Clinical trial results:
A Pharmacokinetic and Safety Study of Single and Multiple Doses of Rabeprazole in Pediatric Subjects with Gastroesophageal reflux disease (GERD) 1 to 11 Years old, inclusive

Summary

EudraCT number	2008-000451-97
Trial protocol	BE
Global end of trial date	16 September 2009

Results information

Result version number	v1 (current)
This version publication date	01 July 2016
First version publication date	01 July 2016

Trial information

Trial identification

Sponsor protocol code	RABGRD1002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00747695
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Johnson & Johnson Pharmaceutical Research & Development, LLC
Sponsor organisation address	920 US Route 202 Raritan, New Jersey, United States,
Public contact	Clinical Registry Group, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000055-PIP01-07
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 September 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 September 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the study was to evaluate the pharmacokinetics (PK), pharmacodynamics (PD, clinical global impressions [CGI] and formulation palatability) and safety of rabeprazole after single and multiple daily administration at 2 dose levels in children between the ages of 1 to 11 years, inclusive (up to 11 years 364 days), with Gastroesophageal Reflux Disease (GERD). As this study is an exploratory assessment of the pharmacokinetics, pharmacodynamics, and safety of rabeprazole in children, no formal hypothesis testing is applied.

Protection of trial subjects:

Safety evaluations were performed in reference to adverse events, clinical laboratory tests (serum chemistry and hematology), vital signs (blood pressure, pulse, respiratory rate, temperature), electrocardiogram (ECG) and physical examinations including height/length and body weight was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 March 2008
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: 3
Country: Number of subjects enrolled	United States: 25
Worldwide total number of subjects	28
EEA total number of subjects	3

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)	28
Adolescents (12-17 years)	0

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

Subject disposition

Recruitment

Recruitment details:

Total 28 subjects were enrolled in the study, out of which 27 subjects completed the study.

Pre-assignment

Screening details:

Screening of up to 21 days was done in which medical history and evaluation of symptoms were recorded before the beginning of treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Rabeprazole 0.14 milligram per kilogram (mg/kg)

Arm description:

Subjects received rabeprazole sodium 0.14 mg/kg of body weight as single daily oral doses for 5 successive days as a bead formulation.

Arm type	Experimental
Investigational medicinal product name	Rabeprazole Sodium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received rabeprazole sodium 0.14 mg/kg as single daily oral doses for 5 successive days as a bead formulation.

Arm title	Rabeprazole 1.0 mg/kg

Arm description:

Subjects received rabeprazole sodium 1.0 mg/kg as single daily oral doses for 5 successive days as a bead formulation.

Arm type	Experimental
Investigational medicinal product name	Rabeprazole Sodium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received rabeprazole sodium 1.0 mg/kg as single daily oral doses for 5 successive days as a bead formulation.

Arm title	Rabeprazole 0.5 mg/kg

Arm description:

Subjects received rabeprazole sodium 0.5 mg/kg as single daily oral doses for 5 successive days as a bead formulation.

Arm type	Experimental

Investigational medicinal product name	Rabeprazole Sodium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received rabeprazole sodium 0.5 mg/kg as single daily oral doses for 5 successive days as a bead formulation.

Number of subjects in period 1	Rabeprazole 0.14 milligram per kilogram (mg/kg)	Rabeprazole 1.0 mg/kg	Rabeprazole 0.5 mg/kg
Started	8	9	11
Completed	8	9	10
Not completed	0	0	1
Adverse event, non-fatal	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Rabeprazole 0.14 milligram per kilogram (mg/kg)
Reporting group description:	
Subjects received rabeprazole sodium 0.14 mg/kg of body weight as single daily oral doses for 5 successive days as a bead formulation.	
Reporting group title	Rabeprazole 0.5 mg/kg
Reporting group description:	
Subjects received rabeprazole sodium 0.5 mg/kg as single daily oral doses for 5 successive days as a bead formulation.	
Reporting group title	Rabeprazole 1.0 mg/kg
Reporting group description:	
Subjects received rabeprazole sodium 1.0 mg/kg as single daily oral doses for 5 successive days as a bead formulation.	

Reporting group values	Rabeprazole 0.14 milligram per kilogram (mg/kg)	Rabeprazole 0.5 mg/kg	Rabeprazole 1.0 mg/kg
Number of subjects	8	11	9
Title for AgeCategorical Units: subjects			
Children (1-11 years)	8	11	9
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	7.5	6.6	6.1
standard deviation	± 3.74	± 3.85	± 3.86
Title for Gender Units: subjects			
Female	3	4	5
Male	5	7	4

Reporting group values	Total		
Number of subjects	28		
Title for AgeCategorical Units: subjects			
Children (1-11 years)	28		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65 to 84 years	0		
85 years and over	0		
Title for AgeContinuous Units: years			
arithmetic mean			
standard deviation	-		

Title for Gender Units: subjects			
Female	12		
Male	16		

End points

End points reporting groups

Reporting group title	Rabeprazole 0.14 milligram per kilogram (mg/kg)
Reporting group description:	
Subjects received rabeprazole sodium 0.14 mg/kg of body weight as single daily oral doses for 5 successive days as a bead formulation.	
Reporting group title	Rabeprazole 1.0 mg/kg
Reporting group description:	
Subjects received rabeprazole sodium 1.0 mg/kg as single daily oral doses for 5 successive days as a bead formulation.	
Reporting group title	Rabeprazole 0.5 mg/kg
Reporting group description:	
Subjects received rabeprazole sodium 0.5 mg/kg as single daily oral doses for 5 successive days as a bead formulation.	

Primary: Maximum Observed Plasma Concentration (Cmax) of Rabeprazole

End point title	Maximum Observed Plasma Concentration (Cmax) of Rabeprazole[1]
End point description:	
The Cmax is the maximum observed plasma concentration. Here 'n' is equal to number of subjects analyzed for this endpoint at specific time point.	
End point type	Primary
End point timeframe:	
Day 1 and 5	

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: Statistical analysis were not planned to be reported.

End point values	Rabeprazole 0.14 milligram per kilogram (mg/kg)	Rabeprazole 0.5 mg/kg	Rabeprazole 1.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[2]	10[3]	9[4]	
Units: Nanogram per millilitre (ng/ml)				
arithmetic mean (full range (min-max))				
Day 1 (n=7, 10, 7)	2 (1 to 6)	2 (1 to 5.98)	2 (1 to 4)	
Day 5 (n=8, 10, 9)	2 (1 to 4)	1.53 (1 to 2.08)	2 (0.68 to 4)	

Notes:

[2] - Pharmacokinetic Analysis Set

[3] - Pharmacokinetic Analysis Set

[4] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-Time Curve From Time Zero to Time of the Last Quantifiable Concentration (AUClast) of Rabeprazole

End point title	Area Under the Plasma Concentration-Time Curve From Time Zero to Time of the Last Quantifiable Concentration (AUClast) of Rabeprazole[5]

End point description:

AUC(last) is area under the plasma concentration-time curve from time zero to last quantifiable time, C(last) is the last observed quantifiable concentration, and lambda(z) is elimination rate constant. Here 'n' is equal to number of subjects analyzed for this endpoint at specific time point.

End point type	Primary

End point timeframe:

Day 1 and 5

Notes:

[5] - 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: Statistical analysis were not planned to be reported.

End point values	Rabeprazole 0.14 milligram per kilogram (mg/kg)	Rabeprazole 0.5 mg/kg	Rabeprazole 1.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[6]	10[7]	9[8]	
Units: hour*nanogram per millilitre (h.ng/ml)				
arithmetic mean (standard deviation)				
Day 1 (n=3, 9, 7)	169 (± 98.4)	309 (± 78.2)	694 (± 519)	
Day 5 (n=4, 9, 9)	142 (± 57.6)	419 (± 234)	869 (± 579)	

Notes:

[6] - Pharmacokinetic Analysis Set

[7] - Pharmacokinetic Analysis Set

[8] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-Time Curve From Time 0 to the Last Sampling Point (i.e, 12 Hours)of Rabeprazole

End point title	Area Under the Plasma Concentration-Time Curve From Time 0 to the Last Sampling Point (i.e, 12 Hours)of Rabeprazole[9]

End point description:

AUCall is the Area under the plasma concentration-time curve from time 0 to the last sampling point (i.e. 12 hours). Here 'n' is equal to number of subjects analyzed for this endpoint at specific time point.

End point type	Primary

End point timeframe:

Day 1 and 5

Notes:

[9] - 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: Statistical analysis were not planned to be reported.

End point values	Rabeprazole 0.14 milligram per kilogram (mg/kg)	Rabeprazole 0.5 mg/kg	Rabeprazole 1.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[10]	10[11]	9[12]	
Units: h.ng/ml				
arithmetic mean (standard deviation)				
Day 1 (n=3, 5, 7)	181 (± 101)	337 (± 94.1)	716 (± 505)	
Day 5 (n=4, 9, 9)	157 (± 50.4)	429 (± 232)	884 (± 579)	

Notes:

[10] - Pharmacokinetic Analysis Set

[11] - Pharmacokinetic Analysis Set

[12] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-Time Curve From Time 0 to Infinite

End point title	Area Under the Plasma Concentration-Time Curve From Time 0 to Infinite[13]

End point description:

The AUC (0 - infinity) is the area under the plasma concentration-time curve from time zero to infinite time, calculated as the sum of AUC(last) and C(last)/lambda(z). Here 'n' is equal to number of subjects analyzed for this endpoint at specific time point. Standard deviation (SD) for group rabeprazole 0.14 mg/kg was not estimable because only subject was analyzed at day 1 for this end point. Therefore, value mentioned for SD i.e. 99999= NA (Not Applicable). Similarly mean value for group rabeprazole 0.14 mg/kg at day 5 i.e. 999= 185, 224 because only two subjects was analyzed for this endpoint.

End point type	Primary

End point timeframe:

Day 1 and 5

Notes:

[13] - 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: Statistical analysis were not planned to be reported.

End point values	Rabeprazole 0.14 milligram per kilogram (mg/kg)	Rabeprazole 0.5 mg/kg	Rabeprazole 1.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[14]	10[15]	9[16]	
Units: h.ng/mL				
arithmetic mean (standard deviation)				
Day 1(n=1, 5, 6)	261 (± 99999)	346 (± 77.9)	785 (± 526)	
Day 5(n=2, 6, 7)	999 (± 21.6)	490 (± 263)	936 (± 600)	

Notes:

[14] - Pharmacokinetic Analysis Set

[15] - Pharmacokinetic Analysis Set

[16] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Decay Half-Life (t1/2) of Rabeprazole

End point title	Plasma Decay Half-Life (t1/2) of Rabeprazole[17]

End point description:

The t1/2 is the time measured for the plasma concentration to decrease by 1 half to its original concentration. It is associated with the terminal slope of the semi logarithmic drug concentration-time curve, and is calculated as 0.693/lambda(z). Here 'n' is equal to number of subjects analyzed for this endpoint at specific time point. Standard deviation (SD) for group rabeprazole 0.14 mg/kg was not estimable because only subject was analyzed at day 1 and 2 subjects at day 5 for this end point. Therefore, value mentioned for SD i.e. 99999= NA (Not Applicable). Similarly mean value for group rabeprazole 0.14 mg/kg at day 5 i.e. 999= 1.2, 1.4 because only two subjects was analyzed for this endpoint.

End point type	Primary

End point timeframe:

Day 1 and 5

Notes:

[17] - 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: Statistical analysis were not planned to be reported.

End point values	Rabeprazole 0.14 milligram per kilogram (mg/kg)	Rabeprazole 0.5 mg/kg	Rabeprazole 1.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[18]	10[19]	9[20]	
Units: hour				
arithmetic mean (standard deviation)				
Day 1(n=1, 5, 6)	1.3 (± 99999)	1.3 (± 0.4)	1.9 (± 1)	
Day 5(n=2, 6, 7)	999 (± 99999)	1.1 (± 0.4)	1.2 (± 0.6)	

Notes:

[18] - Pharmacokinetic Analysis Set

[19] - Pharmacokinetic Analysis Set

[20] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Ratio of AUCall values on Day 5 versus Day 1 of Rabeprazole

End point title	Ratio of AUCall values on Day 5 versus Day 1 of Rabeprazole[21]

End point description:

AURACall calculated as the ratio of AUCall values on Day 5 versus Day 1 for each subject. Here 'n' is equal to number of subjects analyzed for this endpoint at specific time point. Mean value and standard deviation (SD) for groups rabeprazole 0.14 mg/kg, 0.5 mg/kg and 1 mg/kg were not estimable because zero subject was analyzed at day 1 for this end point. Therefore, value mentioned for mean i.e. 999 and SD i.e. 99999= NA (Not Applicable).

End point type	Primary

End point timeframe:

Day 1 and 5

Notes:

[21] - 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: Statistical analysis were not planned to be reported.

End point values	Rabeprazole 0.14 milligram per kilogram (mg/kg)	Rabeprazole 0.5 mg/kg	Rabeprazole 1.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[22]	10[23]	9[24]	
Units: h.ng/mL				
arithmetic mean (standard deviation)				
Day 1(n=0, 0, 0)	999 (± 99999)	999 (± 99999)	999 (± 99999)	
Day 5(n=3, 7, 7)	1.23 (± 0.69)	1.16 (± 0.49)	1.39 (± 0.83)	

Notes:

[22] - Pharmacokinetic Analysis Set

[23] - Pharmacokinetic Analysis Set

[24] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subject with Clinical Global Impression - Severity of Illness Subscale (CGI-S)

End point title	Percentage of Subject with Clinical Global Impression - Severity of Illness Subscale (CGI-S)

End point description:

The Clinical Global Impression Severity (CGI-S) rating scale is a 7 point global assessment that measures the clinician's impression of the severity of illness exhibited by a participant. A rating of 1 is equivalent to "Normal, not at all ill" and a rating of 7 is equivalent to "Among the most extremely ill participants". Higher scores indicate worsening.

End point type	Secondary

End point timeframe:

Baseline

End point values	Rabeprazole 0.14 milligram per kilogram (mg/kg)	Rabeprazole 0.5 mg/kg	Rabeprazole 1.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	11	9	
Units: Percentage of Subjects				
number (not applicable)				
Mildly ill	5	6	5	
Moderately ill	3	4	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subject with Clinical Global Impression - Global

End point title	Percentage of Subject with Clinical Global Impression - Global

End point description:

The Clinical Global Impression-Change (CGI-C) rating scale is used to rate the change in severity of the Participant's illness compared to baseline on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse).

End point type	Secondary

End point timeframe:

End of Study or Early Withdrawal

End point values	Rabeprazole 0.14 milligram per kilogram (mg/kg)	Rabeprazole 0.5 mg/kg	Rabeprazole 1.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	11	9	
Units: Percentage of subjects				
number (not applicable)				
Very much improved	2	2	0	
Much improved	4	7	6	
Minimally improved	1	1	2	
No change	0	1	1	
Minimally worse	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subject with Global assessment of effectiveness

End point title	Percentage of Subject with Global assessment of effectiveness

End point description:

End point type	Secondary

End point timeframe:

End of study of Early Withdrawal

End point values	Rabeprazole 0.14 milligram per kilogram (mg/kg)	Rabeprazole 0.5 mg/kg	Rabeprazole 1.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	11	9	
Units: Percentage of subjects				
number (not applicable)				
Poor	1	0	0	
Fair	0	2	0	
Good	3	6	6	
Excellent	4	3	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who found Palatibilty of Drug Good of Excellent

End point title	Number of Subjects who found Palatibilty of Drug Good of Excellent

End point description:

End point type	Secondary

End point timeframe:

Day 1, 2, 3, 4, and 5

End point values	Rabeprazole 0.14 milligram per kilogram (mg/kg)	Rabeprazole 0.5 mg/kg	Rabeprazole 1.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	11	9	
Units: Number of Subject				
number (not applicable)				
Day 1: Good	5	2	3	
Day 1: Excellent	1	4	4	
Day 2: Good	7	2	4	
Day 2: Excellent	1	4	4	
Day 3: Good	3	2	4	
Day 3: Excellent	3	4	5	
Day 4: Good	5	2	3	
Day 4: Excellent	2	4	5	
Day 5: Good	4	3	4	
Day 5: Excellent	3	4	5	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to End of Study (Day 5)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups	
Reporting group title	Rabeprazole 0.14 mg/kg
Reporting group description:	
Subjects received rabeprazole sodium 0.14 mg/kg of body weight as single daily oral doses for 5 successive days as a bead formulation.	
Reporting group title	Rabeprazole 1.0 mg/kg
Reporting group description:	
Subjects received rabeprazole sodium 1.0 mg/kg as single daily oral doses for 5 successive days as a bead formulation.	
Reporting group title	Rabeprazole 0.5 mg/kg
Reporting group description:	
Subjects received rabeprazole sodium 0.5 mg/kg as single daily oral doses for 5 successive days as a bead formulation.	

Serious adverse events	Rabeprazole 0.14 mg/kg	Rabeprazole 1.0 mg/kg	Rabeprazole 0.5 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 11 (9.09%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Volvulus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Rabeprazole 0.14 mg/kg	Rabeprazole 1.0 mg/kg	Rabeprazole 0.5 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 8 (62.50%)	7 / 9 (77.78%)	9 / 11 (81.82%)
Investigations			

Blood Gastrin Increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Blood Uric Acid Increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Haemoglobin Decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Cardiac Murmur			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Arthropod Bite			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Excoriation			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 11 (0.00%)
occurrences (all)	0	2	0

Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	2 / 8 (25.00%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Abdominal Pain Upper			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hypergastrinaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pancreatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Regurgitation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	3 / 11 (27.27%)
occurrences (all)	0	0	3
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal			

disorders			
Asthma			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	1 / 11 (9.09%)
occurrences (all)	0	2	1
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Gastritis Viral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pharyngitis Streptococcal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypernatraemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 October 2007	The following major changes were made in the first amendment of protocol: Paper CRF was replaced by eCRF as data were collected electronically. Correction was made to indicate the randomization system. The time and events schedule was updated to reflect changes in PK sample collection, fasting gastrin, and screening physical examination and ECG collection. Total blood volume to be collected was updated. The minimum body weight for enrollment was updated. Updated to indicate the correct laboratory.
02 January 2008	The second amendment was released in order to facilitate enrollment, the requirement for an overnight stay at the study center was made optional.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported