

SYNTAX Five-year Results: Left Main Cohort

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Background

- The SYNTAX trial assessed the optimum revascularisation treatment for patients with de-novo LM or 3VD (or both), by randomly assigning patients to either PCI with a first-generation PES or CABG.
- For the primary endpoint of MACCE at 1 year, PCI did not meet the goal of non-inferiority compared with CABG.
- In the observational hypothesis-generating analysis of patients with LM disease, PCI had safety and efficacy outcomes comparable to CABG at 1 year.





SYNTAX Trial Design SYNTAX 23 US Sites 62 EU Sites Heart Team (surgeon & interventional cardiologist) Amenable for both Amenable for only one treatment approach treatment options Stratification: LM and Diabetes Randomized Arms Two Registry Arms N = 1275N = 1800TAXUS* **CABG CABG** PCI VS n = 897n = 903n = 198n = 10773VD LM LM 3VD n = 549n = 348n = 546n = 357(66.3%)(33.7%)(65.4%)(34.6%)*TAXUS Express

Beware of All-Comers trials!

Evaluating the 'all-comers' design: a comparison of participants in two 'all-comers' PCI trials with non-participants

Sanneke P.M. de Boer, Mattie J. Lenzen, Rohit M. Oemrawsingh, Cihan Simsek, Henricus J. Duckers, Willem J. van der Giessen, Patrick W. Serruys, and Eric Boersma*

Conclusions

- Applying the all-comers design did not result in inclusion of all consecutive patients, as only half of the target population was enrolled.
- This design included more patients than observed in classical RCTs.
- AC-RCT participants and non-participants were different in terms of baseline characteristics and outcome.





