Supplemental Material

Appendix

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Study institutes

Institute	Number of patients
Kurashiki Central Hospital	349
Toho University Ohashi Medical Center	282
Sakurakai Takahashi Hospital	265
Asahi General Hospital	253
Ota Memorial Hospital	218
Miyazaki Medical Association Hospital	202
Ogikubo Hospital	202
Hyogo Brain and Heart Center	157
Kawasaki Medical School	153
Sakakibara Heart Institute	150
Rinku General Medical Center	146
Tokyo Women's Medical University	146
Kansai Rosai Hospital Cardiovascular Center	143
Tokyo Medical University Hachioji Medical Center	143
Juntendo University Shizuoka Hospital	139
Chikamori Hospital	130
Tokyo Women's Medical University Yachiyo Medical Center	124
Ageo Central General Hospital	115
Tokyo Kamata Hospital	114
Fujisawa City Hospital	108
Tokushima Prefectural Central Hospital	102
Hiroshima Prefectural Hospital	100
Saiseikai Utsunomiya Hospital	100

Sakurabashi Watanabe Hospital	100
Shin-Koga Hospital	100
Tokushima Red Cross Hospital	100
Tokushima University Hospital	100
Wakayama Medical University	100
Showa University School of Medicine	97
Yokohama City University Medical Center	97
Japanese Red Cross Okayama Hospital	92
National Hospital Organization Osaka National Hospital	89
Mitsui Memorial Hospital	88
Edogawa Hospital	86
Funabashi Municipal Medical Center Heart and Vascular Institute	86
Nihon University School of Medicine	82
Kurume University Hospital	75
Osaka Police Hospital	74
Showa University Northern Yokohama Hospital	74
Shiga General Hospital	73
Fukui Cardiovascular Center	71
Tenri Hospital	71
Saiseikai Nakatsu Hospital	64
Tokyo Rosai Hospital	63
Matsusaka Central Hospital	56
Kobe City Medical Center General Hospital	54
Yokohama Sakae Kyosai Hospital	53
Tokyo Medical University	52
Fukuoka Sanno Hospital	51

Saiseikai Kawaguchi General Hospital	50
Tokyo Metropolitan Tama Medical Center	45
Fujita Health University Hospital	44
Nagoya University Graduate School of Medicine	43
Hyogo Prefectural Awaji Medical Center	41
University of Occupational and Environmental Health	39
Ogaki Municipal Hospital	36
The Jikei University School of Medicine	35
Saiseikai Kumamoto Hospital	30
St. Luke's International Hospital	29
Kobe University Graduate School of Medicine	28
Odawara Cardiovascular Hospital	28
Dokkyo Medical University	25
Nagoya Kyoritsu Hospital	15
Teikyo University School of Medicine	14
Yokohama City University Hospital	14
Osaka University Graduate School of Medicine	13
Juntendo University Graduate School of Medicine	4

Data S1. Definitions used in this study

Definition of the efficacy events

(1) Death
All deaths from any cause. All-cause death: All deaths are applicable regardless of the cause. Cardiovascular death: Deaths resulting from damage to the cardiac vessels.
(2) Non-fatal myocardial infarction
Non-fatal myocardial infarction is defined as myocardial infarction that is nonfatal based on diagnosis by markers for cardiomyopathy (cardiac enzymes) or electrocardiogram* etc. in the presence of symptoms suggestive of a new onset of acute myocardial infarction or reinfarction after index percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG). *An ST change of $\geq \pm 1$ mm (0.1 mV) (new onset or recurrence) or a new Q wave abnormality is observed.
(3) Non-fatal stroke
A patient has cerebral stroke when neurologic symptoms or signs newly develop and when the culprit lesion is detected by computed tomography (CT) or magnetic resonance imaging (MRI) scans. Cerebral stroke is divided into two major subtypes:

ischemic stroke (cerebral infarction) and nonischemic stroke (e.g., cerebral hemorrhage, subarachnoid hemorrhage). Ischemic stroke (cerebral infarction): A new onset of neurological signs or symptoms with a new infarct lesion related to the neurological signs or symptoms, which is confirmed by CT or MRI scans, regardless of whether the neurological signs or symptoms last at least 24 hours or not. Nonischemic stroke: Cerebral hemorrhage, subarachnoid hemorrhage, etc.
(4) Revascularization
Revascularization is defined as unscheduled (emergent) PCI, CABG, or intracoronary thrombolysis introduced after index PCI or CABG. · Target Lesion Revascularization Repeat PCI or CABG for the target lesion (proximal and distal 5-mm-long segments from the edge of the implanted stent) due to restenosis of the target lesion or other complications. · Target Vessel Revascularization Repeat PCI or CABG for the target vessel due to restenosis of the target vessel or other complications.
(5) Transient ischemic attack (TIA)

TIA is defined as transient episodes of neurologic dysfunction caused by focal cerebral, spinal cord, and retinal ischemia. CT and MRI scans reveal no evidence of acute infarction.
(6) Stent thrombosis
Stent thrombosis is defined as definite, probable, or possible stent thrombosis by the Academic Research Consortium classification.
(7) Peripheral arterial occlusive disease
Peripheral arterial occlusive disease internally or surgically treated due to acute ischemia

Table S1. Study criteria

Inclusion criteria
Patients who met all the following criteria were included in this study: 1. Patients aged ≥20 years when consent was obtained 2. Patients with coronary artery lesions that were visually confirmed by coronary angiography and for which PCI was indicated by drug-eluting stent placement (as judged with reference to the package insert) 3. Patients administered antiplatelet drugs 4. Patients providing written consent after receiving an explanation of the contents of this clinical research (in case of an emergency, consent could be obtained from a designated representative)
Exclusion criteria
Patients who were participating or planning to participate in a clinical study that consisted of a clinical trial or intervention before the follow-up of this study was complete.

Patients who had acute coronary syndrome or coronary artery disease requiring elective intracoronary stenting and who had undergone PCI with DES implantation were eligible for the study. DES = drug-eluting stent, PCI = percutaneous coronary intervention.

Table S2. One-year cumulative incidence of primary and secondary endpoints

	Number of events	Incidence (%)
MACCE	261	4.4
All cause death	156	2.7
Non-fatal myocardial infarction	62	1.0
Non-fatal stroke	51	0.9
Stent thrombosis	17	0.3
Major bleeding (BARC type 3 and 5)	165	2.8
All bleedings	419	7.1

BARC = Bleeding Academic Research Consortium; MACCE = major adverse cardiac and cerebrovascular events.

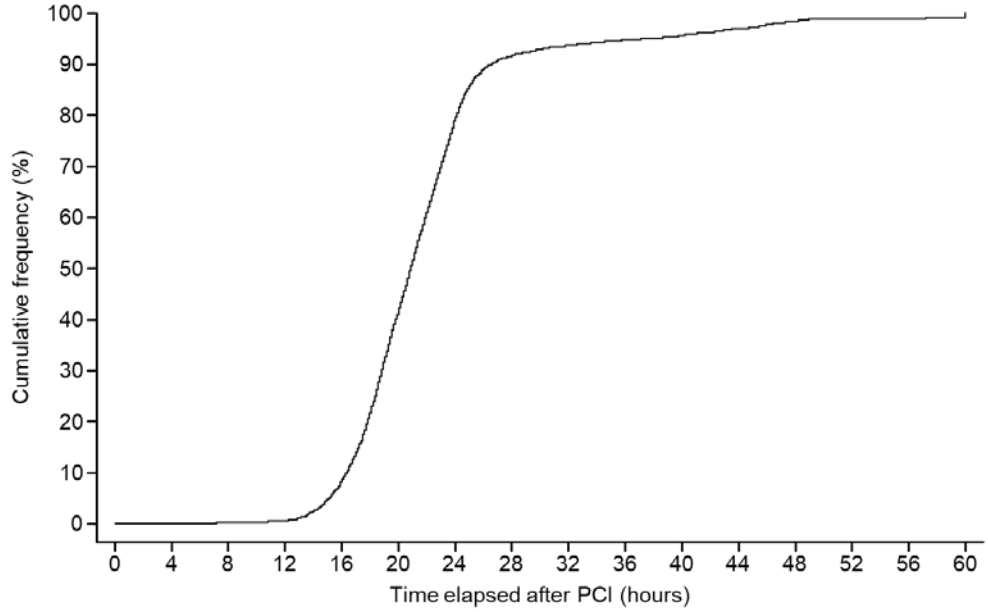

Figure S1. Time to measurement of PRU 12–48 h after PCI

PCI = percutaneous coronary intervention; PRU = $P2Y_{12}$ reaction units.

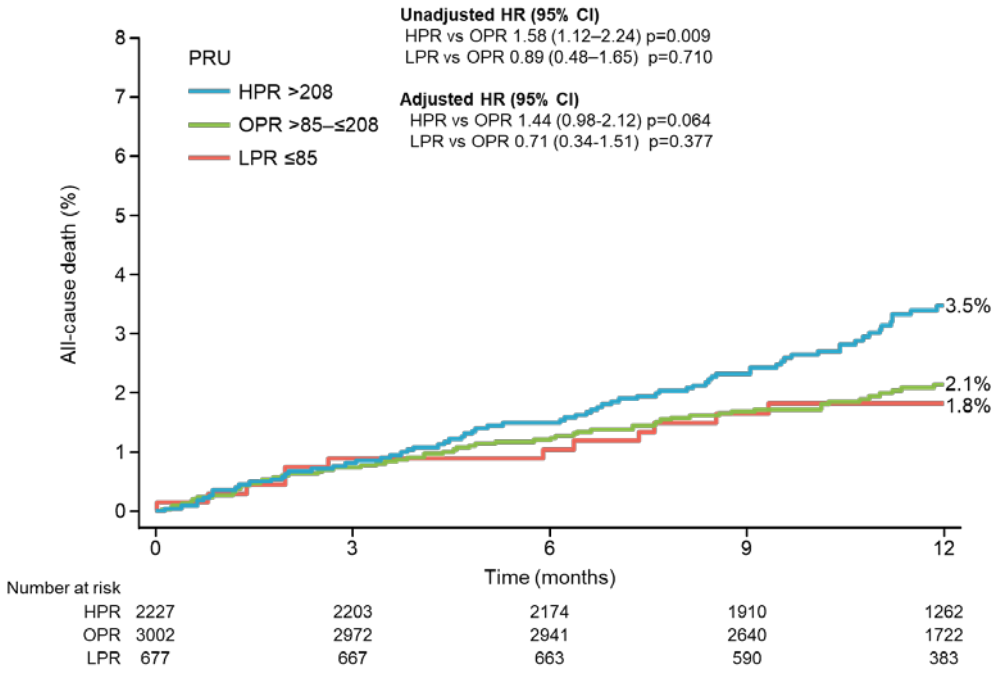

Figure S2A. Time–to–event curves through 1 year for all–cause death according to platelet reactivity

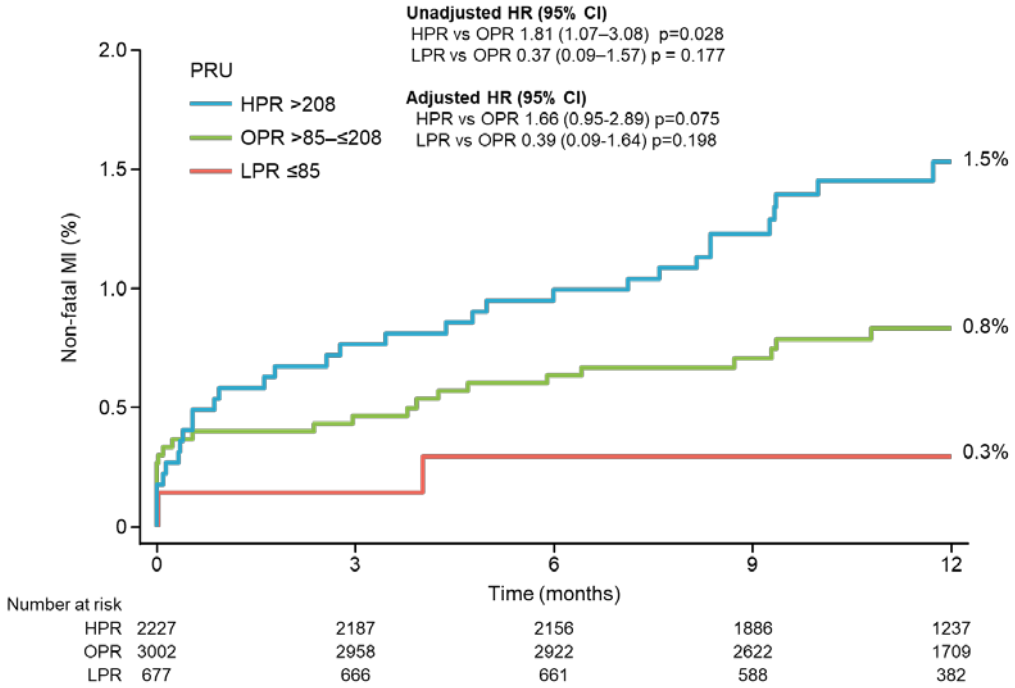

Figure S2B. Time–to–event curves through 1 year for non–fatal MI according to platelet reactivity

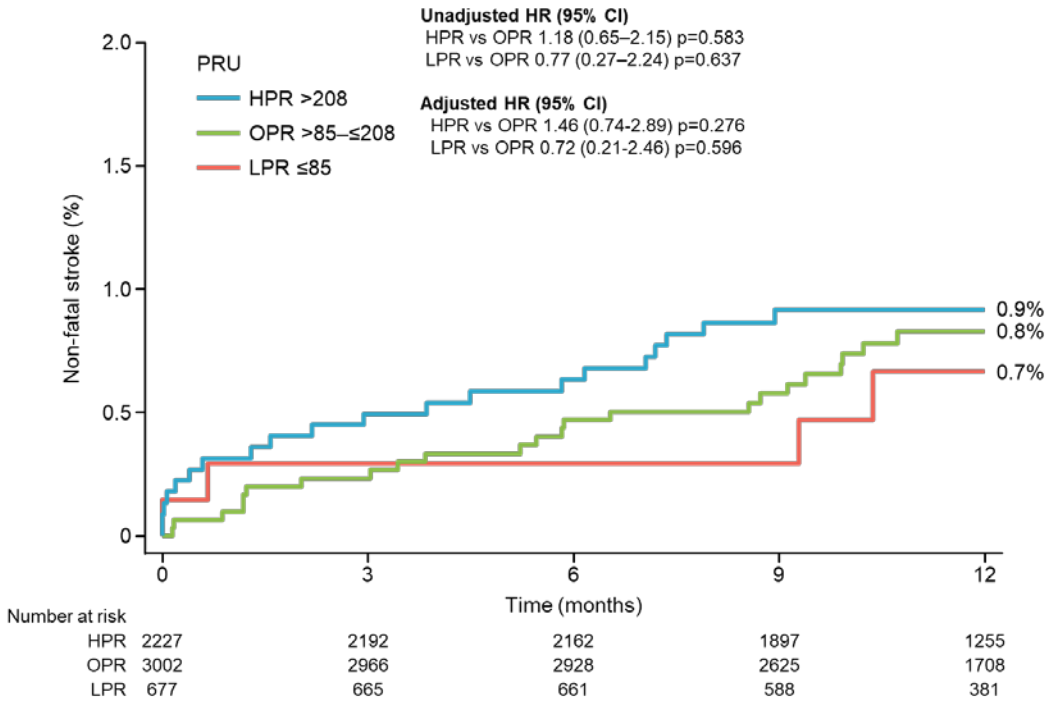

Figure S2C. Time–to–event curves through 1 year for non–fatal stroke according to platelet reactivity

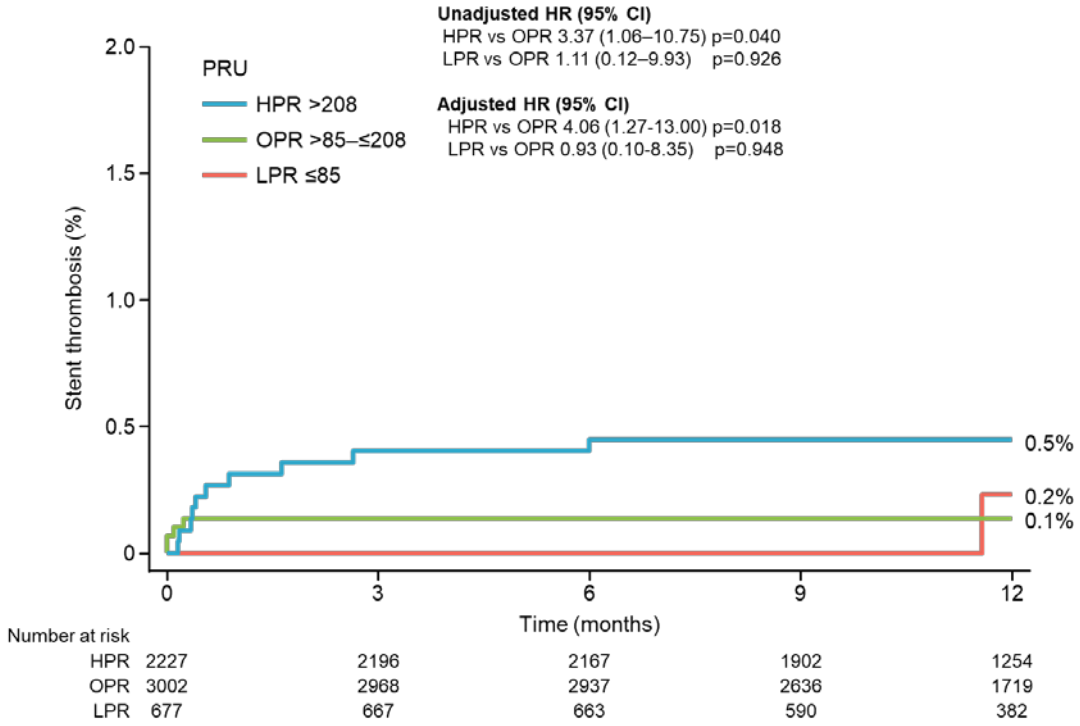

Figure S2D. Time–to–event curves through 1 year for stent thrombosis according to platelet reactivity

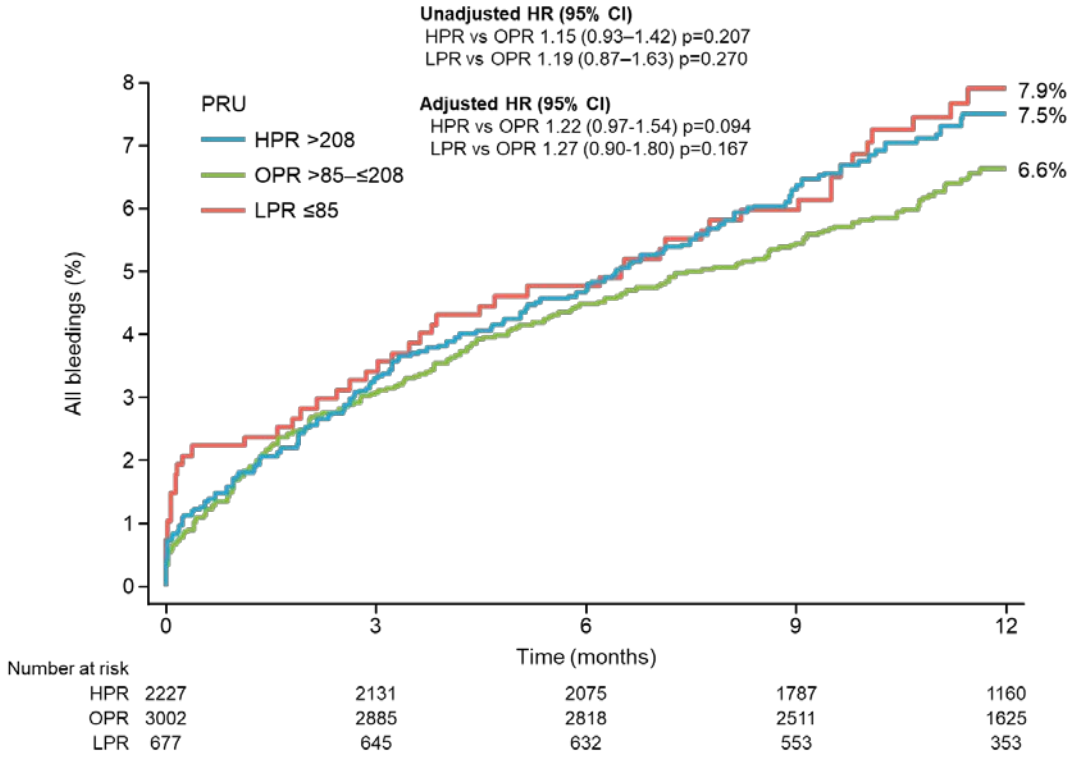

Figure S2E. Time–to–event curves through 1 year for all bleeding according to platelet reactivity

HPR = high $P2Y_{12}$ reaction units; LPR = low $P2Y_{12}$ reaction units; MI = myocardial infarction; OPR = optimal $P2Y_{12}$ reaction units; PRU = $P2Y_{12}$ reaction units.

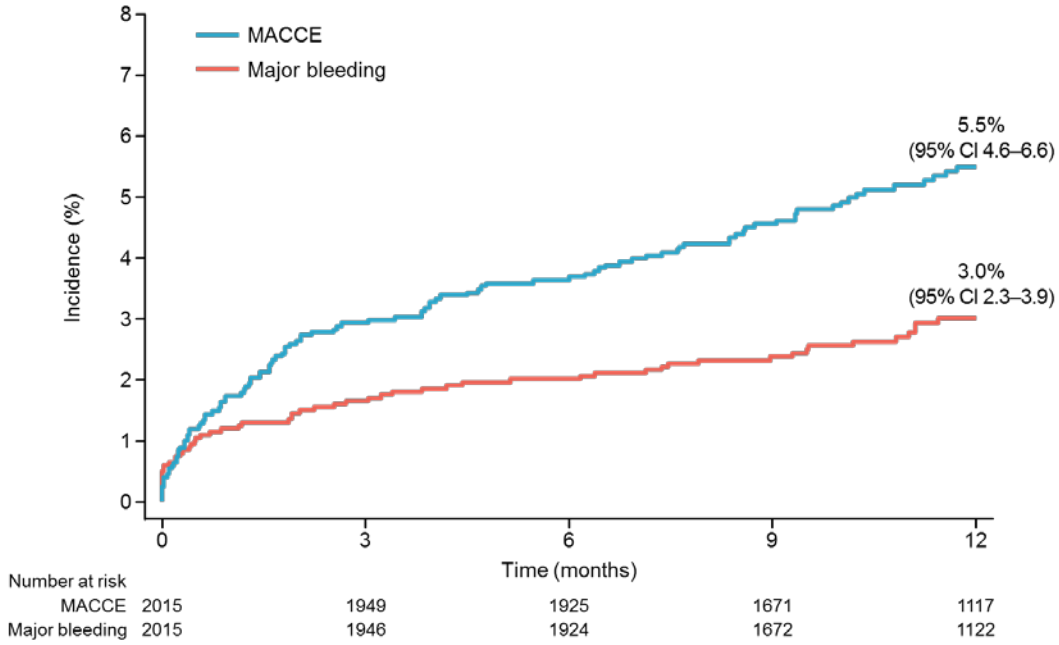

Figure S3A. Time to event curves of ACS and non-ACS groups through 1 year (ACS patients)

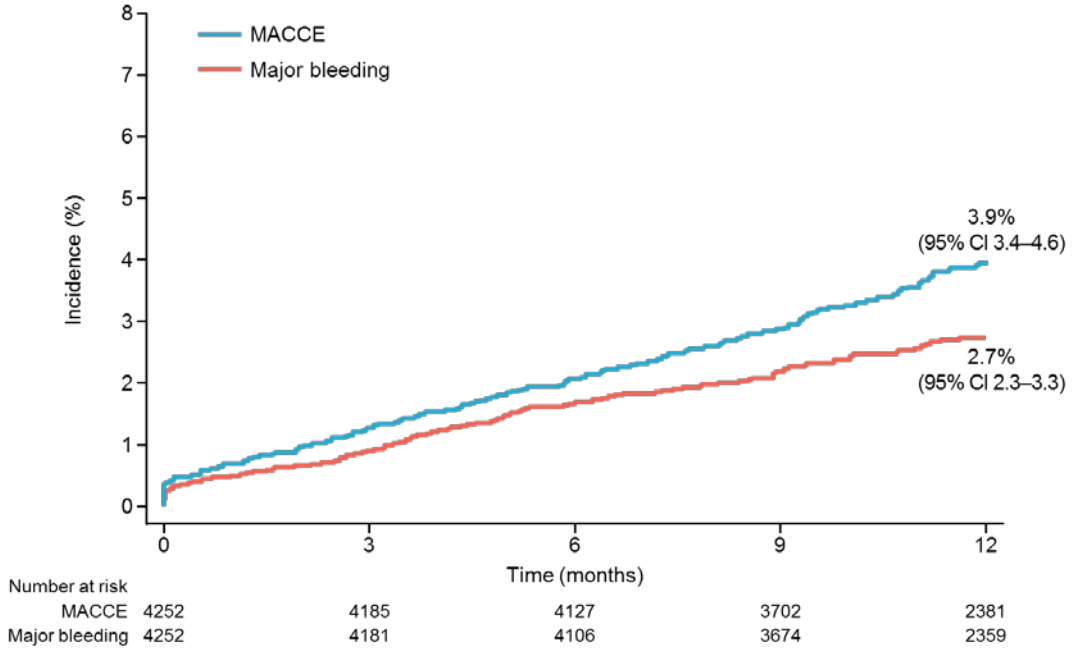

Figure S3B. Time to event curves of ACS and non-ACS groups through 1 year (non-ACS patients)

ACS = acute coronary syndrome; CI = confidence interval; MACCE = major adverse cardiac and cerebrovascular events.

	All			Prasugrel			Clopidogrel		
	LPR	OPR	HPR	LPR	OPR	HPR	LPR	OPR	HPR
N	677	3002	2227	578	2100	1012	95	855	1141
Number of events	19	103	117	16	70	50	2	27	57
Cumulative incidence (%)	3.0	3.6	5.7	3.0	3.6	5.3	2.3	3.3	5.4
Unadjusted HR on OPR	0.82	-	1.55	0.83	-	1.50	0.67	-	1.61
P value	0.420	-	0.001	0.492	-	0.028	0.589	-	0.042
Adjusted HR on OPR	0.71	-	1.53	0.82	-	1.54	0.34	-	1.50
P value	0.241	-	0.004	0.508	-	0.033	0.352	-	0.102

Figure S4A. One-year cumulative incidence of MACCE according to platelet reactivity by P2Y12 inhibitor at discharge

	All			Prasugrel			Clopidogrel		
	LPR	OPR	HPR	LPR	OPR	HPR	LPR	OPR	HPR
N	677	3002	2227	578	2100	1012	95	855	1141
Number of events	19	69	66	13	47	34	5	20	28
Cumulative incidence (%)	3.0	2.5	3.2	2.5	2.4	3.6	5.6	2.5	2.6
Unadjusted HR on OPR	1.23	-	1.30	1.01	-	1.52	2.33	-	1.06
P value	0.427	-	0.125	0.988	-	0.062	0.090	-	0.840
Adjusted HR on OPR	1.26	-	1.36	1.16	-	1.71	2.09	-	0.93
P value	0.417	-	0.103	0.665	-	0.031	0.182	-	0.810

Figure S4B. One-year cumulative incidence of major bleeding according to platelet reactivity by $P2Y_{12}$ inhibitor at discharge

HPR = high $P2Y_{12}$ reaction units; HR = hazard ratio; LPR = low $P2Y_{12}$ reaction units; MACCE = major adverse cardiac and cerebrovascular events; OPR = optimal $P2Y_{12}$ reaction units; PRU = $P2Y_{12}$ reaction units.