



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) | 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 | 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 (C_{max}) of Rabeprazole

| | |
|---|---|
| End point title | Maximum Observed Plasma Concentration (C _{max}) of Rabeprazole ^[1] |
| End point description: The C _{max} 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 (AUC_{last}) 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/lambdaz). 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 Palatibility of Drug Good of Excellent

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