

Supplementary appendix

Supplement to: M. Valgimigli, P. C. Smits, E. Frigoli, et al.

Abbreviated Antiplatelet Therapy After Complex Percutaneous Coronary Intervention In Patients at High Bleeding Risk. A prespecified subgroup analysis from the MASTER-DAPT trial

Supplementary materials: web appendices

MASTER DAPT trial: committees and investigators.....	2
ADDITIONAL INFORMATION ON THE METHODS ¹	10
1. Criteria for High Bleeding Risk	10
2. Inclusion and Exclusion Criteria	10
3. Treatment Regimen	11
3.1. Abbreviated DAPT regimen	11
3.2. Standard DAPT regimen.....	11
3.3. Implementation of randomized study regimens	11
4. Outcome Definitions	11
4.1. Death	11
4.2. Myocardial Infarction.....	15
4.3. Stent Thrombosis.....	16
4.4. Stroke	17
4.5. Bleeding.....	17
Supplemental Table 1. Baseline characteristics of randomised and nonrandomised patients stratified by PCI complexity.....	19
Supplemental Table 2. Procedural characteristics of randomised and nonrandomised patients stratified by PCI complexity.....	22
Supplemental Table 3. Main reason for non-randomisation	25
Supplemental Table 4. Complex PCI criteria.....	26
Supplemental Table 5. Baseline characteristics of all complex and noncomplex PCI patients.....	27
Supplemental Table 6. Procedural characteristics of all complex and noncomplex PCI patients	29
Supplemental Table 7. Dual and Single Antiplatelet therapy	31
Supplemental Table 8 Clinical endpoints at 11 months post-randomisation	34
Supplemental Table 9. Procedural characteristics of abbreviated DAPT vs standard DAPT.....	35
References	43

MASTER DAPT trial: committees and investigators

Executive committee

Coprincipal Investigator	M. Valgimigli
Coprincipal Investigator	P.C. Smits
Sponsor Representative	G.A. Van Es until June 1, 2018
Sponsor Representative	From June, 1 2018, G.B.W.E. Vos
Sponsor Representative	From October 16, 2020, E. Spitzer
Principal Investigators	P. Vrancks; B. Chevalier; Y. Ozaki
Clinical Research Organization Representative	M.C. Morice
Cardiologists	Y. Onuma; E. Frigoli
Bern University Hospital Representative	A. Frenk
Biostatisticians	P. Jüni; J. Tijssen
Terumo Representative (nonvoting member)	D. Paunovic

Steering committee

National Lead Investigators

Bangladesh, India	M.S. Ajit
Kingdom of Bahrain, Saudi Arabia	M. Alasnag
Belgium	J. Bartunek
France	B. Chevalier
Italy	A. Colombo
United Kingdom	D. Hildick-Smith
Portugal, Spain	A. Iñiguez
Austria, Denmark, Estonia, Germany, Sweden	F. Mahfoud
Israel	R. Kornowski
Bulgaria, Czech Republic, Hungary, Poland	M. Lesiak
Singapore, South Korea, Vietnam	P.J. Ong
Japan	Y. Ozaki
Argentina	A.E. Rodriguez
Switzerland	M. Roffi
Australia	C. Schultz
Macedonia, Serbia	G. Stankovic
The Netherlands	P. Tonino

Top enrollers

Inselspital, Bern, Switzerland	Aris Moschovitis
North Estonia Medical Center, Tallinn, Estonia	Peep Laanmets
Interventional Cardiology Unit, Policlinico Casilino, Rome, Italy	Michael Donahue

Data monitoring committee

Chair	M. Bertrand
Biostatistician	S. Pocock
Cardiologist	P. Urban

Clinical events committee

Chair	S. Leonardi
Cardiologists	C. Hanet; R. Lopes; E.P. McFadden; P. Radke; E. Spitzer
Neurologist	R. O. Roine

Safety reporting group (Cardialysis, Rotterdam, The Netherlands)

Boudijn Ladan (Safety Specialist), Laura van der Waal (Safety Assistant), Yvonne Engelbrecht (Safety Assistant), Fred Paddenburg (Safety Manager), Ben Ren, M.D., Ph.D. (Medical Reviewer).

CEC management group (Cardialysis, Rotterdam, The Netherlands)

Ingrid de Zwart (Data Manager), Liliane Elshout (Data Manager), Judith Jonk (Data Manager), Tessa Rademaker-Havinga (Statistician).

Project management

Ria van Vliet (Project Manager, ECRI, Rotterdam, The Netherlands). Marie-Claude Morice (Medical Director, CERC, France), Phani Krishna Kondamudi (Clinical Project Leader, CERC, France), Laure Morsiani (Clinical Operations Manager, CERC, France), Ute Windhövel (Regulatory Affairs Manager, CERC, France). Anita van der Wal (Project Manager, Cardialysis, Rotterdam, the Netherlands), Chantal Bakker (Project Manager, Cardialysis, Rotterdam, The Netherlands). Kazuhiro Minagawa (Project Manager, CVQuest, Tokyo, Japan).

Countries, investigators, and numbers of patients enrolled

Country	Site name	Principal investigator	Patients randomised (n=4579)	Patients consented but not randomised (n=625)
Argentina			16	1
	Buenos Aires, Otamendi Hospital	Dr Juan Mieres	8	
	Buenos Aires, Instituto Cardiovascular de Buenos Aires	Dr Fernando Cura	5	1
	Buenos Aires, Clinica IMA	Dr Carlos Fernandez-Pereira	3	
Australia			142	19
	Perth, Royal Perth Hospital-Cardiology Research	Prof. Carl Schultz	66	7
	Wollongong, Wollongong Hospital	Dr Astin Lee	55	6
	Sydney, Prince of Wales Hospital	Dr Nigel Jepson	8	2
	Fitzroy, St Vincent Hospital	Prof. Robert Whitbourn	7	
	Chermside, The Prince Charles Hospital	Dr Owen Christopher Raffel	6	4
Austria			44	11
	Vienna, Wilhelminenspital	Prof. Kurt Huber	29	9
	Vienna, Rudolfstiftung Hospital	Prof. Franz Weidinger	15	2
Bangladesh	Dhaka, National Heart Foundation Hospital & Research Institute	Prof. Fazila-Tun-Nesa Malik	39	1
Belgium			302	51
	Hasselt, Jessa Ziekenhuis	Prof. Pascal Vranckx	91	14
	Bonheiden, Imelda Ziekenhuis	Dr Willem Dewilde	90	14
	Charleroi, CHU de Charleroi – Hopital Civil Marie Curie	Dr Adel Aminian	48	3
	Aalst, OLV Ziekenhuis	Prof. Emanuele Barbato---- from 6th Sep 2018 Dr Jozef Bartunek	47	7
	Liege, CHR La Citadelle	Dr Suzanne Pourbaix	24	11
	Brussels, CHU St. Pierre UMC St. Pieter	Dr Panagiotis Xaplanteris	2	2
Bulgaria			183	11
	Sofia, UMHAT St. Anna	Dr Vasil Velchev	91	

Country	Site name	Principal investigator	Patients randomised (n=4579)	Patients consented but not randomised (n=625)
	Plovdiv, MHAT "Sveta Karidad" Plovdiv	Dr Dimitar Karageorgiev	60	10
	Sofia, National Heart Hospital	Dr Hristo Mateev	23	1
	Sofia, Tokuda Hospital	Prof. Valeri Gelev	9	
Czech Republic			134	17
	Brno, University Hospital Brno	Prof. Petr Kala	120	17
	Praha, Na Homolce Hospital	Dr Martin Mates	14	
Denmark	Roskilde, Roskilde Hospital Kogevej	Dr Henning Kelbæk	13	
Estonia	Tallinn, North-Estonia Medical Centre Foundation	Dr Peep Laanmets	259	12
France			578	67
	Massy, Hopital Prive Jacques Cartier	Dr Thomas Hovasse	129	19
	Montauban, Clinique du Pont de Chaume	Dr Laurent Delorme	124	7
	Marseille, CHU La Timone	Prof. Thomas Cuisset	41	
	Annecy, Centre Hospitalier Annecy Genvois	Dr Loïc Belle	37	
	Caen, Centre hospitalier regional universitaire de Caen	Prof. Farzin Beygui	33	9
	Nantes, Hopital Prive le Confluent	Dr Ashok Tirouvanziam	31	
	Montpellier, Clinique du Millenaire	Prof. Christophe Piot	30	4
	Caen, Hopital Prive Saint Martin	Dr Jean François Morelle	27	4
	Rouen, Clinique Saint-Hilaire	Dr Rene Koning	27	7
	Metz, Hopital de Mercy	Dr Mathieu Valla	24	3
	Dijon, GCIDB – Hopital Prive Dijon Bourgogne	Dr Philippe Brunel	23	5
	Nimes, CHU Caremeau	Dr Guillaume Cayla	18	4
	Creteil, Centre Hospitalier Universitaire Henri-Mondor	Prof. Emmanuel Teiger	12	2
	Paris, Hopital Universitaire Pitie-Salpetriere	Prof. Gilles Montalescot	10	2
	Paris, Hopital Europeen Georges-Pompidou	Prof. Christian Spaulding	9	1
	Saint-Denis, Centre Cardiologique du Nord	Dr Phillipe Guyon	3	
Germany			24	6
	Homburg, Saarland University	Prof. Felix Mahfoud	20	6
	Landshut, Landshut-Archdorf Krankenhaus	Dr Pyxaras, Stylianos	4	

Country	Site name	Principal investigator	Patients randomised (n=4579)	Patients consented but not randomised (n=625)
Hungary			68	5
	Budapest, Semmelweis University Heart and Vascular Center	Prof. Béla Merkely	46	5
	Szeged, Invasive Cardiology Unit University of Szeged	Dr Imre Ungi	22	
India			147	11
	Coimbatore, G Kuppuswamy Naidu Memorial Hospital	Dr Rajpal K Abhaichand	94	10
	Surat, Shri BD Mehta Mahavir Heart Institute	Dr Atul Damodar Abhyankar	33	
	Chennai, Apollo Hospitals, Chennai	Dr Sengottuvelu. G	13	1
	Chennai, Madras Medical Mission	Dr Ajit Mullasari .S	7	
Israel			100	33
	Safed, Ziv Medical Center, Cardiology Department	Dr Halabi Majdi	37	9
	Petach Tikva, Rabin MC	Prof. Ran Kornowski	34	11
	Haifa, Rambam Medical Center	Prof. Ariel Roguin----from 14th Oct 2018 Dr Yair Feld	16	6
	Jerusalem, Hadassah Ein Karem Medical Center	Prof. Chaim Lotan	13	7
Italy			276	37
	Rome, Policlinico Casilino	Dr Michael Donahue	99	6
	Vimercate, Ospedale di Vimercate	Dr Stefano Garducci	48	3
	Rozzano, Humanitas Research Hospital	Dr Bernhard Reimers	30	2
	Rome, Policlinico Umberto I	Dr Gennaro Sardella	20	2
	Milan, San Raffaele Hospital	Dr Antonio Colombo---from 20th June 2019 Dr Alaide Chieffo	12	1
	Catania, Ferrarotto Hospital	Prof. Corrado Tamburino	9	2
	Messina, AOU Policlinico Martino	Dr Giuseppe Andò	8	4
	Milan, Policlinico San Donato	Dr Luca Testa	8	4
	Milan, Sacco Hospital	Dr Maurizio Di Biasi	8	6
	Rome, Ospedale Sandro Pertini	Dr Alessandro Sciahbasi	8	3
	Caserta, Azienda Ospedaliera di Caserta Sant Anna e San Sebastiano	Prof.Dr Paolo Calabro	6	1
	Andria, Ospedale Lorenzo Bonomo	Dr Gianluigi Minervini	5	
	Cagliari, Azienda Ospedaliera Brotzu	Dr Bruno Loi	5	

Country	Site name	Principal investigator	Patients randomised (n=4579)	Patients consented but not randomised (n=625)
	Milan, Centro Cardiologico Monzino IRCCS	Dr Franco Fabbilocchi	5	
	Milan, ASST Grande Ospedale Metropolitano Niguarda	Dr Jacopo Oreglia	4	3
	Treviglio, ASST Bergamo Ovest	Dr Paolo Sganzerla	1	
Japan			188	17
	Toyoake, Fujita Health University Hospital	Prof. Yukio Ozaki	60	2
	Kokura, Fukuoka Kokura Memorial Hospital	Dr Kenji Ando	43	2
	Osaka, Osaka Police Hospital	Dr Yoshiharu Higuchi	22	4
	Tokyo, Sakakibara Heart Institute	Dr Mamoru Nanasato	13	1
	Kanagawa, St. Marianna University School of Medicine	Dr Yuki Ishibashi	11	1
	Gifu, Gifu Heart Center	Dr Hitoshi Matsuo	10	
	Nagoya, Japanese Red Cross Nagoya Daini Hospital	Dr Ruka Yoshida	8	2
	Ichinomiya, Ichinomiya municipal hospital	Dr Kiyokazu Shimizu	6	2
	Nagoya, Japanese Red Cross Nagoya	Dr Haruo Kamiya	4	2
	634 – Japan, Tokyo, St. Lukes International Hospital	Dr Nobuyuki Komiyama	4	1
	Nagakuteshi, Aichi Medical University Hospital	Dr Tetsuya Amano	3	
	Nagoya, Nagoya University Hospital	Dr Toyoaki Murohara	2	
	Sapporo, Sapporo Higashi Tokushukai Hospital	Dr Seiji Yamazaki	2	
Kingdom of Bahrain	Riffa, Bahrain Defence Force Hospital	Dr Husam Noor	7	1
Macedonia	Skopje, University Clinic of Cardiology	Dr Sasko Kedev	120	3
Poland			177	7
	Krakow, Institute Of Cardiology Jagiellonian University	Dr Jakub Podolec	69	4
	Poznan, Szpital Kliniczny Przemienienia Panskiego	Prof. Maciej Lesiak	50	1
	Wroclaw, 4 Wojskowy Szpital Kliniczny	Dr Krzysztof Reczuch	33	1
	Lubin, Miedziowe Centrum Zdrowia SA	Dr Adian Włodarczak	18	1

Country	Site name	Principal investigator	Patients randomised (n=4579)	Patients consented but not randomised (n=625)
	Krakow, University Hospital Krakow Poland	Prof. Dariusz Dudek	7	
Portugal	Lisbon, Hospital de Santa Maria	Dr Pedro Canas da Silva	1	
Saudi Arabia	King Fahd Armed Forces Hospital	Dr Mirvat Alasnag	16	1
Serbia			138	11
	Belgrade, Institute for Cardiovascular Disease Dedinje	Dr Ljupco Mangovski – from 17 April 2019 Dr Dragan Topic	67	4
	Belgrade, Clinical Center of Serbia	Prof. Goran Stankovic	61	7
	Sremska Kamenica, Institute of Cardiovascular Diseases	Dr Dragan Debeljacki	10	
Singapore			46	10
	Singapore, Tan Tock Seng Hospital	Prof. Paul Ong Jau Lueng	38	10
	Singapore, KhooTeck Puat Hospital	Dr Syed Saqib Imran	8	
South Korea	Seoul, Asan Medical Center	Dr Park Seung-Jung	15	
Spain			196	10
	Huelva, Juan Ramon Jimenez Hospital	Dr José Francisco Diaz Fernandez	47	1
	Vigo, Alvaro Cunqueiro	Prof. Andrés Iniguez	40	2
	Barcelona, Hospital Vall Hebron	Dr Bruno Garcia del Blanco	27	
	Alicante, Hospital General Universitario de Alicante	Dr Vicente Mainar	19	2
	Madrid, Hospital 12 de Octubre	Dr Ivan Gomez Blazquez	17	
	El Palmar, Universitario Virgen de la Arrixaca	Dr Eduardo Pinar	15	1
	Madrid, Hospital Clinico San Carlos	Prof. Javier Escaned Barbosa	11	2
	Barcelona, Bellvitge University Hospital	Dr Joan Antoni Gomez Hospital	10	2
	Santander, Hospital Universitario Valdecilla	Dr Fermin Sainz	9	
	Majadahonda, Hospital Universitario Puerta de Hierro	Dr Javier Goicolea	1	
Sweden			8	
	Orebro, Orebro University Hospital	Dr Ole Fröbert	6	
	Gavle, Gavle Hospital	Dr Robert Kastberg	2	
Switzerland			499	111
	Bern, Inselspital	Dr Aris Moschovitis---from 20th Oct 2020 Prof. Stephan Windecker	308	61
	Liestal, Kantonsspital Baselland	Dr Gregor Leibundgut	68	14

Country	Site name	Principal investigator	Patients randomised (n=4579)	Patients consented but not randomised (n=625)
	Lugano, Cardiocentro Ticino	Dr Giovanni Pedrazzini	31	9
	Geneva, University Hospital	Prof. Marco Roffi	29	13
	Bern, Lindenhofspital	Dr Ali Garachemani	28	3
	Zurich, University Hospital Zurich	Dr Patrick Siegrist	18	7
	Fribourg, HFR Hopital cantonal	Prof. Stéphane Cook	17	4
Netherlands			539	122
	Rotterdam, Maasstad Ziekenhuis	Dr Peter Smits	233	79
	Terneuzen, Zorgsaam	Dr Al Mafragi	87	5
	Emmen, Treant Zorggroep	PI Dr Jessurun---from 1st July 2020 Dr Ruifrok	67	9
	Eindhoven, Catharina Ziekenhuis	Dr Pim Tonino	54	10
	Arnhem, Rijnstate Ziekenhuis	Dr Peter Danse	29	8
	Hertogenbosch, Jeroen Bosch Ziekenhuis	Dr J. Polad	21	3
	Dordrecht, Albert Schweitzer Ziekenhuis	Dr Floris Kauer	20	6
	Enschede, Medisch Spectrum Twente	Dr Clemens von Birgelen	19	
	Nieuwegein, Antonius Ziekenhuis Nieuwegein	Dr Jurrien ten Berg	5	1
	Breda, Amphia Ziekenhuis	Dr Sander Ijsselmuiden	3	
	Den Haag, Hagahospital	Dr Samer Somi	1	1
United Kingdom			279	48
	Bristol, Bristol Heart Institute	Dr Tom Johnson	55	13
	Worcester, Worcestershire Royal Hospital	Dr Helen Routledge	43	8
	Brighton, Brighton & Sussex University Hospitals Trust	Dr David Hildick-Smith	40	3
	Bournemouth, Royal Bournemouth Hospital	Dr Jehangir Din	34	7
	Wolverhampton, Heart and Lung Centre – New Cross Hospital	Dr Shahzad Munir	22	6
	Blackburn, Royal Blackburn Hospital	Dr John McDonald	20	1
	Stevenage, Lee Haynes Research Institute, Lister Hospital	Dr Neville Kukreja	20	1
	Stoke on Trent, Royal Stoke University Hospital	Prof. Mamas Mamas	20	5
	Newcastle upon Tyne, Freeman Hospital	Dr Rajiv Das	13	1

Country	Site name	Principal investigator	Patients randomised (n=4579)	Patients consented but not randomised (n=625)
	Manchester, Wythenshawe Hospital	Dr Hussain Contractor	8	3
	Derry, Altnagelvin Hospital	Dr Aaron Peace	2	
	London, St. George's Hospitals	Dr Rupert Williams	2	
Vietnam	Vietnam National Heart Institute – Bach Mai Hospital Hanoi	Prof. Nguyen Ngoc Quang	25	2

ADDITIONAL INFORMATION ON THE METHODS¹

1. Criteria for High Bleeding Risk

Post-percutaneous coronary intervention (PCI), patients are at high bleeding risk if at least one of the following criteria applies:

1. Clinical indication for treatment with oral anticoagulant (OAC) for at least 12 months.
2. Recent (<12 months) nonaccess site bleeding episode(s) that required medical attention (i.e. actionable bleeding).
3. Previous bleeding episode(s) that required hospitalization if the underlying cause had not been definitively treated (i.e. surgical removal of the bleeding source).
4. Age ≥ 75 years.
5. Systemic conditions associated with an increased bleeding risk (e.g. hematological disorders, including a history of current thrombocytopenia defined as a platelet count $<100.00/\text{mm}^3$ ($<100 \times 10^9/\text{L}$) or any known coagulation disorder associated with increased bleeding risk).
6. Documented anemia, defined as repeated hemoglobin levels <11 g/dL or transfusion during the 4 weeks before inclusion.
7. Need for chronic treatment with steroids or nonsteroidal anti-inflammatory drugs.
8. Diagnosed malignancy (other than skin) considered at high bleeding risk including gastrointestinal, genitourinary/renal and pulmonary.
9. Stroke at any time or transient ischemic attack in the previous 6 months.
10. PRECISE-DAPT score ≥ 25 .

2. Inclusion and Exclusion Criteria

Inclusion Criteria

Inclusion criteria after index PCI

1. Age ≥ 18 years
2. At least one high bleeding risk criterion (listed above)
3. All coronary lesions successfully treated with Ultimaster stent
4. Free of any flow-limiting angiographic complications that required prolonged dual antiplatelet therapy (DAPT) duration based on operator's decision
5. All stages of PCI were complete and no further PCI was planned

Inclusion criteria at 1-month randomization visit (30–44 days after qualifying index PCI)

1. At least one high bleeding risk criterion (listed above) or on the basis of post-PCI actionable nonaccess-site related bleeding episode
2. Uneventful 30-day clinical course (i.e. freedom from any new episode of acute coronary syndrome, symptomatic restenosis, stent thrombosis, stroke, any revascularization requiring prolonged DAPT)
3. If not on OAC:
 - a) Patient was on DAPT regimen of aspirin and a P2Y₁₂ inhibitor;
 - b) Patient with one type of P2Y₁₂ inhibitor for at least 7 days
4. If on OAC:
 - a) Patient was on the same type of OAC for at least 7 days;
 - b) Patient was on clopidogrel for at least 7 days

Exclusion Criteria

Patients were not eligible if any of the following applied:

1. Treated with stent other than Ultimaster stent within 6 months prior to index PCI
 2. Treated for in-stent restenosis or stent thrombosis at index PCI or within 6 months before
 3. Treated with a bioresorbable scaffold at any time prior to index procedure
 4. Incapable of providing written informed consent
 5. Under judicial protection, tutorship or curatorship
 6. Unable to understand and follow study-related instructions or unable to comply with study protocol
 7. Active bleeding requiring medical attention (Bleeding Academic Research Consortium [BARC] ≥ 2) on randomization visit
 8. Life expectancy less than 1 year
 9. Known hypersensitivity or allergy to aspirin, clopidogrel, ticagrelor, prasugrel, cobalt chromium or sirolimus
 10. Any planned and anticipated PCI
 11. Participation in another trial
-

3. Treatment Regimen

Patients were treated according to the randomized regimen from the day of randomization until 11 months after randomization (12 months after the index procedure). After 11 months post randomization, antiplatelet therapy was at the discretion of treating physician.

3.1. Abbreviated DAPT regimen

In patients not on OAC: DAPT was discontinued, and a single antiplatelet agent (SAPT) was continued until at least 11 months post randomization (i.e. 12 months after index PCI).

In patients on OAC: DAPT was discontinued. Either aspirin or clopidogrel was continued until 5 months post randomization (i.e. 6 months after index PCI). OAC was continued until at least 11 months post randomization (i.e. 12 months after index PCI).

3.2. Standard DAPT regimen

In patients not on OAC: Aspirin was continued until at least 11 months post randomization (i.e. 12 months after index PCI). The P2Y12 inhibitor being taken at the time of randomization was continued for at least 5 months and up to 11 months post randomization (i.e. 12 months after index PCI).

In patients on OAC: Aspirin and clopidogrel were continued for at least 2 months (i.e. 3 months after index PCI) and up to 11 months post randomization (i.e. 12 months after index PCI). Thereafter, either aspirin or clopidogrel was continued up to 11 months post randomization (i.e. 12 months after index PCI). OAC was continued until at least 11 months post randomization (i.e. 12 months after index PCI).

The rationale for mandating clopidogrel as the only acceptable P2Y12 inhibitor in the OAC population in both study arms came from the absence of safety and efficacy data regarding the combination of ticagrelor or prasugrel with aspirin and OAC (as patients requiring OAC were excluded from approval RCT) and a recommendation of Class III (i.e. not indicated) in the European guidelines.

3.3. Implementation of randomized study regimens

Study regimens were implemented by regular drug prescription as described above. The investigators provided the necessary prescription to the study participants. The following are recommended according to the current guidelines and local practice.

- Aspirin is prescribed at the standard dose of at least 75 mg/day and up to 162 mg/day.
- Clopidogrel is prescribed in standard dose of 75 mg once daily.
- Prasugrel is prescribed at the standard dose of 10 mg/day or 5 mg/day in patients weighing less than 60 kg or who are over 75 years old. In regions where other standard dose exists (i.e. Japan), prasugrel dosage is adjusted according to the locally approved dose.
- Ticagrelor is prescribed at the standard dose of 180 mg/day (90 mg b.i.d.).
- Vitamin K antagonist is dosed to keep the international normalized ratio within the guideline range.
- Nonvitamin K oral antagonist oral anticoagulants (NOAC; rivaroxaban, edoxaban, dabigatran and apixaban) are given in locally approved doses.
- Switching from a vitamin K antagonist to NOAC or vice-versa is not allowed unless there are clinical and well documented reasons for doing so. Similarly, switching from a NOAC to a VKA during the course of the study is not allowed, unless dictated by a clinical and documented reason (e.g. change in renal function during the course of the investigation), which will be captured in the eCRF.

Prescribed units of aspirin, clopidogrel, prasugrel, ticagrelor and OAC were recorded in the eCRF. Patients are queried on general drug adherence.

4. Outcome Definitions

4.1. Death

All deaths were categorized as cardiovascular, noncardiovascular, or undetermined based on the definitions below.

4.1.1. Cardiovascular death

Cardiovascular death was defined as death resulting from an acute myocardial infarction, sudden cardiac death, death due to heart failure, death due to stroke, death due to cardiovascular procedures, death due to cardiovascular hemorrhage, and death due to other cardiovascular causes.

4.1.2. Death due to acute myocardial infarction

Death due to acute myocardial infarction was death by any mechanism (arrhythmia, heart failure, low output) within 30 days after a myocardial infarction related to the immediate consequences of the myocardial infarction, such as progressive congestive heart failure (CHF), inadequate cardiac output, or refractory arrhythmia. If these events occurred after a “break” (e.g. a CHF- and arrhythmia-free period of at least a week), they were designated by the immediate cause, even though the myocardial infarction may have increased the risk of that event (e.g. late arrhythmic death becomes more likely after an acute myocardial infarction). The acute myocardial infarction was verified to the extent possible by the diagnostic criteria outlined for acute myocardial infarction or by autopsy findings showing recent myocardial infarction or recent coronary thrombus. Sudden cardiac death, if accompanied by symptoms suggestive of myocardial ischemia, new ST elevation, new left bundle branch block (LBBB), or evidence of fresh thrombus by coronary angiography and/or at autopsy should be considered death resulting from an acute myocardial infarction, even if death occurs before blood samples or 12-lead electrocardiogram (ECG) could be obtained, or at a time before the appearance of cardiac biomarkers in the blood. Death resulting from a procedure to treat a myocardial infarction (i.e. PCI, coronary artery bypass graft surgery [CABG]), or to treat a complication resulting from myocardial infarction, should also be considered death due to acute myocardial infarction. Death resulting from an elective coronary procedure to treat myocardial ischemia (i.e. chronic stable angina) or death due to a myocardial infarction that occurred as a direct consequence of a cardiovascular investigation/procedure/operation should be considered as a death due to a cardiovascular procedure.

4.1.3. Sudden cardiac death

Sudden cardiac death was death that occurred unexpectedly, not following an acute myocardial infarction, and included the following:

- Death witnessed and occurring without new or worsening symptoms.
- Death witnessed within 60 min of the onset of new or worsening cardiac symptoms, unless documented (i.e. by ECG or other objective) to be due to acute myocardial infarction.
- Death witnessed and attributed to an identified arrhythmia (e.g. captured on an ECG recording, witnessed on a monitor, or unwitnessed but found on implantable cardioverter-defibrillator review).
- Death after unsuccessful resuscitation from cardiac arrest. Death after successful resuscitation from cardiac arrest and without identification of a noncardiac etiology.
- Unwitnessed death without other cause of death (information regarding the patient’s clinical status preceding death should be provided, if available).

4.1.3.1. GENERAL CONSIDERATIONS

A subject seen alive and clinically stable 24 h prior to being found dead without any evidence or information of a specific cause of death was classified as “sudden cardiac death.” Typical scenarios included:

- Subject well the previous day but found dead in bed the next day
- Subject found dead at home on the couch with the television on
- Deaths for which there was no information beyond “Patient found dead at home” may be classified as “death due to other cardiovascular causes”.

4.1.4. Death due to heart failure or cardiogenic shock

Death due to congestive heart failure referred to a death in association with clinically worsening symptoms and/or signs of heart failure not following an acute myocardial infarction. Deaths due to heart failure could have various etiologies, including single or recurrent myocardial infarctions, ischemic or nonischemic cardiomyopathy, hypertension, or valvular disease. Cardiogenic shock not occurring in the context of an acute myocardial infarction or as the consequence of an arrhythmia occurring in the absence of worsening heart failure was defined as systolic blood pressure (SBP) <90 mm Hg for greater than 1 hour, not responsive to fluid resuscitation and/or heart rate correction, and felt to be secondary to cardiac dysfunction and associated with at least one of the following signs of hypoperfusion:

- Cool, clammy skin or

- Oliguria (urine output <30 mL/h) or
- Altered sensorium or
- Cardiac index <2.2 L/min/m²
- Cardiogenic shock could also be defined if SBP <90 mm Hg and increased to ≥90 mm Hg in less than 1 hour with positive inotropic or vasopressor agents alone and/or with mechanical support.

