Supplementary Appendix

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

Supplement to: Gibson CM, Mehran R, Bode C, et al. Prevention of bleeding in patients with atrial fibrillation undergoing PCI. N Engl J Med. DOI: 10.1056/NEJMoa1611594

SUPPLEMENTARY APPENDIX

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Full Inclusion and Exclusion Criteria

A. Inclusion Criteria:

1. Subjects must ≥18 years of age

2. Must have undergone a PCI (with stent placement) for primary atherosclerotic disease

3. Must have documented medical history of atrial fibrillation defined as:

   - Electrocardiogram, Holter monitor, pacemaker/defibrillator, or any device that provides a rhythm strip documenting paroxysmal, persistent, or permanent non-valvular AF within 1 year before screening.

     OR

   - Electrocardiogram, Holter monitor, pacemaker/defibrillator, or any device that provides a rhythm strip documenting paroxysmal, persistent, or permanent non-valvular AF that was performed more than 1 year before screening if the subject has been receiving oral anticoagulation therapy (VKA or a novel oral anticoagulant) for the AF for 3 months immediately before the index PCI.

4. If a woman, before entry she must be postmenopausal, defined as > 45 years of age with amenorrhea for at least 18 months, or surgically sterile (have had a hysterectomy or bilateral oophorectomy, tubal ligation, or otherwise be incapable of pregnancy), or if heterosexually active and menstrual, practicing a highly effective method of birth control. Women must agree to continue using methods of contraception throughout the study.

5. If a woman of childbearing potential, she must have a negative urine □-human chorionic gonadotropin pregnancy test at screening. Serum pregnancy testing may be performed if required by local regulation.

B. Exclusion Criteria:

Major exclusion criteria include any condition that contraindicates anticoagulant therapy or would confer an unacceptable risk of bleeding, such as, but not limited to:

1. Has any condition that, in the opinion of the investigator, contraindicates anticoagulant therapy or would have an unacceptable risk of bleeding, such as, but not limited to, the following:
   - active internal bleeding, clinically significant bleeding, bleeding at a non-compressible site, or bleeding diathesis within 30 days before randomization
   - platelet count <90,000/μL at screening or pre-randomization
   - history of intracranial hemorrhage
   - clinically significant gastrointestinal bleeding within 12 months before randomization

- except for subjects who are taking a VKA at the time of screening, a PT test result that is higher than the upper limit of normal at the time of screening that suggests underlying coagulation disorder
- any other condition known to increase the risk of bleeding

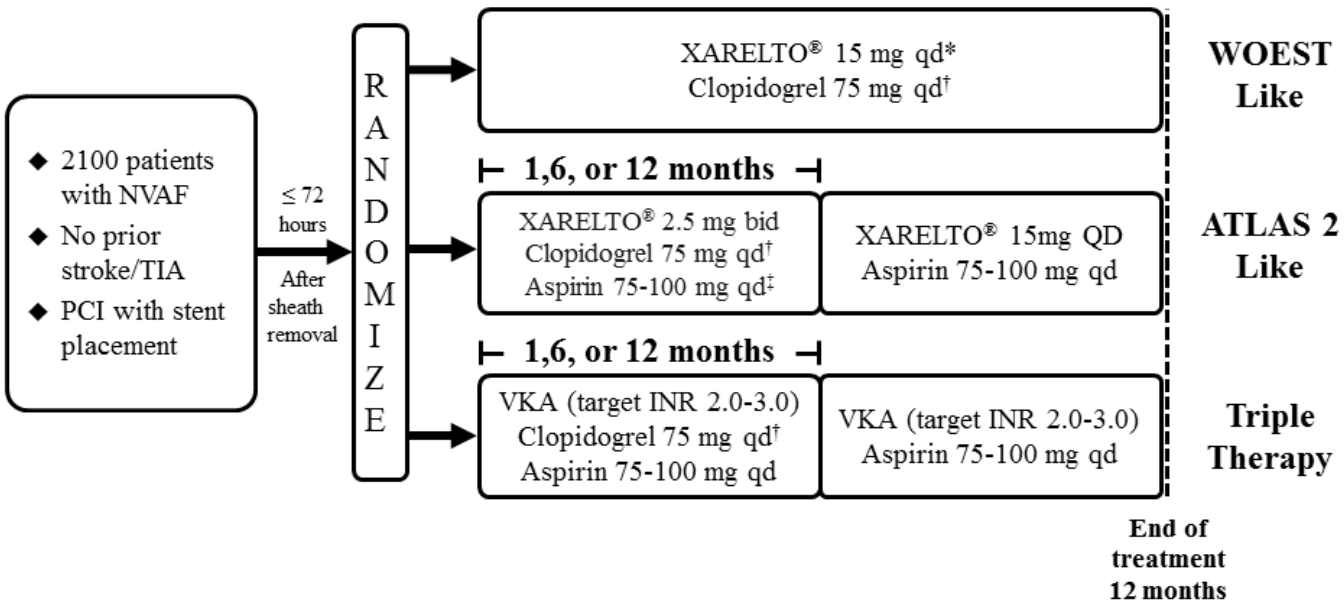
2. Has a history of stroke or TIA
3. Has cardiogenic shock at the time of randomization
4. Has ventricular arrhythmias refractory to treatment at the time of randomization
5. Has calculated CrCl <30 mL/min at screening or pre-randomization
6. Has known significant liver disease (e.g., acute hepatitis, chronic active hepatitis, cirrhosis), or liver function test (LFT) abnormalities at screening (confirmed with repeat testing): alanine transaminase (ALT) >5 times the upper limit of normal or ALT >3 times the upper limit of normal plus total bilirubin >2 times the upper limit of normal
7. Has anemia of unknown cause with a hemoglobin level <10 g/dL (<6.21 mmol/L) at screening or pre-randomization
8. Has a known clinical history of human immunodeficiency virus (HIV) infection
9. Has a current substance abuse (drug or alcohol) problem or a history within the previous 6 months
10. Has any severe condition that would limit life expectancy to less than 12 months
11. Has had major surgery, biopsy of a parenchymal organ, or serious trauma (including head trauma) within the past 30 days.
12. Has a suspected or documented stent thrombosis during the index procedure OR has a PCI with stent placement for a previously stented lesion (stent within a stent) during the index procedure or within the previous 12 months
13. Has an incomplete staged PCI procedure (once the completion of the staged procedure has occurred, the final PCI may become the index event and is allowed)
14. Has a CABG planned
15. Has contraindications to the use of VKAs, ASA, or $P2Y_{12}$ platelet inhibitors (clopidogrel, prasugrel, or ticagrelor), per prescribing information.
16. Has transient AF caused by a reversible disorder (e.g., thyrotoxicosis, pulmonary embolism, recent surgery)
17. Has condition(s) other than paroxysmal, persistent, or permanent non-valvular AF requiring long term anticoagulation with VKAs during the conduct of the study, including but not limited to moderate to severe mitral valve stenosis, mechanical heart valves, deep vein thrombosis, pulmonary embolism, or left ventricular thrombus
18. Is receiving systemic treatment with strong inhibitors of both cytochrome P450 (CYP) 3A4 and p-glycoprotein (P-gp; e.g., the azole-antimycotic ketoconazole and the HIV protease inhibitor ritonavir). Treatment with the azole-antimycotic fluconazole is allowed.
19. Has known allergies, hypersensitivity, or intolerance to rivaroxaban or its excipients
20. Uses disallowed therapies such as: VKAs (other than for subjects randomly assigned to the VKA strategy), heparin, low molecular weight heparin, dabigatran, and FXa inhibitors other than rivaroxaban study drug, any dose of ASA after randomization to Group 1 (rivaroxaban 15 mg once-daily treatment strategy), doses of ASA greater than 100 mg per day after randomization in the rivaroxaban 2.5 mg twice daily and VKA treatment strategies, systemic treatment with drugs that are combined P-gp and

strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, lopinavir/ritonavir, ritonavir, indinavir/ritonavir, and conivaptan), and systemic treatment with drugs that are combined P-gp and strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin, St. John's wort)

21. Has an anticipated need for chronic (more than 4 weeks) therapy with nonsteroidal anti-inflammatory drugs
22. Has received an investigational drug (including investigational vaccines) or used an invasive investigational medical device within 30 days before the planned first dose of study drug or is currently enrolled in an investigational study
23. Is a woman who is pregnant or breast-feeding or planning to become pregnant while enrolled in this study
24. Has any active malignancy
25. Has any condition that, in the opinion of the investigator, would make participation not be in the best interest (e.g., compromise the well-being) of the subject or that could prevent, limit, or confound the protocol-specified assessments
26. Is an employee of the investigator or study site, with direct involvement in the proposed study or other studies under the direction of that investigator or study site, as well as family members of the employees or the investigator

Figure S1

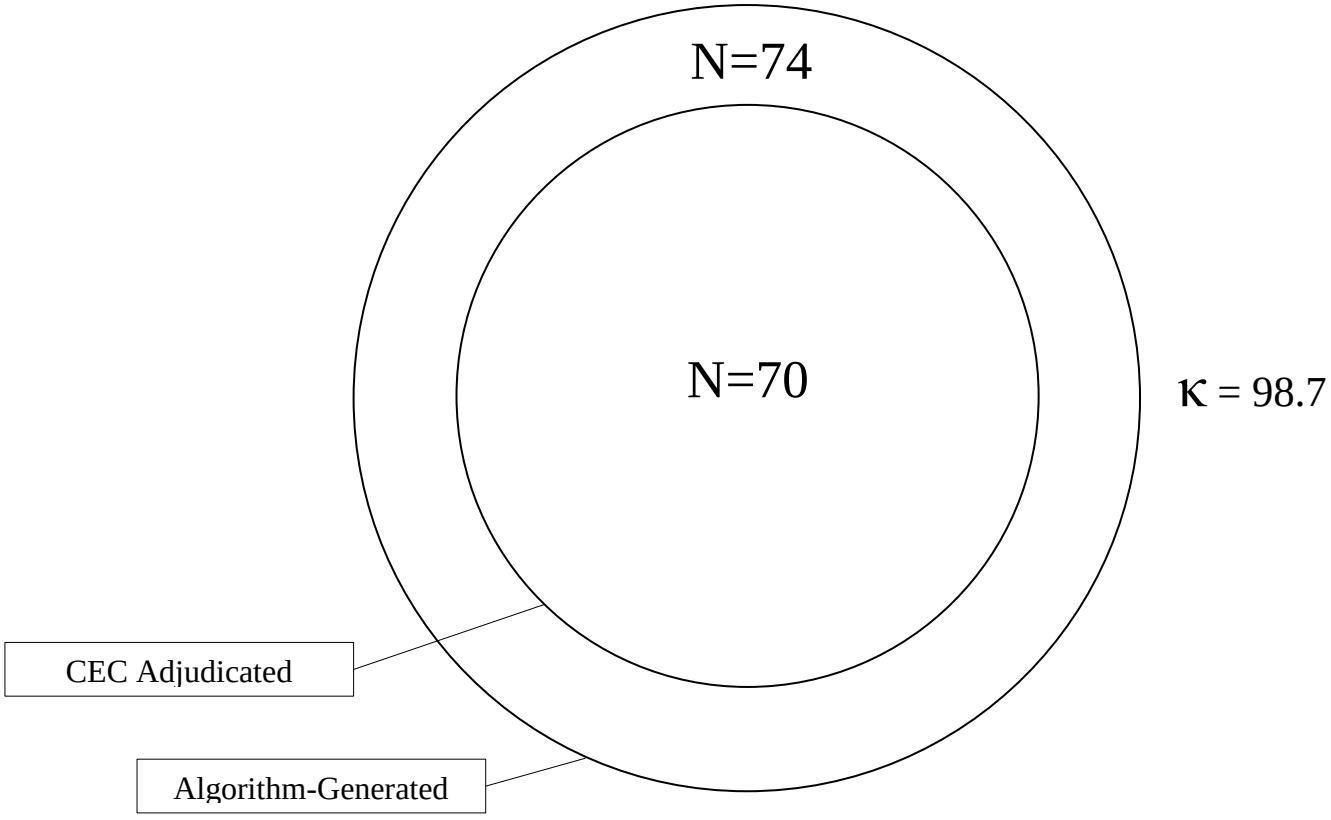
Study Design Figure



*XARELTO® dosed at 10 mg once daily in patients with CrCl of 30 to <50 mL/min.
†Alternative $P2Y_{12}$ inhibitors: 10 mg once-daily prasugrel or 90 mg twice-daily ticagrelor.
‡Low-dose aspirin (75-100 mg/d).

Figure S2

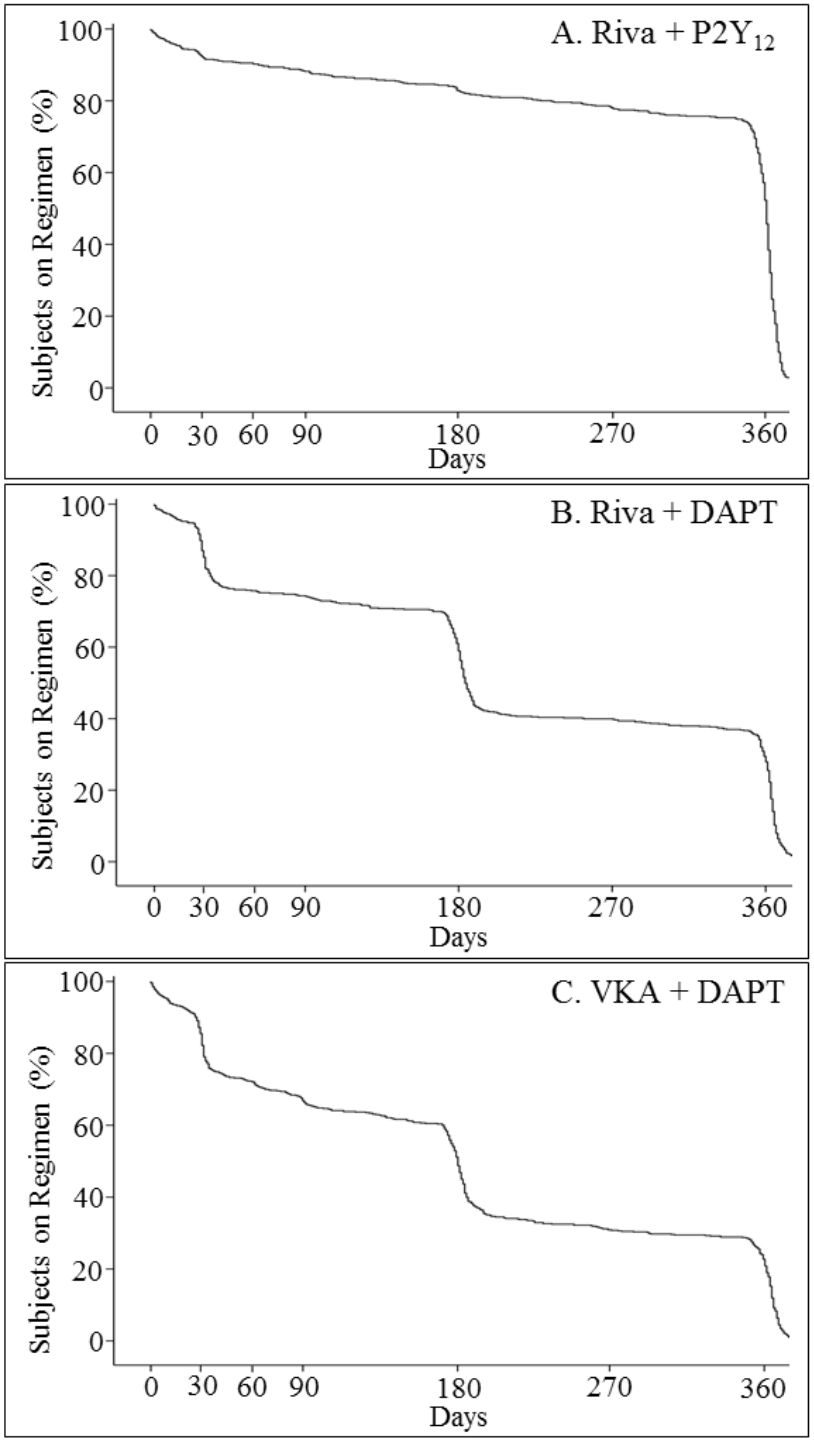
Concordance of BRMA Adjudication and Kappa



Note: All TIMI major and TIMI minor bleeding events and any events that required transfusions of blood were fully adjudicated by the CEC. In addition, a 15% systematic sampling of the Bleeding Requiring medical attention events were also fully adjudicated by the CEC.
Note: Kappa agreement was calculated using Cohen's Kappa.

Figure S3

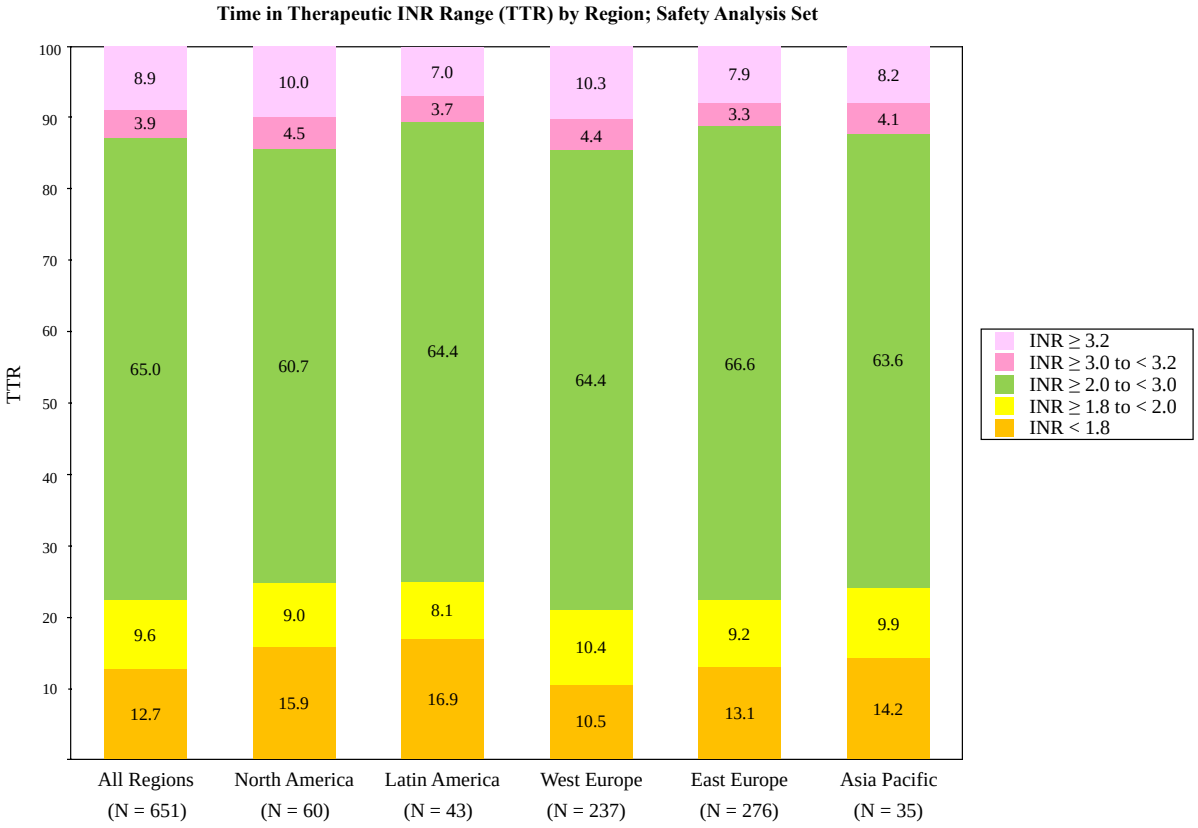
Adherence to Regiment by Treatment Group



Note: This analysis was conducted in the safety population.

Figure S4

Percentage of time in therapeutic INR range (TTR) by region

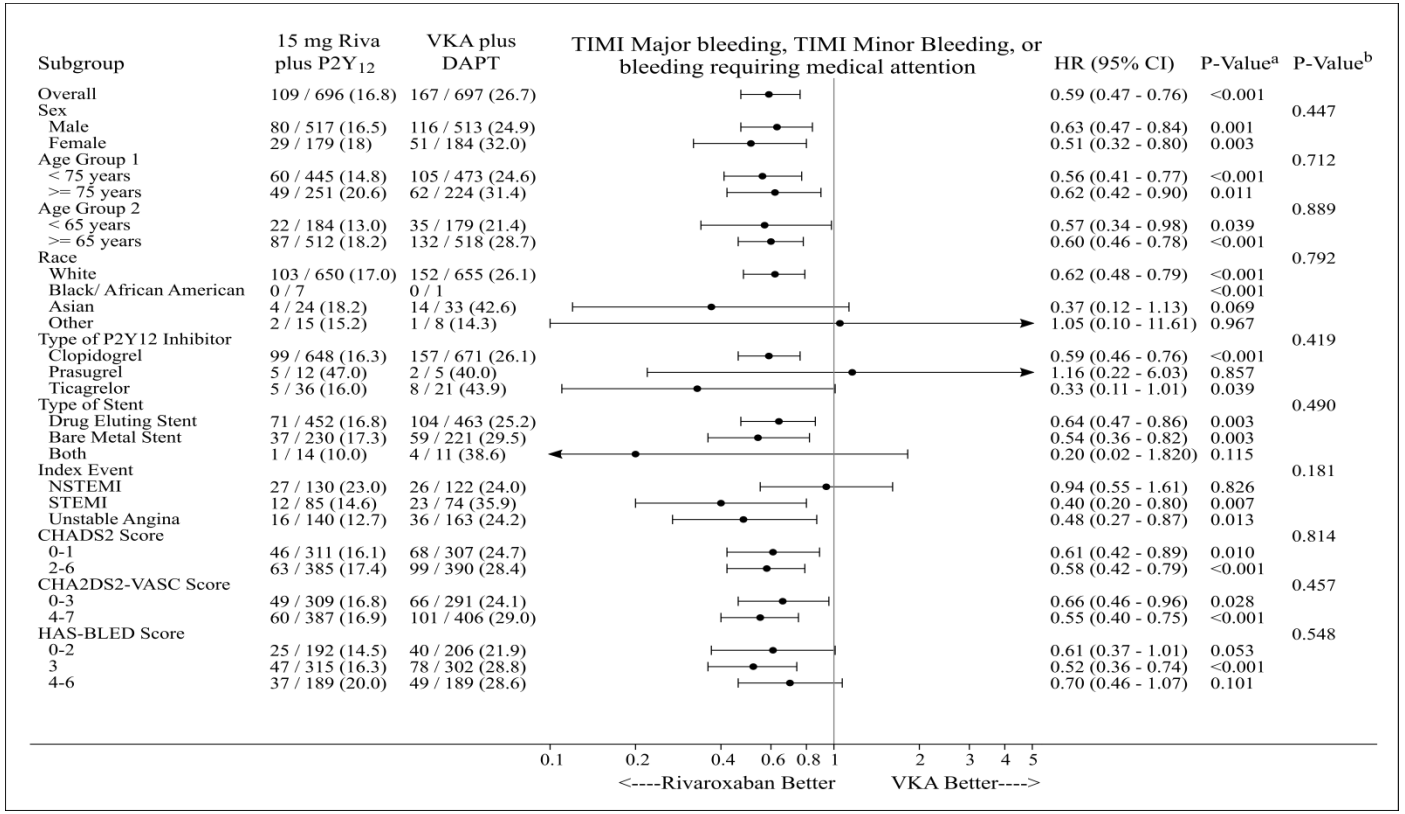


Note: Excluding the First 14 days of Exposure.
Note: Proportion calculated within each subject firstly and then average across subjects within each region.

Figure S5

Subgroup Analysis of the Clinically Significant Bleeding (TIMI Major, TIMI minor, Bleeds Requiring Medical Attention)

15 mg Rivaroxaban plus $P2Y_{12}$ inhibitor vs. VKA plus DAPT

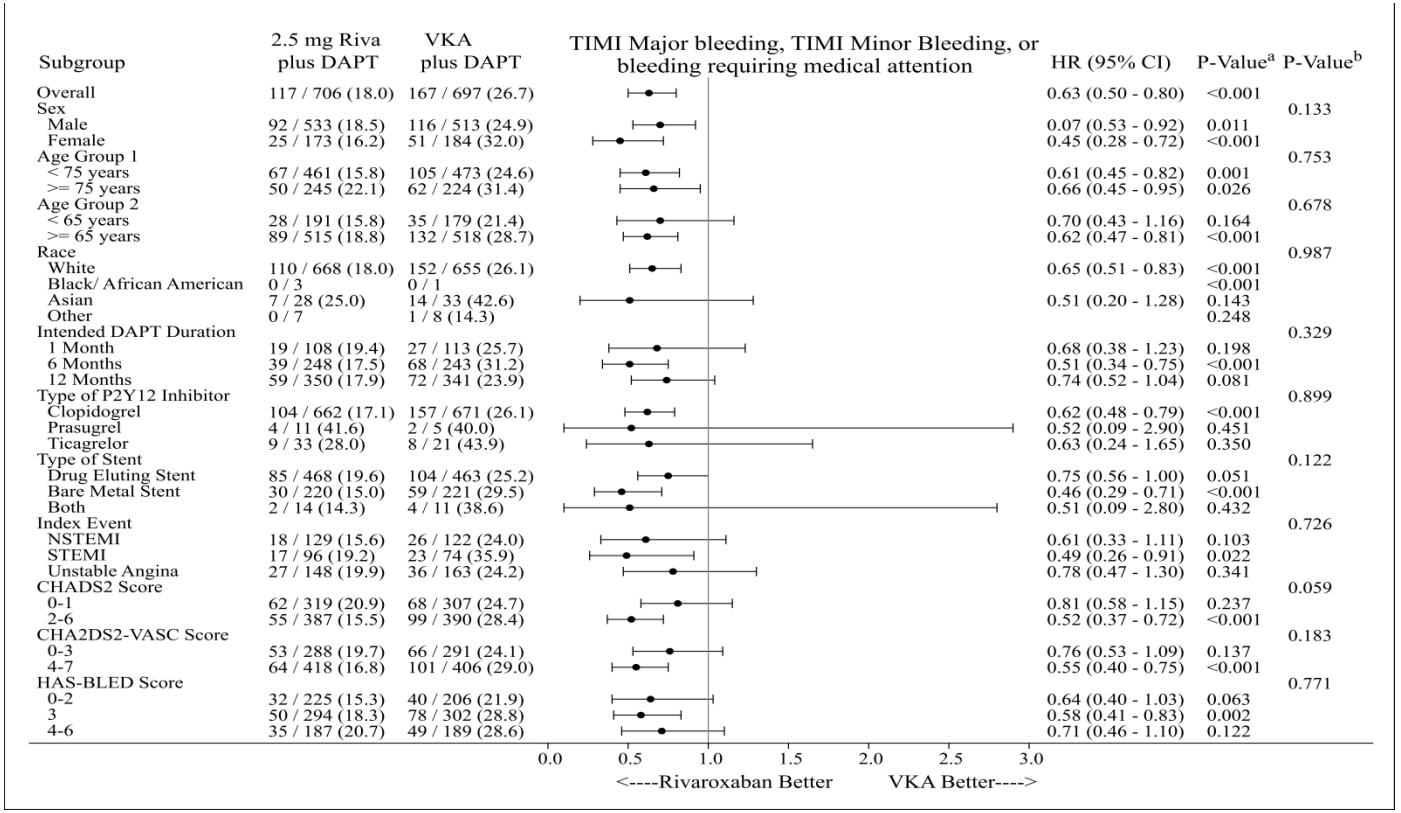


Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Note: A subject could have more than one component event. n = number of subjects with events, N = number of subjects at risk, % = Kaplan-Meier estimates.
Note: Hazard ratios as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Note: BRMA = Bleeding requiring medical attention, TIMI = Thrombolysis in myocardial infarction.
[a]Log-Rank P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.
[b]P-Value for Interaction based on the Cox proportional Hazard joint test.

Figure S6

Subgroup Analysis of the Clinically Significant Bleeding (TIMI Major, TIMI minor, Bleeds Requiring Medical Attention)

2.5 mg Rivaroxaban plus DAPT vs. VKA plus DAPT



Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.

Note: A subject could have more than one component event. n = number of subjects with events, N = number of subjects at risk, % = Kaplan-Meier estimates.

Note: Hazard ratios as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.

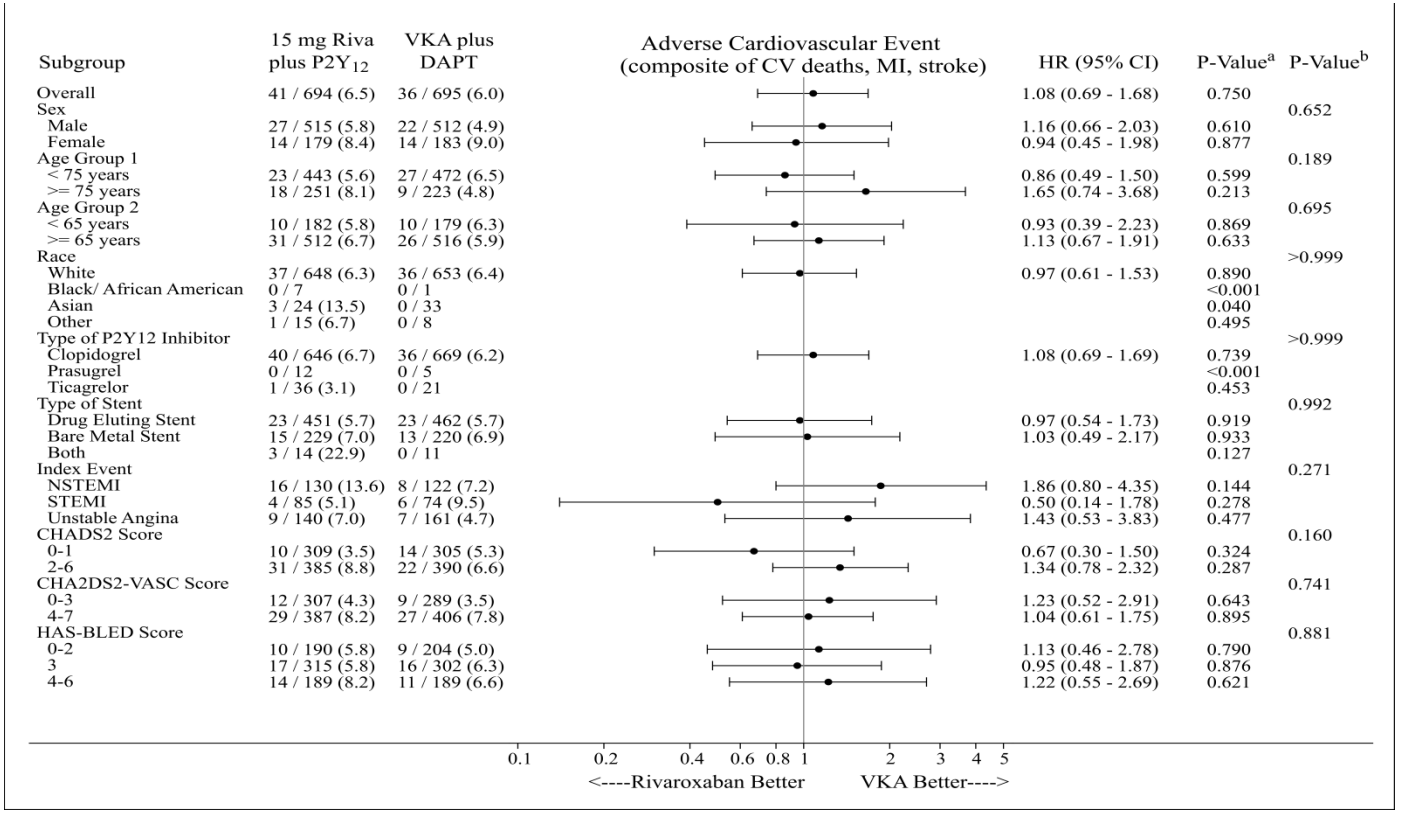
Note: BRMA = Bleeding requiring medical attention, TIMI = Thrombolysis in myocardial infarction.

[a] P-Value for Interaction based on the Cox proportional Hazard joint test.

Figure S7

Subgroup Analysis of the Major Adverse Cardiovascular Events (Cardiovascular Death, MI, Stroke)

15 mg Rivaroxaban plus $P2Y_{12}$ inhibitor vs. VKA plus DAPT

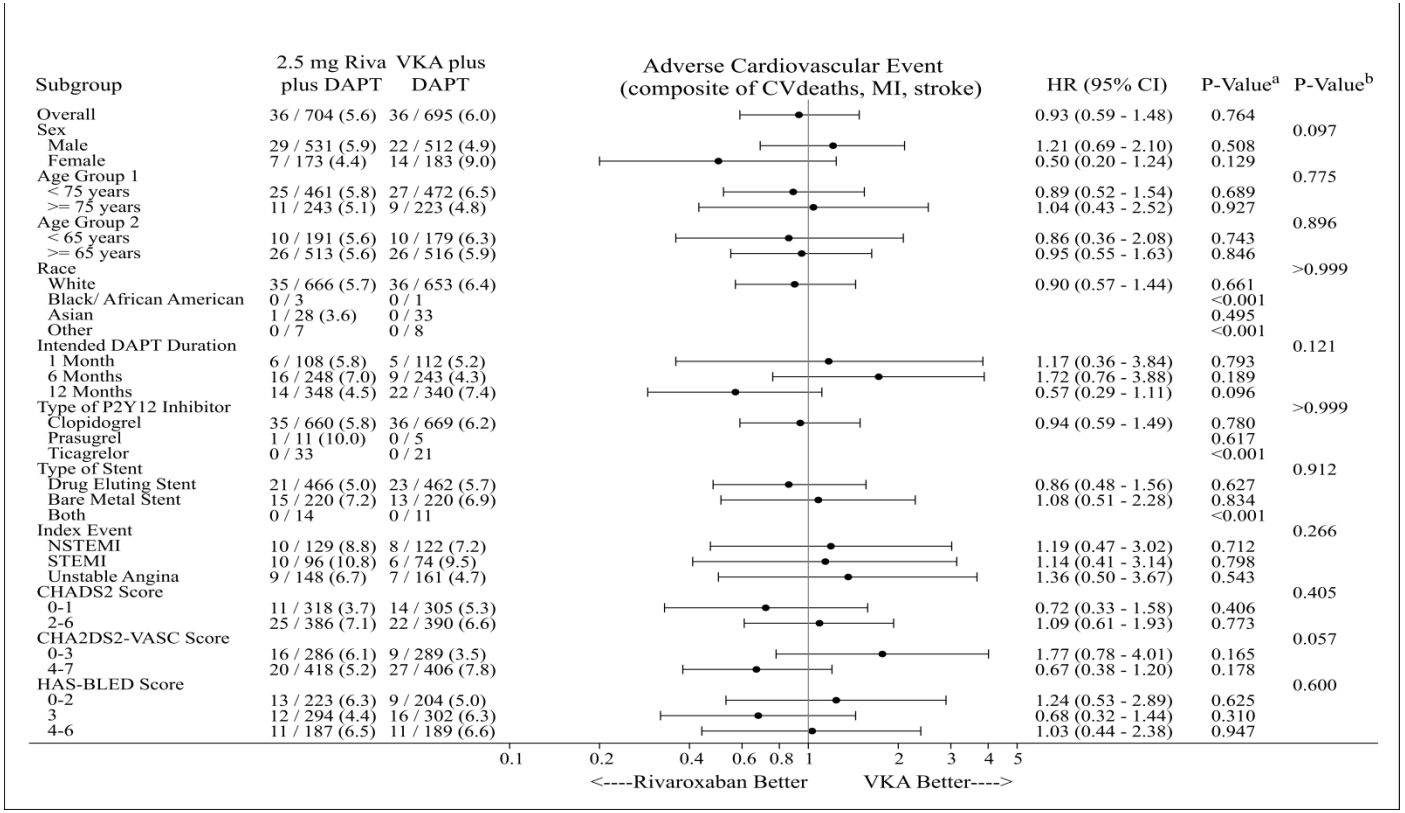


Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Note: A subject could have more than one component event. n = number of subjects with events, N = number of subjects at risk, % = Kaplan-Meier estimates.
Note: Hazard ratios as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Note: 6 subjects from one site were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines.
Note: CV = Cardiovascular, MI = Myocardial Infarction, CI = Confidence Interval, DAPT = Dual Antiplatelet Therapy, HR = Hazard Ratio, VKA = Vitamin K Antagonist.
[a]Log-Rank P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.
[b]P-Value for Interaction based on the Cox proportional Hazard joint test.

Figure S8

Subgroup Analysis of the Major Adverse Cardiovascular Events (Cardiovascular Death, MI, Stroke)

2.5 mg Rivaroxaban plus DAPT vs. VKA plus DAPT



Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Note: A subject could have more than one component event. n = number of subjects with events, N = number of subjects at risk, % = Kaplan-Meier estimates.
Note: Hazard ratios as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Note: 6 subjects from one site were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines.
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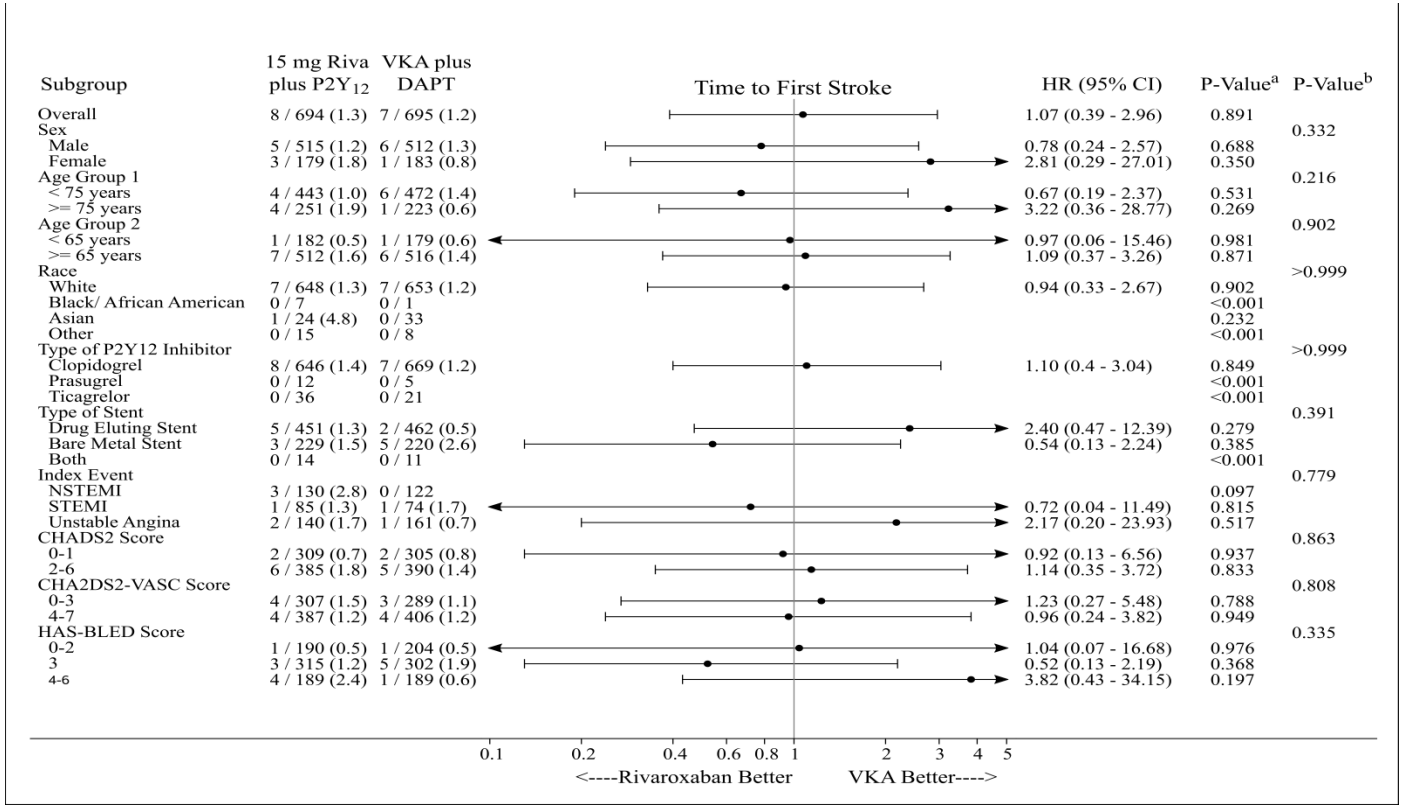
[a]Log-Rank P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.
[b]P-Value for Interaction based on the Cox proportional Hazard joint test.

Figure S9

Subgroup Analysis of Time to First Stroke

15 mg Rivaroxaban plus $P2Y_{12}$ vs. VKA plus DAPT

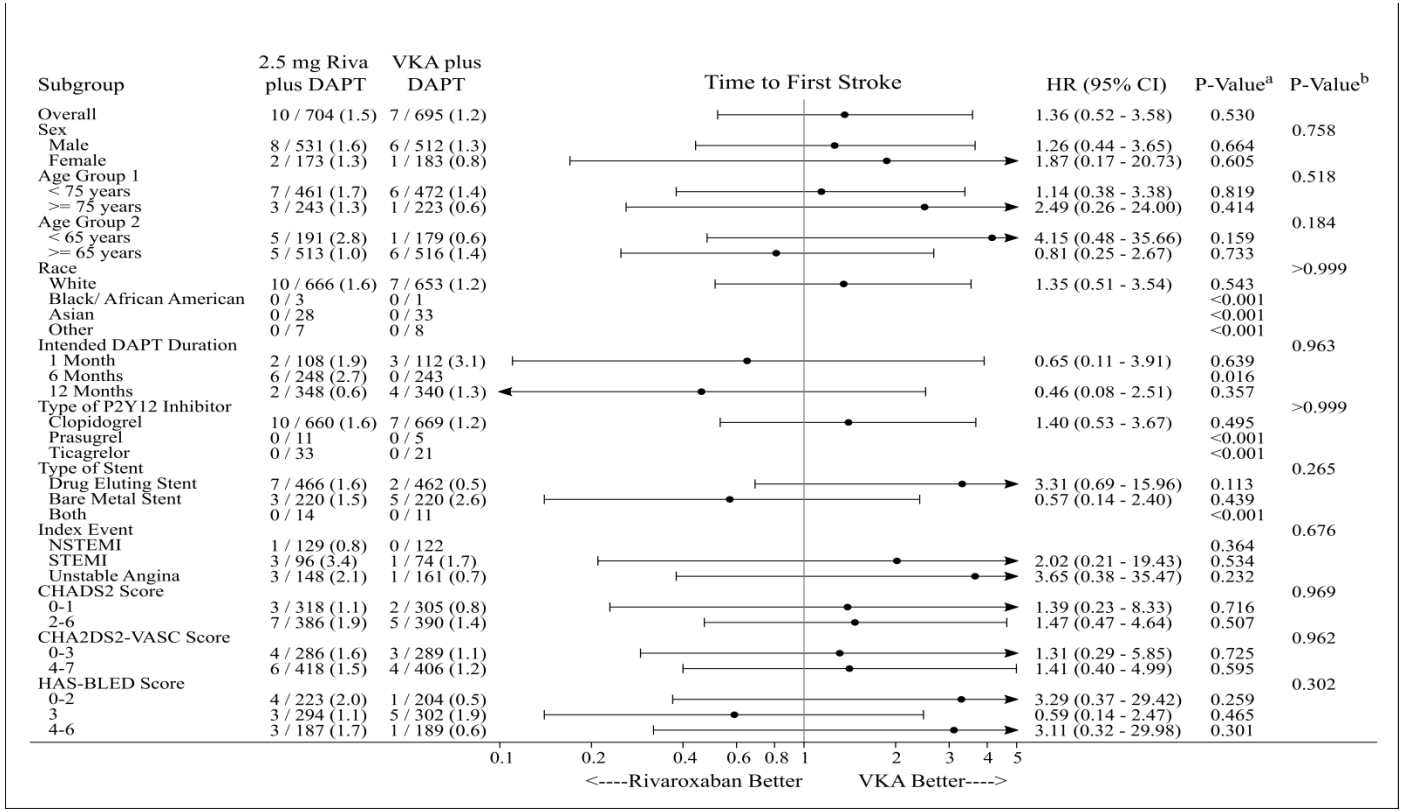


Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Note: A subject could have more than one component event. n = number of subjects with events, N = number of subjects at risk, % = Kaplan-Meier estimates.
Note: Hazard ratios as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Note: 6 subjects from one site were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines.
Note: CI = Confidence Interval, DAPT = Dual Antiplatelet Therapy, HR = Hazard Ratio, VKA = Vitamin K Antagonist.
[a]Log-Rank P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.
[b]P-Value for Interaction based on the Cox proportional Hazard joint test.

Figure S10

Subgroup Analysis of Time to First Stroke

2.5 mg Rivaroxaban plus DAPT vs. VKA plus DAPT

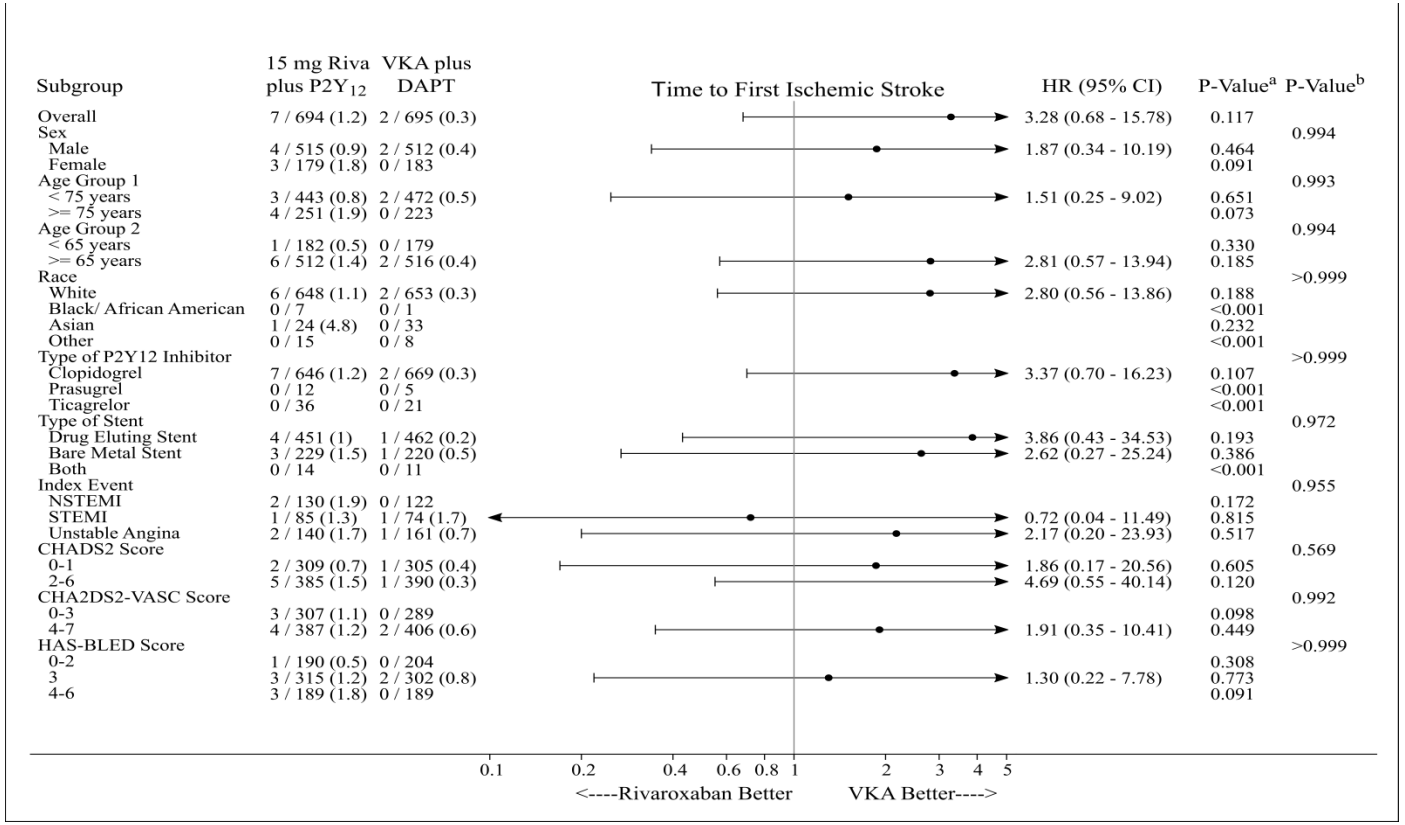


Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Note: A subject could have more than one component event. n = number of subjects with events, N = number of subjects at risk, % = Kaplan-Meier estimates.
Note: Hazard ratios as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Note: 6 subjects from one site were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines.
Note: CI = Confidence Interval, DAPT = Dual Antiplatelet Therapy, HR = Hazard Ratio, VKA = Vitamin K Antagonist.
[a]Log-Rank P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.
[b]P-Value for Interaction based on the Cox proportional Hazard joint test.

Figure S11

Subgroup Analysis of Time to First Ischemic Stroke

15 mg Rivaroxaban plus $P2Y_{12}$ Inhibitor vs. VKA plus DAPT

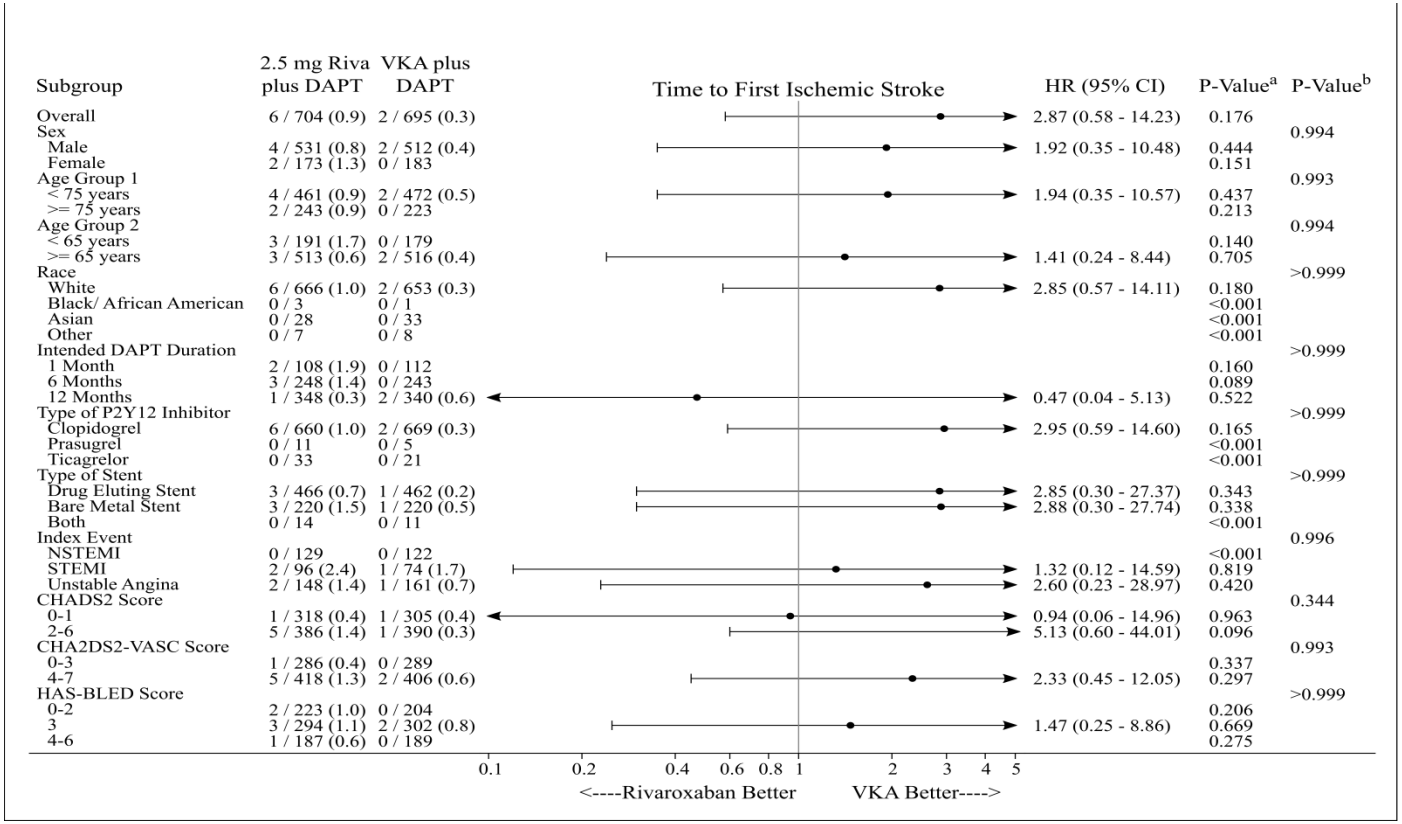


Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Note: A subject could have more than one component event. n = number of subjects with events, N = number of subjects at risk, % = Kaplan-Meier estimates.
Note: Hazard ratios as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Note: 6 subjects from one site were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines.
Note: CI = Confidence Interval, DAPT = Dual Antiplatelet Therapy, HR = Hazard Ratio, VKA = Vitamin K Antagonist.
[a]Log-Rank P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.
[b]P-Value for Interaction based on the Cox proportional Hazard joint test.

Figure S12

Subgroup Analysis of Time to First Ischemic Stroke

2.5 mg Rivaroxaban plus DAPT vs. VKA plus DAPT



Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Note: A subject could have more than one component event. n = number of subjects with events, N = number of subjects at risk, % = Kaplan-Meier estimates.
Note: Hazard ratios as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Note: 6 subjects from one site were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines.
Note: I = Confidence Interval, DAPT = Dual Antiplatelet Therapy, HR = Hazard Ratio, VKA = Vitamin K Antagonist.
[a]Log-Rank P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.
[b]P-Value for Interaction based on the Cox proportional Hazard joint test.

Table S1

Sample size and power calculation of major adverse cardiovascular events required to detect a ≥ 15% risk reduction at a two-sided significance level of 0.05

Endpoint	Event rate	No. per group to attain 90% power	Power with 700 subjects per group
Overall			
Adverse CV event	6.0%	13,598	11.4%
CV death	1.8%	47,196	6.8%
MI	3.5%	23,883	8.6%
Stroke	1.2%	71,195	6.2%
Stent thrombosis	0.7%	122,620	5.7%
DAPT 1 month			
Adverse CV event	5.1%	16,139	10.4%
CV death	2.2%	38,469	7.2%
MI	1.1%	77,740	6.1%
Stroke	3.1%	27,068	8.2%
Stent thrombosis	1.1%	77,740	6.1%
DAPT 6 months			
Adverse CV event	4.3%	19,291	9.5%
CV death	1.9%	44,670	6.9%
MI	2.9%	28,990	8.0%
Stroke	0.0%	–	–
Stent thrombosis	0.4%	215,185	5.4%
DAPT 12 months			
Adverse CV event	7.4%	10,874	13.0%
CV death	1.7%	50,019	6.7%
MI	4.8%	17,198	10.0%
Stroke	1.3%	65,656	6.3%
Stent thrombosis	0.8%	107,192	5.8%

Note: Sample size and power are calculated based on the observed event rate in the VKA arm using the Pearson's chi-square test.
Note: For the power calculation both the treatment and control arms are standardized to 700 subjects.

Table S2

TIMI, ISTH and GUSTO Bleeding Definitions

TIMI Bleeding Definitions	
Type of Bleeding Event	**Definition of Bleeding Event**
TIMI Major Bleeding Event	A TIMI Major bleeding event is defined as: • any symptomatic intracranial hemorrhage, or • clinically overt signs of hemorrhage (including imaging) associated with a drop in hemoglobin of ≥ 5 g/dL (or when the hemoglobin concentration is not available, an absolute drop in hematocrit of ≥ 15%)
TIMI Minor Bleeding Event	A TIMI minor bleeding event is defined as any clinically overt sign of hemorrhage (including imaging) that is associated with a fall in hemoglobin concentration of 3 to < 5 g/dL (or, when hemoglobin concentration is not available, a fall in hematocrit of 9 to < 15%).
Bleeding Events Requiring Medical Attention (BRMA)	A bleeding event requiring medical attention is defined as any bleeding event that requires medical treatment, surgical treatment, or laboratory evaluation and does not meet criteria for a major or minor bleeding event, as defined above. Examples of medical treatment, surgical treatment, or laboratory evaluation include the following: • Laboratory evaluation • CT or MRI • Nasal packing • Endoscopy • Colonoscopy • Cystoscopy • Bronchoscopy • Compression • Ultrasound guided closure of an aneurysm • Coil embolization • Pericardiocentesis • Ionotropic support • Stopping the study medication (either temporarily or permanently) • Reducing or removing antiplatelet therapies • Surgery
Insignificant Bleeding Events	An insignificant bleeding event is defined as a reported blood loss or bleeding event episode not meeting any of the above criteria.
ISTH Bleeding Definitions	
Type of Bleeding Event	**Definition of Bleeding Event**
ISTH Major Bleeding Events	A major bleeding event is defined using ISTH criteria as clinically overt bleeding that is associated with: 1. A fall in hemoglobin of 2 g/dL or more, or 2. A transfusion of 2 or more units of packed red blood cells or whole blood, or 3. A critical site: intracranial, intraspinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome, retroperitoneal, or 4. A fatal outcome.
Clinically Relevant Nonmajor	A clinically-relevant nonmajor bleeding event is defined as an overt

Bleeding Events	bleeding event not meeting the criteria for a major bleeding event, but associated with medical intervention, unscheduled contact (visit or telephone call) with a physician, (temporary) cessation of study drug treatment, or associated with discomfort for the subject such as pain or impairment of activities of daily life. Specific examples of clinically relevant non-major bleeding include the following: • Unscheduled contact (visit or telephone call) with a physician • Study drug temporarily discontinued • Study drug permanently discontinued • Epistaxis if it lasts for more than 5 minutes, if it is repetitive (e.g., 2 or more episodes within 24 hours), or leads to an intervention (e.g., packing, electrocautery) • Gingival bleeding if it occurs spontaneously (i.e., unrelated to tooth brushing or eating), or if it lasts for more than 5 minutes • Hematuria if it is macroscopic, and either spontaneous or lasts for more than 24 hours after instrumentation (e.g., catheter placement or surgery) • Macroscopic gastrointestinal hemorrhage: at least 1 episode of melena or hematemesis, if clinically apparent • Rectal blood loss, if more than a few spots • Hemoptysis • Intramuscular hematoma • Subcutaneous if the size is larger than 25 cm2 or larger than 100 cm2 if provoked • Multiple sources of bleeding • Surgery
Minimal Bleeding Events	All other overt bleeding events not meeting the criteria for major or clinically relevant nonmajor bleeding events will be classified as minimal bleeding events

GUSTO Bleeding Definitions

Type of Bleeding Event	**Definition of Bleeding Event**
Severe or Life Threatening	Severe or life-threatening bleeding is defined as either an intracranial hemorrhage or bleeding that causes hemodynamic compromise and requires intervention.
Moderate	Moderate bleeding is defined as bleeding that requires blood transfusion but does not result in hemodynamic compromise.
Mild	Mild bleeding is defined as bleeding that does not meet criteria for either severe or moderate bleeding.

Table S3

Baseline Characteristics (cont.)

Characteristic	**Group 1** Rivaroxaban 15 mg QD + $P2Y_{12}$ Inhibitor (N=709)	**Group 2** Rivaroxaban 2.5 mg BID + DAPT (N=709)	**Group 3** VKA *plus* DAPT (N=706)
BMI, median (IQR) †	28.6 (25.7 – 32.4)	28.4 (25.6 – 32.1)	29.0 (25.8 – 32.8)
Urgency of Revascularization – no. (%)			
Elective	428 (60.4)	430 (60.6)	449 (63.6)
Urgent	281 (39.6)	279 (39.4)	257 (36.4)
$CHADS_2$ risk of stroke – no. (%)			
0	99 (14.0)	90 (12.7)	83 (11.8)
1	220 (31.0)	232 (32.7)	227 (32.2)
2	246 (34.7)	256 (36.1)	273 (38.7)
3	128 (18.1)	118 (16.6)	107 (15.2)
4	16 (2.3)	13 (1.8)	16 (2.3)
5	0 (0.0)	0 (0.0)	0 (0.0)
6	0 (0.0)	0 (0.0)	0 (0.0)
HAS Bled Score – no. (%)			
0	2 (0.3)	2 (0.3)	0 (0.0)
1	28 (4.0)	43 (6.1)	26 (3.7)
2	166 (23.4)	182 (25.7)	182 (25.8)
3	321 (45.3)	294 (41.5)	308 (43.6)
4	160 (22.6)	157 (22.1)	157 (22.2)
5	31 (4.4)	30 (4.2)	31 (4.4)
6	1 (0.1)	1 (0.1)	2 (0.3)
Comorbidities – no. (%)			
Congestive heart failure	180 (25.4)	187 (26.4)	175 (24.8)
Hypertension	520 (73.3)	519 (73.2)	532 (75.4)
Diabetes mellitus	204 (28.8)	199 (28.1)	221 (31.3)
Hypercholesterolemia	302 (42.6)	295 (41.6)	316 (44.8)
Previous myocardial infarction	140 (19.8)	180 (25.4)	157 (22.2)
Peripheral vascular disease	30 (4.2)	42 (5.9)	35 (5.0)
Gastrointestinal bleeding	7 (1.0)	9 (1.3)	5 (0.7)
Medications – no. (%)			
Aspirin¥	9 (1.3)	702 (99.7)	699 (99.6)
Beta-blocker	586 (82.7)	541 (76.3)	537 (76.1)
ACE inhibitor or ARB	571 (80.5)	532 (75.0)	537 (76.1)
Statin	596 (84.1)	557 (78.6)	552 (78.2)
Proton pump inhibitor			
Omeprazole or esomeprazole	74 (10.4)	78 (11.0)	79 (11.2)
Other	200 (28.2)	198 (27.9)	180 (25.5)

Note: Plus-minus values are mean ± SD. There were no significant differences among the three groups. ACE denotes angiotensin-converting enzyme, ACS acute coronary syndrome, ARB angiotensin-receptor blocker, BMI denotes body mass index, PCI percutaneous coronary intervention, NSTEMI non-ST-segment elevation myocardial infarction, STEMI ST-segment elevation myocardial infarction. Numbers based upon all randomized subjects.

¥ Aspirin use was calculated as administration of aspirin no more than 4 days after PCI procedure for index event.

There were significant differences across groups in the following categories; previous myocardial infarction (p=0.039), aspirin use (p<0.001), beta-blocker use (p=0.003 overall, p=0.002 Group 1 v Group 3), ACE inhibitor or ARB use (p=0.032 overall, p=0.042 Group 1 v Group 3) and statin use (p=0.008 overall, p=0.005 Group 1 v Group 3). All other p-values were not significant.

Table S4

Baseline Characteristics by DAPT Stratum for subjects (Group 2 or Group 3)

Characteristic	DAPT 1 Month (N = 224)	DAPT 6 Months (N=494)	DAPT 12 Months (N = 697)	p-value
Demographics				
Age				
Mean ─ yr	71.7 ± 8.7	69.9 ± 8.7	69.4 ± 9.0	0.003
≥ 65 yr ─ no. (%)	176 (78.6)	368 (74.5)	498 (71.5)	0.095
≥ 75 yr ─ no. (%)	95 (42.4)	163 (33.0)	217 (31.1)	0.008
Female sex ─ no. (%)	48 (21.4)	127 (25.7)	187 (26.8)	0.272
Race*─ no. (%)				0.172
White	216 (96.4)	457 (92.5)	662 (95.0)	
Black or African-American	1 (0.5)	1 (0.2)	2 (0.3)	
Asian	5 (2.2)	31 (6.3)	25 (3.6)	
American Indian or Alaska Native	0 (0.0)	0 (0.0)	0 (0.0)	
Other or unknown	2 (0.9)	5 (1.0)	8 (1.2)	
BMI†				
Median	27.8	29.1	28.6	0.259
Interquartile range	25.4 – 32.5	25.8 – 32.6	25.8 – 32.4	
Active smokers – no. (%)	13 (5.8)	37 (7.5)	54 (7.8)	0.618
Creatinine clearance ─ ml/min‡				
Mean	75.9 ± 33.4	79.6 ± 29.8	79.8 ± 30.9	0.255
< 60 to ≥ 30 ml/min ─ no. (%)	68 (31.9)	138 (28.9)	165 (25.1)	0.104
<30 ml/min ─ no. (%)	2 (0.9)	1 (0.2)	6 (0.9)	0.276
P2Y12 inhibitor at baseline – no. (%)				0.056
Clopidogrel	221 (98.7)	467 (94.5)	656 (94.1)	
Prasugrel	1 (0.5)	4 (0.8)	11 (1.6)	
Ticagrelor	2 (0.9)	23 (4.7)	30 (4.3)	
Index Event				
Type of Index Event – no. (%)				0.089
NSTEMI	28 (12.8)	96 (19.6)	128 (18.6)	
STEMI	18 (8.3)	65 (13.3)	88 (12.8)	
Unstable Angina	53 (24.3)	107 (21.9)	152 (22.1)	
Type of Stent – no. (%)				<0.001
Drug-eluting stent	67 (29.9)	374 (75.9)	498 (72.0)	
Bare metal stent	156 (69.6)	114 (23.1)	174 (25.1)	
Drug-eluting and bare metal stents	1 (0.5)	5 (1.0)	20 (2.9)	
Urgency of Revascularization – no. (%)				<0.001
Elective	157 (70.1)	324 (65.6)	398 (57.1)	
Urgent	67 (29.9)	170 (34.4)	299 (42.9)	
Type of Atrial Fibrillation ─ no. (%)				0.037

Characteristic	DAPT 1 Month (N = 224)	DAPT 6 Months (N=494)	DAPT 12 Months (N = 697)	p-value
Persistent	52 (23.2)	121 (24.5)	122 (17.5)	
Permanent	78 (34.8)	154 (31.2)	249 (35.8)	
Paroxysmal	94 (42.0)	219 (44.3)	325 (46.7)	
Bleed Risk Scores				
$CHADS_2$ risk of stroke – no. (%)				0.270
0	28 (12.5)	53 (10.7)	92 (13.2)	
1	74 (33.0)	147 (29.8)	238 (34.2)	
2	82 (36.6)	204 (41.3)	243 (34.9)	
3	32 (14.3)	81 (16.4)	112 (16.1)	
4	8 (27.6)	9 (1.8)	12 (1.7)	
5	0 (0.0)	0 (0.0)	0 (0.0)	
6	0 (0.0)	0 (0.0)	0 (0.0)	
CHA_2DS_2-VASc risk of stroke – no. (%)				0.457
0	3 (1.3)	4 (0.8)	10 (1.4)	
1	16 (7.1)	32 (6.5)	61 (8.8)	
2	34 (15.2)	55 (11.1)	100 (14.4)	
3	45 (20.1)	92 (18.6)	133 (19.1)	
4	48 (21.4)	121 (24.5)	158 (22.7)	
5	43 (19.2)	103 (20.9)	142 (20.4)	
6	32 (14.3)	72 (14.6)	72 (10.3)	
7	3 (1.3)	15 (3.0)	21 (3.0)	
HAS Bled Score – no. (%)				0.031
0	0 (0.0)	1 (0.2)	1 (0.1)	
1	8 (3.6)	15 (3.0)	46 (6.6)	
2	46 (20.5)	128 (25.9)	190 (27.3)	
3	103 (46.0)	200 (40.5)	299 (42.9)	
4	54 (24.1)	122 (24.7)	138 (19.8)	
5	13 (5.8)	27 (5.5)	21 (3.0)	
6	0 (0.0)	1 (0.2)	2 (0.3)	
Comorbidities				
Congestive heart failure	46 (20.5)	135 (27.3)	181 (26.0)	0.147
Hypertension	165 (73.7)	508 (72.9)	378 (76.5)	0.359
Diabetes mellitus	60 (26.8)	158 (32.0)	202 (29.0)	0.314
Hypercholesterolemia	97 (43.3)	225 (45.6)	289 (41.5)	0.374
Previous myocardial infarction	47 (21.0)	111 (22.5)	179 (25.7)	0.244
Peripheral vascular disease	11 (4.9)	27 (5.5)	39 (5.6)	0.925
Gastrointestinal bleeding	1 (0.5)	4 (0.8)	9 (1.3)	0.620
Medications				
Aspirin[¥]	222 (99.1)	493 (99.8)	695 (99.7)	0.309
Beta-blocker	175 (78.1)	375 (75.9)	528 (75.8)	0.757
ACE inhibitor or ARB	168 (75.0)	385 (77.9)	516 (74.0)	0.297

Characteristic	DAPT 1 Month (N = 224)	DAPT 6 Months (N=494)	DAPT 12 Months (N = 697)	p-value
Statin	164 (73.2)	374 (75.7)	571 (81.9)	0.005
Proton pump inhibitor				0.406
Omeprazole or esomeprazole	27 (12.1)	53 (10.7)	77 (11.1)	
Other	59 (26.3)	118 (23.9)	200 (28.7)	

Note: Plus-minus values are mean ± SD. ACE denotes angiotensin-converting enzyme, ACS acute coronary syndrome, ARB angiotensin-receptor blocker, BMI denotes body mass index, PCI percutaneous coronary intervention, NSTEMI non-ST-segment elevation myocardial infarction, STEMI ST-segment elevation myocardial infarction. Numbers based upon all randomized subjects.
*Race was self-reported.
† Body mass index (BMI) is the weight (kg) divided by the square of the height (m).
‡ Creatinine clearance calculated using the Cockcroft-Gault equation.
¥ Aspirin use was calculated as administration of aspirin no more than 4 days after PCI procedure for index event.

Table S4A

Baseline Characteristics by DAPT Duration (1 month) and Treatment

Characteristic	**Group 2** Rivaroxaban 2.5 mg BID + DAPT (N=109)	**Group 3** VKA *plus* DAPT (N=115)	**p-value**
Demographics			
Age			
Mean ─ yr	70.8 ± 9.6	72.6 ± 7.8	0.126
≥ 65 yr ─ no. (%)	80 (73.4)	96 (83.5)	0.066
≥ 75 yr ─ no. (%)	44 (40.4)	51 (44.4)	0.547
Female sex ─ no. (%)	24 (22.0)	24 (20.9)	0.834
Race*─ no. (%)			0.791
White	105 (96.3)	111 (96.5)	
Black or African-American	0 (0.0)	1 (0.9)	
Asian	2 (1.8)	3 (2.6)	
American Indian or Alaska Native	0 (0.0)	0 (0.0)	
Other or unknown	2 (1.8)	0 (0.0)	
BMI†			
Median	27.8	27.7	0.654
Interquartile range	25.5 – 33.2	25.4 – 32.0	
Active smokers – no. (%)	5 (4.6)	8 (7.0)	0.448
Creatinine clearance ─ ml/min‡			
Mean	78.3 ± 37.1	73.5 ± 29.3	0.302
< 60 to ≥ 30 ml/min ─ no. (%)	28 (26.7)	40 (37.0)	0.105
<30 ml/min ─ no. (%)	2 (1.9)	0 (0.0)	0.242
P2Y12 inhibitor at baseline – no. (%)			0.236
Clopidogrel	107 (98.2)	114 (99.1)	
Prasugrel	0 (0.0)	1 (0.9)	
Ticagrelor	2 (1.8)	0 (0.0)	
Index Event			
Type of Index Event – no. (%)			0.385
NSTEMI	16 (14.8)	12 (10.9)	
STEMI	9 (8.3)	9 (8.2)	
Unstable Angina	21 (19.4)	32 (29.1)	
Type of Stent – no. (%)			0.611
Drug-eluting stent	34 (31.2)	33 (28.7)	
Bare metal stent	74 (67.9)	82 (71.3)	
Drug-eluting and bare metal stents	1 (0.9)	0 (0.0)	
Urgency of Revascularization – no. (%)			0.908
Elective	76 (69.7)	81 (70.4)	
Urgent	33 (30.3)	34 (29.6)	
Type of Atrial Fibrillation ─ no. (%)			0.176

Characteristic	Group 2 Rivaroxaban 2.5 mg BID + DAPT (N=109)	Group 3 VKA *plus* DAPT (N=115)	p-value
Persistent	20 (18.4)	32 (27.8)	
Permanent	43 (39.5)	35 (30.4)	
Paroxysmal	46 (42.2)	48 (41.7)	
Bleed Risk Scores			
$CHADS_2$ risk of stroke – no. (%)			0.184
0	16 (14.7)	12 (10.4)	
1	39 (35.8)	35 (30.4)	
2	32 (29.4)	50 (43.5)	
3	19 (17.4)	13 (11.3)	
4	3 (2.8)	5 (4.4)	
5	0 (0.0)	0 (0.0)	
6	0 (0.0)	0 (0.0)	
CHA_2DS_2-VASc risk of stroke – no. (%)			0.180
0	2 (1.8)	1 (0.9)	
1	12 (11.0)	4 (3.5)	
2	13 (11.9)	21 (18.3)	
3	19 (17.4)	26 (22.6)	
4	20 (18.4)	28 (24.4)	
5	23 (21.1)	20 (17.4)	
6	19 (17.4)	13 (11.3)	
7	1 (0.9)	2 (1.7)	
HAS Bled Score – no. (%)			0.671
0	0 (0.0)	0 (0.0)	
1	5 (4.6)	3 (2.6)	
2	23 (21.1)	23 (20.0)	
3	45 (41.3)	58 (50.4)	
4	29 (26.6)	25 (21.7)	
5	7 (6.4)	6 (5.2)	
6	0 (0.0)	0 (0.0)	
Comorbidities			
Congestive heart failure	21 (19.3)	25 (21.7)	0.647
Hypertension	77 (70.6)	88 (76.5)	0.318
Diabetes mellitus	30 (27.5)	30 (26.1)	0.808
Hypercholesterolemia	38 (34.9)	59 (51.3)	0.013
Previous myocardial infarction	19 (17.4)	28 (24.4)	0.204
Peripheral vascular disease	7 (6.4)	4 (3.5)	0.308
Gastrointestinal bleeding	0 (0.0)	1 (0.9)	>0.999
Medications			
Aspirin[¥]	108 (99.1)	114 (99.1)	>0.999
Beta-blocker	87 (79.8)	88 (76.5)	0.551

Characteristic	Group 2 Rivaroxaban 2.5 mg BID + DAPT (N=109)	Group 3 VKA *plus* DAPT (N=115)	p-value
ACE inhibitor or ARB	83 (76.2)	85 (73.9)	0.700
Statin	79 (72.5)	85 (73.9)	0.808
Proton pump inhibitor			0.107
Omeprazole or esomeprazole	9 (8.3)	18 (15.7)	
Other	34 (31.2)	25 (21.7)	

Note: Plus-minus values are mean ± SD. ACE denotes angiotensin-converting enzyme, ACS acute coronary syndrome, ARB angiotensin-receptor blocker, BMI denotes body mass index, PCI percutaneous coronary intervention, NSTEMI non-ST-segment elevation myocardial infarction, STEMI ST-segment elevation myocardial infarction. Numbers based upon all randomized subjects.
*Race was self-reported.
† Body mass index (BMI) is the weight (kg) divided by the square of the height (m).
‡ Creatinine clearance calculated using the Cockcroft-Gault equation.
¥ Aspirin use was calculated as administration of aspirin no more than 4 days after PCI procedure for index event.

Table S4B

Baseline Characteristics by DAPT Duration (6 months) and Treatment

Characteristic	**Group 2** Rivaroxaban 2.5 mg BID + DAPT (N=248)	**Group 3** VKA *plus* DAPT (N=246)	**p-value**
Demographics			
Age			
Mean ─ yr	70.2 ± 9.1	69.6 ± 8.3	0.403
≥ 65 yr ─ no. (%)	183 (73.8)	185 (75.2)	0.719
≥ 75 yr ─ no. (%)	90 (36.3)	73 (29.7)	0.118
Female sex ─ no. (%)	65 (26.2)	62 (25.2)	0.798
Race*─ no. (%)			0.039
White	235 (94.8)	222 (90.2)	
Black or African-American	1 (0.4)	0 (0.0)	
Asian	11 (4.4)	20 (8.1)	
American Indian or Alaska Native	0 (0.0)	0 (0.0)	
Other or unknown	1 (0.4)	4 (1.6)	
BMI†			
Median	28.7	29.4	0.297
Interquartile range	25.7 – 32.3	25.8 – 32.8	
Active smokers – no. (%)	21 (8.5)	16 (6.5)	0.407
Creatinine clearance ─ ml/min‡			
Mean	77.5 ± 30.0	81.8 ± 29.5	0.114
< 60 to ≥ 30 ml/min ─ no. (%)	78 (32.2)	60 (25.5)	0.108
<30 ml/min ─ no. (%)	1 (0.4)	0 (0.0)	>0.999
$P2Y_{12}$ inhibitor at baseline – no. (%)			0.370
Clopidogrel	231 (93.2)	236 (95.9)	
Prasugrel	3 (1.2)	1 (0.4)	
Ticagrelor	14 (5.7)	9 (3.7)	
Index Event			
Type of Index Event – no. (%)			0.451
NSTEMI	51 (20.7)	45 (18.5)	
STEMI	38 (15.5)	27 (11.1)	
Unstable Angina	52 (21.1)	55 (22.6)	
Type of Stent – no. (%)			0.509
Drug-eluting stent	187 (75.7)	187 (76.0)	
Bare metal stent	56 (22.7)	58 (23.6)	
Drug-eluting and bare metal stents	4 (1.6)	1 (0.4)	
Urgency of Revascularization – no. (%)			0.101
Elective	154 (62.1)	170 (69.1)	
Urgent	94 (37.9)	76 (30.9)	
Type of Atrial Fibrillation ─ no. (%)			0.932

Characteristic	**Group 2** Rivaroxaban 2.5 mg BID + DAPT (N=248)	**Group 3** VKA *plus* DAPT (N=246)	**p-value**
Persistent	60 (24.2)	61 (24.8)	
Permanent	76 (30.7)	78 (31.7)	
Paroxysmal	112 (45.2)	107 (43.5)	
Bleed Risk Scores			
$CHADS_2$ risk of stroke – no. (%)			0.676
0	26 (10.5)	27 (11.0)	
1	74 (29.8)	73 (29.7)	
2	108 (43.6)	96 (39.0)	
3	35 (14.1)	46 (18.7)	
4	5 (2.0)	4 (1.6)	
5	0	0	
6	0	0	
CHA_2DS_2-VASc risk of stroke – no. (%)			0.381
0	2 (0.8)	2 (0.8)	
1	20 (8.1)	12 (4.9)	
2	24 (9.7)	31 (12.6)	
3	51 (20.6)	41 (16.7)	
4	55 (22.2)	66 (26.8)	
5	56 (22.6)	47 (19.1)	
6	35 (14.1)	37 (15.0)	
7	5 (2.0)	10 (4.1)	
HAS Bled Score – no. (%)			0.673
0	1 (0.4)	0 (0.0)	
1	10 (4.0)	5 (2.0)	
2	64 (25.8)	64 (26.0)	
3	100 (40.3)	100 (40.7)	
4	60 (24.2)	62 (25.2)	
5	12 (4.8)	15 (6.1)	
6	1 (0.4)	0 (0.0)	
Comorbidities			
Congestive heart failure	67 (27.0)	68 (27.6)	0.876
Hypertension	188 (75.8)	190 (77.2)	0.708
Diabetes mellitus	70 (28.2)	88 (35.8)	0.072
Hypercholesterolemia	109 (44.0)	116 (47.2)	0.475
Previous myocardial infarction	62 (25.0)	49 (19.9)	0.176
Peripheral vascular disease	12 (4.8)	15 (6.1)	0.538
Gastrointestinal bleeding	2 (0.8)	2 (0.8)	>0.999
Medications			
Aspirin[¥]	248 (100.0)	245 (99.6)	0.498
Beta-blocker	193 (77.8)	182 (74.0)	0.319

Characteristic	Group 2 Rivaroxaban 2.5 mg BID + DAPT (N=248)	Group 3 VKA *plus* DAPT (N=246)	p-value
ACE inhibitor or ARB	199 (80.2)	186 (75.6)	0.215
Statin	194 (78.2)	180 (73.2)	0.190
Proton pump inhibitor			0.108
Omeprazole or esomeprazole	30 (12.1)	23 (9.4)	
Other	67 (27.0)	51 (20.7)	

Note: Plus-minus values are mean ± SD. ACE denotes angiotensin-converting enzyme, ACS acute coronary syndrome, ARB angiotensin-receptor blocker, BMI denotes body mass index, PCI percutaneous coronary intervention, NSTEMI non-ST-segment elevation myocardial infarction, STEMI ST-segment elevation myocardial infarction. Numbers based upon all randomized subjects.
*Race was self-reported.
† Body mass index (BMI) is the weight (kg) divided by the square of the height (m).
‡ Creatinine clearance calculated using the Cockcroft-Gault equation.
¥ Aspirin use was calculated as administration of aspirin no more than 4 days after PCI procedure for index event.

Table S4C

Baseline Characteristics by DAPT Duration (12 months) and Treatment

Characteristic	**Group 2** Rivaroxaban 2.5 mg BID + DAPT (N=352)	**Group 3** VKA *plus* DAPT (N=345)	**p-value**
Demographics			
Age			
Mean ─ yr	69.5 ± 9.0	69.3 ± 9.1	0.721
≥ 65 yr ─ no. (%)	253 (71.9)	245 (71.0)	0.801
≥ 75 yr ─ no. (%)	111 (31.5)	106 (30.7)	0.818
Female sex ─ no. (%)	85 (24.2)	102 (29.6)	0.107
Race*─ no. (%)			0.256
White	331 (94.0)	331 (95.9)	
Black or African-American	2 (0.6)	0 (0.0)	
Asian	15 (4.3)	10 (2.9)	
American Indian or Alaska Native	0 (0.0)	0 (0.0)	
Other or unknown	4 (1.1)	4 (1.2)	
BMI†			
Median	28.4	29.1	**0.035**
Interquartile range	25.6 – 31.6	26.1 – 32.9	
Active smokers – no. (%)	30 (8.5)	24 (7.0)	0.480
Creatinine clearance ─ ml/min‡			
Mean	77.3 ± 31.4	82.3 ± 30.3	**0.037**
< 60 to ≥ 30 ml/min ─ no. (%)	90 (27.0)	75 (23.1)	0.280
<30 ml/min ─ no. (%)	4 (1.2)	2 (0.6)	0.686
$P2Y_{12}$ inhibitor at baseline – no. (%)			0.180
Clopidogrel	326 (92.6)	330 (95.7)	
Prasugrel	8 (2.3)	3 (0.9)	
Ticagrelor	18 (5.1)	12 (3.5)	
Index Event			
Type of Index Event – no. (%)			0.639
NSTEMI	62 (17.8)	66 (19.5)	
STEMI	50 (14.3)	38 (11.2)	
Unstable Angina	75 (21.5)	77 (22.8)	
Type of Stent – no. (%)			0.834
Drug-eluting stent	250 (71.6)	248 (72.3)	
Bare metal stent	90 (25.8)	84 (24.5)	
Drug-eluting and bare metal stents	9 (2.6)	11 (3.2)	
Urgency of Revascularization – no. (%)			0.879
Elective	200 (56.8)	198 (57.4)	
Urgent	152 (43.2)	147 (42.6)	
Type of Atrial Fibrillation ─ no. (%)			0.481

Characteristic	Group 2 Rivaroxaban 2.5 mg BID + DAPT (N=352)	Group 3 VKA *plus* DAPT (N=345)	p-value
Persistent	66 (18.8)	56 (16.3)	
Permanent	119 (33.8)	130 (37.8)	
Paroxysmal	167 (47.4)	158 (45.9)	
Bleed Risk Scores			
$CHADS_2$ risk of stroke – no. (%)			0.522
0	48 (13.6)	44 (12.8)	
1	119 (33.8)	119 (34.5)	
2	116 (33.0)	127 (36.8)	
3	64 (18.2)	48 (13.9)	
4	5 (1.4)	7 (2.0)	
5	0	0	
6	0	0	
CHA_2DS_2-VASc risk of stroke – no. (%)			0.035
0	6 (1.7)	4 (1.2)	
1	33 (9.4)	28 (8.1)	
2	56 (15.9)	44 (12.8)	
3	52 (14.8)	81 (23.5)	
4	78 (22.2)	80 (23.2)	
5	84 (23.9)	58 (16.8)	
6	31 (8.8)	41 (11.9)	
7	12 (3.4)	9 (2.6)	
HAS Bled Score – no. (%)			0.520
0	1 (0.3)	0 (0.0)	
1	28 (8.0)	18 (5.2)	
2	95 (27.0)	95 (27.5)	
3	149 (42.3)	150 (43.5)	
4	68 (19.3)	70 (20.3)	
5	11 (3.1)	10 (2.9)	
6	0 (0.0)	2 (0.6)	
Comorbidities			
Congestive heart failure	99 (28.1)	82 (23.8)	0.190
Hypertension	254 (72.2)	254 (73.6)	0.664
Diabetes mellitus	99 (28.1)	103 (29.9)	0.615
Hypercholesterolemia	148 (42.1)	141 (40.9)	0.753
Previous myocardial infarction	99 (28.1)	80 (23.2)	0.136
Peripheral vascular disease	23 (6.5)	16 (4.6)	0.276
Gastrointestinal bleeding	7 (2.0)	2 (0.6)	0.177
Medications			
Aspirin[¥]	351 (99.7)	344 (99.7)	>0.999
Beta-blocker	261 (74.2)	267 (77.4)	0.318

Characteristic	Group 2 Rivaroxaban 2.5 mg BID + DAPT (N=352)	Group 3 VKA *plus* DAPT (N=345)	p-value
ACE inhibitor or ARB	250 (71.0)	266 (77.1)	0.067
Statin	284 (80.7)	287 (83.2)	0.390
Proton pump inhibitor			0.792
Omeprazole or esomeprazole	39 (11.1)	38 (11.0)	
Other	97 (27.6)	103 (29.9)	

Note: Plus-minus values are mean ± SD. ACE denotes angiotensin-converting enzyme, ACS acute coronary syndrome, ARB angiotensin-receptor blocker, BMI denotes body mass index, PCI percutaneous coronary intervention, NSTEMI non-ST-segment elevation myocardial infarction, STEMI ST-segment elevation myocardial infarction. Numbers based upon all randomized subjects.
*Race was self-reported.
† Body mass index (BMI) is the weight (kg) divided by the square of the height (m).
‡ Creatinine clearance calculated using the Cockcroft-Gault equation.
¥ Aspirin use was calculated as administration of aspirin no more than 4 days after PCI procedure for index event.

Table S5

Baseline Characteristics by Completion Status

Characteristic	Discontinued (N = 525)	Completed (N=1599)	p-value
Demographics			
Age			
Mean ─ yr	71.2 ± 8.7	69.7 ± 9.0	0.001
≥ 65 yr ─ no. (%)	409 (77.9)	1156 (72.3)	0.011
≥ 75 yr ─ no. (%)	202 (38.5)	527 (33.0)	0.021
Female sex ─ no. (%)	148 (28.2)	395 (24.7)	0.112
Race*─ no. (%)			0.582
White	496 (94.5)	1501 (93.9)	
Black or African-American	2 (0.4)	9 (0.6)	
Asian	20 (3.8)	66 (4.1)	
American Indian or Alaska Native	1 (0.2)	0 (0.0)	
Other or unknown	6 (1.1)	23 (1.4)	
BMI†			0.763
Median	28.6	28.7	
Interquartile range	25.7 – 32.4	25.7 ± 32.4	
Active smokers – no. (%)	34 (6.5)	107 (6.7)	0.863
Creatinine clearance ─ ml/min‡			
Mean	74.4 ± 28.8	80.2 ± 31.6	<0.001
< 60 to ≥ 30 ml/min ─ no. (%)	168 (34.9)	397 (25.8)	<0.001
<30 ml/min ─ no. (%)	5 (1.0)	12 (0.8)	0.572
P2Y12 inhibitor at baseline – no. (%)			0.759
Clopidogrel	492 (93.7)	1512 (94.6)	
Prasugrel	8 (1.5)	20 (1.3)	
Ticagrelor	25 (4.8)	67 (4.2)	
Index Event			
Type of Index Event – no. (%)			0.270
NSTEMI	108 (21.1)	274 (17.3)	
STEMI	59 (11.5)	198 (12.5)	
Unstable Angina	105 (20.5)	352 (22.3)	
Type of Stent – no. (%)			0.924
Drug-eluting stent	350 (66.9)	1053 (66.0)	
Bare metal stent	163 (31.2)	512 (32.1)	
Drug-eluting and bare metal stents	10 (1.9)	30 (1.9)	
Urgency of Revascularization – no. (%)			0.841
Elective	325 (61.9)	982 (61.4)	
Urgent	200 (38.1)	617 (38.6)	

Characteristic	Discontinued (N = 525)	Completed (N=1599)	p-value
Type of Atrial Fibrillation ─ no. (%)			0.285
Persistent	108 (20.6)	333 (20.8)	
Permanent	170 (32.4)	573 (35.9)	
Paroxysmal	246 (47.0)	692 (43.3)	
Bleed Risk Scores			
$CHADS_2$ risk of stroke – no. (%)			0.368
0	61 (11.6)	211 (13.2)	
1	158 (30.1)	521 (32.6)	
2	196 (37.3)	579 (36.2)	
3	100 (19.1)	253 (15.8)	
4	10 (1.9)	35 (2.2)	
5	0	0	
6	0	0	
CHA_2DS_2-VASc risk of stroke – no. (%)			0.260
0	5 (1.0)	23 (1.4)	
1	38 (7.2)	137 (8.6)	
2	71 (13.5)	230 (14.4)	
3	90 (17.1)	305 (19.1)	
4	108 (20.6)	357 (22.3)	
5	115 (21.9)	313 (19.6)	
6	77 (14.7)	192 (12.0)	
7	21 (4.0)	42 (2.6)	
HAS Bled Score – no. (%)			0.242
0	1 (0.2)	3 (0.2)	
1	26 (5.0)	71 (4.4)	
2	120 (22.9)	410 (25.6)	
3	225 (42.9)	698 (43.7)	
4	125 (23.8)	349 (21.8)	
5	25 (4.8)	67 (4.2)	
6	3 (0.6)	1 (0.1)	
Comorbidities			
Congestive heart failure	130 (24.8)	412 (25.8)	0.647
Hypertension	386 (73.5)	1185 (74.1)	0.791
Diabetes mellitus	170 (32.4)	454 (28.4)	0.082
Hypercholesterolemia	213 (40.6)	700 (43.8)	0.198
Previous myocardial infarction	129 (24.6)	348 (21.8)	0.181
Peripheral vascular disease	37 (7.1)	70 (4.4)	0.015
Gastrointestinal bleeding	5 (1.0)	16 (1.0)	0.923
Medications			
Aspirin[¥]	364 (69.3)	1055 (70.0)	0.157
Beta-blocker	415 (79.1)	1249 (78.1)	0.651

Characteristic	Discontinued (N = 525)	Completed (N=1599)	p-value
ACE inhibitor or ARB	393 (74.9)	1247 (78.0)	0.138
Statin	419 (79.8)	1286 (80.4)	0.758
Proton pump inhibitor			0.087
Omeprazole or esomeprazole	56 (10.7)	175 (10.9)	
Other	162 (30.9)	415 (26.0)	

Note: Plus-minus values are mean ± SD. ACE denotes angiotensin-converting enzyme, ACS acute coronary syndrome, ARB angiotensin-receptor blocker, BMI denotes body mass index, PCI percutaneous coronary intervention, NSTEMI non-ST-segment elevation myocardial infarction, STEMI ST-segment elevation myocardial infarction. Numbers based upon all randomized subjects.
*Race was self-reported.
† Body mass index (BMI) is the weight (kg) divided by the square of the height (m).
‡ Creatinine clearance calculated using the Cockcroft-Gault equation.
¥ Aspirin use was calculated as administration of aspirin no more than 4 days after PCI procedure for index event.

Table S6

Primary Reason for Early Discontinuation from Treatment Period

Reason	Group 1 (N=696)	Group 2 (N=706)	Combined (N=1402)	Group 3 (N=697)	**Group 1 vs. Group 3** Rivaroxaban *plus* $P2Y_{12}$ Inhibitor vs. VKA *plus* DAPT **p-value**	**Group 2 vs. Group 3** Rivaroxaban *plus* DAPT vs. VKA *plus* DAPT **p-value**	**Combined vs. Group 3 p-value**
Completed treatment period	550 (79.0)	557 (78.9)	1107 (78.9)	492 (70.6)	<0.001	<0.001	<0.001
Early Discontinued	146 (21.0)	149 (21.1)	295 (21.0)	205 (29.4)			
Adverse Event	87 (12.5)	75 (10.6)	162 (11.6)	76 (10.9)	0.354	0.865	0.658
Bleeding Adverse Event	33 (4.7)	32 (4.5)	65 (4.6)	44 (6.3)	0.199	0.141	0.103
Death	20 (2.9)	22 (3.1)	42 (3.0)	22 (3.2)	0.758	0.966	0.840
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Noncompliance with study drug	5 (0.7)	8 (1.1)	13 (0.9)	16 (2.3)	0.016	0.093	0.011
Physician decision	8 (1.1)	5 (0.7)	13 (0.9)	12 (1.7)	0.369	0.083	0.114
Pregnancy	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Protocol violation	3 (0.4)	7 (1.0)	10 (0.7)	7 (1.0)	0.342	0.981	0.484
Study terminated by sponsor	0 (0.0)	1 (0.1)	1 (<0.1)	2 (0.3)	0.500	0.622	0.258
Subject decision	14 (2.0)	20 (2.8)	34 (2.4)	50 (7.2)	<0.001	<0.001	<0.001
Withdrawal of consent	3 (0.4)	3 (0.4)	6 (0.4)	3 (0.4)	>0.999	>0.999	>0.999
Other	6 (0.9)	8 (1.1)	14 (1.0)	17 (2.4)	0.021	0.065	0.010

Note: This analysis was conducted in the safety population.
Note: Percentages calculated with the number of subjects in each stratum and treatment group as denominator.
Note: Physician Decision: Physician has decided to discontinue subject from study treatment, however, subject will allow Month 12 follow up.
Note: Subject Decision: Subject no longer wants to participate in the study, but will allow Month 12 follow-up.
Note: Withdrawal of Consent: Subject no longer wants to participate in the study and will NOT allow Month 12 follow up.

Table S7

Time in Therapeutic Range (TTR) by Region

INR range	Total (N=651)	North America (N=60)	Latin America (N=43)	West Europe (N=237)	East Europe (N=276)	Asia Pacific (N=35)	Overall P-value
< 2.0	22.3 (21.8)	24.8 (24.4)	25.0 (24.3)	21.0 (20.8)	22.2 (22.1)	24.1 (16.9)	0.63
≥ 2.0 to < 3.0	65.0 (24.8)	60.7 (25.7)	64.4 (23.9)	64.4 (24.5)	66.6 (25.4)	63.6 (20.9)	0.53
≥ 3.0	12.8 (16.7)	14.5 (17.6)	10.6 (10.5)	14.6 (18.9)	11.2 (15.7)	12.2 (12.1)	0.15

Note: To adjust for subjects reaching the therapeutic range of VKA, the INR values in the first 14 days after the first dose of study drug are excluded from the analysis.
Note: The TTR values are expressed as mean (SD).
Note: Overall P-value is calculated by the one-way ANOVA test.
Note: Pairwise comparisons using West Europe as the reference: P = 0.02 for East Europe (INR ≥ 3.0); P = NS for all other comparisons.

Table S8

First Occurrence of Clinically Significant Bleeding Events (ITT Analysis)

			Event Rate		Group 1 vs. Group 3 Rivaroxaban *plus* $P2Y_{12}$ Inhibitor **vs.** VKA *plus* DAPT		Group 2 vs. Group 3 Rivaroxaban *plus* DAPT **vs.** VKA *plus* DAPT		Combined vs. Group 3	
	Group 1	**Group 2**	**Combined**	**Group 3**	**RR (95% CI)**	**p-value***	**RR (95% CI)**	**p-value***	**RR (95% CI)**	**p-value***
Overall	N= 709	N= 709	N=1418	N= 706						
Clinically Significant Bleeding	113 (15.9)	118 (16.6)	231 (16.3)	170 (24.0)	0.66 (0.53-0.82)	<.0001	0.69 (0.56-0.85)	<0.001	0.68 (0.57-0.81)	<.0001
TIMI Major	15 (2.1)	13 (1.8)	28 (2.0)	21 (3.0)	0.71 (0.37-1.37)	0.305	0.62 (0.31-1.22)	0.161	0.67 (0.38-1.16)	0.150
TIMI Minor	7 (1.0)	7 (1.00)	14 (1.0)	14 (2.0)	0.50 (0.20-1.23)	0.122	0.50 (0.20-1.23)	0.122	0.50 (0.24-1.04)	0.059
BRMA	96 (13.5)	102 (14.4)	198 (14.0)	141 (19.9)	0.68 (0.53-0.86)	0.001	0.72 (0.57-0.91)	0.005	0.70 (0.58-0.85)	<0.001

Note: Cochran–Mantel–Haenszel p-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA).
Note: Clinically Significant Bleeding is a composite of TIMI Major bleeding, TIMI minor bleeding, and BRMA.
Note: BRMA = Bleed requiring medical attention, TIMI = Thrombolysis in myocardial infarction.
Note: Planned treatment was used for this analysis.
Note: A combination of CEC adjudicated events inside the open-label treatment period and *patient* reported events outside the open label period through end of study (EOS) + 2 days and who discontinued drug early were counted in this analysis.

Table S9

Primary Safety Endpoint and its Components – Event Rates

	Overall				DAPT – 1 month		DAPT – 6 months		DAPT – 12 months	
	Group 1 Rivaroxaban *plus* $P2Y_{12}$ Inhibitor	Group 2 Rivaroxaban *plus* DAPT	Combined	Group 3 VKA *plus* DAPT	Group 2 Rivaroxaban *plus* DAPT	Group 3 VKA *plus* DAPT	Group 2 Rivaroxaban *plus* DAPT	Group 3 VKA *plus* DAPT	Group 2 Rivaroxaban *plus* DAPT	Group 3 VKA *plus* DAPT
Endpoint	**N= 696**	**N= 706**	**N=1402**	**N= 697**	**N=108**	**N=113**	**N=248**	**N=243**	**N=350**	**N=341**
Clinically significant bleeding	109 (15.7)	117 (16.6)	226 (16.1)	167 (24.0)	19 (17.6)	27 (23.9)	39 (15.7)	68 (28.0)	59 (16.9)	72 (21.1)
TIMI major	14 (2.0)	12 (1.7)	26 (1.9)	20 (2.9)	1 (0.9)	5 (4.4)	7 (2.8)	9 (3.7)	4 (1.1)	6 (1.8)
TIMI minor	7 (1.0)	7 (1.0)	14 (1.0)	13 (1.9)	1 (0.9)	2 (1.8)	1 (0.4)	6 (2.5)	5 (1.4)	5 (1.5)
BRMA	93 (13.4)	102 (14.4)	195 (13.9)	139 (19.9)	18 (16.7)	21 (18.6)	32 (12.9)	56 (23.0)	52 (14.9)	62 (18.2)

Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Note: Primary safety endpoint (Clinically significant bleeding) is the composite of TIMI major, TIMI minor, and BRMA events.
Note: Log-Rank p-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.
Note: BRMA = Bleed requiring medical attention, TIMI = Thrombolysis in myocardial infarction, CI = Confidence Interval, DAPT = Dual Antiplatelet Therapy, HR = Hazard Ratio, VKA = Vitamin K Antagonist.

Table S10

Primary Safety Endpoint and its Components (Investigator Reported Events)

	Kaplan Meier Estimates				**Group 1 vs. Group 3** Rivaroxaban *plus* $P2Y_{12}$ Inhibitor **vs.** VKA *plus* DAPT		**Group 2 vs. Group 3** Rivaroxaban *plus* DAPT **vs.** VKA *plus* DAPT		**Combined vs. Group 3**	
	Group 1	**Group 2**	**Combined**	**Group 3**	**HR (95% CI)**	**p-value***	**HR (95% CI)**	**p-value***	**HR (95% CI)**	**p-value***
Overall	N= 696	N= 706	N=1402	N= 697						
Clinically significant bleeding	105 (16.3)	96 (14.8)	201 (15.6)	144 (23.1)	0.68 (0.53 - 0.87)	0.002	0.61 (0.47 - 0.79)	<0.001	0.64 (0.52 - 0.80)	<0.001
TIMI major	15 (2.3)	7 (1.1)	22 (1.7)	20 (3.3)	0.71 (0.36 - 1.39)	0.312	0.33 (0.14 - 0.78)	0.008	0.51 (0.28 - 0.94)	0.028
TIMI minor	20 (3.1)	20 (3.2)	40 (3.1)	22 (3.6)	0.87 (0.47 - 1.59)	0.650	0.86 (0.47 - 1.57)	0.612	0.86 (0.51 - 1.45)	0.572
BRMA	74 (11.9)	74 (11.5)	148 (11.7)	107 (17.6)	0.64 (0.48 - 0.86)	0.003	0.64 (0.47 - 0.86)	0.003	0.64 (0.50 - 0.82)	<0.001
DAPT – 1 month		N= 108		N= 113						
Clinically significant bleeding		16 (16.5)		27 (25.8)			0.57 (0.31 - 1.05)	0.069		
TIMI major		1 (1.1)		7 (7.1)			0.14 (0.02 - 1.12)	0.030		
TIMI minor		3 (3.1)		6 (5.9)			0.49 (0.12 - 1.97)	0.306		
BRMA		14 (14.6)		15 (14.9)			0.92 (0.44 - 1.91)	0.824		
DAPT – 6 months		N= 248		N= 243						
Clinically significant bleeding		31 (13.9)		57 (26.4)			0.49 (0.32 - 0.76)	0.001		
TIMI major		3 (1.4)		7 (3.4)			0.41 (0.11 - 1.58)	0.178		
TIMI minor		6 (2.8)		7 (3.3)			0.82 (0.27 - 2.43)	0.716		
BRMA		23 (10.4)		45 (21.1)			0.47 (0.28 - 0.77)	0.002		

DAPT – 12 months		N= 350		N= 341						
Clinically significant bleeding		49 (14.9)		60 (20.0)			0.74 (0.51 - 1.08)	0.118		
TIMI major		3 (1.0)		6 (2.0)			0.45 (0.11 - 1.81)	0.248		
TIMI minor		11 (3.4)		9 (3.1)			1.12 (0.46 - 2.69)	0.806		
BRMA		37 (11.4)		47 (16.1)			0.71 (0.46 - 1.09)	0.116		

Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Note: Primary safety endpoint (Clinically significant bleeding) is the composite of TIMI major, TIMI minor, and BRMA events.
Note: A subject could have more than one component event. n = number of subjects with events, N = number of subjects at risk, % represents KM estimate at the end of study.
Note: Hazard ratios as compared to the VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Note: Log-Rank p-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.
Note: BRMA = Bleed requiring medical attention, TIMI = Thrombolysis in myocardial infarction, CI = Confidence Interval, DAPT = Dual Antiplatelet Therapy, HR = Hazard Ratio, VKA = Vitamin K Antagonist.
Note: 6 subjects from one site were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines.

Table S11

Bleeding Events according to Bleeding Classifications

	Group 1 (N=696)	**Group 2 (N=706)**	**Combined (N=1402)**	**Group 3 (N=697)**	**Group 1 vs. Group 3** Rivaroxaban *plus* $P2Y_{12}$ Inhibitor vs. VKA *plus* DAPT **p-value**	**Group 2 vs. Group 3** Rivaroxaban *plus* DAPT vs. VKA *plus* DAPT **p-value**	**Combined vs. Group 3 p-value**
Total Fatal Bleeds	2 (0.3)	2 (0.3)	4 (0.3)	6 (0.9)	0.288	0.176	0.092
TIMI Classification							
Overall Clinically Significant Bleeding	109 (15.7)	117 (16.6)	226 (16.1)	167 (24.0)	<0.001	<0.001	<0.001
TIMI Major Bleeding	14 (2.0)	12 (1.7)	26 (1.9)	20 (2.9)	0.300	0.142	0.135
TIMI Minor Bleeding	7 (1.0)	7 (1.0)	14 (1.0)	13 (1.9)	0.178	0.168	0.097
Bleeding Requiring Medical Attention	93 (13.4)	102 (14.5)	195 (13.9)	139 (19.9)	0.001	0.006	<0.001
Insignificant Bleeding	126 (18.1)	152 (21.5)	278 (19.8)	167 (24.0)	0.007	0.278	0.029
ISTH Classification							
Major Bleeding	27 (3.9)	25 (3.5)	52 (3.7)	48 (6.9)	0.013	0.005	0.001
Hemoglobin Drop*	21 (3.0)	19 (2.7)	40 (2.9)	34 (4.9)	0.075	0.032	0.018
Transfusion†	15 (2.2)	13 (1.8)	28 (2.0)	15 (2.2)	0.997	0.677	0.813
Critical Organ Bleeding‡	6 (0.9)	5 (0.7)	11 (0.8)	11 (1.6)	0.224	0.125	0.093
Death	2 (0.3)	2 (0.3)	4 (0.3)	5 (0.7)	0.452	0.285	0.167
Clinically Relevant Non-major Bleeding	90 (12.9)	97 (13.7)	187 (13.3)	130 (18.7)	0.003	0.013	0.001
Minimal Bleeding	123 (17.7)	151 (21.4)	274 (19.5)	163 (23.4)	0.008	0.369	0.041
GUSTO Classification							
Severe	7 (1.0)	10 (1.4)	17 (1.2)	20 (2.9)	0.012	0.060	0.007
Moderate	13 (1.9)	10 (1.4)	23 (1.6)	9 (1.3)	0.388	0.839	0.539
Mild	193 (27.7)	214 (30.3)	407 (29.0)	255 (36.6)	<0.001	0.013	<0.001
BARC Classification							
Type 0	9 (1.3)	14 (2.0)	23 (1.6)	10 (1.4)	0.820	0.428	0.721
Type 1	125 (18.0)	153 (21.7)	278 (19.8)	167 (24.0)	0.006	0.307	0.029
Type 2	92 (13.2)	91 (12.9)	183 (13.1)	126 (18.1)	0.013	0.007	0.002
Type 3a	8 (1.2)	7 (1.0)	15 (1.1)	12 (1.7)	0.369	0.237	0.212
Type 3b	13 (1.9)	16 (2.3)	29 (2.1)	26 (3.7)	0.035	0.108	0.025
Type 3c	2 (0.3)	5 (0.7)	7 (0.5)	4 (0.6)	0.687	>0.999	0.760
Type 4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Type 5a	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	>0.999	0.497	.554
Type 5b	1 (0.1)	2 (0.3)	3 (0.2)	7 (1.0)	0.070	0.106	0.019

Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Note: BARC denotes Bleeding Academic Research Consortium, GUSTO Global Utilization Of Streptokinase and Tpa For Occluded Arteries, ISTH International Society on Thrombosis and Haemostasis, TIMI Thrombolysis in Myocardial Infarction.
* Hemoglobin drop = a fall in hemoglobin of 2 g/dL or more.
† Transfusion = a transfusion of 2 or more units of packed red blood cells or whole blood.
‡ Critical organ bleeding are cases where *investigator*-reported bleeding site is either intracranial, intraspinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome or retroperitoneal.

Table S12

First Occurrence of Major Adverse Cardiovascular Events (ITT Analysis)

			Event Rate		Group 1 vs. Group 3 Rivaroxaban *plus* $P2Y_{12}$ Inhibitor **vs.** VKA *plus* DAPT		Group 2 vs. Group 3 Rivaroxaban *plus* DAPT **vs.** VKA *plus* DAPT		Combined vs. Group 3	
	Group 1	**Group 2**	**Combined**	**Group 3**	**RR (95% CI)**	**p-value***	**RR (95% CI)**	**p-value***	**RR (95% CI)**	**p-value***
Overall	N= 707	N= 707	N=1414	N= 704						
CV Death, MI, Stroke	46 (6.5)	42 (5.9)	88 (6.2)	45 (6.4)	1.02 (0.68-1.51)	0.930	0.93 (0.62-1.40)	0.725	0.98 (0.69-1.38)	0.890
CV Death	19 (2.7)	16 (2.3)	35 (2.5)	18 (2.6)	1.05 (0.56-1.99)	0.878	0.89 (0.46-1.72)	0.719	0.97 (0.55-1.70)	0.916
MI	19 (2.7)	21 (3.0)	40 (2.8)	25 (3.6)	0.76 (0.42-1.36)	0.351	0.84 (0.47-1.48)	0.539	0.80 (0.49-1.31)	0.369
Stroke	10 (1.4)	13 (1.8)	23 (1.6)	10 (1.4)	1.00 (0.42-2.38)	0.992	1.29 (0.57-2.93)	0.535	1.15 (0.55-2.40)	0.714

*Cochran–Mantel–Haenszel P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA).
Note: 6 patients from one site were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines.
Note: Intent – to –Treat population is defined as the combination of CEC adjudicated events inside the open-label treatment period and *patient* reported events outside the open label period through end of study (EOS) + 2 days.

Table S13

Major Adverse Cardiovascular Events – Event Rates

	Overall			DAPT – 1 month		DAPT – 6 months		DAPT – 12 months	
	Group 1 Rivaroxaban *plus* $P2Y_{12}$ inhibitor	Group 2 Rivaroxaban *plus* DAPT	Group 3 VKA *plus* DAPT	Group 2 Rivaroxaban *plus* DAPT	Group 3 VKA *plus* DAPT	Group 2 Rivaroxaban *plus* DAPT	Group 3 VKA *plus* DAPT	Group 2 Rivaroxaban *plus* DAPT	Group 3 VKA *plus* DAPT
Endpoint	**N= 694**	**N= 704**	**N= 695**	**N=108**	**N=112**	**N=248**	**N=243**	**N=348**	**N=340**
Adverse CV Events	41 (5.9)	36 (5.1)	36 (5.2)	6 (5.6)	5 (4.5)	16 (6.5)	9 (3.7)	14 (4.0)	22 (6.5)
CV Death	15 (2.2)	14 (2.0)	11 (1.6)	2 (1.9)	2 (1.8)	6 (2.4)	4 (1.6)	6 (1.7)	5 (1.5)
MI	19 (2.7)	17 (2.4)	21 (3.0)	3 (2.8)	1 (0.9)	7 (2.8)	6 (2.5)	7 (2.0)	14 (4.1)
Stroke	8 (1.2)	10 (1.4)	7 (1.0)	2 (1.9)	3 (2.7)	6 (2.4)	0 (0.0)	2 (0.6)	4 (1.2)
Stent Thrombosis	5 (0.7)	6 (0.9)	4 (0.6)	2 (1.9)	1 (0.9)	4 (1.6)	1 (0.4)	0 (0.0)	2 (0.6)
Adverse CV Events + Stent Thrombosis	41 (5.9)	36 (5.1)	36 (5.2)	6 (5.6)	5 (4.5)	16 (6.5)	9 (3.7)	14 (4.0)	22 (6.5)

Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Note: Composite of adverse CV events is composite of CV death, MI, and stroke.
Note: A subject could have more than one component event. n = number of subjects with events, N = number of subjects at risk.
Note: 6 subjects from one site were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines.
Note: CV = Cardiovascular, MI = Myocardial Infarction, CI = Confidence Interval, DAPT = Dual Antiplatelet Therapy, HR = Hazard Ratio, VKA = Vitamin K Antagonist.

Table S14

Major Adverse Cardiovascular Events (Investigator Reported Events)

	Kaplan-Meier Estimates			**Group 1 vs. Group 3** Rivaroxaban *plus* $P2Y_{12}$ Inhibitor **vs.** VKA *plus* DAPT		**Group 2 vs. Group 3** Rivaroxaban *plus* DAPT **vs.** VKA *plus* DAPT	
	Group 1	**Group 2**	**Group 3**	**HR (95% CI)**	**p-value***	**HR (95% CI)**	**p-value***
Overall	N= 694	N= 704	N= 695				
Adverse CV Events	41 (6.4)	31 (4.8)	32 (5.3)	1.21 (0.76 - 1.92)	0.420	0.91 (0.55 - 1.49)	0.703
CV Death	15 (2.4)	14 (2.2)	10 (1.7)	1.41 (0.63 - 3.15)	0.395	1.31 (0.58 - 2.94)	0.516
MI	17 (2.7)	11 (1.7)	14 (2.3)	1.15 (0.57 - 2.33)	0.698	0.74 (0.34 - 1.63)	0.452
Stroke	11 (1.8)	10 (1.5)	10 (1.7)	1.03 (0.44 - 2.44)	0.937	0.94 (0.39 - 2.26)	0.895
Stent Thrombosis	6 (0.9)	5 (0.7)	3 (0.5)	1.90 (0.47 - 7.60)	0.356	1.60 (0.38 - 6.69)	0.516
Adverse CV Events + Stent thrombosis	41 (6.4)	31 (4.8)	32 (5.3)	1.21 (0.76 - 1.92)	0.420	0.91 (0.55 - 1.49)	0.703
DAPT – 1 month		N= 108	N= 112				
Adverse CV Events		5 (4.9)	4 (4.2)			1.23 (0.33 - 4.57)	0.76
CV Death		2 (2.1)	2 (2.2)			0.96 (0.13 - 6.8)	0.966
MI		1 (0.9)	0 (0.0)			-	0.306
Stroke		2 (1.9)	3 (3.1)			0.65 (0.11 - 3.91)	0.639
Stent Thrombosis		2 (1.9)	0 (0.0)			-	0.155
Adverse CV Events + Stent thrombosis		5 (4.9)	4 (4.2)			1.23 (0.33 - 4.57)	0.76
DAPT – 6 months		N= 248	N= 243				
Adverse CV Events		15 (6.6)	7 (3.3)			2.07 (0.85 - 5.08)	0.103
CV Death		6 (2.8)	4 (1.9)			1.45 (0.41 - 5.14)	0.563

MI		6 (2.6)	2 (0.9)			2.94 (0.59 - 14.57)	0.166
Stroke		6 (2.7)	2 (1.0)			2.89 (0.58 - 14.33)	0.173
Stent Thrombosis		3 (1.3)	1 (0.4)			2.94 (0.31 - 28.22)	0.328
Adverse CV Events + Stent thrombosis		15 (6.6)	7 (3.3)			2.07 (0.85 - 5.08)	0.103
DAPT – 12 months		N= 348	N= 340				
Adverse CV Events		11 (3.5)	21 (7.1)			0.47 (0.23 - 0.98)	0.038
CV Death		6 (1.9)	4 (1.4)			1.34 (0.38 - 4.76)	0.646
MI		4 (1.3)	12 (4.1)			0.30 (0.10 - 0.92)	0.025
Stroke		2 (0.6)	5 (1.7)			0.37 (0.07 - 1.88)	0.209
Stent Thrombosis		0 (0.0)	2 (0.7)			-	0.132
Adverse CV Events + Stent thrombosis		11 (3.5)	21 (7.1)			0.47 (0.23 - 0.98)	0.038

Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Note: Composite of adverse CV events is composite of CV death, MI, and stroke.
Note: A subject could have more than one component event. n = number of subjects with events, N = number of subjects at risk, % represents KM estimate at the end of the study.
Note: Hazard ratios as compared to VKA group are based on the (stratified, only for the 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Note: Log-Rank p-values as compared to the VKA group are based on the (stratified, only for the 2.5 mg BID/115 mg QD comparing VKA) two-sided log rank test.
Note: All of the 15 stent thrombotic events occurred on the same day as another cardiovascular event (CV Death, MI, Stroke).
Note: 6 subjects from one site were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines.
Note: CV = Cardiovascular, MI = Myocardial Infarction, CI = Confidence Interval, DAPT = Dual Antiplatelet Therapy, HR = Hazard Ratio, VKA = Vitamin K Antagonist.

Table S15

Kaplan-Meier Estimates, Hazard Ratio and 95% Confidence Interval for Time to the First Occurrence of Overall Stroke and its Components

	Event Rate			**Group 1 vs. Group 3** Rivaroxaban *plus* $P2Y_{12}$ Inhibitor **vs.** VKA *plus* DAPT		**Group 2 vs. Group 3** Rivaroxaban *plus* DAPT **vs.** VKA *plus* DAPT	
	Group 1	**Group 2**	**Group 3**	**HR (95% CI)**	**p-value***	**HR (95% CI)**	**p-value***
Overall	N= 694	N= 704	N= 695				
Overall Stroke	8 (1.3)	10 (1.5)	7 (1.2)	1.07 (0.39 - 2.96)	0.891	1.36 (0.52 - 3.58)	0.530
Ischemic Stroke	7 (1.2)	6 (0.9)	2 (0.3)	3.28 (0.68 – 15.78)	0.117	2.87 (0.58 – 14.23)	0.176
Ischemic Stoke with hemorrhagic transformation	0 (0.0)	1 (0.1)	1 (0.1)	-	0.318	0.97 (0.06 – 15.50)	0.983
Primary Hemorrhagic Stroke	1 (0.2)	2 (0.3)	3 (0.5)	0.31 (0.03 – 3.00)	0.286	0.63 (0.11 – 3.79)	0.614
Uncertain Stroke	0 (0.0)	1 (0.2)	1 (0.2)	-	0.296	0.93 (0.06 – 14.83)	0.957
DAPT 1 Month		N= 108	N= 112				
Overall Stroke	-	2 (1.9)	3 (3.1)	-	-	0.65 (0.11 – 3.91)	0.639
Ischemic Stroke	-	2 (1.9)	0 (0.0)	-	-	-	0.160
Ischemic Stoke with hemorrhagic transformation	-	0 (0.0)	0 (0.0)	-	-	-	-
Primary Hemorrhagic Stroke	-	0 (0.0)	2 (2.0)	-	-	-	0.152
Uncertain Stroke	-	0 (0.0)	1 (1.2)	-	-	-	0.312
DAPT 6 Months		N= 248	N= 243				
Overall Stroke	-	6 (2.7)	0 (0.0)	-	-	-	0.016
Ischemic Stroke	-	3 (1.4)	0 (0.0)	-	-	-	0.089

Ischemic Stoke with hemorrhagic transformation	-	1 (0.4)	0 (0.0)	-	-	-	0.327
Primary Hemorrhagic Stroke	-	2 (0.9)	0 (0.0)	-	-	-	0.164
Uncertain Stroke	-	0 (0.0)	0 (0.0)	-	-	-	-
DAPT 12 Months		N= 348	N= 340				
Overall Stroke	-	2 (0.6)	4 (1.3)	-	-	0.46 (0.08 – 2.51)	0.357
Ischemic Stroke	-	1 (0.3)	2 (0.6)	-	-	0.47 (0.04 – 5.13)	0.522
Ischemic Stoke with hemorrhagic transformation	-	0 (0.0)	1 (0.3)	-	-	-	0.312
Primary Hemorrhagic Stroke	-	0 (0.0)	1 (0.4)	-	-	-	0.284
Uncertain Stroke	-	1 (0.3)	0 (0.0)	-	-	-	0.349

Note: Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Note: A subject could have more than one component event. n = number of subjects with events, N = number of subjects at risk, % represents KM estimate at the end of the study.
Note: Log-Rank p-values as compared to the VKA group are based on the two-sided log rank test.
Note: 6 subjects from one site were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines.