Supplementary Online Content

Hahn J-Y, Song YB, Oh J-H, et al. Efficacy of P2Y12 inhibitor monotherapy vs dual antiplatelet therapy on cardiovascular events in patients undergoing percutaneous coronary intervention: the SMART-CHOICE randomized clinical trial. Published June 25, 2019. *JAMA*. doi:10.1001/jama.2019.8146

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Inclusion and Exclusion Criteria

Inclusion criteria	
1.	Patients must be at least 20 years of age.
2.	Patients are able to verbally confirm understandings of risks, benefits and treatment alternatives of receiving percutaneous coronary intervention and he/she or his/her legally authorized representative provides written informed consent prior to any study related procedure.
3.	Patients should have undergone successful percutaneous coronary intervention with drug-eluting stent for stable ischemic heart disease or acute coronary syndrome
4.	Patients must have one or more coronary stenosis of 50% or more in a native coronary artery with visually estimated diameter of ≥2.25 mm and ≤4.25 mm eligible for stent implantation.
5.	Target lesion(s) must be amenable for percutaneous coronary intervention
Exclusion criteria	
1.	Patients with a known hypersensitivity or contraindication to any of the following medications: Aspirin, Clopidogrel, Prasugrel, Ticagrelor, Everolimus, or Sirolimus
2.	Hemodynamic instability or cardiogenic shock
3.	Patients with active pathologic bleeding including gastrointestinal or genitourinary bleeding
4.	Drug-eluting stent implantation within 12 months before index procedure
5.	Female of childbearing potential, unless a recent pregnancy test is negative, who possibly plan to become pregnant any time after enrollment into this study.
6.	Non-cardiac co-morbid conditions are present with life expectancy <2 year or that may result in protocol non-compliance (per site investigator's medical judgment).
7.	Patients who are actively participating in another drug or device investigational study, which have not completed the primary endpoint follow-up period.

eTable 2. Discharge medication

	P2Y12 inhibitor monotherapy (n=1495)	DAPT (n=1498)
Discharge medication, No. (%)		
Aspirin	1492/1495 (99.8)	1496/1498 (99.9)
P2Y12 receptor inhibitor	1493/1495 (99.9)	1496/1498 (99.9)
Clopidogrel	1149/1495 (76.9)	1163/1498 (77.6)
Prasugrel	62/1495 (4.1)	67/1498 (4.5)
Ticagrelor	284/1495 (19.0)	268/1498 (17.9)
Statin	1416/1495 (94.7)	1408/1497 (94.1)
ACE inhibitor	271/1492 (18.2)	256/1495 (17.1)
ARB	601/1492 (40.3)	560/1496 (37.4)
β-blocker	795/1494 (53.2)	783/1496 (52.3)

There were no significant between-group differences in discharge medication.
Abbreviations: ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; DAPT, dual antiplatelet therapy.

eTable 3. Clinical outcomes by per-protocol analysis

Outcome	P2Y12 inhibitor monotherapy (n=1185)[a]	Dual antiplatelet therapy (n=1426)[a]	Estimate of Difference (95% 1-Sided CI)	*P* Value for noninferiority
Primary end point				
MACCE[b], No. (%)	36 (3.1)	35 (2.5)	0.6% (-∞% to 1.5%)	.02
Secondary end points			**Hazard Ratio (95% CI)**	***P* Value**
Death, No. (%)	21 (1.8%)	18 (1.3%)	1.42 (0.75-2.66)	.28
Myocardial infarction, No. (%)	10 (0.9%)	17 (1.2%)	0.72 (0.33-1.56)	.40
Stroke, No. (%)	6 (0.5%)	4 (0.3%)	1.82 (0.51-6.46)	.35
Cardiac death, No. (%)	11 (0.9%)	13 (0.9%)	1.03 (0.46-2.29)	.95
Stent thrombosis, No. (%)	3 (0.3%)	2 (0.1%)	1.81 (0.30-10.8)	.52
Bleeding BARC type 2-5, No. (%)	21 (1.8%)	44 (3.1%)	0.58 (0.34-0.97)	.04
Major bleeding[c], No. (%)	8 (0.7%)	12 (0.8%)	0.81 (0.33-1.98)	.65
Post hoc analysis				
Death or myocardial infarction, No. (%)	30 (2.5%)	32 (2.3%)	1.14 (0.69-1.87)	.61
Cardiac death or myocardial infarction, No. (%)	21 (1.8%)	27 (1.9%)	0.95 (0.53-1.67)	.85
Net adverse clinical and cerebral events[d], No. (%)	53 (4.5%)	75 (5.3%)	0.85 (0.60-1.21)	.38

Abbreviations: BARC, Bleeding Academic Research Consortium; CI, confidence interval; HR, hazard ratio; and MACCE, major adverse cardiac and cerebrovascular events.

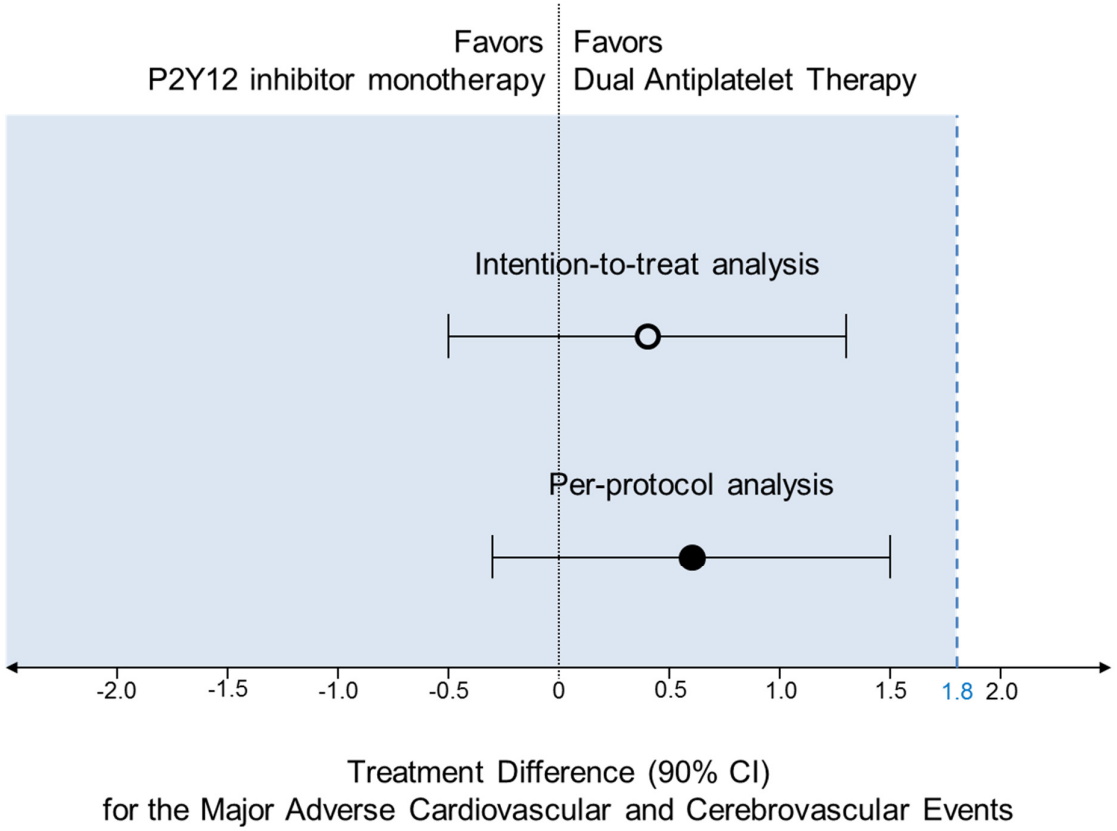
[a] Data are presented for the intention-to-treat population. The percentages are Kaplan–Meier estimates.

[b] A composite of all-cause mortality, myocardial infarction, or stroke.

[c] BARC type 3-5 bleeding.

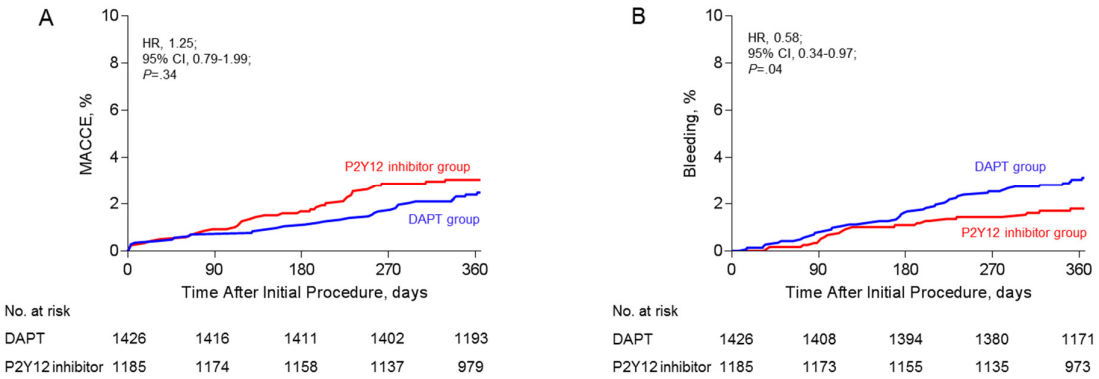
[d] MACCE plus BARC type 2-5 bleeding.

eFigure 1. Treatment Difference for the Major Adverse Cardiovascular and Cerebrovascular Events



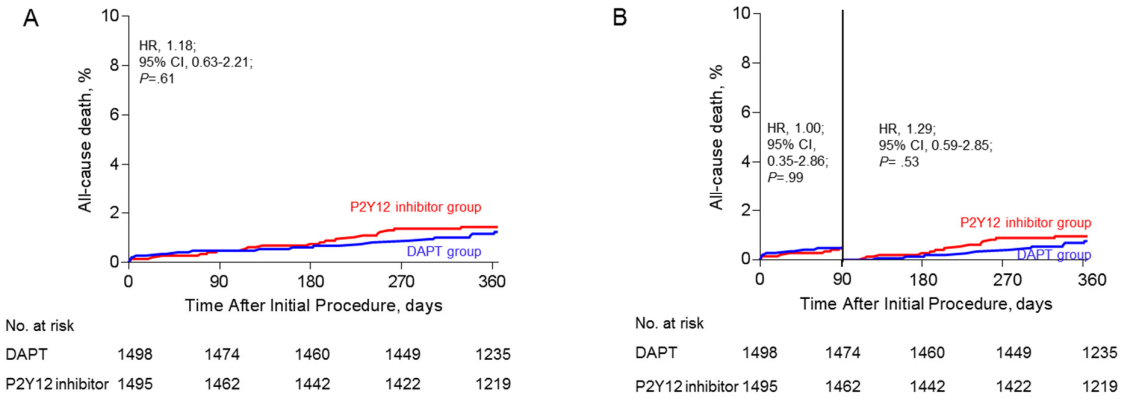
"Blue dashed line at treatment difference = 1.8 indicates noninferiority margin; blue-tinted region to the left of treatment difference = 1.8 indicates values for which P2Y12 inhibitor monotherapy would be considered noninferior to dual antiplatelet therapy. CI indicates confidence interval."

eFigure 2. Time-to-event curves for the end points in the per-protocol population



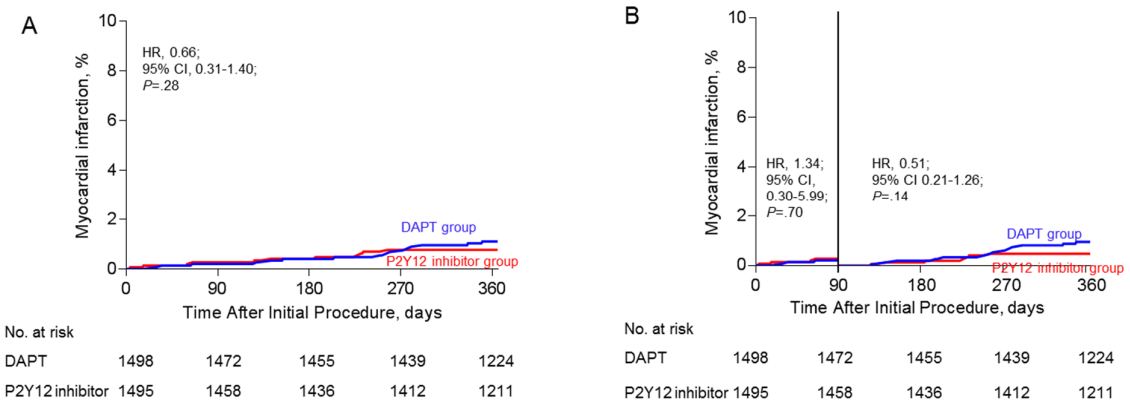
Panel A shows the results of the analysis of the primary end point of major adverse cardiovascular and cerebrovascular events (a composite of death, myocardial infarction, or stroke) at 12 months. Panel B shows the results of the analysis of the bleeding at 12 months. Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses. Hazard ratios are for the patients in the P2Y12 inhibitor monotherapy group. CI indicates confidence interval; DAPT, dual antiplatelet therapy; HR, hazard ratio; MACCE, major adverse cardiac and cerebrovascular events.

eFigure 3. Time-to-event curves and landmark analysis for all-cause death in the intention-to-treat population



Panel A shows the results of the analysis of the all-cause death at 12 months. Results of the landmark analysis at 3 months of the all-cause death are shown in Panel B. Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses. Hazard ratios are for the patients in the P2Y12 inhibitor monotherapy group. CI indicates confidence interval; DAPT, dual antiplatelet therapy; HR, hazard ratio.

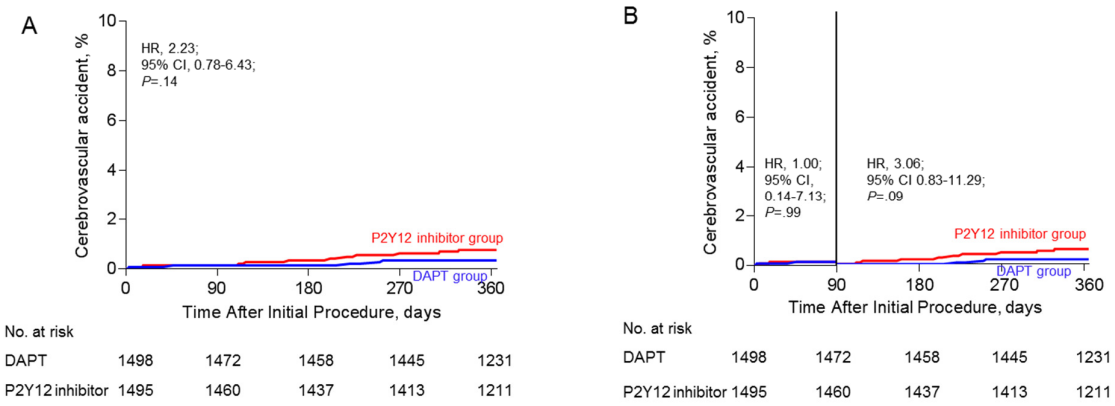
eFigure 4. Time-to-event curves and landmark analysis for myocardial infarction in the intention-to-treat population



No. at risk					
DAPT	1498	1472	1455	1439	1224
P2Y12 inhibitor	1495	1458	1436	1412	1211

Panel A shows the results of the analysis of the myocardial infarction at 12 months. Results of the landmark analysis at 3 months of the myocardial infarction are shown in Panel B. Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses. Hazard ratios are for the patients in the P2Y12 inhibitor monotherapy group. CI indicates confidence interval; DAPT, dual antiplatelet therapy; HR hazard ratio.

eFigure 5. Time-to-event curves and landmark analysis for stroke in the intention-to-treat population



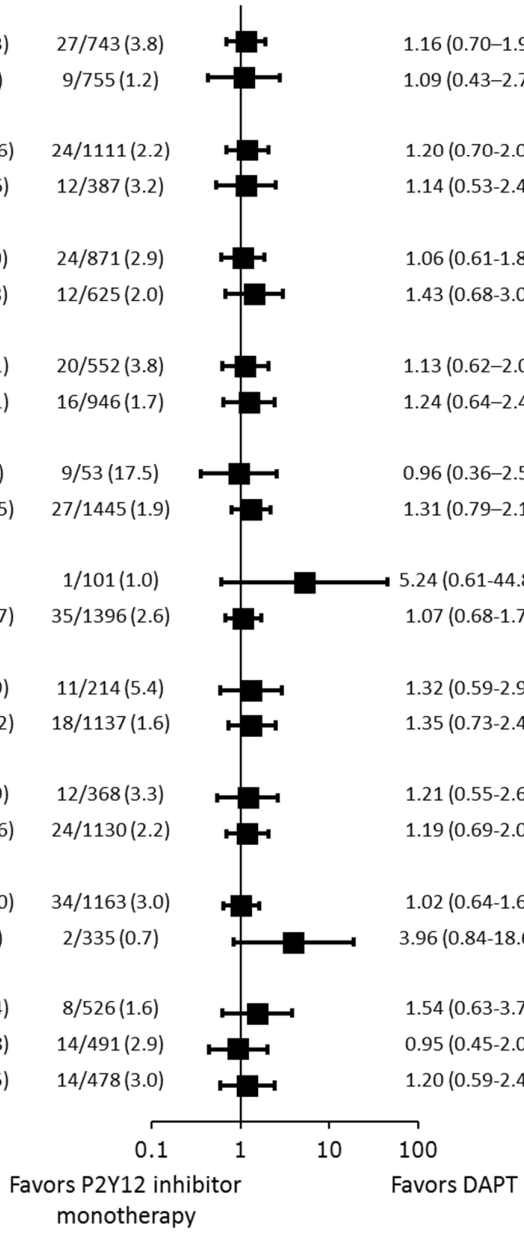
No. at risk

DAPT	1498	1472	1458	1445	1231
P2Y12 inhibitor	1495	1460	1437	1413	1211

Panel A shows the results of the analysis of the stroke at 12 months. Results of the landmark analysis at 3 months of the stroke shown in Panel B. Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses. Hazard ratios are for the patients in the P2Y12 inhibitor monotherapy group. CI indicates confidence interval; DAPT, dual antiplatelet therapy; HR, hazard ratio.

eFigure 6. Subgroup Analyses of the Major Adverse Cardiovascular and Cerebrovascular Events (Primary End Point) at 12 Months

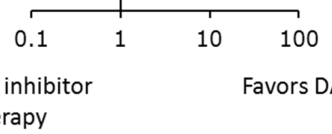
Subgroup	Patients	MACCE (%) P2Y12 inhibitor monotherapy	MACCE (%) DAPT	Hazard ratio (95% CI)	*P* for interaction
Age					.90
≥65 years	1534	33/791 (4.3)	27/743 (3.8)	1.16 (0.70–1.93)	
<65 years	1459	9/704 (1.3)	9/755 (1.2)	1.09 (0.43–2.74)	
Sex					.92
Male	2198	28/1087 (2.6)	24/1111 (2.2)	1.20 (0.70-2.07)	
Female	795	14/408 (3.6)	12/387 (3.2)	1.14 (0.53-2.47)	
ACS					.52
Yes	1741	25/870 (3.0)	24/871 (2.9)	1.06 (0.61-1.85)	
No	1250	17/625 (2.8)	12/625 (2.0)	1.43 (0.68-3.00)	
Diabetes					.84
Yes	1122	23/570 (4.1)	20/552 (3.8)	1.13 (0.62–2.05)	
No	1868	19/922 (2.1)	16/946 (1.7)	1.24 (0.64–2.40)	
CRF					.60
Yes	97	7/44 (16.5)	9/53 (17.5)	0.96 (0.36–2.58)	
No	2895	35/1450 (2.5)	27/1445 (1.9)	1.31 (0.79–2.16)	
Previous stroke					.16
Yes	201	5/99 (5.2)	1/101 (1.0)	5.24 (0.61-44.84)	
No	2790	37/1394 (2.7)	35/1396 (2.6)	1.07 (0.68-1.70)	
LV ejection fraction					.98
<50%	412	13/198 (6.9)	11/214 (5.4)	1.32 (0.59-2.95)	
≥50%	2275	24/1138 (2.2)	18/1137 (1.6)	1.35 (0.73-2.49)	
Multivessel PCI					.98
Yes	705	13/337 (3.9)	12/368 (3.3)	1.21 (0.55-2.65)	
No	2288	29/1158 (2.6)	24/1130 (2.2)	1.19 (0.69-2.05)	
P2Y12 inhibitor					.10
Clopidogrel	2312	34/1149 (3.0)	34/1163 (3.0)	1.02 (0.64-1.65)	
New P2Y12 inhibitor	681	8/346 (2.4)	2/335 (0.7)	3.96 (0.84-18.66)	
Type of DES					.71
CoCr-EES	1051	12/525 (2.4)	8/526 (1.6)	1.54 (0.63-3.78)	
BP-SES	972	13/481 (2.8)	14/491 (2.9)	0.95 (0.45-2.02)	
PtCr-EES	967	17/489 (3.5)	14/478 (3.0)	1.20 (0.59-2.44)	



Data are shown as the number of primary end-point events per total number of patients in that subgroup and the event rate. Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses. Hazard ratios are for the patients in the P2Y12 inhibitor monotherapy group. The P value for interaction represents the likelihood of interaction between the variable and the treatment. ACS indicates acute coronary syndrome; BP-SES, bioresorbable polymer- sirolimus-eluting stent; CoCr-EES, cobalt-chromium everolimus eluting stent; CRF, chronic renal failure; DAPT, dual antiplatelet therapy; DES, drug-eluting stents; LV, left ventricular; PCI, percutaneous coronary intervention; PtCr-EES, platinum-chromium everolimus-eluting stent.

eFigure 7. Subgroup Analyses of BARC type 2-5 Bleeding at 12 Months

Subgroup	Patients	BARC type 2-5 bleeding (%) P2Y12 inhibitor monotherapy	BARC type 2-5 bleeding (%) DAPT	Hazard ratio (95% CI)	*P* for interaction
Age					.10
≥65 years	1534	20/791 (2.7)	24/743 (3.4)	0.79 (0.44–1.43)	
<65 years	1459	8/704 (1.2)	25/755 (3.4)	0.34 (0.16–0.76)	
Sex					.42
Male	2198	21/1087 (2.0)	33/1111 (2.9)	0.65 (0.38-1.12)	
Female	795	7/408 (1.9)	16/387 (4.3)	0.42 (0.17-1.03)	
ACS					.90
Yes	1741	15/870 (1.8)	27/871 (3.2)	0.56 (0.30-1.05)	
No	1250	13/625 (2.2)	22/625 (3.6)	0.59 (0.30-1.18)	
Diabetes					.17
Yes	1122	14/570 (2.6)	16/552 (3.0)	0.85 (0.41–1.74)	
No	1868	14/922 (1.6)	33/946 (3.6)	0.44 (0.23–0.82)	
CRF					.44
Yes	97	2/44 (5.3)	2/53 (4.0)	1.22 (0.17–8.64)	
No	2895	26/1450 (1.9)	47/1445 (3.4)	0.55 (0.34–0.89)	
Previous stroke					.28
Yes	201	2/99 (2.1)	1/101 (1.0)	2.10 (0.19-23.16)	
No	2790	26/1394 (1.9)	48/1396 (3.6)	0.54 (0.34-0.88)	
LV ejection fraction					.75
<50%	412	4/198 (2.2)	9/214 (4.5)	0.49 (0.15-1.59)	
≥50%	2275	21/1138 (1.9)	35/1137 (3.2)	0.60 (0.35-1.04)	
Multivessel PCI					.42
Yes	705	5/337 (1.6)	14/368 (3.9)	0.40 (0.14-1.11)	
No	2288	23/1158 (2.1)	35/1130 (3.2)	0.64 (0.38-1.09)	
P2Y12 inhibitor					.15
Clopidogrel	2312	23/1149 (2.1)	33/1163 (2.9)	0.71 (0.42-1.21)	
New P2Y12 inhibitor	681	5/346 (1.5)	16/335 (5.0)	0.31 (0.11-0.83)	
Type of DES					.80
CoCr-EES	1051	9/525 (1.8)	18/526 (3.5)	0.51 (0.23-1.13)	
BP-SES	972	13/481 (2.8)	19/491 (4.0)	0.69 (0.34-1.40)	
PtCr-EES	967	6/489 (1.3)	12/478 (2.6)	0.49 (0.19-1.32)	



Data are shown as the number of BARC type 2-5 bleeding per total number of patients in that subgroup and the event rate. Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses. Hazard ratios are for the patients in the P2Y12 inhibitor monotherapy group. The P value for interaction represents the likelihood of interaction between the variable and the treatment. ACS indicates acute coronary syndrome; BP-SES, bioresorbable polymer- sirolimus-eluting stent; CoCr-EES, cobalt-chromium everolimus eluting stent; CRF, chronic renal failure; DAPT, dual antiplatelet therapy; DES, drug-eluting stents; LV, left ventricular; PCI, percutaneous coronary intervention; PtCr-EES, platinum-chromium everolimus-eluting stent.