LM intervention: PCI or CABG ? Lessons

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BACKGROUND

Left main coronary artery disease is associated with high morbidity and mortality owing to the large amount of myocardium at risk.

European and U.S. guidelines recommend that most patients with left main coronary artery disease undergo coronary-artery bypass grafting (CABG).

Randomized trials have suggested that percutaneous coronary intervention (PCI) with drug-eluting stents might be an acceptable alternative for selected patients with left main coronary disease.

Randomized studies of PCI vs Surgery for LMCA disease

Study (references)	*n* (PCI)	*n* (CABG)	Outcome
LEMANS[46]	52	53	EF improved in PCI group at 1 y
SYNTAX[13]	357	348	MACCE at 1 y was similar
PRECOMBAT[47]	300	300	PCI was noninferior to CABG at 1 y
Boudriot et al[48]	100	101	PCI was inferior to CABG at 1 y

JACC Cardiovasc Interv. 2016 Feb 22;9(4):318-27. doi: 10.1016/j.jcin.2015.10.044.

Left Main Stenting in Comparison With Surgical Revascularization: 10-Year Outcomes of the (Left Main Coronary Artery Stenting) LE MANS Trial.

Abstract

OBJECTIVES: This study has reported 10-year clinical follow-up of patients enrolled in the prospective, randomized LE MANS (Left Main Stenting) trial.

BACKGROUND: The very long-term outcome after left main stenting in comparison with surgical revascularization remains unknown.

METHODS: In this prospective, multicenter trial, we randomly assigned 105 patients with unprotected left main coronary artery stenosis with low and medium complexity of coexisting coronary artery disease according to SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score to percutaneous coronary intervention (PCI) with stenting (n = 52) or coronary artery bypass grafting (CABG) (n = 53). Drug-eluting stents were implanted in 35%, whereas arterial grafts to the left anterior descending artery were utilized in 81%. Currently, the mean long-term follow-up was collected at 9.8 ± 1.0 years. Follow up for all-cause mortality is complete, whereas the incidence of major adverse cardiovascular and cerebral events (MACCE) was reported from 90% of patients. Ambulatory follow-up was completed in 46 (43.9%) patients.

RESULTS: At 10 years, there was a trend toward higher ejection fraction in stenting when compared with surgery (54.9 ± 8.3% vs. 49.8 ± 10.3%; p = 0.07). The mortality (21.6% vs. 30.2%; p = 0.41) and MACCE (51.1% vs. 64.4%; p = 0.28) were statistically not different between groups; however, numerically the difference was in favor of stenting. Similarly, there was no difference in the occurrence of myocardial infarction (8.7 vs. 10.4%; p = 0.62), stroke (4.3 vs. 6.3%; p = 0.68), and repeated revascularization rates (26.1% vs. 31.3%; p = 0.64). The probability of very long-term survival up to 14 years was comparable between PCI and CABG (74.2% vs. 67.5%; p = 0.34; hazard ratio: 1.45, 95% confidence interval: 0.67 to 3.13); however, there was a trend toward higher MACCE-free survival in the PCI group (34.7% vs. 22.1%; p = 0.06; hazard ratio: 1.71, 95% confidence interval: 0.97 to 2.99).

CONCLUSIONS: In patients with unprotected left main coronary artery stenosis with low and medium complexity of coexisting coronary artery disease, stenting offers numerically, but statistically nonsignificant, favorable long-term outcome up to 10 years in terms of safety and efficacy outcome measures, therefore, constitutes an alternative therapy for CABG.

J Am Coll Cardiol. 2015 May 26;65(20):2198-206. doi: 10.1016/j.jacc.2015.03.033. Epub 2015 Mar 15.

Randomized Trial of Stents Versus Bypass Surgery for Left Main Coronary Artery Disease: 5-Year Outcomes of the PRECOMBAT Study.

BACKGROUND: In a previous randomized trial, we found that percutaneous coronary intervention (PCI) was not inferior to coronary artery bypass grafting (CABG) for the treatment of unprotected left main coronary artery stenosis at 1 year.

