Name of Sponsor/Company: Bristol-Myers Squibb	Individual Study Table Referring to the Dossier	*(For National Authority Use Only)*
Name of Finished Product:		
Name of Active Ingredient: Apixaban		

SYNOPSIS

Final Clinical Study Report for Study CV185035

TITLE OF STUDY: A Phase 3, Randomized, Double-blind, Active-controlled, Parallel-group, Multi-center Study to Evaluate the Safety and Efficacy of Apixaban in Subjects Undergoing Elective Total Hip Replacement Surgery (The ADVANCE-3 study Apixaban Dosed Orally Versus ANtiCoagulation with Injectable Enoxaparin to Prevent Venous Thromboembolism)

INVESTIGATORS/STUDY CENTERS: 160 study sites in 21 countries.

PUBLICATIONS: None

STUDY PERIOD: Study Initiation Date: 08-Mar-2007 **CLINICAL PHASE:** 3

Study Completion Date: 05-Sep-2009

OBJECTIVES:

Primary Objective: To compare the effect of apixaban 2.5 mg twice daily (BID) orally (PO) vs. enoxaparin 40 mg once daily (QD) subcutaneously (SC) on the composite endpoint of adjudicated asymptomatic and symptomatic deep vein thrombosis (DVT), non-fatal pulmonary embolism (PE), and all cause death at the end of the double-blind Intended Treatment Period in subjects undergoing elective total hip replacement (THR) surgery.

Secondary Efficacy Objectives: The key secondary objective was to compare the effect of apixaban 2.5 mg BID PO vs. enoxaparin 40 mg QD SC on the composite endpoint of adjudicated proximal DVT, nonfatal PE, and venous thromboembolism (VTE)-related death at the end of the double-blind Intended Treatment Period.

Other efficacy objectives of the study were to assess the effect of oral apixaban 2.5 mg BID versus SC enoxaparin 40 mg QD on the:

- Composite of adjudicated asymptomatic and symptomatic DVT, non-fatal PE, and VTE-related death
- Composite of adjudicated proximal DVT, non-fatal PE, and all cause death
- Single adjudicated endpoints of distal DVT, proximal DVT, non-fatal PE, VTE-related deaths, and all-cause death

at the end of the double-blind Intended Treatment Period.

Pharmacokinetic Objectives: Amendment 3 to the study protocol added the following pharmacokinetic (PK) objectives:

- To characterize the population PK of apixaban and variability in PK parameters in subjects undergoing total hip replacement surgery
- To characterize the relationship between plasma anti-factor Xa (FXa) activity and apixaban concentration
- To quantify the effect of selected covariates on variability in apixaban PK parameters in subjects undergoing total hip replacement surgery
- To characterize the exposure-response relationships for primary efficacy endpoints, as well as selected clinically relevant secondary efficacy and safety endpoints
- To assess the impact of selected covariates on the exposure response relationships.

Safety Objectives: To assess the effect of oral apixaban 2.5 mg BID versus SC enoxaparin 40 mg QD on:

- adjudicated major bleeding
- composite of adjudicated major and clinically relevant non-major (CRNM) bleeding
- adjudicated clinically relevant non-major bleeding

at the end of the double-blind Treatment Period.

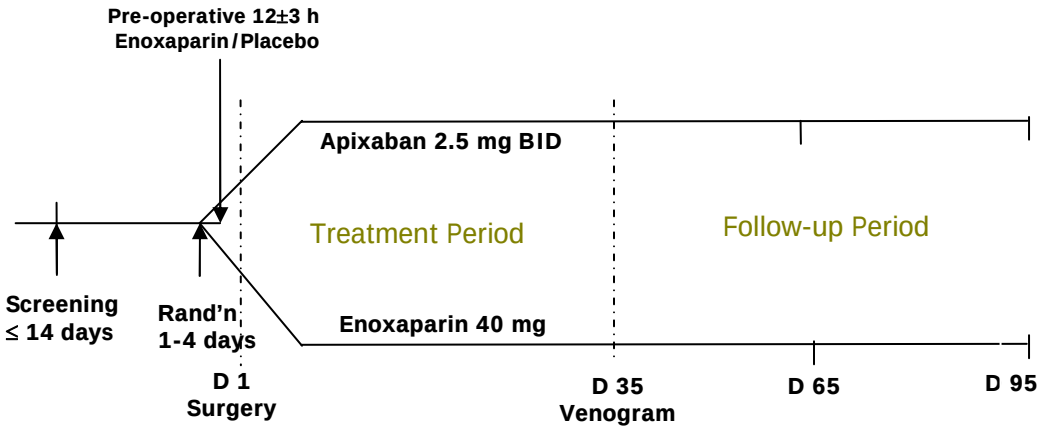
Other safety objectives were to assess the overall safety and tolerability of apixaban and enoxaparin during the double-blind Treatment Period.

METHODOLOGY:

This was a Phase 3, multicenter, randomized, parallel-group study to evaluate the efficacy and safety of apixaban 2.5 mg BID PO compared to enoxaparin 40 mg QD SC, a drug approved and widely used for VTE prophylaxis following total knee replacement and total hip replacement surgeries.

Subjects were randomized to double-blind treatment with (1) apixaban 2.5 mg BID or (2) enoxaparin 40 mg QD.

The study included: (1) a screening period that began no more than 14 days prior to randomization, (2) a randomization period 1 to 4 days prior to surgery, (3) a treatment period, starting with the first dose of SC study drug 12 (± 3) hours prior to surgery and extending through 34 days (± 3 days) after the surgery day, and (4) a 60 (± 5) day follow-up period starting the day after the last dose of study drug.



All apixaban-treated subjects received a matching enoxaparin-placebo injection. All enoxaparin-treated subjects received matching apixaban-placebo tablets.

A mandatory bilateral ascending contrast venogram was to be obtained on Day 35 (± 3 days). The result of this venogram contributed to the primary endpoint of the protocol. Subjects who were shown to have asymptomatic DVT upon venography were to be treated for DVT according to the investigator's standard of care.

NUMBER OF SUBJECTS (Planned and Analyzed): The study was planned to randomize 5406 subjects (approximately 2703 subjects per treatment; changed per Protocol Amendment 4). The number of subjects enrolled was 5765, and the final number randomized was 5407 (apixaban 2708; enoxaparin 2699). A total of 5332 subjects (apixaban 2673; enoxaparin 2659) were treated with blinded study drug and 3866 subjects (apixaban: 1949; enoxaparin: 1917) were included in the primary efficacy data set. A total of 17 subjects had serial plasma samples taken of apixaban PK and anti-Xa activity; this group is referred to as the intensive PK group. In addition, 65 subjects had a small number of plasma samples take for apixaban PK and anti-Xa activity; this group is referred to as the sparse PK group. The results of the PK and pharmacodynamic analyses obtained from these samples are summarized within this report, and are reported separately as a pooled analysis with other Phase 3 apixaban studies.

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION: Males and females, including women of childbearing potential, ≥ 18 years of age, scheduled to undergo elective total hip replacement surgery who met the inclusion/exclusion criteria.

TEST PRODUCT, DOSE AND MODE OF ADMINISTRATION, DURATION OF TREATMENT, BATCH NUMBERS: Apixaban 2.5 mg or matching apixaban-placebo tablets. First PO dose 12 to 24 hours after completing skin wound closure; BID dosing through 34 days after the surgery day. Apixaban batch numbers were 6E17717, 7A28991, 7B29116, 7H25317, and 8B41849. Matching apixaban-placebo batch numbers were 6E18428, 7A28986, 7A29111, and 7C28811.

REFERENCE THERAPY, DOSE AND MODE OF ADMINISTRATION, DURATION OF TREATMENT, BATCH NUMBERS: Enoxaparin 40 mg SC or matching enoxaparin-placebo injections. Initial dose injected 12 ± 3 hours prior to surgery. The next dose was injected after skin wound closure as

per investigator standard of care; QD dosing through 34 days after the surgery day. Enoxaparin batch numbers were 19417, 19427, 6F21444, 6J19616, 6M08763, 7D21822, 7H25787, 7L29290, and 8F33265. Matching enoxaparin-placebo batch numbers were 6G20198, 6G20204, 6G20210, 6G20216, 6G20219, 6H13900, 7D24030, 7D24033, 7D24036, 7D24046, 7D24047, 7E31035, 7E31036, 7F30130, 7F30141, and 7H22703.

CRITERIA FOR EVALUATION: Within the analysis and reporting period, an Independent Central Adjudication Committee (ICAC) adjudicated all venograms, suspected symptomatic DVT and PE, acute clinically overt bleeding events, suspected thrombocytopenia, suspected acute myocardial infarction (MI), suspected acute stroke, and cause of death.

Efficacy: The primary efficacy endpoint was the composite of all adjudicated VTE (PE, symptomatic DVT, asymptomatic DVT) and all-cause death during the Intended Treatment Period. The key secondary efficacy endpoint was the composite of adjudicated asymptomatic and symptomatic proximal DVT, non-fatal PE, and VTE-related death during the Intended Treatment Period.

Safety: Bleeding was the primary safety endpoint, and included the following, if occurring during the Treatment Period (1) confirmed adjudicated major bleeding events, (2) composite of confirmed adjudicated major bleeding and clinically relevant non-major (CRNM) bleeding events, and (3) all bleeding events reported by the investigator.

Secondary Safety Endpoints: adverse events (AEs), vital signs, abnormal standard clinical laboratory test results, and events of special interest (adjudicated thrombocytopenia, adjudicated MI, adjudicated stroke, AEs related to liver function test [LFT] increases, and neurologic AEs).

Pharmacokinetics: The peak plasma concentration (Cmax), minimum plasma concentration (Cmin), and the time to reach the peak concentration (Tmax) were obtained from experimental observations. The area under the concentration-time curve in 1 dosing interval, AUC(TAU), was calculated by using linear trapezoidal and log-trapezoidal methods. The complete results of the population PK and effect of covariates assessment will be presented separately in a pooled analysis from multiple Phase 3 apixaban studies. The complete results of the population PK and effect of covariates assessment will be presented separately in a pooled analysis from multiple Phase 3 apixaban studies.

Pharmacodynamics: Apixaban peak anti-factor Xa activity (peak anti-FXa), trough anti-FXa and the time to reach the observed peak anti-FXa activity (Tmax) were obtained from experimental observations.

STATISTICAL CONSIDERATIONS: The primary and key secondary efficacy analyses were performed on the Primary Efficacy Data Set defined as all randomized subjects who during the Intended Treatment Period, had an adjudicated and evaluable bilateral venogram; or had an adjudicated VTE; or died due to any cause. Subjects were categorized to the treatment group to which they had been assigned by the IVRS, regardless of the treatment they actually received.

In order to control the overall type-I error rate, a sequential test procedure was performed to compare the effect of apixaban vs. enoxaparin on the primary and key secondary efficacy endpoints.

Non-inferiority (NI) of apixaban vs. enoxaparin for the primary efficacy endpoint was tested first at a 1-sided $\alpha = 0.025$ level:

- If NI for the primary efficacy endpoint was demonstrated, NI of apixaban vs. enoxaparin for the key secondary efficacy outcome was tested at the 1-sided $\alpha = 0.025$ level
- If NI of apixaban vs. enoxaparin was demonstrated for the key secondary efficacy endpoint, superiority of apixaban vs. enoxaparin was then tested for the primary efficacy endpoint at a 1-sided $\alpha = 0.025$ level
- If superiority for the primary efficacy endpoint was demonstrated, superiority for the key secondary efficacy endpoint was tested at the 1-sided $\alpha = 0.025$ level.

NI for apixaban on the primary efficacy endpoint would be demonstrated if the upper bound of the 2-sided 95% confidence interval (CI) for relative risk (RR) was < 1.25.

NI for apixaban on the key secondary efficacy endpoint would be demonstrated if the upper bound of the 2-sided 95% CI for RR was < 1.5.

Superiority for an efficacy outcome would be demonstrated if the upper bound of the 2-sided 95% CI for relative risk was < 1.

The safety analysis included all treated subjects. For each primary safety endpoint, point estimates and 95% CIs for event rates were presented by treatment group, together with point estimates and 95% CIs for the difference of event rates between the apixaban and enoxaparin groups. The complete results of the PK exposure / response and effect of covariates assessment will be presented separately in a pooled analysis from multiple Phase 3 apixaban studies.

SUMMARY OF RESULTS:

Disposition and Baseline/Demographic Characteristics:

A total of 5407 subjects were randomized to active study drug (Table 1). For randomized subjects, discontinuation rates from the Treatment Period were similar in both groups. Study discontinuation rates due to AEs were also similar for the apixaban and enoxaparin groups.

Baseline demographic characteristics were balanced between treatment groups. Most subjects were female and White was the most common race. The mean age was 61 years. Approximately 12% of subjects were ≥ 75 years of age.

There were no clinically meaningful differences in the incidence or type of risk factors at baseline between the groups (Table 2). The majority of subjects in both groups had no risk factors at baseline. Of those subjects who did have risk factors at baseline, most had only 1 risk factor.

Table 1: **Subject Disposition at the End of the Treatment Period - Randomized Subjects**

	Apix 2.5mg BID N = 2708	Enox 40mg QD N = 2699
SUBJECTS	2708	2699
SUBJECTS COMPLETING THE PERIOD (%)	2484 (91.7)	2447 (90.7)
SUBJECTS NOT COMPLETING THE PERIOD (%)	224 (8.3)	252 (9.3)
REASON FOR NOT COMPLETING THE PERIOD (%)		
LACK OF EFFICACY	0	0
DEATH	2 (<0.1)	0
ADVERSE EVENT	93 (3.4)	112 (4.1)
STROKE	1 (<0.1)	4 (0.1)
THROMBOCYTOPENIA	0	3 (0.1)
MI	5 (0.2)	2 (<0.1)
BLEEDING	15 (0.6)	13 (0.5)
DVT	3 (0.1)	6 (0.2)
PE	2 (<0.1)	6 (0.2)
OTHER	66 (2.4)	77 (2.9)
SUBJECT WITHDREW CONSENT	86 (3.2)	99 (3.7)
LOST TO FOLLOW-UP	4 (0.1)	3 (0.1)
POOR/NON-COMPLIANCE	1 (<0.1)	1 (<0.1)
PREGNANCY	0	0
SUBJECT NO LONGER MEETS STUDY CRITERIA	15 (0.6)	15 (0.6)
ADMINISTRATIVE REASON BY SPONSOR	0	0
OTHER	23 (0.8)	22 (0.8)
SUBJECTS CONTINUING THE STUDY (%)	2525 (93.2)	2484 (92.0)
SUBJECTS NOT CONTINUING THE STUDY (%)	183 (6.8)	215 (8.0)

The denominator to calculate each percentage is the number of randomized subjects.

Table 2: Summary of Risk Factors at Baseline - Randomized Subjects

	Apix 2.5mg BID N = 2708	Enox 40mg QD N = 2699	Total N = 5407
ANY RISK FACTOR? (%)			
YES	873 (32.2)	873 (32.3)	1746 (32.3)
NO	1835 (67.8)	1826 (67.7)	3661 (67.7)
NOT REPORTED	0	0	0
TYPE OF RISK FACTOR (%)			
KNEE REPLACEMENT	124 (4.6)	116 (4.3)	240 (4.4)
HIP REPLACEMENT	624 (23.0)	623 (23.1)	1247 (23.1)
HIP OR KNEE FRACTURE SURGERY	194 (7.2)	195 (7.2)	389 (7.2)
DVT	41 (1.5)	47 (1.7)	88 (1.6)
PE	17 (0.6)	11 (0.4)	28 (0.5)

The denominator to calculate each percentage is the total number of randomized subjects in the treatment group(s).

Exposure: The extent of exposure to double-bind study drug was similar for subjects in both treatment groups (Table 3).

Table 3: Extent of Exposure from First Through Last Day of Dosing, Not Taking Into Account Interruptions - Treated Subjects

Length of Exposure Days (%)	Apix 2.5mg BID N = 2673	Enox 40mg QD N = 2659
=<3	62 (2.3)	64 (2.4)
4 - =<6	37 (1.4)	30 (1.1)
7 - =<9	29 (1.1)	33 (1.2)
10 - =<14	29 (1.1)	37 (1.4)
15 - =<21	17 (0.6)	19 (0.7)
22 - =<28	21 (0.8)	24 (0.9)
29 - =<31	25 (0.9)	42 (1.6)
32 - =<38	2242 (83.9)	2223 (83.6)
>38	211 (7.9)	187 (7.0)
MEAN(SD)	34.0 (7.68)	33.9 (7.79)
MEDIAN	36.0	36.0
MIN,MAX	1.0, 46.0	1.0, 60.0
TOTAL PATIENT-MONTHS	2987.1	2962.8

The denominator to calculate each percentage is the total number of treated subjects within each treatment group

Efficacy Results: Superiority of apixaban relative to enoxaparin for the primary efficacy endpoint was demonstrated (1-sided p-value < 0.0001) (Table 4). Superiority of apixaban relative to enoxaparin for the key secondary efficacy endpoint was also demonstrated (1-sided p-value = 0.0054) (Table 5).

Table 4: Summary of Adjudicated VTE Events and All-Cause Death with Onset During the Intended Treatment Period - Primary Subjects

	Apix 2.5 mg BID N=1949	Enox 40 mg QD N=1917
ALL VTE/ALL-CAUSE DEATH, N	27	74
EVENT RATE (%)	1.39	3.86
95% CI FOR EVENT RATE	(0.95, 2.02)	(3.08, 4.83)
RELATIVE RISK (APIX/ENOX)	0.36	
95% CI FOR RELATIVE RISK	(0.22, 0.54)	
ONE-SIDED P-VALUE FOR NON-INFERIORITY TEST ON RR	<0.0001*	
TWO-SIDED P-VALUE FOR NON-INFERIORITY TEST ON RR	<0.0001**	
RISK DIFFERENCE (%) (APIX-ENOX)	-2.47	
95% CI FOR RISK DIFFERENCE	(-3.54,- 1.50)	
ONE-SIDED P-VALUE FOR SUPERIORITY TEST ON RR	<0.0001*	
TWO-SIDED P-VALUE FOR SUPERIORITY TEST ON RR	<0.0001**	

* denotes that the result is statistically significant at the one-sided 0.025 level
** denotes that the result is statistically significant at the two-sided 0.05 level

Table 5: Summary of Adjudicated Proximal DVT, Non-fatal PE and VTE-related Death with Onset During the Intended Treatment Period

	Apix 2.5 mg BID N=2199	Enox 40 mg QD N=2195
PROXIMAL DVT/NON-FATAL PE/VTE-RELATED DEATH, n/N	10	25
EVENT RATE (%)	0.45	1.14
95% CI FOR EVENT RATE	(0.24, 0.85)	(0.77, 1.69)
RELATIVE RISK (APIX/ENOX)	0.40	
95% CI FOR RELATIVE RISK	(0.15, 0.80)	
ONE-SIDED P-VALUE FOR NON-INFERIORITY TEST ON RR	<0.0001*	
TWO-SIDED P-VALUE FOR NON-INFERIORITY TEST ON RR	0.0001**	
RISK DIFFERENCE (%) (APIX-ENOX)	-0.68	
95% CI FOR RISK DIFFERENCE	(-1.27,- 0.17)	
ONE-SIDED P-VALUE FOR SUPERIORITY TEST ON RR	0.0054*	
TWO-SIDED P-VALUE FOR SUPERIORITY TEST ON RR	0.0107**	

Data set = Randomized subjects with either an adjudicated and evaluable bilateral proximal venogram or an adjudicated event associated with the endpoint, during the Intended Treatment Period
* denotes that the result is statistically significant at the one-sided 0.025 level
** denotes that the result is statistically significant at the two-sided 0.05 level

Safety Results: The event rates for deaths, AEs, bleeding-related AEs, serious AEs, and discontinuations due to AEs were similar for both groups during the Treatment Period (starting with the active enoxaparin or matching placebo pre-surgery dose of study drug) (Table 6). Three (0.1%) deaths occurred in the apixaban group and 2 (< 0.1%) in the enoxaparin group from first dose through 30 days after last dose of study drug. Two deaths occurred during the Follow-up Period (both in the apixaban group).

Table 6: Summary of Safety During the Treatment Period - Treated Subjects

	Apix 2.5mg BID N = 2673	Enox 40mg QD N = 2659
AE (%)	1752(65.5)	1811(68.1)
SAE (%)	184(6.9)	172(6.5)
Bleeding AE (%)	268(10.0)	268(10.1)
Discontinuations due to AE (%)	91(3.4)	111(4.2)
Deaths (%)	3(0.1)	2(<0.1)

The denominator to calculate each percentage is the total number of treated subjects within each treatment group

There were no fatal bleeding events in the study. Event rates for major bleeding, composite of major and CRNM, and all bleeding were similar for apixaban 2.5 mg BID and enoxaparin 40 mg QD during the Treatment Period. Table 7 summarizes bleeding endpoints starting with the first pre-surgery dose of enoxaparin (for enoxaparin-treated subjects) or matching placebo injection (for apixaban-treated subjects); this summary includes bleeding events in the apixaban group that occurred prior to the first dose of apixaban.

Table 8 summarizes bleeding endpoints starting with the first post-surgery dose (thereby including all bleeding events that occurred after the first dose with apixaban for apixaban-treated subjects but excluding all bleeding events that occurred before the first-post-surgery dose of enoxaparin for enoxaparin-treated subjects).

Table 7: Summary of Bleeding Endpoints During the Treatment Period - Treated Subjects

	Apix 2.5 mg BID N=2673	Enox 40 mg QD N=2659
MAJOR BLEEDING, N	22	18
EVENT RATE (%)	0.82	0.68
95% CI	(0.54, 1.25)	(0.42, 1.08)
DIFF OF EVENT RATES (APIX-ENOX) (%)	0.15	
95% CI	(-0.33, 0.64)	
TWO-SIDED P-VALUE (%)	0.54	
CLINICALLY RELEVANT NON-MAJOR BLEEDING, N	109	120
EVENT RATE (%)	4.08	4.51
95% CI	(3.39, 4.90)	(3.79, 5.38)
DIFF OF EVENT RATES (APIX-ENOX) (%)	-0.44	
95% CI	(-1.53, 0.66)	
TWO-SIDED P-VALUE (%)	0.43	
MAJOR OR CLINICALLY RELEVANT NON-MAJOR BLEEDING, N	129	134
EVENT RATE (%)	4.83	5.04
95% CI	(4.08, 5.71)	(4.27, 5.94)
DIFF OF EVENT RATES (APIX-ENOX) (%)	-0.21	
95% CI	(-1.38, 0.95)	
TWO-SIDED P-VALUE (%)	0.72	
ANY BLEEDING, N	313	334
EVENT RATE (%)	11.71	12.56
95% CI	(10.55, 12.99)	(11.36, 13.88)
DIFF OF EVENT RATES (APIX-ENOX) (%)	-0.85	
95% CI	(-2.61, 0.90)	
TWO-SIDED P-VALUE (%)	0.34	

Table 8: Summary of Bleeding Endpoints During the Post-Surgery Treatment Period - Treated Subjects

	Apix 2.5 mg BID N=2673	Enox 40 mg QD N=2659
MAJOR BLEEDING, N	9	11
EVENT RATE (%)	0.34	0.41
95% CI	(0.17, 0.65)	(0.22, 0.75)
DIFF OF EVENT RATES (APIX-ENOX) (%)	-0.08	
95% CI	(-0.44, 0.27)	
TWO-SIDED P-VALUE (%)	0.65	
CLINICALLY RELEVANT NON-MAJOR BLEEDING, N	88	105
EVENT RATE (%)	3.29	3.95
95% CI	(2.68, 4.05)	(3.27, 4.76)
DIFF OF EVENT RATES (APIX-ENOX) (%)	-0.66	
95% CI	(-1.67, 0.35)	
TWO-SIDED P-VALUE (%)	0.20	
MAJOR OR CLINICALLY RELEVANT NON-MAJOR BLEEDING, N	96	115
EVENT RATE (%)	3.59	4.32
95% CI	(2.95, 4.37)	(3.61, 5.17)
DIFF OF EVENT RATES (APIX-ENOX) (%)	-0.73	
95% CI	(-1.79, 0.32)	
TWO-SIDED P-VALUE (%)	0.17	
ANY BLEEDING, N	261	293
EVENT RATE (%)	9.76	11.02
95% CI	(8.70, 10.95)	(9.88, 12.27)
DIFF OF EVENT RATES (APIX-ENOX) (%)	-1.25	
95% CI	(-2.90, 0.38)	
TWO-SIDED P-VALUE (%)	0.13	

Arterial thromboembolic events (MI or stroke) during the combined Treatment and Follow-up Periods were confirmed by adjudication for 10 (0.4%) subjects in the apixaban group and for 9 (0.3%) subjects in the enoxaparin group. During the Treatment Period, these included 5 MIs and 1 stroke in the apixaban group and 3 MIs and 4 strokes in the enoxaparin group. Thrombocytopenia during the combined Treatment and Follow-up Periods was confirmed by adjudication for 3 (0.1%) subjects in the apixaban group and for 5 (0.2%) subjects in the enoxaparin group. During the Treatment Period, these included 2 in the apixaban group and 3 in the enoxaparin group.

Pharmacokinetic Results:

After 3 days of apixaban treatment, apixaban plasma concentrations appeared to have reached steady state, with plasma concentration around 49 to 50 ng/mL before dosing and 46 to 57 ng/mL 12 or 24 hours after dosing. The observed Tmax of 4 hours for the intensive sampling group was within the 2 to 5 hour peak concentration window of sparse sampling group. The Cmax in the intensive sampling group was similar to the peak concentration in the sparse sampling groups.

Pharmacodynamic Results:

Overall the anti-FXa activity vs. time profiles were similar to that of the apixaban PK profiles, for both sparse and intensive sampling groups. The mean maximal anti-FXa activity levels were 1.36 to 1.52 IU/mL in the peak sampling window and 0.75 to 0.98 IU/mL in the trough window.

There is a direct linear relationship observed between the anti-FXa activity and the apixaban plasma concentrations.

CONCLUSIONS:

- Apixaban 2.5 mg BID was statistically significantly superior to enoxaparin 40 mg QD for the prevention of the composite endpoint of VTE/All-cause death
- Apixaban 2.5 mg BID was statistically significantly superior to enoxaparin 40 mg QD for the prevention of the composite endpoint of proximal DVT/non-fatal PE/VTE-related death
- Event rates for major bleeding, composite of major and CRNM, and all bleeding were similar for apixaban 2.5 mg BID and enoxaparin 40 mg QD
- The overall safety profile (AEs, SAEs, discontinuation due to AEs, LFT increases) of apixaban 2.5 mg BID appears to be similar to that of enoxaparin 40 mg QD
- The number of deaths, myocardial infarction, stroke or thrombocytopenia in the study was low
- Apixaban exposure reached steady-state on Day 3
- Plasma anti-Xa activity was directly correlated with apixaban plasma concentrations indicating that anti-Xa activity is a useful surrogate for apixaban exposure.

DATE OF REPORT: 21-Dec-2009