



Clinical trial results:

Open-label safety and tolerability study of dabigatran etexilate given for 3 days at the end of standard anticoagulant therapy in children aged 12 years to less than 18 years

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2008-006866-27 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 16 February 2012 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 20 June 2016 |
| First version publication date | 16 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | 1160.88 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00844415 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Boehringer Ingelheim |
| Sponsor organisation address | Binger Strasse 173 , Ingelheim am Rhein , Germany, 55216 |
| Public contact | QRPE Processes and Systems Coordination Clinical Trial Information Disclosure , Boehringer Ingelheim Pharma GmbH & Co. KG , +1 8002430127 , clintriage.rdg@boehringer-ingelheim.com |
| Scientific contact | QRPE Processes and Systems Coordination Clinical Trial Information Disclosure , Boehringer Ingelheim Pharma GmbH & Co. KG , +1 8002430127 , clintriage.rdg@boehringer-ingelheim.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000081-PIP01-07 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 15 March 2012 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 16 February 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 February 2012 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To investigate tolerability and safety of dabigatran etexilate capsules in adolescents. To explore preliminary pharmacokinetic and pharmacodynamic parameters in adolescents.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all patients as required.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 02 March 2009 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | Canada: 9 |
| Worldwide total number of subjects | 9 |
| EEA total number of subjects | 0 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 9 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Adolescent (12 to <18years) patients who successfully completed planned treatment with either low molecular weight heparins or oral anticoagulation for primary venous thrombotic event (VTE).

Pre-assignment

Screening details:

All subjects were screened for eligibility to participate in the trial. Subjects attended specialist sites which would then ensure that they (the subject) met all strictly implemented inclusion/exclusion criteria. Subjects were not assigned to trial treatment if any one of the specific entry criteria were violated.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

Open-label study, only one investigational product used

Arms

| | |
|-----------|--------------|
| Arm title | All patients |
|-----------|--------------|

Arm description:

Dabigatran was administered twice daily for three consecutive days (total 6 doses). All patients received an initial oral dose of 1.71mg/kg of dabigatran (80 percent of the adult dose of 150 mg/70 kg adjusted for the patient's weight). Based on thrombin time (TT) and clinical assessment, the dose was adjusted to the target dose of 2.14 mg/kg of dabigatran (100 percent of the adult dose adjusted for the patient's weight). Three patients received 75 mg dabigatran (first dose) followed by 100 mg twice daily (BID). Three patients took dabigatran 100 mg (first dose) followed by 125 mg BID. Two patients received a dose of 125 mg dabigatran followed by 150 mg BID. One patient received only a single dose of dabigatran (75 mg).

| | |
|--|----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dabigatran etexilate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Dose 1: 50 mg capsule BID (100 mg daily)

Dose 2: 75 mg capsule BID (150 mg daily)

Dose 3: 2 X 50 mg capsules BID (200 mg daily)

Dose 4: 50 mg capsule & 75 mg capsule BID (250 mg daily)

Dose 5: 2 X 75 mg capsules BID (300 mg daily)

Maximum dose 150 mg BID

| | |
|---|------------------|
| Number of subjects in period 1 | All patients |
| Started | 9 |
| Pat. received 75 mg followed by 100 mg | 3 ^[1] |
| Pat. received 100 mg followed by 125 mg | 3 ^[2] |

| | |
|---|------------------|
| Pat. received 125 mg followed by 150 mg | 2 ^[3] |
| Pat. received single dose 75 mg | 1 ^[4] |
| Completed | 8 |
| Not completed | 1 |
| Consent withdrawn by subject | 1 |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Since the dose was adjusted by body weight, patients could receive different doses of dabigatran.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Since the dose was adjusted by body weight, patients could receive different doses of dabigatran.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Since the dose was adjusted by body weight, patients could receive different doses of dabigatran.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Since the dose was adjusted by body weight, patients could receive different doses of dabigatran.

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | All patients |
|-----------------------|--------------|

Reporting group description:

Dabigatran was administered twice daily for three consecutive days (total 6 doses). All patients received an initial oral dose of 1.71mg/kg of dabigatran (80 percent of the adult dose of 150 mg/70 kg adjusted for the patient's weight). Based on thrombin time (TT) and clinical assessment, the dose was adjusted to the target dose of 2.14 mg/kg of dabigatran (100 percent of the adult dose adjusted for the patient's weight). Three patients received 75 mg dabigatran (first dose) followed by 100 mg twice daily (BID). Three patients took dabigatran 100 mg (first dose) followed by 125 mg BID. Two patients received a dose of 125 mg dabigatran followed by 150 mg BID. One patient received only a single dose of dabigatran (75 mg).

| Reporting group values | All patients | Total | |
|------------------------|--------------|-------|--|
| Number of subjects | 9 | 9 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 15.7 | | |
| standard deviation | ± 1.3 | - | |
| Gender, Male/Female | | | |
| Units: Participants | | | |
| Female | 6 | 6 | |
| Male | 3 | 3 | |

End points

End points reporting groups

| | |
|--|--------------|
| Reporting group title | All patients |
| Reporting group description: | |
| Dabigatran was administered twice daily for three consecutive days (total 6 doses). All patients received an initial oral dose of 1.71mg/kg of dabigatran (80 percent of the adult dose of 150 mg/70 kg adjusted for the patient's weight). Based on thrombin time (TT) and clinical assessment, the dose was adjusted to the target dose of 2.14 mg/kg of dabigatran (100 percent of the adult dose adjusted for the patient's weight). Three patients received 75 mg dabigatran (first dose) followed by 100 mg twice daily (BID). Three patients took dabigatran 100 mg (first dose) followed by 125 mg BID. Two patients received a dose of 125 mg dabigatran followed by 150 mg BID. One patient received only a single dose of dabigatran (75 mg). | |

Primary: Number of patients with adverse events

| | |
|--|---|
| End point title | Number of patients with adverse events ^[1] |
| End point description: | |
| Patients with treatment drug related adverse events (DRAEs) and serious adverse events (SAEs) are reported separately for on-treatment and post-treatment period. Events were considered „on-treatment“ if occurring within 72 hours after last drug administration. | |
| End point type | Primary |
| End point timeframe: | |
| From Screening until 30 days after first drug administration (end of trial visit) | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: According to the exploratory nature of this study only descriptive statistical methods were applied to all endpoints.

| End point values | All patients | | | |
|-----------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 ^[2] | | | |
| Units: Participants | | | | |
| DRAEs on-treatment | 2 | | | |
| SAEs on-treatment | 0 | | | |
| DRAEs post-treatment | 0 | | | |
| SAEs post-treatment | 1 | | | |

Notes:

[2] - Treated Set (TS), all patients dispensed study medication that have taken at least one dose

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with bleeding events (major and minor)

| | |
|---|--|
| End point title | Number of patients with bleeding events (major and minor) ^[3] |
| End point description: | |
| Patients were carefully assessed for signs and symptoms of bleeding. Bleeding was to be classified as major or minor. Major bleeding had to satisfy one or more of the following criteria: Overt bleeding associated with a decrease in haemoglobin of at least 2 g/dL in 24 hours, Overt bleeding requiring a transfusion of red blood cells, Overt bleeding which was retroperitoneal, intracranial, intraocular, or intraarticular, any overt bleeding deemed by the attending physician to require discontinuation of study | |

medication. Minor bleeds were clinical bleeds that did not fulfill the criteria for major bleeds.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Screening until 30 days after first drug administration (end of trial visit)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: According to the exploratory nature of this study only descriptive statistical methods were applied to all endpoints.

| | | | | |
|-----------------------------|------------------|--|--|--|
| End point values | All patients | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 ^[4] | | | |
| Units: Participants | 0 | | | |

Notes:

[4] - Treated Set (TS), all patients dispensed study medication that have taken at least one dose

Statistical analyses

No statistical analyses for this end point

Primary: Plasma concentration of free dabigatran

| | |
|-----------------|--|
| End point title | Plasma concentration of free dabigatran ^[5] |
|-----------------|--|

End point description:

Plasma concentration of free dabigatran measured at 72 hours after first dose

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

3 days

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: According to the exploratory nature of this study only descriptive statistical methods were applied to all endpoints.

| | | | | |
|---|------------------|--|--|--|
| End point values | All patients | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 ^[6] | | | |
| Units: ng/ml | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Patients with 75mg dose followed by 100mg (N=3) | 28 (± 12.8) | | | |
| Patients with 100mg dose followed by 125mg (N=3) | 41.6 (± 66.5) | | | |

Notes:

[6] - Treated Set, all patients taking >= one dose. Statistics reported only for groups with > 2 patients

Statistical analyses

No statistical analyses for this end point

Primary: Plasma concentration of total dabigatran

| | |
|-----------------|---|
| End point title | Plasma concentration of total dabigatran ^[7] |
|-----------------|---|

End point description:

Plasma concentration of total dabigatran measured at 72 hours after first dose

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 3

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: According to the exploratory nature of this study only descriptive statistical methods were applied to all endpoints.

| End point values | All patients | | | |
|---|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 ^[8] | | | |
| Units: ng/ml | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Patients with 75mg dose followed by 100mg (N=3) | 34.2 (± 3.56) | | | |
| Patients with 100mg dose followed by 125mg (N=3) | 58.2 (± 48.7) | | | |

Notes:

[8] - Treated Set, all patients taking \geq one dose. Statistics reported only for groups with > 2 patients

Statistical analyses

No statistical analyses for this end point

Primary: Thrombin time (TT) centrally measured

| | |
|-----------------|--|
| End point title | Thrombin time (TT) centrally measured ^[9] |
|-----------------|--|

End point description:

Measurement of TT was performed centrally by Hemoclot Thrombin Inhibitor clotting assay.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 3

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: According to the exploratory nature of this study only descriptive statistical methods were applied to all endpoints.

| End point values | All patients | | | |
|--|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 ^[10] | | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| Patients with 75mg dose followed by 100mg (N=3) | 36.9 (± 3.61) | | | |
| Patients with 100mg dose followed by 125mg (N=3) | 37.4 (± 3.97) | | | |

Notes:

[10] - Treated Set, all patients taking \geq one dose. Statistics reported only for groups with > 2 patients

Statistical analyses

No statistical analyses for this end point

Primary: TT locally measured

| | |
|-----------------|-------------------------------------|
| End point title | TT locally measured ^[11] |
|-----------------|-------------------------------------|

End point description:

Measurement of TT was performed locally by Hemoclot Thrombin Inhibitor clotting assay.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 3

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: According to the exploratory nature of this study only descriptive statistical methods were applied to all endpoints.

| End point values | All patients | | | |
|--|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 ^[12] | | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| Patients with 75mg dose followed by 100mg (N=3) | 33.5 (± 2.15) | | | |
| Patients with 100mg dose followed by 125mg (N=3) | 36.8 (± 5.72) | | | |

Notes:

[12] - Treated Set, all patients taking \geq one dose. Statistics reported only for groups with > 2 patients

Statistical analyses

No statistical analyses for this end point

Secondary: Activated Partial Thromboplastin Time (aPTT) centrally measured at 72 hours after first dose

| | |
|-----------------|--|
| End point title | Activated Partial Thromboplastin Time (aPTT) centrally measured at 72 hours after first dose |
|-----------------|--|

End point description:

Measurement of aPTT was performed centrally using validated assays.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 3

| End point values | All patients | | | |
|---|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 ^[13] | | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| Patients with 75mg dose followed by 100mg (N=3) | 38.6 (± 2.94) | | | |

| | | | | |
|--|---------------|--|--|--|
| Patients with 100mg dose followed by 125mg (N=3) | 47.4 (± 4.42) | | | |
|--|---------------|--|--|--|

Notes:

[13] - Treated Set, all patients taking \geq one dose. Statistics reported only for groups with > 2 patients

Statistical analyses

No statistical analyses for this end point

Secondary: aPTT locally measured

| | |
|---|-----------------------|
| End point title | aPTT locally measured |
| End point description: Measurement of aPTT was performed locally using validated assays. | |
| End point type | Secondary |
| End point timeframe: Day 3 | |

| End point values | All patients | | | |
|--|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 ^[14] | | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| Patients with 75mg dose followed by 100mg (N=3) | 29.9 (± 2.68) | | | |
| Patients with 100mg dose followed by 125mg (N=3) | 33.6 (± 0.896) | | | |

Notes:

[14] - Treated Set, all patients taking \geq one dose. Statistics reported only for groups with > 2 patients

Statistical analyses

No statistical analyses for this end point

Secondary: Ecarin Clotting Time (ECT) centrally measured

| | |
|--|---|
| End point title | Ecarin Clotting Time (ECT) centrally measured |
| End point description: Measurement of ECT was performed centrally using validated assays. Descriptive statistics are only performed for the centrally measured ECT. | |
| End point type | Secondary |
| End point timeframe: Day 3 | |

| End point values | All patients | | | |
|--|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 ^[15] | | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| Patients with 75mg dose followed by 100mg (N=3) | 43.3 (± 1.31) | | | |
| Patients with 100mg dose followed by 125mg (N=3) | 49.6 (± 11.6) | | | |

Notes:

[15] - Treated Set, all patients taking >= one dose. Statistics reported only for groups with > 2 patients

Statistical analyses

No statistical analyses for this end point

Secondary: Patients with clinically relevant changes in any laboratory parameter, Electrocardiogram (ECG) or vital signs

| | |
|--|---|
| End point title | Patients with clinically relevant changes in any laboratory parameter, Electrocardiogram (ECG) or vital signs |
| End point description: Changes in any laboratory parameter, ECG or vital signs were judged clinically relevant by the investigator. | |
| End point type | Secondary |
| End point timeframe: Baseline and 3 days | |

| End point values | All patients | | | |
|-----------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 ^[16] | | | |
| Units: Participants | 0 | | | |

Notes:

[16] - Treated Set (TS), all patients dispensed study medication that have taken at least one dose

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrences of clinical outcome

| | |
|---|---------------------------------|
| End point title | Occurrences of clinical outcome |
| End point description: Occurrences of clinical outcomes including recurrent venous thrombotic event (VTE), post thrombotic syndrome (PTS), pulmonary emboli (PEs), and total and VTE related mortality objectively assessed for example by ultrasound, venography or computed chromatography (CT) scan (based on the thrombus location). Number of patients with particular clinical outcome are reported. | |
| End point type | Secondary |
| End point timeframe: 3 days | |

| | | | | |
|--------------------------------------|-------------------|--|--|--|
| End point values | All patients | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 ^[17] | | | |
| Units: Participants | | | | |
| Patients with recurrent VTE | 1 | | | |
| Patients with PTS | 0 | | | |
| Patients with PE | 0 | | | |
| Patients with VTE related death | 0 | | | |
| Patients with other death | 0 | | | |
| Patients with other clinical outcome | 0 | | | |

Notes:

[17] - Treated Set (TS), all patients dispensed study medication that have taken at least one dose

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 3 days

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 14.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | All patients |
|-----------------------|--------------|

Reporting group description:

Dabigatran was administered twice daily for three consecutive days (total 6 doses). All patients received an initial oral dose of 1.71mg/kg of dabigatran (80 percent of the adult dose of 150 mg/70 kg adjusted for the patient's weight). Based on thrombin time (TT) and clinical assessment, the dose was adjusted to the target dose of 2.14 mg/kg of dabigatran (100 percent of the adult dose adjusted for the patient's weight). Three patients received 75 mg dabigatran (first dose) followed by 100 mg twice daily (BID). Three patients took dabigatran 100 mg (first dose) followed by 125 mg BID. Two patients received a dose of 125 mg dabigatran followed by 150 mg BID. One patient received only a single dose of dabigatran (75 mg).

| Serious adverse events | All patients | | |
|---|---------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | All patients | | |
|---|----------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Abdominal pain | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 06 March 2009 | Amendment 1 (06 March 2009) was implemented immediately as this amendment added verapamil to the list of restricted medications when new information became available concerning a potential interaction with dabigatran. There was also an administrative change to allow for analysis of screening/baseline TT and ECT. |
| 29 September 2009 | Amendment 2 (29 Sep 2009) was implemented to: 1.) Request parental consent / child assent for any left over plasma from local analyses and for an additional sample to be taken to be preserved for future research in coagulation studies performed by one of the Coordinating Investigators, Lesley Mitchell at the University of Alberta. This change to the protocol required Health Canada approval and REB approval prior to implementation. 2.) Provide clarification of some protocol requirements and to make administrative changes. These administrative changes to the protocol could be implemented without approval from Health Canada or institutional REBs. |
| 19 February 2010 | Amendment 3 (19Feb10), was implemented immediately when the results of two interaction study results became available. Total dabigatran concentrations were increased up to 2.5-fold by ketoconazole, a P-glycoprotein inhibitor. Rifampicin, a strong P-glycoprotein inducer, showed reductions in dabigatran concentrations by about 67%. A few minor administrative changes were also implemented. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported