Left Main PCI: Anticipating EXCEL

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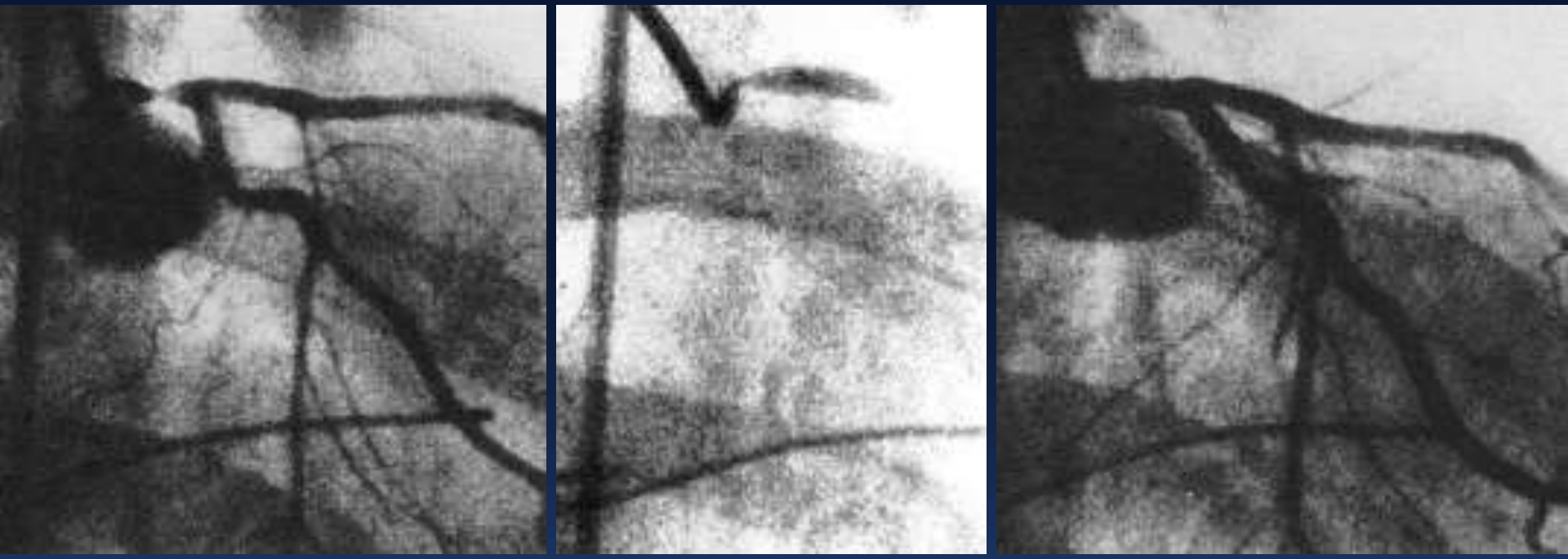
Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

None

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.

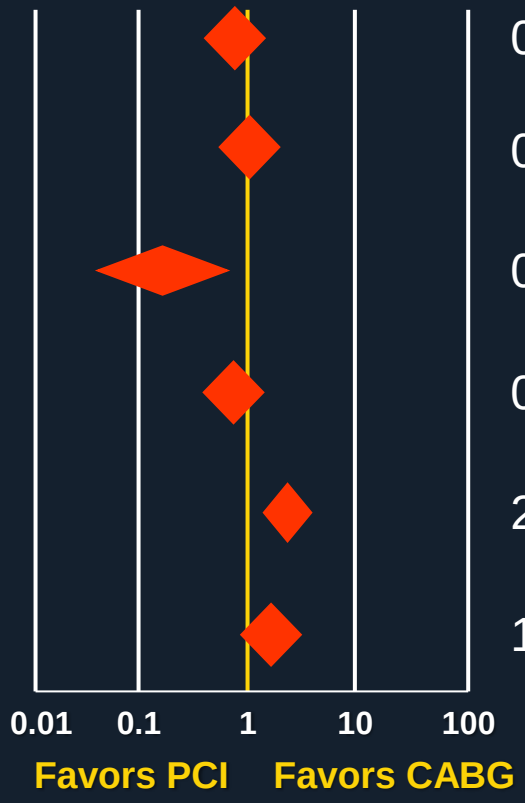
Gruntzig A. Lancet 1978;1:263.

PCI (1st gen DES) vs. CABG for Left Main Ds.
Meta-analysis of 4 RCTs, 1,611 Patients

Trial	LEMANS	SYNTAX LM	Boudriot et al.	PRECOMBAT
Year	2008	2009	2010	2011
N total	105	705	201	600
Age, mean years	61	65	68	62
Male	67%	74%	75%	77%
Diabetes	18%	25%	36%	32%
Distal LM involved	58%	61%	71%	65%
+0/1/2/3 VD, %	0/9/23/68	13/20/31/36	29/31/27/14	10/17/32/41
Syntax Score, mean	25	30	24	25
Log Euroscore, mean	3.4	3.9	2.5	2.7
LIMA-LAD	81%	97%	99%	94%

PCI (1st gen DES) vs. CABG for Left Main Ds.
Meta-analysis of 4 RCTs, 1,611 Patients
1-Year Outcomes

	PCI	CABG	OR (95%CI)	*p*-Value
Death	3.0% (24/807)	4.1% (32/790)	0.74 (0.43-1.28)	0.29
MI	2.8% (23/807)	2.9% (23/790)	0.98 (0.54-1.78)	0.95
Stroke	0.1% (1/707)	1.7% (12/689)	0.15 (0.03-0.67)	0.01
Death, MI, or stroke	5.3% (35/655)	6.8% (43/636)	0.77 (0.48-1.22)	0.26
Repeat Revasc	11.4% (92/807)	5.4% (43/790)	2.25 (1.54-3.28)	<0.001
MACCE	14.5% (117/807)	11.8% (93/790)	1.28 (0.95-1.72)	0.11

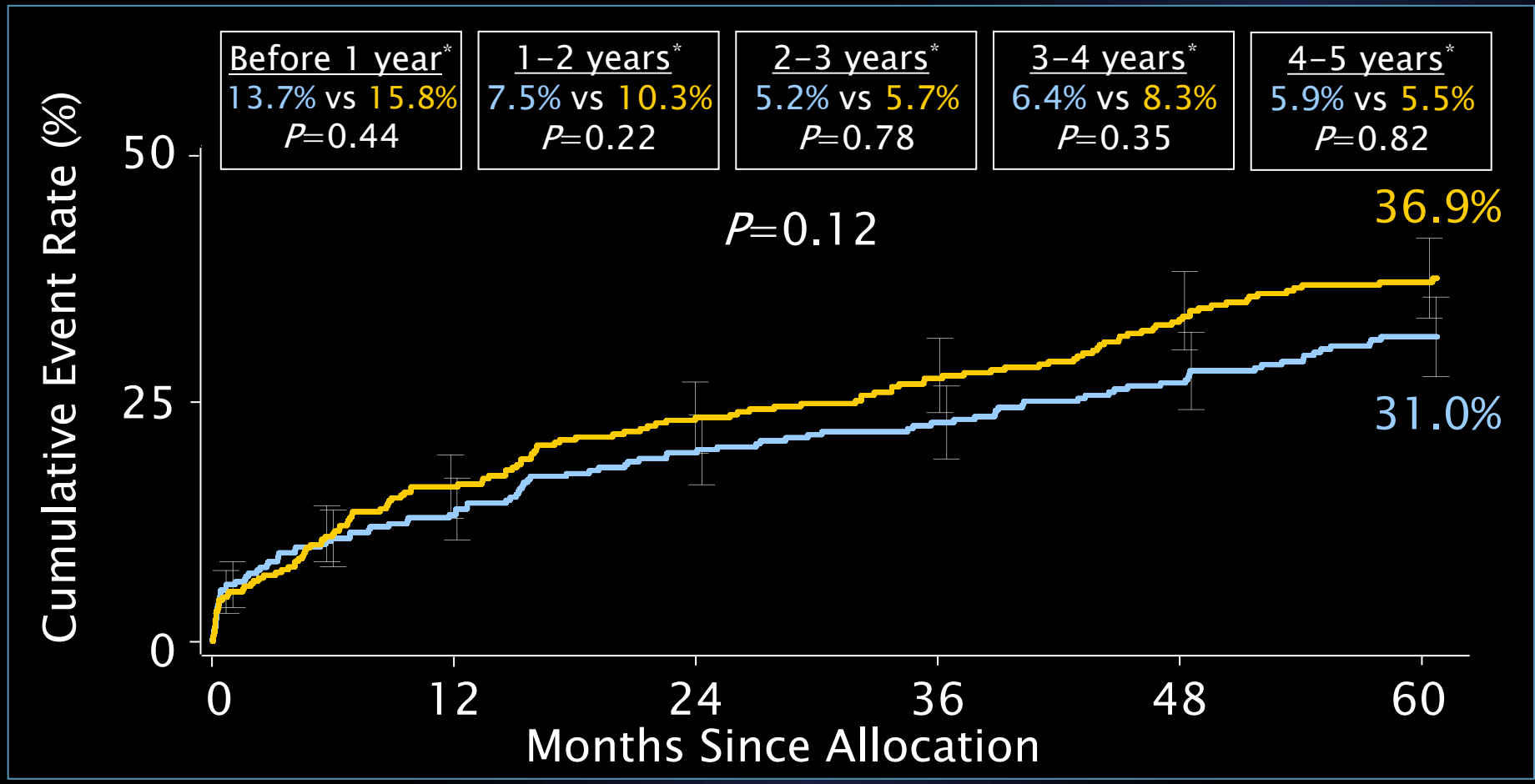


Capodanno D et al. *JACC* 2011;58:1426-32

MACCE to 5 Years
Left Main Subset

SYNTAX

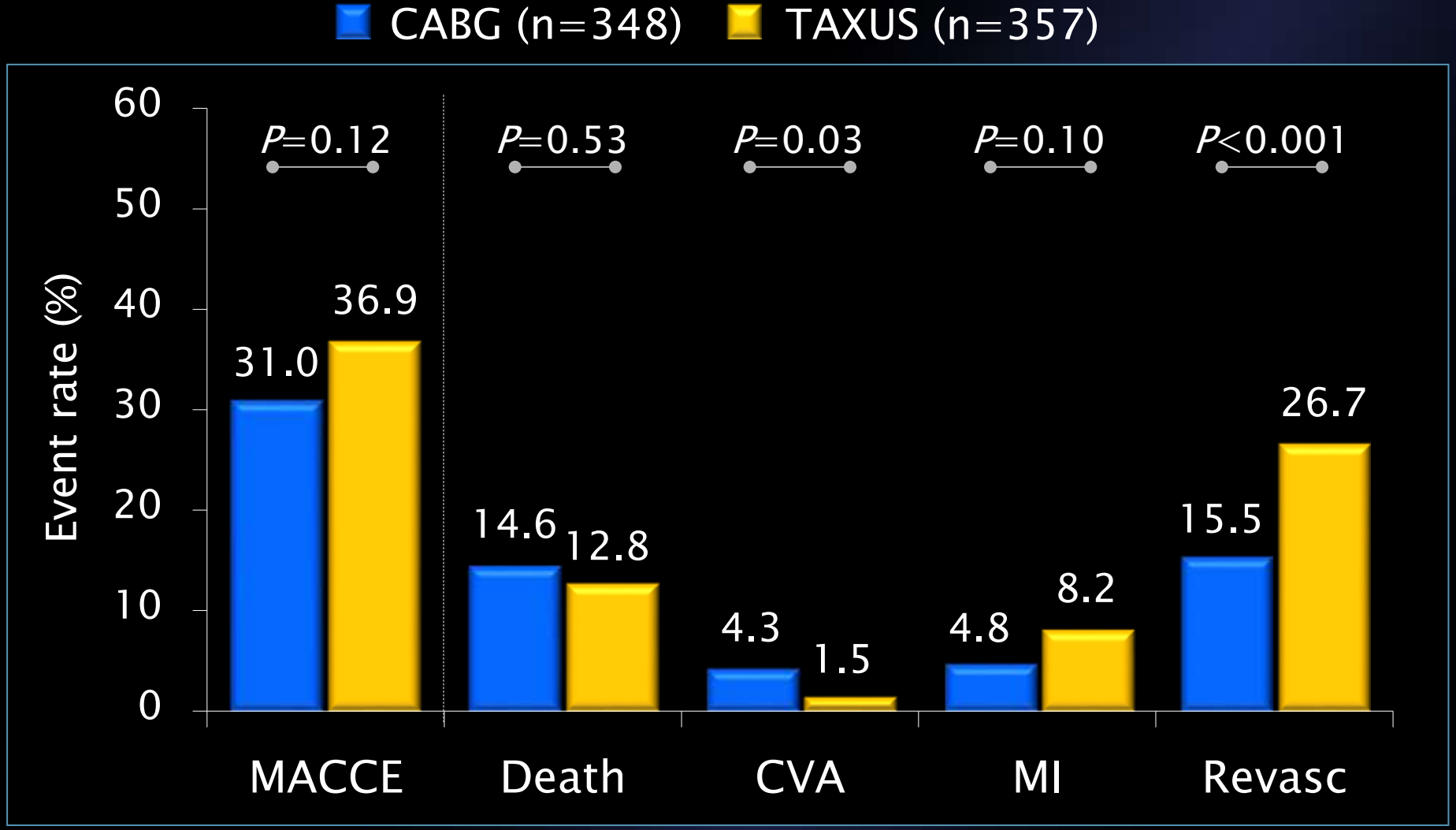
CABG (N=348) TAXUS (N=357)



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

Serruys PW et al. Lancet 2013;381:629–38

MACCE to 5 Years
Left Main Subset

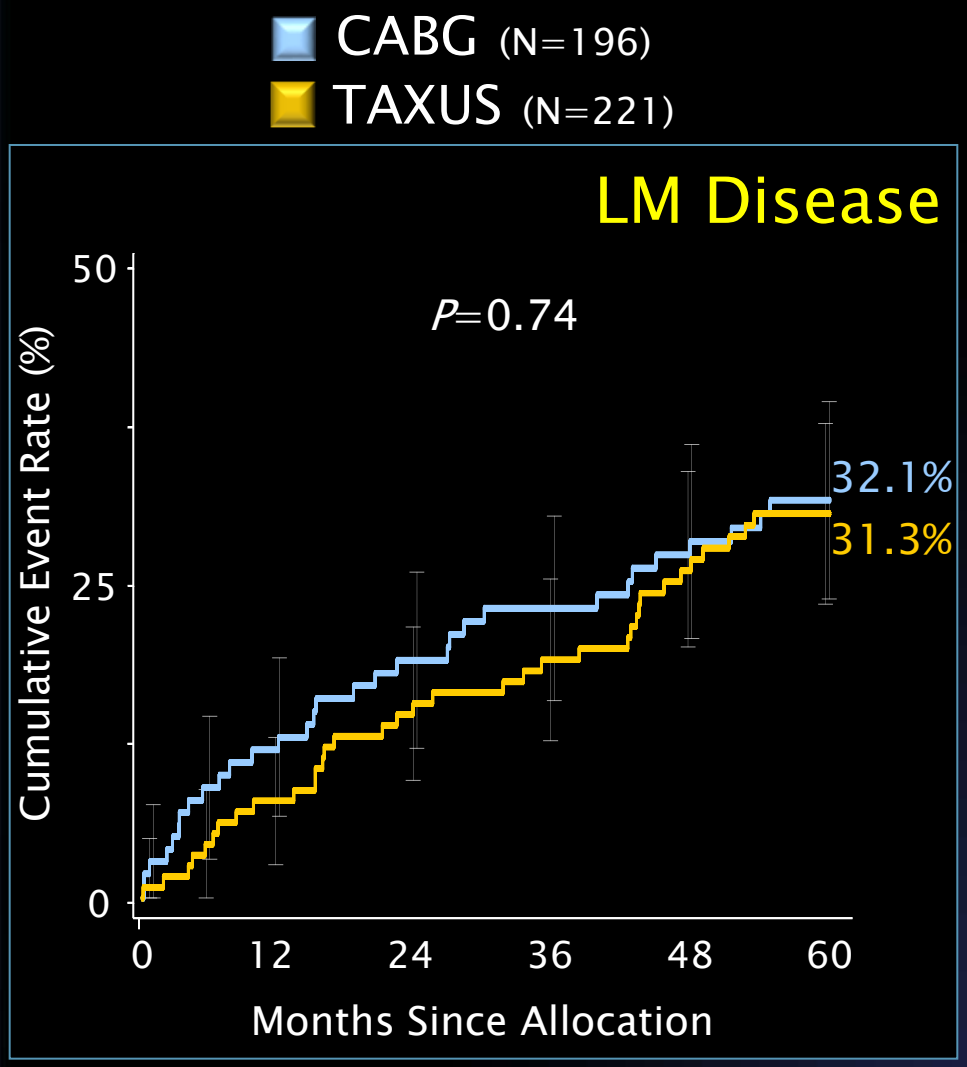


Cumulative KM Event Rate
Log-rank *P* value

Serruys PW et al. Lancet 2013;381:629-38

MACCE to 5 Years by SYNTAX Score Tercile

LM Subset Low to Intermediate Scores (0–32)

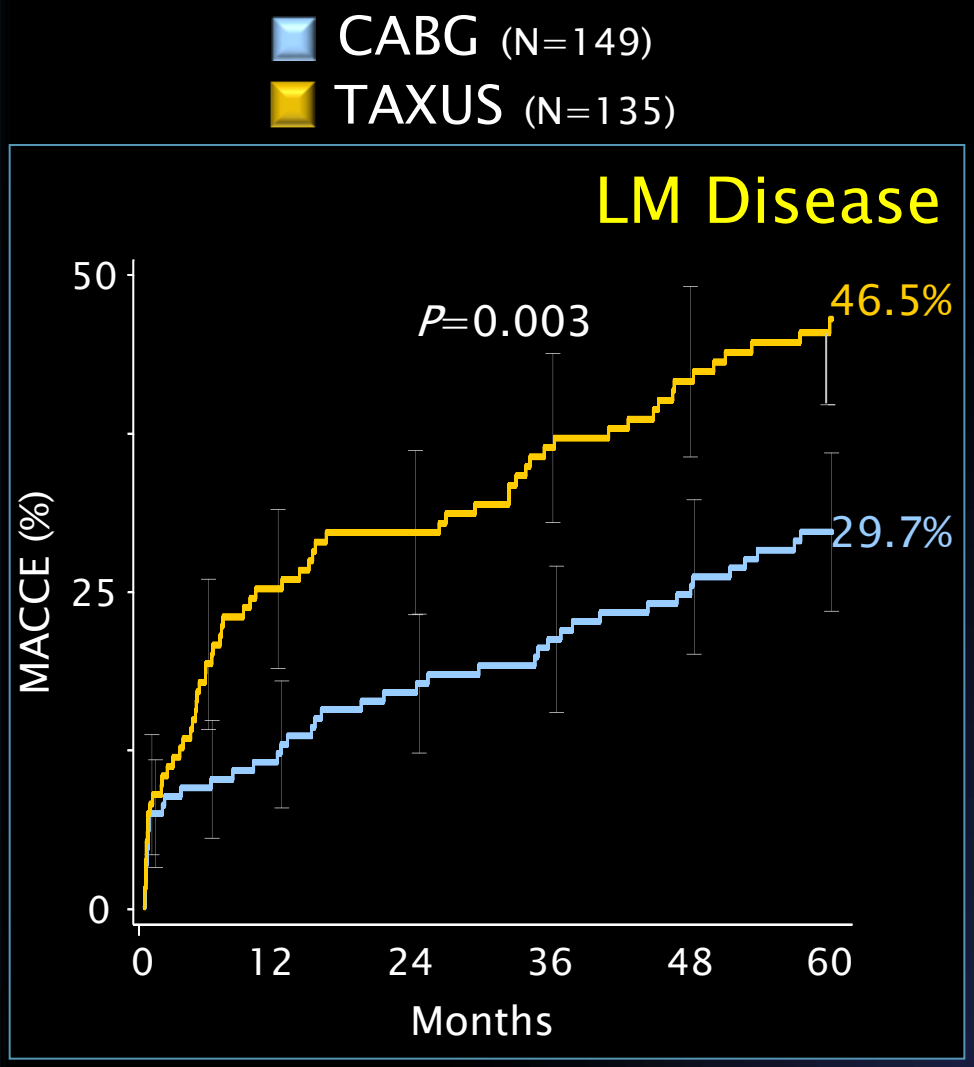


	CABG	PCI	*P* value
Death	15.1%	7.9%	0.02
CVA	3.9%	1.4%	0.11
MI	3.8%	6.1%	0.33
Death, CVA or MI	19.8%	14.8%	0.16
Revasc.	18.6%	22.6%	0.36

Serruys PW et al. Lancet 2013;381:629–38

MACCE to 5 Years by SYNTAX Score Tercile

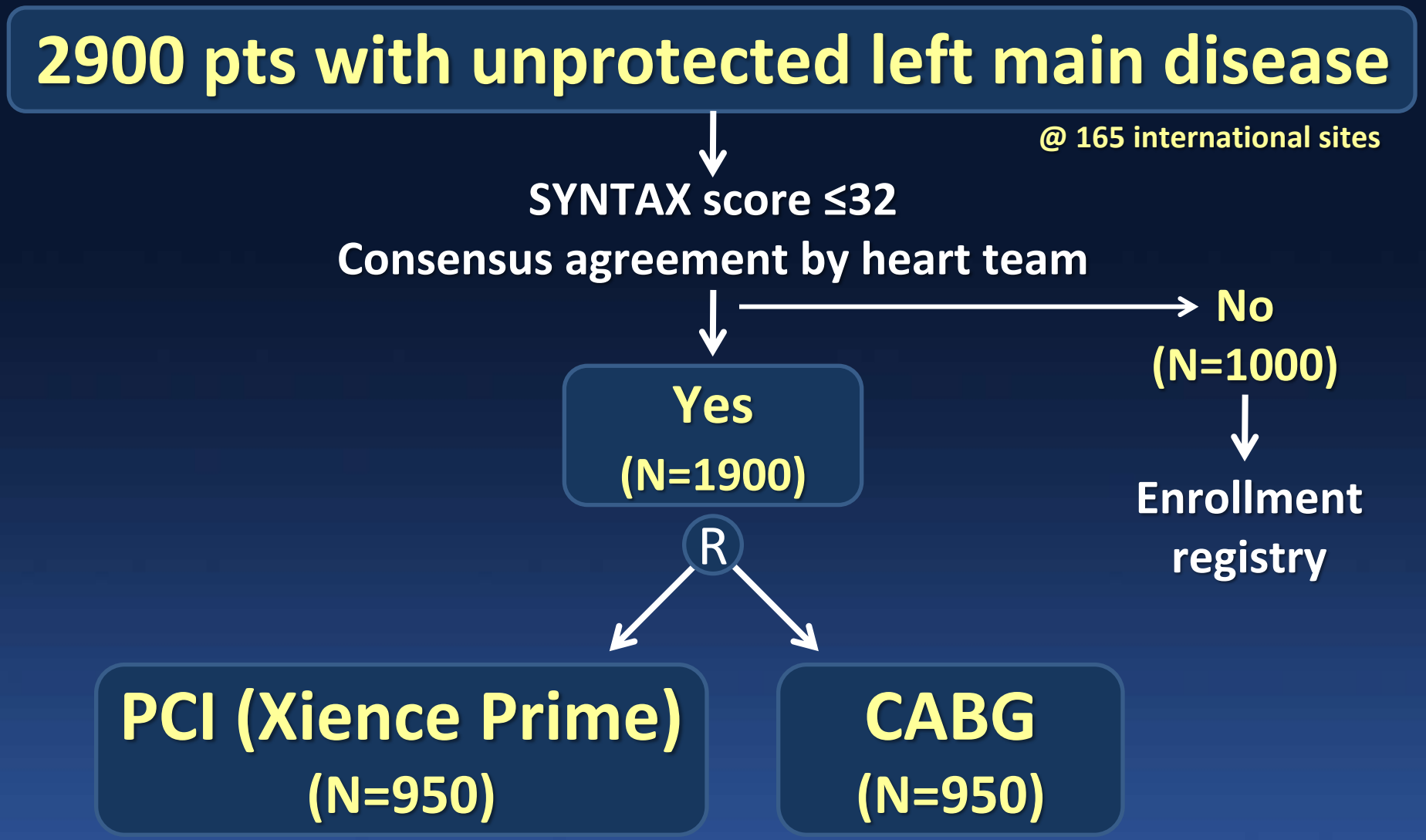
LM Subset High Scores ≥33



	CABG	PCI	*P* value
Death	14.1%	20.9%	0.11
CVA	4.9%	1.6%	0.13
MI	6.1%	11.7%	0.13
Death, CVA or MI	22.1%	26.1%	0.40
Revasc.	11.6%	34.1%	<0.001

Serruys PW et al. Lancet 2013;381:629–38

EXCEL: Study Design



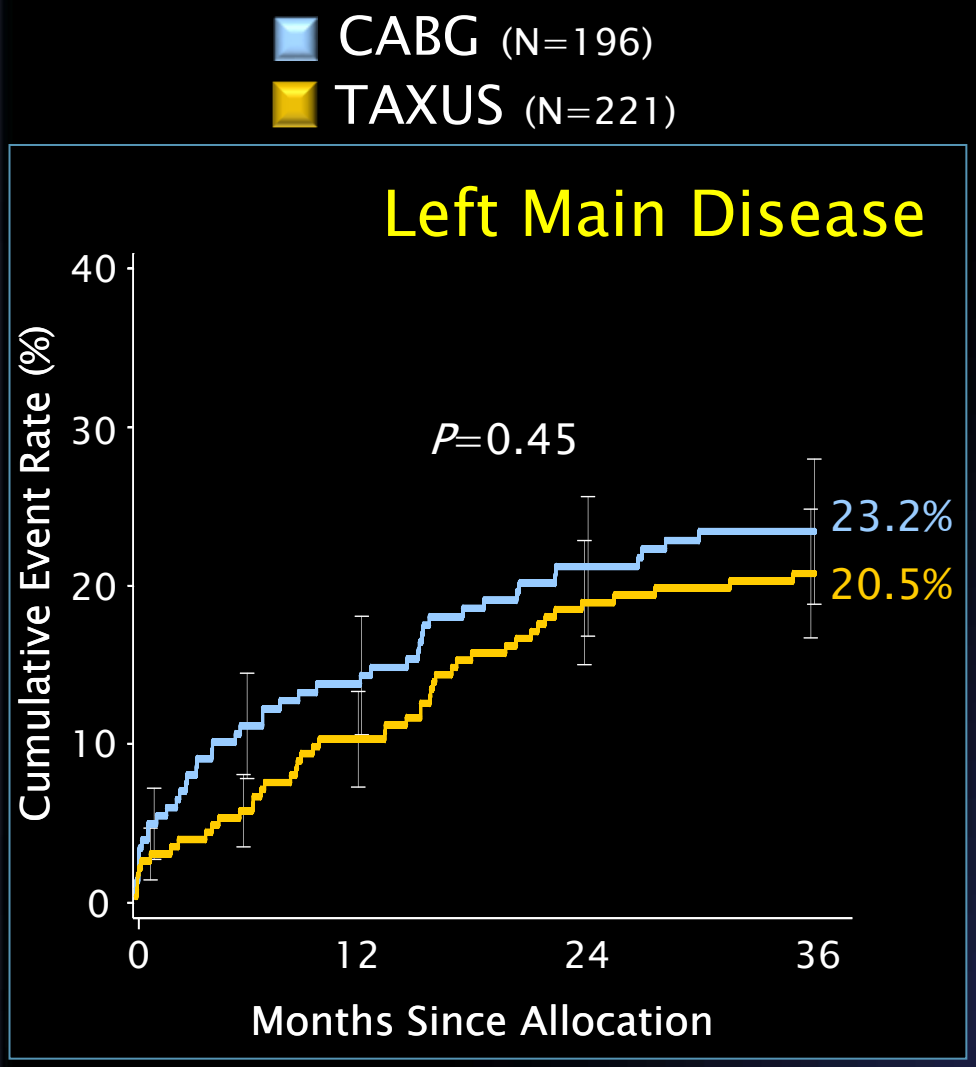
Clinical follow-up:
1 mo, 6 mo and yearly through 5 years

What is Novel About EXCEL?

Restriction of enrollment to Syntax Score ≤32

MACCE to 3 Years by SYNTAX Score Tercile

LM Subset 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

What is Novel About EXCEL?

The primary endpoint:
Death, MI or stroke at 3 years

EXCEL Primary Endpoint

Death, MI or stroke at median FU 3 years

Sequential noninferiority and superiority testing

Noninferiority - Assuming:

- 11.0% event rate in each arm
- non-inferiority margin Δ = 4.2%
- 8% lost to follow-up at 3 years
- one-sided alpha = 0.025

→ 1900 subjects (1300 per arm) provides 80% power to demonstrate non-inferiority of PCI to CABG

Superiority - Assuming:

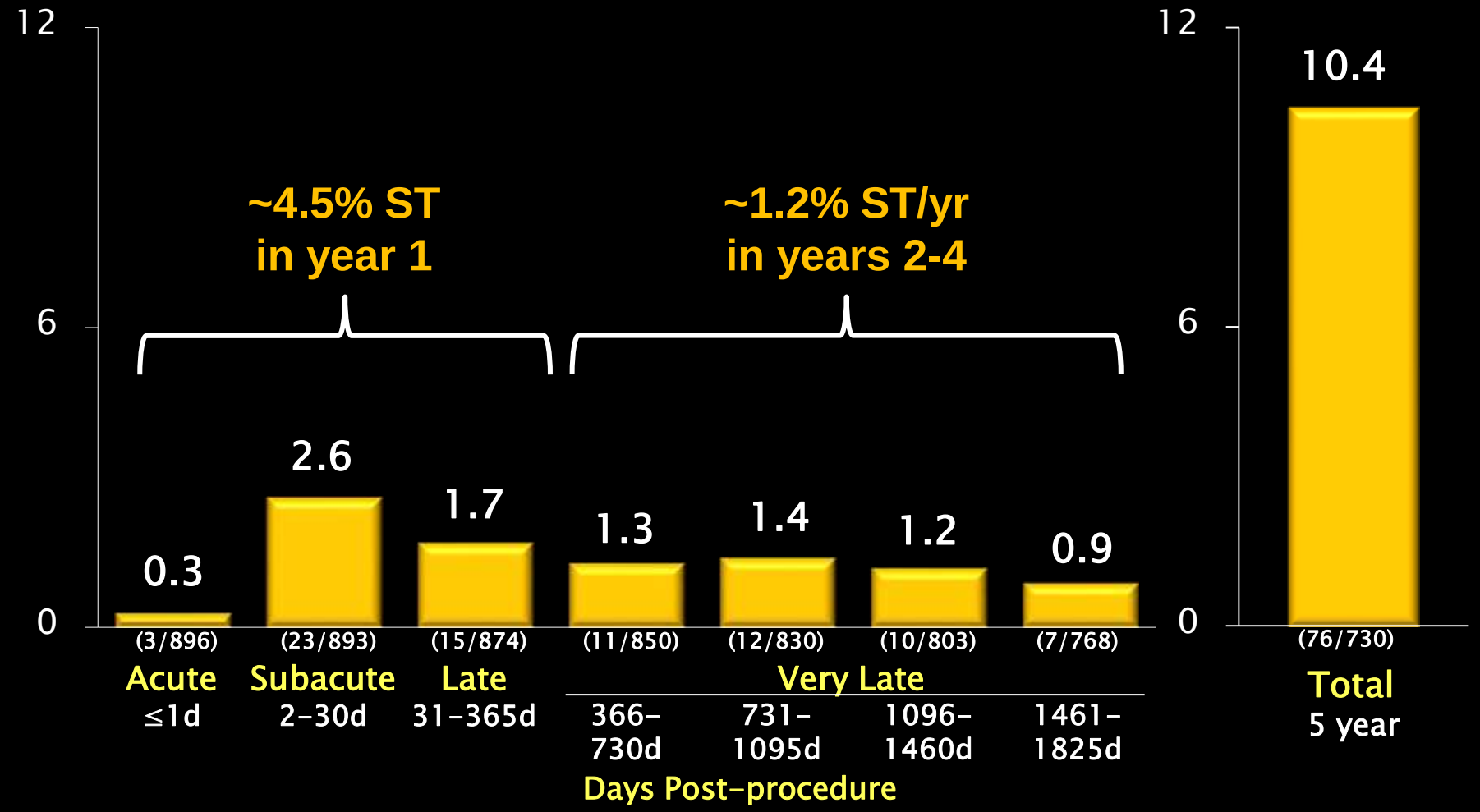
- 11.0% event rate with CABG
- 7.16% event rate with PCI
- 8% lost to follow-up at 3 years
- two-sided alpha = 0.05

→ 1900 subjects (1300 per arm) provides 80% power to demonstrate superiority of PCI to CABG

What is Novel About EXCEL?

Use of best in class DES

SYNTAX: Definite/Probable ARC Stent Thrombosis to 5 Years *(Per Patient)*

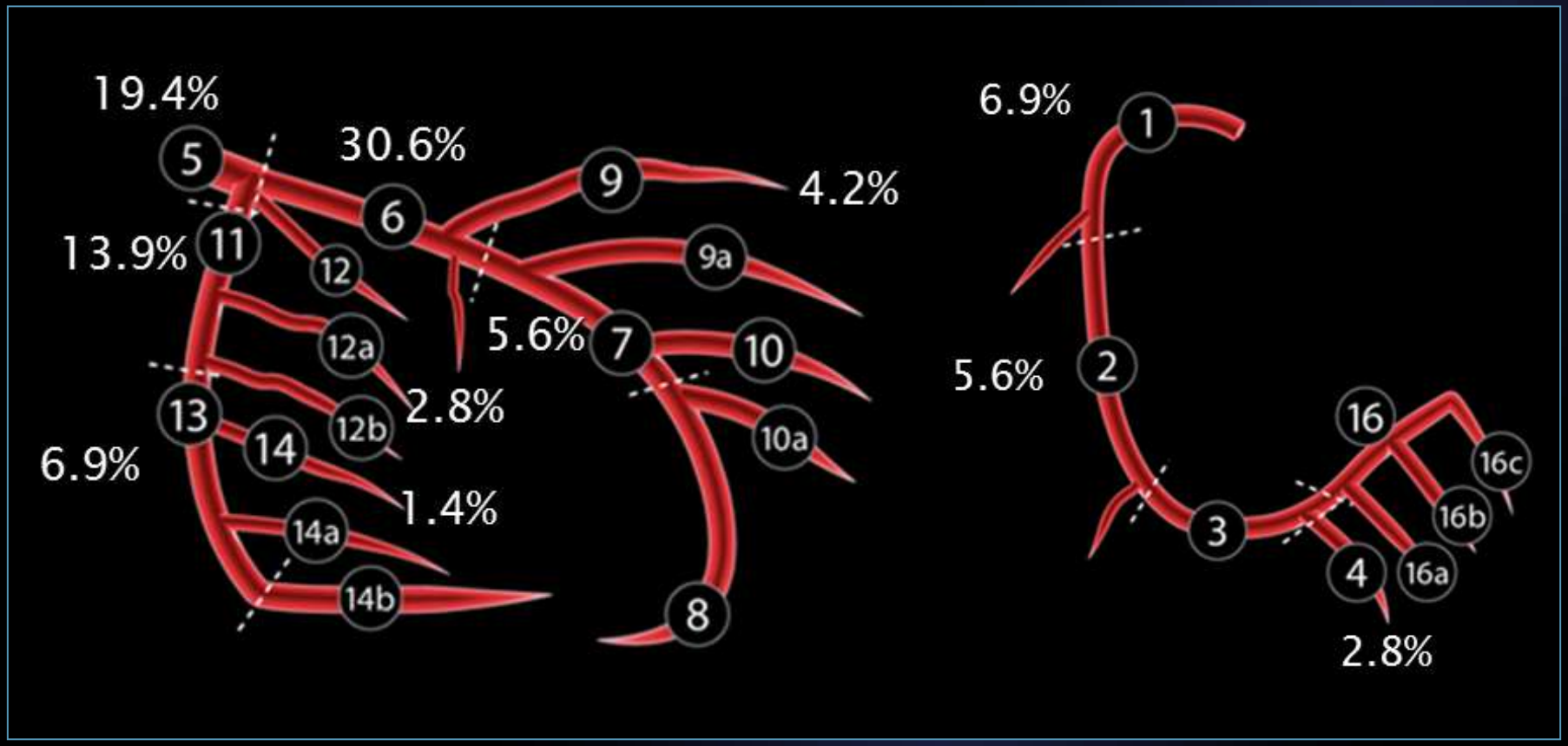


Rate was ~ same in the LM and 3VD cohorts, and roughly independent of Syntax Score

