Clinical outcomes of State-of-the-Art percutaneous coronary revascularisation in patients with de novo three vessel disease.

Results of the SYNTAX II Trial.

Javier Escaned MD, PhD, FESC
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on behalf of the SYNTAX II Investigators.

Potential conflicts of interest

Speaker's name: Javier Escaned

I have the following potential conflicts of interest to report:

Speaker at educational events and consultancies: Abbott, AstraZeneca, Biosensors, Boston Scientific, Medtronic, OrbusNeich, Philips Healthcare

The SYNTAX II study was funded through unrestricted grants from Boston Scientific and Philips Volcano.

Background

- The management of patients with 3-vessel disease (3VD) according to ESC guidelines is largely influenced by the results of the pivotal SYNTAX trial.
- However, since the completion of that trial major technical and procedural advances, influencing PCI outcomes, have taken place:
  - New risk stratification tools.
  - 2nd generation DES.
  - Physiology- and imaging PCI guidance.
  - Improved CTO PCI techniques.

Extent of CAD	PCI		CABG	
3VD with a SYNTAX Score >32	I	A	I	B
3VD with a SYNTAX Score 23-32	I	A	III	B
3VD with a SYNTAX Score >32	I	A	III	B

Windecker S et al. EHJ 2014;35:2541-619
Escaned J et al. EuroIntervention. 2016 Jun 12;12(2):e224-34

Objective of the SYNTAX II study

To investigate if recent technical and procedural developments in PCI (incorporated to form the SYNTAX II strategy) significantly influence outcomes in appropriately selected patients with three-vessel (3VD) coronary artery disease.

Components of the SYNTAX II strategy

- SYNTAX Score II (incorporating clinical and anatomical variables) to guide Heart Team decisions on myocardial revascularisation.
- Physiology-based revascularisation (hybrid use of iFR and FFR).
- Second generation DES (thin strut, biodegradable polymer, everolimus-eluting Synergy™ stent [EES]).
- IVUS-guided optimisation of stent deployment (modified MUSIC criteria).
- Contemporary CTO revascularization techniques.
- Guideline-directed medical therapy.

Escaned J et al. EuroIntervention. 2016 Jun 12;12(2):e224-34

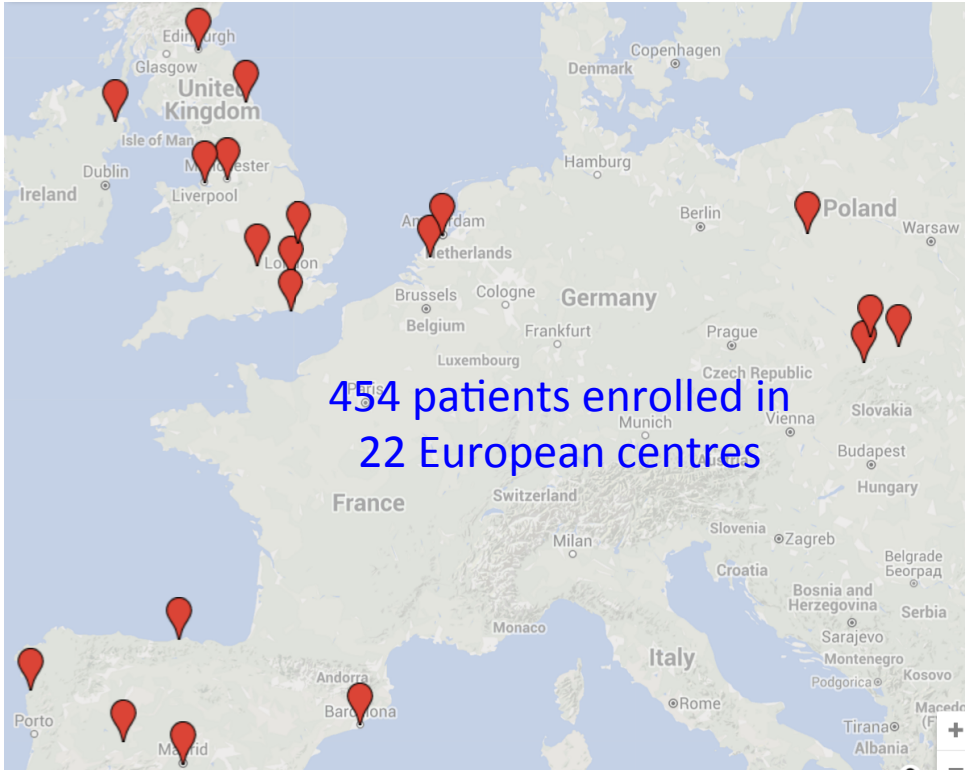
Design and eligibility

- Multicenter, prospective, single-arm, open-label trial of patients with *de-novo* 3VD without left-main stem involvement
- Inclusion if the SYNTAX score II recommends either CABG or PCI (equipoise in 4-year mortality) or PCI, irrespective of anatomic SYNTAX score.
- Sample size: 450 patients (90% power to show superiority in terms of use of 2nd generation EES over PES + attrition).
- Control group: Matched patients with 3VD from the SYNTAX I trial with a SYNTAX Score II showing equipoise between PCI and CABG.

Study design: Escaned J et al. EuroIntervention. 2016 Jun 12;12(2):e224-34. ClincalTrials.gov identifier: NCT02015832.

Participating sites

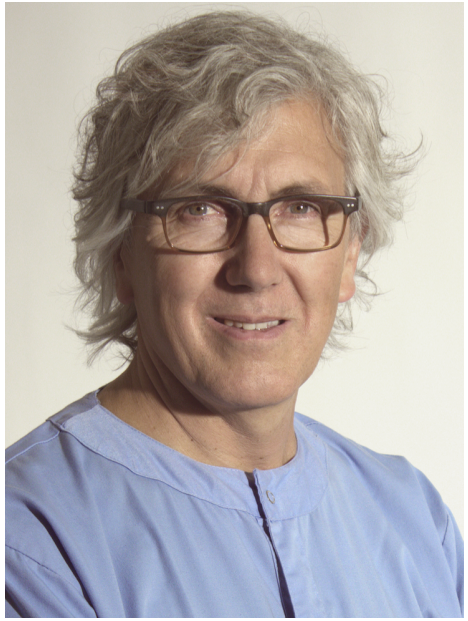
- Belfast Health & Social Care Trust, UK
- Hospital Clínico San Carlos IDISSC, Spain
- John Radcliffe Hospital, Oxford, UK
- Hospital Clinic I Provincial de Barcelona, Spain
- Imperial College Healthcare NHS Trust, UK
- Szpital Kliniczny, Poland
- Hospital Universitario La Paz, Spain
- Hospital Clinico Salamanca, Spain
- Papworth Hospital, UK
- Academisch Medisch Centrum, The Netherlands
- Liverpool Heart and Chest Hospital, UK
- Manchester Royal Infirmary, UK
- Freeman Hospital Newcastle, UK
- Erasmus MC, The Netherlands
- The Royal Infirmary of Edinburgh, UK
- Hospital Universitario Marqués de Valdecilla, Spain
- American Heart of Poland (PAK), Poland
- Hospital Meixoeiro, Spain
- Hospital Puerta de Hierro, Spain
- Brighton & Sussex University Hospitals NHS Trust, UK
- Gornoslaskie Centrum Medycnze, Poland
- St Raphael Hospital, Poland



