ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 07/17/2013

ClinicalTrials.gov ID: NCT00743444

Study Identification

Unique Protocol ID:	D9120C00020
Brief Title:	TLESR-impedance Study in Patients
Official Title:	A Double-blind, Placebo Controlled, Randomized, Two Centre Phase IIA Pharmacodynamic Cross-over Study to Assess the Effect of AZD3355, 65 mg Bid, on Transient Lower Esophageal Sphincter Relaxations (TLESRs) in GERD Patients With an Incomplete Response to PPI Treatment
Secondary IDs:	

Study Status

Record Verification:	July 2013
Overall Status:	Completed
Study Start:	February 2007
Primary Completion:	February 2008 [Actual]
Study Completion:	February 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: ML4004 Board Name: Commissie Medische Ethiek Board Affiliation: Commissie Medische Ethiek Phone: +32 16 34 86 00 Email: ec@uzleuven.be
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Belgium: Federal Agency for Medicinal Products and Health Products

Study Description

Brief Summary:	The purpose of the study is to compare frequency and content of reflux episodes in patients with gastroesophageal reflux disease.
Detailed Description:	

Conditions

Conditions:	Reflux Episodes
Keywords:	GERD transient lower esophageal sphincter relaxations (TLESRs) reflux

Study Design

Study Type:	Interventional
Primary Purpose:	Basic Science
Study Phase:	Phase 2
Intervention Model:	Crossover Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized

Endpoint Classification: Efficacy Study

Enrollment: 27 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1 AZD3355	Drug: AZD3355 65 mg capsules, oral, 3 single doses Other Names: • Lesogaberan
Placebo Comparator: 2	Drug: Placebo capsules, oral, 3 single doses

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 70 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Provision of written consent
- GERD patients, age 18-70 years, females must be postmenopausal or surgically sterilised
- 6 months history of GERD and incomplete response to PPI treatment

Exclusion Criteria:

- Insufficient symptom burden of the reflux disease evaluated by questionnaires
- S-creatinine >1.2 times upper limit of normal
- History of heart disease
- Prior surgery of the upper GI tract

Contacts/Locations

Study Officials: Eva Ersdal, PhD

Study Director
AstraZeneca R&D, Mölndal, Sweden

Daniel Sifrim, MD, PhD
Study Principal Investigator
Center for Gastroenterological Research, Belgium

Locations:

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	42 patients in 2 countries were enrolled in the study. 27 patients were randomised to treatment. 2 patients discontinued prematurely, 1 due to low Lower Esophageal Sphincter Pressure (LESP)/catheter placement problems, and 1 due to nausea/vomiting. Thus, 25 patients completed the study, 10 in Belgium and 15 in the Netherlands.

Reporting Groups

	Description
AZD3355 First, Then Placebo	65 mg drug or placebo capsules, oral, 3 single doses
Placebo First, Then AZD3355	65 mg drug or placebo capsules, oral, 3 single doses

First Intervention

	AZD3355 First, Then Placebo	Placebo First, Then AZD3355
Started	14	13
Completed	14	12
Not Completed	0	1

	AZD3355 First, Then Placebo	Placebo First, Then AZD3355
Catheter placement problems	0	1

Washout Period

	AZD3355 First, Then Placebo	Placebo First, Then AZD3355
Started	14	12
Completed	14	11
Not Completed	0	1
Adverse Event	0	1

Second Intervention

	AZD3355 First, Then Placebo	Placebo First, Then AZD3355
Started	14	11
Completed	14	11
Not Completed	0	0

Baseline Characteristics

Reporting Groups

	Description
Entire Study Population	Includes groups randomized to received Drug first and Placebo first.

Baseline Measures

	Entire Study Population
Number of Participants	27
Age, Continuous [units: years] Mean (Standard Deviation)	51.6 (10.2)
Gender, Male/Female [units: Participants]	
Female	11
Male	16

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Transient Lower Esophageal Sphincter Relaxations (TLESRs) 0-3 Hours Post Meal, Post Third Dose
Measure Description	The number of relaxations for each patient in each period was determined from manometric tracings according to previously published criteria (R.H. Holloway, R. Penagini and A.C. Ireland, Criteria for objective definition of transient lower esophageal sphincter relaxation, Am J Physiol 268 (1995), pp. G128-G133). The analysis of the number of TLESRs was based on an analysis of variance (ANOVA) for log-transformed data. The 95% level confidence interval (CI) limits were transformed back to the original scale to give CIs for the geometric mean for each treatment.
Time Frame	0-3 hours post meal, post third dose
Safety Issue?	No

Analysis Population Description

Per Protocol Analysis Set (PP). From the safety analysis set with 27 patients, the PP excludes 2 patients since they discontinued prematurely from the study. Additionally, 4 patients were excluded from the primary analysis; 1 due to catheter placement problems, 1 due to error in dose administration, 1 due to low LESP, 1 due to multiple swallowing.

Reporting Groups

	Description
AZD3355	65 mg drug capsules, oral, 3 single doses
Placebo	placebo capsules, oral, 3 single doses

Measured Values

	AZD3355	Placebo
Number of Participants Analyzed	21	21
Number of Transient Lower Esophageal Sphincter Relaxations (TLESRs) 0-3 Hours Post Meal, Post Third Dose [units: Relaxations] Geometric Mean (95% Confidence Interval)	11.6 (9.40 to 14.3)	15.5 (12.6 to 19.1)

2. Secondary Outcome Measure:

Measure Title	Total Number Reflux Episodes 0-24 Hours Post First Dose

Measure Description	Number of reflux episodes assessed during the 24-hour ambulatory impedance-pH recording.
Time Frame	0-24 hours
Safety Issue?	No

Analysis Population Description

Per Protocol Analysis Set (PP). From the safety analysis set with 27 patients, the PP excludes 2 patients since they discontinued prematurely from the study. Additionally, 4 patients were excluded from this analysis; 1 due to catheter placement problems, 1 due to error in dose administration, 2 due to insufficient impedance/pH recording time.

Reporting Groups

	Description
AZD3355	65 mg drug capsules, oral, 3 single doses
Placebo	placebo capsules, oral, 3 single doses

Measured Values

	AZD3355	Placebo
Number of Participants Analyzed	21	21
Total Number Reflux Episodes 0-24 Hours Post First Dose [units: Episodes] Geometric Mean (95% Confidence Interval)	30.6 (20.9 to 44.9)	50.5 (34.5 to 74.1)

3. Secondary Outcome Measure:

Measure Title	Area Under the Plasma Concentration vs. Time Curve (AUCtau) During 0-12 Hours Post First Dose Calculated by the Log/Linear Trapezoidal Method.
Measure Description	The AUCtau was calculated for each patient in the period with AZD3355 treatment by the Log-Linear Trapezoidal Method. The descriptive geometric mean of the individual AUCtau values is reported here.
Time Frame	0-12 hours post first dose
Safety Issue?	No

Analysis Population Description

Per Protocol Analysis Set (PP). From the safety analysis set with 27 patients, the PP excludes 2 patients since they discontinued prematurely from the study. Additionally, 1 patient was excluded from the pharmacokinetic analysis due to error in dose administration at dose 2.

Reporting Groups

	Description
AZD3355	65 mg drug capsules, oral, 3 single doses

Measured Values

	AZD3355
Number of Participants Analyzed	24
Area Under the Plasma Concentration vs. Time Curve (AUCtau) During 0-12 Hours Post First Dose Calculated by the Log/Linear Trapezoidal Method. [units: µmol*hours / L] Geometric Mean (Standard Deviation)	7.16 (2.36)

Reported Adverse Events

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

Reporting Groups

	Description
AZD3355	65 mg drug capsules, oral, 3 single doses
Placebo	placebo capsules, oral, 3 single doses

Serious Adverse Events

	AZD3355	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/25 (0%)	0/27 (0%)

Other Adverse Events

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

	AZD3355	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	16/25 (64%)	18/27 (66.67%)
Gastrointestinal disorders		
Abdominal Distension [A] *	3/25 (12%)	1/27 (3.7%)
Flatulence [A] *	2/25 (8%)	1/27 (3.7%)
Nausea [A] *	2/25 (8%)	5/27 (18.52%)
General disorders		
Feeling Hot [A] *	2/25 (8%)	1/27 (3.7%)
Infections and infestations		
Nasopharyngitis [A] *	1/25 (4%)	2/27 (7.41%)
Nervous system disorders		
Dizziness [A] *	3/25 (12%)	1/27 (3.7%)
Headache [A] *	8/25 (32%)	11/27 (40.74%)
Paraesthesia [A] *	5/25 (20%)	3/27 (11.11%)
Skin and subcutaneous tissue disorders		
Hyperhidrosis [A] *	0/25 (0%)	2/27 (7.41%)
Vascular disorders		
Hot Flush [A] *	3/25 (12%)	1/27 (3.7%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA 11.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

There is an agreement between PI and Sponsor (AZ) or its agents that restricts the PI's right to discuss/publish trial results after the trial is completed. The PI agrees to collaborate in good faith with AZ with regards to content and formation of any publication or disclosure to be made by PI and to pay due consideration to opinions offered by AZ.

Results Point of Contact:

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