4.1.5. Death due to stroke

Death due to stroke referred to death after a stroke that was either a direct consequence of the stroke or a complication of the stroke. Acute stroke was verified to the extent possible by the diagnostic criteria outlined for stroke.

4.1.6. Death due to cardiovascular procedures

Death due to cardiovascular procedures referred to death caused by the immediate complications of a cardiac procedure and excluded death resulting from procedures to treat an acute myocardial infarction or the complications resulting from an acute myocardial infarction.

4.1.7. Death due to cardiovascular hemorrhage

Death due to cardiovascular hemorrhage referred to death related to hemorrhage such as a nonstroke intracranial hemorrhage, nonprocedural or nontraumatic vascular rupture (e.g. aortic aneurysm), or hemorrhage causing cardiac tamponade.

4.1.8. Death due to other cardiovascular causes

Death due to other cardiovascular causes referred to a cardiovascular death not included in the above categories (e.g. pulmonary embolism or peripheral artery disease).

4.1.9. Noncardiovascular death

Noncardiovascular death was defined as any death that was not thought to be due to a cardiovascular cause. The following categories may be collected.

4.1.9.1. NONMALIGNANT CAUSES

- Pulmonary
- Renal
- Gastrointestinal
- Hepatobiliary
- Pancreatic
- Infection (includes sepsis)
- Noninfectious (e.g. systemic inflammatory response syndrome)
- Hemorrhage*, excluding hemorrhagic strokes and bleeding in the setting of coronary revascularization
- Noncardiovascular procedure or surgery
- Accidental (e.g. physical accidents or drug overdose) or trauma
- Suicide
- Prescription drug error (e.g. prescribed drug overdose, use of inappropriate drug, or drug-drug interaction)
- Neurological process that was not a stroke or hemorrhage
- Other noncardiovascular, specify: _____

**Examples: Death due to gastrointestinal bleeding was not considered a cardiovascular death. Death due to retroperitoneal hematoma following PCI was considered cardiovascular death. Death due to intracerebral hemorrhage was considered cardiovascular death.*

4.1.9.2. MALIGNANT CAUSES

Death from a malignant cause was that resulting directly from the cancer, or death resulting from a complication of the cancer (e.g. infection, complication of surgery / chemotherapy / radiotherapy), or death resulting from withdrawal of other therapies because of concerns relating to the poor prognosis associated with the cancer.

Cancer deaths that arose from cancers that were present prior to randomization or which developed subsequently were further classified (worsening prior malignancy; new malignancy).

4.1.10. Undetermined cause of death

Undetermined cause of death referred to a death not attributable to one of the above categories of cardiovascular death or to a noncardiovascular cause, due to absence of any information (e.g. the only available information is "patient died"). The use of this category of death was discouraged and should have only applied to a minimal number of cases when no information at all on the circumstances of death were available (i.e. found on obituary of local newspaper). In all circumstances the reviewer used all available information to attribute to one of the categories based on best clinical judgment.

For each death event an assessment was made as to whether the event was caused (on the basis of the totality of the evidence) by a bleeding (i.e. a fatal bleeding occurred) or not.

4.2. Myocardial Infarction

For the primary analysis, the myocardial infarction outcome was defined based on the Third Universal Definition of myocardial infarction with the exception of periprocedural myocardial infarction after PCI, which was defined according to the Society for Cardiovascular Angiography and Intervention (SCAI) definition. For secondary analyses, PCI-related myocardial infarction according to the Third Universal Definition (type 4a) was also adjudicated.

4.2.1. Spontaneous myocardial infarction (>48 h after intervention, myocardial infarction type 1)

Symptoms suggestive of ischemia/infarction in association with ECG, cardiac biomarker, or pathologic evidence of infarction were as follows:

- Detection of a rise and/or fall of cardiac biomarker values (preferably cardiac troponin T or I) with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following:
 - Symptoms of ischemia
 - New or presumed new significant ST segment-T wave (ST-T) changes or new LBBB
 - Development of new Q waves in the ECG
 - Evidence of new loss of viable myocardium or new regional wall motion abnormality
 - Identification of an intracoronary thrombus by angiography or autopsy

Spontaneous myocardial infarction typically occurs after the periprocedural period and may be secondary to late stent complications or progression of native disease (e.g. nonculprit lesion plaque rupture). Performance of ECG and angiography supports adjudication to either a target or nontarget vessel or lesion in most cases.

4.2.2. Type 2 myocardial infarction

In instances of myocardial injury with necrosis where a condition other than coronary artery disease (CAD) contributes to an imbalance between myocardial oxygen supply and/or demand, e.g. coronary endothelial dysfunction, coronary artery spasm, coronary embolism, tachy/bradyarrhythmias, anemia, respiratory failure, hypotension, and hypertension with or without left ventricular hypertrophy.

4.2.3. Type 3 myocardial infarction

Cardiac death with symptoms suggestive of myocardial ischemia and presumed new ischemic ECG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased.

4.2.4. Type 4a myocardial infarction (not used for primary analysis, see section 4.8 for primary definition of periprocedural myocardial infarction)

Type 4a myocardial infarction was defined by elevation of cardiac troponin (cTn) values ($>5 \times \text{URL}$) occurring within 48 h of the procedure in patients with normal baseline values ($\leq \text{URL}$) or a rise of cTn values $>20\%$ if the baseline values are elevated and are stable or falling. In addition, at least one of the following was required:

- Symptoms suggestive of myocardial ischemia
- New ischemic ECG changes
- Angiographic findings consistent with a procedural complication
- Imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality.

4.2.5. Type 4b myocardial infarction

Type 4b myocardial infarction was defined as stent thrombosis associated with myocardial infarction when detected by coronary angiography or autopsy in the setting of evidence of myocardial ischemia and with a rise and/or fall of cardiac biomarker values with at least one value above the URL.

4.2.6. Type 4c myocardial infarction

Type 4c myocardial infarction was defined as spontaneous myocardial infarction where a restenosis was the only angiographic explanation.

4.2.7. Type 5 myocardial infarction

4.2.7.1. CORONARY ARTERY BYPASS GRAFTING-RELATED MYOCARDIAL INFARCTION

Coronary artery bypass grafting (CABG) related myocardial infarction was defined by elevation of troponin values ($>10 \times \text{URL}$) occurring within 48 h of the procedure in patients with normal baseline cTn values ($\leq \text{URL}$). In addition, at least one of the following was required:

- New pathological Q waves or new LBBB
- Angiographic documented new graft or new native coronary artery occlusion
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

4.2.8. Periprocedural myocardial infarction after PCI (within 48 h of PCI)

Periprocedural myocardial infarction was defined based on the SCAI definitions as follows:

- 1) In patients with normal baseline creatine kinase-MB (CK-MB): The peak CK-MB measured within 48 h of the procedure rises to $\geq 10 \times$ the local laboratory ULN, or to $\geq 5 \times$ ULN with new pathologic Q-waves in ≥ 2 contiguous leads or new persistent LBBB, OR in the absence of CK-MB measurements and a normal baseline cTn, a cTn (I or T) level measured within 48 h of the PCI rises to $\geq 70 \times$ the local laboratory ULN, or $\geq 35 \times$ ULN with new pathologic Q-waves in ≥ 2 contiguous leads or new persistent LBBB.
- 2) In patients with elevated baseline CK-MB (or cTn) in whom the biomarker levels are stable or falling: The CK-MB (or cTn) rises by an absolute increment equal to those levels recommended above from the most recent preprocedure level.
- 3) In patients with elevated CK-MB (or cTn) in whom the biomarker levels have not been shown to be stable or falling: The CK-MB (or cTn) rises by an absolute increment equal to those levels recommended above plus new ST-segment elevation or depression plus signs consistent with a clinically relevant myocardial infarction, such as new onset or worsening heart failure or sustained hypotension.

4.2.9. Target-vessel vs. nontarget-vessel myocardial infarction

Any myocardial infarction not clearly attributable to a nontarget vessel was considered as target-vessel myocardial infarction.

4.3. Stent Thrombosis

Stent thrombosis was defined by the Academic Research Consortium as follows:

4.3.1. Definite stent thrombosis

Definite stent thrombosis was considered to have occurred by either angiographic or pathological confirmation:

a. Angiographic confirmation of stent thrombosis (the incidental angiographic documentation of stent occlusion in the absence of clinical signs or symptoms was not considered a confirmed stent thrombosis [silent occlusion])

The presence of an intracoronary thrombus that originates in the stent or in the segment 5 mm proximal or distal to the stent and presence of at least 1 of the following criteria within a 48-h time window:

- Acute onset of ischemic symptoms at rest
- New ischemic ECG changes that suggest acute ischemia
- Typical rise and fall in cardiac biomarkers (refer to definition of spontaneous myocardial infarction: Troponin or CK-MB $>99\text{th}$ percentile of URL)
- Nonocclusive thrombus. Intracoronary thrombus was defined as a (spheric, ovoid, or irregular) noncalcified filling defect or lucency surrounded by contrast material (on 3 sides or within a coronary stenosis) seen in multiple projections, or persistence of contrast material within the lumen, or a visible embolisation of intraluminal material downstream
- Occlusive thrombus Thrombolysis In Myocardial Infarction (TIMI) 0 or TIMI 1 intrastent or proximal to a stent up to the most adjacent proximal side branch or main branch (if originates from the side branch)

b. Pathological confirmation of stent thrombosis

- Evidence of recent thrombus within the stent determined at autopsy or via examination of tissue retrieved following thrombectomy

4.3.2. Probable stent thrombosis

Clinical definition of probable stent thrombosis was considered to have occurred after intracoronary stenting in the following cases:

- Any unexplained death within the first 30 days.
- Irrespective of the time after the index procedure, any myocardial infarction related to documented acute ischemia in the territory of the implanted stent without angiographic confirmation of stent thrombosis and in the absence of any other obvious cause.

4.3.3. Possible stent thrombosis

Clinical definition of possible stent thrombosis was considered to have occurred with any unexplained death from 30 days following intracoronary stenting until end of trial follow-up.

4.4. Stroke

Stroke was defined as an acute episode of focal or global neurological dysfunction caused by central nervous system (CNS) vascular injury as a result of hemorrhage or infarction. CNS included brain, spinal cord and retina. Stroke was defined as follows.

4.4.1. Ischemic stroke

Ischemic stroke was defined as an acute episode of focal cerebral, spinal, or retinal dysfunction caused by CNS infarction. Evidence of infarction was defined as "Pathological, imaging, or other objective evidence of acute cerebral, spinal cord, or retinal focal ischemic injury in a defined vascular distribution; or in the absence of the above (i.e. imaging or autopsy unavailable), clinical evidence of cerebral, spinal cord, or retinal focal ischemic injury was based on symptoms persisting for ≥ 24 h or until death, and other etiologies excluded. Hemorrhagic infarction, defined as a parenchymal hemorrhage after CNS infarction, was considered an ischemic stroke

4.4.2. Cerebral hemorrhage

Hemorrhages in the CNS were classified as stroke if they were nontraumatic, caused by a vascular event, and resulted in injury to the CNS. In contrast, traumatic hemorrhages were not characterized as stroke. Subdural hematoma was not classified as a stroke. The diagnoses included in this section were intracerebral hemorrhage (intraparenchymal and intraventricular) and subarachnoid hemorrhage (both aneurysmal and nonaneurysmal).

4.4.3. Stroke caused by intracerebral hemorrhage

Rapidly developing clinical signs of neurological dysfunction (focal or global) attributable to a focal collection of blood within the brain parenchyma or ventricular system that was not caused by trauma.

4.4.4. Stroke caused by subarachnoid hemorrhage

Rapidly developing signs of neurological dysfunction (focal or global) and/or headache because of bleeding into the subarachnoid space (the space between the arachnoid membrane and the pia mater of the brain or spinal cord), which was not caused by trauma. Hemorrhages could be further classified according to location (example, supratentorial, subtentorial, etc.)

4.4.5. Stroke not otherwise specified

An episode of acute neurological dysfunction presumed to be caused by ischemia or hemorrhage, persisting ≥ 24 h or until death, but without sufficient evidence to be classified as one of the above.

4.5. Bleeding

All potential bleeding events were primarily adjudicated according to Bleeding Academic Research Consortium (BARC) classification.

Type 0	No bleeding
Type 1	Bleeding that is not actionable and does not cause the patient to seek unscheduled performance of studies, hospitalization, or treatment by a health care professional. May include episodes leading to self-discontinuation of medical therapy by the patient, without consulting a health care professional.
Type 2	Any overt, actionable sign of hemorrhage (e.g. more bleeding than would be expected for a clinical circumstance; including bleeding found by imaging alone) that does not fit the criteria for Types 3, 4, or 5 but does meet at least one of the following criteria: Requiring nonsurgical, medical intervention by a health care professional Leading to hospitalization of increased level of care

- Prompting evaluation
- Type 3a Overt bleeding plus hemoglobin drop of 3 to <5* g/dL (provided hemoglobin drop is related to bleed)
Any transfusion with overt bleeding
- Type 3b Overt bleeding plus hemoglobin drop ≥5* g/dL (provided hemoglobin drop is related to bleed)
Cardiac tamponade
Bleeding requiring surgical intervention for control (excluding dental / nasal / skin / hemorrhoid)
Bleeding requiring intravenous vasoactive agents
- Type 3c Intracranial hemorrhage (does not include microbleeds or hemorrhagic transformation; does include intraspinal)
Subcategories: confirmed by autopsy or imaging or lumbar puncture
Intra-ocular bleed compromising vision
- Type 4 CABG-related bleeding
Perioperative intracranial bleeding within 48 h
Reoperation following closure of sternotomy for the purpose of controlling bleeding
Transfusion of ≥5 units of whole blood or packed red blood cells within 48 hour period†
Chest tube output ≥2 L within a 24 hour period
- Type 5a Probable fatal bleeding; no autopsy or imaging confirmation, but clinically suspicious
- Type 5b Definite fatal bleeding: overt bleeding or autopsy or imaging confirmation
- Platelet transfusions were recorded and reported, and were not included in these definitions until further information was obtained about the relationship to outcomes.
- *Corrected for transfusion (1 unit packed red blood cells or 1 unit whole blood=1g/dL hemoglobin).
- †Cell saver products were not counted.

Supplemental Table 1. Baseline characteristics of randomised and nonrandomised patients stratified by PCI complexity

	Complex PCI			Noncomplex PCI			interaction
	Randomised	Nonrandomised	P-value	Randomised	Nonrandomised	P-value	p-value
	N=1196	N=163		N=3383	N=462		
Age, years (mean±SD)	n=1196, 76.65±8.24	n=163, 78.44±7.51	0.009	n=3383, 75.82±8.90	n=462, 77.71±8.01	<0.001	0.906
Male sex (n [%]) (Female)	n=1196, 847 (70.8%)	n=163, 115 (70.6%)	0.927	n=3383, 2324 (68.7%)	n=462, 302 (65.4%)	0.150	0.496
Body mass index, kg/m ² (mean±SD)	n=1196, 27.57±4.61	n=163, 26.91±4.69	0.084	n=3383, 27.27±4.75	n=458, 26.98±5.28	0.227	0.413
Family history of coronary artery disease (n [%])	n=1196, 310 (25.9%)	n=161, 36 (22.4%)	0.386	n=3383, 799 (23.6%)	n=458, 105 (22.9%)	0.769	0.503
Known Arterial hypertension (n [%])	n=1196, 941 (78.7%)	n=162, 120 (74.1%)	0.189	n=3383, 2612 (77.2%)	n=461, 362 (78.5%)	0.553	0.144
Uncontrolled hypertension (n [%])	n=1196, 58 (4.8%)	n=162, 5 (3.1%)	0.426	n=3383, 178 (5.3%)	n=461, 23 (5.0%)	0.911	0.431
Known Diabetes mellitus (n [%])	n=1196, 405 (33.9%)	n=162, 53 (32.7%)	0.791	n=3383, 1133 (33.5%)	n=462, 143 (31.0%)	0.292	0.756
Known Hyperlipidemia (n [%])	n=1196, 823 (68.8%)	n=162, 107 (66.0%)	0.472	n=3383, 2274 (67.2%)	n=462, 293 (63.4%)	0.114	0.838
Smoker (n [%])	n=1195,	n=155,	0.714	n=3371,	n=448,	0.113	0.626
no - never smoked	623 (52.1%)	79 (51.0%)	0.798	1801 (53.4%)	216 (48.2%)	0.039	
yes - previous smoker	486 (40.7%)	62 (40.0%)	0.931	1242 (36.8%)	182 (40.6%)	0.131	
yes - current smoker	86 (7.2%)	14 (9.0%)	0.415	328 (9.7%)	50 (11.2%)	0.354	
Known Peripheral/Vascular disease* (n [%])	n=1196, 137 (11.5%)	n=162, 22 (13.6%)	0.435	n=3383, 348 (10.3%)	n=462, 63 (13.6%)	0.036	0.662
Known Carotid artery disease* (n [%])	n=1196, 70 (5.9%)	n=162, 7 (4.3%)	0.586	n=3383, 194 (5.7%)	n=462, 33 (7.1%)	0.246	0.218
History of heart failure (n [%])	n=1196, 235 (19.6%)	n=162, 35 (21.6%)	0.600	n=3383, 632 (18.7%)	n=461, 84 (18.2%)	0.848	0.534
Left ventricular ejection fraction, % (mean±SD)	n=1140, 52.65±11.48	n=144, 49.70±12.34	0.004	n=3157, 53.43±11.65	n=417, 51.91±12.39	0.013	0.233
Prior myocardial infarction (n [%])	n=1196, 269 (22.5%)	n=162, 29 (17.9%)	0.224	n=3383, 595 (17.6%)	n=462, 96 (20.8%)	0.106	0.048
Prior PCI (n [%])	n=1196, 312 (26.1%)	n=162, 42 (25.9%)	1.000	n=3383, 876 (25.9%)	n=462, 133 (28.8%)	0.195	0.484
Prior cerebrovascular event reported (n [%])	n=1196, 155 (13.0%)	n=162, 19 (11.7%)	0.802	n=3383, 415 (12.3%)	n=462, 75 (16.2%)	0.021	0.133
Stroke (n [%])	n=1196, 114 (9.5%)	n=162, 11 (6.8%)	0.311	n=3383, 296 (8.7%)	n=462, 49 (10.6%)	0.193	0.112

TIA (n [%])	n=1196, 45 (3.8%)	n=162, 7 (4.3%)	0.665	n=3383, 125 (3.7%)	n=462, 26 (5.6%)	0.054	0.528
Undetermined Cerebrovascular event (n [%])	n=1196, 8 (0.7%)	n=162, 3 (1.9%)	0.134	n=3383, 21 (0.6%)	n=462, 8 (1.7%)	0.018	0.993
Known History of Arterial thromboembolism (n [%])	n=1196, 24 (2.0%)	n=162, 5 (3.1%)	0.380	n=3383, 31 (0.9%)	n=462, 11 (2.4%)	0.013	0.388
Known History of Venous thromboembolism (n [%])	n=1196, 75 (6.3%)	n=162, 10 (6.2%)	1.000	n=3383, 164 (4.8%)	n=462, 23 (5.0%)	0.908	0.914
Prior CABG (n [%])	n=1196, 92 (7.7%)	n=162, 16 (9.9%)	0.352	n=3383, 249 (7.4%)	n=462, 50 (10.8%)	0.012	0.649
Prior Prosthetic mechanical heart valve (n [%])	n=1196, 19 (1.6%)	n=162, 5 (3.1%)	0.194	n=3383, 82 (2.4%)	n=462, 15 (3.2%)	0.270	0.517
Known Aortic Valve Stenosis (n [%])	n=1068, 53 (5.0%)	n=147, 13 (8.8%)	0.077	n=3052, 142 (4.7%)	n=406, 31 (7.6%)	0.015	0.809
Prior bleeding before/after qualifying PCI (n [%])	n=1196, 73 (6.1%)	n=162, 24 (14.8%)	<0.001	n=3383, 286 (8.5%)	n=462, 71 (15.4%)	<0.001	0.288
Known Chronic pulmonary disease (n [%])	n=1196, 144 (12.0%)	n=162, 24 (14.8%)	0.310	n=3383, 394 (11.6%)	n=462, 75 (16.2%)	0.006	0.595
Known Chronic Renal Failure (n [%])	n=1196, 253 (21.2%)	n=162, 44 (27.2%)	0.086	n=3383, 623 (18.4%)	n=462, 121 (26.2%)	<0.001	0.579
Known Liver disease (n [%])	n=1196, 16 (1.3%)	n=162, 5 (3.1%)	0.095	n=3383, 45 (1.3%)	n=462, 13 (2.8%)	0.023	0.883
Atrial fibrillation (n [%])	n=1196, 361 (30.2%)	n=162, 70 (43.2%)	0.001	n=3383, 1129 (33.4%)	n=462, 198 (42.9%)	<0.001	0.415
Known History of cancer (n [%])	n=1196, 196 (16.4%)	n=162, 31 (19.1%)	0.371	n=3383, 503 (14.9%)	n=462, 72 (15.6%)	0.677	0.601
Known Active cancer (n [%])	n=1196, 74 (6.2%)	n=162, 10 (6.2%)	1.000	n=3383, 162 (4.8%)	n=462, 29 (6.3%)	0.171	0.476
Known Haematological or Coagulation Disorders (n [%])	n=1196, 165 (13.8%)	n=162, 28 (17.3%)	0.232	n=3383, 413 (12.2%)	n=462, 87 (18.8%)	<0.001	0.344
Chronic treatment with steroids or NSAIDS (n [%])	n=1196, 128 (10.7%)	n=162, 15 (9.3%)	0.683	n=3383, 313 (9.3%)	n=462, 34 (7.4%)	0.195	0.796
Prior VKA (n [%])	n=1196, 131 (11.0%)	n=162, 21 (13.0%)	0.427	n=3383, 495 (14.6%)	n=462, 83 (18.0%)	0.061	0.850
Need for current treatment with OAC (n [%])	n=1196, 415 (34.7%)	n=162, 81 (50.0%)	<0.001	n=3383, 1254 (37.1%)	n=462, 214 (46.3%)	<0.001	0.201
Clinical indication for 12 months OAC (n [%])	n=1196, 414 (34.6%)	n=163, 82 (50.3%)	<0.001	n=3383, 1252 (37.0%)	n=462, 214 (46.3%)	<0.001	0.177
OAC treatment at randomization (n [%])	n=414, 412 (99.5%)	n=82, 80 (97.6%)	0.129	n=1252, 1244 (99.4%)	n=214, 206 (96.3%)	0.001	0.888
PRECISE DAPT score¶ (mean±SD)	n=1196, 27.02±11.06	n=163, 29.28±12.24	0.016	n=3383, 26.67±10.95	n=462, 29.43±12.18	<0.001	0.649
Prior bleeding (n [%])	n=1196, 66 (5.5%)	n=163, 13 (8.0%)	0.211	n=3383, 254 (7.5%)	n=462, 38 (8.2%)	0.575	0.417
Hemoglobin, g/L (mean±SD)	n=1196, 13.07±1.80	n=163, 13.04±1.92	0.797	n=3383, 13.27±1.78	n=462, 12.94±1.89	<0.001	0.103
White blood cell count WBC¶, 109/L (mean±SD)	n=1195, 8.39±15.36	n=163, 8.26±2.57	0.914	n=3383, 8.09±3.64	n=462, 8.37±4.68	0.138	0.601
Creatinine clearance MDRD, ml/min/1.73 m² (mean±SD)	n=1196, 69.72±24.26	n=163, 69.14±26.00	0.776	n=3383, 71.26±23.95	n=462, 67.68±25.40	0.003	0.202

Reported are means with standard deviations (\pm SD), counts (% of patients). TIA: transient ischemic attack; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; NSAIDs: non steroidal anti inflammatory drugs; OAC: oral anticoagulation medication (vitamin K-antagonist VKA or NOAC). ¶ Calculated at screening visit. n=1 PRECISE Score calculated without risk due to WBC.

Supplemental Table 2. Procedural characteristics of randomised and nonrandomised patients stratified by PCI complexity

	Complex PCI			Noncomplex PCI			interaction p-value
	Randomised	Nonrandomised	p-value	Randomised	Nonrandomised	p-value	
	N=1196	N=163		N=3383	N=462		
Indication* (n [%])	n=1196,	n=163,	0.010	n=3383,	n=462,	0.001	0.035
Stable angina	496 (41.5%)	53 (32.5%)	0.033	1353 (40.0%)	161 (34.8%)	0.037	
Silent ischemia	129 (10.8%)	17 (10.4%)	1.000	390 (11.5%)	50 (10.8%)	0.697	
NSTEMI	334 (27.9%)	56 (34.4%)	0.097	819 (24.2%)	153 (33.1%)	<0.001	
STEMI	124 (10.4%)	28 (17.2%)	0.016	414 (12.2%)	45 (9.7%)	0.126	
Unstable angina	113 (9.4%)	9 (5.5%)	0.109	407 (12.0%)	53 (11.5%)	0.819	
Clinical status*							
Killip II, III or IV	n=1196, 112 (9.4%)	n=163, 20 (12.3%)	0.258	n=3383, 394 (11.6%)	n=462, 43 (9.3%)	0.159	0.073
Cardiac arrest	n=1196, 17 (1.4%)	n=163, 1 (0.6%)	0.713	n=3383, 41 (1.2%)	n=462, 3 (0.6%)	0.358	0.855
Heart rate, beats/min (mean±SD)	n=1194, 73.73±16.30	n=163, 76.51±19.24	0.047	n=3380, 73.63±16.54	n=461, 74.01±18.02	0.643	0.141
Systolic blood pressure, mmHg (mean±SD)	n=1193, 139.51±25.81	n=163, 132.29±27.66	0.001	n=3374, 136.31±25.33	n=459, 137.67±25.79	0.280	0.001
Procedural specifications*							
Arterial access site (n [%])	n=1196,	n=163,	0.707	n=3383,	n=462,	0.127	0.835
femoral	205 (17.1%)	30 (18.4%)	0.660	448 (13.2%)	75 (16.2%)	0.083	
radial	987 (82.5%)	133 (81.6%)	0.743	2927 (86.5%)	387 (83.8%)	0.114	
brachial	4 (0.3%)	0 (0.0%)	1.000	8 (0.2%)	0 (0.0%)	0.607	
IABP (n [%])	n=1196, 15 (1.3%)	n=163, 1 (0.6%)	0.710	n=3383, 39 (1.2%)	n=462, 6 (1.3%)	0.816	0.455
LVAD (n [%])	n=1196, 3 (0.3%)	n=163, 0 (0.0%)	1.000	n=3383, 5 (0.1%)	n=462, 1 (0.2%)	0.536	
Total amount of contrast, cc (mean±SD)	n=1188, 211.00±89.12	n=161, 199.72±82.50	0.129	n=3349, 152.05±70.18	n=454, 159.77±73.82	0.029	0.010
Medications during the procedure* (n [%])							
Unfractionated heparin	n=1196, 1149 (96.1%)	n=163, 158 (96.9%)	0.827	n=3382, 3207 (94.8%)	n=461, 436 (94.6%)	0.823	0.561

Bivalirudin	n=1196, 2 (0.2%)	n=163, 0 (0.0%)	1.000	n=3382, 5 (0.1%)	n=461, 0 (0.0%)	1.000	
Low molecular weight heparin	n=1196, 30 (2.5%)	n=163, 5 (3.1%)	0.601	n=3382, 97 (2.9%)	n=461, 20 (4.3%)	0.110	0.687
Cangrelor	n=1196, 1 (0.1%)	n=163, 1 (0.6%)	0.226	n=3382, 10 (0.3%)	n=461, 2 (0.4%)	0.647	0.318
Glycoprotein II/IIIa inhibitors	n=1196, 47 (3.9%)	n=163, 5 (3.1%)	0.827	n=3382, 115 (3.4%)	n=461, 17 (3.7%)	0.685	0.533
Total number of PCIs¶ (n [%])	n=1196,	n=163,	0.872	n=3383,	n=462,	0.572	0.402
one	888 (74.2%)	118 (72.4%)	0.634	3271 (96.7%)	449 (97.2%)	0.675	
two	293 (24.5%)	43 (26.4%)	0.629	112 (3.3%)	13 (2.8%)	0.675	
three	15 (1.3%)	2 (1.2%)	1.000	0 (0.0%)	0 (0.0%)		
Total nr of vessels treated per patient¥ (n [%])	n=1196,	n=163,	0.302	n=3383,	n=462,	0.434	0.314
one	429 (35.9%)	68 (41.7%)	0.165	2936 (86.8%)	407 (88.1%)	0.462	
two	577 (48.2%)	69 (42.3%)	0.181	447 (13.2%)	55 (11.9%)	0.462	
three	190 (15.9%)	26 (16.0%)	1.000	0 (0.0%)	0 (0.0%)		
Treated vessel(s) per patient (n [%])							
Left main	n=1196, 150 (12.5%)	n=163, 19 (11.7%)	0.899	n=3383, 110 (3.3%)	n=462, 19 (4.1%)	0.334	0.367
Left arterial descending artery	n=1196, 761 (63.6%)	n=163, 106 (65.0%)	0.794	n=3383, 1750 (51.7%)	n=462, 222 (48.1%)	0.150	0.300
Left circumflex artery	n=1196, 526 (44.0%)	n=163, 67 (41.1%)	0.502	n=3383, 815 (24.1%)	n=462, 122 (26.4%)	0.273	0.238
Right coronary artery	n=1196, 643 (53.8%)	n=163, 78 (47.9%)	0.181	n=3383, 1017 (30.1%)	n=462, 128 (27.7%)	0.329	0.543
Bypass graft	n=1196, 25 (2.1%)	n=163, 9 (5.5%)	0.015	n=3383, 51 (1.5%)	n=462, 10 (2.2%)	0.317	0.228
Total nr of treated lesions per patient	n=1196,	n=163,	0.747	n=3383,	n=462,	0.775	0.952
one	336 (28.1%)	49 (30.1%)	0.643	2779 (82.1%)	377 (81.6%)	0.796	
two	421 (35.2%)	59 (36.2%)	0.794	604 (17.9%)	85 (18.4%)	0.796	
three or more	439 (36.7%)	55 (33.7%)	0.488	0 (0.0%)	0 (0.0%)		
Total stented lesions per patient	n=1196,	n=163,	0.432	n=3383,	n=462,	0.706	0.705
one	351 (29.3%)	49 (30.1%)	0.855	2825 (83.5%)	389 (84.2%)	0.738	
two	435 (36.4%)	66 (40.5%)	0.341	558 (16.5%)	73 (15.8%)	0.738	
three or more	410 (34.3%)	48 (29.4%)	0.251	0 (0.0%)	0 (0.0%)		
At least one complex lesion B2 or C (n [%])	n=1196, 1115 (93.2%)	n=163, 148 (90.8%)	0.254	n=3383, 2026 (59.9%)	n=462, 275 (59.5%)	0.880	0.307
Number of stents per patient (mean±SD)	n=1196, 3.14±1.26	n=163, 3.28±1.36	0.215	n=3383, 1.26±0.45	n=462, 1.26±0.45	0.737	0.091

Total stent length per patient (mean±SD)	n=1196, 75.00±32.87	n=163, 75.95±37.45	0.733	n=3383, 26.96±11.83	n=462, 26.66±11.65	0.606	0.516
Any overlapping stenting (n [%])	n=1196, 657 (54.9%)	n=163, 89 (54.6%)	0.933	n=3383, 281 (8.3%)	n=462, 36 (7.8%)	0.787	0.822
Any Bifurcation or trifurcation stenting§ (n [%])	n=1196, 184 (15.4%)	n=163, 22 (13.5%)	0.641	n=3383, 0 (0.0%)	n=462, 0 (0.0%)	.	

PCI: percutaneous coronary intervention; IABP: intra-aortic balloon pump used; LVAD: left-ventricular assist device used; DAPT and SAPT: Dual and Single antiplatelet treatment.

*Data from first PCI only.

¶One PCI and up to two staged PCIs - the last PCI was the qualifying PCI one month before the randomisation.

¥Left main counted as two vessels; LIMA/RIMA/Radial grafts counted as one vessel; SVG grafts counted with the vessel as follows: LCX = 1MO, 2M0, PL(Cx) AL branch, or DG; LAD = LAD; RCA = RCA or Posterior descending RC.

§into both main- and side-branch, MADS classes 3, 4, 5, 9, 10, 11, 12, 15, 16, 17, 21, 22, 23, 24

Supplemental Table 3. Main reason for non-randomisation

	Complex PCI	Noncomplex PCI	
	Nonrandomised	Nonrandomised	p-value
If not randomized. give the main reason	n=163.	n=462.	
not eligible	76 (46.6%)	232 (50.2%)	0.466
medical reasons	7 (4.3%)	47 (10.2%)	0.023
death before M1	12 (7.4%)	15 (3.2%)	0.041
patient was lost to follow-up	6 (3.7%)	27 (5.8%)	0.415
patient withdrew consent	62 (38.0%)	141 (30.5%)	0.081

Supplemental Table 4. Complex PCI criteria

	All patients	Abbreviated DAPT	Standard DAPT
	N=4579	N=2295	N=2284
Complex PCI (Giustino) (yes)	n=4579, 1196 (26%)	n=2295, 588 (26%)	n=2284, 608 (27%)
Nr of Complex PCI criteria (Giustino)	n=4579,	n=2295,	n=2284,
0	3383 (74%)	1707 (74%)	1676 (73%)
1	397 (9%)	194 (8%)	203 (9%)
2	349 (8%)	172 (7%)	177 (8%)
3	254 (6%)	125 (5%)	129 (6%)
4	154 (3%)	79 (3%)	75 (3%)
5	37 (1%)	15 (1%)	22 (1%)
6	5 (0%)	3 (0%)	2 (0%)
Bifurcation or trifurcation stenting with two or more stents§	n=4579, 184 (4%)	n=2295, 83 (4%)	n=2284, 101 (4%)
Chronic total occlusion (≥3months or unknown)	n=4579, 214 (5%)	n=2295, 102 (4%)	n=2284, 112 (5%)
3 Vessels treated	n=4579, 190 (4%)	n=2295, 96 (4%)	n=2284, 94 (4%)
3 Stents or more implanted	n=4579, 860 (19%)	n=2295, 429 (19%)	n=2284, 431 (19%)
3 Lesions or more treated	n=4579, 439 (10%)	n=2295, 213 (9%)	n=2284, 226 (10%)
Total stent length >60mm	n=4579, 801 (17%)	n=2295, 399 (17%)	n=2284, 402 (18%)

Reported are counts (% of patients). Data from 1st, 2nd (staged) and 3rd (staged) PCI combined (as applicable).

see Giustino et al. 2016 for Complex PCI criteria; only treated lesions were considered.

§into both main- and side-branch, MADS classes 3, 4, 5, 9, 10, 11, 12, 15, 16, 17, 21, 22, 23, 24

Supplemental Table 5. Baseline characteristics of all complex and noncomplex PCI patients

	All Complex PCI	All Noncomplex PCI	P-value
	N=1196	N=3383	
Age, years (mean±SD)	n=1196, 76.65±8.24	n=3383. 75.82±8.90	0.005
Male sex (n [%]) (Female)	n=1196, 847 (70.8%)	n=3383. 2324 (68.7%)	0.177
Body mass index, kg/m ² (mean±SD)	n=1196, 27.57±4.61	n=3383. 27.27±4.75	0.053
Family history of coronary artery disease (n [%])	n=1196, 310 (25.9%)	n=3383. 799 (23.6%)	0.116
Known Arterial hypertension (n [%])	n=1196, 941 (78.7%)	n=3383. 2612 (77.2%)	0.313
Uncontrolled hypertension (n [%])	n=1196, 58 (4.8%)	n=3383. 178 (5.3%)	0.648
Known Diabetes mellitus (n [%])	n=1196, 405 (33.9%)	n=3383. 1133 (33.5%)	0.831
Known Hyperlipidemia (n [%])	n=1196, 823 (68.8%)	n=3383. 2274 (67.2%)	0.314
Smoker (n [%])	n=1195,	n=3371.	0.007
no - never smoked	623 (52.1%)	1801 (53.4%)	0.458
yes - previous smoker	486 (40.7%)	1242 (36.8%)	0.020
yes - current smoker	86 (7.2%)	328 (9.7%)	0.008
Known Peripheral/Vascular disease* (n [%])	n=1196, 137 (11.5%)	n=3383. 348 (10.3%)	0.274
Known Carotid artery disease* (n [%])	n=1196, 70 (5.9%)	n=3383. 194 (5.7%)	0.885
History of heart failure (n [%])	n=1196, 235 (19.6%)	n=3383. 632 (18.7%)	0.466
Left ventricular ejection fraction, % (mean±SD)	n=1140, 52.65±11.48	n=3157. 53.43±11.65	0.054
Prior myocardial infarction (n [%])	n=1196, 269 (22.5%)	n=3383. 595 (17.6%)	<0.001
Prior PCI (n [%])	n=1196, 312 (26.1%)	n=3383. 876 (25.9%)	0.908
Prior cerebrovascular event reported (n [%])	n=1196, 155 (13.0%)	n=3383. 415 (12.3%)	0.541
Stroke (n [%])	n=1196, 114 (9.5%)	n=3383. 296 (8.7%)	0.410
TIA (n [%])	n=1196, 45 (3.8%)	n=3383. 125 (3.7%)	0.929
Undetermined Cerebrovascular event (n [%])	n=1196, 8 (0.7%)	n=3383. 21 (0.6%)	0.834
Known History of Arterial thromboembolism (n [%])	n=1196, 24 (2.0%)	n=3383. 31 (0.9%)	0.005
Known History of Venous thromboembolism (n [%])	n=1196, 75 (6.3%)	n=3383. 164 (4.8%)	0.059
Prior CABG (n [%])	n=1196, 92 (7.7%)	n=3383. 249 (7.4%)	0.701
Prior Prosthetic mechanical heart valve (n [%])	n=1196, 19 (1.6%)	n=3383. 82 (2.4%)	0.108
Known Aortic Valve Stenosis (n [%])	n=1068, 53 (5.0%)	n=3052. 142 (4.7%)	0.676
Prior bleeding before/after qualifying PCI (n [%])	n=1196, 73 (6.1%)	n=3383. 286 (8.5%)	0.009
Known Chronic pulmonary disease (n [%])	n=1196, 144 (12.0%)	n=3383. 394 (11.6%)	0.715
Known Chronic Renal Failure (n [%])	n=1196, 253 (21.2%)	n=3383. 623 (18.4%)	0.040
Known Liver disease (n [%])	n=1196, 16 (1.3%)	n=3383. 45 (1.3%)	1.000
Atrial fibrillation (n [%])	n=1196, 361 (30.2%)	n=3383. 1129 (33.4%)	0.044
Known History of cancer (n [%])	n=1196, 196 (16.4%)	n=3383. 503 (14.9%)	0.207
Known Active cancer (n [%])	n=1196, 74 (6.2%)	n=3383. 162 (4.8%)	0.068
Known Haematological or Coagulation Disorders (n [%])	n=1196, 165 (13.8%)	n=3383. 413 (12.2%)	0.156

Chronic treatment with steroids or NSAIDS (n [%])	n=1196, 128 (10.7%)	n=3383, 313 (9.3%)	0.154
Prior VKA (n [%])	n=1196, 131 (11.0%)	n=3383, 495 (14.6%)	0.001
Need for current treatment with OAC (n [%])	n=1196, 415 (34.7%)	n=3383, 1254 (37.1%)	0.152
Clinical indication for 12 months OAC (n [%])	n=1196, 414 (34.6%)	n=3383, 1252 (37.0%)	0.142
OAC treatment at randomization (n [%])	n=414, 412 (99.5%)	n=1252, 1244 (99.4%)	1.000
PRECISE DAPT score¶ (mean±SD)	n=1196, 27.02±11.06	n=3383, 26.67±10.95	0.349
Prior bleeding (n [%])	n=1196, 66 (5.5%)	n=3383, 254 (7.5%)	0.021
Hemoglobin, g/L (mean±SD)	n=1196, 13.07±1.80	n=3383, 13.27±1.78	0.001
White blood cell count WBC¶, 109/L (mean±SD)	n=1195, 8.39±15.36	n=3383, 8.09±3.64	0.304
Creatinine clearance MDRD, ml/min/1.73 m ² (mean±SD)	n=1196, 69.72±24.26	n=3383, 71.26±23.95	0.057

Reported are means with standard deviations (±SD), counts (% of patients).

TIA: transient ischemic attack; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; NSAIDS: non steroidal anti inflammatory drugs; OAC: oral anticoagulation medication (vitamin K-antagonist VKA or NOAC).

¶calculated at screening visit. n=1 PRECISE Score calculated without risk due to WBC.

Supplemental Table 6. Procedural characteristics of all complex and noncomplex PCI patients

	All Complex PCI	All Noncomplex PCI	p-value
	N=1196	N=3383	
Indication* (n [%])	n=1196,	n=3383,	0.009
Stable angina	496 (41.5%)	1353 (40.0%)	0.373
Silent ischemia	129 (10.8%)	390 (11.5%)	0.524
NSTEMI	334 (27.9%)	819 (24.2%)	0.012
STEMI	124 (10.4%)	414 (12.2%)	0.085
Unstable angina	113 (9.4%)	407 (12.0%)	0.015
Clinical status*			
Killip II, III or IV	n=1196, 112 (9.4%)	n=3383, 394 (11.6%)	0.032
Cardiac arrest	n=1196, 17 (1.4%)	n=3383, 41 (1.2%)	0.551
Heart rate, beats/min (mean±SD)	n=1194, 73.73±16.30	n=3380, 73.63±16.54	0.845
Systolic blood pressure, mmHg (mean±SD)	n=1193, 139.51±25.81	n=3374, 136.31±25.33	<0.001
Procedural specifications*			
Arterial access site (n [%])	n=1196,	n=3383,	0.003
femoral	205 (17.1%)	448 (13.2%)	0.001
radial	987 (82.5%)	2927 (86.5%)	0.001
brachial	4 (0.3%)	8 (0.2%)	0.524
IABP (n [%])	n=1196, 15 (1.3%)	n=3383, 39 (1.2%)	0.757
LVAD (n [%])	n=1196, 3 (0.3%)	n=3383, 5 (0.1%)	0.438
Total amount of contrast, cc (mean±SD)	n=1188, 211.00±89.12	n=3349, 152.05±70.18	<0.001
Medications during the procedure* (n [%])			
Unfractionated heparin	n=1196, 1149 (96.1%)	n=3382, 3207 (94.8%)	0.1
Bivalirudin	n=1196, 2 (0.2%)	n=3382, 5 (0.1%)	1
Low molecular weight heparin	n=1196, 30 (2.5%)	n=3382, 97 (2.9%)	0.608
Cangrelor	n=1196, 1 (0.1%)	n=3382, 10 (0.3%)	0.308
Glycoprotein II/IIIa inhibitors	n=1196, 47 (3.9%)	n=3382, 115 (3.4%)	0.413
Total number of PCIs¶ (n [%])	n=1196,	n=3383,	<0.001
one	888 (74.2%)	3271 (96.7%)	<0.001
two	293 (24.5%)	112 (3.3%)	<0.001
three	15 (1.3%)	0 (0.0%)	<0.001
Total nr of vessels treated per patient§ (n [%])	n=1196,	n=3383,	<0.001
one	429 (35.9%)	2936 (86.8%)	<0.001
two	577 (48.2%)	447 (13.2%)	<0.001
three	190 (15.9%)	0 (0.0%)	<0.001
Treated vessel(s) per patient (n [%])			

Left main	n=1196, 150 (12.5%)	n=3383, 110 (3.3%)	<0.001
Left arterial descending artery	n=1196, 761 (63.6%)	n=3383, 1750 (51.7%)	<0.001
Left circumflex artery	n=1196, 526 (44.0%)	n=3383, 815 (24.1%)	<0.001
Right coronary artery	n=1196, 643 (53.8%)	n=3383, 1017 (30.1%)	<0.001
Bypass graft	n=1196, 25 (2.1%)	n=3383, 51 (1.5%)	0.188
Total nr of treated lesions per patient	n=1196,	n=3383,	<0.001
one	336 (28.1%)	2779 (82.1%)	<0.001
two	421 (35.2%)	604 (17.9%)	<0.001
three or more	439 (36.7%)	0 (0.0%)	<0.001
Total stented lesions per patient	n=1196,	n=3383,	<0.001
one	351 (29.3%)	2825 (83.5%)	<0.001
two	435 (36.4%)	558 (16.5%)	<0.001
three or more	410 (34.3%)	0 (0.0%)	<0.001
At least one complex lesion B2 or C (n [%])	n=1196, 1115 (93.2%)	n=3383, 2026 (59.9%)	<0.001
Number of stents per patient (mean±SD)	n=1196, 3.14±1.26	n=3383, 1.26±0.45	<0.001
Total stent length per patient (mean±SD)	n=1196, 75.00±32.87	n=3383, 26.96±11.83	<0.001
Any overlapping stenting (n [%])	n=1196, 657 (54.9%)	n=3383, 281 (8.3%)	<0.001
Any Bifurcation or trifurcation stenting§ (n [%])	n=1196, 184 (15.4%)	n=3383, 0 (0.0%)	<0.001
Any OCT of treated lesion	n=1196, 53 (4.4%)	n=3382, 81 (2.4%)	0.001
Any IVUS of treated lesion	n=1196, 109 (9.1%)	n=3382, 178 (5.3%)	<0.001

PCI: percutaneous coronary intervention; IABP: intra-aortic balloon pump used; LVAD: left-ventricular assist device used; DAPT and SAPT: Dual and Single antiplatelet treatment.

*Data from first PCI only.

¶One PCI and up to two staged PCIs - the last PCI was the qualifying PCI one month before the randomisation.

¥Left main counted as two vessels; LIMA/RIMA/Radial grafts counted as one vessel; SVG grafts counted with the vessel as follows: LCX = 1MO, 2M0, PL(Cx) AL branch, or DG; LAD = LAD; RCA = RCA or Posterior descending RC.

§into both main- and side-branch, MADS classes 3, 4, 5, 9, 10, 11, 12, 15, 16, 17, 21, 22, 23, 24.

Supplemental Table 7. Dual and Single Antiplatelet therapy

	Complex PCI			Noncomplex PCI		
	Abbreviated DAPT	Standard DAPT	p-value	Abbreviated DAPT	Standard DAPT	p-value
	N=588	N=608		N=1707	N=1676	
at 1 month visit (before randomisation)						
DAPT	n=588, 585 (99.5%)	n=608, 605 (99.5%)	1.000	n=1707, 1696 (99.4%)	n=1676, 1667 (99.5%)	0.823
Clopidogrel	n=588, 436 (74.1%)	n=608, 428 (70.4%)	0.156	n=1707, 1381 (80.9%)	n=1676, 1365 (81.4%)	0.692
Prasugrel	n=588, 17 (2.9%)	n=608, 17 (2.8%)	1.000	n=1707, 42 (2.5%)	n=1676, 39 (2.3%)	0.823
Ticagrelor	n=588, 132 (22.4%)	n=608, 160 (26.3%)	0.122	n=1707, 273 (16.0%)	n=1676, 263 (15.7%)	0.814
SAPT	n=588, 3 (0.5%)	n=608, 3 (0.5%)	1.000	n=1707, 11 (0.6%)	n=1676, 9 (0.5%)	0.823
Acetylsalicylic acid	n=588, 1 (0.2%)	n=608, 0 (0.0%)	0.492	n=1707, 2 (0.1%)	n=1676, 1 (0.1%)	1.000
Clopidogrel	n=588, 2 (0.3%)	n=608, 3 (0.5%)	1.000	n=1707, 9 (0.5%)	n=1676, 8 (0.5%)	1.000
Prasugrel	n=588, 0 (0.0%)	n=608, 0 (0.0%)	.	n=1707, 0 (0.0%)	n=1676, 0 (0.0%)	.
Ticagrelor	n=588, 0 (0.0%)	n=608, 0 (0.0%)	.	n=1707, 0 (0.0%)	n=1676, 0 (0.0%)	.
at 1 month visit (after randomisation)						
DAPT	n=588, 13 (2.2%)	n=608, 605 (99.5%)	<0.001	n=1707, 39 (2.3%)	n=1676, 1667 (99.5%)	<0.001
Clopidogrel	n=588, 8 (1.4%)	n=608, 432 (71.1%)	<0.001	n=1707, 31 (1.8%)	n=1676, 1366 (81.5%)	<0.001
Prasugrel	n=588, 1 (0.2%)	n=608, 15 (2.5%)	<0.001	n=1707, 0 (0.0%)	n=1676, 40 (2.4%)	<0.001
Ticagrelor	n=588, 4 (0.7%)	n=608, 158 (26.0%)	<0.001	n=1707, 8 (0.5%)	n=1676, 261 (15.6%)	<0.001
SAPT	n=588, 574 (97.6%)	n=608, 2 (0.3%)	<0.001	n=1707, 1660 (97.2%)	n=1676, 7 (0.4%)	<0.001
Acetylsalicylic acid	n=588, 140 (23.8%)	n=608, 0 (0.0%)	<0.001	n=1707, 520 (30.5%)	n=1676, 1 (0.1%)	<0.001
Clopidogrel	n=588, 310 (52.7%)	n=608, 2 (0.3%)	<0.001	n=1707, 926 (54.2%)	n=1676, 6 (0.4%)	<0.001
Prasugrel	n=588, 12 (2.0%)	n=608, 0 (0.0%)	<0.001	n=1707, 15 (0.9%)	n=1676, 0 (0.0%)	<0.001
Ticagrelor	n=588, 112 (19.0%)	n=608, 0 (0.0%)	<0.001	n=1707, 199 (11.7%)	n=1676, 0 (0.0%)	<0.001
at 3 months visit						
DAPT	n=578, 22 (3.8%)	n=602, 504 (83.7%)	<0.001	n=1684, 49 (2.9%)	n=1652, 1433 (86.7%)	<0.001
Clopidogrel	n=578, 15 (2.6%)	n=602, 336 (55.8%)	<0.001	n=1684, 41 (2.4%)	n=1652, 1151 (69.7%)	<0.001
Prasugrel	n=578, 1 (0.2%)	n=602, 16 (2.7%)	<0.001	n=1684, 0 (0.0%)	n=1652, 40 (2.4%)	<0.001
Ticagrelor	n=578, 6 (1.0%)	n=602, 152 (25.2%)	<0.001	n=1684, 8 (0.5%)	n=1652, 242 (14.6%)	<0.001
SAPT	n=578, 553 (95.7%)	n=602, 96 (15.9%)	<0.001	n=1684, 1627 (96.6%)	n=1652, 214 (13.0%)	<0.001
Acetylsalicylic acid	n=578, 135 (23.4%)	n=602, 25 (4.2%)	<0.001	n=1684, 510 (30.3%)	n=1652, 63 (3.8%)	<0.001
Clopidogrel	n=578, 305 (52.8%)	n=602, 71 (11.8%)	<0.001	n=1684, 913 (54.2%)	n=1652, 149 (9.0%)	<0.001
Prasugrel	n=578, 10 (1.7%)	n=602, 0 (0.0%)	0.001	n=1684, 15 (0.9%)	n=1652, 0 (0.0%)	<0.001
Ticagrelor	n=578, 104 (18.0%)	n=602, 0 (0.0%)	<0.001	n=1684, 189 (11.2%)	n=1652, 2 (0.1%)	<0.001
at 6 months visit						

DAPT	n=576, 27 (4.7%)	n=592, 375 (63.3%)	<0.001	n=1654, 43 (2.6%)	n=1628, 997 (61.2%)	<0.001
Clopidogrel	n=576, 21 (3.6%)	n=592, 219 (37.0%)	<0.001	n=1654, 37 (2.2%)	n=1628, 748 (45.9%)	<0.001
Prasugrel	n=576, 0 (0.0%)	n=592, 17 (2.9%)	<0.001	n=1654, 0 (0.0%)	n=1628, 36 (2.2%)	<0.001
Ticagrelor	n=576, 6 (1.0%)	n=592, 139 (23.5%)	<0.001	n=1654, 6 (0.4%)	n=1628, 213 (13.1%)	<0.001
SAPT	n=576, 507 (88.0%)	n=592, 212 (35.8%)	<0.001	n=1654, 1466 (88.6%)	n=1628, 614 (37.7%)	<0.001
Acetylsalicylic acid	n=576, 136 (23.6%)	n=592, 82 (13.9%)	<0.001	n=1654, 472 (28.5%)	n=1628, 239 (14.7%)	<0.001
Clopidogrel	n=576, 260 (45.1%)	n=592, 128 (21.6%)	<0.001	n=1654, 799 (48.3%)	n=1628, 371 (22.8%)	<0.001
Prasugrel	n=576, 10 (1.7%)	n=592, 0 (0.0%)	0.001	n=1654, 17 (1.0%)	n=1628, 0 (0.0%)	<0.001
Ticagrelor	n=576, 102 (17.7%)	n=592, 2 (0.3%)	<0.001	n=1654, 178 (10.8%)	n=1628, 4 (0.2%)	<0.001
at 12 months visit						
DAPT	n=560, 32 (5.7%)	n=585, 211 (36.1%)	<0.001	n=1625, 69 (4.2%)	n=1582, 559 (35.3%)	<0.001
Clopidogrel	n=560, 24 (4.3%)	n=585, 120 (20.5%)	<0.001	n=1625, 55 (3.4%)	n=1582, 418 (26.4%)	<0.001
Prasugrel	n=560, 1 (0.2%)	n=585, 12 (2.1%)	0.003	n=1625, 0 (0.0%)	n=1582, 10 (0.6%)	0.001
Ticagrelor	n=560, 7 (1.3%)	n=585, 79 (13.5%)	<0.001	n=1625, 14 (0.9%)	n=1582, 131 (8.3%)	<0.001
SAPT	n=560, 363 (64.8%)	n=585, 309 (52.8%)	<0.001	n=1625, 1009 (62.1%)	n=1582, 876 (55.4%)	<0.001
Acetylsalicylic acid	n=560, 149 (26.6%)	n=585, 218 (37.3%)	<0.001	n=1625, 462 (28.4%)	n=1582, 558 (35.3%)	<0.001
Clopidogrel	n=560, 135 (24.1%)	n=585, 89 (15.2%)	<0.001	n=1625, 408 (25.1%)	n=1582, 315 (19.9%)	<0.001
Prasugrel	n=560, 9 (1.6%)	n=585, 0 (0.0%)	0.002	n=1625, 17 (1.0%)	n=1582, 0 (0.0%)	<0.001
Ticagrelor	n=560, 70 (12.5%)	n=585, 2 (0.3%)	<0.001	n=1625, 122 (7.5%)	n=1582, 3 (0.2%)	<0.001

Depicted are counts (% of patients medication assessed).

DAPT and SAPT: Dual and Single AntiPlatelet Treatment.

Note: patients switched to routine care around 12 months visit post-qualifying PCI; and switching was allowed inside a 14 days window.

Supplemental Table 8. SAPT at last contact in Abbreviated DAPT patients

	Aspirin therapy¶	Clopidogrel therapy¶	Prasugrel therapy¶	Ticagrelor therapy¶
Antiplatelet therapy before randomisation				
SAPT at last contact in all Abbreviated DAPT patients				
Clinical indication for OAC				
<i>Aspirin monotherapy</i>	2	0	0	0
<i>Clopidogrel*</i>	190	643	0	0
<i>Prasugrel*</i>	0	0	0	0
<i>Ticagrelor*</i>	2	3	0	3
No clinical indication for OAC				
<i>Aspirin monotherapy</i>	1	0	0	0
<i>Clopidogrel*</i>	477	507	0	2
<i>Prasugrel*</i>	33	0	26	0
<i>Ticagrelor*</i>	150	31	2	209
SAPT at last contact in Abbreviated DAPT patients with Complex PCI				
Clinical indication for OAC				
<i>Aspirin monotherapy</i>	1	0	0	0
<i>Clopidogrel*</i>	44	151	0	0
<i>Prasugrel*</i>	0	0	0	0
<i>Ticagrelor*</i>	0	0	0	2
No clinical indication for OAC				
<i>Aspirin monotherapy</i>	0	0	0	0
<i>Clopidogrel*</i>	113	128	0	0
<i>Prasugrel*</i>	6	0	11	0
<i>Ticagrelor*</i>	38	9	1	82
SAPT at last contact in Abbreviated DAPT patients with Noncomplex PCI				
Clinical indication for OAC				
<i>Aspirin monotherapy</i>	1	0	0	0
<i>Clopidogrel*</i>	146	492	0	0
<i>Prasugrel*</i>	0	0	0	0
<i>Ticagrelor*</i>	2	3	0	1
No clinical indication for OAC				
<i>Aspirin monotherapy</i>	1	0	0	0
<i>Clopidogrel*</i>	364	379	0	2
<i>Prasugrel*</i>	27	0	15	0
<i>Ticagrelor*</i>	112	22	1	127

* including few patients on P2Y12 inhibitor monotherapy; ¶ SAPT at last contact

Supplemental Table 9 Clinical endpoints at 11 months post-randomisation at univariate analysis

	All Complex PCI	All Noncomplex PCI	Hazard ratio (95% CI)	p- value
	N = 1196	N = 3383		
Net Adverse Clinical Events	98 (8.22)	256 (7.60)	1.08 (0.86-1.36)	0.517
Major Adverse Cardiac and Cerebral Events	79 (6.62)	197 (5.85)	1.13 (0.87-1.47)	0.343
Major or Clinically Relevant Nonmajor Bleeding (MCB)	90 (7.62)	269 (8.06)	0.94 (0.74-1.19)	0.614
Death	37 (3.10)	119 (3.54)	0.87 (0.60-1.26)	0.477
Cardiovascular death	19 (1.60)	62 (1.86)	0.86 (0.52-1.44)	0.572
Non-cardiovascular death	13 (1.10)	44 (1.33)	0.83 (0.45-1.54)	0.558
Undetermined death	5 (0.43)	13 (0.39)	1.08 (0.39-3.04)	0.880
Cardiovascular or Undetermined death	24 (2.03)	75 (2.24)	0.90 (0.57-1.43)	0.654
Cerebrovascular Accident	9 (0.77)	40 (1.21)	0.63 (0.31-1.30)	0.212
Stroke¶	7 (0.60)	28 (0.84)	0.70 (0.31-1.61)	0.403
ischemic Stroke	6 (0.51)	23 (0.69)	0.73 (0.30-1.80)	0.498
hemorrhagic Stroke	1 (0.08)	5 (0.15)	0.56 (0.07-4.81)	0.599
TIA	2 (0.17)	12 (0.36)	0.47 (0.10-2.09)	0.321
Myocardial infarction	42 (3.56)	67 (2.02)	1.78 (1.21-2.61)	0.004
Definite or Probable Stent Thrombosis	10 (0.85)	13 (0.39)	2.17 (0.95-4.94)	0.066
Definite Stent Thrombosis	8 (0.68)	10 (0.30)	2.25 (0.89-5.71)	0.087
Probable Stent Thrombosis	2 (0.17)	3 (0.09)	1.87 (0.31-11.22)	0.491
Bleeding BARC classification				
Type 1	51 (4.32)	123 (3.68)	1.17 (0.84-1.62)	0.357
Type 2	68 (5.76)	186 (5.59)	1.03 (0.78-1.36)	0.829
Type 3	27 (2.29)	85 (2.55)	0.89 (0.58-1.38)	0.606
Type 3a	19 (1.61)	37 (1.11)	1.45 (0.83-2.52)	0.189
Type 3b	6 (0.51)	35 (1.05)	0.48 (0.20-1.14)	0.098
Type 3c	3 (0.26)	13 (0.39)	0.65 (0.18-2.28)	0.500
Type 4	0 (0.00)	0 (0.00)		
Type 5	2 (0.17)	8 (0.24)	0.70 (0.15-3.31)	0.656
Type 5a	0 (0.00)	2 (0.06)	0.57 (0.03-11.86)	1.000
Type 5b	2 (0.17)	6 (0.18)	0.94 (0.19-4.64)	0.936
Type 3 or 5	29 (2.46)	93 (2.79)	0.88 (0.58-1.33)	0.533

Hazard ratio (95% CI) from Cox's time-to-first event analyses in ITT population. Continuity corrected risk ratios (95% CI) in case of zero events with Fisher's exact test p-value. Interaction p-value testing for modifying effect of Complex PCI (yes or no) on the hazard ratio scale.

¶includes undetermined Strokes.

NACE = Co-primary composite endpoint of all-cause death, myocardial infarction, stroke and bleeding BARC 3 or 5

MCB = Co-primary composite endpoint of bleeding BARC 2, 3 or 5

Supplemental Table 10. Procedural characteristics of abbreviated DAPT vs standard DAPT

	Abbreviated DAPT		Standard DAPT		Complex	Noncomplex
	Complex PCI	Noncomplex PCI	Complex PCI	Noncomplex PCI	p-value	p-value
	N=588	N=1707	N=608	N=1676		
Indication* (n [%])	n=588,	n=1707,	n=608,	n=1676,	0.792	0.402
Stable angina	239 (40.6%)	683 (40.0%)	257 (42.3%)	670 (40.0%)	0.597	1.000
Silent ischemia	66 (11.2%)	179 (10.5%)	63 (10.4%)	211 (12.6%)	0.642	0.059
NSTEMI	172 (29.3%)	423 (24.8%)	162 (26.6%)	396 (23.6%)	0.334	0.446
STEMI	59 (10.0%)	214 (12.5%)	65 (10.7%)	200 (11.9%)	0.776	0.600
Unstable angina	52 (8.8%)	208 (12.2%)	61 (10.0%)	199 (11.9%)	0.491	0.792
Clinical status*						
Killip II, III or IV	n=588, 60 (10.2%)	n=1707, 192 (11.2%)	n=608, 52 (8.6%)	n=1676, 202 (12.1%)	0.372	0.486
Cardiac arrest	n=588, 11 (1.9%)	n=1707, 15 (0.9%)	n=608, 6 (1.0%)	n=1676, 26 (1.6%)	0.228	0.084
Heart rate, beats/min (mean±SD)	n=588, 74.10±16.48	n=1706, 73.33±16.46	n=606, 73.38±16.13	n=1674, 73.92±16.63	0.445	0.298
Systolic blood pressure, mmHg (mean±SD)	n=587, 140.84±26.17	n=1702, 136.22±25.63	n=606, 138.23±25.40	n=1672, 136.39±25.04	0.082	0.845
Procedural specifications*						
Arterial access site (n [%])	n=588,	n=1707,	n=608,	n=1676,	0.109	0.014
femoral	106 (18.0%)	254 (14.9%)	99 (16.3%)	194 (11.6%)	0.443	0.005
radial	482 (82.0%)	1448 (84.8%)	505 (83.1%)	1479 (88.2%)	0.648	0.004
brachial	0 (0.0%)	5 (0.3%)	4 (0.7%)	3 (0.2%)	0.125	0.726
IABP (n [%])	n=588, 11 (1.9%)	n=1707, 13 (0.8%)	n=608, 4 (0.7%)	n=1676, 26 (1.6%)	0.071	0.036
LVAD (n [%])	n=588, 2 (0.3%)	n=1707, 0 (0.0%)	n=608, 1 (0.2%)	n=1676, 5 (0.3%)	0.619	0.030
Total amount of contrast, cc (mean±SD)	n=585, 215.89±89.88	n=1690, 151.64±69.66	n=603, 206.25±88.20	n=1659, 152.47±70.73	0.062	0.733
Medications during the procedure* (n [%])						
Unfractionated heparin	n=588, 565 (96.1%)	n=1707, 1619 (94.8%)	n=608, 584 (96.1%)	n=1675, 1588 (94.8%)	1.000	1.000

Bivalirudin	n=588, 2 (0.3%)	n=1707, 3 (0.2%)	n=608, 0 (0.0%)	n=1675, 2 (0.1%)	0.241	1.000
Low molecular weight heparin	n=588, 17 (2.9%)	n=1707, 46 (2.7%)	n=608, 13 (2.1%)	n=1675, 51 (3.0%)	0.462	0.607
Cangrelor	n=588, 0 (0.0%)	n=1707, 8 (0.5%)	n=608, 1 (0.2%)	n=1675, 2 (0.1%)	1.000	0.109
Glycoprotein II/IIIa inhibitors	n=588, 25 (4.3%)	n=1707, 61 (3.6%)	n=608, 22 (3.6%)	n=1675, 54 (3.2%)	0.656	0.635
Total number of PCIs¶ (n [%])	n=588,	n=1707,	n=608,	n=1676,	0.168	0.067
one	433 (73.6%)	1660 (97.2%)	455 (74.8%)	1611 (96.1%)	0.644	0.069
two	144 (24.5%)	47 (2.8%)	149 (24.5%)	65 (3.9%)	1.000	0.069
three	11 (1.9%)	0 (0.0%)	4 (0.7%)	0 (0.0%)	0.071	
Total nr of vessels treated per patient¥ (n [%])	n=588,	n=1707,	n=608,	n=1676,	0.332	0.169
one	221 (37.6%)	1495 (87.6%)	208 (34.2%)	1441 (86.0%)	0.228	0.171
two	271 (46.1%)	212 (12.4%)	306 (50.3%)	235 (14.0%)	0.148	0.171
three	96 (16.3%)	0 (0.0%)	94 (15.5%)	0 (0.0%)	0.693	
Treated vessel(s) per patient (n [%])						
Left main	n=588, 69 (11.7%)	n=1707, 57 (3.3%)	n=608, 81 (13.3%)	n=1676, 53 (3.2%)	0.432	0.846
Left arterial descending artery	n=588, 372 (63.3%)	n=1707, 868 (50.8%)	n=608, 389 (64.0%)	n=1676, 882 (52.6%)	0.810	0.302
Left circumflex artery	n=588, 265 (45.1%)	n=1707, 387 (22.7%)	n=608, 261 (42.9%)	n=1676, 428 (25.5%)	0.484	0.054
Right coronary artery	n=588, 315 (53.6%)	n=1707, 539 (31.6%)	n=608, 328 (53.9%)	n=1676, 478 (28.5%)	0.908	0.056
Bypass graft	n=588, 10 (1.7%)	n=1707, 28 (1.6%)	n=608, 15 (2.5%)	n=1676, 23 (1.4%)	0.421	0.574
Total nr of treated lesions per patient	n=588,	n=1707,	n=608,	n=1676,	0.941	0.380
one	167 (28.4%)	1412 (82.7%)	169 (27.8%)	1367 (81.6%)	0.847	0.394
two	208 (35.4%)	295 (17.3%)	213 (35.0%)	309 (18.4%)	0.904	0.394
three or more	213 (36.2%)	0 (0.0%)	226 (37.2%)	0 (0.0%)	0.764	
Total stented lesions per patient	n=588,	n=1707,	n=608,	n=1676,	0.837	0.428
one	177 (30.1%)	1434 (84.0%)	174 (28.6%)	1391 (83.0%)	0.611	0.431
two	213 (36.2%)	273 (16.0%)	222 (36.5%)	285 (17.0%)	0.952	0.431
three or more	198 (33.7%)	0 (0.0%)	212 (34.9%)	0 (0.0%)	0.670	
At least one complex lesion B2 or C (n [%])	n=588, 553 (94.0%)	n=1707, 1009 (59.1%)	n=608, 562 (92.4%)	n=1676, 1017 (60.7%)	0.301	0.362
Number of stents per patient (mean±SD)	n=588, 3.16±1.28	n=1707, 1.25±0.45	n=608, 3.13±1.23	n=1676, 1.26±0.45	0.614	0.360

Total stent length per patient (mean±SD)	n=588, 75.98±33.66	n=1707, 26.65±11.66	n=608, 74.05±32.10	n=1676, 27.28±11.99	0.309	0.124
Any overlapping stenting (n [%])	n=588, 346 (58.8%)	n=1707, 142 (8.3%)	n=608, 311 (51.2%)	n=1676, 139 (8.3%)	0.009	1.000
Any Bifurcation or trifurcation stenting§ (n [%])	n=588, 83 (14.1%)	n=1707, 0 (0.0%)	n=608, 101 (16.6%)	n=1676, 0 (0.0%)	0.262	
Any OCT of treated lesion	n=588, 23 (3.9%)	n=1707, 39 (2.3%)	n=608, 30 (4.9%)	n=1675, 42 (2.5%)	0.403	0.736
Any IVUS of treated lesion	n=588, 53 (9.0%)	n=1707, 82 (4.8%)	n=608, 56 (9.2%)	n=1675, 96 (5.7%)	0.92	0.248

PCI: percutaneous coronary intervention; IABP: intra-aortic balloon pump used; LVAD: left-ventricular assist device used; DAPT and SAPT: Dual and Single antiplatelet treatment.

*Data from first PCI only.

¶One PCI and up to two staged PCIs - the last PCI was the qualifying PCI one month before the randomisation.

¥Left main counted as two vessels; LIMA/RIMA/Radial grafts counted as one vessel; SVG grafts counted with the vessel as follows: LCX = 1M0, 2M0, PL(Cx) AL branch, or DG; LAD = LAD; RCA = RCA or Posterior descending RC

§into both main- and side-branch, MADS classes 3, 4, 5, 9, 10, 11, 12, 15, 16, 17, 21, 22, 23, 24.

Supplemental Table 11 BARC bleeding endpoints at 11 months post-randomization under competing risk of death

	Complex PCI					Noncomplex PCI					inter action p-value	All Complex PCI	All Noncomplex PCI	Difference (95% CI)	Subdistribution hazard ratio (95% CI)*	p-value
	Abbreviated DAPT	Standard DAPT	Difference (95% CI)	Subdistribution hazard ratio (95% CI)*	p-value	Abbreviated DAPT	Standard DAPT	Difference (95% CI)	Subdistribution hazard ratio (95% CI)*	p-value						
	N = 588	N = 608				N =1707	N =1676					N = 1196	N = 3383			
Bleeding BARC classification																
Type 1	19(3.23)	32(5.28)	-2.04 [-4.32to0.25]	0.61 (0.34-1.07)	0.083	46(2.70)	77(4.61)	-1.90 [-3.17to-0.64]	0.58 (0.40-0.84)	0.003	0.894	51(4.25)	123(3.65)	0.62 [-0.69to1.94]	1.17 (0.84-1.62)	0.351
Type 2	26(4.41)	42(6.94)	-2.49 [-5.11to0.13]	0.63 (0.39-1.02)	0.061	76(4.47)	110(6.59)	-2.12 [-3.66to-0.58]	0.67 (0.50-0.90)	0.007	0.821	68(5.69)	186(5.52)	0.18 [-1.35to1.70]	1.03 (0.78-1.36)	0.826
Type 3	11(1.87)	16(2.64)	-0.76 [-2.45to0.92]	0.71 (0.33-1.52)	0.372	42(2.47)	43(2.58)	-0.10 [-1.16to0.96]	0.96 (0.63-1.46)	0.836	0.496	27(2.26)	85(2.52)	-0.26 [-1.26to0.74]	0.89 (0.58-1.38)	0.613
Type 3a	9(1.53)	10(1.65)	-0.11 [-1.53to1.31]	0.93 (0.38-2.28)	0.869	17(1.00)	20(1.20)	-0.20 [-0.90to0.51]	0.83 (0.44-1.59)	0.579	0.850	19(1.59)	37(1.10)	0.49 [-0.30to1.29]	1.45 (0.83-2.52)	0.187
Type 3b	2(0.34)	4(0.66)	-0.32 [-1.12to0.48]	0.52 (0.09-2.81)	0.444	19(1.12)	16(0.96)	0.16 [-0.52to0.85]	1.17 (0.60-2.27)	0.651	0.380	6(0.50)	35(1.04)	-0.54 [-1.06to-0.01]	0.48 (0.20-1.15)	0.099
Type 3c	1(0.17)	2(0.33)	-0.16 [-0.73to0.41]	0.52 (0.05-5.68)	0.588	6(0.35)	7(0.42)	-0.07 [-0.49to0.35]	0.84 (0.28-2.50)	0.756	0.716	3(0.25)	13(0.39)	-0.13 [-0.49to0.22]	0.65 (0.19-2.28)	0.502
Type 5	0(0.00)	2(0.33)				2(0.12)	6(0.36)	-0.24 [-0.57to0.09]	0.33 (0.07-1.62)	0.170		2(0.17)	8(0.24)	-0.07 [-0.35to0.21]	0.70 (0.15-3.32)	0.658
Type 2, 3 or 5	35(5.93)	55(9.11)	-3.10 [-6.08to-0.12]	0.64 (0.42-0.98)	0.039	113(6.64)	156(9.36)	-2.70 [-4.53to-0.87]	0.70 (0.55-0.89)	0.004	0.724	90(7.53)	269(7.99)	-0.45 [-2.20to1.31]	0.94 (0.74-1.19)	0.614
Type 3 or 5	11(1.87)	18(2.97)	-1.09 [-2.83to0.65]	0.63 (0.30-1.32)	0.221	44(2.59)	49(2.94)	-0.35 [-1.45to0.76]	0.88 (0.58-1.32)	0.530	0.437	29(2.43)	93(2.76)	-0.33 [-1.37to0.70]	0.88 (0.58-1.33)	0.539
Type 2 or 3	35(5.93)	53(8.78)	-2.77 [-5.72to0.18]	0.67 (0.43-1.02)	0.061	111(6.52)	150(9.00)	-2.46 [-4.26to-0.65]	0.71 (0.56-0.91)	0.007	0.775	88(7.37)	261(7.75)	-0.38 [-2.11to1.36]	0.95 (0.74-1.21)	0.667

Nr of events (cumulative incidence function% under competing risk)

Subhazard ratio (95% CI) from competing risk event analyses in ITT population using the Fine&Gray* (1999) approach. Interaction p-value testing for modifying effect of Complex PCI (yes or no) on the subhazard ratio scale.

Only the first occurrence of each bleeding BARC type per patient is considered. Endpoints with BARC5 shown for completeness.

*Fine, J. P., and R. J. Gray. 1999. A proportional hazards model for the subdistribution of a competing risk. Journal of the American Statistical Association 94: 496-509.

Supplemental Table 12. Clinical endpoints at 11 months post-randomization at a more comprehensive complex pci definition*

	Complex PCI					Noncomplex PCI					interaction p-value
	Abbreviat ed DAPT	Standard DAPT	Hazard ratio (95% CI)	p-value	Com-Nogue Risk Difference (95% CI)	Abbreviate d DAPT	Standard DAPT	Hazard ratio (95% CI)	p- value	Com-Nogue Risk Difference (95% CI)	
	N = 673	N = 684				N =1622	N =1600				
Net Adverse Clinical Events	60(8.93)	59(8.65)	1.03(0.72-1.47)	0.883	0.29 [-2.73 to 3.30]	112(6.94)	123(7.73)	0.89(0.69-1.15)	0.388	-0.79 [-2.59 to 1.02]	0.536
Major Adverse Cardiac and Cerebral Events	52(7.74)	45(6.60)	1.18(0.79-1.75)	0.428	1.15 [-1.60 to 3.90]	86(5.33)	93(5.85)	0.91(0.68-1.22)	0.528	-0.52 [-2.11 to 1.08]	0.311
Major or Clinically Relevant Nonmajor Bleeding	44(6.62)	59(8.73)	0.74(0.50-1.09)	0.130	-2.11 [-4.96 to 0.73]	104(6.50)	152(9.63)	0.66(0.52-0.85)	0.001	-3.12 [-5.01 to -1.23]	0.635
Death	24(3.57)	23(3.37)	1.06(0.60-1.87)	0.846	0.20 [-1.75 to 2.15]	51(3.16)	58(3.65)	0.86(0.59-1.26)	0.449	-0.48 [-1.74 to 0.77]	0.564
Cardiovascular death	11(1.65)	14(2.07)	0.80(0.36-1.76)	0.573	-0.41 [-1.86 to 1.03]	26(1.62)	30(1.90)	0.85(0.50-1.44)	0.551	-0.28 [-1.19 to 0.64]	0.889
Non-cardiovascular death	8(1.20)	8(1.18)	1.01(0.38-2.70)	0.978	0.02 [-1.14 to 1.18]	21(1.32)	20(1.27)	1.03(0.56-1.90)	0.919	0.04 [-0.75 to 0.83]	0.975
Undetermined death	5(0.76)	1(0.15)	5.07(0.59-43.36)	0.139	0.61 [-0.12 to 1.33]	4(0.25)	8(0.51)	0.49(0.15-1.63)	0.247	-0.26 [-0.69 to 0.17]	0.063
Cardiovascular or Undetermined death	16(2.40)	15(2.21)	1.08(0.53-2.19)	0.827	0.18 [-1.42 to 1.79]	30(1.87)	38(2.40)	0.78(0.48-1.25)	0.300	-0.53 [-1.54 to 0.47]	0.445
Cerebrovascular Accident	5(0.76)	6(0.90)	0.85(0.26-2.77)	0.782	-0.14 [-1.11 to 0.84]	12(0.75)	26(1.66)	0.45(0.23-0.90)	0.023	-0.90 [-1.66 to -0.14]	0.369
Stroke¶	3(0.45)	5(0.75)	0.61(0.15-2.54)	0.496	-0.29 [-1.12 to 0.54]	9(0.56)	18(1.15)	0.49(0.22-1.09)	0.082	-0.58 [-1.23 to 0.06]	0.797
ischemic Stroke	3(0.45)	3(0.45)	1.01(0.20-5.02)	0.988	0.01 [-0.72 to 0.73]	8(0.50)	15(0.96)	0.52(0.22-1.24)	0.141	-0.46 [-1.05 to 0.13]	0.476
hemorrhagic Stroke	0(0.00)	2(0.30)	0.20(0.01-4.16)	0.500	-0.30 [-0.71 to 0.12]	1(0.06)	3(0.19)	0.33(0.03-3.15)	0.334	-0.13 [-0.38 to 0.12]	
TIA	2(0.30)	1(0.15)	2.03(0.18-22.39)	0.563	0.15 [-0.36 to 0.67]	3(0.19)	8(0.51)	0.37(0.10-1.39)	0.140	-0.32 [-0.73 to 0.10]	0.222
Myocardial infarction	28(4.23)	23(3.42)	1.24(0.71-2.15)	0.451	0.81 [-1.24 to 2.87]	32(2.01)	26(1.66)	1.21(0.72-2.04)	0.463	0.35 [-0.58 to 1.29]	0.962
Definite or Probable Stent Thrombosis	5(0.76)	6(0.89)	0.85(0.26-2.77)	0.781	-0.13 [-1.10 to 0.83]	9(0.57)	3(0.19)	2.96(0.80-10.93)	0.104	0.37 [-0.05 to 0.80]	0.164
Definite Stent Thrombosis	5(0.76)	4(0.59)	1.27(0.34-4.72)	0.724	0.16 [-0.72 to 1.04]	6(0.38)	3(0.19)	1.97(0.49-7.88)	0.337	0.19 [-0.19 to 0.56]	0.651
Probable Stent Thrombosis	0(0.00)	2(0.30)	0.20(0.01-4.16)	0.500	-0.30 [-0.71 to 0.11]	3(0.19)	0(0.00)	6.91(0.36-133.67)	0.250	0.19 [-0.02 to 0.40]	
Bleeding BARC classification											
Type 1	21(3.17)	33(4.90)	0.64(0.37-1.10)	0.108	-1.73 [-3.84 to 0.38]	44(2.74)	76(4.81)	0.56(0.39-0.82)	0.002	-2.07 [-3.39 to -0.74]	0.703

Type 2	32(4.82)	44(6.52)	0.73(0.46-1.14)	0.168	-1.70 [-4.18 to 0.78]	70(4.38)	108(6.86)	0.63(0.47-0.85)	0.003	-2.48 [-4.08 to -0.88]	0.607
Type 3	15(2.26)	17(2.52)	0.89(0.44-1.78)	0.740	-0.26 [-1.90 to 1.38]	38(2.38)	42(2.66)	0.89(0.57-1.38)	0.595	-0.28 [-1.37 to 0.81]	0.998
Type 3a	11(1.66)	10(1.48)	1.11(0.47-2.62)	0.809	0.18 [-1.16 to 1.51]	15(0.94)	20(1.27)	0.74(0.38-1.44)	0.371	-0.33 [-1.05 to 0.40]	0.458
Type 3b	4(0.61)	5(0.74)	0.81(0.22-3.02)	0.754	-0.14 [-1.01 to 0.74]	17(1.07)	15(0.95)	1.11(0.56-2.23)	0.759	0.11 [-0.58 to 0.81]	0.674
Type 3c	1(0.15)	2(0.30)	0.51(0.05-5.59)	0.579	-0.15 [-0.66 to 0.36]	6(0.38)	7(0.44)	0.84(0.28-2.51)	0.760	-0.07 [-0.51 to 0.38]	0.705
Type 4	0(0.00)	0(0.00)				0(0.00)	0(0.00)				
Type 5	0(0.00)	3(0.45)	0.15(0.01-2.90)	0.249	-0.45 [-0.96 to 0.06]	2(0.13)	5(0.32)	0.39(0.08-2.03)	0.265	-0.19 [-0.52 to 0.14]	
Type 5a	0(0.00)	0(0.00)				0(0.00)	2(0.13)	0.20(0.01-4.16)	0.247	-0.13 [-0.30 to 0.05]	1.000
Type 5b	0(0.00)	3(0.45)	0.15(0.01-2.90)	0.249	-0.45 [-0.96 to 0.06]	2(0.13)	3(0.19)	0.66(0.11-3.92)	0.644	-0.06 [-0.34 to 0.22]	1.000
Type 3 or 5	15(2.26)	20(2.97)	0.76(0.39-1.48)	0.412	-0.70 [-2.41 to 1.01]	40(2.51)	47(2.98)	0.83(0.55-1.27)	0.402	-0.47 [-1.61 to 0.67]	0.804

* analysis performed adding left main or left internal mammary artery or saphenous vein graft treatment as additional criteria into the complex PCI definition; ¶ includes undetermined Strokes;

Supplemental Table 13 BARC bleeding endpoints at 11 months post-randomization with Complex PCI or Acute Coronary Syndrome at 1st PCI under competing risk with death

	Complex PCI or ACS				Noncomplex PCI and no ACS				interaction p-value
	Abbreviated DAPT	Standard DAPT	Subhazard ratio (95% CI)	p-value	Abbreviated DAPT	Standard DAPT	Subhazard ratio (95% CI)	p-value	
	N =1433	N =1403			N = 862	N = 881			
Bleeding BARC classification									
Type 1	40(2.80)	72(5.15)	0.54 (0.36-0.79)	0.002	25(2.91)	37(4.21)	0.69 (0.41-1.14)	0.146	0.451
Type 2	59(4.12)	84(6.02)	0.68 (0.49-0.94)	0.022	43(5.01)	68(7.74)	0.64 (0.44-0.94)	0.021	0.818
Type 3	30(2.10)	34(2.44)	0.86 (0.53-1.40)	0.543	23(2.68)	25(2.85)	0.94 (0.53-1.65)	0.826	0.815
Type 3a	16(1.12)	23(1.65)	0.68 (0.36-1.28)	0.231	10(1.17)	7(0.80)	1.46 (0.56-3.84)	0.440	0.192
Type 3b	12(0.84)	8(0.57)	1.47 (0.60-3.59)	0.401	9(1.05)	12(1.37)	0.77 (0.32-1.82)	0.545	0.305
Type 3c	3(0.21)	3(0.21)	0.98 (0.20-4.84)	0.978	4(0.47)	6(0.68)	0.68 (0.19-2.41)	0.553	0.729
Type 5	2(0.14)	5(0.36)	0.39 (0.08-2.01)	0.260	0(0.00)	3(0.34)			
Type 2, 3 or 5	86(5.99)	117(8.41)	0.70 (0.53-0.93)	0.013	62(7.23)	94(10.71)	0.66 (0.48-0.91)	0.012	0.778
Type 3 or 5	32(2.24)	39(2.80)	0.80 (0.50-1.27)	0.342	23(2.68)	28(3.19)	0.84 (0.48-1.45)	0.527	0.894
Type 2 or 3	84(5.86)	112(8.04)	0.72 (0.54-0.95)	0.022	62(7.22)	91(10.37)	0.68 (0.50-0.95)	0.021	0.820

Nr of events (cumulative incidence function% under competing risk)

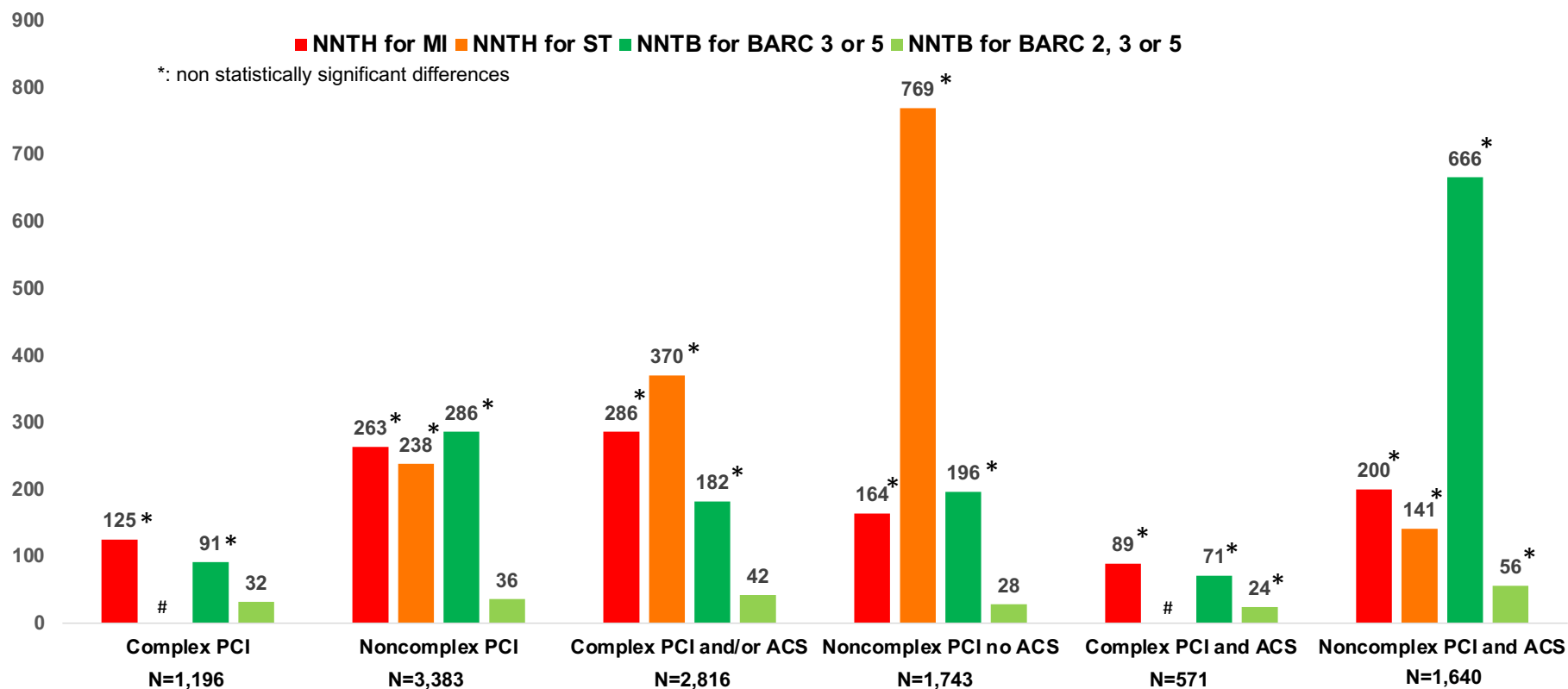
Subhazard ratio (95% CI) from competing risk event analyses in ITT population using the Fine&Gray* (1999) approach. Interaction p-value testing for modifying effect of Complex PCI or ACS (yes or no) on the subhazard ratio scale. Only the first occurrence of each bleeding BARC type per patient is considered.

ACS = STEMI, NSTEMI and Unstable angina.

*Fine, J. P., and R. J. Gray. 1999. A proportional hazards model for the subdistribution of a competing risk. Journal of the American Statistical Association 94: 496-509.

Supplemental Figure 1: Number needed to treat for harm (NNTH) /number needed to treat for benefit (NNTB) at 335 days

ACS, acute coronary syndrome; ST, definite or probable stent thrombosis; MI, myocardial infarction; BARC, bleeding academic research consortium;



References

1. D'Agostino RB, Lee ML, Belanger AJ, Cupples LA, Anderson K, Kannel WB. Relation of pooled logistic regression to time dependent Cox regression analysis: the Framingham Heart Study. *Stat Med* 1990;**9**:1501-15.
2. Valgimigli M, Garcia-Garcia HM, Vrijens B, Vranckx P, McFadden EP, Costa F, Pieper K, Vock DM, Zhang M, Van Es GA, Tricoci P, Baber U, Steg G, Montalescot G, Angiolillo DJ, Serruys PW, Farb A, Windecker S, Kastrati A, Colombo A, Feres F, Juni P, Stone GW, Bhatt DL, Mehran R, Tijssen JGP. Standardized classification and framework for reporting, interpreting, and analysing medication non-adherence in cardiovascular clinical trials: a consensus report from the Non-adherence Academic Research Consortium (NARC). *Eur Heart J* 2019;**40**:2070-85.