ORIGINAL ARTICLE

Rivaroxaban versus aspirin for secondary prevention of ischaemic stroke in patients with cancer: a subgroup analysis of the NAVIGATE ESUS randomized trial

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Background and purpose: Cancer is a frequent finding in ischaemic stroke patients. The frequency of cancer amongst participants in the NAVIGATE ESUS randomized trial and the distribution of outcome events during treatment with aspirin and rivaroxaban were investigated.

Methods: Trial participation required a recent embolic stroke of undetermined source. Patients' history of cancer was recorded at the time of study entry. During a mean follow-up of 11 months, the effects of aspirin and rivaroxaban treatment on recurrent ischaemic stroke, major bleeding and all-cause mortality were compared between patients with cancer and patients without cancer.

Results: Amongst 7213 randomized patients, 543 (7.5%) had cancer. Of all patients, 3609 were randomized to rivaroxaban [254 (7.0%) with cancer] and 3604 patients to aspirin [289 (8.0%) with cancer]. The annual rate of recurrent ischaemic stroke was 4.5% in non-cancer patients in the rivaroxaban arm and 4.6% in the aspirin arm [hazard ratio (HR) 0.98, 95% confidence interval (CI) 0.78–1.24]. In cancer patients, the rate of recurrent ischaemic stroke was 7.7% in the rivaroxaban arm and 5.4% in the aspirin arm (HR 1.43, 95% CI 0.71–2.87). Amongst cancer patients, the annual rate of major bleeds was non-significantly higher for rivaroxaban than aspirin (2.9% vs. 1.1%; HR 2.57, 95% CI 0.67–9.96; *P* for interaction 0.95). All-cause mortality was similar in both groups.

Conclusions: Our exploratory analyses show that patients with embolic stroke of undetermined source and a history of cancer had similar rates of recurrent ischaemic strokes and all-cause mortality during aspirin and rivaroxaban treatments and that aspirin appeared safer than rivaroxaban in cancer patients regarding major bleeds. www.clinicaltrials.gov (NCT02313909).

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Introduction

Embolic stroke of undetermined source (ESUS) is a subset of cryptogenic stroke and a diagnostic label proposed for an ischaemic stroke that occurs without an identifiable and specifically treatable underlying stroke aetiology [1]. The NAVIGATE ESUS (New Approach Rivaroxaban Inhibition of Factor Xa in a Global Trial versus ASA to Prevent Embolism in Embolic Stroke of Undetermined Source) trial is an international randomized phase III trial. The design of the trial and the baseline characteristics of the 7213 enrolled individuals have recently been reported [2,3]. Rivaroxaban was not superior to aspirin in preventing recurrent ischaemic strokes in the NAVIGATE ESUS trial [4]. Moreover, it was associated with a higher risk of bleeding [4]. Whilst the NAVIGATE ESUS participants share a common diagnosis of ischaemic stroke and ESUS, they vary with respect to the underlying potential embolic sources.

Previous studies have demonstrated a correlation between cancer and hypercoagulability, an important factor predisposing not only to ischaemic stroke but also to other thromboembolisms [5,6]. The prevalence of previous cancer can be up to 16% in ischaemic stroke patients [7]. Moreover, a nationwide US-based study reported that 10% of hospitalized ischaemic stroke patients had comorbid cancer [8]. Several factors such as elevated D-dimer and specific cancer types are associated with recurrent strokes [9,10]. Not surprisingly, both short-term and long-term overall mortality are higher in stroke patients with active cancer [11,12]. Patients with lung cancer showed a doubled risk for ischaemic stroke within 1 year of cancer diagnosis compared to matched controls, and the highest risk for ischaemic stroke was in patients with very advanced cancer, reaching a 10-fold risk compared to controls [13]. Embolic strokes are the commonest type of stroke in this patient group [14], whilst cancer-associated cryptogenic stroke might be associated with reduced survival [15]. Active cancer can also predispose to intracranial haemorrhage, often from unique mechanisms such as intratumoural haemorrhage or coagulopathy [16].

The optimal secondary prevention in cancer patients with acute ischaemic stroke has been unclear with a few studies demonstrating reduction in recurrent events, D-dimer levels and transcranial Doppler microembolism with anticoagulant treatment [17]. However, increased risk of bleeding might outweigh these potential benefits. Thus, both the high prevalence of cancer amongst ischaemic stroke patients and the several-fold risk of stroke in cancer patients lead to the important question of optimal long-term antithrombotic treatment in this subgroup of patients. Here, in a *post hoc* exploratory analysis of the large NAVIGATE ESUS trial the baseline characteristics of participants with a history of cancer and the differences of outcome events under rivaroxaban or aspirin treatment were investigated.

Patients and methods

The design of the NAVIGATE ESUS trial (www.clinicaltrials.gov NCT02313909) and the characteristics of the trial patient population have been described previously [2,3]. Briefly, the NAVIGATE ESUS trial is an international randomized phase III trial comparing rivaroxaban (an oral factor Xa inhibitor) versus aspirin in patients with recent ESUS. After qualifying for ESUS according to the trial protocol, the patients were enrolled no later than 6 months after the index stroke and randomized to receive either rivaroxaban 15 mg or aspirin 100 mg once daily.

In addition to relevant baseline characteristics, a history of cancer was solicited, the type of cancer, and whether the diagnosis was made within the previous year before the date of randomization or earlier. Of note, life expectancy of <6 months was an exclusion criterion in the trial. The diagnosis and the type of cancer were based mainly on participant self-report and were not confirmed. No information about staging or anti-cancer treatment was collected. Because superficial skin cancers are not expected to present an increased risk for recurrent ischaemic strokes, major bleeding or death, these patients were grouped together with non-cancer patients. Definitions of relevant outcomes were described previously [2].

In our study, the baseline characteristics and the annual rate of recurrent ischaemic strokes, major bleeds, self-reported quality of life measured with a five-dimensional three-level generic measure (EQ-5D) recorded at the beginning and first recurrent ischaemic stroke or end of the study, and all-cause mortality, between cancer and non-cancer patients as well as between cancer patients in the rivaroxaban and the aspirin arms, were compared.

Written informed consent was obtained from all participants. NAVIGATE ESUS has been approved by the local research ethics committees at each recruiting institution.

Statistical analyses

Normally distributed continuous variables were summarized using the mean and the standard deviation (SD), and comparisons between such variables were performed using the *t* test. Non-normally distributed continuous variables were summarized using the median and the interquartile range, and the comparisons between such

variables were performed using the Wilcoxon test. Frequency tables were analysed with the Pearson chi-squared test or Fisher's exact test as appropriate. Life tables regarding recurrent ischaemic stroke, major bleeds and overall survival between the treatment groups were analysed using a Cox proportional-hazards model; the hazard ratio (HR) and the 95% confidence interval (CI) are reported. All tests are two-sided and conducted at the 0.05 level of significance. All statistical analyses were conducted using the SAS 9.4 statistical package (SAS Institute Inc., Cary, NC, USA).

Results

Baseline characteristics

In all, 7213 patients from 459 sites located in 31 countries between 24 December 2014 and 20 September 2017, of whom 543 (7.5%) had cancer (mean age 72.1 ± 8.2 years; 41% were females), were enrolled. The baseline characteristics of the whole study population have been reported in detail elsewhere [3]. Of them, 3609 patients were randomized to rivaroxaban [254 (7.0%) with cancer] and 3604 patients were randomized to aspirin [289 (8.0%) with cancer].

Frequent cancer types included prostate [107 (19.7%)], breast [101 (18.6%)], colon [66 (12.2%)] and lung [30 (5.5%)] cancers. Cancer was diagnosed less than 1 year prior to the index stroke in 49 (9%) cases. Most of the patients with prior cancer were recruited in the USA, Canada and Western Europe (Table 1).

Cancer patients were older, had a lower body mass index and were less frequently current smokers than non-cancer patients. Moreover, they more often had infarcts in multiple vascular territories. Comparison between cancer and non-cancer patients showed no differences in sex (male 59% and 62%, $P = 0.1436$, respectively) or in relevant comorbidities such as diabetes, heart failure and previous transient ischaemic attack, but hypertension was slightly more frequent in non-cancer patients. The arterial territory of the index stroke was similar in both groups, but non-cancer patients had more subcortical infarcts as their only ischaemic lesion. Furthermore, cancer patients had a lower National Institutes of Health Stroke Scale (NIHSS) score at randomization but no difference in modified Rankin Scale. The self-reported health status was also similar between the two groups. These comparisons are summarized in Table 1.

Baseline patient characteristics by the site of cancer

Comparisons according to the site of cancer showed that patients with lung cancer had been diagnosed in the last year more frequently and had more comorbidities [heart failure (13%) and prior stroke or transient ischaemic attack (30%)]. Lung cancer was associated with multiple ischaemic lesions (27%), whilst colon cancer patients more frequently had anterior circulation strokes (80%). There were no differences in sex, other comorbidities or the NIHSS score at randomization or in the modified Rankin Scale score at randomization between subgroups of cancer patients (Table 2).

Outcomes by the presence of cancer, duration of cancer diagnosis and treatment allocation

In non-cancer patients, the annualized rate of recurrent ischaemic stroke was 4.6% in the aspirin group and 4.5% in the rivaroxaban arm (HR 0.98, 95% CI 0.78–1.24), whereas in the subset of cancer patients the rate of recurrent ischaemic stroke was 5.4% in the aspirin arm and 7.7% in the rivaroxaban arm (HR 1.43, 95% CI 0.71–2.87, $P = 0.31$ for interaction) (Table 3). Cancer patients in the rivaroxaban arm had a non-significantly higher risk for major bleeding compared to the aspirin arm, similar to the overall trial population (HR 2.57, 95% CI 0.67–9.96, P for interaction 0.9539). Finally, also all-cause mortality showed no difference between these subgroups (Table 3). The cumulative risks of these major outcomes are depicted in Fig. 1. There was no association between the duration since cancer diagnosis and the recurrence rate of ischaemic stroke (Table S1). The anatomical distribution of recurrent ischaemic strokes did not differ between cancer and non-cancer patients. Furthermore, the difference between self-reported health status (EQ-5D score) at baseline and after first ischaemic stroke was similar between cancer and non-cancer patients (Table S2). Cancer patients' health status was also similar between the aspirin and rivaroxaban arms (Table S3).

Rate of new cancer diagnosis in ESUS patients

In the whole study population, 124 (1.7%) had a newly diagnosed cancer during the 11-month follow-up. Table S4 shows the frequency of newly diagnosed cancers during the 11-month follow-up in patients with no prior cancer history. Seventy (2.1%) patients in the rivaroxaban arm and 54 (1.6%) in the aspirin arm were diagnosed with a first-ever cancer and the rate of first recurrent ischaemic stroke was similar in both treatment arms.

DISCUSSION

Our exploratory subgroup analyses suggest that ESUS patients with a history of cancer did not receive

Table 1 Baseline features and outcomes of participants with versus without cancer

Characteristic	Cancer (+) (N = 543)	Cancer (−) (N = 6670)	P value
Age, years	72.1 (8.2)	66.5 (9.8)	<0.0001
Age < 60 years	37 (7)	1679 (25)	<0.0001
Male sex	318 (59)	4118 (62)	0.1436
Cancer diagnosed < 1year	48 (9)	Not applicable	Not applicable
Race			
White only	384 (71)	4832 (72)	0.3875
Black only	8 (1)	103 (2)	0.8973
East Asian only	106 (20)	1308 (20)	0.9599
Others (includes not reported/multiracial)	45 (8)	427 (6)	0.0875
BMI, kg/m^2	26.5 (4.8)	27.3 (5.0)	0.0002
<25 kg/m^2	218 (40)	2282 (34)	0.0053
≥25 to <30 kg/m^2	222 (41)	2753 (41)	0.8489
≥30 kg/m^2	101 (19)	1606 (24)	0.0038
Weight, kg	73.6 (15.9)	76.4 (16.5)	0.0002
Medical history			
Hypertension	397 (73)	5188 (78)	0.0123
Diabetes mellitus	141 (26)	1665 (25)	0.6034
Current tobacco use	70 (13)	1414 (21)	<0.0001
Coronary artery disease	30 (6)	442 (7)	0.3181
Heart failure	16 (3)	222 (3)	0.6320
Prior stroke or TIA	98 (18)	1165 (17)	0.7317
Global region			
USA and Canada	91 (17)	827 (12)	0.0034
Latin America	32 (6)	714 (11)	0.0004
Western Europe	274 (50)	2807 (42)	0.0001
Eastern Europe	44 (8)	1074 (16)	<0.0001
East Asia	102 (19)	1248 (19)	0.9661
Qualifying stroke			
Arterial territory of qualifying stroke			
Anterior circulation	384 (71)	4803 (72)	0.5199
Posterior circulation	176 (32)	2093 (31)	0.6181
Cerebral hemisphere with cortical involvement	327 (60)	3708 (56)	0.0367
Cerebral hemisphere, subcortical only	71 (13)	1447 (22)	<0.0001
Brainstem only	16 (3)	315 (5)	0.0572
Cerebellum only	55 (10)	506 (8)	0.0334
Multiple locations	74 (14)	689 (10)	0.0163
NIHSS score at randomization	0.0 (0.0–2.0)	1.0 (0.0–2.0)	<0.0001
NIHSS score ≤ 5	523 (96)	6403 (96)	0.7623
Modified Rankin Scale (mRS) at randomization			
mRS 0 or 1	365 (67)	4305 (65)	0.2110
mRS 2	111 (20)	1561 (23)	0.1154
mRS ≥ 3	67 (12)	803 (12)	0.8375
EQ-5D score at randomization	73.8 (7.2)	74 (6.1)	0.8934
Time from qualifying stroke to randomization, days	42.0 (16.0–92.0)	36.0 (14.0–88.0)	0.1647
First ischaemic stroke, n (100 person-years)	32 (6.5)	283 (4.6)	
First major bleed, n (100 person-years)	10 (2.0)	75 (1.2)	
All-cause mortality, n (100 person-years)	18 (3.5)	99 (1.5)	

BMI, body mass index; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischaemic attack. Data expressed as n (%), mean (standard deviation) or median (interquartile range). Participants with skin cancer only (n = 77) are included in the 'no cancer' group.

additional benefit from rivaroxaban (an anticoagulant) for the prevention of recurrent ischaemic strokes compared with aspirin (an antiplatelet agent), but as reported in the total population aspirin was safer regarding major bleedings. Overall mortality was similar in both treatment arms. Thus, the outcomes in this subgroup analysis of rivaroxaban compared to aspirin are consistent with the overall trial results.

The most frequent cancer types in our study were prostate, breast, colon and lung cancers. Previous studies have shown the high frequency of these types, but also pancreatic cancer, in first-ever and recurrent

Table 2 Baseline features of participants according to site of cancer

Characteristic	No cancer (N = 6670)	Prostate cancer (N = 107)	Breast cancer (N = 101)	Colon cancer (N = 66)	Lung cancer (N = 30)	Other cancer (N = 239)
Age, years	66.5 (9.8)	73.8 (6.2)	73.4 (7.2)	74.6 (8.1)	71.7 (7.4)	70.0 (9.1)
Age < 60 years	1679 (25)	1 (1)	5 (5)	1 (2)	0 (0)	30 (13)
Male sex	4118 (62)	107 (100)	1 (1)	41 (62)	19 (63)	150 (63)
Cancer diagnosed < 1 year	0 (0)	14 (13)	7 (7)	5 (8)	6 (20)	16 (7)
Race						
White only	4832 (72)	78 (73)	80 (79)	45 (68)	17 (57)	164 (69)
Black only	103 (2)	3 (3)	1 (1)	1 (2)	2 (7)	1 (0)
East Asian only	1308 (20)	11 (10)	13 (13)	18 (27)	8 (27)	56 (23)
Others (includes not reported/multiracial)	427 (6)	15 (14)	7 (7)	2 (3)	3 (10)	18 (8)
BMI, kg/m^2	27.3 (5.0)	26.6 (3.5)	27.0 (4.4)	26.2 (4.6)	23.8 (3.6)	26.6 (5.5)
<25 kg/m^2	2282 (34)	35 (33)	40 (40)	27 (41)	19 (63)	97 (41)
≥25 to <30 kg/m^2	2753 (41)	56 (52)	40 (40)	29 (44)	10 (33)	87 (37)
≥30 kg/m^2	1606 (24)	16 (15)	21 (21)	10 (15)	1 (3)	53 (22)
Weight, kg	76.4 (16.5)	79.0 (11.7)	68.9 (13.0)	73.5 (17.6)	66.4 (13.3)	74.1 (17.6)
Medical history						
Hypertension	5188 (78)	73 (68)	81 (80)	47 (71)	21 (70)	175 (73)
Diabetes mellitus	1665 (25)	31 (29)	20 (20)	19 (29)	6 (20)	65 (27)
Current tobacco use	1414 (21)	9 (8)	6 (6)	8 (12)	5 (17)	42 (18)
Coronary artery disease	442 (7)	9 (8)	5 (5)	4 (6)	3 (10)	9 (4)
Heart failure	222 (3)	1 (1)	4 (4)	2 (3)	4 (13)	5 (2)
Prior stroke or TIA	1165 (17)	10 (9)	23 (23)	16 (24)	9 (30)	40 (17)
Arterial territory of qualifying stroke						
Anterior circulation	4803 (72)	74 (69)	72 (71)	53 (80)	22 (73)	163 (68)
Posterior circulation	2093 (31)	37 (35)	31 (31)	14 (21)	10 (33)	84 (35)
Cerebral hemisphere with cortical involvement	3708 (56)	71 (66)	63 (62)	45 (68)	17 (57)	131 (55)
Cerebral hemisphere, subcortical only	1447 (22)	11 (10)	16 (16)	9 (14)	3 (10)	32 (13)
Brainstem only	315 (5)	4 (4)	3 (3)	0 (0)	0 (0)	9 (4)
Cerebellum only	506 (8)	9 (8)	10 (10)	4 (6)	2 (7)	30 (13)
Multiple locations	689 (10)	12 (11)	9 (9)	8 (12)	8 (27)	37 (15)
NIHSS score at randomization	1.0 (0.0–2.0)	0.0 (0.0–2.0)	0.0 (0.0–1.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)	0.0 (0.0–2.0)
NIHSS score ≤ 5	6403 (96)	105 (98)	96 (95)	64 (97)	28 (93)	230 (96)
Modified Rankin Scale (mRS) at randomization						
mRS 0 or 1	4305 (65)	70 (65)	64 (63)	43 (65)	17 (57)	171 (72)
mRS 2	1561 (23)	25 (23)	24 (24)	10 (15)	8 (27)	44 (18)
mRS ≥ 3	803 (12)	12 (11)	13 (13)	13 (20)	5 (17)	24 (10)
Time from qualifying stroke to randomization, days	36.0 (14.0–88.0)	48.0 (16.0–101.0	44.0 (20.0–102.0	42.5 (20.0–87.0)	33.0 (11.0–58.0)	39.0 (14.0–88.0)

BMI, body mass index; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischaemic attack. Data expressed as n (%), mean (standard deviation) or median (interquartile range). Participants with skin cancer only (n = 77) are included in the 'no cancer' group.

strokes [5,9,10,14]. Cancer patients had more frequently multiple acute cerebral ischaemic lesions, which is also supported by previous studies [14,18]. Patients with cancer were also older than non-cancer patients and they were less frequently current smokers, but no other relevant differences were seen in other comorbidities between cancer and non-cancer patients except for a slightly higher prevalence of hypertension in the latter group. Non-cancer patients also had a higher NIHSS score at randomization but no difference in modified Rankin Scale. A history of cancer was not an independent predictor of a higher rate of recurrent ischaemic stroke after adjustment for age and other factors [19]. Interestingly, self-reported health status EQ-5D score data collected at baseline did not differ between cancer and non-cancer patients probably reflecting that a major portion of the patients with cancer were already healed or under control with treatment and that the patients with cancer and expectedly poor prognosis were left out of the study.

Our study suggests that there was no difference in cancer patients' rate of recurrent ischaemic stroke between the rivaroxaban and aspirin arms, which is in agreement with the results of the overall NAVIGATE

Table 3 Rate of major outcomes and response to treatment[a]

	Rivaroxaban assigned (N = 3609)		Aspirin assigned (N = 3604)			
	Number of randomized patients	Number of events (event rate[b])	Number of randomized patients	Number of events (event rate[b])	Hazard ratio (95% CI)	P value (interaction)[c]
Recurrent ischaemic stroke						
Cancer (+)	254	18 (7.7)	289	14 (5.4)	1.43 (0.71, 2.87)	
Cancer (−)	3355	141 (4.5)	3315	142 (4.6)	0.98 (0.78, 1.24)	0.3137
First ISTH major bleed						
Cancer (+)	254	7 (2.9)	289	3 (1.1)	2.57 (0.67, 9.96)	
Cancer (−)	3355	55 (1.7)	3315	20 (0.6)	2.75 (1.65, 4.59)	0.9539
All-cause death						
Cancer (+)	254	9 (3.7)	289	9 (3.3)	1.10 (0.44, 2.78)	
Cancer (−)	3355	56 (1.7)	3315	43 (1.3)	1.30 (0.87, 1.93)	0.7733

CI, confidence interval; ISTH, International Society on Thrombosis and Haemostasis. [a]Intention-to-treat analyses. [b]Event rates reported in 100 person-years. [c]Hazard ratio, 95% CI, and P for interaction not reported if hazard ratio is ≥10 or cannot be computed.

ESUS population [4]. Also, patients with ESUS and cancer had similar serious complications and all-cause mortality under rivaroxaban and aspirin and treatments compared to the overall population, but showed a higher rate of major bleeds in the rivaroxaban arm. The difference did not reach significance in patients with cancer but is in line with the total population.

Only a few previous studies have compared antithrombotic treatments in stroke patients with cancer. The TEACH pilot trial randomized 20 cancer patients to enoxaparin or aspirin arms and showed no differences in the cumulative rates of major bleeding, thromboembolic events and survival between the groups [20]. Furthermore, a recent study comparing direct oral anticoagulants and low-molecular-weight heparin in the treatment of 48 cryptogenic ischaemic stroke patients with active cancer also showed similar clinical outcomes between the treatment arms [21]. However, these studies were limited by their small size. Jang *et al.* [22] found in a retrospective single-centre observational study that enoxaparin may be more effective for lowering the serum D-dimer levels compared to warfarin in patients with cancer-associated strokes, but no difference was seen in the rates of major bleeding. In our study, both treatment arms had a similar frequency of newly diagnosed cancers during the 11-month follow-up. All new cancers were reported as adverse events in trial, but no data were available on cancer stage or treatments.

The most notable strength of our study is the large size of the cohort in an international randomized phase III trial. Furthermore, it is one of the largest studies comparing secondary preventive strategies in ischaemic stroke patients. Data of prior cancers, primary events, serious complications and new cancers were systematically reported by investigators. However, despite the large size of the NAVIGATE ESUS cohort, it represents patients who are willing, able and invited to participate in a clinical trial and therefore may be subject to limitations on generalizability, both overall and within subgroups. Life expectancy less

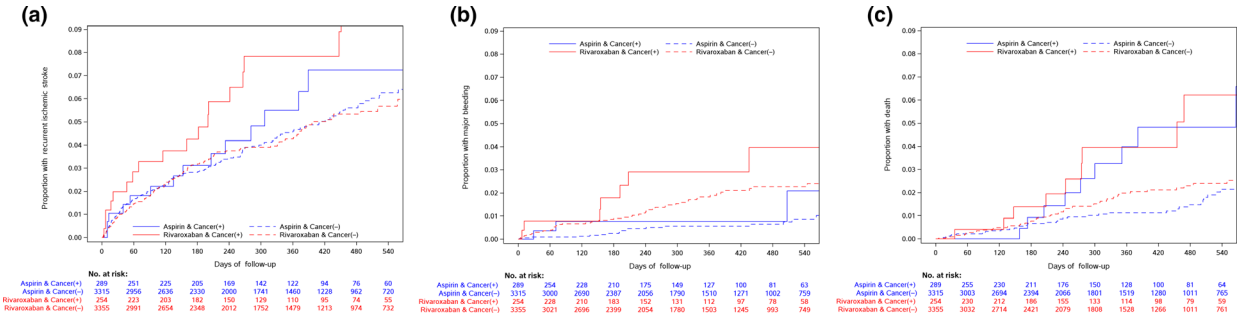

Figure 1 Kaplan–Meier curves of the cumulative risks in cancer patients treated with rivaroxaban or aspirin for (a) recurrent ischaemic stroke, (b) major bleeds and (c) all-cause death.

than 6 months was an exclusion criterion and probably excluded patients with pancreatic cancer and metastatic cancers already diagnosed at the randomization stage. Therefore, it is also possible that those patients who were included in the NAVIGATE ESUS trial had a less severe cancer or they were disease-free. This bias could be an additional explanation for the similar outcome between cancer and non-cancer patients. The diagnosis and the type of cancer were based on participant self-report and were not confirmed, and no information about cancer staging or anti-cancer treatment was collected. Further, diagnostic testing may affect outcome analysis as patients in higher income countries may have undergone more extensive pre-enrolment investigations than those in middle or lower income countries. No data were available on specific biological markers, since additional blood samples were only rarely collected. Patients with venous thrombosis at baseline were also excluded due to the clear indication for anticoagulation.

This subgroup analysis of the NAVIGATE ESUS trial shows that the efficacy and safety profile of rivaroxaban compared with aspirin in ESUS patients with cancer was similar to the overall population of the trial. However, due to the limited number of end-points in cancer patients leading to underpowered subgroup analyses, these results should be interpreted with caution. The results of this analysis could still be helpful for the design of future trials of thromboprophylaxis in patients with cancer, which is a population with simultaneously high thrombotic and high bleeding risk.

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Disclosure of conflicts of interest

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Rate of first recurrent ischaemic stroke and response to treatment: on-treatment analysis

Table S2. Comparison of mean change in EQ-5D scores between cancer and non-cancer patients

Table S3. Comparison of mean change in EQ-5D scores of cancer patients in the rivaroxaban and aspirin arms

Table S4. Rate of first recurrent ischaemic stroke and response to treatment amongst those without cancer at baseline

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