# EU Clinical Trials Register

## Clinical trial results:
## A multicentre, randomised, double-blind, two arm, parallel group, placebo controlled pivotal study to assess the effect of a sodium alginate liquid suspension as add-on therapy in GORD patients with inadequate response to once daily proton pump inhibitor treatment.

### Summary

| EudraCT number | 2014-003174-17 |
|---|---|
| Trial protocol | GB |
| Global end of trial date | 24 December 2015 |

### Results information

| Result version number | v1 (current) |
|---|---|
| This version publication date | 19 November 2017 |
| First version publication date | 19 November 2017 |

### Trial information

#### Trial identification

| Sponsor protocol code | GA1405 |
|---|---|

#### Additional study identifiers

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

Notes:

#### Sponsors

| Sponsor organisation name | Reckitt Benckiser Healthcare (UK) Ltd |
|---|---|
| Sponsor organisation address | Dansom Lane, Hull, United Kingdom, HU8 7DS |
| Public contact | Clinical Research Director, Clinical Research, Reckitt Benckiser Healthcare (UK) Limited, clinicalrequests@rb.com |
| Scientific contact | Clinical Research Director, Clinical Research, Reckitt Benckiser Healthcare (UK) Limited, clinicalrequests@rb.com |

Notes:

#### Paediatric regulatory details

| Is trial part of an agreed paediatric investigation plan (PIP) | No |
|---|---|
| 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 | 17 March 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 24 December 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 December 2015 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the efficacy of sodium alginate liquid suspension compared with matched placebo liquid in the suppression of GORD symptoms in patients whose symptoms are inadequately controlled by once daily PPI therapy alone.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice(GCP) and the ethical principles contained within the Declaration of Helsinki, as referenced in EU Directive 2001 / 20 / EC.

| | |
|---|---|
| Background therapy: - | |
| Evidence for comparator: - | |
| Actual start date of recruitment | 28 April 2015 |
| 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 Kingdom: 227 |
| Country: Number of subjects enrolled | Germany: 169 |
| Worldwide total number of subjects | 396 |
| EEA total number of subjects | 396 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 106 |
| From 65 to 84 years | 290 |

| 85 years and over | 0 |
| --- | --- |

# Subject disposition

## Recruitment

Recruitment details:

This study was conducted in 19 primary care sites in the United Kingdom (UK) and Germany.

## Pre-assignment

Screening details:

A total of 396 patients were screened for the study; 371 patients entered the run-in period and 133 patients were discontinued prior to randomization. Randomized subjects were 263.

One subject from placebo group was lost to follow-up. This subject was excluded from ITT population as it is unknown whether any medication was taken by this subject.

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 396 |
| Intermediate milestone: Number of subjects | Run-in period: 371 |
| Number of subjects completed | 263 |

### Pre-assignment subject non-completion reasons

| | |
|---|---|
| Reason: Number of subjects | Screen failure: 133 |

## Period 1

| | |
|---|---|
| Period 1 title | Overall (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Gaviscon® Double Action Liquid |

Arm description:

Gaviscon® Double Action 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Gaviscon® Double Action Liquid |
| Investigational medicinal product code | |
| Other name | sodium alginate liquid suspension |
| Pharmaceutical forms | Oral suspension in sachet |
| Routes of administration | Oral use |

Dosage and administration details:

Gaviscon® Double Action (sodium alginate 1000 mg, sodium bicarbonate 426 mg and calcium carbonate 650 mg) 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

Placebo 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days

| | |
|---|---|
| Arm type | Placebo |

| Investigational medicinal product name | Placebo |
|---|---|
| Investigational medicinal product code | |
| Other name | Matched placebo liquid |
| Pharmaceutical forms | Oral suspension in sachet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days

| Number of subjects in period 1[1] | Gaviscon® Double Action Liquid | Placebo |
|---|---|---|
| Started | 131 | 132 |
| Completed | 128 | 130 |
| Not completed | 3 | 2 |
|     Adverse event | 3 | 1 |
|     Lost to follow-up | - | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 396 patients were screened for the study; 371 patients entered the run-in period and 133 patients were discontinued prior to randomization. Randomized subjects were 263.

## Baseline characteristics

### Reporting groups

| | |
|---|---|
| Reporting group title | Gaviscon® Double Action Liquid |
| Reporting group description: | |
| Gaviscon® Double Action 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Placebo 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days | |

| Reporting group values | Gaviscon® Double Action Liquid | Placebo | Total |
|---|---|---|---|
| Number of subjects | 131 | 132 | 263 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 27 | 32 | 59 |
| From 65-84 years | 104 | 100 | 204 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 54.28 | 52.36 | |
| standard deviation | ± 12.62 | ± 14.41 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 82 | 76 | 158 |
| Male | 49 | 56 | 105 |
| Race | | | |
| Units: Subjects | | | |
| Caucasian (White) | 129 | 132 | 261 |
| Asian | 2 | 0 | 2 |
| Height | | | |
| Units: cm | | | |
| arithmetic mean | 168.56 | 171.15 | |
| standard deviation | ± 9.6 | ± 9.82 | - |
| Weight | | | |
| Units: kg | | | |
| arithmetic mean | 83.75 | 85.82 | |
| standard deviation | ± 17.5 | ± 19.63 | - |
| BMI | | | |
| BMI - Body mass index | | | |
| Units: kg/m2 | | | |
| arithmetic mean | 29.41 | 29.28 | |
| standard deviation | ± 5.32 | ± 6.25 | - |

# End points

## End points reporting groups

| Reporting group title | Gaviscon® Double Action Liquid |
|---|---|
| Reporting group description: |
| Gaviscon® Double Action 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days | |
| Reporting group title | Placebo |
| Reporting group description: |
| Placebo 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days | |

## Primary: Number of subjects with Reduction of at least 3 days in HRDQ (heartburn & regurgitation) score >0.7 during 7-day treatment period compared to baseline (7-day run-in period)

| End point title | Number of subjects with Reduction of at least 3 days in HRDQ (heartburn & regurgitation) score >0.7 during 7-day treatment period compared to baseline (7-day run-in period) |
|---|---|

End point description:

Intention-to-treat (ITT) population: All subjects in the safety set who were recruited into the study and had at least 1 day of complete HRDQ scores (severity and frequency scores for both Heartburn and Regurgitation) for both the run-in and treatment periods. Subjects were assigned to the treatment groups as randomised. This population was used for summaries of efficacy and baseline data.

Heartburn Regurgitation and Dyspepsia Questionnaire (HRDQ): HRDQ symptom severity was recorded: 0 (no symptoms), 1 (mild), 2 (moderate) and 3 (severe) and the frequency was scored as 0 (none), 1 (once), 2 (twice), 3 (thrice), 4 (4 or 5 times), 5 (6 – 10 times) and 6 (more than 10 times or constant). In addition, the HRDQ questionnaire required patients to record the duration of their symptoms and whether or not they had experienced night-time symptoms.

| End point type | Primary |
|---|---|

End point timeframe:

Up to Day 7 (treatment period)

| End point values | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: Subjects | | | | |
| Reduction in HRDQ Score >0.7: Less than 3 days | 64 | 68 | | |
| Reduction in HRDQ Score >0.7: 3 days | 16 | 24 | | |
| Reduction in HRDQ Score >0.7: 4 days | 13 | 9 | | |
| Reduction in HRDQ Score >0.7: 5 days | 17 | 13 | | |
| Reduction in HRDQ Score >0.7: 6 days | 12 | 7 | | |
| Reduction in HRDQ Score >0.7: 7 days | 9 | 10 | | |
| Reduction in HRDQ Score >0.7: 3 to 7 days | 67 | 63 | | |

## Statistical analyses

| Statistical analysis title | Reduction in HRDQ Score >0.7: Gaviscon vs Placebo |
|---|---|
| Comparison groups | Placebo v Gaviscon® Double Action Liquid |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5939 |
| Method | Regression, Logistic |

## Secondary: Change in mean daily HRDQ score (heartburn and regurgitation) from baseline (7-day run-in period)

| End point title | Change in mean daily HRDQ score (heartburn and regurgitation) from baseline (7-day run-in period) |
|---|---|
| End point description: | |
| ITT population. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Day 7 (treatment period) | |

| End point values | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: unit on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Run-in Period | 1.79 (± 0.84) | 1.64 (± 0.71) | | |
| Treatment Period | 0.91 (± 0.8) | 0.84 (± 0.67) | | |
| Change from run-in to treatment periods | -0.89 (± 0.8) | -0.8 (± 0.68) | | |

## Statistical analyses

| Statistical analysis title | HRDQ Score: Gaviscon vs Placebo |
|---|---|
| Statistical analysis description: | |
| HRDQ Score (Heartburn & Regurgitation) | |
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8435 |
| Method | ANCOVA |

## Secondary: Change in mean daily heartburn and regurgitation score from baseline (7-day run-in period)

| End point title | Change in mean daily heartburn and regurgitation score from baseline (7-day run-in period) |
|---|---|
| End point description: | |
| ITT population. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Day 7 (treatment period) | |

| End point values | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: Unit on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Heartburn - Run-in Period | 0.94 (± 0.51) | 0.85 (± 0.41) | | |
| Heartburn - Treatment Period | 0.45 (± 0.45) | 0.41 (± 0.34) | | |
| Heartburn - Change from run-in to treatment period | -0.49 (± 0.45) | -0.43 (± 0.39) | | |
| Regurgitation - Run-in period | 0.85 (± 0.47) | 0.79 (± 0.43) | | |
| Regurgitation - Treatment period | 0.46 (± 0.43) | 0.43 (± 0.4) | | |
| Regurgitation-Change b/w run-in & treatment period | -0.4 (± 0.42) | -0.36 (± 0.36) | | |

## Statistical analyses

| Statistical analysis title | HRDQ Heartburn - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8537 |
| Method | ANCOVA |

| Statistical analysis title | HRDQ Regurgitation - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8409 |
| Method | ANCOVA |

## Secondary: Change in mean daily frequency of individual symptoms (heartburn & regurgitation) from baseline (7-day run-in period)

| | |
|---|---|
| End point title | Change in mean daily frequency of individual symptoms (heartburn & regurgitation) from baseline (7-day run-in period) |
| End point description: | |
| ITT population. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Day 7 (treatment period) | |

| End point values | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: Unit on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Heartburn Frequency - Run-in Period | 3.98 (± 2.5) | 3.46 (± 1.89) | | |
| Heartburn Frequency - Treatment Period | 1.97 (± 2.02) | 1.81 (± 1.56) | | |
| Heartburn Frequency - Change from baseline | -2.01 (± 1.97) | -1.65 (± 1.62) | | |
| Regurgitation Frequency - Run-in period | 3.82 (± 2.53) | 3.44 (± 2.18) | | |
| Regurgitation Frequency - Treatment period | 2.26 (± 2.36) | 2.02 (± 2.08) | | |
| Regurgitation Frequency -Change from baseline | -1.56 (± 1.89) | -1.42 (± 1.44) | | |

## Statistical analyses

| Statistical analysis title | HRDQ Heartburn Frequency - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5847 |
| Method | ANCOVA |

| Statistical analysis title | HRDQ Regurgitation Frequency - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8618 |
| Method | ANCOVA |

## Secondary: Change in mean daily severity of individual symptoms (heartburn & regurgitation) from baseline (7-day run-in period)

| End point title | Change in mean daily severity of individual symptoms (heartburn & regurgitation) from baseline (7-day run-in period) |
|---|---|
| End point description: | |
| ITT population. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Day 7 (treatment period) | |

| End point values | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: Unit on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Heartburn Severity - Run-in Period | 1.65 (± 0.63) | 1.56 (± 0.57) | | |
| Heartburn Severity - Treatment Period | 0.94 (± 0.68) | 0.92 (± 0.56) | | |
| Heartburn Severity - Change from baseline | -0.71 (± 0.68) | -0.64 (± 0.57) | | |
| Regurgitation Severity - Run-in period | 1.53 (± 0.6) | 1.45 (± 0.58) | | |
| Regurgitation Severity - Treatment period | 0.92 (± 0.65) | 0.88 (± 0.61) | | |
| Regurgitation Severity -Change from baseline | -0.61 (± 0.64) | -0.57 (± 0.57) | | |

## Statistical analyses

| Statistical analysis title | HRDQ Heartburn Severity - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7243 |
| Method | ANCOVA |

| Statistical analysis title | HRDQ Regurgitation Severity - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.935 |
| Method | ANCOVA |

## Secondary: Change in mean daily duration of symptoms (heartburn & regurgitation) from baseline (7-day run-in period)

| End point title | Change in mean daily duration of symptoms (heartburn & regurgitation) from baseline (7-day run-in period) |
|---|---|

End point description:

ITT population.

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

End point timeframe:

Up to Day 7 (treatment period)

| End point values | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: minutes | | | | |
| arithmetic mean (standard deviation) | | | | |
| Run-in period | 253.08 (± 295.08) | 203.37 (± 244.58) | | |
| Treatment period | 136.05 (± 209.04) | 126.14 (± 190.68) | | |
| Change from run-in to treatment periods | -117.022 (± 217.499) | -77.231 (± 166.587) | | |

## Statistical analyses

| Statistical analysis title | HRDQ Daily Symptoms Duration - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3304 |
| Method | ANCOVA |

## Secondary: Change from baseline (7-day run-in period) in patient satisfaction scores at end of study

| | |
|---|---|
| End point title | Change from baseline (7-day run-in period) in patient satisfaction scores at end of study |

End point description:

ITT population.

Patient satisfaction with medication in controlling their symptoms was assessed in response to the question: 'Thinking back over the past 7 days and the medication you received, how satisfied are you with the control of your symptoms?' The patient had to draw a perpendicular line on a 100 mm Visual Analogue Scale (VAS), with anchors at 0 = 'Very Dissatisfied' and 100 = 'Very Satisfied.'

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

End point timeframe:

Up to Day 8 (End of Study visit)

| **End point values** | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: Unit on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Run-in period | 30.99 (± 21.86) | 36.23 (± 20.82) | | |
| Treatment period | 61.22 (± 29.93) | 63.96 (± 27.96) | | |
| Change from run-in to treatment periods | 30.2 (± 35.08) | 27.84 (± 28.51) | | |

## Statistical analyses

| **Statistical analysis title** | Patient Satisfaction scores - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9028 |
| Method | ANCOVA |

## Secondary: Change in mean reflux disease questionnaire (RDQ) symptom scores for GORD dimension from baseline (7-day run-in period)

| End point title | Change in mean reflux disease questionnaire (RDQ) symptom scores for GORD dimension from baseline (7-day run-in period) |
|---|---|

End point description:

ITT population.

RDQ consists of 12 items that describe 3 dimensions for assessment of heartburn, dyspepsia, & regurgitation. Heartburn and regurgitation can be combined into a GORD dimension. Each dimension includes 4 items measuring the frequency and severity of following questions:
• A burning feeling behind your breastbone (heartburn)
• Pain behind your breastbone (heartburn)
• An acid taste in your mouth (regurgitation)
• Unpleasant movement of material upwards from the stomach (regurgitation)
• A burning feeling in the center of the upper stomach (dyspepsia)
• A pain in the center of the upper stomach (dyspepsia)

Response options are scaled with scores 0, 1, 2, 3, 4, 5 for frequencies (Did not have, 1 day, 2 days, 3-4 days, 5-6 days, Daily), whereas for Severity a 6-grade Likert scale is used (0=Did not have, 1=Very mild, 2=Mild, 3=Moderate, 4=Moderately severe, & 5=Severe).

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

End point timeframe:

Up to Day 7 (treatment period)

| **End point values** | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: Unit on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Run-in period | 2.87 (± 1.05) | 2.72 (± 0.99) | | |
| Treatment period | 1.71 (± 1.17) | 1.62 (± 1.16) | | |
| Change from run-in to treatment periods | -1.15 (± 1.14) | -1.1 (± 1.15) | | |

## Statistical analyses

| **Statistical analysis title** | RDQ Scores for GORD Dimension -Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8288 |
| Method | ANCOVA |

## Secondary: Change in mean RDQ scores for Heartburn and Regurgitation from baseline (7-day run-in period)

| End point title | Change in mean RDQ scores for Heartburn and Regurgitation |
|---|---|

from baseline (7-day run-in period)

| End point description: | |
|---|---|
| ITT population. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Day 7 (treatment period) | |

| **End point values** | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: Unit on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Heartburn - Run-in Period | 2.76 (± 1.36) | 2.63 (± 1.3) | | |
| Heartburn - Treatment Period | 1.72 (± 1.39) | 1.7 (± 1.39) | | |
| Heartburn - Change from baseline | -1.03 (± 1.39) | -0.95 (± 1.32) | | |
| Regurgitation - Run-in period | 2.98 (± 1.31) | 2.81 (± 1.26) | | |
| Regurgitation - Treatment period | 1.7 (± 1.38) | 1.55 (± 1.37) | | |
| Regurgitation - Change from baseline | -1.27 (± 1.37) | -1.26 (± 1.35) | | |

**Statistical analyses**

| **Statistical analysis title** | RDQ Heartburn - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8854 |
| Method | ANCOVA |

| **Statistical analysis title** | RDQ Regurgitation - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Placebo v Gaviscon® Double Action Liquid |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6107 |
| Method | ANCOVA |

**Secondary: Change in mean RDQ frequency scores for heartburn and regurgitation from baseline (7-day run-in period)**

| End point title | Change in mean RDQ frequency scores for heartburn and |
|---|---|

| regurgitation from baseline (7-day run-in period) | |
|---|---|

| End point description: | |
|---|---|
| ITT population. | |

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

| End point timeframe: | |
|---|---|
| Up to Day 7 (treatment period) | |

| **End point values** | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: Unit on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Heartburn frequency - Run-in Period | 2.93 (± 1.56) | 2.82 (± 1.52) | | |
| Heartburn frequency - Treatment Period | 1.83 (± 1.57) | 1.87 (± 1.61) | | |
| Heartburn frequency - Change from baseline | -1.09 (± 1.62) | -0.97 (± 1.56) | | |
| Regurgitation frequency - Run-in period | 3.13 (± 1.46) | 2.97 (± 1.45) | | |
| Regurgitation frequency - Treatment period | 1.81 (± 1.54) | 1.64 (± 1.55) | | |
| Regurgitation frequency - Change from baseline | -1.31 (± 1.51) | -1.31 (± 1.58) | | |

**Statistical analyses**

| **Statistical analysis title** | RDQ Heartburn frequency - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7026 |
| Method | ANCOVA |

| **Statistical analysis title** | RDQ Regurgitation frequency - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Placebo v Gaviscon® Double Action Liquid |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5541 |
| Method | ANCOVA |

**Secondary: Change in mean RDQ severity scores for heartburn and regurgitation**

## from baseline (7-day run-in period)

| End point title | Change in mean RDQ severity scores for heartburn and regurgitation from baseline (7-day run-in period) |
|---|---|
| End point description: | |
| ITT population. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Day 7 (treatment period) | |

| End point values | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: Unit on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Heartburn Severity - Run-in Period | 2.59 (± 1.29) | 2.45 (± 1.2) | | |
| Heartburn Severity - Treatment Period | 1.61 (± 1.33) | 1.53 (± 1.28) | | |
| Heartburn Severity - Change from baseline | -0.98 (± 1.33) | -0.93 (± 1.24) | | |
| Regurgitation Severity - Run-in period | 2.82 (± 1.29) | 2.66 (± 1.24) | | |
| Regurgitation Severity - Treatment period | 1.58 (± 1.33) | 1.45 (± 1.29) | | |
| Regurgitation Severity -Change from baseline | -1.24 (± 1.4) | -1.21 (± 1.28) | | |

## Statistical analyses

| Statistical analysis title | RDQ Heartburn Severity - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8724 |
| Method | ANCOVA |

| Statistical analysis title | RDQ Regurgitation Severity - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6732 |
| Method | ANCOVA |

## Secondary: Change in mean HRDQ scores for number of nights with symptoms from baseline (7-day run-in period)

| End point title | Change in mean HRDQ scores for number of nights with symptoms from baseline (7-day run-in period) |
|---|---|
| End point description: | |
| ITT population. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Day 7 (treatment period) | |

| End point values | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: Unit on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Run-in period | 4.07 (± 2.67) | 4.25 (± 2.52) | | |
| Treatment period | 2.57 (± 2.67) | 2.69 (± 2.61) | | |
| Change from run-in to treatment periods | -1.49 (± 2.48) | -1.56 (± 2.42) | | |

### Statistical analyses

| Statistical analysis title | HRDQ Night symptoms - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Poisson regression model |

## Secondary: Number of subjects with night-time symptoms

| End point title | Number of subjects with night-time symptoms |
|---|---|
| End point description: | |
| ITT population. | |
| End point type | Secondary |
| End point timeframe: | |
| At baseline (7-day run-in period) and Day 7 (treatment period) | |

| End point values | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: Subjects | | | | |
| Run-in period - Yes | 107 | 115 | | |
| Run-in period - No | 24 | 16 | | |
| Treatment period - Yes | 83 | 89 | | |
| Treatment period - No | 48 | 42 | | |

## Statistical analyses

| Statistical analysis title | HRDQ subjects count with Night symptoms |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4158 |
| Method | Cochran-Mantel-Haenszel |

## Secondary: Days free from Heartburn and Regurgitation symptoms

| End point title | Days free from Heartburn and Regurgitation symptoms |
|---|---|

End point description:

ITT population.

Symptom-free day is defined as a day where the respective symptoms (heartburn and regurgitation — all derived from the HRDQ) had a value for frequency of 0.

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

End point timeframe:

Up to Day 7 (treatment period)

| End point values | Gaviscon® Double Action Liquid | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 131 | 131 | | |
| Units: Days | | | | |
| arithmetic mean (standard deviation) | | | | |
| Run-in period | 0.1 (± 0.49) | 0.19 (± 0.5) | | |
| Treatment period | 1.45 (± 2.15) | 1.45 (± 2.04) | | |

| Change from run-in to treatment periods | 1.35 (± 2.1) | 1.26 (± 2) | | |
|---|---|---|---|---|

## Statistical analyses

| Statistical analysis title | HRDQ Symptom free days - Gaviscon vs Placebo |
|---|---|
| Comparison groups | Gaviscon® Double Action Liquid v Placebo |
| Number of subjects included in analysis | 262 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Poisson regression model |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to Day 8 (visit 3, End of Study)

Adverse event reporting additional description:

Treatment-Emergent Adverse Events (TEAEs) for SAF population.

Safety (SAF) population includes all subjects who were recruited into the study and received at least one dose of the study medication.

| Assessment type | Systematic |
|---|---|

### Dictionary used

| Dictionary name | MedDRA |
|---|---|
| Dictionary version | 18 |

### Reporting groups

| Reporting group title | Overall study |
|---|---|

Reporting group description: -

| Serious adverse events | Overall study | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

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

| Non-serious adverse events | Overall study | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 108 / 263 (41.06%) | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| Malaise | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 263 (0.76%) | | |
| occurrences (all) | 2 | | |
| **Respiratory, thoracic and mediastinal disorders** | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 4 / 263 (1.52%) | | |
| occurrences (all) | 4 | | |
| Throat irritation | | | |
| subjects affected / exposed | 3 / 263 (1.14%) | | |
| occurrences (all) | 3 | | |
| **Psychiatric disorders** | | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| **Injury, poisoning and procedural complications** | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 4 / 263 (1.52%) | | |
| occurrences (all) | 4 | | |
| Epicondylitis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| Laceration | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| Overdose | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| **Nervous system disorders** | | | |
| Headache | | | |
| subjects affected / exposed | 20 / 263 (7.60%) | | |
| occurrences (all) | 20 | | |
| Lethargy | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| **Ear and labyrinth disorders** | | | |
| Vertigo | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 2 / 263 (0.76%) | | | |
| occurrences (all) | 2 | | | |

**Eye disorders**

Visual impairment

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 263 (0.38%) | | | |
| occurrences (all) | 1 | | | |

**Gastrointestinal disorders**

Abdominal discomfort

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 3 / 263 (1.14%) | | | |
| occurrences (all) | 3 | | | |

Abdominal distension

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 3 / 263 (1.14%) | | | |
| occurrences (all) | 3 | | | |

Abdominal pain

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 4 / 263 (1.52%) | | | |
| occurrences (all) | 4 | | | |

Abdominal pain upper

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 8 / 263 (3.04%) | | | |
| occurrences (all) | 8 | | | |

Defaecation urgency

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 263 (0.38%) | | | |
| occurrences (all) | 1 | | | |

Diarrhoea

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 10 / 263 (3.80%) | | | |
| occurrences (all) | 10 | | | |

Dyspepsia

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 263 (0.38%) | | | |
| occurrences (all) | 1 | | | |

Flatulence

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 6 / 263 (2.28%) | | | |
| occurrences (all) | 6 | | | |

Nausea

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 11 / 263 (4.18%) | | | |
| occurrences (all) | 11 | | | |

Regurgitation

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 263 (0.76%) | | |
| occurrences (all) | 2 | | |
| **Skin and subcutaneous tissue disorders** | | | |
| Erythema | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| **Renal and urinary disorders** | | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| **Musculoskeletal and connective tissue disorders** | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 263 (0.76%) | | |
| occurrences (all) | 2 | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 263 (0.76%) | | |
| occurrences (all) | 2 | | |
| **Infections and infestations** | | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 263 (1.14%) | | |
| occurrences (all) | 3 | | |

| | | | |
|---|---|---|---|
| Sinusitis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |
| | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | | |
| occurrences (all) | 1 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol?  Yes

| Date | Amendment |
|---|---|
| 31 July 2015 | The following changes to the study protocol were made:<br>1. The creation of additional subsections to accommodate the addition of an exploratory endpoint section.<br>2. The clarification of an existing secondary endpoint.<br>3. The reclassification of some secondary endpoints into exploratory endpoints.<br>4. The addition of a new endpoint to newly created exploratory endpoints section.<br>5. Changes to the compliance, calculations and which data to be used.<br>6. Correction to text for classification of AEs.<br>7. Administrative correction to Table 11-1.<br>This amendment was considered to be substantial due to the impact on the scientific integrity of the study that the following changes had:<br>The secondary endpoint was amended to specify the symptoms from which patients had to experience alleviation within the 7-day treatment period.<br>The addition of a new secondary endpoint which specified the symptoms from which patients had to experience alleviation within the 7-day treatment period.<br>Changes made had no impact on the conduct of the study. These were purely in relation to the analysis of data and/or correction to text. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial?  No

### Limitations and caveats

 None reported

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/28464343