ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 08/17/2011

ClinicalTrials.gov ID: NCT00616629

Study Identification

Unique Protocol ID:	D3190C00005
Brief Title:	Cardiac Electrophysiological Study
Official Title:	A Multi-centre, Double-blind, Randomised, Placebo-controlled, Singledose, Phase II Study to Assess the Effects on Atrial and Ventricular Refractoriness and Haemodynamics of an Intravenous Infusion of AZD1305 in Patients Undergoing an Invasive Electrophysiological Procedure
Secondary IDs:	2007-0003455-36 (EudraCT No)

Study Status

Record Verification:	August 2011
Overall Status:	Completed
Study Start:	January 2008
Primary Completion:	June 2008 [Actual]
Study Completion:	June 2008 [Actual]

Sponsor/Collaborators

Sponsor:	AstraZeneca
Responsible Party:	
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: M185-07 Board Name: Regional Ethics Committee in Linköping Board Affiliation: Regional Ethics Committee in Linköping, Sweden Phone: +46 (0)13 227030 Email: anna.alexandersson@linkoping.epn.se
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Sweden: Medical Products Agency Norway: Norwegian Medicines Agency Denmark: Danish Medicines Agency Finland: Finnish Medicines Agency

Study Description

Brief Summary:	The purpose of the study is to measure the effects of AZD1305 on cardiac electrophysiological properties and intracardiac pressures
Detailed Description:	

Conditions

Conditions:	Atrial Flutter
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Double Blind (Subject, Investigator)

Allocation:	Randomized
Endpoint Classification:	Pharmacodynamics Study
Enrollment:	55 [Actual]

Arms and Interventions

Intervention Details:
Drug: AZD1305
Intravenous infusion

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	20 Years
Maximum Age:	80 Years
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- Patients with atrial flutter (with a ventricular rate of <100 beats/minute at enrolment), scheduled for curative catheter ablation
- Sinus rhythm at randomisation

Exclusion Criteria:

- QTc (Fridericia, QTcF) >450 ms measured in sinus rhythm at randomisation,
- Serum potassium below 3.8 or above 5.0 mmol/L or plasma potassium below 3.6 or above 5.0 mmol/L
- QRS duration >120 ms at randomisation

Contacts/Locations

Study Officials: Lauri Toivonen, MD
Study Principal Investigator
Helsinki University Hospital

Locations: Denmark
Research Site

Aalborg, Denmark

Research Site
Arhus, Denmark

Research Site
Hellerup, Denmark

Research Site
København, Denmark

Finland
Research Site
Helsinki, Finland

Research Site
Kuopio, Finland

Research Site
Oulu, Finland

Norway
Research Site
Bergen, Norway

Research Site
Oslo, Norway

Sweden
Research Site
Gŏteborg, Sweden

Research Site
Linkŏping, Sweden

Research Site
Ŏrebro, Sweden

Research Site
Umea, Sweden

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	A total of 68 patients were enrolled into the study. The study randomised 55 patients and 50 of those patients received study drug. All patients who received study drug completed the study.
Pre-Assignment Details	At the pre-entry visit, which took place within 14 days before the planned catheter ablation (Study Day), patients underwent a full clinical assessment including a physical examination, ECG recording, Bood pressure(BP)/heart rate measurement, routine laboratory tests, and transthoracic echocardiography (TTE, if not done within the prior 6 months).

Reporting Groups

	Description
AZD1305 Dose Group 1	Loading dose 15 min at 43.5 mg/h, Maintenance dose maximum 60 additional min at 19.6 mg/h
AZD1305 Dose Group 2	Loading dose 15 min at 130.4 mg/h, Maintenance dose maximum 60 additional min at 58.7 mg/h
AZD1305 Dose Group 3	Loading dose 15 min at 325.9 mg/h, Maintenance dose maximum 60 additional min at 146.6 mg/h
AZD1305 Dose Group 4	Loading dose 15 min at 488.8 mg/h, Maintenance dose maximum 60 additional min at 220.0 mg/h
Placebo	Corresponding placebo

Overall Study

	AZD1305 Dose Group 1	AZD1305 Dose Group 2	AZD1305 Dose Group 3	AZD1305 Dose Group 4	Placebo
Started	13 [1]	14 [1]	14 [2]	2	12
Completed	11	12	13	2	12
Not Completed	2	2	1	0	0
Protocol Violation	1	2	1	0	0
AV-block	1	0	0	0	0

