

**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) | EMA-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 (C_{max})

| | |
|--|--|
| End point title | Maximum Observed Plasma Concentration (C _{max}) ^[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 Intra gastric pH

| | |
|-----------------|--|
| End point title | Percentage Duration With An Intra gastric 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: Intra gastric pH<4 | 69.894 (± 28.5873) | | | |
| Day 5: Intra gastric pH<4 | 68.49 (± 26.056) | | | |
| Day 1: Intra gastric pH<3 | 60.84 (± 57.367) | | | |
| Day 5: Intra gastric 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 occurrences (all) | 0 / 2 (0.00%) 0 | 1 / 10 (10.00%) 1 | 1 / 18 (5.56%) 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 occurrences (all) | 0 / 2 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Infections and infestations | | | |
| Bronchiolitis subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 1 / 10 (10.00%) 1 | 0 / 18 (0.00%) 0 |
| Diarrhoea Infectious subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 0 / 10 (0.00%) 0 | 1 / 18 (5.56%) 1 |
| Gastroenteritis Viral subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 2 / 10 (20.00%) 2 | 0 / 18 (0.00%) 0 |
| Nosocomial Infection subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 0 / 10 (0.00%) 0 | 1 / 18 (5.56%) 1 |
| Otitis Media subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | 0 / 10 (0.00%) 0 | 1 / 18 (5.56%) 1 |
| Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 1 / 10 (10.00%) 1 | 1 / 18 (5.56%) 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 occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Blood Gastrin Increased subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 2 | 0 / 1 (0.00%) 0 | 0 / 9 (0.00%) 0 |

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

| | | | |
|--|---------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 2 | 0 / 1 (0.00%) 0 | 2 / 9 (22.22%) 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