ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 06/25/2014

An Explorative Trial to Evaluate the Pharmacodynamic Effect of SPD557 on Reflux Parameters in Refractory GERD Patients

This study has been terminated.
(This study was terminated early due to recruitment difficulties. There were no safety concerns.)

Sponsor:	Shire
Collaborators:	
Information provided by (Responsible Party):	Shire
ClinicalTrials.gov Identifier:	NCT01370863

Purpose

The purpose of this trial is to investigate the pharmacodynamic effect on reflux parameters of SPD557 tablets (0.5 mg t.i.d., on top of PPI treatment) in patients with Gastroesophageal Reflux Disease (GERD) with persistent symptoms despite taking a stable dose of proton pump inhibitors. Additionally the effect on symptoms will be explored and safety and tolerability will be evaluated.

Condition	Intervention	Phase
Gastroesophageal Reflux Disease	Drug: SPD557 Drug: placebo	Phase 2

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized
Official Title: An Explorative, Randomized, Placebo-controlled, DB, Parallel-group Trial, to Evaluate the Pharmacodynamic Effect of SPD557 on Reflux Parameters in Subjects With GERD & With Persistent Symptoms Despite Taking a Stable Dose of PPIs

Further study details as provided by Shire:

Primary Outcome Measure:

- Change From Baseline in the Number of Liquid-containing Reflux Events (pH/MII Monitoring) at 4 Weeks [Time Frame: Baseline and 4 weeks] [Designated as safety issue: No]
  This is used to characterize gastric reflux events. The measurements were made over a 24-hour period at baseline and again at week 4.

Secondary Outcome Measures:

- Change From Baseline in the Number of Days With Heartburn and/or Regurgitation at 4 Weeks [Time Frame: Baseline and 4 weeks] [Designated as safety issue: No]
- Change From Baseline in the Patient Assessment of Upper Gastrointestinal Symptom Severity Index (PAGI-SYM) Questionnaire at 4 Weeks [Time Frame: Baseline and 4 weeks] [Designated as safety issue: No]
  The PAGI-SYM contains 20 items and the scores range from 0 (no symptoms)-5 (very severe symptoms) for each item with a total score of 0-100. Higher scores indicate more severe gastrointestinal symptoms.

Enrollment: 67
Study Start Date: December 2010
Primary Completion Date: May 2012
Study Completion Date: May 2012

Arms	Assigned Interventions
Experimental: SPD557	Drug: SPD557 0.5 mg tablet t.i.d. for 4 weeks on top of stable PPI treatment
Placebo Comparator: Placebo	Drug: placebo matching placebo tablet t.i.d. for 4 weeks on top of stable PPI treatment

Eligibility

Ages Eligible for Study: 18 Years to 70 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion criteria:

1. Written ICF signed voluntarily before the first trial related activity.
2. Subjects with a history of GERD symptoms (i.e., heartburn and/or regurgitation) during the last 6 months
3. Subjects on a stable dose of PPIs, compliant for at least 6 weeks prior to screening.
4. ≥3 days per week with heartburn and/or regurgitation symptoms of at least moderate severity and a minimum of 25 liquid containing reflux events over 24h (pH/MII monitoring).

Exclusion criteria:

1. Subjects with prior endoscopic anti-reflux procedure or major GI surgery or subjects with major GI disorders.

2. Presence of severe and clinically uncontrolled cardiovascular, liver or lung disease, neurologic, cancer or AIDS.
3. Alarm symptoms suggestive of malignancies or organic disease.

Contacts and Locations

Locations

- Belgium
  - Cliniques universitaires Saint Luc
    - Bruxelles, Belgium, 1200
  - UZ Leuven, Belgium
    - Leuven, Belgium, 3000
  - CUB Hôpital Erasme
    - Brussels, Bruxelles, Belgium, 1070
- France
  - CHU de Bordeaux - Hôpital Saint André
    - Bordeaux Cedex, France, 33075
  - CHU de Lyon - Groupement Hospitalier Edouard Herriot
    - Lyon, France, 69437
  - Hôtel Dieu - CHU de Nantes
    - Nantes Cedex 1, France, 44093
- Germany
  - Klinikum Garmisch-Partenkirchen GmbH
    - Garmisch-Partenkirchen, Germany, 82467
  - Otto-von-Guericke University
    - Magdeburg, Germany, 39120
- Netherlands
  - Academisch Medisch Centrum (AMC)
    - Amsterdam, Netherlands, 1105 AZ
- Switzerland
  - Inselspital Bern (Bern University Hopsital)
    - Bern, Switzerland, BHH D140
  - Kantonsspital St. Gallen
    - St. Gallen, Switzerland, 9007
  - University Hospital Zurich
    - Zurich, Switzerland, CH-8091
- United Kingdom
  - Addenbrooke's Hospital
    - Cambridge, United Kingdom, CB2 0QQ
  - Wingate Institute of Neurogastroenterology
    - London, United Kingdom, E12AJ
  - Queen's Medical Center (Nottingham University Hospital)
    - Nottingham, United Kingdom, NG7 2UH

Investigators

Study Director:	An Rykx, PhD	Shire-Movetis
Principal Investigator:	Prof. Jan Tack, M.D.	KUL, Herestraat 49, 3000 Leuven

More Information

Responsible Party:	Shire
Study ID Numbers:	SPD557-202 2010-021397-12 [EudraCT Number]
Health Authority:	Belgium: Federal Agency for Medicinal Products and Health Products France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) Netherlands: The Central Committee on Research Involving Human Subjects (CCMO) Switzerland: Federal Office of Public Health Germany: Federal Institute for Drugs and Medical Devices United Kingdom: Medicines and Healthcare Products Regulatory Agency

Study Results

Participant Flow

Reporting Groups

	Description
SPD557	0.5 mg tablet administered 3 times daily (t.i.d.) for 4 weeks in addition to stable proton pump inhibitor (PPI) treatment
Placebo	Matching placebo tablet administered three times daily (t.i.d.) for 4 weeks in addition to stable PPI treatment

Overall Study

	SPD557	Placebo
Started	34	33
Completed	32	30
Not Completed	2	3
Adverse Event	1	1

	SPD557	Placebo
Did not want second pH/MII monitoring	1	1
Not meeting inclusion/exclusion criteria	0	1

Baseline Characteristics

Analysis Population Description

The Safety Population was used defined as all subjects randomized into the study with at least 1 administration of the investigational product. Two subjects never received investigational product (n = 65).

Reporting Groups

	Description
SPD557	0.5 mg tablet t.i.d. for 4 weeks in addition to stable proton pump inhibitor (PPI) treatment
Placebo	Matching placebo tablet t.i.d. for 4 weeks in addition to stable PPI treatment

Baseline Measures

	SPD557	Placebo	Total
Number of Participants	34	31	65
Age, Continuous [units: years] Mean (Standard Deviation)	43.8 (16.04)	45.8 (14.50)	44.8 (15.24)
Age, Customized Between 18 and 70 years inclusive [units: participants]	34	31	65
Gender, Male/Female [units: participants]			
Female	19	17	36
Male	15	14	29
Region of Enrollment [1] [units: participants]			
France	13	13	26
Belgium	8	7	15
Netherlands	2	3	5
Germany	4	4	8

	SPD557	Placebo	Total
United Kingdom	3	4	7
Switzerland	4	2	6

[1] All randomized subjects (n = 67).

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline in the Number of Liquid-containing Reflux Events (pH/MII Monitoring) at 4 Weeks
Measure Description	This is used to characterize gastric reflux events. The measurements were made over a 24-hour period at baseline and again at week 4.
Time Frame	Baseline and 4 weeks
Safety Issue?	No

Analysis Population Description

Pharmacodynamics Population (PD) defined as all randomized subjects with at least 1 administration of the investigational product and with both a baseline and post-baseline PD assessment.

Reporting Groups

	Description
SPD557	0.5 mg tablet t.i.d. for 4 weeks in addition to stable proton pump inhibitor (PPI) treatment
Placebo	Matching placebo tablet t.i.d. for 4 weeks in addition to stable PPI treatment

Measured Values

	SPD557	Placebo
Number of Participants Analyzed	31	29
Change From Baseline in the Number of Liquid-containing Reflux Events (pH/MII Monitoring) at 4 Weeks [units: Number of Reflux Events] Mean (Standard Deviation)	-17.9 (59.88)	-13.7 (37.58)

Statistical Analysis 1 for Change From Baseline in the Number of Liquid-containing Reflux Events (pH/MII Monitoring) at 4 Weeks

Statistical Analysis Overview	Comparison Groups	SPD557, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.869
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Difference in LS Mean]
	Estimated Value	-1.452
	Confidence Interval	(2-Sided) 95% -19.054 to 16.149
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Number of Days With Heartburn and/or Regurgitation at 4 Weeks
Measure Description	
Time Frame	Baseline and 4 weeks
Safety Issue?	No

Analysis Population Description

Pharmacodynamics Population (PD) defined as all randomized subjects with at least 1 administration of the investigational product and with both a baseline and post-baseline PD assessment.

Reporting Groups

	Description
SPD557	0.5 mg tablet t.i.d. for 4 weeks in addition to stable proton pump inhibitor (PPI) treatment
Placebo	Matching placebo tablet t.i.d. for 4 weeks in addition to stable PPI treatment

Measured Values

	SPD557	Placebo
Number of Participants Analyzed	31	29
Change From Baseline in the Number of Days With Heartburn and/or Regurgitation at 4 Weeks [units: Number of days] Mean (Standard Deviation)	-0.90 (1.434)	-0.88 (1.610)

Statistical Analysis 1 for Change From Baseline in the Number of Days With Heartburn and/or Regurgitation at 4 Weeks

Statistical Analysis Overview	Comparison Groups	SPD557, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.487
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Diference in LS means]
	Estimated Value	0.264
	Confidence Interval	(2-Sided) 95% -0.495 to 1.024
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Patient Assessment of Upper Gastrointestinal Symptom Severity Index (PAGI-SYM) Questionnaire at 4 Weeks
Measure Description	The PAGI-SYM contains 20 items and the scores range from 0 (no symptoms)-5 (very severe symptoms) for each item with a total score of 0-100. Higher scores indicate more severe gastrointestinal symptoms.
Time Frame	Baseline and 4 weeks
Safety Issue?	No

Analysis Population Description

Pharmacodynamics Population (PD) defined as all randomized subjects with at least 1 administration of the investigational product and with both a baseline and post-baseline PD assessment.

Reporting Groups

	Description
SPD557	0.5 mg tablet t.i.d. for 4 weeks in addition to stable proton pump inhibitor (PPI) treatment
Placebo	Matching placebo tablet t.i.d. for 4 weeks in addition to stable PPI treatment

Measured Values

	SPD557	Placebo
Number of Participants Analyzed	31	29
Change From Baseline in the Patient Assessment of Upper Gastrointestinal Symptom Severity Index (PAGI-SYM) Questionnaire at 4 Weeks [units: Units on a scale] Mean (Standard Deviation)	-0.41 (0.943)	-0.37 (0.760)

Statistical Analysis 1 for Change From Baseline in the Patient Assessment of Upper Gastrointestinal Symptom Severity Index (PAGI-SYM) Questionnaire at 4 Weeks

Statistical Analysis Overview	Comparison Groups	SPD557, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.637
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other [Difference in LS means]
	Estimated Value	-0.087
	Confidence Interval	(2-Sided) 95%

		-0.501 to 0.326
	Estimation Comments	[Not specified]

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	The Safety Population was defined as all subjects randomized into the study with at least 1 administration of the investigational product. Two subjects never received investigational product (n = 65).

Reporting Groups

	Description
SPD557	0.5 mg tablet t.i.d. for 4 weeks in addition to stable proton pump inhibitor (PPI) treatment
Placebo	Matching placebo tablet t.i.d. for 4 weeks in addition to stable PPI treatment

Serious Adverse Events

	SPD557	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/34 (0%)	0/31 (0%)

Other Adverse Events

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

	SPD557	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	25/34 (73.53%)	16/31 (51.61%)
Gastrointestinal disorders		
Abdominal distension	0/34 (0%)	2/31 (6.45%)
Abdominal pain	3/34 (8.82%)	2/31 (6.45%)
Abdominal pain upper	2/34 (5.88%)	0/31 (0%)
Diarrhea	13/34 (38.24%)	2/31 (6.45%)
Dyspepsia	2/34 (5.88%)	1/31 (3.23%)
Nausea	3/34 (8.82%)	2/31 (6.45%)

	SPD557	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
General disorders		
Edema peripheral	0/34 (0%)	2/31 (6.45%)
Infections and infestations		
Influenza	1/34 (2.94%)	2/31 (6.45%)
Nasopharyngitis	3/34 (8.82%)	1/31 (3.23%)
Pharyngitis	0/34 (0%)	2/31 (6.45%)
Nervous system disorders		
Dizziness	2/34 (5.88%)	2/31 (6.45%)
Headache	12/34 (35.29%)	4/31 (12.9%)

Limitations and Caveats

Results data should be interpreted with caution since the study’s early termination affects the statistical power to detect true differences between treatment groups.

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.

If a multicenter publication is not submitted within twelve (12) months after conclusion, abandonment or termination of the Study at all sites, or after Sponsor confirms there shall be no multicenter Study publication, the Institution and/or such Principal Investigator may publish the results from the Institution site individually.

Results Point of Contact:

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