What's Known and Unknown about LM PCI: Transitioning from SYNTAX to EXCEL

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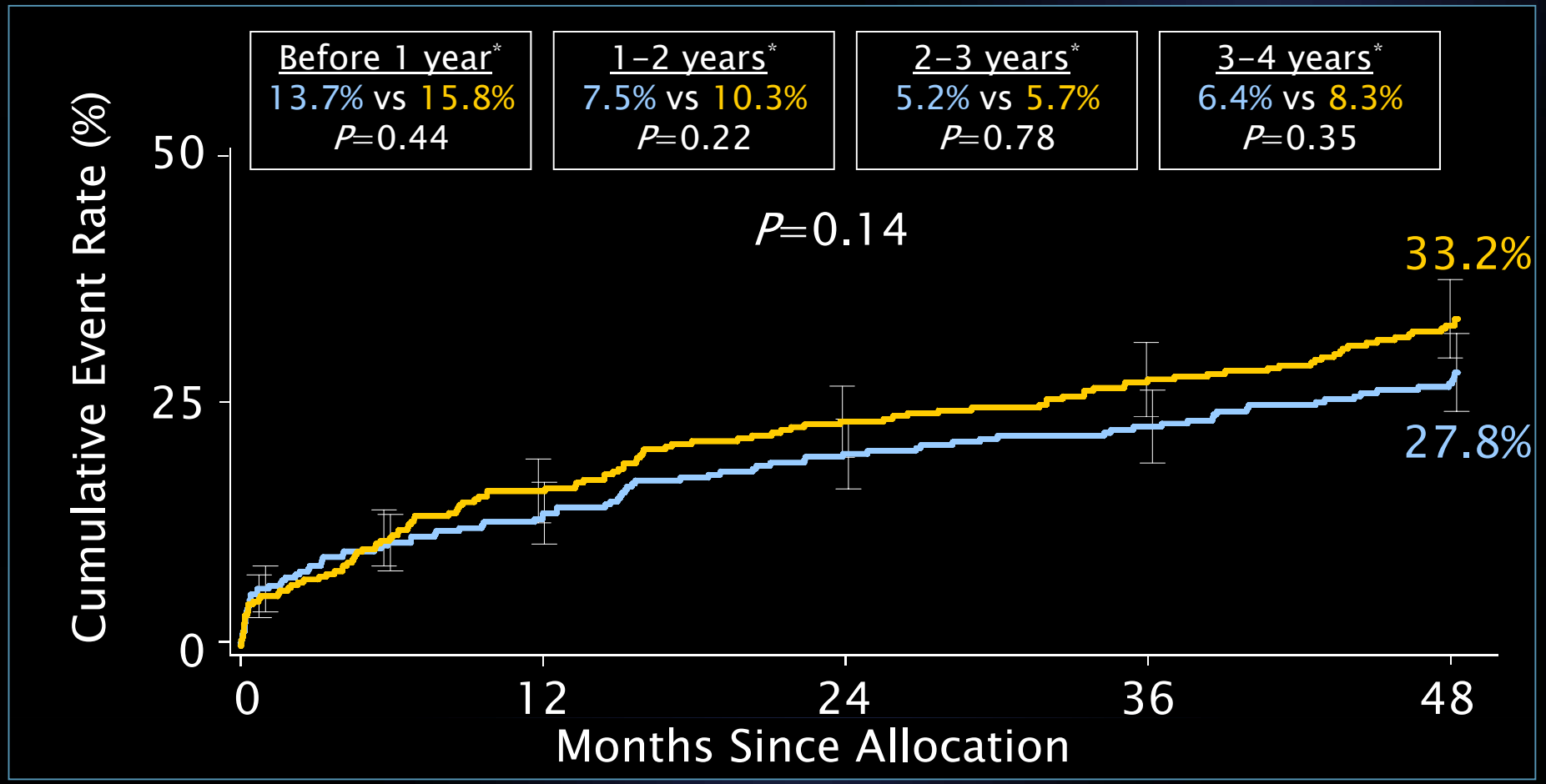
MACCE to 4 Years
Left Main Subset

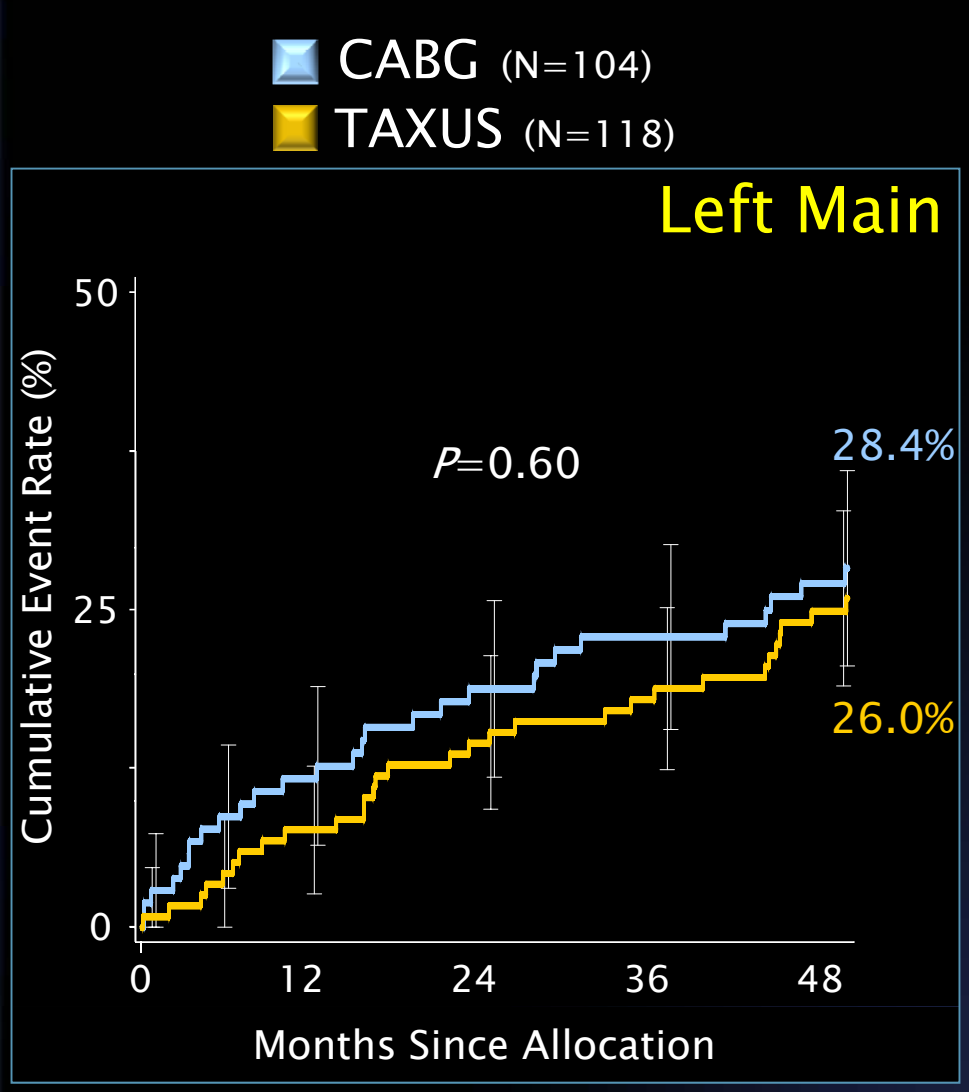
SYNTAX

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

Before 1 year*	1–2 years*	2–3 years*	3–4 years*
13.7% vs 15.8%	7.5% vs 10.3%	5.2% vs 5.7%	6.4% vs 8.3%
P=0.44	*P*=0.22	*P*=0.78	*P*=0.35

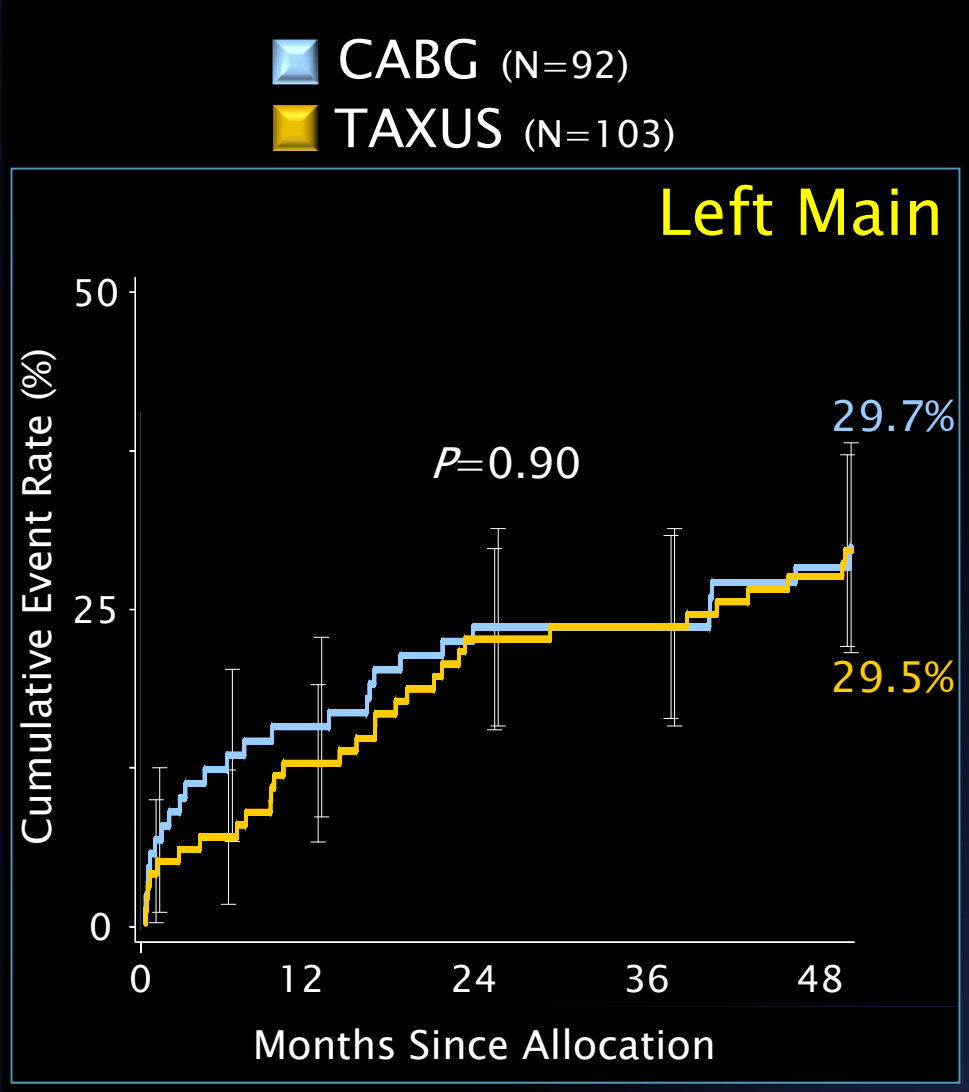


MACCE to 4 Years by SYNTAX Score Tercile *Low Scores (0–22)*



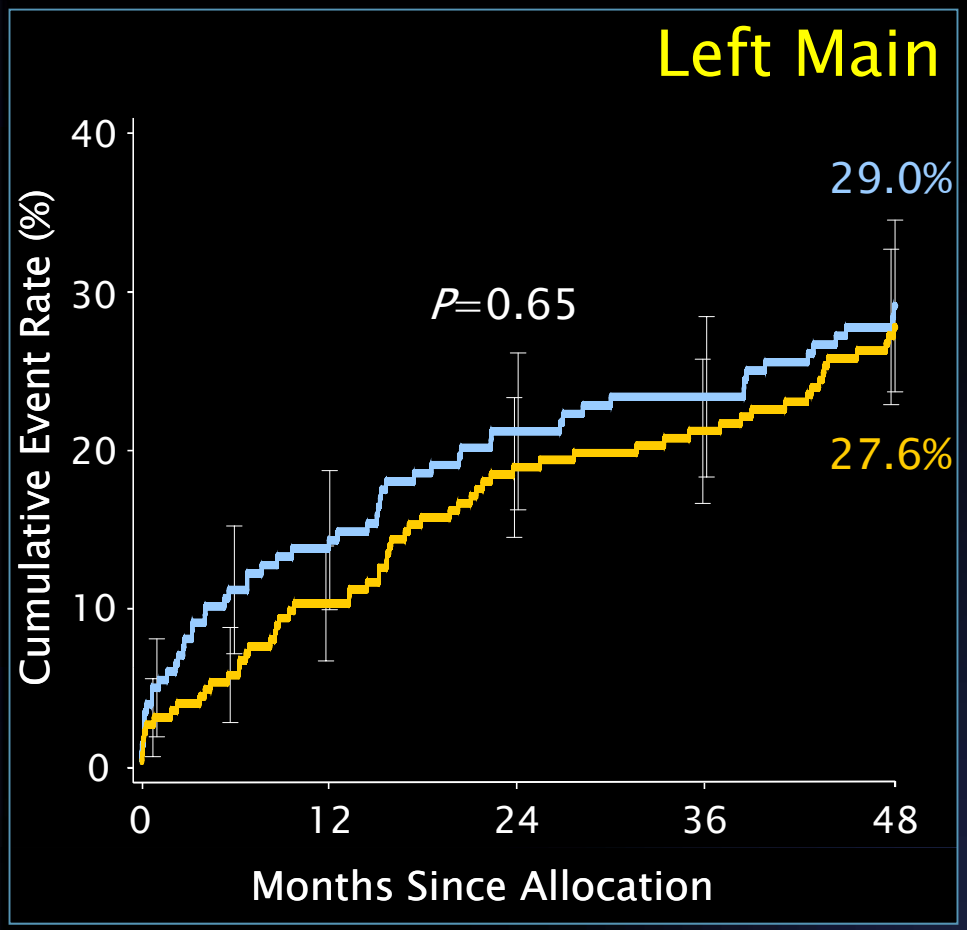
	CABG	PCI	*P* value
Death	9.2%	7.1%	0.54
CVA	4.1%	1.8%	0.28
MI	3.1%	4.3%	0.64
Death, CVA or MI	14.2%	12.3%	0.60
Revasc.	16.8%	18.2%	0.64

MACCE to 4 Years by SYNTAX Score Tercile *Intermediate Scores (23–32)*



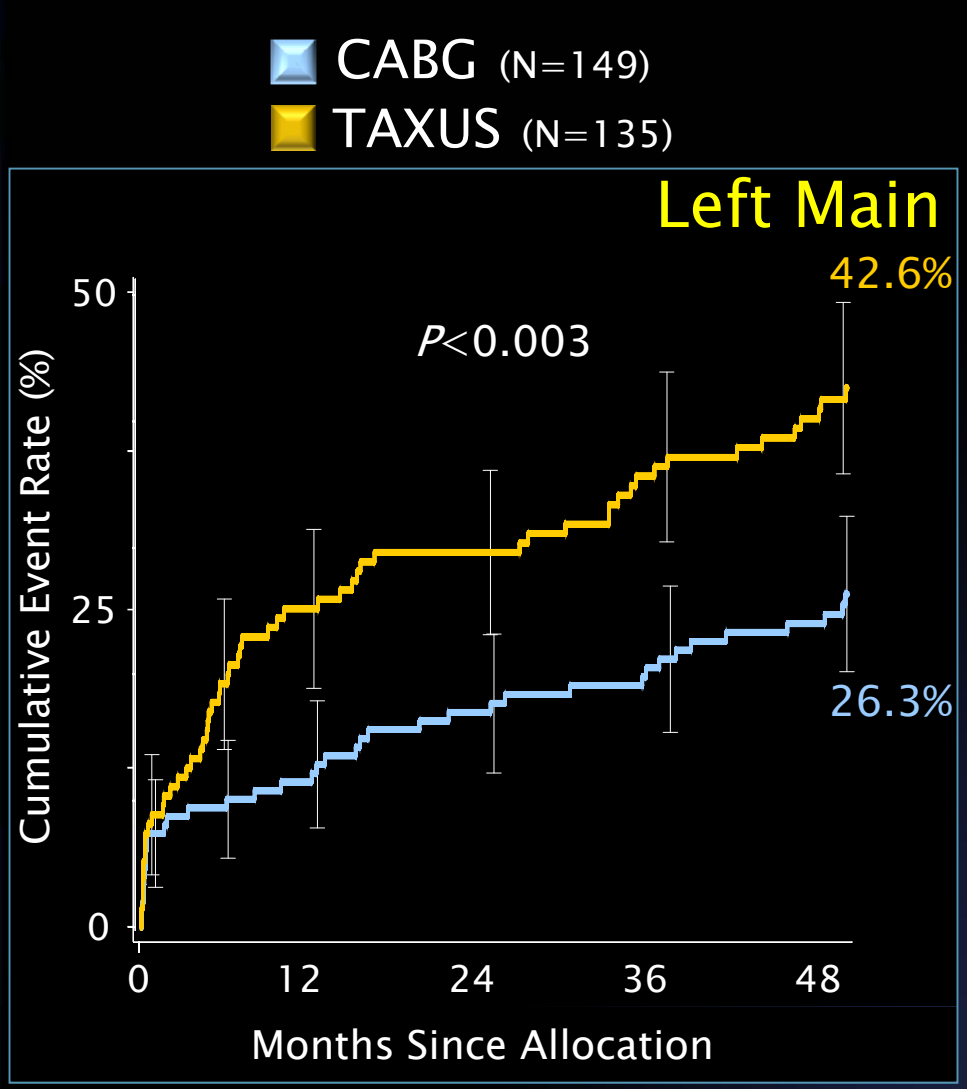
	CABG	PCI	*P* value
Death	14.7%	8.0%	0.12
CVA	3.6%	1.0%	0.23
MI	4.6%	6.0%	0.71
Death, CVA or MI	20.3%	14.8%	0.28
Revasc.	17.0%	20.2%	0.60

MACCE to 4 Years by SYNTAX Score Tercile *Low to Intermediate Scores (0–32)*



	CABG	PCI	*P* value
Death	11.8%	> 7.5%	0.12
CVA	3.9%	> 1.4%	0.11
MI	3.8%	< 5.1%	0.55
Death, CVA or MI	17.1%	> 13.5%	0.25
Revasc.	16.9%	< 19.1%	0.57

MACCE to 4 Years by SYNTAX Score Tercile *High Scores (≥33)*



	CABG	PCI	*P* value
Death	10.5%	17.9%	0.06
CVA	4.9%	1.6%	0.14
MI	6.1%	10.9%	0.18
Death, CVA or MI	18.5%	23.1%	0.33
Revasc.	11.8%	31.3%	<0.001

What Does SYNTAX *Not* Tell Us?

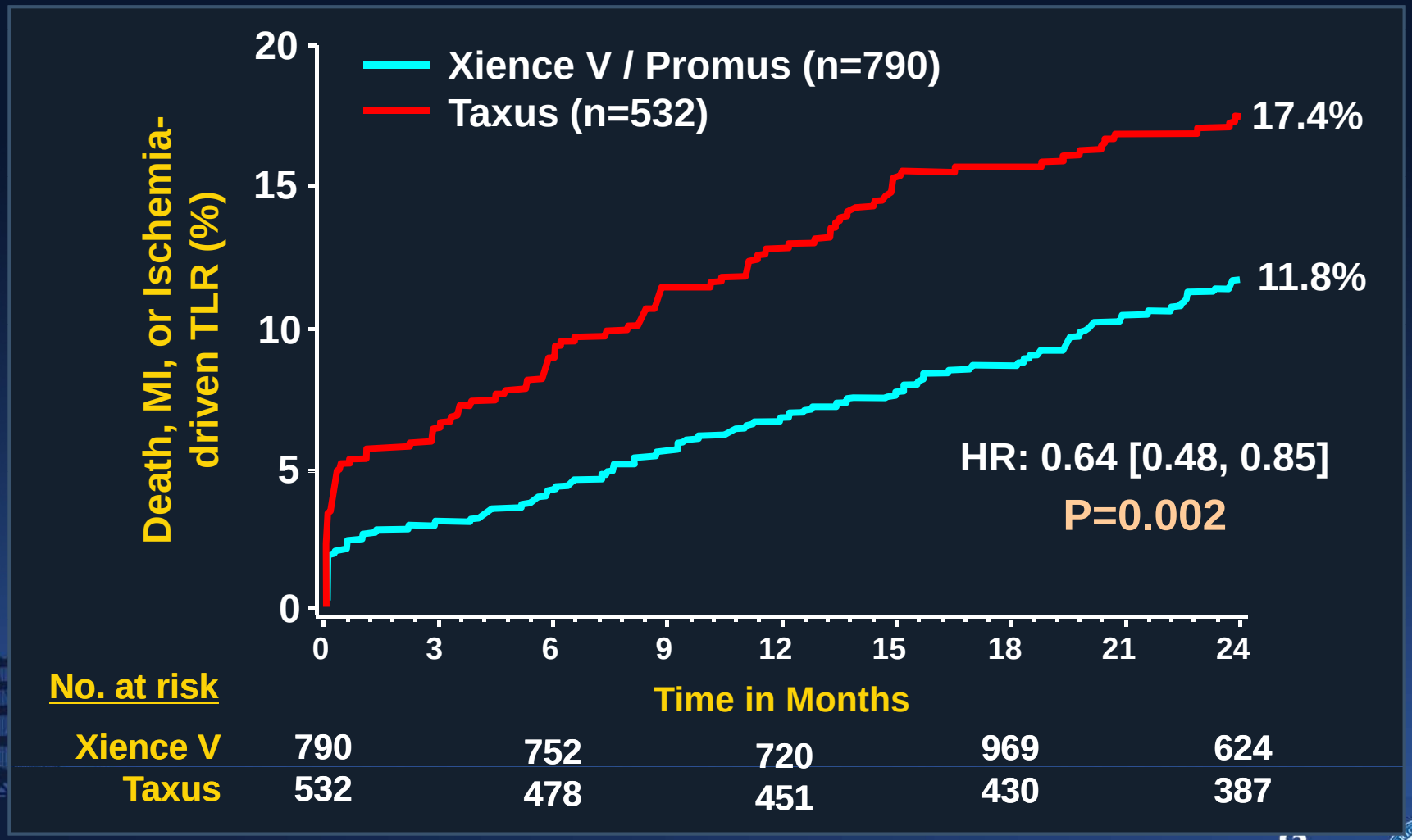
- Can PCI outcomes be improved by…..?
  - Use of better DES? (e.g. XIENCE V)
  - Use of better pharmacotherapy (e.g. bivalirudin)
  - IVUS/FFR? (used in <10% in SYNTAX)
  - More frequent staging? (14% in SYNTAX)
  - Avoidance of routine angiographic FU*?
- Can CABG outcomes be further improved?
- Is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

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

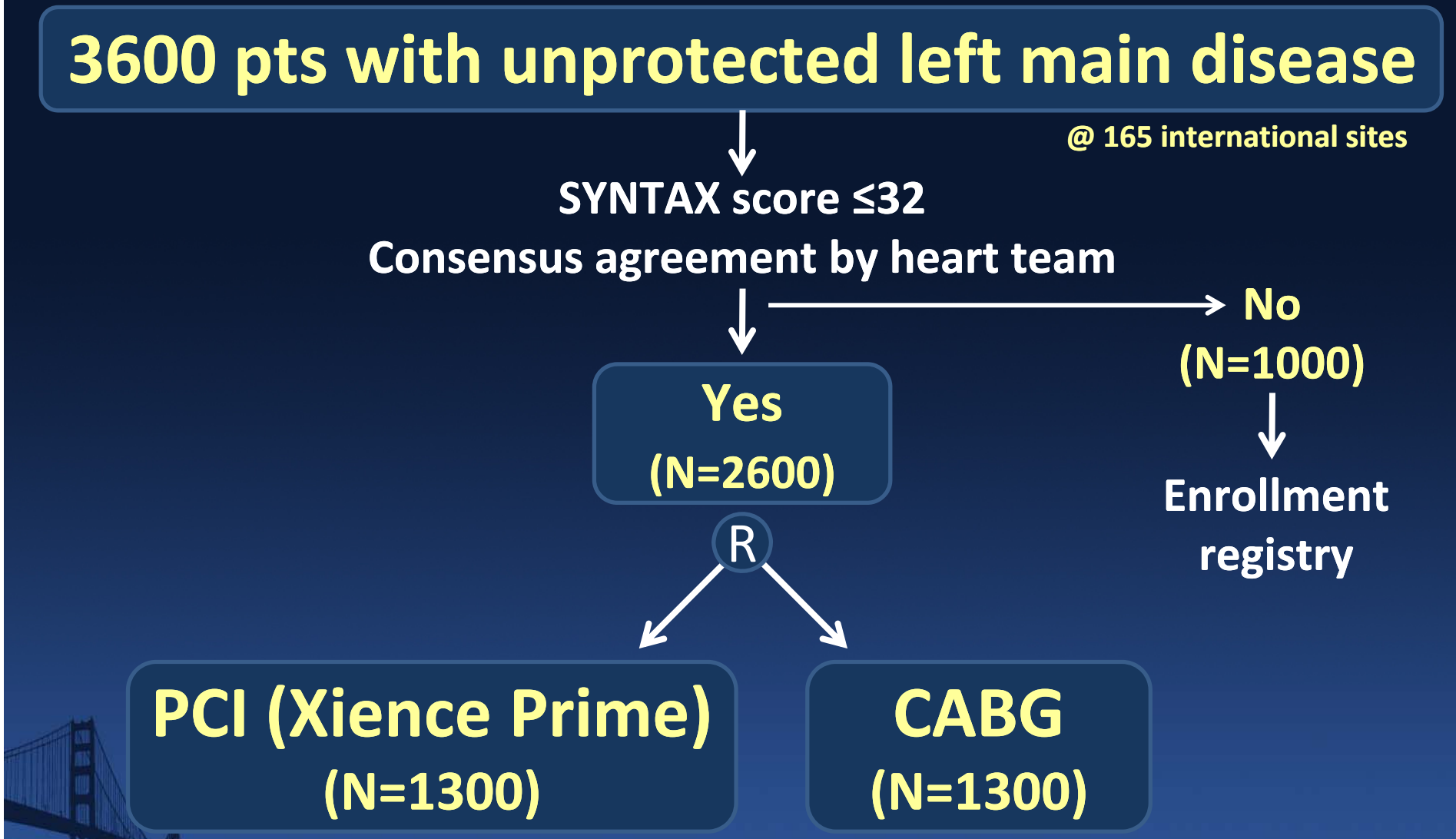
EES vs. PES: SPIRIT II, III, IV and COMPARE RCTs

Pooled database analysis – 2 year results

Patients with multivessel PCI (n=1,322)



EXCEL: Study Design



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

EXCEL: Inclusion Criteria

- Clinical and anatomic eligibility for both PCI and CABG by heart team consensus
- Silent ischemia, stable angina, unstable angina or recent MI
- 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

EXCEL: Principal 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
- Left main RVD <2.25 mm or >4.5 mm

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: Principal Endpoints

- **Primary endpoint: Death, MI, or stroke at 3 year FU - Powered for sequential noninferiority and superiority testing**
- Major secondary endpoints (powered):
  1. Death, MI, or stroke at 30 days
  2. Stroke at 30 days
  3. Unplanned repeat revascularization for ischemia at 3 years
- Additional secondary endpoint (powered):
  1. Death, MI, stroke or unplanned revascularization for ischemia at 3 years
- 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
- **Optimal Therapy Committee Chairs:**
  - PCI: Martin B. Leon
  - Surgery: David Taggart
  - Medical: Bernard Gersh
- **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
- **Sponsor:** Abbott Vascular (Kunal Sampat, lead)

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

EXCEL: Status

- EXCEL was designed and approved at this meeting 3 years ago
- ~160 sites from 16 countries have been chosen and are being initiated
- **As of April 22nd, 86 sites have been initiated, and 414 pts have been randomized!**