ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 12/21/2011

ClinicalTrials.gov ID: NCT00643448

## Study Identification

| | |
|---|---|
| Unique Protocol ID: | D3190C00019 |
| Brief Title: | Explorative Study of AZD1305 in Atrial Fibrillation Patients |
| Official Title: | A Randomised, Placebo-controlled, Double-blind, Parallel-group, Multicentre, Phase IIa Study to Explore the Relationship Between QTcF Interval at First Dose (Loading Dose) and at Steady State After Treatment With AZD1305 Extended-release Tablets or Placebo When Given to Patients With Documented AF |
| Secondary IDs: | 2007-007058-79 |

## Study Status

| | |
|---|---|
| Record Verification: | December 2011 |
| Overall Status: | Completed |
| Study Start: | March 2008 |
| Primary Completion: | August 2008 [Actual] |
| Study Completion: | August 2008 [Actual] |

## Sponsor/Collaborators

| | |
|---|---|
| Sponsor: | AstraZeneca |
| Responsible Party: | Sponsor |
| Collaborators: | |

## Oversight

| | |
|---|---|
| FDA Regulated?: | Yes |

| | |
|---|---|
| Applicable Trial?: | Section 801 Clinical Trial? Yes<br>Delayed Posting? No |
| IND/IDE Protocol?: | No |
| Review Board: | Approval Status: Approved<br>Approval Number: 021-08<br>Board Name: Regional Ethics Committee in Gothenburg<br>Board Affiliation: Regional Ethics Committee in Gothenburg, Sweden<br>Phone: +46 31 786 68 22<br>Email: inger.hellstrom@gu.se |
| Data Monitoring?: | No |
| Plan to Share Data?: | |
| Oversight Authorities: | Sweden: Medical Products Agency<br>Norway: Norwegian Medicines Agency<br>Denmark: Danish Medicines Agency<br>Slovakia: State Institute for Drug Control<br>Russia: Ministry of Health of the Russian Federation<br>Poland: Ministry of Health |

## Study Description

| | |
|---|---|
| Brief Summary: | Explorative study in Atrial Fibrillation patients to assess Safety and Pharmacokinetics at initiation of treatment and at steady state |
| Detailed Description: | |

## Conditions

| | |
|---|---|
| Conditions: | Atrial Fibrillation |
| Keywords: | |

## Study Design

| | |
|---|---|
| Study Type: | Interventional |
| Primary Purpose: | Treatment |
| Study Phase: | Phase 2 |
| Intervention Model: | Parallel Assignment |
| Number of Arms: | 3 |

| | |
|---|---|
| Masking: | Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor) |
| Allocation: | Randomized |
| Endpoint Classification: | Safety Study |
| Enrollment: | 65 [Actual] |

## Arms and Interventions

| Arms | Assigned Interventions |
|---|---|
| Experimental: AZD1305 loading dose 250 mg + 125 mg Tablets | Drug: AZD1305<br>AZD1305 loading dose 250 mg + 125 mg evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |
| Experimental: AZD1305 loading dose 500 mg + placebo Tablets | Drug: AZD1305<br>AZD1305 loading dose 500 mg + placebo evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |
| Placebo Comparator: Placebo corresponding to AZD1305 loading dose Tablets | Drug: Placebo<br>Placebo corresponding to AZD1305 loading dose + evening dose on Study Day 1, maintenance dose twice daily from Study Day 2 |

## Outcome Measures

[See Results Section.]

## Eligibility

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

- Documented Atrial Fibrillation but in stable SR for at least 2 h and a maximum of 28 days.
- Sinus rhythm at randomisation

Exclusion Criteria:

- Haemodynamically unstable condition as judged by the Investigator, systolic BP <100 mmHg or >180 mmHg, or diastolic BP >105 mmHg at randomisation
- Personal or family history of Torsades de Pointes (TdP), any other polymorphic ventricular tachycardia (PVT), sustained ventricular tachycardia, long QT syndrome and/or Brugada syndrome
- Sinus bradycardia (<50 beats per minute (bpm)) at randomisation

- 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
- Use of any antiarrhythmic drug class I and/or III, digitalis glycoside, QT prolonging drug and/or drug that inhibits CYP3A4, as well as St John's Worth

## Contacts/Locations

Study Officials: Kenneth Egstrup
Study Principal Investigator
Svendborg Sygehus, Forsknings-og udviklingsafd.

Locations: Denmark
Research Site
Aalborg, Denmark

Research Site
Esbjerg, Denmark

Research Site
Hvidovre, Denmark

Research Site
Kobenhavn, Denmark

Research Site
Silkeborg, Denmark

Research Site
Svendborg, Denmark

Norway
Research Site
Oslo, Norway

Research Site
RUD, Norway

Research Site
Tynset, Norway

Poland
Research Site
Bytom, Poland

Research Site
Warszawa, Poland

Russian Federation
Research Site
Moscow, Russian Federation

Research Site
Saint-petersburg, Russian Federation

Slovakia
Research Site
Kosice, Slovakia

Research Site
Nitra, Slovakia

Research Site
Nove Zamky, Slovakia

Research Site
Rimavska Sobota, Slovakia

Sweden
Research Site
Goteborg, Sweden

## References

Citations:

Links:

Study Data/Documents:

# Study Results

## Participant Flow

| | |
|---|---|
| Pre-Assignment Details | All patients will attend a pre-entry Visit 3-28 days before the planned randomisation. At this Visit, the Investigator ensures that a signed Informed Consent Form has been obtained before any study specific procedures are conducted. Patients who have given their consent to participate in the study will then undergo a full clinical assessment |

Reporting Groups

| | Description |
|---|---|
| AZD1305 Group A | AZD1305 group A loading dose 250 mg + 125 mg evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |
| AZD1305 Group B | AZD1305 loading dose 500 mg + placebo evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |
| Placebo | Placebo corresponding to AZD1305 loading dose + evening dose on Study Day 1, maintenance dose twice daily from Study Day 2 |

Overall Study

| | AZD1305 Group A | AZD1305 Group B | Placebo |
|---|---|---|---|
| Started | 21 | 22 | 22 |
| Completed | 17 | 17 | 16 |
| Not Completed | 4 | 5 | 6 |
| Lack of Efficacy | 2 | 0 | 4 |
| Adverse Event | 2 | 2 | 2 |
| QTcF>550 ms | 0 | 3 | 0 |

## Baseline Characteristics

Reporting Groups

| | Description |
|---|---|
| AZD1305 Group A | AZD1305 group A loading dose 250 mg + 125 mg evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |

| | Description |
|---|---|
| AZD1305 Group B | AZD1305 loading dose 500 mg + placebo evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |
| Placebo | Placebo corresponding to AZD1305 loading dose + evening dose on Study Day 1, maintenance dose twice daily from Study Day 2 |

Baseline Measures

| | AZD1305 Group A | AZD1305 Group B | Placebo | Total |
|---|---|---|---|---|
| Number of Participants | 21 | 22 | 22 | 65 |
| Age, Continuous<br>Age (years) [units: Years]<br>Mean (Standard Deviation) | 65 (10) | 64 (10) | 64 (9) | 64.5 (9.5) |
| Gender, Male/Female<br>[units: Participants] | | | | |
| Female | 8 | 10 | 8 | 26 |
| Male | 13 | 12 | 14 | 39 |

## Outcome Measures

1. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Maximum QTcF |
| Measure Description | Maximum of all QTcF values obtained for any given patient from randomisation until the intended end of the study drug period, day 10. |
| Time Frame | During treatment days 2-10 |
| Safety Issue? | Yes |

Analysis Population Description

[Not Specified]

Reporting Groups

| | Description |
|---|---|
| AZD1305 Group A and AZD1305 Group B | AZD1305 group A loading dose 250 mg + 125 mg evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 AZD1305 Group B loading dose 500 mg + placebo evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |
| Placebo | Placebo corresponding to AZD1305 loading dose + evening dose on Study Day 1, maintenance dose twice daily from Study Day 2 |

Measured Values

| | AZD1305 Group A and AZD1305 Group B | Placebo |
|---|---|---|
| Number of Participants Analyzed | 21 | 22 |
| Maximum QTcF<br>[units: ms]<br>Mean (Full Range) | 461 (417 to 536) | 427 (383 to 465) |

2. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Adverse Events (AE) |
| Measure Description | Number of patients who had at least one AE according to the definition in the study protocol |
| Time Frame | During treatment days 2-10 |
| Safety Issue? | Yes |

Analysis Population Description

[Not Specified]

Reporting Groups

| | Description |
|---|---|
| AZD1305 Group A and AZD1305 Group B | AZD1305 group A loading dose 250 mg + 125 mg evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 AZD1305 Group B loading dose 500 mg + placebo evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |
| Placebo | Placebo corresponding to AZD1305 loading dose + evening dose on Study Day 1, maintenance dose twice daily from Study Day 2 |

Measured Values

| | AZD1305 Group A and AZD1305 Group B | Placebo |
|---|---|---|
| Number of Participants Analyzed | 43 | 21 |
| Adverse Events (AE)<br>[units: Participants] | 22 | 13 |

3. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Estimated Cmax (Maximum Plasma Concentration) (PK Modeling) at Steady-state |
| Measure Description | Population PK model parameter estimates derived from plasma concentrations of AZD1305 |
| Time Frame | During treatment days 1-10 |
| Safety Issue? | No |

Analysis Population Description
[Not Specified]

Reporting Groups

| | Description |
|---|---|
| AZD1305 Group A | AZD1305 group A loading dose 250 mg + 125 mg evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |
| AZD1305 Group B | AZD1305 loading dose 500 mg + placebo evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |
| Placebo | Placebo corresponding to AZD1305 loading dose + evening dose on Study Day 1, maintenance dose twice daily from Study Day 2 |

Measured Values

| | AZD1305 Group A | AZD1305 Group B | Placebo |
|---|---|---|---|
| Number of Participants Analyzed | 17 | 17 | 0 |
| Estimated Cmax (Maximum Plasma Concentration) (PK Modeling) at Steady-state<br>[units: µmol/L]<br>Mean (Full Range) | 0.41 (0.17 to 0.83) | 0.45 (0.24 to 0.84) | |

4. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Compliance With Trans Telephonic Monitoring (TTM) |
| Measure Description | Percentage of twice daily TTM recordings (individual compliance) transmitted and available for analysis |
| Time Frame | During treatment days 1-10 |
| Safety Issue? | No |

Analysis Population Description
[Not Specified]

Reporting Groups

| | Description |
|---|---|
| AZD1305 Group A | AZD1305 group A loading dose 250 mg + 125 mg evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |
| AZD1305 Group B | AZD1305 loading dose 500 mg + placebo evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |
| Placebo | Placebo corresponding to AZD1305 loading dose + evening dose on Study Day 1, maintenance dose twice daily from Study Day 2 |

Measured Values

| | AZD1305 Group A | AZD1305 Group B | Placebo |
|---|---|---|---|
| Number of Participants Analyzed | 21 | 22 | 22 |
| Compliance With Trans Telephonic Monitoring (TTM)<br>[units: Percentage of recordings analysed]<br>Mean (Full Range) | 97.4 (80 to 100) | 96.4 (68.2 to 100) | 98.3 (72.7 to 100) |

## Reported Adverse Events

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

Reporting Groups

| | Description |
|---|---|
| AZD1305 Group A | AZD1305 group A loading dose 250 mg + 125 mg evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |
| AZD1305 Group B | AZD1305 loading dose 500 mg + placebo evening dose on Study Day 1, maintenance dose 125 mg twice daily from Study Day 2 |
| Placebo | Placebo corresponding to AZD1305 loading dose + evening dose on Study Day 1, maintenance dose twice daily from Study Day 2 |

Serious Adverse Events

| | AZD1305 Group A | AZD1305 Group B | Placebo |
|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Total | 0/ | 3/ | 0/ |
| Blood and lymphatic system disorders | | | |
| Neutropenia [A] † | 0/21 (0%) | 1/22 (4.55%) | 0/22 (0%) |
| Cardiac disorders | | | |
| Polymorphic Ventricular Tachycardia [A] † | 0/21 (0%) | 1/22 (4.55%) | 0/22 (0%) |
| Ventricular Bigeminy [A] † | 0/21 (0%) | 1/22 (4.55%) | 0/22 (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%

| | AZD1305 Group A | AZD1305 Group B | Placebo |
|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Total | 10/ | 12/ | 9/ |
| Cardiac disorders | | | |
| Atrial Fibrillation [A] † | 1/21 (4.76%) | 0/22 (0%) | 2/22 (9.09%) |
| Bradycardia [A] † | 1/21 (4.76%) | 2/22 (9.09%) | 1/22 (4.55%) |
| Palpitation [A] † | 2/21 (9.52%) | 1/22 (4.55%) | 3/22 (13.64%) |
| General disorders | | | |
| Application Site Reaction [A] † | 2/21 (9.52%) | 3/22 (13.64%) | 0/22 (0%) |
| Nausea [A] † | 2/21 (9.52%) | 1/22 (4.55%) | 2/22 (9.09%) |
| Oedema Peripheral [A] † | 2/21 (9.52%) | 0/22 (0%) | 0/22 (0%) |
| Qt Interval Prolonged [A] † | 0/21 (0%) | 3/22 (13.64%) | 0/22 (0%) |
| Nervous system disorders | | | |
| Dizziness [A] † | 2/21 (9.52%) | 4/22 (18.18%) | 0/22 (0%) |

| | AZD1305 Group A | AZD1305 Group B | Placebo |
|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Headache [A] † | 4/21 (19.05%) | 4/22 (18.18%) | 2/22 (9.09%) |

† 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
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