SUPPLEMENTARY DATA

Appendix A. CHA_2DS_2-VASc and HAS-BLED scores calculations.

The CHA_2DS_2-VASc score was calculated by assigning 1 point for congestive heart failure/left ventricular dysfunction, hypertension/uncontrolled hypertension, diabetes mellitus, vascular disease (coronary artery disease, previous myocardial infarction, peripheral artery disease, or complex aortic plaque), age 65-74 and female sex [1 point each]; and 2 points for prior stroke/transient ischemic attack (TIA)/thromboembolism and age ≥75. The HAS-BLED score was calculated by assigning 1 point (each) for hypertension, abnormal renal or liver function (1 point each), stroke, bleeding history or predisposition to bleeding, age ≥65 years, medications predisposing to bleeding (antiplatelets or non-steroidal anti-inflammatory drugs), and alcohol use. Based on the characteristics of the cohort at entry (see inclusion criteria), the baseline labile INR criterion was quantified as 0 in all patients.[1, 2]

Appendix B. Primary outcomes definitions.

The primary endpoints were ischemic strokes/transient ischemic attacks (TIAs) and major bleeding. Ischemic stroke was defined as the sudden onset of a focal neurologic deficit in a location consistent with the territory of a major cerebral artery resulting from an obstruction documented by imaging, surgical intervention, or autopsy. TIA was defined as a transient episode of neurologic dysfunction due to the focal brain, spinal cord, or retinal ischemia, without acute infarction or tissue injury, typically lasting less than an hour. Major bleeding was defined as a fatal bleeding, and/or symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome, and/or bleeding causing a fall in hemoglobin levels of 1.24 mmol/L (≥20 g/L) or more, or leading to a

transfusion of ≥2 units of whole blood or red cells, based on 2005 International Society on Thrombosis and Haemostasis (ISTH) criteria.[3] The investigators identified, confirmed, and recorded all clinical outcomes.

Appendix C. Primary outcomes and predictive abilities.

Of the 156 (11.5%) patients who suffered an ischemic stroke/TIA, 57 (4.2%) suffered it during the period from the inclusion to 2-year, 60 (4.4%) had the ischemic stroke/TIA during the period from 2 to 4-years, and 39 (2.9%) patients suffered the outcome during the period from 4 to 6-years. Also, of the 269 (19.8%) patients who suffered a major bleeding, 86 (6.3%) patients suffered the bleeding event during the period from baseline to 2-year, while 135 (9.9%) experienced the major bleeding during the period from 2 to 4-year, and 72 (5.3%) had it during the period from 4 to 6-years.

Table 1 of the supplementary data.

Incidence rate and unadjusted incidence rate ratio of the different clinical outcomes among periods.

	First period (from inclusion to 2-years)		**Second period (from 2 to 4-years)**		**Third period (from 4 to 6-years)**		**Incidence rate ratio 2-year *vs*. 4-year**		**Incidence rate ratio 4-year *vs*. 6-year**	
	Person-Year	**Incidence rate (95%CI)**	**Person-Year**	**Incidence rate (95%CI)**	**Person-Year**	**Incidence rate (95%CI)**	**IRR (95 % CI)**	**p-value**	**IRR (95 % CI)**	***P***
Ischemic stroke/TIA	114	2.09 (1.59-2.71)	120	2.44 (1.86-3.14)	78	1.84 (1.31-2.51)	0.86 (0.59-1.26)	0.414	1.33 (0.87-2.04)	.168
Major bleeding	172	3.16 (2.53-3.90)	270	5.48 (4.60-6.49)	144	3.39 (2.65-4.27)	0.57 (0.43-0.76)	<0.001	1.62 (1.21-2.18)	< .001
Mortality	260	4.78 (4.00-5.67)	338	6.86 (5.87-7.98)	346	8.15 (6.98-9.45)	0.69 (0.55-0.88)	0.002	0.84 (0.68-1.05)	.114

Table 2 of the supplementary data.

Risk of ischemic stroke/TIA of baseline and dynamic CHA_2DS_2-VASc scores based on Cox regression analyses.

	Hazard Ratio	95%CI	*P*
Univariate analyses			
Baseline CHA_2DS_2-VASc	1.41	1.28-1.56	< .001
CHA_2DS_2-VASc at 2-years	1.69	1.52-1.88	< .001
CHA_2DS_2-VASc at 4-years	2.13	1.86-2.43	< .001
Multivariate analyses			
Baseline CHA_2DS_2-VASc	1.14	0.99-1.32	.069
CHA_2DS_2-VASc at 2-years	1.69	1.46-1.96	< .001
CHA_2DS_2-VASc at 4-years	2.31	1.96-2.73	< .001

Covariates included in multivariate models: baseline age, sex, history of prior ischemic stroke.

Table 3 of the supplementary data.

Risk of major bleeding of baseline and dynamic HAS-BLED scores based on Cox regression analyses.

	Hazard Ratio	**95%CI**	***P***
Univariate analyses			
Baseline HAS-BLED	1.74	1.59-1.90	< .001
HAS-BLED at 2-years	2.01	1.81-2.24	< .001
HAS-BLED at 4-years	2.22	1.96-2.51	< .001
Multivariate analyses			
Baseline HAS-BLED	1.13	1.01-1.28	.040
HAS-BLED at 2-years	1.31	1.14-1.50	< .001
HAS-BLED at 4-years	1.63	1.40-1.89	< .001

Covariates included in multivariate models: baseline age, sex, history of prior bleeding.

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3. Schulman S, Kearon C. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. *J Thromb Haemost.* 2005;3:692-694.