SUPPLEMENTAL MATERIAL:

(1) Inclusion and exclusion criteria
(2) Committees
(3) Study assessments (Supplemental Methods)
(4) Figure S1: Color consort diagram
(5) Table S1: Reasons for ineligibility
(6) Figures S2A and S2B: Monthly rate of recruitment (A) and cumulative enrolment (B)
(7) Table S2: Sinus involvement by treatment arm
(8) Figure S3: Color graph of delay from timing of diagnosis to randomization
(9) Table S3A, S3B, S3C: Event rates for all define study populations at day 180 (Table S3A) and day 365 (Table S3B), and rates of other events of interest (Table S3C)
(10) Table S4: Estimates of time in therapeutic range

Inclusion and exclusion criteria:

Inclusion

a) Patients aged 18 and above
b) New diagnosis of symptomatic CVT as confirmed on CT/CT venogram (CTV) or MRI/MR venogram (MRV)
c) Ability to randomize within 14 days of neuroimaging-confirmed diagnosis
d) The treating clinician is of the opinion that the patient is appropriate for oral anticoagulation as per standard of care
e) Patient of legally acceptable representative is able to provide signed informed consent

Exclusion

a) Patient has known antiphospholipid antibody syndrome (APLS; lupus anticoagulant, anti-beta 2-glycoprotein I antibodies, and anticardiolipin antibody) by Sapporo-Sydney criteria* with a previous history of venous or arterial thrombosis
b) Patient is anticipated to require invasive procedure (e.g. lumbar puncture, thrombectomy, hemicraniectomy) prior to initiation of oral anticoagulation**
c) Patient is unable to swallow due to depressed level of consciousness†
d) Impaired renal function (i.e., CrCl < 30 mL/min using Cockroft-Gault equation)
e) Pregnancy; if a woman is of childbearing potential a urine or serum beta human chorionic gonadotropin (β-hCG) test is positive
f) Breastfeeding at the time of randomization
g) Bleeding diathesis or other contraindication to anticoagulation
h) Any concurrent medical condition requiring mandatory antiplatelet or anticoagulant use
i) Concomitant use of strong CYP3A4 inducers (e.g., ongoing use of dilantin, carbamazepine, HIV protease inhibitors) or CYP3A4 inhibitors (e.g., diltiazem, ketoconazole)
j) Patient has a severe or fatal comorbid illness that will prevent improvement, or cannot complete follow-up due to the same, or cannot complete follow-up due to co-morbid non-fatal illness, non-residence in the city, or for any other known reason for which follow-up would be impossible.

*At least one *clinical* AND one *laboratory* criterion of:

Clinical: (1) Arterial, venous or small vessel vascular thrombosis, (2) Pregnancy morbidity (one or more unexplained deaths of a morphologically normal fetus at 10 weeks' gestation or later; one or more premature births of a morphologically normal neonate prior to 34 weeks' gestation due to eclampsia, severe pre-eclampsia, or placental insufficiency; or three or more unexplained spontaneous abortions before 10 weeks' gestation with normal maternal anatomic and hormonal and parental chromosomal causes excluded).

Laboratory (present on 2 or more occasions ≥12 weeks apart): (1) Lupus anticoagulant in plasma, (2) Anticardiolipin antibodies (IgG and/or IgM) in serum or plasma in moderate or high titer, (3) Anti-beta2-glycoprotein-I antibody (IgG and/or IgM) in serum or plasma.

**Patients who have received an invasive procedure and/or whose level of consciousness improves such that it does not interfere with their ability to take oral medication may be subsequently enrolled into the trial if the investigator deems that the patient is otherwise eligible within the first 14 days after symptom onset.

†A patient without depressed level of consciousness requiring an NG tube for dysphagia who is otherwise eligible does not meet exclusion criterion b).

Committees:

Steering Committee - Dr. Thalia Field (University of British Columbia, Vancouver, BC), Dr. Michael Hill (University of Calgary, Calgary, AB), Dr. Andrew Demchuk (University of Calgary, Calgary AB), Dr. Dar Dowlatshahi (University of Ottawa, Ottawa, ON), Dr. Sylvain Lanthier (Universite de Montreal, Montreal QC), Dr. Agnes Lee (University of British Columbia, Vancouver BC), Dr. Jennifer Mandzia (University of Western Ontario, London ON), Dr. Deepa Suryanarayan (University of Calgary, Calgary AB), Dr. Jeff Weitz (McMaster University, Hamilton, ON), Dr. Hubert Wong (University of British Columbia, Vancouver BC)

Clinical events adjudication committee - Dr. Oscar Benavente (University of British Columbia, Vancouver, BC), Dr. Stephen Van Gaal (University of British Columbia, Vancouver, BC), Dr. Deepa Suryanarayan (University of Calgary, Calgary AB)

Neuroimaging adjudication committee - Dr. Mohammed Almekhlafi (University of Calgary, Calgary AB), Dr. Fouzi Bala (University of Calgary, Calgary AB), Dr. Ibrahim Alhabli (University of Calgary, Calgary AB)

Data Safety and Monitoring Board- Dr. Kenneth Butcher (University of New South Wales, Sydney, Australia), Dr. Cheryl Bushnell (Duke University, Chapel Hill, North Carolina, USA), Dr. Diana Aguiar de Sousa (Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal), Dr. Hubert Wong (University of British Columbia)

Schedule of assessments and description:

	Screening	Random-ization	Day 30 (±5 d)	Day 90 (±14 d)	Day 180 (±14 d)	Day 365 (±14 d)
Informed consent	X					
Attempt at regained capacity informed consent[Ω]		X	X	X	X	X
History and examination, demographics		X				
Review of risk factors		X	Collected to Day 365 visit*			
Weight		X (Actual)				
Telephone follow-up			X			
Vital Signs (BP, HR, Temp)		X		X	X	X
Randomization/ Study drug administration		X				
Mortality/Vital statistics review			X	X	X	X
NIHSS		X		X	X	X
mRS	X[¶]	X	X	X	X	X
PHQ-9, Fatigue assessment Scale, EQ-5D-5L, HIT-6[#]		X	X	X	X	X
Cognitive assessments[†]		X		X	X	X
CT/CTV, MRI/MRV **	X	X		X^	X	X^^
CBC, INR, aPTT, serum creatinine, blood urea nitrogen and serum glucose	X‡					
Pregnancy test	X‡‡					
Societal costs and health care resource utilization assessment including COVID-19 form (as of Aug 2020)		X	X	X	X	X
AE and SAE assessment		Collected to Day 365 visit + 30 days				
Prior medications	X[§]					
Concomitant medications	Collected to Day 365 visit					

[Ω] For subjects for whom the LAR completed the original consent (and if required), research staff will make ongoing efforts until (1) regained capacity consent is obtained from subject, (2) death, or (3) completion of the Day 365 assessment.

¶ Historical (pre-stroke) score

* Re-review with availability of additional investigations as per the treating physician's clinical judgement (e.g., thrombophilia workup, malignancy workup)

Patient Health Questionnaire-9 (PHQ-9) to assess for depression, Fatigue Assessment Scale, EuroQoL-5-dimensional score (EQ-5D-5L), The Headache Impact Test (HIT-6™)

† NIH Toolkit Cognitive Battery, Montreal Cognitive Assessment (MoCA)©, Boston Cookie theft picture

**CT or MR imaging will be done as per standard of care at the institution. The diagnostic scan can be the randomization scan as long as it is within 72h prior to randomization.

^ At the discretion of the investigator

^^ Day 365 CTV/MRV is not performed if there is complete recanalization on Day 180 scan

‡ Blood should be drawn prior to randomization and then subsequent draws following standard of care at the institution.

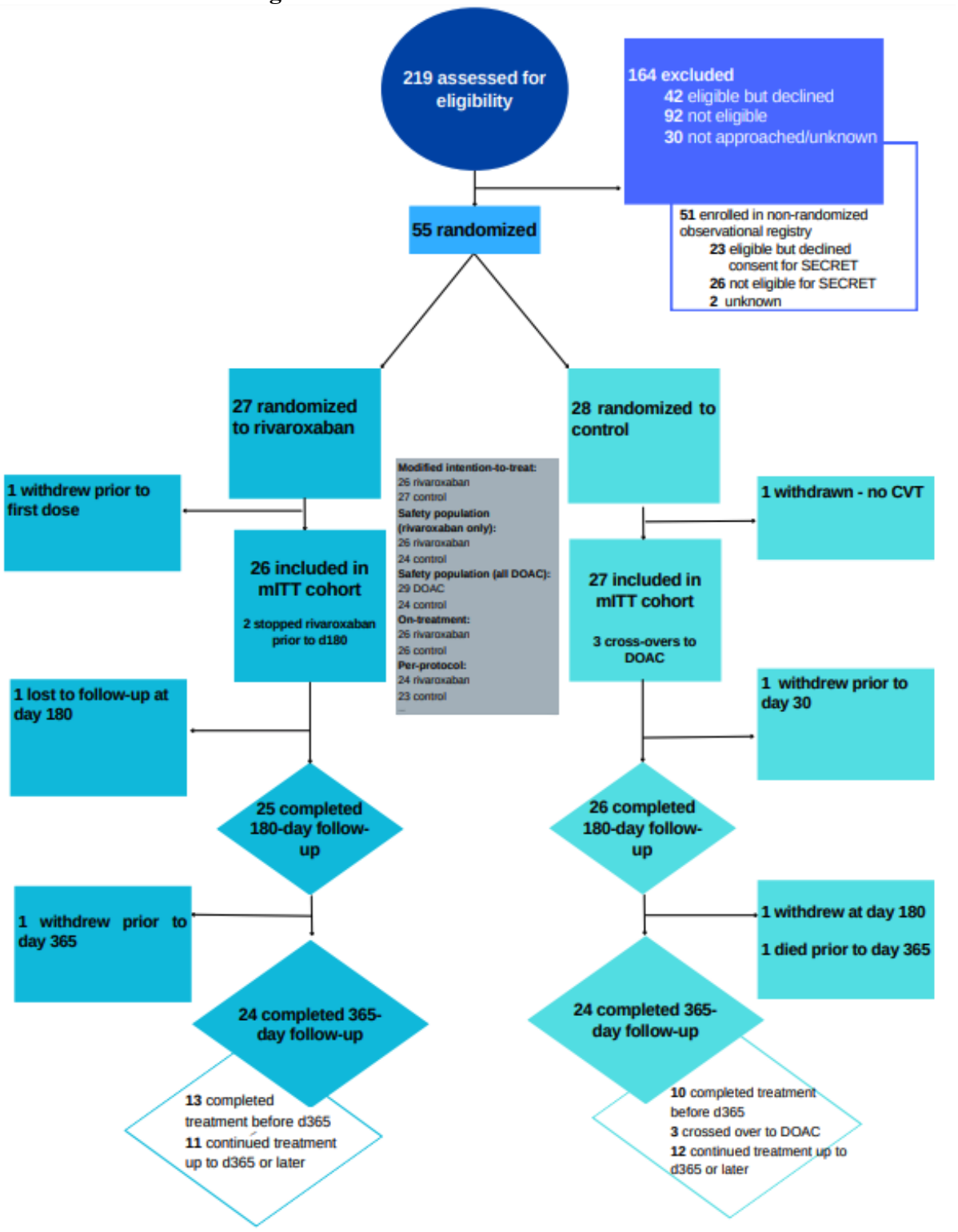
‡‡ If the subject is female and of childbearing potential, a pregnancy test (urine or serum point-of-care pregnancy test) must be completed and the result must be negative in order to be eligible for study participation

[§] Prior medications should be documented prior to randomization.

d = days; h = hours, CTV = CT venogram, MRV = MR venogram

Follow-up visits were at day 30, day 90, day 180 and day 365, with a further safety follow-up visit 30 days after the day 365 follow-up. Prior to the COVID-19 pandemic, only the day 30 visit was intended to be a telephone visit; following resumption of research in the context of the COVID-19 pandemic, all follow-up visits were able to be conducted in-person or remotely. Presenting and past medical history, vitals, standard-of-care blood and concomitant medications were reviewed at the randomization visit. The day 30(+/- 5) phone call reviewed functional outcome as per the mRS, EQ5D-5L, the PHQ-9, the FAS and the HIT-6. Follow-up visits at day 90, 180 and 365 included a vitals assessment if in-person, mRS assessment and repeat administration of the EQ5D-5L, PHQ-9, FAS and HIT-6. All visits included a review for adverse and severe adverse events and concomitant medications. Assessments were by trained personnel who were unaware of the treatment-group assignments. There were no study-specific neuroimaging protocols apart from a parenchymal scan within the 72 hours prior to randomization, timed follow-up vascular neuroimaging at 180 days, and, if complete recanalization had not occurred at 180 days, again at 365 days. Investigators were encouraged to use a consistent neuroimaging modality for follow-up. Recanalization was assessed with standard-of-care vascular neuroimaging (CT venography or contrast-enhanced MR venography) at 180 days, and, if there was not complete recanalization of all vessels, again at day 365. Those participants who discontinued study medication early continued to be followed with usual study assessments unless they withdrew informed consent. Apart from a mandatory pregnancy test at baseline for participants of child-bearing potential, all laboratory investigations were as per standard of care.

Figure S1: Color consort diagram



Supplementary Table S1: Reasons for ineligibility (N = 92)

Reason for ineligibility	**N (%)**
Poor prognosis	9 (9.7)
No CVT	2 (2.2)
Cannot participate in assessments and/or follow-up	7 (7.6)
Outside of two-week window, including chronic CVT	24 (26.1)
Physician preference or indication for a particular antithrombotic strategy	32 (34.8)
Age < 18	1 (1.1)
Depressed level of consciousness	3 (3.3)
Planned invasive procedure/surgery	3 (3.3)
Met criteria for Vaccine-Induced Thrombosis with Thrombocytopenia (VITT) or post-vaccination CVT[28]	10 (10.9%; 6 VITT; 4 post-vaccination non-VITT)

Figures S2A and S2B:
Monthly rate of recruitment (A) and cumulative enrolment (B).
Research operations and recruitment were disrupted nationally following public health orders related to the COVID-19 pandemic during the second week of March 2020, briefly slowing recruitment rates. Recruitment rate in 2019 was 1 patient/10 sites/month, 2.5 patients/10 sites/month in 2020 and 1.6 patients/10 sites/month in 2021.

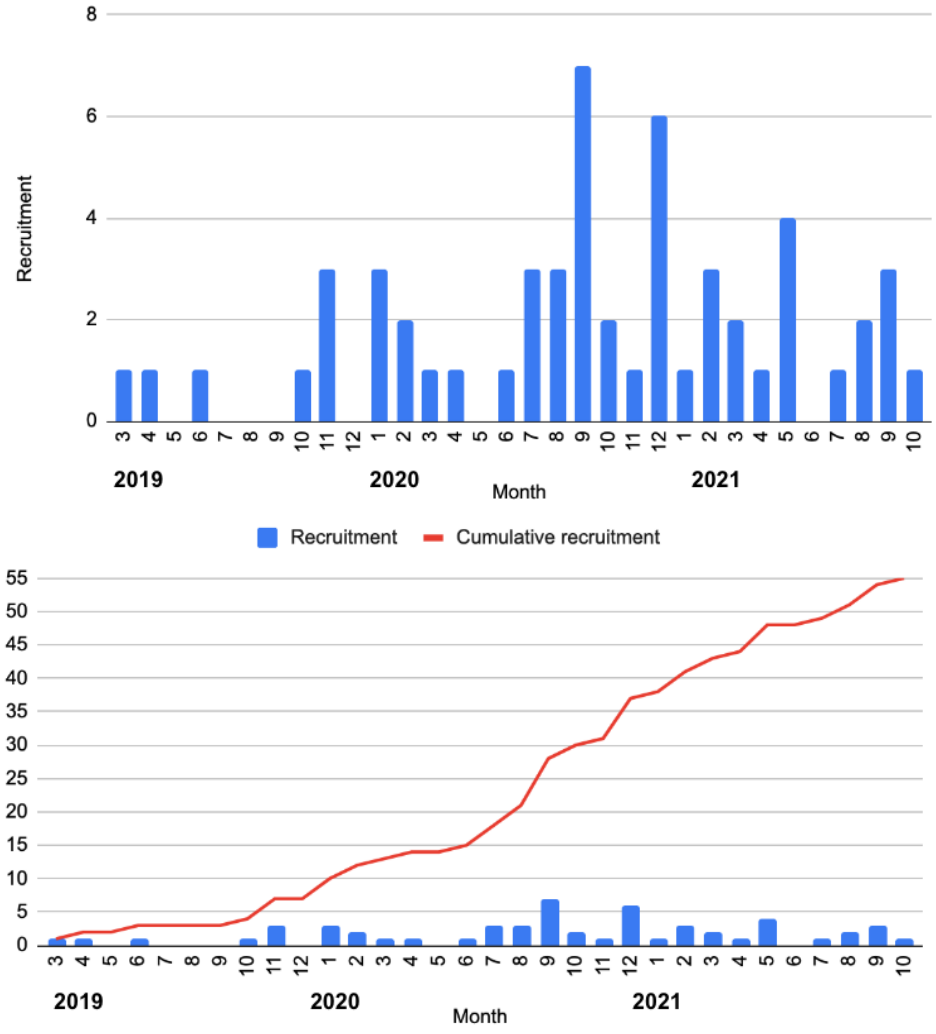


Figure S3: Color graph of delay from timing of diagnosis to randomization

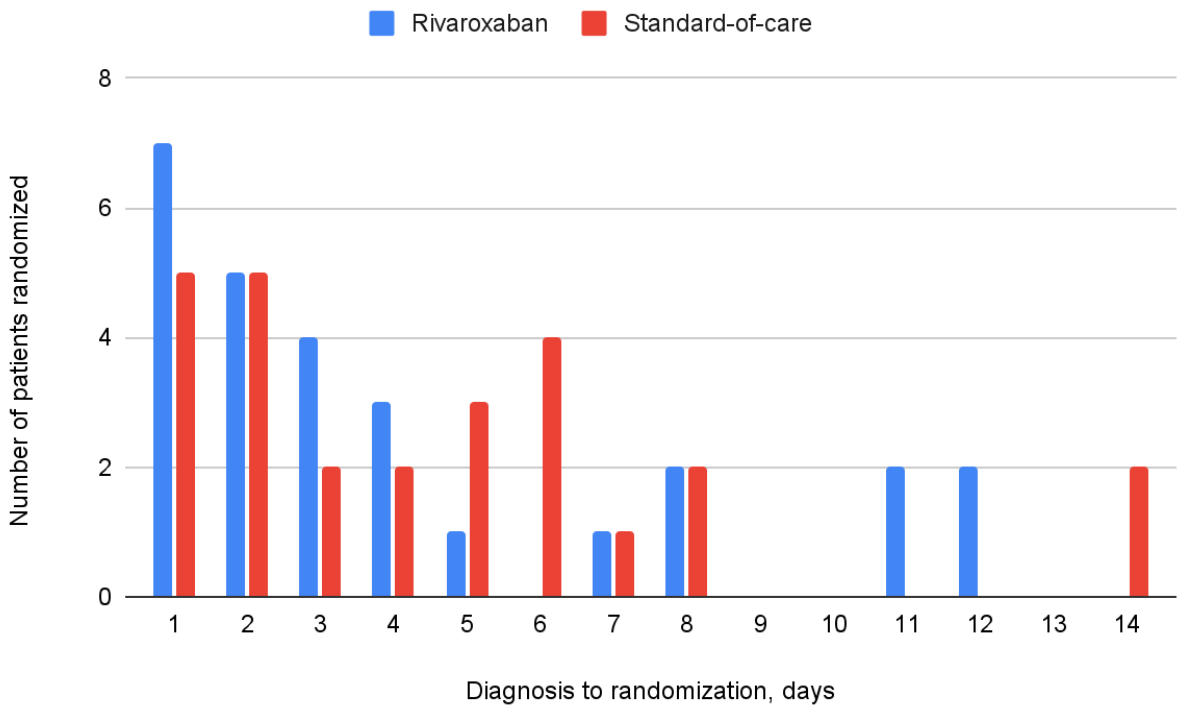


Table S2. Sinus involvement by treatment arm

	Rivaroxaban (N = 26)	Standard of care (N = 27)	All in mITT population (N = 53)
Sinuses involved, N(%)			
Superior sagittal sinus	9 (34.6)	10 (37.0)	19 (37.2)
Left transverse	10 (38.4)	11 (40.7)	21 (41.1)
Right transverse	7 (26.9)	13 (48.1)	20 (39.2)
Left sigmoid	10 (38.4)	10 (37.0)	20 (39.2)
Right sigmoid	7 (26.9)	10 (37.0)	17 (33.3)
Torcula	9 (34.6)	11 (40.7)	20 (39.2)
Straight sinus	5 (19.2)	4 (14.8)	9 (17.6)
Left jugular	8 (30.8)	7 (25.9)	15 (29.4)
Right jugular	6 (23.1)	6 (22.2)	12 (23.5)
Deep venous system	3 (11.5)	2 (7.4)	5 (9.8)
Cortical veins left	10 (38.5)	10 (3.7)	20 (39.2)
Cortical veins right	7 (26.9)	8 (29.6)	15 (29.4)
Cavernous sinus left	1 (3.8)	1 (3.7)	2 (3.9)
Cavernous sinus right	1 (3.8)	1 (3.7)	2 (3.9)
Cerebellar veins left	0 (0)	0 (0)	0 (0)
Cerebellar veins right	0 (0)	0 (0)	0 (0)

Table S3A:

Primary and secondary events at day 180 for Intention-to-treat (ITT), modified intention-to-treat (mITT), safety (rivaroxaban-only; S-R), safety (all DOAC; S-D), on-treatment (OT) and per-protocol (PP) populations

Primary event	# Events	Rivaroxaban (N)	Proportion	95% CI lower	95% CI upper	# Events	Control (N)	Proportion	95% CI lower	95% CI upper	Difference in proportions	95%CI lower	95%CI upper
ITT	1	27	0.03703703704	0.001	0.19	0	28	0	0	0.123	0.03703703704	-0.034	0.11
mITT	1	26	0.03846153846	0.001	0.196	0	27	0	0	0.128	0.03846153846	-0.035	0.112
Safety - Rivaroxaban	1	26	0.03846153846	0.001	0.196	0	24	0	0	0.143	0.03846153846	-0.035	0.112
Safety - DOACs	1	29	0.03448275862	0.001	0.178	0	24	0	0	0.143	0.03448275862	-0.032	0.101
On treatment	1	26	0.03846153846	0.001	0.196	0	26	0	0	0.143	0.03846153846	-0.035	0.112
Per protocol	1	23	0.04347826087	0.001	0.22	0	23	0	0	0.148	0.04347826087	-0.04	0.129
Symptomatic intracranial hemorrhage	**# Events**	**Rivaroxaban (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**# Events**	**Control (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**Difference in proportions**	**95%CI lower**	**95%CI upper**
ITT	1	27	0.03703703704	0.001	0.19	0	28	0	0	0.123	0.03703703704	-0.034	0.11
mITT	1	26	0.03846153846	0.001	0.196	0	27	0	0	0.128	0.03846153846	-0.035	0.11
Safety - Rivaroxaban	1	26	0.03846153846	0.001	0.196	0	24	0	0	0.143	0.03846153846	-0.035	0.112
Safety - DOACs	1	29	0.03448275862	0.001	0.178	0	24	0	0	0.143	0.03448275862	-0.032	0.101
On treatment	1	26	0.03846153846	0.001	0.196	0	26	0	0	0.143	0.03846153846	-0.035	0.112
Per protocol	1	23	0.04347826087	0.001	0.22	0	23	0	0	0.148	0.04347826087	-0.04	0.129
all ICH	**# Events**	**Rivaroxaban (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**# Events**	**Control (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**Difference in proportions**	**95%CI lower**	**95%CI upper**
ITT	2	27	0.07407407407	0.009	0.243	0	28	0	0	0.123	0.07407407407	-0.025	0.173
mITT	2	26	0.07692307692	0.01	0.251	0	27	0	0	0.128	0.07692307692	-0.026	0.179
Safety - Rivaroxaban	2	26	0.07692307692	0.01	0.251	0	24	0	0	0.143	0.07692307692	-0.026	0.179
Safety - DOACs	2	29	0.06896551724	0.009	0.0228	0	24	0	0	0.143	0.06896551724	-0.023	0.161
On treatment	2	26	0.07692307692	0.01	0.251	0	26	0	0	0.143	0.07692307692	-0.026	0.179
Per protocol	2	23	0.08695652174	0.011	0.28	0	23	0	0	0.148	0.08695652174	-0.028	0.202
Clinically relevant non-major bleeding	**# Events**	**Rivaroxaban (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**# Events**	**Control (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**Difference in proportions**	**95%CI lower**	**95%CI upper**
ITT	2	27	0.07407407407	0.009	0.243	0	28	0	0	0.123	0.07407407407	-0.025	0.173
mITT	2	26	0.07692307692	0.01	0.251	0	27	0	0	0.128	0.07692307692	-0.026	0.179
Safety - Rivaroxaban	2	26	0.07692307692	0.01	0.251	0	24	0	0	0.143	0.07692307692	-0.026	0.179

Safety - DOACs	2	29	0.06896551724	0.009	0.0228	0	24	0	0	0.143	0.06896551724	-0.023	0.161
On treatment	2	26	0.07692307692	0.01	0.251	0	26	0	0	0.143	0.07692307692	-0.026	0.179
Per protocol	2	23	0.08695652174	0.011	0.28	0	23	0	0	0.148	0.08695652174	-0.028	0.202
Major and clinically relevant non-major bleeding	**# Events**	**Rivaroxaban (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**# Events**	**Control (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**Difference in proportions**	**95%CI lower**	**95%CI upper**
ITT	3	27	0.1111111111	0.024	0.292	0	28	0	0	0.123	0.1111111111	-0.007	0.23
mITT	3	26	0.1153846154	0.025	0.302	0	27	0	0	0.128	0.1153846154	-0.007	0.238
Safety - Rivaroxaban	3	26	0.1153846154	0.025	0.302	0	24	0	0	0.143	0.1153846154	-0.007	0.238
Safety - DOACs	3	29	0.1034482759	0.022	0.274	0	24	0	0	0.143	0.1034482759	-0.007	0.213
On treatment	3	26	0.1153846154	0.025	0.302	0	26	0	0	0.143	0.1153846154	-0.007	0.238
Per protocol	3	23	0.1304347826	0.028	0.336	0	23	0	0	0.148	0.1304347826	-0.007	0.268
VTE Recurrence	**# Events**	**Rivaroxaban (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**# Events**	**Control (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**Difference in proportions**	**95%CI lower**	**95%CI upper**
ITT	1	27	0.03703703704	0.001	0.19	0	28	0	0	0.123	0.03703703704	-0.034	0.11
mITT	1	26	0.03846153846	0.001	0.196	0	27	0	0	0.128	0.03846153846	-0.035	0.112
Safety - Rivaroxaban	1	26	0.03846153846	0.001	0.196	0	24	0	0	0.143	0.03846153846	-0.035	0.112
Safety - DOACs	1	29	0.03448275862	0.001	0.178	0	24	0	0	0.143	0.03448275862	-0.032	0.101
On treatment	0	26	0	0	0.143	0	26	0	0	0.143	0		
Per protocol	0	23	0	0	0.148	0	23	0	0	0.148	0		
VTE Recurrence and CVT extension	**# Events**	**Rivaroxaban (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**# Events**	**Control (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**Difference in proportions**	**95%CI lower**	**95%CI upper**
ITT	1	27	0.03703703704	0.001	0.19	0	28	0	0	0.123	0.03703703704	-0.034	0.11
mITT	1	26	0.03846153846	0.001	0.196	1	27	0	0	0.128	0.03846153846	-0.035	0.112
Safety - Rivaroxaban	1	26	0.03846153846	0.001	0.196	1	24	0.04166666667	0.001	0.211	-0.003205128205	-0.112	0.106
Safety - DOACs	1	29	0.03448275862	0.001	0.178	1	24	0.04166666667	0.001	0.211	-0.007183908046	-0.111	0.097
On treatment	0	26	0	0	0.143	1	26	0.03846153846	0.001	0.196	-0.03846153846	-0.112	0.034
Per protocol	0	23	0	0	0.148	1	23	0.04347826087	0.001	0.22	-0.04347826087	-0.127	0.04

Table S3B:

Secondary events at day 365 for Intention-to-treat, modified intention-to-treat, on-treatment and per-protocol populations

Symptomatic intracranial hemorrhage	# Events	Rivaroxaban (N)	Proportion	95% CI lower	95% CI upper	# Events	SOC (N)	Proportion	95% CI lower	95% CI upper	Difference in proportions	95%CI lower	95%CI upper
ITT	1	27	0.03703703704	0.001	0.19	1	28	0.03571428571	0.001	0.184	0.001322751323	-0.1	0.1
mITT	1	26	0.03846153846	0.001	0.196	1	27	0.03703703704	0.001	0.19	0.001424501425	-0.101	0.104
Safety - Rivaroxaban	1	26	0.03846153846	0.001	0.196	1	24	0.04166666667	0.001	0.211	-0.003205128205	-0.112	0.106
Safety - DOACs	1	29	0.03448275862	0.001	0.178	1	24	0.04166666667	0.001	0.211	-0.007183908046	-0.111	0.097
On treatment	1	26	0.03846153846	0.001	0.196	1	26	0.03846153846	0.001	0.196	0		
Per protocol	1	23	0.04347826087	0.001	0.22	1	23	0.04347826087	0.001	0.22	0		
all ICH	**# Events**	**Rivaroxaban (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**# Events**	**SOC (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**Difference in proportions**	**95%CI lower**	**95%CI upper**
ITT	2	27	0.07407407407	0.009	0.243	1	28	0.03571428571	0.001	0.184	0.03835978836	-0.082	0.159
mITT	2	26	0.07692307692	0.01	0.251	1	27	0.03703703704	0.001	0.19	0.03988603989	-0.085	0.165
Safety - Rivaroxaban	2	26	0.07692307692	0.01	0.251	1	24	0.04166666667	0.001	0.211	0.03525641026	-0.095	0.165
Safety - DOACs	2	29	0.06896551724	0.009	0.0228	1	24	0.04166666667	0.001	0.211	0.02729885057	-0.095	0.149
On treatment	2	26	0.07692307692	0.01	0.251	1	26	0.03846153846	0.001	0.196	0.03846153846	-0.088	0.165
Per protocol	2	23	0.08695652174	0.011	0.28	1	23	0.04347826087	0.001	0.22	0.04347826087	-0.099	0.186
Clinically relevant non-major bleeding	**# Events**	**Rivaroxaban (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**# Events**	**SOC(N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**Difference in proportions**	**95%CI lower**	**95%CI upper**
ITT	2	27	0.07407407407	0.009	0.243	1	28	0.03571428571	0.001	0.184	0.03835978836	-0.082	0.159
mITT	2	26	0.07692307692	0.01	0.251	1	27	0.03703703704	0.001	0.19	0.03988603989	-0.085	0.165
Safety - Rivaroxaban	2	26	0.07692307692	0.01	0.251	1	24	0.04166666667	0.001	0.211	0.03525641026	-0.095	0.165
Safety - DOACs	2	29	0.06896551724	0.009	0.0228	1	24	0.04166666667	0.001	0.211	0.02729885057	-0.095	0.149
On treatment	2	26	0.07692307692	0.01	0.251	1	26	0.03846153846	0.001	0.196	0.03846153846	-0.067	0.22
Per protocol	2	23	0.08695652174	0.011	0.28	1	23	0.04347826087	0.001	0.22	0.04347826087	-0.099	0.186
Major and clinically relevant non-major bleeding	**# Events**	**Rivaroxaban (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**# Events**	**SOC (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**Difference in proportions**	**95%CI lower**	**95%CI upper**

ITT	3	27	0.1111111111	0.024	0.292	1*	28	0.03571428571	0.001	0.184	0.0753968254	-0.062	0.212
mITT	3	26	0.1153846154	0.025	0.302	1*	27	0.03703703704	0.001	0.19	0.07834757835	-0.064	0.22
Safety - Rivaroxaban	3	26	0.1153846154	0.025	0.302	1*	24	0.04166666667	0.001	0.211	0.07371794872	-0.073	0.22
Safety - DOACs	3	29	0.1034482759	0.022	0.274	1*	24	0.04166666667	0.001	0.211	0.0617816092	-0.075	0.198
On treatment	3	26	0.1153846154	0.025	0.302	1*	26	0.03846153846	0.001	0.196	0.07692307692	-0.067	0.22
Per protocol	3	23	0.1304347826	0.028	0.336	1*	23	0.04347826087	0.001	0.22	0.08695652174	-0.074	0.248
VTE Recurrence	**# Events**	**Rivaroxaban (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**# Events**	**SOC (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**Difference in proportions**	**95%CI lower**	**95%CI upper**
ITT	1	27	0.03703703704	0.001	0.19	0	28	0	0	0.123	0.03703703704	-0.034	0.11
mITT	1	26	0.03846153846	0.001	0.196	0	27	0	0	0.128	0.03846153846	-0.035	0.112
Safety - Rivaroxaban	1	26	0.03846153846	0.001	0.196	0	24	0	0	0.143	0.03846153846	-0.035	0.112
Safety - DOACs	1	29	0.03448275862	0.001	0.178	0	24	0	0	0.143	0.03448275862	-0.032	0.101
On treatment	0	26	0	0	0.143	0	26	0	0	0.143	0		
Per protocol	0	23	0	0	0.148	0	23	0	0	0.148	0		
VTE Recurrence and CVT extension	**# Events**	**Rivaroxaban (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**# Events**	**SOC (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**Difference in proportions**	**95%CI lower**	**95%CI upper**
ITT	1	27	0.03703703704	0.001	0.19	1	28	0.03571428571	0.001	0.184	0.001322751323	-0.098	0.1
mITT	1	26	0.03846153846	0.001	0.196	1	27	0.03703703704	0.001	0.19	0.001424501425	-0.1	0.104
Safety - Rivaroxaban	1	26	0.03846153846	0.001	0.196	1	24	0.04166666667	0.001	0.211	-0.003205128205	-0.112	0.106
Safety - DOACs	1	29	0.03448275862	0.001	0.178	1	24	0.04166666667	0.001	0.211	-0.007183908046	-0.111	0.097
On treatment	0	26	0	0	0.143	1	26	0.03846153846	0.001	0.196	-0.03846153846	-0.112	0.034
Per protocol	0	23	0	0	0.148	1	23	0.04347826087	0.001	0.22	-0.04347826087	-0.127	0.04
Composite outcome (sICH, major extracranial hemorrhage, death)	**# Events**	**Rivaroxaban (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**# Events**	**SOC (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**Difference in proportions**	**95%CI lower**	**95%CI upper**
ITT	1	27	0.03703703704	0.001	0.19	1	28	0.03571428571	0.001	0.184	0.001322751323	-0.098	0.1
mITT	1	26	0.03846153846	0.001	0.196	1	27	0.03703703704	0.001	0.19	0.001424501425	-0.1	0.104
Safety - Rivaroxaban	1	26	0.03846153846	0.001	0.196	1	24	0.04166666667	0.001	0.211	-0.003205128205	-0.112	0.106

Safety - DOACs	1	29	0.03448275862	0.001	0.178	1	24	0.04166666667	0.001	0.211	-0.007183908046	-0.111	0.097
On treatment	1	26	0.03846153846	0.001	0.196	1	26	0.03846153846	0.001	0.196	0		
Per protocol	1	23	0.04347826087	0.001	0.22	1	23	0.04347826087	0.001	0.22	0		
Death	**# Events**	**Rivaroxaban (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**# Events**	**SOC (N)**	**Proportion**	**95% CI lower**	**95% CI upper**	**Difference in proportions**	**95%CI lower**	**95%CI upper**
ITT	0	27	0	0	0.128	1	28	0.03571428571	0.001	0.184	-0.03571428571	-0.105	0.033
mITT	0	26	0	0	0.132	1	27	0.03703703704	0.001	0.19	-0.03703703704	-0.108	0.034
Safety - Rivaroxaban	0	26	0	0	0.132	1	24	0.04166666667	0.001	0.211	-0.04166666667	-0.122	0.038
Safety - DOACs	0	29	0	0	0.119	1	24	0.04166666667	0.001	0.211	-0.04166666667	-0.122	0.038
On treatment	0	26	0	0	0.143	1	26	0.03846153846	0.001	0.196	-0.03846153846	-0.112	0.034
Per protocol	0	23	0	0	0.148	1	23	0.04347826087	0.001	0.22	-0.04347826087	-0.127	0.4

SOC - standard of care

***Major and clinically relevant non-major bleeding event happened simultaneously in this subject (scalp bleeding and subdural hemorrhage) and are counted as one event for combined major bleeding and clinically relevant non-major bleeding*

Table S3C:
Rates of other events of interest, modified intention-to-treat population

	Rivaroxaban N=26	Standard-of-care N=27	Difference in proportions, % (95% CI)
d 180			
Other bleeding, N(%)	2 (7.7)	1 (3.7)	
% (95% CI)	7.7 (0.9 - 25.1)	3.7 (0.1 - 19)	4.0 (-8.5 - 16.5)
Recurrent seizure, N(%)	1 (3.8)	1 (3.7)	
% (95% CI)	3.8 (0.1 - 19.6)	3.7 (0.1 - 19)	0.1 (-10.1 - 10.4)
Ischemic stroke/Myocardial infarction, N(%)	0	1 (3.7)	
% (95% CI)	0 (0, 13.2)	3.7 (0.1 - 19)	-3.7 (-10.8 - 3.4)
d 365			
Other bleeding, N(%)	3 (11.5)	4 (14.8)	
%, (95% CI)	11.5 (2.4 - 30.2)	14.8 (4.2 - 33.7)	-3.3 (-21.5 - 14.9)
Recurrent seizure, N(%)	2 (7.7%)	2 (7.4%)	
% (95%CI)	7.7 (0.9 - 25.1)	7.4 (0.9 - 24.3)	0.3 (-13.9 - 14.5)
Ischemic stroke/Myocardial infarction, N(%)	0	1 (3.7)	
% (95%CI)	0 (0 - 13.2)	3.7 (0.1 - 19)	-3.7 (-10.8 - 3.4)
Vision loss, N(%)	1 (3.8)	2 (7.4)	
% (95% CI)	3.8 (0.1 - 19.6)	7.4 (0.9 - 24.3)	-3.6 (-15.9 - 8.8)
New JAK2 mutation diagnosis, N(%)	1 (3.8)	2 (7.4)	
% (95% CI)	3.8 (0.1 - 19.6)	7.4 (0.9 - 24.3)	-3.6 (-15.9 - 8.8)
New cancer diagnosis, N(%)	1 (3.8)	0 (0)	
% (95% CI)	3.8 (0.1 - 19.6)	0 (0.0 - 12.8)	3.8 (-3.5 - 11.2)

Table S4: Estimates of times in therapeutic range (TTR) using cross-section-of-the-files methodology.[32, 33]

Scenario	Estimated TTR up to day 180	Up to day 365
Available data only	83.3%	84.8%
Worst-case scenario (all missing data imputed as subtherapeutic)	58.5%	58.5%
Best-case scenario (all missing data imputed as therapeutic)	86.7%	87.9%
Medium scenario (half of missing data imputed as therapeutic; half subtherapeutic)	72.6%	73.2%