The EXCEL Trial
Design, Status, and Timelines

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TCT2011

CARDIOVASCULAR RESEARCH FOUNDATION
a passion for innovation

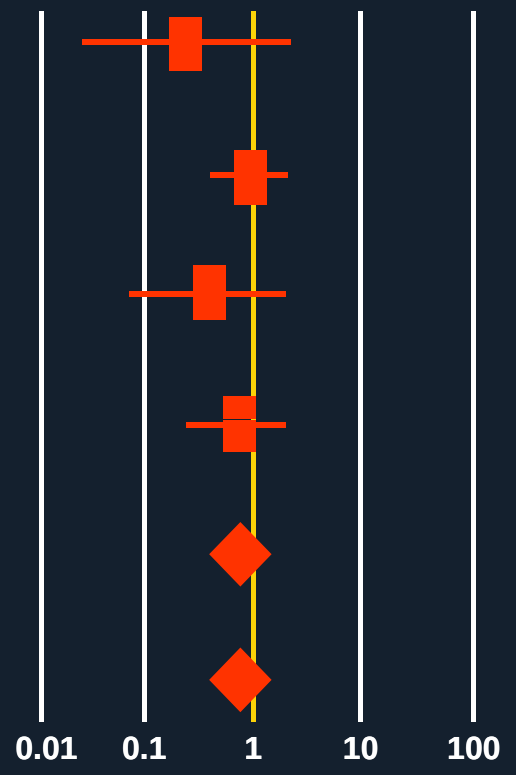
PCI vs. CABG for Left Main Disease
Meta-analysis of 4 RCTs, 1,611 Patients

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%

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

PCI vs. CABG for Left Main Disease
Meta-analysis of 4 RCTs, 1,611 Patients
1-Year Death

	PCI	CABG	OR (95%CI)	*p*-Value
LEMANS	1/52	4/53	0.24 (0.03-2.23)	0.21
SYNTAX left main	15/355	15/336	0.94 (0.45-1.96)	0.88
Boudriot et al.	2/100	5/101	0.39 (0.07-2.07)	0.27
PRECOMBAT	6/300	8/300	0.75 (0.26-2.17)	0.59
Fixed effects estimate	3.0% (24/807)	4.1% (32/790)	0.74 (0.43-1.28)	0.29
Random effects estimate			0.74 (0.43-1.28)	0.29

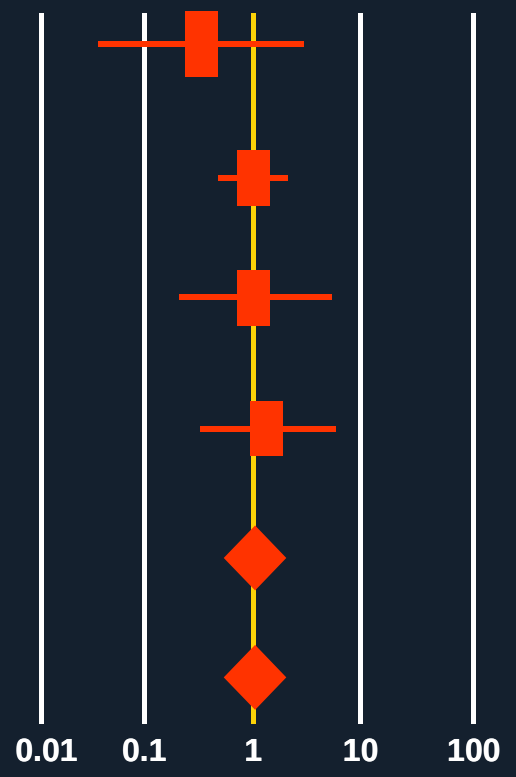


I^2=0%

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

PCI vs. CABG for Left Main Disease
Meta-analysis of 4 RCTs, 1,611 Patients
1-Year MI

	PCI	CABG	OR (95%CI)	*p*-Value
LEMANS	1/52	3/53	0.33 (0.03-3.25)	0.34
SYNTAX left main	15/355	14/336	1.02 (0.48-2.14)	0.97
Boudriot et al.	3/100	3/101	1.01 (0.20-5.13)	0.99
PRECOMBAT	4/300	3/300	1.34 (0.30-6.03)	0.71
Fixed effects estiamate	2.8% (23/807)	2.9% (23/790)	0.98 (0.54-1.78)	0.95
Random effects estimate			0.98 (0.54-1.78)	0.95

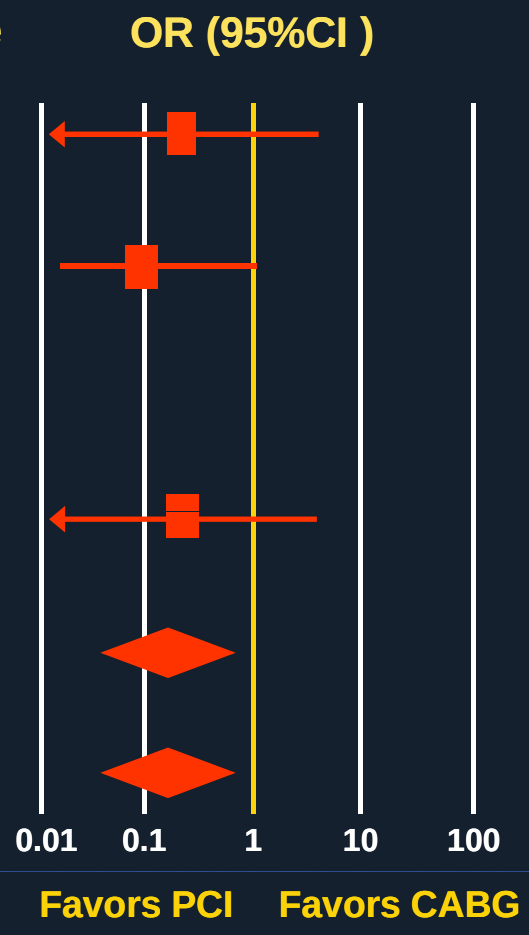


I^2=0%

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

PCI vs. CABG for Left Main Disease
Meta-analysis of 4 RCTs, 1,611 Patients
1-Year Stroke

	PCI	CABG	OR (95%CI)	*p*-Value
LEMANS	0/52	2/53	0.20 (0.01-4.09)	0.30
SYNTAX left main	1/355	8/336	0.12 (0.01-0.93)	0.04
Boudriot et al.				
PRECOMBAT	0/300	2/300	0.20 (0.01-4.16)	0.30
Fixed effects estiamate	0.1% (1/707)	1.7% (12/689)	0.15 (0.03-0.67)	0.01
Random effects estimate			0.15 (0.03-0.67)	0.01

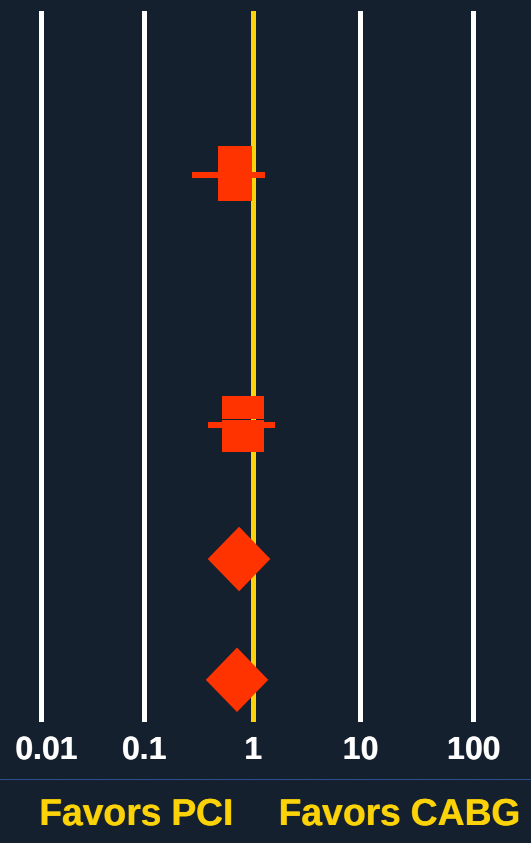


I^2=0%

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

PCI vs. CABG for Left Main Disease
Meta-analysis of 4 RCTs, 1,611 Patients
1-Year Death, MI or Stroke

	PCI	CABG	OR (95%CI)	*p*-Value
LEMANS				
SYNTAX left main	25/355	31/336	0.75 (0.43-1.29)	0.29
Boudriot et al.				
PRECOMBAT	10/300	12/300	0.83 (0.35-1.95)	0.66
Fixed effects estiamate	5.3% (35/655)	6.8% (43/636)	0.77 (0.48-1.22)	0.26
Random effects estimate			0.77 (0.48-1.22)	0.26

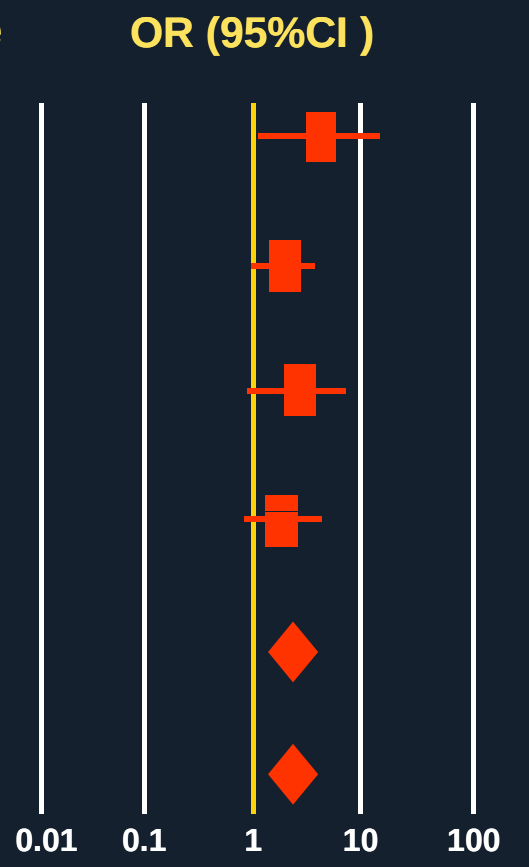


I^2=0%

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

PCI vs. CABG for Left Main Disease
Meta-analysis of 4 RCTs, 1,611 Patients
1-Year Repeat Revascularization

	PCI	CABG	OR (95%CI)	*p*-Value
LEMANS	15/52	5/53	3.89 (1.30-11.68)	0.02
SYNTAX left main	45/355	22/336	2.07 (1.22-3.53)	0.007
Boudriot et al.	14/100	6/101	2.58 (0.95-7.01)	0.06
PRECOMBAT	18/300	10/300	1.85 (0.84-4.08)	0.13
Fixed effects estiamate	11.4% (92/807)	5.4% (43/790)	2.25 (1.54-3.28)	<0.001
Random effects estimate			2.25 (1.54-3.28)	<0.001

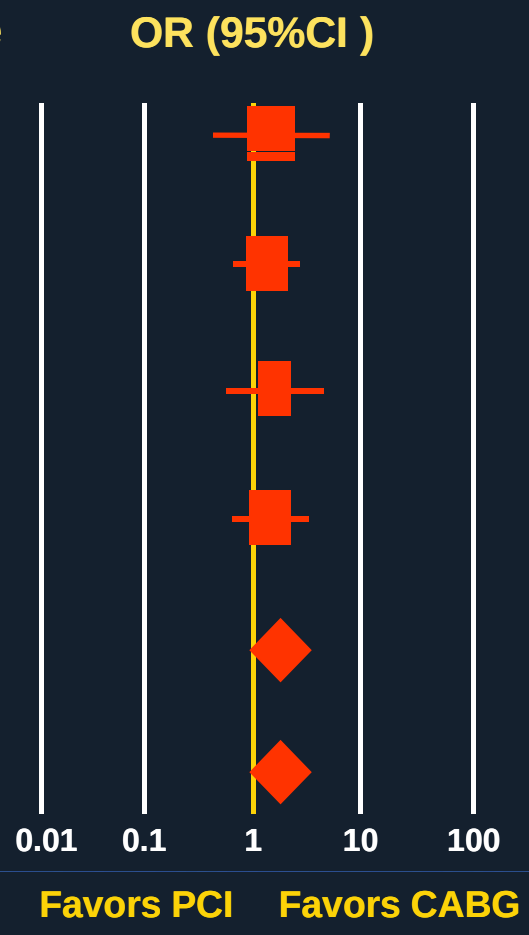


I^2=0%

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

PCI vs. CABG for Left Main Disease
Meta-analysis of 4 RCTs, 1,611 Patients
1-Year MACCE

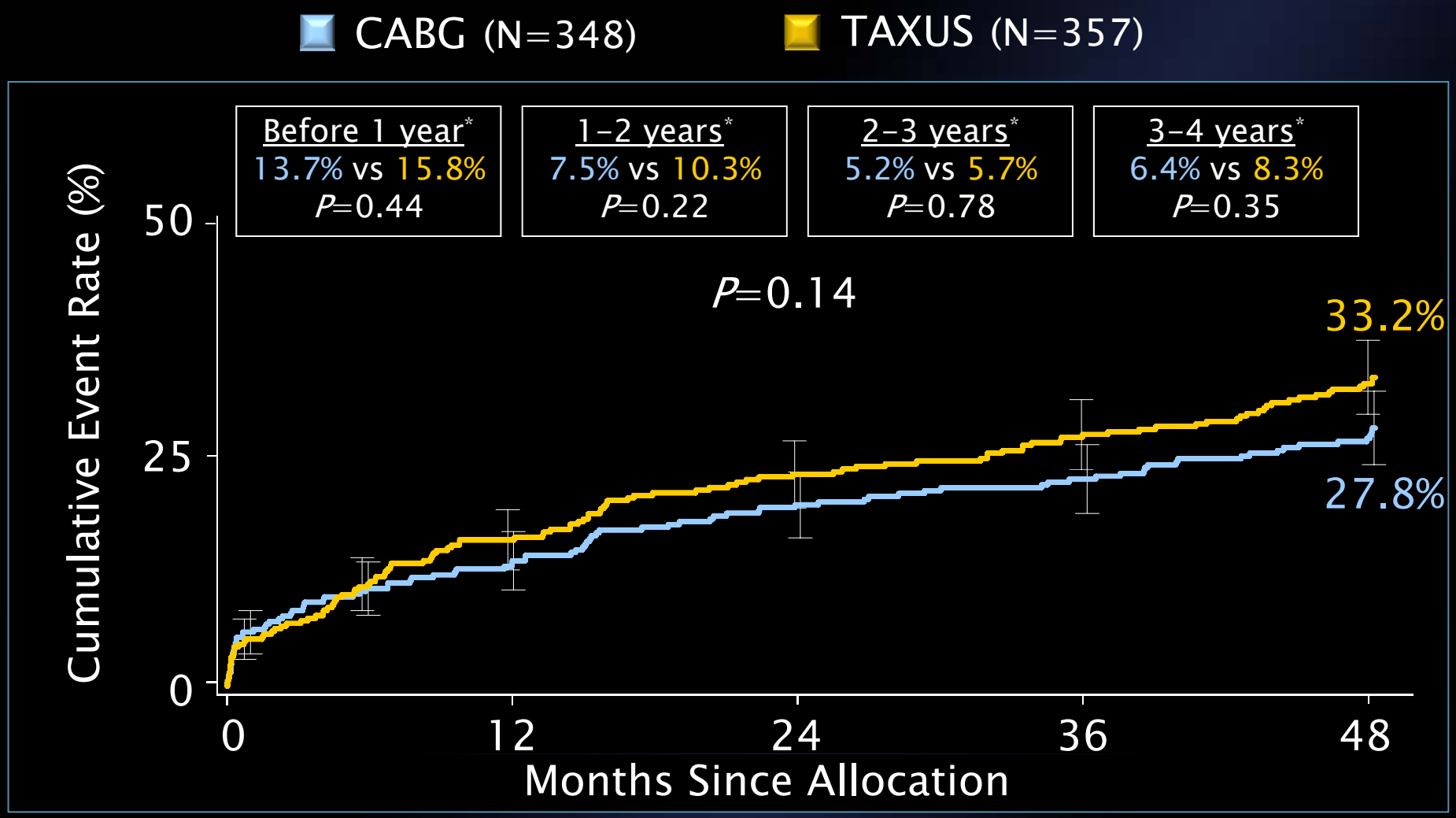
	PCI	CABG	OR (95%CI)	*p*-Value
LEMANS	16/52	13/53	1.37 (0.58-3.23)	0.48
SYNTAX left main	56/355	46/336	1.18 (0.77-1.80)	0.44
Boudriot et al.	19/100	14/101	1.46 (0.69-3.10)	0.33
PRECOMBAT	26/300	20/300	1.33 (0.73-2.44)	0.36
Fixed effects estiamate	14.5% (117/807)	11.8% (93/790)	1.28 (0.95-1.72)	0.11
Random effects estimate			1.28 (0.95-1.72)	0.11



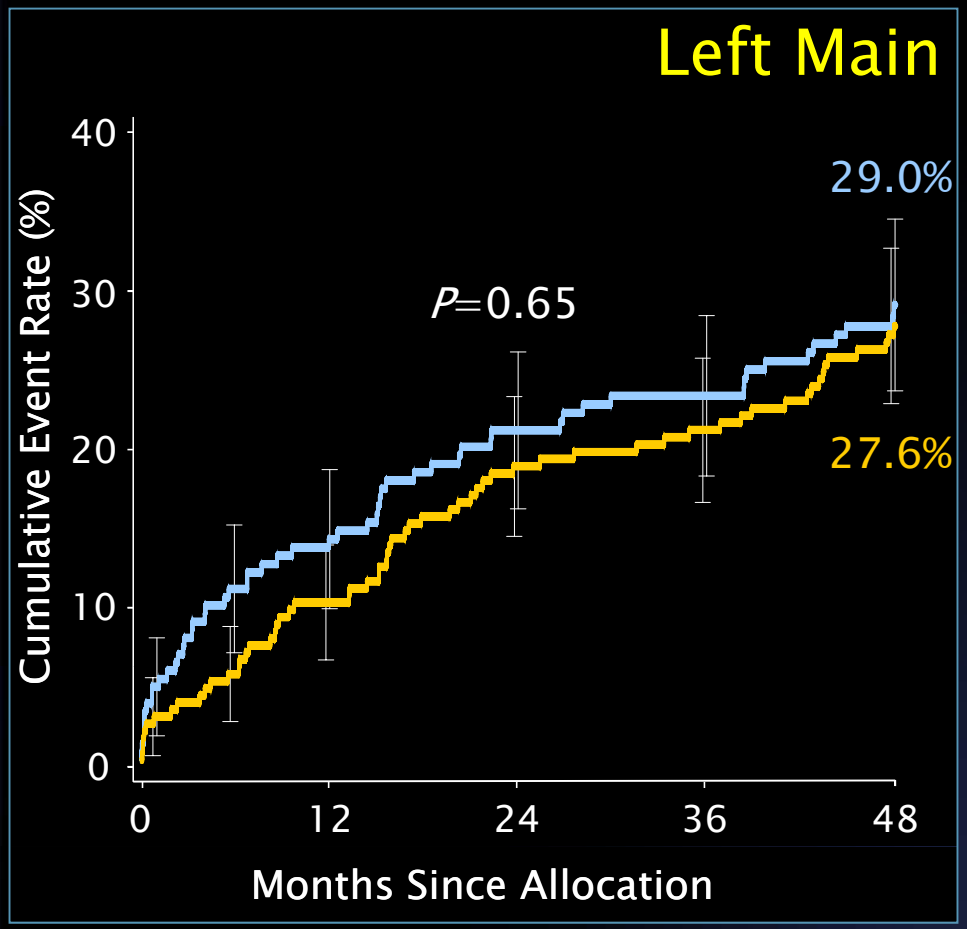
I^2=0%

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

MACCE to 4 Years
Left Main Subset

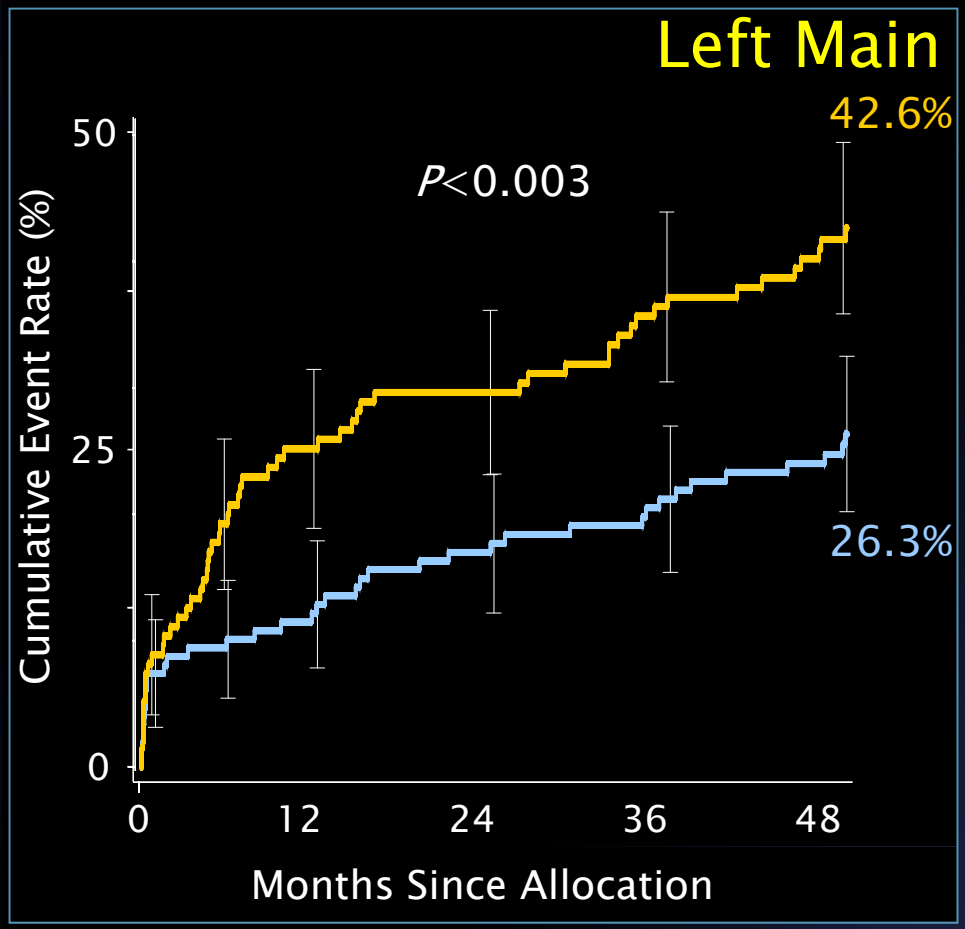


MACCE to 4 Years by SYNTAX Score Tercile *Low to Intermediate Scores (0–32)*



	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

ESC/EACTS Guidelines on Myocardial Revascularization

IIa

B

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

IIb

B

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

III

B

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

Eur Heart J 2010;31:2501-2555

ACC/AHA Guidelines

IIa

B

Left main PCI for NSTEMI/unstable angina:

- If not a CABG candidate (otherwise CABG)

IIa

C

Left main PCI for STEMI:

- When distal coronary flow is TIMI flow grade <3 and PCI can be performed more rapidly and safely than CABG

2011 ACCF/AHA/SCAI Guidelines for PCI
JACC 2011;58;e44-e122;

ACC/AHA Guidelines

IIa

B

Left main PCI for SIHD - Both must be present:

- Anatomic conditions associated with a low risk of PCI procedural complications and a high likelihood of good long-term outcome (e.g., a low SYNTAX score of ≤22, ostial or trunk left main CAD)
- Clinical characteristics that predict a significantly increased risk of adverse surgical outcomes (e.g. STS-predicted risk of operative mortality ≥5%)

2011 ACCF/AHA/SCAI Guidelines for PCI
JACC 2011;58;e44-e122;

ACC/AHA Guidelines

IIb

B

Left main PCI for SIHD - Both must be present:

- Anatomic conditions associated with a low to intermediate risk of PCI procedural complications and an intermediate to high likelihood of good long-term outcome (e.g., low-intermediate SYNTAX score of <33, bifurcation left main CAD)
- Clinical characteristics that predict an increased risk of adverse surgical outcomes (e.g., moderate-severe COPD, disability from prior stroke, or prior cardiac surgery; STS-predicted risk of operative mortality >2%)

2011 ACCF/AHA/SCAI Guidelines for PCI
JACC 2011;58;e44-e122;

ACC/AHA Guidelines

III

B

Left main PCI for SIHD: HARM

- In patients with unfavorable anatomy for PCI (e.g. Syntax score ≥33) and who are good candidates for CABG (vs. performing CABG)

2011 ACCF/AHA/SCAI Guidelines for PCI
JACC 2011;58;e44-e122;

EXCEL: Study Design

3600 pts with unprotected left main disease

@ 165 international sites

↓

SYNTAX score ≤32

Consensus agreement by heart team

↓ → No (N=1000) → Enrollment registry

Yes (N=2600)

R

↙ ↘

PCI (Xience Prime) (N=1300)

CABG (N=1300)

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

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!**