Clinical Study Synopsis

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The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

Bayer HealthCare

Clinical Trial Results Synopsis

Study Design Description		
Study Sponsor:	Bayer HealthCare Pharmaceuticals Inc.	
Study Number:	11899	NCT00439725
Study Phase:	III	
Official Study Title:	Once-daily oral direct factor Xa inhibitor rivaroxaban in the long-term prevention of recurrent symptomatic venous thromboembolism in subjects with symptomatic deep vein thrombosis or pulmonary embolism. The Einstein extension study.	
Therapeutic Area:	Cardiology/Coagulation	
Test Product		
Name of Test Product:	Rivaroxaban (Xarelto, BAY59-7939)	
Name of Active Ingredient:	Rivaroxaban	
Dose and Mode of Administration:	20 mg tablet once daily, administered orally	
Reference Therapy/Placebo		
Reference Therapy:	Matching placebo	
Dose and Mode of Administration:	Matching placebo tablet once daily, administered orally	
Duration of Treatment:	Six or 12 months (determined individually before randomization). The study was terminated once a total of at least 30 confirmed recurrent thromboembolic events had been reached. If the number of events were reached before all subjects had completed the intended study treatment duration, the last included subjects had to be treated until they reached a total treatment duration of at least 3 months.	
Studied period:	**Date of first subjects' first visit:**	28 FEB 2007
	Date of last subjects' last visit:	17 SEP 2009
Premature Study Suspension / Termination:	No	
Substantial Study Protocol Amendments:	Amendment no. 1 (dated 21 MAR 2007) was locally valid only for centers in Germany. Before enrollment of the first subject in Germany, it implemented a clarification to the exclusion criterion regarding contraceptive measures that had been requested by the health authority in Germany. The clarification was "Proper contraceptive measures were defined as a method of contraception with a failure rate<1% during the course of the study (including the observational period). These methods of contraception according to the note for guidance on non-clinical safety studies for the conduct of human trials for pharmaceuticals (CPMP/ICH/286/95, modification) include consistent and correct use of hormone-containing implants and injectables, combined oral contraceptives, hormone-containing intrauterine devices, surgical sterilization, sexual abstinence, and vasectomy." Amendment no. 2 (dated 05 JUL 2007) was globally implemented after study results concerning the pharmacokinetic interaction	

	between the CYP3A4 inducer rifampicin and rivaroxaban had become available. The amendment specified the addition of strong CYP3A4 inhibitors to the list of prohibited concomitant medications and limitation of strong CYP3A4 inducers. Amendment no. 3 (dated 11 OCT 2007) was globally implemented and it specified more flexibility regarding previous treatment with vitamin K antagonist (VKA) for subjects coming from outside the EINSTEIN venous thromboembolism (VTE) treatment program: 6 to 14 months were accepted rather than only 6 + 2 months or 12 ± 2 months.
Study Centre(s):	The study was conducted in 173 centers: Australia (18), Austria (7), Belgium (5), Brazil (6), China (8), Czech Republic (7), Denmark (3), France (18), Germany (7), Hungary (7), India (4), Indonesia (1), Israel (7), Italy (11), Malaysia (1), the Netherlands (5), New Zealand (5), Norway (3), Philippines (2), Poland (7), Singapore (2), South Africa (10), Spain (6), Sweden (6), Switzerland (2), Thailand (2), the United Kingdom (3), and the United States (10).
Methodology:	The primary efficacy outcome was the composite of recurrent deep vein thrombosis (DVT) or non-fatal or fatal pulmonary embolism (PE). The primary efficacy analysis was based on the time to the first event for the primary efficacy outcome. Recurrent DVT/PE, bleeding events, death, and vascular events were evaluated by a central, blinded, independent adjudication committee (CIAC). All such events cited in this report were adjudicated and confirmed by the CIAC unless otherwise described. The principal safety variable was major bleeding events.
Indication/ Main Inclusion Criteria:	Indication Long-term prevention of recurrent symptomatic VTE Main Inclusion Criteria Subjects with confirmed symptomatic DVT or PE • Who either had been treated for 6 or 12 months with VKA or rivaroxaban in study 11702 (Einstein DVT and Einstein PE) or • Who had been treated for 6 to 14 months with VKA (either warfarin or acenocoumarol) outside study 11702.
Study Objectives:	**Primary:** To evaluate whether rivaroxaban is superior to placebo in the long-term prevention of recurrent symptomatic VTE in subjects with symptomatic DVT or PE • Who either had been treated for 6 or 12 months with VKA or rivaroxaban in the 11702 study *or* • Who had been treated for 6 to 14 months with VKA (either warfarin or acenocoumarol) outside study 11702 The principal safety objective was to compare major bleeding events between treatment groups. **Secondary:** Not applicable

Evaluation Criteria:	**Efficacy (Primary):** Primary efficacy outcome: composite of recurrent DVT or non-fatal or fatal PE **Efficacy (Secondary):** • Percentage of subjects with the composite variable comprising recurrent DVT, non-fatal PE and all-cause mortality until the intended end of study treatment • Percentage of subjects with the composite variable comprising recurrent DVT, non-fatal PE, all-cause mortality, strokes and myocardial infarctions until the intended end of study treatment • Percentage of subjects with net clinical benefit as composite of recurrent DVT or non-fatal or fatal PE and major bleeding events until the intended end of study treatment • Percentage of subjects with recurrent VTE (PE or DVT) until the intended end of study treatment • Percentage of subjects with recurrent DVT until the intended end of study treatment • Percentage of subjects with major bleeding • Percentage of subjects with clinically relevant bleeding • Percentage of subjects with all death • Percentage of subjects with other vascular events Other pre-specified outcome measures included: • Percentage of subjects with death (PE) until the intended end of study treatment • Percentage of subjects with death (PE cannot be excluded) until the intended end of study treatment • Percentage of subjects with symptomatic recurrent PE until the intended end of study treatment • Percentage of subjects with symptomatic recurrent VTE (i.e., the composite of recurrent DVT or fatal or non-fatal PE) during observational period • Percentage of subjects with symptomatic recurrent PE during observational period • Percentage of subjects with the composite variable comprising recurrent DVT, non-fatal PE and all-cause mortality during observational period • Percentage of subjects with the composite variable comprising recurrent DVT, non-fatal PE, all-cause mortality, strokes and myocardial infarctions during observational period • Percentage of subjects with net clinical benefit as composite of recurrent DVT or non-fatal or fatal PE and major bleeding events during observational period • Percentage of subjects with recurrent VTE (PE or DVT) during observational period • Percentage of subjects with recurrent DVT during observational period

	Safety: Principal safety variable: major bleeding events Secondary safety variables: all clinically relevant bleeding events (i.e., major bleeding events and other clinically relevant non-major bleeding events), all deaths, and other vascular events.
Statistical Methods:	**Efficacy (Primary):** For the primary efficacy analysis, all events were considered up to the pre-planned duration of treatment (6 or 12 months) irrespective of the actual treatment duration. The time to the first event of the composite primary efficacy outcome was analyzed using a Cox's proportional hazards model stratified for planned treatment duration and adjusted for previous treatment (rivaroxaban vs VKAs). The impact of baseline covariates on the primary efficacy outcome was described by calculating adjusted hazard ratios and 95% confidence intervals (CIs) of the treatment effect. The frequencies of the separate components contributing to the primary efficacy outcome were described. **Efficacy (Secondary):** The following hierarchy for statistical testing of the secondary efficacy outcomes was applied. If significance was proven for the primary efficacy outcome, the secondary efficacy outcome 1 was tested for confirmation. If this was proven significant, the secondary efficacy outcome 2 was tested for confirmation. Finally, if this was also proven significant, the secondary efficacy outcome 3 was tested for confirmation. **Safety:** If rivaroxaban was superior to placebo, the time to the first event for the principal safety variable was compared between treatment groups using a Cox's proportional hazard model. Additionally, time to all clinically relevant bleeding events was also tested using a Cox's proportional hazard model. Adverse events (AEs) were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 12.0. Incidence/prevalence of pre-specified abnormalities, the differences between treatment groups, and the 95% CI on the differences were displayed as exploratory analysis.
Number of Subjects:	Planned: 1300 subjects (650 per treatment group) expected to reach 30 confirmed recurrent thromboembolic events. Analyzed: 1196 (intention-to-treat analysis: 602 rivaroxaban and 594 placebo) 1188 (safety analysis: 598 rivaroxaban and 590 placebo) 1104 (per-protocol (PP) analysis: 550 rivaroxaban and 554 placebo)

Study Results
Results Summary — Subject Disposition and Baseline
In this study, 1200 subjects were enrolled, of which 1197 were randomized at 173 study centers in 28 countries: 602 subjects were randomized to rivaroxaban 20 mg od treatment and 595 to placebo. Of these, 1 subject in the placebo group was excluded from the intent-to-treat (ITT) population due to invalid informed consent. From the safety population, 84 subjects (48 in the rivaroxaban and 36 in the placebo group) were excluded from the per-protocol (PP) population for supportive efficacy evaluations. From the safety population, 232 rivaroxaban subjects (39%) and 241 placebo subjects (41%) did not continue their study medication until the scheduled end of treatment. The most frequently reported reason for premature termination of treatment was the study design: the study was stopped once the required number of at least 30 confirmed recurrent thromboembolic events had been reached, after which the last randomized subjects had to be treated until they reached a total treatment duration of at least 3 months. The premature termination of the study affected 156 subjects (26%) in the rivaroxaban group and 148 subjects (25%) in the placebo group. Other frequent reasons for premature termination of treatment included adverse events (39 subjects [7%] in the rivaroxaban and 18 subjects [3%] in the placebo group), reaching the clinical endpoint (6 subjects [1%] in the rivaroxaban and 50 subjects [9%] in the placebo group), and withdrawal of consent (22 subjects [4%] in the rivaroxaban and 19 subjects [3%] in the placebo group). For one subject in each treatment group (<1%), the reason documented for premature discontinuation of treatment was loss to follow-up. With regard to the ITT population, there were no relevant differences between treatment groups for the baseline and demographic parameters. About 58% of subjects were male. The race of about 78% of subjects was described as White, for about 8% as Asian, and for about 2% as Black. For just over 11% of subjects, no information was available as in some participating countries it is not permitted to collect data on subjects' race. Age ranged from 18 - 89 years in the rivaroxaban group and from 19 - 96 years in the placebo group, with a mean of approximately 58 years in both groups. With respect to the age groups, about 15% of subjects were between 18 and 40 years of age, about 46% between 40 and 65 years, about 23% between 65 and 75 years, and about 16% over 75 years. Mean body weight was about 83 kg, with ranges from 39 to 163 kg. The mean body mass index (BMI) was about 28 kg/m^2, with ranges from approximately 15 to 54 kg/m^2. As an index event at baseline, about 60% of subjects had proximal DVT without PE. About 29% had PE without symptomatic DVT. With respect to prior treatment with VKAs or rivaroxaban, about 55% of subjects had previously been treated with warfarin; about 28% of subjects had been treated with rivaroxaban in study 11702; and about 18% of subjects had been treated with acenocoumarol. Elevated liver function tests (LFTs) (as judged by the investigator) were documented at baseline for 27 subjects in the rivaroxaban group (4.5%) and for 26 subjects in the placebo group (4.4%). Of all the randomized subjects, 314 subjects (52%) in the rivaroxaban group and 318 subjects (53%) in the placebo group had previously taken part in study 11702 (Einstein DVT or Einstein PE); 286 subjects (48%) in the rivaroxaban group and 274 subjects (46%) in the placebo came from outside study 11702.

Results Summary — Efficacy

Percentage of subjects with symptomatic recurrent VTE (i.e., the composite of recurrent DVT or fatal or non-fatal PE until the intended end of study treatment

The incidence rate of the primary efficacy outcome was 1.3% (8/602) in the rivaroxaban group and 7.1% (42/594) in the placebo group until the end of planned treatment for the ITT population. Note that after the termination of the study, subjects still in the study had to be treated until they reached a total treatment duration of at least 3 months. There were 13 events for the primary efficacy outcome that occurred after the day of randomization of the last subject. In addition, there was a lag period between the occurrence of the 30th event for the primary efficacy outcome and the point in time at which the decision was made to stop the study. This was due to the time needed for the regular adjudication and confirmation procedure. Therefore, the total number of subjects with events for primary efficacy in the study was greater than 30. Regarding individual components of the primary efficacy outcome, the incidence rates were 0% (no cases) in the rivaroxaban group and 0.2% (1/594) in the placebo group for death due to PE; 0.2% (1/602) in the rivaroxaban group and 0% (no cases) in the placebo group for death for which PE could not be excluded as the reason; 0.3% (2/602) in the rivaroxaban group and 2.2% (13/594) in the placebo group for symptomatic recurrent PE; and 0.8% (5/602) in the rivaroxaban group and 5.2% (31/594) in the placebo group for symptomatic recurrent DVT.

As primary analysis, a Cox's proportional hazard model stratified for planned treatment duration and adjusted for previous treatment (rivaroxaban vs. VKA with or without rivaroxaban) was employed. The comparison of rivaroxaban vs placebo treatment yielded a hazard ratio of 0.185 (81% relative risk reduction). The 95% confidence interval (CI) of 0.087 - 0.393 ($p<0.0001$) indicated a statistically significant effect. The comparison of prior VKA with or without rivaroxaban treatment with prior rivaroxaban treatment suggested that there was no statistically significant difference between these types of prior treatment (hazard ratio 0.906, 95% CI 0.488 - 1.683).

Percentage of subjects with the composite variable comprising recurrent DVT, non-fatal PE, and all-cause mortality until the intended end of study treatment (Secondary efficacy variable 1)

The secondary efficacy outcome 1 was a composite variable comprising recurrent DVT, non-fatal PE and all-cause mortality.

The incidence rates of the secondary efficacy outcome 1 until the end of planned treatment were 1.3% (8/602) in the rivaroxaban group and 7.2% (43/594) in the placebo group for the ITT population

In the Cox's proportional hazard model stratified for planned treatment duration and adjusted for previous treatment (rivaroxaban vs VKAs), the comparison of rivaroxaban vs placebo treatment yielded a hazard ratio of 0.180. The 95% confidence interval (CI) of 0.085 - 0.383 ($p<0.0001$) indicated a statistically significant effect.

Percentage of subjects with the composite variable comprising recurrent DVT, non-fatal PE, all-cause mortality, strokes, and myocardial infarctions until the intended end of study treatment (Secondary efficacy variable 2)

The secondary efficacy outcome 2 was a composite variable comprising recurrent DVT, non-fatal PE, all-cause mortality, strokes and myocardial infarctions.

The incidence rates of the secondary efficacy outcome 2 until the end of planned treatment were 1.5% (9/602) in the rivaroxaban group and 7.4% (44/594) in the placebo group for the

ITT population.

In the Cox's proportional hazard model stratified for planned treatment duration and adjusted for previous treatment (rivaroxaban vs VKAs), the comparison of rivaroxaban vs placebo treatment yielded a hazard ratio of 0.198. The 95% confidence interval (CI) of 0.096 - 0.405 ($p<0.0001$) indicated a statistically significant effect.

Percentage of subjects with net clinical benefit as composite of recurrent DVT or non-fatal or fatal PE and major bleeding events until the intended end of study treatment (Secondary efficacy variable 3)

The secondary efficacy outcome 3 was net clinical benefit as composite of recurrent DVT or non-fatal or fatal PE (the primary efficacy outcome) and major bleeding events.

The incidence rates of the secondary efficacy outcome 3 until the end of planned treatment were 2.0% (12/602) in the rivaroxaban group and 7.1% (42/594) in the placebo group for the ITT population

In the Cox's proportional hazard model stratified for planned treatment duration and adjusted for previous treatment (rivaroxaban vs VKAs), the comparison of rivaroxaban vs placebo treatment yielded a hazard ratio of 0.278. The 95% confidence interval (CI) of 0.146 - 0.528 ($p<0.0001$) indicated a statistically significant effect.

Percentage of subjects with recurrent VTE (PE or DVT) until the intended end of study treatment (Secondary efficacy variable 4)

The percentage of subjects with recurrent VTE (PE or DVT) was 1.2% in the rivaroxaban group and 7.1% in the placebo group.

Percentage of subjects with recurrent DVT until the intended end of study treatment (Secondary efficacy variable 5)

The percentage of subjects with recurrent DVT until the intended end of study treatment was 0.8% in the rivaroxaban group and 5.2% in the placebo group.

Percentage of subjects with major bleeding (Safety variable)

The incidence of the principal safety variable, treatment-emergent major bleeding events was low (0.7% [4/598] rivaroxaban versus 0% placebo). The difference between the treatment groups was statistically not significant (2-sided exact log-rank test: p-value 0.1121). No fatal bleeding event was reported. All post-randomization treatment-emergent bleeding events were 0.7% in the rivaroxaban group and 0.2% in the placebo group.

Percentage of subjects with clinically relevant bleeding

The incidence rates of the secondary safety variable, treatment-emergent major or clinically relevant non-major bleeding events were 6.0% (36/598) in the rivaroxaban group and 1.2% (7/590) in the placebo group. The difference between the treatment groups was statistically significant ($p<0.0001$) in favor of the placebo group (hazard ratio: 5.185, 95% CI: 2.307 - 11.652). The bleeding events mainly contributing to this difference were of urogenital, nasal and rectal origin. All post-randomization clinically relevant bleeding events were 6.0% in the rivaroxaban group and 1.9% in the placebo group.

Percentage of subjects with all death

There were 3 deaths in the safety population (1 rivaroxaban and 2 placebo). An additional death was documented in a subject randomized to placebo who had an invalid informed

consent and was not included in the safety population. The incidence rates of treatment-emergent deaths were 0.2% in the rivaroxaban group and 0.2% in the placebo group.

Percentage of subjects with other vascular events

On-treatment events were those events that had an onset not later than 1 day after the last intake of double-blind study medication. In contrast, off-treatment events were events that had an onset > 1 day after last intake of double-blind study medication. The rates indicated a low cardiovascular event rate during both the on-treatment and the off-treatment periods. During the on-treatment period, 3/598 (0.5%) subjects in the rivaroxaban 20 mg o.d. group and 4/590 (0.7%) subjects in the placebo group had vascular events; during the off-treatment period, the number of subjects was 2 in the rivaroxaban group and none in the placebo group. All post-randomization other vascular events were 0.8% in the rivaroxaban group and 0.7% in the placebo group.

Percentage of subjects with death (PE) until the intended end of study treatment

The incidence rates of death, treatment-emergent were 0% in the rivaroxaban group and 0.2% in the placebo group.

Percentage of subjects with death (PE cannot be excluded) until the intended end of study treatment

The incidence rates of death (PE cannot be excluded) until the intended end of study treatment were 0.2% in the rivaroxaban group and 0.0% in the placebo group.

Percentage of subjects with symptomatic recurrent PE until the intended end of study treatment

The incidence rates of symptomatic recurrent PE were 0.3% in the rivaroxaban group and 2.2% in the placebo group.

Percentage of subjects with symptomatic recurrent VTE (i.e., the composite of Recurrent DVT or fatal or non-fatal PE) during observational period

The incidence rates of symptomatic recurrent venous thromboembolism were 1.2% in the rivaroxaban group and 0.9% in the placebo group.

Percentage of subjects with the composite variable comprising recurrent DVT, non-fatal PE and all-cause mortality during observational period

The incidence rates of recurrent DVT, non-fatal PE and all-cause mortality during the observational period were 1.2% in the rivaroxaban group and 1.1% in the placebo group.

Percentage of subjects with the composite variable comprising recurrent DVT, non-fatal PE, all-cause mortality, strokes and myocardial infarctions during observational period

The incidence rates of the composite variable comprising recurrent DVT, non-fatal PE, all-cause mortality, strokes and myocardial infarctions during observational period were 1.4% in the rivaroxaban group and 1.1% in the placebo group.

Percentage of subjects with net clinical benefit as composite of recurrent DVT or non-fatal or fatal PE and major bleeding events during observational period

The percentage of subjects with net clinical benefit as composite of recurrent DVT or non-fatal or fatal PE and major bleeding events during observational period was 1.2% in the

rivaroxaban group and 0.9% in the placebo group.

Percentage of subjects with recurrent VTE (PE or DVT) during observational period

The incidence rates recurrent VTE (PE or DVT) during observational period were 1.2% in the rivaroxaban group and 0.9% in the placebo group.

Percentage of subjects with recurrent DVT during observational period

The incidence rates recurrent DVT during observational period were 0.9% in the rivaroxaban group and 0.7% in the placebo group.

Results Summary — Safety

Of the 1197 randomized subjects, 1188 were included in the safety population; a total of 598 subjects were exposed to rivaroxaban 20 mg od and 590 to placebo. The results indicated an acceptable safety profile of rivaroxaban when compared to placebo. This conclusion is based on the following findings:

- There were 3 deaths in the safety population (1 rivaroxaban and 2 placebo). An additional death was documented in a subject randomized to placebo, who had an invalid informed consent and was not included in the safety population.
- The incidence of the principal safety variable, treatment-emergent major bleeding events, was low (0.7% [4/598] rivaroxaban versus 0% placebo). The difference between the treatment groups was statistically not significant (2-sided exact log-rank test: p-value 0.1121). No fatal bleeding event was reported. The major bleeding events were either gastrointestinal bleeding events (n=3) or menometrorrhagia (n=1), which were clinically manageable and had an outcome of "resolved".
- The incidence rates of the secondary safety variable, treatment-emergent major or clinically relevant non-major bleeding events, were 6.0% (36/598) in the rivaroxaban group and 1.2% (7/590) in the placebo group. The difference between the treatment groups was statistically significant in favor of the placebo group (hazard ratio: 5.185, 95% CI: 2.307-11.652). The bleeding events mainly contributing to this difference were of urogenital, nasal, and rectal origin.
- The incidence rates of treatment-emergent major or clinically relevant non-major bleeding events within the pre-specified subgroups were consistent with the overall incidence rates in the respective treatment groups. An increased risk for such bleeding events in both treatment groups was observed in the subgroup of subjects who concomitantly received platelet aggregation inhibitors (PAI) and/or acetyl salicylic acid (ASA) (18.6% [8/43] in the rivaroxaban treatment group vs 3.8% [2/53] in the placebo group) and in the subgroup who received non-steroidal anti-inflammatory drugs (NSAIDs) (14.3% [6/42] in the rivaroxaban treatment group vs 2.7% [1/37] in the placebo group). The relative increase of these bleeding events in the rivaroxaban treatment group compared to placebo was consistent with the overall relative increase.
- The incidence of treatment-emergent adverse events (56% rivaroxaban versus 55% placebo) was comparable between the 2 treatment groups. The incidence of drug-related treatment-emergent adverse events was 16% in the rivaroxaban group versus 11% in the placebo group. *Note that, recurrent DVT and non-fatal PE were not regarded as AEs or serious adverse events (SAEs).*
- The incidence of treatment-emergent adverse events excluding the bleeding events was comparable between the treatment groups (51% rivaroxaban versus 53% placebo), as were those assessed as treatment-related (7% rivaroxaban versus 6% placebo).
- The incidence of treatment-emergent serious adverse events was 9% in the rivaroxaban group vs 8% in the placebo group, compared to 7% in the rivaroxaban group and 8% in the placebo group when bleeding events were excluded.
- A total of 6.5% of the subjects on rivaroxaban versus 3.4% on placebo prematurely

discontinued the study medication due to treatment-emergent AEs.

- There was no fatal outcome related to liver function test abnormalities, nor was there an occurrence of the pre-specified abnormality with alanine transaminase (ALT)>3 x ULN combined with total bilirubin>2 x upper limit of normal (ULN). Observed ALT abnormalities (>3 x ULN; 11/591 rivaroxaban treated subjects [1.9%] vs 3/586 placebo subjects [0.5%]) were transient and either improved or returned to normal during continued treatment (6/11 of rivaroxaban treated subjects) or after stop of study medication (5/11 of rivaroxaban treated subjects). The liver function test abnormalities observed in rivaroxaban treated subjects were asymptomatic and as such clinically not detectable. The differences between the treatment groups of reported adverse events categorized as hepatic disorders (based on the hepatic disorder standardized MedDRA query [SMQ]) were small in this placebo controlled study. Most of the differences were related to laboratory abnormalities.
- During the treatment period, 3/598 subjects (0.5%) in the rivaroxaban 20 mg od group and 4/590 subjects (0.7%) in the placebo group had vascular events as pre-defined in the study protocol and confirmed by the CIAC; during the off-treatment period, the number of subjects was 2/598 (0.3%) in the rivaroxaban 20 mg od group and none in the placebo group. No vascular death occurred. This placebo-controlled study did not present differences in incidence rates of vascular events occurring either on- or off-treatment, taking into account the low number of reported vascular events.

Conclusion(s)

In this study, treatment with rivaroxaban 20 mg od showed superior efficacy when compared to placebo in subjects who had completed a conventional treatment-period with anticoagulant medication for symptomatic VTE. In the safety profile, rivaroxaban showed an expected increased incidence rate of bleeding events when compared to placebo. These events were clinically manageable. Thus, the study supports the extended treatment with rivaroxaban in subjects with symptomatic VTE.

Publication(s):	Cohen AT, Dobromirski M. The use of rivaroxaban for short- and long-term treatment of venous thromboembolism. Thromb Haemost. 2012 Jun;107(6):1035-43. doi: 10.1160/TH11-12-0859. Epub 2012 Feb 28. PMID: 22371186 EINSTEIN Investigators; Bauersachs R, Berkowitz SD, Brenner B, Buller HR, Decousus H, Gallus AS, Lensing AW, Misselwitz F, Prins MH, Raskob GE, Segers A, Verhamme P, Wells P, Agnelli G, Bounameaux H, Cohen A, Davidson BL, Piovella F, Schellong S. Oral rivaroxaban for symptomatic venous thromboembolism. N Engl J Med. 2010 Dec 23;363(26):2499-510. Epub 2010 Dec 3. PMID: 21128814

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Investigational Site List

Marketing Authorization Holder in Germany	
Name	Bayer Pharma AG
Postal Address	D-13342 Berlin Deutschland
Sponsor in Germany (if applicable)	
Legal Entity Name	Bayer HealthCare AG
Postal Address	D-51368 Leverkusen, Germany

List of Investigational Sites

No	Facility Name	Street	ZIP Code	City	Country
1	Concord Repatriation General Hospital	Hospital Road Concord	2139	Sydney	AUSTRALIA
2	Eastern Clinical Research Unit - Box Hill	Eastern Clinical Research Unit Level 1 5 Arnold Street	3128	Box Hill	AUSTRALIA
3	Flinders Medical Centre	Level 6 Flinders Medical Centre Flinders Drive Bedford Park	5042	Adelaide	AUSTRALIA
4	Geelong Hospital	The Andrew Love Cancer Centre Haematology 70 Swanston St	3220	Geelong	AUSTRALIA
5	Gosford Hospital	Holden Street	2250	Gosford	AUSTRALIA
6	Lismore Base Hospital	Uralba Street	2480	LISMORE	AUSTRALIA
7	Maroondah Hospital	Davey Drive Ringwood East	3135	Melbourne	AUSTRALIA

8	Monash Medical Centre	246 Clayton Road	3168	Clayton	AUSTRALIA
9	Princess Alexandra Hospital	Department of Vascular Medicine 1st Floor, Building 1, Room 1BS 19.1 Ipswich Road	4102	Woolloongabba	AUSTRALIA
10	Queen Elizabeth Hospital	28 Woodville Road Woodville	5011	Adelaide	AUSTRALIA
11	Redcliffe Hospital	Research Department Redcliffe Hospital Anzac Avenue	4020	Redcliffe	AUSTRALIA
12	Royal Brisbane & Women's Hospital	Dept Internal Medicine Level 4, James Mayne Building Butterfield St Herston	4029	Brisbane	AUSTRALIA
13	Royal North Shore Hospital	Pacific Highway	2065	St Leonards	AUSTRALIA
14	Royal Perth Hospital	Thrombosis & Haemophilia Service Kirkman House 10 Murray St	6000	Perth	AUSTRALIA
15	St George Hospital	Gray Street	2217	Kogarah	AUSTRALIA
16	Sutherland Hospital & Community Health Service	430 The Kingsway Caringbah	2229	Sydney	AUSTRALIA
17	The Avenue Cardiovascular Centre	42 The Avenue Windsor	3181	Melbourne	AUSTRALIA
18	The Canberra Hospital	Department of Haematology Bldg 10 Gilmore Crescent	2605	Garran	AUSTRALIA

19	Allgemeines Krankenhaus der Stadt Wien Universitätskliniken	Univ. Klinik f. innere Med I Klin. Abt. f. Hämatologie und Hämostaseologie Währinger Gürtel 18-20	1090	Wien	AUSTRIA
20	Hanusch-Krankenhaus Wien	Heinrich-Collin-Straße 30	1140	Wien	AUSTRIA
21	Landeskrankenhaus Feldkirch	Carinagasse 47	6807	Feldkirch	AUSTRIA
22	Landeskrankenhaus Salzburg	Universitätsklinikum der PMU Müllner Hauptstrasse 48	5020	Salzburg	AUSTRIA
23	Medizinische Universität Graz	Med. Universitätsklinik klin. Abteilung f. Angiologie Auenbruggerplatz 15	8036	Graz	AUSTRIA
24	Universitätsklinikum Innsbruck	Anichstraße 35	6020	Innsbruck	AUSTRIA
25	AKH - Universitätskliniken	Univ.-Klinik für Innere Medizin II Klinische Abteilung für Kardiologie Währinger Gürtel 18-20	1090	Wien	AUSTRIA
26	AZ St-Elisabeth	Godveerdegemstraat 96	9620	ZOTTEGEM	BELGIUM
27	CHU de Liège	Hôpital du Sart Tilman Service Cardiologie Domaine Universitaire du Sart Tilman Bâtiment B35	4000	LIEGE	BELGIUM
28	Hôpital Erasme/Erasmus Ziekenhuis	Route de Lennik 808 Lenniksebaan	1070	BRUXELLES - BRUSSEL	BELGIUM
29	UZ Gent	De Pintelaan 185	9000	GENT	BELGIUM

30	UZ Leuven Gasthuisberg	Dienst Inwendige Geneeskunde Bloedings - en Vaatziekten Herestraat 49	3000	LEUVEN	BELGIUM
31	Hosp. Dr Helio Angotti - Assoc. Combate ao Cancer Br Central	Rua Governador Valadares, 640	38010 380	Uberaba	BRAZIL
32	Hospital da Beneficiência Portuguesa	Rua Maestro Cardim , 769 - Paraiso	01323-001	São Paulo	BRAZIL
33	Hospital Universitário Cajuru da PUC PR	Avenida São José, 300	80050-350	Curitiba	BRAZIL
34	Hospital Universitario Pedro Ernesto	Av. 28 de Setembro, 77 - 20551-030		Rio de Janeiro	BRAZIL
35	Hospital Universitário Regional do Norte do Paraná	Av. Robert Koch, 60 - Vl Operário	86038440	Londrina	BRAZIL
36	Inst. de Assistência Médica ao Sérvidor Público Estadual	Rua Pedro de Toledo, 1800	04039-004	São Paulo	BRAZIL
37	Beijing Anzhen Hospital of the Capital University of Medical	Anzhenli, Andingmenwai, Chaoyang Disctrict,	100029	Beijing	CHINA
38	Peking Union Medical College Hospital	No.1 Shuai Fuyuan, Dongcheng District, No.41 Damucang Hutong, Xicheng District,	100730	Beijing	CHINA

39	Respiratory Diseases Institute, Beijing Chaoyang Hospital	8 Bai Jiazhuang Road, Chaoyang District,	100020	beijing	CHINA
40	Shanghai Pulmonary Hospital, Tongji University	No.507, Zhengmin Road,	200433	Shanghai	CHINA
41	Shanghai Renji Hospital	145 Middle Shangdong Road,	200001	shanghai	CHINA
42	The 2nd Affiliated Hospital of Soochow University	Department of Vascular Surgery, No.1055, Sanxiang Road,	215004	Suzhou	CHINA
43	the People's Hospital of Liaoning Province	33 Wenyi Road Shenhe District,	110016	shenyang	CHINA
44	Vascular Surgical Institute, Shanghai Zhongshan Hospital	180 Fenglin Road, Xuhui District,	200032	Shanghai	CHINA
45	Fakultni nemocnice Motol	Clinic of Internal Medicine V uvalu 84	150 00	Prague 5	CZECH REPUBLIC
46	Fakultni nemocnice s poliklinikou Ostrava	Interni klinika 17 Listopadu 1790	708 52	Ostrava-Poruba	CZECH REPUBLIC
47	Hospital Kladno	Interni oddeleni Vancurova 1548	27259	Kladno	CZECH REPUBLIC
48	Masaryk Hospital Usti n/L	II Dpt. of Internal Medicine Socialni pece 12/A	401 13	Usti nad Lebem	CZECH REPUBLIC
49	Mestska nemocnice Ostrava	Oddeleni interna II Nemocnicni 20	728 80	Ostrava	CZECH REPUBLIC
50	Nemocnice Na Fratisku	Interni Oddeleni Na frantisku 847/8	110 00	Praha 1	CZECH REPUBLIC

51	Vseobecna fakultni nemocnice	II Interni Klinika VFN a 1.LF UK U nemocnice 499/2	12800	Praha 2	CZECH REPUBLIC
52	Aarhus Amstsygehus	Medical-Cardiological dept. A Tage Hansens Gade 2	8000	Aarhus C	DENMARK
53	Bredstrup sygehus	Thrombosis Center Medical dept.	8740	Braedstrup	DENMARK
54	H:S Frederiksberg Hospital	Dept. of Cardiology and Endocrinology Nedre Fasanvej 57	2000F	Frederiksberg	DENMARK
55	Centre Hospitalier - Arras	Centre Hospitalier Service de Cardiologie Boulevard Georges Besnier	62000	ARRAS	FRANCE
56	Centre hospitalier Intercommunal - Vernon	Centre Hospitalier Intercommunal Eure Seine Service de Pneumologie 5 rue du Docteur Burnet	27200	VERNON	FRANCE
57	Centre Hospitalier Universitaire - Angers	Centre Hospitalier Universitaire Service d'Accueil des Urgences 4, rue Larrey	49033	ANGERS CEDEX 01	FRANCE

58	Centre Hospitalier Universitaire Brabois	Centre Hospitalier Universitaire Brabois Hopital d'adultes Unité de médecine Interne, Thromboses, Maladies Vasculaires (Pole Cardiovasculaire) Rue du Morvan	54511	VANDOEUVRE LES NANCY	FRANCE
59	Centre Hospitalier Universitaire - Grenoble	Centre Hospitalier Universitaire Hôpital Michalon Centre d'Investigation Clinique BP 217	38043	GRENOBLE	FRANCE
60	Clinique du Parc	Clinique du Parc service d'angiologie	34170	CASTELNAU LE LEZ	FRANCE
61	Groupe Hospitalier Sud - Amiens	C.H.U. Groupe Hospitalier Sud Chirurgie Vasculaire Avenue René Laennec	80000	AMIENS	FRANCE
62	Hôpital Antoine Béclère - Clamart	Hôpital Antoine Béclère Service de Pneumologie 157, rue de la Porte Trivaux	92141	CLAMART	FRANCE
63	Hôpital Civil - Strasbourg	Hôpitaux Universitaires Hôpital Civil Service d'Hypertension et Maladies Vasculaires 1, place de l'Hôpital	67091	STRASBOURG CEDEX	FRANCE

64	Hôpital du Bocage - Dijon	C.H.R.U. Dijon Service d'Hématologie Hôpital du Bocage 2 boulevard de Lattre de Tassigny	21000	DIJON	FRANCE
65	Hôpital Dupuytren - Limoges Cedex	C.H.R.U. Hôpital Dupuytren Service de Chirurgie Thoracique et cardiovasculaire 2, avenue Martin Luther King	87042	LIMOGES	FRANCE
66	Hôpital Gabriel Montpied - Clermont Ferrand	Hôpital Gabriel Montpied Service d'Accueil des Urgences 58 rue Montalembert	63000	CLERMONT FERRAND	FRANCE
67	Hopital Général - Agen	Hopital Général Département des Urgences - SAMU/SMUR Route de Villeneuve	47923	AGEN CEDEX 9	FRANCE
68	Hôpital Hôtel Dieu - Nantes Cedex	C.H.U. Nantes Hôpital Hôtel Dieu Service d'Accueil des Urgences 2, place Alexis Ricordeau	44000	NANTES	FRANCE
69	Hôpital La Cavale Blanche - Brest Cedex	Hôpital La Cavale Blanche Service de Médecine I et Pneumologie Boulevard Tanguy Prigent	29609	BREST CEDEX	FRANCE

70	Hôpital Louis Mourier - Colombes Cedex	Hôpital Louis Mourier Service de médecine interne V 178, rue des Renouillers	92700	COLOMBES	FRANCE
71	Hôpital Nord-SAINT ETIENNE	Hôpital Bellevue Unité de Pharmacologie Clinique boulevard Pasteur	42055	SAINT ETIENNE	FRANCE
72	Hôpital Saint-Eloi - Montpellier Cedex	Hôpital Saint Eloi Service de Médecine Interne et Maladies Vasculaires 80 avenue Augustin Fliche	34295	MONTPELLIER CEDEX	FRANCE
73	Brüderkrankenhaus St. Josef	Innere Medizin Husener Str. 46	33098	Paderborn	GERMANY
74	Klinikum Mannheim gGmbH	IV. Medizinische Klinik Schwerpunkt Gastroenterologie/Hepatologie Theodor-Kutzer-Ufer 1-3	68167	Mannheim	GERMANY
75	Praxis für Innere Medizin u. Gefäßkrankheiten HBE	Halberstädter Strasse 49	39112	Magdeburg	GERMANY
76	Praxis Hr. Dr. P. Baron von Bilderling	Gefäßpraxis Tal 13	80331	München	GERMANY
77	SRH Klinikum-Karlsbad-Langensteinbach gGmbH	Innere Medizin Guttmannstr. 1	76307	Karlsbad	GERMANY
78	St. Josefskrankenhaus	Innere Medizin Landhausstr. 25	69115	Heidelberg	GERMANY

79	Zentralklinikum Augsburg	I. Medizinische Klinik Kardiologie, Pneumonologie, Intensivmedizin, Endokrinologie Stenglinstraße 2	86156	Augsburg	GERMANY
80	Bacs-Kiskun Country Hospital	II Belgyogyaszat Nyiri u. 38	6000	Kecskemet	HUNGARY
81	Borsod County Hospital	III Sz. Belgyogyszat-Angiologia Szntpeteri kapu 72-76	3526	Miskolc	HUNGARY
82	Dr Bugyi Istvan Hospital	I Internal Medicine Department Sima Ferenc u. 44-58	6600	Szentes	HUNGARY
83	Flor Ferenc Hospital	II Dept. of Internal Medicine Semmelweis ter. 1	2143	Kistarcsa	HUNGARY
84	Szent Imre Hospital	Angiologiai Profil Tetenyi ut. 12-16	1115	Budapest	HUNGARY
85	University of Debrecen Medical&Health Science Center	II Internal Medicine Department Nagyerdei krt. 98.	4032	Debrecen	HUNGARY
86	Vas Megyei Markusovszky Korhaz	I Belgyogyaszat Markusovszky ut. 3	9700	Szombathely	HUNGARY
87	Amrita Institute of Medical Sciences	Dept. of Vascular Surgery	682026	Kochi	INDIA
88	Nizam's Institute of Medical Sciences	Department of Vascular Surgery NIMS	500082	Hyderabad	INDIA
89	Ruby Hall Clinic	Department of Vascular Surgery	411001	Pune	INDIA

90	Sir Ganga Ram Hospital	R.No.100, Department of Vascular & Endovascular Surgery, Sir Ganga Ram Hospital, Rajinder Nagar, -	110060	New Delhi	INDIA
91	St Elisabeth Hospital	Antithrombotic Clinic St Elisabeth Hospital Jl. H. Misbah No. 7	20152	Medan	INDONESIA
92	Barzilai Medical Center	3, Hahistadrut Street	78278	Ashkelon	ISRAEL
93	Edith Wolfson Medical Center	62 Halochamim Street P.O.B. 5	58100	Holon	ISRAEL
94	Haemek Medical Center	Rabin Road	18101	Afula	ISRAEL
95	Lady Davis Carmel Medical Center	7, Michal Street	34362	Haifa	ISRAEL
96	Meir Medical Center	Clalit Health Services 59, Tchernichovsky Street	44281	Kfar Saba	ISRAEL
97	Rambam Medical Center	8, Haaliya Hashniya St. Bat Galim	31096	Haifa	ISRAEL
98	Tel Aviv Sourasky Medical Center	Tel Aviv Sourasky Medical Center 6, Weizmann Street	64239	Tel Aviv	ISRAEL
99	A.O. di Padova	Dip. Scienze Mediche e Chirurgiche Clinica Medica II Viale Ospedale Civile, 105	35128	Padova	ITALY
100	A.O. San Paolo Polo Universitario	Ematologia e Trombosi Via A. Di Rudinì, 8	20142	Milano	ITALY

101	A.O.U. di Bologna	Angiologia e Malattie della Coagulazione Policlinico S.Orsola-Malpighi Via Albertoni, 15	40138	Bologna	ITALY
102	A.O.U. di Parma	Medicina Interna ad indir. Angiologico e Coagulativo Via Gramsci, 14	43100	Parma	ITALY
103	A.O.U. Federico II	CRR Emocoagulopatie Dip. Medicina Clinica e Sperimentale Via S. Pansini, 5	80131	Napoli	ITALY
104	A.O.U. Policlinico Giaccone	Malattie Cardiovascolari e Nefrourologiche Dip. Medicina Interna Via del Vespro, 129	90127	Palermo	ITALY
105	AULSS 12 Veneziana - Veneto	Medicina I P.O. SS Giovanni e Paolo Castello 6776	30122	Venezia	ITALY
106	AUSL 2 Lanciano-Vasto-Chieti - Abruzzo	Medicina Interna Ospedale Clinicizzato SS. Annunziata Via dei Vestini, 31	66013	Chieti	ITALY
107	AUSL Piacenza - Emilia Romagna	Centro Emostasi e Trombosi Medicina Interna Area Critica Ospedale Guglielmo da Saliceto Via Taverna, 49	29100	Piacenza	ITALY

108	IRCCS Fondazione San Raffaele	Laboratorio Coagulazione ed Unità Ricerca Trombosi Istituto Scientifico Universitario San Raffaele Via Olgettina, 60	20132	Milano	ITALY
109	IRCCS Policlinico San Matteo	Angiologia - Malattie Tromboemboliche Piazzale Golgi, 19	27100	Pavia	ITALY
110	Hospital Ampang	Department of Hematology, Jalan Mewah Utara, Pandan Mewah, Ampang 68000	68000	Selangor	MALAYSIA
111	Academisch Medisch Centrum Universiteit van Amsterdam	Afd. Interne geneeskunde, Meibergdreef 9	1105 AZ	AMSTERDAM	NETHERLANDS
112	Isala Klinieken, Locatie Sophia	Afdeling Haematologie, Dr. van Heesweg 2	8025 AB	ZWOLLE	NETHERLANDS
113	Spaarne Ziekenhuis	Afdeling Interne Geneeskunde, Spaarnepoort 1	2134 TM	HOOFDDORP	NETHERLANDS
114	Universitair Medisch Centrum Groningen	Afdeling Interne Geneeskunde, Hanzeplein 1	9713 GZ	GRONINGEN	NETHERLANDS
115	Ziekenhuis Rijnstate	Afd. Inwendige Geneeskunde - Wagnerlaan 55	6815 AD	ARNHEM	NETHERLANDS

116	Haematology Service, Canterbury Health Laboratories	corner Hagley Avenue and Tuam Street Christchurch Central	8011	Christchurch	NEW ZEALAND
117	North Shore Hospital	Shakespeare Road Takapuna North Shore City	0622	Auckland	NEW ZEALAND
118	Palmerston North Hospital	50 Ruahine Street Roslyn	4414	Palmerston North	NEW ZEALAND
119	Thrombosis Unit	Regional Cancer and Blood Services Level 6, Building 8, Auckland City Hospital Park Road Grafton	1023	Auckland	NEW ZEALAND
120	Wellington Hospital	Riddiford Street Newtown	6021	Wellington South	NEW ZEALAND
121	Oslo Universitetssykehus HF, Ullevål	Hematologisk avdeling Kirkeveien 166	0407	Oslo	NORWAY
122	Östfold Hospital Trust Fredrikstad	Dept of Medicine PO Box 16	1603	Fredrikstad	NORWAY
123	Sykehuset Asker og Bærum	Dept of Medicine Munthe Kaasvei 100	1309	Rud	NORWAY
124	Philippine Heart Centre	Room 409, Medical Arts Building	0850	Quezon City	PHILIPPINES
125	St. Luke's Medical Centre Cathedral Heights	Heart Institute E. Rodriguez Sr. Blvd. Philippines	1102	Quezon City	PHILIPPINES
126	Instytut Gruzlicy i Chorob Pluc	Oddzial Intensywnej Terapii Pneumonologiczno-Kardiologicznej ul. Plocka 26	01-138	Warszawa	POLAND

127	SP Szpital Kliniczny AM w Bialymstoku	Klinika Hematologii z pododdzialem Chorób Naczyn UM w Bialymstoku Uniwersytecki Szpital Kliniczny w Bialymstoku ul. Marii Sklodowskiej-Curie 24a	15-276	Bialystok	POLAND
128	Szpital im. N. Barlickiego	Klinika Chirurgii Ogólnej i Transplantacyjnej ul. Kopcinskiego 22	90-153	Lodz	POLAND
129	Szpital Kliniczny	Katedra i Klinika Chirurgii Naczyniowej, Ogolnej i Transplantacyjnej ul. Poniatowskiego 2	50-326	Wroclaw	POLAND
130	Szpital Kliniczny	Katedra i Klinika Angiologii, Nadcisnienia Tetniczego i Diabetologii ul. Poniatowskiego 2	50-326	Wroclaw	POLAND
131	Szpital Uniwersytecki w Krakowie	Oddzial Autoimmunologii i Zaburzen Hemostazy ul. Skawinska 8	31-066	Krakow	POLAND

132	Wojewodzki Szpital Specjalistyczny	Oddzial Kardiologiczny z Pododzialem Intensywnego Nadzoru Kardiologicznego ul. Kamienskiego 73A	51-124	Wroclaw	POLAND
133	Singapore General Hospital	Department of Haematology Block 6 Level 5,	169608	Singapore	SINGAPORE
134	Tan Tock Seng Hospital	Department of General Medicine CSO 5B, 11 Jalan Tan Tock Seng,	308433	Singapore	SINGAPORE
135	Clinical Projects Research SA	42 Russell Street	6850	Worcester	SOUTH AFRICA
136	Folateng Charlotte Maxeke Johannesburg Academic Hospital	Johannesburg Hosptial Folateng Private Section 7 York Road Parktown	2193	Johannesburg	SOUTH AFRICA
137	Helderberg Medical Clinical Trials	7G Arun Place Sir Lowry's Pass Road	7130	Somerset West	SOUTH AFRICA
138	Little Company of Mary Hospital	50 Totius St Groenkloof	0181	Pretoria	SOUTH AFRICA
139	Mayo Clinic	William Nicol Drive Floracliffe	1724	Roodepoort	SOUTH AFRICA
140	Pretoria Academic Hospital Ethics Committee	H.W. Snyman Building Level 2/34 Prinshof / Gazena	0084	Pretoria	SOUTH AFRICA
141	Sandton Medi Clinic	Cnr Hendrik Verwoerd & Peter Place Bryanson	2191	Johannesburg	SOUTH AFRICA
142	Sunninghill Hospital	c/o Nanuke & Witkoppen Drive Sunninghill	2157	Johannesburg	SOUTH AFRICA

143	Unitas Hospital	Unitas Hospital Clifton Ave Lyttleton Centurion	0157	Pretoria	SOUTH AFRICA
144	University of Witwatersrand	University of the Witwatersrand Charlotte Maxeke Johannesburg Academic Hospital Medical School 7 York Road Parktown	2132	Johannesburg	SOUTH AFRICA
145	Hospital Clínic i Provincial de Barcelona	Servicio de Medicina Interna C/ Villarroel, 170	08036	Barcelona	SPAIN
146	Hospital de la Mútua de Terrassa	Servei d'Hematologia Plaza del Dr. Robert 5	08221	Terrassa	SPAIN
147	Hospital de la Santa Creu i de Sant Pau	Servei de Hematología Pabelló Nostra Senyora de Montserrat Avda. Sant Antoni María Claret, 167	08025	Barcelona	SPAIN
148	Hospital Josep Trueta	Servicio de Medicina Interna 8ª Planta B Avda. de França, s/n	17007	Girona	SPAIN
149	Hospital Lluís Alcanyís de Xátiva	Servicio de Hematología Ctra Xàtiva a Silla km 2	46800	Xàtiva	SPAIN
150	Hospital Virgen del Camino	Servicio de Medicina Interna. Planta 6ª C/ Irunlarrea, 4	31008	Pamplona	SPAIN
151	Länssjukhuset Ryhov	Kardiosektionen/Medicinkliniken	551 85	Jönköping	SWEDEN

152	Länssjukhuset Sundsvall-Härnösand	Medicinkliniken	851 86	Sundsvall	SWEDEN
153	Sahlgrenska Universitetssjukhuset	Medicinkliniken	413 45	Göteborg	SWEDEN
154	Södra Älvsborgs Sjukhus	Medicinkliniken	501 82	Borås	SWEDEN
155	SU/Östra	Medicinkliniken	416 85	Göteborg	SWEDEN
156	Västerviks Sjukhus	Medicinkliniken	593 81	Västervik	SWEDEN
157	Hôpital Cantonal Universitaire de Genève	Division d'angiologie et d'hémostase Unité d'angiologie Rue Gabrielle-Perret-Gentil 4	1211	Genéve 14	SWITZERLAND
158	Luzerner Kantonsspital	Angiologie Spitalstrasse	6000	Luzern	SWITZERLAND
159	Chulalongkorn University Hospital	Division of Hematology Department of Internal Medicine Chulaongkorn University	10330	Pathumwan, Bangkok	THAILAND
160	Ramathibodhi Hospital	Division of Hematology Department of Medicine Ramathibodi Hospital Rama VI Road	10400	Bangkok	THAILAND
161	Kings College Hospital	Department of Vascular Sugery 2nd Floor, West Entresol (off Hambledon Wing) Bessemer Road Denmark Hill	SE5 9RS	London	UNITED KINGDOM
162	North Middlesex Hospital	Department of Haematology Sterling Way Edmonton		London	UNITED KINGDOM

163	West Middlesex University Hospital	Twickenham Road	TW7 6AF	Isleworth	UNITED KINGDOM
164	Cancer Care Centers of South Texas	4411 Medical Drive	78229	San Antonio	UNITED STATES
165	Eastern Idaho Medical Consultants	3200 Channing Way Suite 205	83404	Idaho Falls	UNITED STATES
166	Lovelace Health Systems	Gibson Healthcare Center Clinical Thrombosis Center 3rd Floor/Elev. B 5400 Gibson Boulevard SE	87108	Albuquerque	UNITED STATES
167	Moses H. Cone Memorial Hospital	Dep't. of Critical Care Medicine 1200 North Elm Street	27401	Greensboro	UNITED STATES
168	Oklahoma University Health Science Center	OU Medical Center 1200 N. Everett Drive	73104	Oklahoma City	UNITED STATES
169	Sinai Hospital of Baltimore	Department of Medicine 2435 West Belvedere Avenue Suite 22	21215-5271	Baltimore	UNITED STATES
170	Spokane Respiratory Center	104 West Fifth Avenue	99204	Spokane	UNITED STATES
171	The Western Pennsylvania Hospital	4800 Friendship Avenue Suite MZ-52	15224	Pittsburgh	UNITED STATES
172	University of North Carolina	UNC Hospitals Department of Medicine Div. of Hematology-Oncology 903 Mary Ellen Jones Bldg.	27599-7035	Chapel Hill	UNITED STATES
173	Wesley Long Community Hospital	501 North Elam Avenue	27403	Greensboro	UNITED STATES

Product Identification Information

Product Type	Drug
US Brand/Trade Name(s)	Xarelto
Brand/Trade Name(s) ex-US	Xarelto
Generic Name	rivaroxaban
Main Product Company Code	BAY59-7939
Other Company Code(s)	
Chemical Description	IUPAC Name: 5-Chloro-N-({(5S)-2-oxo-3-[4-(3-oxo-4-morpholinyl)phenyl]-1,3-oxazolidin-5-yl}methyl)-2-thiophenecarboxamide
Other Product Aliases	

Date of last Update/Change: 04 Mar 2013