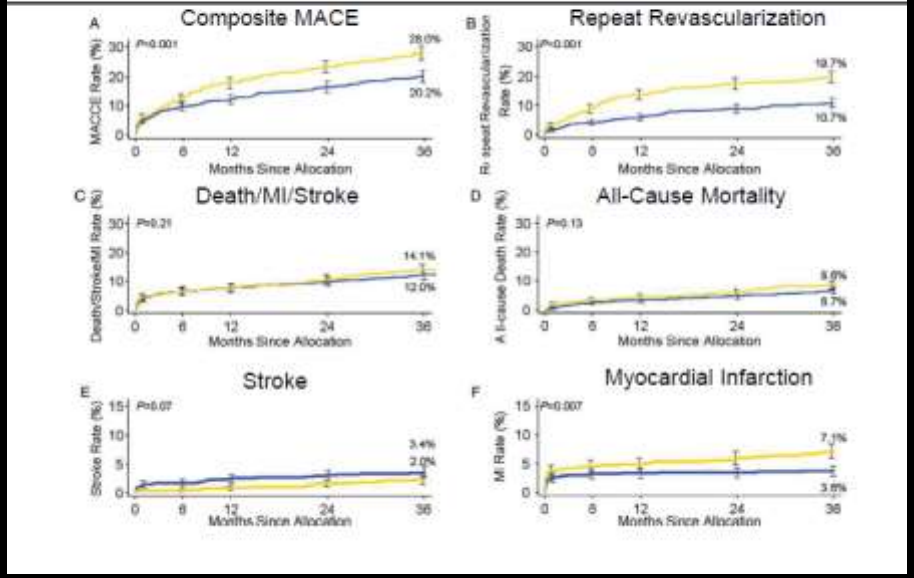
OBJECTIVES: This study sought to determine the 5-year outcomes of PCI compared with CABG for the treatment of unprotected left main coronary artery stenosis.

METHODS: We randomly assigned 600 patients with unprotected left main coronary artery stenosis to undergo PCI with a sirolimus-eluting stent (n = 300) or CABG (n = 300). The primary endpoint was a major adverse cardiac or cerebrovascular event (MACCE: a composite of death from any cause, myocardial infarction, stroke, or ischemia-driven target vessel revascularization) and compared on an intention-to-treat basis.

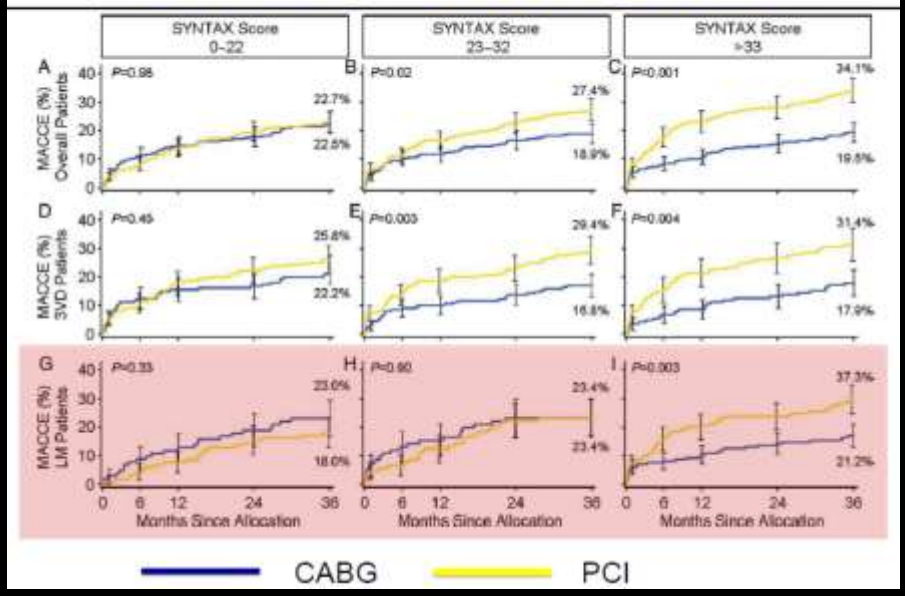
RESULTS: At 5 years, MACCE occurred in 52 patients in the PCI group and 42 patients in the CABG group (cumulative event rates of 17.5% and 14.3%, respectively; hazard ratio [HR]: 1.27; 95% confidence interval [CI]: 0.84 to 1.90; p = 0.26). The 2 groups did not differ significantly in terms of death from any cause, myocardial infarction, or stroke as well as their composite (8.4% and 9.6%; HR, 0.89; 95% CI, 0.52 to 1.52; p = 0.66). Ischemia-driven target vessel revascularization occurred more frequently in the PCI group than in the CABG group (11.4% and 5.5%, respectively; HR: 2.11; 95% CI: 1.16 to 3.84; p = 0.012).

