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

ClinicalTrials.gov ID: NCT00645853

Study Identification

Unique Protocol ID:	D1250C00042
Brief Title:	Long-term Safety in Atrial Fibrillation Patients
Official Title:	Long-term Treatment With the Oral Direct Thrombin Inhibitor AZD0837, Compared to Vitamin-K Antagonists, as Stroke Prevention in Patients With Non-valvular Atrial Fibrillation and One or More Risk Factors for Stroke and Systemic Embolic Events. A 5-year Follow-up Study
Secondary IDs:	

Study Status

Record Verification:	March 2012
Overall Status:	Completed
Study Start:	October 2007
Primary Completion:	May 2009 [Actual]
Study Completion:	May 2009 [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: 89, 05 June 2007 Board Name: National Ethic Committee Board Affiliation: The Federal Board for Drug Quality Control Phone: 47-495-625-4386 Email:
Data Monitoring?:	Yes
Plan to Share Data?:	
Oversight Authorities:	Denmark: Danish Medicines Agency Norway: Norwegian Medicines Agency Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products Russia: Ministry of Health of the Russian Federation Sweden: Medical Products Agency Austria: Agency for Health and Food Safety Hungary: National Institute of Pharmacy

Study Description

Brief Summary:	The purpose of this study is to provide safety and tolerability data for AZD0837 during long-term treatment (5 years) in patients with non-valvular atrial fibrillation (AF) and one or more additional risk factors for stroke and systemic embolic events (moderate to high risk patients).
Detailed Description:	

Conditions

Conditions:	Persistent or Permanent Nonvalvular Atrial Fibrillation
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Prevention
Study Phase:	Phase 2

Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Non-Randomized
Endpoint Classification:	Safety Study
Enrollment:	523 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1	Drug: AZD0837 Treatment with AZD0837 starting with 4 different doses, 150 mg od, 300 mg od, 200 mg bid or 450 mg od and then switching to one general common dose, 300 mg od
Active Comparator: 2	Drug: VKA INR 2-3 Vitamin K antagonists (VKA), titrated to an international normalised ratio (INR) of 2.0 to 3.0 with a target value of 2.5 Other Names: • warfarin

Outcome Measures

[See Results Section.]

Eligibility

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

- Patients with paroxysmal, persistent or permanent Non Valvular Atrial Fibrillation with one or more additional risk factors for stroke and systemic embolic event
- completing treatment with study drug in D1250C00008.

Exclusion Criteria:

- Atrial Fibrillation secondary to reversible disorders, eg hyperthyroidism
- Presence of a valvular heart disease, mechanical heart valves, active endocarditis, left ventricular aneurysm or thrombus, atrial myxoma or any condition other than Atrial Fibrillation requiring chronic anticoagulation treatment
- Myocardial infarction, heart surgery or percutaneous coronary intervention (PCI) within the previous three months prior to inclusion; Stroke and/or systemic embolism within the previous 30 days prior to inclusion
- Conditions associated with increased risk of major bleeding.

Contacts/Locations

Study Officials: Lars Hvilstedt Rasmussen, MD, PhD, FESC
Study Principal Investigator
Head of Cardiology at Heart Centre Aalborg Aarhus University Hospital DK 9100 Aalborg Denmark

Locations:

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 25 October 2007 to 20 May 2008 at medical clinics in Europe.
Pre-Assignment Details	All participants had previously participated in the Prevention of Stroke and Systemic Embolic Events in Patients With Atrial Fibrillation (NCT00684307) study

Reporting Groups

	Description
AZD0837	Treatment with AZD0837 starting with 4 different doses, 150 mg od, 300 mg od, 200 mg bid or 450 mg od, then switching to one general common dose, 300 mg od.

	Description
VKA, INR 2-3	Vitamin K antagonists (VKA), titrated to an international normalised ratio (INR) of 2.0 to 3.0 with a target value of 2.5

Overall Study

	AZD0837	VKA, INR 2-3
Started	288	235
No of Patients After Dose Switch	209 [1]	188 [2]
Discontinued Patient No Due to Closure	196 [3]	178 [3]
AZ Study Closure in Hungary	60	40
Completed	196	178
Not Completed	92	57
Adverse Event	18	7
AZ study closure in Hungary	60	40
Withdrawal by Subject	5	2
Protocol Violation	0	2
Discontinuation criteria	2	2
recall of ICF, planned operation, death	7	4

[1] All patients in the AZD0837 arm switched from their initial doses, to a general dose of 300 mg od
[2] No changes for VKA patients
[3] No of patients discontinued due the study termination caused tablet formulation stability problems

Baseline Characteristics

Reporting Groups

	Description
AZD0837	Treatment with AZD0837 starting with 4 different doses, 150 mg od, 300 mg od, 200 mg bid or 450 mg od, then switching to one general common dose, 300 mg od.
VKA, INR 2-3	Vitamin K antagonists (VKA), titrated to an international normalised ratio (INR) of 2.0 to 3.0 with a target value of 2.5

Baseline Measures

	AZD0837	VKA, INR 2-3	Total
Number of Participants	288	235	523
Age, Continuous [units: Years] Mean (Full Range)	69.9 (34 to 93)	68.0 (33 to 86)	68.95 (33 to 93)
Gender, Male/Female [units: Participants]			
Female	90	73	163
Male	198	162	360

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Bleeding: Number of Patients With Any Bleeding Event, During Treatment Period
Measure Description	Participants
Time Frame	154-711 days on treatment
Safety Issue?	Yes

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD0837	Treatment with AZD0837 starting with 4 different doses, 150 mg od, 300 mg od, 200 mg bid or 450 mg od, then switching to one general common dose, 300 mg od.
VKA, INR 2-3	Vitamin K antagonists (VKA), titrated to an international normalised ratio (INR) of 2.0 to 3.0 with a target value of 2.5

Measured Values

	AZD0837	VKA, INR 2-3
Number of Participants Analyzed	288	235
Bleeding: Number of Patients With Any Bleeding Event, During Treatment Period [units: Participants]	55	56

2. Secondary Outcome Measure:

Measure Title	Alanine Transaminase (ALAT): Number of Patients With ALAT>=3xULN, Post Baseline
Measure Description	ULN=Upper limit of Normal
Time Frame	From baseline to Follow up
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD0837	Treatment with AZD0837 starting with 4 different doses, 150 mg od, 300 mg od, 200 mg bid or 450 mg od, then switching to one general common dose, 300 mg od.
VKA, INR 2-3	Vitamin K antagonists (VKA), titrated to an international normalised ratio (INR) of 2.0 to 3.0 with a target value of 2.5

Measured Values

	AZD0837	VKA, INR 2-3
Number of Participants Analyzed	288	235
Alanine Transaminase (ALAT): Number of Patients With ALAT>=3xULN, Post Baseline [units: Participants]	9	6

3. Secondary Outcome Measure:

Measure Title	Bilirubin: Number of Patients With Bilirubin>=2xULN, Post Baseline
Measure Description	
Time Frame	From baseline to Follow up
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD0837	Treatment with AZD0837 starting with 4 different doses, 150 mg od, 300 mg od, 200 mg bid or 450 mg od, then switching to one general common dose, 300 mg od.
VKA, INR 2-3	Vitamin K antagonists (VKA), titrated to an international normalised ratio (INR) of 2.0 to 3.0 with a target value of 2.5

Measured Values

	AZD0837	VKA, INR 2-3
Number of Participants Analyzed	288	235
Bilirubin: Number of Patients With Bilirubin>=2xULN, Post Baseline [units: Participants]	3	3

4. Secondary Outcome Measure:

Measure Title	Creatinine: Absolute Change From Baseline, at End of Treatment
Measure Description	
Time Frame	Baseline and End of treatment
Safety Issue?	Yes

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD0837	Treatment with AZD0837 starting with 4 different doses, 150 mg od, 300 mg od, 200 mg bid or 450 mg od, then switching to one general common dose, 300 mg od.
VKA, INR 2-3	Vitamin K antagonists (VKA), titrated to an international normalised ratio (INR) of 2.0 to 3.0 with a target value of 2.5

Measured Values

	AZD0837	VKA, INR 2-3
Number of Participants Analyzed	288	235

	AZD0837	VKA, INR 2-3
Creatinine: Absolute Change From Baseline, at End of Treatment [units: µmol/L] Mean (Full Range)	3.70 (-67.0 to 120.0)	-1.17 (-56.0 to 116)

5. Secondary Outcome Measure:

Measure Title	D-dimer:Median and Quartile Range at End of Treatment
Measure Description	Median (Lower Quartile-Upper Quartile), ng/mL
Time Frame	End of treatment
Safety Issue?	Yes

Analysis Population Description

Only patients who switched to one common dose, 300 mg od, are included in the AZD0837 analysis

Reporting Groups

	Description
AZD0837	Treatment with AZD0837 starting with 4 different doses, 150 mg od, 300 mg od, 200 mg bid or 450 mg od, then switching to one general common dose, 300 mg od.
VKA, INR 2-3	Vitamin K antagonists (VKA), titrated to an international normalised ratio (INR) of 2.0 to 3.0 with a target value of 2.5

Measured Values

	AZD0837	VKA, INR 2-3
Number of Participants Analyzed	193	232
D-dimer:Median and Quartile Range at End of Treatment [units: ng/mL] Median (Inter-Quartile Range)	68.9 (43.3 to 128.4)	54.9 (31.9 to 99.0)

6. Secondary Outcome Measure:

Measure Title	Activated Partial Thromboplastin Time (APTT): Absolute Change From Baseline to End of Treatment

Measure Description	Median Full range, Seconds
Time Frame	Baseline and End of treatment
Safety Issue?	Yes

Analysis Population Description

Only patients who switched to one common dose, 300 mg od, are included in the AZD0837 analysis

Reporting Groups

	Description
AZD0837	Treatment with AZD0837 starting with 4 different doses, 150 mg od, 300 mg od, 200 mg bid or 450 mg od, then switching to one general common dose, 300 mg od.

Measured Values

	AZD0837
Number of Participants Analyzed	173
Activated Partial Thromboplastin Time (APTT): Absolute Change From Baseline to End of Treatment [units: sec] Median (Full Range)	12.9 (-62 to 43)

7. Secondary Outcome Measure:

Measure Title	Electroconvulsive Therapy (ECT): Absolute Change From Baseline to End of Treatment
Measure Description	
Time Frame	Baseline and End of Treatment
Safety Issue?	Yes

Analysis Population Description

Only patients who switched to one dose, 300 mg od, are included in the AZD0837 analysis

Reporting Groups

	Description
AZD0837	Treatment with AZD0837 starting with 4 different doses, 150 mg od, 300 mg od, 200 mg bid or 450 mg od, then switching to one general common dose, 300 mg od.

Measured Values

	AZD0837
Number of Participants Analyzed	129
Electroconvulsive Therapy (ECT): Absolute Change From Baseline to End of Treatment [units: sec] Median (Full Range)	49.0 (-5 to 96)

8. Secondary Outcome Measure:

Measure Title	AZD0837: Plasma Concentration of AZD0837 at End of Treatment
Measure Description	
Time Frame	End of treatment
Safety Issue?	No

Analysis Population Description

Only patients who switched to one dose, 300 mg od, are included in the AZD0837 analysis

Reporting Groups

	Description
AZD0837	Treatment with AZD0837 starting with 4 different doses, 150 mg od, 300 mg od, 200 mg bid or 450 mg od, then switching to one general common dose, 300 mg od.

Measured Values

	AZD0837
Number of Participants Analyzed	195
AZD0837: Plasma Concentration of AZD0837 at End of Treatment [units: nmol/L] Median (Full Range)	675 (10 to 4090)

9. Secondary Outcome Measure:

Measure Title	AR-H067637XX, the Active Major Metabolite of AD0837: Plasma Concentration of AR-H067637XX, at End of Treatment

Measure Description	
Time Frame	154-711 days on treatment
Safety Issue?	No

Analysis Population Description

Only patients who switched to one dose, 300 mg od, are included in the AZD0837 analysis

Reporting Groups

	Description
AZD0837	Treatment with AZD0837 starting with 4 different doses, 150 mg od, 300 mg od, 200 mg bid or 450 mg od, then switching to one general common dose, 300 mg od.

Measured Values

	AZD0837
Number of Participants Analyzed	195
AR-H067637XX, the Active Major Metabolite of AD0837: Plasma Concentration of AR-H067637XX, at End of Treatment [units: nmol/L] Median (Full Range)	341 (10 to 929)

Reported Adverse Events

Time Frame	154-711 days on treatment
Additional Description	[Not specified]

Reporting Groups

	Description
AZD0837	Treatment with AZD0837 starting with 4 different doses, 150 mg od, 300 mg od, 200 mg bid or 450 mg od and then switching to one general common dose, 300 mg od
VKA INR 2-3	Vitamin K antagonists (VKA), titrated to an international normalised ratio (INR) of 2.0 to 3.0 with a target value of 2.5

Serious Adverse Events

	AZD0837	VKA INR 2-3
	Affected/At Risk (%)	Affected/At Risk (%)
Total	73/288 (25.35%)	61/235 (25.96%)
Blood and lymphatic system disorders		
Neutropenia [A] †	1/288 (0.35%)	0/235 (0%)
Cardiac disorders		
Acute Coronary Syndrome [A] †	0/288 (0%)	1/235 (0.43%)
Angina Pectoris [A] †	2/288 (0.69%)	1/235 (0.43%)
Angina Unstable [A] †	0/288 (0%)	3/235 (1.28%)
Atrial Fibrillation [A] †	4/288 (1.39%)	4/235 (1.7%)
Atrial Flutter [A] †	0/288 (0%)	1/235 (0.43%)
Bradyarrhythmia [A] †	0/288 (0%)	1/235 (0.43%)
Bradycardia [A] †	3/288 (1.04%)	2/235 (0.85%)
Cardiac Failure [A] †	7/288 (2.43%)	6/235 (2.55%)
Cardiac Failure Congestive [A] †	1/288 (0.35%)	0/235 (0%)
Chordae Tendinae Rupture [A] †	0/288 (0%)	1/235 (0.43%)
Coronary Artery Stenosis [A] †	1/288 (0.35%)	0/235 (0%)
Heart Valve Incompetence [A] †	1/288 (0.35%)	0/235 (0%)
Myocardial Ischaemia [A] †	0/288 (0%)	1/235 (0.43%)
Palpitations [A] †	0/288 (0%)	1/235 (0.43%)
Sick Sinus Syndrome [A] †	2/288 (0.69%)	1/235 (0.43%)
Tachyarrhythmia [A] †	0/288 (0%)	1/235 (0.43%)
Tachycardia [A] †	1/288 (0.35%)	1/235 (0.43%)
Ventricular Tachycardia [A] †	0/288 (0%)	1/235 (0.43%)

	AZD0837	VKA INR 2-3
	Affected/At Risk (%)	Affected/At Risk (%)
Endocrine disorders		
Hyperthyroidism [A] †	1/288 (0.35%)	0/235 (0%)
Eye disorders		
Cataract [A] †	1/288 (0.35%)	2/235 (0.85%)
Eye Haemorrhage [A] †	0/288 (0%)	1/235 (0.43%)
Glaucoma [A] †	0/288 (0%)	1/235 (0.43%)
Retinal Artery Embolism [A] †	1/288 (0.35%)	0/235 (0%)
Gastrointestinal disorders		
Abdominal Hernia [A] †	1/288 (0.35%)	0/235 (0%)
Abdominal Pain [A] †	0/288 (0%)	1/235 (0.43%)
Abdominal Pain Lower [A] †	0/288 (0%)	1/235 (0.43%)
Anal Haemorrhage [A] †	1/288 (0.35%)	0/235 (0%)
Anal Ulcer [A] †	0/288 (0%)	1/235 (0.43%)
Diarrhoea [A] †	0/288 (0%)	1/235 (0.43%)
Gastric Ulcer [A] †	0/288 (0%)	2/235 (0.85%)
Gastritis [A] †	0/288 (0%)	1/235 (0.43%)
Gastrointestinal Haemorrhage [A] †	0/288 (0%)	3/235 (1.28%)
Haematemesis [A] †	0/288 (0%)	1/235 (0.43%)
Inguinal Hernia [A] †	1/288 (0.35%)	1/235 (0.43%)
Melaena [A] †	0/288 (0%)	1/235 (0.43%)
Nausea [A] †	1/288 (0.35%)	0/235 (0%)
Periodontal Disease [A] †	0/288 (0%)	1/235 (0.43%)
General disorders		

	AZD0837	VKA INR 2-3
	Affected/At Risk (%)	Affected/At Risk (%)
Asthenia [A] †	1/288 (0.35%)	0/235 (0%)
Death [A] †	2/288 (0.69%)	0/235 (0%)
Non-Cardiac Chest Pain [A] †	0/288 (0%)	2/235 (0.85%)
Hepatobiliary disorders		
Cholecystitis Chronic [A] †	0/288 (0%)	1/235 (0.43%)
Cholelithiasis [A] †	0/288 (0%)	1/235 (0.43%)
Jaundice Cholestatic [A] †	0/288 (0%)	1/235 (0.43%)
Immune system disorders		
Corneal Graft Rejection [A] †	0/288 (0%)	1/235 (0.43%)
Infections and infestations		
Abscess Limb [A] †	1/288 (0.35%)	0/235 (0%)
Bronchitis [A] †	2/288 (0.69%)	3/235 (1.28%)
Endocarditis [A] †	0/288 (0%)	1/235 (0.43%)
Erysipelas [A] †	3/288 (1.04%)	1/235 (0.43%)
Gastroenteritis [A] †	1/288 (0.35%)	1/235 (0.43%)
Intervertebral Discitis [A] †	0/288 (0%)	1/235 (0.43%)
Laryngitis [A] †	1/288 (0.35%)	0/235 (0%)
Pneumonia [A] †	3/288 (1.04%)	3/235 (1.28%)
Pyelonephritis [A] †	1/288 (0.35%)	0/235 (0%)
Respiratory Tract Infection [A] †	1/288 (0.35%)	0/235 (0%)
Sinusitis [A] †	1/288 (0.35%)	0/235 (0%)
Urinary Tract Infection [A] †	0/288 (0%)	1/235 (0.43%)

	AZD0837	VKA INR 2-3
	Affected/At Risk (%)	Affected/At Risk (%)
Urosepsis [A] †	0/288 (0%)	1/235 (0.43%)
Injury, poisoning and procedural complications		
Concussion [A] †	0/288 (0%)	1/235 (0.43%)
Contusion [A] †	0/288 (0%)	1/235 (0.43%)
Foreign Body Trauma [A] †	0/288 (0%)	1/235 (0.43%)
Head Injury [A] †	0/288 (0%)	1/235 (0.43%)
Joint Dislocation [A] †	1/288 (0.35%)	0/235 (0%)
Post Procedural Haemorrhage [A] †	0/288 (0%)	1/235 (0.43%)
Subdural Haematoma [A] †	0/288 (0%)	1/235 (0.43%)
Tibia Fracture [A] †	1/288 (0.35%)	0/235 (0%)
Investigations		
Alanine Aminotransferase Increased [A] †	2/288 (0.69%)	1/235 (0.43%)
Blood Alkaline Phosphatase Increased [A] †	0/288 (0%)	1/235 (0.43%)
Blood Glucose Increased [A] †	0/288 (0%)	1/235 (0.43%)
Haemoglobin Decreased [A] †	1/288 (0.35%)	2/235 (0.85%)
International Normalised Ratio Increased [A] †	0/288 (0%)	1/235 (0.43%)
Metabolism and nutrition disorders		
Dehydration [A] †	1/288 (0.35%)	1/235 (0.43%)
Diabetes Mellitus [A] †	2/288 (0.69%)	1/235 (0.43%)
Hyperkalaemia [A] †	1/288 (0.35%)	0/235 (0%)
Hypoglycaemia [A] †	1/288 (0.35%)	0/235 (0%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	1/288 (0.35%)	0/235 (0%)

	AZD0837	VKA INR 2-3
	Affected/At Risk (%)	Affected/At Risk (%)
Arthritis [A] †	0/288 (0%)	2/235 (0.85%)
Back Pain [A] †	1/288 (0.35%)	1/235 (0.43%)
Bursitis [A] †	1/288 (0.35%)	0/235 (0%)
Inguinal Mass [A] †	0/288 (0%)	1/235 (0.43%)
Muscle Atrophy [A] †	0/288 (0%)	1/235 (0.43%)
Muscular Weakness [A] †	1/288 (0.35%)	0/235 (0%)
Myalgia [A] †	0/288 (0%)	1/235 (0.43%)
Osteitis [A] †	1/288 (0.35%)	0/235 (0%)
Osteoarthritis [A] †	2/288 (0.69%)	0/235 (0%)
Rheumatoid Arthritis [A] †	0/288 (0%)	1/235 (0.43%)
Scleroderma [A] †	1/288 (0.35%)	0/235 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Basal Cell Carcinoma [A] †	1/288 (0.35%)	0/235 (0%)
Colon Adenoma [A] †	0/288 (0%)	1/235 (0.43%)
Colon Cancer [A] †	3/288 (1.04%)	0/235 (0%)
Colon Cancer Metastatic [A] †	0/288 (0%)	1/235 (0.43%)
Metastases To Central Nervous System [A] †	1/288 (0.35%)	0/235 (0%)
Nervous system disorders		
Cerebral Artery Embolism [A] †	0/288 (0%)	1/235 (0.43%)
Cerebrovascular Accident [A] †	1/288 (0.35%)	1/235 (0.43%)
Dizziness [A] †	1/288 (0.35%)	1/235 (0.43%)
Encephalitis [A] †	1/288 (0.35%)	0/235 (0%)

	AZD0837	VKA INR 2-3
	Affected/At Risk (%)	Affected/At Risk (%)
Epilepsy [A] †	1/288 (0.35%)	0/235 (0%)
Headache [A] †	0/288 (0%)	2/235 (0.85%)
Ischaemic Stroke [A] †	1/288 (0.35%)	0/235 (0%)
Status Epilepticus [A] †	1/288 (0.35%)	0/235 (0%)
Syncope [A] †	3/288 (1.04%)	1/235 (0.43%)
Transient Ischaemic Attack [A] †	1/288 (0.35%)	2/235 (0.85%)
Vascular Encephalopathy [A] †	1/288 (0.35%)	0/235 (0%)
Vertebrobasilar Insufficiency [A] †	1/288 (0.35%)	0/235 (0%)
Psychiatric disorders		
Delusional Disorder, Persecutory Type [A] †	1/288 (0.35%)	0/235 (0%)
Dysthymic Disorder [A] †	1/288 (0.35%)	0/235 (0%)
Renal and urinary disorders		
Dysuria [A] †	1/288 (0.35%)	0/235 (0%)
Haematuria [A] †	2/288 (0.69%)	1/235 (0.43%)
Renal Failure [A] †	1/288 (0.35%)	0/235 (0%)
Urinary Bladder Haemorrhage [A] †	0/288 (0%)	1/235 (0.43%)
Reproductive system and breast disorders		
Postmenopausal Haemorrhage [A] †	1/288 (0.35%)	0/235 (0%)
Respiratory, thoracic and mediastinal disorders		
Dyspnoea [A] †	2/288 (0.69%)	1/235 (0.43%)
Dyspnoea Exertional [A] †	1/288 (0.35%)	0/235 (0%)
Haemoptysis [A] †	0/288 (0%)	1/235 (0.43%)
Pleural Effusion [A] †	1/288 (0.35%)	1/235 (0.43%)

	AZD0837	VKA INR 2-3
	Affected/At Risk (%)	Affected/At Risk (%)
Skin and subcutaneous tissue disorders		
Rash [A] †	0/288 (0%)	1/235 (0.43%)
Vascular disorders		
800003Varicose Vein [A] †	1/288 (0.35%)	0/235 (0%)
Arterial Occlusive Disease [A] †	1/288 (0.35%)	0/235 (0%)
Arterial Stenosis Limb [A] †	1/288 (0.35%)	0/235 (0%)
Hypertension [A] †	1/288 (0.35%)	0/235 (0%)
Orthostatic Hypotension [A] †	1/288 (0.35%)	0/235 (0%)
Peripheral Artery Aneurysm [A] †	1/288 (0.35%)	0/235 (0%)
Peripheral Embolism [A] †	1/288 (0.35%)	0/235 (0%)
Subclavian Vein Thrombosis [A] †	1/288 (0.35%)	0/235 (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	VKA INR 2-3
	Affected/At Risk (%)	Affected/At Risk (%)
Total	125/288 (43.4%)	106/235 (45.11%)
Gastrointestinal disorders		
Diarrhoea [A] †	37/288 (12.85%)	18/235 (7.66%)
Flatulence [A] †	20/288 (6.94%)	1/235 (0.43%)
General disorders		
Fatigue [A] †	19/288 (6.6%)	9/235 (3.83%)
Oedema Peripheral [A] †	25/288 (8.68%)	20/235 (8.51%)

	AZD0837	VKA INR 2-3
	Affected/At Risk (%)	Affected/At Risk (%)
Infections and infestations		
Bronchitis [A] †	14/288 (4.86%)	18/235 (7.66%)
Nasopharyngitis [A] †	35/288 (12.15%)	30/235 (12.77%)
Urinary Tract Infection [A] †	13/288 (4.51%)	15/235 (6.38%)
Injury, poisoning and procedural complications		
Fall [A] †	4/288 (1.39%)	12/235 (5.11%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	9/288 (3.12%)	13/235 (5.53%)
Back Pain [A] †	15/288 (5.21%)	12/235 (5.11%)
Nervous system disorders		
Dizziness [A] †	24/288 (8.33%)	17/235 (7.23%)

† 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.

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