ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 11/22/2012

ClinicalTrials.gov ID: NCT01396226

Study Identification

Unique Protocol ID:	D4120C00002
Brief Title:	A Multi-centre Study Comparing the Effects of AZD2927 and Placebo on the Electrical Activity in the Heart in Patients
Official Title:	A Multi-Centre, Double-Blind, Randomised, Placebo-Controlled Phase II Study to Assess the Effects on Atrial and Ventricular Refractoriness of an Intravenous Infusion of AZD2927 in Patients Undergoing an Invasive Electrophysiological Procedure
Secondary IDs:	2011-001716-59 [EudraCT Number]

Study Status

Record Verification:	November 2012
Overall Status:	Completed
Study Start:	September 2011
Primary Completion:	January 2012 [Actual]
Study Completion:	January 2012 [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: 2011/272-31 Board Name: Regionala etikprövningsnämnden I Linköping Board Affiliation: c/o Hälsouniversitetets kansli Phone: +46 (0)10 103 70 30 Email: registrator@linkoping.epn.se
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Norway: Norwegian Medicines Agency Sweden: Medical Products Agency

Study Description

Brief Summary:	Medical Products Agency
Detailed Description:	• A Multi-Centre, Double-Blind, Randomised, Placebo-Controlled Phase II Study to Assess the Effects on Atrial and Ventricular Refractoriness of an Intravenous Infusion of AZD2927 in Patients Undergoing an Invasive Electrophysiological Procedure. • The study has an adaptive design. In the 1st dose group the planned number of randomised patients is 24. The tentative number of randomised patients in the optional 2nd dose group is 12, 24 or 36 and thus a total maximum of 60 patients will be randomised in the study.

Conditions

Conditions:	Arrhythmia
Keywords:	Atrial refractoriness cardiac electrophysiology IKACh

Study Design

Study Type:	Interventional
Primary Purpose:	Basic Science
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment

Number of Arms: 2

Masking: Double Blind (Subject, Investigator)

Allocation: Randomized

Endpoint Classification: Safety Study

Enrollment: 20 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1 A single dose of AZD2927 administered as an iv infusion	Drug: AZD2927 A single dose of AZD2927 administered as an iv infusion
Placebo Comparator: 2 A single dose of placebo administered as an iv infusion	Drug: Placebo A single dose of placebo administered as an iv infusion

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 20 Years

Maximum Age: 80 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- male or postmenopausal female, aged 20 to 80 years inclusive,
- clinical indication for catheter ablation of atrial flutter,
- history of paroxysmal atrial flutter, with or without paroxysmal AF. Single episodes of persistent atrial flutter or AF requiring cardioversion do not exclude the patient from the study,
- sinus rhythm at randomisation,
- adequate anticoagulation or antithrombotic treatment according to ESC guidelines 2010 or national guideline,

Exclusion Criteria:

- cardioversion within 14 days before randomisation,
- history of stroke or transient ischaemic attack (TIA). History of significant head trauma, epilepsy or other disorders increasing the risk for seizures,
- QTcF >450 ms or <350 ms measured in sinus rhythm at randomisation,

- history and/or signs of clinically significant sinus node dysfunction. Sinus bradycardia (50 beats per minute or less) at randomisation,
- personal or family history of Torsades de Pointes (TdP), any other polymorphic ventricular tachycardia, long QT syndrome, short QT syndrome, Brugada syndrome, or personal history of sustained (>30 s) monomorphic ventricular tachycardia.

Contacts/Locations

Study Officials: Stefan C Carlsson, MD, PHD
Study Director
AstraZeneca

Hakan Walfridsson, MD, PHD
Study Principal Investigator
University Hospital Linkoping Sweden

Locations: Sweden
Research Site
Linköping, Sweden

Research Site
Örebro, Sweden

Norway
Research Site
Oslo, Norway

Sweden
Research Site
Stockholm, Sweden

Research Site
Umeå, Sweden

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	The study had enrolled 20 patients. A total of 18 patients were randomised of which 12 patients received AZD2927. All patients who received treatment completed the study.
Pre-Assignment Details	None

Reporting Groups

	Description
AZD2927	AZD2927 solution for infusion
PLACEBO	Placebo solution for infusion

Overall Study

	AZD2927	PLACEBO
Started	12	6
Patients Who Received Treatment	12	6
Patients Who Completed Treatment	12	6
Completed	12	6
Not Completed	0	0

Baseline Characteristics

Reporting Groups

	Description
AZD2927	AZD2927 solution for infusion
PLACEBO	Placebo solution for infusion

Baseline Measures

	AZD2927	PLACEBO	Total
Number of Participants	12	6	18
Age, Continuous [units: Years] Mean (Standard Deviation)	57.9 (7.7)	63.8 (8.3)	59.9 (8.2)

	AZD2927	PLACEBO	Total
Gender, Male/Female [units: Participants]			
Female	1	1	2
Male	11	5	16
Race/Ethnicity, Customized White [units: Participants]	12	6	18

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Left Atrial Effective Refractory Period
Measure Description	Change in LAERP from before IP infusion to 1st and 2nd assessments during IP infusion
Time Frame	Baseline to last assessment during IP infusion
Safety Issue?	No

Analysis Population Description
Full A analysis Set (FAS)

Reporting Groups

	Description
Arm 1 - AZD2927	AZD2927 solution for intravenous (i.v.) infusion
Arm 2 - PLACEBO	Placebo solution for intravenous (i.v.) infusion

Measured Values

	Arm 1 - AZD2927	Arm 2 - PLACEBO
Number of Participants Analyzed	12	6
Left Atrial Effective Refractory Period [units: msec] Mean (Standard Deviation)		
1st Assessment	2.5 (8.9)	5 (23)
2nd Assessment	2.5 (9.7)	10.8 (34.4)

2. Primary Outcome Measure:

Measure Title	Left Atrial Effective Refractory Period
Measure Description	Change in LAERP from before IP infusion to 1st and 2nd assessments during IP infusion
Time Frame	Baseline to last assessment during IP infusion
Safety Issue?	No

Analysis Population Description
Per Protocol (PP)

Reporting Groups

	Description
Arm 1 - AZD2927	AZD2927 solution for intravenous (i.v.) infusion
Arm 2 - PLACEBO	Placebo solution for intravenous (i.v.) infusion

Measured Values

	Arm 1 - AZD2927	Arm 2 - PLACEBO
Number of Participants Analyzed	11	6
Left Atrial Effective Refractory Period [units: msec] Mean (Standard Deviation)		
1st Assessment	2.7 (9.3)	5 (23)
2nd Assessment	2.7 (10.1)	10.8 (34.4)

3. Secondary Outcome Measure:

Measure Title	Ventricular Effective Refractory Period
Measure Description	Change in VERP from before IP infusion to 1st and 2nd assessments during IP infusion
Time Frame	Baseline to last assessment during IP infusion
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Arm 1 - AZD2927	AZD2927 solution for intravenous (i.v.) infusion
Arm 2 - PLACEBO	Placebo solution for intravenous (i.v.) infusion

Measured Values

	Arm 1 - AZD2927	Arm 2 - PLACEBO
Number of Participants Analyzed	12	6
Ventricular Effective Refractory Period [units: msec] Mean (Standard Deviation)	-0.8 (9)	1.7 (7.5)

4. Secondary Outcome Measure:

Measure Title	Paced QT Interval
Measure Description	Change in CS Paced QT interval (P600 MS) from before and after IP infusion during electrophysiological measurements
Time Frame	Baseline to last assessment during IP infusion
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Arm 1 - AZD2927	AZD2927 solution for intravenous (i.v.) infusion
Arm 2 - PLACEBO	Placebo solution for intravenous (i.v.) infusion

Measured Values

	Arm 1 - AZD2927	Arm 2 - PLACEBO
Number of Participants Analyzed	12	6
Paced QT Interval [units: msec] Mean (Standard Deviation)	-0.9 (8.7)	6.3 (8.4)

5. Secondary Outcome Measure:

Measure Title	Atrio-ventricular Effective Refractory Period
Measure Description	Change from observation before IP infusion to during 1st and 2nd LAERP Mean
Time Frame	Baseline to last assessment during IP infusion
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Arm 1 - AZD2927	AZD2927 solution for intravenous (i.v.) infusion
Arm 2 - PLACEBO	Placebo solution for intravenous (i.v.) infusion

Measured Values

	Arm 1 - AZD2927	Arm 2 - PLACEBO
Number of Participants Analyzed	8	6
Atrio-ventricular Effective Refractory Period [units: msec] Mean (Standard Deviation)		
During IP 1st LAERP Mean	-16.9 (18.1)	1.7 (18.1)
During IP 2nd LAERP Mean	-19.4 (17.6)	3.2 (16.5)

6. Secondary Outcome Measure:

Measure Title	PA Interval
Measure Description	Reflects intra-atrial conduction and is defined as the interval from the onset of the P wave in the surface ECG to the onset of atrial activation (A) in the His bundle electrogram. Change from observation before IP infusion to 30 min after IP start
Time Frame	Baseline to last assessment during IP infusion
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Arm 1 - AZD2927	AZD2927 solution for intravenous (i.v.) infusion
Arm 2 - PLACEBO	Placebo solution for intravenous (i.v.) infusion

Measured Values

	Arm 1 - AZD2927	Arm 2 - PLACEBO
Number of Participants Analyzed	12	6
PA Interval [units: msec] Mean (Standard Deviation)	1.7 (12)	9.3 (15.4)

7. Secondary Outcome Measure:

Measure Title	AH Interval
Measure Description	Change from observation before IP infusion to 30 mins after IP start. AH interval- the conduction time from the low right atrium at the inter-atrial septum through the AV node to the His bundle, ie, intra-nodal conduction time.
Time Frame	Baseline to last assessment during IP infusion
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Arm 1 - AZD2927	AZD2927 solution for intravenous (i.v.) infusion
Arm 2 - PLACEBO	Placebo solution for intravenous (i.v.) infusion

Measured Values

	Arm 1 - AZD2927	Arm 2 - PLACEBO
Number of Participants Analyzed	12	6
AH Interval	0 (14.2)	-2.2 (12.1)

	Arm 1 - AZD2927	Arm 2 - PLACEBO
[units: msec] Mean (Standard Deviation)		

8. Secondary Outcome Measure:

Measure Title	HV Interval
Measure Description	Change from observation before IP infusion to 30 mins after IP start. HV interval - represents conduction time from the proximal His bundle to the ventricular myocardium, ie, infra-nodal conduction time.
Time Frame	Baseline to last assessment during IP infusion
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Arm 1 - AZD2927	AZD2927 solution for intravenous (i.v.) infusion
Arm 2 - PLACEBO	Placebo solution for intravenous (i.v.) infusion

Measured Values

	Arm 1 - AZD2927	Arm 2 - PLACEBO
Number of Participants Analyzed	12	6
HV Interval [units: msec] Mean (Standard Deviation)	-3.5 (8.9)	3.5 (4.9)

9. Secondary Outcome Measure:

Measure Title	PR Interval
Measure Description	Interval from the onset of the P-wave to the start of the QRS complex. Change from observation before IP infusion to 6 to 8 hours and 20 to 24 hours after IP infusion
Time Frame	Baseline to last assessment during IP infusion

Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Arm 1 - AZD2927	AZD2927 solution for intravenous (i.v.) infusion
Arm 2 - PLACEBO	Placebo solution for intravenous (i.v.) infusion

Measured Values

	Arm 1 - AZD2927	Arm 2 - PLACEBO
Number of Participants Analyzed	12	6
PR Interval [units: msec] Mean (Standard Deviation)		
06:00-08:00	-5.1 (17.0)	19.3 (17.9)
20:00-24:00	-8.0 (18.6)	4.3 (21.4)

10. Secondary Outcome Measure:

Measure Title	QRS Duration
Measure Description	Change from observation before IP infusion to 6 to 8 hours and 20 to 24 hours after IP infusion
Time Frame	Baseline to last assessment during IP infusion
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Arm 1 - AZD2927	AZD2927 solution for intravenous (i.v.) infusion
Arm 2 - PLACEBO	Placebo solution for intravenous (i.v.) infusion

Measured Values

	Arm 1 - AZD2927	Arm 2 - PLACEBO
Number of Participants Analyzed	12	6
QRS Duration [units: msec] Mean (Standard Deviation)		
06:00-08:00	-1.2 (6.1)	-0.3 (8.5)
20:00-24:00	-2.5 (9.6)	-2.5 (7.3)

11. Secondary Outcome Measure:

Measure Title	RR Interval
Measure Description	Change from observation before IP infusion to 6 to 8 hours and 20 to 24 hours after IP infusion
Time Frame	Baseline to last assessment during IP infusion
Safety Issue?	No

Analysis Population Description

FAS

Reporting Groups

	Description
Arm 1 - AZD2927	AZD2927 solution for intravenous (i.v.) infusion
Arm 2 - PLACEBO	Placebo solution for intravenous (i.v.) infusion

Measured Values

	Arm 1 - AZD2927	Arm 2 - PLACEBO
Number of Participants Analyzed	12	6
RR Interval [units: msec] Mean (Standard Deviation)		
06:00-08:00	21.3 (170.4)	57.2 (74.2)
20:00-24:00	-11.5 (202)	-8.3 (139.9)

12. Secondary Outcome Measure:

Measure Title	Ventricular Effective Refractory Period
Measure Description	Change in VERP from before IP infusion to 1st and 2nd assessments during IP infusion
Time Frame	Baseline to last assessment during IP infusion
Safety Issue?	No

Analysis Population Description
PP

Reporting Groups

	Description
Arm 1 - AZD2927	AZD2927 solution for intravenous (i.v.) infusion
Arm 2 - PLACEBO	Placebo solution for intravenous (i.v.) infusion

Measured Values

	Arm 1 - AZD2927	Arm 2 - PLACEBO
Number of Participants Analyzed	11	6
Ventricular Effective Refractory Period [units: msec] Mean (Standard Deviation)	-0.9 (9.4)	1.7 (7.5)

13. Secondary Outcome Measure:

Measure Title	Paced QT Interval
Measure Description	Change in CS Paced QT interval (P600 MS) from before and after IP infusion during electrophysiological measurements
Time Frame	Baseline to last assessment during IP infusion
Safety Issue?	No

Analysis Population Description
PP

Reporting Groups

	Description
Arm 1 - AZD2927	AZD2927 solution for intravenous (i.v.) infusion
Arm 2 - PLACEBO	Placebo solution for intravenous (i.v.) infusion

Measured Values

	Arm 1 - AZD2927	Arm 2 - PLACEBO
Number of Participants Analyzed	11	6
Paced QT Interval [units: msec] Mean (Standard Deviation)	-1.0 (9.1)	6.3 (8.4)

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
AZD2927	AZD2927 solution for infusion
PLACEBO	Placebo solution for infusion

Serious Adverse Events

	AZD2927	PLACEBO
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/12 (0%)	0/6 (0%)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	AZD2927	PLACEBO
	Affected/At Risk (%)	Affected/At Risk (%)
Total	2/12 (16.67%)	1/6 (16.67%)
Cardiac disorders		
ATRIAL FIBRILLATION [A] †	1/12 (8.33%)	1/6 (16.67%)
Atrial Flutter [A] †	0/12 (0%)	1/6 (16.67%)
Injury, poisoning and procedural complications		
MEDICAL DEVICE COMPLICATION [A] †	1/12 (8.33%)	0/6 (0%)

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA 14.1

Limitations and Caveats

Not applicable

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 more than 60 days but less than or equal to 180 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:

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