CONCLUSIONS: During 5 years of follow-up, our study did not show significant difference regarding the rate of MACCE between patients who underwent PCI with a sirolimus-eluting stent and those who underwent CABG. However, considering the limited power of our study, our results should be interpreted with caution. (Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease [PRECOMBAT]; NCT00422968).

Clinical outcomes with CABG or PCI for Left Main Disease up to 3 years - SYNTAX



SYNTAX – 3 Year Results



Clinical Outcomes	PRECOMBAT TRIAL-5 YRS				SYNTAX TRIAL-5 YRS			
	Surgery (*N* = 300)	Stents (*N* = 300)	HR (95% CI)	*P* value	Surgery (*N* = 348)	Stents (*N* = 357)	HR (95% CI)	*P* value
MACCE	14%	18%	1.27 (0.84-1.90)	.26	31%	37%	1.23 (0.95-1.59)	.12
All death/stroke/MI	10%	8%	0.89 (0.52-1.52)	.66	21%	19%	0.91 (0.65-1.27)	.57
All death	8%	6%	0.73 (0.39-1.37)	.32	15%	13%	0.88 (0.58-1.32)	.53
Cardiac death	7%	4%	0.54 (0.26-1.13)	.10	7%	9%	1.23 (0.71-2.11)	.46
Stroke	1%	1%	0.99 (0.14-7.02)	.99	4%	2%	0.33 (0.12-0.92)	.03
MI	2%	2%	1.20 (0.37-3.93)	.76	5%	8%	1.67 (0.91-3.10)	.10
Revascularization	5.5%	11.4%	2.11 (1.16-3.84)	.01	16%	27%	1.82 (1.28-2.57)	<.001

Guidelines	Class of Recommendation	LOE
ACC/AHA 2011	IIa—For SIHD when both of the following are present:	B
	1.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 [≤22], ostial or trunk left main stenosis) 1.Clinical characteristics that predict a significantly increased risk of adverse surgical outcomes (e.g., STS-predicted risk of operative mortality ≥ 5%)	
	IIb—For SIHD when both of the following are present:	B
	1.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 <33, bifurcation left main stenosis) 1.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%)	
	III—For SIHD in patients (vs. performing CABG) with unfavorable anatomy for PCI and who are good candidates for CABG	B
ESC 2014	IIa—Left main (isolated or 1VD, ostium/shaft)	B
	IIb—Left main (isolated or 1VD, bifurcation)/left main + 2VD or 3VD, SYNTAX score ≤32	B
	IIIb—Left main + 2VD or 3VD, SYNTAX score ≥33	

CABG vs. PCI in Stable CAD with Suitable Anatomy for Both Procedures

Recommendation for the type of revascularization (CABG or PCI) in patients with SCAD with suitable coronary anatomy for both procedures and low predicted surgical mortality

Recommendations according to extent of CAD	CABG		PCI		
	Class[a]	Level[b]	Class[a]	Level[b]	Ref[c]
One or two-vessel disease without proximal LAD stenosis	IIb	C	I	C	
One-vessel disease with proximal LAD stenosis	I	A	I	A	107,108,160, 161,178,179
Two-vessel disease with proximal LAD stenosis	I	B	I	C	108,133,137
Left main disease with a SYNTAX score ≤ 22	I	B	I	B	17,134,170
Left main disease with a SYNTAX score 23–32	I	B	IIb	B	17
Left main disease with a SYNTAX score >32	I	B	III	B	17
Three-vessel disease with a SYNTAX score ≤ 22	I	A	I	B	17,157,175,176
Three-vessel disease with a SYNTAX score 23–32	I	A	IIa	B	17,157,175,176
Three-vessel disease with a SYNTAX score >32	I	A	IIb	B	17,157,175,176

CABG = coronary artery bypass grafting; LAD = left anterior descending coronary artery; PCI = percutaneous coronary intervention; SCAD = stable coronary artery disease.
[a]Class of recommendation.
[b]Level of evidence.
[c]References.

Conclusions of the data available

- At one year and longer, CABG and PCI appear to have similar rates of the combined end point of death from any cause, MI, stroke.
- As the complexity of associated coronary artery disease increases, assessed either by the SYNTAX score or as the number of vessels that need revascularization, the benefit in favour of CABG over PCI with stenting increases.

For patients with lower complexity coronary disease who can undergo PCI at an acceptable risk and with reasonable probability for success, PCI may be an acceptable or even preferred option.

Still more data are available to validate this approach,

However, guidelines indicate that CABG should remain the preferred option.

Conclusions of the data available

CABG is associated with a significantly higher incidence of adverse in-hospital outcomes, including death, MI, and stroke. However, the long-term rates of death, MI, and stroke are comparable or better depending on severity of associated coronary artery disease.

PCI with stenting is associated with a higher incidence of target vessel revascularization at long-term follow-up.

WHY A NEW TRIAL??

The outcomes of PCI were acceptable only in the patients with coronary artery disease of low or intermediate anatomical complexity.

Because SYNTAX results represented a subgroup of a subgroup, they were hypothesis generating.

PRECOMBAT and others were not adequately powered.

Routine angiographic follow up in PRECOMBAT

Moreover, contemporary metallic drug-eluting stents have a better safety and efficacy profile than do the first-generation stents used in earlier trials.

Surgical techniques and outcomes have also continued to improve, and an evaluation of alternative methods of revascularization for patients with left main coronary artery disease is warranted in a contemporary trial.

EXCEL

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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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Joseph F. Sabik, Patrick W. Serruys, Charles A. Simonton, Philippe Généreux, John Puskas, David E. Kandzari, Marie-Claude Morice, Nicholas Lembo, W. Morris Brown, III, David P. Taggart, Adrian Banning, Béla Merkely, Ferenc Horkay, Piet W. Boonstra, Ad Johannes van Boven, Imre Ungi, Gabor Bogáts, Samer Mansour, Nicolas Noiseux, Manel Sabaté, Jose Pomar, Mark Hickey, Anthony Gershlick, Pawel Buszman, Andrzej Bochenek, Erick Schampaert, Pierre Pagé, Ovidiu Dressler, Ioanna Kosmidou, Roxana Mehran, Stuart J. Pocock, and Arie Pieter Kappetein, for the EXCEL Trial Investigators

NCT01205776

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Study Design

2900 pts with unprotected left main disease

↓

SYNTAX score ≤32

Consensus agreement of eligibility and equipoise by heart team

→ No (N=1000) → Enrollment registry

↓ Yes (N=1900)

Stratified by diabetes, SYNTAX score and center R

↙ PCI (Xience EES) (N=950)

↘ CABG (N=950)

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

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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

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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

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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

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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

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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

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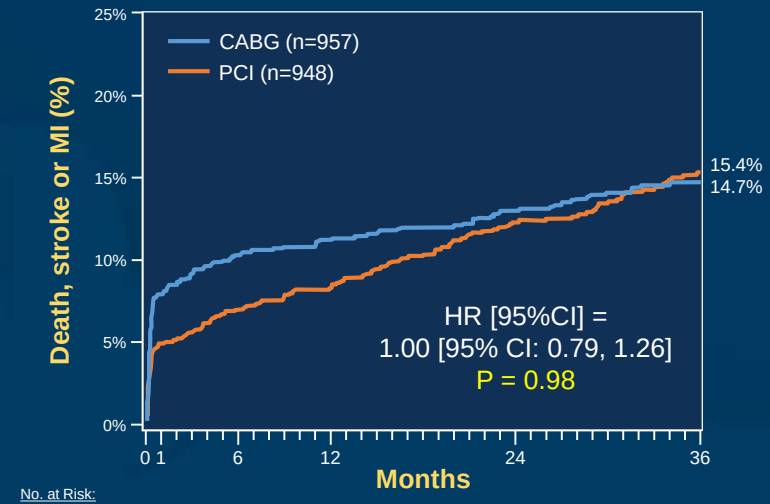
Primary Endpoint
Death, Stroke or MI at 3 Years



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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.

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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

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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

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

THANK YOU