EXCEL

A Prospective, Randomized Trial Comparing Everolimus-Eluting Stents and Bypass Graft Surgery in Selected Patients with Left Main Coronary Artery Disease

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NCT01205776

Disclosures

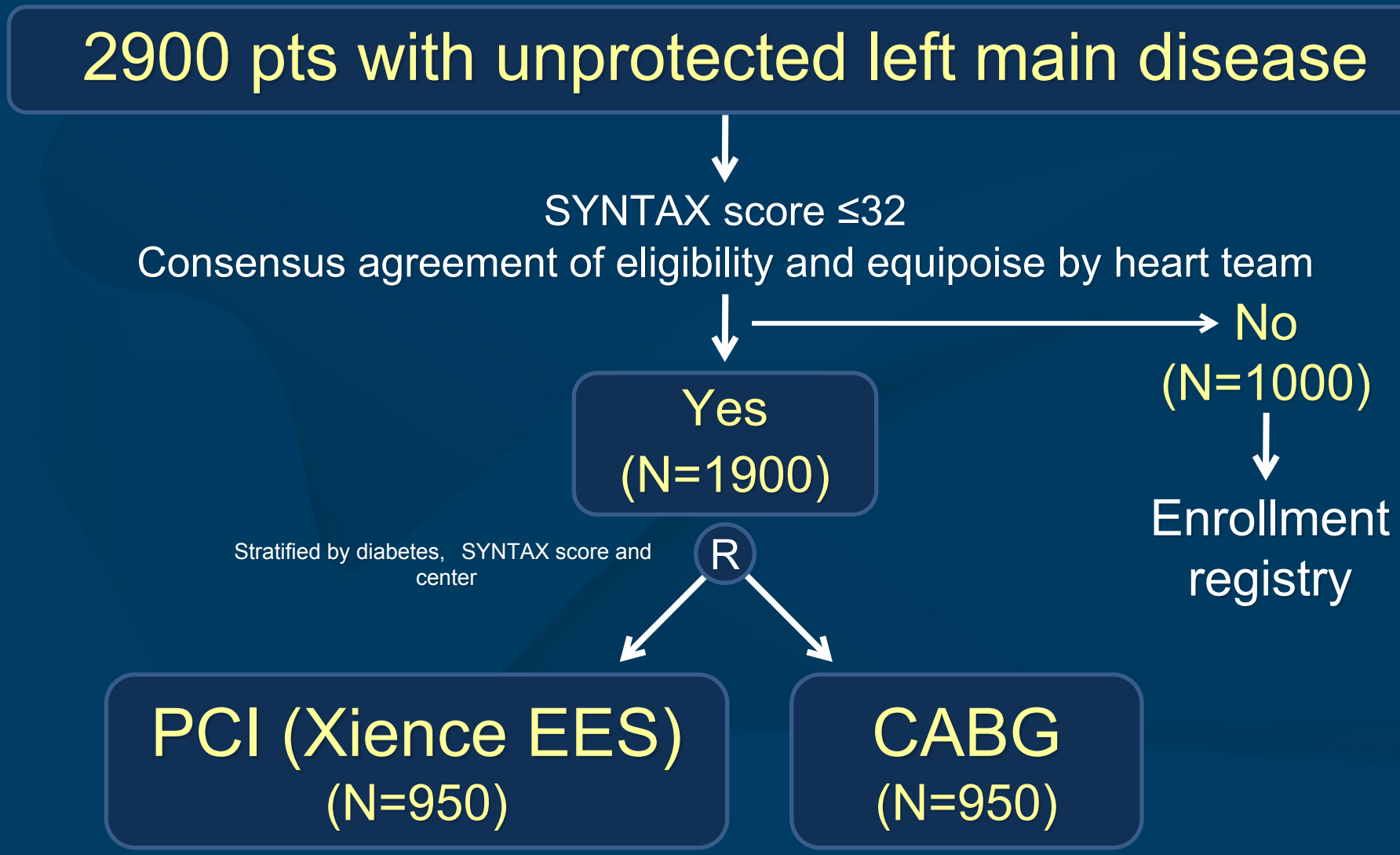
Gregg W. Stone

None

Background

- Patients with left main coronary artery disease (LMCAD) have high morbidity and mortality due to the large amount of myocardium at risk
- Most pts with LMCAD are treated with CABG
- Subset analysis from the SYNTAX trial suggested that DES may be an acceptable option for pts with LMCAD and low or moderate CAD complexity
- Since SYNTAX, PCI and surgical outcomes have both improved, necessitating a contemporary trial examining revascularization alternatives in LMCAD

Study Design



Follow-up: 1 month, 6 months, 1 year, annually through 5 years

Primary endpoint: Measured at a median 3-yr FU, minimum 2-yr FU

Design Imperatives

- Academically-driven trial organized and led equally by interventional cardiologists and cardiac surgeons
- PCI and CABG arms utilize best available devices and techniques
- Large enough for a meaningful primary endpoint:
  - Death, stroke or MI (without revascularization) at a median follow-up duration of 3 years
  - MI definition is prognostically important, identical for PCI and CABG, and chosen to minimize ascertainment bias
- Screening registry incorporated to evaluate the generalizability of the trial results

Major Inclusion Criteria

- Unprotected LMCAD with ≥70% DS, *or* ≥50% - <70% with either i) non-invasive evidence of LM ischemia, ii) IVUS MLA ≤6.0 mm^2, or iii) FFR ≤0.80
- Syntax score ≤32
- Clinical and anatomic eligibility for both PCI and CABG as agreed to by the local Heart Team

Major Exclusion Criteria

- Prior CABG or LM PCI anytime
- Prior non-LM PCI within 1 year
- Need for cardiac surgery other than CABG
- Inability to tolerate DAPT for 1 year
- CK-MB >ULN

Protocol Procedures

PCI recommendations

- Complete revasc of all ischemic territories with EES
- Provisional LM bifurcation treatment preferred
- IVUS guidance strongly recommended
- DAPT pre-loading and treatment for ≥1 year
- Routine angiographic follow-up not permitted

CABG recommendations

- Performed w/ or w/o CPB per operator discretion
- Complete anatomic revascularization of all vessels ≥1.5 mm in diameter with ≥50% DS
- Arterial grafts strongly recommended
- Epi-aortic ultrasound and TEE recommended
- Clopidogrel use during FU allowed but not mandatory

Guideline-directed medical therapy for both groups

Primary and Secondary Endpoints

Tested hierarchically to preserve alpha

Endpoint	Timing of follow-up	Powered for
Primary endpoint: Death, stroke or MI	Median 3 years, minimum 2 years	Non-inferiority
Secondary endpoint #1: Death, stroke or MI	30 days	Non-inferiority
Secondary endpoint #2a: Death, stroke, MI or IDR	Median 3 years, minimum 2 years	Non-inferiority
Secondary endpoint #2b: Death, stroke or MI	Median 3 years, minimum 2 years	Superiority

If the primary endpoint and secondary endpoint #1 both pass, secondary endpoints #2a and #2b are tested simultaneously

IDR = ischemia-driven revascularization

Primary Endpoint Definitions

- Death: Adjudicated due to CV, non-CV, or undetermined causes
- Peri-procedural MI (<72 hrs): CK-MB >10x URL, *or* >5x URL *plus* either i) new pathological Q waves in ≥2 contiguous leads *or* new LBBB, *or* ii) angio documented graft or coronary artery occlusion or new severe stenosis with thrombosis, *or* iii*)* imaging evidence of new loss of viable myocardium or new regional wall motion abnormality
- Spontaneous MI (≥72 hrs): CK-MB or troponin >1x URL *plus* new ST -segment elevation or depression *or* other findings as above
- Stroke: Requires: 1) Rapid onset of a focal/global neurological deficit with no other readily identifiable non-stroke cause; 2) Duration ≥24 hrs, or <24 hrs if i) pharmacologic or non-pharmacologic Rx; *or* ii) positive brain imaging; *or* iii) death; 3) Confirmation by neurologist *plus* confirmatory brain imaging or LP; 4) ≥1 increase in modified Rankin Scale (mRS)

Primary and Secondary Endpoints

Power and statistical analysis

Endpoint	Event rate assumptions	Delta	Alpha	Power (1900 pts)
Primary endpoint: Death, stroke or MI at 3 years	PCI: 11% CABG: 11%	4.2%	1-sided 0.025	80%
Secondary endpoint #1: Death, stroke or MI at 30 days	PCI: 3% CABG: 3%	2.0%	1-sided 0.05	80%
Secondary endpoint #2a: Death, stroke, MI or IDR at 3 years	PCI: 22% CABG: 22%	8.4%	1-sided 0.05	99%
Secondary endpoint #2b: Death, stroke or MI at 3 years	PCI: 7.2% CABG: 11%	-	2-sided 0.05	80%

Non-inferiority is calculated using the Com-Nougue approach to estimating the Z-statistic for the Kaplan-Meier failure rates with standard errors estimated by Greenwood's formula. Time-to-first event rates at 30 days and 3 years are estimated using the Kaplan-Meier method. Sample sizes assume 99% 30-day follow-up and 92% 3-year follow-up. IDR = ischemia-driven revascularization.

Study Organization (i)

- Principal Investigators: Arie Pieter Kappetein, Joseph F. Sabik, Patrick W. Serruys, Gregg W. Stone
- Executive Committee: PIs plus Gerrit-Anne van Es, Stuart J. Pocock, Martin B. Leon, Roxana Mehran, David Taggart, Marie-Claude Morice, Bernard Gersh, Seemant Chaturvedi, Peter-Paul Kint
- PCI Committee: Martin B. Leon (chair), Erick Schampaert, Marco Valgimigli, Antonio Colombo, Marco Costa, Carlo Di Mario, Stephen Ellis, Jean Fajadet, William Fearon, Dean Kereiakes, Raj Makkar, Gary S. Mintz, Jeffrey W. Moses, Paul Teirstein
- CABG Committee: David Taggart (chair), John Puskas, Greg Fontana, Marc Ruel, Paul Sergeant, Michael Mack, Patrick Nataf, Craig Smith
- Optimal Medical Therapy Committee: Bernard Gersh (chair), Bill Boden, Keith Fox, David Maron, P. Gabriel Steg
- Statistical Committee: Stuart J. Pocock (chair), Eugene Blackstone, Peter Juni, Helen Parise

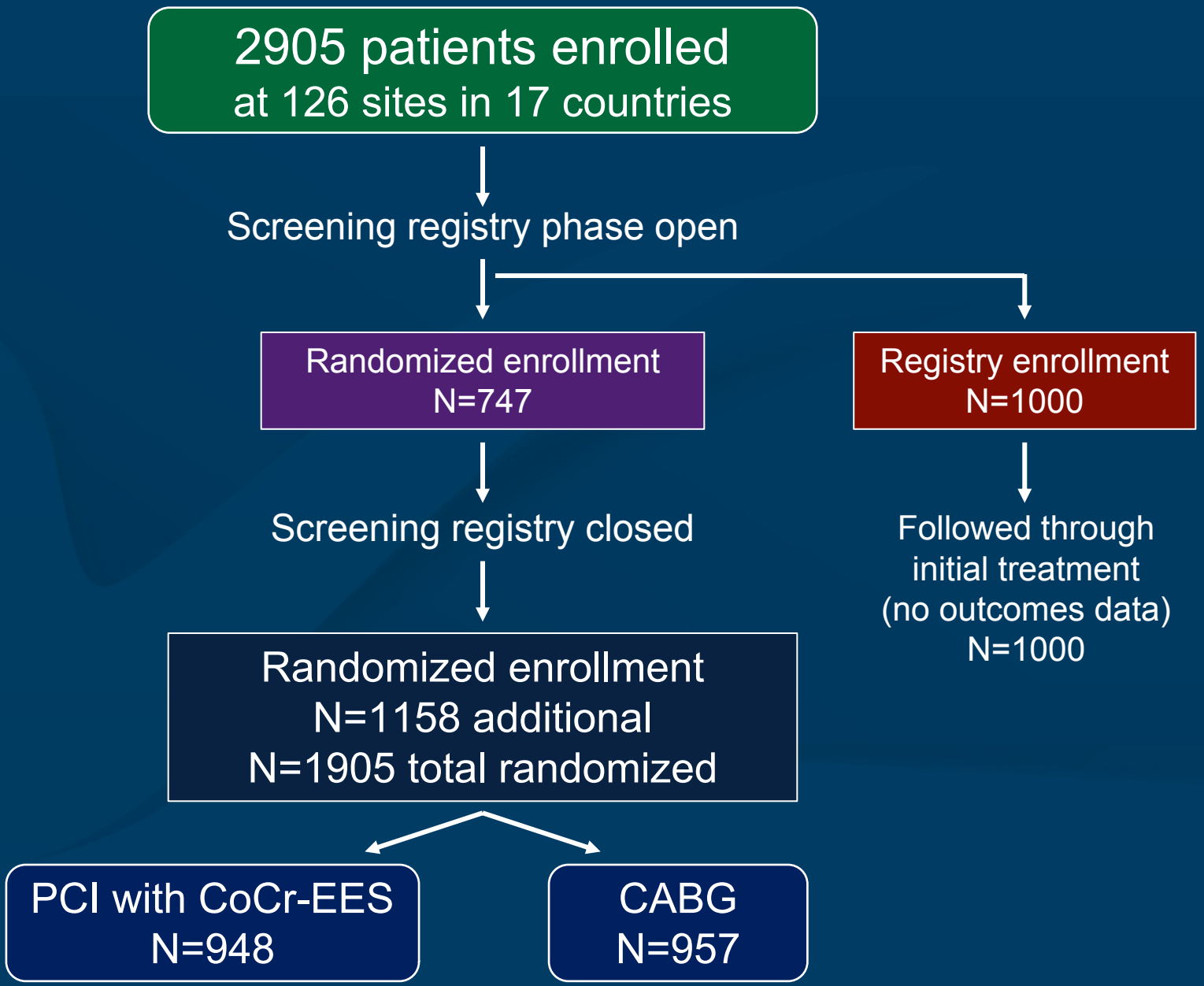
Study Organization (ii)

- Academic Research Organizations: Cardialysis - Gerrit-Anne van Es (Director); The Cardiovascular Research Foundation (CRF) - Ori-Ben Yehuda (Executive Director Clinical Trials Center)
- Site Management and Data Monitoring: Novella Clinical
- Data Management: Cardialysis - Rob Schneijdenberg, Jacintha Ronden, Judith Jonk, Anja Jonkman, Eric van Remortel, Ingrid de Zwart, Liliane Elshout, Ton de Vries, Rick Andreae, Judith Tol van, Eva Teurlings; CRF - Ovidiu Dressler, Saranya Balachandran
- Biostatistics and Data Analysis: CRF - Ovidiu Dressler, Aurora Breazna, Saranya Balachandran, Paul Jenkins, Tom McAndrew
- Clinical Endpoints Committee: CRF - Ioanna Kosmidou (Director), Steven O. Marx and Mark W. Connolly (chairs)
- Electrocardiographic Core Laboratory: CRF - Joe Dizon (Director)
- Angiographic Core Laboratory: CRF - Philippe Généreux (Director)
- IVUS Core Laboratory Analysis: CRF - Akiko Maehara (Director)
- Cost-effectiveness and QoL Assessment: Saint Luke's Mid America Heart Institute - David J. Cohen (Medical Director), Elizabeth Magnuson (Director)
- Sponsor: Abbott Vascular

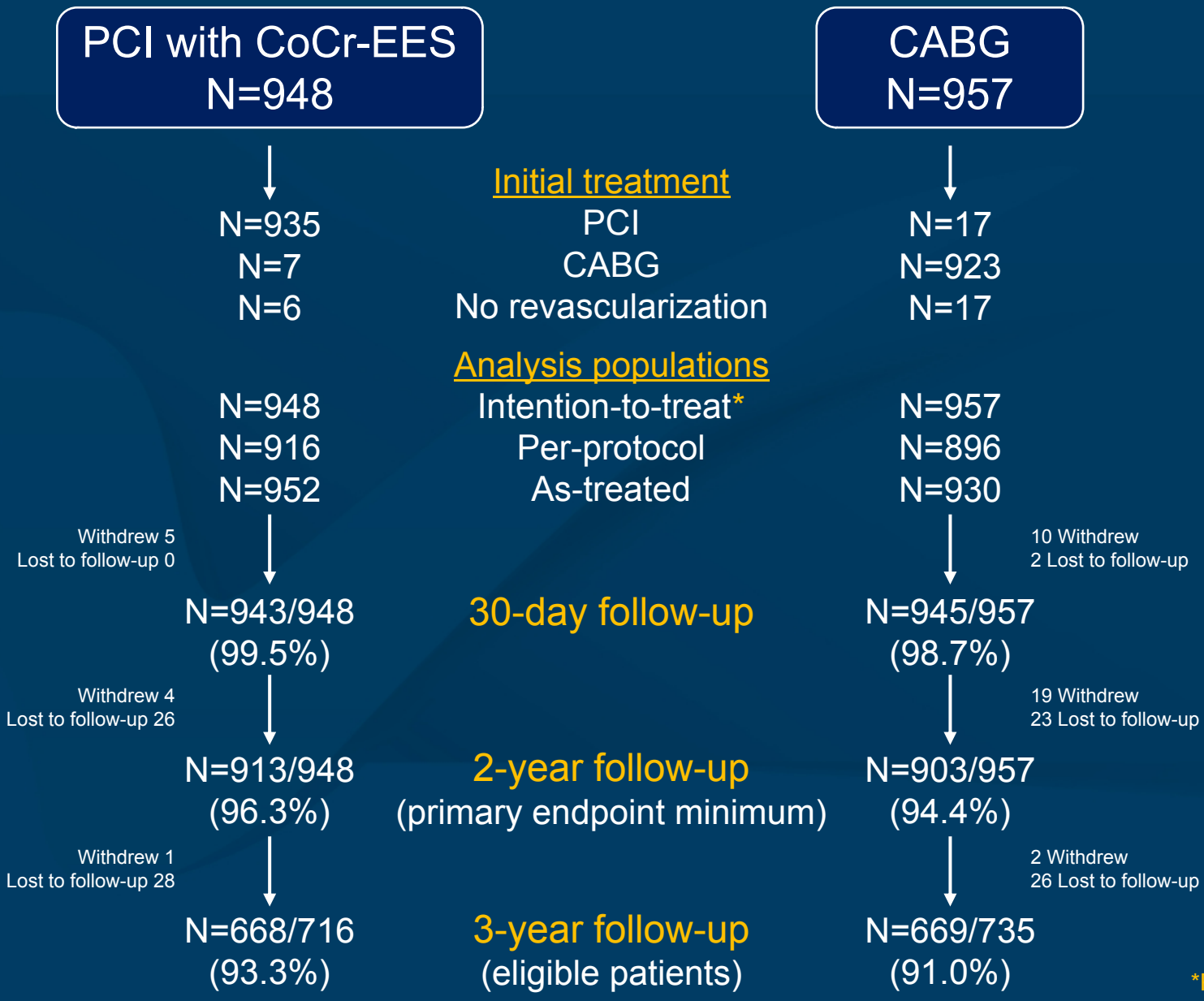
Enrollment

Between Sept. 2010 and March 2014, 2905 pts with LMCAD were recruited at 126 sites in 17 countries, including 1905 randomized and 1000 registry pts

Enrollment


2905 patients enrolled
at 126 sites in 17 countries
Screening registry phase open
Randomized enrollment
N=747
Registry enrollment
N=1000
Screening registry closed
Followed through
initial treatment
(no outcomes data)
N=1000
Randomized enrollment
N=1158 additional
N=1905 total randomized
PCI with CoCr-EES
N=948
CABG
N=957

Enrollment



*Primary analysis population

Top 10 Enrolling Heart Teams

Heart Team	Institution	City/State/Country	N randomized
Nick Lembo Morris Brown	Piedmont Hospital	Atlanta, GA, USA	135
Adrian Banning David Taggart	Oxford University Hospital	Oxford, UK	106
Bela Merkely Ferenc Horkay	Semmelweis University	Budapest, Hungary	88
Ad Johannes van Boven Piet W. Boonstra	Medisch Centrum Leeuwarden	Leeuwarden, NL	80
Imre Ungi Gabor Bogáts	Cardiology Center University of Szeged	Szeged, Hungary	66
Samer Mansour Nicholas Noiseux	Hôpital Hôtel-Dieu de Montréal	Montréal, Canada	57
Manel Sabaté Jose Pomar	Hospital Clinic	Barcelona, Spain	51
Mark Hickey Anthony Gershlick	University Hospitals of Leicester NHS Trust	Leicester, UK	47
Pawel Buszman Andrzej Bochenek	Medical University of Silesia	Katowice , Poland	44
Erick Schampaert Pierre Page	Hôpital du Sacré-Coeur de Montréal	Montréal, Canada	42

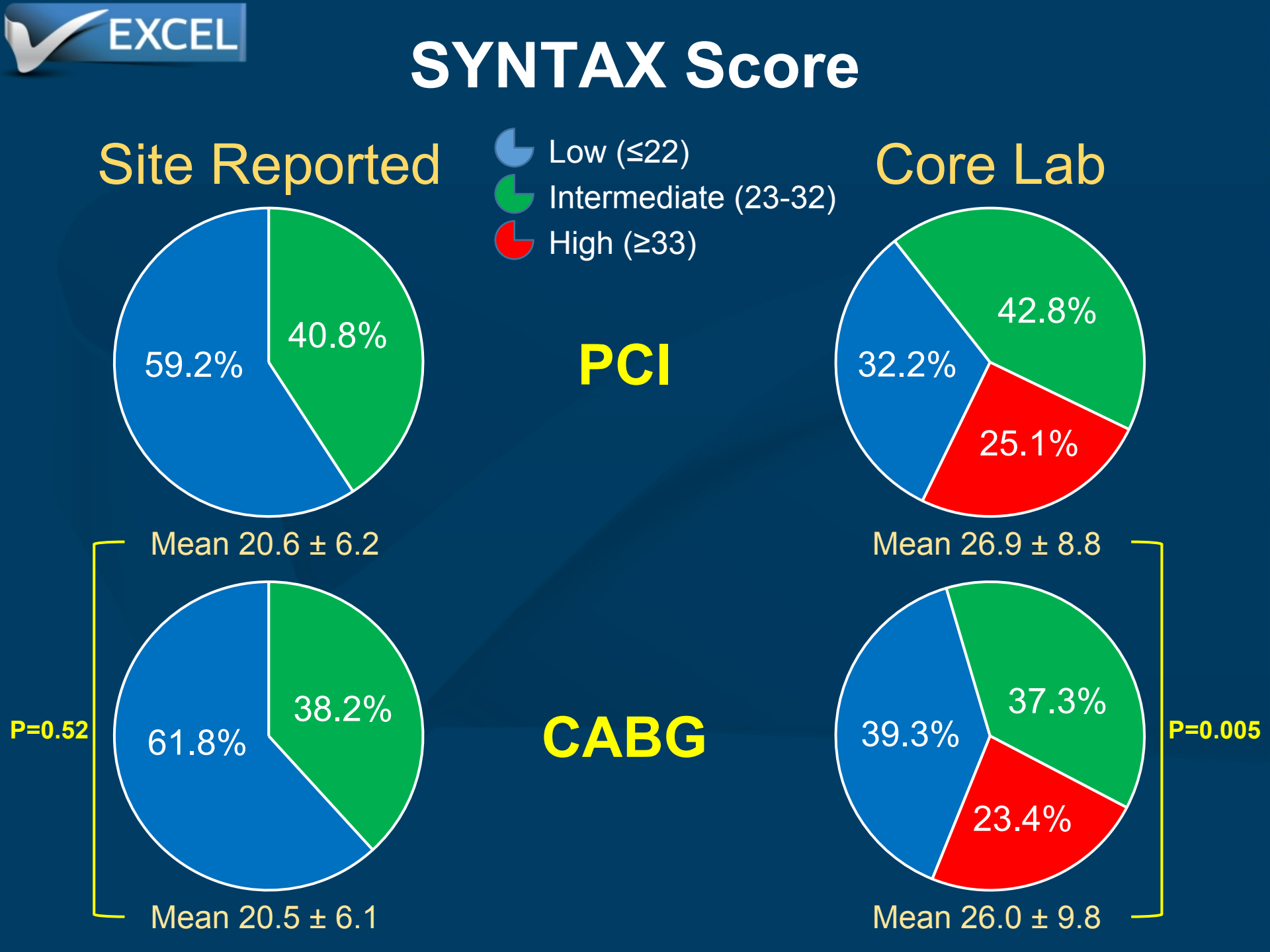
Baseline Data (i)

	PCI (N=948)	CABG (N=957)
Age (years)	66.0 ± 9.6	65.9 ± 9.5
Male	76.2%	77.5%
Country of enrollment		
- Europe	56.3%	56.5%
- North America	40.2%	38.8%
- Other	3.5%	4.7%
Diabetes	30.2%	28.0%
- Insulin-treated	7.7%	7.7%
Hypertension, medically treated	74.5%	73.9%
Hyperlipidemia, medically treated	71.5%	69.3%
Current smoker	24.1%	20.8%
Prior PCI	18.4%	15.9%
Congestive heart failure	7.1%	6.2%
Prior stroke or TIA	5.5%	7.0%

Baseline Data (ii)

	PCI (N=948)	CABG (N=957)
Peripheral vascular disease	10.3%	8.8%
COPD	6.9%	8.5%
Clinical presentation		
- Recent MI (within 7 days)	15.0%	14.8%
- Unstable angina, biomarker negative	24.2%	24.6%
- Stable angina	53.1%	53.2%
- Silent ischemia or other	7.7%	7.4%
Body mass index (kg/m^2)	28.6 ± 5.0	28.8 ± 4.9
Renal insufficiency (CrCl <60 mL/min)	17.6%	15.4%
Anemia (WHO criteria)	26.9%	22.6%
Thrombocytopenia (<150,000 cells/mm^3)	7.0%	7.0%
Left ventricular ejection fraction (%)	57.0 ± 9.6	57.3 ± 9.0

SYNTAX Score



Core Lab Data

	PCI (N=942)	CABG (N=936)
Qualifying LM lesion*		
- LM coronary segment	97.6%	97.0%
- LM equivalent disease**	1.2%	1.5%
- Neither	1.3%	1.5%
Distal LM bifurcation or trifurcation ds.	81.8%	79.2%
# Diseased non-LM coronary arteries*		
- 0	17.3%	17.8%
- 1	31.0%	31.2%
- 2	34.5%	31.5%
- 3	17.2%	19.4%

*DS ≥50% by QCA
**DS of both the ostial left LAD and ostial LCX ≥50% by QCA

PCI Procedure

935 patients, 1021 planned procedures, 2287 stents

Planned staged procedures	9.1%
Arterial access site*	
- Femoral	72.9%
- Radial	26.9%
- Brachial	0.2%
IVUS guidance	77.2%
FFR assessment	9.0%
Hemodynamic support device*	5.2%
Contrast use* (cc)	256 ± 127
Fluoroscopy time* (min)	24 ± 16

# Vessels treated per pt*†	1.7 ± 0.8
- LM	100.0%**
- LAD	28.3%
- LCX	16.6%
- RCA	26.7%
# Lesions treated per pt*	1.9 ± 1.1
# Stents implanted per pt*	2.4 ± 1.5
- Total stent length (mm)*	49.1 ± 35.6
Type of stents implanted*	
- DES	99.8%
- EES	99.2%
- XIENCE	98.4%

*All procedures (index + planned staged); **Excludes pts with LM equivalent ds;
†Max 4 vessels, including LM as a separate vessel

CABG Procedure

923 patients and procedures

Off-pump CABG	29.4%
On-pump bypass duration (min)	83 ± 45
- Cross clamp duration (min)	55 ± 27
Epi-aortic ultrasound	13.1%
Transesophageal ultrasound	42.3%
Hemodynamic support device	3.5%

# Conduits per pt	2.6 ± 0.8
- Arterial conduits	1.4 ± 0.6
- Venous conduits	1.2 ± 0.9
Any IMA used	98.8%
Bilateral IMA used	28.8%
Any radial artery used	6.0%
Only arterial conduits used	24.8%
Vessels bypassed per pt	
- LAD	98.8%
- LCX	88.2%
- RCA	37.8%

Peri-procedural Medications

	PCI (n=935)	CABG (n=923)	P-value
Aspirin pre-procedure	98.0%	76.2%	<0.001
P2Y12 receptor inhibitor pre-procedure	97.3%	-	-
- Clopidogrel or ticlopidine*	73.9%	-	-
- Prasugrel or ticagrelor*	26.8%	-	-
Heparin anticoagulation*†	77.9%	-	-
Bivalirudin anticoagulation*†	33.5%	-	-
Glycoprotein IIb/IIIa inhibitor use	6.9%	-	-

*Some pts received more than one agent; †All procedures, including index and planned staged (1021 procedures in 935 PCI pts with one or more procedures)

Discharge Medications

	PCI (n=931)	CABG (n=911)	P-value
Aspirin	98.5%	98.0%	0.43
P2Y12 receptor inhibitor	97.6%	32.6%	<0.001
- Clopidogrel or ticlopidine	72.0%	32.1%	<0.001
- Prasugrel or ticagrelor	25.7%	0.5%	<0.001
Beta-blocker	83.4%	92.5%	<0.001
ACE inhibitors or receptor blocker	56.8%	42.2%	<0.001
Calcium channel blocker	5.9%	7.1%	0.29
Diuretic	3.6%	24.4%	<0.001
Aldosterone antagonist	0.1%	0.8%	0.04
Anti-arrhythmic agent	0.5%	11.6%	<0.001
Statin	96.7%	92.4%	<0.001
Chronic oral anticoagulant	1.3%	4.3%	<0.001

Primary and Hierarchical Secondary Clinical Outcomes

	PCI (n=948)	CABG (n=957)	Diff [upper confidence limit]	P_{NI}	HR [95%CI]	P_{Sup}
Primary endpoint						
Death, stroke or MI at 3 years						
Secondary endpoints						
Death, stroke or MI at 30 days						
Death, stroke, MI or ischemia-driven revasc at 3 years						
Death, stroke or MI at 3 years						

The pre-specified non-inferiority margins (deltas) were 4.2% for death, stroke or MI at 3 years, 2.0% for death, stroke or MI at 30 days, and 8.4% for death, stroke, MI or ischemia-driven revascularization at 3 years.
†Upper 97.5% confidence limit; ††Upper 95.0% confidence limit.

Primary and Hierarchical Secondary Clinical Outcomes

	PCI (n=948)	CABG (n=957)	Diff [upper confidence limit]	P_{NI}	HR [95%CI]	P_{Sup}
Primary endpoint						
Death, stroke or MI at 3 years	15.4%	14.7%	0.7% [4.0%]†	0.018	-	-
Secondary endpoints						
Death, stroke or MI at 30 days						
Death, stroke, MI or ischemia-driven revasc at 3 years						
Death, stroke or MI at 3 years						

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Primary endpoint						
Death, stroke or MI at 3 years	15.4%	14.7%	0.7% [4.0%]†	0.018	-	-
Secondary endpoints						
Death, stroke or MI at 30 days	4.9%	7.9%	-3.1% [-1.2%]††	<0.001	-	-
Death, stroke, MI or ischemia-driven revasc at 3 years						
Death, stroke or MI at 3 years						

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Primary endpoint						
Death, stroke or MI at 3 years	15.4%	14.7%	0.7% [4.0%]†	0.018	-	-
Secondary endpoints						
Death, stroke or MI at 30 days	4.9%	7.9%	-3.1% [-1.2%]††	<0.001	-	-
Death, stroke, MI or ischemia-driven revasc at 3 years	23.1%	19.1%	4.0% [7.2%]††	0.01	-	-
Death, stroke or MI at 3 years						

The pre-specified non-inferiority margins (deltas) were 4.2% for death, stroke or MI at 3 years, 2.0% for death, stroke or MI at 30 days, and 8.4% for death, stroke, MI or ischemia-driven revascularization at 3 years.
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Death, stroke or MI at 3 years	15.4%	14.7%	0.7% [4.0%]†	0.018	-	-
Secondary endpoints						
Death, stroke or MI at 30 days	4.9%	7.9%	-3.1% [-1.2%]††	<0.001	-	-
Death, stroke, MI or ischemia-driven revasc at 3 years	23.1%	19.1%	4.0% [7.2%]††	0.01	-	-
Death, stroke or MI at 3 years	15.4%	14.7%	-	-	1.00 [0.79, 1.26]	0.98

The pre-specified non-inferiority margins (deltas) were 4.2% for death, stroke or MI at 3 years, 2.0% for death, stroke or MI at 30 days, and 8.4% for death, stroke, MI or ischemia-driven revascularization at 3 years.
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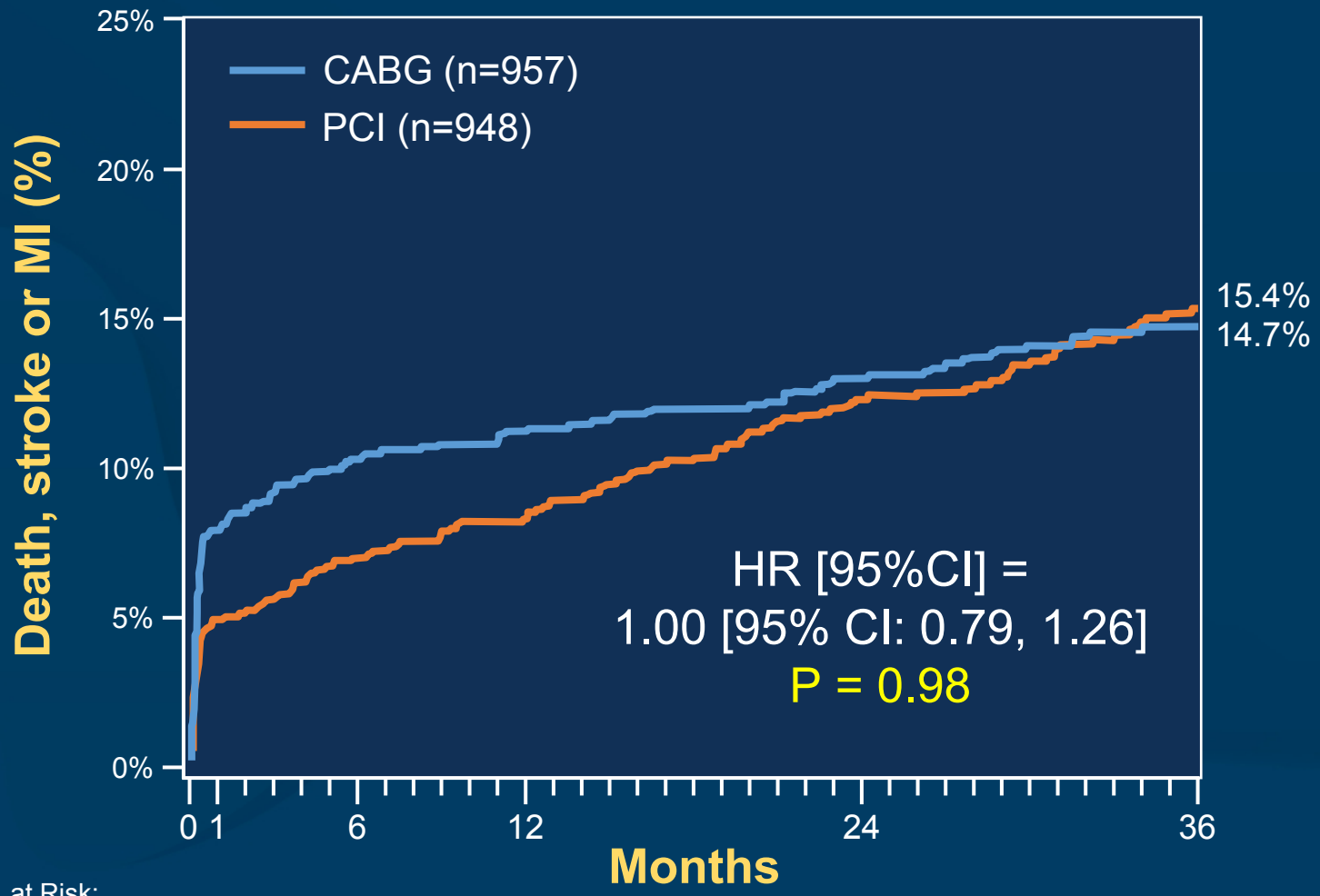
Primary Endpoint

Death, Stroke or MI at 3 Years



No. at Risk:

PCI	948	896	875	850	784	445
CABG	957	868	836	817	763	458

Adjudicated Outcomes at 30 Days

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
Death, stroke or MI	4.9%	7.9%	0.61 [0.42, 0.88]	0.008
- Death	1.0%	1.1%	0.90 [0.37, 2.22]	0.82
- Stroke	0.6%	1.3%	0.50 [0.19, 1.33]	0.15
- MI	3.9%	6.2%	0.63 [0.42, 0.95]	0.02
- Peri-procedural	3.6%	5.9%	0.61 [0.40, 0.93]	0.02
- Spontaneous	0.3%	0.3%	1.00 [0.20, 4.95]	1.00
- STEMI	0.7%	2.3%	0.32 [0.14, 0.74]	0.005
- Non-STEMI	3.2%	3.9%	0.82 [0.50, 1.32]	0.41
Death, stroke, MI or IDR	4.9%	8.4%	0.57 [0.40, 0.82]	0.002
- Ischemia-driven revasc (IDR)	0.6%	1.4%	0.46 [0.18, 1.21]	0.11
Stent thrombosis, def/prob	0.6%	0.0%	-	0.01
Graft occlusion, symptomatic	0.0%	1.2%	-	<0.001
Definite stent thrombosis or symptomatic graft occlusion	0.3%	1.2%	0.27 [0.08, 0.97]	0.03

Major Adverse Events Within 30 Days

	PCI (n=948)	CABG (n=957)	RR [95%CI]	P-value
Peri-procedural MAE, any	8.1%	23.0%	0.35 [0.28, 0.45]	<0.001
- Death*	0.9%	1.0%	0.91 [0.39, 2.23]	0.83
- Stroke*	0.6%	1.3%	0.50 [0.19, 1.34]	0.16
- Myocardial infarction*	3.9%	6.2%	0.63 [0.42, 0.95]	0.02
- Ischemia-driven revascularization*	0.6%	1.4%	0.47 [0.18, 1.22]	0.11
- TIMI major/minor bleeding	3.7%	8.9%	0.42 [0.28, 0.61]	<0.001
- Transfusion ≥2 units	4.0%	17.0%	0.24 [0.17, 0.33]	<0.001
- Major arrhythmia**	2.1%	16.1%	0.13 [0.08, 0.21]	<0.001
- Surgery/radiologic procedure	1.3%	4.1%	0.31 [0.16, 0.59]	<0.001
- Renal failure†	0.6%	2.5%	0.25 [0.10, 0.61]	<0.001
- Sternal wound dehiscence	0.0%	2.0%	0.03 [0.00, 0.43]	<0.001
- Infection requiring antibiotics	2.5%	13.6%	0.18 [0.12, 0.28]	<0.001
- Prolonged intubation (>48 hours)	0.4%	2.9%	0.14 [0.05, 0.41]	<0.001
- Post-pericardiotomy syndrome	0.0%	0.4%	0.11 [0.01, 2.08]	0.12

*Adjudicated events; others are site-reported. **SVT requiring cardioversion, VT or VF requiring treatment, or bradyarrhythmia requiring temporary or permanent pacemaker.
†Serum creatinine increased by ≥0.5 mg/dL from baseline or need for dialysis.

Adjudicated Outcomes at 3 Years (i)

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
Death, stroke or MI (1˚ endpoint)	15.4%	14.7%	1.00 [0.79, 1.26]	0.98
- Death	8.2%	5.9%	1.34 [0.94, 1.91]	0.11
- Definite cardiovascular	3.7%	3.4%	1.10 [0.67, 1.80]	0.71
- Definite non-cardiovascular	3.9%	2.3%	1.60 [0.91, 2.80]	0.10
- Undetermined cause	0.8%	0.3%	2.00 [0.50, 7.98]	0.32
- Stroke	2.3%	2.9%	0.77 [0.43, 1.37]	0.37
- MI	8.0%	8.3%	0.93 [0.67, 1.28]	0.64
- Peri-procedural	3.8%	6.0%	0.63 [0.42, 0.96]	0.03
- Spontaneous	4.3%	2.7%	1.60 [0.95, 2.70]	0.07
- STEMI	1.3%	2.8%	0.46 [0.23, 0.91]	0.02
- Non-STEMI	7.0%	5.9%	1.15 [0.80, 1.65]	0.46

Adjudicated 3-Year Death

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
All-cause death	8.2%	5.9%	1.34 [0.94, 1.91]	0.11
- Definite cardiovascular	3.7%	3.4%	1.10 [0.67, 1.80]	0.71
- Sudden cardiac death	1.4%	0.7%		0.11
- Myocardial infarction	0.7%	0.6%		0.56
- HF or cardiogenic shock	0.3%	0.6%		0.48
- Stroke	0.8%	0.8%		1.00
- Bleeding	0.0%	0.3%		0.08
- Other CV cause	0.4%	0.4%		0.70
- Definite non-cardiovascular	3.9%	2.3%	1.60 [0.91, 2.80]	0.10
- Pulmonary	0.3%	0.1%		0.56
- Infection (includes sepsis)	1.5%	0.7%		0.11
- Gastrointestinal	0.1%	0.3%		0.57
- Malignancy	1.7%	0.9%		0.27
- Accident/trauma	0.2%	0.1%		0.57
- Non-CV organ failure	0.1%	0.0%		0.32
- Other non-CV cause	0.0%	0.2%		0.16
- Undetermined cause	0.8%	0.3%	2.00 [0.50, 7.98]	0.32

Adjudicated Outcomes at 3 Years (ii)

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
Death, stroke, MI or IDR	23.1%	19.1%	1.18 [0.97, 1.45]	0.10
- Ischemia-driven revasc (IDR)	12.6%	7.5%	1.72 [1.27, 2.33]	<0.001
- PCI	10.3%	6.8%	1.57 [1.13, 2.18]	0.006
- CABG	3.5%	0.8%	4.29 [1.88, 9.77]	<0.001
All revascularization	12.9%	7.6%	1.72 [1.27, 2.33]	<0.001
Stent thrombosis, def/prob	1.3%	0.0%	-	<0.001
- Definite	0.7%	0.0%	-	0.01
- Probable	0.7%	0.0%	-	0.01
- Early (0 - 30 days)	0.7%	0.0%	-	0.008
- Late (30 days – 1 year)	0.1%	0.0%	-	0.32
- Very late (1 year - 3 years)	0.5%	0.0%	-	0.05
Graft occlusion, symptomatic	0.0%	5.4%	-	<0.001
Definite stent thrombosis or symptomatic graft occlusion	0.7%	5.4%	0.12 [0.05, 0.28]	<0.001

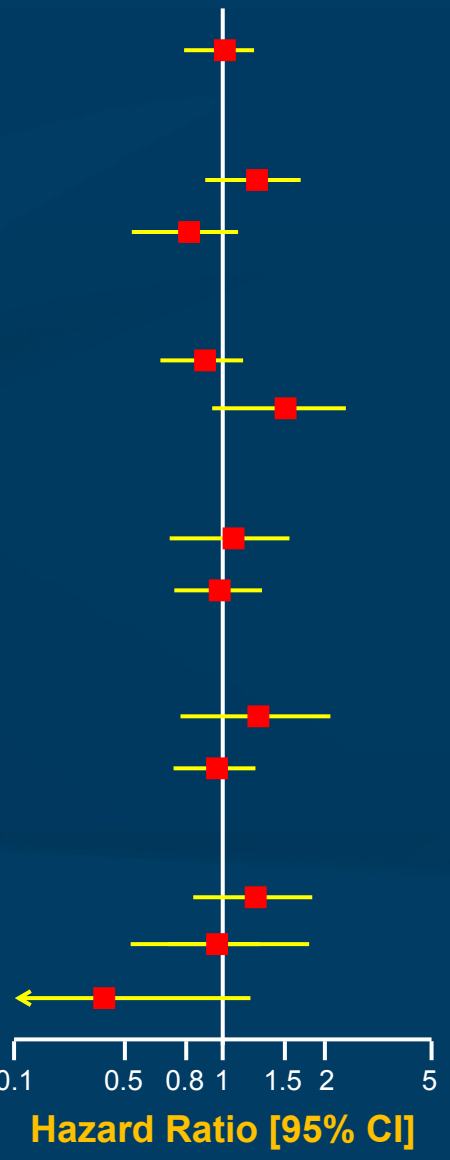
Primary Endpoint Landmark Analysis (post hoc)

	From randomization to 30 days				From 30 days to 3 years			
	PCI (n=948)	CABG (n=957)	HR [95%CI]	P value	PCI (n=939)	CABG (n=947)	HR [95%CI]	P value
Death, stroke or MI	4.9%	7.9%	0.61 [0.42, 0.88]	0.008	11.5%	7.9%	1.44 [1.06, 1.96]	0.02
- Death	1.0%	1.1%	0.90 [0.37, 2.22]	0.82	7.3%	4.9%	1.44 [0.98, 2.13]	0.06
- Stroke	0.6%	1.3%	0.50 [0.19, 1.33]	0.15	1.8%	1.8%	1.00 [0.49, 2.05]	1.00
- MI	3.9%	6.2%	0.63 [0.42, 0.95]	0.02	4.2%	2.5%	1.71 [1.00, 2.93]	0.05

Stroke and MI rates are non-hierarchical; i.e. include fatal and non-fatal events. The 30-day to 3-year landmark period includes all randomized pts at day 30 except those who died before day 30. Thus there may be some patients with a stroke or MI within 30 days who have a second event between 30 days and 3 years.

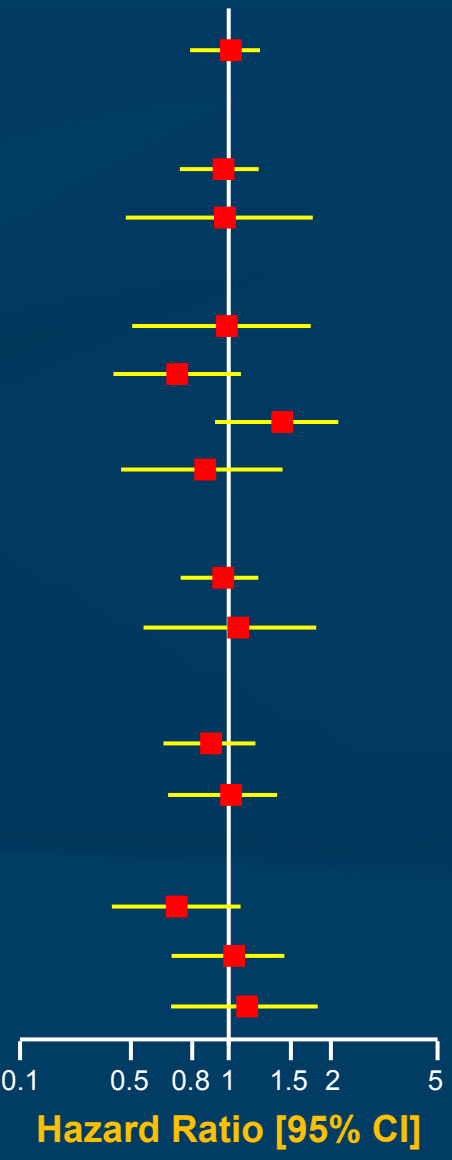
3-Year Death, Stroke or MI

Subgroup	PCI (N=948)	CABG (N=957)	HR [95% CI]	P (Int)
All patients	15.4%	14.7%	1.00 [0.79, 1.26]	
Age (median cutoff)				
- ≥67 years	18.7%	15.0%	1.22 [0.89, 1.69]	0.07
- <67 years	12.2%	14.4%	0.78 [0.55, 1.11]	
Gender				
- Male	14.0%	14.9%	0.87 [0.66, 1.14]	0.06
- Female	19.7%	14.1%	1.48 [0.93, 2.41]	
Diabetes mellitus				
- Yes	21.2%	19.4%	1.04 [0.70, 1.55]	0.77
- No	13.3%	13.1%	0.97 [0.72, 1.30]	
Chronic kidney disease				
- eGFR ≤60 ml/min	24.5%	19.3%	1.24 [0.75, 2.07]	0.36
- eGFR >60 ml/min	13.5%	13.6%	0.95 [0.72, 1.25]	
Geographic location				
- North America	15.5%	12.4%	1.22 [0.82, 1.82]	0.14
- Europe	15.5%	15.6%	0.95 [0.69, 1.29]	
- Other	9.5%	22.2%	0.37 [0.08, 1.20]	



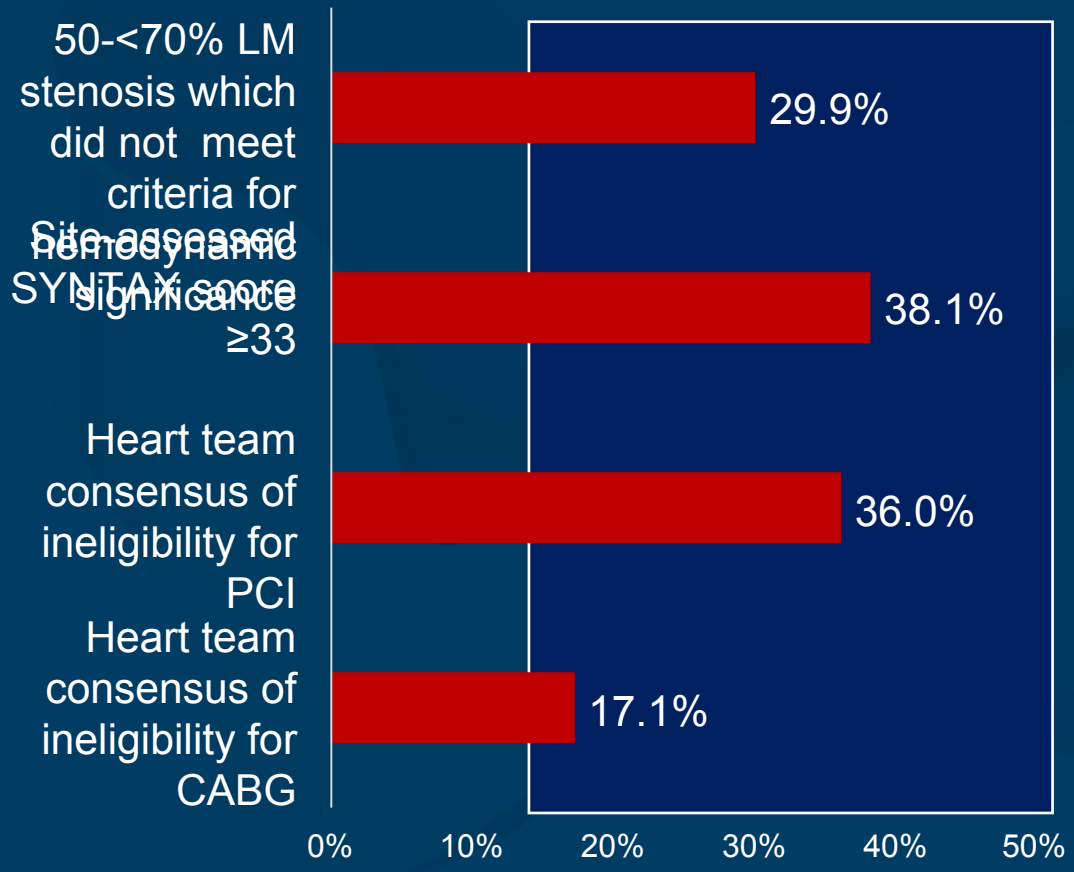
3-Year Death, Stroke or MI

Subgroup	PCI (N=948)	CABG (N=957)	HR [95% CI]	P (Int)
All patients	15.4%	14.7%	1.00 [0.79, 1.26]	
Left ventricular ejection fraction				
- ≥50%	14.7%	14.4%	0.98 [0.75, 1.27]	0.99
- <50%	20.4%	18.2%	0.98 [0.52, 1.83]	
Non-LM diseased coronary arteries				
- 0	14.6%	14.4%	0.99 [0.54, 1.79]	
- 1	12.3%	16.0%	0.72 [0.46, 1.12]	0.78
- 2	18.8%	12.7%	1.44 [0.96, 2.21]	
- 3	15.2%	16.8%	0.87 [0.50, 1.48]	
LM bifurcation or trifurcation stenosis ≥50%				
- Yes	15.6%	15.3%	0.98 [0.75, 1.27]	0.82
- No	14.8%	12.9%	1.05 [0.59, 1.87]	
Syntax score (site reported)				
- ≤22	14.3%	14.4%	0.95 [0.70, 1.31]	0.70
- 23 - 32	17.0%	15.4%	1.05 [0.73, 1.51]	
Syntax score (core lab assessment)				
- ≤22	10.3%	13.3%	0.71 [0.44, 1.13]	
- 23 - 32	17.6%	16.5%	1.02 [0.71, 1.47]	0.49
- ≥33	16.9%	14.3%	1.15 [0.71, 1.87]	

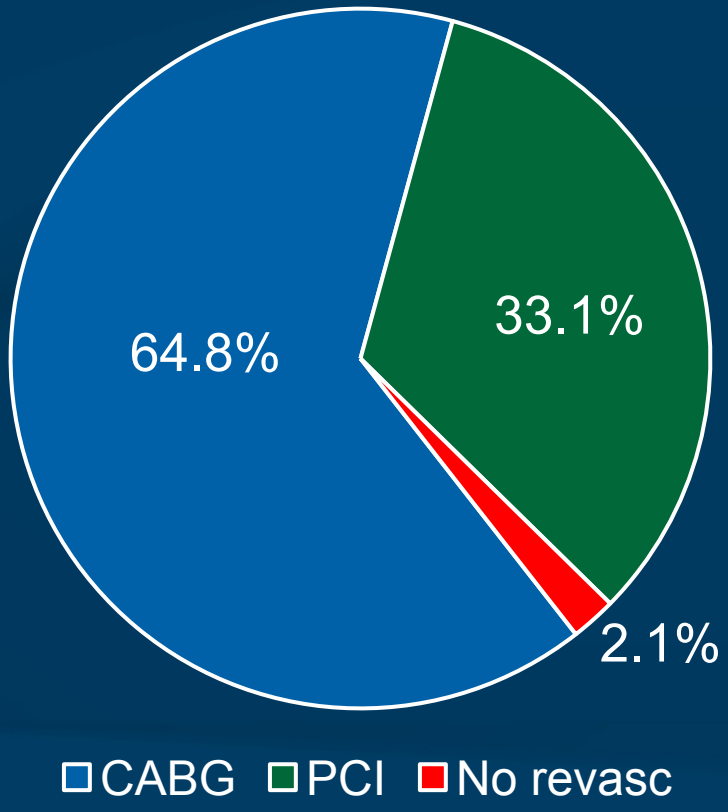


Registry (n=1000)

Major reasons for exclusion from randomization



Treatment of registry patients



Of the 1747 pts enrolled during the registry period, 62% were eligible for PCI (1078; 331 reg + 747 rand), and 80% were eligible for CABG (1395; 648 reg + 747 rand)

Limitations

- Blinding not possible; some degree of event ascertainment bias cannot be excluded
- Not powered for low frequency events; e.g. mortality
- Under-powered for subgroups; e.g. primary endpoint results were consistent in high SYNTAX score subgroup - however, further studies are required to determine whether PCI is an acceptable alternative to CABG in LMCAD pts with high anatomic complexity
- Longer-term FU (ongoing through 5 years) is required to examine whether additional differences emerge

Conclusions

- Treatment of patients with LMCAD and low or intermediate SYNTAX scores with CoCr-EES resulted in similar rates of the primary endpoint of death, stroke or MI at 3 years, with fewer adverse events within 30 days compared to CABG
- PCI may thus be considered an acceptable or even preferred revascularization modality for selected patients with LMCAD, a decision which should be made after heart team discussion, taking into account each patient's individual circumstances and preferences

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ORIGINAL ARTICLE

Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease

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