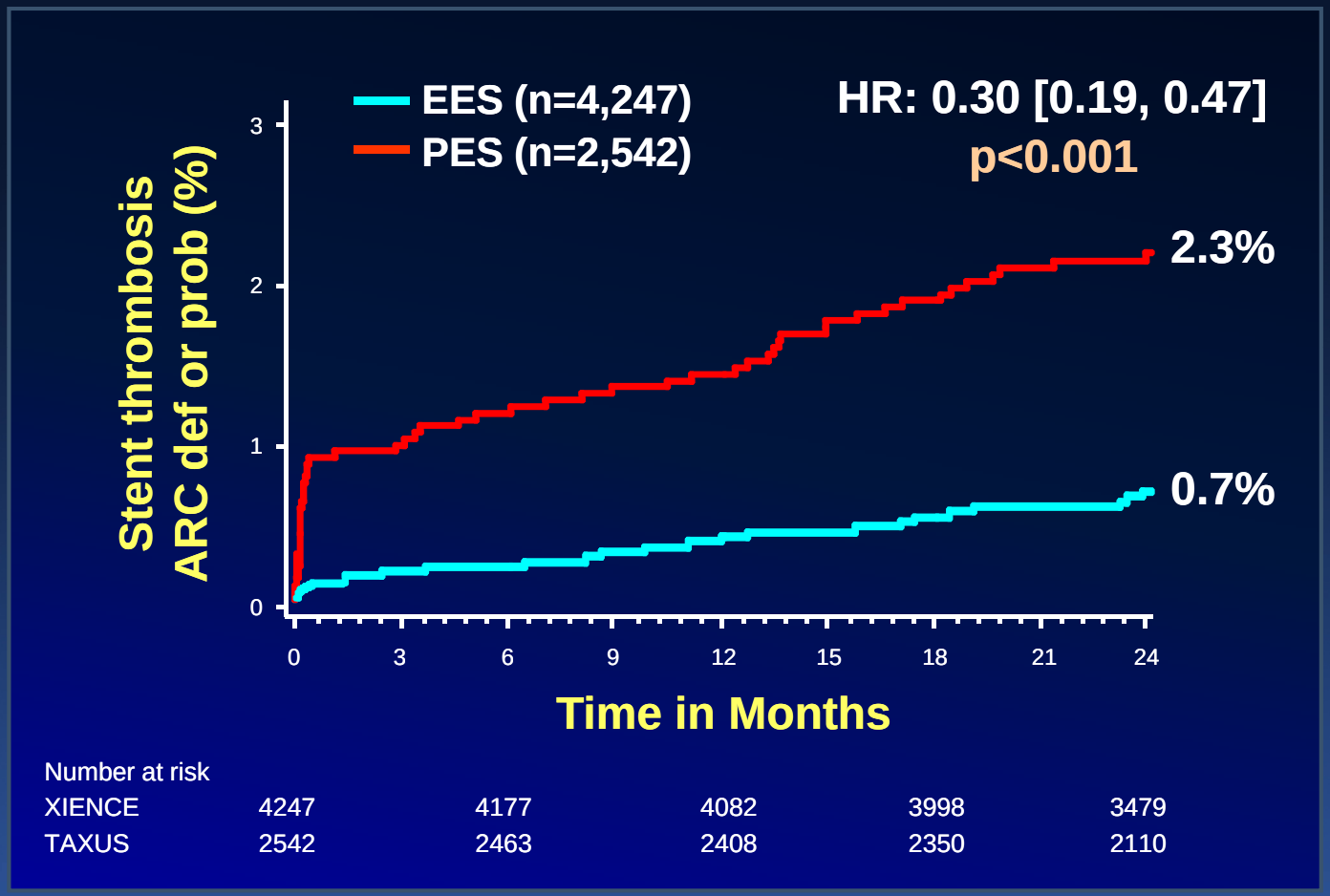
SPIRIT II, III, IV and COMPARE trials
Pooled database analysis (n=6,789)
Cardiac death or MI