Patient Disposition to 5 Years LM Subset Intent-to-Treat



CABG n=348 RCT: *Enrolled* N=705

PCI* n=357

CABG n=336 RCT: 1 Year Follow-up
CABG 96.6% PCI 99.4%

PCI* n=355

CABG n=331 RCT: 2 Year Follow-up
CABG 92.0% PCI 97.1%

PCI* n=533

CABG n=502 RCT: 3 Year Follow-up
CABG 95.1% PCI 98.6%

PCI* n=352

CABG n=325 RCT: 4 Year Follow-up
CABG 93.4% PCI 97.8%

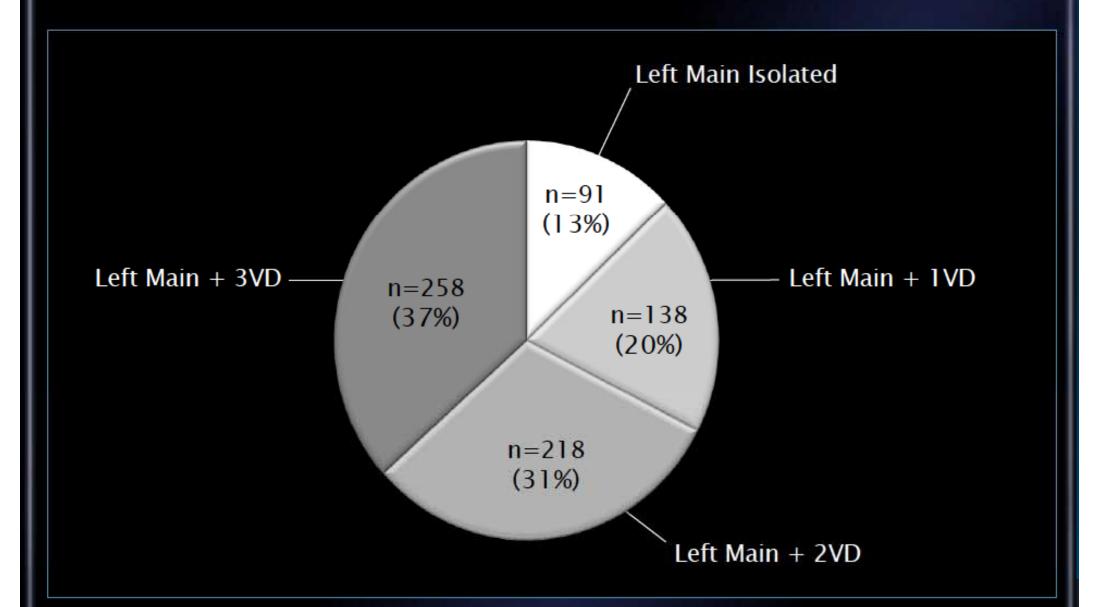
PCI* n=349

CABG n=322 RCT: 5 Year Final Follow-up
CABG 92.5% PCI 96.9%

PCI* n=346

Heterogeneity in the Left Main Group





Site-reported data

Patient Characteristics LM Subset



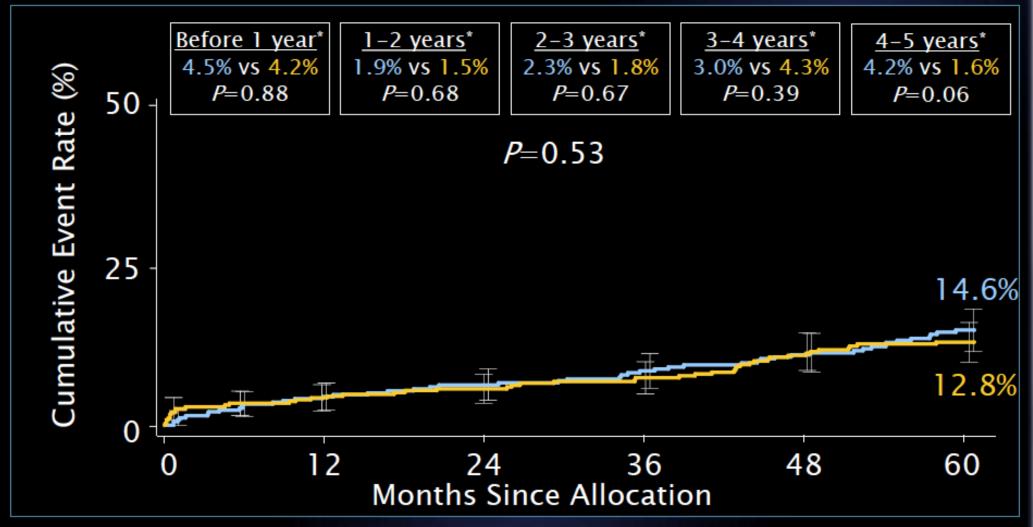
	CABG N=348	TAXUS N=357	<i>P</i> value
Age*, mean ± SD (y)	65.6 ± 10.1	65.4 ± 9.8	0.78
Medically treated diabetes*, %	22.4	21.8	0.86
BMI, mean ± SD	27.7 ± 5.0	28.2 ± 4.9	0.24
Additive euroSCORE*, mean ± SD	3.9 ± 2.9	3.9 ± 2.8	0.91
Total Parsonnet score*, mean ± SD	9.1 ± 7.4	8.9 ± 7.8	0.77
Total SYNTAX Score, mean ± SD	26.7 ± 11.5	28.1 ± 12.4	0.13
No. lesions, mean ± SD	3.2 ± 1.9	3.3 ± 1.8	0.89

All-Cause Death to 5 Years Left Main Subset



■ CABG (N=348)

■ TAXUS (N=357)



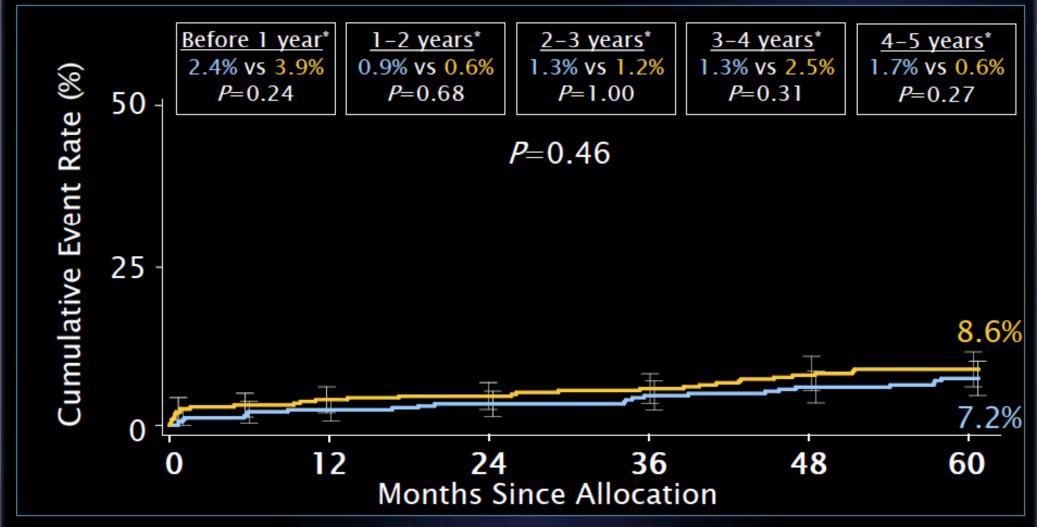
Cumulative KM Event Rate \pm 1.5 SE; log-rank Pvalue; *Binary rates

Cardiac Death to 5 Years Left Main Subset



 \blacksquare CABG (N=348)

■ TAXUS (N=357)



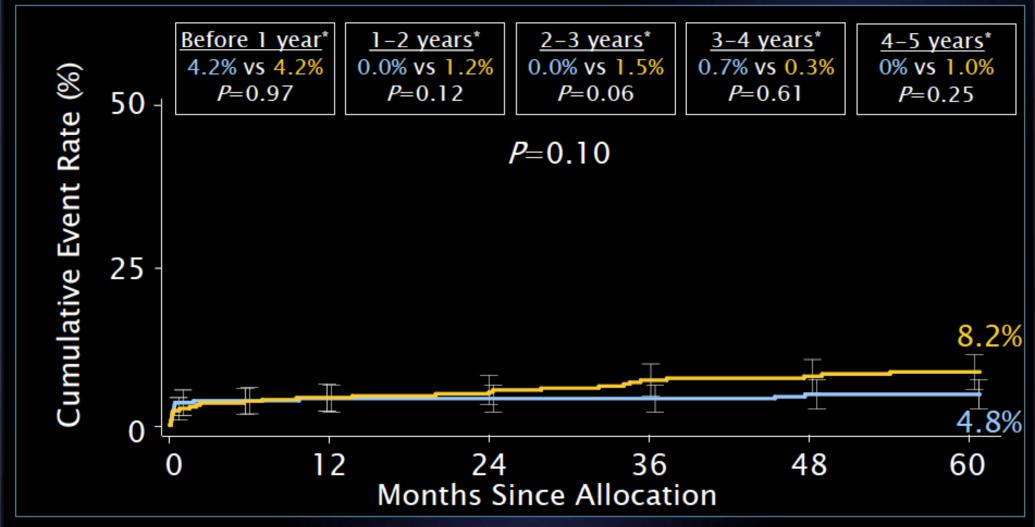
Cumulative KM Event Rate \pm 1.5 SE; log-rank Pvalue;*Binary rates

Myocardial Infarction to 5 Years *Left Main Subset*



 \blacksquare CABG (N=348)

■ TAXUS (N=357)



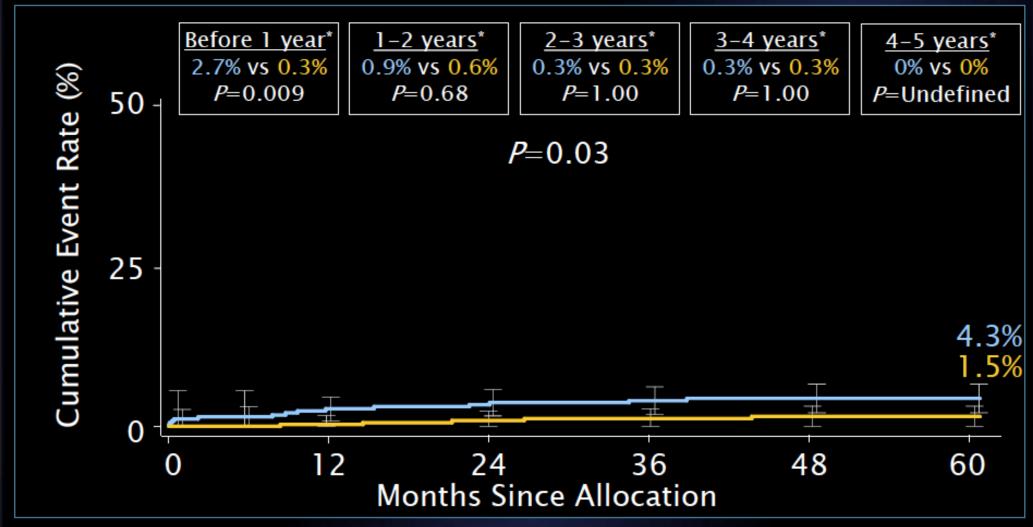
Cumulative KM Event Rate \pm 1.5 SE; log-rank Pvalue; Binary rates

CVA to 5 Years Left Main Subset



■ CABG (N=348)

TAXUS (N=357)



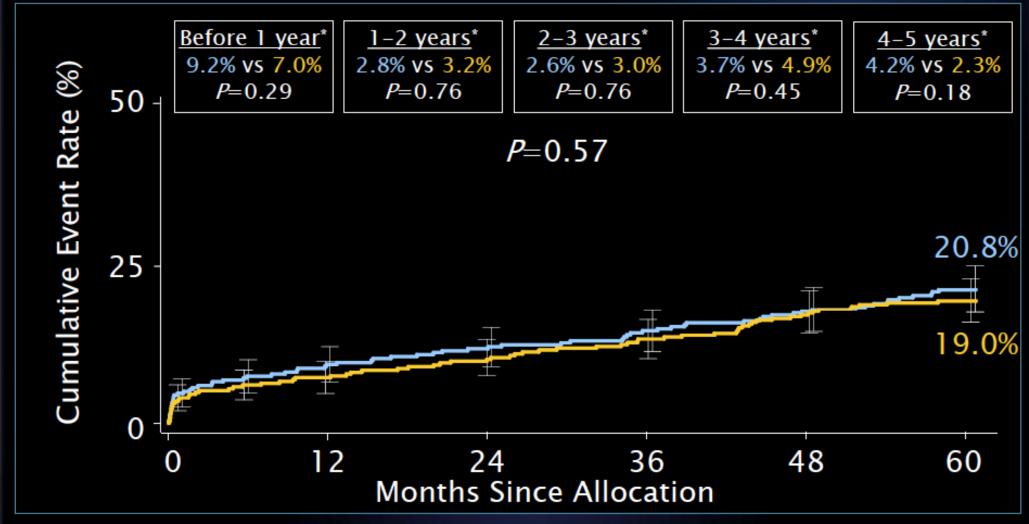
Cumulative KM Event Rate \pm 1.5 SE; log-rank Pvalue; Binary rates

All-Cause Death/CVA/MI to 5 Years Left Main Subset



 \blacksquare CABG (N=348)

■ TAXUS (N=357)



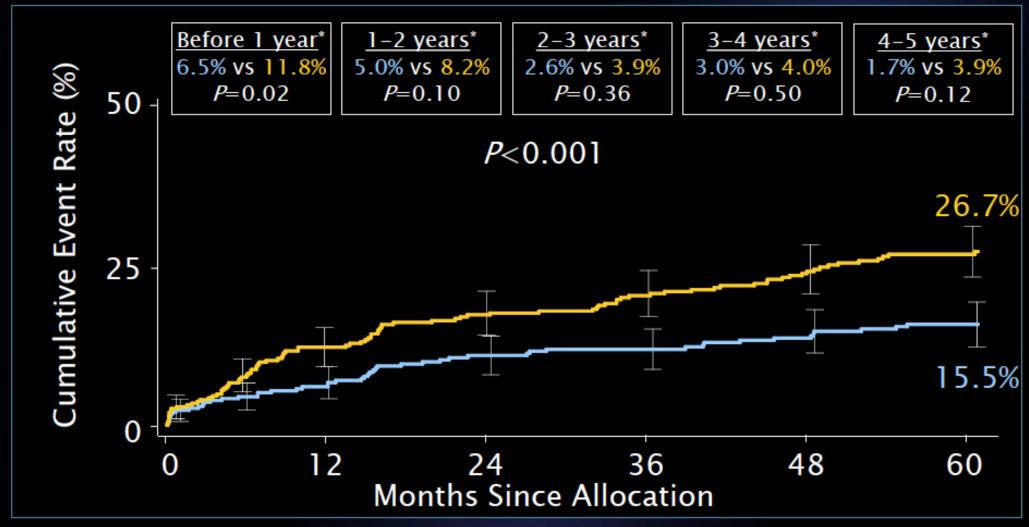
Cumulative KM Event Rate \pm 1.5 SE; log-rank *P* value; *Binary rates

Repeat Revascularization to 5 Years Left Main Subset



 \blacksquare CABG (N=348)

■ TAXUS (N=357)



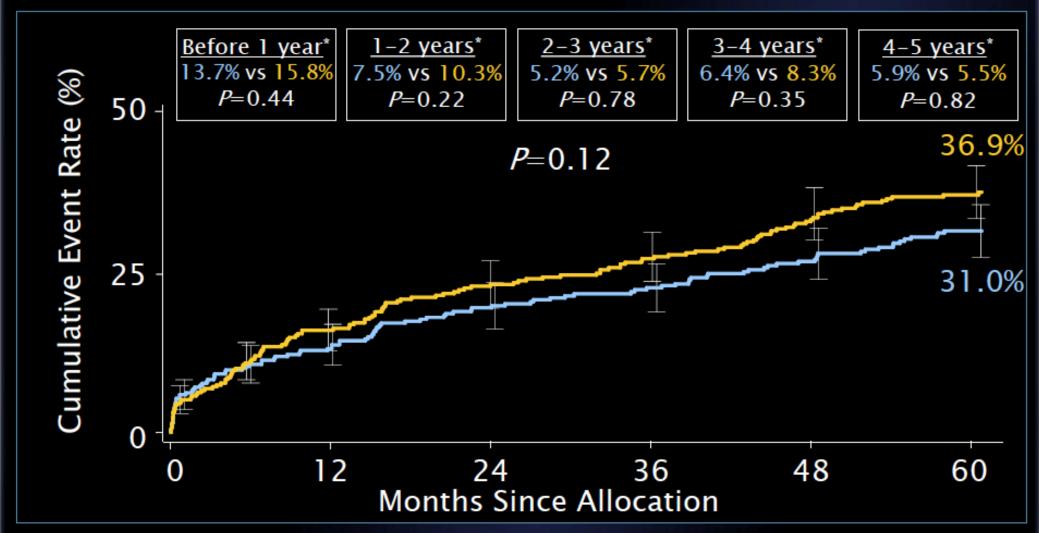
Cumulative KM Event Rate \pm 1.5 SE; log-rank Pvalue; Binary rates

MACCE to 5 Years Left Main Subset



 \blacksquare CABG (N=348)

■ TAXUS (N=357)

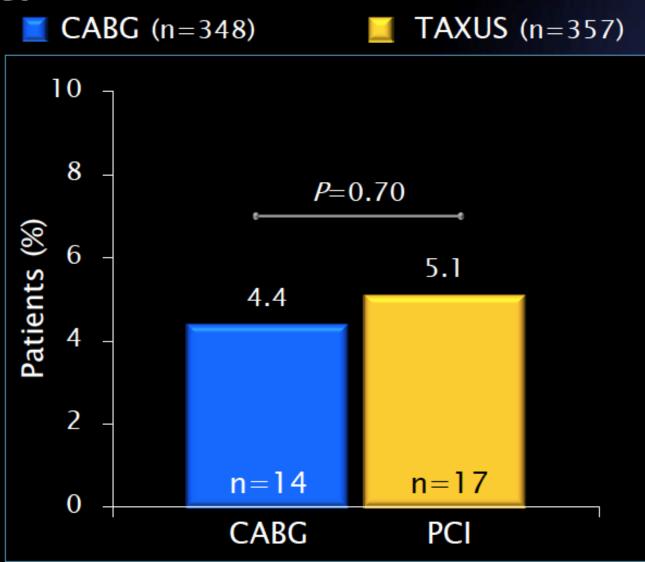


Cumulative KM Event Rate \pm 1.5 SE; log-rank Pvalue; Binary rates

Symptomatic Graft Occlusion & Stent Thrombosis to 5 Years

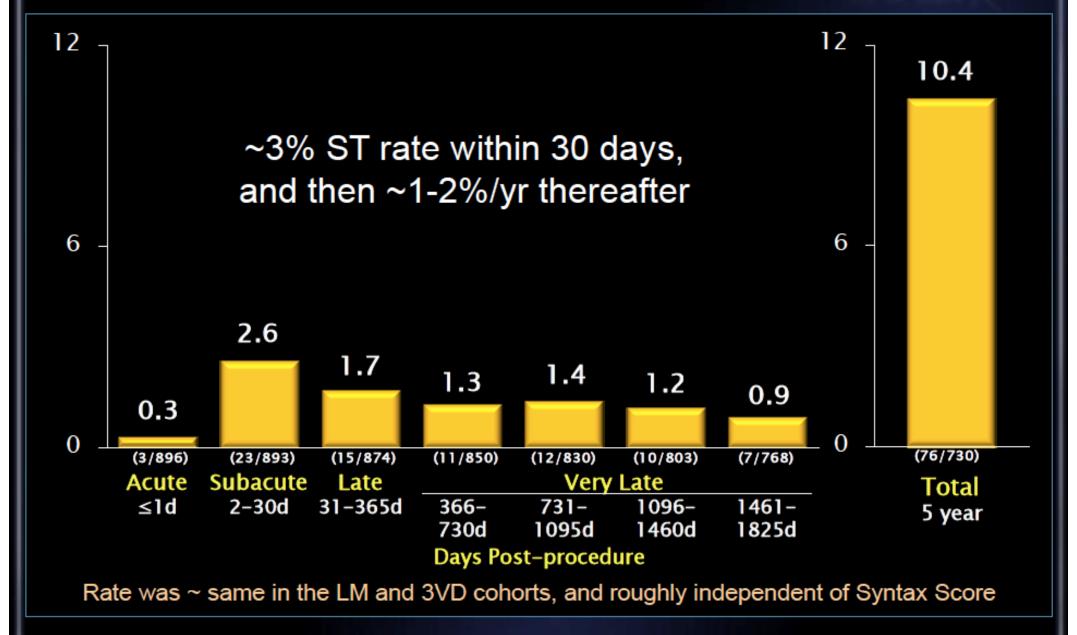


LM Subset



SYNTAX: Definite/Probable ARC Stent Thrombosis to 5 Years (Per Patient)

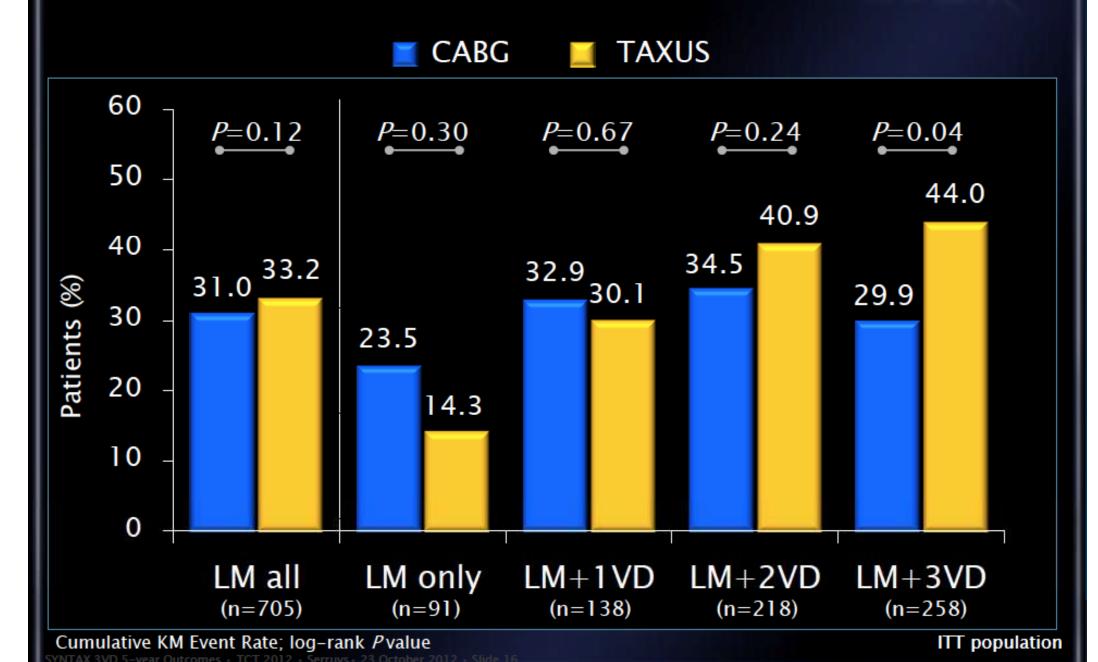




Serruys PW. TCT2012

MACCE to 5 Years Left Main Subsets

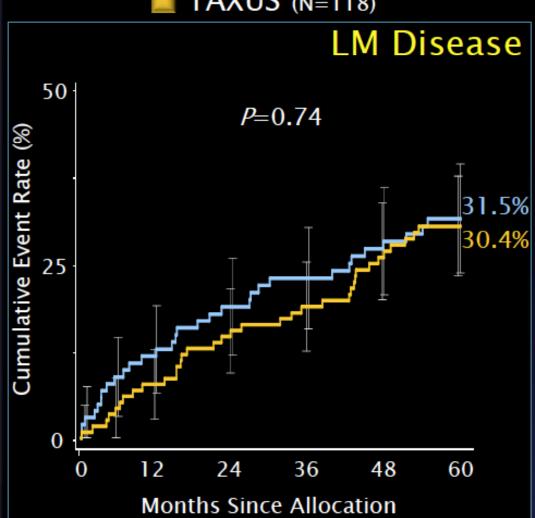




MACCE to 5 Years by SYNTAX Score Tercile LM Subset Low Scores 0-22 SYNTAX



■ TAXUS (N=118)



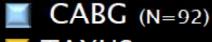
	CABG	PCI	<i>P</i> value
Death	11.3%	7.0%	0.28
CVA	4.1%	1.8%	0.28
MI	3.1%	6.2%	0.32
Death, CVA or MI	15.2%	13.9%	0.71
Revasc.	20.3%	23.0%	0.65

Cumulative KM Event Rate \pm 1.5 SE; log-rank Pvalue

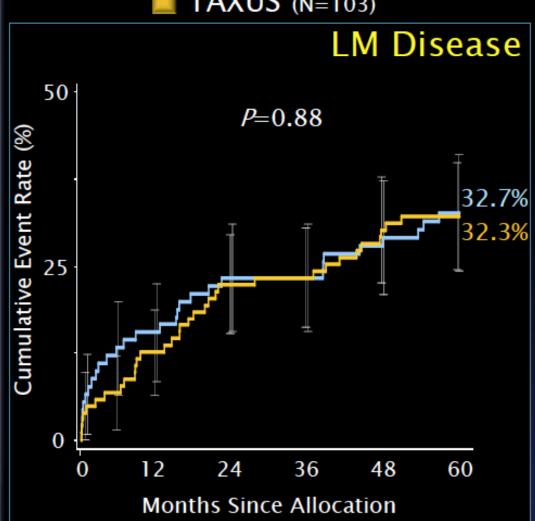
Site-reported Data; ITT population

SVNTAY 3VD 5-year Outcomes - TCT 2012 - Serring - 23 October 2012 - Slide 17

MACCE to 5 Years by SYNTAX Score Tercile LM Subset Intermediate Scores 23-32 SYNTA



TAXUS (N=103)



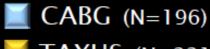
	CABG	PCI	<i>P</i> value
Death	19.3%	8.9%	0.04
CVA	3.6%	1.0%	0.23
MI	4.6%	6.0%	0.71
Death, CVA or MI	24.9%	15.7%	0.11
Revasc.	16.6%	22.2%	0.40

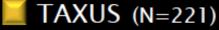
Cumulative KM Event Rate \pm 1.5 SE; log-rank Pvalue

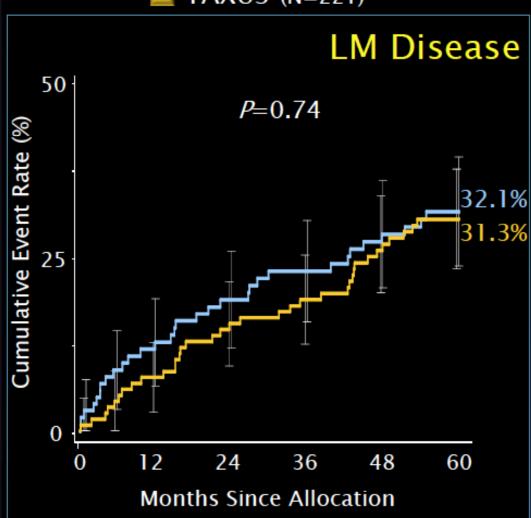
Site-reported Data; ITT population

MACCE to 5 Years by SYNTAX Score Tercile Low to Intermediate Scores (0-32)







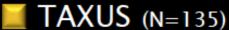


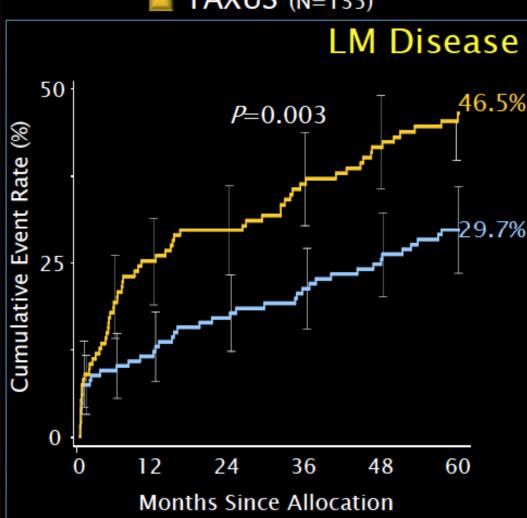
	CABG	PCI	<i>P</i> value
Death	15.1%	7.9%	0.02
CVA	3.9%	1.4%	0.11
MI	3.8%	6.1%	0.33
Death, CVA or MI	19.8%	14.8%	0.16
Revasc.	18.6%	22.6%	0.36

Serruys PW et al. Lancet 2013;381:629-38

MACCE to 5 Years by SYNTAX Score Tercile LM Subset High Scores ≥33 SYNTAX







	CABG	PCI	<i>P</i> value
Death	14.1%	20.9%	0.11
CVA	4.9%	1.6%	0.13
MI	6.1%	11.7%	0.13
Death, CVA or MI	22.1%	26.1%	0.40
Revasc.	11.6%	34.1%	<0.001

Cumulative KM Event Rate \pm 1.5 SE; log-rank Pvalue

Site-reported Data; ITT population

Summary Left Main Subset



- At 5 years, overall MACCE in the PCI group was comparable with CABG (31.0% CABG vs 36.9% PCI)
- Similar overall safety outcomes (Death/CVA/MI) between CABG and PCI at 5 years (20.8% CABG vs 19.0% PCI)
- There was a higher rate of revascularization in the PCI group (15.5% CABG vs 26.7% PCI), driven primarily by patients with high baseline SYNTAX scores
- A higher rate of CVA in the CABG group (4.3% CABG vs 1.5% PCI) was driven mostly by periprocedural events, with no difference between groups after 1 year
- PCI outcomes are excellent relative to CABG in LM isolated and LM+1VD

SYNTAX (2009-2013): Which Legacy?

The NEW ENGLAND JOURNAL of MEDICINE

MARCH 5, 2009

Percutaneous Coronary Intervention versus Coronary-Artery Bypass Grafting for Severe Coronary Artery Disease

Patrick W. Serruys, M.D., Ph.D., Marie-Claude Morice, M.D., A. Pieter Kappetein, M.D., Ph.D., Antonio Colombo, M.D., David R. Holmes, M.D., Michael J. Mack, M.D., Elisabeth Stähle, M.D. Ted E. Feldman, M.D., Marcel van den Brand, M.D., Eric J. Bass, B.A., Nic Van Dyck, R.N., Katrin Leadley, M.D., Keith D. Dawkins, M.D., and Friedrich W. Mohr, M.D., Ph.D., for the SYNTAX Investigators*

ABSTRACT

Percutaneous coronary intervention (PCI) involving drug-eluting stents is increasingly used to treat complex coronary artery disease, although coronary-artery bypass grafting (CABG) has been the treatment of choice historically. Our trial compared PCI and CABG for treating patients with previously untreated three-vessel or left main coronary artery disease (or both).

We randomly assigned 1800 patients with three-vessel or left main coronary artery tal Evanston, IL (T.E.E.): Boston Scientific disease to undergo CABG or PCI (in a 1:1 ratio). For all these patients, the local cardiac surgeon and interventional cardiologist determined that equivalent anatomical revascularization could be achieved with either treatment. A noninferiority comparison of the two groups was performed for the primary end point - a major adverse the Eramus University Medical Center cardiac or cerebrovascular event (i.e., death from any cause, stroke, myocardial infarction, or repeat revascularization) during the 12-month period after randomization. Patients for whom only one of the two treatment options would be beneficial. because of anatomical features or clinical conditions, were entered into a parallel,

Most of the preoperative characteristics were similar in the two groups. Rates of major adverse cardiac or cerebrovascular events at 12 months were significantly higher in the PCI group (17.8%, vs. 12.4% for CABG; P=0.002), in large part because of published on February 18, 2009, and up an increased rate of repeat revascularization (13.5% vs. 5.9%, Pc0.001); as a result. the criterion for noninferiority was not met. At 12 months, the rates of death and N Engl J Med 2009;360:961-72. myocardial infarction were similar between the two groups; stroke was significantly Copyrigh © 2008 Minorchaeth Medical 2 more likely to occur with CABG (2.2%, vs. 0.6% with PCI; P=0.003).

CABG remains the standard of care for patients with three-vessel or left main coronary artery disease, since the use of CABG, as compared with PCI, resulted in lower rates of the combined end point of major adverse cardiac or cerebrovascular events at 1 year. (ClinicalTrials.gov number, NCT00114972.)

N ENGL J MED 350(10 NEJM.ORG MARCH 5, 2009)

(P.W.S., A.P.K., M.B.): Institut Cardio San Raffaele Scientific Institute, Milan (A.C.): Mann Clinic Rochester MN (M.J.M.); University Hospital Uppsala, opsala, Sweden (E.S.): Evanston Hosp K.D.D.); and Herzzentrum Universität Leipzig, Leipzig, Germany (F.W.M.). Ad-Rottenfam, Gravendilioval 230, 3015 CE serruys@erasmusmc.nl.

and Cardiac Surgery (SYNTAX) investi-

dated on February 7, 2013, at NEJM.org.

Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease

and left main coronary disease: 5-year follow-up of the

randomised, clinical SYNTAX trial

Friedrich W.Mohr, Marie-Claude Morice, A. Piet er Kappetein, Tedis Feldman, Elisabeth Stähle, Antonio Colombo, Michael J.Mask, David R.Holmes Jr, Marie-anable Marel, Nic Van Dydr, Vidri M Houle, Keith D Dawláns, Patrick W Serruss

Background We report the 5-year results of the SYNTAX trial, which compared coronary artery bypass graft surgery Loncet 2013; 381:629-38 or three-vessel disease, to confirm findings at 1 and 3 years.

Methods The randomised, clinical SYNTAX trial with nested registries took place in 85 centres in the USA and Lateria being being form Europe. A cardiac surgeon and interventional cardiologist at each centre assessed consecutive patients with do-novo (Prof W More MO); Maptal three-vessel disease or left main coronary disease to determine suitability for study treatments. Eligible patients suitable for either treatment were randomly assigned [1:1] by an interactive voice response system to either PCI with a first-generation paclitaxel-cluting stent or to CABG. Patients suitable for only one treatment option were entered into either the PCI-only or CABG-only registries. We analysed a composite rate of major adverse cardiac and cerebrovascular events (MACCE) at 5-year follow-up by Kaplan-Meier analysis on an intention-to-treat basis. This study is registered with ClinicalTrials.gov, number NCT00114972.

s 1800 patients were randomly assigned to CABG (n=897) or PCI (n=903). More patients who were assig Findings 1000 patients were randomly assigned to CABC withdraw consent than did those assigned to PCI (50 w 11). After 5 years follow-up, Kaplan-Meier estimates of MACCE were 26-9% in the CABG group and 37-3% in the PCI group (p-0-0001). Estimates of sentificiation, Mus., Bay myocardial infarction (3.8% in the CABG group vs 9.7% in the PCI group; p<0.0001) and repeat revascularisation (13.7% vs 25.9%; p<0.0001) were significantly increased with PCI versus CABG. All-cause death (11.4% in the CABG group vs 13.9% in the PCI group; p=0.10) and stroke (3.7% vs 2.4%; p=0.09) were not significantly different CARG group vs 13-79-38 uses to grover, rebetween group, 28-6% of patients in the CARG group with low SYNTAX scores had MACCE versus 32-1% of
patients in the PCI group [ep-0.43] and 31-0% in the CARG group with left main coronary disease had MACCE
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tion CABG should remain the standard of care for patients with complex lesions (high or intermediate SYNTAX scores). For patients with less complex disease (low SYNTAX scores) or left main coronary disease (low or intermediate SYNTAX scores). PCI is an acceptable alternative. All patients with complex multivessel coronary artery disease should be reviewed and discussed by both a cardiac surgeon and interventional cardiologist to reach co

Coronary artery bypass graft surgery (CABG) has been patients has been a matter of debate, with many pubthought to be appropriate only for patients with single-tical power. The SYNergy between percutaneous con disease, such as multivessel and left main coronary or three-vessel disease (or both), by randomly assign-

the standard of care for revascularisation of patients lished trials comparing outcomes of CABG and PCI with with complex coronary artery disease since its drug-eluting stents (DES).11 Most of these trials have introduction in 1968.1 When percutaneous coronary been limited by non-randomised patient selection, intervention (PCI) was introduced in 1977,2 it was inclusion of less complex disease, or insufficient statisvessel disease, but as operator ability and device intervention with TAXus and cardiac surgery (SYNTAX) technologies have advanced, the use of PCI has trial* assessed the optimum revascularisation treatment expanded to treat patients with increasingly complex for patients with de-novo left main coronary disease

Articles

V M House PhQ K D Davetire MC

ncetcom Vol 381 February 23, 2013

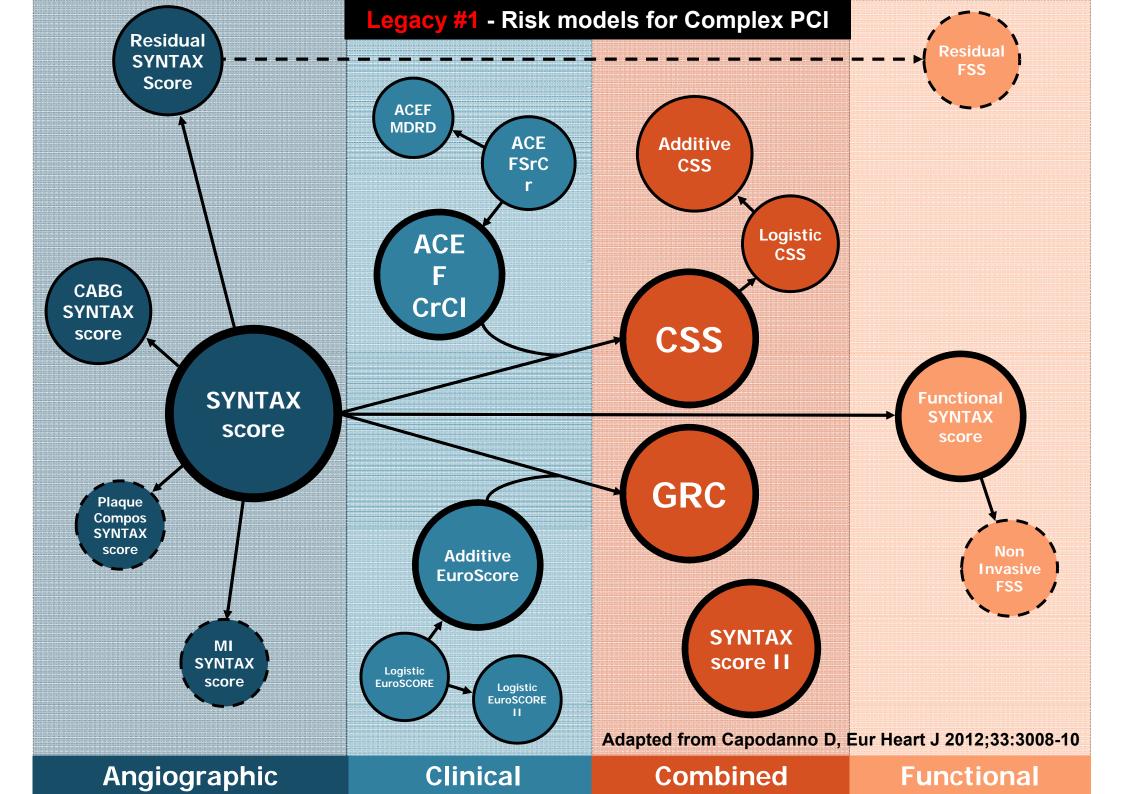
1-Year Outcomes

5-Year Outcomes









Legacy #2 – SYNTAX Advanced Our understanding On How to Improve The Outcomes of LM PCI

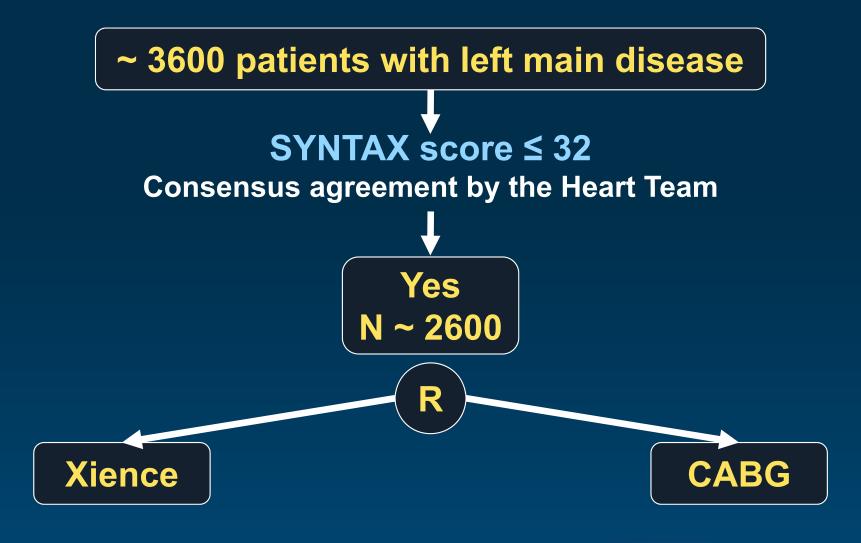
- Use best in class DES
- Thienopyridine pre-loading
- Optimal pharmacotherapy
 Statin pre-loading
 - Bivalirudin anticoagulation
- IVUS/FFR to assess the intermediate LM Isn
- FFR to avoid unnecessary stenting, but also to ensure complete ischemic revascularization
- IVUS guided LM stenting
- 1- vs 2-stent techniques
- Debulking
- Optimal LM stent technique
 Hemodynamic support

 - Staging
 - Routine angiographic FU





Legacy #3 – From the Ashes of the SYNTAX, a New Trial: The EXCEL







Legacy #4 - The Heart Team Approach

The rationale for Heart Team decision-making for patients with stable complex coronary artery disease

Stuart J. Head¹, Sanjay Kaul², Michael J. Mack³, Patrick W. Serruys¹,

David P. Taggart⁴, David R. Holmes Jr⁵, Martin B. Leon^{6,7}, Jean Marco⁸,

Ad J.J.C. Bogers¹, and A. Pieter Kappetein^{1*}

The Heart Team of Cardiovascular Care

David R. Holmes, JR, MD,* Jeffrey B. Rich, MD,† William A. Zoghbi, MD,‡ Michael J. Mack, MD,§

- Initially introduced in revascularization trials to select patients for randomization. The Coronary Heart Team consists of a clinical/non-invasive cardiologist, an interventional cardiologist, and a cardiac surgeon. Other physicians with specific expertise can be added if necessary.
- The Heart Team has recently become a class 1C recommendation in European and American guidelines on myocardial revascularization





5-Year from SYNTAX... key messages

For patients with left main disease

- Revascularization with PCI has comparable safety and efficacy outcomes to CABG
- -Although formally unproved at this stage, PCI seems a reasonable treatment alternative in this patient population, in particular, when the SYNTAX Score is low (≤22) or intermediate (23-32)

Legacies from SYNTAX include evolving concepts in trial design and decision making for LM PCI