* Centers listed by number of enrolled patients

SYNTAX II

Principal Investigators and Study Chairmen



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Chairman

Vasim Farooq MB ChB PhD
Manchester Royal Infirmary
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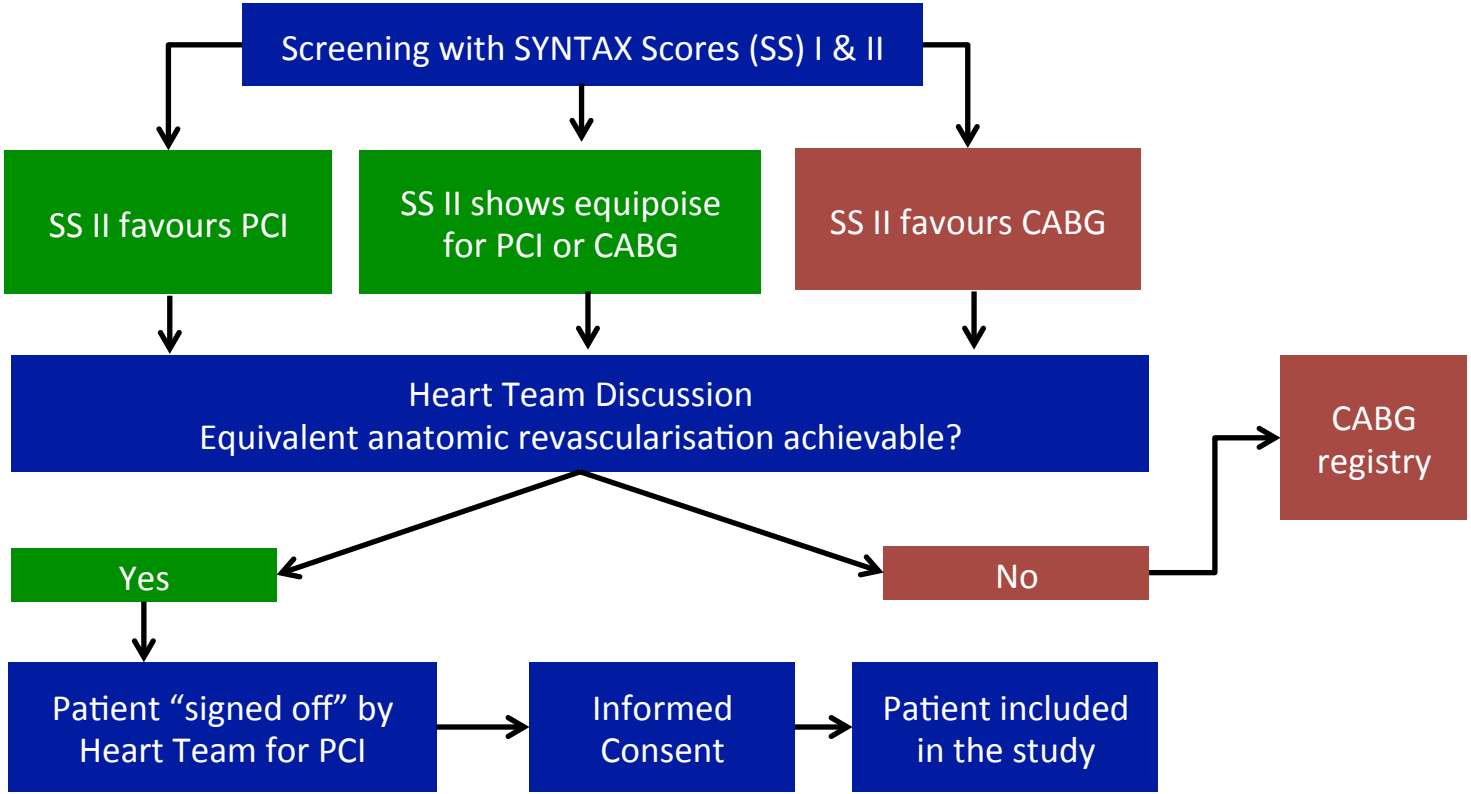
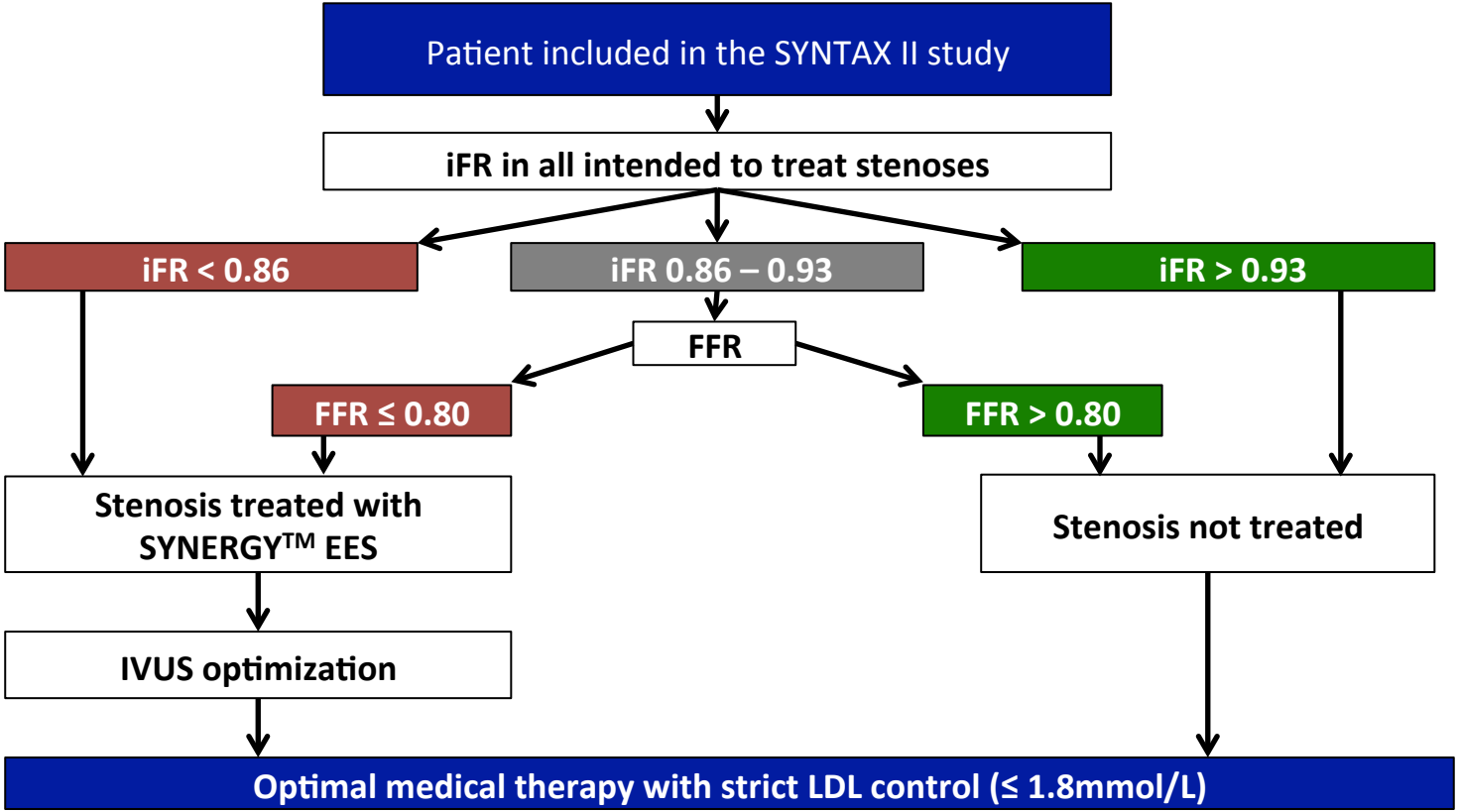
Deputy Chairman

Study flowchart: patient inclusion



Study flowchart: PCI procedure



Primary endpoint: comparison with PCI

- **Primary endpoint:** Composite of major adverse cardiac and cerebrovascular events (MACCE) at one-year follow-up.

- **Comparator:** Predefined PCI cohort (n=315) from the original SYNTAX-I trial selected on the basis of equipoise 4-year mortality between CABG and PCI

Exploratory endpoint: comparison with CABG

- **Exploratory endpoint:** Composite of major adverse cardiac and cerebrovascular events (MACCE) at one-year follow-up.

- **Comparator:** Predefined CABG cohort (n=334) from the original SYNTAX-I trial selected on the basis of equipoise 4-year mortality between CABG and PCI.

Baseline characteristics

	SYNTAX II (n=454)	SYNTAX I PCI arm (n=315)	P value
Age (years)	66.7 ± 9.7	66.7 ± 9.1	0.99
Male	93.2%	93.0%	0.93
BMI (kg/m²)	28.9 ± 4.7	28.2 ± 4.4	0.032
DM	30.3%	29.2%	0.75
Current Smoker	14.7%	17.8%	0.26
Previous MI	12.5%	28.7%	<0.001
Previous Stroke	5.6%	1.9%	0.010
Hypertension	77.0%	73.4%	0.26
Hyperlipidemia	77.3%	74.4%	0.35
Clinical Presentation			<0.001
Silent Ischemia	5.5%	13.3%	
Stable angina	68.8%	61.6%	
Unstable angina	25.6%	25.1%	

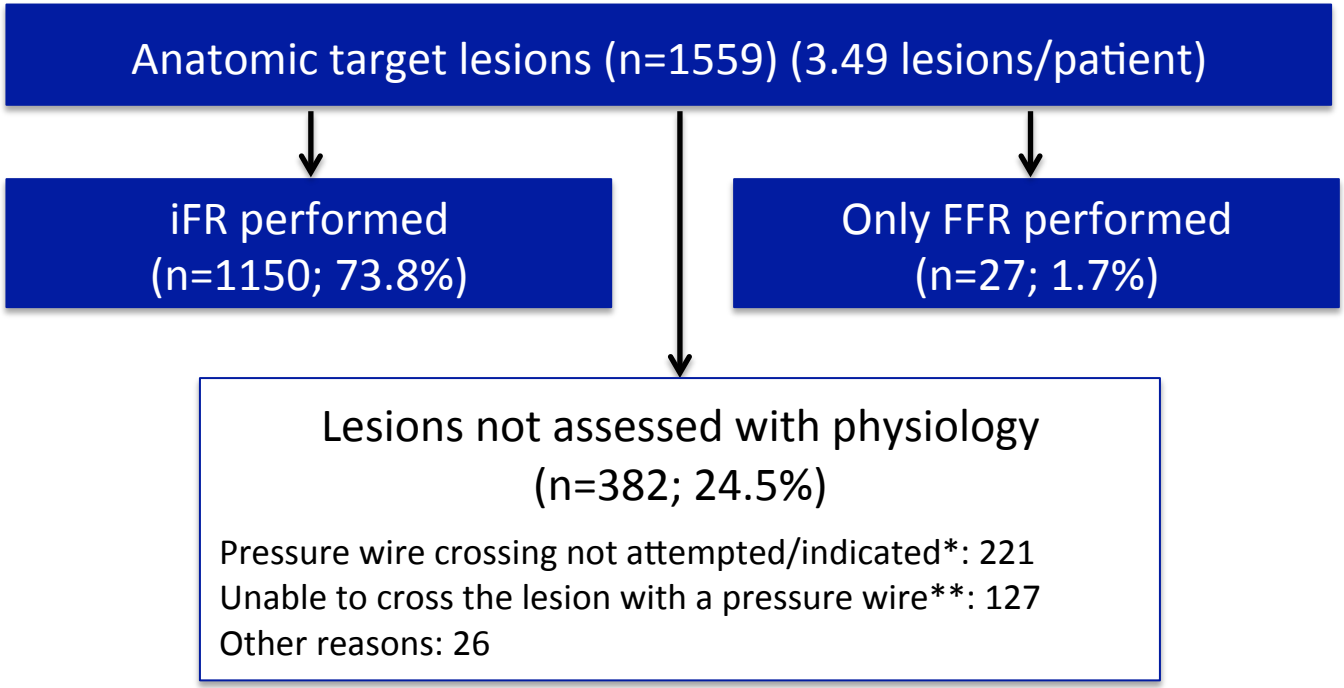
SYNTAX Score II

	SYNTAX II	SYNTAX I PCI arm	P value
Components of the SYNTAX Score II			
Age	66.7 ± 9.7	66.7 ± 9.1	0.99
Gender (Male)	93.2%	93.0%	0.93
Cr Clearance (ml/min)	82.0 ± 26.9	87.3 ± 28.5	0.008
Ejection Fraction (%)	58.1 ± 8.3	61.8 ± 11.3	<0.001
Peripheral Vascular Disease	7.7%	9.5%	0.37
COPD	10.8%	12.7%	0.42
Anatomic SYNTAX Score	20.3 ± 6.4	22.8 ± 8.7	<0.001

SYNTAX Score II PCI	**30.2 ± 8.6**	**30.6 ± 8.7**	**0.528**
Predicted 4-yr mortality PCI (%)	8.9 ± 8.8%	9.2 ± 8.7%	0.640
SYNTAX Score II CABG	**29.1 ± 10.4**	**29.1 ± 9.6**	**1.0**
Predicted 4-yr mortality CABG (%)	9.0 ± 9.3	8.5 ± 8.1	0.440

SYNTAX II

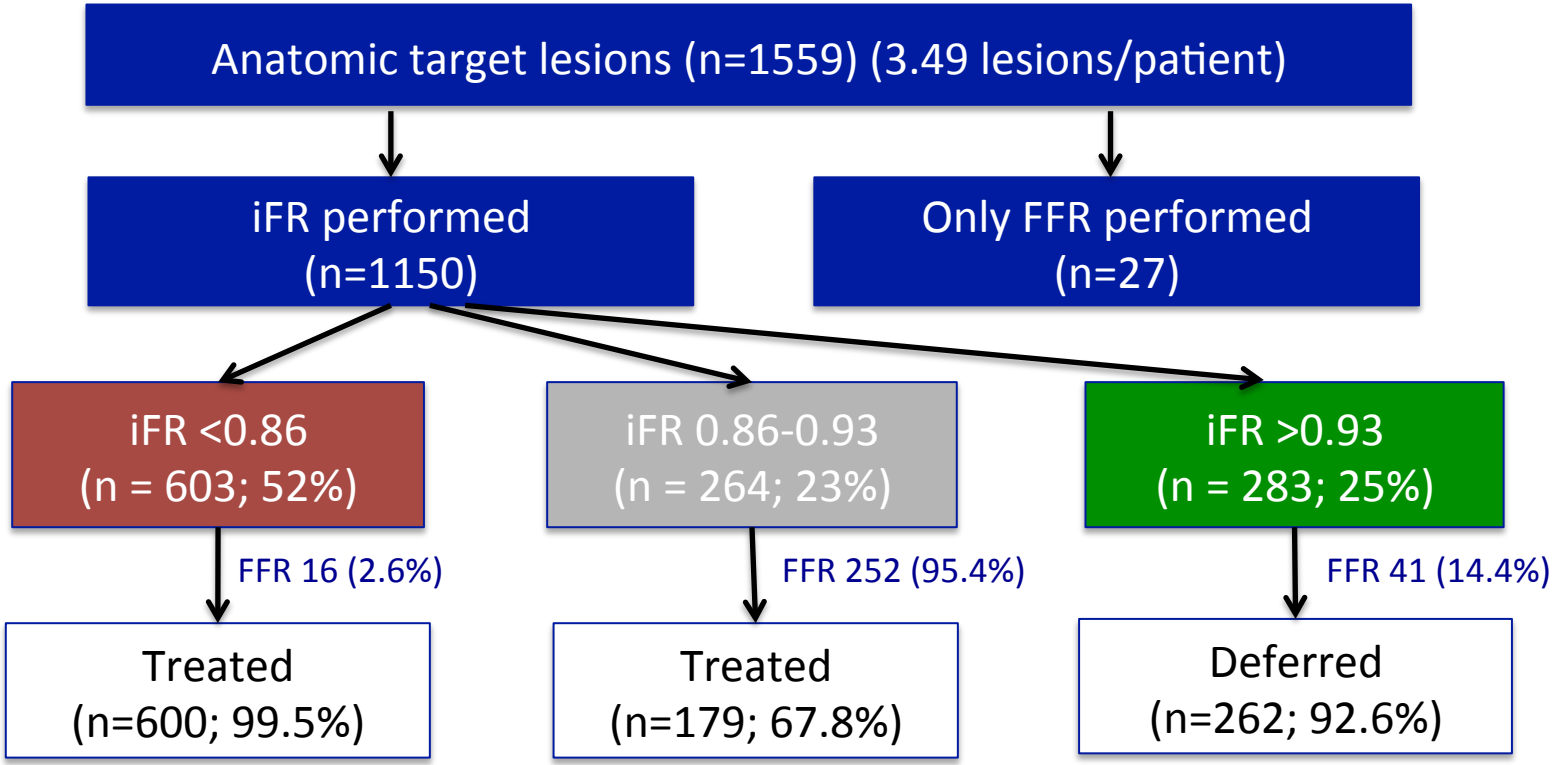
Physiological stenosis interrogation



*Use of pressure guidewire in CTOs was not indicated.
**Physiological interrogation was prompted irrespective of angiographic lesion severity.

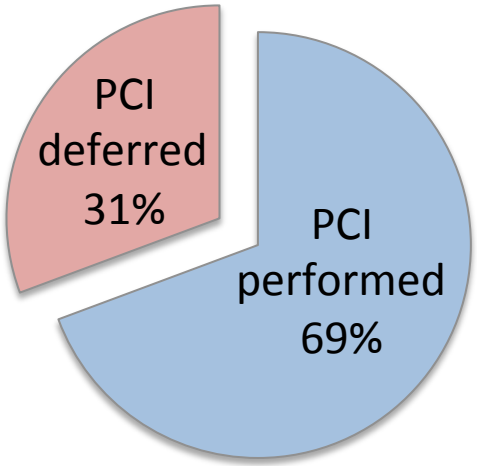
SYNTAX II

Physiological stenosis interrogation



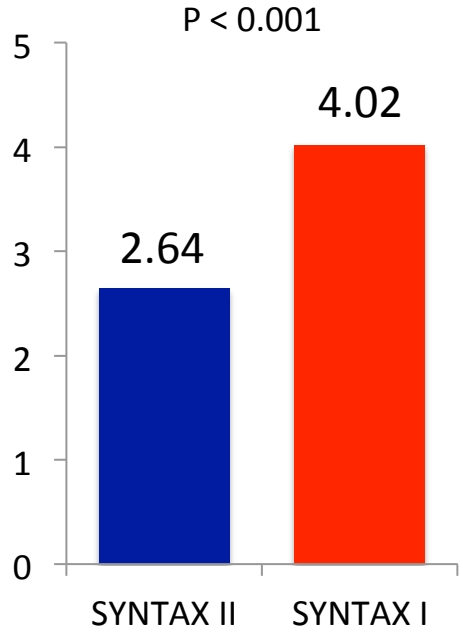
Impact of intracoronary physiology on PCI

Lesion treatment after iFR/FFR interrogation (n=1177)

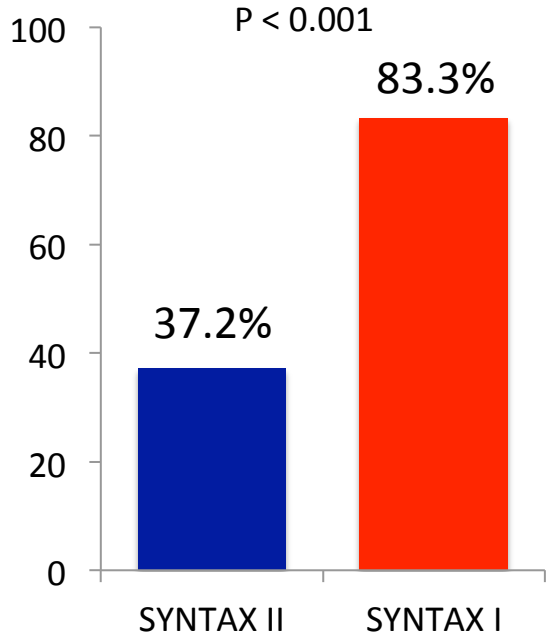


SYNTAX II

Lesions treated per patient (n) in SYNTAX II and SYNTAX I

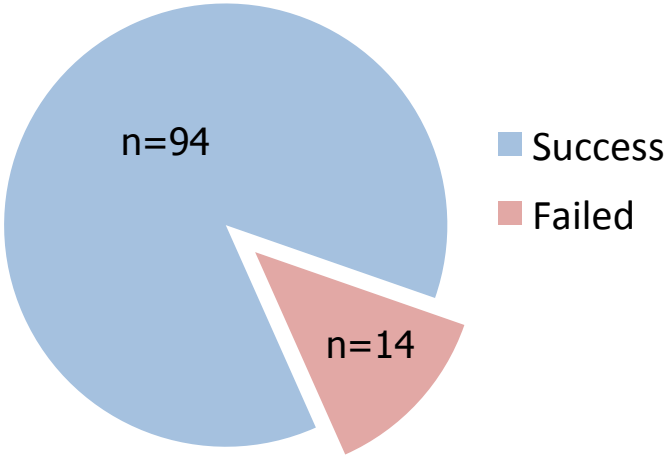


Cases of three-vessel PCI (%) in SYNTAX II and SYNTAX I



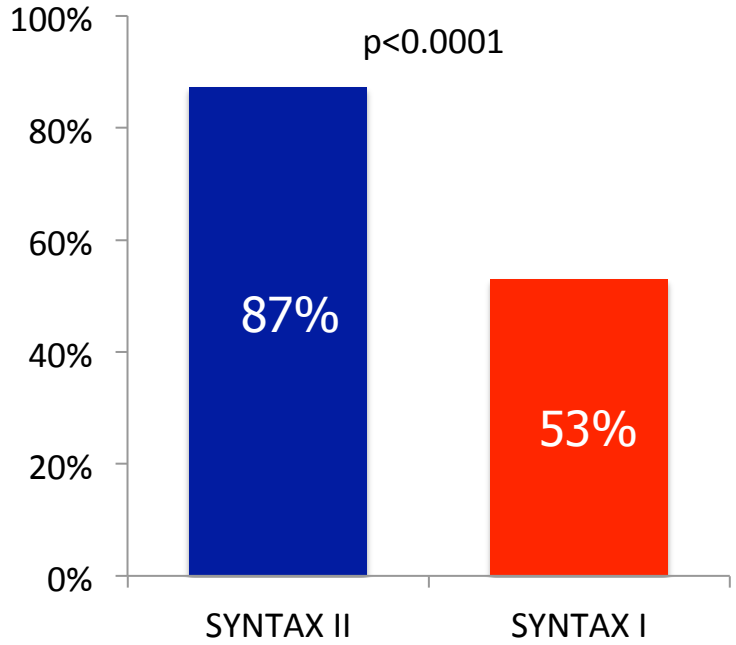
Treatment of chronic total occlusions (CTO)

CTO PCI procedural success rate in SYNTAX II: 87%

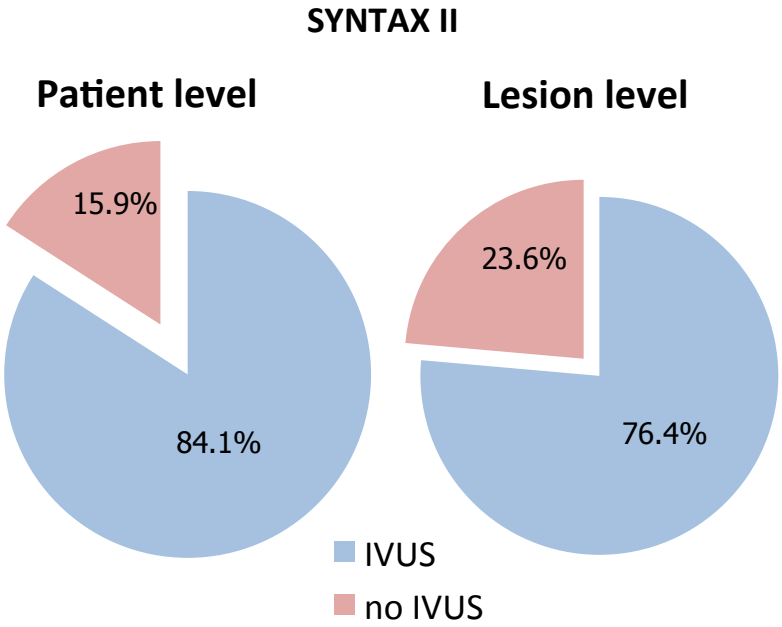


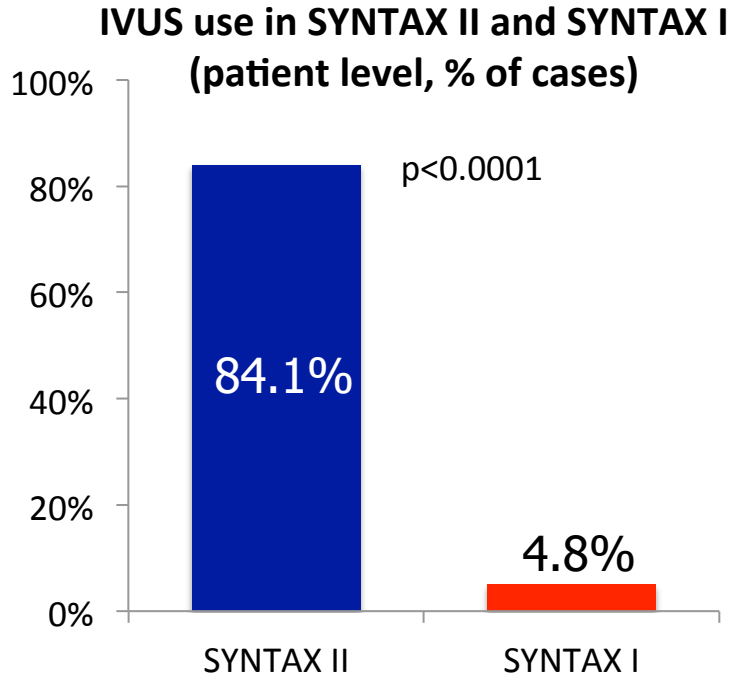
SYNTAX II CTO PCI

CTO revascularisation in SYNTAX II and SYNTAX I



Use of intravascular ultrasound (IVUS)



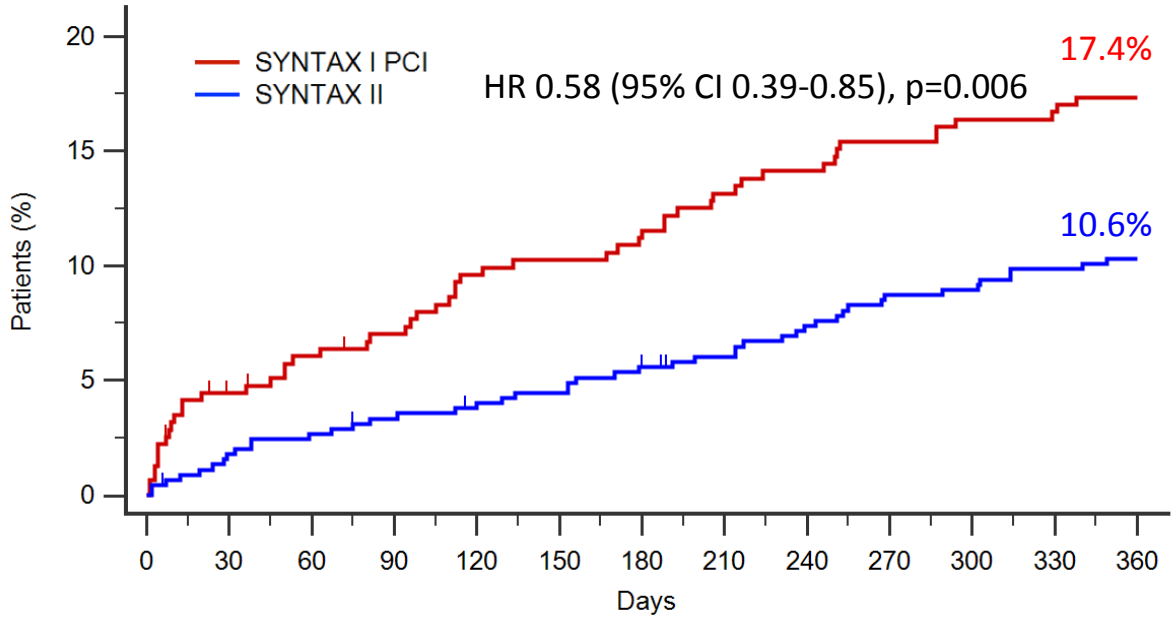


Post-implantation IVUS led to further optimisation of the stented lesion in 30.2%.

One year follow up results

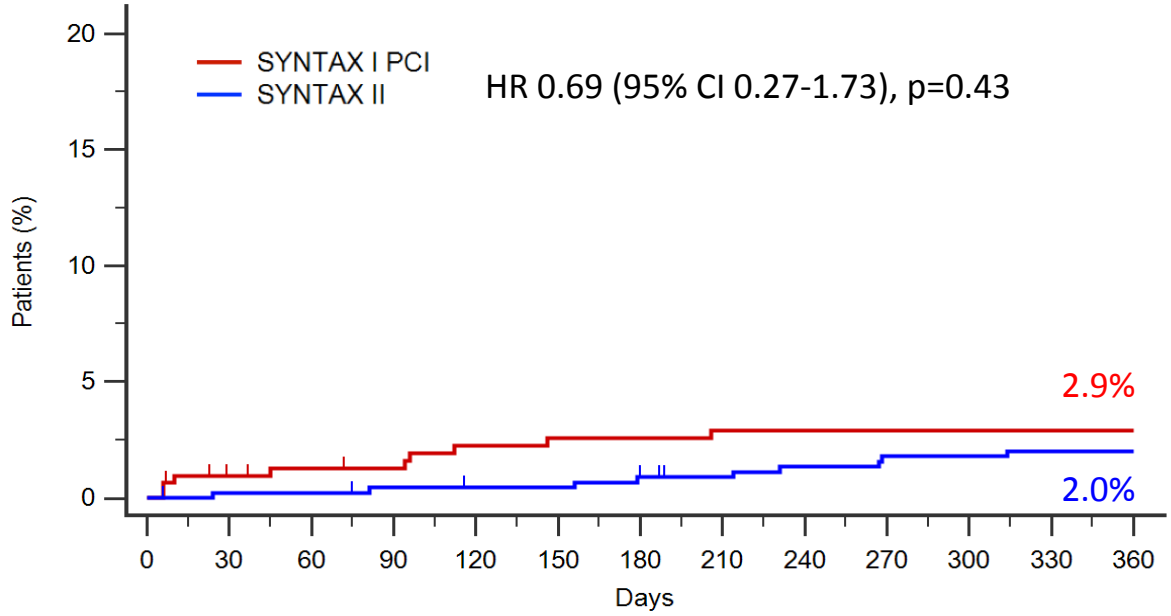
Comparison with PCI

Primary endpoint: MACCE



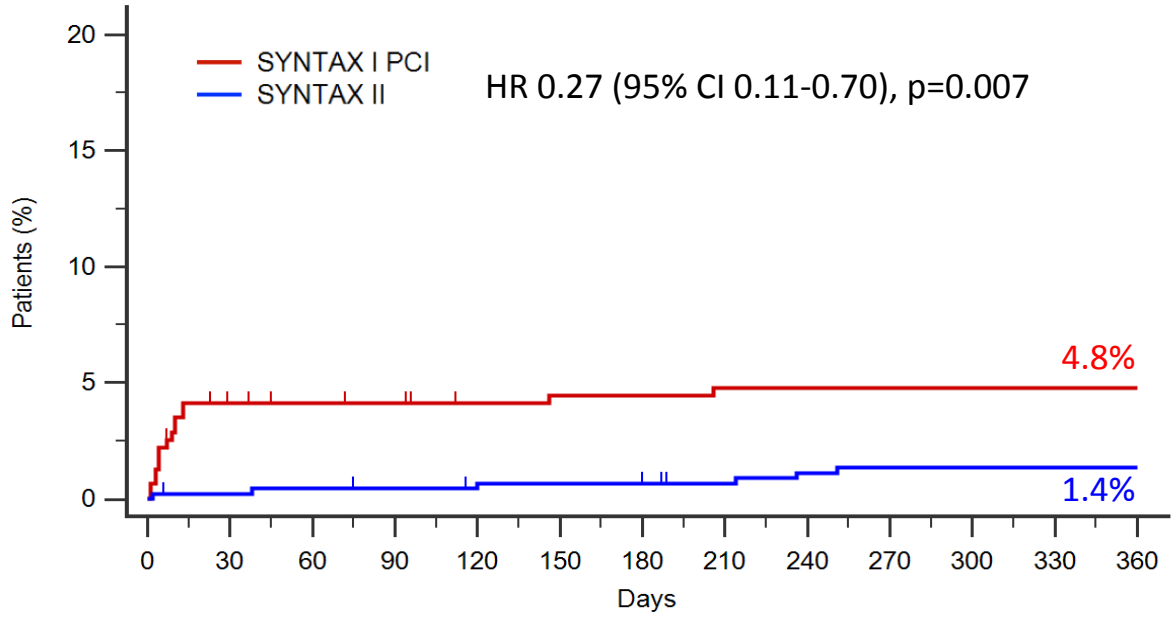
SYNTAX I PCI	315	298	292	288	280	278	274	269	266	262	259	258	256
SYNTAX II	450	441	437	433	429	427	421	417	411	405	404	400	398

All-cause death



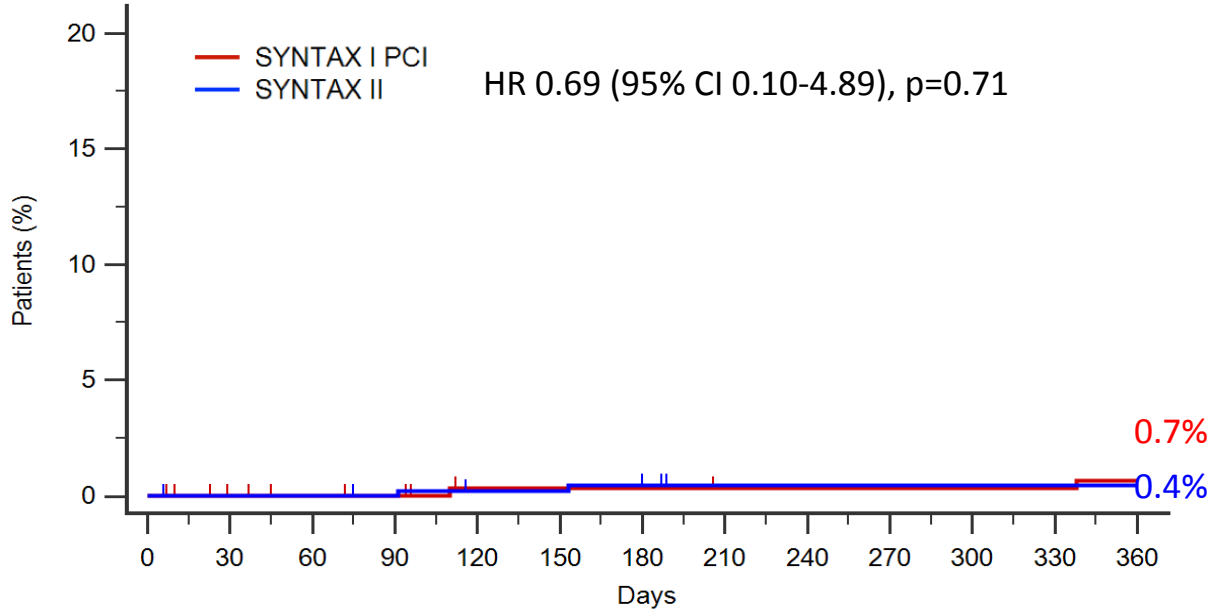
SYNTAX I PCI	315	309	307	306	303	302	302	301	301	301	301	301	301
SYNTAX II	450	448	448	446	445	445	442	440	438	436	436	435	435

Myocardial infarction



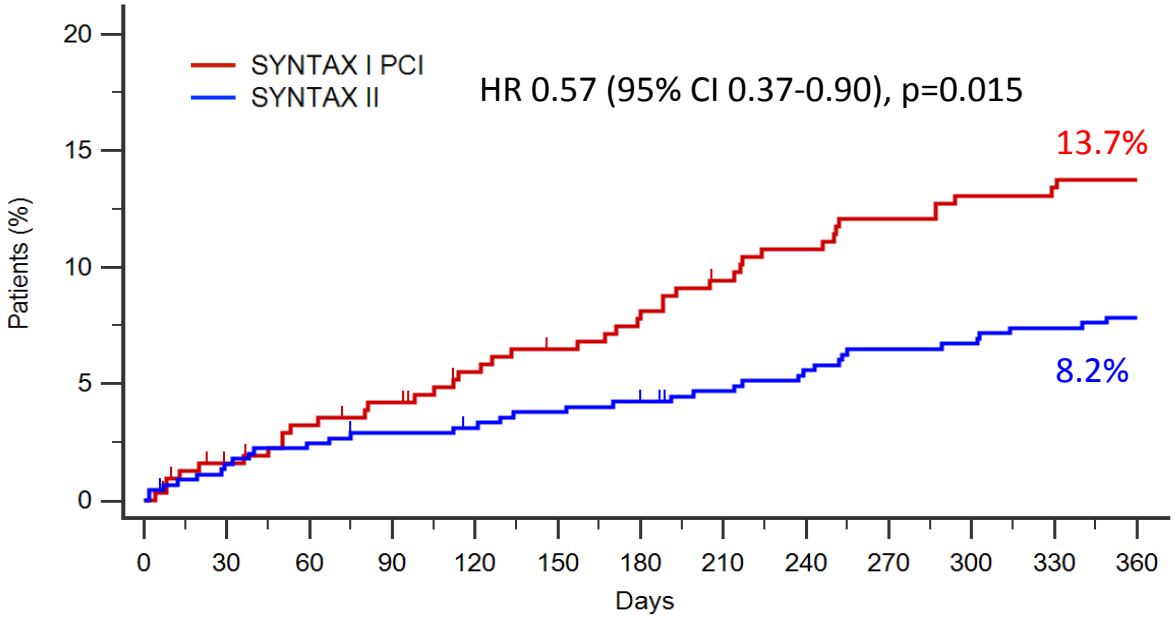
SYNTAX I PCI	315	299	297	296	293	292	292	291	291	291	291	291	291
SYNTAX II	450	448	447	446	444	444	443	441	439	438	438	438	438

Stroke



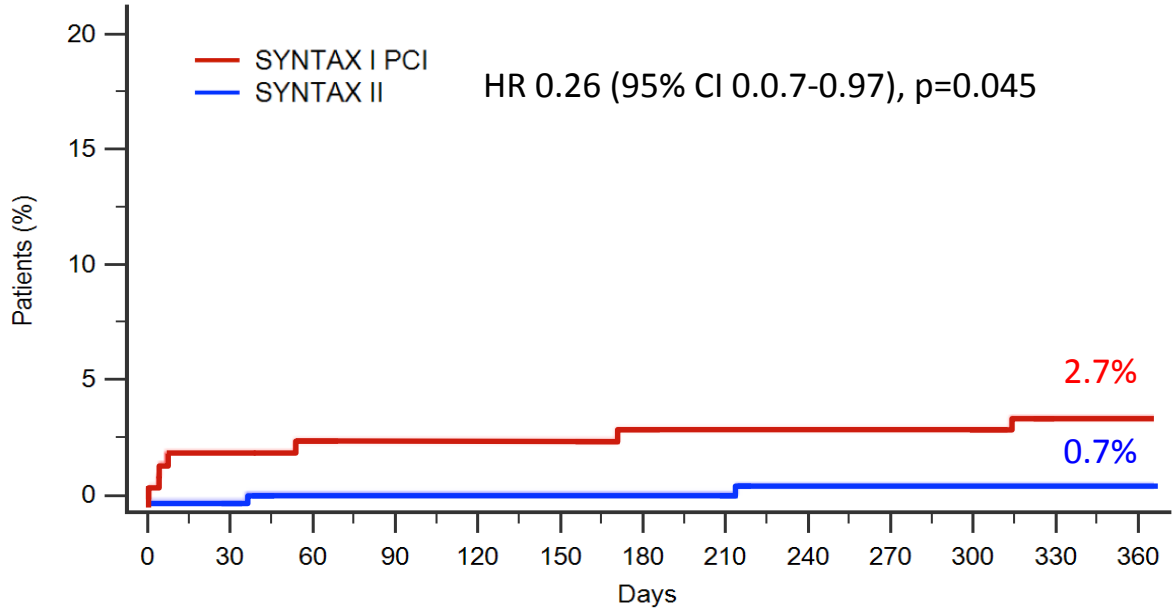
SYNTAX I PCI	315	309	307	306	302	302	302	301	301	301	301	301	300
SYNTAX II	450	449	449	448	446	446	444	442	442	442	442	442	442

Any repeat revascularisation



SYNTAX I PCI	315	305	299	295	288	284	279	274	270	266	263	262	261
SYNTAX II	450	442	438	435	433	430	427	423	419	415	414	411	409

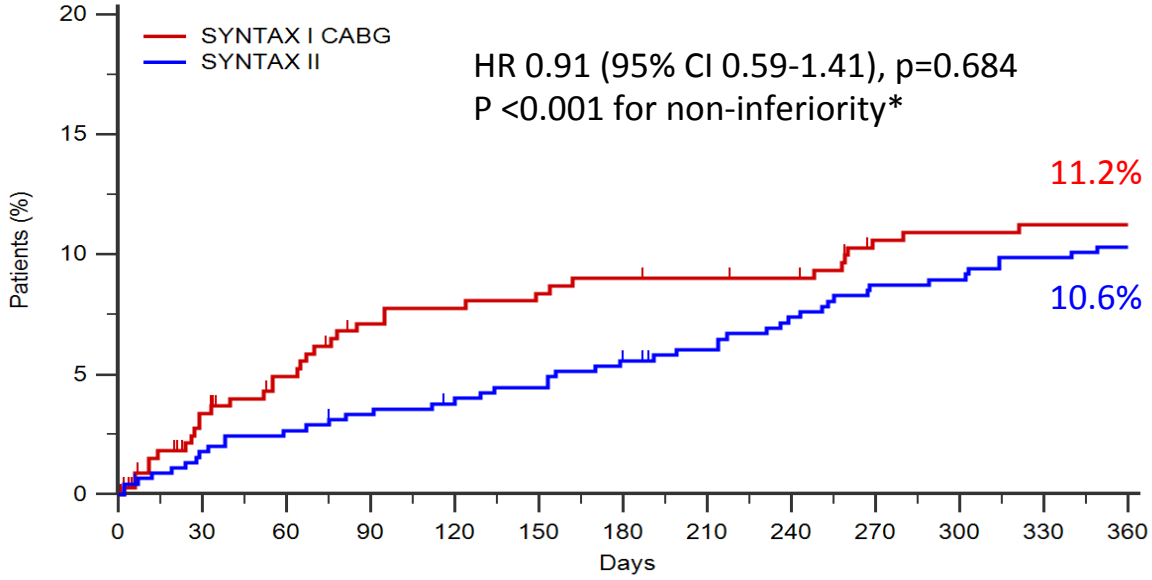
Definite stent thrombosis



SYNTAX I PCI	315	299	297	296	292	292	292	291	291	291	291	291	290
SYNTAX II	450	447	446	444	441	441	437	435	431	428	428	427	427

One year follow up results
Comparison with CABG

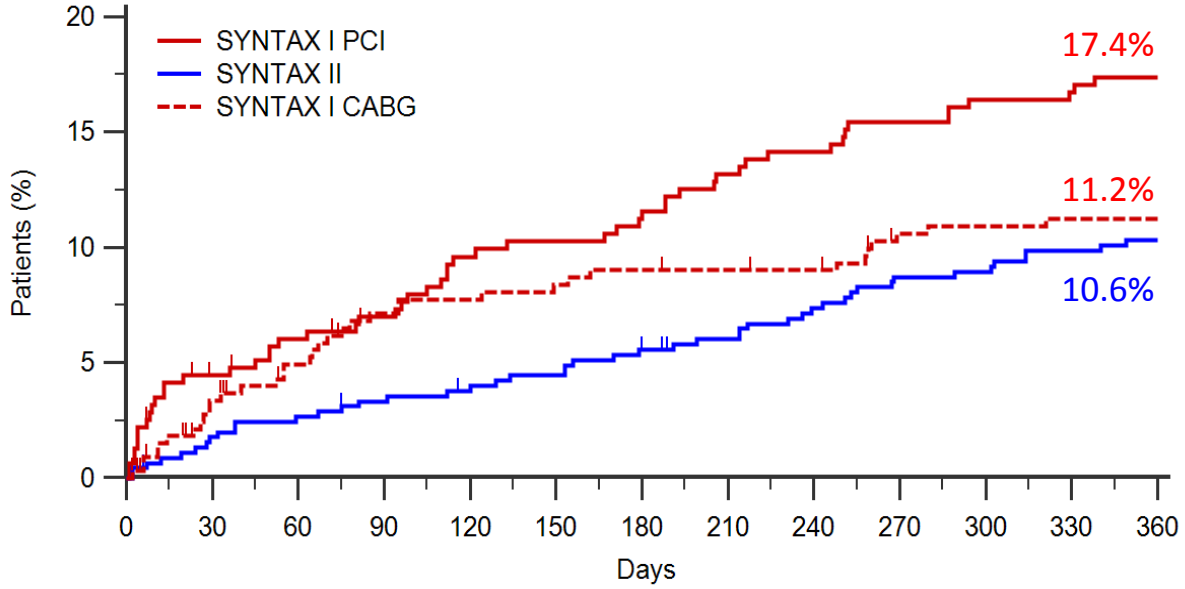
Exploratory End-Point: MACCE PCI vs. CABG



SYNTAX I CABG	334	313	304	295	293	291	289	288	287	279	278	277	277
SYNTAX II	450	441	437	433	429	427	421	417	411	405	404	400	398

*Non-inferiority margin of 5% with a one-sided alpha of 5%

MACCE SYNTAX II and SYNTAX I PCI / CABG

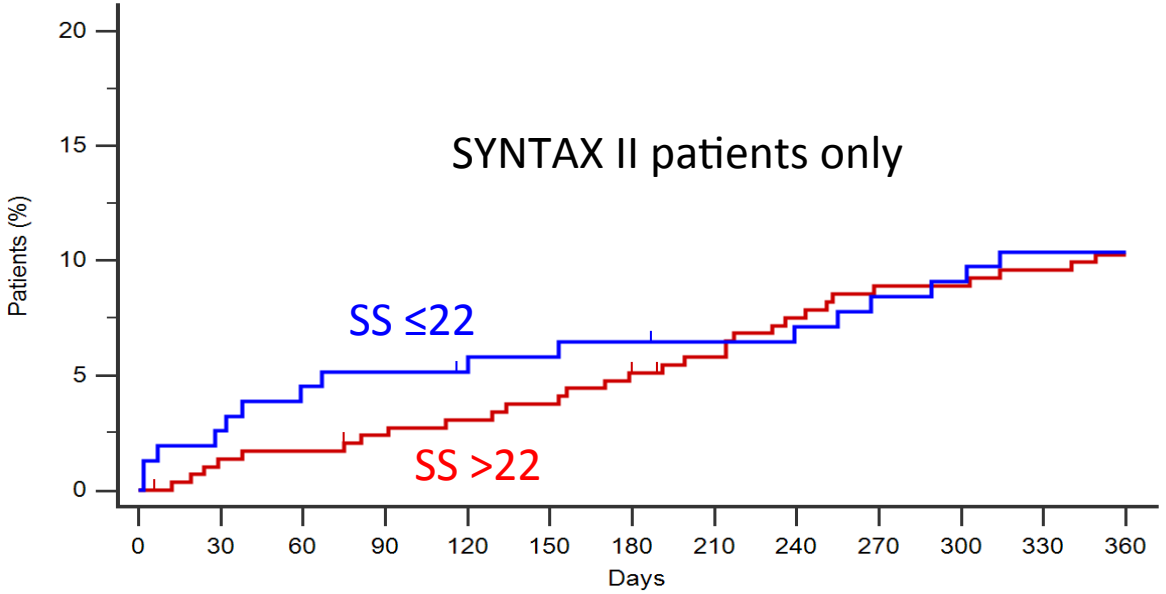


SYNTAX I PCI	315	298	292	288	280	278	274	269	266	262	259	258	256
SYNTAX II	450	441	437	433	429	427	421	417	411	405	404	400	398
SYNTAX I CABG	334	313	304	295	293	291	289	288	287	279	278	277	277

One year follow up results

Influence of anatomic SS on MACCE

SYNTAX II MACCE in SS I ≤22 and >22



SYNTAX SCORE >22	295	290	289	286	284	282	277	274	269	265	265	263	261
SYNTAX SCORE ≤22	155	151	148	147	145	145	144	143	142	140	139	137	137

Conclusions (I)

- In patients with 3VD the use of the SYNTAX-II strategy was associated with improved clinical outcomes at one year, compared to matched patients treated percutaneously in the original SYNTAX-I trial.

- The one-year exploratory comparison between SYNTAX II and matched CABG patients from the original SYNTAX-I trial suggests non-inferiority of PCI when the SYNTAX-II strategy is followed.

Conclusions (II)

- Compared to SYNTAX I, contemporary state-of-art PCI in SYNTAX II led to significantly fewer lesions treated with PCI, and significantly higher success rates in CTO revascularisation.

- One-year outcomes of patients with SYNTAX score >22, treated with PCI using the SYNTAX score II risk stratification, were similar to those observed in patients with low anatomical risk (SYNTAX score ≤22).

SYNTAX II trial organisation

Principal Investigators

PIs: A Banning, J Escaned

Study Chairman: PW Serruys

Deputy Chairman: V Farooq

Co-PIs: AP Kappetein, D Taggart (Surgeons)

Steering Committee

A Banning, J Escaned, V Farooq, AP Kappetein, PW Serruys, D Taggart, GA van Es

Sponsor

ECRI - European Cardiovascular Research Institute

Grant givers

Volcano and Boston Scientific

Data & Safety Monitoring Board

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Clinical Events Committee

JP Herrman, E McFadden, V Thijs, P Vranckx

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Core Laboratory

Coronary physiology: N. Ryan

IVUS: G. De Maria

Coronary CTA: C. Collet, Y. Miyazaki

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FASTTRACK CLINICAL RESEARCH
ESC Late Breaking Science in PCI 1

Interventional cardiology

Clinical outcomes of state-of-the-art percutaneous coronary revascularization in patients with *de novo* three vessel disease: 1-year results of the SYNTAX II study

Javier Escaned[1], Carlos Collet[2], Nicola Ryan[1], Giovanni Luigi De Maria[3], Simon Walsh[4], Manel Sabate[5], Justin Davies[6], Maciej Lesiak[7], Raul Moreno[8], Ignacio Cruz-Gonzalez[9], Stephan P. Hoole[10], Nick Ej West[10], J. J. Piek[2], Azfar Zaman[11], Farzin Fath-Ordoubadi[12], Rodney H. Stables[13], Clare Appleby[13], Nicolas van Mieghem[14], Robert Jm. van Geuns[14], Neal Uren[15], Javier Zueco[16], Pawel Buszman[17], Andres Iniguez[18], Javier Goicolea[19], David Hildick-Smith[20], Andrzej Ochala[21], Dariusz Dudek[22], Colm Hanratty[4], Rafael Cavalcante[14], Arie Pieter Kappetein[14], David P. Taggart[3], Gerrit-Anne van Es[23,24], Marie-Angele Morel[23], Ton de Vries[23], Yoshinobu Onuma[14,23], Vasim Farooq[12], Patrick W. Serruys[6]*, and Adrian P. Banning[3]

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Thank you for your attention

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Back up slides

Centres, site investigators and enrolled patients

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Hospital Clinico San Carlos Javier Escaned	50	
John Radcliffe Hospital Adrian Banning	35	
Hospital Clinic I Provincial Manel Sabaté	32	
Imperial College Healthcare Justin Davies	27	
Holy Transfiguration Hospital Maciej Lesiak	20	
Hospital Universitario La Paz Raul Moreno	20	
Hospital Clinico Salamanca Ignacio Cruz	20	
Papworth Hospital Nick West	20	
Academisch Medisch Centrum Jan Piek	20	
Liverpool Heart and Chest Hospital Clare Appleby & Rod Stables	19	
Manchester Royal Infirmary Farzin Fath-Ordoubadi & Vasim Farooq	19	
Freeman Hospital Newcastle Azfar Zaman	19	
Erasmus Medical Center Nicolas van Mieghem	16	
The Royal Infirmary of Edinburgh Neal Uren	15	
Hospital Universitario Valdecilla Javier Zueco	12	
American Heart of Poland (PAK), Pawel Buszman	10	
Hospital Meixoeiro Andres Iñiguez	8	
Hospital Puerta de Hierro Javier Goicolea	8	
Brighton & Sussex University Hospitals David Hildick-Smith	6	
Gornoslaskie Centrum Medycnze, Andrzej Ochala	4	
St Raphael Hospital Dariusz Dudek	3	

Definitions

- **MACCE:** All-cause death, stroke, any myocardial infarction (MI) or any revascularisation.
- **Periprocedural MI:** CK-MB ≥5xULN (or Tn ≥35 ULN if CK-MB not available) and new pathological Q-waves in the ECG within 7 days post PCI.
- **Spontaneous MI:** New Q-waves or one plasma level of CK-MB 5x ULN (or Tn ≥35 ULN if CK-MB not available) in the context of clinical syndrome consistent with ACS.
- **Stent Thrombosis:** According to the Academic Research Consortium.

SYNTAX II

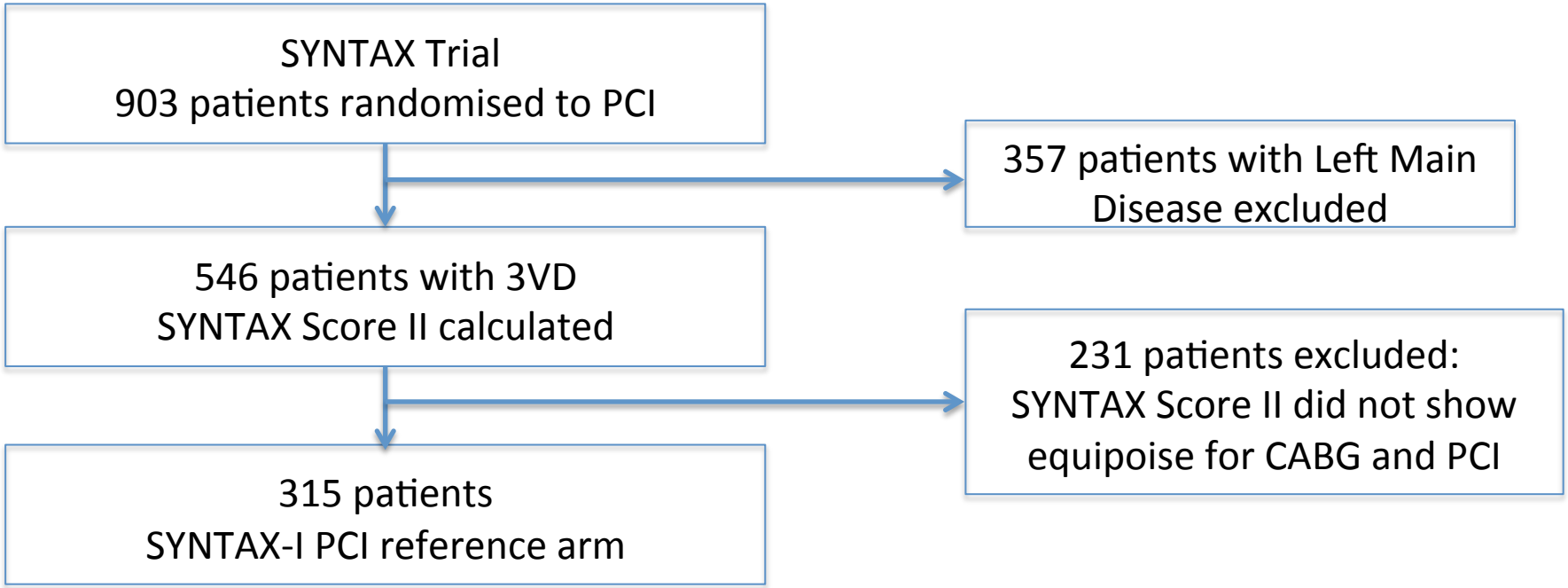
Medical therapy

	SYNTAX II	SYNTAX I PCI arm	P value
Aspirin			
At discharge	99.8% (448/449)	96.2% (302/314)	<0.001
At 1 Year	95.6% (413/432)	92.1% (278/302)	0.046
P2Y12 inhibitor			
At discharge	99.3% (446/449)	98.4% (309/314)	0.234
Clopidogrel	66.8% (298/446)	N/A	
Prasugrel	4.5% (20/446)	N/A	
Ticagrelor	28.7% (128/446)	N/A	
At 1 Year	61.8% (267/432)	72.2% (218/302)	0.0034
Beta-blocker at discharge	75.7% (339/448)	77.1% (242/314)	0.6550
Statin at discharge	97.3% (437/449)	85.4% (268/314)	<0.001

Use of coronary stents

	SYNTAX II	SYNTAX I PCI arm	P value
Stents per patient	3.78±1.92 (440)	5.19±2.04 (308)	<0.001
Stents per lesion	1.43±0.76 (1165)	1.28±0.65 (1251)	<0.001
Mean stent length (per stent, mm)	24.43±9.18 (1663)	18.82±7.04 (1599)	<0.001
Total stent length (per patient, mm)	92.32±52.78 (440)	97.71±43.66 (308)	0.13

Selection of the SYNTAX I PCI Reference Arm



Selection of the SYNTAX I CABG Reference Arm