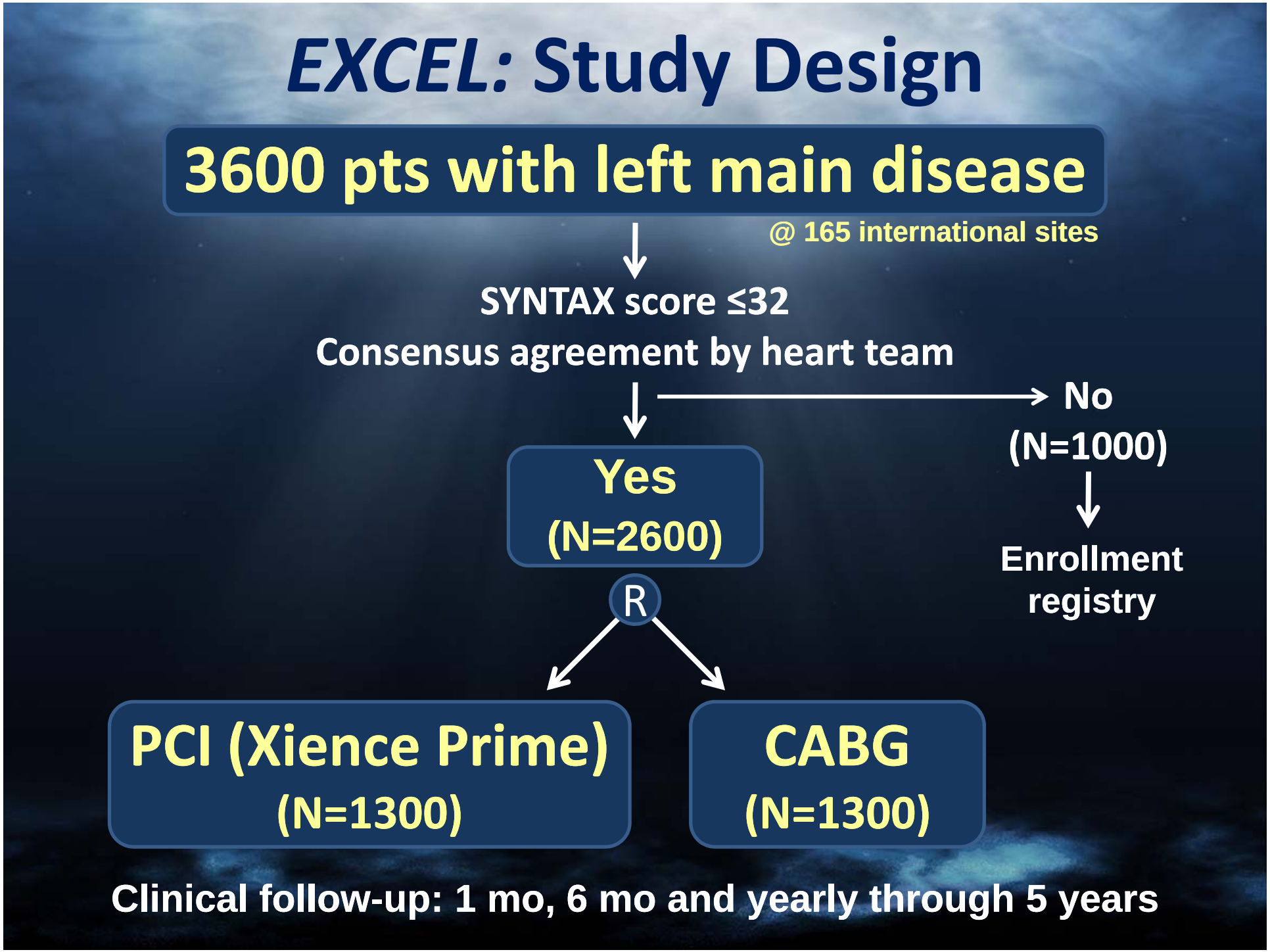
SPIRIT II, III, IV and COMPARE trials
Pooled database analysis (n=6,789)
Ischemic TLR



SPIRIT II, III, IV and COMPARE trials
Pooled database analysis (n=6,789)
Stent thrombosis (ARC definite/probable)



EXCEL: Study Design



EXCEL: Principal Endpoints

- **Primary endpoint: Death, MI, or stroke at a median follow-up of 3 years**

  - Powered for sequential noninferiority and superiority testing

- Major secondary endpoints:

  1. Stroke at 30 days (powered for superiority and noninferiority testing of CABG vs. PCI)
  2. Unplanned repeat revascularization for ischemia at a median follow-up of 3 years (powered for superiority and noninferiority testing of PCI vs. CABG)

- Quality of life and cost-effectiveness assessments:
  At baseline, 1 month, 1 year, 3 years and 5 years

EXCEL: Organization (i)

Academically driven study; 50% interventionalists, 50% cardiac surgeons

- Principal Investigators:
  - Interventional: Patrick W. Serruys, Gregg W. Stone
  - Surgical: A. Pieter Kappetein, Joseph F. Sabik
- Executive Operations Committee:
  - 4 principal investigators, Peter-Paul Kint, Martin B. Leon, Alexandra Lansky, Roxana Mehran, Marie-Angèle Morel, Chuck Simonton, David Taggart, Lynn Vandertie, Gerrit-Anne van Es, Marie-Claude Morice, Jessie Coe, Poornima Sood, Ali Akavand, Krishnankutty Sudhir
- Optimal Therapy Committee Chairs
  - PCI: Martin B. Leon
  - Surgery: David Taggart
  - Medical: Bernard Gersh
- Sponsor: Abbott Vascular

EXCEL: Organization (ii)

- Countries and Country Leaders (PCI and CABG)
  - United States: David Kandzari and John Puskas
  - Europe (10): Marie-Claude Morice and David Taggart
  - Brazil: Alex Abizaid and Luis Carlos Bento Sousa
  - Argentina: Jorge Belardi and Daniel Navia
  - Canada: Erick Schampaert and Marc Ruel
  - S. Korea: Seung-Jung Park and Jay-Won Lee
  - Australia: Ian Meredith and Julian Smith
  - China: TBD
- Statistical Committee: Stuart Pocock, Chair
- Data Safety and Monitoring Board: Lars Wallentin, Chair
- Academic Research Organizations
  - Cardiovascular Research Foundation and Cardialysis
- QOL and Cost-Effectiveness Analysis: David J. Cohen

EXCEL: Status

- After 2 years of preparation the protocol and CRF are finalized
- ~160 sites from 17 countries have been chosen and are being initiated
- FDA meetings and global regulatory submissions are ongoing
- The trial has begun: 28 pts have been randomized!