Introducing EXCEL: The Definitive Unprotected Left Main Randomized Trial

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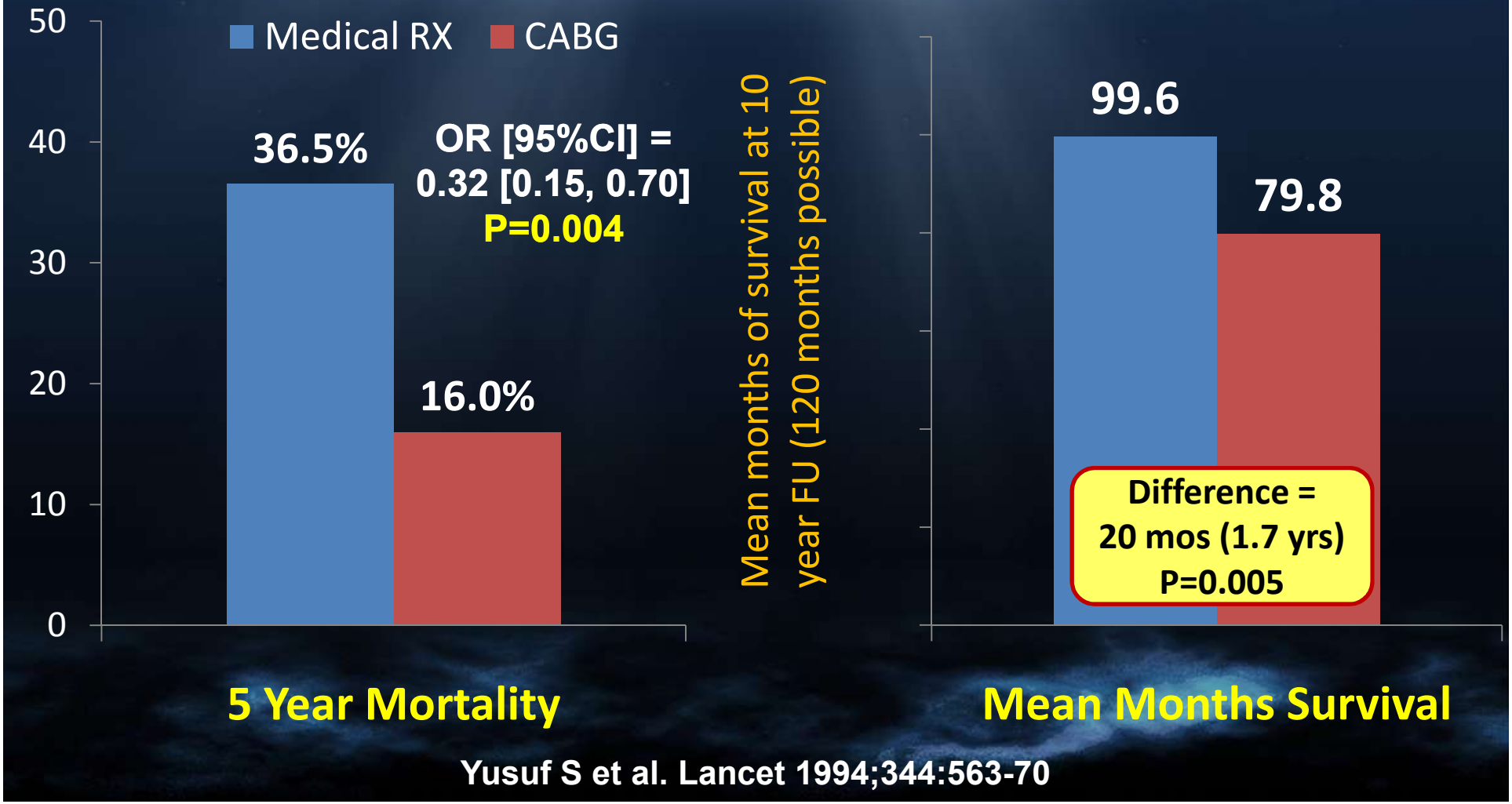
CABG vs. Medical Therapy in LM Ds.

175 pts with left main disease were randomized to CABG vs. medical therapy in 2 studies (VA and EU)

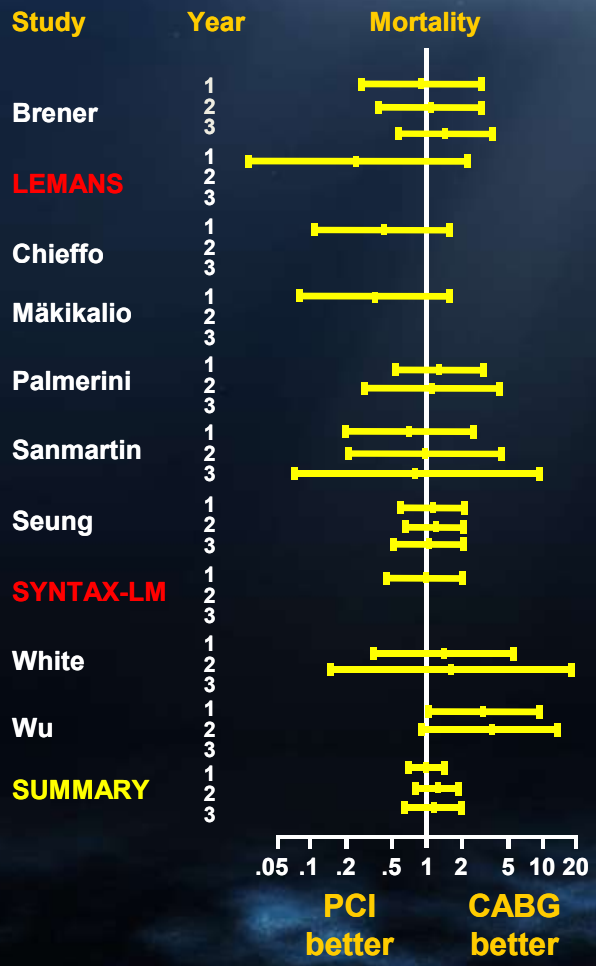


Yusuf S et al. Lancet 1994;344:563-70

Meta-analysis of PCI vs. CABG for LM Ds.

10 studies (2 RCTs, 8 observational [7 matched or adjusted])

N=3,773 pts (2,114 CABG and 1,659 PCI [78.7% DES])



OR [95%CI] for mortality at each year

	Year 1	Year 2	Year 3
Random effects	1.00 [0.70-1.41]	1.27 [0.83-1.94]	1.11 [0.66-1.86]
Fixed effects	0.97 [0.71-1.33]	1.28 [0.84-1.94]	1.11 [0.66-1.85]
Heterogeneity	P=0.38	P=0.77	P=0.81

Year 1: 1,393 PCI pts and 1,932 CABG pts;
Year 2: 528 PCI pts and 890 CABG pts;
Year 3: 263 PCI pts and 578 CABG pts.

Naik H et al. *JACC CV Interv* 2009;8:739-47

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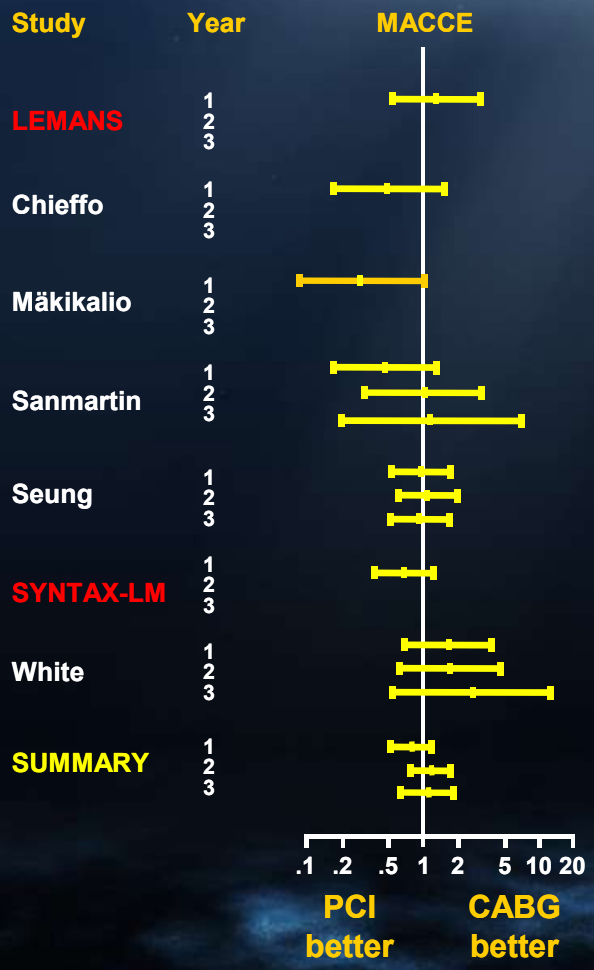

OR [95%CI] for D/CVA/MI at each year

	Year 1	Year 2	Year 3
Random effects	0.84 [0.57-1.22]	1.25 [0.81-1.94]	1.16 [0.68-1.98]
Fixed effects	0.82 [0.62-1.09]	1.25 [0.81-1.94]	1.16 [0.68-1.96]
Heterogeneity	P=0.18	P=0.70	P=0.48

Year 1: 1,239 PCI pts and 1,614 CABG pts;
Year 2: 432 PCI pts and 652 CABG pts;
Year 3: 236 PCI pts and 451 CABG pts.

Naik H et al. *JACC CV Interv* 2009;8:739-47

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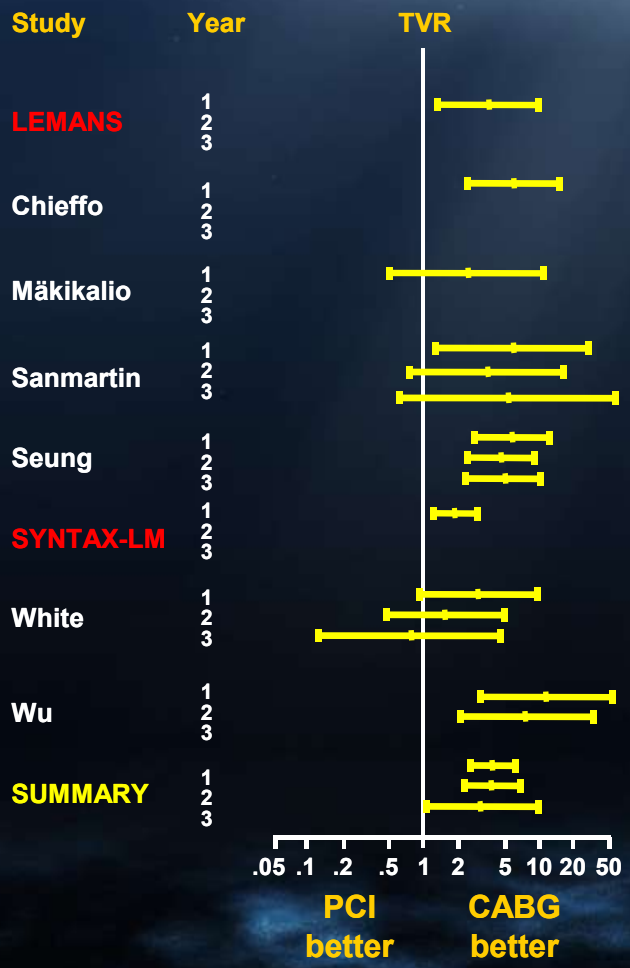


OR [95%CI] for TVR at each year

	Year 1	Year 2	Year 3
Random effects	4.36 [2.60-7.32]	4.20 [2.21-7.97]	3.30 [0.96-11.33]
Fixed effects	3.84 [2.77-5.33]	4.35 [2.54-7.44]	4.01 [2.01-7.98]
Heterogeneity	P=0.38	P=0.38	P=0.38

Year 1: 1,240 PCI pts and 1,692 CABG pts;
Year 2: 417 PCI pts and 699 CABG pts;
Year 3: 211 PCI pts and 447 CABG pts.

Naik H et al. *JACC CV Interv* 2009;8:739-47

SYNTAX Eligible Patients

SYNTAX

De novo disease (n=1800)

Limited Exclusion Criteria

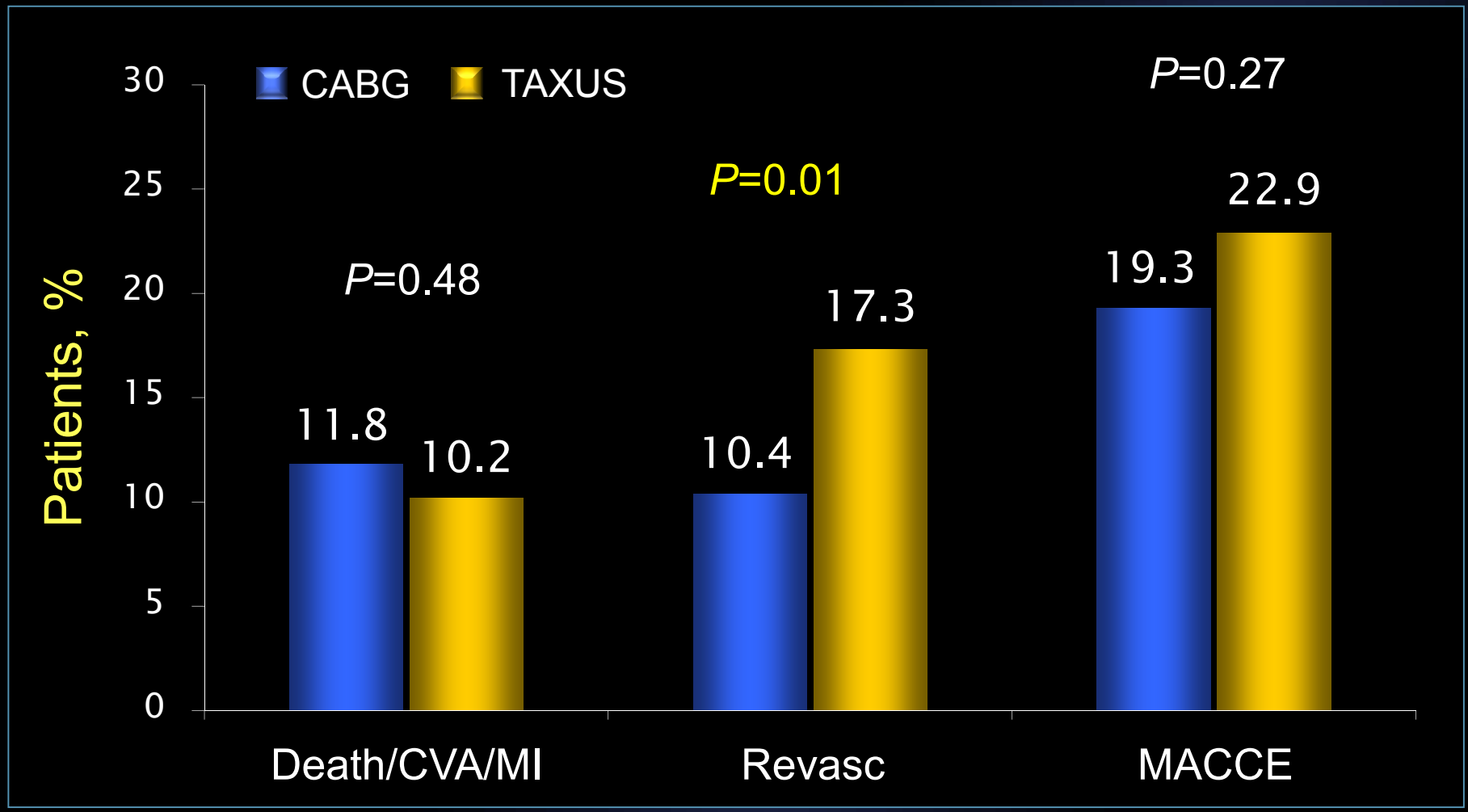
- Previous interventions
- Acute MI with CPK>2x
- Concomitant cardiac surgery

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

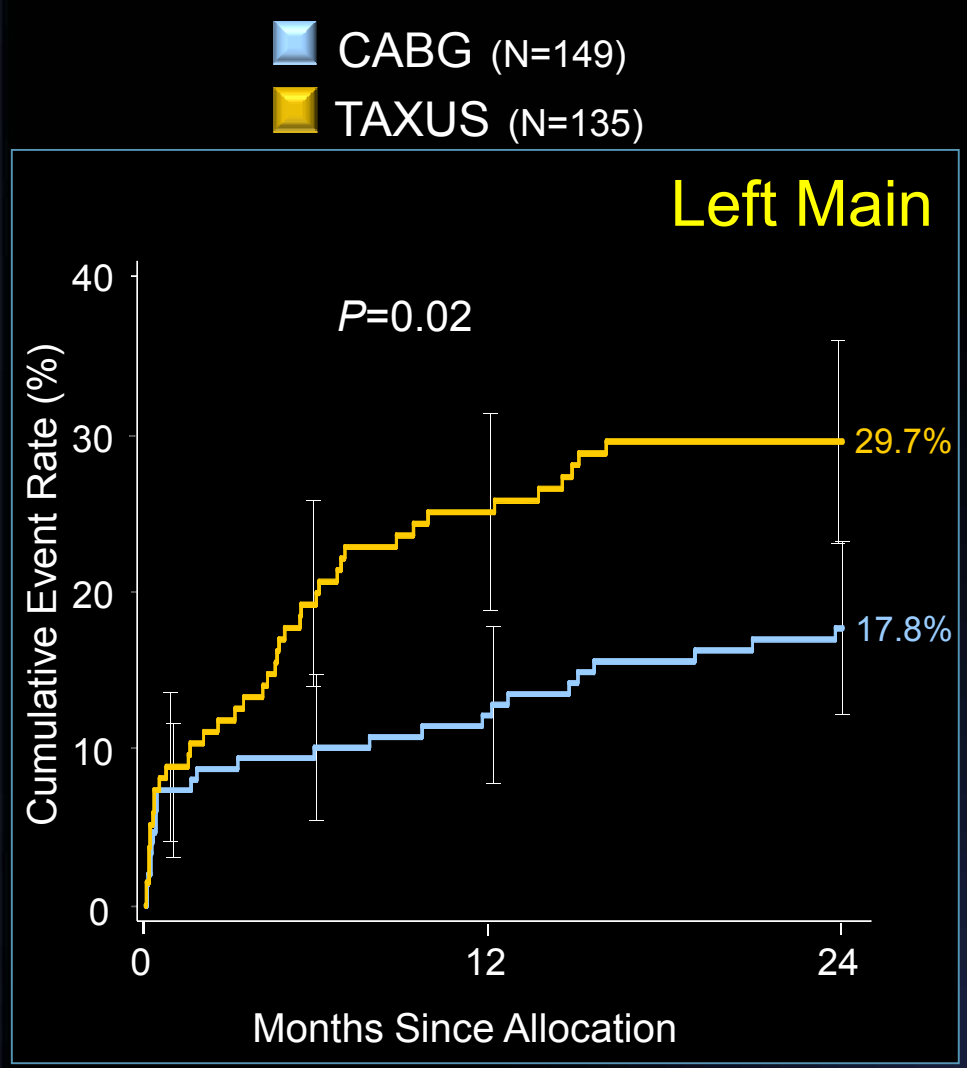
Serruys PW et al. NEJM 2009;360:961-72

SYNTAX: 2 Year Outcomes in the LM Subgroup (N=705)



MACCE to 2 Years by SYNTAX Score Tercile

Left Main SYNTAX Score ≥33

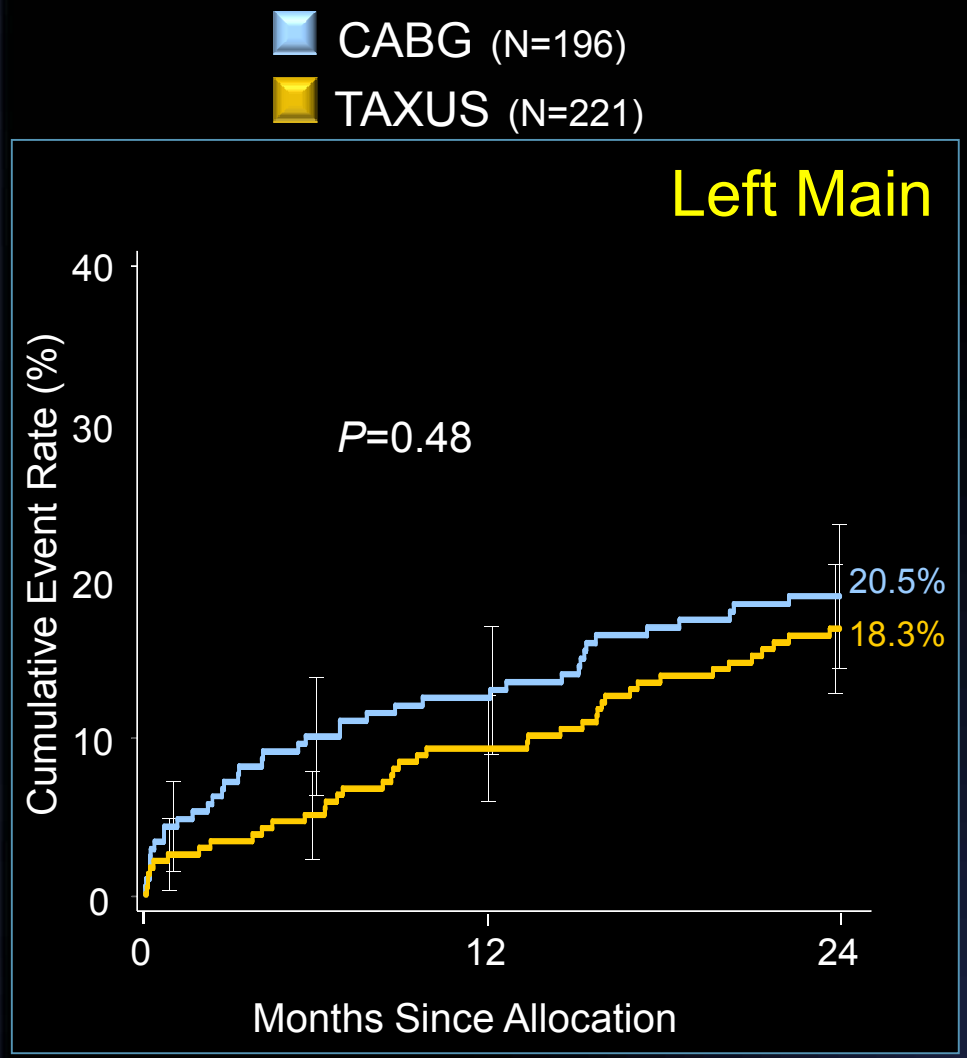


	CABG	PCI	*P*-value
Death	4.1%	10.4%	0.04
CVA	4.2%	0.8%	0.08
MI	6.1%	8.4%	0.48
Death, CVA or MI	11.5%	15.6%	0.32
Revasc.	9.2%	21.8%	0.003

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

Site-reported data; ITT population

MACCE to 2 Years by SYNTAX Score Tercile *Left Main SYNTAX Scores 0–32*



	CABG	PCI	*P*–value
Death	7.9%	2.7%	0.02
CVA	3.3%	0.9%	0.09
MI	2.6%	3.8%	0.59
Death, CVA or MI	12.1%	6.9%	0.06
Revasc.	11.4%	14.3%	0.44

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

Site-reported Data; ITT population

ACC/AHA Guidelines Post SYNTAX

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

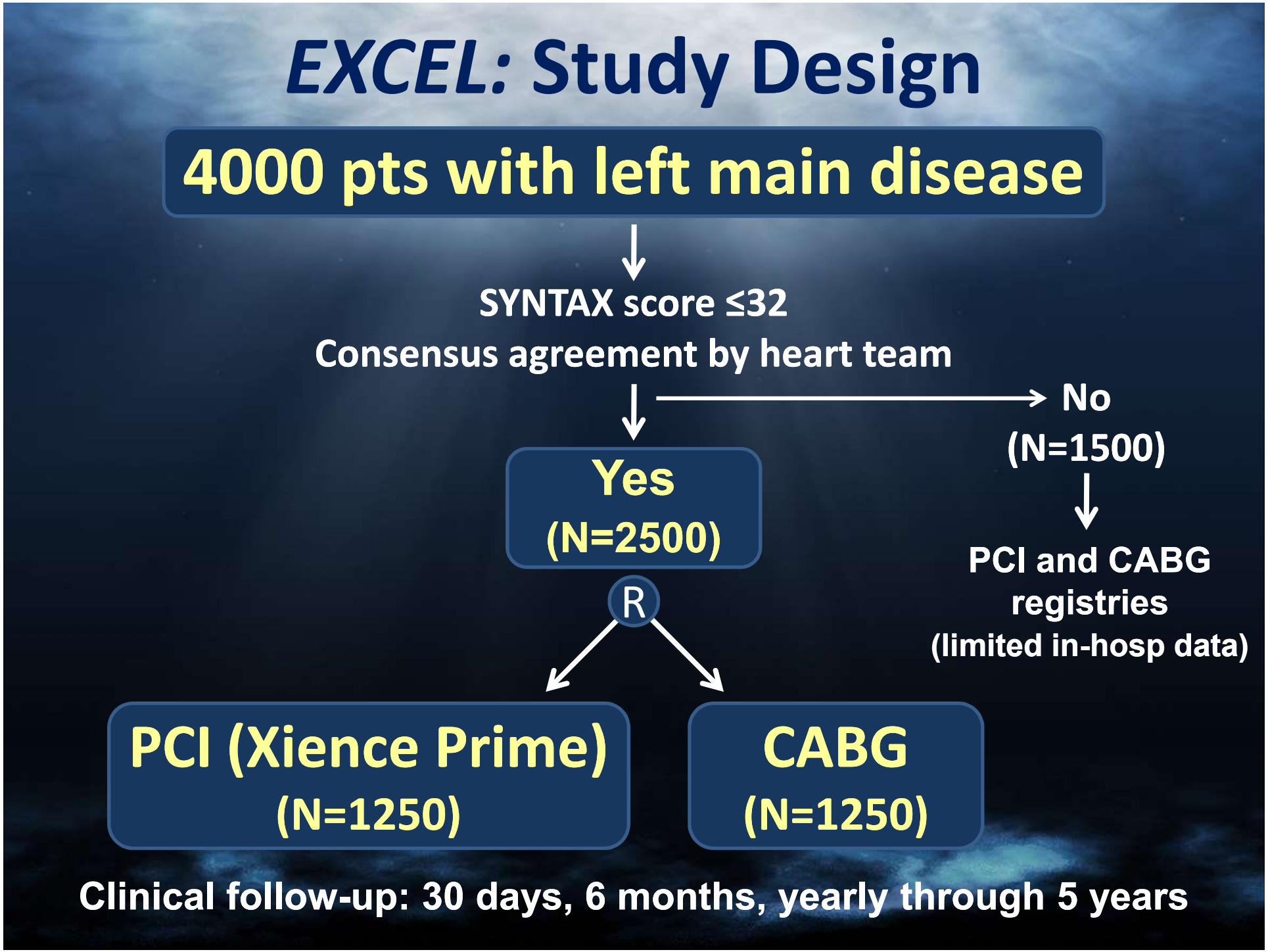
IIb = “may or might be considered; may or might be reasonable; usefulness/effectiveness is unknown/unclear/uncertain or not well established”

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

What Would an Informative Trial of Left Main DES vs. CABG Look Like?

- It wouldn't be an all-comers trial!
  - Exclude pts who clearly should go to CABG, e.g. high SYNTAX scores
- Optimize PCI technique
  - Pre-specify when/how to use IVUS, staged procedures, RX of distal bifurcation, no routine angio FU, etc.
  - Use the best stent and adjunctive pharmacology
- Optimize CABG technique
  - Minimize waiting time to CABG, maximize pan-arterial revascularization, adjunctive pharmacology, etc.
- Use a meaningful 1º endpoint: Death, CVA or MI
- ~2500 randomized pts

EXCEL: Study Design



EXCEL: Inclusion Criteria

- Significant LM ds. by heart team consensus
  - Angiographic DS ≥70%, or
  - Angiographic DS ≥50% to <70% with
    - a markedly positive noninvasive study, and/or
    - IVUS MLA <6.0 mm^2, and/or
    - FFR <0.80
- Clinical and anatomic eligibility for both PCI and CABG by heart team consensus
- Silent ischemia, stable angina, unstable angina or recent MI

EXCEL: Clinical Exclusion Criteria

- Prior PCI within 1 year, or prior LM PCI anytime
- Prior CABG anytime
- Need for any cardiac surgery other than CABG
- Additional surgery required within 1 year
- Unable to tolerate, obtain or comply with dual antiplatelet therapy for 1 year
- Non cardiac co-morbidities with life expectancy < 3 years
- Clinical equipoise not present

EXCEL: Angiographic Exclusion Criteria

- Left main DS <50% (visually assessed)
- SYNTAX score ≥33
- Left main RVD <2.25 mm or >4.5 mm

EXCEL: Use of XIENCE Prime

Enhanced stent
New SDS

-More flexible and deliverable

- Shorter balloon tapers

- Higher RBP

EXCEL: Endpoints

- Primary endpoint: Death, MI, or stroke at median follow-up of 3 years
- Major secondary endpoint: Death, MI, stroke or unplanned revascularization at median follow-up of 3 years
  - ❖ Power analysis: Both endpoints are powered for sequential noninferiority and superiority testing
- Quality of life and cost-effectiveness assessments: At regular intervals

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, Jessie Coe, Poornima Sood, Ali Akavand, Krishnankutty Sudhir, Thomas Engels
- Optimal Therapy Committee Chairs
  - PCI: Martin B. Leon
  - Surgery: David Taggart
  - Medical: Bernard Gersh

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
- Statistical Committee
  - Stuart Pocock, Chair
- Data Safety and Monitoring Board
  - Lars Wallentin, Chair
- Academic Research Organizations
  - Cardiovascular Research Foundation and Cardialysis
- Sponsor: Abbott Vascular

EXCEL: Status

- After 12 months of preparation the protocol is finalized
- The site selection process is underway
- FDA meetings and global regulatory submissions are being prepared
- First patient enrolled: 3rd Quarter 2010

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