

SUPPLEMENTAL MATERIAL

Table S1. Selected Baseline Characteristics.

Characteristic	Ticagrelor (n = 6930)	Clopidogrel (n = 6955)
Median age (Q1-Q3), years	66 (60, 72)	66 (60, 73)
Female sex, n (%)	1908 (27.5)	1980 (28.5)
Geographic region, n (%)		
Asia	806 (11.6)	796 (11.4)
Central/South America	871 (12.6)	869 (12.5)
Europe	3739 (54.0)	3759 (54.0)
North America	1514 (21.8)	1531 (22.0)
PAD inclusion criterion, n (%)		
Revascularization >30 days prior to randomization	3923 (56.6)	3952 (56.8)
Abnormal ankle-brachial index and no prior revascularization	3007 (43.4)	3003 (43.2)
Median ankle-brachial index (Q1-Q3)	0.70 (0.58, 0.82)	0.70 (0.58, 0.82)
Medical history, n (%)		
Coronary or carotid revascularization	1914 (27.6)	1901 (27.3)
Coronary stent implantation	1004 (14.5)	964 (13.9)
Coronary artery disease*	2019 (29.1)	2013 (28.9)
Number of vascular territories affected†		
1	3874 (55.9)	3930 (56.5)
2	2333 (33.7)	2355 (33.9)
3	723 (10.4)	670 (9.6)
Medications before randomization, n (%)		

Aspirin	4667 (67.3)	4604 (66.2)
Clopidogrel	2193 (31.6)	2280 (32.8)
Statin	5058 (73.0)	5123 (73.7)
Angiotensin-converting-enzyme inhibitor	2826 (40.8)	2809 (40.4)
Angiotensin-receptor blocker	1741 (25.1)	1747 (25.1)

*Coronary artery disease is defined as myocardial infarction, percutaneous coronary intervention (PCI), or coronary-artery bypass grafting (CABG).

†An affected vascular territory was defined by the presence of peripheral artery disease, coronary artery disease, or cerebrovascular disease (including previous stroke, transient ischemic attack, carotid-artery stenosis, or carotid revascularization).

Table S2. On-treatment Analyses of Total Cardiovascular and Limb Events and Procedures by Event Type.

Event	Total Events per 100 Patient-Years		HR (95% CI)	p-value
	Ticagrelor	Clopidogrel		
Cardiovascular and limb events	16.4	17.6	0.93 (0.86-1.01)	0.09
Acute cardiovascular and limb events	6.6	6.6	0.99 (0.89-1.10)	0.79
Cardiovascular death	1.2	1.2	1.05 (0.85-1.29)	0.66
Non-fatal myocardial infarction	1.8	1.8	0.96 (0.80-1.16)	0.20
Non-fatal ischemic stroke	0.7	0.9	0.87 (0.67-1.13)	0.30
Acute limb ischemia	0.7	0.7	1.08 (0.79-1.47)	0.65
Unstable angina	1.8	1.9	0.97 (0.79-1.18)	0.74
Transient ischemic attack	0.3	0.2	1.11 (0.68-1.83)	0.67
Procedures	9.8	10.9	0.90 (0.81-0.99)	0.0260
Coronary revascularization	1.9	2.1	0.91 (0.76-1.09)	0.29
Carotid revascularization	0.5	0.5	0.93 (0.66-1.31)	0.67
Peripheral revascularization	6.3	7.2	0.87 (0.78-0.98)	0.0192
Amputation for symptomatic PAD	1.1	1.0	1.03 (0.79-1.35)	0.81

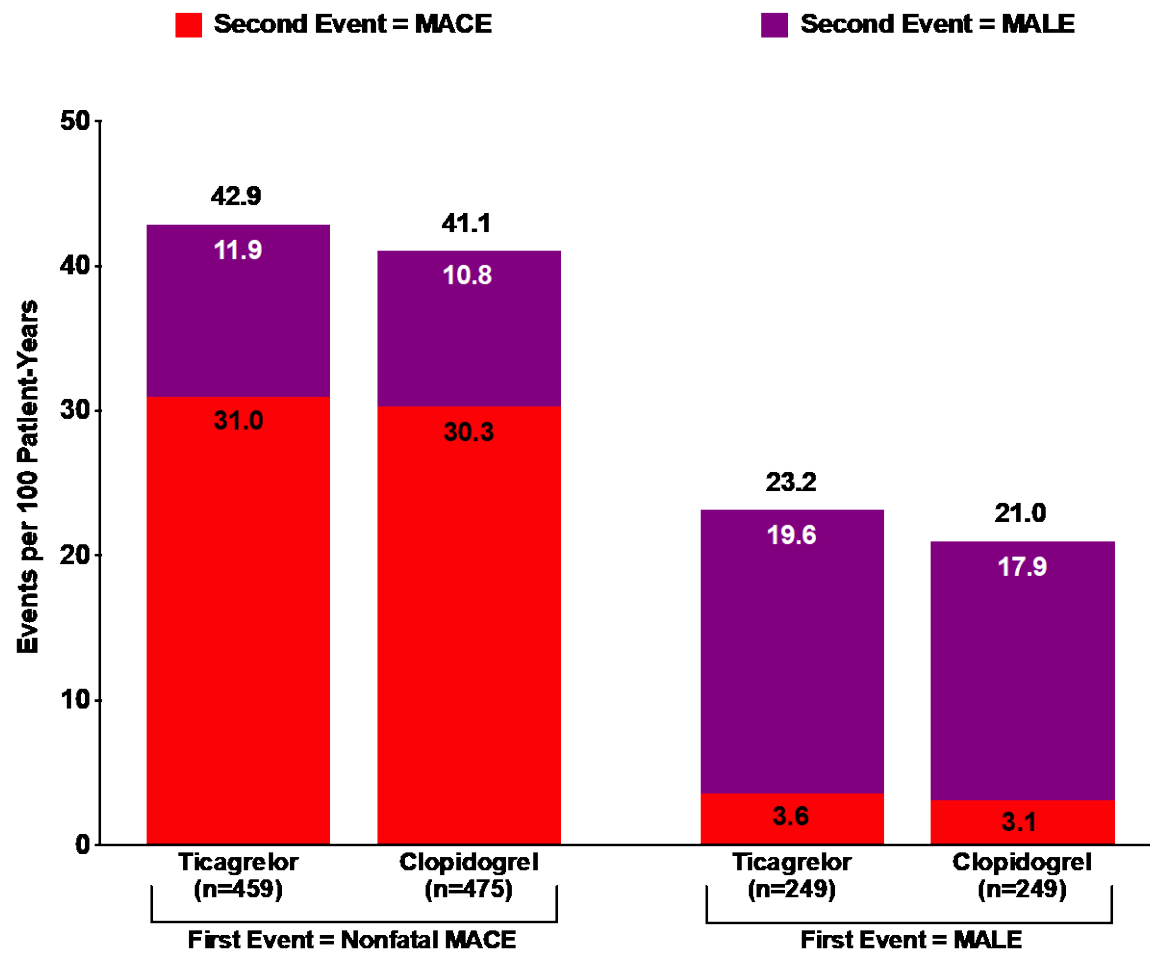
Table S3. Subgroup Analyses for Total MACE.

Subgroup	Total Events per 100 Patient-Years		HR (95% CI)	Interaction p-value
	Ticagrelor	Clopidogrel		
PAD inclusion criterion				0.84
ABI/TBI	4.9	4.8	1.01 (0.86-1.20)	
Prior revascularization	5.7	5.8	0.99 (0.87-1.14)	
Ankle-brachial index				0.78
Quartile 1 (<0.58)	6.8	6.6	1.04 (0.86-1.26)	
Quartile 2 (0.58 to <0.70)	5.1	5.0	1.03 (0.83-1.28)	
Quartile 3 (0.70 to <0.82)	5.4	5.3	1.01 (0.81-1.25)	
Quartile 4 (\geq 0.82)	4.2	4.7	0.90 (0.72-1.13)	
History of coronary stent implantation				0.14
Yes	7.5	8.7	0.85 (0.67-1.08)	
No	5.0	4.8	1.04 (0.92-1.17)	
History of coronary artery disease				0.68
Yes	7.9	8.1	0.97 (0.83-1.15)	
No	4.3	4.2	1.02 (0.89-1.17)	
Number of vascular territories affected				0.67
1	3.9	3.8	1.05 (0.90-1.23)	
2	6.2	6.5	0.95 (0.80-1.12)	
3	10.3	10.5	0.98 (0.76-1.26)	

Table S4. Subgroup Analyses for Total MALE.

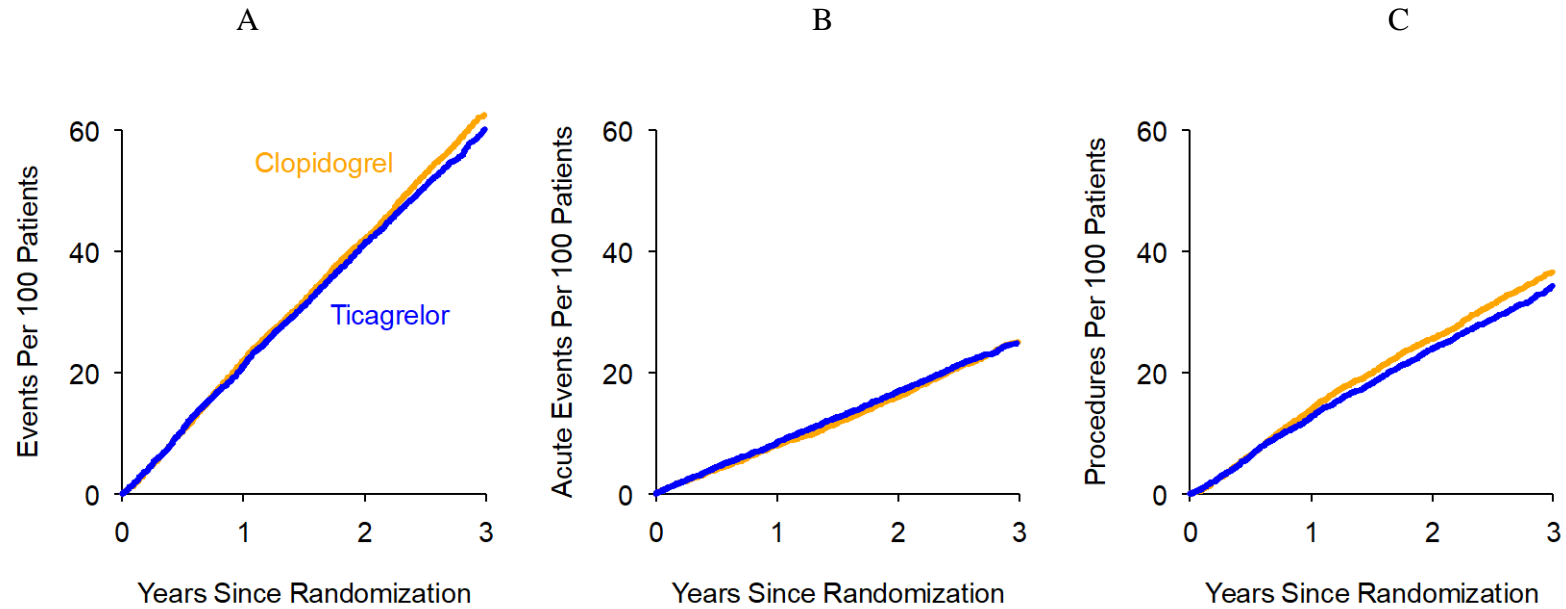
Subgroup	Total Events per 100 Patient-Years		HR (95% CI)	Interaction p-value
	Ticagrelor	Clopidogrel		
PAD inclusion criterion				0.28
ABI/TBI	1.3	1.5	0.86 (0.62-1.20)	
Prior revascularization	2.9	2.6	1.08 (0.86-1.35)	
Ankle-brachial index				0.0472
Quartile 1 (<0.58)	2.8	3.7	0.77 (0.57-1.06)	
Quartile 2 (0.58 to <0.70)	1.7	1.9	0.86 (0.58-1.27)	
Quartile 3 (0.70 to <0.82)	1.7	1.3	1.37 (0.90-2.08)	
Quartile 4 (\geq 0.82)	2.5	1.8	1.39 (0.93-2.08)	
History of coronary stent implantation				0.98
Yes	1.6	1.5	1.01 (0.60-1.70)	
No	2.3	2.2	1.01 (0.83-1.24)	
History of coronary artery disease				0.60
Yes	1.9	2.0	0.93 (0.65-1.34)	
No	2.3	2.2	1.04 (0.84-1.30)	
Number of vascular territories affected				0.57
1	2.4	2.2	1.10 (0.86-1.40)	
2	1.9	2.1	0.89 (0.64-1.25)	
3	2.0	2.2	0.91 (0.49-1.69)	

Figure S1. Rates of Second MACE or MALE Events by Type of First Nonfatal MACE or MALE Event.



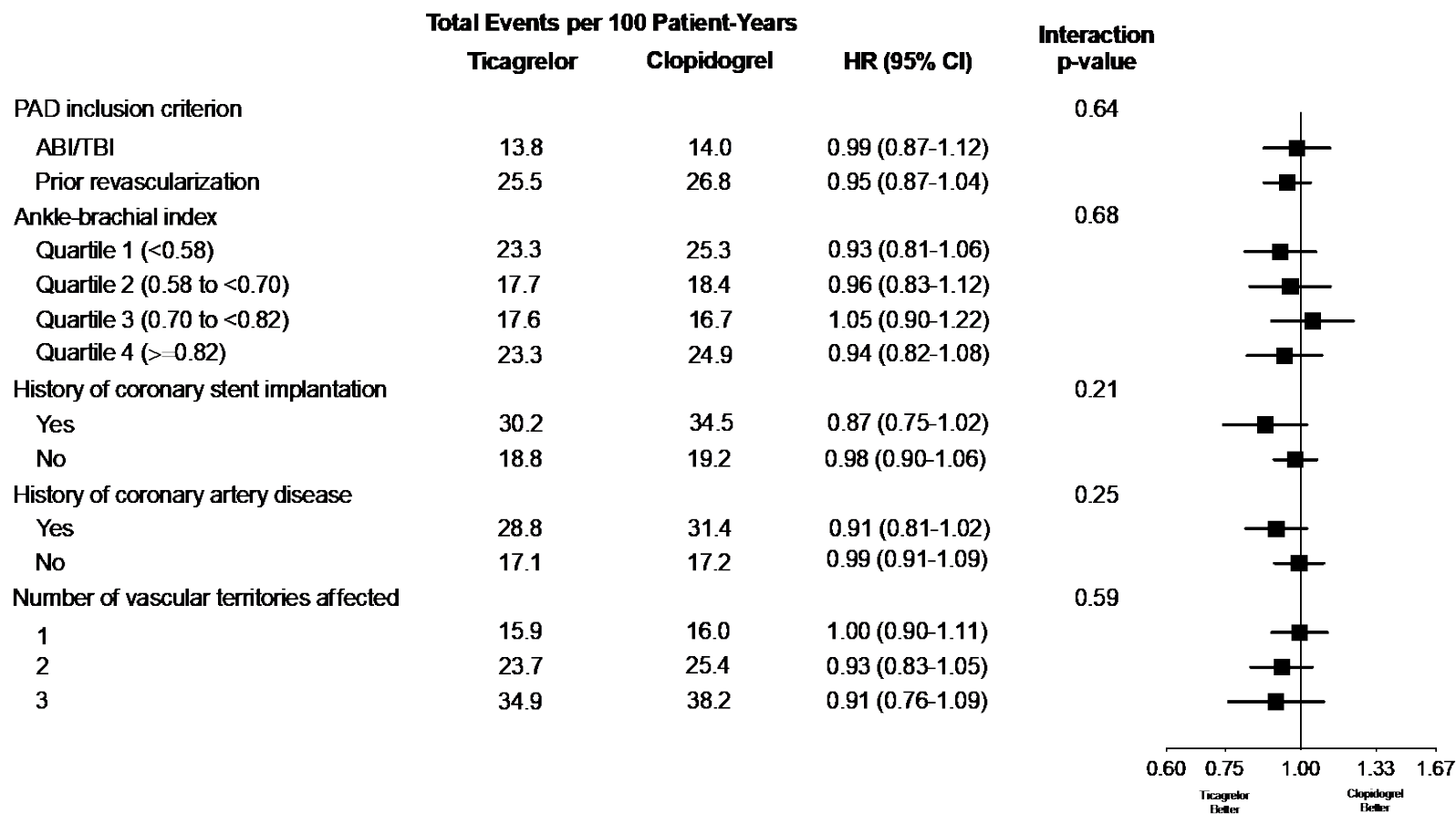
Values above bars are the sum of the rates of cardiovascular events and procedures as a second event. Values within bars are the rates of MACE or the rates of MALE as a second event. MACE, major adverse cardiovascular event; MALE, major adverse limb events.

Figure S2. Mean Cumulative Functions.



Panel A: total cardiovascular and limb events and procedures. Panel B: total acute cardiovascular and limb events. Panel C: total procedures. The estimated numbers of events per 100 patients in the ticagrelor and clopidogrel groups at 3 years were 60.0 and 62.5 for cardiovascular and limb events, 24.8 and 25.0 for acute cardiovascular and limb events, and 34.2 and 36.6 for procedures, respectively.

Figure S3. Subgroup Analyses for Total Cardiovascular and Limb Events and Procedures.



Marginal proportional hazard regression models with terms for the interaction between treatment and subgroups were constructed to estimate subgroup treatment effects and heterogeneity with respect to total cardiovascular and limb events and procedures. CI, confidence interval; HR, hazard ratio.