Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

This clinical study synopsis is provided in line with **Boehringer Ingelheim's *Policy on Transparency and Publication of Clinical Study Data***.

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 Trial Report**	Boehringer Ingelheim
Name of finished product: Pradaxa®		**EudraCT No.:** 2011-002285-21	
Name of active ingredient: Dabigatran etexilate (BIBR 1048)		**Page:** 1 of 5	**Synopsis No.:**
Module:		**Volume:** {hyperlink }	
Disclosure Synopsis date: 23 JUL 2014	**Trial No. / U No.:** 1160.138 / U13-2746-01	**Date of trial:** 01 FEB 2012 – 07 JUN 2013	**Date of revision:** Not applicable

Title of trial:	Evaluation of the long term safety of the use of dabigatran etexilate in patients with a bileaflet mechanical heart valve **(RE-ALIGN-EX)** This trial was prematurely discontinued.
Coordinating Investigators:	[redacted]
Trial sites:	Multicentre trial in 30 sites in 9 countries
Publication (reference):	Werf F van de, Brueckmann M, Connolly SJ et al. Am Heart J 2012;163(6):931-937.e1 and Eikelboom JW, Connolly SJ, Brueckmann M et al. NEJM 2013;369:1206-1214. Any discrepancies noted between the results from the CTR 1160.138 and the publication are due to the pooled analysis in the publication and the different analysis sets.
Clinical phase:	II
Objectives:	The primary objective of this trial was to obtain long-term safety data regarding the use of dabigatran etexilate (DE) compared with warfarin in patients having received a mechanical bileaflet heart valve.
Methodology:	This open label, active-controlled study was the long-term extension for patients previously enrolled in study 1160.113 (RE-ALIGN). Patients were to continue on the treatment they received in RE-ALIGN (DE or warfarin) and were to be followed for up to 84 months (i.e. 3 months in 1160.113 and up to 81 months in 1160.138). This study was terminated prematurely due to safety concerns arising during the conduct of both trials. Following an unblinded interim safety review it was decided as of 11 Oct 2012 that only patients in Population B should continue study treatment whereas patients in Population A were discontinued and immediately transitioned to an alternative anticoagulant. As of 28 Nov 2012, the study was completely terminated due to safety concerns. All remaining ongoing patients were immediately transitioned to a non-study anticoagulant.

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No. of subjects:

planned: entered: up to 650 patients

actual: enrolled: 159 patients

entered: 158 patients

Treatment	Entered	Treated
DE 150 mg b.i.d.	13	13
DE 220 mg b.i.d.	33	33
DE 300 mg b.i.d.	53	53
All DE	99	99
Warfarin	59	59

DE: dabigatran etexilate; b.i.d.: twice daily

Diagnosis and main criteria for inclusion:	Patients with bileaflet mechanical heart valve in place who completed RE-ALIGN and who were in need for continued anticoagulation
Test product:	Dabigatran etexilate
doses:	1 capsule of 150 mg (150 mg), 2 capsules of 110 mg (220 mg), or 2 capsules of 150 mg (300 mg) twice daily
mode of admin.:	Oral
batch nos.:	201437 (110 mg), 201666 (150 mg)
Reference therapy:	Warfarin
doses:	Tablet strengths were 1 mg, 3 mg, or 5 mg. Warfarin was dosed according to the target International Normalisation Ratio as recommended in guidelines and as deemed appropriate by the investigator.
mode of admin.:	Oral
batch nos.:	0B52UP (1 mg), 0B38UW (3 mg), 0C21UG (5 mg)
Duration of treatment:	Up to 84 months (including 12 weeks of treatment in RE-ALIGN)

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Criteria for evaluation:

Efficacy / clinical pharmacology: No primary or secondary efficacy endpoints were defined. Instead the following clinical efficacy outcome events were analysed descriptively: all-cause death, venous thromboembolism (VTE), MIs, transient ischaemic attack (TIA), stroke, systemic embolism, and valve thrombosis.

Safety: No primary of secondary safety endpoints were defined. Instead the following clinical safety outcome events were analysed descriptively: adverse events (AEs), serious adverse events (SAEs), AEs leading to discontinuation, bleeding events, and major bleeding events (MBEs).

Statistical methods: Descriptive statistics

SUMMARY – CONCLUSIONS:

Efficacy / clinical pharmacology results:

Disposition

A total of 159 patients were enrolled (i.e. 65% of the treated patients in study 1160.113) and 158 patients received at least 1 dose of trial medication (1 patient was not treated due to active infective endocarditis [exclusion criterion]). The study was terminated prematurely by the sponsor due to safety concerns; 153 patients completed the trial i.e. participated in the 6 months follow-up as introduced by the urgent safety memos dated 11 Oct 2012 and 28 Nov 2012. Five patients discontinued from the trial prematurely; the reasons were withdrawn consent (2 patients), lost to follow-up (2 patients), and other AEs (1 patient).

Demographic characteristics, exposure, and compliance

Overall, the treated patients had a mean age (SD) of 57.2 years (8.8), with a mean BMI of 27.7 kg/m^2. Most of the patients were male (64.6%) and most patients were White (89.2%). Median exposure to the study drug (excluding interruptions) was similar for patients treated with DE (all DE: 123 days) and warfarin (119 days). Overall, mean compliance of patients treated with DE ranged from 90% to 103%. For patients on warfarin, the INR was within the target range as defined by the investigator for a mean of 60.8% of time (SD=29.32).

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Efficacy / clinical pharmacology results (continued):

Pharmacokinetics

The gMean trough concentration of total dabigatran was approximately 123 ng/mL at the beginning of the study and approximately 108 ng/mL at the end-of-treatment visit. The trough concentrations appeared stable over time and largely overlapped between Populations A and B. Higher concentrations were seen in female patients and in patients taking P-gp inhibitors. The difference by creatinine clearance in patients with better renal function was not as pronounced because the dosing algorithm was optimised for renal function. Due to the low number of events, no statistical concentration-response analyses were performed.

Efficacy outcome events

Overall, 7 patients were adjudicated with at least 1 efficacy OE during on- and intermittent off-treatment periods (i.e. 2 patients with low risk and 5 patients with intermediate to high risk), see table below. Of these, 1 patient who died was treated with warfarin; all other OEs occurred in patients treated with DE. There were no patients with VTE or systemic embolism reported in this trial.

Summary of patients with adjudicated efficacy OEs (on- and intermittent off−treatment events) / treated set

	DE 150	DE 220	DE 300	All DE	Warfarin	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Treated patients	13 (100)	34 (100)	53 (100)	99 (100)	59 (100)	158 (100)
Death	0	0	0	0	1 (1.7)	1 (0.6)
VTE	0	0	0	0	0	0
MI	0	1 (2.9)	0	1 (1.0)	0	1 (0.6)
TIA	1 (7.7)	0	0	1 (1.0)	0	1 (0.6)
Stroke	0	0	3 (5.7)	3 (3.0)	0	3 (1.9)
Systemic embolism	0	0	0	0	0	0
Valve thrombosis	0	2 (5.9)	0	2 (2.0)	0	2 (1.3)

Due to dose reductions on DE, patients could appear in more than 1 DE column, but were counted in the 'All DE' and 'Total' columns only once. Events occurring from first study drug intake until last study drug intake + 6 days were considered.

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Safety results:

Adverse events

Overall, 38.6% of the treated patients were reported with any AE during the on-treatment period (all DE: 39.4%, warfarin: 37.3%). The most frequently reported AE (on preferred term level) was hypertension (all DE: 5.1%, warfarin: 6.8%), followed by bronchitis, dyspepsia, gastrooesophageal reflux, palpitations, peripheral oedema, dyspnoea, and haematuria (1.9% of patients each). AEs leading to discontinuation of study drug were reported by 3.8% of patients (all DE: 5.1%, warfarin: 1.7%). On preferred term level, AEs leading to discontinuation were reported by at most 1 patient. A total of 4.4% of patients reported with SAEs; none of them were fatal, or leading to disability/incapacity or congenital anomaly. One patient treated with warfarin died during this trial due to sudden cardiac death; this event was considered as not related to study drug intake. Due to the OE and SAE reporting strategy in this trial, the event was only captured as an OE and not as an SAE.

Bleeding events (safety outcome events)

In total, there were 6 patients (3.8%) with bleeding OEs during the on- and intermittent off-treatment periods in this trial. Of these, 5 patients (5.1%) were treated with DE and 1 patient (1.7%) received warfarin. One of the 5 patients treated with DE reduced the dose from DE 300 to DE 220 and had a bleeding event during intake of both DE doses; therefore the numbers of patients with bleeding events during intake of DE were 1 patient (DE 150), 2 patients (DE 220), and 3 patients (DE 300). Of the 6 patients with bleeding events, 2 patients were classified with low risk. Overall, 5 patients had protocol-defined minor bleeding events and 1 patient who reduced the DE dose had a clinically relevant non major bleeding event both during intake of DE 300 as well as DE 220. No major bleeding event or life-threatening bleeding events occurred during this trial.

Conclusions:

Overall, incidences of thromboembolic events and bleeding events were higher in patients treated with DE as compared with patients receiving warfarin in trials 1160.113 and 1160.138, leading to premature termination of both trials. In conclusion, dabigatran etexilate should not be used in patients with mechanical heart valves for the prevention of thromboembolic events.

Trial Synopsis - Appendix

The appended table on the following pages supplements the trial results presented in the Trial Synopsis. The primary objective of this trial was to obtain long-term safety. To comply with disclosure requirements, the primary endpoint was defined as patients with any AEs; additional secondary endpoints were defined as:

- Patients with AEs leading to discontinuation of trial drug
- Patients with serious AEs

The appended table provides the additional primary and secondary endpoints, as summarised below.

Results for	presented in
Adverse event overall summary – treated set	Table 15.3.2: 1

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: All patients

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	99 (100.0)	59 (100.0)	158 (100.0)
Patients with any AE	39 (39.4)	22 (37.3)	61 (38.6)
Patients with severe AEs	4 (4.0)	2 (3.4)	6 (3.8)
Patients with investigator defined drug-related AEs	7 (7.1)	1 (1.7)	8 (5.1)
Patients with other significant AEs (according to ICH E3)	5 (5.1)	1 (1.7)	6 (3.8)
Patients with AEs leading to discontinuation of trial drug	5 (5.1)	1 (1.7)	6 (3.8)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	3 (3.0)	4 (6.8)	7 (4.4)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	3 (3.0)	4 (6.8)	7 (4.4)
Prol.hospitalisation	1 (1.0)	0 (0.0)	1 (0.6)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Population A

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	78 (100.0)	48 (100.0)	126 (100.0)
Patients with any AE	30 (38.5)	20 (41.7)	50 (39.7)
Patients with severe AEs	2 (2.6)	2 (4.2)	4 (3.2)
Patients with investigator defined drug-related AEs	4 (5.1)	1 (2.1)	5 (4.0)
Patients with other significant AEs (according to ICH E3)	3 (3.8)	1 (2.1)	4 (3.2)
Patients with AEs leading to discontinuation of trial drug	3 (3.8)	1 (2.1)	4 (3.2)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	2 (2.6)	4 (8.3)	6 (4.8)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	2 (2.6)	4 (8.3)	6 (4.8)
Prol.hospitalisation	1 (1.3)	0 (0.0)	1 (0.8)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
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Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Population B

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	21 (100.0)	11 (100.0)	32 (100.0)
Patients with any AE	9 (42.9)	2 (18.2)	11 (34.4)
Patients with severe AEs	2 (9.5)	0 (0.0)	2 (6.3)
Patients with investigator defined drug-related AEs	3 (14.3)	0 (0.0)	3 (9.4)
Patients with other significant AEs (according to ICH E3)	2 (9.5)	0 (0.0)	2 (6.3)
Patients with AEs leading to discontinuation of trial drug	2 (9.5)	0 (0.0)	2 (6.3)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	1 (4.8)	0 (0.0)	1 (3.1)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	1 (4.8)	0 (0.0)	1 (3.1)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Aortic

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	68 (100.0)	44 (100.0)	112 (100.0)
Patients with any AE	26 (38.2)	18 (40.9)	44 (39.3)
Patients with severe AEs	2 (2.9)	2 (4.5)	4 (3.6)
Patients with investigator defined drug-related AEs	4 (5.9)	1 (2.3)	5 (4.5)
Patients with other significant AEs (according to ICH E3)	3 (4.4)	1 (2.3)	4 (3.6)
Patients with AEs leading to discontinuation of trial drug	3 (4.4)	1 (2.3)	4 (3.6)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	2 (2.9)	2 (4.5)	4 (3.6)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	2 (2.9)	2 (4.5)	4 (3.6)
Prol.hospitalisation	1 (1.5)	0 (0.0)	1 (0.9)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Mitral

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	29 (100.0)	14 (100.0)	43 (100.0)
Patients with any AE	13 (44.8)	4 (28.6)	17 (39.5)
Patients with severe AEs	2 (6.9)	0 (0.0)	2 (4.7)
Patients with investigator defined drug-related AEs	3 (10.3)	0 (0.0)	3 (7.0)
Patients with other significant AEs (according to ICH E3)	2 (6.9)	0 (0.0)	2 (4.7)
Patients with AEs leading to discontinuation of trial drug	2 (6.9)	0 (0.0)	2 (4.7)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	1 (3.4)	2 (14.3)	3 (7.0)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	1 (3.4)	2 (14.3)	3 (7.0)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Aortic plus Mitral

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	2 (100.0)	1 (100.0)	3 (100.0)
Patients with any AE	0 (0.0)	0 (0.0)	0 (0.0)
Patients with severe AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with investigator defined drug-related AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with other significant AEs (according to ICH E3)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with AEs leading to discontinuation of trial drug	0 (0.0)	0 (0.0)	0 (0.0)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	0 (0.0)	0 (0.0)	0 (0.0)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Low risk

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	30 (100.0)	18 (100.0)	48 (100.0)
Patients with any AE	10 (33.3)	6 (33.3)	16 (33.3)
Patients with severe AEs	1 (3.3)	0 (0.0)	1 (2.1)
Patients with investigator defined drug-related AEs	1 (3.3)	0 (0.0)	1 (2.1)
Patients with other significant AEs (according to ICH E3)	2 (6.7)	0 (0.0)	2 (4.2)
Patients with AEs leading to discontinuation of trial drug	2 (6.7)	0 (0.0)	2 (4.2)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	1 (3.3)	0 (0.0)	1 (2.1)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	1 (3.3)	0 (0.0)	1 (2.1)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Intermediate to high risk

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	69 (100.0)	41 (100.0)	110 (100.0)
Patients with any AE	29 (42.0)	16 (39.0)	45 (40.9)
Patients with severe AEs	3 (4.3)	2 (4.9)	5 (4.5)
Patients with investigator defined drug-related AEs	6 (8.7)	1 (2.4)	7 (6.4)
Patients with other significant AEs (according to ICH E3)	3 (4.3)	1 (2.4)	4 (3.6)
Patients with AEs leading to discontinuation of trial drug	3 (4.3)	1 (2.4)	4 (3.6)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	2 (2.9)	4 (9.8)	6 (5.5)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	2 (2.9)	4 (9.8)	6 (5.5)
Prol.hospitalisation	1 (1.4)	0 (0.0)	1 (0.9)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Pre CTP amendment 2

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	95 (100.0)	58 (100.0)	153 (100.0)
Patients with any AE	38 (40.0)	22 (37.9)	60 (39.2)
Patients with severe AEs	4 (4.2)	2 (3.4)	6 (3.9)
Patients with investigator defined drug-related AEs	7 (7.4)	1 (1.7)	8 (5.2)
Patients with other significant AEs (according to ICH E3)	5 (5.3)	1 (1.7)	6 (3.9)
Patients with AEs leading to discontinuation of trial drug	5 (5.3)	1 (1.7)	6 (3.9)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	3 (3.2)	4 (6.9)	7 (4.6)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	3 (3.2)	4 (6.9)	7 (4.6)
Prol.hospitalisation	1 (1.1)	0 (0.0)	1 (0.7)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Source data: Appendix 16.2, Listing 7.4, 7.5, 7.6, 7.7, 7.8 ctr\eot_xae1_.sas 20NOV2013

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Post CTP amendment 2

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	4 (100.0)	1 (100.0)	5 (100.0)
Patients with any AE	1 (25.0)	0 (0.0)	1 (20.0)
Patients with severe AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with investigator defined drug-related AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with other significant AEs (according to ICH E3)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with AEs leading to discontinuation of trial drug	0 (0.0)	0 (0.0)	0 (0.0)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	0 (0.0)	0 (0.0)	0 (0.0)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Pre CTP amendment 2 - Population A

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	78 (100.0)	48 (100.0)	126 (100.0)
Patients with any AE	30 (38.5)	20 (41.7)	50 (39.7)
Patients with severe AEs	2 (2.6)	2 (4.2)	4 (3.2)
Patients with investigator defined drug-related AEs	4 (5.1)	1 (2.1)	5 (4.0)
Patients with other significant AEs (according to ICH E3)	3 (3.8)	1 (2.1)	4 (3.2)
Patients with AEs leading to discontinuation of trial drug	3 (3.8)	1 (2.1)	4 (3.2)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	2 (2.6)	4 (8.3)	6 (4.8)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	2 (2.6)	4 (8.3)	6 (4.8)
Prol.hospitalisation	1 (1.3)	0 (0.0)	1 (0.8)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Source data: Appendix 16.2, Listing 7.4, 7.5, 7.6, 7.7, 7.8 ctr\eot_xae1_.sas 20NOV2013

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Pre CTP amendment 2 - Population B

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	17 (100.0)	10 (100.0)	27 (100.0)
Patients with any AE	8 (47.1)	2 (20.0)	10 (37.0)
Patients with severe AEs	2 (11.8)	0 (0.0)	2 (7.4)
Patients with investigator defined drug-related AEs	3 (17.6)	0 (0.0)	3 (11.1)
Patients with other significant AEs (according to ICH E3)	2 (11.8)	0 (0.0)	2 (7.4)
Patients with AEs leading to discontinuation of trial drug	2 (11.8)	0 (0.0)	2 (7.4)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	1 (5.9)	0 (0.0)	1 (3.7)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	1 (5.9)	0 (0.0)	1 (3.7)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Source data: Appendix 16.2, Listing 7.4, 7.5, 7.6, 7.7, 7.8 ctr\eot_xae1_.sas 20NOV2013

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Pre CTP amendment 2 - Aortic valve surgery

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	68 (100.0)	44 (100.0)	112 (100.0)
Patients with any AE	26 (38.2)	18 (40.9)	44 (39.3)
Patients with severe AEs	2 (2.9)	2 (4.5)	4 (3.6)
Patients with investigator defined drug-related AEs	4 (5.9)	1 (2.3)	5 (4.5)
Patients with other significant AEs (according to ICH E3)	3 (4.4)	1 (2.3)	4 (3.6)
Patients with AEs leading to discontinuation of trial drug	3 (4.4)	1 (2.3)	4 (3.6)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	2 (2.9)	2 (4.5)	4 (3.6)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	2 (2.9)	2 (4.5)	4 (3.6)
Prol.hospitalisation	1 (1.5)	0 (0.0)	1 (0.9)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Pre CTP amendment 2 - Mitral valve surgery

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	25 (100.0)	14 (100.0)	39 (100.0)
Patients with any AE	12 (48.0)	4 (28.6)	16 (41.0)
Patients with severe AEs	2 (8.0)	0 (0.0)	2 (5.1)
Patients with investigator defined drug-related AEs	3 (12.0)	0 (0.0)	3 (7.7)
Patients with other significant AEs (according to ICH E3)	2 (8.0)	0 (0.0)	2 (5.1)
Patients with AEs leading to discontinuation of trial drug	2 (8.0)	0 (0.0)	2 (5.1)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	1 (4.0)	2 (14.3)	3 (7.7)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	1 (4.0)	2 (14.3)	3 (7.7)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Pre CTP amendment 2 - Aortic plus Mitral valve surgery

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	2 (100.0)	0 (0.0)	2 (100.0)
Patients with any AE	0 (0.0)	0 (0.0)	0 (0.0)
Patients with severe AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with investigator defined drug-related AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with other significant AEs (according to ICH E3)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with AEs leading to discontinuation of trial drug	0 (0.0)	0 (0.0)	0 (0.0)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	0 (0.0)	0 (0.0)	0 (0.0)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Pre CTP amendment 2 - Low risk

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	30 (100.0)	18 (100.0)	48 (100.0)
Patients with any AE	10 (33.3)	6 (33.3)	16 (33.3)
Patients with severe AEs	1 (3.3)	0 (0.0)	1 (2.1)
Patients with investigator defined drug-related AEs	1 (3.3)	0 (0.0)	1 (2.1)
Patients with other significant AEs (according to ICH E3)	2 (6.7)	0 (0.0)	2 (4.2)
Patients with AEs leading to discontinuation of trial drug	2 (6.7)	0 (0.0)	2 (4.2)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	1 (3.3)	0 (0.0)	1 (2.1)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	1 (3.3)	0 (0.0)	1 (2.1)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Source data: Appendix 16.2, Listing 7.4, 7.5, 7.6, 7.7, 7.8 ctr\eot_xae1_.sas 20NOV2013

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Pre CTP amendment 2 - Intermediate to high risk

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	65 (100.0)	40 (100.0)	105 (100.0)
Patients with any AE	28 (43.1)	16 (40.0)	44 (41.9)
Patients with severe AEs	3 (4.6)	2 (5.0)	5 (4.8)
Patients with investigator defined drug-related AEs	6 (9.2)	1 (2.5)	7 (6.7)
Patients with other significant AEs (according to ICH E3)	3 (4.6)	1 (2.5)	4 (3.8)
Patients with AEs leading to discontinuation of trial drug	3 (4.6)	1 (2.5)	4 (3.8)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	2 (3.1)	4 (10.0)	6 (5.7)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	2 (3.1)	4 (10.0)	6 (5.7)
Prol.hospitalisation	1 (1.5)	0 (0.0)	1 (1.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Post CTP amendment 2 - Population B

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	4 (100.0)	1 (100.0)	5 (100.0)
Patients with any AE	1 (25.0)	0 (0.0)	1 (20.0)
Patients with severe AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with investigator defined drug-related AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with other significant AEs (according to ICH E3)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with AEs leading to discontinuation of trial drug	0 (0.0)	0 (0.0)	0 (0.0)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	0 (0.0)	0 (0.0)	0 (0.0)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Post CTP amendment 2 - Mitral valve surgery

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	4 (100.0)	0 (0.0)	4 (100.0)
Patients with any AE	1 (25.0)	0 (0.0)	1 (25.0)
Patients with severe AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with investigator defined drug-related AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with other significant AEs (according to ICH E3)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with AEs leading to discontinuation of trial drug	0 (0.0)	0 (0.0)	0 (0.0)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	0 (0.0)	0 (0.0)	0 (0.0)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Post CTP amendment 2 - Aortic plus Mitral valve surgery

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	0 (0.0)	1 (100.0)	1 (100.0)
Patients with any AE	0 (0.0)	0 (0.0)	0 (0.0)
Patients with severe AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with investigator defined drug-related AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with other significant AEs (according to ICH E3)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with AEs leading to discontinuation of trial drug	0 (0.0)	0 (0.0)	0 (0.0)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	0 (0.0)	0 (0.0)	0 (0.0)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Post CTP amendment 2 - Intermediate to high risk

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	4 (100.0)	1 (100.0)	5 (100.0)
Patients with any AE	1 (25.0)	0 (0.0)	1 (20.0)
Patients with severe AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with investigator defined drug-related AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with other significant AEs (according to ICH E3)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with AEs leading to discontinuation of trial drug	0 (0.0)	0 (0.0)	0 (0.0)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	0 (0.0)	0 (0.0)	0 (0.0)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Population A - Aortic valve surgery

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	68 (100.0)	44 (100.0)	112 (100.0)
Patients with any AE	26 (38.2)	18 (40.9)	44 (39.3)
Patients with severe AEs	2 (2.9)	2 (4.5)	4 (3.6)
Patients with investigator defined drug-related AEs	4 (5.9)	1 (2.3)	5 (4.5)
Patients with other significant AEs (according to ICH E3)	3 (4.4)	1 (2.3)	4 (3.6)
Patients with AEs leading to discontinuation of trial drug	3 (4.4)	1 (2.3)	4 (3.6)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	2 (2.9)	2 (4.5)	4 (3.6)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	2 (2.9)	2 (4.5)	4 (3.6)
Prol.hospitalisation	1 (1.5)	0 (0.0)	1 (0.9)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Population A - Mitral valve surgery

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	9 (100.0)	4 (100.0)	13 (100.0)
Patients with any AE	4 (44.4)	2 (50.0)	6 (46.2)
Patients with severe AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with investigator defined drug-related AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with other significant AEs (according to ICH E3)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with AEs leading to discontinuation of trial drug	0 (0.0)	0 (0.0)	0 (0.0)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	0 (0.0)	2 (50.0)	2 (15.4)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	0 (0.0)	2 (50.0)	2 (15.4)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Population A - Aortic plus Mitral valve surgery

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	1 (100.0)	0 (0.0)	1 (100.0)
Patients with any AE	0 (0.0)	0 (0.0)	0 (0.0)
Patients with severe AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with investigator defined drug-related AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with other significant AEs (according to ICH E3)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with AEs leading to discontinuation of trial drug	0 (0.0)	0 (0.0)	0 (0.0)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	0 (0.0)	0 (0.0)	0 (0.0)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Population A - Low risk

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	30 (100.0)	18 (100.0)	48 (100.0)
Patients with any AE	10 (33.3)	6 (33.3)	16 (33.3)
Patients with severe AEs	1 (3.3)	0 (0.0)	1 (2.1)
Patients with investigator defined drug-related AEs	1 (3.3)	0 (0.0)	1 (2.1)
Patients with other significant AEs (according to ICH E3)	2 (6.7)	0 (0.0)	2 (4.2)
Patients with AEs leading to discontinuation of trial drug	2 (6.7)	0 (0.0)	2 (4.2)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	1 (3.3)	0 (0.0)	1 (2.1)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	1 (3.3)	0 (0.0)	1 (2.1)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Population A - Intermediate to high risk

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	48 (100.0)	30 (100.0)	78 (100.0)
Patients with any AE	20 (41.7)	14 (46.7)	34 (43.6)
Patients with severe AEs	1 (2.1)	2 (6.7)	3 (3.8)
Patients with investigator defined drug-related AEs	3 (6.3)	1 (3.3)	4 (5.1)
Patients with other significant AEs (according to ICH E3)	1 (2.1)	1 (3.3)	2 (2.6)
Patients with AEs leading to discontinuation of trial drug	1 (2.1)	1 (3.3)	2 (2.6)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	1 (2.1)	4 (13.3)	5 (6.4)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	1 (2.1)	4 (13.3)	5 (6.4)
Prol.hospitalisation	1 (2.1)	0 (0.0)	1 (1.3)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Population B - Mitral valve surgery

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	20 (100.0)	10 (100.0)	30 (100.0)
Patients with any AE	9 (45.0)	2 (20.0)	11 (36.7)
Patients with severe AEs	2 (10.0)	0 (0.0)	2 (6.7)
Patients with investigator defined drug-related AEs	3 (15.0)	0 (0.0)	3 (10.0)
Patients with other significant AEs (according to ICH E3)	2 (10.0)	0 (0.0)	2 (6.7)
Patients with AEs leading to discontinuation of trial drug	2 (10.0)	0 (0.0)	2 (6.7)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	1 (5.0)	0 (0.0)	1 (3.3)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	1 (5.0)	0 (0.0)	1 (3.3)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Population B - Aortic plus Mitral valve surgery

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	1 (100.0)	1 (100.0)	2 (100.0)
Patients with any AE	0 (0.0)	0 (0.0)	0 (0.0)
Patients with severe AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with investigator defined drug-related AEs	0 (0.0)	0 (0.0)	0 (0.0)
Patients with other significant AEs (according to ICH E3)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with AEs leading to discontinuation of trial drug	0 (0.0)	0 (0.0)	0 (0.0)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	0 (0.0)	0 (0.0)	0 (0.0)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.

Table 15.3.2: 1 Adverse event overall summary by sub group - TRT

Sub group: Population B - Intermediate to high risk

	Dabigatran N (%)	Warfarin N (%)	Total N (%)
Number of patients	21 (100.0)	11 (100.0)	32 (100.0)
Patients with any AE	9 (42.9)	2 (18.2)	11 (34.4)
Patients with severe AEs	2 (9.5)	0 (0.0)	2 (6.3)
Patients with investigator defined drug-related AEs	3 (14.3)	0 (0.0)	3 (9.4)
Patients with other significant AEs (according to ICH E3)	2 (9.5)	0 (0.0)	2 (6.3)
Patients with AEs leading to discontinuation of trial drug	2 (9.5)	0 (0.0)	2 (6.3)
Patients with significant AEs (pre-specified events)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with serious AEs	1 (4.8)	0 (0.0)	1 (3.1)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	1 (4.8)	0 (0.0)	1 (3.1)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 16.0
Population A: patients who, prior to 1160.113, had recently undergone surgery for implantation of bileaflet mechanical heart valve(s) and had not yet started oral anticoagulation therapy.
Population B: patients who have had surgery for implantation of a mitral bileaflet mechanical heart valve at least three months prior to randomisation into 1160.113 and were currently taking an oral VKA.
Low risk: aortic valves with no additional risk factors.
Intermediate to high risk: aortic valves with additional risk factors or mitral valves.
Patients are presented according to the treatment they received except for 2 patients, 650001 and 800151, who mistakenly switched to study warfarin part way through the study. These patients are presented under the DE columns only.