EXCEL

Evaluation of Xience Prime versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization

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The Cardiovascular Research Foundation

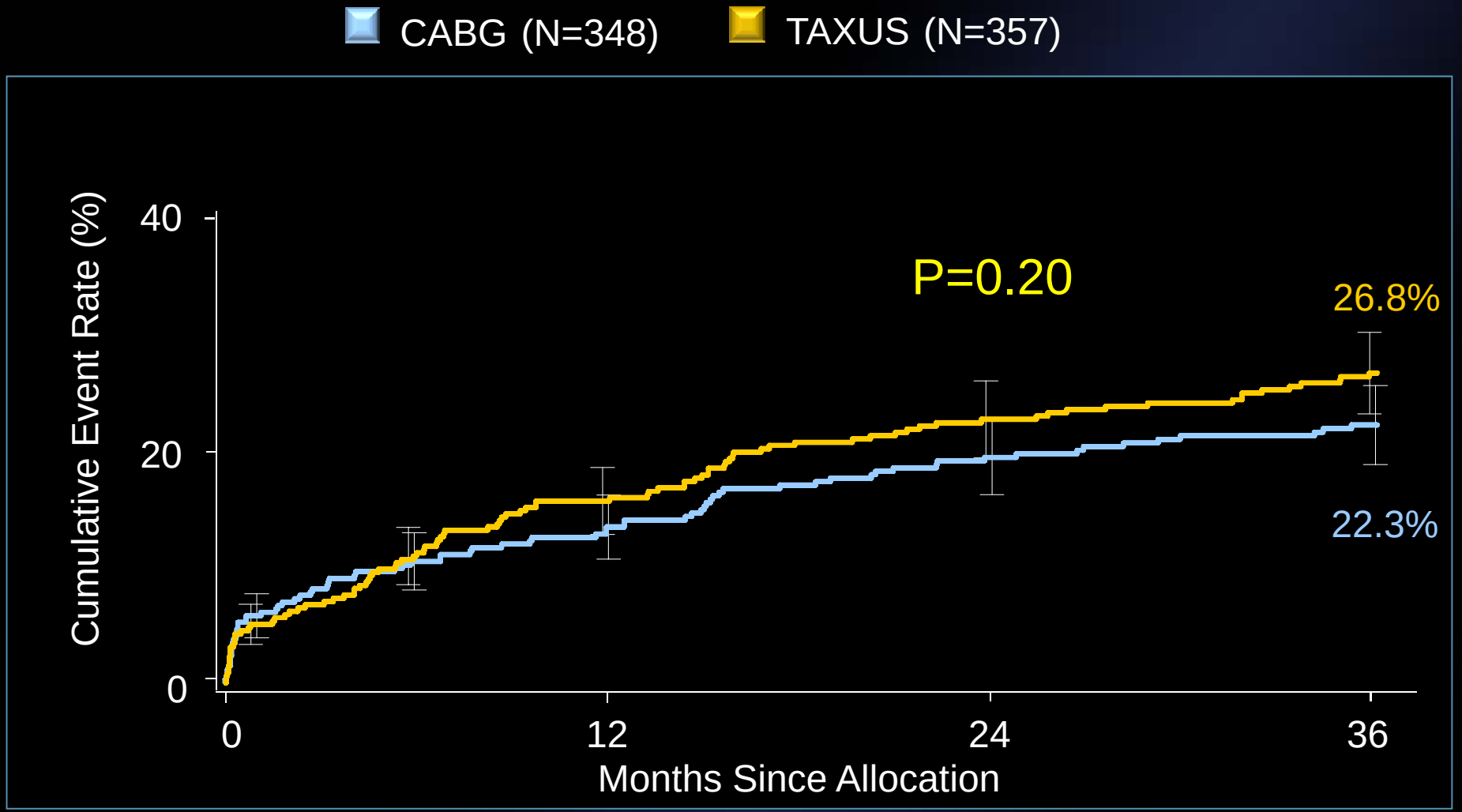
Disclosures

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

Consultant to Medtronic

MACCE to 3 Years

Left Main Subset

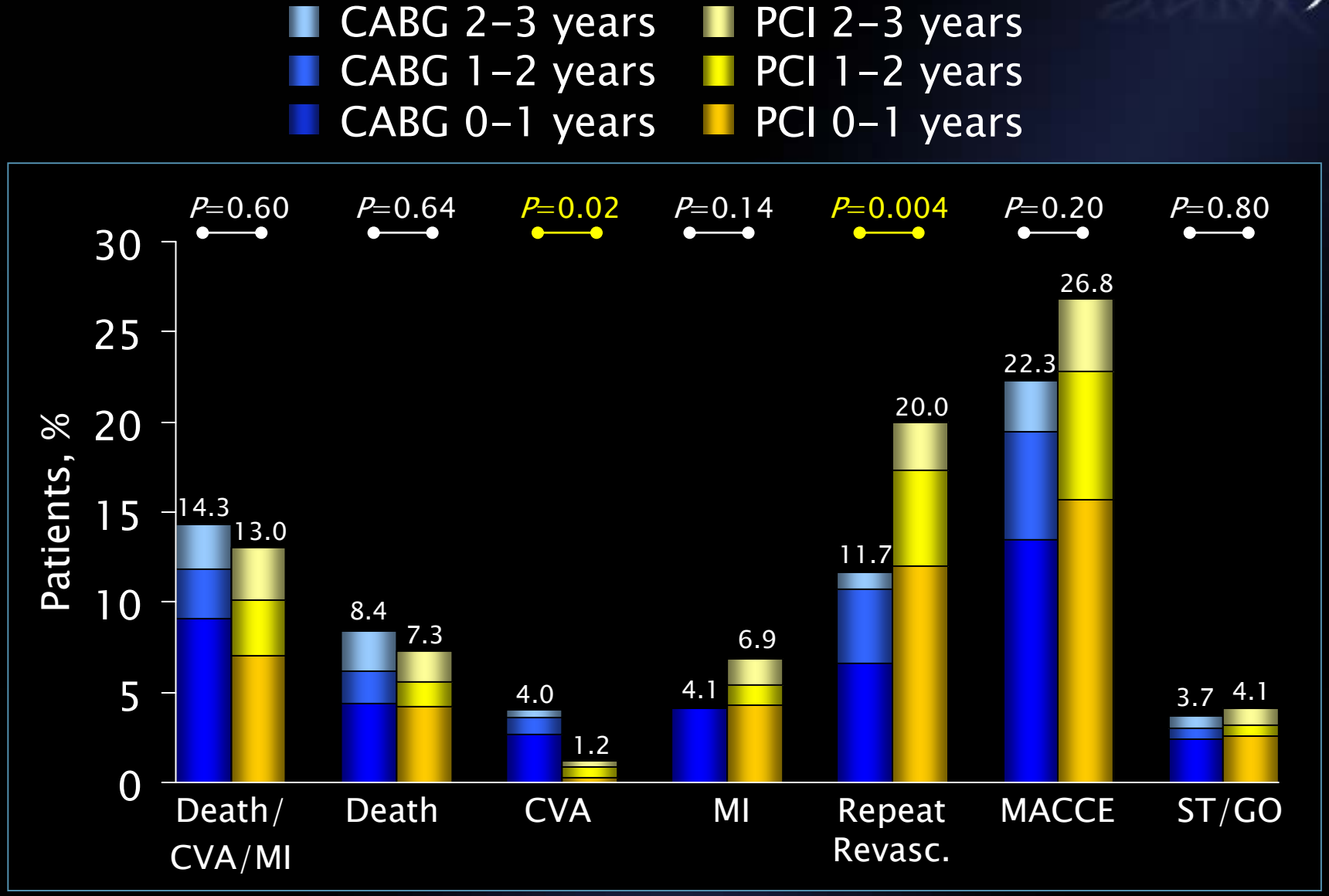


Cumulative KM Event Rate ± 1.5 SE;

Serruys PW. TCT2010

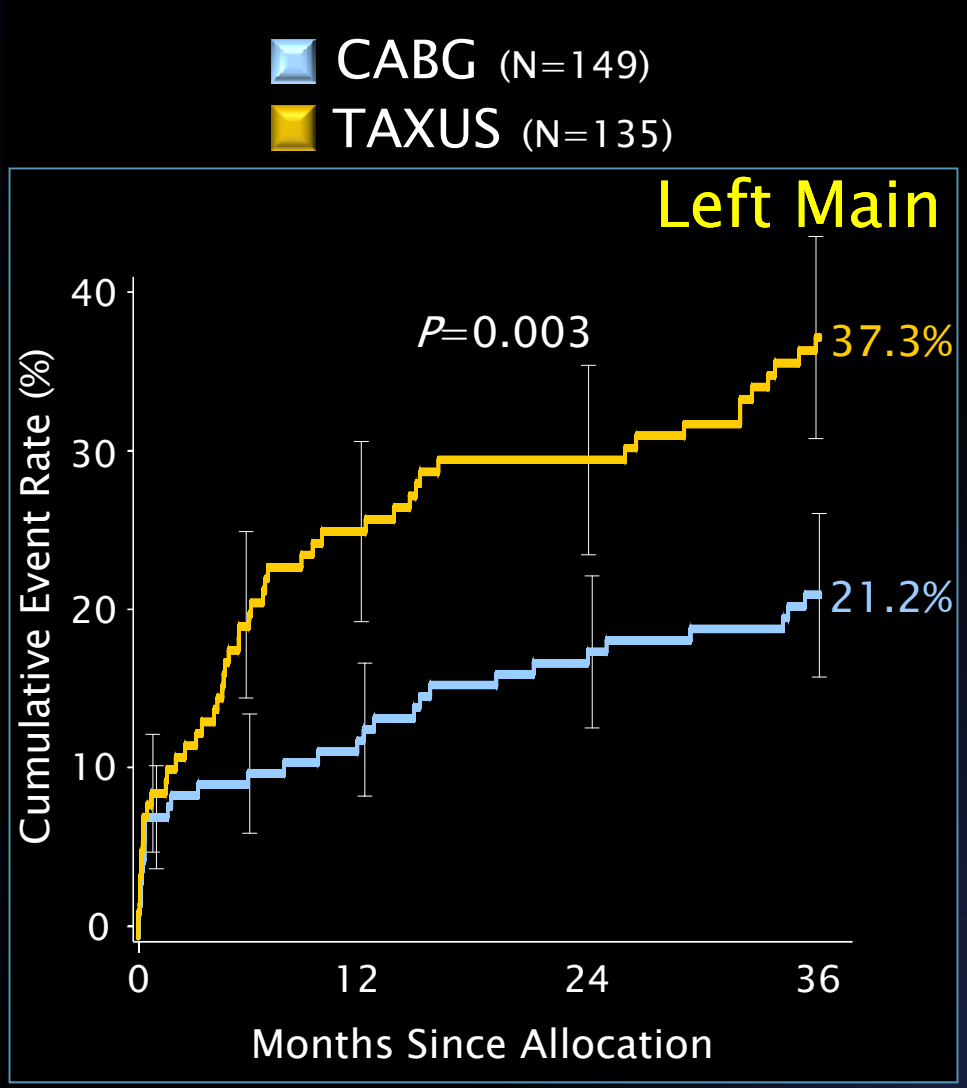
ITT population

3-Year Outcomes: *Left Main Subset*



Serruys PW. TCT2010

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

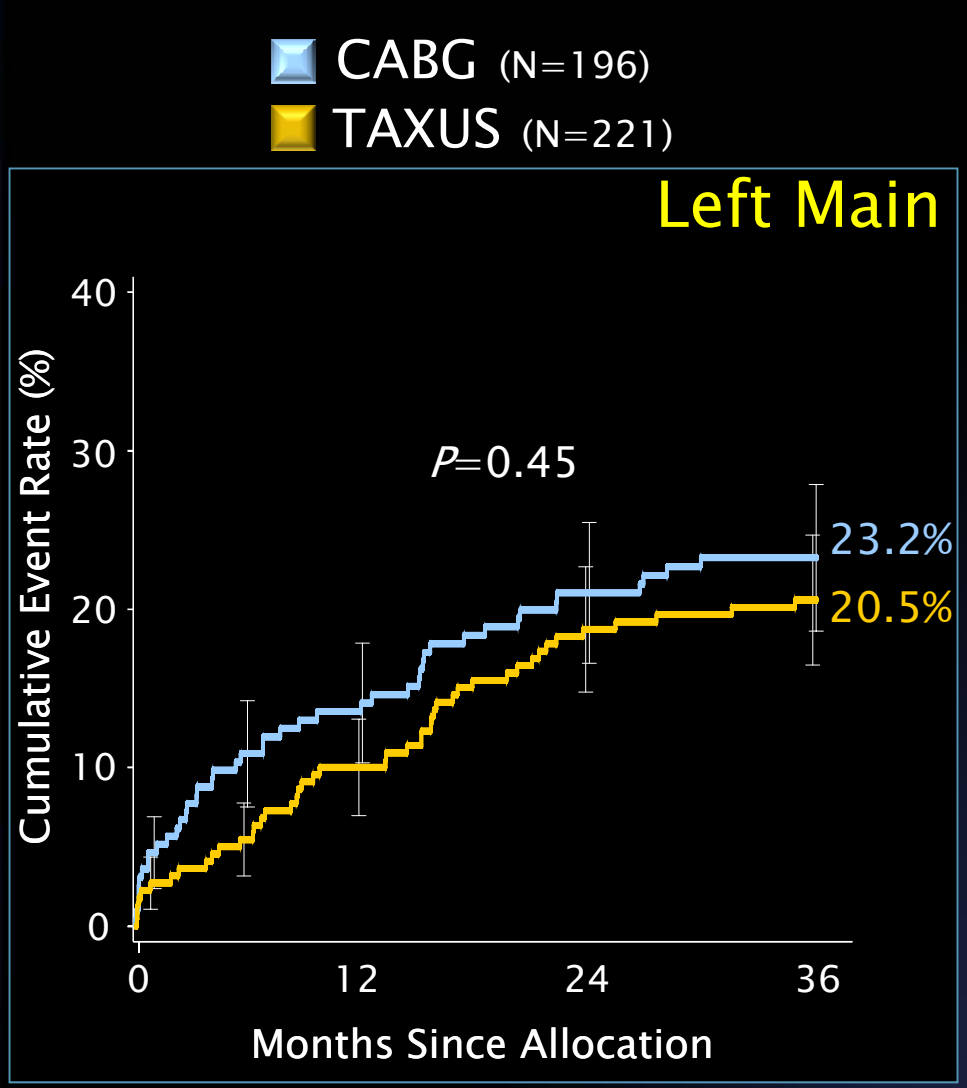


	CABG	PCI	*P* value
Death	7.6%	13.4%	0.10
CVA	4.9%	1.6%	0.13
MI	6.1%	10.9%	0.18
Death, CVA or MI	15.7%	20.1%	0.34
Revasc.	9.2%	27.7%	<0.001

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

Site-reported Data; ITT population

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

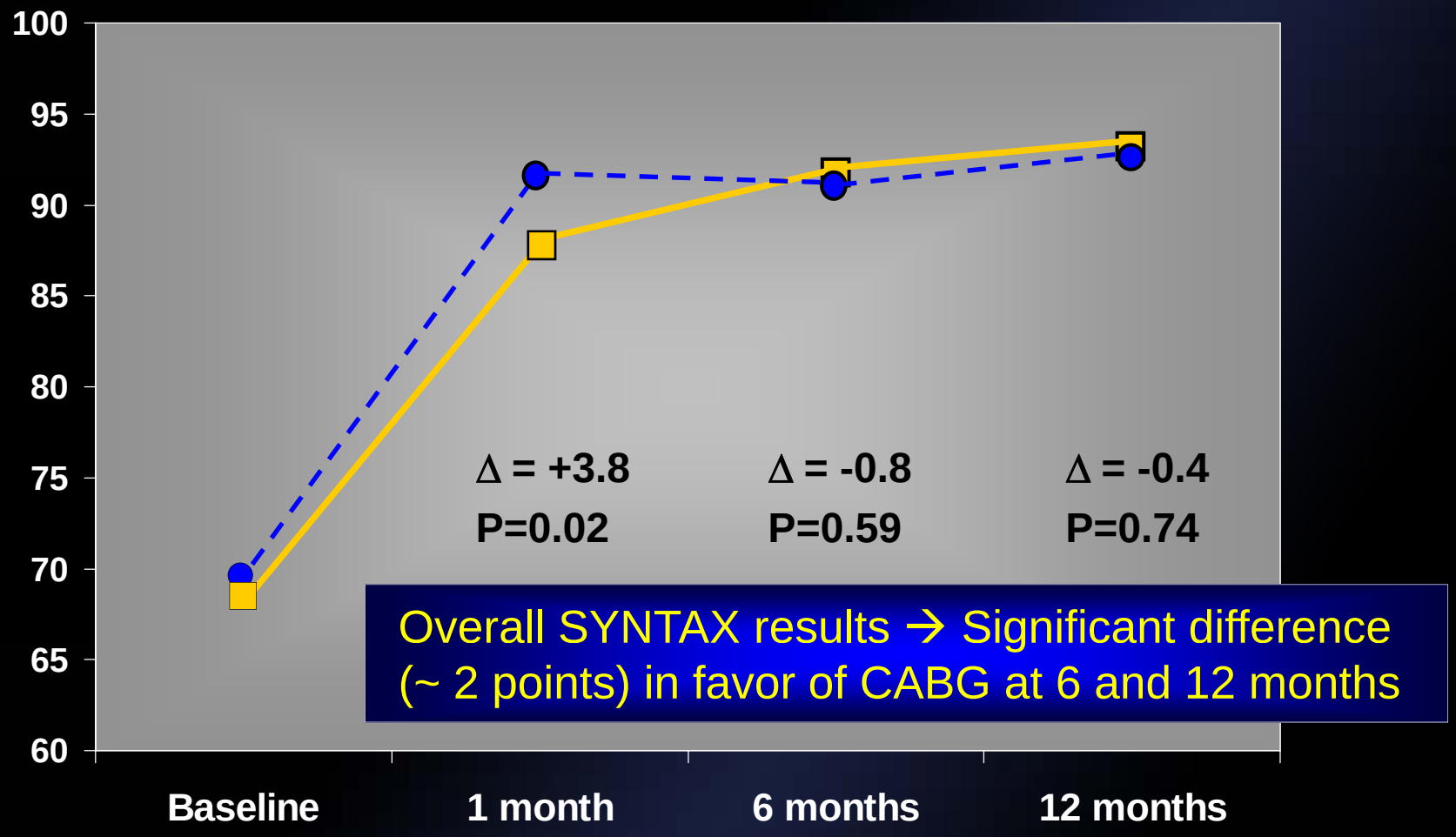


	CABG	PCI	*P* value
Death	9.0%	3.7%	0.02
CVA	3.3%	0.9%	0.09
MI	2.6%	4.6%	0.33
Death, CVA or MI	13.2%	8.7%	0.12
Revasc.	13.7%	15.7%	0.61

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

Site-reported Data; ITT population

LM Subset – Primary QOL Endpoint: SAQ-Angina Frequency

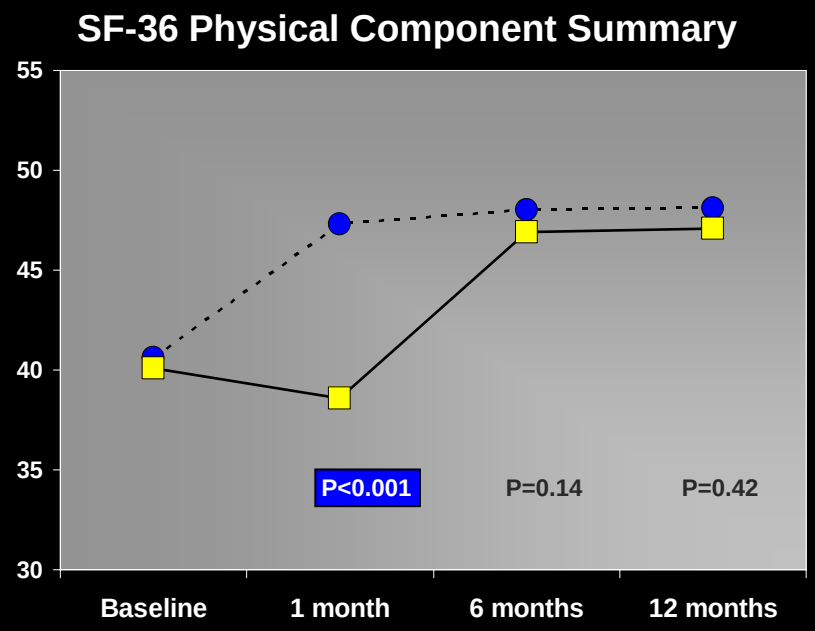


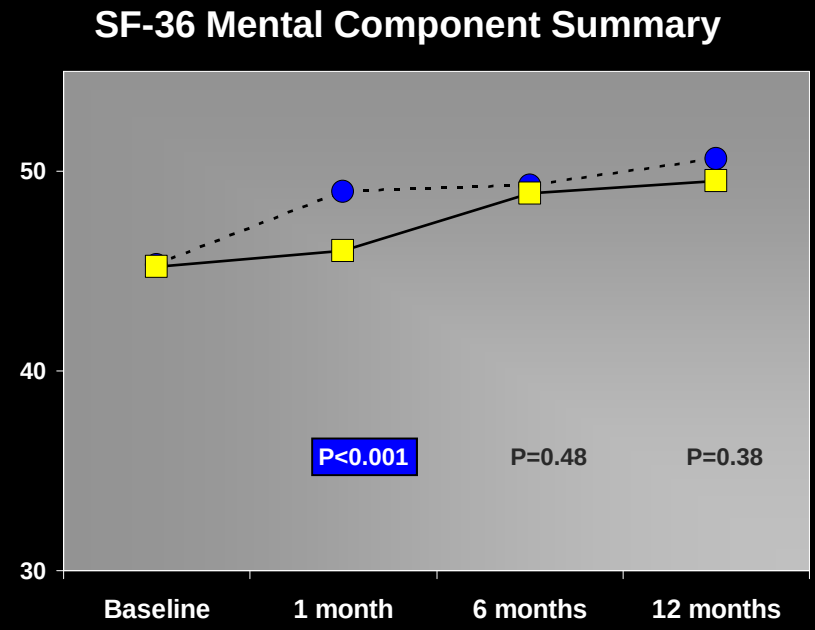
Overall SYNTAX results → Significant difference (~ 2 points) in favor of CABG at 6 and 12 months

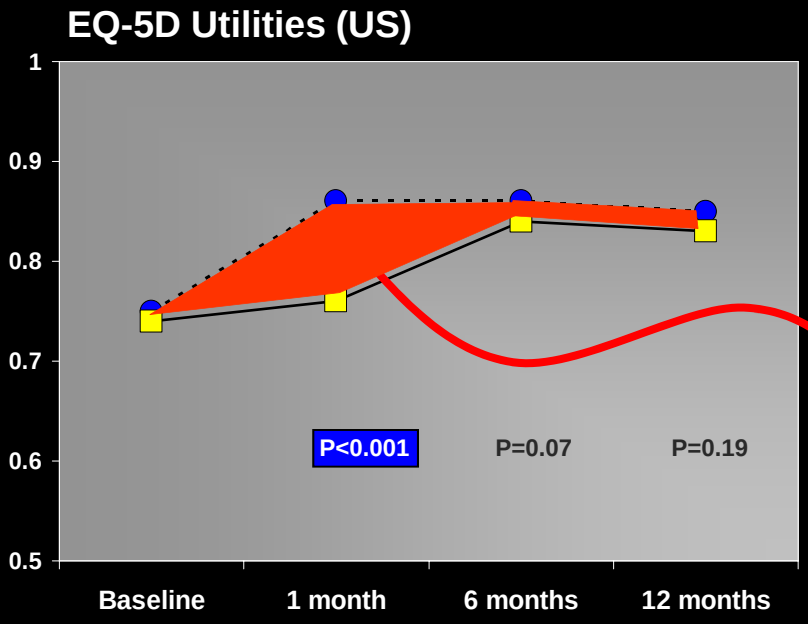
Cohen DJ. LM Summit NYC Feb. 2011.

LM Subset – Generic QOL and Utilities

Left Main







PCI

CABG

Quality Adjusted Life Years

Δ = 0.03 (P<0.01)

Cohen DJ. LM Summit NYC Feb. 2011.

LM Subset – Total 1-Year Costs

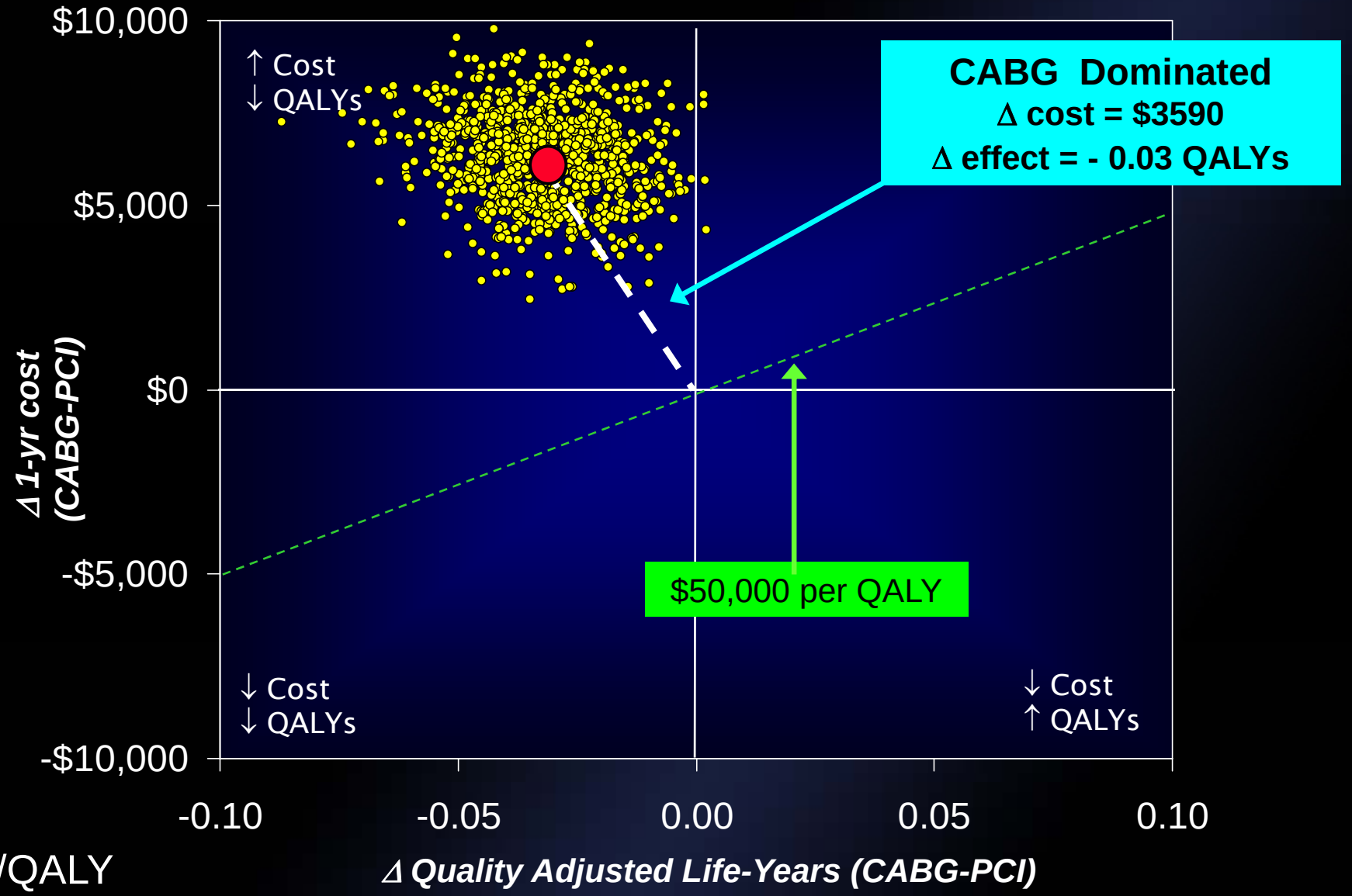
Left Main SYNTAX

Cohen DJ. LM Summit NYC Feb. 2011.

Cost-Effectiveness of CABG vs. PCI*

Left Main Subgroup

Left Main SYNTAX



*$/QALY

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

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

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

What Does SYNTAX Not Tell Us?

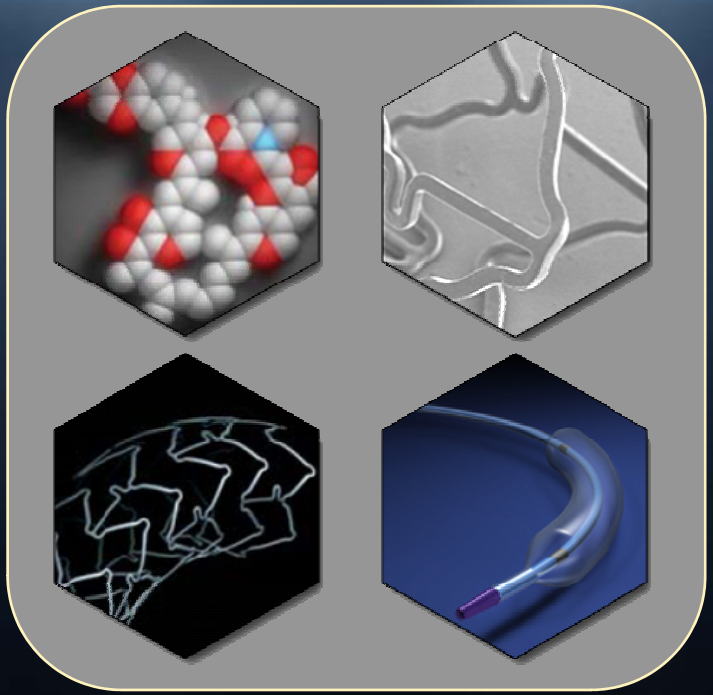
- **Can PCI outcomes be improved by…..?**
  - Use of better DES? (e.g. XIENCE V)
  - Use of better pharmacotherapy (e.g. bivalirudin)
  - IVUS/FFR? (used in <10% in SYNTAX)
  - More frequent staging? (14% in SYNTAX)
  - Avoidance of routine angiographic FU*?
- **Can CABG outcomes be further improved?**
- **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

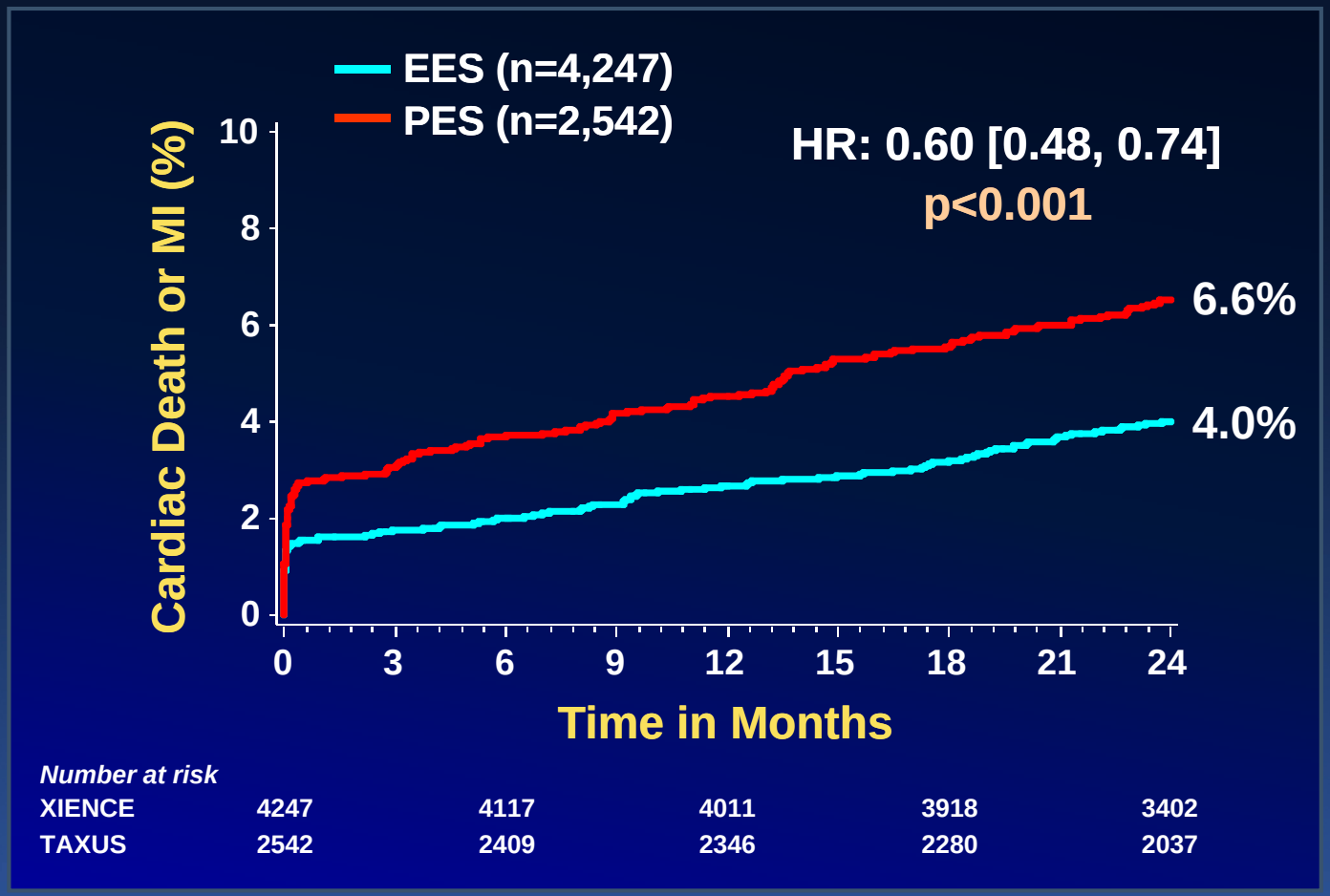


Durable
Fluorinated
Copolymer

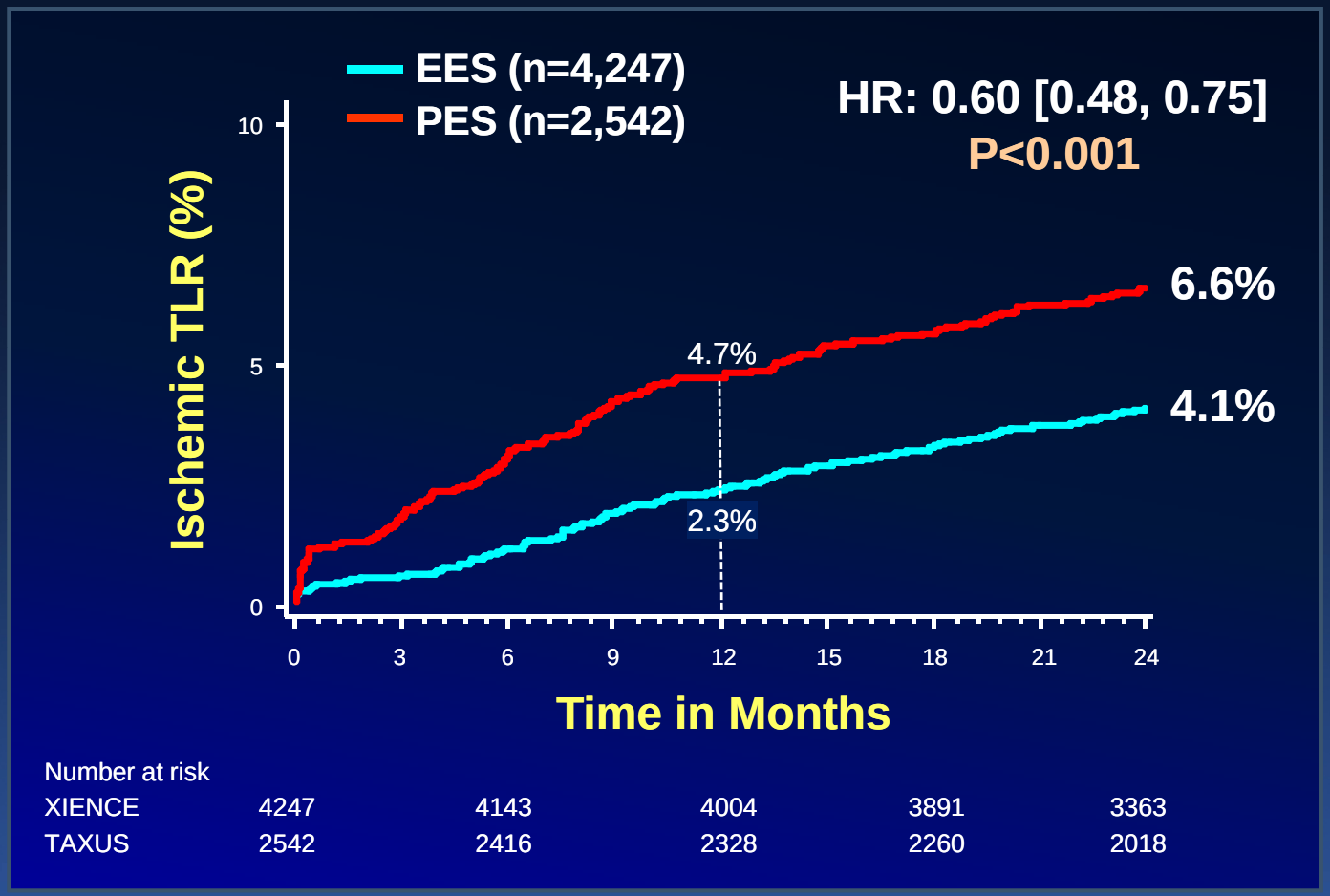
ML VISION
Stent Delivery
System

EES vs. PES
SPIRIT and COMPARE
Clinical Trials

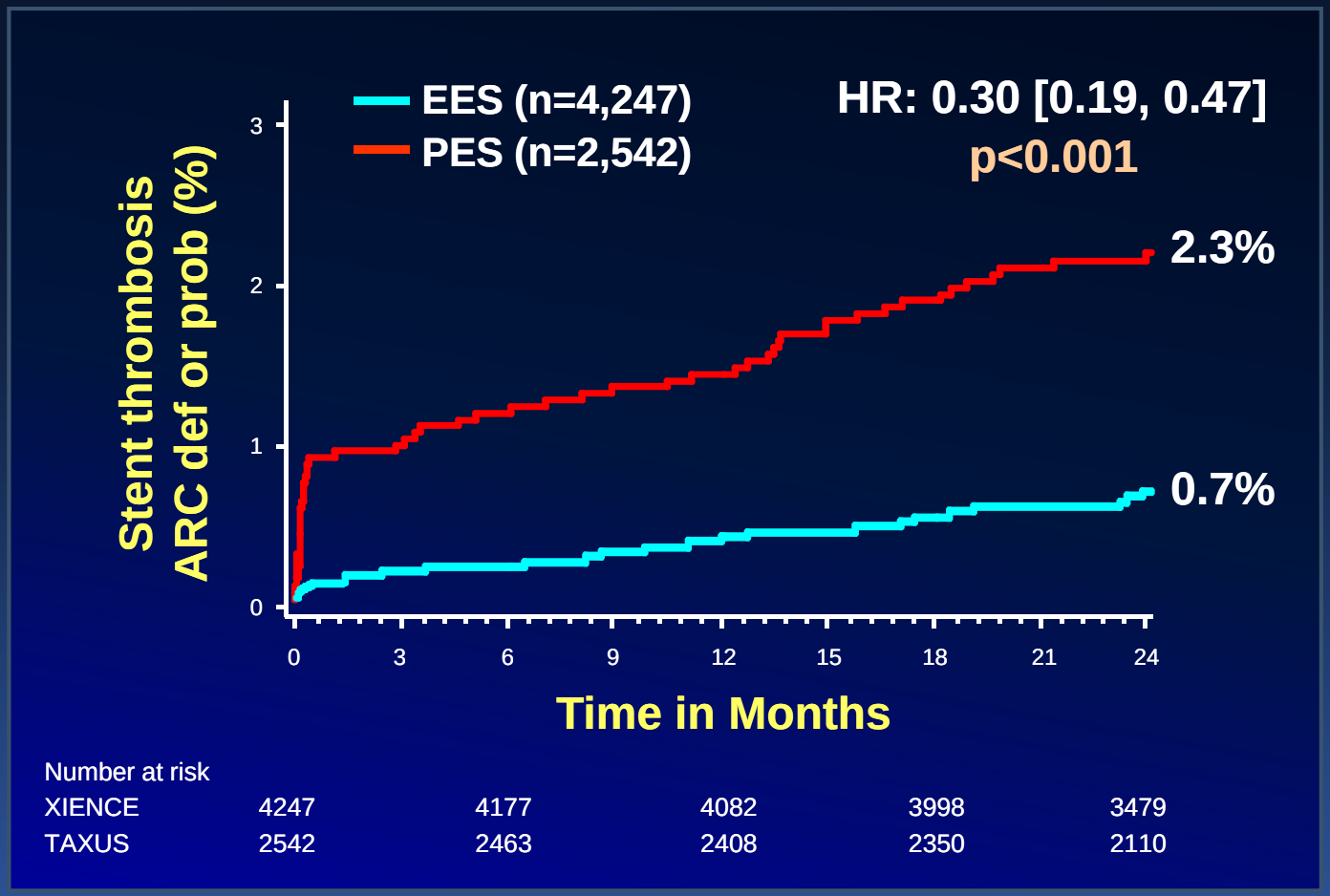
SPIRIT II, III, IV and COMPARE trials
Pooled database analysis (n=6,789)
Cardiac death or MI



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)



The XIENCE Prime Stent

Enhanced stent
New SDS

-More flexible and deliverable

- Shorter balloon tapers

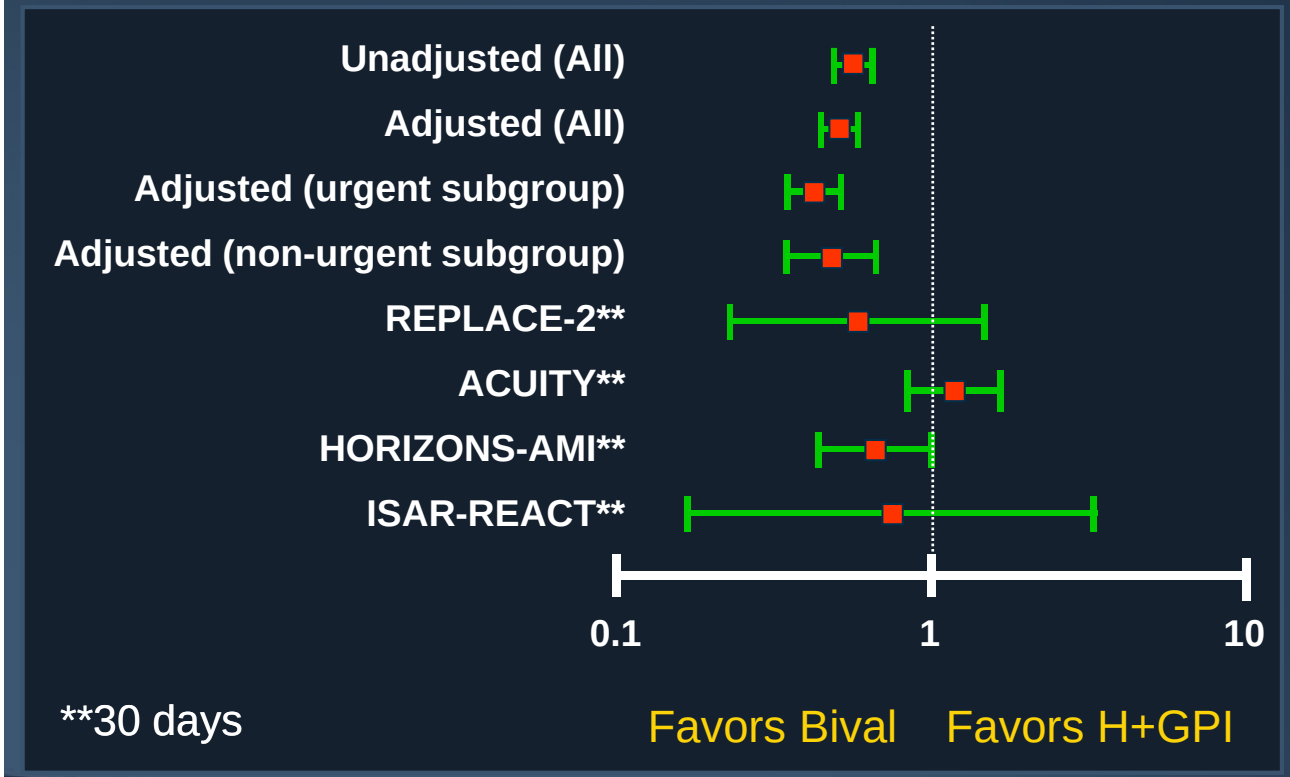
- Higher RBP

Bivalirudin vs. Heparin + GPIIb/IIIa

N = 127,185 pts undergoing PCI 2003-2006

(Premier Perspective Database, ~1/6th of all US hosps; bival in 26%)

In-hospital death



Bivalirudin	H+GPI
0.8%	2.1%

Adjusted HR [95%CI]

0.51 [0.44 – 0.60]

49% ⇩ Death

Rassen JA et al. EHJ 2009;On-line

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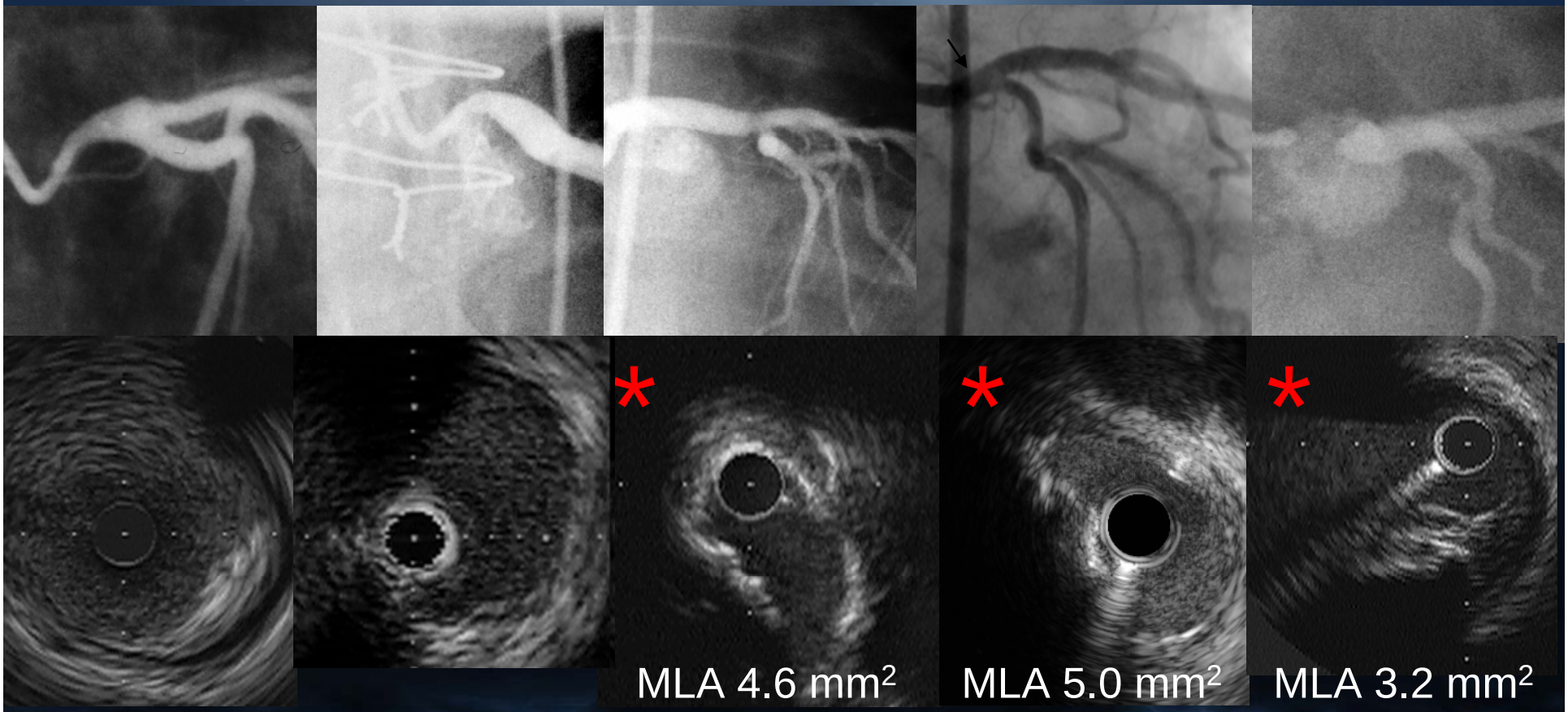
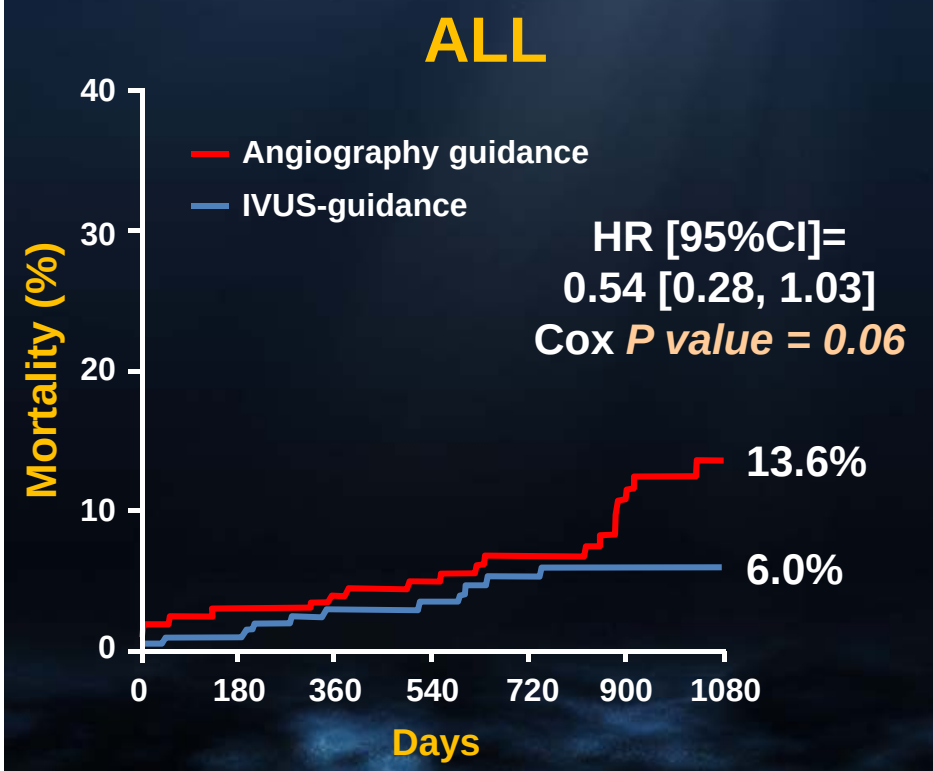
Which of these LMCA lesions are significant and therefore should be treated? And which are not??

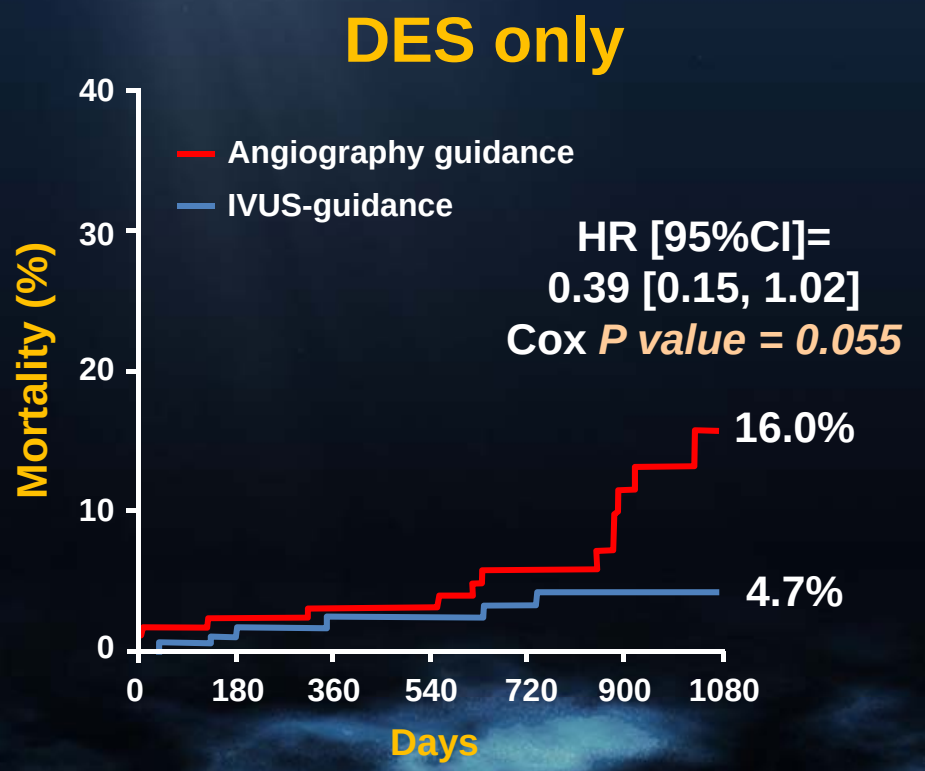


LMCA IVUS usually shows either insignificant or critical disease

Impact of IVUS Guidance on Left Main Stenting: MAIN-COMPARE

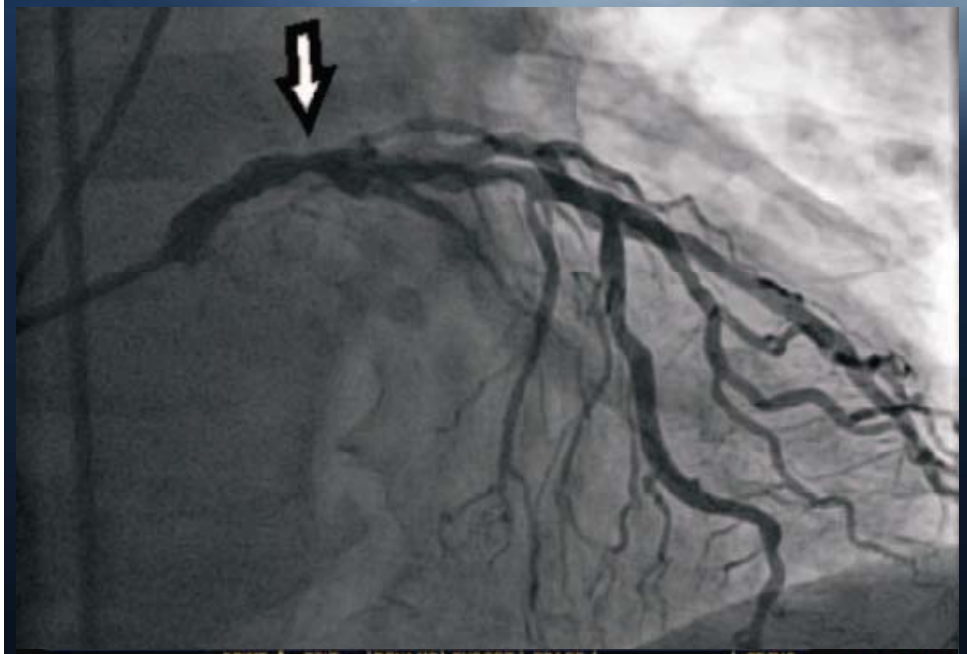
IVUS guidance was used in 756/975 pts undergoing unprotected LM stenting. **Propensity matching was used to create 201 matched pairs (145 DES pairs).**

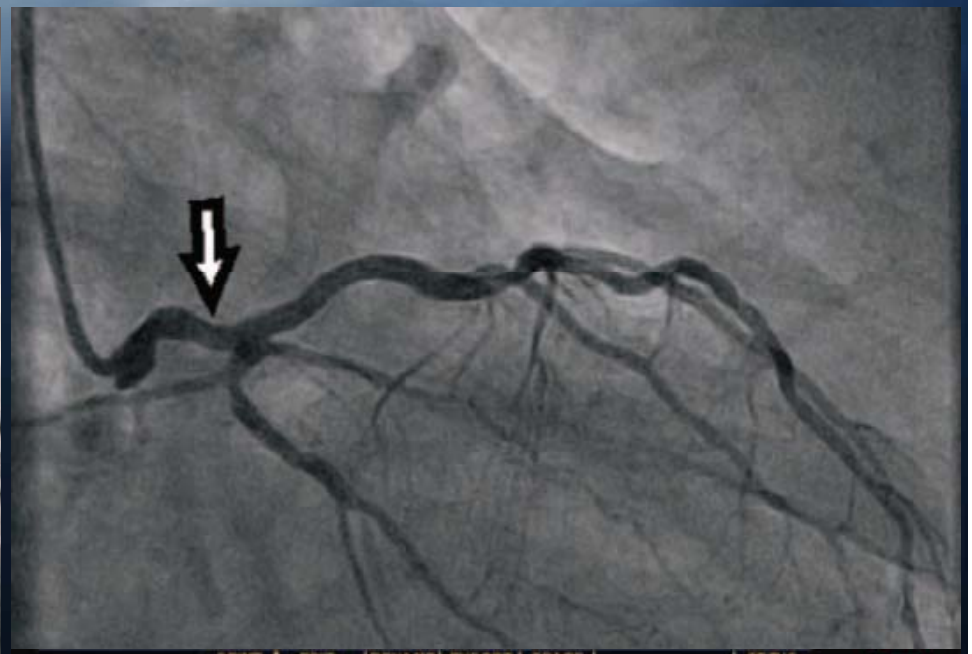


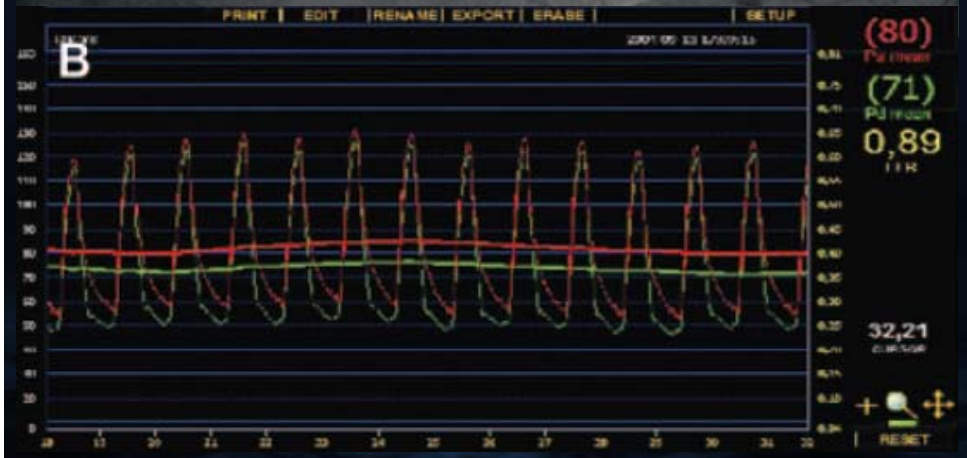


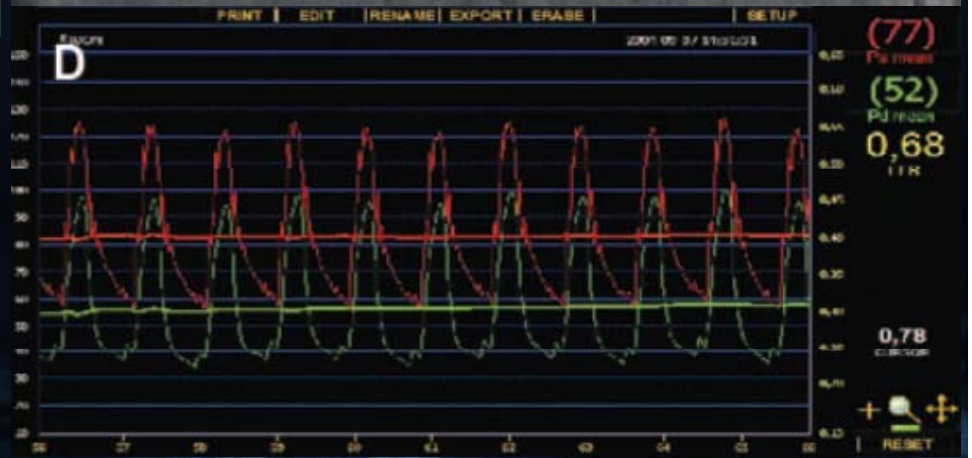
Park SJ et al. *Circ CV Int* 2009;2:167-177

Correlation between angiography and FFR in unprotected left main disease





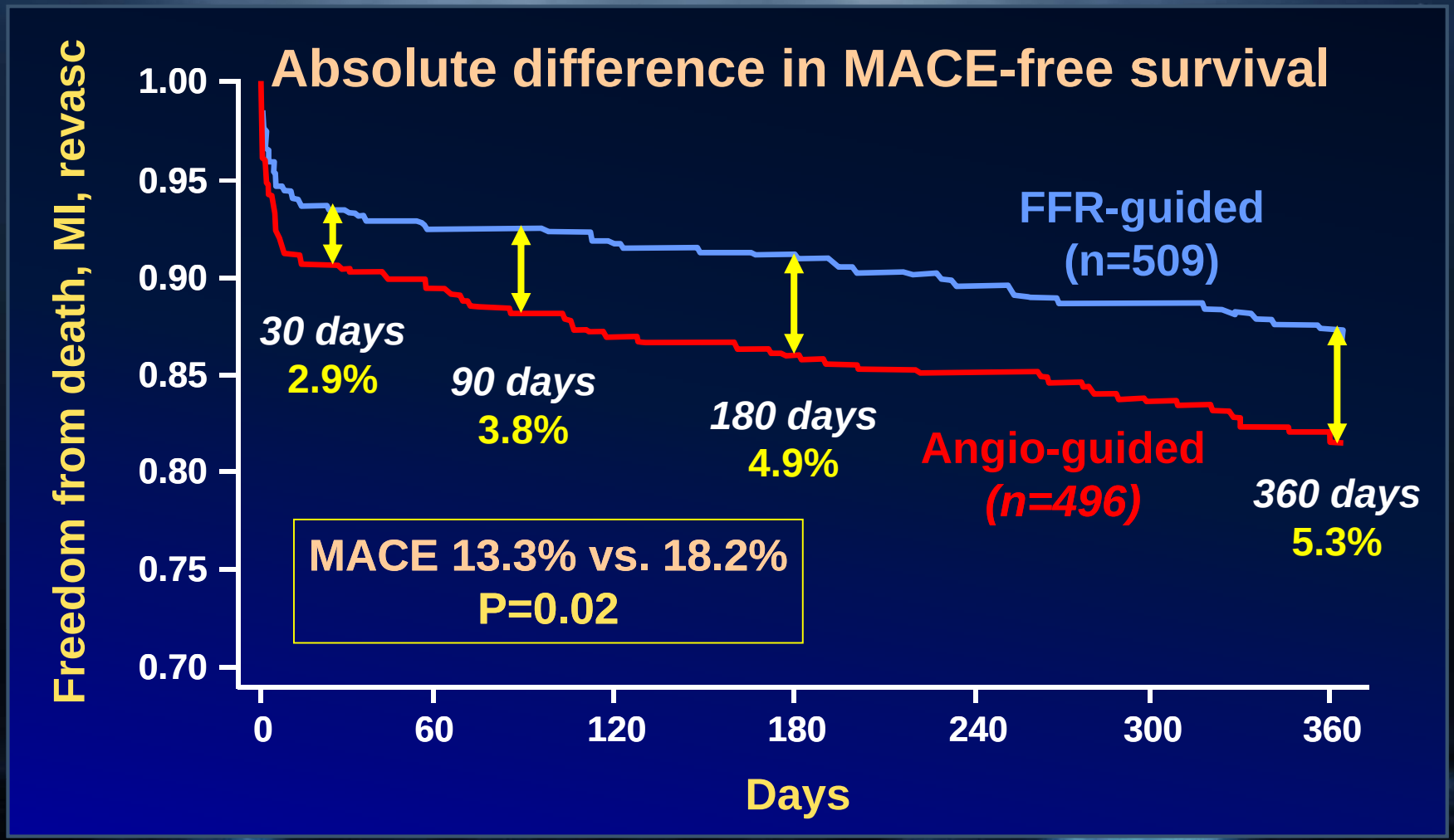




Hamilos M et al. Circulation. 2009;120:1505-1512.

FAME: Primary Endpoint

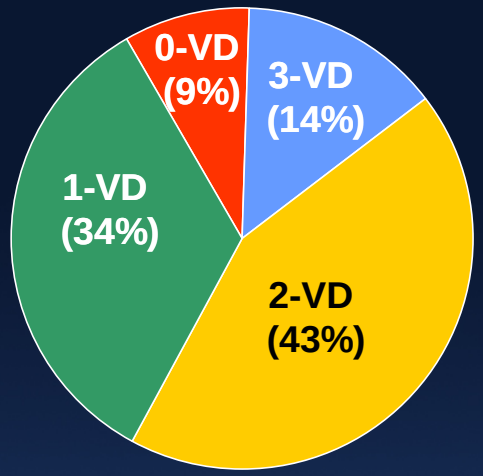
1005 pts with MVD undergoing PCI with DES were randomized to FFR-guided vs. angio-guided intervention



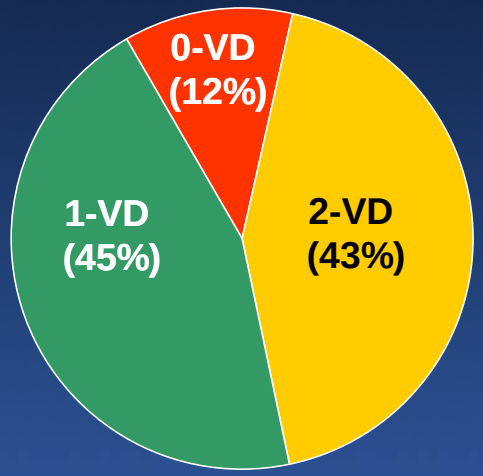
Tonino PAL et al. NEJM 2009;360:213–24

FAME:
Angiographic vs. Functional NDV

Pts with angiographic 3VD
(%DS >50%)
N=115

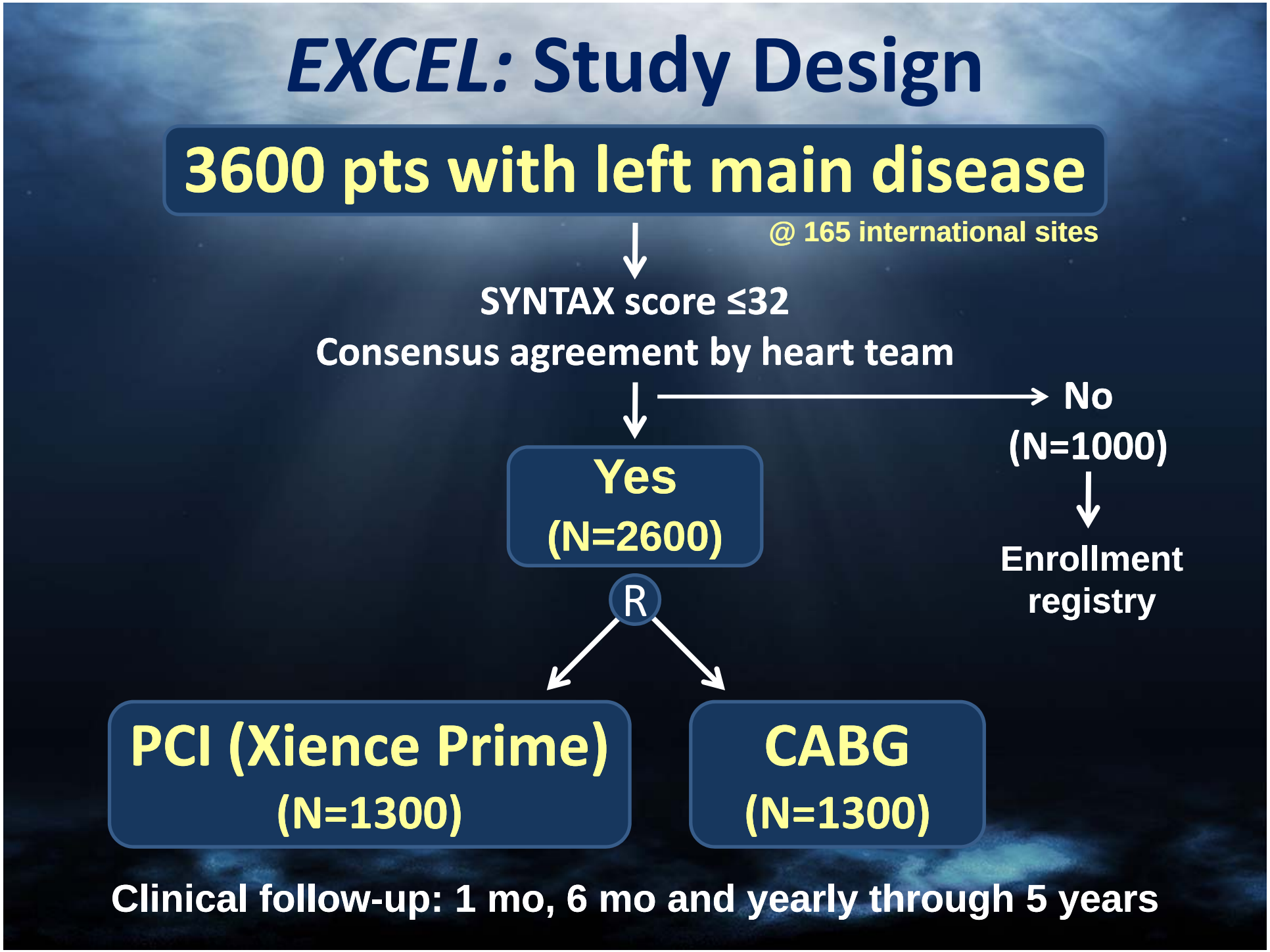


Pts with angiographic 2VD
(%DS >50%)
N=394



Tonino PAL et al. *JACC* 2010;55:2816–21

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

PCI Medications

- **Aspirin:** Preloading 300 to 325 mg at least 2 hrs before the PCI is mandatory (even if on chronic ASA).
- **ADP antagonist:** Preloading is mandatory (even if on chronic ADP antagonist).
  - Clopidogrel 600 mg >6 hrs before PCI, or 300mg >12 hrs before PCI; or
  - Prasugrel 60 mg >1 hr before PCI; or
  - Ticagrelor with dosing per labeling >1 hr before PCI
- **Statin:** Mandatory, with first dose at least 12 hours before PCI
  - Atorvastatin 80 mg daily or rosuvastatin 40 mg daily
- **Procedural anticoagulation**: Bivalirudin (recommended), UFH or LMWH; GPIIb/IIIa is discouraged

PCI Procedure: Highlights

- **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: 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!