Serruys PW. JACC 2013:on-line

SYNTAX: Location of Stent Thrombosis

(Per Vessel)



87.2% of 1st ST occurred in vessels treated at the index procedure

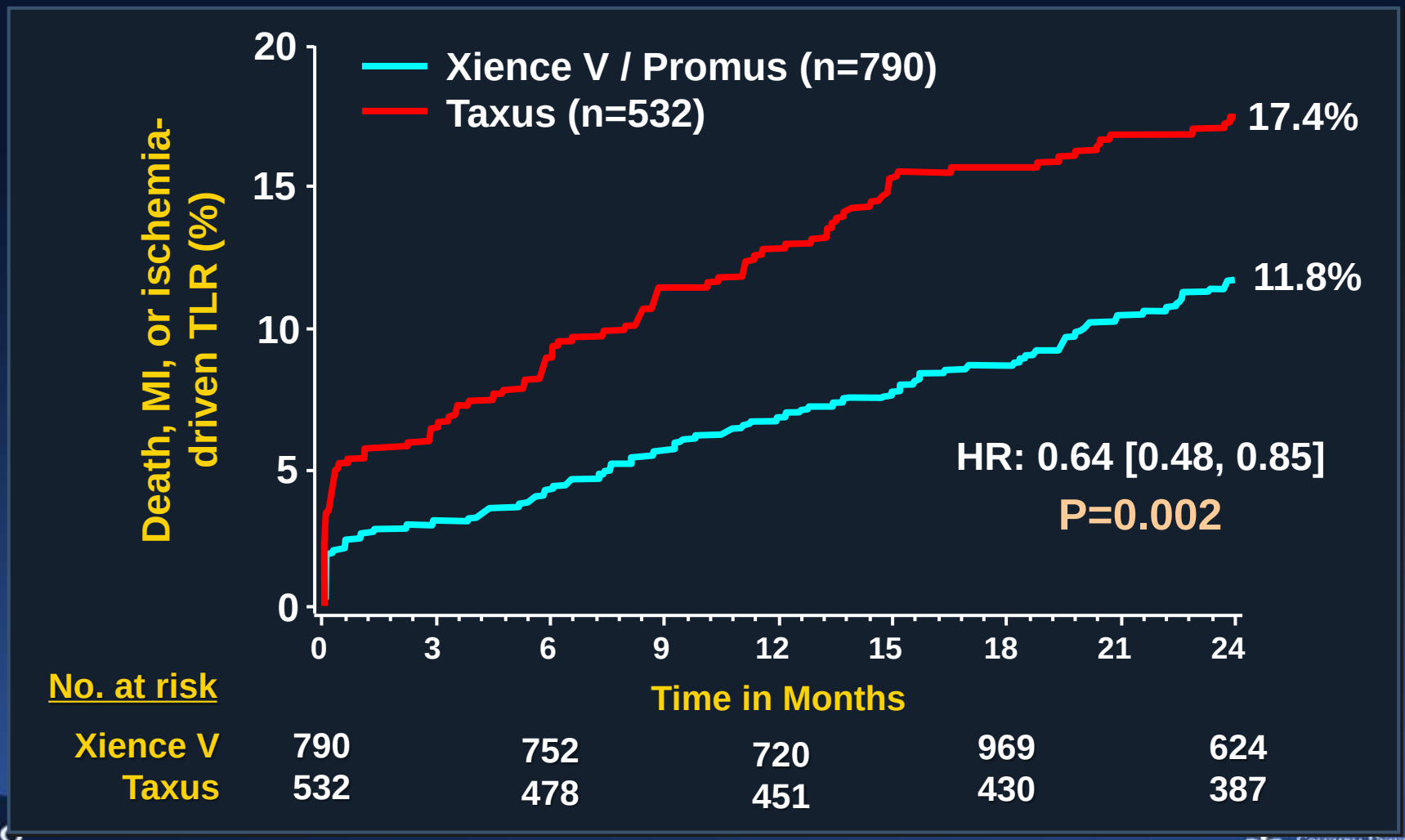
Note: Some ST in multiple vessels

Serruys PW. JACC 2013:on-line

EES vs. PES: SPIRIT II, III, IV and COMPARE RCTs

Pooled database analysis – 2 year results

Patients with multivessel PCI (n=1,322)

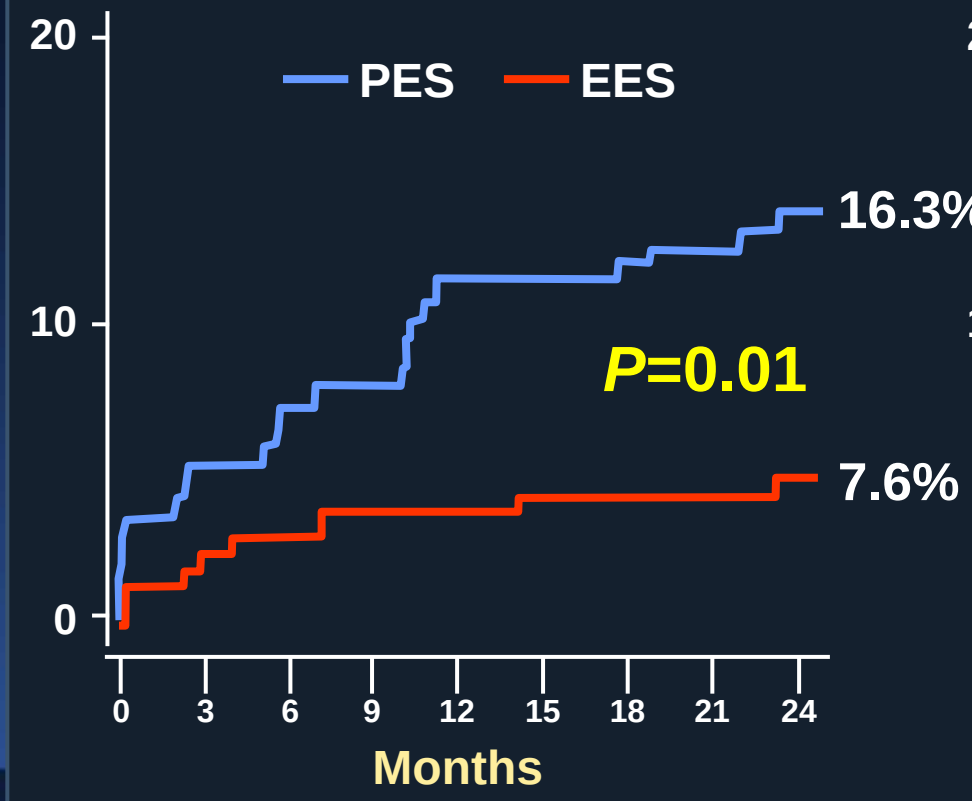


Stone GW. TCT 2012

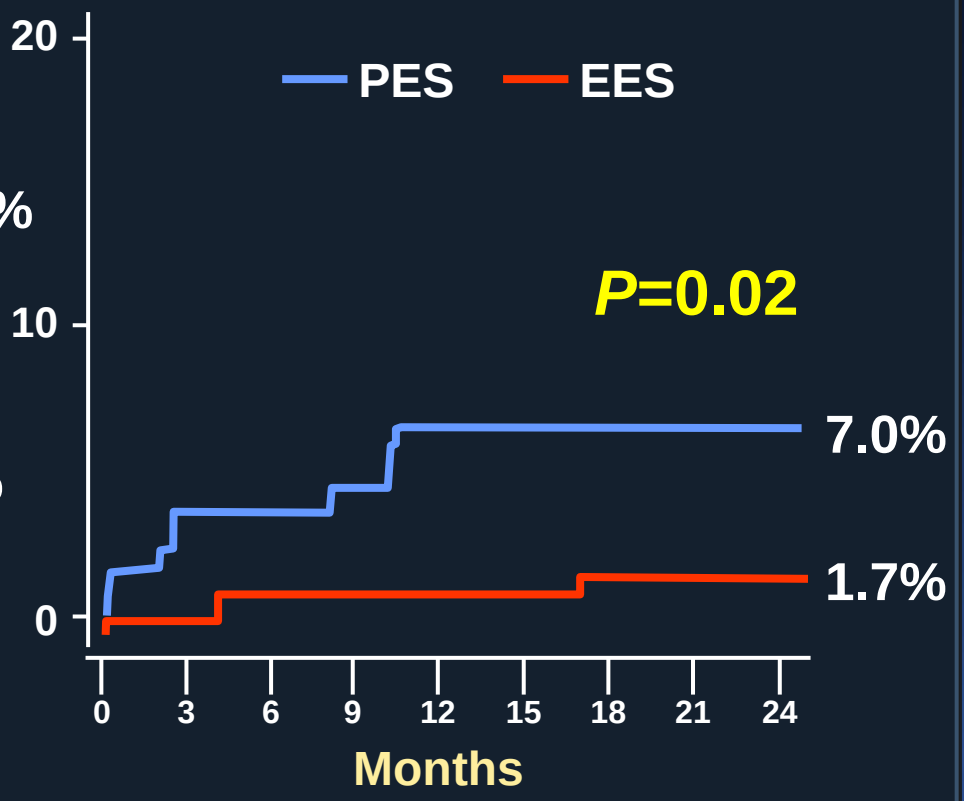
LEMAX: Propensity-matched Comparison of PES and EES in ULM ds.

- 172 matched pts in each group -

Target lesion failure



Stent thrombosis (any)



Moynagh A et al. *EuroIntervention* 2013;9:452-62

What is Novel About EXCEL?

Optimal PCI and CABG Technique

EXCEL: PCI Procedure Highlights

- **DAPT and statin pre-loading:** Required
- **IVUS:** Strongly recommended to guide LM PCI
- **FFR:** Strongly recommended to assess borderline lesions
- **Lesion preparation:** Direct stenting strongly discouraged
- **Distal LM bifurcation:** Provisional stenting recommended
- **Hemodynamic support:** Permitted, not usually required
- **Vascular access and closure:** Operator discretion
- **Staging:** Liberal use permitted (<2 weeks preferred)
- **Routine FU angiography:** Not permitted

EXCEL: CABG Procedure Highlights

- **On-pump vs. off-pump:** Operator discretion
  - If on-pump: Arrested heart or beating heart; single cross-clamp technique strongly recommended
- **Ascending aorta assessment**: Intra-operative assessment TEE and/or epi-aortic echo strongly recommended
- **Intra-op TEE:** Strongly recommended prior to cannulation to assess LV function, cardiac valves, and ascending aorta
- **Arterial grafts are the preferred conduits**: LIMA to LAD very strongly recommended – then RIMA (free or in-situ) > radial, in-situ gastroepiploic, and free inferior epigastric arteries > SVG – but use local practice and expertise

EXCEL: Study Design

2900 pts with unprotected left main disease

@ 165 international sites

SYNTAX score ≤32

Consensus agreement by heart team

No (N=1000) → **Enrollment registry**

Yes (N=1900)

R

PCI (Xience Prime) (N=950)

CABG (N=950)

Enrollment closed on March 6th, 2014
1905 pts randomized
Results at TCT 2016

Clinical follow-up: Through 5 years

Primary endpoint: Death/CVA/MI at median 3 yr FU

NOBLE: Study Design

1200 pts with unprotected left main disease

@ 26 EU sites

With ≤3 additional non-complex lesions
(excludes length >25 mm, CTO,
2-stent bifurcation, calcified or tortuous vessels)

R

PCI (Biomatrix BES)
(N=600)

CABG
(N=600)

Clinical follow-up: Through 5 years

Results at TCT 2016