Clinical trial results:
Comparison of two methods for in vivo diagnosis of Helicobacter pylori infection, by means of a tablet of 13C-Urea.

Summary

EudraCT number	2016-001598-33
Trial protocol	IT
Global end of trial date	29 December 2016

Results information

Result version number	v1 (current)
This version publication date	15 February 2018
First version publication date	15 February 2018
Summary attachment (see zip file)	Clinical Trial Summary Report (PSC-DS-BRETEX - Clinical Trial Summary Report.pdf)

Trial information

Trial identification

Sponsor protocol code	PSC-DS-BRETEX

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	SOFAR S.p.A.
Sponsor organisation address	Via Firenze 40, Trezzano Rosa, Italy, 20060
Public contact	Divisione Medica, SOFAR S.p.A., +39 029093621, laura.patrucco@sofarfarm.it
Scientific contact	Divisione Medica, SOFAR S.p.A., +39 029093621, laura.patrucco@sofarfarm.it

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	31 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 December 2016
Global end of trial reached?	Yes
Global end of trial date	29 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Concordance between the results obtained with the two methods in the diagnosis of H. pylori

Protection of trial subjects:

Participation in the study did not entail any additional risk for patients than would have been expected with the execution of the examination with a single method, as only one 100 mg tablet of EXPIROBACTER® was taken, dissolved in a solution in which a 1.4 g sachet of citric acid was dissolved. The patients had indication to perform urea Breath tests for the determination of H. pylori infection. Once the marker was taken, non-invasive methods of expired air sampling were performed.
The risks associated with intake are limited to a possible not known intolerance to EXPIROBACTER® or citric acid. In any case, these are limited risks, which are acceptable against the benefit of accessing a non-invasive diagnostic evaluation.

Background therapy:

None

Evidence for comparator:

The different distribution of the isotopes ^{13}C (carbon-13) and ^{12}C (carbon-12) in the molecules of exhaled carbon dioxide, expressed as $^{12}C/^{13}C$ ratio, gives a rationale for ^{13}C-based test.
In normal conditions, the assumption of urea enriched in ^{13}C does not change $^{12}C/^{13}C$ ratio, because only 1% of the carbon is represented by ^{13}C.
Conversely, in case of H. pylori infection, the assumption of ^{13}C-urea changes the $^{12}C/^{13}C$ ratio, since the presence of the bacterium increases urease activity, leading to the formation of ^{13}C carbon dioxide. ^{13}C carbon dioxide passes to the blood and can be measured by exhaled breath analysis.

Actual start date of recruitment	22 November 2016
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	Italy: 46
Worldwide total number of subjects	46
EEA total number of subjects	46

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)	45
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients have been recruited between 22-Nov-2016 and 29-Dec-2016 in an Italian clinical site.

Pre-assignment

Screening details:

Subjects enrolled underwent to Urea Breath Test, performed with EXPIROBACTER®, to confirm or exclude H. pylori infection.
Subjects were fasting and did not take food or drink or smoke during the duration of the examination.
All patients performed, during the same session, the test with the two different methods.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

The patients were diagnosed using both methods. Blinding was not needed.

Arms

Arm title	Classic and BreathID Method

Arm description:

The patients underwent the breath test using both the classic method, requiring basal exhalation sampling before EXPIROBACTER® ingestion and a second exhalation sampling 30 minutes after, according to the Summary of the Product Characteristics, and a second method based on a continuous analysis of exhaled breath performed by Exalenz BreathID medical device.

Arm type	Both Experimental and Comparator
Investigational medicinal product name	EXPIROBACTER ® 100 mg.
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The patient was administered orally 1 tablet of 100 mg of EXPIROBACTER®, dissolved in a solution in which a 1.4 g sachet of citric acid was solubilized.

Number of subjects in period 1	Classic and BreathID Method
Started	46
Completed	46

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	46	46	
Age categorical Units: Subjects			
Adults (18-64 years)	45	45	
From 65-84 years	1	1	
Age continuous Units: years			
arithmetic mean	32.22		
standard deviation	± 11.48	-	
Gender categorical Units: Subjects			
Female	36	36	
Male	10	10	
Previous H. pylori test			
The presence of any H. pylori test previously performed was reported, together with the result of the test (positive/negative)			
Units: Subjects			
No	38	38	
Yes - Positive	4	4	
Yes - Negative	4	4	
Symptoms leading to the current test for H. pylori			
The presence of at least one symptoms leading to the current test for H. Pylori was registered			
Units: Subjects			
No symptoms	32	32	
At least one symptom	14	14	

Subject analysis sets

Subject analysis set title	BreathID
Subject analysis set type	Full analysis

Subject analysis set description:

The patients underwent the breath test using a method based on a continuous analysis of exhaled breath performed by Exalenz BreathID medical device.

Subject analysis set title	Classic method
Subject analysis set type	Full analysis

Subject analysis set description:

The patients underwent the breath test using the classic method, requiring basal exhalation sampling before EXPIROBACTER® ingestion and a second exhalation sampling 30 minutes after, according to the Summary of the Product Characteristics

Reporting group values	BreathID	Classic method	
Number of subjects	46	46	
Age categorical Units: Subjects			
Adults (18-64 years)	45	45	
From 65-84 years	1	1	
Age continuous Units: years			
arithmetic mean	32.22	32.22	
standard deviation	± 11.48	± 11.48	
Gender categorical Units: Subjects			
Female	36	36	
Male	10	10	
Previous H. pylori test			
The presence of any H. pylori test previously performed was reported, together with the result of the test (positive/negative)			
Units: Subjects			
No	38	38	
Yes - Positive	4	4	
Yes - Negative	4	4	
Symptoms leading to the current test for H. pylori			
The presence of at least one symptoms leading to the current test for H. Pylori was registered			
Units: Subjects			
No symptoms	32	32	
At least one symptom	14	14	

End points

End points reporting groups

Reporting group title	Classic and BreathID Method

Reporting group description:

The patients underwent the breath test using both the classic method, requiring basal exhalation sampling before EXPIROBACTER® ingestion and a second exhalation sampling 30 minutes after, according to the Summary of the Product Characteristics, and a second method based on a continuous analysis of exhaled breath performed by Exalenz BreathID medical device.

Subject analysis set title	BreathID
Subject analysis set type	Full analysis

Subject analysis set description:

The patients underwent the breath test using a method based on a continuous analysis of exhaled breath performed by Exalenz BreathID medical device.

Subject analysis set title	Classic method
Subject analysis set type	Full analysis

Subject analysis set description:

The patients underwent the breath test using the classic method, requiring basal exhalation sampling before EXPIROBACTER® ingestion and a second exhalation sampling 30 minutes after, according to the Summary of the Product Characteristics

Primary: Evaluation of results concordance

End point title	Evaluation of results concordance[1]

End point description:

The primary endpoint of this study was the evaluation of the overlap between the results obtained by molecular correlation spectrometry (BreathID) and those obtained by mass spectrometry (classic method) to perform H. pylori test. The concordance (agreement) between the two methods was assessed using Cohen's kappa.
Correlation between the two methods was excellent: both methods allowed to identify 41 negative and 5 positive patients (K=1.00) (Table 1).

End point type	Primary

End point timeframe:

The diagnosis was performed with both methods at the same time

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: The primary analysis was an agreement analysis between the two diagnostic metods using Cohen's kappa. It was not possible to report the results of such a statistical analysis in the Clinical Trials Register. Results are repoted in the attached Table 1.

End point values	Classic and BreathID Method	BreathID	Classic method	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	46	46	46	
Units: concordant tests	46	46	46	

Attachments (see zip file)	Table 1 - Concordance between the two methods/PSC-DS-

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's satisfaction

End point title	Patient's satisfaction

End point description:

Patient's satisfaction was measured by a Visual Analogue Scale (0-100 mm).

End point type	Secondary

End point timeframe:

Day 1

End point values	BreathID	Classic method		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	46		
Units: mm				
arithmetic mean (standard deviation)	90.17 (± 8.54)	82.35 (± 16.52)		

Statistical analyses

Statistical analysis title	T-test on mean patient's satisfaction

Statistical analysis description:

The mean patient's satisfaction with the classic method and the BreathID, was compared.

Comparison groups	BreathID v Classic method
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [2]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	7.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.35
upper limit	12.3

Notes:

[2] - The difference between the two diagnostic methods was statistically significant at $p < 0.01$

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse events were to be reported during the duration of the study

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Classic and BreathID Method

Reporting group description:

The patients underwent the breath test using both the classic method, requiring basal exhalation sampling before EXPIROBACTER® ingestion and a second exhalation sampling 30 minutes after, according to the Summary of the Product Characteristics, and a second method based on a continuous analysis of exhaled breath performed by Exalenz BreathID medical device.

Serious adverse events	Classic and BreathID Method		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 46 (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	Classic and BreathID Method		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 46 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No adverse event occurred during the study.

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