Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

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The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country..

Additional information on this study and the drug concerned may be provided upon request based on **Boehringer Ingelheim's Policy on Transparency and Publication of Clinical Study Data**.

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		
Name of finished product: Pradaxa				
Name of active ingredient: Dabigatran etexilate mesilate		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:**		**Addendum No.:**
Disclosure Synopsis Date: 06 Dec 2013	**Number:** U06-1617	**Study period (dates):** 3 NOV 04 to 15 MAY 06		

Title of study:	A phase III, randomised, parallel-group, double-blind, active controlled study to investigate the efficacy and safety of two different dose regimens of orally administered dabigatran etexilate capsules [150 or 220 mg once daily starting with a half dose (i.e.75 or 110 mg) on the day of surgery] compared to subcutaneous enoxaparin 40 mg once daily for 8 ±2 days, in prevention of venous thromboembolism in patients with primary elective total knee replacement surgery RE-MODEL (Thromboembolism prevention after knee surgery)
Investigator:	[redacted]
Study center(s):	Multicentre, multinational study involving 105 study centers in 15 countries on 3 continents (Europe, Africa, Australia).
Publication (reference):	Data from this trial were not yet published.
Clinical phase:	III
Objectives:	To determine the comparative efficacy and safety of two different dose regimens of dabigatran etexilate administered orally (capsules), compared with enoxaparin 40 mg once daily given as subcutaneous injection for a treatment period of 8 ±2 days, in prevention of venous thromboembolism in patients with primary elective total knee replacement surgery.
Methodology:	Randomised, parallel-group, double-blind, double-dummy, active-control study of two different dose regimens of dabigatran etexilate compared with enoxaparin.
No. of subjects: **planned:** **actual:**	entered: 2010 enrolled: 2183 Dabigatran 220 mg: entered: 693 treated: 679 analysed (for primary endpoint): 503 Dabigatran 150 mg: entered: 708 treated: 703 analysed (for primary endpoint): 526 Enoxaparin 40 mg: entered: 699 treated: 694 analysed (for primary endpoint): 512
Diagnosis and main criteria for inclusion:	Patients with primary elective total knee replacement surgery who provided written informed consent.

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Test product:	Dabigatran etexilate
dose:	Regimen 1: Dabigatran etexilate 75 mg on the day of surgery, 150 mg once daily (qd) thereafter. Regimen 2: Dabigatran etexilate 110 mg on the day of surgery, 220 mg once daily thereafter.
mode of admin.:	Oral (p.o.)
batch no.:	Dabigatran etexilate 75 mg: 404323, 9040225; Dabigatran etexilate 110 mg: 404331,9040226 Dabigatran-matching placebo capsules: 9040167, 9040224
Duration of treatment:	8 ±2 days including the day of surgery
Reference therapy:	Enoxaparin
dose:	40 mg qd (to be started on the day before surgery)
mode of admin.:	Subcutaneous injection (s.c.)
batch no.:	Enoxaparin 40 mg: E109, E111 Enoxaparin-matching syringes: B040311, B040406,B040312, B040405, B040716
Criteria for evaluation:	
Efficacy:	Primary efficacy endpoint: A composite endpoint consisting of total Venous Thromboembolic Events (VTE) and all-cause mortality during the treatment period. Total VTE was defined as the composite incidence of proximal and distal deep venous thrombosis (DVT) detected by routine venography; symptomatic DVT, and pulmonary embolism (PE). Secondary efficacy endpoints (during the treatment period): 1. Composite endpoint of major VTE (defined as proximal DVT and PE) and VTE related mortality 2. Proximal DVTs 3. Total DVTs 4. Symptomatic DVT 5. Pulmonary Embolism (PE) 6. Deaths Additionally, a composite endpoint of total VTE and all-cause mortality during the follow-up period was evaluated.

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Safety:	1. Frequency of bleeding events (see section 5.2.2 for definition) a) Frequency of Major Bleeding Events (MBE) b) MBE and clinically relevant bleeding events c) Any bleeding events (major, clinically relevant and minor) 2. Volume of blood loss 3. Blood transfusion 4. Adverse events 5. Discontinuation due to adverse events 6. Laboratory measures 7. Physical examination All safety endpoints were assessed during the treatment phase, in the post treatment phase, and post study.
Additional endpoints	It was planned to analyse a tertiary endpoint which was the resource utilization of each treatment group during the treatment and follow-up period (health economic assessment). However, this analysis will not be presented in this report but in a separate report.
Statistical methods:	Testing for non-inferiority defined as a 9.2% absolute difference in the rate of the primary endpoint between treatment groups. This study aimed to show (1) non-inferiority of the high dabigatran dose regimen versus enoxaparin, (2) non-inferiority of the low dabigatran dose regimen versus enoxaparin, (3) superiority of the high dabigatran dose regimen versus enoxaparin, and (4) superiority of the low dabigatran dose regimen versus enoxaparin for the primary efficacy endpoint. The overall significance level was controlled by a-priori ordering of hypotheses. The planned sample size had 90% of power to claim non-inferiority with one-sided alpha=0.025. The calculation assumed that the incidence of the primary endpoint to be 1% lower for dabigatran treatment compared with enoxaparin. The explored control rates ranged from 30% to 48% based on the published rates of LMWH and the enoxaparin rates from more recent active-controlled trials. It was also assumed that 25% of the venograms would be non-evaluable.
SUMMARY – CONCLUSIONS:	

Efficacy results:	Overall, 2101 patients were randomised; 2076 patients were randomised and received treatment (safety set) and 2056 patients were randomised, treated, and underwent surgery (FAS-op); of these 1541 patients (dabigatran 220 mg: 503 patients, dabigatran 150 mg: 526 patients, enoxaparin: 512 patients) were evaluable for the primary endpoint (FAS); i.e. 75.0% of patients in the FAS-op population. Overall, the mean age was 67.7 years; almost all patients were white (98.7%), and 66.0% of patients were female. The majority of patients (55.3%) had normal kidney function (CrCl ≥80 mL/min), mild impairment (CrCl 50-80 mL/min) was observed in 34.9%, and moderate impairment (CrCl 30-50 mL/min) was seen in 6.3% of patients overall. The majority of patients had received spinal anaesthesia (54.8%) and both oral study drug (within 1- 4 hours post surgery, 82.0%) and subcutaneous injection (pre-surgery, 89.4%) were administered according to the protocol in almost all patients. The incidences of total VTE and all-cause mortality were 36.4% (dabigatran 220 mg), 40.5% (dabigatran 150 mg), and 37.7% (enoxaparin). The risk difference (95% CI) versus enoxaparin was -1.3% (-7.3, 4.6) in the dabigatran 220 mg group and +2.8% (-3.1, 8.7) in the dabigatran 150 mg group; the respective odds ratios (95% CI) were 0.9 (0.7, 1.2) and 1.1 (0.9, 1.4). Thus the incidences of total VTE and all-cause mortality in both dabigatran dose groups were within the pre-specified non-inferiority margin of 9.2%. The strongest contribution to the primary endpoint came from asymptomatic DVTs detected by venography with incidences of 36.0% (dabigatran 220 mg), 39.5% (dabigatran 150 mg), and 35.9% (enoxaparin). Symptomatic DVTs were rare events in all treatment groups; the incidences were 0.2% (dabigatran 220 mg), 0.6% (dabigatran 150 mg) and 1.6% (enoxaparin). In each treatment group 1 patient had a PE and 1 patient died during the treatment period. The incidence of total VTE and all-cause mortality appeared to be lower in patients <70 years of age than in patients ≥70 years in all treatment groups. Patients with a lean BMI of <25 kg/m^2 appeared to have lower total VTE rates than obese patients (BMI 30 to 35 kg/m^2). In regard to renal function, patients with moderate impairment appeared to have somewhat higher incidences of total VTE than patients with normal creatinine clearance. This effect was more pronounced in the dabigatran 220 mg group. The incidence of the primary endpoint was lower in male patients than in female patients independent of the treatment. The incidence of major VTE and VTE-related mortality was also similar in all treatment groups with 2.6% (dabigatran 220 mg), 3.8% (dabigatran 150 mg), and 3.5% (enoxaparin) as was the incidence of proximal DVTs with 2.6% (dabigatran 220 mg), 3.4% (dabigatran 150 mg), and 3.3% (enoxaparin). The incidence of symptomatic DVTs during the treatment period was very low in all treatment groups. In the dabigatran 220 mg group only 1 patient, in the dabigatran 150 mg group 3 patients, and in the enoxaparin group 8 patients had a symptomatic DVT. The p-values for the comparison of dabigatran 220 mg versus enoxaparin was 0.0385, and for the dabigatran 150 mg group versus enoxaparin 0.1414. The incidence of total VTE and all-cause mortality during the follow-up was very low; 3 (dabigatran 220 mg), 3 (dabigatran 150 mg), and 2 (enoxaparin) patients had an event.
Safety results:	The extent of exposure to study medication was similar in all treatment groups and the total exposure was 27.4 years (dabigatran 220 mg), 28.1 years (dabigatran 150 mg), and 27.2 years (enoxaparin).

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Safety results (continued):

The indcidences of major bleeding events (MBE) were similar in all treatment groups: During the treatment period, 10 patients (1.5%) in the dabigatran 220 mg group, 9 patients (1.3%) in the dabigatran 150 mg group, and 9 patients (1.3%) in the enoxaparin group had MBEs. A statistical test for treatment differences of the dabigatran groups versus enoxaparin yielded p-values of 0.8209 (dabigatran 220 mg) and 1.00 (dabigatran 150 mg). Most MBEs occurred in the early post-operative period of Days 1-3, and allmost all MBEs were at the surgical site. When analysed by worst bleeding, similar proportions of patients in all treatment groups had clinically-relevant bleeding events (CRBE) and minor bleeding events. In the dabigatran 220 mg group 40 patients (5.9%), in the dabigatran 150 mg group 48 patients (6.8%), and in the enoxaparin group 37 patients (5.3%) had CRBEs; 8.8% (dabigatran 220 mg), 8.4% (dabigatran 150 mg), and 9.9% (enoxaparin) of patients had minor bleedings. Statistical testing for differences between the dabigatran groups and the enoxaparin group indicated no difference. When MBEs and CRBEs were combined, minimally higher incidences were apparent in the dabigatran groups (dabigatran 220 mg: 7.4%; dabigatran 150 mg: 8.1%) than in the enoxaparin group (6.6%). However, a statistical test for differences between the dabigatran groups and the enoxaparin group yielded p-values of 0.5933 (dabigatran 220 mg) and 0.2895 (dabigatran 150 mg). An analysis of MBEs and CRBEs based on events showed that there were 60 bleeding events in 50 patients in the dabigatran 220 mg group, 59 bleeding events in 57 patients in the dabigatran 150 mg group, and 50 events in 46 patients; overall, there were 14 patients with multiple bleeding events, 8 patients in the dabigatran 220 mg group, 2 patients in the dabigatran 150 mg group, and 4 patients in the enoxaparin group. The majority of MBEs or CRBEs occurred at the surgical site in all treatment groups: 37/60 (61.7%) in the dabigatran 220 mg group, 35/59 (59.3%) in the dabigatran 150 mg group, and 42/50 (84.0%) in the enoxaparin group. Conversely the proportion of bleeding events at other sites was higher in the dabigatran groups than in the enoxaparin group (35.0% and 39.0% vs. 16%).

The overall incidence of treatment-emergent adverse events was similar in all treatment groups with 78.2% (dabigatran 220 mg), 79.7% (dabigatran 150 mg), and 80.0% (enoxaparin) of patients. The majority of adverse events were of mild or moderate intensity, only 2.8% (dabigatran 220 mg), 2.6% (dabigatran 150 mg), and 1.9% (enoxaparin) of patients reported adverse events of severe intensity. The frequency of adverse events that lead to discontinuation from the study was also similar in all treatment groups with 3.7% (dabigatran 220 mg), 3.7% (dabigatran 150 mg), and 4.6% (enoxaparin). In the opinion of the investigator, 10.2% (dabigatran 220 mg), 9.8% (dabigatran 150 mg), and 10.5% of patients experienced adverse events that were related to study drug.

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Safety resuls (continued):

In general, the frequencies of adverse events by system organ class as well as by preferred term were similar in all treatment groups. The most frequent adverse events were gastrointestinal disorders with similar frequencies in all treatment groups (dabigatran 220 mg: 40.4%; dabigatran 150 mg: 41.1%; enoxaparin: 44.1%). Within this system organ class, nausea (range: 19.6% to 24.9%), vomiting (16.1% to 17.1%), and constipation (9.2% to 11.1%) were the most frequent adverse events with slightly higher incidences in the enoxaparin group than in the dabigatran groups. The second most frequent adverse events were vascular disorders (dabigatran 220 mg: 24.0%; dabigatran 150 mg: 29.9%; enoxaparin: 29.8%).Within this system organ class deep vein thrombosis was the most frequent event.

The proportion of patients who experienced serious adverse events was slightly lower in the dabigatran 220 mg group (4.6%) than in the dabigatran 150 mg group (6.3%), or in the enoxaparin group (6.2%). Vascular disorders were the most frequent SAEs affecting 9 patients (1.3%) in the dabigatran 220 mg group, 16 patients (2.3%) in the dabigatran 150 mg group, and 14 patients (2.0%) in the enoxaparin group. Within this system organ class, DVT was the most frequent event. The system organ class with the second highest incidence were cardiac disorders which were reported by 5 patients (0.7%) in the dabigatran 220 mg group, 9 patients (1.3%) in the dabigatran 150 mg group, and 5 patients (0.7%) in the enoxaparin group.

Overall 9 patients died in the course of the study, 3 patients died in the wash-out period of the treatment period, i.e. within 3 days after last drug administration, and 4 patients died in the post-treatment period, and 2 patients died after they had completed the study. During the treatment period which includes the wash-out period, 1 patient in each treatment group died. In the post-treatment group, 2 patients in the dabigatran 220 mg group and 2 patients in the enoxaparin group died. In no case was the adverse event that led to death assessed as being related to study drug by the treating physician.

In regard to clinical laboratory, no unexpected findings were observed for haematology parameters, electrolytes, and substrates. Liver enzyme elevations were rare events; overall, there were 18 patients, 6 patients in each treatment group, with ALT-elevations above 5x ULN including 2 patients in the dabigatran 150 mg group with extreme elevations (>20x ULN). However, the ALT-elevations returned to baseline in all but one patient.

AST-elevations were less frequent than ALT-elevations. At any time post baseline 2 patients (dabigatran 220 mg), 5 patients (dabigatran 150 mg), and 2 patients hadt AST-elevations >5x ULN. The majority of AST-elevations occurred in the immediate post-operative period and returned to baseline in all patients.

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Safety results (continued).	Overall, elevations of total bilirubin levels were rare events. Even in the immediate post-operative period only very few patients in all treatment groups had elevated total bilirubin levels. At any time post-baseline, 2 patients (dabigatran 220 mg), 2 patients (dabigatran 150 mg), and 3 patients (enoxaparin) had total bilirubin elevations of more than 2x ULN. There was 1 patient [patient number 1621] in the dabigatran 150 mg group who had both elevation of total bilirubin above 2x ULN and ALT-elevation of more than 3x ULN.
Conclusions:	With both dabigatran doses of 220 mg per day and 150 mg per day the pre-specified non-inferiority margin in comparison with enoxaparin for the primary endpoint, the incidence of total VTE and all-cause mortality, was reached. The incidence of total VTE and all-cause mortality was lowest in the dabigatran 220 mg group, intermediate in the enoxaparin group, and highest in the dabigatran 150 mg group. A slight propensity in the dabigatran 220 mg dose group towards higher incidences and greater severity of bleeding events was observed compared with the dabigatran 150 mg group and the enoxaparin group. Thus, a dose-response relationship in the 2 dabigatran doses was observed with slightly greater efficacy but increased frequency of bleedings in the higher dose group; enoxaparin data were generally intermediate between those of both dabigatran treatment groups. It can be concluded that once daily dabigatran (150 mg and 220 mg) is non-inferior to enoxaparin 40 mg once daily when administered for 6-14 days in patients undergoing total knee replacement surgery. Generally, the safety profile was comparable in all 3 treatment groups.

Trial Synopsis – Appendix

The result tables on the following pages supplement the trial results presented in the Trial Synopsis. The number of secondary endpoints defined for this trial was too large to allow meaningful presentation in this format. The appended tables provide complete disposition results and results of additional secondary endpoints, as summarised below.

Results for	**presented in**
Disposition of patients	Table 15.1.1: 1
Major VTE and VTE-related mortality during treatment period	Table 15.2.2: 1
Incidence of proximal DVTs during treatment period	Table 15.2.3: 1
Symptomatic DVTs during treatment period	Table 15.2.5: 1
Total DVTs during treatment period	Table 15.2.4: 1
PE during treatment period	Table 15.2.6: 1
Deaths during treatment period	Table 15.2.7: 1
Total VTE and all cause mortality during follow-up period	Table 15.2.8: 1

Table 15.1.1: 1 Patient disposition at the end of treatment

	Dabigatran 220mg	Dabigatran 150mg	Enoxaparin	Total
Enrolled				2183
Not entered randomised				82
Entered/ randomised	693	708	699	2101
Not treated&	14	5	5	25
Treated	679 (100.0)	703 (100.0)	694 (100.0)	2076 (100.0)
Completed treatment	630 (92.8)	647 (92.0)	632 (91.1)	1909 (92.0)
Discontinued treatment	49 (7.2)	56 (8.0)	62 (8.9)	167 (8.0)
Reason for discontinued treatment				
AE: worsening of disease under study*	1 (0.1)	1 (0.1)	7 (1.0)	9 (0.4)
AE: worsening of other pre-existing disease	1 (0.1)	1 (0.1)	2 (0.3)	4 (0.2)
AE: other (including bleeding events)	23 (3.4)	24 (3.4)	23 (3.3)	70 (3.4)
Bleeding events~	7 (1.0)	9 (1.3)	2 (0.3)	18 (0.9)
Other than bleeding events§	16 (2.4)	15 (2.1)	21 (3.0)	52 (2.5)
Non compliant with protocol (investigator assessment)	3 (0.4)	5 (0.7)	5 (0.7)	13 (0.6)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Consent withdrawn	3 (0.4)	7 (1.0)	8 (1.2)	18 (0.9)
Other	18 (2.7)	18 (2.6)	17 (2.4)	53 (2.6)
Deaths during treatment period^	1	1	1	3

*:I.e. symptomatic DVT or PE
The investigator terminated treatment prematurely due to DVT or PE, which was not centrally confirmed by the adjudication committees for 1 patient receiving Dabigatran150mg, 1 patient receiving Dabigatran220mg and 4 patients receiving Enoxaparin
~:Bleeding includes patients who discontinued due to any bleeding event which did or did not clinically require cessation of study drug
§:This line only counts patients who discontinued due to an other AE but who did not discontinue due to a bleeding
^:The date of death determines whether the patient is counted during treatment period or not
&:Patient [redacted] was randomized to Dabigatran 220mg (kit no 1915) by the investigator but never received any treatment. The investigator re-assigned the kit to patient [redacted]. Therefore, this patient is counted in the total column but not in the Dabigatran 220mg column

Source data: Appendix 16.2, Listing 1.1, 1.2, 1.3 safety\disp.sas 06NOV2006

Table 15.2.2: 1 Comparative analysis of major VTE and VTE related mortality during treatment period (FAS−major)

	Dabigatran 220mg	Dabigatran 150mg	Enoxaparin
FAS−mDVT	506	527	511
Incidence			
n	13	20	18
%	2.6	3.8	3.5
95% CI*	(1.2, 3.9)	(2.2, 5.4)	(1.9, 5.1)
Risk difference(%) vs. Enoxaparin			
estimate*	−1.0	0.3	
95% CI*	(−3.1, 1.2)	(−2.0, 2.6)	
p−value*	0.3760	0.8151	
Relative risk over Enoxaparin#			
estimate	0.73	1.08	
95% CI	(0.36, 1.47)	(0.58, 2.01)	
Odds ratio over Enoxaparin@			
estimate	0.7	1.1	
95% CI	(0.4, 1.5)	(0.6, 2.1)	

*: based on normal approximation of independent binomial distribution without stratification,
p−value is for testing no difference between two treatment groups
#: based on normal approximation of log relative risk without continuity correction
@: based on logistic regression including the main factor of treatment,
derived from contrast that compared the two treatments

Table 15.2.3: 1 Comparative analysis of proximal DVT during treatment period (FAS)

	Dabigatran 220mg	Dabigatran 150mg	Enoxaparin
FAS-pDVT	506	525	510
Incidence			
n	13	18	17
%	2.6	3.4	3.3
95% CI*	(1.2, 3.9)	(1.9, 5.0)	(1.8, 4.9)
Risk difference(%) vs. Enoxaparin			
estimate*	-0.8	0.1	
95% CI*	(-2.8, 1.3)	(-2.1, 2.3)	
p-value*	0.4715	0.9325	
Relative risk over Enoxaparin#			
estimate	0.77	1.03	
95% CI	(0.38, 1.57)	(0.54, 1.97)	
Odds ratio over Enoxaparin@			
estimate	0.8	1.0	
95% CI	(0.4, 1.6)	(0.5, 2.0)	

*: based on normal approximation of independent binomial distribution without stratification,
p-value is for testing no difference between two treatment groups
#: based on normal approximation of log relative risk without continuity correction
@: based on logistic regression including the main factor of treatment,
derived from contrast that compared the two treatments

Table 15.2.5: 1 Comparative analysis of symptomatic DVT during the treatment period (FAS-op)

	Dabigatran 220mg	Dabigatran 150mg	Enoxaparin
FAS-op	675	696	685
Incidence			
n	1	3	8
%	0.1	0.4	1.2
95% CI*	(0.0, 0.8)	(0.1, 1.3)	(0.5, 2.3)
Comparison vs. Enoxaparin			
p-value*	0.0385	0.1414	
Comparison vs. Dabigatran 150mg			
p-value*	0.6246		

*: exact 95% CI by Clopper and Pearson, p-value based on Fisher's exact test

Table 15.2.4: 1 Comparative analysis of total DVT during treatment period (FAS−tDVT)

	Dabigatran 220mg	Dabigatran 150mg	Enoxaparin
FAS−tDVT	503	524	511
Incidence			
n	182	211	192
%	36.2	40.3	37.6
95% CI*	(32.0, 40.4)	(36.1, 44.5)	(33.4, 41.8)
Risk difference(%) vs. Enoxaparin			
estimate*	−1.4	2.7	
95% CI*	(−7.3, 4.5)	(−3.2, 8.6)	
p−value*	0.6463	0.3740	
Relative risk over Enoxaparin#			
estimate	0.96	1.07	
95% CI	(0.82, 1.13)	(0.92, 1.25)	
Odds ratio over Enoxaparin@			
estimate	0.9	1.1	
95% CI	(0.7, 1.2)	(0.9, 1.4)	

*: based on normal approximation of independent binomial distribution without stratification,
p−value is for testing no difference between two treatment groups
#: based on normal approximation of log relative risk without continuity correction
@: based on logistic regression including the main factor of treatment,
derived from contrast that compared the two treatments

Table 15.2.6: 1 Comparative analysis of PE during the treatment period (FAS-op)

	Dabigatran 220mg	Dabigatran 150mg	Enoxaparin
FAS-op	675	696	685
Incidence			
n	0	1	1
%	0.0	0.1	0.1
95% CI*	[0.0, 0.5)	(0.0, 0.8)	(0.0, 0.8)
Comparison vs. Enoxaparin			
p-value*	1.0000	1.0000	
Comparison vs. Dabigatran 150mg			
p-value*	1.0000		

*: exact 95% CI by Clopper and Pearson, p-value based on Fisher's exact test

Table 15.2.7: 1 Comparative analysis of death during the treatment period (FAS−op)

	Dabigatran 220mg	Dabigatran 150mg	Enoxaparin
FAS−op	675	696	685
Incidence			
n	1	1	1
%	0.1	0.1	0.1
95% CI*	(0.0, 0.8)	(0.0, 0.8)	(0.0, 0.8)
Comparison vs. Enoxaparin			
p−value*	1.0000	1.0000	
Comparison vs. Dabigatran 150mg			
p−value*	1.0000		

*: exact 95% CI by Clopper and Pearson, p−value based on Fisher’s exact test

Table 15.2.8: 1 Summary of total VTE and all-cause mortality during the follow-up* period (FAS-op)

	Dabigatran 220mg	Dabigatran 150mg	Enoxaparin
Treated and operated (FAS-op)	675	696	685
Any data available during the follow-up period*	658	679	665
Number of patients observed for:			
<20 days	8	13	13
20 to 40 days	31	19	22
41 to 60 days	33	36	31
>60 days	586	611	599
Incidence	4	3	2
asymptomatic DVT°	0	1	0
symptomatic DVT	1	2	0
PE	2	0	0
death	1	0	2

*: includes the period from the end of treatment to the end of study (3 months follow-up)
°: asymptomatic DVT detected by delayed routine venography

Note: patients were counted only once in the most severe category in subcategories of DVT, PE and death