[1] Two patients never received study drug

[2] One patient never received study drug

Baseline Characteristics

Reporting Groups

	Description
AZD1305 Dose Group 1	Loading dose 15 min at 43.5 mg/h, Maintenance dose maximum 60 additional min at 19.6 mg/h
AZD1305 Dose Group 2	Loading dose 15 min at 130.4 mg/h, Maintenance dose maximum 60 additional min at 58.7 mg/h
AZD1305 Dose Group 3	Loading dose 15 min at 325.9 mg/h, Maintenance dose maximum 60 additional min at 146.6 mg/h
AZD1305 Dose Group 4	Loading dose 15 min at 488.8 mg/h, Maintenance dose maximum 60 additional min at 220.0 mg/h
Placebo	Corresponding placebo

Baseline Measures

	AZD1305 Dose Group 1	AZD1305 Dose Group 2	AZD1305 Dose Group 3	AZD1305 Dose Group 4	Placebo	Total
Number of Participants	11	12	13	2	12	50
Age, Continuous Age (years) [units: Years] Mean (Standard Deviation)	60 (14)	62 (6)	60 (8)	50 (23)	62 (6)	56 (14.5)
Gender, Male/Female [units: Participants]						
Female	2	2	2	0	0	6
Male	9	10	11	2	12	44

Outcome Measures

1. Primary Outcome Measure:

Measure Title	LAERP (Left Atrial Effective Refractory Period (ie, the Longest S1-S2 Interval That Fails to Result in Atrial Depolarisation))
Measure Description	Absolute change, after - before infusion
Time Frame	Measurements were obtained twice, from the invasive electrophysiological measurements made before and 20 min (or more) after the start of administration of the investigational product
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD1305 Dose Group 1	Loading dose 15 min at 43.5 mg/h, Maintenance dose maximum 60 additional min at 19.6 mg/h
AZD1305 Dose Group 2	Loading dose 15 min at 130.4 mg/h, Maintenance dose maximum 60 additional min at 58.7 mg/h
AZD1305 Dose Group 3	Loading dose 15 min at 325.9 mg/h, Maintenance dose maximum 60 additional min at 146.6 mg/h
AZD1305 Dose Group 4	Loading dose 15 min at 488.8 mg/h, Maintenance dose maximum 60 additional min at 220.0 mg/h
Placebo	Corresponding placebo

Measured Values

	AZD1305 Dose Group 1	AZD1305 Dose Group 2	AZD1305 Dose Group 3	AZD1305 Dose Group 4	Placebo
Number of Participants Analyzed	11	11	13	2	11
LAERP (Left Atrial Effective Refractory Period (ie, the Longest S1-S2 Interval That Fails to Result in Atrial Depolarisation)) [units: ms] Mean (Full Range)	11 (-15 to 40)	43 (0 to 210)	55 (-5 to 85)	50 (40 to 60)	-10 (-90 to 30)

2. Secondary Outcome Measure:

Measure Title	RAERP (Right Atrial Effective Refractory Period)
Measure Description	Absolute change, after - before infusion
Time Frame	Measurements were obtained twice, from the invasive electrophysiological measurements made before and 20 min (or more) after the start of administration of the investigational product
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD1305 Dose Group 1	Loading dose 15 min at 43.5 mg/h, Maintenance dose maximum 60 additional min at 19.6 mg/h

	Description
AZD1305 Dose Group 2	Loading dose 15 min at 130.4 mg/h, Maintenance dose maximum 60 additional min at 58.7 mg/h
AZD1305 Dose Group 3	Loading dose 15 min at 325.9 mg/h, Maintenance dose maximum 60 additional min at 146.6 mg/h
AZD1305 Dose Group 4	Loading dose 15 min at 488.8 mg/h, Maintenance dose maximum 60 additional min at 220.0 mg/h
Placebo	Corresponding placebo

Measured Values

	AZD1305 Dose Group 1	AZD1305 Dose Group 2	AZD1305 Dose Group 3	AZD1305 Dose Group 4	Placebo
Number of Participants Analyzed	11	12	12	2	11
RAERP (Right Atrial Effective Refractory Period) [units: ms] Mean (Full Range)	19 (-5 to 40)	42 (0 to 75)	84 (-30 to 165)	135 (100 to 170)	-12 (-90 to 40)

3. Secondary Outcome Measure:

Measure Title	VERP (Ventricular Effective Refractory Period)) and Other Electrophysiological and Electrocardiographic Variables; RR, P Wave Duration, PR, QRS, QTend, QTcF, QTtop, QTend - QTtop)
Measure Description	Absolute change, after - before infusion
Time Frame	Measurements were obtained twice, from the invasive electrophysiological measurements made before and 20 min (or more) after the start of administration of the investigational product
Safety Issue?	Yes

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD1305 Dose Group 1	Loading dose 15 min at 43.5 mg/h, Maintenance dose maximum 60 additional min at 19.6 mg/h
AZD1305 Dose Group 2	Loading dose 15 min at 130.4 mg/h, Maintenance dose maximum 60 additional min at 58.7 mg/h
AZD1305 Dose Group 3	Loading dose 15 min at 325.9 mg/h, Maintenance dose maximum 60 additional min at 146.6 mg/h
AZD1305 Dose Group 4	Loading dose 15 min at 488.8 mg/h, Maintenance dose maximum 60 additional min at 220.0 mg/h
Placebo	Corresponding placebo

Measured Values

	AZD1305 Dose Group 1	AZD1305 Dose Group 2	AZD1305 Dose Group 3	AZD1305 Dose Group 4	Placebo
Number of Participants Analyzed	11	12	13	2	11
VERP (Ventricular Effective Refractory Period)) and Other Electrophysiological and Electrocardiographic Variables; RR, P Wave Duration, PR, QRS, QTend, QTcF, QTtop, QTend - QTtop) [units: ms] Mean (Full Range)	11 (-25 to 30)	41 (5 to 145)	59 (25 to 110)	65 (45 to 85)	3 (-25 to 40)

4. Secondary Outcome Measure:

Measure Title	QTcF (Interval From the Beginning of the Q or R Wave to the End of the T Wave in the Surface ECG, Corrected for Changes in RR Interval Using Fridericia' Formula =QT/RR1/3 Interval in Seconds)
Measure Description	Absolute change, after - before infusion
Time Frame	Measurements were obtained twice, from the invasive electrophysiological measurements made before and 20 min (or more) after the start of administration of the investigational product. ECG measurements, including QTcF, are available from several additiona
Safety Issue?	Yes

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD1305 Dose Group 1	Loading dose 15 min at 43.5 mg/h, Maintenance dose maximum 60 additional min at 19.6 mg/h
AZD1305 Dose Group 2	Loading dose 15 min at 130.4 mg/h, Maintenance dose maximum 60 additional min at 58.7 mg/h
AZD1305 Dose Group 3	Loading dose 15 min at 325.9 mg/h, Maintenance dose maximum 60 additional min at 146.6 mg/h
AZD1305 Dose Group 4	Loading dose 15 min at 488.8 mg/h, Maintenance dose maximum 60 additional min at 220.0 mg/h
Placebo	Corresponding placebo

Measured Values

	AZD1305 Dose Group 1	AZD1305 Dose Group 2	AZD1305 Dose Group 3	AZD1305 Dose Group 4	Placebo
Number of Participants Analyzed	11	12	13	2	12
QTcF (Interval From the Beginning of the Q or R Wave to the End of the T Wave in the Surface ECG, Corrected for Changes in RR Interval Using Fridericia' Formula =QT/RR1/3 Interval in Seconds) [units: ms] Mean (Full Range)	20 (-2 to 42)	65 (13 to 150)	79 (31 to 128)	65 (59 to 70)	4 (-51 to 47)

5. Secondary Outcome Measure:

Measure Title	Cmax Observed for AZD1305
Measure Description	A total of 13 scheduled PK samples for each patient during and after infusion
Time Frame	During and after infusion
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD1305 Dose Group 1	Loading dose 15 min at 43.5 mg/h, Maintenance dose maximum 60 additional min at 19.6 mg/h
AZD1305 Dose Group 2	Loading dose 15 min at 130.4 mg/h, Maintenance dose maximum 60 additional min at 58.7 mg/h
AZD1305 Dose Group 3	Loading dose 15 min at 325.9 mg/h, Maintenance dose maximum 60 additional min at 146.6 mg/h
AZD1305 Dose Group 4	Loading dose 15 min at 488.8 mg/h, Maintenance dose maximum 60 additional min at 220.0 mg/h
Placebo	Corresponding placebo

Measured Values

	AZD1305 Dose Group 1	AZD1305 Dose Group 2	AZD1305 Dose Group 3	AZD1305 Dose Group 4	Placebo
Number of Participants Analyzed	11	12	13	2	0
Cmax Observed for AZD1305 [units: umol/L]	0.178 (0.104 to 0.279)	0.692 (0.368 to 1.82)	1.46 (0.931 to 2.81)	2.41 (2.24 to 2.58)	

	AZD1305 Dose Group 1	AZD1305 Dose Group 2	AZD1305 Dose Group 3	AZD1305 Dose Group 4	Placebo
Mean (Full Range)					

6. Secondary Outcome Measure:

Measure Title	AUC Total of AZD1305 (Umol*h/L)
Measure Description	A total of 13 scheduled PK samples for each patient during and after infusion
Time Frame	Based on PK samples during and after infusion
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD1305 Dose Group 1	Loading dose 15 min at 43.5 mg/h, Maintenance dose maximum 60 additional min at 19.6 mg/h
AZD1305 Dose Group 2	Loading dose 15 min at 130.4 mg/h, Maintenance dose maximum 60 additional min at 58.7 mg/h
AZD1305 Dose Group 3	Loading dose 15 min at 325.9 mg/h, Maintenance dose maximum 60 additional min at 146.6 mg/h
AZD1305 Dose Group 4	Loading dose 15 min at 488.8 mg/h, Maintenance dose maximum 60 additional min at 220.0 mg/h
Placebo	Corresponding placebo

Measured Values

	AZD1305 Dose Group 1	AZD1305 Dose Group 2	AZD1305 Dose Group 3	AZD1305 Dose Group 4	Placebo
Number of Participants Analyzed	11	12	13	2	0
AUC Total of AZD1305 (Umol*h/L) [units: umol*h/L] Mean (Full Range)	1.54 (0.97 to 2.21)	4.97 (2.70 to 10.0)	10.3 (5.71 to 18.9)	17.3 (16.5 to 18.2)	

7. Secondary Outcome Measure:

Measure Title	Number of Patients Who Had at Least One AE

Measure Description	Number of patients
Time Frame	During active treatment period
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD1305 Dose Group 1	Loading dose 15 min at 43.5 mg/h, Maintenance dose maximum 60 additional min at 19.6 mg/h
AZD1305 Dose Group 2	Loading dose 15 min at 130.4 mg/h, Maintenance dose maximum 60 additional min at 58.7 mg/h
AZD1305 Dose Group 3	Loading dose 15 min at 325.9 mg/h, Maintenance dose maximum 60 additional min at 146.6 mg/h
AZD1305 Dose Group 4	Loading dose 15 min at 488.8 mg/h, Maintenance dose maximum 60 additional min at 220.0 mg/h
Placebo	Corresponding placebo

Measured Values

	AZD1305 Dose Group 1	AZD1305 Dose Group 2	AZD1305 Dose Group 3	AZD1305 Dose Group 4	Placebo
Number of Participants Analyzed	11	12	13	2	12
Number of Patients Who Had at Least One AE [units: Participants]	2	2	2	1	1

Reported Adverse Events

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

Reporting Groups

	Description
AZD1305 Dose Group 1	Loading dose 15 min at 43.5 mg/h, Maintenance dose maximum 60 additional min at 19.6 mg/h
AZD1305 Dose Group 2	Loading dose 15 min at 130.4 mg/h, Maintenance dose maximum 60 additional min at 58.7 mg/h

	Description
AZD1305 Dose Group 3	Loading dose 15 min at 325.9 mg/h, Maintenance dose maximum 60 additional min at 146.6 mg/h
AZD1305 Dose Group 4	Loading dose 15 min at 488.8 mg/h, Maintenance dose maximum 60 additional min at 220.0 mg/h
Placebo	Corresponding placebo

Serious Adverse Events

	AZD1305 Dose Group 1	AZD1305 Dose Group 2	AZD1305 Dose Group 3	AZD1305 Dose Group 4	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/11 (0%)	1/12 (8.33%)	1/13 (7.69%)	0/2 (0%)	1/12 (8.33%)
Vascular disorders					
Bradycardia And Hypotension [A] †	0/11 (0%)	1/12 (8.33%)	1/13 (7.69%)	0/2 (0%)	1/12 (8.33%)

† 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%

	AZD1305 Dose Group 1	AZD1305 Dose Group 2	AZD1305 Dose Group 3	AZD1305 Dose Group 4	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	2/	1/	1/	1/	0/
Cardiac disorders					
Atrial Fibrillation [A] †	1/11 (9.09%)	0/12 (0%)	0/13 (0%)	0/2 (0%)	0/12 (0%)
Eye disorders					
Vision Blurred [A] †	0/11 (0%)	1/12 (8.33%)	0/13 (0%)	0/2 (0%)	0/12 (0%)
Gastrointestinal disorders					
Vomiting [A] †	0/11 (0%)	0/12 (0%)	0/13 (0%)	1/2 (50%)	0/12 (0%)
Musculoskeletal and connective tissue disorders					
Muscoskeletal Chest Pain [A] †	1/11 (9.09%)	0/12 (0%)	0/13 (0%)	0/2 (0%)	0/12 (0%)
Nervous system disorders					

	AZD1305 Dose Group 1	AZD1305 Dose Group 2	AZD1305 Dose Group 3	AZD1305 Dose Group 4	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Syncope Vasovagal [A] †	0/11 (0%)	0/12 (0%)	1/13 (7.69%)	0/2 (0%)	0/12 (0%)

† 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:

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