Supplemental Tables for Apixaban compared with warfarin to prevent thrombosis in thrombotic antiphospholipid syndrome: a randomized trial

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Supplement Table 1: Detailed patient characteristics with study outcomes

ID	Age	Sex	BMI	Study Arm (dose, mg)	Clinical History	Antibody Positivity	APS Category	Outcome Event	Days to Event	Warfarin Days	Apixaban 2.5 mg BID Days	Apixaban 5.0 mg BID Days
1	43	Female	36.9	Apixaban 2.5	DVT	Triple	Definite	Stroke	67	0	67	0
2	47	Female	19.4	Apixaban 2.5	Stroke, TIA, DVT, pregnancy loss	Double	Likely	Stroke	37	0	37	0
3	69	Female	23.2	Apixaban 2.5	Stroke, pregnancy loss	N/A	Historical	Stroke	6	0	6	0
4	51	Female	25.5	Apixaban 2.5 & 5.0	Stroke, other arterial thrombosis, DVT, PE	Triple	Definite	Stroke	316	0	234	82
5	40	Female	39.3	Apixaban 2.5 & 5.0	Stroke, DVT, PE, pregnancy loss	Single	Likely	Stroke	156	0	123	33
6	66	Male	39.3	Apixaban 5.0	DVT	N/A	Historical	Stroke	104	0	0	104
7	62	Female	30.5	Warfarin	Stroke, DVT, PE	N/A	Historical	Major Bleed	319	319	0	0
8	60	Male	38.9	Apixaban 2.5 & 5.0	DVT, PE	Double	Definite	none	-	0	204	161
9	29	Female	24.4	Apixaban 2.5 & 5.0	DVT, pregnancy loss	Double	Definite	none	-	0	204	161
10	53	Female	22.4	Apixaban 2.5 & 5.0	DVT, PE	Double	Likely	none	-	0	183	182
11	47	Female	29.9	Apixaban 2.5 & 5.0	Stroke	Single	Likely	none	-	0	209	156
12	45	Male	30.9	Apixaban 2.5 & 5.0	DVT, PE	Single	Likely	none	-	0	182	183
13	36	Female	20.5	Apixaban 2.5 & 5.0	PE	Single	Likely	none	-	0	154	211
14	47	Female	35.9	Apixaban 2.5 & 5.0	DVT, PE	N/A	Historical	none	-	0	124	241

15	36	Male	49.6	Apixaban 2.5 & 5.0	DVT, PE	N/A	Historical	none	-	0	91	274
16	30	Female	46.5	Apixaban 5.0	DVT, PE	Triple	Definite	none	-	0	0	365
17	43	Female	27.7	Apixaban 5.0	PE, pregnancy loss	Triple	Definite	none	-	0	0	365
18	45	Female	29.3	Apixaban 5.0	DVT, pregnancy loss	Triple	Likely	none	-	0	0	365
19	44	Female	28.9	Apixaban 5.0	DVT	Triple	Definite	none	-	0	0	365
20	32	Female	25.7	Apixaban 5.0	DVT, pregnancy loss	Triple	Definite	none	-	0	0	365
21	61	Female	27.1	Apixaban 5.0	DVT	Single	Likely	none	-	0	0	365
22	52	Female	27.6	Apixaban 5.0	MI	N/A	Historical	none	-	325	0	40
23	27	Female	38.8	Apixaban 5.0	DVT	N/A	Historical	none	-	0	0	365
24	56	Female	30.8	Apixaban 5.0	PE	N/A	Historical	none	-	0	0	365
25	60	Female	37.1	Warfarin	Stroke, TIA	Triple	Definite	none	-	365	0	0
26	20	Male	29.8	Warfarin	DVT, PE	Triple	Definite	none	-	365	0	0
27	57	Female	33.4	Warfarin	Stroke, TIA, pregnancy loss	Triple	Definite	none	-	365	0	0
28	35	Male	30.1	Warfarin	Other arterial thrombosis	Triple	Definite	none	-	365	0	0
29	61	Female	31.6	Warfarin	MI, DVT, PE, pregnancy loss	Triple	Definite	none	-	365	0	0
30	34	Female	33.1	Warfarin	DVT	Triple	Likely	none	-	365	0	0
31	25	Female	44.6	Warfarin	DVT	Triple	Definite	none	-	365	0	0
32	47	Female	33.8	Warfarin	TIA, DVT	Double	Definite	none	-	365	0	0
33	42	Female	30.8	Warfarin	Stroke, TIA	Double	Definite	none	-	365	0	0
34	43	Female	26.2	Warfarin	DVT	Single	Definite	none	-	365	0	0
35	54	Male	32.6	Warfarin	DVT, PE	Single	Definite	none	-	365	0	0
36	66	Female	31.2	Warfarin	PE	Single	Likely	none	-	365	0	0
37	41	Female	45.1	Warfarin	Stroke, pregnancy loss	Single	Likely	none	-	365	0	0

38	42	Female	20.7	Warfarin	Stroke, TIA	Single	Likely	none	-	365	0	0
39	31	Female	26.1	Warfarin	DVT	Single	Definite	none	-	365	0	0
40	47	Female	37.5	Warfarin	DVT	Single	Definite	none	-	365	0	0
41	61	Female	28	Warfarin	Stroke, TIA, pregnancy loss	N/A	Historical	none	-	365	0	0
42	55	Female	41	Warfarin	DVT	N/A	Historical	none	-	365	0	0
43	52	Female	22	Warfarin	DVT	N/A	Historical	none	-	365	0	0
44	70	Female	27.1	Warfarin	DVT	N/A	Historical	none	-	365	0	0
45	73	Male	31.1	Warfarin	Other arterial thrombosis, DVT, PE	N/A	Historical	none	-	365	0	0
46	40	Female	35.9	Warfarin	DVT, PE	N/A	Historical	none	-	365	0	0
47	63	Female	36	Warfarin	DVT	N/A	Historical	none	-	365	0	0
48	32	Female	31.6	Warfarin	Other arterial thrombosis, DVT, pregnancy loss	N/A	Historical	none	-	365	0	0

APS: antiphospholipid syndrome; BID: twice daily; BMI: body mass index; DVT: Deep vein thrombosis; MI: myocardial infarction; PE: pulmonary embolism; TIA: transient ischemic attack

*Dose of apixaban the time of the outcome event

^Patients with APS where characterized as having *definite APS* defined as radiology verified thrombosis plus a qualifying laboratory result[#] *likely APS* was defined as radiology verified thrombosis plus at least 1 qualifying laboratory result; or *historical APS* was defined as a report of a qualifying thrombosis event along with a reported history of abnormal laboratory testing, but results were not available for confirmation

$Derived from Sapporo Criteria: the presence of lupus anticoagulant or anticardiolipin IgG or IgM or anti-β-2-glycoprotein-1 IgG or IgM >40 IgG phospholipid Units (GPL) or IgM Phospholipid Units (MPL) or > the 99th percentile, on 2 separate occasions at least 12 weeks apart

N/A: not applicable as patient with historical APS

Supplemental Table 2: Unscheduled encounters and adverse outcomes during the study

Event type	Apixaban, n	Warfarin, n
Encounter type		
Emergency department	11	8
Unplanned doctor visit	10	10
Outcome		
Nuisance bleeding*	1	2
New cancer diagnosis	0	2
Isolated distal DVT	1	0

*Bleeding that did not meet criteria as a major or clinically relevant nonmajor bleed
DVT: deep vein thrombosis

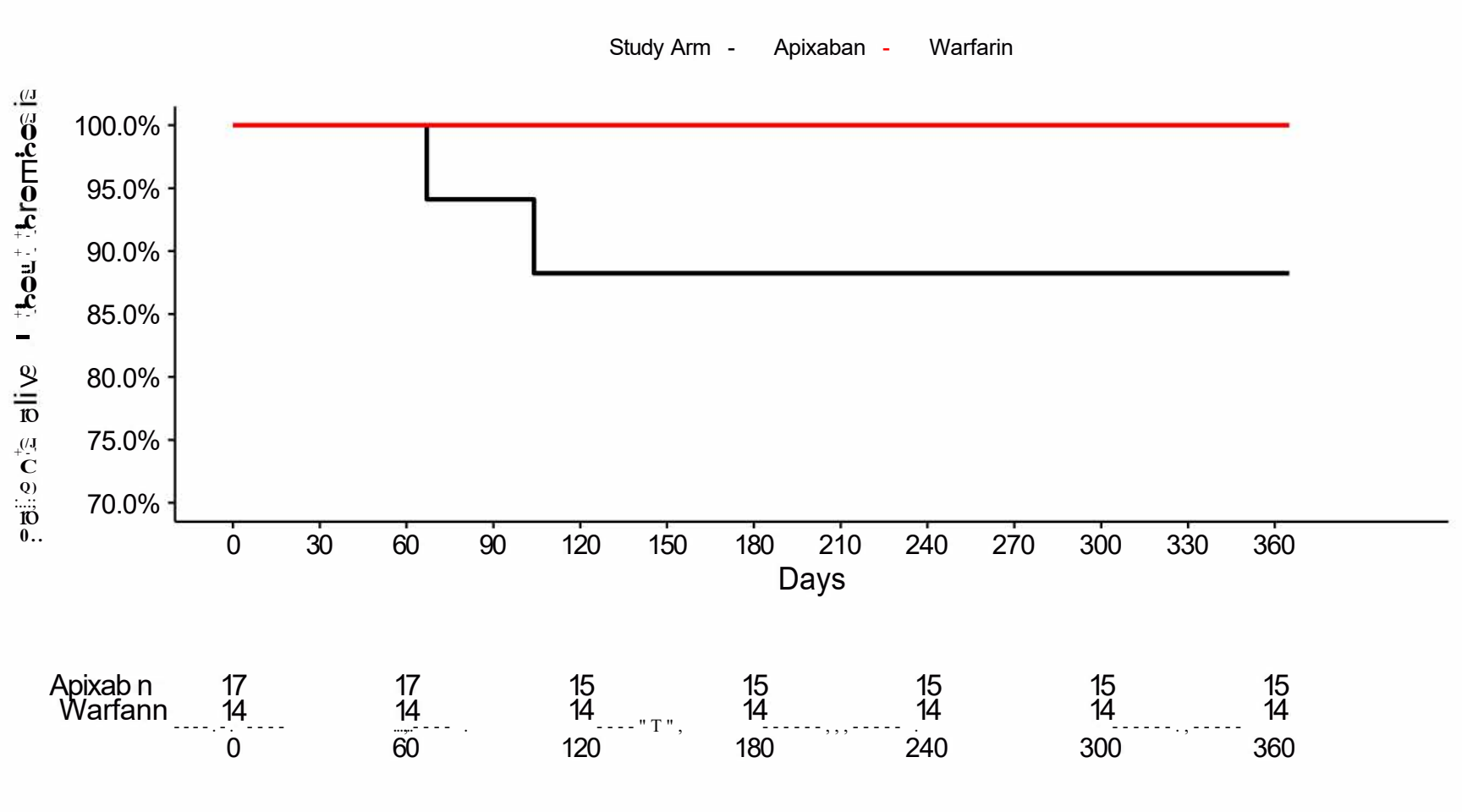
Supplemental Table 3: Details for each participant that experienced a thrombotic *or major bleed* event during the study

Patient Study Identification	24	16	12	2	32	3	27
Demographic Information							
Sex	Female	Female	Female	Female	Male	Female	Female
Age	40	43	47	51	66	69	62
BMI	39.3	36.9	19.4	25.5	39.3	23.2	30.5
Treatment	Apixaban	Apixaban	Apixaban	Apixaban	Apixaban	Apixaban	Warfarin
Level	Single	Triple	Double	Triple	-	-	-
Type	Likely^	Definite^	Likely^	Definite^	Historical ^	Historical ^	Historical ^
Adverse Events							
Outcome Event Type	Stroke	Stroke	Stroke	Stroke	Stroke	Stroke	Major Bleed
Days to event	156	67	37	316	104	6	319
Stroke Distribution	Right anterior frontal lacunar	Anterior and posterior, unilateral	Bilateral anterior	Right frontal	Multifocal left frontal	Right parietal	-
Single v. Multiple Lesions on MRI	Single	Multiple	Multiple	Single with multiple chronic infarcts	Multiple	Single	-
MRI DWI (Normal or Abnormal)	Abnormal DWI	Abnormal DWI	Abnormal DWI	Abnormal DWI	Abnormal DWI	Abnormal DWI	-
Hemorrhage Present	No	Yes T2W on MRI	No	No	No	No	
TOAST Classification	Undetermined etiology	Undetermined etiology	Undetermined etiology	Undetermined etiology	Cardioembolic (atrial fibrillation)	Undetermined etiology	-
Laboratory Diagnostics							
Lupus Anticoagulant Detected	X	X	X				
Anticardiolipin IgG positive*		X	X	X			

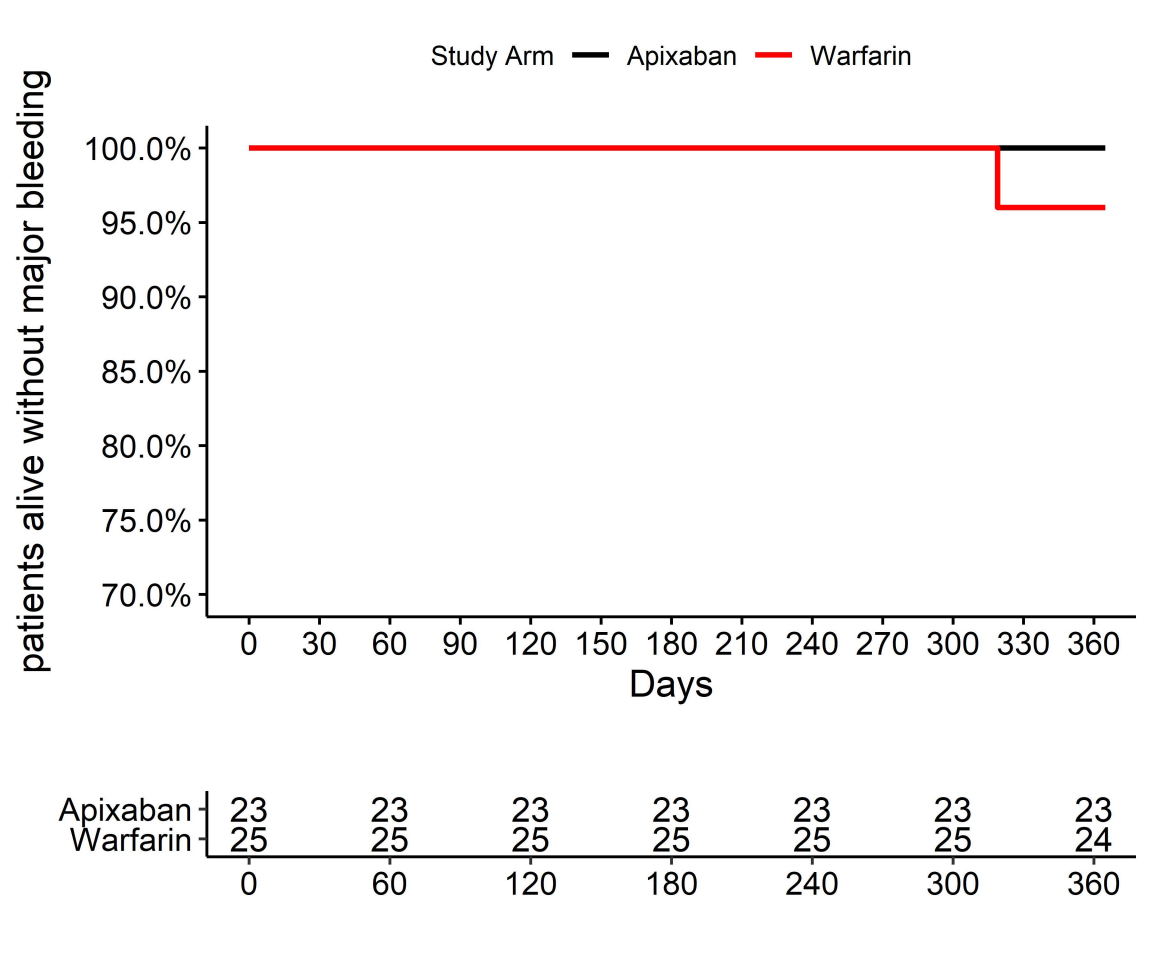
Patient Study Identification	24	16	12	2	32	3	27
Anticardiolipin IgM positive*		X		X			
Anti-beta-2-Glycoprotein-1 IgG positive*		X	X	X			
Anti-beta-2-Glycoprotein-1 IgM positive*		X		X			
Previous Thrombotic Events	X	X	X	X	X	X	X
Arterial Events	X		X	X		X	X
Myocardial infarction							
Stroke	X		X	X		X	X
Other				X			
Venous Events	X	X	X	X	X		X
Deep vein thrombosis	X	X	X	X	X		X
Pulmonary embolism	X			X			X
Pregnancy morbidity	X		X			X	
Risk Factors							
Smoking	X		X				
Hypertension		X				X	
Diabetes							
Dyslipidemia						X	
Heritable thrombophilia				X			X
Charlson comorbidity index	2		1	6	7	4	2
Comorbidities							
Systemic lupus erythematosus							
Autoimmune disease		X		X			
Depression/Anxiety			X	X			X
Migraine/Headache			X	X			X
GERD		X		X		X	X
Reactive airway/COPD			X				
Chronic pain syndrome						X	X
TIA/Stroke	X						
Medications							

Patient Study Identification	24	16	12	2	32	3	27
Aspirin							
Statin						X	
Hydroxychloroquine	X	X					X
Other immunosuppressant	X	X					X
Antihypertensive	X	X		X	X		
Calcium		X		X			
Vitamin D	X	X		X		X	
Antidepressant/Anxiolytic			X			X	
Prescription analgesic		X				X	X
Other vitamin supplement			X	X		X	
Diabetic medication							
Asthma/Reactive airway			X		X		
Oral Contraceptive							

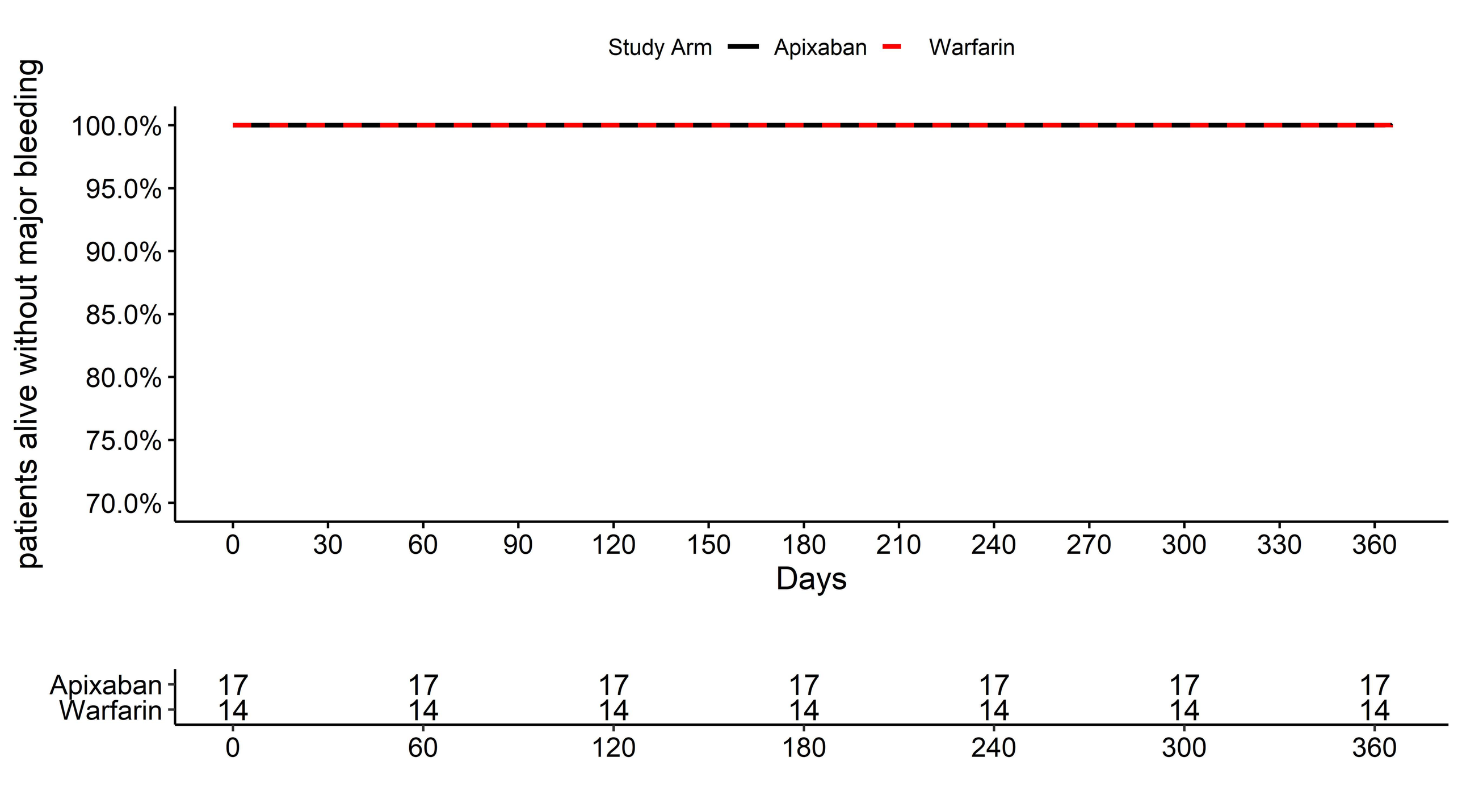
APS: antiphospholipid syndrome; COPD: chronic obstructive pulmonary disease; GERD: gastroesophageal reflux disease; SD: standard deviation; TIA: transient ischemic attack
MRI: magnetic resonance imaging
DWI: Diffusion weighted imaging
*At the time of enrollment
^Patients with APS where characterized as having *definite APS* defined as radiologically verified thrombosis plus a qualifying laboratory result[#] *likely APS* was defined as radiologically verified thrombosis plus at least 1 qualifying laboratory result; or *historical APS* was defined as a report of a qualifying thrombosis event along with a reported history of abnormal laboratory testing, but results were not available for confirmation
[#]Derived from Sapporo Criteria: the presence of lupus anticoagulant or anticardiolipin IgG or IgM or anti-β-2-glycoprotein-1 IgG or IgM >40 IgG phospholipid Units (GPL) or IgM Phospholipid Units (MPL) or > the 99th percentile, on 2 separate occasions at least 12 weeks apart


Study Arm - Apixaban - Warfarin
100.0%
95.0%
90.0%
85.0%
80.0%
75.0%
70.0%
0
30
60
90
120
150
180
210
240
270
300
330
360
Days
Apixaban 17 17 15 15 15 15 15
Warfarin 14 14 14 14 14 14 14
0
60
120
180
240
300
360

Supplemental Figure 1: Kaplan–Meier cumulative event rate for major bleeding The solid black line is for apixaban and solid red line is for warfarin.


Study Arm
Apixaban
Warfarin
patients alive without major bleeding
100.0%
95.0%
90.0%
85.0%
80.0%
75.0%
70.0%
0
30
60
90
120
150
180
210
240
270
300
330
360
Days
Apixaban
Warfarin
23
25
23
25
23
25
23
25
23
25
23
25
23
24
0
60
120
180
240
300
360

Supplemental Figure 2: Kaplan–Meier cumulative event rate of thrombosis and vascular death in the subgroup that did not have a history of arterial thrombosis. This Kaplan-Meier figure represents the 1-year event rate of thrombosis outcome (stroke) among only subjects enrolled with no prior history of arterial thrombosis. The black and red lines display apixaban and warfarin; respectively.


Study Arm
Apixaban
Warfarin
patients alive without major bleeding
100.0%
95.0%
90.0%
85.0%
80.0%
75.0%
70.0%
0
30
60
90
120
150
180
210
240
270
300
330
360
Days
Apixaban
Warfarin
17
14
0
60
120
180
240
300
360

Supplemental Figure 3: Kaplan–Meier cumulative event rate of major and clinically relevant non-major bleeding in the subgroup that did not have a history of arterial thrombosis. This Kaplan-Meier figure represents the 1-year event rate of major bleeding outcome among only subjects enrolled with no prior history of arterial thrombosis. The black and red lines display apixaban and warfarin; respectively.