ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 03/20/2012

ClinicalTrials.gov ID: NCT00623779

Study Identification

Unique Protocol ID:	D1250C00051
Brief Title:	Atrial Fibrillation (AF) Patients Not Taking Vitamin-K Antagonist (VKA)
Official Title:	A Controlled, Randomized, Parallel , Multi-centre Feasibility Study of the Oral Direct Thrombin Inhibitor, AZD0837, Given as ER Formulation, in the Prevention of Stroke and Systolic Embolic Events in Patients With Atrial Fibrillation, Who Are Appropriate for But Unable/Unwilling to Take VKA Therapy
Secondary IDs:	

Study Status

Record Verification:	March 2012
Overall Status:	Completed
Study Start:	October 2007
Primary Completion:	October 2008 [Actual]
Study Completion:	October 2008 [Actual]

Sponsor/Collaborators

Sponsor:	AstraZeneca
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes

Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 07/H0720/99 Board Name: National Research Ethics Service Board Affiliation: Royal Free Hospital NHS Trust Phone: 44-020-7794-0581 Email: Thomas.McQuillan@royalfree.nhs.uk
Data Monitoring?:	Yes
Plan to Share Data?:	
Oversight Authorities:	Denmark: Danish Medicines Agency Norway: Norwegian Medicines Agency Poland: Ministry of Health Russia: Ministry of Health of the Russian Federation Sweden: Medical Products Agency United Kingdom: Medicines and Healthcare Products Regulatory Agency

Study Description

Brief Summary:	The purpose of this study is to assess the safety and tolerability of AZD0837 in patients with atrial fibrillation who are unable or unwilling to take vitamin K antagonist therapy for up to 3 months.
Detailed Description:	

Conditions

Conditions:	Persistent or Permanent Non-valvular Atrial Fibrillation
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Prevention
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	1

Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety Study
Enrollment:	128 [Actual]

Arms and Interventions

Intervention Details:
- Drug: AZD0837
  - ER formulation
- Drug: Aspirin
  - Oral form

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No

Criteria: Inclusion Criteria:

- Either one of the following risk factors is sufficient for inclusion (high risk patient)
- Previous cerebral ischaemic attack (stroke or transient ischaemic attack (TIA), >30 days prior to randomization)
- Previous systemic embolism or at least one of the following risk factors are needed for inclusion: Age ≥75 years
- Symptomatic congestive heart failure
- Impaired left ventricular systolic function
- Diabetes mellitus; Hypertension requiring anti-hypertensive treatment
- In addition to AF the patient must be appropriate for but unable or unwilling to take VKA therapy

Exclusion Criteria:

- Presence of a clinically significant valvular heart disease;; Stroke or TIA and/or systemic embolism within the previous 30 days prior to randomization
- Conditions associated with increased risk of major bleeding

Contacts/Locations

Study Officials: Gregory Y Lip, MD
Study Principal Investigator
Birmingham City Hospital

Locations: Denmark
Research Site
Aalborg, Denmark

Research Site
Copenhagen, Denmark

Research Site
Silkeborg, Denmark

Research Site
Horsens, Denmark

Research Site
Kobenhavn, Denmark

Research Site
Arhus N, Denmark

Research Site
Frederikssund, Denmark

Research Site
Esbjerg, Denmark

Research Site
Svendborg, Denmark

Norway
Research Site
Gjettum, Norway

Research Site
Straume, Norway

Research Site
Oslo, Norway

Research Site

Elverum, Norway

Research Site
Stovner, Norway

Research Site
Kongsberg, Norway

Poland
Research Site
Warszawa, Poland

Research Site
Sopot, Poland

Research Site
Bytom, Poland

Research Site
Lodz, Poland

Research Site
Ruda Slaska, Poland

Research Site
Otwock, Poland

Research Site
Krakow, Poland

Research Site
Wroclaw, Poland

Research Site
Plock, Poland

Research Site
Ostrow Mazowiecka, Poland

Research Site
Czestochowa, Poland

Research Site
Lublin, Poland

Research Site

Torun, Poland

Russian Federation
Research Site
St. Petersburg, Russian Federation

Research Site
Moscow, Russian Federation

Sweden
Research Site
Lund, Sweden

Research Site
Molndal, Sweden

Research Site
Stockholm, Sweden

Research Site
Boras, Sweden

Research Site
Malmo, Sweden

Research Site
Goteborg, Sweden

United Kingdom
Research Site
Birmingham, United Kingdom

Research Site
Newcastle Upon Tyne, United Kingdom

Research Site
Eastbourne, United Kingdom

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	The study population included male and female participants >18 years of age with chronic non-valvular Atrial Fibrillation. The participants were recruited during the time period from 22 October 2007 to 21 October 2008 at medical clinics in Europe.
Pre-Assignment Details	For participants treated with Vitamin K Antagonists (VKA) at the time of enrollment, VKA treatment was to be adjusted (and stopped before randomisation) to ensure that INR was below 2.0 at randomisation. If this was not achieved the participant was discontinued from the study.

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Overall Study

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Started	41	42	45
Completed	38	39	44
Not Completed	3	3	1
Adverse Event	1	3	0
Criteria from CSR	2	0	1

Baseline Characteristics

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Baseline Measures

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy	Total
Number of Participants	41	42	45	128
Age, Continuous [units: Years] Mean (Standard Deviation)	72.5 (8)	71.6 (8.51)	68.8 (9.36)	70 (8.68)
Gender, Male/Female [units: Participants]				
Female	16	16	17	49
Male	25	26	28	79

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Premature Discontinuation of Study or Study Drug Due to Any Reason
Measure Description	The premature discontinuation of study or study drug due to any reason
Time Frame	28 week (randomisation visit to last follow up visit in study) according to protocols
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	41	42	45
Premature Discontinuation of Study or Study Drug Due to Any Reason [units: Participants]	4	6	3

2. Primary Outcome Measure:

Measure Title	Premature Discontinuation of Study Drug Due to Any Reason
Measure Description	The premature discontinuation of study drug due to any reason
Time Frame	24 weeks (randomisation visit to last treatment visit)
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	41	42	45
Premature Discontinuation of Study Drug Due to Any Reason [units: Participants]	3	3	1

3. Primary Outcome Measure:

Measure Title	Premature Discontinuation of Study Due to Any Reason
Measure Description	|The premature discontinuation of study due to any reason
Time Frame	28 weeks (randomisation visit to last follow up visit)
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	41	42	45
Premature Discontinuation of Study Due to Any Reason [units: Participants]	4	4	2

4. Primary Outcome Measure:

Measure Title	Compliance With Study Drug
Measure Description	[(number of doses dispensed-number of doses returned)/number of days between visits]*100
Time Frame	24 weeks (randomisation visit to last treatment visit) according to protocol
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	41	39	0
Compliance With Study Drug	96.95 (16.503)	99.82 (11.383)	

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
[units: Percentage] Mean (Standard Deviation)			

5. Primary Outcome Measure:

Measure Title	Compliance With Study Visits/Assessments
Measure Description	(number of visits attended acroos the time of study divided by the number of expected visits according to the time of entry into study)*100
Time Frame	28 weeks (randomisation visit to last follow up visit) according to protocol
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	41	42	45
Compliance With Study Visits/Assessments [units: Percentage] Mean (Standard Deviation)	93.3 (15.01)	95.6 (10.45)	97.5 (6.8)

6. Secondary Outcome Measure:

Measure Title	Bleeding Events
Measure Description	Number of patients with a bleeding event while on study drug. Patients with multiple bleeding events are counted once

Time Frame	24 weeks (randomisation visit to last treatment visit) according to protocol. For patients who discontinued treatment the time frame was <24 weeks. Mean number of weeks was 7 weeks (baseline to end of treatment visit)
Safety Issue?	Yes

Analysis Population Description

41 + 42 + 45 participants were randomized into the study to treatment arm 1, arm 2 and arm 3 respectively. However, one of the participants randomized to arm 2 was treated according to treatment arm 3

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	41	41	46
Bleeding Events [units: Participants]	0	5	2

7. Secondary Outcome Measure:

Measure Title	Change in Creatinine Level
Measure Description	Individual change in Creatinine level (umil/L) from baseline to week 4 visit for patients while on study drug (week 4 visit-baseline)
Time Frame	4 weeks according to protocol (randomisation visit to week 4 visit)
Safety Issue?	Yes

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg

	Description
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	37	40	45
Change in Creatinine Level [units: umol/L] Mean (Standard Deviation)	6.2 (8.64)	3.6 (13.21)	2.6 (12.90)

8. Secondary Outcome Measure:

Measure Title	Alanine Aminotransferase (ALAT)
Measure Description	Number of patients while on study drug with Alanine aminotransferase (ALAT)>=3 times upper limit of normal.
Time Frame	24 weeks (randomisation visit to last treatment visit) according to protocol. For patients who discontinued treatment the time frame was <24 weeks. Mean number of weeks was 7 weeks (baseline to end of treatment visit)
Safety Issue?	Yes

Analysis Population Description

41 + 42 + 45 participants were randomized into the study to treatment arm 1, arm 2 and arm 3 respectively. However, one of the participants randomized to arm 2 was treated according to treatment arm 3

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	41	41	46
Alanine Aminotransferase (ALAT) [units: Participants]	0	0	1

9. Secondary Outcome Measure:

Measure Title	Bilirubin
Measure Description	Number of patients while on study drug with Bilirubin>=2 times upper limit of normal.
Time Frame	24 weeks (randomisation visit to last treatment visit) according to protocol. For patients who discontinued treatment the time frame was <24 weeks. Mean number of weeks was 7 weeks (baseline to end of treatment visit)
Safety Issue?	Yes

Analysis Population Description

41 + 42 + 45 participants were randomized into the study to treatment arm 1, arm 2 and arm 3 respectively. However, one of the participants randomized to arm 2 was treated according to treatment arm 3

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	41	41	46
Bilirubin [units: Participants]	1	0	0

10. Secondary Outcome Measure:

Measure Title	Plasma Concentration of AZD0837 (Prodrug)
Measure Description	Assessment of plasma concentration of AZD0837 (prodrug) made on the week 4 visit
Time Frame	4 weeks after baseline according to protocol
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	24	26	0
Plasma Concentration of AZD0837 (Prodrug) [units: nmol/L] Median (Full Range)	596.0 (5.0 to 2920.0)	636.0 (18.2 to 5920.0)	

11. Secondary Outcome Measure:

Measure Title	Plasma Concentration of AR-H067637XX (Active Metabolite)
Measure Description	Assessment of plasma concentration of AR-H067637XX (active metabolite) made on the week 4 visit
Time Frame	4 weeks after baseline according to protocol
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	24	26	0
Plasma Concentration of AR-H067637XX (Active Metabolite) [units: nmol/L] Median (Full Range)	258.5 (5.0 to 539.0)	368.5 (159.0 to 776.0)	

12. Secondary Outcome Measure:

Measure Title	Change in D-Dimer Level
Measure Description	Individual change in D-Dimer level (ng/ml) from baseline to week 4 visit for patients while on study drug (week 4 visit-baseline)
Time Frame	4 weeks according to protocol.(baseline to week 4 visit)
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	38	38	43
Change in D-Dimer Level [units: ng/ml] Median (Full Range)	-33.484 (-78.37 to 288.13)	-41.445 (-92.61 to 130.00)	4.853 (-80.12 to 793.56)

13. Secondary Outcome Measure:

Measure Title	Activated Partial Thromboplastin Time (APTT)
Measure Description	Individual change in Activated partial thromboplastin time (APTT) (sec) from baseline to week 4 visit for patients while on study drug (week 4 visit-baseline)
Time Frame	4 weeks according to protocol.(baseline to week 4 visit)
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	25	20	0
Activated Partial Thromboplastin Time (APTT) [units: sec] Median (Full Range)	31.74 (-17.8 to 105.8)	51.51 (3.1 to 75.1)	

14. Secondary Outcome Measure:

Measure Title	Ecarin Clotting Time (ECT)
Measure Description	Individual change in Ecarin clotting time (ECT) (sec) from baseline to week 4 visit for patients while on study drug (week 4 visit-baseline)
Time Frame	4 weeks according to protocol.(baseline to week 4 visit)
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Measured Values

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
Number of Participants Analyzed	24	18	0
Ecarin Clotting Time (ECT) [units: sec] Median (Full Range)	125.6 (6 to 274)	179.1 (7 to 341)	

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	41 + 42 + 45 participants were randomized into the study to treatment arm 1, arm 2 and arm 3 respectively. However, one of the participants randomized to arm 2 was treated according to treatment arm 3

Reporting Groups

	Description
AZD0837 150 mg	AZD0837 150 mg
AZD0837 300 mg	AZD0837 300 mg
Standard Therapy	Standard Therapy

Serious Adverse Events

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	2/41 (4.88%)	3/41 (7.32%)	2/46 (4.35%)
Cardiac disorders			
Cardiac Failure [A] †	0/41 (0%)	1/41 (2.44%)	0/46 (0%)

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Gastrointestinal disorders			
Gastrointestinal Disorder [A] †	0/41 (0%)	0/41 (0%)	1/46 (2.17%)
General disorders			
Drug Intolerance [A] †	0/41 (0%)	1/41 (2.44%)	0/46 (0%)
Metabolism and nutrition disorders			
Podagra [A] †	0/41 (0%)	0/41 (0%)	1/46 (2.17%)
Renal and urinary disorders			
Renal Failure [A] †	1/41 (2.44%)	0/41 (0%)	0/46 (0%)
Vascular disorders			
Deep Vein Thrombosis [A] †	0/41 (0%)	1/41 (2.44%)	0/46 (0%)
Hypotension [A] †	1/41 (2.44%)	0/41 (0%)	0/46 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 10.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	AZD0837 150 mg	AZD0837 300 mg	Standard Therapy
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	3/41 (7.32%)	1/41 (2.44%)	1/46 (2.17%)
Infections and infestations			
Bronchitis [A] †	3/41 (7.32%)	1/41 (2.44%)	1/46 (2.17%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 10.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Results Point of Contact:

Name/Official Title: Gerard Lynch
Organization: AstraZeneca
Phone: +44 1509 645895
Email: aztrial_results_posting@astrazeneca.com