Clinical trial results:
A Pharmacokinetic, Pharmacodynamic and Safety Study of Single and Multiple Doses of Rabeprazole in Pediatric Subjects with Gastroesophageal Reflux Disease (GERD) 1 to 11 Months old, Inclusive

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2008-000452-27
Trial protocol	BE GB
Global end of trial date	29 February 2012

Results information

Result version number	v2 (current)
This version publication date	01 July 2016
First version publication date	05 August 2015
Version creation reason	• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	RABGRD1003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00747526
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, L.L.C.
Sponsor organisation address	920 Route 202, PO Box 300,, Raritan, New Jersey, United States, 08869
Public contact	Clinical Registry Group, Clinical Registry Group, +31 71524 21 66, ClinicalTrialsEU@its.jnj.com
Scientific contact	Janssen-Cilag International NV, Janssen-Cilag International NV, +31 71524 21 66, 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	29 February 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 February 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this trial is to evaluate the pharmacokinetics, pharmacodynamics (intraesophageal/intragastric pH, clinical global impressions, formulation palatability and GERD daily symptom diary) and safety of Rabeprazole (RAB) after single and multiple daily administration at 2 dose levels in children between the ages of 1 and 11 months (inclusive up to 11 months 29 days), with GERD. As this 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 was assessed through monitoring of concomitant therapies and adverse events (AEs) throughout the study; and clinical laboratory testing at baseline and post treatment including hematology, clinical chemistry, and urinalysis assessment. Vital signs, 12-lead electrocardiogram, and physical examination including body weight and length were also performed before and after treatment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 April 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	Brazil: 6
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	United States: 28
Worldwide total number of subjects	49
EEA total number of subjects	15

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	49
Children (2-11 years)	0
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:

The study was initiated from 14 April 2008 and completed on 29 February 2012 in which subjects from 5 countries were enrolled.

Pre-assignment

Screening details:

A total 49 subjects were enrolled in the study out of these 47 subjects completed the study and 2 subjects withdrew the study.

Period 1

Period 1 title	Open Label Treatment Phase (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	Part 1 - Rabeprazole 0.14 milligram per kilogram (mg/kg)

Arm description:

Subject received Rabeprazole 0.14 milligram/kilogram (mg/kg) of body weight capsule orally.

Arm type	Experimental
Investigational medicinal product name	Rabeprazole Sodium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subject received Rabeprazole 0.14 milligram/kilogram (mg/kg) of body weight capsule orally.

Arm title	Part 1 - Rabeprazole 0.5 mg/kg

Arm description:

Subject received Rabeprazole 0.5 mg/kg of body weight capsule orally.

Arm type	Experimental
Investigational medicinal product name	Rabeprazole Sodium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subject received Rabeprazole 0.5 mg/kg of body weight capsule orally.

Arm title	Part 2 - Rabeprazole 5 mg

Arm description:

Subject received Rabeprazole 5 mg capsule orally.

Arm type	Experimental
Investigational medicinal product name	Rabeprazole Sodium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
Subject received Rabeprazole 5 mg capsule orally.

Arm title	Part 2 - Rabeprazole 10 mg

Arm description:
Subject received Rabeprazole 10 mg capsule orally.

Arm type	Experimental
Investigational medicinal product name	Rabeprazole Sodium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
Subject received Rabeprazole 10 mg capsule orally.

Arm title	Part 2 - Placebo

Arm description:
Subject received the Placebo matching with Rabeprazole.

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

Dosage and administration details:
Subject received the matched modal dose of Placebo

Arm title	Part 2 - Placebo + Rabeprazole 5 mg

Arm description:
Subject received oral capsule of Placebo in combination with Rabeprazole 5 mg capsule orally.

Arm type	Experimental
Investigational medicinal product name	Rabeprazole Sodium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
Subject received orally Rabeprazole 5 mg capsule orally.

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

Dosage and administration details:
Subject received matched dose of oral capsule of Placebo

Number of subjects in period 1	Part 1 - Rabeprazole 0.14 milligram per kilogram (mg/kg)	Part 1 - Rabeprazole 0.5 mg/kg	Part 2 - Rabeprazole 5 mg
Started	2	10	9
Completed	2	10	9
Not completed	0	0	0
Adverse event, serious non-fatal	-	-	-
Lack of efficacy	-	-	-

Number of subjects in period 1	Part 2 - Rabeprazole 10 mg	Part 2 - Placebo	Part 2 - Placebo + Rabeprazole 5 mg
Started	9	18	1
Completed	9	16	1
Not completed	0	2	0
Adverse event, serious non-fatal	-	1	-
Lack of efficacy	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Part 1 - Rabeprazole 0.14 milligram per kilogram (mg/kg)
Reporting group description:	
Subject received Rabeprazole 0.14 milligram/kilogram (mg/kg) of body weight capsule orally.	
Reporting group title	Part 1 - Rabeprazole 0.5 mg/kg
Reporting group description:	
Subject received Rabeprazole 0.5 mg/kg of body weight capsule orally.	
Reporting group title	Part 2 - Rabeprazole 5 mg
Reporting group description:	
Subject received Rabeprazole 5 mg capsule orally.	
Reporting group title	Part 2 - Rabeprazole 10 mg
Reporting group description:	
Subject received Rabeprazole 10 mg capsule orally.	
Reporting group title	Part 2 - Placebo
Reporting group description:	
Subject received the Placebo matching with Rabeprazole.	
Reporting group title	Part 2 - Placebo + Rabeprazole 5 mg
Reporting group description:	
Subject received oral capsule of Placebo in combination with Rabeprazole 5 mg capsule orally.	

Reporting group values	Part 1 - Rabeprazole 0.14 milligram per kilogram (mg/kg)	Part 1 - Rabeprazole 0.5 mg/kg	Part 2 - Rabeprazole 5 mg
Number of subjects	2	10	9
Title for AgeCategorical			
Units: subjects			
Infants and Toddlers (28 days - 23 months)	2	10	9
Title for AgeContinuous			
Units: months			
arithmetic mean	5	6.5	5.6
standard deviation	± 4.24	± 2.55	± 3.13
Title for Gender			
Units: subjects			
Female	0	7	3
Male	2	3	6

Reporting group values	Part 2 - Rabeprazole 10 mg	Part 2 - Placebo	Part 2 - Placebo + Rabeprazole 5 mg
Number of subjects	9	18	1
Title for AgeCategorical			
Units: subjects			
Infants and Toddlers (28 days - 23 months)	9	18	1
Title for AgeContinuous			
Units: months			
arithmetic mean	4.4	4.8	1
standard deviation	± 2.83	± 2.73	± 0

Title for Gender Units: subjects			
Female	3	8	1
Male	6	10	0

Reporting group values	Total		
Number of subjects	49		
Title for AgeCategorical Units: subjects			
Infants and Toddlers (28 days - 23 months)	49		
Title for AgeContinuous Units: months arithmetic mean standard deviation	--		
Title for Gender Units: subjects			
Female	22		
Male	27		

End points

End points reporting groups

Reporting group title	Part 1 - Rabeprazole 0.14 milligram per kilogram (mg/kg)
Reporting group description: Subject received Rabeprazole 0.14 milligram/kilogram (mg/kg) of body weight capsule orally.	
Reporting group title	Part 1 - Rabeprazole 0.5 mg/kg
Reporting group description: Subject received Rabeprazole 0.5 mg/kg of body weight capsule orally.	
Reporting group title	Part 2 - Rabeprazole 5 mg
Reporting group description: Subject received Rabeprazole 5 mg capsule orally.	
Reporting group title	Part 2 - Rabeprazole 10 mg
Reporting group description: Subject received Rabeprazole 10 mg capsule orally.	
Reporting group title	Part 2 - Placebo
Reporting group description: Subject received the Placebo matching with Rabeprazole.	
Reporting group title	Part 2 - Placebo + Rabeprazole 5 mg
Reporting group description: Subject received oral capsule of Placebo in combination with Rabeprazole 5 mg capsule orally.	
Subject analysis set title	Safety Analysis Population
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects who were randomized and received at least 1 dose of study drug.	
Subject analysis set title	Pharmacodynamic Analysis Population
Subject analysis set type	Sub-group analysis
Subject analysis set description: All subjects who were randomized, received study drug, and had at least one PD measurement.	
Subject analysis set title	pH Analysis Set
Subject analysis set type	Sub-group analysis
Subject analysis set description: All subjects who were randomized, received study drug, and had pH measurements for at least one day.	

Primary: Maximum Observed Plasma Concentration (Cmax)

End point title	Maximum Observed Plasma Concentration (Cmax)[1]
End point description:	
End point type	Primary
End point timeframe: Baseline up to day 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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Part 1 - Rabeprazole 0.14 milligram per kilogram (mg/kg)	Part 1 - Rabeprazole 0.5 mg/kg	Part 2 - Rabeprazole 5 mg	Part 2 - Rabeprazole 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	0[3]	0[4]	0[5]
Units: nanogram per milliliter (ng/ml)				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[2] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

[3] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

[4] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

[5] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

End point values	Part 2 - Placebo	Part 2 - Placebo + Rabeprazole 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: nanogram per milliliter (ng/ml)				
arithmetic mean (standard deviation)	()	()		

Notes:

[6] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

[7] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Maximum Observed Plasma Concentration (Tmax)

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax)[8]

End point description:

End point type	Primary

End point timeframe:

Baseline up to Day 5

Notes:

[8] - 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 were done, no inferential statistical analyses were performed

End point values	Part 1 - Rabeprazole 0.14 milligram per kilogram (mg/kg)	Part 1 - Rabeprazole 0.5 mg/kg	Part 2 - Rabeprazole 5 mg	Part 2 - Rabeprazole 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[9]	0[10]	0[11]	0[12]
Units: Hours				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[9] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

[10] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

[11] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

[12] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

End point values	Part 2 - Placebo	Part 2 - Placebo + Rabeprazole 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[13]	0[14]		
Units: Hours				
median (full range (min-max))	(to)	(to)		

Notes:

[13] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

[14] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

Statistical analyses

No statistical analyses for this end point

Primary: Dose Normalized Area Under the Plasma Concentration-Time Curve From Time Zero to Last Quantifiable Time (AUC [0-last]) of Rabeprezole

End point title	Dose Normalized Area Under the Plasma Concentration-Time Curve From Time Zero to Last Quantifiable Time (AUC [0-last]) of Rabeprezole[15]

End point description:

End point type	Primary

End point timeframe:

Day 1 and Day 5

Notes:

[15] - 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 were done, no inferential statistical analyses were performed

End point values	Part 1 - Rabeprazole 0.14 milligram per kilogram (mg/kg)	Part 1 - Rabeprazole 0.5 mg/kg	Part 2 - Rabeprazole 5 mg	Part 2 - Rabeprazole 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[16]	0[17]	0[18]	0[19]
Units: nanogram*hour per milliliter				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[16] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

[17] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

[18] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

[19] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

End point values	Part 2 - Placebo	Part 2 - Placebo + Rabeprazole 5 mg		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[20]	0[21]		
Units: nanogram*hour per milliliter				
arithmetic mean (standard deviation)	()	()		

Notes:

[20] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

[21] - No descriptive statistics of pharmacokinetic data was performed due to small number of subjects.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage Duration With An Intragastric pH

End point title	Percentage Duration With An Intragastric pH[22]

End point description:

End point type	Primary

End point timeframe:

Day 1 and Day 5

Notes:

[22] - 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 were done, no inferential statistical analyses were performed

End point values	pH Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	15[23]			
Units: Percentage of Time in a 24 Hour Period				
arithmetic mean (standard deviation)				
Day 1: Intragastric pH<4	69.894 (± 28.5873)			
Day 5: Intragastric pH<4	68.49 (± 26.056)			
Day 1: Intragastric pH<3	60.84 (± 57.367)			
Day 5: Intragastric pH<5	28.7609 (± 24.9894)			

Notes:

[23] - pH analysis set.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage Duration With An Intraesophageal pH

End point title	Percentage Duration With An Intraesophageal pH[24]

End point description:

End point type	Primary

End point timeframe:

Day 1 and Day 5

Notes:

[24] - 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 were done, no inferential statistical analyses were performed

End point values	pH Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: Percentage of Time in a 24 Hour Period				
arithmetic mean (standard deviation)				
Day 1	12.853 (± 19.3117)			
Day 5	10.027 (± 20.9011)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Clinical Global Impression Severity (CGI-S) Score

End point title	Percentage of Subjects With Clinical Global Impression Severity (CGI-S) Score [25]

End point description:

The Clinical Global Impression Severity (CGI-S) rating scale is a 7 point (1-absent, 2-minimal, 3-mild, 4-moderate, 5-moderate severe, 6-severe, 7-extreme) 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	Primary

End point timeframe:

At Baseline

Notes:

[25] - 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 were done, no inferential statistical analyses were performed

End point values	Part 1 - Rabeprazole 0.14 milligram per kilogram (mg/kg)	Part 1 - Rabeprazole 0.5 mg/kg	Part 2 - Rabeprazole 5 mg	Part 2 - Rabeprazole 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	10	9	9
Units: Percentage of Subjects				
number (not applicable)				
Normal, not at all ill	1	1	0	0
Borderline ill	0	1	0	1
Mildly ill	0	0	3	4
Moderately ill	1	5	4	2
Markedly ill	0	3	0	2
Severely ill	0	0	2	0

End point values	Part 2 - Placebo	Part 2 - Placebo + Rabeprazole 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	1		
Units: Percentage of Subjects				
number (not applicable)				
Normal, not at all ill	3	0		
Borderline ill	5	0		
Mildly ill	2	0		
Moderately ill	5	0		
Markedly ill	3	1		
Severely ill	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Categorical Scores on Clinical Global Impression of Severity (CGI-S)

End point title	Percentage of Participants With Categorical Scores on Clinical Global Impression of Severity (CGI-S)[26]

End point description:

The Clinical Global Impression (CGI) rating scale is a 7-point global assessment that measures the clinician's impression of the severity of illness exhibited by a participant, which ranges from "very much worse" to "very much improved".

End point type	Primary

End point timeframe:

End of study

Notes:

[26] - 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 were done, no inferential statistical analyses were performed

End point values	Part 1 - Rabeprazole 0.14 milligram per kilogram (mg/kg)	Part 1 - Rabeprazole 0.5 mg/kg	Part 2 - Rabeprazole 5 mg	Part 2 - Rabeprazole 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	10	9	9
Units: Percentage of Subjects				
number (not applicable)				
Much improved	0	0	0	0
Minimally improved	0	0	0	1
No change	1	0	0	0

End point values	Part 2 - Placebo	Part 2 - Placebo + Rabeprazole 5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	1		
Units: Percentage of Subjects				
number (not applicable)				
Much improved	1	1		
Minimally improved	0	0		
No change	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with the Palatability Scores on Day 1 and Day 5

End point title	Number of subjects with the Palatability Scores on Day 1 and Day 5[27]

End point description:

End point type	Primary

End point timeframe:

Day 1 and Day 5

Notes:

[27] - 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 were done, no inferential statistical analyses were performed

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in the Total gastroesophageal reflux disease (GERD) Symptom and Severity Score at Day 5

End point title	Change From Baseline in the Total gastroesophageal reflux disease (GERD) Symptom and Severity Score at Day 5[28]

End point description:

The gastroesophageal reflux disease (GERD) symptom and severity scale measures the frequency (0= Never; 1= 1-2 times; 2= 3-4 times; 3= 5-6 times; 4= 7 or more times) and the severity (1= Mild; 2= Moderate; 3=Severe) of GERD symptoms. The score is defined as the sum of the frequency (0-4) and severity (1-3) of that symptom. The total score is the sum of the scores of all the symptoms and ranges

from 12 to 84. Higher scores indicate more serious condition. For change from baseline, 0 indicates no change; a positive score indicates worsening, while a negative score indicates improvement.

End point type	Primary

End point timeframe:

Day 1 and Day 5

Notes:

[28] - 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 were done, no inferential statistical analyses were performed

End point values	Pharmacodynamic Analysis Population			
Subject group type	Subject analysis set			
Number of subjects analysed	49			
Units: units on a scale				
arithmetic mean (standard deviation)				
Day 1: Times baby regurgitate	2.55 (± 3.156)			
Day 5: Times baby regurgitate	2.35 (± 3.035)			
Day 1: Hours or minutes baby cry or fuss	1.28 (± 2.03)			
Day 5: Hours or minutes baby cry or fuss	0.88 (± 1.658)			
Day 1: Times baby have episodes or arching back	1.86 (± 3.397)			
Day 5: Times baby have episodes or arching back	1.17 (± 2.461)			
Day 1: Times baby cry during a feeding	0.69 (± 1.262)			
Day 5: Times baby cry during a feeding	0.29 (± 0.617)			

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	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1
Reporting groups	
Reporting group title	Part 1 - Rabeprazole 0.14 milligram per kilogram (mg/kg)
Reporting group description: Subject received Rabeprazole 0.14 milligram/kilogram (mg/kg) of body weight capsule orally.	
Reporting group title	Part 1 - Rabeprazole 0.5 mg/kg
Reporting group description: Subject received Rabeprazole 0.5 mg/kg of body weight capsule orally.	
Reporting group title	Part 2 - Placebo
Reporting group description: Subject received the Placebo matching with Rabeprazole.	
Reporting group title	Part 2 - Rabeprazole 10 mg
Reporting group description: Subject received Rabeprazole 10 mg capsule orally.	
Reporting group title	Part 2 - Placebo + Rabeprazole 5 mg
Reporting group description: Subject received oral capsule of Placebo in combination with Rabeprazole 5 mg capsule orally.	
Reporting group title	Part 2 - Rabeprazole 5 mg
Reporting group description: Subject received Rabeprazole 5 mg capsule orally.	

Serious adverse events	Part 1 - Rabeprazole 0.14 milligram per kilogram (mg/kg)	Part 1 - Rabeprazole 0.5 mg/kg	Part 2 - Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	0 / 10 (0.00%)	2 / 18 (11.11%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			

subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Respiratory Syncytial Virus Bronchiolitis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Feeding Disorder			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2 - Rabeprazole 10 mg	Part 2 - Placebo + Rabeprazole 5 mg	Part 2 - Rabeprazole 5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	1 / 9 (11.11%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Respiratory Syncytial Virus Bronchiolitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Feeding Disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	1 / 9 (11.11%)
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	Part 1 - Rabeprazole 0.14 milligram per kilogram (mg/kg)	Part 1 - Rabeprazole 0.5 mg/kg	Part 2 - Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	6 / 10 (60.00%)	8 / 18 (44.44%)
Investigations			
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood Gastrin Increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cardiac Murmur			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Platelet Count Increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Cyanosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Mass			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pyrexia			

subjects affected / exposed	0 / 2 (0.00%)	1 / 10 (10.00%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Eye disorders			
Eye Discharge			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Eye Swelling			
subjects affected / exposed	0 / 2 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	2 / 10 (20.00%)	1 / 18 (5.56%)
occurrences (all)	0	2	2
Haematemesis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Nasal Obstruction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Rhinitis Allergic			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	1 / 2 (50.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 2 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0

Rash Maculo-Papular			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Diarrhoea Infectious			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Gastroenteritis Viral			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 10 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Nosocomial Infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Otitis Media			
subjects affected / exposed	1 / 2 (50.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 10 (10.00%)	1 / 18 (5.56%)
occurrences (all)	0	1	1

Non-serious adverse events	Part 2 - Rabeprazole 10 mg	Part 2 - Placebo + Rabeprazole 5 mg	Part 2 - Rabeprazole 5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)	0 / 1 (0.00%)	4 / 9 (44.44%)
Investigations			
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood Gastrin Increased			
subjects affected / exposed	2 / 9 (22.22%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0

Cardiac Murmur			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Platelet Count Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cyanosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Mass			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye Discharge			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye Swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Haematemesis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vomiting			

subjects affected / exposed	1 / 9 (11.11%)	0 / 1 (0.00%)	2 / 9 (22.22%)
occurrences (all)	2	0	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nasal Obstruction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rhinitis Allergic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rash Maculo-Papular			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Diarrhoea Infectious			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis Viral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 1 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Nosocomial Infection			

subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Otitis Media			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 June 2007	Amendment INT-1 was implemented and included the following changes: a) The enrollment weight specified as minimum weight of 5 kg in pediatric subjects; b) Changes in PK sampling schedule; adjustments in collected blood volume; c) Changes to some assessments in Time and Events schedule; and d) Fasting gastrin sample collection moved from screening visit to predose on Day 1.
02 January 2008	Amendment INT-2 was implemented and included the change in order to facilitate enrollment, the overnight stay requirement was removed for subjects not enrolled in the pH probe component of the study.
19 September 2008	Amendment INT-3 was implemented after the enrollment of 2 subjects and included the changes: a) of dose in Part 1 of the study was increased from 0.14 mg/kg to 0.5 mg/kg; b) In order to facilitate enrollment, subjects were given 2 treatment options (Option 1 with treatment for 5 days and semi-rich PK sampling schedule; Option 2 with treatment up to 14 days and sparse PK sampling) and a lower minimum weight was allowed for one of these treatment options. The total study period was updated for consistency with new treatment options; c) Adjustments in collected blood volume were made; and c) Exclusion criteria were updated.
17 September 2009	Amendment INT-4 was implemented after the enrollment of 11 subjects and included the following changes: a) The total number of subjects planned to be enrolled in Part 1 of the study was reduced from 12 to 9, as data from Part 1 was used to select doses in Part 2; b) Doses used in Part 2 were defined; dosing instructions for Part 2 were added; c) Subjects enrolled in Part 1 were allowed to be enrolled in Part 2; and d) Participation in the pharmacogenomic research portion was made optional.
10 November 2009	Amendment INT-5 was implemented after the enrollment of 11 subjects and included the following change of Volume of blood collection was reduced.
22 October 2010	Amendment INT-6 was implemented after the enrollment of 34 subjects and included the following changes: a) Rationale for commissioning of DMSB was added; b) Guidance was provided regarding dosing in case subjects vomited after drug intake; c) Clarification was made regarding the type of PK analysis to be done; clarification was added regarding PK sample processing; d) Instructions were added to allow pH monitoring at home and additional clarification was provided on pH monitoring; e) Specification on minimum number of subjects was added; and f) A statement was added indicating that the use of PPIs, H2-blockers, antacids and sucralfate was allowed during follow up phase after collection of the last PK sample and discontinuation of study drug administration.
08 February 2011	Amendment INT-7 was implemented after the enrollment of 35 subjects and included the following change of Capillary sampling for PK samples was allowed.
18 May 2011	Amendment INT-8 was implemented after the enrollment of 37 subjects and included the following change: a) The dosing duration in Part 2 of the study was increased from up to 14 days to a maximum of 28 days. A total duration of study for subjects enrolled in Part 2 of 9 weeks was added.
24 August 2011	Amendment INT-9 was implemented after the enrollment of 42 subjects and included the following change of Capillary sampling for clinical laboratory samples was allowed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported