Clinical trial results:
The use of Antacids and Alginates during Pre-Investigation Proton Pump Inhibitor Washout: Impact on Compliance and Symptom Burden

Summary

EudraCT number	2019-004561-41
Trial protocol	GB
Global end of trial date	05 July 2021

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022
Summary attachment (see zip file)	PPI Washout Study Abstract (Summary.docx)

Trial information

Trial identification

Sponsor protocol code	FGC-19-003

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	The Functional Gut Clinic
Sponsor organisation address	8 Dorset Square, London, United Kingdom, NW1 6PU
Public contact	Andres Vales, The Functional Gut Clinic, 0044 204867777, andres@thefunctionalgutclinic.com
Scientific contact	Andres Vales, The Functional Gut Clinic, 0044 204867777, andres@thefunctionalgutclinic.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	05 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 July 2021
Global end of trial reached?	Yes
Global end of trial date	05 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The Gastro-Esophageal Reflux Disease Health Related Quality of Life (GERD-HRQL) (1) score is a validated questionnaire and is commonly used in reflux studies. We will use this questionnaire to ask how patients tolerate stopping their acid reducing medications before reflux testing. We will use this to see if giving them specific instruction about how to use Gaviscon Advance helps patients to tolerate better, versus simply giving them the plain information and allowing them to do it themselves.
(1) Velanovich, V. The development of the GERD-HRQL symptom severity instrument. Diseases of the Esophagus. Volume 20, Issue 2, P130-134. April 2007.

Protection of trial subjects:

The trial site was a clinic with experience in performing gastrointestinal diagnostic tests. Clinicians performing the test are experienced in making the patient feel comfortable and reassured and are HCPC registered. The clinic is inspected in terms of the site and patient pathway every year by the CQC. The clinic is also IQIPS accredited with a yearly thorough inspection of clinical governance and patient dignity etc.

Background therapy:

All patients were asked to follow the "standard information", that is, to stop proton pump inhibitors and H2 receptor antagonists, as per British Society of Gastroenterology guidelines for performing 24 hour pH monitoring.

Evidence for comparator:

Patients were allowed to take over the counter remedies for symptoms of acid reflux and indigestion, aside from those they were asked to stop. There were able to take them up to the night before the test but not during the test. These types of treatments are found not to affect test accuracy as long as they are not taken immediately before the test - Gatta L, Vakil N, Ricci C, Osborn JF, Tampieri A, Perna F, et al. Effect of proton pump inhibitors and antacid therapy on 13C urea breath tests and stool test for Helicobacter pylori infection. Am J Gastroenterol. 2004;99(5):823-9.

Actual start date of recruitment	10 August 2020
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: 60
Worldwide total number of subjects	60
EEA total number of subjects	0

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)	53
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants ≥18 years old were selected from those referred for oesophageal manometry and 24-hour pH/impedance monitoring at The Functional Gut Clinic. When booking in, patients already established on a ≥four-week course of standard or double dose PPI therapy were given information about the study. Recruitment occurred between Aug '20 and June '21

Pre-assignment

Screening details:

Prospective participants were screened over the phone and those with red flag symptoms, known Barrett's oesophagus, grade C/D oesophagitis, peptic ulcer disease, upper gastrointestinal malignancy or those with previous oesophageal or gastric surgery were excluded. Those with allergies to alginates/antacids or on a low salt diet were also excluded.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Control Group

Arm description:

Everyone was given the usual information regarding the washout period, namely stopping proton pump inhibitors and H2 Receptor Antagonists for seven days and advised that antacids/alginates could be taken up to the night before the test.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Group

Arm description:

The treatment group only were given a bottle of Gaviscon Advance (oral suspension, containing 1000 mg sodium alginate and 200 mg potassium bicarbonate per 10 mL dose). They were asked to take 10 mL of suspension, four times a day (after breakfast, lunch, dinner and before bed) from when PPIs were stopped until the night before testing.

Arm type	Active comparator
Investigational medicinal product name	Gaviscon Advance
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for oral suspension
Routes of administration	Oral use

Dosage and administration details:

1000 mg sodium alginate and 200 mg potassium bicarbonate per 10 mL dose

Number of subjects in period 1	Control Group	Treatment Group
Started	30	30
Completed	26	22
Not completed	4	8
Lost to follow-up	4	8

Baseline characteristics

Reporting groups

Reporting group title	Control Group

Reporting group description:

Everyone was given the usual information regarding the washout period, namely stopping proton pump inhibitors and H2 Receptor Antagonists for seven days and advised that antacids/alginates could be taken up to the night before the test.

Reporting group title	Treatment Group

Reporting group description:

The treatment group only were given a bottle of Gaviscon Advance (oral suspension, containing 1000 mg sodium alginate and 200 mg potassium bicarbonate per 10 mL dose). They were asked to take 10 mL of suspension, four times a day (after breakfast, lunch, dinner and before bed) from when PPIs were stopped until the night before testing.

Reporting group values	Control Group	Treatment Group	Total
Number of subjects	30	30	60
Age categorical			
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			
Units: years			
median	50	46	
inter-quartile range (Q1-Q3)	38 to 55	36 to 54	-
Gender categorical			
Units: Subjects			
Female	16	13	29
Male	14	17	31

Subject analysis sets

Subject analysis set title	Control Group Day 0
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Control group for the trial on the last day of taking PPIs and time point when the baseline questionnaire data is collected.

Subject analysis set title	Treatment Group Day 0
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Treatment group for the trial on the last day of taking PPIs and time point when the baseline questionnaire data is collected.

Subject analysis set title	Control Group Day 7
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Control group for the trial 7 days after stopping PPIs and when the repeat questionnaire data is collected.

Subject analysis set title	Treatment Group Day 7
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Treatment group for the trial 7 days after stopping PPIs and when the repeat questionnaire data is collected.

Reporting group values	Control Group Day 0	Treatment Group Day 0	Control Group Day 7
Number of subjects	26	22	26
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
median	52	46	
inter-quartile range (Q1-Q3)	43 to 56	36 to 54	
Gender categorical			
Units: Subjects			
Female	15	9	
Male	11	13	

Reporting group values	Treatment Group Day 7		
Number of subjects	22		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			

Age continuous Units: years median inter-quartile range (Q1-Q3)			
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Control Group

Reporting group description:

Everyone was given the usual information regarding the washout period, namely stopping proton pump inhibitors and H2 Receptor Antagonists for seven days and advised that antacids/alginates could be taken up to the night before the test.

Reporting group title	Treatment Group

Reporting group description:

The treatment group only were given a bottle of Gaviscon Advance (oral suspension, containing 1000 mg sodium alginate and 200 mg potassium bicarbonate per 10 mL dose). They were asked to take 10 mL of suspension, four times a day (after breakfast, lunch, dinner and before bed) from when PPIs were stopped until the night before testing.

Subject analysis set title	Control Group Day 0
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Control group for the trial on the last day of taking PPIs and time point when the baseline questionnaire data is collected.

Subject analysis set title	Treatment Group Day 0
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Treatment group for the trial on the last day of taking PPIs and time point when the baseline questionnaire data is collected.

Subject analysis set title	Control Group Day 7
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Control group for the trial 7 days after stopping PPIs and when the repeat questionnaire data is collected.

Subject analysis set title	Treatment Group Day 7
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Treatment group for the trial 7 days after stopping PPIs and when the repeat questionnaire data is collected.

Primary: Change in GERD-HRQL score - Control Group

End point title	Change in GERD-HRQL score - Control Group

End point description:

Questionnaire score. Minimum score is 0 - no symptoms. Max score is 50 - worst symptoms.

End point type	Primary

End point timeframe:

The GERD-HRQL score was taken on the last day of taking PPIs (Day 0). A repeat score was taken just before the 24 hour pH test (Day 7).

End point values	Control Group Day 0	Control Group Day 7		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	26		
Units: N/A				
median (inter-quartile range (Q1-Q3))	10 (6.3 to 21)	16.5 (13.3 to 25.3)		

Attachments (see zip file)	Fig 2 - HRQL - ITT.png

Statistical analyses

Statistical analysis title	Control Group Wilcoxon Signed Ranks Test
Comparison groups	Control Group Day 0 v Control Group Day 7
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon signed-rank test
Parameter estimate	Median difference (final values)
Point estimate	6.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	7
Variability estimate	Standard deviation

Primary: Change in GERD-HRQL score - Treatment Group

End point title	Change in GERD-HRQL score - Treatment Group

End point description:

Questionnaire score. Minimum score is 0 - no symptoms. Max score is 50 - worst symptoms.

End point type	Primary

End point timeframe:

The GERD-HRQL score was taken on the last day of taking PPIs (Day 0). A repeat score was taken just before the 24 hour pH test (Day 7).

End point values	Treatment Group Day 0	Treatment Group Day 7		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22	22		
Units: N/A				
median (inter-quartile range (Q1-Q3))	19 (12.3 to 24.3)	17.5 (13 to 24)		

Attachments (see zip file)	Fig 2 - HRQL - ITT.png

Statistical analyses

Statistical analysis title	Treatment Group Wilcoxon Signed Ranks Test

Statistical analysis description:

Analysis of the symptoms change from the last day of taking PPIs compared to 7 days later. The null hypothesis was that symptoms would significantly deteriorate.

Comparison groups	Treatment Group Day 0 v Treatment Group Day 7
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon signed-rank test
Parameter estimate	Median difference (final values)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	3.5
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Less than 15 days

Adverse event reporting additional description:

All those responsible for screening patients were instructed in the proper completion of trial documents and signed a declaration to this effect. A form for recording adverse events existed within the Site File and there was a protocol for keeping all site staff up to date with events. Overall responsibility was held by the Principal Investigator.

Assessment type	Non-systematic

Dictionary used

Dictionary name	SNOMED CT
Dictionary version	2018

Reporting groups

Reporting group title	Treatment Group

Reporting group description:

Treatment group for the trial, as previously described.

Serious adverse events	Treatment Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Treatment Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 22 (4.55%)		
Product issues			
Nausea	Additional description: The participant had a severe dislike of the taste of the product (personal preference) and were allowed to stopped taking it. But they were still included in the Intention To Treat analysis.		
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		

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? Yes

Date	Interruption	Restart date
01 March 2020	COVID Pandemic	10 August 2020

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The main limitation of our study is that, despite randomisation, the GERD-HRQL scores between the groups differ at baseline. After investigation, a subversion of the allocation procedure could not be found.

Notes: