Supplemental Materials

Table S1. Baseline Characteristics According to Modified Risk Profile

Characteristics	Low Risk, modified ESER <6 in men and <5 in women			High Risk, modified ESRS ≥6 in men and ≥ 5 in women		
	Ticagrelor -Aspirin (N=2627)	Clopidogrel -Aspirin (N=2668)	*P* value	Ticagrelor -Aspirin (N=578)	Clopidogrel -Aspirin (N=538)	*P* value
Median age (IQR) -yr	63.0(55.9-69.2)	62.8(55.9-69.2)	0.94	73.9(67.7-78.4)	72.4(67.3-77.5)	0.07
Female sex - no. (%)	678(25.8)	680(25.5)	0.79	412 (71.3)	400(74.2)	0.27
Median BMI (IQR), kg/m^2	24.4(22.5-26.6)	24.2(22.5-26.2)	0.94	2533(23.44-27.34)	24.89(2266-27.34)	0.08
Median WC (IQR), cm	85(80-90)	85(80-90)	0.94	90(80-95)	89(80-95)	0.82
Median ESRS (IQR)	2(1-3)	2(1-3)	0.82	4(3-4)	4(3-4)	0.20
ESRS components, no. (%)						
Age						
<65 yr	1537 (58.5)	1571 (58.9)	0.83	65 (11.2)	79 (14.7)	0.05

65-75 yr	820 (31.2)	836 (31.3)		245 (424)	245 (45 .5)	0.05
>75 yr	270(10.3)	261 (9.8)		268 (46.4)	215 (39.9)	
Hypertension	1466 (55.8)	1489 (55.8)	1 .00	510 (88.2)	490 (90.9)	0.14
Diabetes	501 (19.1)	486 (18.2)	0.42	307 (53.1)	269 (49.9)	0.28
Myocardial infarction	30(1.1)	15 (0.6)	0.02	24 (4.2)	27 (5.0)	0. 49
Other heart diseases	92 (3.5)	111 (4.2)	0.21	132 (228)	127 (23.6)	0.77
Peripheral vascular disease	3(0.1)	5 (0.2)	0.49	3 (0.5)	2 (0.4)	0.71
Smoker	1079(41.1)	1116(41.8)	0.58	149 (25.8)	114 (21.2)	0.07
History of TIA or ischemic stroke	461 (17.5)	462 (17.3)	0.82	239 (41.3)	256 (47.5)	0.04
TOAST classification						
LAA	1052 (49.1)	1106 (50.7)	0.39	335 (768)	299 (74 6)	0.41
CE	6 (0.3)	9 (0.4)	0.39	3(0.7)	1 (0.2)	0.41
SAO	1007 (47.0)	989 (454)		74 (17.0)	85 (21.2)	

Other demonstrated etiology	22(1.0)	31 (1.4)		6(1.4)	4(1.0)	
Undetermined etiology	54 (2.5)	45 (2.1)		18(4.1)	12 (3.0)	
WC≥90 cm	859 (32.7)	888 (33.3)	0.65	294 (50.9)	269 (49.9)	0.75
CYP2C19 LOF carriers - no. (%)						
Intermediate metabolizers	2141 (81.5)	2180(81.7)	0.84	436 (75.4)	401 (74 4)	0.69
Poor metabolizers	486 (18.5)	488(18.3)		142 (24.6)	138 (25.6)	0.69
Median time from symptom onset to randomization (IQR) — hr.	13.7(9.0-20.3)	14. 5(9.0 -20.8)	0.10	13.0(8.5-20.6)	13.1(7.7-20.0)	0.77
Qualifying event - no. (%)						
Ischemic stroke	2041 (77.7)	2092 (784)	0.53	445 (77.0)	423 (78.5)	0.55
TIA	586 (22.3)	576 (21.6)		133 (23.0)	116 (21.5)	0.55
Median NIHSS score in patients with qualifying ischemic stroke (IQR) †	2(1-3)	2(1-3)	0.55	2(1-3)	2(1-3)	0.53
Median ABCD^2 score in patients with	4(4-5)	4(4-5)	0.52	5(4-6)	5(4-5)	0.06

qualifying TIA (IQR) ‡						
Previous antiplatelet therapy - no. (%)	237 (9.0)	224 (8.4)	0.42	148 (25.6)	139 (25.8)	0.94
Previous lipid-lowering therapy - no. (%)	154 (5.9)	143 (5.4)	0.43	104 (18.0)	98 (18.2)	0.93

BMI denotes body mass index. CE denotes cardioembolism. ESRS denotes Essen Stroke Risk Score. LAA, Large artery atherosclerosis; IQR denotes interquartile range. IS denotes ischemic stroke. SAO denotes Small artery occlusion. TIA denotes transient ischemic attack. LOF denotes loss-of-function. WC denotes waist circumference.

* National Institutes of Health Stroke Scale (NIHSS) scores range from 0 to 42, with higher scores indicating more severe stroke.

† $ABCD^2$ score assesses the risk of stroke on the basis of age, blood pressure, clinical features, duration of TIA, and presence or absence of diabetes, with scores ranging from 0 to 7 and higher scores indicating greater risk.

‡ Medication within 1 month before symptom onset.

Table S2. Association of Ticagrelor-Aspirin vs Clopidogrel-Aspirin with Clinical Outcomes Stratified by Modified Risk Profile

Outcome	Low risk, modified ESER <6 in men and <5 in women				High Risk, modified ESRS ≥6 in men and ≥ 5 in women				P_{int}
	Ticagrelor-Aspirin, event rate (%)*	Clopidogrel-Aspirin, event rate (%)*	HR (95%CI)	*P* value	Ticagrelor-Aspirin, event rate (%)*	Clopidogrel-Aspirin, event rate (%)*	HR (95%CI)	*P* value	
Primary outcome									
Stroke	136 (5.2)	198 (7.4)	0.69(0.55-0.85)	<0.001	55 (9.5)	45 (8.3)	1.16(0.76-1.79)	0.49	0.03
Secondary outcomes									
Stroke within 30 days	113 (4.3)	166 (6.3)	0.68(0.54-0.87)	<0.001	43 (7.4)	39 (7.2)	1.00(0.63-1.60)	0.99	0.11
Composite vascular events†	163 (6.2)	234 (8.8)	0.70(0.57-0.85)	<0.001	66 (11.4)	59 (10.9)	1.09(0.74-1.60)	0.66	0.05
Ischemic stroke	134 (5.1)	194 (7.3)	0.69(0.55-0.86)	<0.001	55 (9.5)	44 (8.2)	1.19(0.77-1.83)	0.43	0.03
Primary safety outcome									
Severe or moderate bleeding‡	6 (0.2)	9 (0.3)	0.66(0.24-1.87)	0.44	3 (0.5)	2 (0.4)	1.43(0.23-8.75)	0.75	0.45
Secondary safety outcome									

Any bleeding	141 (5.4)	60 (2.2)	2.50(1.84-3.40)	<0.001	29 (5.0)	20 (3.7)	1.10(0.58-2.07)	0.77	0.05

CI denotes confidence interval. ESER denotes Essen Stroke Risk Score. HR denotes hazard ratio. mRS denotes modified Rankin Scale. TIA denotes transient ischemic attack.

* Event rates for ordinal stroke or TIA are raw estimates, whereas event rates for other outcomes are Kaplan-Meier estimates of the percentage of patients with events at 90 days.

† Composite vascular events include ischemic stroke, hemorrhagic stroke, TIA, myocardial infarction, vascular death.

‡ Severe or moderate bleeding and mild bleeding were defined according to GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) criteria.

Table S3. Efficacy and Safety Outcomes of Patients With Different Antiplatelet Therapies Stratified by Risk Profiles in the Per-protocol Population

Outcome	Low risk, ESER <3				High Risk, ESRS ≥3				P_{int}
	Ticagrelor-Aspirin, event rate (%)*	Clopidogrel-Aspirin, event rate (%)*	HR (95%CI)	*P* value	Ticagrelor-Aspirin, event rate (%)*	Clopidogrel-Aspirin, event rate (%)*	HR (95%CI)	*P* value	
Primary outcome									
Stroke	87 (5.1)	136 (7.5)	0.65(0.50-0.86)	<0.001	94 (8.3)	97 (8.5)	0.96(0.72-1.29)	0.80	0.03
Secondary outcomes									
Stroke within 30 days	74 (4.3)	120 (6.6)	0.64(0.48-0.86)	<0.001	74 (6.6)	78 (6.8)	0.96(0.69-1.33)	0.79	0.04
Composite vascular events†	99 (5.8)	153 (8.5)	0.66(0.51-0.85)	<0.001	104 (9.2)	118 (10.3)	0.89(0.67-1.17)	0.40	0.07
Ischemic stroke	87 (5.1)	134 (7.4)	0.67(0.51-0.88)	<0.001	92 (8.1)	94 (8.2)	0.97(0.72-1.30)	0.82	0.04
Primary safety outcome									
Severe or moderate	1 (0.1)	2 (0.1)	0.45(0.04-5.01)	0.52	2 (0.2)	4 (0.3)	0.59(0.11-3.25)	0.55	0.84

bleeding‡									
Secondary safety outcome									
Any bleeding	78 (4.5)	27 (1.5)	3.30(2.10-5.19)	<0.001	44 (3.9)	31 (2.7)	1.33(0.82-2.16)	0.26	0.01

CI denotes confidence interval. ESER denotes Essen Stroke Risk Score. HR denotes hazard ratio. mRS denotes modified Rankin Scale. TIA denotes transient ischemic attack.

* Event rates for ordinal stroke or TIA are raw estimates, whereas event rates for other outcomes are Kaplan-Meier estimates of the percentage of patients with events at 90 days.

† Composite vascular events include ischemic stroke, hemorrhagic stroke, TIA, myocardial infarction, vascular death.

‡ Severe or moderate bleeding and mild bleeding were defined according to GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) criteria.

Table S4. Efficacy and Safety Outcomes of Patients With Different Antiplatelet Therapies Stratified by Modified Risk Profile in the Per-protocol Population

Outcome	Low risk, modified ESER <6 in men and <5 in women				High Risk, modified ESRS ≥6 in men and ≥ 5 in women				P_{int}
	Ticagrelor-Aspirin, event rate (%)*	Clopidogrel-Aspirin, event rate (%)*	HR (95%CI)	*P* value	Ticagrelor-Aspirin, event rate (%)*	Clopidogrel-Aspirin, event rate (%)*	HR (95%CI)	*P* value	
Primary outcome									
Stroke	129 (5.5)	188 (7.7)	0.71(0.57-0.89)	<0.001	52 (10.3)	45 (9.1)	1.13(0.73-1.74)	0.59	0.04
Secondary outcomes									
Stroke within 30 days	108 (4.6)	159 (6.5)	0.71(0.55-0.91)	0.01	40 (7.9)	39 (7.9)	0.96(0.59-1.55)	0.86	0.18
Composite vascular events†	147 (6.3)	216 (8.8)	0.70(0.57-0.86)	<0.001	56 (11.0)	55 (11.1)	1.05(0.70-1.58)	0.81	0.08
Ischemic stroke	127 (5.4)	184 (7.5)	0.72(0.57-0.90)	<0.001	52 (10.3)	44 (8.9)	1.15(0.74-1.79)	0.52	0.04

Primary safety outcome									
Severe or moderate bleeding‡	3 (0.1)	5 (0.2)	0.54(0.13-2.26)	0.40	0 (0.0)	1 (0.2)	NA	1.00	0.99
Secondary safety outcome									
Any bleeding	97 (4.1)	43 (1.8)	2.51(1.74-3.64)	<0.001	25 (4.9)	15 (3.0)	1.12(0.56-2.27)	0.75	0.16

CI denotes confidence interval. ESER denotes Essen Stroke Risk Score. HR denotes hazard ratio. mRS denotes modified Rankin Scale. TIA denotes transient ischemic attack.

* Event rates for ordinal stroke or TIA are raw estimates, whereas event rates for other outcomes are Kaplan-Meier estimates of the percentage of patients with events at 90 days.

† Composite vascular events include ischemic stroke, hemorrhagic stroke, TIA, myocardial infarction, vascular death.

‡ Severe or moderate bleeding and mild bleeding were defined according to GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) criteria.

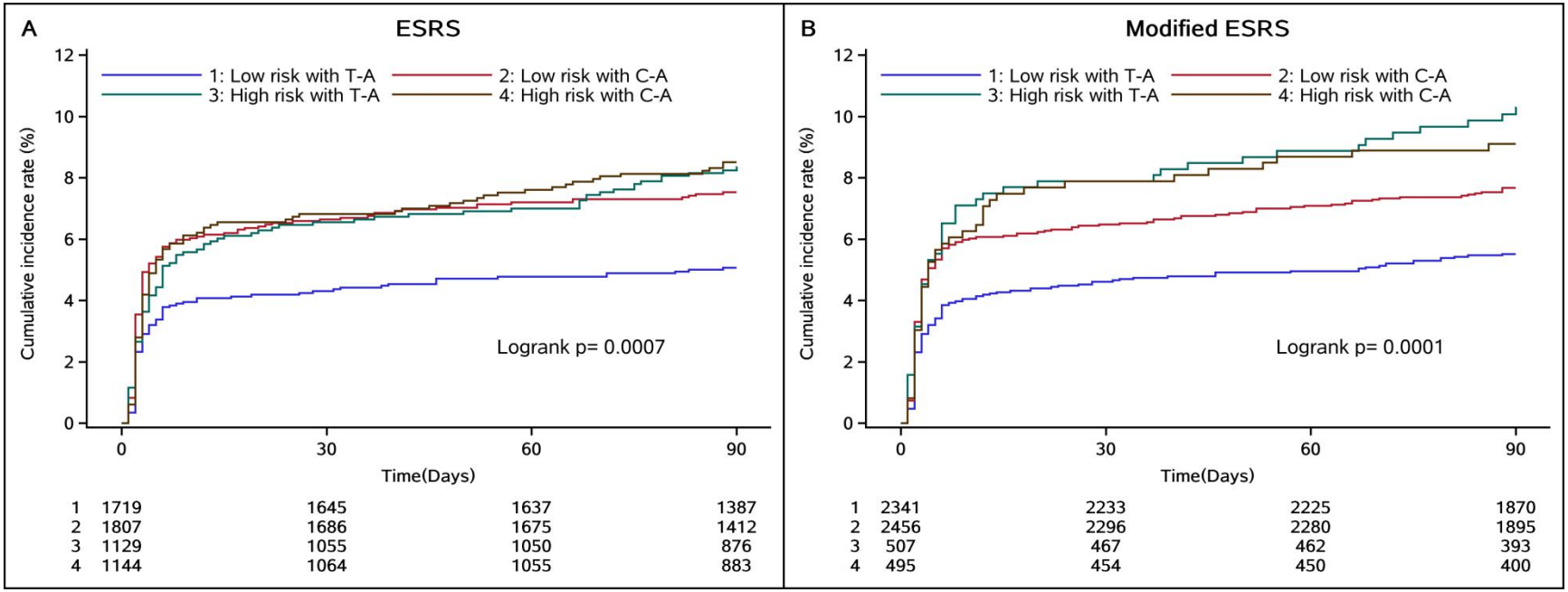

Figure S1. Cumulative Probability of Stroke According to treatment and risk profile in the per-protocol population

C denotes clopidogrel; ESRS denotes Essen Stroke Risk Score; T denotes ticagrelor.