Clinical trial results:
A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group, Phase 2a Study of Oral IW-9179 Administered Once Daily for 14 Days to Patients with Functional Dyspepsia

Summary

EudraCT number	2012-002748-25
Trial protocol	NL BE
Global end of trial date	25 January 2014

Results information

Result version number	v1 (current)
This version publication date	10 March 2021
First version publication date	10 March 2021

Trial information

Trial identification

Sponsor protocol code	ICP-112-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01712412
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ironwood Pharmaceuticals Inc.
Sponsor organisation address	100 Summer Street Suite 2300, Boston, MA, United States, 02110
Public contact	Corporate Communications, Ironwood Pharmaceuticals Inc., +1 6176217722, Info@ironwoodpharma.com
Scientific contact	Corporate Communications, Ironwood Pharmaceuticals Inc., +1 6176217722, Info@ironwoodpharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 January 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 January 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objectives of the study are to determine the safety and efficacy of IW-9179 administered to patients with functional dyspepsia, with and without concomitant proton pump inhibitor and/or H2 receptor antagonist (H2RA) administration.

Protection of trial subjects:

The Screening Period began with the signature of the informed consent form (ICF) at the Screening Visit (which occurred between Day -59 and Day -18).

Background therapy:

Subjects who entered the study on a proton pump inhibitor (PPI) and/or H2 receptor antagonist (H2RA) must have continued the use of those agents without any changes to the dose or frequency throughout the Screening, Pretreatment, Treatment, and Post-treatment Periods.

Evidence for comparator: -	
Actual start date of recruitment	27 November 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Netherlands: 5
Worldwide total number of subjects	10
EEA total number of subjects	10

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	10
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The Screening Period may have lasted up to 42 days. Subjects who met the Rome III criteria for functional dyspepsia (FD) and met all Screening criteria proceeded to the Pretreatment Period. The Pretreatment Period occurred immediately after the Screening Period and consisted of the 14 to 17 days immediately prior to the Randomization Visit.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Blinding implementation details:

Randomization was performed using a computer-generated randomization scheme. The subjects, the investigators, and the sponsor were blinded to the treatment assignments until after the study completion and database lock.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Oral placebo once daily (QD) for 14 days

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

At the Randomization Visit, subjects underwent a meal challenge test consisting of pre-meal symptom measurements and a standardized meal followed by post-meal symptom measurements. The first dose of investigational medicinal product (IMP) was taken at the Randomization Visit after the meal challenge test. Daily administration of IMP continued for a total of 14 days through the End-of-Treatment (EOT) Visit. Subjects repeated the meal challenge test at the EOT Visit receiving the last dose of IMP at the study center during the EOT Visit, just prior to the meal challenge test. Subjects who did not undergo the meal challenge received their first does of IMP at the Randomization Visit and followed the same dosing schedule as those who underwent the meal challenge test.

Arm title	IW-9179 500 µg

Arm description:

IW-9179 500 µg QD for 14 days

Arm type	Experimental
Investigational medicinal product name	IW-9179
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

At the Randomization Visit, subjects underwent a meal challenge test consisting of pre-meal symptom measurements and a standardized meal followed by post-meal symptom measurements. The first dose

of IMP was taken at the Randomization Visit after the meal challenge test. Daily administration of IMP continued for a total of 14 days through the EOT Visit. Subjects repeated the meal challenge test at the EOT Visit receiving the last dose of IMP at the study center during the EOT Visit, just prior to the meal challenge test. Subjects who did not undergo the meal challenge received their first does of IMP at the Randomization Visit and followed the same dosing schedule as those who underwent the meal challenge test.

Number of subjects in period 1	Placebo	IW-9179 500 µg
Started	4	6
Completed	4	4
Not completed	0	2
Adverse event	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: Oral placebo once daily (QD) for 14 days	
Reporting group title	IW-9179 500 µg
Reporting group description: IW-9179 500 µg QD for 14 days	

Reporting group values	Placebo	IW-9179 500 µg	Total
Number of subjects	4	6	10
Age categorical Units: Subjects			
Adults (18-64 years)	4	6	10
Age continuous Units: years			
arithmetic mean	32.3	44.2	
standard deviation	± 8.0	± 14.0	-
Gender categorical Units: Subjects			
Female	1	3	4
Male	3	3	6
Race Units: Subjects			
White	4	6	10
Ethnicity Units: Subjects			
Not Hispanic or Latino	4	6	10

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Oral placebo once daily (QD) for 14 days	
Reporting group title	IW-9179 500 µg
Reporting group description: IW-9179 500 µg QD for 14 days	

Primary: Change From Baseline in Daily Patient Symptom Severity (PSS) Assessment During the Treatment Period: Postprandial Fullness

End point title	Change From Baseline in Daily Patient Symptom Severity (PSS) Assessment During the Treatment Period: Postprandial Fullness[1]

End point description:

PSS assessments were collected daily for the following 11 symptoms: epigastric pain, epigastric burning,epigastric bloating, postprandial fullness, early satiation, nausea, belching, heartburn, regurgitation,nonepigastric pain, and nonepigastric bloating. Subjects assessed the severity of these symptoms (with the exception of early satiation) on an 11-point (0-10) NRS, where 0 = none and 10 = very severe.Early satiation was assessed on a 5-point ordinal scale (none, mild, moderate, severe, and very severe). For each of the daily-assessed symptoms, the PSS for a specified period is the average of the non-missing scores over the treatment period.
Postprandial Fullness

End point type	Primary

End point timeframe:

Baseline, up to Day 14

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics are presented as per the protocol. The study was not powered to detect a statistically significant difference. The other 10 symptom included in the Daily PSS Assessment, are reported out under "Secondary Endpoints".

End point values	Placebo	IW-9179 500 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[2]	6[3]		
Units: units on a scale				
arithmetic mean (standard deviation)	-1.335 (± 0.641)	-2.455 (± 0.735)		

Notes:

[2] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

[3] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Average Post-Meal Symptom Severity (PMSSD) Assessment at EOT (Day 14)

End point title	Change From Baseline in Average Post-Meal Symptom Severity (PMSSD) Assessment at EOT (Day 14)

End point description:

The PMSS assesses the following 7 symptoms: epigastric pain, epigastric burning, epigastric bloating, nausea, belching, heartburn, and regurgitation. Subjects assess the severity of these meal symptoms on an 11-point (0-10) numerical rating scale (NRS), where 0 = none and 10 = very severe. The average PMSSD is obtained by averaging the PMSSDs across all post-meal time points. For each post-meal symptom, change from baseline (Day 1) to the EOT Visit (Day 14) in the average PMSSD was summarized.

End point type	Secondary

End point timeframe:

Baseline, EOT (Day 14): assessments are collected 15 minutes before the meal (t= -15 minutes), just prior to beginning to eat the meal (t=0 minutes), and then every 15 minutes after the meal for the next 4 hours.

End point values	Placebo	IW-9179 500 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[4]	3[5]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Epigastric Pain	-0.331 (± 0.928)	0.592 (± 0.797)		
Epigastric Burning	-0.805 (± 2.643)	-0.125 (± 0.116)		
Epigastric Bloating	1.419 (± 0.939)	-0.581 (± 1.402)		
Nausea	0.156 (± 0.440)	-0.370 (± 0.321)		
Belching	-0.135 (± 3.125)	-0.297 (± 0.911)		
Heartburn	-0.050 (± 0.100)	-0.051 (± 0.089)		
Regurgitation	0.963 (± 1.245)	-0.077 (± 0.133)		

Notes:

[4] - Intent-to-Treat Population: Randomized subjects with a baseline and EOT assessment.

[5] - Intent-to-Treat Population: Randomized subjects with a baseline and EOT assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Daily Patient Symptom Severity (PSS) Assessment During the Treatment Period

End point title	Change From Baseline in Daily Patient Symptom Severity (PSS) Assessment During the Treatment Period

End point description:

PSS assessments were collected daily for the following 11 symptoms: epigastric pain, epigastric burning, epigastric bloating, postprandial fullness, early satiation, nausea, belching, heartburn, regurgitation, nonepigastric pain, and nonepigastric bloating. Subjects assessed the severity of these symptoms (with the exception of early satiation) on an 11-point (0-10) NRS, where 0 = none and 10 = very severe. Early satiation was assessed on a 5-point ordinal scale (none, mild, moderate, severe, and very severe). For each of the daily-assessed symptoms, the PSS for a specified period is the average of the non-missing scores over the treatment period.

End point type	Secondary

End point timeframe:

Baseline, up to Day 14

End point values	Placebo	IW-9179 500 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[6]	6[7]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Early Fullness	-0.404 (± 0.128)	-0.913 (± 0.435)		
Epigastric Pain	-0.798 (± 0.658)	-2.293 (± 0.861)		
Epigastric Burning	-1.020 (± 1.546)	-0.365 (± 0.745)		
Epigastric Bloating	-1.029 (± 1.123)	-2.072 (± 1.794)		
Nausea	0.033 (± 0.476)	-0.613 (± 1.210)		
Belching	-1.273 (± 0.996)	-2.131 (± 1.376)		
Heartburn	-0.128 (± 0.154)	-0.133 (± 0.365)		
Regurgitation	-0.229 (± 0.741)	-0.338 (± 0.612)		
Pain Below Belly Button	-0.649 (± 1.520)	-0.673 (± 0.771)		
Bloating Below Belly Button	-0.288 (± 1.525)	-0.980 (± 0.766)		

Notes:

[6] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

[7] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Were Weekly Symptom Relief (SR) Assessment Responders at Day 7 and Day 14

End point title	Percentage of Subjects Who Were Weekly Symptom Relief (SR) Assessment Responders at Day 7 and Day 14

End point description:

Weekly SR assessments were collected on Day 7 and Day 14 of the Treatment Period. Subjects assessed their degree of relief of dyspepsia symptoms, early satiation, postprandial fullness, epigastric pain, and epigastric burning during the previous week on a 7-point balanced scale (completely relieved, considerably relieved, somewhat relieved, unchanged, somewhat worse, considerably worse, and as bad as I can imagine). For each of the 5 symptoms assessed weekly for degree of relief, an SR Responder was a subject who reported "somewhat relieved", "considerably relieved", or "completely relieved" for both weeks of the Treatment Period.

End point type	Secondary

End point timeframe:

Collected on Day 7 and Day 14 of the Treatment Period

End point values	Placebo	IW-9179 500 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[8]	6[9]		
Units: percentage of subjects				
number (not applicable)				
Dyspepsia Relief	25.0	33.3		
Early Fullness Relief	25.0	33.3		
Postprandial Fullness	25.0	33.3		
Epigastric Pain	0	33.3		
Epigastric Burning Relief	0	16.7		

Notes:

[8] - Intent-to-Treat Population: randomized subjects with an assessment at Days 7 and 14.

[9] - Intent-to-Treat Population: randomized subjects with an assessment at Days 7 and 14.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Nepean Dyspepsia Index (NDI) Questionnaire at EOT (Day 14)

End point title	Change From Baseline in Nepean Dyspepsia Index (NDI) Questionnaire at EOT (Day 14)

End point description:

Subjects completed the Nepean Dyspepsia Index (NDI) questionnaire to indicate the frequency (using a 0 [not at all] to 4 [every day/almost every day] ordinal scale), intensity (using a 0 [not at all] to 5 [very severe] ordinal scale), and bothersomeness (using a 0 [not at all] to 4 [extremely] ordinal scale) of 15 stomach problems they'd had in the last two weeks. For each stomach problem, an NDI symptom score was derived by adding the scores for frequency, intensity, and bothersomeness, for a total score range of 0 to 13 for each stomach problem, with higher scores indicating a worse problems.

End point type	Secondary

End point timeframe:

Baseline, EOT (Day 14)

End point values	Placebo	IW-9179 500 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[10]	3[11]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Epigastric Pain or Ache	-1.750 (± 2.872)	-3.000 (± 8.888)		
Epigastric Discomfort	-2.500 (± 3.317)	-3.333 (± 5.508)		
Epigastric Burning Sensation	-1.500 (± 5.745)	-0.667 (± 2.082)		
Burning Sensation in Chest	-2.000 (± 2.449)	-1.667 (± 1.528)		

Epigastric Cramps	-1.750 (± 4.573)	-2.667 (± 3.055)		
Pain or Ache in Chest	-0.500 (± 2.517)	0.000 (± 0.000)		
Inability to Finish a Regular Meal	-2.500 (± 3.109)	0.000 (± 0.000)		
Bitter/Sour Fluid in Mouth or Throat	-0.750 (± 5.377)	-1.000 (± 1.732)		
Fullness After Eating or Slow Digestion	-3.500 (± 3.873)	-6.000 (± 7.211)		
Epigastric Pressure	-0.667 (± 2.082)	-4.667 (± 4.163)		
Epigastric Bloating	-2.500 (± 4.123)	-8.500 (± 2.121)		
Nausea	-2.000 (± 3.367)	-2.000 (± 2.000)		
Burping/Belching	-2.250 (± 4.992)	-3.667 (± 5.508)		
Vomiting	0.000 (± 0.000)	-1.333 (± 2.309)		
Epigastric Bad Breath	-2.250 (± 2.872)	-2.000 (± 3.464)		

Notes:

[10] - Intent-to-Treat Population: Randomized subjects with a baseline and EOT assessment.

[11] - Intent-to-Treat Population: Randomized subjects with a baseline and EOT assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Rate of Bowel Movements (BMs) During the Treatment Period

End point title	Change From Baseline in Weekly Rate of Bowel Movements (BMs) During the Treatment Period

End point description:

BM data were collected daily. A CBM is a BM that is associated with a sense of complete evacuation.

End point type	Secondary

End point timeframe:

Baseline, End of Treatment (up to Day 14)

End point values	Placebo	IW-9179 500 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[12]	6[13]		
Units: bowel movements per week				
arithmetic mean (standard deviation)	-1.356 (± 4.874)	5.698 (± 5.831)		

Notes:

[12] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

[13] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Rate of Complete Bowel Movements (CBMs) During the Treatment Period

End point title	Change From Baseline in Weekly Rate of Complete Bowel Movements (CBMs) During the Treatment Period

End point description:

BM data were collected daily. A CBM is a BM that is associated with a sense of complete evacuation.

End point type	Secondary

End point timeframe:

Baseline, End of Treatment (up to Day 14)

End point values	Placebo	IW-9179 500 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[14]	6[15]		
Units: CBMs per week				
arithmetic mean (standard deviation)	-0.985 (± 2.025)	3.174 (± 6.674)		

Notes:

[14] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

[15] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Rate of Spontaneous Bowel Movements (SBMs) During the Treatment Period

End point title	Change From Baseline in Weekly Rate of Spontaneous Bowel Movements (SBMs) During the Treatment Period

End point description:

BM data were collected daily. An SBM is a BM that occurs in the absence of laxative, suppository, or enema use. For analysis purposes, BMs occurring within 24 hours of laxative, suppository, or enema use were not considered SBMs.

End point type	Secondary

End point timeframe:

Baseline, End of Treatment (up to Day 14)

End point values	Placebo	IW-9179 500 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[16]	6[17]		
Units: SBMs per week				
arithmetic mean (standard deviation)	-1.356 (± 4.874)	6.009 (± 6.220)		

Notes:

[16] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

[17] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Rate of Complete Spontaneous Bowel Movements (CSBMs) During the Treatment Period

End point title	Change From Baseline in Weekly Rate of Complete Spontaneous Bowel Movements (CSBMs) During the Treatment Period

End point description:

BM data were collected daily. A CSBM is an SBM that is associated with a sense of complete evacuation. An SBM is a BM that occurs in the absence of laxative, suppository, or enema use. For analysis purposes, BMs occurring within 24 hours of laxative, suppository, or enema use were not considered SBMs.

End point type	Secondary

End point timeframe:

Baseline, End of Treatment (up to Day 14)

End point values	Placebo	IW-9179 500 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[18]	6[19]		
Units: CSBMs per week				
arithmetic mean (standard deviation)	-0.985 (± 2.025)	3.485 (± 6.192)		

Notes:

[18] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

[19] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Stool Consistency, as Measured by the Bristol Stool Form Scale During the Treatment Period

End point title	Change From Baseline in Stool Consistency, as Measured by the Bristol Stool Form Scale During the Treatment Period

End point description:

Stool consistency analyses were performed using the 7-point Bristol Stool Form Scale (BSFS), whereby a score of 1 = separate hard lumps like nuts (difficult to pass); 2 = sausage shaped but lumpy; 3 = like a sausage but with cracks on surface; 4 = like a sausage or snake, smooth and soft; 5 = soft blobs with clear-cut edges (passed easily); 6 = fluffy pieces with ragged edges, a mushy stool; and 7 = watery, no solid pieces (entirely liquid).

End point type	Secondary

End point timeframe:

Baseline, End of Treatment (up to Day 14)

End point values	Placebo	IW-9179 500 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[20]	6[21]		
Units: units on a scale				
arithmetic mean (standard deviation)	0.112 (± 0.349)	2.285 (± 1.393)		

Notes:

[20] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

[21] - Intent to Treat Population: randomized subjects with a baseline and post-baseline assessment.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the Randomization Visit (Day 1) through the End-of-Study Visit (Day 22 +3 days).	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.0
Reporting groups	
Reporting group title	Placebo
Reporting group description: matching oral placebo once daily (QD) for 14 days	
Reporting group title	IW-9179 500 µg
Reporting group description: IW-9179 500 µg QD for 14 days	

Serious adverse events	Placebo	IW-9179 500 µg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	IW-9179 500 µg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	5 / 6 (83.33%)	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	4 / 6 (66.67%)	
occurrences (all)	0	4	
Abdominal Discomfort			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Gastrointestinal Sounds Abnormal			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	

Gingivitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Tendonitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 April 2013	The following changes were made to the protocol to allow for a more inclusive patient population: • Treatment group randomization will no longer be stratified on whether or not a patient is currently taking a proton pump inhibitor (PPI) at the time of the Screening Visit. Stratification will now be based on whether or not a patient is currently taking a PPI and/or a H2 receptor agonist (H2RA) at the time of the Pretreatment Visit. • Inclusion #5 was modified to remove the Rome III criteria Postprandial Distress Syndrome (PDS) and Epigastric Pain Syndrome (EPS) subgroup eligibility requirements. It now includes only the Rome III criteria for functional dyspepsia eligibility requirement. • Inclusion #7 was edited to simplify the "worst postprandial fullness" eligibility requirement. • Inclusion #8 now allows concomitant use of H2RA without any changes to the dose or frequency throughout the duration of the study. • Exclusion #1 was revised to add an average daily score for heartburn to the eligibility requirement. • Exclusion #s 8, 9, 10, and 22 were removed. • Exclusion #9 was revised to no longer require IgA and tTg testing. Patients are now excluded if diagnosed with, or suspected of having celiac disease. • Exclusion #20 was modified to allow patients who previously entered the pretreatment period to rescreen based on specific criteria and at the discretion of the Medical Monitor. Other changes made to the protocol can be summarized as follows: • The Screening Period was increased from 28 to 42 days to accommodate the scheduling of esophagogastroduodenoscopies. • Medical history will now include specific details regarding the patient's most recent test for H. pylori (if applicable) at Screening and if antibiotic treatment was given in order to collect information on whether previous H. pylori infection affects treatment response.
25 April 2013	(continued) • The serum alcohol test was moved from the Randomization Visit to the Pretreatment Visit in order to obtain the results prior to Randomization. • The Meal Challenge Test may be waived after discussion with the Medical Monitor if the patient prefers not to complete it. Patients that do not complete the Meal Challenge Test at the Randomization Visit will not undergo this test at the End-of-treatment Visit. This option was included due to the time commitment involved with performing the procedure. • Benzodiazepenes were added to the Prohibited Medications list (Appendix 1) due to their potential effects on endpoint measurements and usual use in a non-stable dosing regiment (i.e. "as needed" use). • Updated the Medical Monitor and associated contact details due to a change in staffing. • Minor administrative changes were made that do not affect the conduct of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported