# Clinical trial results:
# Safety and Efficacy of Rabeprazole in the Treatment of Gastroesophageal Reflux Disease in 12-16 Year Old Patients

## Summary

| | |
|---|---|
| EudraCT number | 2016-001879-73 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 01 May 2006 |

**Results information**

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 31 July 2016 |
| First version publication date | 31 July 2016 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | E3810-A001-202 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00132496 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Eisai Medical Research Inc. |
| Sponsor organisation address | 100 Tice Boulevard, Woodcliff Lake, United States, 07677 |
| Public contact | Eisai Medical Information, Eisai Medical Research Inc., 1 8882742378, esi_medinfo@eisai.com |
| Scientific contact | Eisai Medical Information, Eisai Medical Research Inc., 1 8882742378, esi_medinfo@eisai.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? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 01 May 2006 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 01 May 2006 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To collect safety information on rabeprazole 10 mg and 20 mg in the treatment of gastroesophageal reflux disease (GERD) in children aged 12 to 16 years.

Protection of trial subjects:

This study was conducted in accordance with standard operating procedures (SOPs) of the sponsor (or designee), which are designed to ensure adherence to Good Clinical Practice (GCP) guidelines as required by the following:
- Principles of the World Medical Association Declaration of Helsinki (World Medical Association, 2008)
- International Council on Harmonisation (ICH) E6 Guideline for GCP (CPMP/ICH/135/95) of the European Agency for the Evaluation of Medicinal
Products, Committee for Proprietary Medicinal Products, International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
- Title 21 of the United States (US) Code of Federal Regulations (US 21 CFR) regarding clinical studies, including Part 50 and Part 56 concerning informed subject consent and Institutional Review Board (IRB) regulations and applicable sections of US 21 CFR Part 312
- European Good Clinical Practice Directive 2005/28/EC and Clinical Trial Directive 2001/20/EC for studies conducted within any European Union (EU) country. All suspected unexpected serious adverse reactions were reported, as required, to the Competent Authorities of all involved EU member states.
- Article 14, Paragraph 3, and Article 80-2 of the Pharmaceutical Affairs Law (Law No. 145, 1960) for studies conducted in Japan, in addition to Japan’s GCP Subject Information and Informed Consent.

| | |
|---|---|
| Background therapy: - | |
| Evidence for comparator: - | |
| Actual start date of recruitment | 18 August 2005 |
| 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 | United States: 111 |
| Worldwide total number of subjects | 111 |
| EEA total number of subjects | 0 |

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) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 111 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 119 participants were screened and of these, 111 were enrolled into the study, 54 participants received 10 mg rabeprazole and 57 participants received 20 mg rabeprazole from Week 1 through Week 8.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | 10 mg Rabeprazole sodium |

Arm description:

Participants had a screening evaluation within 2 weeks prior to starting study drug administration. Participants received 10 mg rabeprazole once daily at the same time each day for 8 weeks, with a follow-up visit at Week 10.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Rabeprazole sodium |
| Investigational medicinal product code | E3810 |
| Other name | |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Rabeprazole sodium was administered orally, once per day for up to 8 weeks.

| | |
|---|---|
| **Arm title** | 20 mg Rabeprazole sodium |

Arm description:

Participants had a screening evaluation within 2 weeks prior to starting study drug administration. Participants received 20 mg rabeprazole once daily at the same time each day for 8 weeks, with a follow-up visit at Week 10.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Rabeprazole sodium |
| Investigational medicinal product code | E3810 |
| Other name | AcipHex |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Rabeprazole sodium was administered orally, once per day for up to 8 weeks.

| **Number of subjects in period 1** | 10 mg Rabeprazole sodium | 20 mg Rabeprazole sodium |
|---|---|---|
| Started | 54 | 57 |
| Completed | 52 | 55 |
| Not completed | 2 | 2 |
| Physician decision | 1 | - |
| Consent withdrawn by subject | 1 | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | 10 mg Rabeprazole sodium |
| Reporting group description: | |
| Participants had a screening evaluation within 2 weeks prior to starting study drug administration. Participants received 10 mg rabeprazole once daily at the same time each day for 8 weeks, with a follow-up visit at Week 10. | |
| Reporting group title | 20 mg Rabeprazole sodium |
| Reporting group description: | |
| Participants had a screening evaluation within 2 weeks prior to starting study drug administration. Participants received 20 mg rabeprazole once daily at the same time each day for 8 weeks, with a follow-up visit at Week 10. | |

| Reporting group values | 10 mg Rabeprazole sodium | 20 mg Rabeprazole sodium | Total |
|---|---|---|---|
| Number of subjects | 54 | 57 | 111 |
| Age categorical<br>Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 0 |
| Newborns (0-27 days) | | | 0 |
| Infants and toddlers (28 days-23 months) | | | 0 |
| Children (2-11 years) | | | 0 |
| Adolescents (12-17 years) | | | 0 |
| Adults (18-64 years) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 14.2 | 14.1 | |
| standard deviation | ± 1.29 | ± 1.49 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 27 | 26 | 53 |
| Male | 27 | 31 | 58 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | 10 mg Rabeprazole sodium |
| Reporting group description: | |
| Participants had a screening evaluation within 2 weeks prior to starting study drug administration. Participants received 10 mg rabeprazole once daily at the same time each day for 8 weeks, with a follow-up visit at Week 10. | |
| Reporting group title | 20 mg Rabeprazole sodium |
| Reporting group description: | |
| Participants had a screening evaluation within 2 weeks prior to starting study drug administration. Participants received 20 mg rabeprazole once daily at the same time each day for 8 weeks, with a follow-up visit at Week 10. | |

### Primary: Summary of Adverse Events (AEs)

| | |
|---|---|
| End point title | Summary of Adverse Events (AEs)[1] |
| End point description: | |
| Safety variables included AEs, serious AEs, laboratory evaluations (hematology, clinical chemistry, and urinalysis), vital signs (blood pressure and pulse rate, respiration rate, oral temperature), and physical examinations. The safety of rabeprazole sodium was evaluated based on incidence of treatment-emergent adverse events (TEAEs), critical changes in clinically relevant laboratory values, and physical examinations. AEs were assessed weekly (during study visits and by phone) and laboratory tests were performed at Screening, Baseline and at the end of active study drug treatment (Week 8 or when the participant discontinued the study). The safety population was used and included all participants who received at least one dose of study treatment. | |
| End point type | Primary |
| End point timeframe: | |
| Screening Visit up to Week 12 | |

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 was not done.

| End point values | 10 mg Rabeprazole sodium | 20 mg Rabeprazole sodium | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 57 | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| TEAEs | 31 | 35 | | |
| Treatment-related TEAEs | 8 | 8 | | |
| Serious AEs | 0 | 1 | | |
| Withdrawal due to TEAEs | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in Frequency of GERD Symptoms Between Baseline and Weeks 8

**and 10 and Between Week 10 and Week 8 at Nighttime**

| End point title | Change in Frequency of GERD Symptoms Between Baseline and Weeks 8 and 10 and Between Week 10 and Week 8 at Nighttime |
|---|---|

End point description:

Change in frequency of GERD symptoms was computed as frequency of a symptom collected during a given week visit minus frequency count recorded at baseline. Five primary GERD symptoms were assessed: heartburn, regurgitation, nausea, vomiting, and epigastric pain. The participant was also able to choose two other symptoms of concern from a list of twenty possible symptoms. The participant noted in their diary the number of episodes of each symptom and time of occurrence (daytime and/or nighttime). A negative value indicates a decrease in mean frequency of a symptom. The Intent-to-treat (ITT) population was used and included all participants in the Safety population who also had at least one post-baseline assessment.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline (including Screening values) to Week 8 (Wk 8) and Baseline (including Screening values) to Week 10 (Wk 10)

| **End point values** | 10 mg Rabeprazole sodium | 20 mg Rabeprazole sodium | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 57 | | |
| Units: Change in frequency | | | | |
| arithmetic mean (standard deviation) | | | | |
| Heartburn Week 8 - Baseline (n = 48, 51) | -0.21 (± 0.503) | -0.48 (± 0.727) | | |
| Heartburn Week 10 - Baseline (n = 48, 52) | -0.18 (± 0.462) | -0.4 (± 0.684) | | |
| Heartburn Week 10 - Week 8 (n = 51, 54) | 0.03 (± 0.219) | 0.07 (± 0.196) | | |
| Regurgitation Week 8 - Baseline (n = 48, 51) | -0.1 (± 0.328) | -0.21 (± 0.612) | | |
| Regurgitation Week 10 - Baseline (n = 48, 52) | -0.13 (± 0.34) | -0.15 (± 0.522) | | |
| Regurgitation Week 10 - Week (n = 51, 54) | -0.02 (± 0.126) | 0.05 (± 0.266) | | |
| Nausea Week 8 - Baseline (n = 48, 51) | -0.19 (± 0.686) | -0.24 (± 0.446) | | |
| Nausea Week 10 - Baseline (n = 48, 52) | -0.19 (± 0.68) | -0.17 (± 0.482) | | |
| Nausea Week 10 - Week 8 (n = 51, 54) | -0.02 (± 0.195) | 0.04 (± 0.161) | | |
| Vomiting Week 8 - Baseline (n = 48, 51) | -0.07 (± 0.358) | -0.04 (± 0.283) | | |
| Vomiting Week 10 - Baseline (n = 48, 52) | -0.07 (± 0.351) | -0.01 (± 0.191) | | |
| Vomiting Week 10 - Week 8 (n = 51, 54) | 0.01 (± 0.028) | 0.03 (± 0.121) | | |
| Epigastric Pain Week 8 - Baseline (n = 48, 51) | -0.12 (± 0.62) | -0.29 (± 0.523) | | |
| Epigastric Pain Week 10 - Baseline (n = 48, 52) | -0.17 (± 0.417) | -0.22 (± 0.473) | | |
| Epigastric Pain Week 10 - Week 8 (n = 51, 54) | -0.07 (± 0.485) | 0.06 (± 0.226) | | |
| Other Week 8 - Baseline (n = 38, 45) | -0.21 (± 0.921) | -0.76 (± 1.069) | | |

| | | | | |
|---|---|---|---|---|
| Other Week 10 - Baseline (n = 38, 45) | -0.08 (± 1.479) | -0.57 (± 1.055) | | |
| Other Week 10 - Week 8 (n = 43, 49) | 0.1 (± 0.739) | 0.18 (± 0.408) | | |

## Statistical analyses

| **Statistical analysis title** | Heartburn Frequency at Night Wk 8 - Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest. Analysis of covariance (ANCOVA) was employed.

| | |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[2] |
| P-value | = 0.833 [3] |
| Method | ANCOVA |

Notes:

[2] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[3] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Heartburn Frequency at Night Wk 10 - Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[4] |
| P-value | = 0.737 [5] |
| Method | ANCOVA |

Notes:

[4] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[5] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Heartburn Frequency at Night Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[6] |
| P-value | = 0.196 [7] |
| Method | ANCOVA |

Notes:

[6] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[7] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Regurgitation Frequency at Night Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[8] |
| P-value | = 0.914 [9] |
| Method | ANCOVA |

Notes:

[8] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[9] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Regurgitation Frequency at Night Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[10] |
| P-value | = 0.271 [11] |
| Method | ANCOVA |

Notes:

[10] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[11] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Regurgitation Frequency at Night Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[12] |
| P-value | = 0.072 [13] |
| Method | ANCOVA |

Notes:

[12] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[13] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Nausea Frequency at Night Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[14] |
| P-value | = 0.671 [15] |
| Method | ANCOVA |

Notes:

[14] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[15] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Nausea Frequency at Night Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[16] |
| P-value | = 0.147 [17] |
| Method | ANCOVA |

Notes:

[16] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[17] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Nausea Frequency at Night Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[18] |
| P-value | = 0.139 [19] |
| Method | ANCOVA |

Notes:

[18] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[19] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Vomiting Frequency at Night Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[20] |
| P-value | = 0.821 [21] |
| Method | ANCOVA |

Notes:

[20] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[21] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Vomiting Frequency at Night Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[22] |
| P-value | = 0.047 [23] |
| Method | ANCOVA |

Notes:

[22] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[23] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Vomiting Frequency at Night Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[24] |
| P-value | = 0.105 [25] |
| Method | ANCOVA |

Notes:

[24] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[25] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Epigastric Pain Frequency at Night Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[26] |
| P-value | = 0.304 [27] |
| Method | ANCOVA |

Notes:

[26] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[27] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Epigastric Pain Frequency at Night Wk 10–Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[28] |
| P-value | = 0.795 [29] |
| Method | ANCOVA |

Notes:

[28] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[29] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Epigastric Pain Frequency at Night Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[30] |
| P-value | = 0.098 [31] |
| Method | ANCOVA |

Notes:

[30] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[31] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Other Frequency at Night Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[32] |
| P-value | = 0.026 [33] |
| Method | ANCOVA |

Notes:

[32] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[33] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Other Frequency at Night Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[34] |
| P-value | = 0.125 [35] |
| Method | ANCOVA |

Notes:

[34] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[35] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Other Frequency at Night Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[36] |
| P-value | = 0.117 [37] |
| Method | ANCOVA |

Notes:

[36] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[37] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

## Secondary: Change in Frequency of GERD Symptoms Between Baseline and Weeks 8 and 10 and Between Week 10 and Week 8 at Daytime

| | |
|---|---|
| End point title | Change in Frequency of GERD Symptoms Between Baseline and Weeks 8 and 10 and Between Week 10 and Week 8 at Daytime |

End point description:

Change in frequency of GERD symptoms was computed as frequency of a symptom collected during a given week visit minus frequency count recorded at baseline. Five primary GERD symptoms were assessed: heartburn, regurgitation, nausea, vomiting, and epigastric pain. The participant was also able to choose two other symptoms of concern from a list of twenty possible symptoms. The participant noted in their diary the number of episodes of each symptom and time of occurrence (daytime and/or nighttime). A negative value indicates a decrease in mean frequency of a symptom. The Intent-to-treat (ITT) population was used and included all participants in the Safety population who also had at least one post-baseline assessment.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline (including Screening values) to Week 8 and Baseline (including Screening values) to Week 10

| **End point values** | 10 mg Rabeprazole sodium | 20 mg Rabeprazole sodium | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 57 | | |
| Units: Change in frequency | | | | |
| arithmetic mean (standard deviation) | | | | |
| Heartburn Week 8 – Baseline (n = 48, 51) | -0.54 (± 1.097) | -0.88 (± 1.147) | | |
| Heartburn Week 10 – Baseline (n = 48, 52) | -0.42 (± 0.953) | -0.46 (± 1.174) | | |
| Heartburn Week 10 – Week 8 (n = 51, 54) | 0.11 (± 0.492) | 0.42 (± 1.253) | | |
| Regurgitation Week 8 – Baseline (n = 48, 51) | -0.3 (± 0.961) | -0.42 (± 1.159) | | |
| Regurgitation Week 10 – Baseline (n = 48, 52) | -0.21 (± 0.939) | -0.2 (± 0.772) | | |
| Regurgitation Week 10 – Week 8 (n = 51, 54) | 0.09 (± 0.49) | 0.21 (± 0.679) | | |
| Nausea Week 8 – Baseline (n = 48, 51) | -0.55 (± 0.978) | -0.41 (± 0.697) | | |
| Nausea Week 10 – Baseline (n = 48, 52) | -0.45 (± 0.963) | -0.3 (± 0.802) | | |
| Nausea Week 10 – Week 8 (n = 51, 54) | 0.07 (± 0.459) | 0.09 (± 0.454) | | |
| Vomiting Week 8 – Baseline (n = 48, 51) | -0.09 (± 0.458) | -0.04 (± 0.246) | | |

| | | | | |
|---|---|---|---|---|
| Vomiting Week 10 – Baseline (n = 48, 52) | -0.09 (± 0.458) | 0.01 (± 0.326) | | |
| Vomiting Week 10 – Week 8 (n = 51, 54) | -0.01 (± 0.069) | 0.05 (± 0.194) | | |
| Epigastric Pain Week 8 – Baseline (n = 48, 51) | -0.5 (± 0.874) | -0.54 (± 0.811) | | |
| Epigastric Pain Week 10 – Baseline (n = 48, 52) | -0.35 (± 0.957) | -0.46 (± 0.8) | | |
| Epigastric Pain Week 10 – Week 8 (n = 51, 54) | 0.12 (± 0.785) | 0.06 (± 0.359) | | |
| Other Week 8 – Baseline (n = 38, 45) | -1.73 (± 2.136) | -2.51 (± 9.085) | | |
| Other Week 10 – Baseline (n = 38, 45) | -1.14 (± 2.661) | -2.12 (± 8.819) | | |
| Other Week 10 – Week 8 (n = 43, 49) | 0.5 (± 2.777) | 0.37 (± 0.803) | | |

## Statistical analyses

| **Statistical analysis title** | Heartburn Frequency at Daytime Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[38] |
| P-value | = 0.282 [39] |
| Method | ANCOVA |

Notes:

[38] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[39] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Heartburn Frequency at Daytime Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[40] |
| P-value | = 0.817 [41] |
| Method | ANCOVA |

Notes:

[40] - Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

[41] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity

and therefore should be interpreted with caution.

| **Statistical analysis title** | Heartburn Frequency at Daytime Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[42] |
| P-value | = 0.125 [43] |
| Method | ANCOVA |

Notes:

[42] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[43] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Regurgitation Frequency at Daytime Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[44] |
| P-value | = 0.588 [45] |
| Method | ANCOVA |

Notes:

[44] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[45] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Regurgitation Frequency at Daytime Wk 10 –Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[46] |
| P-value | = 0.94 [47] |
| Method | ANCOVA |

Notes:

[46] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[47] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity

and therefore should be interpreted with caution.

| **Statistical analysis title** | Regurgitation Frequency at Daytime Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[48] |
| P-value | = 0.622 [49] |
| Method | ANCOVA |

Notes:

[48] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[49] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Nausea Frequency at Daytime Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[50] |
| P-value | = 0.728 [51] |
| Method | ANCOVA |

Notes:

[50] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[51] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Nausea Frequency at Daytime Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[52] |
| P-value | = 0.715 [53] |
| Method | ANCOVA |

Notes:

[52] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[53] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity

and therefore should be interpreted with caution.

| **Statistical analysis title** | Nausea Frequency at Daytime Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[54] |
| P-value | = 0.868 [55] |
| Method | ANCOVA |

Notes:

[54] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[55] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Vomiting Frequency at Daytime Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[56] |
| P-value | = 0.104 [57] |
| Method | ANCOVA |

Notes:

[56] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[57] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Vomiting Frequency at Daytime Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[58] |
| P-value | = 0.039 [59] |
| Method | ANCOVA |

Notes:

[58] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[59] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity

and therefore should be interpreted with caution.

| **Statistical analysis title** | Vomiting Frequency at Daytime Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[60] |
| P-value | = 0.038 [61] |
| Method | ANCOVA |

Notes:

[60] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[61] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Epigastric Pain Frequency at Daytime Wk 8–Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[62] |
| P-value | = 0.986 [63] |
| Method | ANCOVA |

Notes:

[62] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[63] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Epigastric Pain Frequency at Daytime Wk10–Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[64] |
| P-value | = 0.59 [65] |
| Method | ANCOVA |

Notes:

[64] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[65] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity

and therefore should be interpreted with caution.

| **Statistical analysis title** | Epigastric Frequency at Daytime Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[66] |
| P-value | = 0.513 [67] |
| Method | ANCOVA |

Notes:

[66] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[67] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Other Frequency at Daytime Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[68] |
| P-value | = 0.412 [69] |
| Method | ANCOVA |

Notes:

[68] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[69] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Other Frequency at Daytime Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[70] |
| P-value | = 0.547 [71] |
| Method | ANCOVA |

Notes:

[70] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[71] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity

and therefore should be interpreted with caution.

| **Statistical analysis title** | Other Frequency at Daytime Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[72] |
| P-value | = 0.618 [73] |
| Method | ANCOVA |

Notes:

[72] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[73] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

## Secondary: Change in Severity of GERD Symptoms Between Baseline and Weeks 8 and 10 and Between Week 10 and Week 8

| End point title | Change in Severity of GERD Symptoms Between Baseline and Weeks 8 and 10 and Between Week 10 and Week 8 |
|---|---|

End point description:

Participants were instructed to start recording severity of GERD symptoms in the daily diary. The change in severity was computed as the difference between a given symptom week score and baseline score. The severity of GERD symptoms were recorded as the maximum severity of the symptom (heartburn, regurgitation, nausea, vomiting, and epigastric pain) each day as reported by the participant in their daily diary using the 5-point Likert scale. The participant was also able to choose two other symptoms of concern from a list of twenty possible symptoms. Intent-to-treat population included all participants in the Safety population who also had at least one post-baseline assessment.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline (including Screening values) to Week 8 and Baseline (including Screening values) to Week 10

| **End point values** | 10 mg Rabeprazole sodium | 20 mg Rabeprazole sodium | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 57 | | |
| Units: Change in severity | | | | |
| arithmetic mean (standard deviation) | | | | |
| Heartburn Week 8 – Baseline (n = 48, 51) | -0.57 (± 0.815) | -0.87 (± 0.768) | | |
| Heartburn Week 10 – Baseline (n = 48, 52) | -0.46 (± 0.772) | -0.63 (± 0.779) | | |
| Heartburn Week 10 – Week 8 (n = 51, 54) | 0.11 (± 0.382) | 0.23 (± 0.47) | | |
| Regurgitation Week 8 – Baseline (n = 48, 51) | -0.39 (± 0.697) | -0.42 (± 0.749) | | |
| Regurgitation Week 10 – Baseline (n = 48, 52) | -0.31 (± 0.751) | -0.31 (± 0.617) | | |

| | | | | |
|---|---|---|---|---|
| Regurgitation Week 10 – Week 8 (n = 51, 54) | 0.07 (± 0.295) | 0.1 (± 0.318) | | |
| Nausea Week 8 – Baseline (n = 48, 51) | -0.41 (± 0.706) | -0.55 (± 0.704) | | |
| Nausea Week 10 – Baseline (n = 48, 52) | -0.33 (± 0.714) | -0.41 (± 0.794) | | |
| Nausea Week 10 – Week 8 (n = 51, 54) | 0.05 (± 0.358) | 0.12 (± 0.436) | | |
| Vomiting Week 8 – Baseline (n = 48, 51) | -0.13 (± 0.518) | -0.09 (± 0.346) | | |
| Vomiting Week 10 – Baseline (n = 48, 52) | -0.12 (± 0.508) | -0.02 (± 0.325) | | |
| Vomiting Week 10 – Week 8 (n = 51, 54) | 0 (± 0.109) | 0.06 (± 0.202) | | |
| Epigastric Pain Week 8 – Baseline (n = 48, 51) | -0.4 (± 0.574) | -0.59 (± 0.681) | | |
| Epigastric Pain Week 10 – Baseline (n = 48, 52) | -0.37 (± 0.57) | -0.52 (± 0.665) | | |
| Epigastric Pain Week 10 – Week 8 (n = 51, 54) | 0 (± 0.24) | 0.05 (± 0.195) | | |
| Other Week 8 – Baseline (n = 38, 45) | -0.74 (± 0.725) | -0.81 (± 0.746) | | |
| Other Week 10 – Baseline (n = 38, 45) | -0.66 (± 0.715) | -0.63 (± 0.745) | | |
| Other Week 10 – Week 8 (n = 43, 49) | 0.04 (± 0.381) | 0.16 (± 0.318) | | |

## Statistical analyses

| **Statistical analysis title** | Heartburn Frequency Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[74] |
| P-value | = 0.431 [75] |
| Method | ANCOVA |

Notes:

[74] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[75] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Heartburn Frequency Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[76] |
| P-value | = 0.628 [77] |
| Method | ANCOVA |

Notes:

[76] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[77] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Heartburn Frequency Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[78] |
| P-value | = 0.117 [79] |
| Method | ANCOVA |

Notes:

[78] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[79] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Regurgitation Frequency Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[80] |
| P-value | = 0.753 [81] |
| Method | ANCOVA |

Notes:

[80] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[81] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Regurgitation Frequency Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[82] |
| P-value | = 0.707 [83] |
| Method | ANCOVA |

Notes:

[82] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[83] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Regurgitation Frequency Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[84] |
| P-value | = 0.941 [85] |
| Method | ANCOVA |

Notes:

[84] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[85] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Nausea Frequency Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[86] |
| P-value | = 0.368 [87] |
| Method | ANCOVA |

Notes:

[86] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[87] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Nausea Frequency Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[88] |
| P-value | = 0.852 [89] |
| Method | ANCOVA |

Notes:

[88] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[89] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Nausea Frequency Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[90] |
| P-value | = 0.795 [91] |
| Method | ANCOVA |

Notes:

[90] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[91] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Vomiting Frequency Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[92] |
| P-value | = 0.468 [93] |
| Method | ANCOVA |

Notes:

[92] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[93] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Vomiting Frequency Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[94] |
| P-value | = 0.023 [95] |
| Method | ANCOVA |

Notes:

[94] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[95] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Vomiting Frequency Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[96] |
| P-value | = 0.031 [97] |
| Method | ANCOVA |

Notes:

[96] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[97] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Epigastric Pain Frequency Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[98] |
| P-value | = 0.66 [99] |
| Method | ANCOVA |

Notes:

[98] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[99] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Epigastric Pain Frequency Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[100] |
| P-value | = 0.738 [101] |
| Method | ANCOVA |

Notes:

[100] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[101] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Epigastric Pain Frequency Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[102] |
| P-value | = 0.528 [103] |
| Method | ANCOVA |

Notes:

[102] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[103] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Other Frequency Wk 8 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[104] |
| P-value | = 0.377 [105] |
| Method | ANCOVA |

Notes:

[104] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[105] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Other Frequency Wk 10 – Baseline |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[106] |
| P-value | = 0.914 [107] |
| Method | ANCOVA |

Notes:

[106] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[107] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Other Frequency Wk 10 – Wk 8 |
|---|---|

Statistical analysis description:

Testing of hypotheses on efficacy parameters was conducted for exploratory purposes and P-values were calculated without multiplicity adjustment for multiple endpoints. Appropriate parametric and/or nonparametric statistics were applied. All tests were two-sided. A P-value of <0.05 indicated a significant difference between the two treatment groups in the parameter of interest.

| | |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[108] |
| P-value | = 0.17 [109] |
| Method | ANCOVA |

Notes:

[108] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[109] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

## Secondary: Percentage of Participants Who Took Six or Fewer Antacids Per Day

| End point title | Percentage of Participants Who Took Six or Fewer Antacids Per Day |
|---|---|

End point description:

A 2-week supply of antacids was dispensed at the Screening and Baseline Visits. At the Baseline Visit, participants were instructed to begin completing daily drug administration diaries with the time of medication dosing and to note any rescue antacids (number of tablets in each 24-hour period) or other concomitant medications used. The participant responded to the question "Did participant take 6 or fewer antacids per day?" The shift in antacid use at postbaseline visits were compared to baseline. The ITT population was used and included all participants in the Safety population who also had at least one post-baseline assessment.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to Week 2, Baseline to Week 4, Baseline to Week 6, Baseline to Week 8, and Baseline to Week 10

| **End point values** | 10 mg Rabeprazole sodium | 20 mg Rabeprazole sodium | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 42 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Baseline - Yes | 100 | 97.7 | | |
| Baseline - No | 0 | 2.3 | | |

| | | | | |
|---|---|---|---|---|
| Week 2 - Yes | 98.1 | 100 | | |
| Week 2 - No | 1.9 | 0 | | |
| Week 4 - Yes | 100 | 100 | | |
| Week 4 - No | 0 | 0 | | |
| Week 6 - Yes | 100 | 98.1 | | |
| Week 6 - No | 0 | 1.9 | | |
| Week 8 - Yes | 100 | 98.2 | | |
| Week 8 - No | 0 | 1.8 | | |
| Week 10 - Yes | 100 | 98.1 | | |
| Week 10 - No | 0 | 1.9 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in the Psychological General Well-Being Index (PGWBI) Scores

| End point title | Change from Baseline in the Psychological General Well-Being Index (PGWBI) Scores |
|---|---|

End point description:

At the bi-weekly study center visit, a quality of life (QOL) assessment was conducted using the PSWBI scales, which has been validated in ages 12 years and older. Change in quality of life domains was computed as QOL domain score at a given week visit minus baseline score. The PGWBI is composed of 22 items and was analyzed to 7 dimensions; Anxiety (ANX) (score range 0-25), Depressed Mood (DEP) (score range 0-15), Positive well-being (PWB) (score range 0-20), Self-control (SC) (score range 0-15), General Health (GH) (score range 0-15), Vitality (VT) (score range 0-20), and Raw Index Score (score range 0-110). Each item in the questionnaire has a 6-point scale from 0-5 where a higher score indicates a more positive rating and a lower score means a more negative rating. The ITT population was used and included all participants in the Safety population who also had at least one post-baseline assessment.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 2, 4, 6, 8, and 10

| **End point values** | 10 mg Rabeprazole sodium | 20 mg Rabeprazole sodium | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 57 | | |
| Units: Scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Anxiety; Week 2 - Baseline (n = 47, 50) | 4.9 (± 16.95) | 5.6 (± 17.52) | | |
| Anxiety; Week 4 - Baseline (n = 51, 52) | 5.8 (± 17.01) | 9 (± 14.98) | | |
| Anxiety; Week 6 - Baseline (n = 52, 51) | 8.5 (± 16.19) | 8.8 (± 17.51) | | |
| Anxiety; Week 8 - Baseline (n = 52, 54) | 11 (± 15.3) | 7.8 (± 17.42) | | |
| Anxiety; Week 10 - Baseline (n = 48, 52) | 10 (± 16.19) | 9.7 (± 18.12) | | |
| Depressed mood; Week 2 - Baseline (n = 47, 50) | 4.8 (± 12.33) | 2.5 (± 13.12) | | |
| Depressed mood; Week 4 - Baseline (n = 51, 52) | 5.2 (± 12.81) | 2.3 (± 13.96) | | |

| | | | | |
|---|---|---|---|---|
| Depressed mood; Week 6 - Baseline (n = 52, 51) | 6.7 (± 14.94) | 5 (± 16.16) | | |
| Depressed mood; Week 8 - Baseline (n = 52, 54) | 6.5 (± 16.03) | 2.8 (± 18.97) | | |
| Depressed mood; Week 10 - Baseline (n = 48, 52) | 5.4 (± 15.72) | 5.5 (± 18.09) | | |
| Positive well-being; Week 2 - Baseline (n= 47, 50) | 4.6 (± 13.51) | 2.9 (± 14.25) | | |
| Positive well-being; Week 4 - Baseline (n= 51, 52) | 5.8 (± 16.47) | 4.9 (± 17.05) | | |
| Positive well-being; Week 6 - Baseline (n= 52, 51) | 8.8 (± 16.97) | 8.3 (± 17.25) | | |
| Positive well-being; Week 8 - Baseline (n= 52, 54) | 9.1 (± 18.22) | 8.9 (± 19.37) | | |
| Positive well-being; Week 10 - Baseline (n=48, 52) | 8.1 (± 16.9) | 8.5 (± 18.41) | | |
| Self control; Week 2 - Baseline (n = 47, 50) | 2.3 (± 16.98) | 1.9 (± 10.17) | | |
| Self control; Week 4 - Baseline (n = 51, 52) | 2 (± 18.87) | 2.6 (± 10.57) | | |
| Self control; Week 6 - Baseline (n = 52, 51) | 7.6 (± 19.13) | 4.8 (± 11.71) | | |
| Self control; Week 8 - Baseline (n = 52, 54) | 4.7 (± 21.05) | 3 (± 13.93) | | |
| Self control; Week 10 - Baseline (n = 48, 52) | 5.6 (± 16.52) | 4.9 (± 15.57) | | |
| General health; Week 2 - Baseline (n = 47, 50) | 7 (± 16.56) | 7.5 (± 16.64) | | |
| General health; Week 4 - Baseline (n = 51, 52) | 9.8 (± 16.13) | 9.1 (± 13.66) | | |
| General health; Week 6 - Baseline (n = 52, 51) | 14.1 (± 13.57) | 8.6 (± 17.85) | | |
| General health; Week 8 - Baseline (n = 52, 54) | 12.1 (± 16.39) | 11.6 (± 15.33) | | |
| General health; Week 10 - Baseline (n = 48, 52) | 11.1 (± 13.84) | 9.1 (± 14.94) | | |
| Vitality; Week 2 - Baseline (n = 47, 50) | 0.2 (± 14.82) | 6.7 (± 15.34) | | |
| Vitality; Week 4 - Baseline (n = 51, 52) | 1.1 (± 17.42) | 8 (± 19.08) | | |
| Vitality; Week 6 - Baseline (n = 52, 51) | 4.2 (± 13.45) | 10.9 (± 19.07) | | |
| Vitality; Week 8 - Baseline (n = 52, 54) | 4.9 (± 17.16) | 10.3 (± 19.84) | | |
| Vitality; Week 10 - Baseline (n = 48, 52) | 4.7 (± 18.52) | 9.4 (± 20.71) | | |
| Raw index score; Week 2 - baseline (n = 47, 50) | 3.9 (± 11.16) | 4.6 (± 10.3) | | |
| Raw index score; Week 4 - baseline (n = 51, 52) | 4.9 (± 12.09) | 6.3 (± 10.36) | | |
| Raw index score; Week 6 - baseline (n = 52, 51) | 8.2 (± 10.3) | 8 (± 11.52) | | |
| Raw index score; Week 8 - baseline (n = 52, 54) | 8.2 (± 11.98) | 7.6 (± 13.25) | | |
| Raw index score; Week 10 - baseline (n = 48, 52) | 7.6 (± 12.06) | 8.1 (± 13.58) | | |

## Statistical analyses

| **Statistical analysis title** | Anxiety; Week 2 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[110] |
| P-value | = 0.658 [111] |
| Method | ANCOVA |

Notes:

[110] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[111] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Anxiety; Week 4 - Baseline |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[112] |
| P-value | = 0.152 [113] |
| Method | ANCOVA |

Notes:

[112] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[113] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Anxiety; Week 6 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[114] |
| P-value | = 0.245 [115] |
| Method | ANCOVA |

Notes:

[114] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[115] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Anxiety; Week 8 - Baseline |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[116] |
| P-value | = 0.564 [117] |
| Method | ANCOVA |

Notes:

[116] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[117] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Anxiety; Week 10 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[118] |
| P-value | = 0.226 [119] |
| Method | ANCOVA |

Notes:

[118] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[119] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Depressed mood; Week 2 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[120] |
| P-value | = 0.671 [121] |
| Method | ANCOVA |

Notes:

[120] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[121] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Depressed mood; Week 4 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[122] |
| P-value | = 0.833 [123] |
| Method | ANCOVA |

Notes:

[122] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[123] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Depressed mood; Week 6 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[124] |
| P-value | = 0.395 [125] |
| Method | ANCOVA |

Notes:

[124] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[125] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Depressed mood; Week 8 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[126] |
| P-value | = 0.835 [127] |
| Method | ANCOVA |

Notes:

[126] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[127] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Depressed mood; Week 10 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[128] |
| P-value | = 0.147 [129] |
| Method | ANCOVA |

Notes:

[128] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[129] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Positive well-being; Week 2 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[130] |
| P-value | = 0.675 [131] |
| Method | ANCOVA |

Notes:

[130] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[131] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Positive well-being; Week 4 - Baseline |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[132] |
| P-value | = 0.226 [133] |
| Method | ANCOVA |

Notes:

[132] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[133] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Positive well-being; Week 6 - Baseline |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[134] |
| P-value | = 0.075 [135] |
| Method | ANCOVA |

Notes:

[134] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[135] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Positive well-being; Week 8 - Baseline |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[136] |
| P-value | = 0.123 [137] |
| Method | ANCOVA |

Notes:

[136] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[137] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Positive well-being; Week 10 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[138] |
| P-value | = 0.17 [139] |
| Method | ANCOVA |

Notes:

[138] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[139] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Self control; Week 2 - Baseline |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[140] |
| P-value | = 0.234 [141] |
| Method | ANCOVA |

Notes:

[140] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[141] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Self control; Week 4 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[142] |
| P-value | = 0.112 [143] |
| Method | ANCOVA |

Notes:

[142] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[143] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Self control; Week 6 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[144] |
| P-value | = 0.421 [145] |
| Method | ANCOVA |

Notes:

[144] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[145] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Self control; Week 8 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[146] |
| P-value | = 0.524 [147] |
| Method | ANCOVA |

Notes:

[146] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[147] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Self control; Week 10 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[148] |
| P-value | = 0.412 [149] |
| Method | ANCOVA |

Notes:

[148] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[149] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | General health; Week 2 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[150] |
| P-value | = 0.742 [151] |
| Method | ANCOVA |

Notes:

[150] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[151] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | General health; Week 4 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[152] |
| P-value | = 0.765 [153] |
| Method | ANCOVA |

Notes:

[152] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[153] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | General health; Week 6 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[154] |
| P-value | = 0.266 [155] |
| Method | ANCOVA |

Notes:

[154] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[155] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | General health; Week 8 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[156] |
| P-value | = 0.388 [157] |
| Method | ANCOVA |

Notes:

[156] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[157] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | General health; Week 10 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[158] |
| P-value | = 0.849 [159] |
| Method | ANCOVA |

Notes:

[158] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[159] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Vitality; Week 2 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[160] |
| P-value | = 0.026 [161] |
| Method | ANCOVA |

Notes:

[160] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[161] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Vitality; Week 4 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[162] |
| P-value | = 0.031 [163] |
| Method | ANCOVA |

Notes:

[162] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[163] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Vitality; Week 6 - Baseline |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[164] |
| P-value | = 0.011 [165] |
| Method | ANCOVA |

Notes:

[164] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[165] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Vitality; Week 8 - Baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[166] |
| P-value | = 0.026 [167] |
| Method | ANCOVA |

Notes:

[166] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[167] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Vitality; Week 10 - Baseline |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[168] |
| P-value | = 0.073 [169] |
| Method | ANCOVA |

Notes:

[168] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[169] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Raw index score; Week 2 - baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[170] |
| P-value | = 0.367 [171] |
| Method | ANCOVA |

Notes:

[170] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[171] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Raw index score; Week 4 - baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[172] |
| P-value | = 0.181 [173] |
| Method | ANCOVA |

Notes:

[172] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[173] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Raw index score; Week 6 - baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |

| | |
|---|---|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[174] |
| P-value | = 0.196 [175] |
| Method | ANCOVA |

Notes:

[174] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[175] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Raw index score; Week 8 - baseline |
|---|---|
| Comparison groups | 20 mg Rabeprazole sodium v 10 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[176] |
| P-value | = 0.382 [177] |
| Method | ANCOVA |

Notes:

[176] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[177] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Raw index score; Week 10 - baseline |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[178] |
| P-value | = 0.138 [179] |
| Method | ANCOVA |

Notes:

[178] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[179] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

## Secondary: Change from Baseline in the Medical Outcomes Study 10-item Short form Questionnaire (SF-10) Scores

| End point title | Change from Baseline in the Medical Outcomes Study 10-item Short form Questionnaire (SF-10) Scores |
|---|---|

End point description:

At the bi-weekly study center visit, a quality of life (QOL) assessment was conducted using a pediatric form of the SF-10 scales, which has been validated for children ages 12 years and older. Change in quality of life domains was computed as QOL domain score at a given week visit minus baseline score. This was a 10-item questionnaire in which scores were analyzed based on two main categories, Physical and Psychological summary scores. A higher score indicates more favorable physical and psychological functioning. The ITT population was used and included all participants in the Safety population who also had at least one post-baseline assessment.

| End point type | Secondary |
|---|---|

End point timeframe:

Screening Visit, Baseline Visit (if greater than 72 hours after Screening), Weeks 2, 4, 6, 8, and 10

| End point values | 10 mg Rabeprazole sodium | 20 mg Rabeprazole sodium | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 57 | | |
| Units: Scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Physical summary score Week 2 (n = 48, 50) | 3.7 (± 8.47) | 2 (± 10.67) | | |
| Physical summary score Week 4 (n = 49, 51) | 3 (± 7.1) | 3.9 (± 9.42) | | |
| Physical summary score Week 6 (n = 50, 54) | 3.7 (± 8.65) | 4.5 (± 11.07) | | |
| Physical summary score Week 8 (n = 50, 54) | 2.9 (± 7.75) | 4.4 (± 10.58) | | |
| Physical summary score Week 10 (n = 47, 53) | 3.8 (± 6.53) | 4.3 (± 9.45) | | |
| Psychological summary score Week 2 (n = 48, 50) | 3.1 (± 8.85) | -0.2 (± 10.15) | | |
| Psychological summary score Week 4 (n = 49, 51) | 2.8 (± 9.05) | 1.9 (± 7.74) | | |
| Psychological summary score Week 6 (n = 50, 54) | 2.7 (± 9.35) | 2.5 (± 7.24) | | |
| Psychological summary score Week 8 (n = 50, 54) | 3.7 (± 9.57) | 2.1 (± 8.33) | | |
| Psychological summary score Week 10 (n = 47, 53) | 3.6 (± 10.39) | 1.8 (± 9.43) | | |

**Statistical analyses**

| Statistical analysis title | Physical summary score Week 2 |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[180] |
| P-value | = 0.054 [181] |
| Method | ANCOVA |

Notes:

[180] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[181] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| Statistical analysis title | Physical summary score Week 4 |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[182] |
| P-value | = 0.955 [183] |
| Method | ANCOVA |

Notes:

[182] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[183] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as

covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Physical summary score Week 6 |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[184] |
| P-value | = 0.8 [185] |
| Method | ANCOVA |

Notes:

[184] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[185] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Physical summary score Week 8 |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[186] |
| P-value | = 0.641 [187] |
| Method | ANCOVA |

Notes:

[186] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[187] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Physical summary score Week 10 |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[188] |
| P-value | = 0.783 [189] |
| Method | ANCOVA |

Notes:

[188] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[189] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Psychological summary score Week 2 |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[190] |
| P-value | = 0.139 [191] |
| Method | ANCOVA |

Notes:

[190] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[191] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity

and therefore should be interpreted with caution.

| **Statistical analysis title** | Psychological summary score Week 4 |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[192] |
| P-value | = 0.876 [193] |
| Method | ANCOVA |

Notes:

[192] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[193] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Psychological summary score Week 6 |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[194] |
| P-value | = 0.236 [195] |
| Method | ANCOVA |

Notes:

[194] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[195] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Psychological summary score Week 8 |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[196] |
| P-value | = 0.608 [197] |
| Method | ANCOVA |

Notes:

[196] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[197] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity and therefore should be interpreted with caution.

| **Statistical analysis title** | Psychological summary score Week 10 |
|---|---|
| Comparison groups | 10 mg Rabeprazole sodium v 20 mg Rabeprazole sodium |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | other[198] |
| P-value | = 0.697 [199] |
| Method | ANCOVA |

Notes:

[198] - This was an open-label trial testing two dosages of rabeprazole sodium for safety and efficacy.

[199] - P-value from ANCOVA taking treatment and center as fixed factors, and baseline values as covariates. P-values reported as statistically significant (ie, P<0.05) were not adjusted for multiplicity

and therefore should be interpreted with caution.

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Adverse events were collected for up to 12 weeks. | |
| Adverse event reporting additional description: | |
| Treatment-emergent adverse events were reported. The Safety Population was used and included all participants who received at least 1 dose of study treatment. | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 8.0 |

| Reporting groups | |
|---|---|
| Reporting group title | 10 mg Rabeprazole sodium |
| Reporting group description: | |
| Participants had a screening evaluation within 2 weeks prior to starting study drug administration. Participants received 10 mg rabeprazole once daily at the same time each day for 8 weeks, with a follow-up visit at Week 10. | |
| Reporting group title | 20 mg Rabeprazole sodium |
| Reporting group description: | |
| Participants had a screening evaluation within 2 weeks prior to starting study drug administration. Participants received 20 mg rabeprazole once daily at the same time each day for 8 weeks, with a follow-up visit at Week 10. | |

| Serious adverse events | 10 mg Rabeprazole sodium | 20 mg Rabeprazole sodium | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 54 (0.00%) | 1 / 57 (1.75%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Psychiatric disorders | | | |
| Mood swings | | | |
| subjects affected / exposed | 0 / 54 (0.00%) | 1 / 57 (1.75%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | 10 mg Rabeprazole sodium | 20 mg Rabeprazole sodium | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 21 / 54 (38.89%) | 26 / 57 (45.61%) | |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Headache | | | |
| subjects affected / exposed | 5 / 54 (9.26%) | 6 / 57 (10.53%) | |
| occurrences (all) | 6 | 6 | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 54 (0.00%) | 3 / 57 (5.26%) | |
| occurrences (all) | 0 | 3 | |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | 3 / 57 (5.26%) | |
| occurrences (all) | 1 | 3 | |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | 2 / 57 (3.51%) | |
| occurrences (all) | 3 | 2 | |
| Nausea | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | 2 / 57 (3.51%) | |
| occurrences (all) | 3 | 2 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 5 / 54 (9.26%) | 3 / 57 (5.26%) | |
| occurrences (all) | 5 | 3 | |
| Nasal congestion | | | |
| subjects affected / exposed | 4 / 54 (7.41%) | 4 / 57 (7.02%) | |
| occurrences (all) | 4 | 4 | |
| Pharyngolaryngeal pain | | | |
| subjects affected / exposed | 6 / 54 (11.11%) | 5 / 57 (8.77%) | |
| occurrences (all) | 6 | 5 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | 2 / 57 (3.51%) | |
| occurrences (all) | 3 | 2 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | 4 / 57 (7.02%) | |
| occurrences (all) | 1 | 4 | |
| Otitis media | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 54 (1.85%) | 3 / 57 (5.26%) | |
| occurrences (all) | 1 | 3 | |
| Pharyngitis | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | 2 / 57 (3.51%) | |
| occurrences (all) | 3 | 2 | |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | 3 / 57 (5.26%) | |
| occurrences (all) | 2 | 4 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 54 (7.41%) | 3 / 57 (5.26%) | |
| occurrences (all) | 4 | 3 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported