Clinical trial results:
A multi-centre, randomised, double-blind, two arm, parallel group, placebo-controlled study to assess the effect of Sodium Alginate Chewable Tablets on symptoms of gastro-oesophageal reflux disease.

Summary

EudraCT number	2014-005261-69
Trial protocol	GB DE IT
Global end of trial date	30 August 2016

Results information

Result version number	v1 (current)
This version publication date	17 September 2017
First version publication date	17 September 2017

Trial information

Trial identification

Sponsor protocol code	GA1402

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	07 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 August 2016
Global end of trial reached?	Yes
Global end of trial date	30 August 2016
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 Chewable Tablets compared to matched placebo tablets in the reduction of the symptoms of GORD as assessed using the Reflux Disease Questionnaire (RDQ).

Protection of trial subjects:

This study was conducted in accordance with the 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	21 September 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: 93
Country: Number of subjects enrolled	Germany: 288
Country: Number of subjects enrolled	Italy: 43
Worldwide total number of subjects	424
EEA total number of subjects	424

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)	333
From 65 to 84 years	88

85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited at sites in the United Kingdom, Germany and Italy.

Pre-assignment

Screening details:

Total 526 subjects were screened; 99 subjects were screening failures; 427 subjects were randomized & 426 subjects were treated (1 subject was randomized in error). Subject included in analysis were 424 (2 lost to follow-up subjects from both groups were also excluded from analysis due to no treatment evidence & evaluable data for any visits).

Period 1

Period 1 title	Overall trial (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

Arm description:

Gaviscon Double Action Tablets, 4 tablets by mouth 4 times daily for 7 - 10 days

Arm type	Experimental
Investigational medicinal product name	Gaviscon Double Action Tablets
Investigational medicinal product code	
Other name	Sodium alginate chewable tablets
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Gaviscon Double Action Tablets, 4 tablets by mouth 4 times daily for 7 - 10 days

Arm title	Placebo

Arm description:

Placebo (matching tablets) 4 tablets 4 times daily for 7 - 10 days

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

Dosage and administration details:

Placebo (matching tablets), 4 tablets 4 times daily for 7 - 10 days

Number of subjects in period 1	Gaviscon	Placebo
Started	212	212
Completed	200	199
Not completed	12	13
Consent withdrawn by subject	1	-
Adverse event, non-fatal	9	9
Lack of efficacy	1	2
Protocol deviation	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Gaviscon
Reporting group description:	
Gaviscon Double Action Tablets, 4 tablets by mouth 4 times daily for 7 - 10 days	
Reporting group title	Placebo
Reporting group description:	
Placebo (matching tablets) 4 tablets 4 times daily for 7 - 10 days	

Reporting group values	Gaviscon	Placebo	Total
Number of subjects	212	212	424
Age categorical			
ITT population			
Units: Subjects			
Adults (18-64 years)	172	161	333
From 65-84 years	38	50	88
85 years and over	2	1	3
Age continuous			
ITT population			
Units: years			
arithmetic mean	50	50.1	
standard deviation	± 15.51	± 16.47	-
Gender categorical			
ITT population			
Units: Subjects			
Female	110	115	225
Male	102	97	199
Ethnicity			
ITT population			
Units: Subjects			
Asian	2	2	4
Black or African American	1	1	2
Other	0	0	0
White	209	209	418
Smoking history			
ITT population			
Units: Subjects			
Current smoker	45	46	91
Ex-smoker	58	52	110
Never smoked	109	114	223
Alcohol consumer			
ITT population			
Units: Subjects			
No	91	107	198
Yes	121	105	226

Height			
ITT population			
Units: cm			
arithmetic mean	171.3	170.1	
standard deviation	± 9.39	± 10.32	-
Weight			
ITT population			
Units: kg			
arithmetic mean	82.2	80.2	
standard deviation	± 18.07	± 17.56	-

End points

End points reporting groups

Reporting group title	Gaviscon
Reporting group description:	
Gaviscon Double Action Tablets, 4 tablets by mouth 4 times daily for 7 - 10 days	
Reporting group title	Placebo
Reporting group description:	
Placebo (matching tablets) 4 tablets 4 times daily for 7 - 10 days	

Primary: Number of subjects with a reduction of at least 1.5 points in the RDQ GORD dimension from baseline

End point title	Number of subjects with a reduction of at least 1.5 points in the RDQ GORD dimension from baseline

End point description:

Intent-to-treat (ITT) population: All randomized subjects (minus three subjects with no evaluable data).

Reflux Disease Questionnaire (RDQ) is a validated 12-item self-assessment questionnaire in which subjects are asked to rate the frequency and severity of 6 symptoms covering the two dimensions of Gastro-Oesophageal Reflux Disease (GORD) – regurgitation and heartburn – and dyspepsia on 6-point Likert scales ranging from 0 = None to 5 = Daily and 0 = none to 5 = Severe, respectively.

Response = Reduction of RDQ GORD dimension score ≥1.5.
Responder = Subject with a reduction from baseline of 1.5 points in the RDQ GORD dimension score.

End point type	Primary

End point timeframe:

Visit 2 (baseline) to visit 3

End point values	Gaviscon	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	212		
Units: Participants				
Non-responders	101	132		
Responders	111	80		

Statistical analyses

Statistical analysis title	RDQ GORD responses

Statistical analysis description:

Number of subjects with a reduction of at least 1.5 points in the RDQ GORD dimension from baseline

Comparison groups	Gaviscon v Placebo

Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0031
Method	ANCOVA

Secondary: Change from baseline in RDQ GORD dimension score

End point title	Change from baseline in RDQ GORD dimension score
End point description: ITT population	
End point type	Secondary
End point timeframe: Visit 2 (baseline) to visit 3	

End point values	Gaviscon	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	212		
Units: Participants				
arithmetic mean (standard deviation)				
Baseline (Visit 2)	3.1 (± 0.93)	3 (± 0.9)		
End of treatment (Visit 3)	1.4 (± 1.2)	1.7 (± 1.21)		
Change from Baseline	-1.7 (± 1.27)	-1.3 (± 1.16)		

Statistical analyses

Statistical analysis title	RDQ GORD dimension score
Comparison groups	Gaviscon v Placebo
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	ANCOVA

Secondary: Change from baseline in RDQ heartburn score

End point title	Change from baseline in RDQ heartburn score
End point description: ITT population	
End point type	Secondary
End point timeframe: Visit 2 (baseline) to visit 3	

End point values	Gaviscon	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	212		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Baseline (Visit 2)	3 (± 1.29)	2.9 (± 1.19)		
End of treatment (Visit 3)	1.5 (± 1.37)	1.8 (± 1.41)		
Change from Baseline	-1.6 (± 1.58)	-1.2 (± 1.36)		

Statistical analyses

Statistical analysis title	RDQ heartburn score
Comparison groups	Gaviscon v Placebo
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019
Method	ANCOVA

Secondary: Change from baseline in RDQ regurgitation score	
End point title	Change from baseline in RDQ regurgitation score
End point description: ITT population	
End point type	Secondary
End point timeframe: Visit 2 (baseline) to visit 3	

End point values	Gaviscon	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	212		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Baseline (Visit 2)	3.1 (± 1.16)	3.1 (± 1.19)		
End of treatment (Visit 3)	1.3 (± 1.4)	1.7 (± 1.39)		
Change from Baseline	-1.8 (± 1.45)	-1.5 (± 1.45)		

Statistical analyses

Statistical analysis title	RDQ regurgitation score
Comparison groups	Gaviscon v Placebo
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029
Method	ANCOVA

Secondary: Change from baseline in RDQ dyspepsia score	
End point title	Change from baseline in RDQ dyspepsia score
End point description: ITT population	
End point type	Secondary
End point timeframe: Visit 2 (baseline) to visit 3	

End point values	Gaviscon	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	212		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Baseline (Visit 2)	2.6 (± 1.41)	2.5 (± 1.29)		
End of treatment (Visit 3)	1.3 (± 1.36)	1.6 (± 1.41)		
Change from Baseline	-1.4 (± 1.51)	-1 (± 1.44)		

Statistical analyses

Statistical analysis title	RDQ dyspepsia score
Comparison groups	Gaviscon v Placebo
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	ANCOVA

Secondary: Overall Treatment Evaluation (OTE)	
End point title	Overall Treatment Evaluation (OTE)
End point description: ITT population.	

OTE questionnaire is a validated scale which asks subjects to rate the degree of changes in their symptoms after 7 days of drug administration on a 15-point Likert-scale ranging from -7 = Extremely deteriorated to +7 = Extremely improved. In case of change, subjects are asked to rate the importance of the change on a 7-point scale ranging from 1 = Not important to 7 = Extremely important.

End point type	Secondary

End point timeframe:

Visit 2 (baseline) to visit 3

End point values	Gaviscon	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	212		
Units: Participants				
-7 extremely deteriorated	1	4		
-6 significantly deteriorated	2	4		
-5 relatively deteriorated	4	6		
-4 moderately deteriorated	1	4		
-3 a little deteriorated	1	5		
-2 slightly deteriorated	4	3		
-1 almost not deteriorated	1	2		
0 no change	34	37		
+1 almost not improved	12	16		
+2 slightly improved	24	17		
+3 a little improved	13	25		
+4 moderately improved	21	26		
+5 relatively improved	27	29		
+6 significantly improved	39	25		
+7 extremely improved	26	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in number of nights (out of the last 7 nights) when the subject experienced night time symptoms

End point title	Change from baseline in number of nights (out of the last 7 nights) when the subject experienced night time symptoms

End point description:

ITT population.

Before treatment, subjects were asked as to how many nights over the last 7 nights they had experienced night time symptoms (‘How many nights did you have night time symptoms over the last 7 nights?’). The answer was documented in the eCRF. During the treatment period, subjects recorded night time symptoms in the subject diary, prompted by the question ‘Did you have any night time symptoms last night?’ The number of nights with night time symptoms during treatment was calculated from these data.

End point type	Secondary

End point timeframe:

Visit 2 (baseline) to visit 3

End point values	Gaviscon	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	212		
Units: Night				
arithmetic mean (standard deviation)				
Baseline (Visit 2)	4 (± 2.67)	3.9 (± 2.55)		
End of treatment (Visit 3)	1.7 (± 2.2)	1.7 (± 2.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in subject ratings of the degree (magnitude) and the importance of changes in symptoms

End point title	Change from baseline in subject ratings of the degree (magnitude) and the importance of changes in symptoms

End point description:

ITT population.

'Symptom change after 7 days administration' ranged from -7 = Extremely deteriorated over 0 = No change to +7 = Extremely improved.

'Importance of symptom change to subject' ranged from 0 = No improvement to 7 = extremely important.

End point type	Secondary

End point timeframe:

Visit 2 (baseline) to visit 3

End point values	Gaviscon	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	212		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Symptom change after 7 days administration	3.2 (± 3.08)	2.2 (± 3.34)		
Importance of symptom change for subject	4 (± 2.6)	3.5 (± 2.72)		

Statistical analyses

Statistical analysis title	Symptom change after 7 days administration
Comparison groups	Gaviscon v Placebo

Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	two-sided Wilcoxon two-sample test

Statistical analysis title	Importance of symptom change for subject
Comparison groups	Gaviscon v Placebo
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.068
Method	two-sided Wilcoxon two-sample test

Secondary: Number of subjects with Adverse Events (AEs)

End point title	Number of subjects with Adverse Events (AEs)

End point description:

Safety population.

ADR = Adverse Drug Reaction
SAE = Serious Adverse Event

End point type	Secondary

End point timeframe:

Up to Visit 3

End point values	Gaviscon	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	212		
Units: Participants				
All Adverse Events (AEs):	109	115		
Non-treatment emergent adverse events:	12	14		
Treatment emergent adverse events (TEAEs):	104	107		
IMP-related adverse events (ADRs):	66	54		
Serious TEAEs (SAEs):	0	1		
IMP-related serious TEAEs (serious ADRs):	0	0		
TEAEs with death as outcome:	0	0		
TEAEs leading to dose withdrawal:	9	8		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to Visit 3	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0
Reporting groups	
Reporting group title	Gaviscon
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Gaviscon	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	
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	Gaviscon	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	104 / 212 (49.06%)	107 / 212 (50.47%)	
Nervous system disorders			
Headache			

subjects affected / exposed	28 / 212 (13.21%)	30 / 212 (14.15%)	
occurrences (all)	29	31	
Gastrointestinal disorders			
Flatulence			
subjects affected / exposed	36 / 212 (16.98%)	37 / 212 (17.45%)	
occurrences (all)	37	38	
Diarrhoea			
subjects affected / exposed	23 / 212 (10.85%)	17 / 212 (8.02%)	
occurrences (all)	23	17	
Nausea			
subjects affected / exposed	16 / 212 (7.55%)	20 / 212 (9.43%)	
occurrences (all)	17	21	
Abdominal pain upper			
subjects affected / exposed	17 / 212 (8.02%)	18 / 212 (8.49%)	
occurrences (all)	18	25	

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